Industria y Comercio

SUPERINTENDENCIA

PCT

Delegatura de propiedad Industrial

División de Nuevas Creaciones

SOLICITUD

PATENTE DE INVENCIÓN

21. **EXPEDIENTE No.** 05-21462

54. **TÍTULO** 1,2,4'' OXIDIAZOLES COMO MODULADORES DE RECEPTOR - 5. METABOTROPICO GLUTAMATO

51. **CLASIFICACIÓN INTERNACIONAL** C07 D 271/00 AGIK 31/4245 AGIP25/00

71. **SOLICITANTE** 1. ASTRAZENECA AB 2. NPS PHARMACEUTICALS, INC.

DOMICILIO 1. SODERTALJE SUECIA, 2 SALT LAKE, CITY, ESTADOS UNIDOS.

74. **APODERADO** D ILIA MARIA RODRIGUEZ D' ALEMAN

22. **BOGOTÁ, D. C.,** M. 4/05

(59)

(FORMA P-10)

05- 21462

1

PETITORIO

SUPERINDUSTRIA Y COMERCIO
Radicacion : 05021462 00000000 Folios: 1364
Fecha (dd/mm/aaaa): 2005-03-08 16:48:20
Tramite : 911 PCT-PATENT 379 PAGS MAL 411 PRESENTA
Dependencia: 0200 DIVISION DE NUEVAS SOLICITUDES

Industria y Comercio
SUPERINTENDENCIA

FORMULARIO ÚNICO DE SOLICITUD DE PATENTE
PCT
ENTRADA EN FASE NACIONAL 09-03-2005

1) SOLICITUD DE:

☒ Patente de invención ☐ Patente de Modelo de Utilidad

☐ Capitulo I. ☒ Capitulo II.

2) SOLICITANTE (71)	**Nombre: 1. ASTRAZENECA AB** **2. NPS PHARMACEUTICALS, INC.** **Dirección: 1. S-151 85 Södertälje Suecia** **2. 383 Colorow Drive Salt Lake City, Ut 84108 Estados Unidos** **Nacionalidad o domicilio: 1. Södertälje Suecia** **2. Salt Lake City, Utah, Estados Unidos** **Lugar de constitución: 1. Suecia** **2. Utah, Estados Unidos**	**IDENTIFICACIÓN** **C.C.** ☐ **NIT:** ☐ **C.E.** ☐ **OTRO** ☐ **Cual** _____ **NÚMERO** _____
	Teléfono: **Fax:** **E. Mail:**	
3) REPRESENTANTE O APODERADO	**Nombre:** DILIA MARIA RODRIGUEZ D´ALEMAN **Dirección:** Carrera 11 N°. 93-43 Of. 404 Bogotá D.C. **Teléfono:** 6350835 **Fax:** 6350824 **E. Mail:** clarkemodet@clarkemodet.com.co	**IDENTIFICACIÓN** **C.C.** ☒ **NIT:** ☐ **C.E.** ☐ **OTRO** ☐ **NÚMERO:** 41.654.882 **TP:** 20824 CSJ
4) INVENTOR (ES) (72)	**Nombre: (VER LISTA ADJUNTA)** **Nacionalidad o Domicilio:**	

5) PCT (86)
Solicitud Internacional No. PCT/US2003/024846 Fecha: Agosto 8, 2003

Publicación Internacional No. WO 2004/014881 A 2 Fecha: Febrero 19, 2004

6)Titulo (54) 1,2,4" OXIDIAZOLES COMO MODULADORES DE RECEPTOR-5 METABOTROPICO DE GLUTAMATO

7) Clasificación Internacional: C07D 271/00 A61K31/4245 · A61P 25/00

8) PRIORIDAD	**33) País de Origen**	**(32) Fecha**	**(31) Número de Solicitud**
SI ☒ **NO** ☐	**Estados Unidos**	**Agosto 9, 2002**	**60/402,040**

9) Comprobante de pago N°. 05-12,932 Fecha: febrero 17, 2005

Instrucciones para el diligenciamiento del presente formulario. Ver reverso de esta pagina

2
2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 05 - 12,932
FECHA : FEBRERO 17 DE 2005

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

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CLARKE MODET Y CO. COLOMBCONSIGNACION		BANCO POPULAR	050-00110-6	37881667	17/02/2005	2,294,000.00

C O N C E P T O

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

SON: CUATROCIENTOS CUARENTA Y TRES MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

P615

10) ANEXOS

- [X] Comprobante de pago de la tasa de presentación de la solicitud
- [ ] Comprobante de pago por reivindicación de prioridad
- [ ] Documento que acredita la existencia y representación legal cuando el solicitante sea persona Jurídica
- [X] Poderes, si fuera el caso
- [X] Documento de cesión del inventor al solicitante o a su causante
- [ ] Declaraciones
- [X] Copia de la solicitud Internacional. (Resumen, descripción, reivindicación, Dibujos).
- [X] Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicación, Dibujos)
- [ ] Copia 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 12 x 12 y 6 x 6 cm
- [ ] De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionados parcial o totalmente con la invención de esta solicitud.
- [X] Otros:
  1. Opinión escrita
  2. PCT Capítulo II
  3. Solicitud PCT
  4. Notificación de la transmisión del reporte de búsqueda
  5. Notificación de la recepción del examen preeliminar
  6. Notificación de la modificación de las reivindicaciones
  7. Información sobre oficinas designadas
  8. Notificación de la transmisión del reporte de búsqueda
  9. Notificación de la transmisión del documento de prioridad
  10. Notificación del recibo de la copia de la prioridad
  11. Notificación del numero y fecha de la presentación internacional

11) FIGURA CARACTERÍSTICA:

12) Solicitud concesión de la patente,

NOMBRE: DILIA RODRÍGUEZ D´ALEMAN

FIRMA:

C.C. 41.654.882 de Bogota TP 20824 CSJ

Instrucciones para el diligenciamiento del presente formulario. Ver reverso de esta pagina

05-21962

#4

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18. OSTERWALL, CHristoffer – Sueco
C/o AstraZeneca AB
S-151 85 Södertälje, Suecia

6 1471

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
085747-0270		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 03/24846	08/08/2003	09/08/2002
Applicant		
ASTRAZENECA AB		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written 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

2. [X] Certain claims were found unsearchable (See Box I).

3. [ ] Unity of invention is lacking (see Box II).

4. With regard to the title,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

'1,2,4!OXADIAZOLES AS MODULATORS OF METABOTROPIC GLUTAMATE RECEPTOR-5

5. With regard to the abstract,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/24846

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/24846

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D413/12 C07D413/14 C07D417/14 A61K31/4245 A61P25/00

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 26927 A (STORMANN THOMAS M ;DELMAR ERIC G (US); MOE SCOTT T (US); SMITH DAR) 3 June 1999 (1999-06-03) page 5, line 30 - line 34; claims 1,15,16 figure 1, compound 5	1-27
X	EP 0 397 365 A (PFIZER) 14 November 1990 (1990-11-14) claims 1,14 examples	1-27
X	US 5 140 034 A (BAKER RAYMOND ET AL) 18 August 1992 (1992-08-18) column 1, line 5 - line 15; claim 1 column 4, line 25 - line 42	1-27

-/--

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 December 2003	16/04/2004

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

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

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 422 369 A (BAYER AG) 17 April 1991 (1991-04-17) page 4, line 26 - line 44; claims 1,10; table 1	1-17,28
X	WO 00 35913 A (AVENTIS CROPSCIENCE GMBH) 22 June 2000 (2000-06-22) page 22; claims 1,9; table 1	1-24,28
X	HOLLA B S ET AL: "Synthesis and antibacterial studies of a new series of 1,2-bis(1,3,4-oxadiazol-2-yl)ethanes and 1,2-bis(4-amino-1,2,4-triazo 1-3-yl)ethanes" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 35, no. 2, February 2000 (2000-02), pages 267-271, XP004330420 ISSN: 0223-5234 compounds 4 and 5 tables I,II	1-24
X	GÜNAY N S ET AL: "5-Nitroimidazole derivatives as possible antibacterial and antifungal agents" IL FARMACO, vol. 54, 1999, pages 826-831, XP002264297 ROME, IT ISSN: 0014-827X tables 1,2	1-24
X	MADRONERO R ET AL: "Tetrazole analogues of arylthiazolylacetic acids. Synthesis and pharmacological study" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY., vol. 9, no. 4, 1974, pages 445-448, XP009022649 EDITIONS SCIENTIFIQUE ELSEVIER, PARIS., FR ISSN: 0223-5234 scheme 1 abstract	1-27
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4885431 XP002264298 5,5'-(1,2-ethanediyl)-bis'3-(m-tolyl)-1,2,4-oxadiazole! & ORG. MASS SPECTROM. (1991), 26(11), 1017-1018,	1-17

-/—

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4208871 XP002264299 & SYNTH. COMMUN. (1990), 20(12), 1811-1817,	1-17
P,X	DATABASE CHEMCATS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002264300 Order numbers: SPB 01075, SEW 03694, BTB 02953 & "Maybridge HTS" 14 May 2003 (2003-05-14) , MAYBRIDGE PLC , TINTAGEL, CORNWALL, PL34 0HW, UK	1-17

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

The present application contains four separate independent compound claims of overlapping scope (see claims 1, 2, 16 and 17). The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection (Article 6 PCT). A further lack of clarity arises owing to the fact that a seemingly arbitrary selection of compounds have been disclaimed in claim 2 but not in the broader claim 1. Many of the variables in the claims are so ill-defined that it is impossible to determine the subject-matter for which protection is sought. For example, it is not clear whether the definition of X4 in claim 2 as being C0-C4alkylR5R6 is intended to imply that X4 may be absent (i.e. for C0-alkyl).

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved (see search report for a selection of documents) that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to compounds of formula I as defined in claim 2 wherein X1, X2 and X3 are as defined in claim 5, M2 is as defined in claim 7 and X4 is defined as in claim 10.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/24846

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

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

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

Although claims 26 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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

see FURTHER INFORMATION sheet PCT/ISA/210

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

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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

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

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

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

Remark on Protest

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

[ ] No protest accompanied the payment of additional search fees.

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9926927	A	03-06-1999	AU	1531799 A	15-06-1999
			CA	2311131 A1	03-06-1999
			CN	1285820 T	28-02-2001
			EP	1037878 A2	27-09-2000
			JP	2001524468 T	04-12-2001
			NZ	505207 A	31-10-2003
			WO	9926927 A2	03-06-1999
			US	2003013715 A1	16-01-2003
			US	6429207 B1	06-08-2002
EP 0397365	A	14-11-1990	US	4914207 A	03-04-1990
			AT	102197 T	15-03-1994
			CA	2016181 A1	09-11-1990
			DE	69006907 D1	07-04-1994
			DE	69006907 T2	09-06-1994
			DK	397365 T3	24-05-1994
			EP	0397365 A1	14-11-1990
			ES	2062354 T3	16-12-1994
			FI	94639 B	30-06-1995
			IE	62936 B1	08-03-1995
			JP	1958887 C	10-08-1995
			JP	3002180 A	08-01-1991
			JP	6092404 B	16-11-1994
US 5140034	A	18-08-1992	GB	2229182 A ,B	19-09-1990
EP 0422369	A	17-04-1991	DE	3929673 A1	14-03-1991
			EP	0422369 A2	17-04-1991
			JP	3099066 A	24-04-1991
WO 0035913	A	22-06-2000	DE	19858193 A1	21-06-2000
			AU	1974100 A	03-07-2000
			WO	0035913 A1	22-06-2000
			EP	1140922 A1	10-10-2001
			JP	2002532497 T	02-10-2002
			US	2003162812 A1	28-08-2003

[redacted]ATENT C PERATI N TREAT[redacted]

14

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
FOLEY & LARDNER
Attn. Bent, Stephen A.
Washington Harbour
3000 K Street N.W., Suite 500
Washington, D.C. 20007-5101
UNITED STATES OF AMERICA

COMMUNICATION IN CASES FOR WHICH
NO OTHER FORM IS APPLICABLE

Applicant's or agent's file reference 085747-0270	Date of mailing (day/month/year) 16/04/2004
International application No. PCT/US 03/24846	REPLY DUE See paragraph 1 below
Applicant ASTRAZENECA AB	International filing date (day/month/year) 08/08/2003

1. [ ] REPLY DUE within _____ [illegible]days from the above date of mailing

   [X] NO REPLY DUE

2. COMMUNICATION:

The international search report mailed to you on 23/01/04 was not accompanied by the modified abstract mentioned on form PCT/ISA/210 (first sheet).

Please find enclosed the missing sheet. The deadline for comments on the modified abstract will, of course, be calculated from the date of mailing of this letter.

We wish to apologise for any inconvenience caused.

A copy of this letter and its enclosures has been sent to the International Bureau of Geneva.

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

Form PCT/ISA/224 (January 1994)

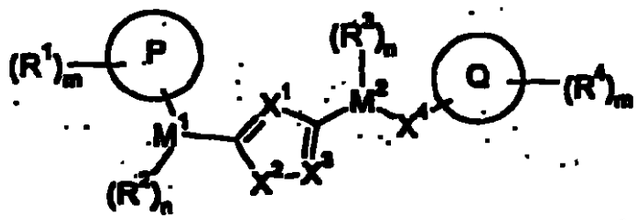
Correct version

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/24846

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to new compounds of formula I,



(I)

a process for their preparation and new intermediates prepared therein, pharmaceutical formulations containing said compounds and to the use of said compounds in therapy.

In particular there are compounds according to the present invention that are potent and selective for the mGluR Group I receptor and more particularly for mGluR5.

Thus, it is expected that the compounds of the invention are well suited for the prevention and/or treatment of mGluR5 receptor-mediated disorders such as acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:
BENT, Stephen A.
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, D.C. 20007-5143
ETATS-UNIS D'AMERIQUE

+ipea408

NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence and Administrative Instructions, Section 601(a))

Date of mailing (day/month/year)	19-03-2004

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
085747-0270	

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US03/24846	08/08/2003	09/08/2002

Applicant

ASTRAZENECA AB et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

04/03/2004

2. This date of receipt is:

[X] the actual date of receipt of the demand by this Authority (Rule 61.1(b)).

[ ] the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).

[ ] the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. [ ] ATTENTION: That date of receipt is after the expiration of 19 months from the priority date. Consequently, in respect of some Offices, the demand does not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)) and the acts for entry into the national phase must therefore be performed within 20 months from the priority date (or later in some Offices). However, in respect of some other Offices, the time limit of 30 months (or later) may nevertheless apply. See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

[ ] *(If applicable)* This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	LODOLO F Tel. (+49-89) 2399-2039

Form PCT/IPEA/402 (April 2002; reprint January 2004) (16/03/2004)

Europäisches Patentamt · European Patent Office · Office européen des brevets

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING THE FILING OF AMENDMENTS OF THE CLAIMS

(PCT Administrative Instructions, Section 417)

To:

BENT, Stephen, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year) 29 March 2004 (29.03.2004)	
Applicant's or agent's file reference 085747-0270	IMPORTANT NOTIFICATION
International application No. PCT/US2003/024846	International filing date (day/month/year) 08 August 2003 (08.08.2003)
Applicant ASTRA ZENECA AB et al	

1. The applicant is hereby notified that amendments to the claims under Article 19 were received by the International Bureau on:

   18 March 2004 (18.03.2004)

2. This date is within the time limit under Rule 46.1.

   Consequently, the international publication of the international application will contain the amended claims according to Rule 48.2(f), (h) and (i).

3. The applicant is reminded that the international application (description, claims and drawings) may be amended during the international preliminary examination under Chapter II, according to Article 34, and in any case, before each of the designated Offices, according to Article 28 and Rule 52, or before each of the elected Offices, according to Article 41 and Rule 78.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No. (41-22) 338.90.90

Authorised officer

Isabelle DÉPREZ (Fax 338 9090)
Telephone No. (41-22) 338 8398

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

To:

BENT, Stephen, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year)	
29 March 2004 (29.03.2004)	
Applicant's or agent's file reference	**IMPORTANT INFORMATION**
065747-0270	

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US2003/024846	08 August 2003 (08.08.2003)	09 August 2002 (09.08.2002)

Applicant
ASTRA ZENECA AB et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

   EP :AT,BE,BG,CH,CY,CZ,DE,DK,EE,ES,FI,FR,GB,GR,HU,IE,IT,LU,MC,NL,PT,RO,SE,
   SI,SK,TR
   National :BG,CA,CN,DE,GB,IL,JP,KP,KR,MN,NO,PL,RO,RU,SK,US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

   AP :GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZM,ZW
   EA :AM,AZ,BY,KG,KZ,MD,RU,TJ,TM
   OA :BF,BJ,CF,CG,CI,CM,GA,GN,GQ,GW,ML,MR,NE,SN,TD,TG
   National :AE,AG,AL,AM,AT,AU,AZ,BA,BB,BR,BY,BZ,CH,CO,CR,CU,CZ,DK,DM,DZ,EC,
   EE,ES,FI,GD,GE,GH,GM,HR,HU,ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,
   MG,MK,MW,MX,MZ,NI,NZ,OM,PG,PH,PT,SC,SD,SE,SG,SL,SY,TJ,TM,TN,TR,TT,TZ,UA,
   UG,UZ,VC,VN,YU,ZA,ZM,ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing , if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

   Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

   The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 338.90.90

Authorized officer:
Isabelle DÉPREZ (Fax 338 9090)

Telephone No. (41-22) 338 8389

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

BENT, Stephen, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, DC 20007-5101
ETATS-UNIS D'AMERIQUE

Date of mailing *(day/month/year)* 19 February 2004 (19.02.2004)		
Applicant's or agent's file reference 085747-0270	IMPORTANT NOTICE	
International application No. PCT/US2003/024846	International filing date *(day/month/year)* 08 August 2003 (08.08.2003)	Priority date *(day/month/year)* 09 August 2002 (09.08.2002)
Applicant ASTRA ZENECA AB et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this notice:

   AU, AZ, BY, CH, CN, CO, DZ, EP, HU, JP, KG, KP, KR, MD, MK, MZ, RU, TM, US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

   AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, SC, SD, SE, SG, SK, SL, SY, TJ, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-*bis*)).

3. Enclosed with this notice is a copy of the international application as published by the International Bureau on 19 February 2004 (19.02.2004) under No. WO 2004/014881

4. **TIME LIMITS for filing a demand for international preliminary examination and for entry into the national phase**

   The applicable time limit for entering the national phase will, subject to what is said in the following paragraph, be **30 MONTHS** from the priority date, not only in respect of any elected Office if a demand for international preliminary examination is filed before the expiration of 19 months from the priority date, but also in respect of any designated Office, in the absence of filing of such demand, where Article 22(1) as modified with effect from 1 April 2002 applies in respect of that designated Office. For further details, see *PCT Gazette* No. 44/2001 of 1 November 2001, pages 19926, 19932 and 19934, as well as the *PCT Newsletter*, October and November 2001 and February 2002 issues.

   In practice, time limits other than the 30-month time limit will continue to apply, for various periods of time, in respect of certain designated or elected Offices. For regular updates on the applicable time limits (20, 21, 30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at http://www.wipo.int/pct/en/index.html.

   For filing a demand for international preliminary examination, see the *PCT Applicant's Guide*, Volume I/A, Chapter IX. Only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

   It is the applicant's sole responsibility to monitor all these time limits.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Gijsbertus Beijer - Carlos Roy
Facsimile No.(41-22) 740.14.35	Telephone No.(41-22) 338.91.11

Form PCT/IB/308 (April 2002)

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
FOLEY & LARDNER
Attn. Bent, Stephen A.
Washington Harbour
3000 K Street N.W., Suite 500
Washington, D.C. 20007-5101
UNITED STATES OF AMERICA

Applicant's or agent's file reference 085747-0270	Date of mailing (day/month/year) 23/01/2004
International application No. PCT/US 03/24846	FOR FURTHER ACTION See paragraphs 1 and 4 below
Applicant ASTRAZENECA AB	International filing date (day/month/year) 08/08/2003

1. [x] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

   When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

   Where? Directly to the International Bureau of WIPO
   34, chemin des Colombettes
   1211 Geneva 20, Switzerland
   Facsimile No.: (41-22) 740.14.35

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Further action(s): The applicant is reminded of the following:

   Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

   Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Kerstin G^tz

Form PCT/ISA/220 (July 1998)

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The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 085747-0270	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 03/24846	International filing date *(day/month/year)* 08/08/2003	(Earliest) Priority Date *(day/month/year)* 09/08/2002
Applicant ASTRAZENECA AB		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written 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 readble 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

2. [X] Certain claims were found unsearchable (See Box I).

3. [ ] Unity of invention is lacking (see Box II).

4. With regard to the title,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

1,2,4 OXADIAZOLES AS MODULATORS OF METABOTROPIC GLUTAMATE RECEPTOR-5

5. With regard to the abstract,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/24846

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Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/24846 24

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D413/12 C07D413/14 C07D417/14 A61K31/4245 A61P25/00

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 26927 A (STORMANN THOMAS M ;DELMAR ERIC G (US); MOE SCOTT T (US); SMITH DAR) 3 June 1999 (1999-06-03) page 5, line 30 - line 34; claims 1,15,16 figure 1, compound 5	1-27
X	EP 0 397 365 A (PFIZER) 14 November 1990 (1990-11-14) claims 1,14 examples	1-27
X	US 5 140 034 A (BAKER RAYMOND ET AL) 18 August 1992 (1992-08-18) column 1, line 5 - line 15; claim 1 column 4, line 25 - line 42	1-27

-/—

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 December 2003	23/01/2004

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

1

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 422 369 A (BAYER AG) 17 April 1991 (1991-04-17) page 4, line 26 - line 44; claims 1,10; table 1	1-17,28
X	WO 00 35913 A (AVENTIS CROPSCIENCE GMBH) 22 June 2000 (2000-06-22) page 22; claims 1,9; table I	1-24,28
X	HOLLA B S ET AL: "Synthesis and antibacterial studies of a new series of 1,2-bis(1,3,4-oxadiazol-2-yl)ethanes and 1,2-bis(4-amino-1,2,4-triazo 1-3-yl)ethanes" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 35, no. 2, February 2000 (2000-02), pages 267-271, XP004330420 ISSN: 0223-5234 compounds 4 and 5 tables I,II	1-24
X	GÜNAY N S ET AL: "5-Nitroimidazole derivatives as possible antibacterial and antifungal agents" IL FARMACO, vol. 54, 1999, pages 826-831, XP002264297 ROME, IT ISSN: 0014-827X tables 1,2	1-24
X	MADRONERO R ET AL: "Tetrazole analogues of arylthiazolylacetic acids. Synthesis and pharmacological study" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY., vol. 9, no. 4, 1974, pages 445-448, XP009022649 EDITIONS SCIENTIFIQUE ELSEVIER, PARIS., FR ISSN: 0223-5234 scheme 1 abstract	1-27
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4885431 XP002264298 5,5'-(1,2-ethanediyl)-bis'3-(m-tolyl)-1,2,4-oxadiazole! & ORG. MASS SPECTROM. (1991), 26(11), 1017-1018,	1-17

-/—

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4208871 XP002264299 & SYNTH. COMMUN. (1990), 20(12), 1811-1817,	1-17
P,X	DATABASE CHEMCATS 'Online! . CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002264300 Order numbers: SPB 01075, SEW 03694, BTB 02953 & "Maybridge HTS" 14 May 2003 (2003-05-14) , MAYBRIDGE PLC , TINTAGEL, CORNWALL, PL34 0HW, UK	1-17

1

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

The present application contains four separate independent compound claims of overlapping scope (see claims 1, 2, 16 and 17). The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection (Article 6 PCT). A further lack of clarity arises owing to the fact that a seemingly arbitrary selection of compounds have been disclaimed in claim 2 but not in the broader claim 1. Many of the variables in the claims are so ill-defined that it is impossible to determine the subject-matter for which protection is sought. For example, it is not clear whether the definition of X4 in claim 2 as being CO-C4alkylR5R6 is intended to imply that X4 may be absent (i.e. for CO-alkyl).

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved (see search report for a selection of documents) that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to compounds of formula I as defined in claim 2 wherein X1, X2 and X3 are as defined in claim 5, M2 is as defined in claim 7 and X4 is defined as in claim 10.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/24846

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

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

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

Although claims 26 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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

see FURTHER INFORMATION sheet PCT/ISA/210

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

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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

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

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

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

Remark on Protest

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

[ ] No protest accompanied the payment of additional search fees.

International Application No
PCT/US 03/24846

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9926927 A	03-06-1999	AU 1531799 A	15-06-1999
		CA 2311131 A1	03-06-1999
		CN 1285820 T	28-02-2001
		EP 1037878 A2	27-09-2000
		JP 2001524468 T	04-12-2001
		NZ 505207 A	31-10-2003
		WO 9926927 A2	03-06-1999
		US 2003013715 A1	16-01-2003
		US 6429207 B1	06-08-2002
EP 0397365 A	14-11-1990	US 4914207 A	03-04-1990
		AT 102197 T	15-03-1994
		CA 2016181 A1	09-11-1990
		DE 69006907 D1	07-04-1994
		DE 69006907 T2	09-06-1994
		DK 397365 T3	24-05-1994
		EP 0397365 A1	14-11-1990
		ES 2062354 T3	16-12-1994
		FI 94639 B	30-06-1995
		IE 62936 B1	08-03-1995
		JP 1958887 C	10-08-1995
		JP 3002180 A	08-01-1991
		JP 6092404 B	16-11-1994
US 5140034 A	18-08-1992	GB 2229182 A ,B	19-09-1990
EP 0422369 A	17-04-1991	DE 3929673 A1	14-03-1991
		EP 0422369 A2	17-04-1991
		JP 3099066 A	24-04-1991
WO 0035913 A	22-06-2000	DE 19858193 A1	21-06-2000
		AU 1974100 A	03-07-2000
		WO 0035913 A1	22-06-2000
		EP 1140922 A1	10-10-2001
		JP 2002532497 T	02-10-2002
		US 2003162812 A1	28-08-2003

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

BENT, Stephen, A.
Foley & Lardner
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year) 17 November 2003 (17.11.03)	
Applicant's or agent's file reference 085747-0270	IMPORTANT NOTIFICATION
International application No. PCT/US03/24846	International filing date (day/month/year) 08 August 2003 (08.08.03)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 09 August 2002 (09.08.02)
Applicant ASTRA ZENECA AB et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(a) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(a) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
09 Augu 2002 (09.08.02)	60/402,040	US	19 Sept 2003 (19.09.03)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

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PATENT COOPERATION TREATY

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Washington Harbour
3000 K Street, N.W. Suite 500
Washington, DC 20007-5101
United States of America

Date of mailing (day/month/year)	IMPORTANT NOTIFICATION
01 ctober 2003 (01.10.03)	
Applicant's or agent's file reference	**International application No.**
085747-0270	PCT/US03/24846

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

ASTRA ZENECA AB et al (for all designated States except US)
WENSBO, David et al (for US)

International filing date	:	08 August 2003 (08.08.03)
Priority date(s) claimed	:	09 August 2002 (09.08.02)
Date of receipt of the record copy by the International Bureau	:	22 September 2003 (22.09.03)
List of designated Offices	:	

AP :GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZM,ZW
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ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- [X] time limits for entry into the national phase - see updated important information (as of April 2002)
- [ ] confirmation of precautionary designations (if applicable)
- [X] requirements regarding priority documents (if applicable)

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: Lulu HENRIOD (Fax 338 9090)
Facsimile No. (41-22) 338.90.90	Telephone No. (41-22) 338 8767

File Reference: 085747-0270

IN THE UNITED STATES RECEIVING OFFICE
UNDER THE PATENT COOPERATION TREATY

Applicants	:	**AstraZeneca AB, et al.**
International Application No.	:	PCT/US03/24846
International Filing Date	:	08 August 2003 (08.08.03)
Title of the Invention	:	**New Compounds**

RESPONSE TO INVITATION TO CORRECT DEFECTS
UNDER PCT ARTICLES 3(4)(i) and 14(1) AND RULE 26
IN THE INTERNATIONAL APPLICATION

ATTN: Latrice Russell

Mail Stop PCT
Commissioner of Patent
P.O. Box 1450
Alexandria, Virginia 22313-1450
United States of America

Dear Madame:

In response to Annex A of the Invitation to Correct Defects in the International Application, Form PCT/RO/106, dated 16 September 2003, and the sixteenth-month extension of time dated 03 October 2003, Agent for Applicants respectfully submits two (2) executed General Appointment of Agent for the Applicants: AstraZeneca AB (with authorization statement) and NPS Pharmaceuticals, Inc., also eighteen (18) executed General Appointment of Agent forms for each Applicant/Inventor in connection with the above-identified application. Lastly, please be informed that inventor WALDMAN's first name was misspelled. The correct spelling is **Magnus**, enclosed is a corrected page 5 of the PCT Request.

Respectfully submitted,

Stephen A. Bent
Registration No. 29,768

Date: November 26, 2003
Foley and Lardner
Washington Harbour
3000 K Street N.W., Suite 500
Washington, DC 20007-5109

Continuation of Box. III. FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included n 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.)*

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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: SE

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

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

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This person is:
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Applicant's registration No. with the Office

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

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

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

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This person is:
☐ applicant only
☒ applicant and inventor
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Applicant's registration No. with the Office

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

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SWEDEN

This person is:
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☒ 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: SE

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

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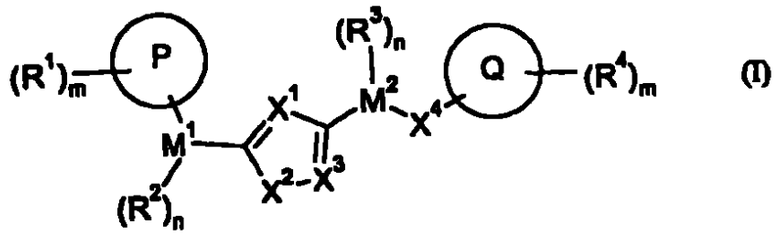
(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH,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

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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.

(54) Title: NEW COMPOUNDS



(I)

(57) Abstract: The present invention relates to new compounds of formula I, (I) a process for their preparation and new intermediates prepared therein, pharmaceutical formulations containing said compounds and to the use of said compounds in therapy.

WO 2004/014881 A2

NEW COMPOUNDS

FIELD OF THE INVENTION

The present invention relates to a new class of compounds, to pharmaceutical formulations containing said compounds and to the use of said compounds in therapy. The present invention further relates to the process for the preparation of said compounds and to new intermediates prepared therein.

BACKGROUND OF THE INVENTION

Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system (CNS). Glutamate produces its effects on central neurons by binding to and thereby activating cell surface receptors. These receptors have been divided into two major classes, the ionotropic and metabotropic glutamate receptors, based on the structural features of the receptor proteins, the means by which the receptors transduce signals into the cell, and pharmacological profiles.

The metabotropic glutamate receptors (mGluRs) are G protein-coupled receptors that activate a variety of intracellular second messenger systems following the binding of glutamate. Activation of mGluRs in intact mammalian neurons elicits one or more of the following responses: activation of phospholipase C; increases in phosphoinositide (PI) hydrolysis; intracellular calcium release; activation of phospholipase D; activation or inhibition of adenyl cyclase; increases or decreases in the formation of cyclic adenosine monophosphate (cAMP); activation of guanylyl cyclase; increases in the formation of cyclic guanosine monophosphate (cGMP); activation of phospholipase A_2; increases in arachidonic acid release; and increases or decreases in the activity of voltage- and ligand-gated ion channels. Schoepp *et al.*, *Trends Pharmacol. Sci. 14*:13 (1993), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Bordi and Ugolini, *Prog. Neurobiol. 59*:55 (1999).

Molecular cloning has identified eight distinct mGluR subtypes, termed mGluR1 through mGluR8. Nakanishi, *Neuron 13*:1031 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995),

Knopfel *et al., J. Med. Chem. 38*:1417 (1995). Further receptor diversity occurs via expression of alternatively spliced forms of certain mGluR subtypes. Pin *et al., PNAS 89*:10331 (1992), Minakami *et al., BBRC 199*:1136 (1994), Joly *et al., J. Neurosci. 15*:3970 (1995).

Metabotropic glutamate receptor subtypes may be subdivided into three groups, Group I, Group II, and Group III mGluRs, based on amino acid sequence homology, the second messenger systems utilized by the receptors, and by their pharmacological characteristics. Group I mGluR comprises mGluR1, mGluR5 and their alternatively spliced variants. The binding of agonists to these receptors results in the activation of phospholipase C and the subsequent mobilization of intracellular calcium.

Attempts at elucidating the physiological roles of Group I mGluRs suggest that activation of these receptors elicits neuronal excitation. Various studies have demonstrated that Group I mGluRs agonists can produce postsynaptic excitation upon application to neurons in the hippocampus, cerebral cortex, cerebellum, and thalamus, as well as other CNS regions. Evidence indicates that this excitation is due to direct activation of postsynaptic mGluRs, but it also has been suggested that activation of presynaptic mGluRs occurs, resulting in increased neurotransmitter release. Baskys, *Trends Pharmacol. Sci. 15*:92 (1992), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al., Neuropharmacology 34*:1(1995), Watkins *et al., Trends Pharmacol. Sci. 15*:33 (1994).

Metabotropic glutamate receptors have been implicated in a number of normal processes in the mammalian CNS. Activation of mGluRs has been shown to be required for induction of hippocampal long-term potentiation and cerebellar long-term depression. Bashir *et al., Nature 363*:347 (1993), Bortolotto *et al., Nature 368*:740 (1994), Aiba *et al., Cell 79*:365 (1994), Aiba *et al., Cell 79*:377 (1994). A role for mGluR activation in nociception and analgesia also has been demonstrated, Meller *et al., Neuroreport 4*: 879 (1993), Bordi and Ugolini, *Brain Res. 871*:223 (1999). In addition, mGluR activation has been suggested to play a modulatory role in a variety of other normal processes including synaptic transmission, neuronal development, apoptotic neuronal death, synaptic plasticity, spatial learning, olfactory memory, central control of cardiac activity, waking, motor control and control of the vestibulo-ocular reflex. Nakanishi, *Neuron 13*: 1031 (1994), Pin *et al., Neuropharmacology 34*:1, Knopfel *et al., J. Med. Chem. 38*:1417 (1995).

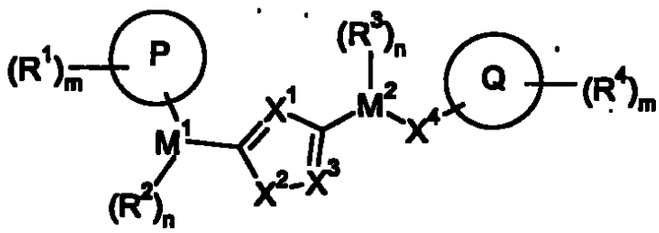
Further, Group I metabotropic glutamate receptors and mGluR5 in particular, have been suggested to play roles in a variety of pathophysiological processes and disorders affecting the CNS. These include stroke, head trauma, anoxic and ischemic injuries, hypoglycemia, epilepsy, neurodegenerative disorders such as Alzheimer's disease and pain. Schoepp *et al.*, *Trends Pharmacol. Sci. 14*:13 (1993), Cunningham *et al.*, *Life Sci. 54*:135 (1994), Hollman *et al.*, *Ann. Rev. Neurosci. 17*:31 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995), Spooren et al., *Trends Pharmacol. Sci. 22*:331 (2001), Gasparini et al. *Curr. Opin. Pharmacol. 2*:43 (2002), Neugebauer *Pain 98*:1 (2002). Much of the pathology in these conditions is thought to be due to excessive glutamate-induced excitation of CNS neurons. Because Group I mGluRs appear to increase glutamate-mediated neuronal excitation via postsynaptic mechanisms and enhanced presynaptic glutamate release, their activation probably contributes to the pathology. Accordingly, selective antagonists of Group I mGluR receptors could be therapeutically beneficial, specifically as neuroprotective agents, analgesics or anticonvulsants.

Recent advances in the elucidation of the neurophysiological roles of metabotropic glutamate receptors generally and Group I in particular, have established these receptors as promising drug targets in the therapy of acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders. Because of their physiological and pathophysiological significance, there is a need for new potent mGluR agonists and antagonists that display a high selectivity for mGluR subtypes, particularly the Group I receptor subtype, most particularly the mGluR5 subtype.

The object of the present invention is to provide compounds exhibiting an activity at metabotropic glutamate receptors (mGluRs), especially at the mGluR5 receptor.

SUMMARY OF THE INVENTION

The present invention provides a compound of formula Ia



(Ia)

wherein:

P is selected from the group consisting of hydrogen, C_{3-7}alkyl or a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$,C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

M^1 is selected from the group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-3}alkyl$(CO)NR^5C_{0-3}$alkyl, C_{0-4}alkylNR^5, C_{0-3}alkylSC_{0-3}alkyl, C_{0-3}alkyl$(SO)C_{0-3}$alkyl or C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^2 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^1, X^2 and X^3 are independently selected from the group consisting of CR, CO, N, NR, O and S;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$, C_{0-3}alkylNR^5R^6 and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{3-7}cycloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5; C_{0-3}alkylSC_{0-3}alkyl, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5, C_{0-4}alkyl(NR^5R^6), C_{0-4}alkyl$(NR^5R^6)=N$, NR^5C_{0-4}alkyl$(NR^5R^6)=N$, NOC_{0-4}alkyl, C_{1-4}alkylhalo, C, O, SO, SO_2 and S;

Q is a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S and which fused ring may be substituted by one or more A;

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, wherein said ring may be substituted by one or more A;

R^5 and R^6 are independently selected from the group consisting of hydrogen, hydroxy, C_{1-6}alkyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, and wherein R^5 and R^6 may together form a 5- or 6-membered ring containing one or more atoms independently selected from the goup consisting of C, N, O and S;

wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl defined under R^1, R^2, R^3, R^4, R^5 and R^6 may be substituted by one or more A;

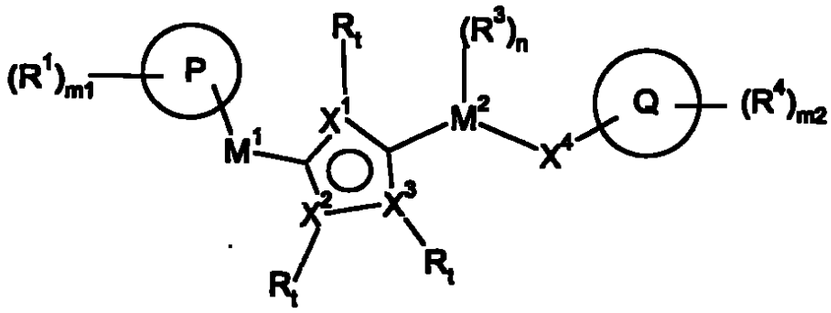
A is selected from the group consisting of hydrogen, hydroxy, oxo, halo, nitro, C_{0-6}alkylcyano, C_{1-4}alkyl, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, OC_{1-6}alkyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, $NR^5(CO)OR^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m is selected from 0, 1, 2, 3 and 4; and

n is selected from 0, 1, 2 and 3,

or salt thereof.

The present invention provides a compound of formula I



(I)

wherein:

P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

M^1 is a bond;

X^1 selected from the group consisting of C, CO, N, O and S;

X^2 is selected from the group consisting of C, N, O and S;

X^3 is i) selected from the group consisting of N, O and S, or

ii) selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H. ;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$ and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any

substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and any suitable carbon atom is optionally substituted with R^4; and

R^4 is selected from the group consisting of C_{0-6}alkylcyano, =NC_{1-4}alkyl, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}alkyl)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, =NR^5, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, (CO)R^5,

$O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m1 is selected from 0, 1, 2, 3 and 4;

m2 is selected from 0, 1, 2 and 3;

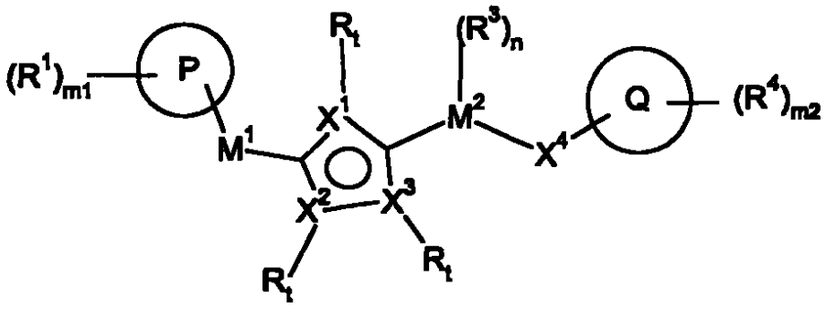
n is selected from 0, 1 and 2; and

t is 0 or 1,

and salts thereof,

with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole, 1,2-di{2-(3-amino-phenyl)-[1,3,4]oxadiazole-yl)ethane, 1,2-di{5-[5-(4-nitro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-bromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-chloro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane and 1,2-di{5-[5-(2,4-dibromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane.

The present invention provides a compound of formula Ib



(Ib)

wherein:

P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

M^1 is a bond;

X^1 selected from the group consisting of C, CO, N, O and S;

X^2 is selected from the group consisting of C, N, O and S;

X^3 is selected from the group consisting of N, O and S, or X^3 is CH when X^2 is N, O or S;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$ and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom; and

R^4 is selected from the group consisting of C_{0-6}alkylcyano, =NC_{1-4}alkyl, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}alkyl)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, =NR^5, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, (CO)R^5, O(CO)R^5, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, O(CO)OR^5, OC_{1-6}alkyl(CO)R^5, C_{1-6}alkyl(CO)R^5, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl(CO)NR^5R^6, OC_{1-6}alkyl(CO)NR^5R^6,

$OC_{2-6}alkylNR^5(CO)R^6$, $C_{0-6}alkylNR^5(CO)R^6$, $C_{0-6}alkylNR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, $C_{0-6}alkyl(SO_2)NR^5R^6$, $OC_{2-6}alkyl(SO_2)NR^5R^6$, $C_{0-6}alkylNR^5(SO_2)R^6$, $OC_{2-6}alkylNR^5(SO_2)R^6$, SO_3R^5, $C_{1-6}alkylNR^5(SO_2)NR^5R^6$, $OC_{2-6}alkyl(SO_2)R^5$, $C_{0-6}alkyl(SO_2)R^5$, $C_{0-6}alkyl(SO)R^5$, $OC_{2-6}alkyl(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m1 is selected from 0, 1, 2, 3 and 4;

m2 is selected from 0, 1, 2 and 3;

n is selected from 0, 1 and 2; and

t is 0 or 1,

and salts thereof,

with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole.

In a further aspect of the invention there is provided pharmaceutical formulations comprising a therapeutically effective amount of a compound of formula I and a pharmaceutically acceptable carrier.

In yet a further aspect of the invention there is provided a pharmaceutical formulation including a compound of formula I for use in the treatment of mGluR5 receptor-mediated disorders, and particularly neurological disorders, psychiatric disorders, acute and chronic pain.

In still a further aspect of the invention there is provided a compound of formula I for use in therapy for the treatment of mGluR5 receptor-mediated disorders, and particularly neurological disorders, psychiatric disorders, acute and chronic pain.

In another aspect of the invention there is provided a process for the preparation of compounds of formula I, and the intermediates provided therein.

These and other aspects of the present invention are described in greater detail herein below.

DETAILED DESCRIPTION OF THE INVENTION

Listed below are definitions of various terms used in the specification and claims to describe the present invention.

For the avoidance of doubt it is to be understood that where in this specification a group is qualified by 'hereinbefore defined', 'defined hereinbefore' or 'defined above' the said group encompasses the first occurring and broadest definition as well as each and all of the other definitions for that group.

For the avoidance of doubt it is to be understood that in this specification 'C_{1-6}' means a carbon group having 1, 2, 3, 4, 5 or 6 carbon atoms.
In this specification "C" means 1 cabon atom.

In this specification, unless stated otherwise, the term "alkyl" includes both straight and branched chain alkyl groups and may be methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, i-pentyl, t-pentyl, neo-pentyl, n-hexyl or i-hexyl, t-hexyl. The term "C_{1-3}alkyl" refers to an alkyl group having 1, 2 or 3 carbon atoms, and may be methyl, ethyl, n-propyl and i-propyl.

In this specification, unless stated otherwise, the term "cycloalkyl" refers to an optionally substituted, saturated cyclic hydrocarbon ring system. The term "C_{3-7}cycloalkyl" may be cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

In this specification, unless stated otherwise, the term "alkenyl" includes both straight and branched chain alkenyl groups. The term "C_{2-6}alkenyl" refers to an alkenyl group having 2 to 6 carbon atoms and one or two double bonds, and may be, but is not limited to vinyl, allyl, propenyl, i-propenyl, butenyl, i-butenyl, crotyl, pentenyl, i-pentenyl and hexenyl.

In this specification, unless stated otherwise, the term "alkynyl" includes both straight and branched chain alkynyl groups. The term C_{2-6}alkynyl having 2 to 6 carbon atoms and one

or two triple bonds, and may be, but is not limited to ethynyl, propargyl, butynyl, i-butynyl, pentynyl, i-pentynyl and hexynyl.

The term "aryl" refers to an optionally substituted monocyclic or bicyclic hydrocarbon ring system containing at least one unsaturated aromatic ring. Examples and suitable values of the term "aryl" are phenyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, indyl and indenyl.

In this specification, unless stated otherwise, the term "heteroaryl" refer to an optionally substituted monocyclic or bicyclic unsaturated, aromatic ring system containing at least one heteroatom selected independently from N, O or S. Examples of "heteroaryl" may be, but are not limited to thiophene, thienyl, pyridyl, thiazolyl, furyl, pyrrolyl, triazolyl, imidazolyl, oxadiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, benzofuryl, indolyl, isoindolyl, pyridonyl, pyridazinyl, pyrimidinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, pyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl.

In this specification, unless stated otherwise, the term "alkylaryl", "alkylheteroaryl " and "alkylcycloalkyl " refer to a substituent that is attached via the alkyl group to an aryl, heteroaryl and cycloalkyl group.

In this specification, unless stated otherwise, a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to furyl, isoxazolyl, isothiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, thiazolyl, thienyl, imidazolyl, imidazolidinyl, imidazolinyl, triazolyl, morpholinyl, piperazinyl, piperidyl, piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, thiomorpholinyl, phenyl, cyclohexyl, cyclopentyl and cyclohexenyl.

In this specification, unless stated otherwise, a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O or S, includes aromatic and

heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to imidazolidinyl, imidazolinyl, morpholinyl, piperazinyl, piperidyl, piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl or thiomorpholinyl, tetrahydrothiopyranyl, furyl, pyrrolyl, isoxazolyl, isothiazolyl, oxazolyl, oxazolidinonyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, thiazolyl, thienyl, imidazolyl, triazolyl, phenyl, cyclopropyl, aziridinyl, cyclobutyl, azetidinyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, cycloheptenyl, cyclooctyl and cyclooctenyl.

In this specification, unless stated otherwise, a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O or S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to naphthyl, norcaryl, chromyl, isochromyl, indanyl, benzoimidazol or tetralinyl, benzooxazolyl, benzothiazolyl, benzofuryl, benzothienyl, benzotriazolyl, indolyl, azaindolyl, indazolyl, indolinyl, isoindolinyl, benzimidazolyl, oxadiazolyl, thiadiazolyl, quinolinyl, quinoxalinyl and benzotriazolyl.

In this specification, unless stated otherwise, the term "$=NR^5$" and "$=NOR^5$" include imino- and oximogroups carrying an R^5 substituent and may be, or be part of, groups including, but not limited to iminoalkyl, iminohydroxy, iminoalkoxy, amidine, hydroxyamidine and alkoxyamidine.

In the case where a subscript is the integer 0 (zero) the group to which the subscript refers, indicates that the group is absent, i.e. there is a direct bond between the groups.

In this specification, unless stated otherwise, the term "bond" is a saturated bond.

In this specification, unless stated otherwise, the term "halo" may be fluoro, chloro, bromo or iodo.

In this specification, unless stated otherwise, the term "alkylhalo" means an alkyl group as defined above, substituted with one or more halo. The term "C_{1-6}alkylhalo" may include, but is not limited to fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl and bromopropyl. The term "OC_{1-6}alkylhalo" may include, but is not limited to fluoromethoxy, difluoromethoxy, trifluoromethoxy, fluoroethoxy and difluoroethoxy.

In one embodiments of the invention P may be hydrogen or C_{3-7} alkyl or P may be a 3- to 8-membered ring containing one or more atoms selected from C, N, O or S said ring may be optionally fused with a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O, or S. In a preferred embodiment of the invention P is selected from 5 and 6 membered aromatic and heteroaromatic rings.
In a further preferred embodiment P is selected from thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5.
In yet a further preferred embodiment of the invention P is phenyl substituted on position 3 or disubstituted on positions 2 and 5.

P is optionally substituted via a carbon atom with 0, 1, 2, 3 or 4 groups R^1, wherein the number of R^1 substituents on the P ring is designated by the term *m1*. In preferred embodiments of the invention *m1* is 1 or 2. In further preferred embodiments of the invention *m1* is 1.
In suitable embodiments of invention R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}

$_{6}$alkylNR^{5}(CO)OR^{6}, SO$_{3}$R^{5} and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S.

In a more suitable embodiment of the invention R^{1} is selected from hydrogen, hydroxy, halo, nitro, C$_{1-6}$alkylhalo, OC$_{1-6}$alkylhalo, C$_{1-6}$alkyl, OC$_{1-6}$alkyl, C$_{2-6}$alkenyl, C$_{0-6}$alkylC$_{3-6}$cycloalkyl, C$_{1-6}$alkylOR^{5}, C$_{1-6}$alkyl(CO)R^{5}, C$_{0-6}$alkylCO$_{2}$R^{5}, C$_{0-6}$alkylcyano, C$_{0-6}$alkylNR^{5}R^{6}, C$_{0-6}$alkylSR^{5} and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C and O.

Any C$_{1-6}$alkyl defined under R^{1} may be substituted by one or more A. In one embodiment of the invention R^{1} is ethyl and A is hydroxyl.

In a further suitable embodiment of the invention R^{1} is selected from hydrogen, methyl, ethyl, cyclopropyl, hydroxy, methoxy, cyano, flouro, chloro, bromo, iodo, trifluoromethyl, difluoromethoxy, trifluoromethoxy, amino, nitro, dimethylamino, methylsulfanyl, vinyl, acetyl, formic acid methyl ester, methoxymethyl, ethanol and furyl.

In a more suitable embodiment of the invention P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl or phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5 and R^{1} is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C$_{1-6}$alkylhalo, OC$_{1-6}$alkylhalo, C$_{1-6}$alkyl, OC$_{1-6}$alkyl, C$_{2-6}$alkenyl, C$_{0-6}$alkylC$_{3-6}$cycloalkyl, C$_{1-6}$alkylOR^{5}, C$_{1-6}$alkyl(CO)R^{5}, C$_{0-6}$alkylCO$_{2}$R^{5}, C$_{0-6}$alkylcyano, C$_{0-6}$alkylNR^{5}R^{6}, C$_{0-6}$alkylSR^{5} and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

In a further suitable embodiment of the invention P is phenyl substituted on position 3 or disubstituted on positions 2 and 5 and R^{1} is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C$_{1-6}$alkylhalo, OC$_{1-6}$alkylhalo, C$_{1-6}$alkyl, OC$_{1-6}$alkyl, C$_{2-6}$alkenyl, C$_{0-6}$alkylC$_{3-6}$cycloalkyl, C$_{1-6}$alkylOR^{5}, C$_{1-6}$alkyl(CO)R^{5}, C$_{0-6}$alkylCO$_{2}$R^{5}, C$_{0-6}$alkylcyano, C$_{0-6}$alkylNR^{5}R^{6}, C$_{0-6}$alkylSR^{5} and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

According to another aspect of the invention the ring P is connected to the core ring by M^{1}, wherein M^{1} can be a bond directly joining P to the core ring. M^{1} can also be a linker C$_{1-3}$alkyl.

In a preferred embodiment of the invention M^{1} is a bond.

When M^1 is not a direct bond M^1 can be further substituted with 0, 1, 2 or 3 substituents R^2 wherein the number of substituents R^2 is designated by the term *n*. The substituents R^2 may be selected from hydrogen, hydroxy, oxo, C_{1-4}alkylhalo, halo and C_{1-4}alkyl. In a preferred embodiment of the invention *n* is 0.

In another aspect of the invention there is provided compounds of formula I wherein X^1 is selected from the group consisting of C, CO, N, O and S. In a further aspect of the invention X^2 is selected from the group consisting of C, N, O and S. In yet a further aspect of the invention X^3 is selected from the group consisting of N, O and S, or X^3 is selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H.

X^1, X^2 and X^3 can be further substituted with 0, 1 or 2 substituents R wherein the number of substituents R is designated by the term *t*. The substituent R may be selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^{5}R^6, C_{0-3}alkyl(CO)OR^5, C_{0-3}alkylNR^{5}R^6 and C_{0-3}alkylaryl. In one embodiment of the invention R is selected from the group consisting of hydrogen, C_{0-3}alkyl and halo.
In a preferred embodiment of the invention X^1 is C, N or O and R is selected from hydrogen, C_{0-3}alkyl and halo. In one embodiment R is selected from hydrogen, chloro or methyl.
In another preferred embodiment of the invention X^1 is N.
In a suitable embodiment X^2 is selected from N, O and S, and R is hydrogen. In another embodiment of the invention X^3 is N, O or S. In a further preferred embodiment of the invention X^1 is O and one of X^2 and X^3 is O and the other is N. In yet a further preferred embodiment of the invention X^1 is N and one of X^2 and X^3 is O and the other is N. In yet another preferred embodiment of the invention X^1 is C or CR and one of X^2 and X^3 is O and the other is N.
In another preferred embodiment of the invention X^2 is O and X^3 is N, and in yet another preferred embodiment of the invention X^2 is N and X^3 is O.
In a further preferred embodiment of the invention X^1 is O and X^2 and X^3 are N.
In another suitable embodiment of the invention the ring containing X^1, X^2 and X^3 forms an oxadiazole, isoxazole, oxazole, chloro-isoxazole or a methyl-isoxazole.

In a preferred embodiment of the invention the ring containing X^1, X^2 and X^3 forms an oxadiazole. In another preferred embodiment of the invention the ring containing X^1, X^2 and X^3 forms an isoxazole.

The ring containing X^1, X^2 and X^3 should not be further annulated onto any other ring.

In a suitable embodiment of the invention M^2 may be a direct bond from the core ring to the variable X^4 or M^2 may be selected from the group consisting of bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl.
In preferred embodiments of the invention M^2 is a bond or C_{1-3}alkyl. In further preferred embodiments of the invention M^2 is C_{1-3}alkyl, preferably methyl or ethyl.

When M_2 is not a direct bond M^2 may be further substituted with 0, 1 or 2 R^3 groups wherein the number of substituents R^3 is designated by the term *n*. In one embodiment of the invention *n* is 1 or 2. In another embodiment of the invention *n* is 0.

In a suitable embodiment of the invention R^3 is selected from the group consisting of R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, =NR^5, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^{5}R^6.
In a preferred embodiment R^3 is selected from hydrogen and C_{1-4}alkyl, preferably methyl or dimethyl.
In another preferred embodiment M^2 may be selected from the group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl and R^3 is selected from hydrogen and C_{1-4}alkyl.
In yet another preferred embodiments of the invention M^2 is a bond or C_{1-3}alkyl and R^3 is hydrogen, methyl or dimethyl.
In a further preferred embodiment M^2 may be selected from the group consisting of a bond, methyl and ethyl and R^3 is hydrogen, methyl or dimethyl.

In a further embodiment of the invention M^2 is nitrogen. In yet a further embodiment of the invention M^2 is oxygen.

According to another aspect of the invention X^4 is selected from the group consisting of $C_{0-4}alkylR^5R^6$, $C_{3-7}cycloalkyl$, $C_{1-4}alkyl(NR^5R^6)$, NR^5, $C_{0-4}alkyl(NR^5R^6)=N$, $NR^5C_{0-4}alkyl(NR^5R^6)=N$, $NOC_{0-4}alkyl$, $C_{1-4}alkylhalo$, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond.

In a preferred embodiment of the invention X^4 is selected from the group consisting of $C_{0-4}alkylR^5R^6$, $C_{3-7}cycloalkyl$, NR^5, O, SO, SO_2 and S and R^5 and R^6 are independently selected from hydrogen and $C_{1-6}alkyl$.

In a further preferred embodiment of the invention X^4 is selected from the group consisting of CH_2, $CHCH_3$, $CH(CH_3)_2$ and NR^5. In a further preferred embodiment of the invention X^4 is NR^5 and R^5 is selected from hydrogen and $C_{1-6}alkyl$. In a preferred embodiment of the invention R^5 is methyl or hydrogen and R^6 is hydrogen.

In still a further preferred embodiment of the invention X^4 is O. In yet another preferred embodiment of the invention X^4 is S.

It is to be understood that the bond between M^2 and X^4 is a single bond in all tautomeric forms.

Embodiments of the present invention include those wherein Q is a 5- or 6-membered ring. When Q is a 5-membered ring, Q is selected from the group consisting of the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom.

In one embodiment the 5 membered ring Q is selected from the group consisting of triazolyl and thiadiazolyl. In another embodiment the 5 membered ring Q is selected from the group consisting of tetrazolyl and oxadiazolyl. In a further embodiment the 5 membered ring Q is imidazolyl.

When Q is a 6-membered ring, Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl,

pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl.

In a preferred embodiment of the invention the 6 membered ring Q is selected from the group consisting of pyridonyl, tetrahydrotriazolopyridyl and tetrahydrotriazolopyrimidinyl. In another embodiment the 6 membered ring Q is pyridazinyl. In a further embodiment the 6 membered ring Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl and imidazopyridyl.

Q can be further substituted with 0, 1, 2 or 3 substituents R^4, wherein the number of R^4 substituents is designated by the term *m2*. In a preferred embodiment *m2* is 1 or 2.

When Q is a 5-membered ring the substituent R^4 is selected from the group consisting of C_{0-6}alkylcyano, =NC_{1-4}alkyl, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl, C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}alkyl)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

In a further embodiment of the invention R^4 on the 5 membered Q ring is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl, C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from

C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

In one embodiment of the invention Q is selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and R^4 is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

In another embodiment of the invention Q selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and R^4 is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S; which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

When Q is a 6-membered ring the substituent R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

In a suitable embodiment of the invention R^4 on the 6 membered Q ring is selected from hydrogen and C_{1-6}alkyl. In a further embodiment of the invention R^4 is hydrogen, methyl, ethyl, propyl, butyl or hexyl.

In a preferred embodiment of the invention Q selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl and R^4 is hydrogen or C_{1-6}alkyl.

In another preferred embodiment of the invention Q selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl and imidazopyridyl, and R^4 is hydrogen or C_{1-6}alkyl.

In a suitable embodiment of the invention R^4 is selected from the group consisting of benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl, dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl,

trifluoromethyl, acetic acid methylester, allyl, amino, benzyl, cyclopropylmethyl, ethyl, fluorobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

Ring Q may be substituted by one or more R^4 on a carbon and/or a nitrogen atom in the ring. When Q is substituted on the carbon atom, R^4 is selected from benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl, dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl and trifluoromethyl.

When Q is substituted on the nitrogen atom, R^4 is selected from acetic acid methylester, allyl, amino, benzyl, cyclopropyl, cyclopropylmethyl, ethyl, flourobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methoxyethyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

When R^4 is a ring R^4 can be substituted with one or more substituents A, wherein A is selected from hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-}

$_{6}$alkyl(SO_2)NR^5R^6, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO)R^5, OC_{2-6}alkyl(SO)R^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S.

In a preferred embodiment A is selected from hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{1-6}alkyl, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

Specific embodiments of the invention include,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole,

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine,

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine,

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole,
3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,
3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,
5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,
2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,
5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole,
2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,
4-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine,
2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine,
2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b],
3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,
3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,
3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,
3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole, or
5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,
or salt thereof.

Further specific embodiments of the invention include,

4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester,

2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole,

5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine,

3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole,

4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole,

4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine,

3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile,

4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole,

4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine,

2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol,

3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol,

5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1;2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester,

5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole,

5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole,

2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide,

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine, or

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

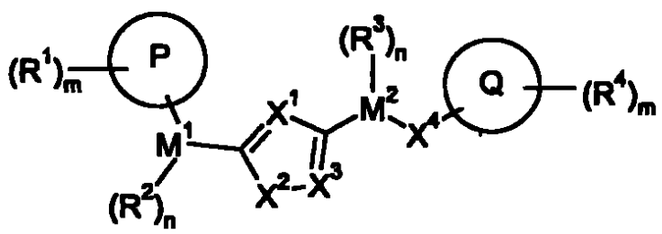
(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester,

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine,

or salt thereof.

Further feasible examples of compounds of formula I are provided by compounds of formula Ia



(Ia)

wherein:

P is selected from the group consisting of hydrogen, C_{3-7}alkyl and a 3- to 8-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO,

$(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, $C_{1-6}alkylOR^5$, $OC_{2-6}alkylOR^5$, $C_{1-6}alkyl(CO)R^5$, $OC_{1-6}alkyl(CO)R^5$, $C_{0-6}alkylCO_2R^5$, $OC_{1-6}alkylCO_2R^5$, $C_{0-6}alkylcyano$, $OC_{2-6}alkylcyano$, $C_{0-6}alkylNR^5R^6$, $OC_{2-6}alkylNR^5R^6$, $C_{1-6}alkyl(CO)NR^5R^6$, $OC_{1-6}alkyl(CO)NR^5R^6$, $C_{0-6}alkylNR^5(CO)R^6$, $OC_{2-6}alkylNR^5(CO)R^6$, $C_{0-6}alkylNR^5(CO)NR^5R^6$, $C_{0-6}alkylSR^5$, $OC_{2-6}alkylSR^5$, $C_{0-6}alkyl(SO)R^5$, $OC_{2-6}alkyl(SO)R^5$, $C_{0-6}alkylSO_2R^5$, $OC_{2-6}alkylSO_2R^5$, $C_{0-6}alkyl(SO_2)NR^5R^6$, $OC_{2-6}alkyl(SO_2)NR^5R^6$,$C_{0-6}alkylNR^5(SO_2)R^6$, $OC_{2-6}alkylNR^5(SO_2)R^6$, $C_{0-6}alkylNR^5(SO_2)NR^5R^6$, $OC_{2-6}alkylNR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, $C_{0-6}alkylNR^5(CO)OR^6$, $OC_{2-6}alkylNR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

M^1 is selected from the group consisting of a bond, $C_{1-3}alkyl$, $C_{2-3}alkenyl$, $C_{2-3}alkynyl$, $C_{0-4}alkyl(CO)C_{0-4}alkyl$, $C_{0-3}alkylOC_{0-3}alkyl$, $C_{0-3}alkyl(CO)NR^5$, $C_{0-3}alkyl(CO)NR^5C_{0-3}alkyl$, $C_{0-4}alkylNR^5$, $C_{0-3}alkylSC_{0-3}alkyl$, $C_{0-3}alkyl(SO)C_{0-3}alkyl$ and $C_{0-3}alkyl(SO_2)C_{0-3}alkyl$;

R^2 is selected from the group consisting of hydrogen, hydroxy, $C_{0-6}alkylcyano$, oxo, $=NR^5$, $=NOR^5$, $C_{1-4}alkylhalo$, halo, $C_{1-4}alkyl$, $O(CO)C_{1-4}alkyl$, $C_{1-4}alkyl(SO)C_{0-4}alkyl$, $C_{1-4}alkyl(SO_2)C_{0-4}alkyl$, $(SO)C_{0-4}alkyl$, $(SO_2)C_{0-4}alkyl$, $OC_{1-4}alkyl$, , $C_{1-4}alkylOR^5$ and $C_{0-4}alkylNR^5R^6$;

X^1, X^2 and X^3 are independently selected from the group consisting of CR, CO, N, NR, O and S;

R is selected from the group consisting of hydrogen, $C_{0-3}alkyl$, halo, $C_{0-3}alkylOR^5$, $C_{0-3}alkylNR^5R^6$, $C_{0-3}alkyl(CO)OR^5$, $C_{0-3}alkylNR^5R^6$ and $C_{0-3}alkylaryl$;

M^2 is selected from the group consisting of a bond, $C_{1-3}alkyl$, $C_{3-7}cycloalkyl$, $C_{2-3}alkenyl$, $C_{2-3}alkynyl$, $C_{0-4}alkyl(CO)C_{0-4}alkyl$, $C_{0-3}alkylOC_{0-3}alkyl$, $C_{0-3}alkylNR^5C_{1-3}alkyl$, $C_{0-3}alkyl(CO)NR^5$, $C_{0-4}alkylNR^5$, $C_{0-3}alkylSC_{0-3}alkyl$, $C_{0-3}alkyl(SO)C_{0-3}alkyl$ and $C_{0-3}alkyl(SO_2)C_{0-3}alkyl$;

R^3 is selected from the group consisting of hydrogen, hydroxy, $C_{0-6}alkylcyano$, oxo, $=NR^5$, $=NOR^5$, $C_{1-4}alkylhalo$, halo, $C_{1-4}alkyl$, $O(CO)C_{1-4}alkyl$, $C_{1-4}alkyl(SO)C_{0-4}alkyl$, $C_{1-4}alkyl(SO_2)C_{0-4}alkyl$, $(SO)C_{0-4}alkyl$, $(SO_2)C_{0-4}alkyl$, $OC_{1-4}alkyl$, $C_{1-4}alkylOR^5$ and $C_{0-4}alkylNR^5R^6$;

X^4 is selected from the group consisting of $C_{0-4}alkylR^5$, $C_{0-4}alkyl(NR^5R^6)$, $C_{0-4}alkyl(NR^5R^6)=N$, $NR^5C_{0-4}alkyl(NR^5R^6)=N$, $NOC_{0-4}alkyl$, $C_{1-4}alkylhalo$, C, O, SO, SO_2 and S;

Q is a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S and which fused ring may be substituted by one or more A;

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, wherein said ring may be substituted by one or more A;

R^5 and R^6 are independently selected from the group consisting of hydrogen, hydroxy, C_{1-6}alkyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, and wherein R^5 and R^6 may together form a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S;

wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl defined under R^1, R^2, R^3, R^4, R^5 and R^6 may be substituted by one or more A; and

A is selected from the group consisting of hydrogen, hydroxy, oxo, halo, nitro, C_{0-6}alkylcyano, C_{1-4}alkyl, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, OC_{1-6}alkyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, $NR^5(CO)OR^6$, C_{0-6}alkyl(SO_2)NR^5R^6, OC_{2-6}alkyl(SO_2)NR^5R^6, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO_2)R^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S;

m is selected from 0, 1, 2, 3 and 4; and

n is selected from 0, 1, 2 and 3,

or salt thereof.

The present invention relates to the use of compounds of formula I and IA as hereinbefore defined as well as to the salts thereof. Salts for use in pharmaceutical formulations will be pharmaceutically acceptable salts, but other salts may be useful in the production of the compounds of formula I and Ia.

Examples of pharmaceutically acceptable salts may be, but are not limited to hydrochloride, 4-aminobenzoate, anthranilate, 4-aminosalicylate, 4-hydroxybenzoate, 3,4-dihydroxybenzoate, 3-hydroxy-2-naphthoate, nitrate and trifluoroacetate. Other pharmaceutically acceptable salts and methods of preparing these salts may be found in, for example, Remington's Pharmaceutical Sciences (18th Edition, Mack Publishing Co.).

Some compounds of formula I may have chiral centres and/or geometric isomeric centres (E- and Z- isomers), and it is to be understood that the invention encompasses all such optical, diastereoisomers and geometric isomers.

The invention relates to any and all tautomeric forms of the compounds of formula I.

The invention relates to the following compounds, which may be used as intermediates in the preparation of a compound of formula I;

6-Methylpyridine-4-carboxylic acid,

1-Cyano-3-ethylbenzene,

3-Ethylbenzoic acid,

3-Fluoro-5-methyl-benzoic acid,

3-Methoxymethyl-benzoic acid,

N-Hydroxy-3-methoxy-benzamidine,

N-Hydroxy-benzamidine,

N-Hydroxy-3-methyl-benzamidine,

5-Chloromethyl-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole,

5-Chloromethyl-3-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile,

3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile,

3-Chloromethyl-5-m-tolyl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine,

3-Chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

4-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine,

3-Chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine,

3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole,

3-Chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-pyridin-2-yl-4H-[1,2,4]triazole-3-thiol,

5-(4-Benzyl-morpholin-2-yl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-pyridin-3-yl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol,

5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

5-Chloro-thiophene-3-carboxylic acid,

3-Methylsulfanyl-benzoic acid,

3-Cyclopropyl-benzoic acid,

3-tert-Butoxycarbonylamino-benzoic acid,

3-Acetyl-benzoic acid,

2-Methyl-isonicotinic acid hydrazide,

5-Chloro-2-fluoro-benzoic acid hydrazide.,

3-Cyano-benzoic acid hydrazide,

2-Chloro-isonicotinic acid hydrazide,

2-Fluoro-5-methyl-benzoic acid hydrazide,

Pyrimidine-4-carboxylic acid hydrazide,

3-Fluoro-N-hydroxy-benzamidine,

N-Hydroxy-thiophene-3-carboxamidine,

2-Chloro-N-hydroxy-propionamidine,

3,N-Dihydroxy-benzamidine,

N-Hydroxy-2-methyl-benzamidine,

N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine,

3-Chloro-N-hydroxy-benzamidine,

N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine,

2,5-Difluoro-N-hydroxy-benzamidine,

4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol,

4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

4-(3-Methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

5-Thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

4-Furan-2-ylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

4-Furan-2-ylmethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol,

5-(2-Fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol,

5-(2-Chloro-6-methyl-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(tetrahydro-furan-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,
4-Ethyl-5-thioxo-4,5-dihydro-1H-[1,2,4]triazole-3-carboxylic acid methyl ester,
5-(2-Chloro-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
5-(2-Chloro-6-methoxy-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol,
4-Propyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol,
3-(5-Mercapto-4-methyl-4H-[1,2,4]triazol-3-yl)-benzonitrile,
5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole-3-thiol ,
5-(3,5-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
5-(2,6-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,
5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-pyrimidin-5-yl-2,4-dihydro-[1,2,4]triazole-3-thione,
4-Ethyl-5-furan-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione,
4-(Tetrahydrofuran-2-ylmethyl)-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,
5-Cyclopentyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione,
4-Ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-2,4-dihydro-[1,2,4]triazole-3-thione,
5-(3,5-Dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,
5-(3-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,
5-(4-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl- 5-(3-nitrophenyl)-4H-[1,2,4]triazole-3-thiol,

5-(2,5-Difluorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

5-(3-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

5-(4-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-methoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Methyl-5-pyridin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Allyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(4-methoxy-phenoxymethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-phenoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-hydroxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-methylsulfanylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Ethoxymethyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Furan-3-yl-4-methyl-2,4-dihydro-[1,2,4]triazole-3-thione ,

4-Methyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-pyridazin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-pyridin-4-ylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(6-hydroxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(4-hydroxy-phenyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-p-tolyloxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(6-methoxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(2-methoxy-pyridin-4-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-pyrimidin-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(5-methoxy-pyrimidin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol,

4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol,

4-Cyclopropylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol,

4-Cyclopropyl-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Furan-2-yl-4-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Cyclopropyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

(3-Thiophen-2-yl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-acetic acid methyl ester,

4-Cyclopropylmethyl-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-(2-Methoxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

Thiophen-2-yl-4-(2,2,2-trifluoroethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Cyclopropyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Cyclopropyl-5-pyridin-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-3-methanesulfonyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-(5-Methanesulfonyl-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(2-Hydroxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-(4,5-Dimethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

Methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

3-Pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-Furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3- a]pyrimidine,

4-Ethyl-5-(6-methoxy-pyridazin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(5-methoxy-pyridin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole,

5-Chloromethyl-3-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

5-Chloromethyl-3-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole ,

5-Chloromethyl-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-Chloromethyl-3-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-phenol,

5-Chloromethyl-3-o-tolyl-[1,2,4]oxadiazole,

5-Chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-Chloromethyl-3-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile,

2-Chloro-4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-pyridine,

3-Chloromethyl-5-(2,5-dimethyl-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(2,5-dichloro-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(2-fluoro-5-bromo-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-methyl-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(3-cyclopropyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-carbamic acid tert-butyl ester,

1-[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-ethanone,

5-(5-Chloro-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole,

2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-phenol,

3-Chloromethyl-5-(2-chloro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(2,5-dichloro-thiophen-3-yl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile,

3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole ,

5-(5-Bromo-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-thiophene-3-carbonitrile,

2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-benzonitrile,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-fluoro-benzonitrile,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-fluoro-benzonitrile,

4-Chloro-2-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenol,

3-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(1-Chloro-ethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

3-(1-Chloro-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,2,4]oxadiazole,

[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-methanol,

3-Chloromethyl-5-[1-(toluene-4-sulfonyl)-1H-pyr rol-3-yl]-[1,2,4]oxadiazole,

3-Chloromethyl-5-furan-3-yl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(5-chloro-thiophen-2-yl)-[1,2,4]oxadiazole,

1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethanol,

[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol,

1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethanol,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol,

2-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-Chloromethyl-5-(3-chloro-phenyl)-[1,3,4]oxadiazole,

4-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

2-Chloromethyl-5-m-tolyl-[1,3,4]oxadiazole,

3-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-benzonitrile,

2-Chloro-4-(5-chloromethyl-[1,3,4]oxadiazol-2-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-chloromethyl-[1,3,4]oxadiazole,

2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole,

2-(1-Bromo-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,3,4]oxadiazole,

4-[5-(1-Bromo-ethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

2-(1-Bromo-ethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole,

3-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol,

1-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethanol,

5-(2-Fluoro-5-methyl-phenyl)-isoxazole-3-carboxylic acid methyl ester,

5-Thiophen-3-yl-isoxazole-3-carboxylic acid methyl ester,

5-Phenyl-isoxazole-3-carboxylic acid methyl ester,

5-(3-Chloro-phenyl)-4-methyl-isoxazole-3-carboxylic acid ethyl ester,

5-(5-Chloro-thiophen-3-yl)-isoxazole-3-carboxylic acid methyl ester,

[5-(3-Chloro-phenyl)-isoxazol-3-yl]-methanol,

[2-(3-Chloro-phenyl)-oxazol-4-yl]-methanol,

[3-(3-Chloro-phenyl)-isoxazol-5-yl]-methanol,

5-(Thiophen-3-yl-isoxazol-3-yl)methanol,

[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-methanol,

(5-Phenyl-isoxazol-3-yl)-methanol,

[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-yl]-methanol,

[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-yl)]-methanol,

Methanesulfonic acid 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethyl ester,

Methanesulfonic acid 2-(3-chloro-phenyl)-oxazol-4-ylmethyl ester,

Methanesulfonic acid 3-(3-chloro-phenyl)-isoazol-5-ylmethyl ester,

Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester,

Methanesulfonic acid -phenyl)-isoxazol-5-yl]-ethyl ester,

Methanesulfonic acid 5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-ylmethyl ester,

Methanesulfonic acid 5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester,

Methanesulfonic acid 5-thiophen-3-yl-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-phenyl-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(3-chloro-phenyl)-4-methyl-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(5-chloro-thiophen-3-yl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethyl ester,
Methanesulfonic acid 1-[5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethyl ester,
Methanesulfonic acid 4-chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester,
Pyrimidine-4-carboxylic acid,
3-(3-Chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester,
2-Bromomethyl-5-(3-chloro-phenyl)-oxazole,
2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester,
2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester,
1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethanol,
1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethanol,
[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-methanol,
3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide,
3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide,
3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride,
3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide,
[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide,
(R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide,
3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-3-methyl-butyric acid hydrazide,
3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one,
3-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one,
3-Chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole,
1-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole,
(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetonitrile,
2-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid,
2-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid,

3-(3-Chloro-phenyl)-5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole or,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl-phenyl}-carbamic acid tert-butyl ester.

Pharmaceutical formulations

According to one aspect of the present invention there is provided a pharmaceutical formulation comprising a compound of formula I, or salt thereof, for use in the prevention and/or treatment of metabotropic glutamate receptor subtype 5 receptor (mGluR5) mediated disorders and any disorder listed below.

The composition may be in a form suitable for oral administration, for example as a tablet, pill, syrup, powder, granule or capsule, for parenteral injection (including intravenous, subcutaneous, intramuscular, intravascular or infusion) as a sterile solution, suspension or emulsion, for topical administration as an ointment, patch or cream or for rectal administration as a suppository.

In general the above compositions may be prepared in a conventional manner using one or more conventional excipients, pharmaceutical diluents and/or inert carriers.

According to another aspect of the invention thee is provided a pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound of formula I in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

Suitable daily doses of the compounds of formula I in the treatment of a mammal, including man are approximately 0.01 to 250 mg/kg bodyweight at peroral administration and about 0.001 to 250 mg/kg bodyweight at parenteral administration. The typical daily dose of the active ingredients varies within a wide range and will depend on various factors such as the relevant indication, the route of administration, the age, weight and sex of the patient and may be determined by a physician.

Medical use

It has been found that the compounds according to the present invention, or salts thereof, exhibit a high degree of potency and selectivity for individual metabotropic glutamate receptor (mGluR) subtypes. In particular there are compounds according to the present invention that are potent and selective for the mGluR Group I receptor and more particularly for mGluR5. Accordingly, the compounds of the present invention are expected to be useful in the prevention and/or treatment of conditions associated with excitatory activation of an mGluR Group I receptor and for inhibiting neuronal damage caused by excitatory activation of an mGluR Group I receptor, specifically when the mGluR Group I receptor is mGluR5. The compounds may be used to produce an inhibitory effect of mGluR Group I, especially mGluR5, in mammals, including man.

mGluR5 is highly expressed in the central and peripheral nervous system and in other tissues. Thus, it is expected that the compounds of the invention are well suited for the prevention and/or treatment of mGluR5 receptor-mediated disorders such as acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders.

Further disorders are Alzheimer's disease senile dementia, AIDS-induced dementia, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's Chorea, migraine, epilepsy, schizophrenia, depression, anxiety, acute anxiety, obsessive compulsive disorder, ophthalmological disorders such as retinopathies, diabetic retinopathies, glaucoma, auditory neuropathic disorders such as tinnitus, chemotherapy induced neuropathies, post-herpetic neuralgia and trigeminal neuralgia, tolerance, dependency, addiction and craving disorders, neurodevelopmental disorders including Fragile X, autism, mental retardation, schizophrenia and Down's Syndrome.

The compounds are also well suited for the prevention and/or treatment of pain related to migraine, inflammatory pain, neuropathic pain disorders such as diabetic neuropathies, arthritis and rheumatitiod diseases, low back pain, post-operative pain and pain associated with various conditions including angina, renal or billiary colic, menstruation, migraine and gout.

Other disorders are stroke, head trauma, anoxic and ischemic injuries, hypoglycemia, cardiovascular diseases and epilepsy.

The dose required for the therapeutic or preventive treatment of a particular disorder will necessarily be varied depending on the host treated, the route of administration and the severity of the illness being treated.

The invention relates to compounds of formula I as defined hereinbefore, for use in therapy.

The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of neurological disorders.

The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of psychiatric disorders.

The invention relates to compounds of formula I as defined hereinbefore, , for use in prevention and/or treatment of chronic and acute pain disorders.

The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of mGluR5 receptor-mediated disorders.

The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of Alzheimer's disease senile dementia, AIDS-induced dementia, Parkinson's disease, amylotropic lateral sclerosis, Huntington's Chorea, migraine, epilepsy, schizophrenia, depression, anxiety, acute anxiety, ophthalmological disorders such as retinopathies, diabetic retinopathies, glaucoma, auditory neuropathic disorders such as tinnitus, chemotherapy induced neuropathies, post-herpetic neuralgia and trigeminal neuralgia, tolerance, dependency, Fragile X, autism, mental retardation, schizophrenia and Down's Syndrome.

The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of pain related to migraine, inflammatory pain, neuropathic pain disorders such as diabetic neuropathies, arthritis and rheumatitiod diseases, low back

pain, post-operative pain and pain associated with various conditions including angina, renal or billiary colic, menstruation, migraine and gout.

The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of stroke, head trauma, anoxic and ischemic injuries, hypoglycemia, cardiovascular diseases and epilepsy.

The present invention relates also to the use of a compound of formula I as defined hereinbefore, in the manufacture of a medicament for the prevention and/or treatment of mGluR5 receptor-mediated disorders and any disorder listed above.

The invention also provides a method of treatment and/or prevention of mGluR5 receptor-mediated disorders and any disorder listed above, in a patient suffering from, or at risk of, said condition, which comprises administering to the patient an effective amount of a compound of formula I, as hereinbefore defined.

In the context of the present specification, the term "therapy" includes treatment as well as prevention, unless there are specific indications to the contrary. The terms "therapeutic" and "therapeutically" should be construed accordingly.

In this specification, unless stated otherwise, the term 'antagonist' means a compound that by any means, partly or completely, blocks the transduction pathway leading to the production of a response by the ligand.

The term "disorder", unless stated otherwise, means any condition and disease associated with metabotropic glutamate receptor activity.

<u>Non- Medical use</u>

In addition to their use in therapeutic medicine, the compounds of formula I or salt thereof, are also useful as pharmacological tools in the development and standardisation of *in vitro* and *in vivo* test systems for the evaluation of the effects of inhibitors of mGluR related

activity in laboratory animals such as cats, dogs, rabbits, monkeys, rats and mice, as part of the search for new therapeutics agents.

Pharmacology

The pharmacological properties of the compounds of the invention can be analyzed using standard assays for functional activity. Examples of glutamate receptor assays are well known in the art as described in for example Aramori *et al., Neuron* 8:757 (1992), Tanabe *et* al., *Neuron* 8:169 (1992), Miller *et al., J. Neuroscience* 15: 6103 (1995), Balazs, *et al., J. Neurochemistry* 69:151 (1997). The methodology described in these publications is incorporated herein by reference. Conveniently, the compounds of the invention can be studied by means of an assay that measures the mobilization of intracellular calcium, $[Ca^{2+}]_i$ in cells expressing mGluR5.

Intracellular calcium mobilization was measured by detecting changes in fluorescence of cells loaded with the fluorescent indicator fluo-3. Fluorescent signals were measured using the FLIPR system (Molecular Devices). A two addition experiment was used that could detect compounds that either activate or antagonize the receptor.

For FLIPR analysis, cells expressing human mGluR5d were seeded on collagen coated clear bottom 96-well plates with black sides and analysis of $[Ca^{2+}]_i$ mobilization was done 24 hours after seeding.

FLIPR experiments were done using a laser setting of 0.800 W and a 0.4 second CCD camera shutter speed. Each FLIPR experiment was initiated with 160 µL of buffer present in each well of the cell plate. After each addition of the compound, the fluorescence signal was sampled 50 times at 1 second intervals followed by 3 samples at 5 second intervals. Responses were measured as the peak height of the response within the sample period. EC_{50} and IC_{50} determinations were made from data obtained from 8-point concentration response curves (CRC) performed in duplicate. Agonist CRC were generated by scaling all responses to the maximal response observed for the plate. Antagonist block of the agonist challenge was normalized to the average response of the agonist challenge in 14 control wells on the same plate.

We have validated a secondary functional assay for mGluR5d based on Inositol Phosphate (IP_3) turnover. IP_3 accumulation is measured as an index of receptor mediated phospholipase C turnover. GHEK cells stably expressing the human mGluR5d receptors were incubated with [3H] myo-inositol overnight, washed three times in HEPES buffered saline and pre-incubated for 10 minutes with 10 mM LiCl. Compounds (agonists) were added and incubated for 30 minutes at 37°C. Antagonist activity was determined by pre-incubating test compounds for 15 minutes, then incubating in the presence of glutamate (80μM) or DHPG (30 μM) for 30 minutes. Reactions were terminated by the addition of perchloric acid (5%). Samples were collected and neutralized, and inositol phosphates were separated using Gravity-Fed Ion-Exchange Columns.

A detailed protocol for testing the compounds of the invention is provided below in Pharmaceutical Examples.

Abbreviations

FLIPR	Fluorometric Imaging Plate reader
CCD	Charge Coupled Device
CRC	Concentration Response Curve
GHEK	Human Embrionic Kidney expressing Glutamate Transporter
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (buffer)
IP_3	inositol triphosphate
DHPG	3,5-dihydroxyphenylglycine;
BSA	Bovine Serum Albumin
EDTA	Ethylene Diamine Tetraacetic Acid

Methods of Preparation

Another aspect of the present invention provides a process for preparing a compound of formula I, or salt thereof.

Throughout the following description of such processes it is understood that, where appropriate, suitable protecting groups will be added to, and subsequently removed from,

the various reactants and intermediates in a manner that will be readily understood by one skilled in the art of organic synthesis. Conventional procedures for using such protecting groups as well as examples of suitable protecting groups are described, for example, in "Protective Groups in Organic Synthesis" T.W. Green, P.G.M. Wuts, Wiley-Interscience, New York, 1999.

Unless specified otherwise, are P, Q, X^1, X^2, X^3, X^4, R, R^1, R^2, R^3, R^4, R^5, R^6, M^1, M^2, m and n, defined as in formula I.

All starting materials are commercially available or earlier described in the literature. The ^1H and ^{13}C NMR spectra were recorded either on Bruker 300, Bruker DPX400 or Varian +400 spectrometers operating at 300, 400 and 400 MHz for ^1H NMR respectively, using TMS or the residual solvent signal as reference, in deuterated chloroform as solvent unless otherwise indicated. All reported chemical shifts are in ppm on the delta-scale, and the fine splitting of the signals as appearing in the recordings (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet).

Analytical in line liquid chromatography separations followed by mass spectra detections, were recorded on a Waters LCMS consisting of an Alliance 2795 (LC) and a ZQ single quadropole mass spectrometer. The mass spectrometer was equipped with an electrospray ion source operated in a positive or negative ion mode. The ion spray voltage was ±3 kV and the mass spectrometer was scanned from *m/z* 100-700 at a scan time of 0.8 s. To the column, X-Terra MS, Waters, C8, 2.1 x 50mm, 3.5 µm, was applied a linear gradient from 5 % to 100% acetonitrile in10 mM ammonium acetate (aq.), or in 0.1% TFA (aq.).

Preparative reversed phase chromatography was run on a Gilson autopreparative HPLC with a diode array detector using an XTerra MS C8, 19x300mm, 7µm as column.

MS-triggered preparative reversed phase chromatograpy was run on a Waters autopurification *LC-MS* system with a diode array detector and a ZQ mass detector using an XTerra MS C8, 19x100 mm, 5 µm as column.

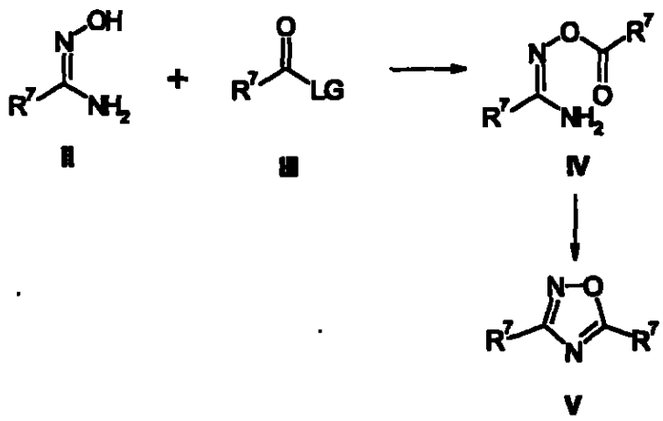
Purification by a chromatotron was performed on rotating silica gel / gypsum (Merck, 60 PF-254 with calcium sulphate) coated glass sheets, with coating layer of 1, 2, or 4 mm using a TC Research 7924T chromatotron.

Purification of products were also done using Chem Elut Extraction Columns (Varian, cat #1219-8002), Mega BE-SI (Bond Elut Silica) SPE Columns (Varian, cat # 12256018; 12256026; 12256034), or by flash chromatography in silica-filled glass columns. Microwave heating was performed in a Smith Synthesizer Single-mode microwave cavity producing continuous irradiation at 2450 MHz (Personal Chemistry AB, Uppsala, Sweden).

Abbreviations:

DMF	*N,N*-dimethylformamide
BOPA	Benzoyl Peroxide
P-BEMP	Polystyrene bound 2-tert-Butylimino-2-diethylamino-1,3-dimethyl-perhydro--1,3,2-diazaphosporine
Deoxofluor	[Bis(2-methoxyethyl)amino]sulfur trifluoride
DAST	(Diethylamino)sulfur trifluoride
EDCI	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
HOBt	1-hydroxybenzotriazole hydrate
THF	tetrahydrofuran
TFA	trifluoroacetic acid
Et	ethyl
Ac	acetyl
DIBAL	diisobutylaluminum hydride
M, N	molar and normal
HBTU	*O*-Benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate
Boc	tert-butoxycarbonyloxy
LDA	Lithium diisopropylamine
LHA	Lithium aluminium hydride
MCPBA	meta-chloroperoxybenzoic acid
SPE	solid phase extraction
Lawesson's Reagent	[2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane--2,4-disulfide

General syntheses of compounds of formula V.



II III IV

V

A compound of formula V, wherein R^7 is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared through cyclization of a compound of formula IV formed from a suitably activated compound of formula III, wherein LG is a leaving group, with a compound of formula II.

The compound of formula II may be prepared from a suitable nitrile by addition of hydroxylamine in a suitable solvent such as, methanol, ethanol, water or mixture thereof, using an appropriate base such as hydroxide, carbonate or acetate.

The compound of formula III may be activated as follows; i) as the acid chloride formed from the acid using a suitable reagent such as oxalyl chloride or thionyl chloride; ii) as an anhydride or mixed anhydride formed from treatment with a reagent such as alkyl chloroformate; iii) using traditional methods to activate acids in amide coupling reactions such as EDCI with HOBt or uronium salts like HBTU; iv) as an alkyl ester when the hydroxyamidine is deprotonated using a strong base like tert-butoxide; v) by any other suitable method of activation for the desired substrate.

The ester formation may be accomplished using an appropriate aprotic solvent such as dichloromethane, tetrahydrofuran, *N,N*-dimethylformamide or toluene, with optionally an appropriate organic base such as triethylamine, diisopropylethylamine and the like or an inorganic base such sodium bicarbonate or potassium carbonate.

The cyclization of the ester to form an oxadiazole may be carried out on the crude ester, with evaporation and replacement of the solvent with a higher boiling solvent such as DMF, or with aqueous extraction to provide a semi-purified material or with material purified by standard chromatographic methods. The cyclization may be accomplished by heating conventionally or by microwave irradiation (100-180°C), in a suitable solvent such as pyridine or *N,N*-dimethylformamide or using a lower temperature method employing reagents like tetrabutylammonium fluoride in tetrahydrofuran or by any other suitable known literature method.

Other compatible non-reacting functional groups suitably protected may also be present in the substrates.

Further examples of the above described reactions can be found in Poulain et al., Tetrahedron Lett., (2001), *42*, 1495-98, Ganglott et al., Tetrahedron Lett., (2001), *42*, 1441-43, which are hereby included as references.

Synthesis of Nitriles and Acids for use in preparation of compounds of formula II and III

Aryl nitriles are available by a variety of methods including cyanation of an aryl halide or triflate under palladium or nickel catalysis using an appropriate cyanide source such as zinc cyanide in an appropriate solvent such as *N,N*-dimethylformamide. The corresponding acid is available from the nitrile by hydrolysis under either acidic or basic conditions in an appropriate solvent such as aqueous alcohols. Aryl acids are also available from a variety of other sources, including iodo- or bromo- lithium exchange followed by trapping with CO_2 to give directly the acid.

The acid may be converted to the primary amide using any compatible method to activate the acid, including via the acid chloride or mixed anhydride, followed by trapping with any source of ammonia, including ammonium chloride in the presence of a suitable base, ammonium hydroxide, methanolic ammonia or ammonia in an aprotic solvent such as dioxane. This amide intermediate may be converted to the nitrile using a variety of dehydration reagents such as oxalyl chloride or thionyl chloride. This reaction sequence to convert an acid into a nitrile may also be applied to non-aromatic acids, including suitably protected amino acid derivatives. A suitable protecting group for an amine, in an amino

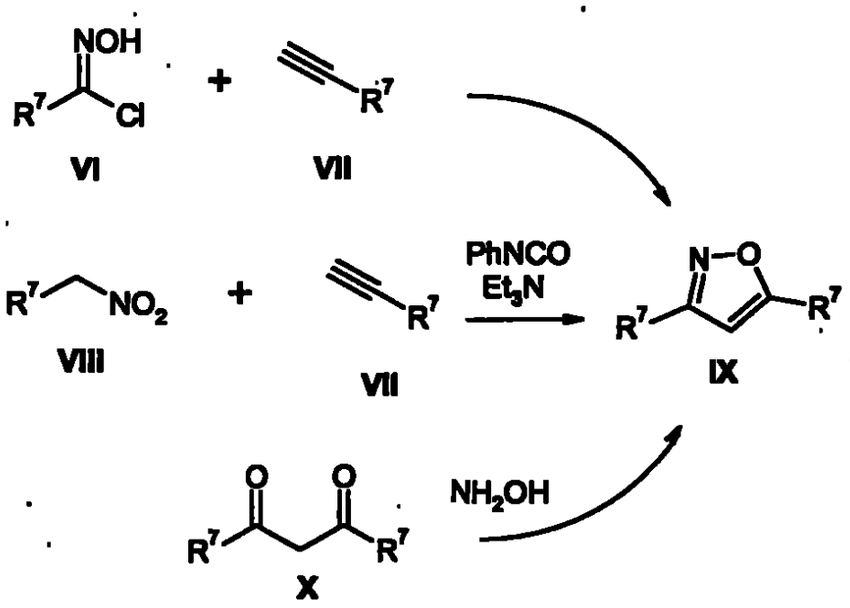
acid or in a remote position of any other acid starting material, may be any group which removes the basicity and nucleophilicity of the amine functionality, including such carbamate protecting group as Boc.

Some acids are more easily prepared taking advantage of commercially available analogs. For example, 6-methylpyridine-4-carboxylic acid is prepared by dechlorination of 2-chloro-6-methylpyridine-4-carboxylic acid. Certain types of substituted fluoro-benzonitriles and benzoic acids are available from bromo-difluoro-benzene via displacement of one fluoro group with a suitable nucleophile such as imidazole in the presence of a base such as potassium carbonate in a compatible solvent such as *N,N*-dimethylformamide at elevated temperatures (80-120°C) for extended periods of time. The bromo group may subsequently be elaborated into the acid or nitrile as above.

1,3-Disubsituted and 1,3,5-trisubstituted benzoic acids and benzonitriles may be prepared by taking advantage of readily available substituted isophthalic acid derivatives. Monohydrolysis of the diester allows selective reaction of the acid with a variety of reagents, most typically activating agents such as thionyl chloride, oxalyl chloride or isobutyl chloroformate and the like. From the activated acid, a number of products are available. In addition to the primary amide used to form the nitrile by dehydration as mentioned above, reduction to the hydroxymethyl analog may be carried out on the mixed anhydride or acid chloride using a variety of reducing agents such as sodium borohydride in a compatible solvent such as tetrahydrofuran. The hydroxymethyl derivative may be further reduced to the methyl analog using catalytic hydrogenation with an appropriate source of catalyst such as palladium on carbon in an appropriate solvent such as ethanol. The hydroxymethyl group may also be used in any reaction suitable for benzylic alcohols such as acylation, alkylation, transformation to halogen and the like. Halomethylbenzoic acids of this type may also be obtained from bromination of the methyl derivative when not commercially available. Ethers obtained by alkylation of the hydroxymethyl derivatives may also be obtained from the halomethylaryl benzoate derivatives by reaction with the appropriate alcohol using an appropriate base such as potassium carbonate or sodium hydroxide in an appropriate solvent such as tetrahydrofuran or the alcohol. When other substituents are present, these may also be employed in standard transformation reactions. Treatment of an aniline with acid and sodium nitrite may yield a diazonium salt, which may be transformed into a halide such as fluoride using tetrafluoroboric acid.

Phenols react in the presence of a suitable base such as potassium carbonate with alkylating agents to form aromatic ethers.

Formation of compounds of formula IX

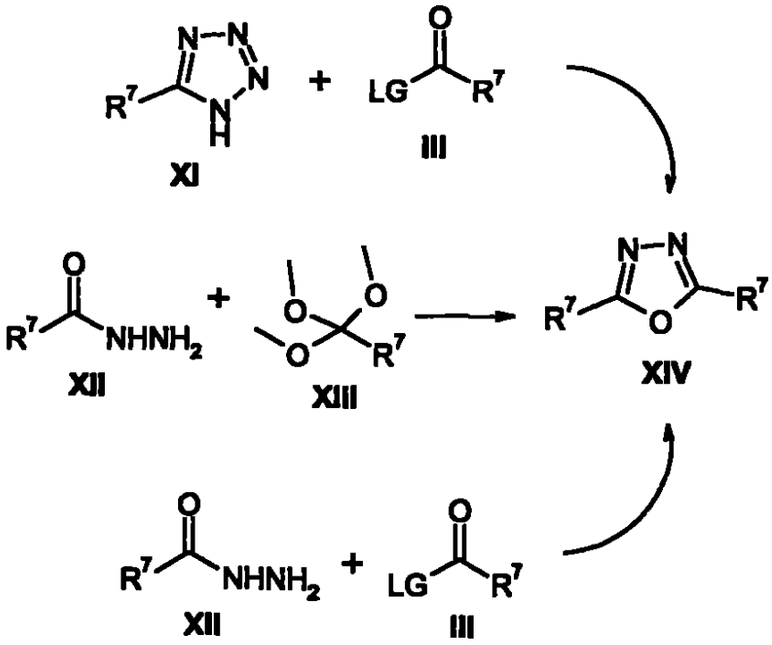


A compound of formula IX, wherein R^7 is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared by a 1,3-dipolar cycloaddition between compounds of formula VI and VII under basic conditions using a suitable base such as sodium bicarbonate or triethylamine at suitable temperatures (0°C – 100°C) in solvents such as toluene. Synthesis of compounds of type VI has previously been described in the literature, e.g. Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57, 6649-50. 1,3-Dipolar cycloaddition with acetylenes of type VII can also be effected using substituted nitromethanes of type VIII via activation with an electrophilic reagent such as PhNCO in the presence of a base such as triethylamine at elevated temperatures (50-100 °C). Li, C-S.; Lacasse, E.; Tetrahedron Lett. (2002) *43*; 3565 - 3568. Several compounds of type VII are commercially available, or may be synthesized by standard methods as known by one skilled in the art.

Alternativley, compounds of formula X, which are available from a Claisen condensation of a methyl keone and an ester using basic conditions using such bases as sodium hydride or potassium tert-butoxide, may yield compounds of formula IX via condensation and subsequent cyclization using hydroxylamine, for example in the form of the hydrochloric acid salt, at elevated temperatures (60-120°C).

It is understood that for both methods subsequent functional group transformations may be necessary. In the case of an ester group, these transformations may include, but is not limited to either of following three procedures: a) Complete reduction using a suitable reducing agent such as LAH in solvents such as THF. b) Partial reduction using a suitable selective reducing agent such as DIBAL followed by alkylation with an alkylhalide. c) Alkylation using an alkylmetal reagent such as an alkyl magnesium halide in solvents such as toluene or THF, followed by reduction with for example sodium borohydride in methanol.

Formation of compounds of formula XIV

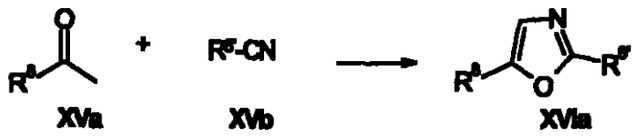


A compound of formula XIV, wherein R^7 is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group,

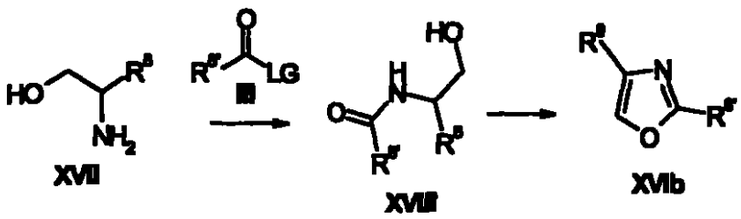
may be prepared from tetrazole compounds of type XI via acylation using an isolable compound of type III such as an acid chloride or anhydride, or a compound of type III wherein the LG may be formed *in situ*, for example from activation of an acid using a reagent such as DCC or EDCI, followed by rearrangement to the 1,3,4-oxadizaole. Jursic, B.S.; Zdravkovski, Z.;. Synth.Commun.; (1994) *24*; 1575-1582.

Alternatively, compounds of formula XIV may also be prepared from acyl hydrazide of type XII via heating in the presence of compounds of formula XIII or III, wherein LG is a leaving group such as chloride or alkoxide, at elevated temperatures (60-130°C) in one step. The reaction of compounds of Formula XIII may be carried out neat or using a suitable aprotic solvent such as benzene or xylene, or a protic solvent such as ethanol or n-butanol, and may be facilitated by the presence of abase such as KOtBu or a acid such as p-toluene sulfonic acid or acetic acid. Se references: Saunders, J.; Cassidy, M.; Freedman, S. B.; Harley, E. A.; Iversen, L.L. J.Med.Chem.; (1990) 33; 1128-1138; Peet, N. P.; Sunder, S. J.Heterocycl.Chem.; (1984) 21; 1807-1816. For compounds of formula III a dehydrating agent such as phosphorous pentoxide may be used to increase cyclization of the formed reaction intermediate as has been previously been decribed for example by Kakefuda, Akio; et al.; Bioorg. Med. Chem. (2002), *10*; 1905-1912.

Formation of compounds of formula XVI



XVa XVb XVIa



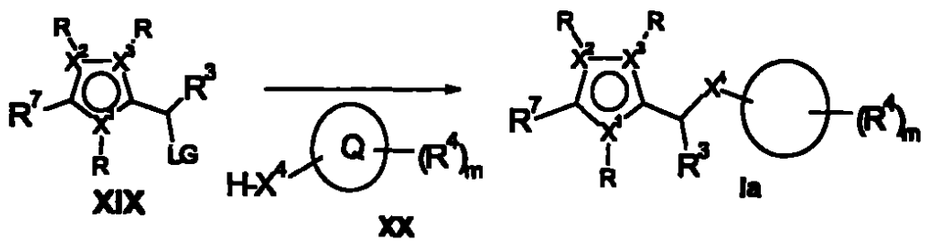
XVII XVIII XVIb

A compound of formula XVI, wherein R^8 as defined above is independently selected from a group consisting of M^1-(R^2)$_n$-P-(R^1)$_{m1}$, M^2-(R^3)$_n$-X^4-Q-(R^4)$_{m2}$, and M^2-(R^3)$_n$-G wherein G

is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared by the reaction of compounds of formula XVa and XVb in the presence of in situ generated Tl(OTf)3 under acidic conditions according to the procedure of Lee and Hong; Tetrahedron Lett., (1997), *38*, 8959-60.

Alternatively compounds of formula III and XVII are reacted as described above for formula V to give an intermediate of formula XVIII. Such an intermediate may give the required oxazole by cyclodehydration with to generate the oxazoline followed by dehydrogenation using $BrCCl_3$ in the same reaction pot. Phillips, A.J.; Uto, Y.; Wipf, P.; Reno, M.J. and Williams, D.R., Organic Letters, (2000) *2*, 1165-8.

Formation of the bond between X^4 and M^2 or Q and M^2 through nucleophilic displacement of a leaving group:



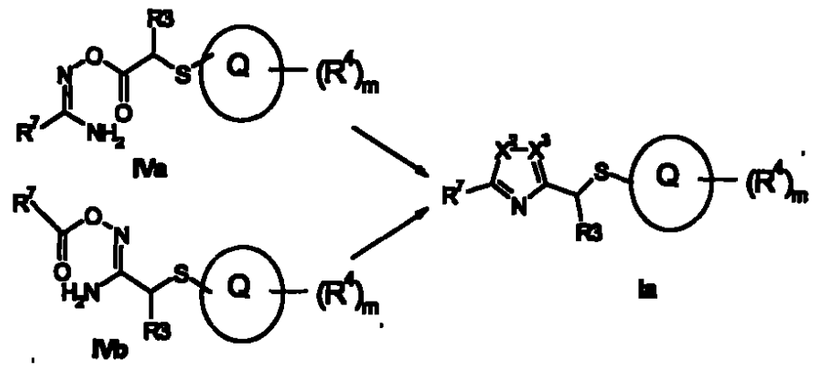
A compound of formula XX, may be used to displace the leaving group LG in compounds of formula XIX (R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$). When X^4 is represented by a heteroatom such as N and S, the reaction is carried out in the presence of an appropriate base such as potassium carbonate, cesium carbonate, sodium hydride, triethylamine or the like, which may facilitate the reaction by deprotonation of the X^4 residue and prevent the formation of any excess acid that would be generated by the reaction in the absence of a base. The reaction may be accomplished using any appropriate solvent such as acetonitrile or DMF, and may be carried out at room temperature or at elevated temperature (35-100°C) to accelerate the reaction.

Such conditions may be used with appropriate modifications of employed equipment for parallel synthesis, using standard techniques known to the one skilled in the art.

Similarly these reaction conditions may be carried out for compounds of formula XX when X^4 = bond and ring Q is a fused bicycle containing a heteroatom such as N as defined

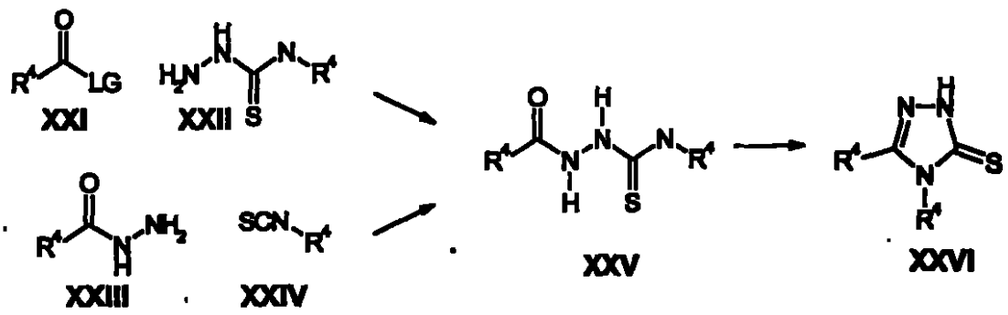
aboved. In either the latter or the above described case with X^4=N, NaH in DMF is preferred as desribed in literature precedences, for example Murdoch, Robert; Tully, W. Roger; Westwood, Robert; *J.Heterocycl.Chem.*; (1986), *23*; 833-841.

For compounds of formula XX containing X^4 = C a stronger base needs to be employed to achieve deprotonation, such as for example LDA, n-butyllithium or any other alkyl metal base in apropriate aprotic solvents such as THF, hexane or toluene at temperatures generally below ambient temperatures, e.g.at –78°C or 0°C.



An alternative procedure for the synthesis of above described type of thiomethyl oxadiazole is to form an acyclic ester IVa and IVb from the combination of a suitably substituted hydroxyamidine and activated acid coupling partner also suitably substituted. Displacement of the chloride using the thiol nucleophile may occur immediately prior to cyclization using one of the methods of oxadiazole formation described above. The displacement can also be carried out on the chloromethyl hydroxyamidine or chloromethyl acid starting materials followed by the two step esterification and cyclization as above. The conditions described may be used with appropriate modifications of employed equipment for parallel synthesis using standard techniques known to the one skilled in the art.

Formation of 4-alkyl-triazoles thiols/thiones:



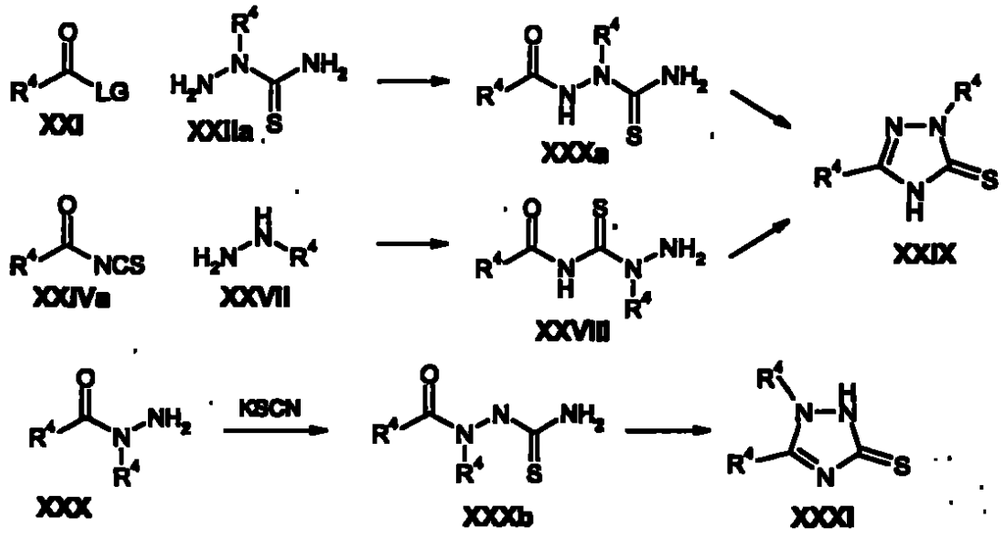
Any suitable acylating agent such as an acid chloride or an activated acid or the corresponding acid under amide coupling conditions as mentioned above, is reacted with a suitable 4-alkyl-3-thiosemicarbazide in the presence of a base such as pyridine or non-nucleophilic amines to form the acyclic intermediate compound of formula XXV, wherein R^4 is as defined above. The same intermediate is also available through reaction of an acyl hydrazide with an alkyl isothiocyanate. Cyclization to give a compound of formula XXVI is easily effected by treatment with an appropriate inorganic base such as hydroxide or bicarbonate at elevated temperature in an appropriate solvent such as water, water-dioxane, an aqueous alcohol or mixture thereof.

Such conditions may be used with appropriate modifications of employed equipment when using a solid phase base instead of above-mentioned ones, such as for example P-BEMP for parallel synthesis using standard techniques known to the one skilled in the art.

The compound of formula XXV reacts through its tautomeric form under the conditions described above with compounds of formula XIX to yield the S-alkylation compounds of the formula Ia.

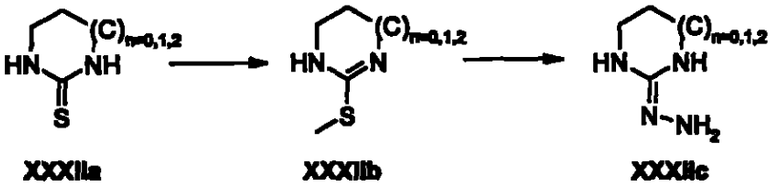
The triazole thiones XXIX and XXXI alkylated on the other nitrogen atoms of the ring (1 and 2) are available through similar procedures. The 2-alkyl triazole thione XXVIII may be obtained by treatment of an aroyl isothiocyanate with an alkyl hydrazine in toluene at elevated temperatures, e.g. 85°C, followed by heating with aqueous bicarbonate. The same product may also be obtained through treatment of the analogous 2-alkyl-3-thiosemicarbazide with an activated acid in the presence of a suitable base such as pyridine

or triethylamine followed by alkaline ring closure in a manner similar to the alkaline ring closure yielding product XXVI above.

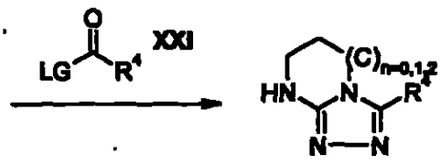


The 1-alkyl triazole thiones XXXI may be prepared by the reaction of a suitable *N*-alkyl-*N*-acylhydrazide with potassium thiocyanate in the presence of an acid such as HCl or other compatible strong acid via the 1-acyl-1-alkyl-3-thiosemicarbazide intermediate which undergoes alkaline ring closure in a manner similar to the alkaline ring closure yielding compounds of formula XXVI above.

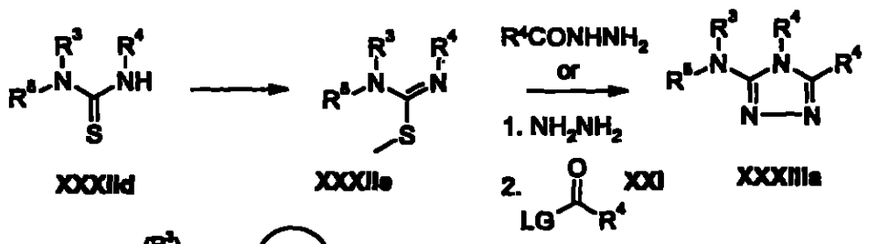
Formation of compounds of formula XXXIII



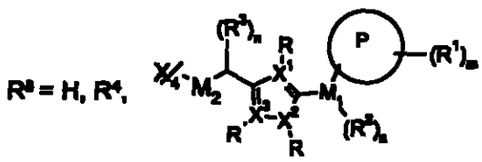
XXXIIa XXXIIb XXXIIc



XXXIII



XXXIId XXXIIe XXXIIIa

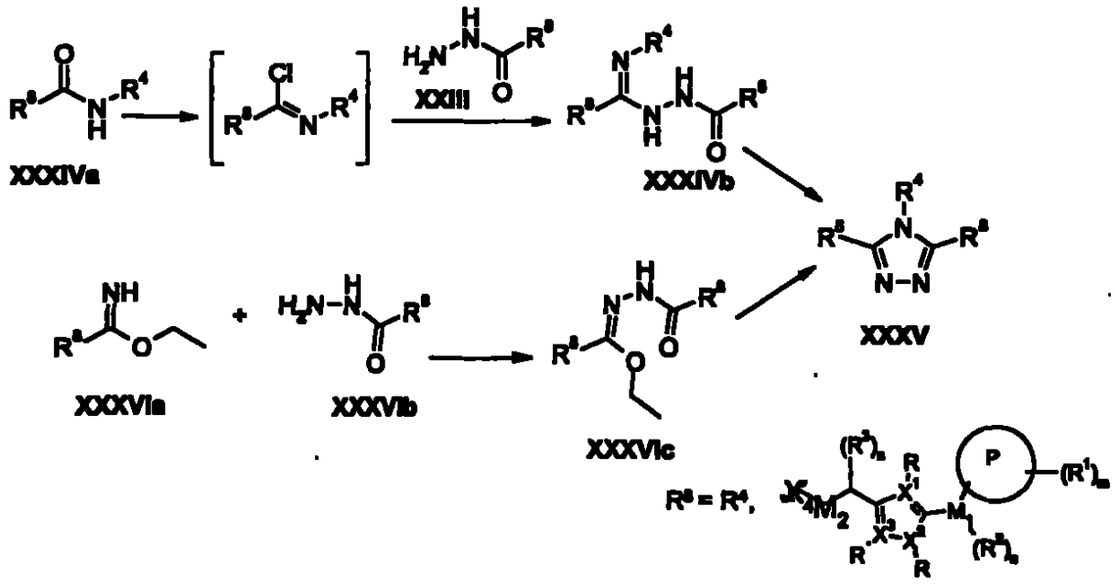


A compound of formula XXXIII may be prepared by alkylation of cyclic thioureas of formula XXXIIa, wherein n is defined as 0,1 or 2, resulting in compound of formula XXXIIb, e.g. 2-methylthio-1,4,5,6-tetrahydropyrimidine in case of n=1. The alkylation with for example methyliodide as alkylating agent can be done in several solvents (DMF, acetone, CH_2Cl_2 etc.) at room temperature or elevated temperatures and will give the product as its hydroiodide salt as has been previously described by Kennedy, Kevin J.; Simandan, Tiberiu L.; Dix, Thomas A.; Synth.Commun.; (1998); *24*; 741-746. Cyclic thioureas are readily available either through synthesis as known by the one skilled in the art, or commercial sources. Compounds of formula XXXIIc result from the hydrazinolysis of the corresponding compounds of type XXXIIb. The hydrazinolysis is preferably done in refluxing EtOH with hydrazine hydrate as described previously by Krezel, Izabella;

Pharmazie; (1994); *94*, 27-31. Finally, fused triazoles of formula XXXIII may be formed through the thermal acylation and condensation reaction between compounds of formula XXI wherein LG is a leaving group as for example a halide, and compounds of formula XXXIIc . Such reactions may be conducted in pyridine or in EtOH or toluene in the presence of base. Normal heating or microwave irradiation may be used. Similarly, XXXIII may be prepared in the presence of a base, such as sodium methoxide in a suitable solvent such as methanol or ethanol at elevated temperatures where XXI may also be an ester or carboxylic acid.

Acyclic thioureas of formula XXXIId , wherein R^5 is defined as in the scheme and R^3 and R^4 are as defined in Formula I, may also be employed using a similar method to obtain compounds of formula XXXIIIa, wherein the introduction of the hydrazine portion may be carried out using either hydrazine followed by acylation, or by using a preformed acyl hydrazine.

Formation of compounds of formula XXXV

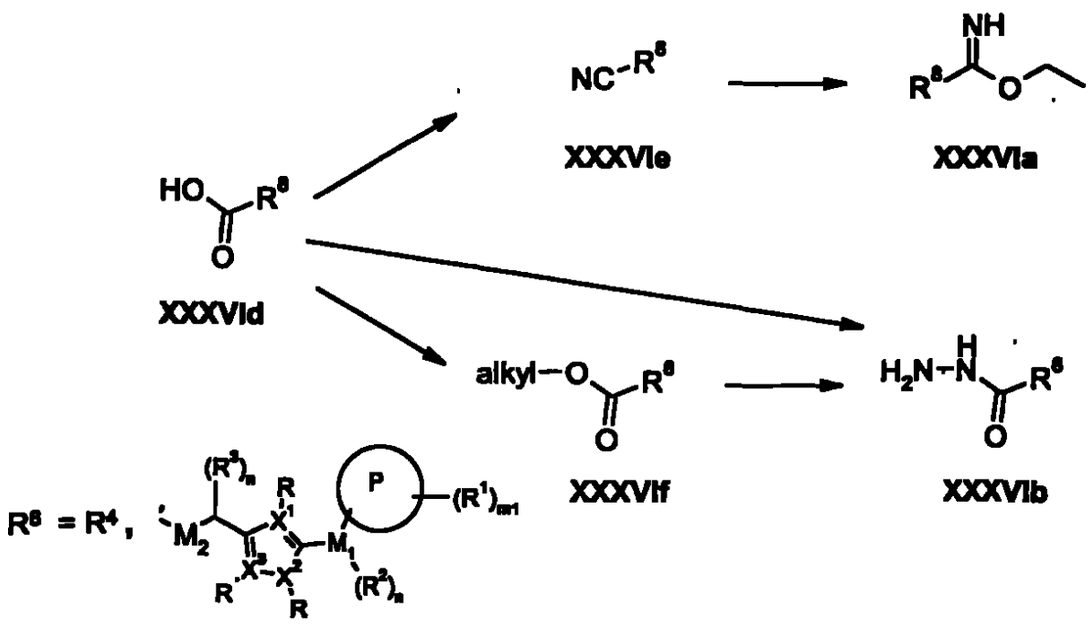


Compounds of formula XXXIVb may be prepared by using similar methods as above, e.g. by activation of XXXIVa to give the corresponding imidoyl chloride by using oxalyl chloride or pentachlorophosphine in the optional presence of a base such as triethylamine. The intermediate may be used in-situ or may be isolated prior to trapping by a compound

of formula XXIII as has been used above. The subsequent product may be cyclized under acidic or basic conditions in a suitable solvent such as DMF to give compounds of formula XXXV. XXXV may be an intermediate used in the formation of compounds of Formula I, or may be the final bioactive compound of Formula I.

A compound of formula XXXV, wherein R^8 is selected independently from a group as depicted above may also be prepared through reaction of compounds of formula XXXVIa (ethyl imidoate is depicted as example) and XXXVIb followed by cyclization at elevated temperatures (40 – 80°C) in the presence of an amine , whereas the amine preferably should have, but is not limited to, a low boiling point such as that it can be used in excess and simplify the work-up procedure. Examples for such amines may be, but are not limited to methylamine or ethylamine which may be used as solutions in for example methanol, THF or dichloromethane.

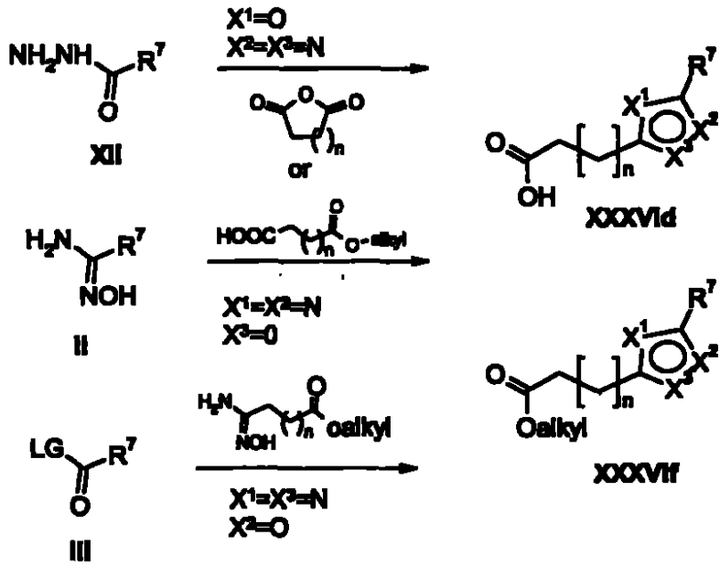
Formation of compounds of formula XXXVIa and XXXVIb



A compound of formula XXXVIa, wherein R^8 is selected independently from a group as depicted above may be prepared through reaction of a nitrile of formula XXXVIe in an alcohol such as ethanol in the presence of a protic acid, for example hydrochloric acid. The nitrile may be obtained from an acid XXXVId as described above. Compounds of formula XXXVId may also be used to prepare acyl hydrazides of formula XXXVIb, wherein R^8 is

selected independently from a group as depicted above. This type of substance XXXVIb may also be formed directly from an acid. There may be advantages to react an intermediate ester of type XXXVIf with either neat hydrazine, hydrazine salt in the presence of a base or hydrazine hydrate in facilitating a simpler workup. However, the direct route via the acid using in situ activation may be advantageous in substrates sensitive to nucleophilic attack and also give the product in a shorter sequence of steps.

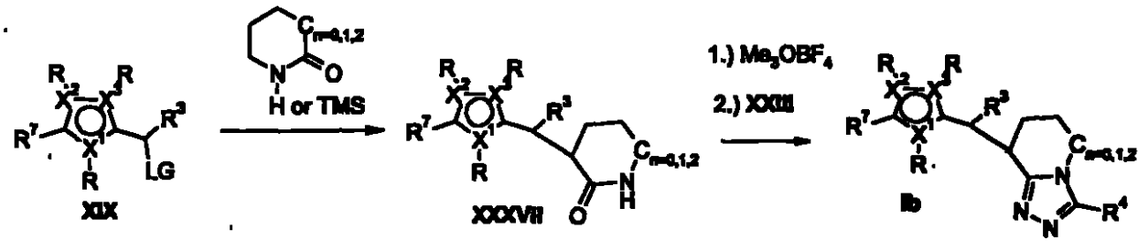
Formation of compounds of formula XXXVId and XXXVIf



Compound of formula XXXVId & XXXVIf, wherein R^7 is a group consisting of M^1-$(R^2)_n$-P-$(R^1)_m$, may be prepared by either of the non-limiting methods: a) reaction of acyl hydrazide compounds of formula XII with a cyclic anhydride or monoesterified diacid followed by the cyclization of the formed intermediate would lead to 1,3,4-oxadiazoles of type XXXVId and XXXVIf respectively (X^1=O, X^2 and X^3=N); b) reaction and cyclization of an hydroxyamidine of Formula II with a cyclic anhydride or with the monoesterified diacid may be used to provide the 1,2,4-oxaziazole analogs XXXVId and XXXVIf wherein X^1 and X^2 =N, X^3=O; c) reaction of a compound of type III with an hydroxamidine type compound, with the exception of the succinyl derivative, may be used to provide the 1,2,4-oxaziazole analogs XXXVIf wherein X^1 and X^3 =N, X^2=O.

Compounds XXXVId and XXXVIf may be interconverted independent of the nature of X^1, X^2 or X^3 as described above.

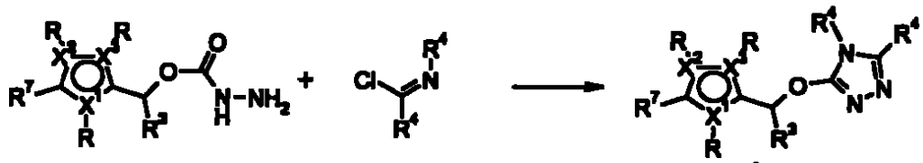
Formation of compounds of formula Ib



A compound of formula Ib, wherein R^7 is selected from a group M^1-$(R^2)_n$-P-$(R^1)_{m1}$ may be prepared from compounds of formula XXXVII, generated from XIV as described below, through selective O alkylation using Me_3OBF_4 or dimethyl sulfate (as described in literature precedences, for example: a) Sheu, Jennline; Smith, Michael B.; Oeschger, Thomas R.; Satchell, Jacqueline; Org.Prep.Proced.Int.; (1992); *24*, 147 – 158; or b) Hutchinson, Ian S.; Matlin, Stephen A.; Mete, Antonio, Tetrahedron Lett.; (2001); *42*; 1773 – 1776). The methoxy group may then be displaced by an acyl hydrazide of type XXIII, followed by a ring closing condensation to form the triazole heterocycle. This may be done in ethanol, toluene, DMF or pyridine under thermal conditions with regular heating or microwave irradiation, as has been previously described by for example Lawson, Edward C.; Hoekstra, William J.; Addo, Michael F.; Andrade-Gordon, Patricia; Damiano, Bruce P.; Kauffman, Jack A.; Mitchell, John A.; Maryanoff, Bruce E.; Bioorg.Med.Chem.Lett.; (2001); *11*; 2619 – 2622.

Compounds of type XXXVII may be prepared by the reaction of cyclic amides, lactams, which are readily alkylated in the α-position to the carbonyl by successive treatment with 2 equivalents of a strong base e.g *n*-Buli to generate the dianion followed by addition of 1 equivalent of compounds of formula XIX, in an aprotic solvent such as THF, as has been previously described by for example Grieco, Paul A.; Kaufman, Michael D.; J.Org.Chem.; (1999); *64*; 6041 – 6048). Alternatively, a N-protected lactam may be used in which only 1 equivalent base e.g. LDA is needed to generate the anion for the alkylation as has been previously described by for example Padwa, Albert; Beall, L. Scott; Heidelbaugh, Todd M.; Liu, Bing; Sheehan, Scott M.; J.Org.Chem.; (2000); *65*; 2684 – 2695.

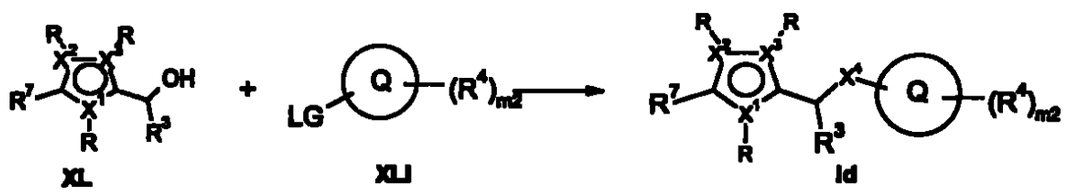
General synthesis of compounds of formula Ic



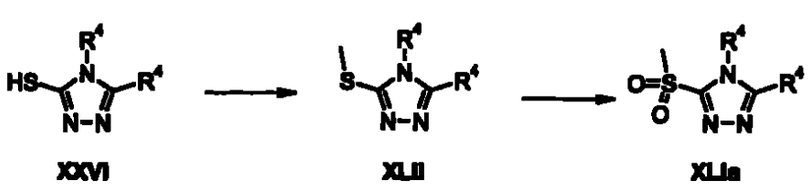
XXXVIII XXXIX Ic

A compound of formula Ic, wherein R^7 is consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, may be prepared through reaction with subsequent cyclization of compounds of formula XXXVIII, with a compound of formula XXXIX. The compound of formula XXXIX may be prepared from a suitable secondary amide using oxalyl chloride or pentachlorophosphine in the optional presence of a base such as triethylamine and used either in-situ or as isolated material as described above from XXXIVa.

Compounds of formula XXXVIII, may be prepared from the corresponding alcohol by reacting it with phosgene or preferably a phosgene analog such as carbonyldiimidazole followed by coupling to hydrazine.



XL XLI Id



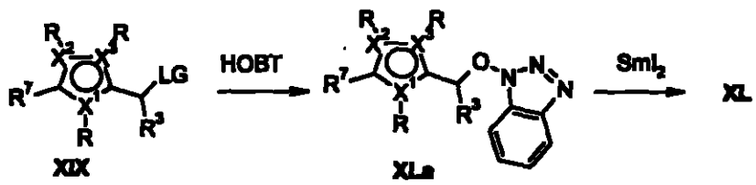
XXVI XLII XLIa

Other means of synthesizing a compound of formula Ic or Id, wherein $X^4 = O$ and wherein R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$, may be by the O-alkylation of compounds of type XL with compounds of type XLI wherein the leaving group may consist of a tosyl-, mesyl-, halo- or any other appropriate group, in the a suitable base such as cesium or potassium carbonate, sodium hydride in solvents such as for example DMF or DMSO.

Compounds of type XLI may be synthesized as exemplified with triazole XXVI by alkylation or arylation of the sulfur group using an apropriate alkylating or arylating

reagent followed by double oxidation of the thiogroup to the corresponding sulfone using oxidants such as MCPBA, hydrogen peroxide in acetic acid or potassium permanganate. Such a sequence has previously been described for example by Åkerblom et al. *J. Med. Chem. 16,* 312 (1973). Alternatively, triazole halides may be synthesized as previously described in the literature by for example Ashton, W.T. et al. *J. Med. Chem. 36,* 591 (1993).

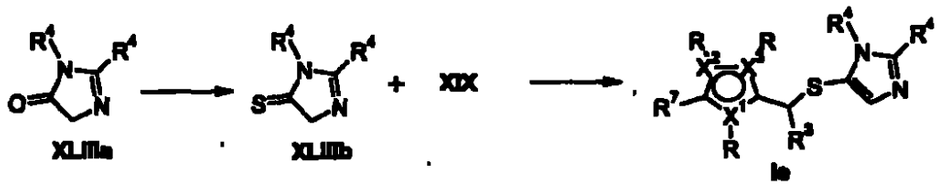
The alcohols may be prepared either directly upon synthesis of the oxadiazole or isoxazole part as described above under general synthesis of compounds of formula V. Alternatively they may be prepared from an oxadiazole or isoxazole unit with an appropriate leaving group such as a halide, e.g. chloride, using a three step sequence as described by Palazzo et al. *J. Heterocycl. Chem.* (1979) 16:1469, followed by a standard reduction protocol of the resulting aldehyde (or hydrate thereof) using for example sodium borohydride in methanol.



Yet another method may involve the reaction of a compound of structure XIV unit containing an appropriate leaving group such as a halide, e.g. chloride with hydroxybenzotriazole in the presence of a suitable base such as potassium carbonate or triethylamine in a suitable solvent such as DMSO, acetonitrile, acetone, DMF to give compounds of type XLa. Alternatively XLa may be obtained if hydroxybenzotriazole is present during cyclization to the oxadiazole, either as a co-activator with EDCI or as a result of a byproduct from a coupling reagent such as HBTU as described above under the reaction of compounds of formula II - V. XLa may be converted to the alcohol by the addition of samarium diiode, preferably over an elongated period of time (5-360 minutes) in a suitable solvent such as tetrahydrofuran, methanol, water or mixtures thereof, with THF being a preferred solvent, at an appropriate temperature (-75°C - +75°C).

The cleavage of the N-O bond can alternatively be done using commonly used hydrogenation methods in the presence of a suitable catalyst such as raney-nickel as known by the one skilled in the art. In compounds of formula XLa the oxobenzotriazole functionality may also serve as a leaving group. Thus compounds XLa may react with compounds XX as described above.

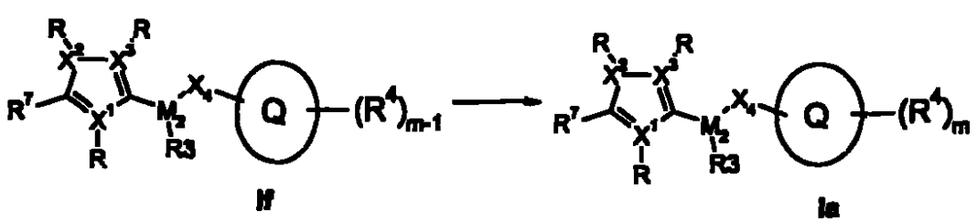
Formation of compounds of type Ie



A compound of formula Ie, wherein R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$, may be prepared through nucleophilic substitution of compounds of type XLIIIb with compounds of type XIX as described above. Compounds of type XLIIIb may be prepared by reaction of their oxo-analogues XLIIIa using P_2S_{10} or Lawesson's reagent under thermal conditions. Synthesis of compounds of type XLIIIa has been described by Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989); *45*; 6375-6386.

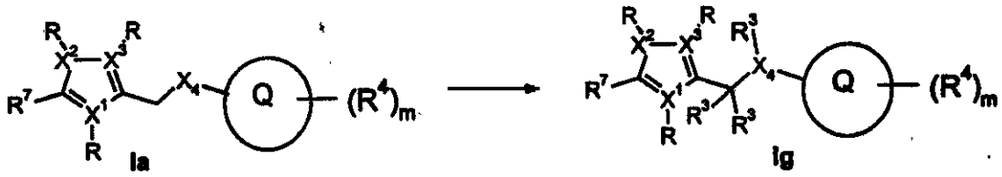
Introduction of substitution in the Q ring:

If substitution on the Q ring is desired, one may choose an appropriately substituted aryl or heteroaryl thiol to use for the displacement reaction. The same is valid for other nucleophilic reagents other than substituted or non-substituted aryl or heteroaryl thiols serving to substitute the same in the final compounds. If the aryl or heteroaryl residue has an amenable reactive moiety, either directly introduced or as a result of a deprotection reaction, including but not limited to a free NH site as in aniline, imidazole, benzimidazole, indole and the like, a compound of formula If (R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$) may be substituted with R^4 using a suitable base such as an alkyllithium or alkali-metal hydride or hydroxide to deprotonate the NH residue, followed by the addition of a suitable electrophilic reagent such as an alkyl halides, acid chlorides or anhydrides, chloroformates, carbamoyl chlorides, sulfonyl chlorides, isocyanates, isothiocyanates and the like to provide the substituted product of Formula Ia.



Introduction of the M^2 substituent(s) and of the X^4 substituent(s):

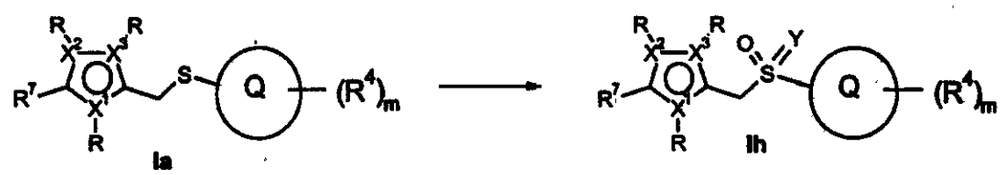
When the most acidic protons are positioned on the atom adjacent to X^4, or on X^4 itself, substitution may be achieved by deprotonation of compound of Formual **Ia** with a strong base such as an alkyllithium or an alkali-metal hydride in a suitable aprotic non-acidic solvent like THF or diethylether followed by trapping of the resulting anion with a suitable electrophile such as alkyl halides, acid chlorides or anhydrides, chloroformates, carbamoyl chlorides, sulfonyl chlorides, isocyanates, isothiocyanates and the like. When an excess of base and electrophile are employed and the reaction is left for sufficient time, two hydrogens may be replaced by the electrophile as illustrated below for the introduction of two R^3-substituents (M^2 exemplified as carbon). Two or more, different or same substituents, might also be introduced accordingly by subsequent deprotonations and reactions with appropriate electrophiles to yield compounds of Formula **Ig**.



Ia **Ig**

Oxidation of S atom of chain (when X^4 is S) or N atoms on substituents:

Oxidation of the sulfur atom to give sulfones (Y=O) and sulfoxides (Y= ":", i.e. a lone pair) may be achieved by direct oxidation using any suitable oxidizing agent including peroxyacids such as MCPBA. In the case of MCPBA oxidation, it is possible to obtain a mixture of products from a single reaction and separate them by standard column chromatography or to obtain selectively the sulfoxide or sulfone by controlling the stoichiometry and temperature of the reaction.



Ia **Ih**

If one of the subsitutents, e.g. R^4 contains one or more nitrogen atoms as for example a pyridine moiety or any other susbtituent as defined above, then oxidation of this nitrogen may occur in the above reaction of **Ia** with an oxidant such as MCPBA to give the

corresponding N-oxide. It is understood to the one skilled in the art that such products may be obtained by separation via standard column chromatography or any other standard purifcation protocol even in the case of mixtures containing for example **Ih** and N-oxide. It is also understood to the skilled in the art that the formation of N-oxides may be reduced by choice of suitable reaction conditions such as using acidic media to protect the nasic amine.

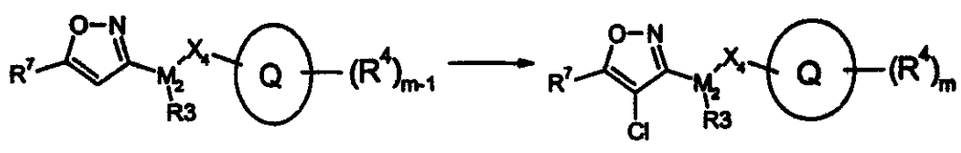
Other miscellaneous reactions:

When the intermediate compounds contain a suitable reactive functionality such as an aryl halide or triflate, the functionality may be employed to further elaborate the product. For example, when 3-halo-phenyl is present in P-$(R^1)_{m1}$, it is possible to use standard Suzuki conditions to couple an aryl boronic acid to yield a diaryl coupling product. Miyaura, N., Yanagi, T., Suzuki, A., Synth.Commun., (1981),11; 7, 513-520.

Other functionalities such as an aliphatic alcohol may for example be converted to a fluoro group by the use of a fluorinating agent such as DAST, or other halide groups by the use of for example triphenylphosphine and either iodine, N-bromosuccinimide or N-chlorosuccinimide These halides may serve as leaving groups for further elaboration or may remain as substituent in active compounds of formula **Ia**.

In a similar fashion alcohols may be transformed to leaving grous such as the non-limiting examples mesyl or tosyl by employing the appropriate sulfonyl halide or sulfonyl anhydride in the presence of a non-nucleophilic base together with the alcohol to obtain the sulfonic ester derivative.

Other funtionalities which may be further elaborated are depicted in the following, non-limiting example (R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$), where halogenation may be undergone on a carbon-atom of an oxazole unit employing a chlorinating agent such as sulfuryl chloride.



Examples

Suitable embodiments of the invention will now be illustrated by the following non-limiting examples.

NMR measurements were made on the delta scale (δ).

The compounds prepared according to Examples 1 to 39 and 100 to 328 are intermediates. The compounds prepared according to Examples 40 to 99 and 329 to 794 are end products.

Intermediates

Example 1

6-Methylpyridine-4-carboxylic acid

A hydrogen filled balloon was attached to a flask containing 2-chloro-6-methylpyridine-4-carboxylic acid (2 g, 12.0 mmol), palladium 10 wt. % on activated carbon (0.5 g), triethyl amine (4.8 ml) and ethanol (24 ml) and then stirred overnight at room temperature. The reaction mixture was filtered through celite, washed with methanol and concentrated. The residue was titurated with dichloromethane and then filtered to afford 6-methylpyridine-4-carboxylic acid as a white solid; 1.05 g (66%). ^{1}H NMR (MeOD) δ (ppm): 8.62 (d, 1H), 7.68 (s, 1H), 7.60 (d, 1H), 2.55 (s, 3H).

Example 2

1-Cyano-3-ethylbenzene

Argon was bubbled into a solution of 1-bromo-3-ethylbenzene (2.5 g, 13.5 mmol) in DMF (37 ml) for 10 min. and then zinc cyanide (1.75 g, 14.9 mmol) and tetrakis(triphenylphosphine)palladium(0) (1.56 g, 1.35 mmol) were added. After stirring at 80°C overnight the reaction mixture was diluted with ethyl acetate (35 ml) then filtered through celite to remove the precipitate. The filtrate was washed with water (3x), saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. The product was purified by flash column chromatography using 2% ethyl acetate in hexane affording a colorless liquid (1.42 g). GC-MS (M+): 131.18.

Example 3

3-Ethylbenzoic acid

6 M Sodium hydroxide (25 ml) was added to 1-cyano-3-ethylbenzene (1 g, 7.62 mmol) in methanol (25 ml) and then heated at 100°C overnight. After concentrating the reaction mixture, the aqueous layer was washed with dichloromethane (2x), then acidified pH about 3 with 12 M HCl. The precipitate was extracted with ethyl acetate then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford 3-ethylbenzoic acid as a colorless oil; 0.770 g (28% yield over 2 steps). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.76 (d, 2H), 7.43 (m, 2H), 2.67 (m, 2H), 1.19 (t, 3H).

Example 4

3-Fluoro-5-methyl-benzoic acid

Concentrated HCl (30 ml) was added to a cooled (-5°C) suspension of dimethyl 5-amino isophthalate (20 g, 95.6 mmol) in water (75 ml), followed by portionwise addition of $NaNO_2$ (7.5 g, 109 mmol). The reaction mixture was then stirred for 15 min., after which HBF_4 (18 ml, 100 mmol, 48% aqueous solution) was added. The resulting mixture was stirred at 0°C for 30 min. and the precipitate formed was collected by filtration and washed with cold methanol (60 ml) and ether (60 ml). The residue was then decomposed by heating in an oil bath (~110°C). The cooled mixture was then diluted with ether, concentrated onto silica gel and purified by flash chromatography with 5% ethyl acetate hexane as eluant giving 9.0 g (44%) of product as a white fluffy solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.57 (s, 1H), 7.95 (d, 2H), 3.97 (s, 6H).

A suspension of 5-fluoro-isophthalic acid dimethyl ester (1.7 g, 8.0 mmol) in methanol (41 ml) was treated with 1.0 N sodium hydroxide (7.2 ml, 7.2 mmol). The reaction was left stirring overnight at room temperature. After the solution was concentrated, the residue was dissolved in water and transferred to a separatory funnel. The aqueous layer was washed with dichloromethane (3 times) and then acidified with 1.0 N HCl to pH 2. Ethyl acetate was used to extract the precipitate, which was then washed with brine and dried over anhydrous sodium sulphate. After removal of solvent in vacuo, a total of 1.3 g (83%) of 5-fluoro-isophthalic acid monomethyl ester was isolated as a white solid. ^{1}H NMR (DMSO), δ (ppm): 8.31 (t, 1H), 7.96 (m, 2H), 3.91 (s, 3H).

Triethylamine (2.2 ml, 16.0 mmol) and isobutyl chloroformate (1.0 ml, 8.0 mmol) were added to an ice-cooled solution of 5-fluoro-isophthalic acid monomethyl ester (1.3 g, 6.7 mmol) in dichloromethane (20 ml) and then warmed to room temperature. After stirring for

2 h, the reaction mixture was filtered and concentrated. The residue was re-dissolved tetrahydrofuran (10 ml) and then sodium borohydride (1.1 g, 29.02 mmol) in water (3ml) was added drop-wise. After 1 h, the reaction was quenched with methanol and then diluted with ethyl acetate, washed with water and brine, dried over anhydrous sodium sulfate, filtered and concentrated. Flash column chromatography on silica gel using 30% ethyl acetate in hexanes afforded 667 mg (54%) of 3-fluoro-5-hydroxymethyl-benzoic acid methyl ester as a colorless oil. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.82 (s, 1H), 7.63 (d, 1H), 7.32 (d, 1H), 4.76 (s, 2H), 3.93 (s, 3H).

Ethanol (2 ml) was added to round bottom flask containing 3-fluoro-5-hydroxymethyl-benzoic acid methyl ester (667 mg, 3.6 mmol) and palladium (10 wt.% on activated carbon, 300 mg) under argon. The flask was evacuated using a water aspirator and then filled with hydrogen from a balloon. After stirring for 2 h, the palladium on carbon was removed by filtration through celite. The filtrate was then concentrated to afford 520 mg (87%) of 3-fluoro-5-methyl-benzoic acid methyl ester. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.65 (s, 1H), 7.51 (d, 1H), 7.08 (d, 1H), 3.91 (s, 3H), 2.40 (s, 3H).

0.5 N Lithium hydroxide (7.4 ml, 3.7 mmol) was added to a solution 3-fluoro-5-methyl-benzoic acid methyl ester (520 mg, 3.1 mmol) in tetrahydrofuran (7.4 ml). The reaction was stirred at 75°C for 2 h and then the solvent was removed in vacuo. The residue was dissolved in a small amount of water and then acidified (pH about 2) by the addition of 10% HCl (aq.). Following extraction of the aqueous layer with ethyl acetate, the organic layer was then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 469 mg (98%) of 3-fluoro-5-methyl-benzoic acid as a white solid. 1H NMR (DMSO), d (ppm): 7.62 (s, 1H), 7.45 (d, 1H), 7.32 (d, 1H), 2.38 (s, 3H).

Example 5

3-Methoxymethyl-benzoic acid

A mixture of 3-bromomethyl-benzoic acid methyl ester (556 mg, 2.4 mmol) and potassium carbonate (670 mg, 4.9 mmol) in methanol (10 ml) and tetrahydrofuran (10 ml) was heated at 55°C for 2 h. After cooling, the reaction mixture was diluted with water and then extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. After drying in vacuo, 3-

methoxymethyl-benzoic acid methyl ester (436 mg, quantitative) was isolated as a white solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.01 (s, 1H), 7.98 (d, 1H), 7.55 (d, 1H), 7.43 (t, 1H), 4.50 (s, 2H), 3.92 (s, 3H), 3.41 (s, 3H).

1 N Sodium hydroxide (3.6 ml, 3.6 mmol) was added to a 3-methoxymethyl-benzoic acid methyl ester (436 mg, 2.4 mmol) in methanol (5 ml) and tetrahydrofuran (5 ml). The reaction was stirred at 70°C for 30 min. and then the solvent was removed in vacuo. The residue was dissolved in a small amount of water and then acidified (pH about 2) by the addition of 1 N HCl (aq.). Following extraction of the aqueous layer with ethyl acetate, the organic layer was then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 395 mg (98%) of 3-methoxymethyl-benzoic acid as a white solid. ^{1}H NMR (DMSO), δ (ppm): 7.90 (s, 1H), 7.87 (d, 1H), 7.56 (d, 1H), 7.48 (t, 1H), 4.48 (s, 2H), 3.31 (s, 3H).

Example 6

***N*-Hydroxy-3-methoxy-benzamidine**

Using the general procedure of Shine et al., J. Heterocyclic Chem. (1989) 26:125-128, hydroxylamine hydrochloride (22 ml, 5 M, 110 mmol) and sodium hydroxide (11 ml, 10 M, 110 mmol) were added to a solution of 3-methoxybenzonitrile (11.5 ml. 94 mmol) in ethanol (130 ml). The reaction mixture was then heated at reflux (80°C) for 12 h. After the mixture was cooled, most of the solvent was removed in vacuo. The crude product was partitioned between ethyl acetate and water, washed with saturated brine, dried over anhydrous sodium sulfate and the solvent was removed in vacuo. Flash chromatography on silica gel using 35-50% ethyl acetate in hexane yielded the title compound (8.05 g, 52%).

Examples 7-9 were prepared in an analogous method to the procedure given in Example 6.

Example 7

***N*-Hydroxy-benzamidine**

N-hydroxy-benzamidine (4.83 g, 91%, white solid) was obtained from benzonitrile (4 g, 38.9 mmol), hydroxylamine hydrochloride (8.89 ml, 44.0 mmol) and sodium hydroxide (4.49 ml, 45.0 mmol) in ethanol (30 ml). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.81 (broad peak, 1H), 7.63 (m, 2H), 7.39 (m, 3H), 4.91 (s, 2H).

Example 8

***N*-Hydroxy-3-methyl-benzamidine**

N-Hydroxy-3-methyl-benzamidine (3.65 g, 94%, white solid) was obtained from m-tolunitrile (3 g, 26.0 mmol), hydroxylamine hydrochloride (5.9 ml, 29.6 mmol), and sodium hydroxide (3.0 ml, 29.9 mmol) in ethanol (20 ml). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.25 (broad peak, 1H), 7.36 (m, 2H), 7.25 (m, 2H), 4.88 (s, 2H), 2.38 (s, 3H).

Example 9

3-Cyano-*N*-hydroxy-benzamidine

3-Cyano-*N*-hydroxy-benzamidine (1.32 g, 52%, white solid) was obtained from isophthalonitrile (2 g, 15.6 mmol), hydroxylamine hydrochloride (3.12 ml, 5 M, 15.6 mmol) and sodium hydroxide (15.6 ml, 1 M, 15.6 mmol) in ethanol (20 ml). Purification was performed by flash column chromatography using 20-50% ethyl acetate in hexanes. ^{1}H NMR (DMSO), δ (ppm): 9.91 (s, 1H), 8.06 (s, 1H), 8.01 (d, 1H), 7.85 (d, 1H), 7.59 (t, 1H), 6.01 (bs, 2H).

Example 10

5-Chloromethyl-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole

Chloroacetyl chloride (0.72 ml, 9.03 mmol) and triethylamine (1.50 ml, 10.23 mmol) were added to *N*-hydroxy-3-methoxy-benzamidine (1 g, 6.02 mmol) in dichloromethane (12.0 ml) at 0°C and the resulting mixture was stirred for 20 min. To effect cyclization to oxadiazole, the solution was concentrated and DMF (20 ml) was added to the residue and heated at 120°C for 5 h. The product was purified by flash chromatography using 10-20% ethyl acetate in hexane affording 0.90 g (66% yield over 2 steps) of the title compound (yellow oil). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.68 (m, 1H), 7.60 (d, 1H), 7.40 (t, 1H), 7.07 (m, 1H), 4.76 (s, 2H), 3.88 (s, 3H).

Examples 11-14 were prepared in an analogous method to the procedure given in Example 10.

Example 11

5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole

5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole (1.62 g, 57% yield over 2 steps, yellow oil) was obtained from chloroacetyl chloride (1.76 ml, 22.05 mmol) and triethylamine (3.32 ml, 24.99 mmol) with *N*-hydroxy-benzamidine (2 g, 14.7mmol) in dichloromethane (29.3 ml). Purification was performed by flash chromatography using 10% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.08 (m, 2H), 7.51 (m, 3H), 4.76 (s, 2H).

Example 12

5-Chloromethyl-3-m-tolyl-[1,2,4]oxadiazole

5-Chloromethyl-3-m-tolyl-[1,2,4]oxadiazole (1.75 g, 62% yield over 2 steps, yellow oil) was obtained from chloroacetyl chloride (1.59 ml, 20.0 mmol) and triethylamine (3.00 ml, 22.7 mmol) with *N*-hydroxy-3-methyl-benzamidine (2 g, 13.3 mmol) in dichloromethane (26.6 ml). Purification was performed by flash chromatography using 10% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.87 (s, 1H), 7.36 (m, 2H), 4.75 (s, 2H), 2.34 (s, 3H)

Example 13

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile (3.57 g, 43%) was obtained from 2-chloro-*N*-hydroxy-acetamidine (4.05 g, 37.4 mmol) and 3-cyanobenzoyl-chloride (6.2 g, 37.4 mmol) in dichloromethane (60 ml) with triethylamine (6.5 ml, 46.7 mmol).. Purification was performed by silica gel chromatography. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.47 (bs, 1H), 8.41 (dd, 1H), 7.91 (dd, 1H), 7.72(t, 1H), 4.70 (s, 2H); GC-MS (M+): 219.

Example 14

3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile

3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile (1.2 g, 87%, light brown solid): 3-cyano-*N*-hydroxy-benzamidine (1.0 g, 6.2 mmol), triethylamine (1.5 ml, 10.6 mmol) and chloroacetyl chloride (0.74 ml, 9.3 mmol) in dichloromethane (12 ml). Purification was performed by decolorizing with silica gel. 1H NMR (CDCl3), d (ppm): 8.40 (s, 1H), 8.32 (d, 1H), 7.82 (d, 1H), 7.64 (t, 1H), 4.77 (s, 2H).

Example 15

3-Chloromethyl-5-*m*-tolyl-[1,2,4]oxadiazole

3-Methyl-benzoyl chloride (0.80 ml, 6.1 mmol) was added to a solution of 2-chloro-*N*-hydroxy-acetamidine (440 mg, 4.1 mmol) in dichloromethane (10 ml) at room temperature and the resulting mixture was stirred for 30 min. Then triethylamine (0.62 ml, 4.5 mmol) was added and the resulting mixture was stirred for 30 min. The product was partitioned into dichloromethane and the organic layer was washed with water and brine and dried over sodium sulfate. Evaporation of the solvent and flash chromatography on silica (10 – 20% ethyl acetate in hexanes) yielded the acyclic ester intermediate (814 mg). A solution of this intermediate in DMF (10 ml) was heated at 135°C for 4 h. The product was partitioned into ethyl acetate and the organic layer was washed with water and brine and dried over sodium sulfate. Evaporation of the solvent and flash chromatography on silica (5% ethyl acetate in hexanes) yielded 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (469 mg, 54% over 2 steps, white solid). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.99 (s, 1H), 7.97 (m, 1H), 7.43 (d, 2H), 4.68 (s, 2H), 2.45 (s, 3H).

Example 16

3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole

DMF (10 ml) was added to a mixture of 3-fluorobenzoic acid (710 mg, 5.07 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (972 mg, 5.07 mmol), 1-hydroxybenzotriazole hydrate (HOBt) (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) at room temperature and then stirred overnight. The reaction mixture was diluted with ethyl acetate, washed with water (3 times) and brine, dried over anhydrous sodium sulfate, filtered and concentrated. DMF (14 ml) was added to the residue and the resulting solution was heated at 135°C for 3.5 h to effect cyclization to oxadiazole. After cooling the reaction mixture was washed with water (3 times) and brine, dried over anhydrous sodium sulfate, filtered and concentrated. 3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole (383 mg, 35% yield over 2 steps, yellow oil) was obtained by flash chromatography on silica gel, using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.96 (d, 1H), 7.86 (m, 1H), 7.54 (m, 1H), 7.33 (m, 1H), 4.68 (s, 2H).

Examples 17-30 were prepared in an analogous method to the procedure given in Example 16.

Example 17

3-Chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole

3-Chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole (197 mg, 20% yield over 2 steps, white solid) was obtained from 3-thiophenecarboxylic acid (700 mg, 4.96 mmol), EDCI (950 mg, 4.96 mmol), HOBt (670 mg, 4.96 mmol) and 2-chloro-*N*-hydroxy-acetamidine (538 mg, 5.46 mmol) in DMF (10 ml). The acyclic product was purified by flash column chromatography eluting with 2:1.2:0.8 dichloromethane:hexane:ethyl acetate. The title compound was purified by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.28 (s, 1H), 7.70 (d, 1H), 7.48 (m, 1H).

Example 18

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine (25 mg, 4% yield over 2 steps) was obtained from 5-methynicotinic acid (472 mg, 3.44 mmol), EDCI (652 mg, 3.44 mmol), HOBt (465 mg, 3.44 mmol) and 2-chloro-*N*-hydroxy-acetamidine (340 mg, 3.13 mmol) in DMF (10 ml). The acyclic intermediate was purified by flash column chromatography using 100% ethyl acetate; 200 mg (30%) of the acyclic ester was also isolated as side product.

Example 19

3-Chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole (335 mg, 30% yield over 2 steps, yellow solid) was obtained from 3-nitrobenzoic acid (847 mg, 5.07 mmol), EDCI (972 mg, 5.07 mmol), HOBt (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) in DMF (10 ml). The acyclic intermediate was purified by flash column chromatography using 100% ethyl acetate. Purification was performed by flash column chromatography using 15% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.03 (t, 1H), 8.50 (t, 2H), 7.79 (t, 1H), 4.71 (s, 2H)

Example 20

4-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine

4-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine (316 mg, 28% yield over 2 steps, yellow oil) was obtained from 6-methylpyridine-4-carboxylic acid (800 mg, 5.8 mmol), EDCI (1.12 g, 5.8 mmol), HOBt (788 mg, 5.8 mmol) and 2-chloro-*N*-hydroxy-acetamidine (575 mg, 5.3 mmol) in DMF (10 ml) plus triethylamine (536 mg, 5.3 mmol). Purification was performed by flash column chromatography using 30% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.75 (d, 1H), 7.88 (s, 1H), 7.79 (d, 1H), 4.70 (s, 2H), 2.70 (s, 3H)

Example 21

3-Chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole (446 mg, 52% yield over 2 steps, yellow oil) was obtained from 3-ethylbenzoic acid (770 mg, 3.81 mmol), EDCI (803 mg, 4.19 mmol), HOBt (566 mg, 4.19 mmol) and 2-chloro-*N*-hydroxy-acetamidine (454 mg, 4.19 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.96 (t, 2H), 7.42 (m, 2H), 4.68 (s, 2H), 2.74 (m, 2H), 1.28 (m, 3H).

Example 22

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine (40 mg, 4% yield over 2 steps, yellow solid) was obtained from 3-(dimethylamino)benzoic acid (656 mg, 3.97 mmol), EDCI (761 mg, 3.97 mmol), HOBt (536 mg, 3.97 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 3.6 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.46 (t, 2H), 7.37 (t, 1H), 6.94 (d, 1H), 4.68 (s, 2H), 3.04 (s, 6H).

Example 23

3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (406 mg, 43% yield over 2 steps, white solid) was obtained from 3-chlorobenzoic acid (708 mg, 4.52 mmol), EDCI (866 mg, 4.52 mmol), HOBt (611 mg, 4.52 mmol) and 2-chloro-*N*-hydroxy-acetamidine (446 mg, 4.11 mmol) in DMF (10 ml). Purification was performed by flash column chromatography

using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.17 (t, 1H), 8.05 (d, 1H), 7.59 (t, 1H), 7.50 (t, 1H), 4.68 (s, 2H).

Example 24

3-Chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole (707 mg, 55% yield over 2 steps, light yellow oil) was obtained from 3-trifluoromethoxybenzoic acid (1.05 g, 5.07 mmol), EDCI (972 mg, 5.07 mmol), HOBt (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

Example 25

5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole

5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole (707 mg, 55% yield over 2 steps, white solid) was obtained from 3-bromobenzoic acid (1.05 g, 5.07 mmol), EDCI (972 mg, 5.07 mmol), HOBt (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. 1H NMR (CDCl3) d (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

Example 26

3-Chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole

3-Chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole (202 mg, 20%, off-white solid) was obtained from thiophene-2-carboxylic acid (649 mg, 5.1 mmol), 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.6 mmol), EDCI (972 mg, 5.1 mmol) and HOBt (684 mg, 5.1 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.00 (s, 1H), 7.83 (d, 1H), 7.19 (t, 1H), 4.13 (s, 2H).

Example 27

3-Chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole (312 mg, 46%, colorless oil) was obtained from 3-fluoro-5-methyl-benzoic acid (469 mg, 3.0 mmol), 2-chloro-*N*-hydroxy-acetamidine (363 mg, 3.3 mmol), EDCI (641 mg, 3.3 mmol) and HOBt (452 mg, 3.3 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.79 (s, 1H), 7.65 (d, 1H), 7.15 (d, 1H), 4.67 (s, 2H), 2.46 (s, 3H).

Example 28

3-Chloromethyl-5-thiazol-4-yl-[1,2,4]oxadiazole

3-Chloromethyl-5-thiazol-4-yl-[1,2,4]oxadiazole (37 mg, 5%, yellow solid) was obtained from thiazole-4-carboxylic acid (500 mg, 3.9 mmol), 2-chloro-*N*-hydroxy-acetamidine (462 mg, 4.3 mmol), EDCI (817 mg, 4.3 mmol) and HOBt (575 mg, 4.3 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 30% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.02 (d, 1H), 8.42 (d, 1H), 4.70 (s, 2H).

Example 29

3-Chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole (2.9 g, 44%, white solid) was obtained from 3-iodo-benzoic acid (5.0 g, 20.2 mmol), 2-chloro-*N*-hydroxy-acetamidine (2.4 g, 22.2 mmol), EDCI (4.3 g, 22.2 mmol) and HOBt (3.0 g, 22.2 mmol) in DMF (10 ml). The acyclic ester intermediate was purified by flash column chromatography using 50–80% ethyl acetate in hexanes. The title compound was purified by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.52 (s, 1H), 8.13 (d, 1H), 7.96 (d, 1H), 7.29 (t, 1H), 4.68 (s, 2H).

Example 30

3-Chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole

3-Chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole (193 mg, 34%, light yellow oil) was obtained from 3-methoxymethyl-benzoic acid (395 mg, 2.4 mmol), 2-chloro-*N*-hydroxy-acetamidine (284 mg, 2.6 mmol), EDCI (501 mg, 2.6 mmol) and HOBt (353 mg, 2.6 mmol) in DMF (5 ml). Purification was performed by SPE (flash)

chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.14 (s, 1H), 8.08 (d, 1H), 7.61 (d, 1H), 7.53 (t, 1H), 4.68 (s, 2H), 4.54 (s, 2H), 3.44 (s, 3H).

Example 31

5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazole-3-thiol

2-Furoyl chloride (0.76 ml, 7.66 mmol) was added in a dropwise manner to a solution of 4-methyl-3-thiosemicarbazide (732 mg, 6.96 mmol) and pyridine (7 ml) and the resulting solution was stirred at room temperature for 4 h. The reaction mixture was diluted with ethyl acetate (100 ml), successively washed with water (3x100 ml) and brine (100 ml). The organic phase was dried (sodium sulfate), filtered and concentrated in-vacuo. The residue was suspended in sodium bicarbonate (70 ml, 69.6 mmol, 1 M water) and left stirring at 100°C overnight. The reaction mixture was cooled to 0°C, then brought to pH about 6 using hydrochloric acid (70 ml, 1 N water). The title compound (298 mg) was collected by filtration as a white solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.4 (bs, 1H), 7.63 (d, 1H), 7.02 (d, 1H), 6.60 (dd, 1H), 3.83 (s, 3H).

Examples 32-35 were prepared in an analogous method to the procedure given in Example 31.

Example 32

4-Methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol

4-Methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol (478 mg, off-white solid) was obtained from 4-methyl-3-thiosemicarbazide (732 mg, 6.96 mmol) and pyridine (7 ml) with benzoyl chloride (0.89 ml, 7.66 mmol). Then sodium bicarbonate (70 ml, 69.6 mmol, 1 M water) was added at 100°C overnight and the title compound was collected by filtration. ^{1}H NMR ($CDCl_3$), δ (ppm): 12.3(bs, 1H), 7.55 (m, 5H), 3.65 (s, 3H).

Example 33

4-Methyl-5-pyridin-2-yl-4*H*-[1,2,4]triazole-3-thiol

4-Methyl-5-pyridin-2-yl-4*H*-[1,2,4]triazole-3-thiol (44 mg, greenish solid) was obtained from 4-methyl-3-thiosemicarbazide (537 mg, 5.11 mmol) and pyridine (7 ml) with 2-pyridinecarbonyl chloride hydrochloride (1.00 g, 5.62 mmol). Then sodium bicarbonate

(51 ml, 1 M water) was added at 100°C overnight and the title compound was collected using extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.1 (bs, 1H), 8.70 (d, 1H), 8.02 (d, 1H), 7.84 (m, 1H), 7.41 (dd, 1H), 4.05 (s, 3H).

Example 34

5-(4-Benzyl-morpholin-2-yl)-4-methyl-4H-[1,2,4]triazole-3-thiol

(83.3 mg, dirty yellow solid) was obtained from 4-methyl-3-thiosemicarbazide (346 mg, 3.29 mmol) and pyridine (7 ml) with 4-benzyl-2-morpholinecarbonyl chloride hydrochloride (1.00 g, 3.62 mmol). Then sodium bicarbonate (33 ml, 1 M water) was added at 100°C overnight and the title compound was collected using extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.48 (bs, 1H), 7.25 (m, 5H), 4.68 (dd, 1H), 3.86 (dAb, 1H), 3.68 (tAB, 1H), 3.59-3.64 (m, 5H), 3.07 (d, 1H), 2.88 (d, 1H), 2.61 (t, 1H), 2.37 (dt, 1H).

Example 35

5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol

5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (2.21 g, 83%, off-white solid) was obtained from 4-methyl-3-thiosemicarbazide (1.80 g, 17.2 mmol) and pyridine (20 ml) with trimethylacetyl chloride (1.92 ml, 15.6 mmol). Then sodium hydroxide (200 ml, 5% water) was added and left stirring at 60°C overnight and the title compound was collected extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.7 (bs, 1H), 3.72 (s, 3H) 1.40 (s, 9H).

Example 36

4-Methyl-5-pyridin-3-yl-4*H*-[1,2,4]triazole-3-thiol

A solution of 4-methyl-3-thiosemicarbazide (902 mg, 8.58 mmol), nicotinic acid (960 mg, 7.80), EDCI (1.64 g, 8.58 mmol), HOBt (1.16 g, 8.58 mmol) in DMF (10 ml) was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate (100 ml), successively washed with hydrochloric acid (50 ml, 10% aqueous), water (50 ml), saturated sodium carbonate (50 ml, aqueous), water (50 ml) and brine (50 ml). The organic phase was dried (sodium sulfate), filtered and concentrated in-vacuo. The residue was stirred in sodium hydroxide (53.4 ml, 66.7 mmol, 5% aqueous) at 60°C overnight. The

reaction mixture was cooled to room temperature, then carefully brought to pH about 6 using hydrochloric acid (1 N water). The aqueous phase was saturated with solid sodium chloride, then extracted with ethyl acetate (4x50 ml). The combined organic phase was washed with brine (100 ml), dried (sodium sulfate), filtered and concentrated in-vacuo (180 mg, off-white solid). ^{1}H NMR ($CDCl_3$), δ (ppm): 11.6 (bs, 1H), 8.94 (s, 1H), 8.83 (dd, 1H), 7.98 (m, 1H), 7.51 (dd, 1H), 3.69 (s, 3H).

Examples 37-39 were prepared in an analogous method to the procedure given in Example 36.

Example 37

4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol

4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol (693 mg, white solid) was obtained from 4-methyl-3-thiosemicarbazide (902 mg, 8.58 mmol), 3-thiophenecarboxylic acid (1 g, 7.80 mmol), EDCI (1.64 g, 8.58 mmol), HOBt (1.16 g, 8.58 mmol) in DMF (10 ml). Then sodium hydroxide (88 ml, 110 mmol, 5% aqueous) at 60°C overnight and the title compound was product collected extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.4 (bs, 1H), 7.77 (dd, 1H), 7.51 (dd, 1H), 7.42 (dd, 1H), 3.61 (s, 3H).

Example 38

4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol

4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol (71.2 mg, sticky yellow oil) was obtained from 4-methyl-3-thiosemicarbazide (902 mg, 8.58 mmol), 4-carboxythiazole (1.01 g, 7.80), EDCI (1.64 g, 8.58 mmol), HOBt (1.16 g, 8.58 mmol) in DMF (10 ml). Then sodium hydroxide (43 ml, 54 mmol, 5% aqueous) at 60°C overnight and the title compound was collected extraction and evaporation.

Example 39

5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol

5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (403 mg, beige solid) was obtained from 4-methyl-3-thiosemicarbazide (1.80 g, 17.2 mmol), cyclohexane carboxylic acid (2 g, 15.6

mmol), EDCI (2.99 g, 17.2 mmol) and HOBt (2.10 g, 17.2 mmol) in DMF(20 ml); then sodium hydroxide (195 ml, 244 mmol, 5% aqueous) at 60°C overnight.

Example 40

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

1*H*-Benzoimidazole-2-thiol (150 mg, 1 mmol) was added to a solution of the 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (30 mg, 0.13 mmol) and potassium carbonate (50 mg, 0.36 mmol) in DMF (2 ml) at room temperature. The solvent was removed in vacuo and the product obtained by flash chromatography using 20-100% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.71 (d, 1H), 7.62 (d, 1H), 7.53 (m, 2H), 7.42 (t, 1H), 7.18 (overlapping , m, 3H), 4.52 (s, 2H), 3.87 (s, 3H).

Examples 41-92 were prepared in an analogous method to the procedure given in Example 40.

Example 41

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

The title compound was prepared from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22 mmol), potassium carbonate (92.4 mg, 0.67 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (52.8 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 30-40% ethyl acetate in hexanes afforded 76 mg (90%) of the title compound as a white solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.68 (d, 1H), 7.57 (t, 1H), 7.49 (m, 2H), 7.41 (t, 1H), 7.15 (m, 2H), 4.53 (s, 2H), 3.85 (s, 3H), 3.72 (s, 3H). LC-MS $(M+1)^+$ 386.3.

Example 42

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile (39 mg, 47%, white solid) was obtained from 3-chloromethyl-3-(5-chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile (50 mg, 0.22 mmol), potassium carbonate

(92.4 mg, 0.67 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (52.8 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.34 (s, 1H), 8.28 (d, 1H), 7.79 (d, 1H), 7.60 (t, 1H), 7.53 (d, 1H), 7.49 (d, 1H), 7.19 (m, 1H), 4.70 (s, 2H), 3.74 (s, 3H). LS-MS (ES+full scan, $C_{17}H_{12}N_6OS_2$) M^+ calc. 380.05, found $(M+1)^+$ 381.04.

Example 43

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole (41.2 mg, 44%, off-white solid) was obtained from 3-chloromethyl-5-phenyl-[1,2,4]oxadiazole (50 mg, 0.26 mmol), potassium carbonate (106 mg, 0.77 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (60.8 mg, 0.31 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.09 (m, 2H), 7.57 (m, 5H), 7.17 (dd, 1H), 4.53 (s, 2H), 3.72 (s, 3H).

Example 44

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole (75.5 mg, 70.5%, white foam) was obtained from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (82 mg, 0.365 mmol), potassium carbonate (210 mg, 1.520 mmol), 2-thiol-5-methyl-1H-benzoimidazole (50 mg, 0.305 mmol) in acetonitrile (3 ml) at room temperature. Purification was performed by SPE flash chromatography using 50% ethyl acetate in hexanes followed by trituration with ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.95 (bs, 1H), 7.80 (d, 1H), 7.70 (s, 1H), 7.52 (m, 2H), 7.21 (dd, 2H), 7.17 (d, 1H), 4.40 (s, 2H), 3.95 (s, 3H), 2.50 (s, 3H).

Example 45

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (76 mg, 85%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99.4 mg, 0.72 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (56.7 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.50 (m, 2H), 7.40 (m, 2H), 7.18 (t, 1H), 4.52 (s, 2H), 3.71 (s, 3H), 2.41 (s, 3H).

Example 46

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole (84 mg, 86%, white solid) was obtained from 3-chloromethyl-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole (60 mg, 0.23 mmol), potassium carbonate (95 mg, 0.69 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (54 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-60% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.38 (s, 1H), 7.29 (d, 1H), 7.86 (d, 1H), 7.68 (t, 1H), 7.50 (t, 2H), 7.19 (m, 1H), 4.57 (s, 2H), 3.75 (s, 3H).

Example 47

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (74.3 mg, 88%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (53.3 mg, 0.27 mmol), 5-chloromethyl-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22) mmol), and potassium carbonate (92.6 mg, 0.67 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.62

(d, 1H), 7.52 (d, 2H), 7.48 (d, 1H), 7.37 (t, 1H), 7.18 (t, 1H), 7.06 (m, 1H), 4.64 (s, 2H), 3.84 (s, 3H), 3.71 (s, 3H). LC-MS (MH+): 386.06.

Example 48

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole (79.9 mg, 87%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (86.8 mg, 0.44 mmol), 5-chloromethyl-3-phenyl-[1,2,4]oxadiazole (50 mg, 0.26 mmol), and potassium carbonate (152.0 mg, 1.1 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.02 (d, 2H), 7.47 (m, 5H), 7.18 (t, 1H).

Example 49

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole (71.8 mg, 91%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (78.9 mg, 0.40 mmol), 5-chloromethyl-3-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol) and potassium carbonate (138.2 mg, 1.0 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 45-65% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.82 (d, 2H), 7.52 (d, 1H), 7.47 (d, 1H), 7.31 (m, 2H), 7.18 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H), 2.39 (s, 3H). LC-MS (MH^+): 370.06.

Example 50

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile (130 mg, 75%) was obtained from 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile (100 mg, 0.45 mmol) with K_2CO_3 (189 mg, 1.36 mmol) and 4-methyl-5-

(2-thienyl)1,2,4-triazole-3-thiol (110 mg, 0.54 mmol) in acetonitrile at room temperature. Purification was performed by flash chromatography using 50% ethyl acetate in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.38 (bs,1H), 8.32 (d,1H), 7.88 (d,1H), 7.68 (t,1H), 7.51 (dd, 2H), 7.18 (dd,1H), 4.56 (s,2H), 3.75 (s,3H); LC-MS $(M+H)^+$: 381.

Example 51

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (82.8 mg, 90%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazole-3-thiol (61 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.96 (s, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.53 (s, 2H), 3.91 (s, 3H), 2.75 (s, 3H), 2.41 (s, 3H).

Example 52

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (89 mg, 99%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(2-methyl-thiazol-4-yl)-[1,3,4]oxadiazole-2-thiol (57.3 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.97 (s, 1H), 7.90 (m, 2H), 7.40 (m, 2H), 4.66 (s, 2H), 2.80 (s, 3H), 2.42 (s, 3H).

Example 53

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole (80 mg, 88%, white solid) was obtained from 3-chloromethyl-5-

thiophen-2-yl-[1,2,4]oxadiazole (50 mg, 0.25 mmol), potassium carbonate (103 mg, 0.75 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (59 mg, 0.30 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.65 (m, 1H), 7.51 (m, 2H), 7.19 (m, 2H), 4.50 (t, 2H), 3.74 (s, 3H).

Example 54

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (54.2 mg, 57%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(2,4-dimethyl-thiazol-5-yl)-4-methyl-4H-[1,2,4]triazole-3-thiol (65.1 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm):: 7.88 (m, 2H), 7.39 (m, 2H), 4.57 (s, 2H), 3.49 (s, 3H), 2.73 (s, 3H), 2.43 (d, 6H).

Example 55

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (77.9 mg, 81%, yellow solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 4-methyl-5-(5-nitro-furan-2-yl)-4H-[1,2,4]triazole-3-thiol (65.1 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (m, 2H), 7.46 (d, 1H), 7.40 (m, 2H), 7.33 (d, 1H), 4.59 (s, 2H), 3.91 (s, 3H), 2.42 (s, 3H).

Example 56

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (66 mg, 75%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol (55.3 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.79 (dd, 2H), 7.89 (m, 2H), 7.63 (dd, 2H), 7.40 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.41 (s, 3H).

Example 57

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole (100 mg, 99%, white waxy solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(4-tert-butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol (71.1 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.57 (m, 4H), 7.39 (d, 2H), 4.55 (s, 2H), 3.61 (s, 3H), 2.40 (s, 3H), 1.35 (s, 9H).

Example 58

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (53.8 mg, 56%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(6-chloro-pyridin-3-yl)-4-methyl-4H-[1,2,4]triazole-3-thiol (65.2 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.67 (d, 1H), 8.02 (dd, 1H), 7.88 (m, 2H), 7.49 (d, 1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.65 (s, 3H), 2.42 (s, 3H).

Example 59

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole (138 mg, 62%) was obtained from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (225.9 mg, 1.11 mmol), benzooxazole-2-thiol (167 mg, 1.00 mmol), potassium carbonate (180 mg, 1.3 mmol) in DMF (4.5 ml) at room temperature overnight. Purification was performed on silica gel using 10-20% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm):: 7.67 (d, 1H), 7.57 (m, 3H), 7.43 (t, 1H), 7.21 (m, 2H), 7.14 (m, 1H), 4.50 (s, 2H), 3.86 (s, 3H).

Example 60

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole (73.6 mg, 73%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (61 mg, 0.31 mmol), 3-chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole (50 mg, 0.28 mmol), and potassium carbonate (115 mg, 0.83 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.20 (d, 1H), 7.64 (d, 1H), 7,48 (m, 3H), 7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H)

Example 61

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (51.0 mg, 76%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40.0 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 5-furan-2-yl-4-methyl-4H-[1,2,4]triazole-3-thiol (41.7 mg, 0.23 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.58 (s, 1H), 7.40 (m, 2H), 7.10 (d, 1H), 6.58 (dd, 1H), 4.51 (s, 2H), 3.77 (s, 3H), 2.41 (s, 3H).

Example 62

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (75.4 mg, 83%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (51 mg, 0.26 mmol), 3-chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole (50 mg, 0.24 mmol) and potassium carbonate (98 mg, 0.71 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 55-60% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.78 (m, 1H), 7.51 (m, 3H), 7.32 (m, 1H), 7.18 (m, 1H), 4.55 (s, 2H), 3.74 (s, 3H)

Example 63

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine (27.3 mg, 96.5%) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (20.8 mg, 0.1 mmol) with pyridine-2-thiol (12.2 mg, 0.11 mmol) and potassium carbonate in DMF (0.8 ml) at room temperature for 15 h. Purification was performed by flash chromatography on silica gel using 20% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.47 (dd, 1H), 7.94 (s, 1H), 7.90 (t, 1H), 7.51 (dt, 1H), 7.38 (d, 2H), 7.26 (dd, 1H), 7.02 (dd, 1H), 4.61 (s, 2H), 2.42 (s, 3H).

Example 64

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine (74.5 mg, 96%) was obtained from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (51.2 mg, 0.25 mmol), 1*H*-imidazo[4,5-b]pyridine-2-thiol (37.5 mg, 0.23 mmol) and potassium carbonate (80 mg, 0.58 mmol) in DMF (1.5 ml) at room temperature overnight. Purification was performed on silica gel using 25-50% ethyl acetate in dichloromethane. ^{1}H-NMR (DMSO-d_6), δ (ppm): 8.24 (br s, 1H), 7.88 br s, 1H), 7.66 (d, 1H), 7.55 (m, 3H), 7.29 (d, 1H), 7.19 (m, 1H), 4.82 (s, 2H), 3.85 (s, 3H).

Example 65

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (58 mg, 68%, white solid) was obtained from 3-chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22 mmol), potassium carbonate (91.5 mg, 0.66 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (52.2 mg, 0.26 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-100% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.70 (s, 1H), 7.58 (d, 1H), 7.52 (m, 1H), 7.49 (m, 1H), 7.18 (m, 1H), 7.12 (d, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 2.42 (s, 3H).

Example 66

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine (19.0 mg, 43%, light yellow solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (26 mg, 0.13 mmol), 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine (25 mg, 0.12 mmol) and potassium carbonate (50 mg, 0.36 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 100% ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.13 (s, 1H), 8.65 (s, 1H), 8.16 (s, 1H), 7.50 (m, 2H), 7.19 (t, 1H) 4.57 (s, 2H), 3.74 (s, 3H), 2.43 (s, 3H)

Example 67

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (55.8 mg, 67%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (48.4 mg, 0.23 mmol), potassium carbonate (96 mg, 0.70 mmol), 4-methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol (44.4 mg, 0.23 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in

hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.64 (m, 2H), 7.50 (m, 3H), 7.39 (m, 2H), 4.56 (s, 2H), 3.61 (s, 3H), 2.41 (s, 3H).

Example 68

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (42.8 mg, 51%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (48.4 mg, 0.23 mmol), potassium carbonate (96 mg, 0.70 mmol), 4-methyl-5-pyridin-2-yl-4*H*-[1,2,4]triazole-3-thiol (44.6 mg, 0.23 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.62 (d, 1H), 8.30 (d, 1H), 7.85 (m, 3H), 7.36 (m, 3H), 4.59 (s, 2H), 4.02 (s, 3H), 2.40 (s, 3H).

Example 69

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine (95.8 mg, 83%, clear oil) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (59.9 mg, 0.29 mmol), potassium carbonate (119 mg, 0.86 mmol), 5-(4-benzyl-morpholin-2-yl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol (83.3 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 10% methanol in ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.31 (m, 7H), 4.75 (dd, 1H), 4.47 (dd, 2H), 3.84 (m, 2H), 3.59 (bs, 5H), 3.20 (d, 1H), 2.72 (m, 2H), 2.43 (s, 3H), 2.30 (dt, 1H).

Example 70

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (24 mg, 34%, white solid) was obtained from 3-chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole (40 mg, 0.20 mmol), potassium carbonate (82.5 mg, 0.60 mmol), 4-

methyl-5-pyridin-4-yl-4*H*-[1,2,4]triazole-3-thiol (38.3 mg, 0.20 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 10% methanol in ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.80 (bs, 2H), 8.20 (dd, 1H), 7.62 (m, 3H), 7.45 (dd, 1H), 4.59 (s, 2H), 3.70 (s, 3H).

Example 71

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole (44 mg, 67%, white solid) was obtained from 3-chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole (37 mg, 0.18 mmol), potassium carbonate (75.3 mg, 0.54 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (43 mg, 0.22 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-100% ethyl acetate in hexanes. ^{1}H NMR (DMSO), δ (ppm): 9.37 (d, 1H), 8.86 (d, 1H), 7.80 (d, 1H), 7.65 (d, 1H), 7.26 (t, 1H), 4.54 (s, 2H), 3.75 (s, 3H).

Example 72

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole (21.1 mg, 13%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (91 mg, 0.46 mmol), 3-chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole (100 mg, 0.42 mmol) and and potassium carbonate (173 mg, 1.25 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 60% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.96 (s, 1H), 8.44 (t, 2H), 7.75 (t, 1H), 7.51 (m, 2H), 7.19 (t, 1H), 4.59 (s, 2H), 3.76 (s, 3H)

Example 73

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine (59.2 mg, 66%, white solid) was obtained from 4-methyl-

5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (51 mg, 0.26 mmol), 4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine (50 mg, 0.24 mmol), and potassium carbonate (100 mg, 0.72 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 100% ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.71 (d, 1H), 7.79 (s, 1H), 7.73 (d, 1H), 7.49 (m, 2H), 7.19 (t, 1H), 4.58 (s, 2H), 3.73 (s, 3H), 2.65 (s, 3H)

Example 74

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine (30 mg, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol (46.1 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 5% methanol in ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.90 (bs, 1H), 8.76 (bs, 1H), 8.03 (m, 1H), 7.88 (m, 2H), 7.46 (dd, 1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.66 (s, 3H), 2.42 (s, 3H).

Example 75

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (60 mg, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 4-methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol (47.3 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 40% ethyl acetate in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.71 (dd, 1H), 7.48 (m, 2H), 7.38 (m, 2H), 4.52 (s, 2H), 3.67 (s, 3H), 2.41 (s, 3H).

Example 76

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (30 mg, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 4-methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol (47.5 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 60% ethyl acetate in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.89 (d, 1H), 8.22 (d, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.55 (s, 2H), 3.94 (s, 3H), 2.41 (s, 3H).

Example 77

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (725 mg, 97%, white solid) was obtained from 3-chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole (500 mg, 1.56 mmol), potassium carbonate (647 mg, 4.68 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (369 mg, 1.87 mmol) in acetonitrile (10 ml) at room temperature. Purification was performed by flash column chromatography on silica gel using 40% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 8.06 (d, 1H), 7.93 (d, 1H), 7.51 (m, 2H), 7.26 (t, 1H), 7.19 (m, 1H), 4.54 (s, 2H), 3.73 (s, 3H).

Example 78

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (28.1 mg, 27%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (59 mg, 0.30 mmol), 3-chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole (60 mg, 0.27 mmol) and potassium carbonate (111 mg, 0.80 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (t, 2H), 7.51 (m, 2H), 7.42 (t, 2H)7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H), 2.70 (m, 2H), 1.26 (t, 3H)

Example 79

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (46.0 mg, 59%, white solid) was obtained from 2-mercaptobenzimidazole (41 mg, 0.27 mmol), 4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine (50 mg, 0.24 mmol), and potassium carbonate (100 mg, 0.72 mmol) in DMF (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 100% ethyl acetate and titurated with ether. ^{1}H NMR (DMSO-d_6), δ (ppm): 8.72 (d, 1H), 7.87 (s, 1H), 7.78 (d, 1H), 7.47 (t, 2H), 7.14 (m, 2H), 4.81 (s, 2H), 2.59 (s, 3H)

Example 80

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (36 mg, 51%, white solid) was obtained from 3-chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole (50 mg, 0.16 mmol), potassium carbonate (65 mg, 0.47 mmol), 1*H*-benzoimidazole-2-thiol (23 mg, 0.16 mmol) in DMF (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-100% ethyl acetate in hexanes followed by trituration with ethyl acetate. ^{1}H NMR (DMSO), δ (ppm): 12.73 (bs, 1H), 8.30 (s, 1H), 8.09 (d, 2H), 7.45 (m, 3H), 7.18 (m, 2H), 4.78 (s, 2H).

Example 81

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (54.3 mg, 80%, clear oil) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 4-methyl-5-trifluromethyl-4*H*-[1,2,4]triazole-3-thiol (35.1 mg, 0.19 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.41 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.43 (s, 3H).

Example 82

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (51.4 mg, 62%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 5-(2,6-dichloro-pyridin-4-yl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol (50.1 mg, 0.19 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.61 (s, 2H), 7.40 (m, 2H), 4.60 (s, 2H), 3.71 (s, 3H), 2.42 (s, 3H).

Example 83

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (57.8 mg, 81%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 4-methyl-5-p-tolyl-4*H*-[1,2,4]triazole-3-thiol (39.4 mg, 0.19 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.53 (d, 2H), 7.39 (m, 2H), 7.30 (d, 2H), 4.55 (s, 2H), 3.59 (s, 3H), 2.42 (d, 6H).

Example 84

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine (28.0 mg, 85%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (18 mg, 0.093 mmol), 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine (20 mg, 0.084 mmol), and potassium carbonate (35 mg, 0.25 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 70% ethyl acetate in

hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.49 (m, 2H), 7.36 (m, 3H), 7.17 (t, 1H), 6.91 (d, 1H), 4.51 (s, 2H), 3.72 (s, 3H), 3.00 (s, 6H)

Example 85

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (76.8 mg, 90%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (47 mg, 0.24 mmol), 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22 mmol), and potassium carbonate (91 mg, 0.66 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.49 (m, 4H), 7.18 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

Example 86

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole (144.0 mg, 91%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (78 mg, 0.39 mmol), 3-chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole (100 mg, 0.36 mmol) and potassium carbonate (149 mg, 1.08 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 55% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.04 (d, 1H), 7.95 (s, 1H), 7.51 (m, 4H), 7.18 (m, 1H), 4.56 (s, 2H), 3.74 (s, 3H)

Example 87

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (10.5 mg, clear oil) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (165 mg, 1.20 mmol), 5-

cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (94.6 mg, 0.48 mmol) in acetonitrile (3 ml) at 60°C overnight. Purification was performed on silica gel using 2% ammonia (2 N methanol) in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.39 (m, 2H), 4.42 (s, 2H), 3.46 (s, 3H), 2.60 (m, 1H), 2.42 (d, 3H), 1.74 (m, 7H), 1.34 (m, 3H).

Example 88

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (56.8 mg, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 5-tert-butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (41 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.40 (m, 2H), 4.46 (s, 2H), 3.63 (s, 3H), 2.43 (m, 3H), 1.45 (s, 9H).

Example 89

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (83.4 mg, 86%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (47 mg, 0.24 mmol), 5-(3-bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole (60 mg, 0.22 mmol), and potassium carbonate (91 mg, 0.66 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 60% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.25 (t, 1H), 8.02 (d, 1H), 7.73 (d, 1H), 7.50 (m, 2H), 7.40 (t, 1H), 7.19 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

Example 90

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (71.1 mg, 84%, white solid) was obtained from 2-mercaptobenzimidazole (35 mg, 0.23 mmol),

5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole (60 mg, 0.22 mmol) and potassium carbonate (91 mg, 0.66 mmol) in DMF (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 35% ethyl acetate in hexane and titurated with ether. ^{1}H NMR (DMSO-d_6), δ (ppm): 12.78 (broad s, 1H), 8.18 (s, 1H), 8.07 (d, 1H), 7.93 (d, 1H), 7.59 (t, 1H), 7.46 (s, 2H), 7.14 (m, 2H), 4.77 (s, 2H)

Example 91

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole (76 mg, 90%, white solid) was obtained from 3-chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole (50 mg, 0.21 mmol), potassium carbonate (87 mg, 0.63 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (50 mg, 0.25 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.06 (s, 1H), 8.01 (d, 1H), 7.59 (d, 1H), 7.50 (m, 3H), 7.18 (t, 1H), 4.54 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H), 3.43 (s, 3H).

Example 92

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (62 mg, 84%, white solid) was obtained from 3-chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole (50 mg, 0.21 mmol), potassium carbonate (87 mg, 0.63 mmol), 1*H*-benzoimidazole-2-thiol (32 mg, 0.21 mmol) in DMF (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-100% ethyl acetate in hexanes. ^{1}H NMR (DMSO), δ (ppm): 8.09 (d, 2H), 7.59 (m, 2H), 7.46 (bs, 2H), 7.14 (m, 2H), 4.77 (s, 2H), 4.51 (s, 2H), 3.35 (s, 3H).

Example 93

4-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine

A solution of isonicotinoyl chloride (2.0 g, 11.2 mmol) in dichloromethane was treated with 2-chloro-*N*-hydroxy-acetamidine (1.58 g, 14.6 mmol), followed by addition of triethylamine (4.67 ml, 33.6 mmol) in a dropwise manner. After stirring at room temperature 1 h, extraction with ethyl acetate using water and brine washes afforded the oxy-acyl intermediate (used without further purification, 150 mg, 0.7 mmol). A solution of the crude product in acetonitrile (2 ml) and DMSO (2 ml) with K_2CO_3 (292 mg, 2.1 mmol) and 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (140 mg, 0.7 mmol) was stirred at room temperature for 24 h followed by 1.5 h at 120°C (sealed tube). Standard aqueous work-up with ethyl acetate using water and brine washes followed by silica gel chromatography afforded the title compound (110 mg, 44%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.41 dd,2H), 7.92 dd,2H), 7.50 dd,1H), 7.47 dd,1H), 7.18 dd,1H), 4.58 (s,2H), 3.74 (s,3H); LC-MS $(M+H)^+$: 357.

Example 94 was prepared in an analogous method to the procedure given in Example 93.

Example 94

4-[5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine

4-[5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine (12 mg, 5%) was obtained from *N*-hydroxy-isonicotinamidine (200 mg, 1.4 mmol) with chloroacetyl chloride (0.11 ml, 1.4 mmol) and triethylamine (0.5 ml, 3.5 mmol); aqueous work-up gave intermediate (150 mg, 0.7 mmol); treated with K_2CO_3 (292 mg, 2.1 mmol), and 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (140 mg, 0.7 mmol). Purification was performed by silica gel chromatography and recrystallization. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.76 (dd,2H), 7.89 (dd,2H), 7.53 (dd,1H), 7.48 (dd,1H), 7.18 (dd,1H), 4.71 (s,2H), 3.73 (s,3H); LC-MS (M+H)+: 357.

Example 95

2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine

and

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b]pyridine

THF (3 ml) was added to a mixture of sodium hydride (60%, 8 mg, 0.2 mmol) and 2-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine (24.6 mg, 0.072 mmol) and the resulting mixture was stirred at 0°C for about 15 min.. Methyl iodide (20 µL, 0.32 mmol) was added the resulting mixture was stirred at 0°C for 2h. The reaction was quenched by the addition of dichloromethane (10 ml) and water (2 ml). After vigorous stirring, the organic extracts (10 ml, plus 3x5 ml) were eluted through a Chem Elut Extraction Column (Varian, cat #1219-8002). Purification using SPE chromatography (5 g silica) using 25/25/50 to 50/25/25 ethyl acetate / dichloromethane / hexane yielded two products. The first product to elute was 2-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine (6 mg, 23%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.46 (d, 1H), 7.72 (d, 1H), 7.62 (d, 1H), 7.55 (d,1H), 7.42 (t,1H), 7.14 (m, 2H), 5.67 (q, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 2.01 (d, 3H).

The second product to elute was 2-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1H-imidazo[4,5-b]pyridine (12 mg, 47%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 7.69 (d, 1H), 7.60 (d, 1H), 7.55 (d, 1H), 7.41 (t, 1H), 7.13 (m, 1H), 4.90 (s, 2H), 3.87 (s, 3H), 3.70 (s, 3H).

Example 96-97 was prepared in an analogous method to the procedure given in Example 95.

Example 96

3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole

3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole (13 mg, 47%) was obtained from 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (25.5 mg, 0.069 mmol) with 60% sodium hydride (37 mg, 0.92 mmol) and methyl iodide (0.10 ml, 1.6 mmol) in THF (3 ml) at room temperature for 2 h. The product was extracted with ethyl acetate and purified by SPE 20-40% ethyl acetate in 1:1 dichloromethane : hexane. ^{1}H NMR ($CDCl_3$),

δ (ppm): 7.83 (br s, 2H), 7.48 (d, 1H), 7.42 (d, 1H), 7.36 (m, 2H), 7.13 (m, 1H), 3.50 (s, 3H), 2.35 (s, 3H), 1.95 (s, 6H).

Example 97

3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole

3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole (6.1 mg, 17%) was obtained from 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (33.8 mg, 0.091 mmol) with 60% sodium hydride (17 mg, 0.42 mmol) and methyl iodide (20 µL, 0.32 mmol) in THF (2.5 ml) at room temperature for 1h. The product was extracted with dichloromethane and purified by SPE 25-40% ethyl acetate in 1:1 chloroform : hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (br s, 2H), 7.50 (d, 1H), 7.46 (d, 1H), 7.38 (m, 2H), 7.16 (m, 1H) , 4.89 (q, 1H), 3.64 (s, 3H), 2.37 (s, 3H), 1.90 (d, 3H).

Example 98

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole and 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

Dichloromethane (2.5 ml) was added to a mixture of 3-chloro-benzenecarboperoxoic acid (57-85%, 49.5 mg, 0.16-0.25 mmol) and 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (45 mg, 0.12 mmol) and the resulting mixture was stirred at room temperature overnight. The reaction was quenched by the addition of dichloromethane (10 ml) and 1 M sodium hydroxide (3 ml). After vigorous stirring, the organic extracts (10 ml, plus 3x5 ml) were eluted through a Chem Elut Extraction Column (Varian, cat #1219-8002). Purification was performed by SPE chromatography (5 g silica) using 10-30% ethyl acetate in 1:1 dichloromethane : hexane yielded two products. The first product to elute was 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (12.3 mg, 25%). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.63 (d, 1H), 7.56 (d, 1H), 7.36 (m, 2H), 7.24 (m, 1H), 5.12 (s, 2H), 3.94 (s, 3H), 2.36 (d, 3H).

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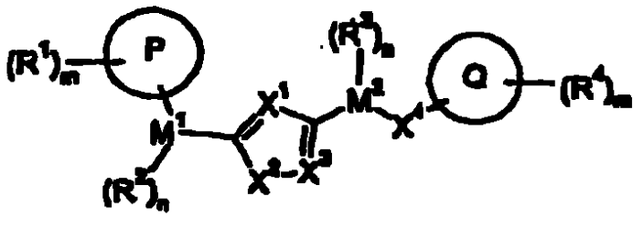
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(54) Title: "1,2,4"OXADIAZOLES AS MODULATORS OF METABOTROPIC GLUTAMATE RECEPTOR-5



(I)

(57) Abstract: The present invention relates to new compounds of formula (I), a process for their preparation and new intermediates prepared therein, pharmaceutical formulations containing said compounds and to the use of said compounds in therapy. In particular, there are compounds according to the present invention that are potent and selective for the mGluR Group I receptor and more particularly for mGluR5. Thus, it is expected that the compounds of the invention are well suited for the prevention and/or treatment of mGluR5 receptor-mediated disorders such as acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders.

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— *with amended claims*

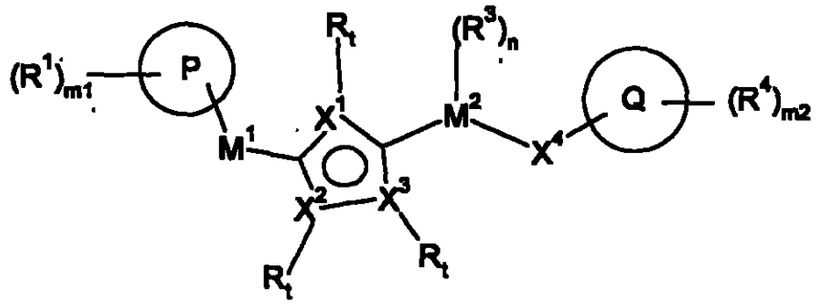
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AMENDED CLAIMS
[received by the International Bureau on 18 March 2004 (18.032004);
original claims 1-28 replaced by amended claims 1-27 (44 pages)]

1. A compound having the formula I



(I)

wherein:

P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

M^1 is a bond;

X^1 selected from the group consisting of C, CO, N, O and S;

X^2 is selected from the group consisting of C, N, O and S;

X^3 is i) selected from the group consisting of N, O and S, or

ii) selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H ;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$ and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and any suitable carbon atom is optionally substituted with R^4; and

R^4 is selected from the group consisting of C_{0-6}alkylcyano, $=NC_{1-4}$alkyl, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkyl$Oaryl$, C_{0-6}alkyl$Oheteroaryl$, C_{0-6}alkyl$Naryl$, C_{0-6}alkyl$Nheteroaryl$, OC_{0-6}alkyl$Oaryl$, OC_{0-6}alkyl$Oheteroaryl$, OC_{0-6}alkyl$Naryl$, OC_{0-6}alkyl$Nheteroaryl$, NC_{0-6}alkyl$Oaryl$, NC_{0-6}alkyl$Oheteroaryl$, NC_{0-6}alkyl$Naryl$, NC_{0-6}alkyl$Nheteroaryl$, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}$alkyl$)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl,

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imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m1 is selected from 0, 1, 2, 3 and 4;

m2 is selected from 0, 1, 2 and 3;

n is selected from 0, 1 and 2; and

t is 0 or 1,

and salts thereof,

with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole, 1,2-di{2-(3-amino-phenyl)-[1,3,4]oxadiazole-yl)ethane, 1,2-di{5-[5-(4-nitro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-bromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-chloro-phenyl)furan-2-yl]-

[1,3,4]oxadiazol-yl)ethane and 1,2-di{5-[5-(2,4-dibromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane.

2. A compound according to claim 1, wherein P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl or phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5 and R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

3. A compound according to claim 2, wherein P is phenyl substituted on position 3 or disubstituted on positions 2 and 5.

4. A compound according to claim 1, wherein X^1 is N and one of X^2 and X^3 is O and the other is N.

5. A compound according to claim 1, wherein the ring containing X^1, X^2 and X^3 forms an oxadiazole, isoxazole, oxazole, chloro-isoxazole or a methyl-isoxazole.

6. A compound according to claim 1, wherein M^2 is a bond or C_{1-3}alkyl and R^3 is hydrogen, methyl or dimethyl.

7. A compound according to claim 1, wherein X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, NR^5, O, SO, SO_2 and S and R^5 and R^6 are independently selected from hydrogen and C_{1-6}alkyl.

8. A compound according to claim 7, wherein X^4 is selected from the group consisting of CH_2, $CHCH_3$, $CH(CH_3)_2$ and NR^5.

9. A compound according to claim 7, wherein X^4 is S.

10. A compound according to claim 1, wherein Q is selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom, and any suitable carbon atom is optionally substituted with R^4 and R^4 is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

11. A compound according to any one of claims 1 or 10, wherein Q is selected from the group consisting of triazolyl and thiadiazolyl.

12. A compound according to claim 1, wherein Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl and R^4 is hydrogen or C_{1-6}alkyl.

13. A compound according to any one of claims 1 or 12, wherein Q is selected from the group consisting of pyridonyl, tetrahydrotriazolopyridyl and tetrahydrotriazolopyrimidinyl.

14. A compound according to claim 1, wherein R^4 is selected from the group consisting of benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl,

dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl, trifluoromethyl, acetic acid methylester, allyl, amino, benzyl, cyclopropylmethyl, ethyl, fluorobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

15. A compound which is selected from the group consisting of

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

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5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole,

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine,

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine,

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole,

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

4-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine,

2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b],

3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole and

5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

or salt thereof.

17. A compound which is selected from the group consisting of

4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester,

2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole,

5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

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3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine,

3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

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3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole,

4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole,

4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine,

3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile,

4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole,

4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine,

2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2.4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol,

3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol,

5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester,

5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole,

5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

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4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole,

2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide,

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine, or

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester,

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine,

or salt thereof.

17. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 16 in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

18. The pharmaceutical formulation according to claim 17, for use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

19. A compound according to any one of claims 1 to 16 for use in therapy.

20. The compound according to claim 19, for use in prevention and/or treatment of mGluR5 receptor-mediated disorders.

21. The compound according to claim 19, for use in prevention and/or treatment of neurological disorders.

22. The compound according to claim 19, for use in prevention and/or treatment of psychiatric disorders.

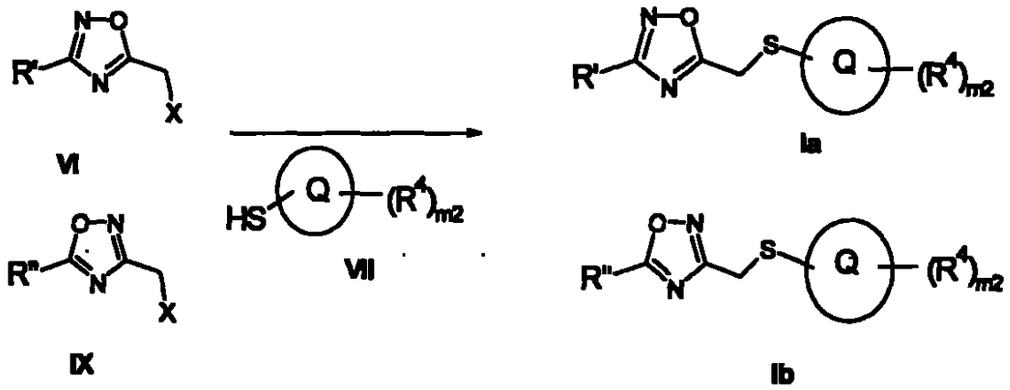
23. The compound according to claim 19, for use in prevention and/or treatment of chronic and acute pain disorders.

24. The use of a compound according to any one of claims 1 to 16 in the manufacture of a medicament for the use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

25. A method of prevention and/or treatment of mGluR5 receptor-mediated disorders, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound according to any one of claims 1 to 16.

26. A method for inhibiting activation of mGluR5 receptors, comprising treating a cell containing said receptor with an effective amount of a compound according to any one of claims 1 to 16.

27. Processes for the preparation of a compound according to claim 2, comprising;



wherein R' and R'' contains either a group represented in Formula I by M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$ or a leaving group such as $(CH_2)_nX$, wherein X is any suitable leaving group such as chloro or mesylate or a group which may subsequently be transformed into a leaving group and Q, X^4, R^3 R^4, M^2, m2 and n are as defined in claim 1.

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(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, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

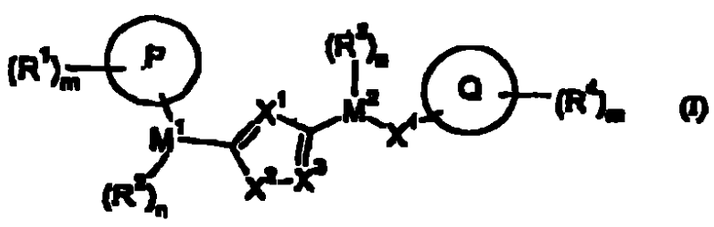
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ,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

Published:
— *with international search report*

(88) Date of publication of the international search report: 27 May 2004

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

(54) Title: "1,2,4"OXADIAZOLES AS MODULATORS OF METABOTROPIC GLUTAMATE RECEPTOR-5



(I)

(57) Abstract: The present invention relates to new compounds of formula (I), a process for their preparation and new intermediates prepared therein, pharmaceutical formulations containing said compounds and to the use of said compounds in therapy. In particular, there are compounds according to the present invention that are potent and selective for the mGluR Group I receptor and more particularly for mGluR5. Thus, it is expected that the compounds of the invention are well suited for the prevention and/or treatment of mGluR5 receptor-mediated disorders such as acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders.

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D413/12 C07D413/14 C07D417/14 A61K31/4245 A61P25/00

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 26927 A (STORMANN THOMAS M ;DELMAR ERIC G (US); MOE SCOTT T (US); SMITH DAR) 3 June 1999 (1999-06-03) page 5, line 30 - line 34; claims 1,15,16 figure 1, compound 5	1-27
X	EP 0 397 365 A (PFIZER) 14 November 1990 (1990-11-14) claims 1,14 examples	1-27
X	US 5 140 034 A (BAKER RAYMOND ET AL) 18 August 1992 (1992-08-18) column 1, line 5 - line 15; claim 1 column 4, line 25 - line 42	1-27

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[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents :

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 December 2003	23/01/2004

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

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 422 369 A (BAYER AG) 17 April 1991 (1991-04-17) page 4, line 26 - line 44; claims 1,10; table 1	1-17,28
X	WO 00 35913 A (AVENTIS CROPSCIENCE GMBH) 22 June 2000 (2000-06-22) page 22; claims 1,9; table 1	1-24,28
X	HOLLA B S ET AL: "Synthesis and antibacterial studies of a new series of 1,2-bis(1,3,4-oxadiazol-2-yl)ethanes and 1,2-bis(4-amino-1,2,4-triazo 1-3-yl)ethanes" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 35, no. 2, February 2000 (2000-02), pages 267-271, XP004330420 ISSN: 0223-5234 compounds 4 and 5 tables I,II	1-24
X	GÜNAY N S ET AL: "5-Nitroimidazole derivatives as possible antibacterial and antifungal agents" IL FARMACO, vol. 54, 1999, pages 826-831, XP002264297 ROME, IT ISSN: 0014-827X tables 1,2	1-24
X	MADRONERO R ET AL: "Tetrazole analogues of arylthiazolylacetic acids. Synthesis and pharmacological study" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY., vol. 9, no. 4, 1974, pages 445-448, XP009022649 EDITIONS SCIENTIFIQUE ELSEVIER, PARIS., FR ISSN: 0223-5234 scheme 1 abstract	1-27
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4885431 XP002264298 5,5'-(1,2-ethanediyl)-bis'3-(m-tolyl)-1,2,4-oxadiazole! & ORG. MASS SPECTROM. (1991), 26(11), 1017-1018,	1-17

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INTERNATI NAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4208871 XP002264299 & SYNTH. COMMUN. (1990), 20(12), 1811-1817,	1-17
P,X	DATABASE CHEMCATS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002264300 Order numbers: SPB 01075, SEW 03694, BTB 02953 & "Maybridge HTS" 14 May 2003 (2003-05-14) , MAYBRIDGE PLC , TINTAGEL, CORNWALL, PL34 0HW, UK	1-17

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

The present application contains four separate independent compound claims of overlapping scope (see claims 1, 2, 16 and 17). The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection (Article 6 PCT). A further lack of clarity arises owing to the fact that a seemingly arbitrary selection of compounds have been disclaimed in claim 2 but not in the broader claim 1. Many of the variables in the claims are so ill-defined that it is impossible to determine the subject-matter for which protection is sought. For example, it is not clear whether the definition of X4 in claim 2 as being C0-C4alkylR5R6 is intended to imply that X4 may be absent (i.e. for C0-alkyl).

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved (see search report for a selection of documents) that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to compounds of formula I as defined in claim 2 wherein X1, X2 and X3 are as defined in claim 5; M2 is as defined in claim 7 and X4 is defined as in claim 10.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

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

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

Although claims 26 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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

see FURTHER INFORMATION sheet PCT/ISA/210

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

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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

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

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

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

Remark on Protest

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

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT/US 03/24846

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The second product to elute was 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (33.2 mg, 71%). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (br s, 2H), 7.59 (d, 1H), 7.54 (d, 1H), 7.38 (m, 2H), 7.22 (m, 1H) , 5.05 (d_{AB}, 1H) , 4.90 (d_{AB}, 1H), 4.03 (s, 3H), 2.39 (d, 3H).

Example 99

5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

To 5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl) -[1,2,4]oxadiazole (50 mg, 0.10 mmol) in a vial was added 3-furan boronic acid (17 mg, 0.16 mmol), tetrakis(triphenylphosphine)palladium(0) (6 mg, 0.0052 mmol), ethylene glycol dimethyl ether (1 ml) and 2 M sodium carbonate (1 ml). The vial was then sealed and heated at 90°C for 1 h with vigorous stirring. The reaction was cooled, diluted with ethyl acetate, washed with water and saturated brine, filtered and concentrated. The residue was purified by flash column chromatography using 70% ethyl acetate in hexanes. Additional purification by trituration with a mixture of diethyl ether and hexanes and then filtration afforded the title compound as a beige solid 25 mg (57%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.18 (s, 1H), 7.98 (d, 1H), 7.79 (s, 1H), 7.71 (d, 1H), 7.51 (m, 4H), 7.17 (m, 1H), 6.74 (s, 1H), 4.55 (s, 2H), 3.73 (s, 3H).

Intermediates

Example 100

Pyrimidine-4-carboxylic acid.

3-Methyl-pyrimidine (9.41 g, 100 mmol), potassium permanganate (26.9 g) and sodium carbonate (10.6 g) was refluxed in water (100 ml) for 72 h followed by filtration through celite. The filtrate was washed with several portions of DCM and EtOAc before acidification with conc. HCl. The formed precipitate was collected and washed with water to yield 1.37 g of the title compound as a white solid. 1H NMR (DMSO-d6) d (ppm): 13.94 (br. s, 1H), 9.37 (d, 1H), 9.07 (d, 1H), 8.01 (dd, 1H).

Example 101

5-Chloro-thiophene-3-carboxylic acid.

Thiophene-3-carboxylic acid (17.51 g, 136.6 mmol) and 1-chloro-pyrrolidine-2,5-dione (23.7 g) was refluxed in acetic acid (200 ml) for 4 h under argon before pouring onto water (700 ml). Repeated extraction with several small portions of DCM, followed by back extraction from the combined organics with several small portions of 2 M aqueous sodium hydroxide, gave a combined alkaline aqueous solution that was washed with DCM before acidified with conc. HCl to precipitate the crude material. This precipitate was recrystallized from water to yield 14.98 g of the title compound as a grey solid contaminated with approximately 20 mol% of a dichlorinated byproduct as judged from MS and 1H-NMR. 1H NMR (DMSO-d6) d (ppm): 8.15 (d, 1H), 7.37 (d, 1H).

Example 102

3-Methylsulfanyl-benzoic acid

Methyl iodide (0.972 mL) was added to a mixture of 3-mercapto-benzoic acid (601 mg, 3.9 mmol) and potassium carbonate (2.7 g, 19.5 mmol) in DMF (8 mL) in an ice-bath. After the reaction was warmed to room temperature and stirred for 1 hour, the reaction mixture was diluted with ethyl acetate, washed with water (3X), dried over anhydrous sodium sulfate, filtered, and concentrated to afford 3-methylsulfanyl-benzoic acid methyl ester (684 mg, 96%, yellow oil). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.80 (d, 1H), 7.44 (d, 1H), 7.35 (t, 1H), 3.92 (s, 3H), 2.53 (s, 3H).

3-Methylsulfanyl-benzoic acid methyl ester (684mg, 3.8 mmol) and 1N NaOH (5.6 mL, 5.6 mmol) in methanol (8 mL) and THF (8 mL) were heated at 70°C for 1 hour. The reaction mixture was concentrated and then the residue was diluted with water. After acidification with 1N HCl to pH ~ 2, the aqueous layer was extracted with ethyl acetate and then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 3-methylsulfanyl-benzoic acid (616 mg, 97%, white solid). ^{1}H NMR (DMSO), δ (ppm): 13.1 (bs, 1H), 7.76 (s, 1H), 7.70 (d, 1H), 7.51 (d, 1H), 7.44 (t, 1H), 2.52 (s, 3H).

Example 103

3-Cyclopropyl-benzoic acid

1.0 M Diethyl zinc in hexanes (27.3 ml, 27.3 mmol) was added to a solution of 2,4,6-trichlorophenol (5.4g, 27.3 mmol) in dichloromethane (100 ml) at –40°C. After stirring for 15 minutes, diiodo-methane (2.2 mL, 27.3 mmol) was added at –40°C and stirred for an additional 15 minutes. 1-Bromo-3-vinyl-benzene (2.5 g, 13.7 mmol) was then added to the reaction mixture, allowed to warm to room temperature, and left stirring overnight. The reaction mixture was diluted with dichloromethane, washed with 1N HCl (2X), saturated sodium bicarbonate (2X), saturated sodium sulfite, 1N sodium hydroxide, and saturated brine, dried over magnesium sulfate, filtered and concentrated. GC-MS revealed that the reaction mixture contained 1-Bromo-3-cyclopropyl-benzene and 1-bromo-3-vinyl-benzene. To remove the bromo-3-vinyl-benzene, the crude mixture was reacted with potassium permanganate. A solution of potassium permanganate/water (1.5 g/20 mL) was added drop-wise to a solution of the crude mixture (~ 3.5 g) in THF (40 mL) at 0°C and then allowed to warm to room temperature. After 1 hour, the reaction was diluted with diethyl ether, washed with water and saturated brine, dried over anhydrous sodium sulfate filtered and concentrated. Purication by flash column chromatography eluted with 100 hexanes afforded 1-bromo-3-cyclopropyl-benzene (2.20g, 81%).

1.6 M n-Butyllithium in hexanes (3.2 mL, 5.1 mmol) was added drop-wise to a solution of 1-bromo-3-cyclopropyl-benzene at –78°C and stirred for 1 hour. This reaction mixture was then transferred via canula to a 250 mL round bottom flask equipped with a stirrer bar approximately ¼ full of solid carbon dioxide and stirred and for 1 hour. The reaction mixture was concentrated and then the residue was diluted with water. The aqueous layer was washed with dichloromethane (3X), acidified with 1 N HCl to pH ~ 2, and extracted with ethyl acetate. The organic phase was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford 3-cyclopropyl-benzoic (356 mg, 43%, white solid). ^{1}H NMR (DMSO), δ (ppm): 12.90 (bs, 1H), 7.71 (d, 1H), 7.64 (s, 1H), 7.34 (m, 2H), 2.01 (m, 1H), 0.99 (m, 2H), 0.70 (m, 2H).

Example 104

3-tert-Butoxycarbonylamino-benzoic acid

To a flask containing ethyl-3-aminobenzoate (1g, 6.05 mmol) added di-*tert*-butyl dicarbonate (3.16 g, 14.5 mmol), triethyl amine (500 mg, 4.94 mmol), and THF (10 mL) and allowed to stir at 60°C for two hours and then overnight at room temperature. The THF was removed *in vacuo*, and the crude ester was partitioned between ethyl acetate and water, washed with saturated brine, dried over anhydrous sodium sulfate and the solvent was removed *in vacuo*. The product was then purified by flash column chromatography using 15% ethyl acetate in hexane affording 2g of 3-tert-butoxycarbonylamino-benzoic aid ethyl ester (white slurry).

To the crude 3-tert-butoxycarbonylamino-benzoic acid ethyl ester (~2.0g, 0.00754 mmol) added THF (15 mL), and 0.5M LiOH (15 mL). The mixture was heated for two hours at 75°C and the THF was removed *in vacuo* after cooling. The precipitate was filtered from the remaining mixture and the filtrate was transferred to a separatory funnel. The aqueous layer was washed with dichloromethane (3x) and was acidified to pH ~5 using 1M HCl. The product was then extracted with ethyl acetate, washed with water, saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. 730mg of 3-tert-Butoxycarbonylamino-benzoic acid (white solid) was isolated. 1H NMR (DMSO-d_6) δ (ppm): 9.58 (s, 1H), 8.16 (s, 1H), 7.63 (d, 1H), 7.54 (d, 1H), 7.37 (t, 1H), 1.49 (s, 9H)

Example 105

3-Acetyl-benzoic acid

6M Sodium hydroxide (25 mL) was added to 3-acetylbenzonitrile (850 mg, 5.82 mmol) in methanol (25 mL) and then heated at 90°C overnight. After concentrating the reaction mixture, the aqueous layer was washed with dichloromethane (2x), then acidified pH ~ 3 with 12M HCl. The precipitate was extracted with ethyl acetate then washed with water and saturated brine, dried over anhydrous sodium sulfate filtered and concentrated to afford 3-ethylbenzoic acid as a colorless oil; 0.800g (92%). 1H NMR ($CDCl_3$) δ (ppm): 8.70 (s, 2H), 8.33 (d, 2H), 8.24 (d, 2H), 7.64 (t, 1H), 2.70 (s, 3H).

Example 106

2-Methyl-isonicotinic acid hydrazide

Dichloromethane (10mL) was added to 2-methyl nicotinic acid hydrochloride salt (1.1g, 6.34 mmol) and oxalyl chloride (6.95mL, 13.9mmol) was added slowly under Argon while the flask was cooled in ice. Dimethylformamide (2 drops) was added and the reaction was allowed to stir overnight during which time it warmed to room temperature. The reaction was concentrated and THF (10mL) was added to the flask and it was placed in an ice bath. Methanol (5mL) was added and the reaction was allowed to stir for one hour. The reaction was concentrated and the residue was partitioned between $NaHCO_3$ (sat) and EtOAc. The product was extracted with EtOAc three times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. Purification was performed by solid phase extraction tube (20% EtOAc/hexanes) gave the title compound as a clear oil. ^1H NMR $CDCl_3$ δ (ppm): 8.51 (d, 1H), 7.57 (d, 1H), 7.51 (d, 1H), 3.82 (s, 3H), 2.50 (s, 3H).

2-Methyl-isonicotinic acid methyl ester (316.5mg, 2.093mmol) was dissolved in MeOH (7mL) under Argon and hydrazine monohydrate 98% (1mL, 20.93mmol) was added. The reaction was allowed to stir under Argon at room temperature for eighteen hours. The reaction was concentrated to give the title compound (271.9mg, 86%) as a white solid. ^1H NMR $CDCl_3$ δ (ppm): 8.59 (d, 1H), 7.50 (s, 1H), 7.38 (d, 1H), 3.09 (br. s, 3H), 2.60 (s, 3H).

Example 107

5-Chloro-2-fluoro-benzoic acid hydrazide.

Step 1: 5-Chloro-2-fluoro-benzoic acid methyl ester: Methanol (20 ml) was added to a solution 5-chloro-2-fluoro-benzoyl chloride (1.2 g, 6.2 mmol) in dichloromethane (10 ml) in an ice-bath. The reaction mixture was warmed to room temperature, stirred for 3 h and then concentrated to afford 5-chloro-2-fluoro-benzoic acid methyl ester (1.17 g, 100%). 1H NMR ($CDCl_3$), δ (ppm): 7.93 (m, 1H), 7.48 (m, 1H), 7.12 (m, 1H), 3.96 (s, 3H). Step 2: 5-Chloro-2-fluoro-benzoic acid hydrazide: A mixture of 5-chloro-2-fluoro-benzoic acid methyl ester (1.17 g, 6.2 mmol) and hydrazine monohydrate (0.451 ml, 9.3 mmol) in ethanol (20 ml) was stirred at room temperature overnight. The reaction mixture was concentrated and then the residue was triturated with diethyl ether to afford 5-chloro-2-

fluoro-benzoic acid hydrazide (497 mg, 42%, white solid). 1H NMR (DMSO), δ (ppm): 9.66 (bs, 1H), 7.58 (m, 2H), 7.36 (m, 1H), 4.58 (bs, 2H).

Example 108 was prepared analogously to example 107.

Example 108

3-Cyano-benzoic acid hydrazide

3-cyano-benzoyl chloride (3g, 18.12 mmol) in dichloromethane (5 mL) and methanol (20 mL) was stirred at room temperature and overnight. The solvent was removed using a rotevaporator to afford a white solid (3.76g). ^{1}H NMR (DMSO) δ (ppm): 8.33 (m, 1H), 8.24 (m, 1H), 8.14 (m, 1H), 7.76 (m, 1H), 3.89 (d, 3H).

A mixture of 3-cyano-benzoic acid methyl ester (2 g, 12 mmol) and hydrazine monohydrate (0.60 mL, 12 mmol) in ethanol (10 mL) was stirred at room temperature overnight. The reaction mixture was concentrated and then the residue was triturated with diethyl ether to afford 3-cyano-benzoic acid hydrazide (1.02 g, 51%, pink solid). ^{1}H NMR (DMSO) δ (ppm): 10.31 (s, 1H), 8.21 (m, 1H), 8.11 (m, 1H), 7.99 (m, 1H), 7.70 (m, 1H), 4.50 (s, 1H).

Example 109

2-Chloro-isonicotinic acid hydrazide

HOBt (823 mg, 6.09 mmol), and EDCI (1.2 g, 6.09 mmol) were added to a suspension of 2-chloro-isonicotinic acid (800 mg, 5.08 mmol) in acetonitrile (10.3 ml) at room temperature. After two h a solution of hydrazine monohydrate (0.493 ml, 10.2 mmol) in acetonitrile (5.0 ml) was added drop-wise at 0°C. After 30 min, the solvent was removed using a roto-evaporator and the residue was diluted with ethyl acetate, quenched with water, dried over sodium sulfate, filtered and concentrated to afford 2-chloro-isonicotinic acid hydrazide (493 mg, 57%, yellow solid). 1H NMR (DMSO) d (ppm): 10.21 (bs, 1H), 8.55 (d, 1H), 7.82 (s, 1H), 7.75 (d, 1H), 4.69 (bs, 2H).

The following compounds were prepared analogously to example 109:

Example No.	Name
110	2-Fluoro-5-methyl-benzoic acid hydrazide

111	Pyrimidine-4-carboxylic acid hydrazide

The following compounds were prepared analogously to Example 6:

Example No.	Name
112	3-Fluoro-N-hydroxy-benzamidine
113	N-Hydroxy-thiophene-3-carboxamidine
114	2-Chloro-N-hydroxy-propionamidine
115	3,N-Dihydroxy-benzamidine
116	N-Hydroxy-2-methyl-benzamidine
117	N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine
118	3-Chloro-N-hydroxy-benzamidine
119	N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine
120	2,5-Difluoro-N-hydroxy-benzamidine

The following compounds were prepared analogously to Example 31:

Example No.	Name
121	4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol
122	4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
123	4-(3-Methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
124	4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
125	4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
126	5-Thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazole-3-thiol
127	4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
128	4-Furan-2-ylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
129	4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
130	4-Ethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol
131	4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
132	4-Furan-2-ylmethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol
133	4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazole-3-thiol

134	4-Ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol
135	4-Ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol
136	5-(2-Fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol
137	4-Ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol
138	4-Ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol
139	5-(2-Chloro-6-methyl-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
140	5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
141	4-Ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol
142	4-Ethyl-5-(tetrahydro-furan-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
143	4-Ethyl-5-thioxo-4,5-dihydro-1H-[1,2,4]triazole-3-carboxylic acid methyl ester

The following compounds were prepared analogously to Example 36:

Example No.	Name
144	5-(2-Chloro-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
145	5-(2-Chloro-6-methoxy-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
146	4-Ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol
147	4-Propyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
148	4-Ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazole-3-thiol
149	4-Ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol
150	3-(5-Mercapto-4-methyl-4H-[1,2,4]triazol-3-yl)-benzonitrile
151	5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
152	5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
153	5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
154	5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
155	5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
156	5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazole-3-thiol
157	5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
158	5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
159	4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole-3-thiol

160	5-(3,5-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
161	5-(2,6-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
162	5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
163	5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazole-3-thiol
164	4-Ethyl-5-pyrimidin-5-yl-2,4-dihydro-[1,2,4]triazole-3-thione
165	4-Ethyl-5-furan-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione
166	4-(Tetrahydrofuran-2-ylmethyl)-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
167	5-Cyclopentyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione
168	4-Ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-2,4-dihydro-[1,2,4]triazole-3-thione

Example 169

5-(3,5-Dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol

3,5-Dichloro-benzoic acid (382 mg, 2 mmol) was mixed with triethylamine (606 mg, 3 mmol) in THF (6 ml) at 10 °C. Then isobutyl chloroformate (300 mg, 2.2 mmol) was added dropwise and stirred for 45 min. To the reaction mixture, 4-methyl-3-thiosemicarbazide (238.4 mg, 2 mmol) was added. After being stirred at room temperature for 10 min, the reaction mixture was heated to 70 °C overnight. Standard work-up. The product was purified by column chromatography with 25~30 % ethyl acetate in hexanes to give 46.4 mg (8.5 %) of 5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol.

The following compounds were prepared analogously to Example 169:

Example No.	Name
170	5-(3-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
171	5-(4-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
172	4-Ethyl- 5-(3-nitrophenyl)-4H-[1,2,4]triazole-3-thiol
173	5-(2,5-Difluorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
174	5-(3-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
175	5-(4-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol

Example 176

4-Ethyl-5-methoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione

Step 1: N-Ethyl-2-(methoxyacetyl)hydrazinecarbothioamide: Methoxyacetic acid (360 mg, 3.99 mmol), 4-ethyl-3- thiosemicarbazide (581 mg, 4.87 mmol), diisopropylcarbodiimide (615 mg, 4.87 mmol) and hydroxybenzotriazole (69.6 mg, 0.51 mmol) were mixed in dimethylformamide (10 ml) and stirred under argon at ambient temperatures for 19 h. After evaporation to dryness the crude was used directly in the next step. MS (ESI) m/z 192 (M+1). Step 2: 4-Ethyl-5-methoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione: N-Ethyl-2-(methoxyacetyl)hydrazinecarbothioamide (760 mg crude, 4 mmol) and sodium bicarbonate (560 mg, 6.6 mmol) were suspended in water (15 ml) and refluxed for 5 h. After cooling and filtration the filtrate was acidified with concentrated hydrochloric acid, followed by extraction with ethyl acetate. After evaporation to dryness the crude was recrystallized in ethyl acetate/heptane. Filtration and recrystallization of the mother liquor gave a combined yield of 325 mg (47%) of the title compound. 1H NMR ($CDCl_3$), δ (ppm): 4.47 (s, 2H), 4.13 (q, 2H), 3.37 (s, 3H), 1.38 (t, 3H).

The following compounds were prepared analogously to Example 176:

Example No.	Name
177	4-Methyl-5-pyridin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
178	4-Allyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
179	4-Ethyl-5-(4-methoxy-phenoxymethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
180	4-Ethyl-5-phenoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione
181	4-Ethyl-5-hydroxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione
182	4-Ethyl-5-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
183	4-Ethyl-5-methylsulfanylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione
184	5-Ethoxymethyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione
185	5-Furan-3-yl-4-methyl-2,4-dihydro-[1,2,4]triazole-3-thione
186	4-Methyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
187	4-Ethyl-5-pyridazin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
188	4-Ethyl-5-pyridin-4-ylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione
189	4-Ethyl-5-(6-hydroxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

190	4-Ethyl-5-(4-hydroxy-phenyl)-2,4-dihydro-[1,2,4]triazole-3-thione
191	4-Ethyl-5-p-tolyloxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione
192	4-Ethyl-5-(6-methoxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
193	4-Ethyl-5-(2-methoxy-pyridin-4-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
194	4-Ethyl-5-pyrimidin-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
195	4-Ethyl-5-(5-methoxy-pyrimidin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

Example 196

4-Furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol

A solution of formic acid hydrazide (439 mg, 7.809 mmol) in pyridine (20 ml) was added to a solution of 2-isothiocyanatomethyl-furan (1 g, 7.185 mmol) in pyridine (20ml). Reaction took place at room temperature overnight, and ethanol (20 ml) was added directly to the reaction and placed in 80C bath overnight. Solvent was evaporated and the title compound (1.09 g, 83%) was obtained from purification by SPE chromatography on silica gel with 500 ml 20%, 250 ml 25%, 250 ml 30%, 250 ml 35%, 250 ml 40%, and 250 ml 50% ethyl acetate in hexanes. 1H NMR (CD3OD), δ (ppm): 14.0 (bs, 1H), 8.19 (s, 1H), 7.52 (q, 1H), 6.52 (m, 1H), 6.42 (m, 1H), 4.90 (s, 2H).

The following compounds were prepared analogously to Example 196:

Example No.	Name
197	4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
198	4-Cyclopropylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol

Example 199

4-Cyclopropyl-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione

To a slurry of thiophene-2-carboxylic acid hydrazide (866 mg, 6.09 mmol) in iPrOH (25 ml) was added isothiocyanato-cyclopropane (602 mg, 6.08 mmol). The mixture was stirred at 70 °C for 72 h and then cooled to room temperature. The white precipitate was filtered off and suspended in a MeOH:H_2O (9:1, 40 ml) together with aq. NaOH (2%, 5 ml). The reaction mixture was stirred at 70 °C overnight and then cooled to room temperature. The pH was adjusted to around 4 with aq. HCl (1N). The formed white precipitate was filtered off, washed with water and dried under vacuum (829 mg, 61%). 1H NMR (CD3OD), δ

(ppm): 7.67 (dd, 1H), 7.63 (dd, 1H), 7.17 (dd, 1H), 3.15 (m, 1H), 1.14 (m, 2H), 0.86 (m, 2H).

The following compounds were prepared analogously to Example 199:

Example No.	Name
200	5-Furan-2-yl-4-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
201	4-Cyclopropyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
202	(3-Thiophen-2-yl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-acetic acid methyl ester
203	4-Cyclopropylmethyl-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
204	4-(2-Methoxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
205	Thiophen-2-yl-4-(2,2,2-trifluoroethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
206	4-Cyclopropyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
207	4-Cyclopropyl-5-pyridin-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione

Example 208

4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazole-3-thiol

To a solution of 4-ethyl-3-thiosemicarbazide(2.38 g, 20 mmol) and triethylamine (6.06 g, 60 mmol) in THF (30 ml), trifluoroacetic anhydride (5.04 g, 24 mmol) was added. The reaction mixture was stirred at room temperature for an h and and heated at 60 °C overnight. Standard work-up, the product was triturated with hexanes to give 564g of as 4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole-3-thiol pale-brown solid. 1H-NMR(CDCl3) d(ppm): 12.64 (w, 1H), 4.22 (q, 2H) and 1.44 (t, 3H).

Example 209

4-Ethyl-3-methanesulfonyl-5-thiophen-2-yl-4H-[1,2,4]triazole

The title compound was synthesized according to the method described in Åkerblom et al. J. Med. Chem. 16, 312 (1973). 4-Ethyl-3-methylsulfanyl-5-thiophen-2-yl-4H-[1,2,4]triazole (1.14 g, 5.06 mmol) was dissolved in glacial acetic acid (20 ml) followed by the addition of 30% hydrogen peroxide (5 ml). After stirring at ambient temperatures for 16 h additional 30% hydrogen peroxide (5 ml) was added. The mixture was stirred for 3 h at ambient temperature, then heated to 100 °C for 2.5 h. After cooling in an ice/water bath

the reaction was neutralized with sodium hydroxide and extracted twice with dichloromethane. The organic layers were combined, evaporated to dryness and dried in vacuo yielding the title compound (0.78 g, 60%). 1H NMR (CDCl3), δ (ppm): 7.60 (d, 1H), 7.56 (d, 1H), 7.22 (m, 1H), 4.51 (q, 2H), 3.58 (s, 3H), 1.55 (t, 3H).

The following compound was prepared analogously to Example 209:

Example No.	Name
210	4-(5-Methanesulfonyl-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine

Example 211

4-(2-Hydroxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione

To a slurry of LAH (38.1 mg, 1.00 mmol) in anhydrous THF (8 ml) was drop wise added (3-thiophen-2-yl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-acetic acid (101 mg, 0.42 mmol) in anhydrous THF (4 ml). The mixture was reacted for 2 h and then quenched with saturated aq. Na_2SO_4 (10 ml). THF was removed under reduced pressure and the residue was made acidic with aq. HCl (3N) and partitioned between EtOAc and water. The aqueous layer was extracted with EtOAc (3 x 20 ml). The combined organic layers were washed with brine (15 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was used without purification in the next step.1H NMR (DMSO-d6), δ (ppm): 13.94 (s, 1H), 7.86 (d, 1H); 7.81 (d, 1H), 7.24 (dd, 1H), 5.09 (t, 1H), 4.16 (t, 2H), 3.76 (app. q, 2H).

Example 212

4-(4,5-Dimethyl-4H-[1,2,4]triazol-3-yl)-pyridine

860 µl (10 mmol) oxalyl chloride was slowly added to a solution of 731 mg (10 mmol) N-methyl-acetamide and 2.33 ml (20 mmol) 2,6-lutidine in 20 ml CH_2Cl_2 at 0°C. After 15 min 1.37 g (10 mmol) isonicotinic acid hydrazide was added in one portion. The resulting mixture was stirred at room temperature for 1h and the neutralized with $NaHCO_3$(sat). The phases were separated and the water phase was extracted with CH_2Cl_2. The combined organic phases were dried and concentrated. The residue was dissolve in 20 ml acetic acid and heated at 120°C for 2h. After cooling the solvent was removed. Flashchromatography

(CH2Cl2/MeOH 10:1) afforded 765 mg (44%) of a grey/white solid. 1H NMR (CDCl3), d (ppm): 2.52 (s, 3 H) 3.66 (s, 3 H) 7.58 (d, 2 H) 8.76 (d, 2 H).

Example 213

Methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine

A mixture of 1000 mg (4.35 mmol) N-amino-N',N''-dimethyl-guanidine hydriodide (Henry; Smith; J.Amer.Chem.Soc.; 73; 1951; 1858) and 774 mg (4.35 mmol) isonicotinoyl chloride hydrochloride in 3ml of pyridine was heated with microwaves for 5 min at 160°C. K_2CO_3(sat) was added and the mixture was extracted 4 times with $CHCl_3$. The organic phase was dried and concentrated. Recrystallization from ethanol, water and EtOAc gave 216 mg (26%) of a yellow white solid. 1H NMR (DMSO), d (ppm): 2.85 (d, 3 H) 3.45 (s, 3 H) 6.25 (d, 1 H) 7.65 (m, 2 H) 8.67 (m, 2 H).

Example 214

3-Pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

A solution of 750 mg (3.1 mmol) (1,4,5,6-tetrahydro-pyrimidin-2-yl)-hydrazine hydroiodide (ref. Krezel, Izabella; Pharmazie; EN; 49; 1; 1994; 27-31) and 552 mg (3.1 mmol) isonicotinoyl chloride hydrochloride in 3 ml pyridine was heated at 120 °C over night. The reaction mixture was cooled and diluted with K_2CO_3(sat) and extracted with 3x10 ml chloroform. The combined organic extracts were dried and concentrated. . Flashchromatography (CH_2Cl_2/MeOH 10:1) afforded 83 mg (18%) of a white solid. 1H NMR ($CDCl_3$), d (ppm): 1.91 (m, 2 H) 3.24 (m, 2 H) 4.13 (m, 2 H) 7.67 (m, 2 H) 8.65 (m, 2 H).

The following compound was prepared analogously to Example 214:

Example No.	Name
215	3-Furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

Example 216

4-Ethyl-5-(6-methoxy-pyridazin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

Step 1: 6-Chloro-pyridazine-3-carboxylic acid: Potassium dichromate (3.3 g, 11.2 mmol) was added in portions to a solution of 3-Chloro-6-methyl-pyridazine (1.2 g, 9.3 mmol) in H_2SO_4 (10 ml). After addition the mixture is stirred at 50 °C on. The reaction was pored on ice and the mixture was extracted three times with diethyl ether. The combined organic phases were dried and concentrated to give the title compound (840 mg, 57%). LC-MS (M++1): 159 and 161 (3:1). Step 2: 6-Chloro-pyridazine-3-carboxylic acid methyl ester: A solution of 6-chloro-pyridazine-3-carboxylic acid (700 mg, 4.53mmol) in thionyl chloride (15 ml) was refluxed for 3 h. The reaction was cooled to ambient temperature and evaporated to dryness. Sodium methoxide (244 mg, 4.53 mmol) in MeOH (20 ml) was added to the residue and the solution was stirred on at room temperature (rt). H_2O was added and the mixture was extracted three times with DCM. The combined organic phases were dried and concentrated. Flashchromatography (SiO_2, Heptane/EtOAc 1:1) afforded 560 mg (72%) of the title compound.1H NMR ($CDCl_3$), δ (ppm): 4.09 (s, 3 H), 7.69 (d, 1 H), 8.18 (d, 1 H).LC-MS (M++1): 173 and 175 (3:1). Step 3: 6-Methoxy-pyridazine-3-carboxylic acid methyl ester: A solution of 6-chloro-pyridazine-3-carboxylic acid methyl ester in NaOMe in MeOH (1M, 10ml) was refluxed on. H_2O was added and the mixture was extracted three times with DCM to give organic phase I. The combined organic phases I were dried and concentrated to give the title compound (40 mg, 10%). The water phase was acidified with concentrated hydrochloric acid and extracted three times with DCM to give organic phase II. The combined organic phases II were dried and concentrated to give 6-methoxy-pyridazine-3-carboxylic acid (LC-MS (M++1): 155) (230 mg, 65%). A solution of 6-methoxy-pyridazine-3-carboxylic acid in thionyl chloride (6 ml) was refluxed for 3 h. The reaction was cooled to ambient temperature and evaporated to dryness. MeOH (10 ml) was added to the residue and the solution was stirred on at rt. Saturated $NaHCO_3$ (aq) was added and the mixture was extracted three times with DCM. The combined organic phases were dried and concentrated to give the title compound (253 mg, 100%).LC-MS (M++1): 169. Step 4: 4-Ethyl-5-(6-methoxy-pyridazin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione: NaOMe (86 mg, 1.6 mmol) was added to a solution of 6-methoxy-pyridazine-3-carboxylic acid methyl ester (210 mg, 1.25 mmol) and 4-ethyl-3-thiosemicarbazide (190 mg, 1.6 mmol) in MeOH (6 ml) and the mixture was heated to 70°C at 72 h. The reaction was cooled to ambient temperature and evaporated to dryness. H_2O (10 ml) was added to the

residue and the mixture was acidified with concentrated hydrochloric acid and the title compound 35 mg (12%) was collected by filtration. LC-MS (M++1): 238.

Example 217

4-Ethyl-5-(5-methoxy-pyridin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

Step 1: 5-Methoxy-pyridine-2-carboxylic acid methyl ester: 5-Methoxy-2-methyl-pyridine (700 mg, 5.69 mmol) was dissolved in H_2O (20 ml) and heated to 80 °C. $KMnO_4$ (4 g, 25.3 mmol) was added in portion to the solution over 1 h. After stirring at 80 °C for 5 h the mixture was filtrated and the filtrate was washed with H_2O (60 °C). The combined water phase was concentrated. DMF (20 ml), K_2CO_3 (785 mg, 5.7 mmol) followed by MeI (540 ml, 8.6 mmol) was added to the remaining residue and the mixture was heated to 80 °C on. The reaction was cooled to ambient temperature and H_2O was added and the mixture was extracted three times with toluene. The combined organic phases were dried and concentrated. Flashchromatography (SiO_2, Heptane/EtOAc 1:1) afforded 210 mg (22%) of the title compound.1H NMR ($CDCl_3$):d ppm 3.93 (s, 3 H) 4.00 (s, 3 H) 7.23 (m, 1 H) 8.13 (d, 1 H) 8.40 (d, 1 H). Step 2: 4-Ethyl-5-(5-methoxy-pyridin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione: NaOMe (4 ml, 4.0 mmol, 1M) was added to a solution of 5-Methoxy-pyridine-2-carboxylic acid methyl ester (200 mg, 1.2 mmol), 4-ethyl-3-thiosemicarbazide (145 mg, 1.2 mmol) in MeOH (10 ml) and the mixture was heated to 70°C on. The reaction was cooled to ambient temperature and evaporated to dryness. H_2O (10 ml) was added to the residue and the mixture was acidified with concentrated hydrochloric acid and the title compound 50 mg (18%) was collected by filtration. LC-MS (M++1): 237.

The following compounds were prepared analogously to example 10:

Example No.	Name
218	5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole
219	5-Chloromethyl-3-(3-fluoro-phenyl)-[1,2,4]oxadiazole
220	5-Chloromethyl-3-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole
221	5-Chloromethyl-3-thiophen-2-yl-[1,2,4]oxadiazole

222	5-Chloromethyl-3-thiophen-3-yl-[1,2,4]oxadiazole
223	3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-phenol
224	5-Chloromethyl-3-o-tolyl-[1,2,4]oxadiazole
225	5-Chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole
226	5-Chloromethyl-3-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole

The following compounds were prepared analogously to example 16:

Example No.	Name
227	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile
228	2-Chloro-4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-pyridine
229	3-Chloromethyl-5-(2,5-dimethyl-phenyl)-[1,2,4]oxadiazole
230	3-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole
231	3-Chloromethyl-5-(2,5-dichloro-phenyl)-[1,2,4]oxadiazole
232	3-Chloromethyl-5-(2-fluoro-5-bromo-phenyl)-[1,2,4]oxadiazole
233	3-Chloromethyl-5-(3-methyl-phenyl)-[1,2,4]oxadiazole
234	3-Chloromethyl-5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole
235	3-Chloromethyl-5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazole
236	3-Chloromethyl-5-(3-cyclopropyl-phenyl)-[1,2,4]oxadiazole
237	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-carbamic acid tert-butyl ester
238	1-[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-ethanone
239	5-(5-Chloro-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole
240	2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-phenol

Example 241

3-Chloromethyl-5-(2-chloro-5-methyl-phenyl)-[1,2,4]oxadiazole

2-Chloro-5-methyl-benzoic acid (1g, 5.8 mmol) was treated with 5 ml thionyl chloride at reflux for two h. Excess thionyl chloride was removed under reduced pressure. The residue was added to a suspension of 2-chloro-N-hydroxy-acetamidine (638 mg, 5.8 mmol) in dichloromethane (10 ml) at room temperature. After stirring for 30 min, triethylamine

(2.04 ml, 14.6 mmol) was added and stirred for an additional h. The reaction mixture was diluted with ethyl acetate, washed with water and brine, dried over anhydrous sodium sulfate, filtered and concentrated. Flash column chromatography using 10 – 20% ethyl acetate in hexanes afforded 460 mg of the acyclic ester intermediate. DMF was added to this intermediate and then heated at 135°C for 4 h to effect cyclization to oxadiazole. After cooling the reaction mixture was washed with water (3 times) and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. Purification by flash column chromatography on silica gel using 5% ethyl acetate in hexanes afforded the title compound 160 mg (12 % over 2 steps) as a white solid. m/z 244 (GCMS).

The following compounds were prepared analogously to Example 241:

Example No.	Name
242	3-Chloromethyl-5-(2,5-dichloro-thiophen-3-yl)-[1,2,4]oxadiazole
243	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile
244	3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole
245	3-Chloromethyl-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole
246	3-Chloromethyl-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole
247	5-(5-Bromo-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole
248	3-Chloromethyl-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole
249	5-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-thiophene-3-carbonitrile
250	2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-benzonitrile
251	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-fluoro-benzonitrile
252	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-fluoro-benzonitrile

253	4-Chloro-2-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenol
254	3-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole
255	3-(1-Chloro-ethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole
256	3-(1-Chloro-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,2,4]oxadiazole

Example 257

[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-methanol

3-Hydroxymethylbenzoic acid, described in Reed, G. A.; Dimmel, D.R.; Malcolm, E. W. J. Org. Chem. 1993, 58 (23), 6372-6376, (175 mg, 1.15 mmol), 2-chloro-N-hydroxy-acetamidine (125 mg, 1.15 mmol) and HBTU was dissolved in anhydrous DMF (4 ml). Triethylamine (0.48 ml, 3.5 mmol) was added and the reaction was stirred at ambient temperature over night. The crude product was partitioned between dichloromethane and $NaHCO_3$ (aq), the organic phase was dried ($MgSO_4$) and the dichloromethane was removed in vacuo. The resulting DMF-solution was heated at 120 °C over night. The reaction mixture was concentrated in vacuo and the title compound (64 mg, 25%) was isolated by flash chromatography using 25-50% ethyl acetate in heptane. 1H NMR (CDCl3), δ (ppm): 8.15 (s, 1H), 8.06 (d, 1H), 7.62 (d, 1H), 7.53 (t, 1H); 4.80 (d, 2H), 4.66 (s, 1H); 1.99 (br. t, 1H).

The following compounds were prepared analogously to Example 257:

Example No.	Name
258	3-Chloromethyl-5-[1-(toluene-4-sulfonyl)-1H-pyr rol-3-yl]-[1,2,4]oxadiazole
259	3-Chloromethyl-5-furan-3-yl-[1,2,4]oxadiazole
260	3-Chloromethyl-5-(5-chloro-thiophen-2-yl)-[1,2,4]oxadiazole

Example 261

1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethanol

Step 1: 1-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-1H-benzotriazole: 2-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole (109 mg, 0.45 mmol), hydroxybenzotriazole (76.4 mg, 0.56 mmol) and potassium iodide (23.0 mg, 0.14 mmol)

were dissolved in DMF (2.5 ml), followed by the addition of potassium carbonate (74.0 mg, 0.53 mmol). After stirring under argon at ambient temperatures for 24 h the reaction mixture was diluted with ethyl acetate and washed with 2N ammonium chloride solution. After reextraction of the aqueous layer with ethyl acetate, the combined organic layers were washed with brine and evaporated to dryness. Column chromatography over 12 g silica using heptane / ethyl acetate = 4/1 gave after drying in vacuo the title compound (129 mg, 84%). 1H NMR ($CDCl_3$), δ (ppm): 7.94 (d, 1 H), 7.82 (m, 1 H), 7.76 (m, 1 H), 7.46 (m, 1 H), 7.39-7.27 (m, 4 H), 5.98 (q, 1 H), 2.04 (d, 3 H). Step 2: 1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethanol: 1-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-1H-benzotriazole (58.4 mg, 0.17 mmol) was dissolved under argon in dry THF (3 ml). To this mixture a 0.1 molar solution of samarium diiodide in THF (5 ml, 0.5 mmol) was slowly added over 20 min. After stirring for 80 min additional samarium diioide solution (4 ml, 0.4 mmol) was added during 5 min. The reaction mixture was quenched after further 15 min of stirring with aqueous $Na_2S_2O_3$, diluted with diethyl ether and washed with 1 molare aqueous hydrochloric acid, dried over sodium sulfate and evaporated to dryness. After drying in vacuo crude title compound was obtained (36.0 mg, 92%) which was used in the next step without further purification.1H NMR ($CDCl_3$), δ (ppm): 7.98-7.75 (m, 2 H), 7.50-7.38 (m, 2 H), 5.25 (q, 1 H), 1.74 (d, 3 H).

The following compounds were prepared analogously to Example 261:

Example No.	Name
262	[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol

Example 263

1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethanol

To a solution of 3.19 g (30.6 mmol) 2,N-dihydroxy-propionamidine in 25 ml pyridine was added 4.3 ml (33.7 mmol) 3-chloro-benzoyl chloride at 0°C. Cooling was removed and the mixture was stirred at room temperature for 25 min and at reflux for 25 min. After cooling the mixture was poured into water and extracted twice with CH_2Cl_2. The organic phase was dried and concentrated. Recrystallization from heptane/EtOAc afforded 4.12 g (60%) of a white solid. 1H NMR ($CDCl_3$), d (ppm): 1.68 (d, 3 H) 2.67 (m, 1 H) 5.09 (m, 1 H) 7.46 (t, 1 H) 7.56 (d, 1 H) 8.01 (d, 1 H) 8.13 (s, 1 H).

Example 264

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol

Step 1: N-{4-[(Z)-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methylene}(oxido)amino]phenyl}-N,N-dimethylamine: The title compound was synthesized according to the method described in Palazzo et.al. J. Heterocycl. Chem. (1979) 16:1469. 1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-pyridinium chloride (1.81 g, 5.87 mmol) was dissolved in water (20 ml). To this solution, 4-nitroso-N,N-dimethylanilin (0.88 g, 5.86 mmol) dissolved in ethanol (50 ml) was added, followed by slow addition of 1 molar aq. sodium hydroxide (5.9 ml, 5.9 mmol) over a 3 min period. After 1 h the formed precipitate was filtered, washed with water and air-dried to give the title compound (2.08 g, wet) which was used immediately in the next step MS (ESI) m/z 344 (M+1). Step 2: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanediol: N-{4-[(Z)-{[5-(3-Chlorophenyl)-1,2,4-oxadiazol-3-yl]methylene}(oxido)amino]phenyl}-N,N-dimethylamine (2.08 g wet) was suspended in diethyl ether (30 ml), followed by the addition of 1 molar aqueous hydrochloric acid. The mixture was stirred vigorously for 20 min, transferred to a separation funnel and diluted with diethyl ether and 1 molar aqueous hydrochloric acid. After extraction, the aqueous layer was extracted two more times with diethyl ether. Combining the organic layers, drying over magnesium sulfate, followed by evaporation to dryness and drying in vacuo gave the title compound as crude (0.56 g, 42% from 1-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-pyridinium chloride). MS (ESI) m/z 227 (M+1). Step 3: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol: Step 3: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol: 1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-pyridinium chloride (99.3 mg, 0.44 mmol) was diasolved in methanol (4 ml) followed by the addition of sodium borohydride (32 mg, 0.84 mmol). More sodium borohydride was added after 2 h and the reaction was allowed to run over night. The reaction mixture was diluted with dichloromethane and aq. ammonium chloride and stirred vigorously. After separation of the layers and washing of the organic layer with brine, followed by evaporation to dryness, crude product was obtained. This was purified by flash chromatography using heptane/ethyl acetate which gave the title compound (32.0 mg, 32%). 1H NMR ($CDCl_3$), δ (ppm): 8.11 (s, 1H), 8.00 (apparent d, 1H), 7.56 (apparent d, 1H), 7.46 (apparent t, 1H), 4.87 (d, 2H), 2.91 (t, 1H).

Example 265

2-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole

2-Fluoro-5-methyl-benzoic acid hydrazide (320 mg, 1.9 mmol) and 2-chloro-1,1,1-triethoxy-ethane (1.9 ml) were heated in a sealed vial at 120°C for 30 min. The reaction mixture was place directly onto a flash column (silica gel) and purified by using 0 - 5% ethyl acetate in hexanes to afford 2-chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole (284.5 mg, 66%). 1H NMR (CDCl3) d (ppm): 7.89 (q, 1H), 7.36 (m, 1H), 7.16 (t, 1H), 4.81 (s, 2H), 2.43 (s, 3H).

The following compounds were prepared analogously to Example 265:

Example No.	Name
266	2-Chloromethyl-5-(3-chloro-phenyl)-[1,3,4]oxadiazole
267	4-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine
268	2-Chloromethyl-5-m-tolyl-[1,3,4]oxadiazole
269	3-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-benzonitrile
270	2-Chloro-4-(5-chloromethyl-[1,3,4]oxadiazol-2-yl)-pyridine
271	2-(5-Chloro-2-fluoro-phenyl)-5-chloromethyl-[1,3,4]oxadiazole

Example 272

2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole

3-Chloro-benzoic acid hydrazide (170 mg, 1 mmol) and 2-bromo-1,1,1-triethoxypropane (1 ml) were heated in a sealed vial at 120°C for 10 min. The reaction mixture was place directly onto a flash column (silica gel) and purified using 0 – 50% dichloromethane in hexanes. The product was re-purified by flash column chromatography using a mixture of ethyl acetate:hexanes:dichloromethane (1:19:20) to afford 2-(1-bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole (93 mg, 32%, colorless oil). 1H NMR ($CDCl_3$) d (ppm): 8.09 (t, 1H), 7.99 (t, 1H), 7.55 (m, 3H), 5.30 (m, 1H), 2.21 (q, 3H).

The following compounds were prepared analogously to Example 272:

Example No.	Name
273	2-(1-Bromo-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,3,4]oxadiazole
274	4-[5-(1-Bromo-ethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine
275	2-(1-Bromo-ethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole
276	2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole

Example 277

3-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole

A solution of 396 mg (2.22 mmol) N-bromosuccinimid in 2 ml THF was added dropwise to a solution of 583 mg (2.22 mmol) triphenylphosphine in 2 ml THF at 0°C. After stirring for 20 min 416 mg (1.85 mmol) 1-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethanol in 2 ml THF was added. Stirring was continued overnight at room temperature before the solvent was removed under reduced pressure. Flash chromatography (heptane/EtOAc 6:1) afforded 168 mg (32%). 1H NMR ($CDCl_3$), d (ppm): 2.12 (d, 3 H) 5.21 (q, 1 H) 7.47 (t, 1 H) 7.57 (m, 1 H) 8.03 (d, 1 H) 8.15 (s, 1 H).

Example 278

1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol

Step 1 4-(3-Chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester: Sodium hydride (60% oil dispersion, 1.24 g, 31.1 mmol) was added in portions to a solution of 3-chloroacetophenone (4.0 g, 25.9 mmol) and diethyl oxalate (4.54 g, 31.1 mmol) in DMF (32 ml) at 0°C. The mixture stirred at room temperature for 1 h and was then heated at 80°C for a half an h. After cooling, the mixture was treated with 3N HCl and then diluted with ethyl acetate. The organic layer was washed with water (3X) and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. The resulting residue was then purified by flash column chromatography on silica using 0 – 10% ethyl acetate in hexanes to afford of 4-(3-chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester (4.43g, 67%, yellow solid). 1H NMR ($CDCl_3$) d (ppm): 15.12 (br s, 1H), 7.98 (s, 1H), 7.88 (d, 1H), 7.58

(d, 1H), 7.47 (t, 1H), 7.05 (s, 1H), 4.39 (m, 2H), 1.41 (m, 3H). Step 2: 5-(3-Chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester: A solution of 4-(3-chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester (3.0 g, 11.8 mmol) and hydroxylamine hydrochloride (2.46 g, 35.4 mmol) in methanol (60 ml) was heated at 80°C for 4 h. After cooling, the mixture was filtered and washed with cold methanol to afford 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (2.0 g, 71%, white solid). 1H NMR ($CDCl_3$) d (ppm): 7.82 (s, 1H), 7.72 (m, 1H), 7.47 (m, 2H), 4.03 (s, 3H). Mixture of both methyl and ethyl ester (mostly methyl). Step 3: 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanone: In a screw cap vial equipped with stir bar added methyl magnesium iodide (3M in diethyl ether) (0.79 ml, 2.38 mmol), toluene (1 ml), tetrahydrofuran (0.39 ml, 4.77 mmol) and triethylamine (1 ml, 7.15 mmol). Cooled the solution down to 0°C and to it added solution of 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (300 mg, 1.19 mmol) in toluene (5 ml). Left the resulting mixture stirring at 0°C for 5 h. Reaction mixture was quenched with 1N hydrochloric acid (aqueous, 6.5 ml, 6.5 mmol), diluted with toluene (35 ml), sequentially washed with water (50 ml), saturated sodium bicarbonate (aqueous, 30 ml), water (50 ml) and brine (30 ml). The organic phase was concentrated, in-vacuo. The isolated residue was dissolved in methanol (8 ml) and 20% potassium hydroxide (aqueous, 1 ml). The mixture was stirred at 45°C for 30 min. At this point the mixture was concentrated, in-vacuo. The isolated residue was dissolved in toluene (60 ml), sequentially washed with water (50 ml), saturated sodium bicarbonate (aqueous, 50 ml) and water (50 ml). The organic phase was concentrated, in-vacuo. The crude residue was purified on silica gel using 2% ethyl acetate in hexanes to isolate the desired compound as a white solid (156 mg, 60%). 1H-NMR ($CDCl_3$), d (ppm): 7.77 (m, 1H), 7.66 (m, 1H), 7.42 (m, 2H), 6.90 (s, 1H), 2.69 (s, 3H). Step 4: 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol: In a screw cap vial equipped with stir bar added 1-[5-(3-chloro-phenyl)-isoxazol-3-yl]-ethanone (100 mg, 0.45 mmol), sodium borohydride (34 mg, 0.90 mmol) and methanol (3 ml). Left the resulting mixture stirring at room temperature for 3 h. Reaction was quenched with water (30 ml) and brine (30 ml), extracted with dichloromethane (3X30 ml). Combined organic phase was dried (sodium sulfate), filtered and concentrated, in-vacuo to isolate 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol as a white solid (110 mg). 1H-NMR (CDCl3), d (ppm): 7.69 (m, 1H), 7.59 (m, 1H), 7.37 (m, 2H), 6.59 (s, 1H), 5.07 (q, 1H), 3.45 (bs, 1H), 1.58 (d, 3H).

The following compound was prepared analogously to Example 278:

Example No.	Name
279	1-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethanol

The following compounds were prepared analogously to 5-(3-Chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (step 2 in the synthesis of Example 279):

Example No.	Name
280	5-(2-Fluoro-5-methyl-phenyl)-isoxazole-3-carboxylic acid methyl ester
281	5-Thiophen-3-yl-isoxazole-3-carboxylic acid methyl ester
282	5-Phenyl-isoxazole-3-carboxylic acid methyl ester
283	5-(3-Chloro-phenyl)-4-methyl-isoxazole-3-carboxylic acid ethyl ester
284	5-(5-Chloro-thiophen-3-yl)-isoxazole-3-carboxylic acid methyl ester

Example 285

[5-(3-Chloro-phenyl)-isoxazol-3-yl]-methanol

Lithium aluminum hydride (320 mg, 8.4 mmol) was slowly added to a solution of 5-(3-chloro-phenyl)-isoxazole-3-carcoxylic acid ethyl ester (2.0 g, 8.4) in THF (100 ml) at room temperature. After 1 h, the reaction mixture was quenched with water and then extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The resulting residue was then purified by flash column chromatography using 15-40% ethyl acetate in hexane to afford [5-(3-chloro-phenyl)-isoxazol-3-yl]-methanol (1.32g, 75%, yellow solid). 1H NMR ($CDCl_3$) d (ppm): 7.78 (s, 1H), 7.68 (m, 1H), 7.43 (m, 2H), 6.63 (s, 1H), 4.84 (d, 2H), 2.23 (t, 1H).

The following compounds were prepared analogously to Example 285:

Example No.	Name
286	[2-(3-Chloro-phenyl)-oxazol-4-yl]-methanol

287	[3-(3-Chloro-phenyl)-isoxazol-5-yl]-methanol
288	5-(Thiophen-3-yl-isoxazol-3-yl)methanol
289	[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-methanol
290	(5-Phenyl-isoxazol-3-yl)-methanol
291	[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-yl]-methanol
292	[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-yl)]-methanol

Example 293

Methanesulfonic acid 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethyl ester

In a screw cap vial equipped with stir bar was added 1-[5-(3-chloro-phenyl)-isoxazol-3-yl]-ethanol (110 mg, 0.49 mmol), dichloromethane (3 ml) and triethylamine (0.34 ml, 2.46 mmol). Cooled the mixture down to 0°C and to it added methane sulfonyl chloride (0.08 ml, 0.98 mmol). Left the reaction mixture stirring at room temperature for 30 min. Reaction was quenched with saturated sodium bicarbonate (aqueous, 40 ml) and extracted with dichloromethane (3X30 ml). Combined organic phase was washed with brine (40 ml), dried (sodium sulfate), filtered and concentrated, in-vacuo to isolate the desired compound as brown oil.

The following compounds were prepared analogously to Example 293:

Example No.	Name
294	Methanesulfonic acid 2-(3-chloro-phenyl)-oxazol-4-ylmethyl ester
295	Methanesulfonic acid 3-(3-chloro-phenyl)-isoazol-5-ylmethyl ester
296	Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester
297	Methanesulfonic acid -phenyl)-isoxazol-5-yl]-ethyl ester
298	Methanesulfonic acid 5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-ylmethyl ester
299	Methanesulfonic acid 5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester
300	Methanesulfonic acid 5-thiophen-3-yl-isoxazol-3-ylmethyl ester
301	Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester

302	Methanesulfonic acid 5-phenyl-isoxazol-3-ylmethyl ester
303	Methanesulfonic acid 5-(3-chloro-phenyl)-4-methyl-isoxazol-3-ylmethyl ester
304	Methanesulfonic acid 5-(5-chloro-thiophen-3-yl)-isoxazol-3-ylmethyl ester
305	Methanesulfonic acid 1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethyl ester
306	Methanesulfonic acid 1-[5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethyl ester

Example 307

Methanesulfonic acid 4-chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester

Sulfuryl chloride (1 ml) was added to methanesulfonic acid 5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester (200 mg, 0.70 mmol) and then stirred at 60°C overnight. The reaction mixture was diluted with dichloromethane, washed saturated sodium bicarbonate, dried over anhydrous sodium sulfate, filtered and concentrated to afford methanesulfonic acid 4-chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester (219 mg,, 97%, light brown solid). 1H NMR ($CDCl_3$) d (ppm): 8.07 (m, 1H), 7.92 (m, 1H), 7.50 (m, 2H), 5.38 (s, 2H), 3.16 (s, 3H).

Example 308

3-(3-Chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester

Step 1: 3-Chloro-N-hydroxy-benzamidine: A solution of 3-chlorobenzaldehyde (3.35 ml, 0.030 mmol) in ethanol (40 ml) was added to a solution of hydroxylamine hydrochloride (2.47 g, 0.036 mmol) and sodium hydroxide (1.42 g, 0.036) in water (20 ml) at room temperature and then heated at 90°C for 24 h. After cooling, the reaction mixture was concentrated, the residue diluted with water and then the precipitate was filtered and dried to afford 3-chloro-N-hydroxy-benzamidine (1.13 g, 93 %). 1H NMR ($CDCl_3$) d (ppm): 8.11 (s, 1H), 7.72 (s, 1H), 7.61 (m, 1H), 7.46 (m, 1H), 7.36 (m, 1H). Step 2: 3-Chloro-N-hydroxy-benzimidoyl chloride: N-chlorosuccinimide (858 mg, 6.4 mmol) was added to a solution of 3-chloro-N-hydroxy-benzamidine (1 g, 6.4 mmol) at room temperature and stirred for 1 h. The reaction mixture was diluted with diethyl ether and then washed with

water (3X), dried over anhydrous magnesium sulfate, filtered, and concentrated to afford the titled compound (1.13 g, 93 %). 1H NMR ($CDCl_3$) d (ppm): 8.03 (s, 1H), 7.87 (m, 1H), 7.76 (m, 1H), 7.43 (m,1H).: Step 3: 3-(3-Chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester: Triethyl amine (0.73 ml, 5.3 mmol) was added drop-wise to a solution of 3-chloro-N-hydroxy-benzimidoyl chloride (1.0 g, 5.3 mmol) and methyl propiolate (2.2 ml, 25.3 mmol) in an ice-bath. The reaction mixture was warmed to room temperature and left to stir overnight. After diluting the reaction with dichloromethane, the organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated. Purification by flash column chromatography eluted with 50% hexanes in ethyl acetate and then recrystallization with methanol afforded 3-(3-chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester (635 mg, 51%, white solid). 1H NMR ($CDCl_3$) d (ppm): 7.86 (m, 1H), 7.74 (m, 1H), 7.46 (2H), 7.2 (s, 1H), 4.05 (s, 3H).

Example 309

2-Bromomethyl-5-(3-chloro-phenyl)-oxazole

Step 1 5-(3-Chloro-phenyl)-2-methyl-oxazole: To a solution of Tl(OAc)3 (4.2 g, 11.1 mmol) in acetonitrile (80 ml), trifluoromethanesulfuric acid (5g, 33.3 mmol) was added dropwise at room temperature and stirred for 15 min. The reaction mixture was then heated to 80°C and 1-(3-chloro-phenyl)-ethanone (1.14 g, 7.4 mmol) in acetonitrile (40 ml) was added. After one h, the reaction was quenched with dichloromethane and saturated sodium bicarbonate. The organic layer was dried, purified by column chromatography with 5~19 % ethyl acetate in hexanes to give 1.2 (83.9 %) g of 5-(3-chloro-phenyl)-2-methyl-oxazole as yellow oil. 1H-NMR($CDCl_3$) d(ppm): 7.60 (s, 1H), 7.48 (d, 1H), 7.29 (m, 2H), 7.23 (s, 1H) and 2.34 (s, 3H). Step 2: 2-Bromomethyl-5-(3-chloro-phenyl)-oxazole: 5-(3-chloro-phenyl)-2-methyl-oxazole (580 mg, 3 mmol) was mixed with NBS (531 mg, 3 mmol) and BPOA (36.3 mg, 0.15 mmol) in CCl_4 at room temperature. The reaction mixture was heated at 75 °C for 2 h and then quenched with water and dichloromethane. The organic layer was dried, concentrated, purified by column chromatography with 2~5 % ethyl acetate in hexanes to give 562 mg (68.3 %) of 2-bromomethyl-5-(3-chloro-phenyl)-oxazole as yellow oil. 1H-NMR($CDCl_3$) d(ppm): 7.67 (s, 1H), 7.54 (d, 1H), 7.35(m, 3H) and 4.56 (s, 2H).

Example 310

2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester

To a mixture of 3-Chlorobenzoic acid (5.0 g, 31.9 mmol), serine methylester hydrochloride (6.1 g, 31.9 mmol) and HOBt (4.31 g, 31.9 mmol) in DMF (100 ml) was added N-methylmorpholine (NMM) (7.0 ml, 63.8 mmol) and EDCI (4.97 g, 31.9 mmol) at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 h. The mixture was diluted with ethyl acetate (300 ml) and then washed with water (3 x 250 ml) followed by brine. The organic extract was dried over Na_2SO_4 (anhydrous) and then concentrated in vacuo giving 2-(3-Chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g, 93%) of a pale yellow solid. 1H NMR ($CDCl_3$) d (ppm): 7.78 (s, 1 H), 7.66 (d, 1 H), 7.45, (dd, 1 H), 7.34 (t, 1 H), 7.25 (br, d, 1H), 4.82 (m, 1 H), 4.08 (m, 2 H), 3.79 (s, 3 H), 3.19 (br, t, 1H).

To a solution of 2-(3-chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g, 29.6 mmol) in CH_2Cl_2 at -20°C was added dropwise De-oxofluor (7.2 g, 32.6 mmol). After stirring at this temperature for 30 min, $BrCCl_3$ (3.6 g, 18.1 mmol) was added dropwise followed by DBU (2.79g, 18.1 mmol). The mixture was then stirred at 2-3°C for 8 h ad then quenched with saturated $NaHCO_3$ followed by extraction with ethyl acetate. The organic extract as then washed with brine and dried over Na_2SO_4 (anhydrous). Purification was performed by flash column chromatography on silica gel using ethyl acetate in hexanes as eluant to afford 2-(3-chloro-phenyl)-oxazole-4-carboxylic acid methyl ester (4.1g, 59%) as a yellow solid. 1H NMR ($CDCl_3$) d (ppm): 8.30 (s, 1 H), 8.12 (d, 1 H), 7.98 (dd, 1 H), 7.45 (m, 2 H), 3.96 (s, 3 H).

Example 311

2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester

To a mixture of 3-Chlorobenzoic acid (5.0 g, 31.9 mmol), serine methylester hydrochloride (6.1 g, 31.9 mmol) and HOBt (4.31 g, 31.9 mmol) in DMF (100 ml) was added N-methylmorpholine (NMM) (7.0 ml, 63.8 mmol) and EDCI (4.97 g, 31.9 mmol) at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 h. The mixture was diluted with ethyl acetate (300 ml) and then washed with water (3 x 250 ml) followed by brine. The organic extract was dried over Na_2SO_4 (anhydrous) and then concentrated in vacuo giving 2-(3-Chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g,

93%) of a pale yellow solid. 1H NMR ($CDCl_3$) d (ppm): 7.78 (s, 1 H), 7.66 (d, 1 H), 7.45, (dd, 1 H), 7.34 (t, 1 H), 7.25 (br, d, 1H), 4.82 (m, 1 H), 4.08 (m, 2 H), 3.79 (s, 3 H), 3.19 (br, t, 1H).

To a solution of 2-(3-chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g, 29.6 mmol) in CH_2Cl_2 at -20°C was added dropwise De-oxofluor (7.2 g, 32.6 mmol). After stirring at this temperature for 30 min, $BrCCl_3$ (3.6 g, 18.1 mmol) was added dropwise followed by DBU (2.79g, 18.1 mmol). The mixture was then stirred at 2-3°C for 8 h ad then quenched with saturated $NaHCO_3$ followed by extraction with ethyl acetate. The organic extract as then washed with brine and dried over Na_2SO_4 (anhydrous). Purification was performed by flash column chromatography on silica gel using ethyl acetate in hexanes as eluant to afford 2-(3-chloro-phenyl)-oxazole-4-carboxylic acid methyl ester (4.1g, 59%) as a yellow solid. 1H NMR ($CDCl_3$) d (ppm): 8.30 (s, 1 H), 8.12 (d, 1 H), 7.98 (dd, 1 H), 7.45 (m, 2 H), 3.96 (s, 3 H).

Example 312

1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethanol

Step 1: 5-(5-Chloro-2-fluoro-phenyl)-isoxazole-3-carbaldehyde: In a 50 ml round bottom flask equipped with stir bar and drying tube added 5-(5-chloro-2-fluoro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (0.78 g, 2.89 mmol) and dichloromethane (10 ml). Cooled the solution down to –78°C and to this stirred solution added diisobutylaluminum hydride (1M hexanes, 5.3 ml, 5.3 mmol). The resulting mixture was left stirring at –78°C for 3 h. Reaction was quenched using sodium sulfate decahydrate. The resulting mixture was stirred at 63°C for 15 min after which it was filtered through a celite pad. The filterate was concentrated in-vacuo to isolate an off-white solid, which was triturated with hexanes to isolate the title compound as a white solid (0.55g, 84%). 1H-NMR ($CDCl_3$), d (ppm): 10.2 (s, 1H), 7.99 (m, 1H), 7.44 (m, 1H), 7.20 (m, 1H), 7.10 (d, 1H). Step 2: 1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethanol: In a 50 ml round bottom flask equipped with stir bar added 5-(5-chloro-2-fluoro-phenyl)-isoxazole-3-carbaldehyde (0.55 g, 2.42 mmol) and tetrahydrofuran (6 ml). Cooled the mixture down to 0°C and to it added methyl magnesium iodide (3M in diethyl ether, 3.23 ml, 9.67 mmol). The resulting mixture was left stirring at 0°C for 3 h. Reaction mixture was quenched with hydrochloric acid (1N, aqueous, 10 ml), extracted with diethyl ether (3X50 ml). Combined organic phase was washed with water

(50 ml), brine (50 ml), dried (sodium sulfate), filtered and concentrated in-vacuo. The crude residue was purified on silica gel using 10% ethyl acetate in hexanes to isolate the desired compound as clear oil (179 mg, 31%).

Example 313

1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethanol

3-Chloro-benzohydroximoyl chloride (e.g. Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57(24), 6649-50) (2.84 g, 14.8 mmol) was suspended in benzene (50 ml) and cooled to 0°C. 3-Butyn-2-ol (2.10 g, 29.9 mmol) and triethylamine (1.89 ml, 26.7 mmol) were added. The mixture was heated to 60°C for 1.5 houes, cooled and diluted with benzene and 1N aqueous hydrochloric acid. After stirring, the separated benzene layer was evaporated to dryness and the crude purified via flash chromatography over silica using heptane/ethyl acetate = 5/1 giving after drying in vacuo the title compound (0.49 g, 15%). 1H NMR ($CDCl_3$), δ (ppm): 1.64 (d, 3 H), 5.07 (dq, 1 H), 6.50 (s, 1 H), 7.40 (m, 2 H), 7.68 (m, 1 H), 7.79 (m, 1 H)

Example 314

[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-methanol

Step 1: (5-Chloro-2-fluoro-phenylethynyl)-trimethyl-silane: In a 250 ml round bottom flask equipped with a stir bar and reflux condenser added 4-chloro-2-bromo-1-fluoro-benzene (5 g, 23.9 mmol), triphenylphosphine (250 mg, 0.10 mmol), (trimethylsilyl)acetylene (5.2 ml, 36.5 mmol)and triethylamine (60 ml). The reaction mixture was purged with argon, followed by addition of palladium (II) acetate (108 mg, 0.05 mmol). The resulting mixture was left stirring at reflux under argon, overnight. The reaction mixture was filtered through a pad of celite using ethyl acetate and the filterate was concentrated in-vacuo. The isolated residue was absorbed on silica gel and filtered using hexanes. The filterate was concentrated in-vacuo to isolate the title compound as brown oil (5.42 g). Step 2: 4-Chloro-2-ethynyl-1-fluoro-benzene: In a 250 ml round bottom flask equipped with stir bar added (5-chloro-2-fluoro-phenylethynyl)-trimethyl-silane (5.42 g, 23.9 mmol), potassium carbonate (16.5 g, 120 mmol) and methanol (60 ml). The reaction mixture was left stirring at room temperature for 1 h. Diluted the reaction mixture with hexanes (200 ml) and washed with water (250 ml). The aqueous phase was extracted

with hexanes (2X100 ml). Combined organic phase was washed with brine (200 ml), dried (sodium sulfate), filtered and concentrated in-vacuo to isolate the desired compound as brown oil (3.56 g). 1H-NMR ($CDCl_3$), d (ppm): 7.47 (dd, 1H), 7.30 (m, 1H), 7.05 (t, 1H), 3.36 (s, 1H). Step 3: Chloro-hydroxyimino-acetic acid ethyl ester: In 1 L round bottom flask equipped with stir bar added amino-acetic acid ethyl ester hydrochloride (20 g, 143 mmol) and water (30 ml). The solution was cooled down to 0°C followed by sequential addition of concentrated hydrochloric acid (11.8 ml, 143 mmol) and dropwise addition of sodium nitrite (9.89 g, 143 mmol) solution in water (15 ml). After 10 min added another equivalent each of concentrated hydrochloric acid and sodium nitrite solution in water. The reaction mixture was left stirring at 0°C for 1 h. Reaction mixture was extracted with ether (4X100 ml). Combined organic phase was dried (sodium sulfate), filtered and concentrated in-vacuo to isolate a lemon yellow solid. The solid was recrystallized from hexanes to isolate a white solid (11 g, 51%). 1H-NMR ($CDCl_3$), d (ppm): 9.98 (bs, 1H), 4.40 (q, 2H), 1.38 (t, 3H). Step 4: 5-(5-Chloro-2-fluoro-phenyl)-isoxazole-3-carboxylic acid ethyl ester: In a 250 ml round bottom flask equipped with stir bar added 4-chloro-2-ethynyl-1-fluoro-benzene (2 g, 12.9 mmol), chloro-hydroxyimino-acetic acid ethyl ester (3.92 g, 25.9 mmol), sodium bicarbonate (7.07 g, 84.1 mmol) and toluene (50 ml). Reaction mixture was left stirring at room temperature for 48 h, after which it was concentrated in-vacuo. Residue was taken up in ethyl acetate (200 ml), sequentially washed with water (150 ml), brine (150 ml), dried (sodium sulfate), filtered and concentrated in-vacuo. The crude residue was purified on silica gel using 3% acetone in hexanes to isolate the title compound as an off-white solid (1.56 g). 1H-NMR ($CDCl_3$), d (ppm): 8.00 (dd, 1H), 7.43 (m, 1H), 7.18 (m, 2H), 4.51 (q, 2H), 1.47 (t, 3H). Step 5: [5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-methanol: In a 50 ml round bottom flask equipped with stir bar and drying tube added 5-(5-chloro-2-fluoro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (0.78 g, 2.89 mmol) and tetrahydrofuran (10 ml). To this stirred solution added solution of lithium aluminum hydride (0.12 g, 2.89 mmol) in tetrahydrfuran (2 ml). The resulting mixture was left stirring at room temperature for 1 h. Reaction was quenched using sodium sulfate decahydrate. The resulting mixture was stirred at 63°C for 15 min after which it was filtered through a celite pad. The filterate was concentrated in-vacuo to isolate the title compound as yellow solid (0.65 g, 99%). 1H-NMR ($CDCl_3$), d (ppm): 7.73 (dd, 1H), 7.27 (m, 1H), 7.24 (t, 1H), 6.73 (d, 1H), 4.77 (s, 2H), 4.45 (bs, 1H).

Example 315

3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide

Step 1: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid: 3-Chloro-benzoic acid hydrazide (3.4 g, 20 mmol) and succinic anhydride (2. g, 20 mmol) was mixed in ethyl acetate (50 ml) at room temperature for 15 min. The reaction mixture was diluted with ether and the precipitate was filtered to give 5.1 g of 4-[N'-(3-chloro-benzoyl)-hydrazino]-4-oxo-butyric acid. 1H-NMR($CDCl_3$ + DMSO-d6) d(ppm): 10.01 (s, 1H), 9.53 (s, 1H), 7.68 (s, 1H), 7.55 (d, 1H), 7.21 (d, 1H), 7.12 (t, 1H) and 2.35 (m, 4H). This solid was mixed with conc. H_2SO_4 and stirred at room temperature for 45 min and the reaction mixture was carefully added to crashed ice (400g). The precipitate was filtered to give 4.07 g (80.6 %) of 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid as white solid. 1H-NMR(DMSO-d6) d(ppm): 12.4 (w, 1H), 7.96 (s, 1H), 7.91 (d, 1H), 7.71 (d, 1H), 7.63 (t, 1H), 3.15 (t, 2H) and 2.82 (t, 2H). Step 2: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid (2.52 g, 10 mmol) was mixed with iodomethane (5.68 g, 40 mmol) and K_2CO_3 (5.52 g, 40 mmol) in DMF (25 ml) at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water 3 times, dried with $MgSO_4$ and concentrated to give.2.57 g of 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid methyl ester. The methyl ester (2.54 g, 9.52 mmol) was mixed with 98% hydrazine hydrate (4.76 g, 95.2 mmol) in methanol (10 ml) for an h. The reaction mixture was concentrated, diluted with water, filtered to give 2.17 g (81.4 %) of 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide as white solid. 1H-NMR($CDCl_3$ + DMSO-d6) d(ppm): 8.75 (w, 1H), 7.91 (s, 1H), 7.82 (d, 1H), 7.42 (m, 2H), 3.45 (w, 2H), 3.19 (t, 2H) and 2.68 (t, 2H).

Example 316

3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide

Step 1: 2-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-malonic acid dimethyl ester: 2-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole (331 mg, 1.36 mmol) was mixed with dimethyl malonate (360 mg, 2/76 mmol) and DBU (207 mg, 1.36 mmol) in acetonitrile (3 ml) at 70 °C overnight. The reaction mixture was dilute with dichloromethane and washed with water. The organic layer was dried and concentrated.

The residue was purified with 5~20 % ethyl acetate in hexanes to give 357 mg (74.3 %) 2-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-malonic acid dimethyl ester as white solid. 1H-NMR($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.95 (d, 1H), 7.53 (d, 1H), 7.47 (t, 1H), 4.06 (d, 1H), 3.95 (m, 1H), 3.84 (s, 3H), 3.74 (s, 3H) and 1.51 (d, 3H). Step 2: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid methyl ester: 2-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-malonic acid dimethyl ester (352.8 mg, 1.0 mmol) was mixed with sodium chloride (76.3 mg, 1.3 mmol) and a drop of water in DMSO (1.5 ml) at 175 °C for an h. The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with water and concentrated. The residue was purified with column chromatography with 10~20 % ethyl acetate in hexanes to give 215 mg (76.8 %)3-[5-(3-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid methyl ester as clear oil. 1H-NMR($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.45 (t, 1H), 3.73 (s, 3H), 3.67 (m, 1H), 3.05 (dd, 1H), 2.73 (dd, 1H) and 1.50 (d, 3H). Step 3: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide (146 mg, %) was obtained from 3-[5-(3-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid methyl ester (215 mg, 0.766 mmol) reacted with hydrazine hydrate (0.74 ml) in methanol (3 ml) at room temperature for 2.5 h. 1H-NMR($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.46 (t, 1H), 7.23 (w, 1H), 3.93 (w, 2H), 3.71 (m, 1H), 2.90 (dd, 1H), 2.57 (dd, 1H) and 1.50 (d, 3H).

Example 317

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride

Step 1: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (1.6 g, 6.33 mmol) was reacted with $SOCl_2$ (10 ml) at room temperature overnight. The reaction mixture was concentrated by vacuum. The residue was mixed with THF (20 ml) and quenched with 28 % $NH_3.H_2O$ (5 ml) at 0 °C. After being stirred for 2 h, the reaction mixture was dilute with dichloromethane and washed with water and brine. The organic layer was dried, concentrate and triturated with hexanes to give 1.21 g (76 %) of 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide. 1H-NMR($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.32 (t, 2H) and 2.87 (t, 2H). Step 2: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-

yl]-propionitrile: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide (1.2 g, 4.77 mmol) was mixed with pyridine (0.829 g, 10.5 mmol) and trifluoroacetic anhydride (1.2 g, 5.72 mmol) in dichloromethane(25 ml) at room temperature for 2 h. The reaction mixture was diluted with dichloromethane and washed with water and brine. The organic layer was dried to give 1.1 g (98%) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionitrile as pale-brown oil. 1H-NMR($CDCl_3$) d(ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.35 (t, 2H) and 3.01 (t, 2H). Step 3: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionitrile (1.1 g, 4.71 mmol) was mixed with 24 % HCl in ethanol (8 ml) overnight. The precipitate was filtered and washed with ether to give 0.99 g (66 %) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride as white solid. 1H-NMR(DMSO-d6) d(ppm): 11.70 (w, 2H), 7.78 (m, 2H), 7.64 (m, 2H), 4.41 (q, 2H), 3.45 (t, 2H), 3.22 (t, 2H) and 1.28 (t, 3H).

Example 318

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide

Step 1: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid: 3-Chloro-N-hydroxy-benzamidine 4.52 g, 26.5 mmol) was heated with succinic anhydride (2.65 mg, 26.5 mmol) in DMF (5 ml) at 150°C for an h. The reaction mixture was cooled down and diluted with ethyl acetate. The organic solution was washed with water and brine, concentrated by vacuum. The residue was triturated with 20 % ethyl acetate in hexanes to give 4.0 g (60 %) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid as white solid.). 1H-NMR($CDCl_3$) d(ppm): 8.08 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.42 (t, 1H), 3.28 (t, 2H) and 3.04 (t, 2H). Step 2: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide: This acid was reacted with iodoethane (1.6g, 10.5 mmol) and K_2CO_3 (1.46 10.5 mmol) in DMF (5 ml) for 5 min to form 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid ethyl ester. The ethyl ester was then treated with 37% hydrazine (2ml) in ethanol (5 ml) at 80 °C for2 h to give 595 mg (65% in 3 steps) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide as off-white solid1H-NMR($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.43 (t, 1H), 7.00 (w, 1H), 3.95 (w, 2H), 3.34 (t, 2H) and 2.79 (t, 2H).

Example 319

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide

Step 1: (N-Hydroxycarbamimidoyl)-acetic acid ethyl ester: To a ethanol solution (40 ml) of cyano-acetic acid ethyl ester (9.9 g, 0.1 mol), the mixture solution of sodium hydroxide (4 g, 0.1 mol) in water (40 ml) and 5 M hydroxylamine hydrochloride (20 ml) was added and the reaction mixture was stirred at 50 °C overnight. After being concentrated, the reaction mixture was diluted with water and extrated with ethyl acetate. The organic layer was dried, concentrated again. The residue was purified by column chromatography with 30~70 % ethyl acetate in hexanes to give 3.32 g (22.7 %) of (N-Hydroxycarbamimidoyl)-acetic acid ethyl ester as white solid. 1H-NMR($CDCl_3$) d(ppm): 5.04 (ws, 2H), 4.20 (q, 2H), 3.19 (s, 2H) and 1.30 (t, 3H). Step 2: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid ethyl ester: To a dichloromethane solution (10 ml) of (N-hydroxycarbamimidoyl)-acetic acid ethyl ester (1.46 g, 10 mmol) and triethylamine, 3-chlorobenzoyl chloride (1.75 g, 10 mmol) was added slowly at 5 °C and the reaction mixture was stirred for 10 min. DMF (8 ml) was added to the reaction mixture was heated to 135 °C for 2 h. Standard work-up, the product was passed column with dichloromethane to give 1.2 g (45 %) of [5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid ethyl ester as pale-yellow oil. 1H-NMR($CDCl_3$) d(ppm): 8.168 (s, 1H), 8.04 (d, 1H), 7.59 (d, 1H), 7.49 (t, 1H), 4.26 (q, 2H), 3.91 (s, 2H) and 1.31 (t, 3H). Step 3: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide: 5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid ethyl ester (0.64 g, 2.4 mmol) was mixed with 37 % hydrazine (1.6 ml) in ethabol (10 ml) at 80 °C for 4 h. The reaction mixture was concentrated and diluted with water. The precipitate was filtered, washed with water to give 0.51 g (83.3 %) of [5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide.

Example 320

(R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide

Step 1: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid methyl ester: To a solution of (R)-2-methylsuccinic acid 4-methyl ester (2.2 g, 15 mmol) and triethylamine (4.54 g, 45 mmol) in THF (30 ml), isobutylchloroformate (2.16 g, 15.8 mmol) was added dropwise at 0 °C. After being stirred for 30 min, the 3-chloro-N-hydroxy-benzamidine (2.56 g, 15 mmol) was added. The reaction mixture was stirred at room temperature for

another 30 min and then heated to 135 °C with DMF for 45 min. The reaction mixture was diluted with ethyl acetate and washed with water and brine. The organic layer was dried and concentrated to give 4.0 g (95 %) of (R)-3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid methyl ester as pale-yellow oil. Step 2: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide (430 mg, 77%) was obtained from (R)-3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid methyl ester (461.4 mg, 2.0 mmol) reacted with hydrazine hydrate (2mL) in methanol (2 mL) at 65 °C for 1 h. 1H-NMR($CDCl_3$) d (ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.46 (m, 2H), 6.98 (w, 1H), 3.93 (w, 2H), 3.78 (m, 1H), 2.86 (dd, 1H), 2.55 (dd, 1H) and 1.59 (d, 3H).

The following compounds were prepared analogously to Example 320:

Example No.	Name
321	3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-3-methyl-butyric acid hydrazide

Example 322

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one

1.33 ml (3.32 mmol) n-BuLi (2.5 M in hexanes) was added dropwise to a solution of 157 mg (1.58 mmol) d-valerolactone in 5,3 ml THF at 0 °C. After stirring for 2 h at 0 °C, 400 mg (1.58 mmol) 3-chloromethyl-5-[3-chloro-phenyl)-[1,2,4]oxadiazole was added in one portion and stirring was continued for 3 h. NH_4Cl(sat) was added to quench the reaction and the mixture was extracted twice with CH_2Cl_2. The combined organic phases were dried and concentrated. Flashchromatography (SiO_2, Heptane/EtOAc 1:8) afforded 113 mg (25%) of a yellow-white solid. 1H NMR ($CDCl_3$):d ppm 1.80 (m, 1 H) 1.89 (m, 1 H) 2.00 (m, 1 H) 2.91 (m, 1 H) 2.98 (m, 1 H) 3.35 (m, 1 H) 3.52 (m, 1 H) 5.83 (s, 1 H) 7.46 (t, 1 H) 7.55 (d, J=8.08 Hz, 1 H) 8.00 (d, 1 H) 8.11 (s, 1 H).

The following compounds were prepared analogously to Example 322:

Example No.	Name
323	3-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one

Example 324

3-Chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole and 1-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole

A solution of 2-chloro-N-hydroxy-acetamidine (781 mg, 7.2 mmol), 5-chloro-thiophene-3-carboxylic acid (1.4 g), HBTU (3.55 g) and DIPEA (1.3 g) in DMF (20 ml) was stirred at ambient temperature for 1 h before heated at 120 °C for 4 h under argon. Removal of the solvent in vacuo followed by silica gel chromatography of the obtained residue using 0-20% EtOAc in n-heptane yielded 38.5 mg of the faster eluting 3-chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole as a syrup, followed by 65 mg of the slower eluting 1-[5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole as a white solid. 3-Chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole: 1H NMR ($CDCl_3$) d (ppm): 8.01 (d, 1H), 7.50 (d, 1H), 4.63 (s, 2H). 1-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole: 1H NMR ($CDCl_3$) d (ppm): 7.97 (m, 2H), 7.52 (dt, 1H), 7.44 (m, 2H), 7.34 (m, 1H), 5.70 (s, 2H).

Example 325

(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetonitrile

4-Methyl-5-thiophene-3-yl-4H-[1,2,4]triazole-3-thiol (197 mg, 1.0 mmol), chloroacetonitile (95 ml, 1.5 mmol), sodium carbonate (424 mg, 4 mmol) and potassium iodide (332mg, 2.0 mmol) were stirred together at 100 °C for 3 h with an additional addition of chloroacetonitrile (60ml, 0.5 mmol) after 2 h. The reaction was cooled, diluted with ethyl acetate and washed with water. The organic solution was dried, filtered and evaporated. Silica gel chromatography (dichloromethane:methanol 19:1) yielded 150 mg of the desired compound.

Example 326

2-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid

(R)-2-chloro-propionic acid (500 mg, 4.6 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (1.09 g, 5.58 mmol) and potassium carbonate (1.94 g, 14.03 mmol) were dissolved in acetonitrile (15 ml) at room temperature. Reaction proceeded for 2.5 h and was partitioned between ethyl acetate (350 ml) and water 3 times, washed with 1 M HCl, once with saturated brine, dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. Reaction was not completed at this stage and the crude was stirred in DMF (10 ml) overnight. Extraction was repeated and purification was performed by SPE (solid phase extraction) chromatography on silica gel using 300 ml ethyl acetate, 100 ml 1%, and 100 ml 3% formic acid in ethyl acetate, yielding title compound (150.7 mg, 12%) 1H-NMR ($CDCl_3$), d (ppm): 7.52 (dd, 2H), 7.19 (m, 1H), 4.21 (q, 1H), 3.78 (s, 3H), 1.64 (d, 3H).

The following compounds were prepared analogously to Example 326:

Example No.	Name
327	2-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid

Example 328

3-(3-Chloro-phenyl)-5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

The title compound (2.08 g, 81.5 %) was obtained form 5-chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole (1.9 g, 8.29 mmol) reacted with 4-methyl-4H-[1,2,4]triazole-3-thiol (1.0 g, 8.71 mmol) and K_2CO_3 (4.58 g, 33.2 mmol) in DMF (19 ml) at room temperature overnight. 1H-NMR($CDCl_3$) d (ppm): 8.21 (s, 1H), 8.05 (s, 1H), 7.94 (d, 1H), 7.49(d, 1H), 7.43 (t, 1H), 4.69 (s, 2H) and 3.64(s, 3H).

Example 329

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl-phenyl}-carbamic acid tert-butyl ester

The title compound was prepared from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (53 mg, 0.27 mmol), 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-carbamic acid tert-butyl ester (75 mg, 0.24 mmol), and potassium carbonate (101 mg, 0.73 mmol) in acetonitrile (2.5 ml). The product was purified by SPE (flash) chromatography using 65% ethyl acetate in hexane (88.0mg, 79%, white solid) . 1H NMR ($CDCl_3$) d (ppm): 8.06 (s, 1H), 7.73 (d, 1H), 7.66 (d, 1H), 7.51 (t, 2H), 7.42 (t, 1H), 7.18 (m, 1H), 6.68 (s, 1H), 4.51 (s, 2H), 3.73 (s, 3H), 1.53 (s, 9H).

The following compounds were prepared analogously to Example 41:

Example No.	Name	1H NMR	MS
330	4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.88 (d, 2H), 7.81 (m, 1H), 7.75 (m, 2H), 7.22 (m, 2H), 5.42 (q, 1H), 3.22 (m, 1H), 1.98 (d, 3H), 1.17 (m, 2H), 0.79 (m, 2H)	
331	4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.69 (m, 2H), 7.6 (m, 1H), 7.52 (m, 3H), 7.35 (t, 1H), 7.04 (m, 1H), 4.93 (q, 1H), 3.78 (t, 3H), 3.55 (s, 3H), 1.86 (d, 3H)	
332	4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.71 (m, 2H), 7.82 (m, 2H), 7.53 (m, 2H), 7.32 (m, 2H), 4.94 (q, 1H), 3.54 (s, 3H), 2.33 (s, 3H), 1.87 (d, 3H)	
333	5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-	2.58 (s, 3 H) 3.70 (s, 3 H) 4.65 (s, 2 H) 7.17 (s,	370.0

	o-tolyl-[1,2,4]oxadiazole	1 H) 7.29 (s, 2 H) 7.36 (s, 1 H) 7.46 (s, 1 H) 7.51 (s, 1 H) 7.90 (s, 1 H)	
334	5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	0.87 (m, 2 H) 1.18 (m, 2 H) 3.47 (ddd, J=6.95, 3.41, 3.28 Hz, 1 H) 4.70 (s, 2 H) 7.23 (m, 1 H) 7.67 (m, 2 H) 7.77 (m, 2 H) 8.04 (d, 2 H)	415.9
335	2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol	2.36 (s, 3 H) 4.03 (t, 2 H) 4.30 (t, 2 H) 4.57 (s, 2 H) 7.11 (m, 2 H) 7.35 (s, 1 H) 7.47 (d, 1 H) 7.64 (d, 1 H) 7.81 (d, 1 H)	417.9
336	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine	1.38 (t, 3 H) 2.34 (s, 3 H) 4.66 (m, 4 H) 7.19 (m, 1 H) 7.47 (m, 1 H) 7.83 (d,1 H) 8.23 (d, 1 H) 8.94 (d, 1 H) 9.28 (s, 1 H)	398.0
337	3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	1.34 (t, 3 H) 2.37 (s, 3 H) 4.06 (q, 2 H) 4.61 (s, 2 H) 6.82 (s, 1 H) 7.12 (m, 1 H) 7.36 (ddd, 1 H) 7.55 (s, 1 H) 7.85 (d, 2 H).	386.0
338	{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-	2.36 (s, 3 H) 3.70 (s, 3 H) 4.46 (s, 2 H) 5.10 (s, 2 H) 7.21 (m, 2 H) 7.47	445.9

	[1,2,4]triazol-4-yl}-acetic acid methyl ester	(m, 2 H) 7.73 (d, 1 H) 7.86 (m, 1 H)	
339	5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	2.26 (s, 3 H) 3.16 (s, 3 H) 3.57 (t, 2 H) 4.42 (t, 2 H) 4.44 (s, 2 H) 6.60 (s, 1 H) 7.10 (m, 2 H) 7.37 (m, 1 H) 7.70 (s, 1 H) 7.73 (d,1 H)	416.0
340	3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	0.87 (m, 2 H) 1.14 (m, 2 H) 2.35 (s, 3 H) 3.39 (dt, 1 H) 4.71 (s, 2 H) 6.72 (s, 1 H) 7.09 (d, 1 H) 7.39 (m, 1 H) 7.56 (m, 1 H) 7.87 (d, 1 H) 7.93 (s, 1 H)	398.0
341	3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	0.32 (m, 2 H) 0.56 (m, 2 H) 1.14 (d, 1 H) 4.00 (d, 2 H) 4.76 (s, 2 H) 7.16 (ddd, 2 H) 7.43 (m, 1 H) 7.50 (t, 2 H) 7.99 (dd, 1 H)	448.1
342	4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	1.40 (t, 3 H) 4.63 (q, 2 H) 4.72 (s, 2 H) 7.20 (m, 1 H) 7.53 (m, 1 H) 8.06 (dd, 1 H) 8.29 (d, 1 H) 8.86 (d, 1 H) 9.26 (s, 1 H).	417.8
343	3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	1.29 (t, 3 H) 1.66 (m, 3 H) 1.87 (m, 2 H) 2.02 (m, 3 H) 2.42 (s, 3 H) 3.01 (s, 2 H) 3.90 (d, 2	370.2

		H) 4.52 (s, 2 H) 7.39 (d, . 2 H) 7.90 (d, 2 H)	
344	3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole	1.18 (t, 3 H) 2.95 (t, 2 H) 3.09 (t, 2 H) 3.72 (q, 2 H) 3.76 (s, 3 H) 4.66 (s, 2 H) 6.81 (d, 2 H) 7.09 (d, 2 H) 7.40 (t, 1 H) 7.47 (m, 1 H) 7.92 (d, 1 H) 8.03 (s, 1 H)	456.1
345	5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.23 (t, 3 H) 2.22 (s, 3 H) 4.02 (d, 2 H) 4.60 (s, 2 H) 5.22 (s, 2 H) 6.92 (d, 2 H) 7.09 (d, 2 H) 7.65 (t, 1 H) 7.79 (d, 1 H) 8.04 (m, 2 H)	442.1
346	5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	3.14 (s, 3 H) 3.57 (t, 2 H) 4.30 (t, 2 H) 4.58 (s, 2 H) 7.23 (m, 1 H) 7.64 (m, 2 H) 7.78 (m, 2 H) 8.03 (d, 2 H)	433.9
347	3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.98 (m, 1H), 7.43 (m, 1H), 7.16 (apparent t, 1H), 4.73 (s, 2H), 4.62 (s, 2H), 4.01 (q, 2H), 3.33 (s, 3H), 1.34 (t, 3H).	384.9
348	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.05 (m, 1H), 7.53 (m, 1H), 7.21 (apparent t, 1H); 4.62 (s, 2H), 4.61 (s, 2H), 4.02 (q, 2H), 3.34 (s, 3H), 1.32 (t,	384.9

		3H).	
349	5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.07 (apparent s, 1H), 7.97 (m, 1H), 7.55 (m, 1H), 7.45 (apparent t, 1H), 4.62 (s, 2H), 4.59 (s, 2H), 4.01 (q, 2H), 3.34 (s, 3H), 1.32 (t, 3H).	366.9
350	3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.02 (m, 1H), 7.92 (m, 1H), 7.46 (m, 1H), 7.39 (apparent t, 1H), 4.71 (s, 2H), 4.62 (s, 2H), 4.01 (q, 2H), 3.34 (s, 3H), 1.34 (t, 3H).	366.9
351	4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	1.82 (d, 3 H), 3.46 (s, 3 H), 4.93 (q, 1 H), 6.33 (s, 1 H), 7.23-7.31 (m, 2 H), 7.44 (d, 2 H), 7.49 (m, 1 H), 7.61 (s, 1 H), 8.63 (d, 2 H).	399.1
352	3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	4.6 (s, 2 H), 4.8 (d, 2 H), 5.0 (d, 1 H), 5.2 (d, 1 H), 5.9 (m, 1 H), 6.5 (m, 1 H), 7.1 (d, 1 H), 7.4 (t, 1 H), 7.5 (m, 2 H), 8.0 (d, 1 H), 8.1 (s, 1 H)	399.95
353	3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	4.5 (s, 2 H) 4.8 (d, 2 H) 5.0 (d, 1 H) 5.2 (d, 1 H) 5.9 (m, 1 H) 6.5 (m, 1 H) 7.0 (d, 1 H) 7.4 (m, 1 H) 7.5 (s, 1 H) 7.6 (d, 1	371.98

		H) 8.2 (m, 1 H)	
354	5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole	4.7 (s, 2 H) 4.8 (m, 2 H) 5.0 (d, 1 H) 5.2 (d, 1 H) 5.9 (m, 1 H) 6.5 (dt, 2 H) 7.1 (dd, 2 H) 7.6 (dd, 2 H)	356.01
355	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.4 (t, 3 H) 3.7 (s, 3 H) 4.1 (q, 2 H) 4.6 (s, 2 H) 5.2 (s, 2 H) 6.8 (d, 2 H) 6.9 (d, 2 H) 7.4 (t, 1 H) 7.6 (d, 1 H) 8.0 (d, 1 H) 8.1 (s, 1 H)	457.91
356	3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.4 (t, 3 H) 3.7 (s, 3 H) 4.1 (q, 2 H) 4.8 (s, 2 H) 5.2 (s, 2 H) 6.8 (d, 2 H) 6.9 (d, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (d, 1 H) 8.0 (s, 1 H)	457.97
357	{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol	1.4 (t, 3 H) 4.2 (d, 2 H) 4.7 (s, 2 H) 4.9 (s, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (d, 1 H) 8.0 (s, 1 H)	352.09
358	3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.3 (t, 3 H) 3.0 (t, 2 H) 3.3 (s, 3 H) 3.8 (t, 2 H) 3.9 (q, 2 H) 4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (ddd, 1 H) 7.9 (dt, 1 H) 8.0 (t, 1 H)	380.12
359	3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-	1.4 (t, 3 H) 2.1 (s, 3 H) 3.8 (s, 2 H) 4.0 (q, 2 H) 4.7 (s, 2 H) 7.4 (t, 1 H)	382.07

	[1,2,4]oxadiazole	7.5 (ddd, 1 H) 7.9 (dt, 1 H) 8.0 (t, 1 H)	
360	3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	.2 (t, 3 H) 1.3 (t, 3 H) 3.5 (q, 2 H) 4.0 (q, 2 H) 4.7 (s, 2 H) 4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (ddd, 1 H) 7.9 (dt, 1 H) 8.0 (t, 1 H)	379.13
361	5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester		
362	2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	1.4 (t 3 H) 4.2 (q, 2 H) 4.7 (s, 2 H) 6.6 (dd, 1 H) 7.1 (d, 1 H) 7.2 (m, 1 H) 7.5 (ddd, 1 H) 7.6 (d, 1 H) 8.0 (dd, 1 H)	406.07
363	2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	0.9 (m, 2 H) 1.2 (m, 2 H) 3.2 (m, 1 H) 4.8 (s, 2 H) 6.6 (m, 1 H) 7.0 (d, 1 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.6 (m, 1 H) 7.9 (m, 1 H) 8.0 (m, 1 H)	399.86
364	5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole	1.3 (t, 3 H) 1.9 (d, 3 H) 2.0 (m, 1 H) 2.1 (m, 1 H) 2.3 (m, 1 H) 2.8 (m, 1 H) 3.8 (m, 2 H) 4.0 (m, 1 H) 4.1 (m, 1 H) 5.0 (m, 1 H) 5.1 (m, 1 H) 7.4 (t, 1 H) 7.6 (m, 1	406.04

		H) 8.0 (m, 1 H) 8.1 (s, 1 H)	
365	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine	1.4 (t, 3 H) 1.9 (d, 3 H) 4.1 (m, 2 H) 5.2 (q, 1 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.8 (m, 1 H) 8.0 (m, 1 H) 8.1 (m, 1 H) 9.4 (m, 1 H) 9.5 (s, 1 H)	414.12
366	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine	1.0 (t, 3 H) 1.9 (d, 3 H) 3.7 (m, 2 H) 4.2 (m, 2 H) 5.0 (q, 1 H) 7.1 (m, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (d, 1 H) 8.1 (s, 1 H) 8.5 (m, 2 H)	427.06
367	5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol	1.3 (t, 3 H) 1.9 (d, 3 H) 3.9 (m, 2 H) 5.1 (q, 1 H) 6.7 (d, 1 H) 7.5 (t, 1 H) 7.6 (m, 1 H) 7.7 (m, 1 H) 7.7 (s, 1 H) 8.0 (d, 1 H) 8.1 (s, 1 H) 13.1 (s, 1 H)	429.1
368	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol	1.2 (t, 3 H) 1.9 (d, 3 H) 3.9 (q, 2 H) 5.1 (q, 1 H) 6.9 (d, 2 H) 7.3 (d, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (m, 1 H) 8.1 (m, 1 H) 10.2 (s, 1 H)	428.08
369	5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-	1.54 (m, 1 H) 1.86 (m, 2 H) 2.02 (m, 1 H) 3.71 (m, 4 H) 3.79 (m, 1 H) 4.13 (m, 3 H) 4.60 (m, 2	

	[1,2,4]oxadiazole	H) 5.30 (s, 2 H) 6.82 (m, 2 H) 6.92 (m, 2 H) 7.44 (t, 1 H) 7.55 (d, 1 H) 7.95 (d, 1 H) 8.07 (s, 1 H)	
370	5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.14 (m, 4 H) 3.10 (s, 1 H) 3.75 (s, 3 H) 4.70 (s, 2 H) 5.21 (s, 2 H) 6.82 (d, 2 H) 6.95 (d, 2 H) 7.45 (t, 1 H) 7.56 (m, 1 H) 7.99 (d, 1 H) 8.10 (s, 1 H)	
371	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.38 (t, 3 H) 4.27 (q, 2 H) 4.64 (s, 2 H) 6.58 (m, 1 H) 7.21 (m, 2 H) 7.53 (m, 1 H) 7.59 (m, 1 H) 8.06 (m, 1 H)	
372	3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	1.29 (t, 3 H) 2.40 (s, 3 H) 3.31 (s, 3 H) 3.99 (m, 2 H) 4.56 (s, 2 H) 4.60 (s, 2 H) 7.37 (m, 2 H) 7.87 (m, 2 H)	346
373	3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole	1.30 (t, 3 H) 1.97 (m, 1 H) 2.10 (m, 1 H) 2.24 (m, 1 H) 2.39 (s, 3 H) 2.80 (m, 1 H) 3.79 (m, 1 H) 3.86 (m, 1 H) 3.99 (m, 1 H) 4.08 (m, 1 H) 4.54 (m, 2 H) 4.98 (m, 1 H) 7.36 (m, 2 H) 7.86 (m, 1 H) 7.88 (s, 1 H)	372

374	2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	1.18 (m, 3 H) 1.95 (d, 3 H) 3.81 (s, 3 H) 3.90 (q, 2 H) 5.15 (q, 1 H) 6.94 (m, 2 H) 7.35 (m, 1 H) 7.45 (m, 3 H) 7.81 (m, 1 H) 7.92 (m, 1 H)	
375	4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	1.43 (t, 3 H), 4.64 (q, 2 H), 4.87 (s, 2 H), 7.18 (m, 2 H), 7.72 (m, 1 H), 8.29 (dd, 1 H), 8.89 (d, 1 H), 9.30 (d, 1 H)	402.1
376	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	4.12 (s, 3 H), 4.64 (s, 2 H), 7.21 (t, 1 H), 7.57 (m, 1 H), 8.06 (dd, 1 H), 8.28 (dd, 1 H), 8.92 (d, 1 H), 9.30 (d, 1 H)	404.1
377	3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.03 (s, 1H), 7.92 (d, 1H), 7.53 (d, 1H), 7.48 (m, 2H), 7.40 (t, 1H), 7.18 (t, 1H), 4.87 (s, 2H), 3.72 (s, 3H).	390.96
378	5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.92 (s, 1H), 7.84 (d, 1H), 7.53 (m, 2H), 7.43 (m, 2H), 7.18 (m, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 2.52 (s, 3H).	
379	2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole		
380	5-(2,5-Dimethyl-phenyl)-3-(4-	7.87 (s, 1H), 7.49 (m,	

	methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	2H), 7.22 (m, 3H), 4.56 (d, 2H), 3.74 (s, 3H), 2.61 (s, 3H), 2.37 (s, 3H).	
381	5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.83 (dd, 1H), 7.49 (m, 2H), 7.35 (m, 1H), 7.16 (m, 2H), 4.53 (s, 2H), 3.73 (s, 3H), 2.35 (s, 3H).	388.10
382	5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.87 (d, 1H), 7.79 (s, 1H), 7.51 (m, 2H), 7.40 (t, 1H), 7.30 (m, 1H), 7.20 (m, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 1.96 (m, 1H), 1.04 (m, 2H), 0.77 (m, 2H).	
383	4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (d, 2H), 8.02 (dd, 1H), 7.88 (dd, 1H), 7.80 (s, 1H), 7.60 (d, 2H), 7.42 (m, 2H), 4.51 (s, 2H), 3.64 (s, 3H).	
384	4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (bs, 2H), 7.90 (m, 1H), 7.66 (m, 3H), 7.22 (m, 1H), 4.58 (s, 2H), 3.73 (s, 3H).	
385	4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (m, 2H), 7.95 (s, 1H), 7.86 (m, 1H), 7.64 (m, 2H), 7.45 (m, 2H), 4.63 (s, 2H), 3.72 (s, 3H), 2.55 (3H).	
386	4-{5-[5-(3-Chloro-phenyl)-	8.83 (d, 2H), 8.11 (s,	

	[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	1H), 8.00 (d, 1H), 7.64 (m, 2H), 7.60 (m, 1H), 7.49 (t, 1H), 4.64 (s, 2H), 3.73 (s, 3H).	
387	2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.82 (d, 2H), 8.74 (d, 1H), 7:82 (s, 1H), 7.76 (d, 1H), 7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s, 3H), 2.68 (s, 3H).	
388	1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone	8.67 (s, 1H), 8.29 (d, 1H) 8.20 (d, 1H), 7.68 (t, 1H), 7.52 (m, 2H), 7.20 (m, 1H), 4.58 (s, 2H), 3.76 (s, 3H), 2.68 (s, 3H).	
389	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (dd, 2H), 7.86 (d, 1H), 7.64 (m, 2H), 7.39 (m, 1H), 7.14 (dd, 1H), 4.63 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H).	383.09
390	2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.68 (dd, 1H), 7.92 (m, 2H), 7.52 (bs, 1H), 7.4 (m, 3H), 4.61 (s, 2H), 3.7 (s, 3H), 2.67 (s, 3H), 2.44 (s, 3913H).	
391	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.76 (s, 1H), 7.68 (m, 1H), 7.54 (m, 1H), 7.48 (m, 1H), 7.40 (m, 2H), 7.20 (m, 1H), 6.76 (s, 1H), 4.56 (s, 2H), 3.70 (s, 3H).	

392	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (m, 2H), 7.76 (m, 1H), 7.65 (m, 3H), 7.41 (m, 2H), 6.77 (s, 1H), 4.61 (s, 2H), 3.69 (s, 3H).	
393	3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.07 (s, 1H), 7.95 (dd, 1H), 7.48 (m, 4H), 7.17 (dd, 1H), 4.59 (s, 2H), 4.05 (t, 2H), 1.67 (m, 2H), 1.30 (m, 2H), 0.88 (t, 3H).	
394	5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.01 (d, 1H), 7.91 (dd, 1H), 7.48 (m, 4H), 7.12 (m, 1H), 4.51 (s, 2H), 4.17 (t, 2H), 3.34 (t, 2H), 3.18 (s, 3H), 1.90 (m, 2H).	
395	3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.09 (s, 1H), 7.97 (dd, 1H), 7.57 (m, 1H), 7.47 (m, 2H), 7.24 (m, 4H), 7.06 (m, 3H), 5.37 (s, 2H), 4.57 (s, 2H).	
396	5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.10 (d, 1H), 8.03 (dd, 1H), 7.55 (m, 4H), 7.38 (s, 1H), 7.20 (dd, 1H), 6.32 (m, 2H), 5.30 (s, 2H), 4.60 (s, 2H).	457.02
397	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.93 (m, 1H), 8.78 (m, 1H), 8.03 (m, 3H), 7.59 (m, 1H), 7.51 (m, 2H), 4.63 (s, 2H), 3.69 (s,	

		3H).	
398	5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (m, 1H), 8.05 (m, 1H), 7.74 (m, 1H), 7.59 (m, 1H), 7.51 (m, 3H), 4.57 (s, 2H), 3.71 (s, 3H).	
399	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine	8.69 (d, 1H), 8.10 (s, 1H), 8.00 (m, 1H), 7.49 (m, 4H), 4.63 (s, 2H), 3.71 (s, 3H), 2.67 (s, 3H).	
400	5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.08 (m, 1H), 7.51 (m, 1H) 7.21 (m, 1H), 4.59 (s, 2H), 3.77 (s, 3H).	409.00
401	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 8.08 (m, 1H) 8.29 (d, 1H), 7.64 (d, 2H), 7.56 (m, 1H), 7.24 (t, 1H), 4.66 (s, 2H), 3.75 (s, 3H).	404.07
402	3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (s, 1H), 8.76 (d, 1H), 8.07 (d, 1H), 7.87 (d, 1H), 7.36 (m, 3H), 4.59 (s, 2H), 3.69 (s, 3H), 2.39 (s, 3H).	
403	5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent): 8.05 (m, 1H), 8.00 (dd, 1H), 7.75 (dd, 1H), 7.58 (m, 1H), 7.54 (m, 1H), 7.53 (m, 1H), 7.26 (m, 1H), 7.22 (m, 1H), 6.86	

		(m, 2H), 5.63 (s, 2H), 4.51 (s, 2H).	
404	5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):8.08 (m, 1H), 8.07 (dd, 1H), 7.75 (m, 1H), 7.67 (m, 1H), 7.60 (m, 2H), 7.28 (dd, 1H), 4.57 (s, 2H), 4.27 (m, 2H), 1.29 (m, 3H).	405.10
405	3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.90 (m, 1H), 8.77 (dd, 1H), 8.03 (m, 1H), 7.78 (m, 1H), 7.48 (m, 1H), 7.28 (m, 1H), 7.12 (m, 1H), 4.73 (s, 2H), 3.68 (s, 3H), 2.36 (s, 3H).	
406	4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (m, 2H), 7.77 (m, 1H), 7.62 (m, 2H), 7.31 (m, 1H), 7.11 (dd, 1H), 4.75 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H).	
407	4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (m, 2H), 8.23 (m, 1H), 7.71 (m, 2H), 7.65 (m, 1H), 7.18 (d, 1H), 4.66 (s, 2H), 3.75 (s, 3H).	448.02
408	3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (m, 1H), 8.76 (m, 1H), 8.22 (m, 1H), 8.05 (m, 1H), 7.50 (m, 1H), 7.48 (m, 1H), 7.17 (dd, 1H), 4.63 (s, 2H), 3.70 (s, 3H).	

409	5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.23 (dd, 1H), 7.70 (m, 1H), 7.52 (m, 2H), 7.19 (m, 2H), 4.49 (s, 2H), 3.77 (s, 3H).	452.90
410	5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole	8.06 (d, 2H) 7.34 (d, 1H), 7.51 (m, 5H), 4.68 (s, 2H), 3.68 (s, 3H).	
411	3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (s, 1H), 8.78 (d, 1H) 8.05 (d, 1H), 7.93 (d, 1H), 7.91 (d, 1H), 7.50 (m, 2H), 7.28 (t, 1H), 4.64 (s, 2H), 3.70 (s, 3H).	
412	4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 7.93 (d, 1H) 7.90 (d, 1H), 7.64 (d, 2H), 7.52 (m, 1H), 7.33 (m, 1H), 4.64 (s, 2H), 3.73 (s, 3H).	
413	5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.90 (d, 1H) 7.82 (d, 1H), 7.74 (d, 1H), 7.51 (m, 3H), 4.58 (s, 2H), 3.71 (s, 3H).	
414	3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.91 (s, 1H), 8.78 (d, 1H) 8.23 (d, 1H), 8.04 (d, 1H), 7.66 (d, 1H), 7.49 (m, 2H), 4.60 (s, 2H), 3.69 (s, 3H).	
415	3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.22 (d, 1H) 7.74 (d, 1H), 7.63 (d, 1H), 7.49 (m, 3H), 4.54 (s, 2H), 3.70 (s, 3H).	

416	2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.92 (s, 1H), 8.78 (d, 1H) 8.65 (d, 1H), 8.04 (t, 2H), 7.89 (d, 1H), 7.51 (m, 1H), 4.69 (s, 2H), 3.71 (s, 3H).	
417	2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.82 (d, 2H), 8.65 (d, 1H) 8.02 (s, 1H), 7.89 (d, 1H), 7.64 (d, 2H), 4.70 (s, 2H), 3.74 (s, 3H).	
418	2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.64 (d, 1H) 8.01 (s, 1H), 7.88 (d, 1H), 7.75 (d, 1H), 7.52 (m, 2H), 4.62 (s, 2H), 3.72 (s, 3H).	
419	4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (d, 2H), 8.12 (d, 2H) 7.63 (m, 3H), 7.55 (m, 2H), 4.63 (s, 2H), 3.72 (s, 3H).	
420	3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole	8.11 (d, 2H) 7.74 (d, 1H), 7.57 (m, 1H), 7.52 (m, 4H), 4.56 (s, 2H), 3.70 (s, 3H).	
421	5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):8.21 (m, 1H), 8.02 (m, 1H), 7.82 (m, 1H), 7.68 (m, 1H), 7.56 (m, 1H), 7.33 (t, 1H), 4.50 (s, 2H), 3.82 (s, 3H).	
422	3-[5-(3-Chloro-phenyl)-isoxazol-3-	(CD3OD as solvent):	404.05

	ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.84 (s, 1H), 7.75 (m, 2H), 7.60 (m, 1H) 7.50 (m, 2H), 7.27 (m, 1H), 6.92 (s, 1H), 4.51 (s, 2H), 4.23 (q, 2H), 1.33 (t, 3H).	
423	2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.64 (d, 1H), 8.01 (s, 1H) 7.98 (d, 1H), 7.54 (d, 1H), 7.50 (d, 1H), 7.20 (m, 1H), 4.61 (s, 2H), 3.76 (s, 3H).	392.00
424	4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (d, 2H), 7.85 (d, 1H) 7.78 (d, 1H), 7.62 (d, 2H), 7.46 (m, 1H), 7.22 (m, 1H), 4.76 (s, 2H), 3.72 (s, 3H).	
425	3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.84 (d, 1H) 7.74 (m, 1H), 7.51 (m, 3H), 7.24 (m, 1H), 4.70 (s, 2H), 3.70 (s, 3H).	
426	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	(CD3OD as solvent):7.89 (m, 2H), 7.76 (m, 1H), 7.60 (m, 1H), 7.47 (m, 2H), 7.27 (m, 1H), 4.55 (s, 2H), 4.25 (q, 2H), 2.41 (s, 3H), 1.32 (s, 3H)	384.13
427	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	(CD3OD as solvent):7.85 (m, 1H), 7.75 (m, 1H), 7.60 (m, 1H), 7.55 (m, 1H), 7.27	402.09

		(m, 1H), 7.22 (m, 1H), 4.57 (s, 2H), 4.27 (q, 2H), 2.36 (s, 3H), 1.33 (s, 3H).	
428	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent):8.75 (m, 2H), 8.04 (m, 2H), 7.78 (m, 2H), 7.66 (m, 1H), 7.60 (m, 1H), 7.37 (m, 1H), 6.30 (m, 2H), 5.42 (s, 2H), 4.56 (s, 2H).	452.10
429	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (m, 2H), 8.09 (m, 1H), 7.98 (m, 1H), 7.58 (m, 3H), 7.50 (dd, 1H), 4.69 (s, 2H), 4.12 (m, 2H), 1.36 (m, 3H).	
430	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent):8.87 (s, 1H), 8.77 (d, 1H), 8.07 (m, 3H), 7.67 (m, 2H), 7.61 (dd, 1H), 4.62 (s, 2H), 4.13 (m, 2H), 1.26 (m, 3H).	400.12
431	5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):7.79 (m, 3H), 7.67 (m, 2H), 7.51 (m, 2H), 4.56 (s, 2H), 4.22 (q, 2H), 1.30 (t, 3H).	405.07
432	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-	(CD3OD as solvent):8.86 (s, 1H), 8.76 (d, 1H), 8.07 (m,	452.12

	ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine	1H), 8.01 (m, 2H), 7.64 (m, 3H), 7.36 (s, 1H), 6.29 (s, 2H), 5.37 (s, 2H), 4.55 (s, 2H).	
433	3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	(CD3OD as solvent):7.87 (m, 2H), 7.73 (m, 1H), 7.63 (m, 1H), 7.45 (m, 3H), 7.25 (m, 1H), 6.31 (m, 2H), 5.42 (s, 2H), 4.49 (s, 2H), 2.40 (s, 3H).	436.16
434	5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):7.75 (dd, 1H), 7.69 (m, 1H), 7.66 (m, 1H), 7.41 (m, 1H), 7.38 (m, 1H), 7.25 (m, 2H), 6.32 (s, 2H), 5.44 (s, 2H), 4.51 (s, 2H), 2.36 (s, 3H).	454.12
435	5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.23 (s, 1H), 8.09 (m, 1H), 7.97 (m, 1H), 7.48 (m, 1H), 7.45 (m, 1H), 7.37 (s, 1H), 6.39 (m, 1H), 6.34 (m, 1H), 5.12 (s, 2H), 4.55 (s, 2H).	375.09
436	3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.92 (s, 1H), 8.78 (d, 1H) 8.43 (s, 1H), 8.35 (d, 1H), 8.05 (d, 1H), 7.91 (d, 1H), 7.72 (t, 1H), 7.52 (m, 1H), 4.67 (s, 2H), 3.71 (s, 3H).	376.20

437	3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.82 (d, 2H), 8.43 (s, 1H) 8.35 (d, 1H), 7.90 (t, 1H), 7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s, 3H).	376.10
438	3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.42 (s, 1H), 8.35 (d, 1H) 7.89 (d, 1H), 7.72 (m, 2H), 7.52 (s, 1H), 4.61 (s, 2H), 3.73 (s, 3H).	
439	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.08 (m, 1H), 7.54 (m, 2H), 7.48 (d, 1H), 7.20 (m, 2H), 4.69 (s, 2H), 4.18 (m, 2H), 1.39 (t, 3H).	423.12
440	2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.64 (d, 1H), 8.02 (s, 1H), 7.89 (d, 1H), 7.53 (d, 1H), 7.48 (d, 1H), 7.20 (t, 1H), 4.69 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	406.00
441	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.23 (s, 1H), 7.66 (d, 1H), 7.53 (d, 1H), 7.48 (m, 2H), 7.19 (t, 1H), 4.63 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	376.10
442	3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	7.93 (m, 2H), 7.71 (m, 1H), 7.49 (m, 2H), 7.42 (m, 2H), 4.63 (s, 2H), 4.10 (q, 2H), 2.43 (s, 3H), 1.36 (t, 3H).	384.10

443	4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.80 (m, 2H), 7.91 (m, 2H), 7.60 (m, 2H), 7.41 (m, 2H), 4.68 (s, 2H), 4.09 (m, 2H), 2.43 (s, 3H), 1.29 (s, 3H).	379.20
444	3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	(CD3OD as solvent):8.87 (s, 1H), 8.77 (d, 1H), 8.02 (m, 1H), 7.92 (m, 2H), 7.49 (m, 1H), 7.42 (m, 2H), 4.67 (s, 2H), 4.05 (q, 2H), 2.43 (s, 3H), 1.35 (t, 3H).	379.20
445	3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	7.88 (dd, 1H), 7.71 (m, 1H), 7.49 (m, 2H), 7.28 (m, 1H), 7.14 (dd, 1H), 4.66 (s, 2H), 4.11 (q, 2H), 2.39 (s, 3H), 1.34 (t, 3H).	
446	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (m, 2H), 7.86 (m, 1H), 7.60 (m, 2H), 7.38 (m, 1H), 7.14 (dd, 1H), 4.70 (s, 2H), 4.11 (q, 2H), 2.39 (s, 3H), 1.36 (t, 3H).	398.20
447	3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.87 (s, 1H), 8.76 (d, 1H), 8.01 (m, 1H), 7.88 (m, 1H), 7.49 (m, 1H), 7.28 (m, 1H), 7.14 (dd, 1H), 4.69 (s, 2H), 4.07 (q, 2H), 2.39 (q, 2H),	

		1.35 (t, 3H).	
448	3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine	(DMSO-D6 as solvent): 8.75 (dd, 2H), 8.05 (m, 4H), 7.79 (m, 1H), 7.66 (dd, 1H), 6.33 (s, 2H), 4.65 (s, 2H).	387.05
449	4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (dd, 2H), 8.24 (m, 1H), 7.71 (m, 1H), 7.61 (m, 2H), 7.18 (dd, 1H), 4.72 (s, 2H), 4.13 (m, 2H), 1.29 (m, 3H).	464.02
450	5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole	7.75 (m, 2H), 7.51 (m, 3H), 7.16 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H).	
451	3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.42 (s, 1H), 8.35 (d, 1H), 7.89 (d, 1H), 7.71 (t, 1H), 7.54 (d, 1H), 7.48 (d, 1H), 7.20 (t, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 1.40 (t, 3H).	395.10
452	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole	8.13 (d, 2H), 7.49 (br m, 5H), 7.20 (m, 1H), 4.65 (s, 2H), 4.16 (m, 2H), 1.40 (t, 3H).	370.09
453	4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine	8.36 (d, 1H), 7.51 (br m, 3H), 7.42 (s, 1H), 7.19 (m, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 1.42 (t, 3H).	
454	3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-	8.06 (s, 1H), 7.95 (d, 1H), 7.54 (m, 1H), 7.49	

	ylsulfanylmethyl)-[1,2,4]oxadiazole	(m, 1H), 7.42 (m, 2H), 7.20 (m, 1H), 4.78 (s, 2H), 4.17 (q, 2H), 1.41 (t, 3H).	
455	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (m, 2H), 7.76 (m, 1H), 7.66 (m, 1H), 7.60 (m, 2H), 7.41 (m, 2H), 6.78 (s, 1H), 4.65 (s, 2H), 4.07 (q, 2H), 1.40 (t, 3H).	399.10
456	2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.73 (d, 1H), 7.81 (s, 1H), 7.75 (s, 2H), 7.51 (m, 2H), 4.60 (s, 2H), 3.71 (s, 3H) 2.68 (s, 3H).	
457	4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.73 (d, 1H), 7.82 (s, 1H), 7.76 (d, 1H), 7.54 (d, 1H), 7.48 (d, 1H), 7.29 (m, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 2.68 (s, 3H), 1.41 (t, 3H).	
458	5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole	7.78 (d, 1H), 7.53 (t, 2H), 7.48 (d, 1H), 7.18 (m, 2H), 4.74 (s, 2H), 4.17 (m, 2H), 1.41 (t, 3H).	376.00
459	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 8.09 (m, 1H), 7.58 (m, 3H), 7.24 (m, 1H), 4.73 (s, 2H), 4.13 (m, 2H), 1.41 (t, 3H).	418.10

460	4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.82 (d, 2H), 8.75 (d, 1H), 7.84 (s, 1H), 7.76 (d, 1H), 7.60 (d, 2H), 4.74 (s, 2H), 4.13 (m, 2H), 1.41 (t, 3H).	
461	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile	8.11 (s, 1H), 7.97 (m, 3H), 7.83 (d, 1H), 7.63(m, 3H), 7.50 (t, 1H), 4.63 (s, 2H) and 3.68 (s, 3H)	
462	5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.67(m, 1H), 7.50 (m, 5H), 4.61 (s, 2H) and 3.66 (s, 3H).	
463	5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.55 (m, 6H), 4.61 (s, 2H) and 3.64 (s, 3H).	
464	4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 8.05 (m, 1H), 7.59 (m, 2H), 7.47 (s, 2H), 4.73 (s, 2H), 4.11 (m, 2H), 1.32 (m, 3H).	
465	5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (dd, 1H), 7.50 (m, 4H), 7.19 (dd, 1H), 4.68 (s, 2H), 4.17 (q, 2H), 1.39 (t, 3H).	
466	5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.80 (dd, 2H), 7.79 (m, 1H), 7.60 (m, 2H), 7.28 (m, 1H), 4.68 (s, 2H), 4.11 (q, 2H), 1.39 (t,	406.10

		3H).	
467	4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	7.80 (m, 1H), 7.52 (m, 1H), 7.48 (m, 1H), 7.20 (m, 4H), 4.68 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	
468	5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.07 (dd, 1H), 7.71 (dd, 1H), 7.49 (m, 4H), 4.69 (s, 2H), 4.12 (m, 2H), 1.38 (t, 3H).	
469	5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.80 (m, 1H), 7.72 (m, 1H), 7.49 (m, 2H), 7.28 (m, 2H), 4.68 (s, 2H), 4.12 (q, 2H), 1.37 (t, 3H).	406.10
470	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 8.11 (m, 1H), 7.99 (m, 1H), 7.57 (m, 3H), 7.48 (t, 1H), 4.70 (s, 2H), 3.99 (q, 2H), 1.72 (m, 2H), 0.91 (t, 3H).	
471	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 7.87 (dd, 1H), 7.58 (m, 2H), 7.39 (m, 1H), 7.15 (q, 1H), 4.70 (s, 2H), 4.01 (m, 2H), 2.40 (s, 3H), 1.70 (m, 2H), 0.87 (t, 3H).	
472	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole	7.91 (d, 1H), 7.67 (d, 1H), 7.52 (d, 1H), 7.48 (d, 1H), 7.20 (m, 2H), 4.62 (s, 2H), 4.18 (m,	376.10

		2H), 1.38 (t, 3H).	
473	3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole	7.90 (s, 1H), 7.74 (d, 1H), 7.67 (d, 1H), 7.52 (m, 2H), 7.21 (m, 1H), 4.60 (s, 2H), 3.71 (s, 3H) 2.68 (s, 3H).	
474	4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (d, 2H), 8.05 (s, 1H), 7.61 (m, 3H), 7.44 (m, 1H), 4.73 (s, 2H), 3.70 (s, 3H).	
475	5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole	8.05 (s, 1H), 7.73 (d, 1H), 7.62 (d, 1H), 7.51 (s, 2H), 7.44 (m, 1H), 4.66 (s, 2H), 3.68 (s, 3H).	
476	5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole	8.05 (d, 1H), 7.62 (d, 1H), 7.53 (d, 1H), 7.47 (d, 1H), 7.44 (m, 1H), 7.19 (m, 1H), 4.75 (s, 2H), 4.15 (m, 2H), 1.40 (t, 3H).	376.10
477	5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile	8.18 (d, 1H), 8.03 (d, 1H), 7.51 (m, 1H), 7.46 (m, 1H), 7.18 (m, 1H), 4.63 (s, 2H), 4.16 (q, 2H), 1.40 (t, 3H).	401.00
478	5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.52(m, 4H), 7.34 (t, 1H), 7.27 (m, 1H), 4.63 (s, 2H) and 3.54 (s, 3H).	

479	5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.52(m, 5H), 7.27 (m, 1H), 4.62 (s, 2H) and 3.66 (s, 3H).	403.00
480	5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7:59(m, 4H), 7.49 (t, 1H), 7.22 (m, H), 4.61 (s, 2H) and 3.64 (s, 3H).	403.10
481	3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.87(m, 2H), 7.72 (s, 1H), 7.58 (d, 1H), 7.45 (m, 3H), 4.60 (s, 2H) and 3.85 (s, 3H).	
482	5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.59(dd, 1H), 7.49 (t, 1H), 7.44 (t, 1H), 7.2 (m, 2H), 7.05 (dd, 1H), 4.60 (s, 2H), 3.88 (s, 3H) and 3.65 (s, 3H).	
483	5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.59(m, 3H), 7.49 (t, 1H), 7.03 (d, 2H), 4.59 (s, 2H), 3.89 (s, 3H) and 3.63 (s, 3H).	415.00
484	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	7.86 (dd, 1H), 7.59 (m, 1H), 7.37 (m, 1H), 7.14 (m, 2H), 6.58 (q, 1H), 4.63 (s, 2H), 4.26 (q, 2H), 2.39 (s, 3H), 1.37 (t, 3H).	386.10

485	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	7.91 (m, 2H), 7.59 (m, 1H), 7.40 (m, 2H), 7.10 (q, 1H), 6.58 (q, 1H), 4.61 (s, 2H), 4.24 (q, 2H), 2.43 (s, 3H), 1.36 (t, 3H).	368.20
486	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	7.97 (m, 1H), 7.47 (m, 1H), 7.16 (t, 1H), 4.72 (d, 2H), 4.16 (m, 2H), 2.41 (d, 3H), 1.37 (m,3H).	
487	3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.72 (m, 2H), 8.17 (m, 2H), 7.86 (dd, 1H), 7.49 (m, 1H), 7.23 (dd, 1H), 4.59 (s, 2H), 2.35 (s, 3H).	
488	3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.05 (s, 1H), 7.84 (dd, 1H), 7.69 (m, 1H), 7.47 (m, 1H), 7.22 (m, 2H), 4.52 (s, 2H), 2.33 (s, 3H).	
489	3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.73 (dd, 2H), 8.17 (dd, 2H), 7.89 (m, 2H), 7.46 (m, 2H), 4.58 (s, 2H), 2.389 (s, 3H).	
490	3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-	(CD3OD as solvent):8.05 (dd, 1H), 7.87 (d, 2H), 7.70 (dd,	

	ylamine	1H), 7.45 (m, 2H), 7.23 (q, 1H), 4.50 (s, 2H), 2.39 (s, 3H).	
491	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.23 (m, 1H), 7.66 (m, 1H), 7.60 (m, 1H), 7.47 (m, 1H), 7.11 (m, 1H), 6.60 (m, 1H), 4.61 (s, 2H), 4.26 (q, 2H), 1.38 (t, 3H).	360.10
492	5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (m, 1H), 8.00 (m, 1H), 7.59 (m, 2H), 7.51 (t, 1H), 7.12 (m, 1H), 6.60 (m, 1H), 4.63 (s, 2H), 4.26 (q, 2H), 1.38 (t, 3H).	389.00
493	4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.73 (d, 1H), 7.82 (s, 1H), 7.75 (m, 1H), 7.60 (m, 1H), 7.12 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.26 (q, 2H), 2.68 (s, 3H), 1.39 (t, 3H).	
494	5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.80 (m, 1H), 7.61 (m, 1H), 7.29 (m, 2H), 7.12 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.28 (q, 2H), 1.39 (t, 3H).	390.09
495	4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (m, 2H), 7.63 (m, 1H), 7.59 (m, 2H), 7.41 (m, 2H), 6.58 (s, 1H), 4.63 (s, 2H), 4.06 (q, 2H), 1.38 (t, 3H).	371.00

496	4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole	7.77 (m, 1H), 7.60 (m, 1H) 7.40 (m, 2H), 7.10 (m, 1H), 6.60 (m, 1H), 6.55 (s, 1H), 4.58 (s, 2H), 4.21 (q, 2H), 1.38 (t, 3H).	359.10
497	5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.60(d, 1H), 7.54 (s, 3H), 7.47 (t, 1H), 4.69 (s, 2H),4.06 (q, 2H) and 1.36 (t, 3H).	
498	5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.53(m, 4H), 7.20 (d, 2H), 4.68 (s, 2H), 4.03 (q, 3H) , 2.45(s, 1H) and 1.32 (t, 3H).	
499	5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.58(d, 1H), 7.29-7.50(m, 5H), 4.66 (s, 2H), 4.02 (q, 2H), 2.45 (s, 1H) and 1.32 (t, 3H).	
500	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.52 (s, 1H), 8.40 (d, 1H), 8.12 (s, 1H), 8.05 (dd, 2H), 7.76(t, 1H),7.60 (d, 1H), 7.50 (t, 1H), 4.72 (s, 2H), 4.10 (q, 2H) and 1.41 (t, 3H).	
501	4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	7.80 (m, 2H), 7.78 (m, 1H), 7.65 (m, 1H), 7.59 (m, 2H), 7.40 (m, 2H),	

		6.65 (s, 1H), 4.67 (s, 2H), 3.64 (s, 3H).	
502	5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.14 (s, 1H), 8.02 (d, 1H), 7.60(d, 1H), 7.52 (t, 1H), 7.32 (m, 1H), 7.23 (m, 2H), 4.70 (s, 2H), 3.96 (q, 2H) and 1.27 (t, 3H).	
503	5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.06 (d, 1H), 7.63(s, 1H), 7.58 (d, 1H), 7.49 (m, 4H), 7.23 (m, 2H), 4.68 (s, 2H), 4.04 (q, 2H) and 1.34 (t, 3H).	
504	5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.3(m, 6H), 4.68 (s, 2H), 4.03 (q, 2H) and 1.34 (t, 3H).	
505	4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.78 (d, 2H), 7.55 (m, 3H), 7.44(m, 1H), 7.29 (m, 3H), 4.69 (s, 2H), 4.04 (q, 2H) and 1.34 (t, 3H).	
506	3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.55 (s, 1H), 7.50 (d, 1H), 7.44(m, 2H), 7.28 (m, 3H), 7.18 (dd, 1H), 4.64 (s, 2H), 4.10 (q, 2H) and 1.35 (t, 3H).	404.00
507	3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.58 (s, 1H), 7.53 (s, 1H), 7.40 (m, 1H), 7.27 (m, 3H), 7.10 (d, 1H),	388.00

		6.68 (d, 1H), 4.62 (s, 2H), 4.19 (q, 2H) and 1.33 (t, 3H).	
508	5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.83 (s, 1H), 7.53 (d, 1H), 7.44 (m, 2H), 7.32 (d, 1H), 7.18 (t, 2H), 4.63 (s, 2H), 4.17 (q, 2H), 2.37 (s, 3H), 1.38 (t, 3H).	
509	4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (m, 2H), 7.78 (m, 1H), 7.66 (m, 1H), 7.57 (m, 2H), 7.41 (m, 2H), 6.67 (s, 1H), 4.71 (s, 2H), 4.03 (q, 2H), 1.36 (t, 3H).	
510	3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.78 (s, 1H), 7.64 (m, 1H) 7.52 (m, 1H), 7.41 (m, 3H), 7.18 (m, 1H), 6.65 (s, 1H), 4.66 (s, 2H), 4.08 (q, 2H), 1.36 (t, 3H).	404.00
511	3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.77 (s, 1H), 7.64 (d, 1H), 7.59 (m, 1H), 7.39 (m, 2H), 7.10 (m, 1H), 6.62 (s, 1H), 6.59 (m, 1H), 4.65 (s, 2H), 4.17 (q, 2H), 1.35 (t, 3H).	388.10
512	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine		

513	5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(DMSO-D6 as solvent): 7.82(dd, 1H), 7.65 (d, 1H), 7.58 (m,1H), 7.25 (m, 1H), 4.60 (s, 2H), 4.16 (q, 2H), 1.24 (t, 3H).	
514	4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.78(d, 2H), 7.71 (d, 2H), 7.68 (m,1H), 4.67 (s, 2H), 4.10 (q, 2H), 1.21 (t, 3H).	
515	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (m, 2H), 7.73 (m, 1H), 7.60 (m, 2H), 7.21 (m, 1H), 7.07 (m, 1H), 6.76 (m, 1H), 4.63 (s, 2H), 4.02 (q, 2H), 2.40 (s, 3H), 1.38 (t, 3H).	
516	4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole	7.71 (d, 1H), 7.53 (m, 1H), 7.47 (m, 1H), 7.46 (m, 2H), 7.07 (m, 1H), 6.77 (d, 1H), 4.63 (s, 2H), 4.12 (q, 2H), 2.40 (s, 3H), 1.39 (t, 3H).	
517	4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole	7.72 (d, 1H), 7.60 (m, 1H), 7.10 (m, 1H), 7.05 (m, 2H), 6.77 (d, 1H), 6.60 (m, 1H), 4.61 (s, 2H), 4.21 (q, 2H), 2.39 (s, 3H), 1.38 (t, 3H).	
518	5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.60 (d, 1H), 7.50 (t, 1H), 4.72(s, 2H), 4.12	391.00

		(q, 2H) and 1.42 (t, 3H).	
519	3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.05 (s, 1H), 7.94 (d, 1H), 7.50 (d, 1H), 7.43 (t, 1H), 4.83(s, 2H), 4.13 (q, 2H) and 1.44 (t, 3H).	
520	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.23 (s, 1H), 7,65 (d, 1H), 7.48 (m, 1H), 4.69 (s, 2H), 4.12 (q, 2H) and 1.41 (t, 3H).	
521	5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole	8.05 (s, 1H), 7,61 (d, 1H), 7.43 (m, 1H), 4.81 (s, 2H), 4.12 (q, 2H) and 1.43 (t, 3H).	
522	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (d, 1H), 8.00 (d, 1H), 7.52 (m, 4H), 7.25 (m, 2H), 4.67 (s, 2H), 4.06 (q, 2H), 1.31 (t, 3H).	
523	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.10 (s, 1H), 7.99 (d, 1H), 7.59 (m, 4H), 7.48 (t, 1H), 7.22 (d, 1H), 4.67 (s, 2H), 4.01 (q, 2H), 1.30 (t, 3H).	
524	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole	7.91 (s, 1H), 7,68 (d, 1H), 7.21 (m, 1H), 4.67 (s, 2H), 4.13 (q, 2H) and 1.41 (t, 3H).	
525	3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile	8.35(m, 2H), 7.89 (d, 1H), 7.87 (t, 1H), 7.58 (d,1H), 7.09 (d,1H), 4.70 (s, 2H), 4.00 (q,	

		2H), 1.27 (t, 3H).	
526	4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 8.01 (d, 1H), 9.93 (m, 1H), 7.59 (m, 2H), 7.52 (m, 1H), 7.47 (m, 1H), 4.83 (s, 2H), 4.11 (q, 2H), 1.40 (t, 3H).	400.10
527	2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.00 (s, 1H), 7.89 (d, 1H), 7.60 (m, 1H), 7.50 (m, 1H), 7.44 (m, 1H), 7.13 (m, 1H), 6.60 (m, 1H), 4.76 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	389.00
528	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.57 (m, 3H), 7.51 (t, 1H), 7.05 (d, 2H), 4.67 (s, 2H), 4.02 (q, 2H), 3.89 (s, 3H), 1.31 (t, 3H).	
529	5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.02 (d, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.35 (d, 2H), 7.23 (s, 1H), 7.22 (d, 1H), 6.19 (s, 1H), 6.04 (s, 1H), 5.13 (s, 2H), 4.61 (s, 2H), 2.37 (s, 3H).	
530	4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.74 (d, 1H), 7,81 (s, 1H), 7.74 (d, 1H), 4.74 (s, 2H), 4.12 (q, 2H) 2.69 (s,1H) and 1.42 (t,	

		3H).	
531	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole	7.70 (d, 1H), 7,60 (s, 1H), 7.44 (t, 1H), 7.16 (d, 1H), 4.70 (s, 2H), 4.12 (q, 2H), 3.90 (s, 3H) and 1.41 (t, 3H).	
532	5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole	7.63 (d, 1H), 7,56 (s, 1H), 7.39 (t, 1H), 7.07 (d, 1H), 4.82 (s, 2H), 4.12 (q, 2H) and 1.42 (t, 3H).	
533	5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole	7.77 (s, 1H), 7,52 (d, 1H), 7.16 (m, 1H), 4.79 (s, 2H), 4.13 (q, 2H) and 1.42 (t, 3H).	
534	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.07 (dd, 1H), 7.56 (m, 1H), 7.24 (dd, 1H), 4.73 (s, 2H), 4.13 (q, 2H) and 1.42 (t, 3H).	
535	3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.40 (s, 1H), 8.34 (d, 1H), 7.91 (d, 1H), 7.01 (t, 1H), 4.73 (s, 2H), 4.12 (q, 2H) and 1.42 (t, 3H).	381.10
536	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole	7.75 (s, 1H), 7.63 (m, 1H), 7.40 (m, 2H), 6.73 (s, 1H), 4.65 (s, 2H), 4.07 (q, 2H) and 1.40 (t, 3H).	
537	3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-	7.58 (s, 1H), 7.46 (d, 1H), 7.32 (d, 3H), 4.74	

	trifluoromethyl-4H-[1,2,4]triazole	(s, 2H), 4.09 (q, 2H) and 1.39 (t, 3H).	
538	4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole	7.78 (s, 1H), 7.39 (m, 1H), 6.53 (d, 1H), 4.63 (s, 2H), 4.07 (q, 2H) and 1.39 (t, 3H).	
539	4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.73 (d, 1H), 7.83 (s, 1H), 7.76 (d, 1H), 7.47 (m, 3H), 7.27 (s, 1H), 4.65 (s, 2H), 3.67 (s, 3H), 2.69 (s, 3H).	
540	4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.74 (d, 1H), 7.82 (s, 1H), 7.67 (d, 1H), 7.56 (d, 1H), 7.51 (m, 1H), 7.48 (m, 1H), 7.46 (s, 1H), 4.65 (s, 2H), 3.67 (s, 3H), 2.69 (s, 3H).	
541	4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.73 (d, 1H), 7.82 (s, 1H), 7.75 (d, 1H), 7.63 (d, 2H), 7.51 (d, 2H), 4.65 (s, 2H), 3.65 (s, 3H), 2.69 (s, 3H).	
542	4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.73 (d, 1H), 7.83 (s, 1H), 7.45 (d, 1H), 7.61 (d, 2H), 7.04 (d, 2H), 4.62 (s, 2H), 3.89 (s, 3H), 3.64 (s, 3H), 2.69 (s, 3H).	
543	4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-	8.74 (d, 1H), 7.85 (s, 1H), 7.77 (d, 1H), 7.51 (d, 2H), 7.32 (d, 2H),	

	pyridine	4.70 (s, 2H), 4.03 (q, 2H), 2.70 (s, 3H), 2.45 (s, 3H), 1.31 (t, 3H).	
544	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole	(DMSO-D6 as solvent): 7.93(m, 1H), 7.86 (m, 2H), 7.80 (m,1H), 7.67 (m, 2H), 7.25 (m,1H), 4.61 (s, 2H), 4.16 (q, 2H), 1.24 (t, 3H).	388.10
545	4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.78(bs, 2H), 7.92 (m, 2H), 7.71 (d, 2H), 7.68 (m,1H), 7.27 (m,1H), 4.70 (s, 2H), 4.10 (q, 2H), 1.39 (t, 3H).	383.10
546	5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.50 (t, 1H), 7.21 (m, 2H), 7.00 (t, 1H), 4.68 (s, 2H), 4.07 (q, 2H), 1.35 (t, 3H).	
547	5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.02 (d, 1H), 7.59 (m, 2H), 7.52 (d, 1H), 7.41 (d, 1H), 7.04 (d, 1H), 4.73 (s, 2H), 4.21 (q, 2H), 1.42 (t, 3H).	
548	2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol	9.89 (s, 1H), 7.70 (s, 1H), 7.56 (d, 1H), 7.54 (d, 1H), 7.30 (m, 1H), 7.18 (m, 1H), 6.98 (d, 1H), 4.66 (s, 2H), 4.12	399.90

		(q, 2H), 2.34 (s, 3H), 1.37 (t, 3H).	
549	3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.73 (bs, 1H), 7.59 (m, 2H), 7.41 (m, 2H), 7.10 (dd, 1H), 6.59 (m, 2H), 5.05 (q, 1H), 4.13 (q, 2H), 1.91 (d, 3H), 1.27 (t, 3H).	401.10
550	4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.8 (dd, 2H), 7.74 (bs, 1H), 7.63 (m, 1H), 7.57 (dd, 2H), 7.40 (m, 2H), 6.62 (s, 2H), 5.15 (q, 1H), 4.05 (q, 2H), 1.95 (d, 3H), 1.34 (t, 3H).	
551	3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.52 (d, 2H), 7.49 (d, 1H), 7.01 (d, 2H), 4.69 (s, 2H), 4.02 (q, 4H), 1.82 (m, 2H), 1.51 (q, 2H), 1.32 (t, 3H), 1.01 (t, 3H).	
552	3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.12 (s, 1H), 8.00 (d, 1H), 7.58 (d, 1H), 7.51 (d, 1H), 7.09 (d, 2H), 6.96 (s, 1H), 6.08 (s, 2H), 4.67 (s, 2H), 4.02 (q, 2H), 1.31 (t, 3H).	
553	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-	8.11 (s, 1H), 7.48 (m, 2H), 7.16 (t, 1H), 4.63 (s, 2H), 4.13 (q, 2H),	391.90

	[1,2,4]oxadiazole	2.82 (s, 3H), 1.37 (t, 3H).	
554	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole	(DMSO-D6 as solvent): 8.21(m, 2H), 7.51 (m, 2H), 7.21 (m,3H), 4.63 (s, 2H), 4.16 (q, 2H), 1.38 (t, 3H).	
555	4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole	7.71 (dd, 1H), 7.59 (dd, 1H), 7.26 (m, 1H), 7.06 (m, 2H), 6.66 (d, 1H), 6.58 (dd, 1H), 5.06 (q, 1H), 4.13 (q, 2H), 2.39 (s, 3H), 1.91 (d, 3H), 1.28 (t, 3H).	
556	4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 7.71 (dd, 1H), 7.59 (dd, 2H), 7.23 (m, 1H), 7.06 (m, 1H), 6.64 (d, 1H), 5.15 (q, 1H), 4.01 (q, 2H), 2.39 (s, 3H), 1.94 (d, 3H), 1.30 (t, 3H).	410.10
557	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.66 (s, 1H), 7.58 (d, 1H), 7.52 (t, 1H), 7.37 (s, 1H), 4.69 (s, 2H), 4.09 (q, 2H), 3.93 (s, 3H), 1.37 (t, 3H).	
558	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.57 (d, 1H), 7.51 (t, 1H), 7.17 (s, 1H), 7.04 (s, 1H), 4.69 (s,	

		2H), 4.56 (q, 2H), 4.12 (s, 3H), 1.40 (t, 3H).	
559	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.65 (s, 1H), 7.57 (d, 1H), 7.48 (d, 2H), 4.60 (s, 2H), 4.50 (q, 2H), 3.79 (s, 3H), 1.36 (t, 3H).	
560	4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (bs, 2H), 7.70 (m, 1H), 7.61 (m, 3H), 7.44 (m, 2H), 4.65 (s, 2H), 4.09 (q, 2H), 2.31 (s, 3H), 1.40 (t, 3H).	
561	3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.70 (s, 1H), 7.60 (m, 2H), 7.43 (m, 2H), 7.10 (m, 1H), 6.59 (m, 1H), 4.59 (s, 2H), 4.23 (q, 2H), 2.28 (s, 3H), 1.38 (t, 3H).	
562	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole	7.61(d, 1H), 7.49 (m, 2H), 7.22 (m,2H), 4.59 (s, 2H), 4.16 (q, 2H),2.32 (s,3H), 1.38 (t, 3H).	
563	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.45 (d, 1H), 7.02 (d, 1H), 4.69 (s, 2H), 3.97 (q, 2H), 2.32 (s, 3H), 1.28 (t, 3H).	
564	5-(3-Chloro-phenyl)-3-[4-ethyl-5-	8.11 (s, 1H), 8.01 (d,	

	(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1H), 7.58 (d, 1H), 7.51 (t, 1H), 7.28 (s, 1H), 6.83 (d, 1H), 4.64 (s, 2H), 4.14 (q, 2H), 2.56 (s, 3H), 1.39 (t, 3H).	
565	4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (d, 2H), 7.99 (m, 1H), 7.90 (m, 1H), 7.60 (m, 2H), 7.48 (m, 2H), 4.65 (s, 2H), 4.10 (q, 2H), 1.39 (t, 3H).	
566	3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.99 (s, 1H), 7.90 (m, 1H), 7.60 (m, 1H), 7.47 (m, 2H), 7.12 (m, 1H), 6.60 (m, 1H), 4.59 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	
567	2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine	8.11 (s, 1H), 8.00 (d, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.40 (d, 2H), 4.71 (s, 2H), 4.10 (q, 2H), 2.64 (s, 3H), 1.40 (t, 3H).	
568	3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 7.99 (d, 1H), 7.58 (d, 1H), 7.51 (t, 1H), 7.07 (d, 1H), 6.52 (d, 1H), 4.64 (s, 2H), 4.23 (q, 2H), 1.40 (t, 3H).	
569	2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-	8.59 (d, 1H), 8.10 (s, 1H), 8.00 (d, 1H), 7.66 (s, 1H), 7.59 (d, 1H),	

	[1,2,4]triazol-3-yl}-pyridine	7.54 (d, 1H), 7.50 (d, 1H), 4.72 (s, 2H), 4.11 (q, 2H), 1.42 (t, 3H).	
570	2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine	8.11 (s, 1H), 8.00 (d, 1H), 7.58 (d, 1H), 7.50 (t, 1H), 7.24 (s, 1H), 6.91 (s, 1H), 4.70 (s, 2H), 4.08 (q, 2H), 4.02 (s, 3H), 1.39 (t, 3H).	464.10
571	2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile	8.02 (s, 1H), 7.76 (d, 2H), 7.47 (m,3H), 7.17 (t, 1H), 4.68 (s, 2H), 4.19 (q, 2H), 2.51 (s, 3H), 1.39 (t, 3H).	
572	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.14 (s, 1H), 8.03 (d, 1H), 7.58 (d, 1H), 7.50 (d, 1H), 7.44 (d, 1H), 6.94 (1H), 4.67 (s, 2H), 4.03 (q, 2H), 3.88 (s, 3H), 1.29 (t, 3H).	
573	3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.61 (m, 1H), 7.52 (d, 1H), 7.21 (d, 1H), 7.11 (m, 1H), 7.61 (m, 1H), 6.55 (s, 1H), 4.57 (s, 2H), 4.21 (q, 2H), 1.38 (t, 3H).	393.10
574	3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile	8.21(m, 1H), 8.04 (dd, 1H), 7.59 (m, 2H), 7.10 (dd,1H), 6.59 (dd,1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	

575	4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole	7.77 (m, 2H), 7.53 (d, 1H), 7.47 (m, 4H), 7.19 (dd, 1H), 6.71 (s, 1H), 4.61 (s, 2H), 4.12 (q, 2H) and 1.39 (t, 3H).	
576	4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole	7.77 (m, 3H), 7.50 (m, 5H), 6.69 (s, 1H), 4.56 (s, 2H) and 3.67 (s, 3H)	
577	4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole	7.77 (m, 2H), 7.61 (s, 1H), 7.46 (m, 3H), 7.14 (d, 1H), 6.69 (s, 1H), 6.60 (d, 1H), 4.60 (s, 2H), 4.22 (q, 2H) and 1.38 (t, 3H).	
578	4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (w, 2H), 7.77 (m, 2H), 7.61 (d, 2H), 7.45 (m, 3H), 6.71 (s, 1H), 4.65 (s, 2H), 4.06 (q, 2H) and 1.39 (t, 3H).	
579	4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (w, 2H), 7.77 (m, 2H), 7.63 (d, 2H), 7.46 (m, 3H), 6.70 (s, 1H), 4.60 (s, 2H) and 3.68 (s, 3H).	
580	2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole	7.80 (m, 2H), 7.70 (m, 1H), 7.35(m, 2H), 7.13 (m, 2H), 6.60 (m, 1H), 4.74 (s, 2H), 4.23 (q, 2H), 2.40 (s, 3H), 1.36 (t, 3H).	368.10
581	4-[4-Methyl-5-(5-m-tolyl-	8.81 (m, 2H), 7.80 (m,	365.10

	[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	2H), 7.61 (d, 2H), 7.39 (m, 2H), 4.74 (s, 2H), 3.71 (s, 3H), 2.4 (s, 3H).	
582	4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (d, 2H), 7.81 (m, 2H), 7.58 (m, 2H), 7.37 (m, 2H), 4.81 (s, 2H), 4.41 (q, 2H), 2.42 (s, 3H), 1.33 (t, 3H).	379.10
583	4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (d, 2H), 7.98 (m, 1H), 7.58 (d, 2H), 7.46 (d,1H), 4.66 (s, 2H), 4.10 (q, 2H), 1.38 (t,3H).	405.90
584	3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.79 (bs, 2H), 8.46 (m, 1H), 7.91 (m, 1H), 7.59 (d,2H), 7.43 (t, 1H), 4.74 (s, 2H), 4.12 (q, 2H), 1.41 (t,3H).	
585	3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.45(dd, 1H), 7.91 (m, 1H), 7.59 (d, 1H), 7.43 (t, 1H), 7.10 (d,1H), 6.58 (dd,1H), 4.65 (s, 2H), 4.27 (q, 2H), 1.39 (t, 3H).	397.10
586	3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.45 (dd, 1H), 7.90 (m, 1H), 7.47 (m,3H), 7.18 (t, 1H), 4.68 (s, 2H), 4.17 (q, 2H), 1.41 (t, 3H).	
587	3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-	8.41 (m, 2H), 7.89 (d, 1H), 7.69 (d, 1H), 7.13	379.10

	[1,2,4]oxadiazol-5-yl]-benzonitrile	(m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.27 (q, 2H), 1.40 (t, 3H).	
588	3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile	8.36 (m, 2H), 7.80 (t, 1H), 7.62 (m, 2H), 7.15 (m, 1H), 6.61 (m, 1H), 4.78 (s, 2H), 4.2 (q, 2H), 1.40 (t, 3H).	379.10
589	3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.41 (m, 2H), 7.90 (m, 1H), 7.72 (t, 1H), 4.68 (s, 2H), 3.73 (s, 3H).	
590	5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.08 (m, 1H), 7.58 (m, 1H), 7.25 (m, 1H), 4.67 (s, 2H), 3.74 (s, 3H).	394.90
591	2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.63 (m, 1H), 8.02 (m, 1H), 7.89 (m, 1H), 7.61 (m, 1H), 7.14 (m, 1H), 6.61 (m, 1H), 4.67 (s, 2H), 4.27 (q, 2H), 1.40 (t, 3H).	390.00
592	2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.63 (d, 1H), 8.00 (d, 1H), 7.88 (m, 1H), 7.62 (d, 1H), 7.14 (d, 1H), 6.61 (m, 1H), 4.60 (s, 2H), 3.82 (s, 3H).	
593	2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	7.98 (m, 2H), 7.89 (d, 1H), 7.49 (m, 1H), 7.44 (m, 1H), 4.69 (s, 2H), 3.92 (s, 3H), 2.77 (s,	

		3H).	
594	2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.91 (s, 1H), 8.24 (s, 1H), 7.98 (s, 1H), 7.91 (d, 1H), 7.49 (m, 1H), 7.43 (m, 1H), 4.72 (s, 2H), 3.96 (s, 3H).	
595	2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.00 (s, 1H), 7.89 (d, 1H), 7.60 (s, 1H), 7.53 (m, 1H), 7.43 (m, 1H), 7.12 (d, 1H), 6.60 (d of d, 1H), 4.68 (s, 2H), 3.80 (s, 3H).	
596	2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.00 (s, 1H), 7.90 (d, 1H), 7.52 (m, 2H), 4.86 (s, 2H), 4.13 (q, 2H), 1.42 (t, 3H).	
597	4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 7.68 (s, 1H), 7.59 (d, 2H), 7.23 (m,1H), 4.63 (s, 2H), 4.10 (q, 2H), 2.32 (d,3H), 1.37 (t,3H).	
598	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole	7.67 (d, 1H), 7.59 (m, 1H), 7.2 (s, 1H), 7.09 (d, 1H), 6.58 (dd,1H), 4.56 (s, 2H), 4.24 (q, 2H), 2.32 (s, 3H), 1.36 (t, 3H).	374.00
599	3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.02 (m, 1H), 7.91 (m, 1H), 7.57 (d, 1H), 7.35 (m, 2H), 7.08 (d, 1H), 6.56 (dd,1H), 4.72 (s,	

		2H), 4.22 (q, 2H), 2.32 (s, 3H), 1.36 (t, 3H).	
600	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (dd, 2H), 8.02 (m,1H), 7.92 (m, 1H), 7.57 (dd, 2H), 7.42 (m,2H), 4.80 (s, 2H), 4.08 (q, 2H), 1.38 (t,3H).	
601	4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.87 (m, 3H), 8.42 (m, 2H), 7.75 (t, 1H), 7.66 (d, 2H), 4.88 (s, 2H), 4.15 (q, 2H), 1.45 (t, 3H).	
602	2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole	8.87 (t, 1H), 8.39 (m, 2H), 7.73 (t, 1H), 7.61 (m, 1H), 7.15 (m, 1H), 6.61 (m, 1H), 4.28 (q, 2H), 1.78 (s, 2H), 1.41 (t, 3H).	
603	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 7.78 (m, 3H), 7.66 (m, 1H), 7.39 (m, 2H), 6.84 (s, 1H), 4.69 (s, 2H), 3.27 (m, 1H), 1.20 (q, 2H), 0.83 (m, 2H).	411.00
604	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole	7.77 (m, 1H), 7.65 (m, 1H), 7.56 (m, 2H), 7.41 (m, 2H), 7.04 (m, 2H), 6.79 (s, 1H), 4.61 (s, 2H), 3.97 (q, 2H), 3.89 (s, 3H), 1.32 (t, 3H).	428.20

605	5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole	8.08 (m, 1H), 7.96 (dd, 1H), 7.45 (m, 4H), 7.17 (m, 1H), 4.93 (q, 1H), 3.67 (s, 3H), 1.91 (d,3H).	404.92
606	5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole	8.1(d, 1H), 7.98 (d, 1H), 7.51 (m,4H), 7.17 (t, 1H), 5.11 (q, 1H), 4.11 (q, 2H), 1.93 (d,3H), 1.34 (t, 3H).	418.90
607	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.08 (m,1H), 7.98 (dd, 1H), 7.59 (m, 3H), 7.46 (t, 1H), 5.05 (q, 1H), 3.66 (s, 3H), 1.94 (d, 3H).	400.07
608	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.10 (m,1H), 7.99 (dd, 1H), 7.58 (m, 3H), 7.47 (t, 1H), 5.20 (q, 1H), 4.06 (q, 2H), 1.96 (d, 3H), 1.33 (t,3H).	414.05
609	3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.84 (s, 2H), 8.30 (m, 2H), 7.85 (m, 1H), 7.66 (m, 3H), 4.84 (s, 2H), 4.14 (q, 2H), 1.43 (t, 3H).	
610	3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.27 (m, 2H), 7.82 (m, 1H), 7.62 (m, 2H), 7.18 (t, 1H), 6.62 (m, 1H), 4.79 (s, 2H), 4.27 (q, 2H), 1.40 (t, 3H).	

611	3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.83 (d, 2H), 8.31 (m, 2H), 7.84 (m, 4H), 4.81 (s, 2H), 3.77 (s, 3H).	
612	3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.82 (s, 2H), 8.33 (m, 2H), 7.86 (t, 3H), 7.67 (t, 1H), 4.91 (d, 2H), 1.24 (m, 3H), 0.88 (m, 2H).	402.20
613	4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent): 8.80 (s (br), 2H), 7.96 (m, 2H), 7.81(d,2H), 7.61 (m, 2H), 4.73 (s, 2H), 3.84 (s, 3H).	
614	4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent): 8.75 (d, 2H), 8.02 (s, 1H), 7.96 (d, 1H), 7.89 (d, 2H), 7.60 (m, 2H), 4.89 (s, 2H), 3.59 (m, 1H), 1.21 (m, 2H), 0.84 (m, 2H).	412.16
615	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	7.80 (m, 2H), 8.04 (m, 1H), 7.77 (d, 2H), 7.51 (m, 1H), 7.21 (t, 1H), 4.92 (s, 2H), 3.32 (m, 1H), 1.21 (m, 2H), 0.85 (m, 2H).	430.11
616	2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	8.02 (m, 1H), 7.52 (m, 3H), 7.20 (t, 1H), 7.04 (m, 2H), 4.81 (s, 2H), 4.03 (q, 2H), 3.89 (s, 3H), 1.33 (t, 3H).	

617	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (d, 2H), 8.03 (m, 1H), 7.65 (m, 2H), 7.51 (m, 1H), 7.20 (t, 1H), 4.78 (s, 2H), 3.75 (s, 3H).	
618	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (bs, 2H), 8.02 (m, 1H), 7.61 (m, 2H), 7.51 (m, 1H), 7.20 (t, 1H), 4.85 (s, 2H), 4.13 (q, 2H), 1.41 (t, 3H).	
619	2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	8.01 (d of d collapsed, 1H), 7.85 (d, 1H), 7.51(m, 4H), 7.00(d, 2H), 4.79 (s, 2H), 4.00 (q, 2H), 3.88 (s, 3H), 1.30 (t, 3H).	
620	2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole	7.97 (s, 1H), 7.84 (d, 1H), 7.58 (d, 1H), 7.49 (m, 1H), 7.40 (m, 1H), 7.12 (d, 1H), 6.59 (d of d, 1H), 5.16 (q, 1H), 4.17 (q, 2H), 2.02 (d, 3H), 1.28 (t, 3H).	
621	5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole	8.06 (m, 1H), 7.54 (m, 3H), 7.23 (m, 2H), 4.93 (q, 1H), 3.72 (s, 3H), 1.91 (d,3H).	
622	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.07 (dd,1H), 7.62 (dd, 2H), 7.54 (m, 1H), 7.21 (t, 1H), 5.07 (q, 1H), 3.69	418.10

		(s, 3H), 1.95 (d, 3H).	
623	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.08 (m,1H), 7.57 (m, 3H), 7.22 (t, 1H), 5.21 (q, 1H), 4.08 (q, 2H), 1.97 (d, 3H), 1.35 (t,3H).	
624	2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.83 (m, 2H), 8.65 (m, 1H), 8.05 (t, 1H), 7.92 (t, 1H), 7.76 (t, 2H), 4.82 (2H), 3.31 (m, 1H), 1.23 (m, 2H), 0.86 (m, 2H).	
625	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (t, 2H), 7.82 (m, 1H), 7.63 (m, 2H), 7.32 (m, 1H), 7.10 (m, 1H), 4.75 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H), 1.61 (d, 1H).	
626	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 7.82 (m, 1H), 7.59 (t, 2H), 7.33 (m, 1H), 7.11 (m, 1H), 4.82 (s, 2H), 4.10 (m, 2H), 2.39 (s, 3H), 1.38 (t, 3H).	397.08
627	4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (s, 2H), 7.84 (m, 1H), 7.76 (d, 2H), 7.32 (m, 1H), 7.12 (q, 1H), 4.91 (s, 2H), 3.31 (m, 1H), 2.39 (d, 3H),1.21 (m, 2H), 0.84 (m, 2H).	409.15
628	2-(4-Ethyl-5-furan-2-yl-4H-	7.77 (m, 1H), 7.61 (m,	

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	[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole	1H), 7.32 (d, 1H), 7.12 (m, 2H), 6.61 (m, 1H), 4.76 (s, 2H), 4.26 (q, 2H), 2.37 (d, 3H), 1.23 (t, 3H).	
629	2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole	7.81 (m, 1H), 7.54 (m, 2H), 7.32 (d, 1H), 7.11 (m, 1H), 7.03 (m, 2H), 4.79 (s, 2H), 4.02 (q, 2H), 3.89 (s, 3H), 2.37 (d, 3H), 1.31 (t, 3H).	426.15
630	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (dd, 2H), 7.91 (dd, 1H), 7.60 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.86 (d, 1H), 4.67 (s, 2H), 4.05 (q, 2H), 1.37 (t, 3H).	417.02
631	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (dd, 2H), 7.91 (dd, 1H), 7.59 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.74 (d, 1H), 5.20 (q, 1H), 4.05 (q, 2H), 1.95 (d, 3H), 1.34 (t, 3H).	431.10
632	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (dd, 2H), 7.91 (dd, 1H), 7.63 (dd, 2H), 7.39 (m, 1H), 7.15 (m, 1H), 6.85 (d, 1H), 4.62 (s, 2H), 3.69 (s, 3H).	403.10
633	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-	8.81 (dd, 2H), 7.91 (dd, 1H), 7.60 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H),	417.10

	[1,2,4]triazol-3-yl)-pyridine	6.72 (d, 1H), 5.06 (q, 1H), 3.64 (s, 3H), 1.93 (d, 3H).	
634	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 7.92 (dd, 1H), 7.76 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.95 (d, 1H), 4.71 (s, 2H), 3.27 (m, 1H), 1.18 (m, 2H), 0.82 (m, 2H).	429.10
635	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (dd, 2H), 7.92 (dd, 1H), 7.76 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.85 (d, 1H), 5.40 (q, 1H), 3.24 (m, 1H),1.98 (d, 3H), 1.88 (m, 2H), 0.80 (m, 2H).	443.20
636	3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.90 (dd, 1H), 7.60 (dd, 1H), 7.39 (m, 1H), 7.11 (m, 2H), 6.85 (d, 1H), 6.59 (dd, 1H), 4.62 (s, 2H), 4.20 (q, 2H), 1.38 (t, 3H).	
637	3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.88 (dd, 1H), 7.59 (dd, 1H), 7.39 (m, 1H), 7.11 (m, 2H), 6.74 (d, 1H), 6.58 (dd, 1H), 5.08 (q, 1H), 4.20 (q, 2H), 1.92 (d, 3H), 1.34 (t, 3H).	
638	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-	1.96 (d, 3 H) 3.61 (s, 3 H) 5.10 (q, 1 H) 7.38 (t, 1 H) 7.47 (m, 1 H) 7.54	

	[1,2,4]triazol-3-yl)-pyridine	(m, 2 H) 7.84 (m, 1 H) 7.93 (m, 1 H) 8.74 (d, 2 H)	
639	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.80 (bs, 2H), 7.99 (m, 1H), 7.90 (m, 1H), 7.58 (d, 2H), 7.51 (m, 1H), 7.46 (t, 1H), 5.31 (q, 1H), 4.06 (q, 2H), 2.04 (d, 3H), 1.31 (t, 3H).	414.10
640	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (bs, 2H), 8.03 (m, 1H), 7.94 (d, 1H), 7.76 (d, 2H), 7.51 (m, 1H), 7.45 (t, 1H), 7.54 (q, 1H), 3.25 (m, 1H), 2.06 (d, 3H), 1.19 (m, 2H), 0.81 (m, 2H).	426.07
641	5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (dd, 1H), 7.60 (d, 1H), 7.55 (m, 1H), 7.22 (t, 1H), 7.09 (d, 1H), 6.58 (m,1H), 4.55 (s, 2H), 3.81 (s, 3H).	
642	5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (dd, 1H), 7.89 (d, 1H), 7.55 (m, 2H), 7.22 (t, 1H), 6.88 (dd,1H), 4.55 (s, 2H), 3.67 (s, 3H).	
643	4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol	10.08(s,1H), 7.88(d, 1H), 7.47 (m, 3H), 7.17 (t,1H), 7.06 (d, 1H), 4.68 (s, 2H), 4.14 (q, 2H), 1.38 (t, 3H).	

644	2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.83 (d, 2H), 8.60 (m, 1H), 7.94 (m, 1H), 7.85 (m, 1H), 7.62 (m, 2H), 4.82 (s, 2H), 3.75 (s, 3H).	
645	2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.82 (d, 2H), 8.60 (m, 1H), 7.94 (m, 1H), 7.86 (m, 1H), 7.59 (m, 2H), 4.87 (s, 2H), 4.12 (q, 2H), 1.43 (t, 3H).	
646	2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.81 (d, 2H), 8.60 (m, 1H), 7.96 (m, 1H), 7.86 (m, 1H), 7.75 (m, 2H), 4.92 (s, 2H), 3.32 (m, 1H), 1.21 (m, 2H), 0.87 (q, 2H).	
647	2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.57 (m, 1H), 7.92 (m, 1H), 7.81 (m, 1H), 7.61 (m, 1H), 7.12 (m, 1H), 6.61 (m, 1H), 4.79 (s, 2H), 4.26 (q, 2H), 1.40 (t, 3H).	
648	2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine	8.59 (m, 1H), 7.94 (m, 1H), 7.84 (m, 1H), 7.55 (m, 2H), 7.05 (m, 2H), 4.83 (s, 2H), 4.02 (q, 2H), 1.34 (t, 3H).	
649	2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	8.00 (m, 1H), 7.87 (d, 1H), 7.53 (m, 3H), 7.42 (t, 1H), 7.01 (m, 2H), 5.07 (q, 1H), 3.88 (s,	

		3H), 3.54 (s, 3H), 2.00 (d, 3H).	
650	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (bs, 2H), 8.01 (m, 1H), 7.63 (d, 2H), 7.50 (m, 1H), 7.18 (m, 1H), 5.17 (q, 1H), 3.69 (s, 3H), 2.02 (d, 3H).	
651	5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.20 (m, 1H), 7.65 (m, 1H), 7.60 (s, 1H), 7.13 (m, 2H), 6.56 (m, 1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	
652	2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	8.02 (d, 1H), 7.90 (d, 1H), 7.50 (m, 4H), 7.03 (d, 2H), 4.71 (s, 2H), 3.88 (s, 3H), 3.61 (s, 3H).	
653	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 8.09 (t, 1H), 7.97 (m, 1H), 7.76 (d, 2H), 7.45 (m, 2H), 4.89 (s, 2H), 3.30 (m, 1H), 1.22 (m, 2H), 0.86 (m, 2H).	412.07
654	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.78 (s, 2H), 8.14 (m, 1H), 8.04 (m, 1H), 7.77 (t, 2H), 7.54 (m, 2H), 4.79 (s, 2H), 3.29 (m, 1H), 1.21 (m, 2H), 0.85 (d, 2H).	
655	4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-	8.79 (s, 2H), 7.79 (t, 1H), 7.61 (t, 2H), 7.33	

	ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	(m, 1H), 7.08 (m, 1H), 5.09 (m, 1H), 3.65 (s, 3H), 2.37 (s, 3H), 2.02 (d, 3H).	
656	4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (m, 2H), 8.23 (m, 1H), 7.79 (d, 2H), 7.32 (m, 1H), 7.09 (m, 1H), 5.28 (m, 1H), 4.07 (m, 2H), 2.37 (s, 3H), 2.04 (d, 3H), 1.24 (m, 3H).	
657	4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (m, 2H), 7.82 (d, 1H), 7.74 (d, 2H), 7.31 (m, 1H), 7.11 (m, 1H), 5.51 (m, 1H), 3.23 (m, 1H), 2.38 (s, 3H), 2.06 (d, 3H), 1.16 (m, 2H), 0.78 (m, 2H).	
658	4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.83 (m, 2H), 7.78 (m, 1H), 7.59 (m, 2H), 7.33 (m, 1H), 7.10 (m, 1H), 5.26 (m, 1H), 3.90 (m, 2H), 2.37 (s, 3H), 2.03 (d, 3H), 0.92 (m, 1H), 0.48 (m, 2H), 0.21 (m, 2H).	
659	2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	7.98 (s, 1H), 7.75 (m, 1H), 7.31 (m, 1H), 7.08 (m, 1H), 5.03 (q, 1H), 3.85 (s, 3H), 2.75 (s, 3H), 2.35 (s, 3H), 1.98 (d, 3H).	

660	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.80 (m, 2H), 8.01 (m, 1H), 7.58 (m, 2H), 7.49 (m, 1H), 7.19 (m, 1H), 5.32 (q, 1H), 4.08 (q, 2H), 2.04 (d, 3H), 1.35 (t, 3H).	
661	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (d, 2H), 8.03 (m, 1H), 7.75 (m, 2H), 7.50 (m, 1H), 7.20 (m, 1H), 5.55 (q, 1H), 3.26 (s, 1H), 2.06 (d, 3H), 1.18 (m, 2H), 0.81 (m, 2H).	
662	2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole	8.97 (m, 1H), 7.59 (m, 1H), 7.47 (m, 1H), 7.17 (m, 1H), 7.12 (m, 1H), 6.59 (m, 1H), 5.18 (q, 1H), 4.21 (q, 2H), 2.00 (d, 3H), 1.33 (t, 3H).	
663	2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	7.99 (s, 1H), 7.96 (m, 1H), 7.48 (m, 1H), 7.17 (t, 1H), 7.06 (q, 1H), 3.86 (s, 3H), 2.75 (s, 3H), 1.98 (d, 3H).	
664	4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (dd, 2H), 7.71 (dd, 1H), 7.58 (dd, 2H), 7.25 (m, 1H), 7.08 (m, 1H), 6.62 (d, 1H), 5.12 (q, 1H), 3.87 (dd, 2H), 2.40 (s, 3H), 1.94 (d, 3H), 0.90 (m, 1H), 0.49 (m, 2H), 0.19 (m, 2H).	

665	4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (bs, 2H), 7.92 (d, 1H), 7.80 (dd, 1H), 7.60 (d, 2H), 7.50 (m,1H), 7.25 (m, 1H), 5.05 (q, 2H), 3.65 (s, 3H), 1.94 (d, 3H).	
666	4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.76 (d, 2H), 7.95 (d, 1H), 7.85 (dd, 1H), 7.75 (d, 2H), 7.50 (m,1H), 7.25 (m, 1H), 5.45 (q, 2H), 3.20 (m, 1H), 1.98 (d, 3H) 1.22 (m, 2H), 0.88 (m, 2H).	
667	4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.65 (d, 1H), 7.71 (s, 1H), 7.63 (d, 1H), 7.54 (d, 2H), 7.00 (d, 2H), 5.10 (q, 1H), 3.87 (s, 3H), 3.53 (s, 3H), 2.58 (s, 3H), 2.00 (d, 3H).	
668	4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.65 (d, 1H), 7.71 (s, 1H), 7.63 (d, 1H), 7.49 (d, 2H), 7.01 (d, 2H), 5.26 (q, 1H), 3.96 (q, 2H), 3.88 (s, 3H), 2.62 (s, 3H), 2.02 (d, 3H), 1.24 (t, 3H).	
669	4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine	8.79 (d, 2H), 8.67 (d, 1H), 7.73 (s, 1H), 7.65 (d, 1H), 7.55 (d, 2H), 5.33 (q, 1H), 4.08 (q, 2H), 2.64 (s, 3H), 2.03	

		(d, 3H), 1.30 (t, 3H).	
670	4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine	8.77 (d, 2H), 8.68 (d, 1H), 7.72 (m, 4H), 5.55 (q, 1H), 3.24 (m, 1H), 2.64 (s, 3H), 2.04 (d, 3H), 1.16 (m, 2H), 0.81 (m, 2H).	
671	4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine	8.61 (d, 1H), 7.57 (m, 3H), 7.08 (d, 1H), 6.57 (d, 1H), 5.02 (q, 1H), 3.70 (s, 3H), 1.96 (d, 3H).	
672	2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	7.99 (s, 1H), 7.94 (m,1H), 7.86 (m, 1H), 7.48 (m, 1H), 7.39 (m, 1H), 5.03 (q, 1H), 3.82 (t, 3H), 2.73 (d, 3H), 1.98 (d, 3H).	
673	3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.88 (s, 1H), 8.76 (d, 1H), 8.00 (m, 2H), 7.90 (d, 1H), 7.48 (m, 3H), 5.14 (q, 1H), 3.60 (s, 3H), 2.02 (d, 3H).	
674	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine	8.66 (d, 1H), 7.99 (m, 1H), 7.88 (m, 1H), 7.51 (m, 1H), 7.43 (m, 2H), 7.34 (d, 1H), 5.13 (q, 1H), 3.61 (s, 3H), 2.63 (s, 3H), 2.00 (d, 3H).	
675	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-	8.68 (dd, 2H), 8.05 (d, 1H), 7.92 (d, 1H), 7.67	

	ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	(dd, 2H), 7.51 (d, 1H), 7.37 (t, 1H) 5.37 (q, 1H), 3.18 (m, 1H), 1.90 (d, 3H), 1.08 (m, 2H), 0.74 (m, 2H).	
676	5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole	8.01 (s, 1H), 7.90 (d, 1H), 7.50 (m, 3H), 7.38 (t, 1H), 6.92 (d, 2H), 4.88 (q, 1H) 3.78 (s, 3H), 3.47 (s, 3H), 1.83 (d, 3H).	
677	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.70 (dd, 2H), 8.05 (m, 1H), 7.67 (m, 2H), 7.46 (m, 1H), 7.18 (m, 1H), 5.41 (q, 1H), 3.18 (m, 1H), 1.90 (d, 3H), 1.08 (m, 2H), 0.74 (m, 2H).	
678	5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole	8.05 (m, 1H), 7.56 (m, 3H), 7.21 (t, 1H), 7.00 (m, 3H), 5.01 (q, 1H), 3.85 (s, 3H), 3.56 (s, 3H), 1.90 (d, 3H).	
679	4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine	8.79 (d, 2H), 8.67 (d, 1H), 7.75 (s, 1H), 7.67 (d, 1H), 7.56 (d, 2H), 4.82 (s, 2H), 4.10 (q, 2H), 2.64 (s, 3H), 1.39 (t, 3H).	
680	4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-	8.78 (d, 3H), 8.68 (d, 1H), 7.74 (m, 4H), 4.90 (s, 2H), 3.30 (m, 1H),	

	2-yl]-2-methyl-pyridine	2.65 (s, 3H), 1.21 (m, 2H), 0.84 (m, 2H).	
681	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 8.12 (m, 1H), 7.76 (m, 2H), 7.57 (m, 1H), 7.25 (m, 1H), 4.81 (s, 2H), 3.31 (m, 1H), 1.20 (m, 2H), 0.85 (m, 2H).	
682	4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine	8.66 (d, 1H), 7.72(s, 1H), 7.65 (d, 1H), 7.60 (d, 1H), 7.11 (d, 1H), 6.60(d of d, 1H), 4.70 (s, 2H), 3.80 (s, 3H), 2.64 (s, 3H).	
683	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (bs, 2H), 7.98 (m, 1H), 7.88 (m, 1H), 7.51 (m, 4H), 5.30 (q, 1H), 3.90 (m, 2H), 2.05 (t, 3H), 0.94 (ms, 1H), 0.50 (m, 2H), 0.19 (m, 2H).	
684	4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.66 (d, 1H), 7.72 (s, 1H), 7.60 (m, 3H), 7.17 (m, 3H), 5.13 (q, 1H), 3.57 (s, 3H), 2.63 (s, 3H), 2.00 (d, 3H).	
685	4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.65 (d, 1H), 7.72 (s, 1H), 7.66 (d, 1H), 7.48-7.20 (m, 4H), 5.15 (q, 1H), 3.60 (s, 3H), 2.63 (s, 3H), 2.01 (d, 3H).	
686	3-[3-(4-Cyclopropyl-5-pyridin-4-yl-	8.77 (dd, 2H), 8.49	

	4H-[1,2;4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	(dd,1H), 7.90 (m, 1H), 7.74 (dd, 2H), 7.43 (t, 1H), 4.81 (s, 2H), 3.31 (m, 1H), 1.21 (m, 2H), 0.83 (m, 2H).	
687	4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol	10.15 (bs, 1H), 8.77 (dd, 2H), 7.89 (d,1H), 7.75 (dd, 2H), 7.45 (dd, 1H), 7.06 (d, 1H), 4.79 (s, 2H), 3.29 (m, 1H), 1.21 (m, 2H), 0.83 (m, 2H).	
688	4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.77 (dd, 2H), 7.72 (m, 3H), 7.62 (dd, 1H), 7.43 (t, 1H), 7.14 (m, 1H), 4.77 (s, 2H), 3.88 (s, 3H), 3.28 (m, 1H), 1.17 (m, 2H), 0.84 (m, 2H).	
689	4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.7 (q, 2H), 7.81 (d, 1H), 7.7 (q, 2H), 7.29 (m, 1H), 7.1 (t, 1H), 4.71 (s, 2H), 3.23 (m, 1H), 2.32 (s, 3H), 1.11 (m, 2H), 0.76 (m, 2H)	
690	4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.67 (m, 2H), 7.82 (m, 1H), 7.72 (m, 1H), 7.66 (m, 1H), 7.42 (m, 1H), 7.21 (m, 1H), 4.68 (s, 1H), 3.23 (m, 1H), 1.11 (m, 2H), 0.75 (m, 2H)	
691	4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-	8.69 (q, 2H), 7.85 (m, 2H), 7.67 (q, 2H), 7.32	

	ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	(m, 2H), 4.69 (s, 2H), 3.2 (m, 1H), 2.35 (s, 3H), 1.11 (m, 2H), 0.76 (m, 2H)	
692	3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.71 (b s, 2H), 8.36 (m, 1H), 8.28 (d, 1H), 7.83 (d d, 1H), 7.67 (m, 3H), 4.72 (s, 2H), 3.23 (m, 1H), 1.14 (m, 2H), 0.77 (m, 2H)	
693	4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.75 (t, 2H), 7.79 (m, 2H), 7.26 (m, 2H), 4.78 (s, 2H), 3.28 (m, 1H), 1.14 (m, 2H), 0.82 (m, 2H)	
694	4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.67 (d d, 2H), 7.87 (m, 2H), 7.67 (d d, 2H), 7.33 (m, 2H), 5.36 (q, 1H), 3.15 (m, 1H), 2.36 (s, 3H), 1.92 (d, 3H), 1.07 (m, 2H), 0.72 (m, 2H)	
695	4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.69 (m, 2H), 7.6 (m, 3H), 7.52 (m, 1H), 7.35 (t, 1H), 7.04 (d d, 1H), 5.35 (q, 1H), 3.81 (s, 3H), 3.15 (m, 1H), 1.91 (d, 3H), 1.11 (m, 2H), 0.7 (m, 2H)	
696	4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-	8.69 (d, 2H), 7.78 (m, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.24 (m, 1H),	

	4H-[1,2,4]triazol-3-yl}-pyridine	4.72 (s, 2H), 3.22 (m, 1H), 2.31 (s, 3H), 1 (m, 2H), 0.76 (m, 2H)	
697	2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol	9.89 (s, 1H), 8.7 (m, 2H), 7.68 (m, 3H), 7.2 (m, 1H), 6.92 (d, 1H), 4.72 (s, 2H), 3.22 (m, 1H), 2.26 (s, 3H), 1.01 (m, 2H), 0.74 (m, 2H)	
698	4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.69 (d d, 2H), 7.8 (q, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.22 (m, 1H), 5.4 (q, 1H), 3.16 (m, 1H), 2.32 (s, 3H), 1.93 (d, 3H), 1.09 (m, 2H), 0.73 (m, 2H)	

Example 699

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol

[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-methanol (32 mg, 0.14 mmol), 4-methyl-5-thiophene-3-yl-4H-[1,2,4]triazole-3-thiol (41 mg, 0.21 mmol) and potassium carbonate (29 mg, 0.21 mmol) was dissolved in anhydrous acetonitrile and refluxed under nitrogen atmosphere for 1 h. The solvent was removed in vacuo and the residue was dissolved in NaHCO3 (aq) and extracted with dichloromethane (*3). The organic phase was dried (MgSO4), filtered and concentrated. The title compound was isolated as an colorless oil (43 mg, 80%) by flash chromatography using 3% methanol in dichloromethane. 1H NMR (CDCl3), δ (ppm): 8.07 (s, 1H), 7.98 (d, 1H), 7.60 (d, 1H), 7.52-7.45 (m, 3H), 7.16 (dd, 1H), 5.29 (s, 2H), 4.75 (s, 2H), 4.50 (s, 2H), 3.71 (s, 1H).

The following compounds were prepared analogously to Example 699:

Example No.	Name	1H NMR	MS
700	3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol		
701	5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.5 (m, 1 H) 1.8 (m, 2 H) 2.0 (m, 1 H) 3.7 (m, 1 H) 3.8 (m, 1 H) 4.1 (s,m, 3 H) 4.5 (dd, 2 H) 7.1 (dd, 1 H) 7.4 (t, 2 H) 7.5 (m, 2 H) 7.9 (dd, 1 H) 8.0 (m, 1 H	460
702	(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol	0.8 (2 d, 6 H) 2.0 (m, 1 H) 3.5 (dd, 1 H) 3.6 (dd, 1 H) 4.5 (s, 2 H) 6.3 (d, 1 H) 7.3 (m, 3 H) 7.5 (apparent triplett, 1 H) 7.6 (m, 2 H) 8.0 (apparent d, 1 H) 8.1 (m, 1 H)	490
703	5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	2.4 (s, 3 H) 4.6 (s, 2 H) 4.8 (q, J=7.7 Hz, 2 H) 7.1 (m, 1 H) 7.2 (m, 1 H) 7.4 (m, 1 H) 7.5 (m, 1 H) 7.6 (m, 1 H) 7.8 (m, 1 H)	455.9

Example 704

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

5-Chloromethyl-3-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole (23 mg, 0.10 mmol) and 4-ethyl-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione (23 mg, 0.11 mmol) was dissolved in anhydrous DMF (1 ml) and potassium carbonate (21 mg, 0.15 mmol) was

added. After stirring for 22 h ethyl acetate was added, the resulting mixture was washed twice with water and once with brine, dried over MgSO4 and evaporated. Flash chromatography using heptane:ethyl acetate 1:1 yielded the title compound (20 mg, 50%). 1H NMR (CDCl3) d (ppm): 7.64 (m, 1H), 7.45 (d, 1H), 7.39 (d, 1H), 7.10 (m, 3H), 4.70 (s, 2H), 4.08 (q, 2H), 1.32 (t, 3H).

The following compounds were prepared analogously to Examples 704:

Example No.	Name	1H NMR	MS
705	5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.71 (s, 3 H) 4.51 (s, 2 H) 6.88 (dd, 1 H) 7.17 (dd, 1 H) 7.48 (dd, 1 H) 7.51 (dd, 1 H) 7.54 (t, 1 H) 8.18 (m, 1 H)	345.92
706	3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.78 (s, 3 H) 4.64 (s, 2 H) 6.57 (dd, 1 H) 7.09 (d, 1 H) 7.38 (t, 1 H) 7.46 (m, 1 H) 7.58 (d, 1 H) 7.91 (d, 1 H) 8.01 (m, 1 H)	373.96
707	3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.63 (s, 3 H) 4.64 (s, 2 H) 6.85 (d, 1 H) 7.39 (t, 1 H) 7.47 (dt, 1 H) 7.56 (t, 1 H) 7.87 (br. s, 1 H) 7.91 (dt, 1 H) 8.01 (t, 1 H)	373.96
708	5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.77 (s, 3 H) 4.50 (s, 2 H) 6.55 (dd, 1 H) 7.07 (d, 1 H) 7.43 (t, 1 H) 7.55 (m, 2 H) 7.95 (dt, 1 H) 8.05 (t, 1 H)	373.96
709	5-(3-Chloro-phenyl)-3-(5-furan-3-	3.63 (s, 3 H) 4.49 (s, 2	373.97

	yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	H) 6.84 (br. s, 1 H) 7.43 (t, 1 H) 7.54 (m, 2 H) 7.87 (s, 1 H) 7.94 (d, 1 H) 8.04 (m, 1 H)	
710	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	4.06 (s, 3 H) 4.63 (s, 2 H) 7.43 (t, 1 H) 7.53 (m, 1 H) 7.95 (d, 1 H) 8.05 (t, 1 H) 8.27 (dd, 1 H) 8.85 (d, 1 H) 9.25 (d, 1 H)	385.97
711	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	4.06 (s, 3 H) 4.75 (s, 2 H) 7.35 (t, 1 H) 7.42 (ddd, 1 H) 7.88 (dt, 1 H) 7.97 (t, 1 H) 8.24 (dd, 1 H) 8.84 (d, 1 H) 9.23 (d, 1 H)	385.97
712	3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.29 (t, 3 H) 4.07 (q, 2 H) 4.68 (s, 2 H) 7.08 (m, 2 H) 7.35 (m, 2 H) 7.44 (dd, 1 H) 7.87 (dd, 1 H)	421.99
713	3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.32 (t, 3 H) 4.18 (q, 2 H) 4.71 (s, 2 H) 6.51 (dd, 1 H) 7.02 (dd, 1 H) 7.10 (dd, 1 H) 7.37 (ddd, 1 H) 7.53 (dd, 1 H) 7.91 (dd, 1 H)	406.02
714	5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.30 (t, 3 H) 4.09 (q, 2 H) 4.47 (s, 2 H) 6.96 (d, 1 H) 7.11 (dd, 1 H) 7.40 (dd, 1 H) 7.47 (dd, 1 H) 7.60 (d, 1 H)	409.92

715	5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.33 (t, 3 H) 4.21 (q, 2 H) 4.52 (s, 2 H) 6.54 (dd, 1 H) 6.98 (d, 1 H) 7.05 (dd, 1 H) 7.55 (dd, 1 H) 7.62 (d, 1 H)	393.96
716	5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.36 (t, 3 H) 4.12 (q, 2 H) 4.58 (s, 2 H) 7.15 (dd, 1 H) 7.43 (m, 2 H) 7.48 (dd, 1 H) 7.94 (d, 1 H)	409.92
717	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol	1.30 (t, 3 H) 4.02 (q, 2 H) 4.51 (s, 2 H) 5.07 (s, 2 H) 6.72 (m, 4 H) 7.39 (t, 1 H) 7.49 (m, 1 H) 7.89 (m, 1 H) 7.99 (t, 1 H)	443.9
718	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol	1.33 (t, 3 H) 4.05 (q, 2 H) 4.70 (s, 2 H) 5.11 (s, 2 H) 6.74 (m, 4 H) 7.13 (t, 1 H) 7.44 (m, 1 H) 7.93 (dd, 1 H)	461.9
719	3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.75 (m, 1H), 7.64 (d, 1H), 7.23 (m, 2H), 7.16 (d, 1H), 6.63 (dd, 1H), 4.80 (s, 2H), 4.29 (q, 2H), 1.43 (t, 3H)	389.9
720	3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.17 (dd, 1H), 7.87 (m, 1H), 7.74 (m, 2H), 7.33 (dd, 1H), 6.95 (dd, 1H), 5.01 (s, 2H), 3.96 (s, 3H)	375.8

721	4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.74 (d, 2 H), 7.97 (s, 1 H), 7.87 (m, 1 H), 7.56 (d, 2 H), 7.44 (m, 1 H), 7.36 (apparent t, 1 H), 5.06 (q, 1 H), 3.58 (s, 3 H), 1.96 (d, 3 H).	400
722	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	0.90 (m, 2 H), 1.22 (m, 2 H), 3.49 (m, 1 H), 4.81 (s, 2 H), 7.26 (t, 1 H), 7.53 (m, 1 H), 8.11 (m, 2 H), 8.88 (d, 1 H) 9.33 (s, 1 H)	430.1
723	2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine	1.32 (t, 3 H), 1.94 (d, 3 H), 4.00 (s, 3H), 4.50 (m, 2 H), 5.20 (q, 1 H), 7.46 (t, 1 H), 7.56 (m, 1 H), 7.99 (d, 1 H), 8.10 (t, 1 H), 8.56 (d, 2 H).	444.1
724	2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine	1.34 (t, 3 H), 1.94 (d, 3 H), 4.50 (m, 2 H), 5.26 (q, 1 H), 7.36 (t, 1 H), 7.46 (t, 1 H), 7.57 (d, 1 H), 7.99 (m, 1 H), 8.10 (m, 1 H), 8.92 (d, 2 H).	414
725	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine	1.32 (t, 3 H), 1.97 (d, 3 H), 3.99 (s, 3H), 4.06 (m, 2 H), 5.19(q, 1 H), 6.98 (bs, 1 H), 7.16 (m, 1 H), 7.47 (t, 1 H), 7.58 (m, 1 H), 7.98 (dt, 1 H), 8.10 (m, 1 H) 8.31 (d, 1	443.1

		H).	
726	5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine	1.30 (t, 3 H), 1.96 (d, 3 H), 3.99(m, 2H), 4.00 (s, 3 H), 5.16 (q, 1 H), 6.87 (d, 1 H), 7.47 (t, 1 H), 7.58 (m, 1 H), 7.86 (dd, 1 H), 8.00 (d, 1 H), 8.11 (t, 1 H) 8.40 (d, 1 H).	443
727	2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine	1.30 (t, 3 H), 1.93 (d, 3 H), 3.92 (s, 3 H), 4.52 (m, 2 H), 5.13 (q, 1 H), 7.32 (dd, 1 H), 7.46 (t, 1 H), 7.56 (m, 1 H), 7.99 (dt, 1 H), 8.10 (t, 1 H), 8.25 (d, 1 H) 8.30 (d, 1 H).	443.1
728	3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine	1.38 (t, 3 H), 1.96 (d, 3 H), 4.20 (s, 3 H), 4.61 (m, 2 H), 5.20 (q, 1 H), 7.12 (d, 1 H), 7.46 (t, 1 H), 7.56 (t, 1 H), 8.00 (d, 1 H), 8.10 (s, 1 H), 8.40 (d, 1 H)	444
729	3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	0.77 (m, 2 H), 1.14 (m, 2 H), 1.99 (d, 3 H), 3.22 (m, 1 H), 5.44 (q, 1 H), 7.45 (m, 2 H), 7.58 (d, 1 H), 8.02 (d, 1 H), 8.15 (m, 2 H), 8.72 (d, 1 H) 9.05 (s, 1 H).	
730	4-{5-[3-(3-Chloro-phenyl)-	3.69 (s, 3 H) 4.73 (s, 2	384.91

	[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	H) 7.39 (t, 1 H) 7.47 (m, 1 H) 7.60 (m, 2 H) 7.92 (m, 1 H) 8.02 (t, 1 H) 8.79 (m, 2 H)	

Example 731

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

The title compound was synthesized according to the method described by Graybill et al. Tetrahedron lett. 2002 43, 5305-5309 from furan-2-carboxylic acid hydrazide (55.2 mg, 0.44 mmol), 1-isothiocyanato-2-methyl-propane (47ml, 0.38 mmol) and 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (45.0 mg, 0.20 mmol) with P-BEMP (136 mg, 0.30 mmol) as base. Purification by flash chromatography (33-66% EtOAc in heptane) gave the product as an oil (12.7 mg, 15.6%).1H NMR ($CDCl_3$) d (ppm): 8.08 (s, 1 H), 7.97 (d, 1H), 7.55 (d, 2H), 7.45 (t, 1H), 7.10 (d, 1H), 6.56 (d, 1H), 4.62 (s, 2H), 4.01 (d, 2H), 2.03 (m, 1H), 0.86 (d, 6H).

General: Thiophene-2-carbohydrazide (1.5 equiv) and an isothiocyanate (1.3 equiv) were dissolved in DMF (1 ml). 2-tert-Butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosporine (1 equiv) on polystyrene was added and the reactions were shaken on a Bohdan miniblock at ambient temperature for 1 h and then for one additional h at 45 °C. The resin was washed with dioxane:water 1:1 several times. The ring closure was carried out at 85 °C for 48 h in dioxane:water 1:1 on the miniblock. The resin was washed with acetonitrile (2´2ml). The 3-(chloromethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole was added to the reaction and shaken in acetonitrile at 50 °C for 2h. The product was filtrated and purified on MS-directed prep-HPLC, gradient 0-100% acetonitrile over 15 min.

The following compounds were prepared analogously to Example 731:

Example No.	Name	1H NMR	MS
732	5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-		464.0

	ylsulfanylmethyl]-[1,2,4]oxadiazole		
733	5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		460.0
734	5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		430.0
735	5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		484.0
736	5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		480.0
737	5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		446.0
738	5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		446.0
739	5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		484.0

Example 740

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol (28.0 mg, 0.13 mmol), 4-ethyl-3-methanesulfonyl-5-thiophen-2-yl-4H-[1,2,4]triazole (35.2 mg, 0.13 mmol) and cesium carbonate (130 mg) were dissolved in dimethylformamide and stirred under argon at ambient temperatures for 46 h. After evaporation to dryness the crude was chromatographed on 12 g silica, heptane/ethyl acetate 4/1 to 2/1. Collection of the appropriate fractions gave after evaporation to dryness and drying in vacuo the title compound (17.0 mg, 33%). 1H NMR ($CDCl_3$), δ (ppm): 8.13 (m, 1H), 8.02 (m, 1H), 7.58 (m, 1H), 7.47 (m, 2H), 7.40 (dd, 1H), 7.14 (dd, 1H), 5.74 (s, 2H), 4.04 (q, 2H), 1.38 (t, 3H).

The following compounds were prepared analogously to Example 740:

Example No.	Name	1H NMR	MS
741	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (s broad, 2 H), 8.12 (apparent dd, 1 H), 7.78 (s, 1 H), 7.56 (s broad, 2 H), 7.25 (apparent t, 1 H), 5.79 (s, 2 H), 3.66 (s, 3 H).	388
742	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.82 (s broad, 2 H), 8.07-7.94 (m, 2 H), 7.69 (s broad, 2 H), 7.47 (m, 2 H), 6.47 (q, 1 H), 3.63 (s, 3 H), 2.02 (d, 3 H).	384.1
743	4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	1.92 (d, 3 H), 3.57 (s, 3 H), 6.36 (q, 1 H), 6.74 (s, 1 H), 7.39 (m, 2 H), 7.60 (m, 2 H), 7.66 (m, 1 H), 7.78 (m, 1 H), 8.75 (m, 2 H)	383.1
744	3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-		

	pyridine		

The following compounds were prepared analogously to Example 740 with the exception that sodium hydride was employed as the base and the reaction was heated at 80°C:

745	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.77 (d, 2H), 8.17 (s, 1H), 8.05 (d, 1H), 7.79 (d, 2H), 7.62 (dd, 1H), 7.52 (t, 1H), 5.79 (s, 2H), 3.25 (m, 1H), 1.14 (d, 2H), 0.89 (m, 2H)	
746	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethoxy]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.77 (d, 2H), 7.79 (m, 3H), 7.7 (m, 1H), 7.44 (m, 2H), 6.84 (s, 1H), 5.71 (s, 2H), 3.21 (m, 1H), 1.13 (d, 2H), 0.82 (m, 2H)	

Example 747

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

HBTU (171 mg, 0.45 mmol) and HOBT (8 mg, 0.06 mmol) were added to a solution of 2-methoxy benzoic acid (68 mg, 0.45 mmol) and DIPEA (192 ml , 1.11 mmol) in DMF (3 ml). After 10 min N-hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine (100 mg, 0.37 mmol) was added. The reaction mixture was stirred at RT for 7 h and then at 110 °C over night. After cooling the reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic phase was dried and concentrated. Flash chromatography (heptane/EtOAc 1:2) afforded 1.9 mg (11%) of the desired product.

1H NMR ($CDCl_3$), d (ppm): 7.99 (m, 1H), 7.53 (m, 1H), 7.50 (m, 1H), 7.47 (m, 1H), 7.16 (m, 1H), 7.04 (m, 2H), 4.52 (s, 2H), 3.94 (s, 3H), 3.71 (s, 3H).

The following compounds were prepared analogously to Example 747:

Example No.	Name	1H NMR	MS
748	5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.72 (s, 3 H) 4.52 (s, 2 H) 6.61 (dd, 1 H) 7.16 (dd, 1 H) 7.30 (dd, 1 H) 7.47 (dd, 1 H) 7.50 (dd, 1 H) 7.67 (dd, 1 H)	345.92
749	3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester		414.0
750	5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		374.0
751	5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		392.0
752	3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole		382.1
753	5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		422.0
754	5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		392.0
755	5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		390.0

756	5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		374.0

Example 757

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole

DMF was added to a mixture of 2-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid (50 mg, 0.186 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (35.7 mg, 0.186 mmol), 1-hydroxybenzotriazole hydrate (HOBT) (28.5 mg, 0.186 mmol) and 3-chloro-N-hydroxy-benzamidine (29.3 mg, 0.172 mmol) at room temperature and stirred overnight. The reaction mixture was diluted with ethyl acetate (75 ml), washed with water 3 times, once with 1.0 M HCl (30 ml), saturated $NaHCO_3$ (30 ml) and saturated brine (30 ml), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. DMF (1 ml) was added to the residue and the resulting solution was heated at 135°C for 3 h to effect cyclization to oxadiazole. After cooling the reaction mixture was diluted with ethyl acetate (75 ml), washed with water 3 times, once with 1.0 M HCl (30 ml), saturated $NaHCO_3$ (30 ml) and saturated brine (30 ml), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The title compound (46.5 mg, 66.9%) was purified by SPE chromatography on silica gel using 50 ml 40%, 150 ml 50% ethyl acetate in hexanes. 1H NMR ($CDCl_3$), δ (ppm): 8.03 (s, 1H), 7.92 (m, 1H), 7.47 (m, 4H), 7.18 (dd, 1H), 4.99 (q, 1H), 3.64 (s, 3H), 1.97 (d, 3H).

The following compounds were prepared analogously to Example 757:

Example No.	Name	1H NMR	MS
758	3-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.88 (d, 1H), 8.76 (dd, 1H), 8.03 (m, 2H), 7.93 (d, 1H), 7.74 (m, 3H), 5.09 (m, 1H), 3.58 (s, 3H), 2.00 (d, 3H)	

The following compounds were prepared analogously to Example 10:

Example No.	Name
759	5-(1-Chloro-ethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole
760	3-(1-Chloro-ethyl)-5-m-tolyl-[1,2,4]oxadiazole
761	3-(1-Chloro-ethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole
762	3-(1-Chloro-ethyl)-5-(2-chloro-5-methyl-phenyl)-[1,2,4]oxadiazole
763	3-(1-Chloro-ethyl)-5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole
764	3-(1-Chloro-ethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole
765	3-[3-(1-Chloro-ethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile

The following compounds were prepared analogously to Example 40:

Example No.	Name	1H NMR	MS
766	4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.74 (d, 2H), 7.79 (s, 1H), 7.57 (d d, 2H), 7.38 (d, 1H), 7.25 (d, 1H), 5 (q, 1H), 3.62 (s, 3H), 2.33 (s, 3H), 1.92 (d, 3H)	
767	4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.67 (d, 2H), 7.7 (m, 1H), 7.57 (d d, 2H), 7.2 (m, 2H), 5 (q, 1H), 3.61 (s, 3H), 1.87 (d, 3H)	
768	4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.77 (d, 2H), 7.85 (m, 1H), 7.61 (m, 2H), 7.38 (m, 1H), 7.06 (t, 1H), 5.02 (q, 1H), 3.66 (s, 3H), 2.37 (s, 3H), 1.94 (d, 3H)	
769	4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-	8.75 (d, 2H), 7.9 (m,	

	5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	1H), 7.74 (m, 2H), 7.38 (m, 1H), 7.13 (m, 1H), 5.45 (q, 1H), 3.24 (m, 1H), 2.39 (s, 3H), 2 (d, 3H), 1.15 (m, 2H), 0.79 (m, 2H)	
770	3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile	8.76 (d d, 2H), 8.4 (s, 1H), 8.32 (d, 1H), 7.87 (d, 1H), 7.65 (t, 1H), 7.59 (m, 2H), 5.07 (q, 1H), 3.67 (s, 3H), 2.59 (s, 2H), 1.91 (d, 3H)	
771	3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile	8.77 (m, 2H), 8.42 (d, 1H), 8.38 (m, 1H), 7.9 (m, 1H), 7.71 (m, 3H), 5.49 (q, 1H), 3.25 (m, 1H), 2 (d, 3H), 1.17 (m, 2H), 0.81 (m, 2H)	
772	3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine	8.77 (br s, 2H), 8.18 (d, 2H), 7.98 (s, 1H), 7.87 (d, 1H), 7.52 (d, 1H), 7.44 (t, 1H), 5.66 (s, 2H), 4.88 (q, 1H), 1.98 (d, 3H)	

The following compounds were prepared analogously to Example 316:

Example No.	Name
773	3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propionic acid hydrazide

774	Rac-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide

The following compounds were prepared analogously to Example 318:

Example No.	Name
775	2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropanecarboxylic acid hydrazide

Example 776

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid hydrazide

3,3-Dimethyl-dihydro-furan-2,5-dione (6.4g) was heated at 50oC in ethanol (150 mL) overnight. The solvent was removed *in vacuo* and the residue triturated with hexane to yield 2,2-Dimethyl-succinic acid 4-ethyl ester (4.66g) which was used without further purification. t-Butanol (7.5 mL) was added to a mixture of 2,2-Dimethyl-succinic acid 4-ethyl ester (2.74g, 15.7mmol) in dichloromethane (62 mL) containing magnesium sulfate (7.5 g) and conc. sulfuric acid (0.85 mL) and the mixture was stirred at room temperature overnight. Saturated sodium bicarbonate solution was added and the product was extracted into dichloromethane, washed with brine solution, dried and concentrated to yield the diested as a colorloess oil (1.89 g). The ethyl ester was hydrolyzed by trating the crude sample with potassium hydroxide (2.75g) in a mixture of ethanol (50 mL) and water (25 mL) at room temperatire for 2h. The reaction was acidified using 1N HCl (aq) and extracted into ether, dried and concentrated to yield 2,2-Dimethyl-succinic acid 1-tert-butyl ester (1.4g). This acid was treated under the conditions of Example 320 (step 1) to yield 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid tert-butyl ester (1.9g). This t-Bu ester was deprotected using formic acid (19 mL) at 50°C for 20 min. The crude product was concentrated and triturated with a mixture of ether and hexane to yield 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid (1.12g). To a solution of 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid (561 mg, 2 mmol) and triethylamine (1.1 mL, 8 mmol) in THF (9 ml), isobutyl chloroformate (0.31 mL, 2.4 mmol) was added dropwise at -78 °C. After being stirred for 1h, hydrazine hydrate (1 mL, 11 mmol) was added. The reaction mixture was stirred at room temperature for 1 h and concentrated. A small amount of ice was added to quence

any excess reagent and precipitate the product, which was collected by filtration to give 482 mg of the title compound.

The following compounds were prepared analogously to Example 320:

Example No.	Name
777	(S)-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-hydrazinocarbonyl-ethyl}-carbamic acid tert-butyl ester

Example 778

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole

Step 1: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (ethoxy-thiophen-2-yl-methylene)-hydrazide: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide (266.69 mg, 1 mmol) was mixed with thiophene-2-carboximidic acid ethyl ester (191.6 mg, 1mmol) in ethanol (6 ml) and stirred at room temperature overnight. The reaction was quenched with water, extracted with ethyl acetate, dried and concentrated in vacuo. The crude product was triturated with hexane to yield 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (ethoxy-thiophen-2-yl-methylene)-hydrazide as a white solid (305 mg, 75%). 1H-NMR($CDCl_3$) d(ppm): 8.99 (ws, 1H), 8.09 (s, 1H), 7.98 (d, 1H), 7.41(m, 4H), 7.08 (dd, 1H), 4.27 (q, 2H), 3.34 (m, 4H) and 1.41 (t, 3H). Step 2: 3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (ethoxy-thiophen-2-yl-methylene)-hydrazide (81 mg, 0.2 mmol) was mixed with 2M methylamine (0.3 ml in THF) in ethanol (2 ml) at 70~80 °C overnight. The reaction mixture was concentrated with silica gel and purified by column chromatography with 0.5~2.0% methanol in ethyl acetate to give 54 mg (72.5 %) of 3-(3-chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole. 1H-NMR($CDCl_3$) d (ppm): 8.08 (s, 1H), 7.97 (d, 1H), 7.41 (m, 4H), 7.20 (dd, 1H), 3.80 (s, 3H), 3.68 (dd, 2H), 3.38 (dd, 2H).

The following compounds were prepared analogously to Example 778:

Example No.	Name	1H NMR	MS
779	3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole	8.08 (s, 1H), 7.97 (d, 1H), 7.47(m, 4H), 7.20 (dd, 1H), 4.20 (q, 2H), 3.72 (dd, 2H), 3.38 (dd, 2H) and 1.47 (t, 3H)	
780	5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.61(s, 1H), 7.58 (d, 1H), 7.48 (t, 1H), 7.11 (d, 1H), 6.59 (m, 1H), 4.48 (s, 2H) and 3.92 (s, 3H)	
781	2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole	8.04 (s, 1H), 7.93 (d, 1H), 7.60(s, 1H), 7.52 (d, 1H), 7.46 (t, 1H), 7.06 (d, 1H), 6.59 (m, 1H), 3.87 (s, 3H), 3.65 (t, 2H) and 3.38 (t, 2H)	
782	2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole	8.05 (s, 1H), 7.94 (d, 1H), 7.60(s, 1H), 7.52 (d, 1H), 7.47 (t, 1H), 7.10 (d, 1H), 6.59 (m, 1H), 4.30 (q, 2H), 3.67 (t, 2H), 3.39 (t, 2H) and 1.43 (t, 3H)	
783	2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole	8.05 (s, 1H), 7.94 (d, 1H), 7.63 (s, 1H), 7.52 (d, 1H), 7.46 (t, 1H), 7.01 (d, 1H), 6.58 (m, 1H), 3.67 (dd, 2H), 3.51 (t, 2H), 3.33 (m, 1H)	383.12

		1.25 (m, 2H) and 0.93 (m, 2H)	

Example 784

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine

Step 1: Isonicotinic acid {4-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-ethoxy-butylidene}-hydrazide: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride (473.3, 1.5 mmol) was mixed with isonicotinic acid hydrazide (205.7 mg, 1.5 mmol) in ethanol (8 ml) at 60 °C for an h and then at room temperature for 2 h. The reaction mixture was diluted with dichloromethane and washed with water. The organic layer was dried, concentrated with vacuum and the residue was triturated with ether to give 490 mg (78.9 %) of isonicotinic acid {4-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-ethoxy-butylidene}-hydrazide as white solid. Step 2: 4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine (47.1 mg, 82 %) as white solid was obtained from isonicotinic acid {4-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-ethoxy-butylidene}-hydrazide (60 mg, 0.15 mmol) reacted with 2M methylamine (0.45 ml, 0.9 mmol) in ethanol (1 ml) at 60 °C overnight. 1H-NMR($CDCl_3$) d(ppm): 8.77 (d, 2H), 8.02 (s, 1H), 7.91 (d, 1H), 7.58(d, 2H), 7.42 (m, 2H), 3.76 (s, 3H), 3.66 (t, 2H) and 3.38 (t, 2H).

The following compounds were prepared analogously to Example 784:

Example No.	Name	1H NMR	MS
785	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (d, 2H), 8.05 (s, 1H), 7.94 (d, 1H), 7.58(d, 2H), 7.43 (m, 2H), 4.16 (q, 2H), 3.72 (t, 2H), 3.40 (t, 2H) and 1.44 (t, 3H)	
786	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-	8.77 (d, 2H), 8.05 (s, 1H), 7.93 (d, 1H),	

	cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	7.73(d, 2H), 7.44 (m, 2H), 3.72(t, 3H), 3.51 (t, 2H), 3.38 (m, 1H), 1.23 (m, 2H) and 0.79 (m, 2H)	

Example 787

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine

Step 1: N-Cyclopropyl-isonicotinamide: Isonicotinic acid ethyl ester (3.0 g, 20 mmol) was mixed with cyclopropylamine (2 ml) at 120 °C in a sealed vial for 40 h. The reaction mixture was triturated with ether to give 1.62 g (50 %) of N-cyclopropyl-isonicotinamide as off-white solid. 1H-NMR($CDCl_3$) d (ppm): 8.73 (d, 2H), 7.60 (d, 2H) and 6.55 (w, 1H), 2.92 (m, 1H), 0.90 (m, 2H) and 0.66 (m, 2H). Step 2: N-Cyclopropyl-isonicotinimidoyl chloride hydrochloride: N-Cyclopropyl-isonicotinamide (1.62 g, 10 mmol) was reacted with SOCl2 (12 g, 100 mol) at 80 °C overnight. The reaction mixture was concentrated and triturated with dichloromethane to give 1.3 g (64%) of N-cyclopropyl-isonicotinimidoyl chloride hydrochloride as yellow solid. Step 3: 4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide (56 mg, 0.2 mmol) was mixed with N-cyclopropyl-isonicotinimidoyl chloride hydrochloride (40.6 mg, 0.2 mmol) and K_2CO_3 (60 mg, 0.43 mmol) in DMF (1 ml) at 100 °C for 3 h. The reaction mixture was dilute with dichloromethane and then washed with water. The organic layer was concentrated and purified with 5~6 % methanol in ethyl acetate to give 32 mg (39%) of the title comound. 1H-NMR($CDCl_3$) d (ppm): 8.78 (d, 2H), 8.05 (s, 1H), 7.96(d, 1H), 7.73(d, 2H), 7.45(m, 2H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.68 (d, 3H), 1.25 (m, 2H) and 0.79 (m, 2H).

The following compounds were prepared analogously to Example 787: It should be noted that some reactions provided 1,3,4-oxadiazole cyclization products with loss of the methylamino or cycopropylamino group instead of or as well as the triazole product.

Example No.	Name	1H NMR	MS
788	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.74 (d, 2H), 8.04 (s, 1H), 7.94 (d, 1H), 7.67 (d, 2H), 7.43 (m, 2H), 3.48(s, 2H), 3.09 (m, 1H), 1.75 (s, 6H), 1.16 (m, 2H) and 0.68 (m, 2H)	
789	4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.76 (w, 2H), 8.03 (s, 1H), 7.92 (d, 1H), 7.72(d, 2H), 7.44 (m, 2H), 4.13(m, 1H), 3.72 (dd, 1H), 3.43 (m, 1H), 3.27 (dd, 1H), 1.66 (d, 3H), 1.25 (m, 2H) and 0.79 (m, 2H)	
790	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (d, 2H), 8.01 (s, 1H), 7.91 (d, 1H), 7.73 (d, 2H), 7.49 (d, 1H), 7.42 (t, 1H), 3.99 (m, 1H), 3.83 (dd, 1H), 3.48 (m, 1H), 3.39 (m, 1H), 1.61 (d, 3H), 1.25 (m, 2H), 0.98 (m, 1H), 0.74 (m, 1H)	
791	cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.73 (d, 2H), 7.88 (s, 1H), 7.78 (d, 1H), 7.65 (d, 2H), 7.41 (d, 1H), 7.34 (t, 1H), 3.20 (m, 1H), 2.89 (m, 2H), 2.54	

		(dd, 1H), 2.00 (td, 1H), 1.20 (m, 2H), 0.83 (m, 2H)	
792	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.82 (m, 2H), 7.98 (s, 1H), 7.90 (m, 3H), 7.47 (d, 1H), 7.39 (t, 1H), 3.51 (s, 2H), 1.70 (s, 6H)	
793	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.76 (d, 2H), 8.07 (s, 1H), 7.97 (d, 1H), 7.77 (d, 2H), 7.49 (dd, 1H), 7.43 (t, 1H), 3.53 (s, 2H), 1.69 (s, 6H)	
794	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.82 (d, 2H), 8.05 (m, 1H), 7.95 (d, 1H), 7.91 (d, 2H), 7.50 (dd, 1H), 7.42 (t, 1H), 3.94 (dd, 1H), 3.67 (dd, 1H), 3.41 (dd, 1H), 1.66 (d, 3H)	
795	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.77 (d, 2H), 7.81 (m, 4H), 7.42 (d, 1H), 7.32 (t, 1H), 3.07 (q, 1H), 2.99 (q, 1H), 2.41 (q, 1H), 2.08 (td, 1H)	
796	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.76 (d, 2H), 7.85 (m, 1H), 7.77 (d, 1H), 7.55 (d, 2H), 7.44 (dd, 1H), 7.34 (t, 1H), 3.70 (s, 3H), 2.89 (m, 1H), 2.72	

		(m, 1H), 2.51 (q, 1H), 2.02 (dt, 1H)	
797	4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (d, 2H), 8.02 (s, 1H), 7.93 (d, 1H), 7.59 (d, 2H), 7.53 (d, 1H), 7.46 (t, 1H), 4.03 (m, 1H), 3.80 (s, 3H), 3.52 (m, 1H), 3.23 (dd, 1H), 1.66 (d, 3H)	
798	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.81 (d, 2H), 8.07 (s, 1H), 7.97 (d, 1H), 7.87 (d, 2H), 7.50 (d, 1H), 7.43 (t, 1H), 3.91 (q, 1H), 3.66 (dd, 1H), 3.44 (dd, 1H), 1.65 (d, 3H)	
799	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.80 (d, 2H), 8.05 (s, 1H), 7.95 (d, 1H), 7.61 (d, 2H), 7.51 (d, 1H), 7.45 (t, 1H), 4.07 (q, 1H), 3.75 (s, 3H), 3.48 (dd, 1H), 3.23 (dd, 1H), 1.68 (d, 3H)	
800	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (d, 2H), 8.05 (s, 1H), 7.96 (d, 1H), 7.74 (d, 2H), 7.50 (dd, 1H), 7.46 (t, 1H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.67 (d, 3H), 1.25 (m, 2H), 0.81 (m,	

		2H)	
801	(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester		

Example 802

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester (135 mg) was mixed with 96 % formic acid (1.3 mL) and heated at 50 °C for 1 h. The reaction mixture was concentrated *in vacuo*. The residue was quenched with saturated sodium bicarbonate and extracted with ethyl acetate. The organic layer was dried with sodium sulfate and concentrated. Purification was performed by flash column silica gel chromatography with 2-3% (2 M ammonia methanol) in dichloromethane to give 106 mg of the title compound as an off-white solid. 1H NMR ($CDCl_3$):d ppm 8.73 (d, 2H), 8.03 (s, 1H), 7.93 (d, 1H), 7.69 (d, 2H), 7.46 (d, 1H), 7.42 (t, 1H), 5.02 (dd, 1H), 3.61 (dd, 1H), 3.49 (dd, 1H), 3.35 (m, 1H), 2.47 (br s, 2H), 1.20 (m, 2H), 0.75 (m, 2H)

Example 803

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine

Sodium cyanoborohydride (0.1 mL, 1M in THF) was added to a solution of (S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine (30 mg) in methanol (0.8 mL) containing 96% formic acid (0.1 mL) and 37% formalin solution (0.1 mL). The residue was quenched with water and extracted with ethyl acetate. The organic layer was dried with sodium sulfate and concentrated. Purification was performed by flash column silica gel chromatography with 3% (2 M ammonia methanol) in dichloromethane to give 22 mg of the title compound.

1H NMR ($CDCl_3$):d ppm 8:76 (d, 2H), 8.06 (s, 1H), 7.97 (d, 1H), 7.73 (d, 2H), 7.47 (d, 1H), 7.45 (t, 1H), 5.00 (dd, 1H), 3.76 (dd, 1H), 3.51 (dd, 1H), 3.42 (m, 1H), 2.45 (br s, 6H), 1.26 (m, 2H), 0.88 (m, 1H), 0.79 (m, 1H)

Example 804

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine

37 mg (0.25 mmol) Me3OBF4 was added to a solution of 60 mg (0.21 mmol) 3-[5-(3-chloro -phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one in 2 ml CH_2Cl_2. The mixture was stirred overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2, washed with NaHCO3 (sat), dried and concentrated. The residue was dissolved in 3 ml EtOH and 22 mg (0.16 mmol) isonicotinic hydrazide was added. The solution was heated with microwaves at 120 °C for 10 min. The reaction mixture was cooled and the volatiles were removed under reduced pressure. The crude product was purified by preparative HPLC to afford 17 mg (20%) of the desired product. 1H NMR ($CDCl_3$):d ppm 1.75 (m, 1 H) 1.99 (m, 1 H) 2.21 (m, 2 H) 3.16 (dd, 1 H) 3.73 (m, 1 H) 3.85 (dd, 1 H) 4.07 (m, 1 H) 4.19 (m, 1 H) 7.47 (t, 1 H) 7.56 (m, 1 H) 7.67 (m, 2 H) 8.01 (m, 1 H) 8.11 m, 1 H) 8.76 (d, 2 H).

The following compounds were prepared analogously to Example 804:

Example No.	Name	1H NMR	MS
805	8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine	1.69 (m, 1 H) 1.99 (m, 1 H) 2.18 (m, 2 H) 3.11 (m, 1 H) 3.67 (m, 1 H) 3.87 (m, 1 H) 4.02 (m, 1 H) 4.24 (m, 1 H) 7.15 (m, 1 H) 7.47 (m, 3 H) 7.56 (m, 1 H) 8.01 (d, J=7.83 Hz, 1 H) 8.12 (d,	

		J=1.77 Hz, 1 H)	
806	8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine	1.76 (m, 1 H) 2.00 (m, 1 H) 2.21 (m, 2 H) 3.22 (dd, , 1 H) 3.74 (m, 1 H) 3.87 (dd, 1 H) 4.09 (m, 1 H) 4.19 (m, 1 H) 7.23 (m, 1 H) 7.53 (m, 1 H) 7.68 (m, 2 H) 8.10 (dd, 1 H) 8.77 (m, 2 H)	

Example 807

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole

3-(3-Chloro-phenyl)-5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole was mixed with 30 ml of chloroform/pyridine(25/1) at room temperature. Then bromine in chloroform (0.5 ml) was added dropwise and the reaction mixture was heated at 70 °C overnight. The reaction mixture was diluted with chloroform and washed with saturated NH_4Cl twice and the organic layer was dried with sodium sulfate, concentrated, the residue was triturated with diethyl ether to give the title compound (1.5 g, 57.5 %, yellow solid). 1H-NMR($CDCl_3$) d(ppm): 8.05 (s, 1H), 7.94 (d, 1H), 7.47(d, 1H), 7.43 (t, 1H), 4.66 (s, 2H) and 3.59 (s, 3H).

Example 808

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine

To {3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)[1,2,4] oxadiazole 5-yl-phenyl}-carbamic acid tert-butyl ester (88.0 mg, 0.19 mmol) in dichloromethane (3 ml) at 0°C added TFA (1.5 ml) and allowed to stir for 1 h. The reaction mixture was warmed to room temperature and the solvent was removed under vacuum. Dichloromethane was added to the resulting residue and the mixture was cooled to 0°C and saturated sodium bicarbonate was added to the stirring solution until turning basic (pH ~ 8). The mixture was then transferred to a separatory funnel and the product was extracted

with dichloromethane, dried using anhydrous sodium sulfate, and concentrated in vacuo. The resulting residue was titurated with ether and 61.1mg (87%) of 3-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine was isolated (light yellow solid). 1H NMR (DMSO-d6) d (ppm): 7.81 (d, 1H), 7.64 (d, 1H), 7.23 (m, 4H), 6.84 (d, 1H), 5.57 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H).

The following compounds were prepared analogously to Example 98:

Example No.	Name	1H NMR	MS
809	5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole		423.01
810	5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole		

The following compounds were prepared analogously to Example 93:

Example No.	Name	1H NMR	MS
811	2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine		

Example 812

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol

HBr (1 ml) and HOAc (1 ml) were added to 4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine (9 mg, 0.02 mmol) and the reaction was stirred at 80 °C on. Saturated $NaHCO_3$ (aq) was added to the reaction and the mixture was extracted three times with dichloromethane. The combined organic phases were dried and concentrated to give the title compound (8.5 mg, 99 %). 1H NMR ($CDCl_3$), δ (ppm): 1.37 (t, 3 H), 1.96 (d, 3 H), 4.10 (q, 2 H), 5.23 (q, 1 H), 6.80 (m, 2 H), 7.49 (t, 2 H), 7.59 (m, 1 H), 7.99 (d, 1 H), 8.11 (s, 1 H).

Example 813

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine

84 microl (0.21 mmol, 2.5 M) n-BuLi was added dropwise to a solution of 37 mg (0.21 mmol) 4-(4,5-dimethyl-4H-[1,2,4]triazol-3-yl)-pyridine in 2.1 ml THF at 0°C. After 20 min a solution of 60 mg (0.21 mmol) 3-(1-bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole was added dropwise. The reaction mixture was allowed to reach room temperature and stirred over night. NH_4Cl(sat) was added and the mixture was extracted twice with EtOAc. The organic phase was dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 20:1) afforded 7.7 mg (10%) of the desired product.
1H NMR ($CDCl_3$), d (ppm): 1.57 (d, 3 H) 3.16 (m, 1 H) 3.38 (m, 1 H) 3.71 (s, 3 H) 3.84 (d, 1 H) 7.46 (t, 1 H) 7.55 (m, 1 H) 7.58 (m, 2 H) 7.98 (m, 1 H) 8.10 (t, 1 H) 8.77 (d, 2 H)

Example 814

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine

10 mg (0.4 mmol) NaH was added to a solution of 38 mg (0.2 mmol) methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine in 3 ml DMF under an atmosphere of nitrogen. After 10 min a solution of 50 mg (0.22 mmol) 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole in 2 ml DMF was added. After stirring for 45 min NH_4Cl(sat) was added and the mixture was extracted twice with $CHCl_3$. The organic phase was dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 20:1) afforded 41 mg (54%) of the desired product. 1H NMR ($CDCl_3$), d (ppm): 3.07 (s, 3 H) 3.71 (s, 3 H) 4.56 (s, 2 H) 7.45 (m, 1 H) 7.55 (m, 1 H) 7.62 (d, 2 H) 7.98 (d, 1 H) 8.09 (m, 1 H) 8.73 (d, 2 H).

Example 815

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

32 mg (1.31 mmol) NaH was added to a solution of 193 mg (0.96 mmol) 3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine in 10 ml DMF at room temperature. After 10 min 200 mg (0.87mmol) 5-(3-chloro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole

was added to the reaction mixture. The reaction mixture was stirred at room temperature over night. The reaction mixture was diluted with NH_4Cl(sat) and extracted twice with EtOAc. The combined organic phases were washed with water, dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 20:1) afforded 111 mg (32%) of a white solid. 1H NMR ($CDCl_3$), d (ppm): 2.24 (m, 2 H) 3.57 (m, 2 H) 4.15 (m, 2 H) 5.01 (s, 2 H) 7.46 (t, 1 H) 7.56 (d, 1 H) 7.62 (d, 2 H) 7.99 (d, 1 H) 8.10 (s, 1 H) 8.70 (d, 2 H).

The following compounds were prepared analogously to Example 815:

Example No.	Name	1H NMR	MS
816	8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine		
817	8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine		
818	8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	1.81 (d, 3 H) 2.19 (m, 2 H) 3.47 (m, 2 H) 4.12 (m, 2 H) 6.07 (q, 1 H) 7.42 (m, 1 H) 7.49 (m, 1 H) 7.61 (m, 2 H) 7.91 (m, 1 H) 8.00 (m, 1 H) 8.70 (m, 2 H)	
819	8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	2.23 (m, 2 H) 3.50 (m, 2 H) 4.20 (m, 2 H) 4.97 (s, 2 H) 6.49 (m, 1 H) 6.89 (d, 1 H) 7.19 (t, 1 H) 7.48 (m, 1 H) 7.51 /m, 1 H) 8.06 (m, 1 H)	
820	8-{1-[5-(3-Chloro-phenyl)-	1.74 (d, 3 H) 2.17 (m, 2	

	[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	H) 3.45 (m, 2 H) 4.10 (m, 2 H) 5.96 (m, 1 H) 7.44 (t, 1 H) 7.53 (m, 1 H) 7.59 (m, 2 H) 7.97 (m, 1 H) 8.08 (m, 1 H) 8.67 (d, 2 H)	

Example 821

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole

3-Chloromethyl-5-[1-(toluene-4-sulfonyl)-1H-pyrrol-3-yl]-[1,2,4]oxadiazole (50 mg) and potassium hydroxide (50 mg) was heated for two h in methanol (5 ml). The mixture was diluted with ethyl acetate (10 ml), washed with water and brine, dried over $MgSO_4$, filtered and concentrated. The title compound was isolated in 57% yield by flash chromatography on silica gel using 40% ethyl acetate in heptane. 1H NMR ($CDCl_3$) d (ppm): 9.8 (s, 1H), 7.5 (m, 2H), 7.4 (d, 1H), 7.2 (dd, 1H), 6.8 (m, 1H), 6.7 (d, 1H), 4.5 (s, 2H), 4.1 (q, 2H), 1.4 (t, 3H).

Example 822

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine and wet 57%-86% MCPBA (52.4 mg, 0.20-0.30 mmol) were dissolved in dichloromethane (4 ml) and stirred for 16 h. The reaction mixture was purified via reversed phase preparative LC to give the title compound (7.5 mg, 8%). 1H NMR ($CDCl_3$), δ (ppm): 8.33 (d, 2 H), 8.06 (m, 1 H), 7.96 (m, 1 H), 7.67 (d, 2 H), 7.57 (m, 1 H), 7.46 (apparent t, 1 H), 4.60 (s, 2 H), 3.71 (s, 3 H).

Example 823

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole

2-Furan-2-yl-3-methyl-3,5-dihydro-imidazol-4-one (described in Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989) 6375-6386) (50 mg, 0.30 mmol) was dissolved in dioxane (3 ml) and Lawesson reagent (136 mg, 0.34 mmol) was added. The reaction mixture was heated to reflux over night and then allowed to room temperature at which time DIPEA (212 ml, 1.22 mmol) and 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (140 mg, 0.61 mmol) was added. The resulting mixture was heated to reflux for 5h and then kept at room temperature over night. Ethyl acetate was added and the reaction mixture was washed with water followed by brine. The organic phase was dried over $MgSO_4$ and evaporated. The title compound (13 mg, 11%) was obtained by flash chromatography using 1% methanol in chloroform.

1H NMR (CD_3OD) d (ppm): 7.96 (m, 1 H), 7.90 (m, 1H), 7.60 (dd, 1H), 7.57 (ddd, 1H), 7.46 (t, 1H), 7.09 (s, 1H), 6.86 (dd, 1H), 6.52 (dd, 1H), 3.95 (s, 2H), 3.74 (s, 3H).

Example 824

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole

To a cooled (-15 °C) solution of 2-{3-[5-(5-chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol (46 mg, 0.11 mmol) in anhydrous THF (15 ml) was dropwise added DAST (32 ml, 0.24 mmol). The mixture was stirred at room temperature for 1.5 h and was then quenched with MeOH (1 ml). The solvent was removed under reduced pressure and the residue was partitioned between brine and EtOAc. The aqueous layer was extracted with EtOAc (2 x 20 ml). The combined organic layers were washed with brine (10 ml), dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography (EtOAc:heptane 2:1) and preparative HPLC afforded the title compound as a white solid (11 mg, 22%). 1H NMR ($CDCl_3$) d (ppm): 8.05 (dd, 1H), 7.52 (m, 3H), 7.20 (m, 1H), 7.16 (m, 1H), 4.75 (t, 1H), 4.63 (m, 3H), 4.45 (m, 2H).

Example 825

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

The title compound was prepared according to method for 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole, with the exception of using molar equivalent cesium carbonate instead of potassium carbonate as the base, from 1-[5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole (32.3 mg, 0.097 mmol) and 4-ethyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione (23 mg) by using 50% EtOAc in n-heptane as chromatography eluent to yield 21 mg. 1H NMR ($CDCl_3$) d (ppm): 7.95 (d, 1H), 7.57 (dd, 1H), 7.44 (d, 1H), 7.07 (dd, 1H), 6.56 (dd, 1H), 4.56 (s, 2H), 4.22 (q, 2H), 1.35 (t, 3H).

Example 826

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile

The title compound was prepared using the general procedure of Rogers et al., Tetrahedron Letters (2002) 43: 3585-3587. To a stirring solution of 3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile (20mg, 0.050 mmol), 2-(methylsulfonyl-ethanol) (9.38 mg, 0.075 mmol), and DMF (0.05 M) at 0 °C was added NaH (5.8 mg, 0.150 mmol). Stirred for 20 min and removed the ice bath. Stirred an additional 20 min while warming to room temperature. The reaction mixture was quenched with 1 N HCl solution and partitioned between ethyl acetate and brine. The organic layer was dried (Na_2SO_4), filtered and concentrated to dryness. The crude organics were purified by flash column chromatography using ethyl acetate followed by 5% methanol in ethyl acetate to give the title compound (8.1 mg, 41%, white solid). 1H NMR ($CDCl_3$), δ (ppm): 8.25 (m, 1H), 7.75 (m, 1H), 7.60 (s, 1H), 7.18 (m, 2H), 6.60 (m, 1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).

Pharmaceutical Examples

FLIPR Assay of Group I receptor antagonist activity

For FLIPR analysis, cells were seeded on collagen coated clear bottom 96-well plates with black sides and analysis of $[Ca^{2+}]_i$ mobilization was performed 24 hours following seeding.

Cell cultures in the 96-well plates were loaded with a 4 μM solution of acetoxymethyl ester form of the fluorescent calcium indicator fluor-3 (Molecular Probes, Eugene, Oregon) in 0.01% pluronic. All assays were performed in a buffer containing 127 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$, 0.7 mM NaH_2PO_4, 2 mM $CaCl_2$, 0.422 mg/ml $NaHCO_3$, 2.4 mg/ml HEPES, 1.8 mg/ml glucose and 1 mg/ml BSA Fraction IV (pH 7.4).
FLIPR experiments were done using a laser setting of 0.800 W and a 0.4 second CCD camera shutter speed with excitation and emission wavelengths of 488 nm and 562 nm, respectively. Each FLIPR experiment was initiated with 160 μL of buffer present in each well of the cell plate. A 40 μL addition from the antagonist plate was followed by a 50 μL addition from the agonist plate. After each addition the fluorescence signal was sampled 50 times at 1 second intervals followed by 3 samples at 5 second intervals. Responses were measured as the peak height of the response within the sample period.
EC_{50}/IC_{50} determinations were made from data obtained from 8 point concentration response curves (CRC) performed in duplicate. Agonist CRC were generated by scaling all responses to the maximal response observed for the plate. Antagonist block of the agonist challenge was normalized to the average response of the agonist challenge in 14 control wells on the same plate.

Measurement of Inositol Phosphate (IP3) Turnover in Intact Whole Cells

GHEK stably expressing the human mGluR5d receptor were seeded onto 24 well poly-L-lysine coated plates at 40 x 10^4 cells /well in media containing 1 μCi/well [3H] myo-inositol. Cells were incubated overnight (16 h), then washed three times and incubated for 1 hour at 37°C in HEPES buffered saline (146 mM NaCl, 4.2 mM KCl, 0.5 mM $MgCl_2$, 0.1% glucose, 20 mM HEPES, pH 7.4) supplemented with 1 unit/ml glutamate pyruvate transaminase and 2 mM pyruvate. Cells were washed once in HEPES buffered saline and pre-incubated for 10 minutes in HEPES buffered saline containing 10 mM LiCl. Compounds (agonists) were added and incubated at 37°C for 30 minutes. Antagonist activity was determined by pre-incubating test compounds for 15 minutes, then incubating in the presence of glutamate (80μM) or DHPG (30 μM) for 30 minutes. The reaction was terminated by the addition of 0.5 ml perchloric acid (5%) on ice, with

incubation at 4°C for at least 30 minutes. Samples were collected in 15 ml Falcon tubes and inositol phosphates were separated using Dowex columns, as described below.

Assay For Inositol Phosphates Using Gravity-Fed Ion-Exchange Columns

a) Preparation of Ion- Exchange Columns

Ion-exchange resin (Dowex AG1-X8 formate form, 200-400 mesh, BIORAD) was washed three times with distilled water and stored at 4°C. 1.6 ml resin was added to each column and washed with 3 ml 2.5 mM HEPES, 0.5 mM EDTA, pH 7.4.

b) Sample Treatment

Samples were collected in 15 ml Falcon tubes and neutralized with 0.375 M HEPES, 0.75 M KOH. 4 ml of HEPES / EDTA (2.5 / 0.5 mM, pH 7.4) were added to precipitate the potassium perchlorate. Supernatant was added to the prepared Dowex columns.

c) Inositol Phosphate Separation

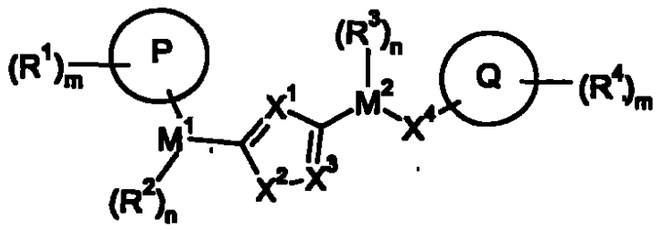
Elute glycero phosphatidyl inositols with 8 ml 30 mM ammonium formate.
Elute total inositol phosphates with 8 ml 700 mM ammonium formate / 100 mM formic acid and collect eluate in scintillation vials. Count eluate mixed with 8 ml scintillant.

Results

Typical IC_{50} values as measured in the assays described above are 10 μM or less. In one aspect of the invention the IC_{50} is below 2 μM. In another aspect of the invention the IC_{50} is below 0.2 μM. In a further aspect of the invention the IC_{50} is below 0.05 μM.

CLAIMS

1. A compound having the formula Ia



(I)

wherein:

P is selected from the group consisting of hydrogen, C_{3-7}alkyl or a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

M^1 is selected from the group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-3}alkyl$(CO)NR^5C_{0-3}$alkyl, C_{0-4}alkylNR^5, C_{0-3}alkylSC_{0-3}alkyl, C_{0-3}alkyl$(SO)C_{0-3}$alkyl or C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^2 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-}

$_4$alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^1, X^2 and X^3 are independently selected from the group consisting of CR, CO, N, NR, O and S;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl(CO)OR^5, C_{0-3}alkylNR^5R^6 and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{3-7}cycloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkylSC_{0-3}alkyl, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl;

R^3 is selected from a group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5, C_{0-4}alkyl(NR^5R^6), C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, C, O, SO, SO_2 and S;

Q is a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S and which fused ring may be substituted by one or more A;

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, wherein said ring may be substituted by one or more A;

R^5 and R^6 are independently selected from the group consisting of hydrogen, hydroxy, C_{1-6}alkyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, and wherein R^5 and R^6 may together form a 5- or 6-membered ring containing one or more atoms independently selected from the goup consisting of C, N, O and S;

wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl defined under R^1, R^2, R^3, R^4, R^5 and R^6 may be substituted by one or more A;

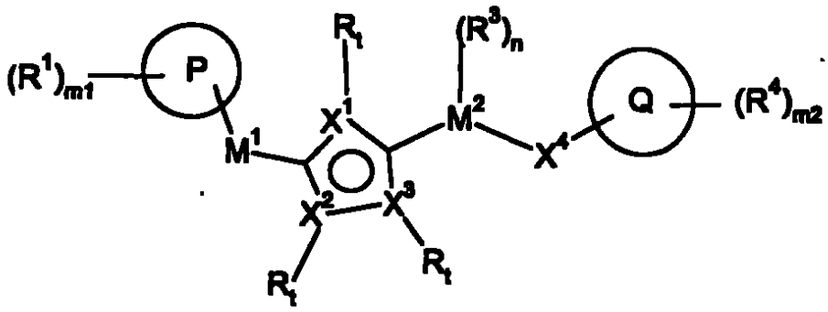
A is selected from the group consisting of hydrogen, hydroxy, oxo, halo, nitro, C_{0-6}alkylcyano, C_{1-4}alkyl, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, OC_{1-6}alkyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, $NR^5(CO)OR^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m is selected from 0, 1, 2, 3 and 4; and

n is selected from 0, 1, 2 and 3,

or salt thereof.

2. A compound having the formula I



(I)

wherein:

P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

M^1 is a bond;

X^1 selected from the group consisting of C, CO, N, O and S;

X^2 is selected from the group consisting of C, N, O and S;

X^3 is i) selected from the group consisting of N, O and S, or

ii) selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H. ;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$ and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any

substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and any suitable carbon atom is optionally substituted with R^4; and

R^4 is selected from the group consisting of C_{0-6}alkylcyano, =NC_{1-4}alkyl, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl, C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylN(C_{1-4}alkyl)$_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, =NR^5, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, (CO)R^5,

$O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m1 is selected from 0, 1, 2, 3 and 4;

m2 is selected from 0, 1, 2 and 3;

n is selected from 0, 1 and 2; and

t is 0 or 1,

and salts thereof,

with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole, 1,2-di{2-(3-amino-phenyl)-[1,3,4]oxadiazole-yl)ethane, 1,2-di{5-[5-(4-nitro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-bromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-chloro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane and 1,2-di{5-[5-(2,4-dibromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane.

3. A compound according to claim 2, wherein P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl or phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5 and R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

4. A compound according to claim 3, wherein P is phenyl substituted on position 3 or disubstituted on positions 2 and 5.

5. A compound according to claim 2, wherein X^1 is N and one of X^2 and X^3 is O and the other is N.

6. A compound according to claim 2, wherein the ring containing X^1, X^2 and X^3 forms an oxadiazole, isoxazole, oxazole, chloro-isoxazole or a methyl-isoxazole.

7. A compound according to claim 2, wherein M^2 is a bond or C_{1-3}alkyl and R^3 is hydrogen, methyl or dimethyl.

8. A compound according to claim 2, wherein X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, NR^5, O, SO, SO_2 and S and R^5 and R^6 are independently selected from hydrogen and C_{1-6}alkyl.

9. A compound according to claim 8, wherein X^4 is selected from the group consisting of CH_2, $CHCH_3$, $CH(CH_3)_2$ and NR^5.

10. A compound according to claim 8, wherein X^4 is S.

11. A compound according to claim 2, wherein Q is selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom, and any suitable carbon atom is optionally substituted with R^4 and R^4 is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

12. A compound according to any one of claims 2 or 11, wherein Q is selected from the group consisting of triazolyl and thiadiazolyl.

13. A compound according to claim 2, wherein Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl and R^4 is hydrogen or C_{1-6}alkyl.

14. A compound according to any one of claims 2 or 13, wherein Q is selected from the group consisting of pyridonyl, tetrahydrotriazolopyridyl and tetrahydrotriazolopyrimidinyl.

15. A compound according to claim 2, wherein R^4 is selected from the group consisting of benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl, dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl, trifluoromethyl, acetic acid methylester, allyl, amino, benzyl, cyclopropylmethyl, ethyl, fluorobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

16. A compound which is selected from the group consisting of 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole,

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine,

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine,

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole,

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,
4-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine,
2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine,
2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b],
3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,
3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,
3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,
3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole and
5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole
or salt thereof.

17. A compound which is selected from the group consisting of
4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,
4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,
4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,
5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole,
5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,
2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester,

2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole,

5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine,

3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole,

4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole,

4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine,

3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile,

4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole,

4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,
2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole,
4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,
4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,
4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,
3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,
3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,
3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,
3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,
3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,
3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,
5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,
2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,
2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,
2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,
2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,
2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2;4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine,

2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol,

3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol,

5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester,

5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole,

5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole,

2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide,

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine, or

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester,

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine,

or salt thereof.

18. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 17 in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

19. The pharmaceutical formulation according to claim 18, for use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

20. A compound according to any one of claims 1 to 17 for use in therapy.

21. The compound according to claim 20, for use in prevention and/or treatment of mGluR5 receptor-mediated disorders.

22. The compound according to claim 20, for use in prevention and/or treatment of neurological disorders.

23. The compound according to claim 20, for use in prevention and/or treatment of psychiatric disorders.

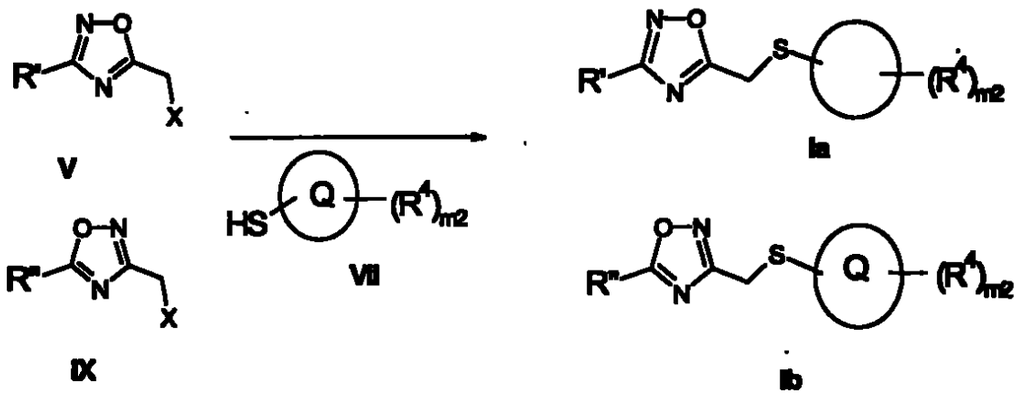
24. The compound according to claim 20, for use in prevention and/or treatment of chronic and acute pain disorders.

25. The use of a compound according to any one of claims 1 to 17 in the manufacture of a medicament for the use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

26. A method of prevention and/or treatment of mGluR5 receptor-mediated disorders, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound according to any one of claims 1 to 17.

27. A method for inhibiting activation of mGluR5 receptors, comprising treating a cell containing said receptor with an effective amount of a compound according to any one of claims 1 to 17.

28. Processes for the preparation of a compound according to claim 2, comprising:



wherein R' and R'' contains either a group represented in Formula I by M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$ or a leaving group such as $(CH_2)_nX$, wherein X is any suitable leaving group such as chloro or mesylate or a group which may subsequently be transformed into a leaving group and Q, X^4, R^3 R^4, M^2, m and n are as defined in claim 1.

"1,2,4" OXADIAZOLES COMO MODULADORES DE RECEPTOR-5 METABOTROPICO DE GLUTAMATO

RESUMEN DE LA INVENCIÓN

La presente invención se refiere a compuestos novedosos de la fórmula I, un procedimiento para su preparación y nuevos intermediarios preparados con el mismo, formulaciones farmacéuticas que contienen a los compuestos y el uso de los compuestos en terapias. En particular, de acuerdo a la presente invención existen compuestos potentes y selectivos para el receptor de mGluR de grupo I y más particularmente para mGluR5. De esta manera, se espera que los compuestos de la invención sean muy adecuados para la prevención y/o tratamiento de transtornos mediados por el receptor mGluR5, tales como trastornos neurológicos y psiquiátricos agudos y crónicos y transtornos de dolor agudos y crónicos.

COMPUESTOS NOVEDOSOS

CAMPO DE LA INVENCION

La presente invención se refiere a una clase novedosa de compuestos, a formulaciones farmacéuticas que contienen a dichos compuestos y al uso de dichos compuestos en terapia. La presente invención también se refiere al procedimiento para la preparación de dichos compuestos y a los intermediarios nuevos preparados en el mismo.

ANTECEDENTES DE LA INVENCION

El glutamato es el principal neurotransmisor excitador en el sistema nervioso central de mamífero (SNC). El glutamato produce su efecto en las neuronas centrales uniéndose a, y por lo tanto activando, los receptores de la superficie celular. Estos receptores se han dividido en dos clases principales, los receptores de glutamato ionotrópicos y los metabotrópicos, tomando como base las características estructurales de las proteínas del receptor, los medios mediante los cuales los receptores transducen las señales al interior de la célula, y los perfiles

farmacológicos.

Los receptores de glutamato metabotrópicos (mGluR) son receptores acoplados a proteína G que activan una variedad de sistemas de segundos mensajeros intracelulares después de la unión del glutamato. La activación de los mGluR en neuronas de mamífero intactas induce una o más de las siguientes respuestas: activación de fosfolipasa C; incremento en la hidrólisis de fosfoinositido (PI); liberación de calcio intracelular; activación de fosfolipasa D; activación o inhibición de adenil ciclasa; incremento o reducción en la formación de monofosfato cíclico de adenosina (cAMP); activación de guanilil ciclasa; incremento en la formación de monofosfato cíclico de guanosina (cGMP); activación de fosfolipasa A_2; incremento en la liberación de ácido araquidónico; e incremento o reducción en la actividad de canales iónicos regulados por voltaje y por ligando. *Schoepp et al., Trends Pharmacol. Sci. 14*:13 (1993), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al., Neuropharmacology 34*:1 (1995), Bordi y Ugolini, *Prog. Neurobiol. 59*:55 (1999).

La clonación molecular ha identificado ocho subtipos distintos de mGluR, denominados mGluR1 a mGluR8. Nakanishi, *Neuron 13*:1031 (1994), Pin *et al.*,

Neuropharmacology 34:1 (1995), Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995). La diversidad de receptor adicional se presenta a través de la expresión de formas empalmadas en forma alternada de algunos subtipos de mGluR. Pin *et al.*, *PNAS 89*:10331 (1992), Minakami *et al.*, *BBRC 199*:1136 (1994), Joly *et al.*, *J. Neurosci. 15*:3970 (1995).

Los subtipos de receptor de glutamato metabotrópicos se pueden subdividir en tres grupos, mGluR de grupo I, grupo II y grupo III, tomando como base la homología de secuencia de aminoácidos, los sistemas de segundos mensajeros utilizados por los receptores, y sus características farmacológicas. El mGluR del grupo I comprende mGluR1, mGluR5 y sus variantes empalmadas en forma alternada. La unión de agonistas a estos receptores da como resultado la activación de fosfolipasa C y la movilización subsiguiente de calcio intracelular.

Los intentos para esclarecer los papeles fisiológicos de los mGluR del grupo I sugieren que la activación de estos receptores induce la excitación neuronal. Varios estudios han demostrado que los agonistas de mGluR del grupo I pueden producir excitación post-sináptica después de aplicación a las neuronas en el hipocampo, corteza cerebral, cerebelo,

hipotálamo, así como en otras regiones del sistema nervioso central. Las evidencias indican que esta excitación se debe a la activación directa de los mGluR post-sinápticos, pero también se ha sugerido que se presenta la activación de los mGluR pre-sinápticos, lo que da como resultado una liberación incrementada de neurotransmisor. Baskys, *Trends Pharmacol. Sci. 15*:92 (1992), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al., Neuropharmacology 34*:1 (1995), Watkins *et al., Trends Pharmacol. Sci. 15*:33 (1994).

Los receptores de glutamato metabotrópicos se han implicado en un número de procesos normales en el SNC de mamífero. Se ha demostrado que es necesaria la activación de los mGluR para la inducción de potenciación a largo plazo del hipocampo y para la depresión a largo plazo del cerebelo. Bashir *et al., Nature 363*:347 (1993), Bortolotto *et al., Nature 368*:740 (1994), Aiba *et al., Cell 79*:365 81994), Aiba *et al., Cell 79*:377 (1994). También se ha demostrado un papel para la activación de mGluR en la nocicepción y analgesia, Meller *et al., Neuroreport 4*:879 (1993), Bordi y Ugolini, *Brain Res. 871*:223 (1999). Además, se ha sugerido que la activación de mGluR desempeña un papel modulador en una variedad de

otros procesos normales incluyendo transmisión sináptica, desarrollo neuronal, muerte neuronal apoptótica, plasticidad sináptica, aprendizaje espacial, memoria olfatoria, control central de la actividad cardiaca, vigilia, control motor y control del reflejo vestíbulo-ocular. Nakanishi, *Neuron 13*:1031 (1994), Pin *et al., Neuropharmacology 34*:1, Knopfel *et al., J. Med. Chem. 38*:1417 (1995).

Asimismo, se ha sugerido que los receptores de glutamato metabotrópico del grupo I y en particular mGluR5, participan en una variedad de procesos y trastornos fisiopatológicos que afectan al SNC. Estos incluyen apoplejía, trauma cefálico, daños anóxicos e isquémicos, hipoglucemia, epilepsia, trastornos neurodegenerativos tales como la enfermedad de Alzheimer, y dolor. Shoepp *et al., Trends Pharmacol. Sci. 14*:13 (1993), Cunningham *et al., Life Sci. 54*:135 (1994), Hollman *et al., Ann. Rev. Neurosci. 17*:31 (1994), Pin *et al., Neuropharmacology 34*:1 (1995), Knopfel *et al., J. Med. Chem. 38*:1417 (1995), Spooren *et al., Trends Pharmacol. Sci. 22*:331 (2001), Gasparini *et al. Curr. Opin. Pharmacol. 2*: 43 (2002), Neugebauer *Pain 98*:1 (2002). Se piensa que mucha de la patología en estas condiciones es ocasionada por una excitación excesiva

de las neuronas del SNC inducida por glutamato. Debido a que los mGluR del grupo I parecen incrementar la excitación neuronal mediada por glutamato a través de mecanismos post-sinápticos y de la liberación incrementada de glutamato pre-sináptica, su activación probablemente contribuya a la patología. Por consiguiente, los antagonistas selectivos de los receptores de mGluR del grupo I podrían ser terapéuticamente benéficos, en específico como agentes neuroprotectores, analgésicos o anti-convulsivos.

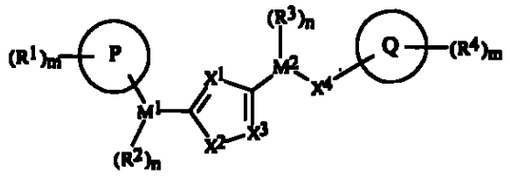
Los avances recientes en el esclarecimiento de los papeles neurofisiológicos de los receptores de glutamato metabotrópicos en general, y en particular del grupo I, han establecido a estos receptores como blancos para fármaco promisorios en la terapia de trastornos neurológicos y psiquiátricos agudos y crónicos, y en trastornos de dolor crónico y agudo. Debido a su significación fisiológica y fisiopatológica, existe la necesidad respecto a nuevos agonistas y antagonistas potentes de mGluR que presenten una alta selectividad para los subtipos de mGluR, en particular el subtipo de receptor del grupo I, de manera más particular el subtipo mGluR5.

El objetivo de la presente invención es proveer compuestos que presenten una actividad en los

receptores de glutamato metabotrópicos (mGluRs), en especial en el receptor mGluR5.

BREVE DESCRIPCIÓN DE LA INVENCION

La presente invención provee un compuesto de la fórmula Ia:



(Ia)

en la cual:

P se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{3-7} o un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6},

O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})-arilo, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, alquil$(C_{1-6})OR^5$, O-alquil$(C_{2-6})OR^5$, alquil$(C_{1-6})(CO)R^5$, O-alquil$(C_{1-6})(CO)R^5$, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil$(C_{0-6})NR^5R^6$, O-alquil$(C_{2-6})NR^5R^6$, alquil(C_{1-6})-$(CO)NR^5R^6$, O-alquil$(C_{1-6})(CO)NR^5R^6$, alquil$(C_{0-6})NR^5$-$(CO)R^6$, O-alquil$(C_{2-6})NR^5(CO)R^6$, alquil$(C_{0-6})NR^5(CO)$-NR^5R^6, alquil$(C_{0-6})SR^5$, O-alquil$(C_{2-6})SR^5$, alquil(C_{0-6})-$(SO)R^5$, O-alquil$(C_{2-6})(SO)R^5$, alquil$(C_{0-6})SO_2R^5$, O-alquil$(C_{2-6})SO_2R^5$; alquil$(C_{0-6})(SO_2)NR^5R^6$, O-alquil(C_{2-6})-$(SO_2)NR^5R^6$, alquil-$(C_{0-6})NR^5(SO_2)R^6$, O-alquil$(C_{2-6})NR^5$-$(SO_2)R^6$, alquil(C_{0-6})-$NR^5(SO_2)NR^5R^6$, O-alquil$(C_{2-6})NR^5$-$(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})-$NR^5(CO)OR^6$, O-alquil-$(C_{2-6})NR^5(CO)OR^6$, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, en el cual dicho anillo puede estar sustituido con uno o más A;

M^1 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil$(C_{0-4})(CO)$alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil$(C_{0-3})(CO)NR^5$,

alquil(C_{0-3})(CO)NR^5-alquilo de C_{0-3}, alquil(C_{0-4})NR^5, alquil(C_{0-3})-S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)-alquilo de C_{0-3} o alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^2 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^1, X^2 y X^3 se seleccionan de manera independiente a partir del grupo que consiste de CR, CO, N, NR, O y S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5, alquil(C_{0-3})NR^5R^6 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, cicloalquilo de C_{3-7}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil-(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5; alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})-(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que

consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5, alquil(C_{0-4})(NR^5R^6), alquil(C_{0-4})-(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halogenoalquilo de C_{1-4}, C, O, SO, SO_2 y S;

Q es un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S y cuyo anillo fusionado puede estar sustituido con uno o más A;

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, NR^5, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-

alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, en el cual dicho anillo puede estar sustituido con uno o más A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno, hidroxi, alquilo de C_{1-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, y en el cual R^5 y R^6 pueden formar juntos un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

en el cual cualquier alquilo de C_{1-6}, alquenilo de C_{2-6}, alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo y alquil(C_{0-6})-heteroarilo definido bajo R^1, R^2, R^3, R^4, R^5 y R^6 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, oxo, halógeno, nitro, alquil(C_{0-6})ciano, alquilo de C_{1-4}, alquil(C_{0-4})cicloalquilo de C_{3-6}, halogenoalquilo de C_{1-6}, O-halógeno-

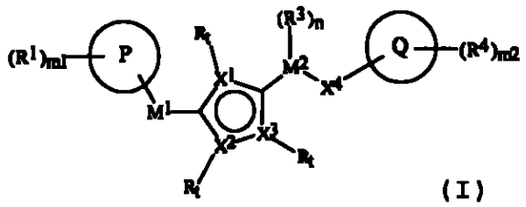
alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquilo de C_{1-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, alquil(C_{0-6})-NR^5R^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})-NR^5(CO)NR^5R^6, O(CO)NR^5R^6, NR^5(CO)OR^6, alquil(C_{0-6})(SO_2)-NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)-NR^5R^6, O-alquil(C_{2-6})(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m se selecciona a partir de 0, 1, 2, 3 y 4; y

n se selecciona a partir de 0, 1, 2 y 3,

o sal del mismo.

La presente invención provee un compuesto de la fórmula I



(I)

en la cual:

P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5;

R^1 está unido a P a través de un átomo de carbono en el anillo P y se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})-(CO)R^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, alquil(C_{0-6})NR^5(CO)R^6, O-

alquil(C_{2-6})$NR^5(CO)R^6$, alquil(C_{0-6})$NR^5(CO)NR^5R^6$, alquil(C_{0-6})-SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})$(SO)R^5$, O-alquil(C_{2-6})-$(SO)R^5$, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})-$(SO_2)NR^5R^6$, O-alquil(C_{2-6})$(SO_2)NR^5R^6$, alquil(C_{0-6})NR^5-$(SO_2)R^6$, O-alquil(C_{2-6})$NR^5(SO_2)R^6$, alquil(C_{0-6})$NR^5(SO_2)$-NR^5R^6, O-alquil(C_{2-6})$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})$NR^5(CO)OR^6$, O-alquil(C_{2-6})$NR^5(CO)$-OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

M^1 es un enlace;

X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S;

X^2 se selecciona a partir del grupo que consiste de C, N, O y S;

X^3 i) se selecciona a partir del grupo que consiste de N, O y S, o

ii) se selecciona a partir de N, O, S, y C cuando X^2 se selecciona a partir de N, O, o S, y cuando X^3 es C, el sustituyente R en X^3 es H;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})$(CO)OR^5$ y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que

consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)-alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo;

Q es i) seleccionada a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en los cuales cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y cualquier átomo de carbono apropiado está opcionalmente sustituido

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con R^4; y

R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})-(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})N-(alquilo de C_{1-4})$_2$ y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N

y O, y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A; o

ii) se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo; y

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A;

R^5 y R^6 se seleccionan de manera independiente

a partir del grupo que consiste de hidrógeno y alquilo de C_{1-6};

en el cual cualquier alquilo de C_{1-6} definido bajo R^1, R^2 y R^4 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})-NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)-NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5-(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m1 se selecciona a partir de 0, 1, 2, 3 y 4;

m2 se selecciona a partir de 0, 1, 2 y 3;

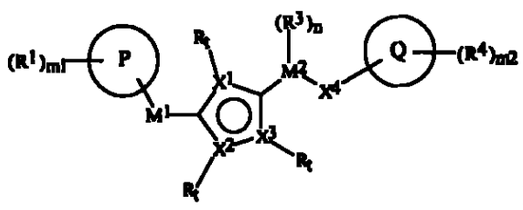
n se selecciona a partir de 0, 1 y 2; y

t es 0 o 1,

y sales de los mismos,

con la condición que el compuesto no sea 5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol, 1,2-di{2-(3-amino-fenil)-[1,3,4]-oxadiazol-il)etano, 1,2-di{5-[5-(4-nitrofenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-bromo-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-cloro-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano y 1,2-di{5-[5-(2,4-dibromofenil)furan-2-il]-[1,3,4]-oxadiazol-il)etano.

La presente invención provee un compuesto de la fórmula Ib



(Ib)

en la cual:

P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5;

R^1 está unido a P a través de un átomo de carbono en el anillo P y se selecciona a partir del

grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, O-alquil(C_{1-6})-$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-$(CO)NR^5R^6$, O-alquil(C_{1-6})$(CO)NR^5R^6$, alquil(C_{0-6})NR^5-$(CO)R^6$, O-alquil(C_{2-6})$NR^5(CO)R^6$, alquil(C_{0-6})$NR^5(CO)$-NR^5R^6, alquil(C_{0-6})SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})-$(SO)R^5$, O-alquil(C_{2-6})$(SO)R^5$, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})$(SO_2)NR^5R^6$, O-alquil(C_{2-6})-$(SO_2)NR^5R^6$, alquil(C_{0-6})$NR^5(SO_2)R^6$, O-alquil(C_{2-6})NR^5-$(SO_2)R^6$, alquil(C_{0-6})$NR^5(SO_2)NR^5R^6$, O-alquil(C_{2-6})NR^5-$(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})-$NR^5(CO)OR^6$, O-alquil(C_{2-6})$NR^5(CO)OR^6$, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

M^1 es un enlace;

X^1 se selecciona a partir del grupo que

consiste de C, CO, N, O y S;

X^2 se selecciona a partir del grupo que consiste de C, N, O y S;

X^3 se selecciona a partir del grupo que consiste de N, O y S, o X^3 es CH cuando X^2 es N, O ó S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)-alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-

alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo ;

Q es i) seleccionada a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno; y

R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})-heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})-heteroarilo, alquil(C_{0-6})O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de

C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})N(alquilo de C_{1-4})$_2$ y un anillo no aromático de 3 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A; o

ii) se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo; y

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se

seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno y alquilo de C_{1-6};

en el cual cualquier alquilo de C_{1-6} definido bajo R^1, R^2 y R^4 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})ciano, O-alquil(C_{1-6})CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{1-6})(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{0-6})-(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5-(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)-NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5(SO_2)R^6,

SO_3R^5, alquil$(C_{1-6})NR^5(SO_2)NR^5R^6$, O-alquil$(C_{2-6})(SO_2)R^5$, alquil$(C_{0-6})(SO_2)R^5$, alquil$(C_{0-6})(SO)R^5$, O-alquil$(C_{2-6})(SO)R^5$ y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m1 se selecciona a partir de 0, 1, 2, 3 y 4;

m2 se selecciona a partir de 0, 1, 2 y 3;

n se selecciona a partir de 0, 1 y 2; y

t es 0 o 1,

y sales de los mismos,

con la condición que el compuesto no sea 5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol.

En un aspecto adicional de la invención, se proveen formulaciones farmacéuticas que comprenden una cantidad terapéuticamente efectiva de un compuesto de la fórmula I y un vehículo farmacéuticamente aceptable.

En un aspecto adicional de la invención se provee una formulación farmacéutica que incluye un compuesto de la fórmula I para ser utilizada en el tratamiento de trastornos mediados por el receptor mGluR5, y en particular trastornos neurológicos, trastornos psiquiátricos, dolor agudo y crónico.

Incluso en una aspecto adicional de la invención, se provee un compuesto de la fórmula I para ser utilizado en terapia para el tratamiento de trastornos mediados por el receptor mGluR5, y en particular trastornos neurológicos, trastornos psiquiátricos, dolor agudo y crónico.

En otro aspecto de la invención se provee un procedimiento para la preparación de compuestos de la fórmula I, y los intermediarios provistos en el mismo.

Estos y otros aspectos de la presente invención se describen con mayor detalle en la misma a continuación.

DESCRIPCION DETALLADA DE LA INVENCION

A continuación se listan las definiciones de diversos términos utilizados en la descripción y reivindicaciones para describir la presente invención.

Con el fin de evitar dudas, se debe entender que en casos en los que en esta descripción se califique a un grupo con "definido anteriormente en la presente invención", "antes definido en la presente invención" o "definido anteriormente" dicho grupo abarca la definición más amplia y que ocurra primero así como todas y cada una de las otras definiciones

para dicho grupo.

Con el fin de evitar dudas, se debe entender que en esta descripción "C_{1-6}" significa un grupo de carbono que tiene 1, 2, 3, 4, 5 o 6 átomos de carbono.

En esta descripción "C" significa un átomo de carbono.

En esta descripción, a menos que se indique lo contrario, el término "alquilo" incluye grupos alquilo de cadena tanto recta como ramificada y puede ser metilo, etilo, n-propilo, i-propilo, n-butilo, i-butilo, s-butilo, t-butilo, n-pentilo, i-pentilo, t-pentilo, neo-pentilo, n-hexilo o i-hexilo, t-hexilo. El término "alquilo de C_{1-3}" se refiere a un grupo alquilo que tiene 1, 2 o 3 átomos de carbono, y puede ser metilo, etilo, n-propilo e i-propilo.

En esta descripción, a menos que se indique lo contrario, el término "cicloalquilo" se refiere a un sistema de anillo de hidrocarburo cíclico, saturado, opcionalmente sustituido. El término "cicloalquilo de C_{3-7}" puede ser ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo y cicloheptilo.

En esta descripción, a menos que se indique lo contrario, el término "alquenilo" incluye grupos alquenilo de cadena tanto recta como ramificada. El

término "alquenilo de C_{2-6}" se refiere a un grupo alquenilo que tiene 2 a 6 átomos de carbono y uno o dos dobles enlaces, y puede ser, pero no se limita a vinilo, alilo, propenilo, i-propenilo, butenilo, i-butenilo, crotilo, pentenilo, i-pentenilo y hexenilo.

En esta descripción, a menos que se indique lo contrario, el término "alquinilo" incluye grupos alquinilo de cadena tanto recta como ramificada. El término "alquinilo de C_{2-6}" tiene de 2 a 6 átomos de carbono y uno o dos triples enlaces, y puede ser, pero no se limita a etinilo, propargilo, butinilo, i-butinilo, pentinilo, i-pentinilo y hexinilo.

El término "arilo" se refiere a un sistema de anillo de hidrocarburo monocíclico o bicíclico, opcionalmente sustituido, que contiene por lo menos un anillo aromático insaturado. Los ejemplos y valores apropiados del término "arilo" son fenilo, naftilo, 1,2,3,4-tetrahidronaftilo, indilo e indenilo.

En esta descripción, a menos que se indique lo contrario, el término "heteroarilo" se refiere a un sistema de anillo aromático, monocíclico o bicíclico, insaturado, opcionalmente sustituido que contiene por lo menos un heteroátomo que se selecciona de manera independiente a partir de N, O ó S. Los ejemplos de "heteroarilo" pueden ser, pero no se

limitan a tiofeno, tienilo, piridilo, tiazolilo, furilo, pirrolilo, triazolilo, imidazolilo, oxadiazolilo, oxazolilo, isoxazolilo, pirazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolo-pirimidinilo, benzofurilo, indolilo, isoindolilo, piridonilo, piridazinilo, pirimidinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, piridilo, imidazo-piridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo.

En esta descripción, a menos que se indique lo contrario, los términos "alquilarilo", "alquil-heteroarilo" y "alquilcicloalquilo" se refieren a un sustituyente que está unido mediante el grupo alquilo a un grupo arilo, heteroarilo y cicloalquilo.

En esta descripción, a menos que se indique lo contrario, un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, incluye anillos aromáticos y heteroaromáticos así como anillos carbocíclicos y heterocíclicos los cuales pueden ser saturados o insaturados. Los ejemplos de dichos anillos pueden ser, pero no se limitan a furilo, isoxazolilo, isotiazolilo, oxazolilo, pirazinilo,

pirazolilo, piridazinilo, piridilo, pirimidilo, pirrolilo, tiazolilo, tienilo, imidazolilo, imidazolidinilo, imidazolinilo, triazolilo, morfolinilo, piperazinilo, piperidilo, piperidonilo, pirazolidinilo, pirazolinilo, pirrolidinilo, pirrolinilo, tetrahidropiranilo, tiomorfolinilo, fenilo, ciclohexilo, ciclopentilo y ciclohexenilo.

En esta descripción, a menos que se indique lo contrario, un anillo de 3 a 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, incluye anillos aromáticos y heteroaromáticos así como anillos carbocíclicos y heterocíclicos los cuales pueden ser saturados o insaturados. Los ejemplos de dichos anillos pueden ser, pero no se limitan a imidazolidinilo, imidazolinilo, morfolinilo, piperazinilo, piperidilo, piperidonilo, pirazolidinilo, pirazolinilo, pirrolidinilo, pirrolinilo, tetrahidropiranilo o tiomorfolinilo, tetrahidrotiopiranilo, furilo, pirrolilo, isoxazolilo, isotiazolilo, oxazolilo, oxazolidinonilo, pirazinilo, pirazolilo, piridazinilo, piridilo, pirimidilo, pirrolilo, tiazolilo, tienilo, imidazolilo, triazolilo, fenilo, ciclopropilo, aziridinilo, ciclobutilo, azetidinilo, ciclopentilo, ciclopentenilo, ciclohexilo, ciclohexenilo, cicloheptilo, cicloheptenilo,

ciclo-octilo y ciclo-octenilo.

En esta descripción, a menos que se indique lo contrario, un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, incluye anillos aromáticos y heteroaromáticos así como anillos carbocíclicos y heterocíclicos los cuales pueden ser saturados o insaturados. Los ejemplos de dichos anillos pueden ser, pero no se limitan a naftilo, norcarilo, cromilo, isocromilo, indanilo, benzoimidazol o tetralinilo, benzo-oxazolilo, benzotiazolilo, benzofurilo, benzotienilo, benzotriazolilo, indolilo, azaindolilo, indazolilo, indolinilo, isoindolinilo, bencimidazolilo, oxadiazolilo, tiadiazolilo, quinolinilo, quinoxalinilo y benzotriazolilo.

En esta descripción, a menos que se indique lo contrario, los términos "$=NR^5$" y "$=NOR^5$" incluyen grupos imino y oximo que portan un sustituyente R^5 y pueden ser, o ser parte de, grupos que incluyen, pero sin limitarse a, iminoalquilo, iminohidroxi, iminoalcoxi, amidina, hidroxiamidina y alcoxiamidina.

En el caso en el cual un subíndice es el número entero 0 (cero) el grupo al cual se refiere el subíndice, indica que el grupo está ausente, es decir que existe un enlace directo entre los grupos.

En esta descripción, a menos que se indique lo contrario, el término "enlace" es un enlace saturado.

En esta descripción, a menos que se indique lo contrario, el término "halógeno" puede ser fluoro, cloro, bromo, o yodo.

En esta descripción, a menos que se indique lo contrario, el término "halogenoalquilo" significa un grupo alquilo como el definido anteriormente, sustituido con uno o más halógenos. El término "halogenoalquilo de C_{1-6}" puede incluir, pero no se limita a fluorometilo, difluorometilo, trifluorometilo, fluoroetilo, difluoroetilo y bromopropilo. El término "O-halogenoalquilo de C_{1-6}" puede incluir, pero no se limita a fluorometoxi, difluorometoxi, trifluorometoxi, fluoroetoxi y difluoroetoxi.

En una modalidad de la invención P puede ser hidrógeno o alquilo de C_{3-7} o P puede ser un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan a partir C, N, O ó S, dicho anillo puede estar fusionado opcionalmente con un anillo de 5 o 6

miembros que contiene 1 o más átomos que se seleccionan de manera independiente a partir de C, N, O, o S. En una modalidad preferida de la invención P se selecciona a partir de anillos aromáticos y hetero-aromáticos de 5 y 6 miembros. En una modalidad preferida adicional, P se selecciona a partir de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5. Incluso en una modalidad preferida de la invención, P es fenilo sustituido en la posición 3 o disustituido en las posiciones 2 y 5.

P está opcionalmente sustituido mediante un átomo de carbono, con 0, 1, 2, 3 o 4 grupos R^1, en el cual el número de sustituyentes R^1 en el anillo P se designa con el término *m1*. En modalidades preferidas de la invención *m1* es 1 o 2. En modalidades preferidas adicionales de la invención, *m1* es 1.

En modalidades apropiadas de la invención R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de

C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, alquil(C_{1-6})-OR^5, O-alquil$(C_{2-6})OR^5$, alquil$(C_{1-6})(CO)R^5$, O-alquil(C_{1-6})-$(CO)R^5$, alquil$(C_{0-6})CO_2R^5$, O-alquil$(C_{1-6})CO_2R^5$, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})ciano, alquil$(C_{0-6})NR^5R^6$, O-alquil(C_{2-6})-NR^5R^6, alquil$(C_{1-6})(CO)NR^5R^6$, O-alquil$(C_{1-6})(CO)NR^5R^6$, alquil$(C_{0-6})NR^5(CO)R^6$, O-alquil$(C_{2-6})NR^5(CO)R^6$, alquil(C_{0-6})-$NR^5(CO)NR^5R^6$, alquil$(C_{0-6})SR^5$, O-alquil$(C_{2-6})SR^5$, alquil$(C_{0-6})(SO)R^5$, O-alquil$(C_{2-6})(SO)R^5$, alquil(C_{0-6})-SO_2R^5, O-alquil$(C_{2-6})SO_2R^5$, alquil$(C_{0-6})(SO_2)NR^5R^6$, O-alquil$(C_{2-6})(SO_2)NR^5R^6$, alquil$(C_{0-6})NR^5(SO_2)R^6$, O-alquil(C_{2-6})-$NR^5(SO_2)R^6$, alquil$(C_{0-6})NR^5(SO_2)NR^5R^6$, O-alquil$(C_{2-6})NR^5$-$(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})-$NR^5(CO)OR^6$, O-alquil$(C_{2-6})NR^5(CO)OR^6$, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S.

En una modalidad más apropiada de la invención R^1 se selecciona a partir de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{1-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, alquil(C_{0-6})ciano, alquil(C_{0-6})-NR^5R^6, alquil(C_{0-6})-SR^5 y un anillo de 5 o 6 miembros que contiene uno o

más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

Cualquier alquilo de C_{1-6} definido bajo R^1 puede estar sustituido con uno o más A. En una modalidad de la invención R^1 es etilo y A es hidroxilo.

En una modalidad apropiada adicional de la invención R^1 se selecciona a partir de hidrógeno, metilo, etilo, ciclopropilo, hidroxi, metoxi, ciano, fluoro, cloro, bromo, iodo, trifluorometilo, difluorometoxi, trifluorometoxi, amino, nitro, dimetilamino, metilsulfanilo, vinilo, acetilo, éster metílico del ácido fórmico, metoximetilo, etanol y furilo.

En una modalidad más apropiada de la invención P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo o fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5 y R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halógeno-alquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{1-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, alquil(C_{0-6})-ciano, alquil(C_{0-6})-NR^5R^6, alquil$(C_{0-6})SR^5$ y un anillo de 5 miembros que contiene uno o más átomos que se

seleccionan de manera independiente a partir del grupo que consiste de C y O.

En una modalidad apropiada adicional de la invención P es fenilo sustituido en la posición 3 o disustituido en las posiciones 2 y 5 y R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{1-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, alquil(C_{0-6})-ciano, alquil(C_{0-6})-NR^5R^6, alquil(C_{0-6})SR^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

De conformidad con otro aspecto de la invención, el anillo P se conecta al anillo central mediante M^1, en el cual M^1 puede ser un enlace que une directamente a P al anillo central. M^1 también puede ser un enlazador de alquilo de C_{1-3}.

En una modalidad preferida de la invención M^1 es un enlace.

Cuando M^1 no sea un enlace directo, M^1 puede estar sustituido también con 0, 1, 2 o 3 sustituyentes R^2, en el cual el número de sustituyentes R^2 se

designa con el término *n*. Los sustituyentes R^2 se pueden seleccionar a partir de hidrógeno, hidroxi, oxo, halogenoalquilo de C_{1-4}, halógeno y alquilo de C_{1-4}. En una modalidad preferida de la invención *n* es 0.

En otro aspecto de la invención, se proveen compuestos de la fórmula I en la cual X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S. En un aspecto adicional de la invención, X^2 se selecciona a partir del grupo que consiste de C, N, O y S. Incluso en un aspecto adicional de la invención, X^3 se selecciona a partir del grupo que consiste de N, O, y S, o X^3 se selecciona a partir de N, O, S, y C cuando X^2 se seleccione a partir de N, O, o S, y cuando X^3 es C, el sustituyente R en X^3 es H.

X^1, X^2 y X^3 también pueden estar sustituidos con 0, 1 o 2 sustituyentes R en el cual el número de sustituyentes R se designa con el término t. El sustituyente R se puede seleccionar a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})-(CO)OR^5, alquil(C_{0-3})NR^5R^6 y alquil(C_{0-3})arilo. En una modalidad de la invención R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3} y halógeno.

En una modalidad preferida de la invención

X^1 es C, N, u O y R se selecciona a partir de hidrógeno, alquilo de C_{0-3} y halógeno. En una modalidad R se selecciona a partir de hidrógeno, cloro o metilo.

En otra modalidad preferida de la invención X^1 es N.

En una modalidad apropiada X^2 se selecciona a partir de N, O y S, y R es hidrógeno. En otra modalidad de la invención X^3 es N, O ó S. En una modalidad preferida adicional de la invención X^1 es O y uno de X^2 y X^3 es O y el otro es N. Incluso en una modalidad preferida adicional de la invención X^1 es N y uno de X^2 y X^3 es O y el otro es N. Incluso en otra modalidad preferida de la invención X^1 es C o CR y uno de X^2 y X^3 es O y el otro es N.

En otra modalidad preferida de la invención X^2 es O y X^3 es N, e incluso en otra modalidad preferida de la invención X^2 es N y X^3 es O.

En una modalidad preferida adicional de la invención X^1 es O y X^2 y X^3 son N.

En otra modalidad apropiada de la invención el anillo que contiene a X^1, X^2 y X^3 forma un oxadiazol, isoxazol, oxazol, cloroisoxazol o un metil-isoxazol.

En una modalidad preferida de la invención el anillo que contiene a X^1, X^2 y X^3 forma un

oxadiazol. En otra modalidad preferida de la invención el anillo que contiene a X^1, X^2 y X^3 forma un isoxazol.

El anillo que contiene a X^1, X^2 y X^3 no debe estar anillado adicionalmente en cualquier otro anillo.

En una modalidad apropiada de la invención M^2 puede ser un enlace directo desde el anillo central hacia la variable X^4 o M^2 se puede seleccionar a partir del grupo que consiste de enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})-(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3}.

En modalidades preferidas de la invención M^2 es un enlace o alquilo de C_{1-3}. En modalidades preferidas adicionales de la invención M^2 es alquilo de C_{1-3}, de preferencia metilo o etilo.

Cuando M^2 no sea un enlace directo M^2 puede estar también sustituido con 0, 1 o 2 grupos R^3 en el cual el número de sustituyentes R^3 se designa con el término *n*. En una modalidad de la invención *n* es 1 o 2. En otra modalidad de la invención *n* es 0.

En una modalidad apropiada de la invención R^3 se selecciona a partir del grupo que consiste de R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halógeno-

alquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)-alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6.

En una modalidad preferida R^3 se selecciona a partir de hidrógeno y alquilo de C_{1-4}, de preferencia metilo o dimetilo.

En otra modalidad preferida M^2 se puede seleccionar a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})-(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3} y R^3 se selecciona a partir de hidrógeno y alquilo de C_{1-4}.

Incluso en otras modalidades preferidas de la invención M^2 es un enlace o alquilo de C_{1-3} y R^3 es hidrógeno, metilo o dimetilo.

En una modalidad preferida adicional M^2 se puede seleccionar a partir del grupo que consiste de un enlace, metilo y etilo y R^3 es hidrógeno, metilo o dimetilo.

En una modalidad adicional de la invención M^2 es nitrógeno. Incluso en una modalidad adicional

de la invención M^2 es oxígeno.

De conformidad con otro aspecto de la invención X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo.

En una modalidad preferida de la invención X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, NR^5, O, SO, SO_2 y S y R^5 y R^6 se seleccionan de manera independiente a partir de hidrógeno y alquilo de C_{1-6}.

En una modalidad preferida adicional de la invención X^4 se selecciona a partir del grupo que consiste de CH_2, $CHCH_3$, $CH(CH_3)_2$ y NR^5. En una modalidad preferida adicional de la invención X^4 es NR^5 y R^5 se selecciona a partir de hidrógeno y alquilo de C_{1-6}. En una modalidad preferida de la invención R^5 es metilo o hidrógeno y R^6 es hidrógeno.

Incluso en otra modalidad preferida adicional de la invención X^4 es O. Incluso en otra modalidad preferida de la invención X^4 es S.

Se debe entender que el enlace entre M^2 y X^4 es un enlace sencillo en todas las formas tautoméricas.

Las modalidades de la presente invención incluyen aquellas en las cuales Q es un anillo de 5 o 6 miembros. Cuando Q es un anillo de 5 miembros, Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en el cual cualquier átomo de nitrógeno susceptible de sustitución en el anillo está sustituido con R^4 en dicho átomo de nitrógeno.

En una modalidad, el anillo de 5 miembros Q se selecciona a partir del grupo que consiste de triazolilo y tiadiazolilo. En otra modalidad, el anillo de 5 miembros Q se selecciona a partir del grupo que consiste de tetrazolilo y oxadiazolilo. En una modalidad adicional, el anillo de 5 miembros Q es imidazolilo.

Cuando Q es un anillo de 6 miembros, Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxaxolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo.

En una modalidad preferida de la invención el anillo de 6 miembros Q se selecciona a partir del

grupo que consiste de piridonilo, tetrahidrotriazolopiridilo y tetrahidrotriazolopirimidinilo. En otra modalidad el anillo de 6 miembros Q es piridazinilo. En una modalidad adicional el anillo de 6 miembros Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo e imidazopiridilo.

Q también puede estar sustituido con 0, 1, 2 o 3 sustituyentes R^4, en el cual el número de sustituyentes R^4 se designa con el término *m2*. En una modalidad preferida *m2* es 1 ó 2.

Cuando Q es un anillo de 5 miembros el sustituyente R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})-heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})-heteroarilo, alquil(C_{0-6})O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)-

alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})-N(alquilo de C_{1-4})$_2$ y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En una modalidad adicional de la invención R^4 en el anillo de 5 miembros Q se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-

arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En una modalidad de la invención Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y R^4 se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo, O-alquil(C_{0-6})-arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})O-arilo, alquil(C_{0-6})-O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-

heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En otra modalidad de la invención Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y R^4 se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-

O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

Cuando Q es un anillo de 6 miembros el sustituyente R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})-arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})-(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo

de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En una modalidad apropiada de la invención R^4 en el anillo Q de 6 miembros se selecciona a partir de hidrógeno y alquilo de C_{1-6}. En una modalidad adicional de la invención R^4 es hidrógeno, metilo, etilo, propilo, butilo o hexilo.

En una modalidad preferida de la invención Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolo-piridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo y R^4 es hidrógeno o alquilo de C_{1-6}.

En otra modalidad preferida de la invención Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo,

piridazinilo y imidazopiridilo,. y R^4 es hidrógeno o alquilo de C_{1-6}.

En una modalidad apropiada de la invención R^4 se selecciona a partir del grupo que consiste de benzo[b]tiofenilo, benzodioxolilo, bromo, bromofurilo, butoxifenilo, clorometoxipiridilo, clorofenilo, clorofenilmetanol, cloropiridilo, clorotiofeno, cianofenilo, ciclohexilo, ciclopentilo, diclorofenilo, dicloropiridilo, difluorofenilo, dimetiltiazolilo, etanol, etoximetilo, fluorometilfenilo, fluorofenilo, éster metílico del ácido fórmico, furilo, hidrógeno, hidroxifenoximetilo, hidroxifenilo, imidazolilo, metoxietilo, metoximetilo, metoxifenoximetilo, metoxifenilo, metoxifeniletilo, metoxipiridazinilo, metoxipiridilo, metoxipirimidinilo, metoxitiofeno, metilimidazolilo, metilpiridilo, metilsulfanilmetilo, metiltiazolilo, metiltiofeno, nitrofurilo, nitrofenilo, fenilo, p-toliloximetilo, piridazinilo, piridinoxidilo, bencilmorfolinilo, piridinolilo, piridilo, piridilmetilo, pirimidinilo, ter-butilfenilo, tetrahidrofurilo, tiazolilo, tiofeno, tolilo, trifluorometilo, éster metílico del ácido acético, alilo, amino, bencilo, ciclopropilmetilo, etilo, fluorobencilo, fluoroetilo, furilmetilo, hidroxietilo, isobutilo, metilo, metilbencilo, metilbutilo, metilsulfanil-

propilo, n-butilo, n-hexilo, n-propilo, tetrahidrofurilmetilo, tiofenilmetilo y trifluoroetilo.

El anillo Q puede estar sustituido con uno o más R^4 en un átomo de carbono y/o un átomo de nitrógeno en el anillo. Cuando Q está sustituido en el átomo de carbono, R^4 se selecciona a partir de benzo[b]tiofenilo, benzodioxolilo, bromo, bromofurilo, butoxifenilo, clorometoxipiridilo, clorofenilo, clorofenilmetanol, cloropiridilo, clorotiofeno, cianofenilo, ciclohexilo, ciclopentilo, diclorofenilo, dicloropiridilo, difluorofenilo, dimetiltiazolilo, etanol, etoximetilo, fluorometilfenilo, fluorofenilo, éster metílico del ácido fórmico, furilo, hidrógeno, hidroxifenoximetilo, hidroxifenilo, imidazolilo, metoxietilo, metoximetilo, metoxifenoximetilo, metoxifenilo, metoxifeniletilo, metoxipiridazinilo, metoxipiridilo, metoxipirimidinilo, metoxitiofeno, metilimidazolilo, metilpiridilo, metilsulfanilmetilo, metiltiazolilo, metiltiofeno, nitrofurilo, nitrofenilo, fenilo, p-toliloximetilo, piridazinilo, piridinoxidilo, bencilmorfolinilo, piridinolilo, piridilo, piridilmetilo, pirimidinilo, ter-butilfenilo, tetrahidrofurilo, tiazolilo, tiofeno, tolilo y trifluorometilo.

Cuando Q está sustituido en el átomo de nitrógeno, R^4 se selecciona a partir de éster

metílico del ácido acético, alilo, amino, bencilo, ciclopropilo, ciclopropilmetilo, etilo, fluorobencilo, fluoroetilo, furilmetilo, hidroxietilo, isobutilo, metoxietilo, metilo, metilbencilo, metilbutilo, metilsulfanilpropilo, *n*-butilo, *n*-hexilo, *n*-propilo, tetrahidrofurilmetilo, tiofenilmetilo y trifluoroetilo.

Cuando R^4 es un anillo R^4 puede estar sustituido con uno o más sustituyentes A, en el cual A se selecciona a partir de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})-cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})ciano, O-alquil(C_{1-6})CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{1-6})(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})-NR^5(CO)NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})-NR^5(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste

de C, N, O y S.

En una modalidad preferida A se selecciona a partir de hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})-arilo, alquil(C_{0-6})OR^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

Las modalidades específicas de la invención incluyen:

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

5-(3-metoxifenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-metil-1*H*-benzoimidazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]-oxadiazol,

3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[4-metil-5-(2-metil-tiazol-4-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-[5-(2-metil-tiazol-4-il)-[1,3,4]oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

3-[4-metil-5-(5-nitro-furan-2-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-[5-(4-ter-butilfenil)-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-benzo-oxazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)piridina,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-imidazo[4,5-b]piridina,

5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

3-metil-5-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-metil-5-fenil-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxa-diazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-morfolina,

4-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,2,4]oxadiazol,

2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(2-metilpiridin-4-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

2-[5-(3-yodofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil}-amina,

5-(3-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-trifluorometoxi-fenil)[1,2,4]-oxadiazol,

3-(5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-bromo-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-benzoimidazol,

5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-[5-(3-metoximetil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

4-[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina,

2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-1-metil-1*H*-imidazo[4,5-b]piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1-metil-1*H*-imidazo[4,5-b],

3-[1-metil-1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]oxadiazol, o

5-(3-furan-3-il-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

o sal de los mismos.

Las modalidades especificas adicionales de la invención incluyen:

4-(4-ciclopropil-5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-

piridina,

4-{4-metil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-o-tolil-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-{3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]-triazol-4-il}-etanol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxa-diazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(4-etil-5-furan-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

Ester metílico del ácido {3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-acético,

5-(2-fluoro-5-metil-fenil)-3-[5-furan-2-il-4-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-

oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-{5-[3-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-ciclopentil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-{4-etil-5-[2-(4-metoxi-fenil)-etil]-4H-[1,2,4]triazol-3-ilsulfanilmetil}-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-toliloximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metoxi-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metoximetil-4H-

[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etil-sulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-furan-2-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenoxi-metil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

3-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenoxi-metil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxa-diazol,

{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-metanol,

3-(3-clorofenil)-5-[4-etil-5-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metilsulfanilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-etoximetil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]-

triazol-3-carboxílico,

2-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-{1-[4-etil-5-(tetrahidrofuran-2-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridazina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-ilmetil)-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-fenol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenoximetil)-4-(tetrahidrofuran-2-ilmetil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-ciclopropil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-il-

sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-[4-etil-5-(tetrahidrofuran-2-il)-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-{5-[3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(3-clorofenil)-5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-metilsulfanil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1H-benzoimidazol,

5-(2,5-dimetil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-ciclopropil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[2-(3-clorofenil)-oxazol-4-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-metil-5-(5-tiofen-2-il-[1,2,4]oxadiazol-3-

ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{4-metil-5-[5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

2-metil-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

1-{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-etanona,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-metil-5-tiofen-2-il-4H-[1,2,4]triazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-2-metil-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-tiofen-2-il-4-tiofen-2-il-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxa-diazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

3-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[4-metil-5-(5-fenil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

2-cloro-4-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[3-(3-fluoro-fenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(3-fluoro-fenil)-5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(5-fluoro-2-metil-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]-

triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

4-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadi-azol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metoxi-piridina,

3-(3-clorofenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-benzonitrilo,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(2,5-diclorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4)oxadiazol,

4-{5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4)triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

4-[4-metil-5-(3-tiofen-3-il-[1,2,4]oxadiazol-5-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-tiofen-3-carbonitrilo,

5-(3-clorofenil)-3-[5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-[5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-ilamina,

3-piridin-4-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-tiofen-2-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(2,5-difluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[4-etil-5-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-etil-3-furan-2-il-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-tolil-4H-[1,2,4]-

triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-m-tolil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-nitro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-[5-(2,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

5-(2-cloro-5-metil-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-{5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-dicloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-tiofen-2-il-4H-[1,2,4]triazol,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-furan-2-il-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-{3-[5-(3-cloro-tiofen-2-il)-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-trifluoro-

metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

4-etil-3-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-5-trifluorometil-4H-[1,2,4]triazol,

4-{3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-[3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

4-{4-etil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-

3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol,

3-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-(5-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-metil-tiazol-4-il)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(4-fluoro-fenil)-[1,2,4]oxadiazol,

4-etil-3-{1-(5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-5-furan-2-il-4H-[1,2,4]triazol,

4-(4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-(4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[4-cloro-5-(3-clorofenil)-isoxazol-3-ilm-etilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[4-cloro-5-(3-clorofenil)-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metil-

piridina,

3-[5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metoxi-piridina,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-benzonitrilo,

5-(3-clorofenil)-3-[4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-[5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-5-fluorobenzonitrilo,

4-etil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-2-il-4H-[1,2,4]triazol,

4-metil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-3-il-4H-[1,2,4]triazol,

4-etil-3-furan-2-il-5-(5-fenil-isoxazol-3-il-metilsulfanil)-4H-[1,2,4]triazol,

4-[4-etil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-[4-metil-5-(5-fenil-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,3,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-[4-etil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{5-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-[3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tri-

fluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-cloro-4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-(3-clorofenil)-5-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-metil-5-tiazol-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

4-{4-etil-5-[5-(4-metiltiofen-2-il)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(3-nitro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-

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ilsulfanilmetil)-5-(3-nitro-fenil)-[1,3,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[1-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-

piridina,

4-{5-[5-(5-cloro-2-fluor6-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-(5-cloro-2-fluorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-

piridina,

2-cloro-4-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4)triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol,

2-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-

il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4(5-(1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-cloro-2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]tri-

azol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

2-cloro-4-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-furan-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-{5-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol-2-il}-piridina,

2-(3-clorofenil)-5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-(5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4)triazol-3-il}-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-etil-5-{1-[5-(2-fluoro-5-metilfenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

2-(2-fluoro-5-metil-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

2-(5-cloro-2-fluoro-fenil)-5-[1-(4-etil-5-furan-

2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

2-(5-cloro-2-fluoro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(3-fluorofenil)-[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-{5-[1-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

4-{5-[1-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

4-{5-[1-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

2-(3-clorofenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

3-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol,

4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-(1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-[5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropilmetil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil}-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

4-cloro-2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

4-{4-ciclopropil-5-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-

piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(3-fluoro-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-ciclopropil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il)-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

4-{4-ciclopropil-5-[5-(2,5-difluorofenil)[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[1-(5-m-tolil-[1,2,4]oxadi-azol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-(4-ciclopropil-5-{1-[5-(3-metoxifenil)[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]tri-azol-3-ilsulfanilmetil)(1,2,4]oxadiazol-5-il]-4-metilfenol,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-metanol,

3-[5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-fenol,

5-(3-clorofenil)-3-[4-(tetrahidro-furan-2-il-metil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

(2-clorofenil)-{5-[5-(3-clorofenil)-(1,2,4]oxadiazol-3-ilmetilsulfanil]-4-isobutil-4H-[1,2,4]triazol-3-il}-metanol,

5-(2-fluoro-5-metil-fenil)-3-[5-tiofen-2-il-4-(2,2,2-trifluoro-etil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-3-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-

[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(5-furan-2-il-4-metil-

4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridazina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-furan-2-il-4-isobutil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metilsulfanil-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-hexil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-iloximetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadi-

azol-3-ilmetoxi]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(2-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-2-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzoico,

5-(2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-vinil-fenil)-[1,2,4]oxadiazol,

5-(3-difluorometoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metoxi-tiofen-3-il)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-

[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(3-clorofenil)-5-[2-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[2-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-tiofen-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]piridina,

5-(5-bromo-4-metil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-(3-clorofenil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfonilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfinilmetil)-[1,2,4]oxadiazol,

2-metil-6-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{2-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-

propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)amina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(1H-pirrol-3-il)-[1,2,4]oxadiazol,

1-óxido de 4-{5-[5-(3-clorofenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-

piridina,

5-(3-clorofenil)-3-(2-furan-2-il-3-metil-3H-imidazol-4-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[4-(2-fluoro-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-hidroxi-benzonitrilo,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina, o

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etoxi}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil--4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

3-{3-[1-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-{3-[1-(4-ciclopropil-5-piridin4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

3-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

cis-4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il)-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

Ester ter-butílico del ácido (S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico,

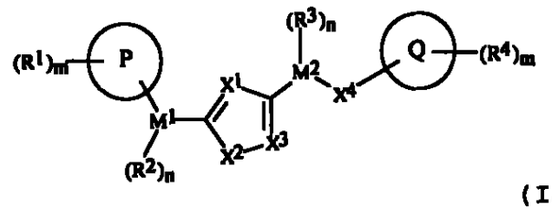
(S)-1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-

(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil-amina,

(S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-dimetil-amina,

o sal de los mismos.

Los ejemplos adicionales factibles de compuestos de la fórmula I son provistos por compuestos de la fórmula Ia



(Ia)

en la cual:

P se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{3-7} y un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})-arilo, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, alquil(C_{1-6})OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})$(CO)R^5$, O-alquil(C_{1-6})$(CO)R^5$, alquil(C_{0-6})CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})(CO)-NR^5R^6, O-alquil(C_{1-6})$(CO)NR^5R^6$, alquil(C_{0-6})$NR^5(CO)R^6$, O-alquil(C_{2-6})$NR^5(CO)R^6$, alquil(C_{0-6})$NR^5(CO)NR^5R^6$, alquil(C_{0-6})SR^5 O-alquil(C_{2-6})SR^5, alquil(C_{0-6})$(SO)R^5$, O-alquil(C_{2-6})$(SO)R^5$, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})-SO_2R^5, alquil(C_{0-6})$(SO_2)NR^5R^6$, O-alquil(C_{2-6})$(SO_2)NR^5R^6$, alquil(C_{0-6})$NR^5(SO_2)R^6$, O-alquil(C_{2-6})$NR^5(SO_2)R^6$, alquil(C_{0-6})$NR^5(SO_2)NR^5R^6$, O-alquil(C_{2-6})$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})$NR^5(CO)OR^6$, O-alquil(C_{2-6})$NR^5(CO)OR^6$, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, en el cual dicho anillo puede estar sustituido con uno o más A;

M^1 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-3})(CO)NR^5 alquilo de C_{0-3}, alquil(C_{0-4})NR^5, alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^2 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^1, X^2 y X^3 se seleccionan de manera independiente a partir del grupo que consiste de CR, CO, N, NR, O y S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5, alquil(C_{0-3})NR^5R^6 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, cicloalquilo de C_{3-7}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo

de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})-(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)-alquilo de C_{0-3};

R^3 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5, alquil(C_{0-4})(NR^5R^6), alquil(C_{0-4})-(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halogenoalquilo de C_{1-4}, C, O, SO, SO_2 y S;

Q es un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S y cuyo anillo fusionado puede estar sustituido con uno o más A;

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano,

oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})-arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, en el cual dicho anillo puede estar sustituido con uno o más A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno, hidroxi, alquilo de C_{1-6}, alquil(C_{0-6})cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, y en el cual R^5 y R^6 pueden formar juntos un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S;

en el cual cualquier alquilo de C_{1-6} alquenilo de C_{2-6}, alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo y alquil(C_{0-6})-heteroarilo definido bajo R^1, R^2, R^3, R^4, R^5 y R^6 puede estar sustituido con uno o más A; y

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, oxo, halógeno, nitro, alquil(C_{0-6})-ciano, alquilo de C_{1-4}, alquil(C_{0-4})-cicloalquilo de C_{3-6}, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquilo de C_{1-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})SR^5 O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})NR^5(CO)NR^5R^6, O(CO)NR^5R^6, NR^5(CO)OR^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)-NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})-(SO)R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S;

m se selecciona a partir de 0, 1, 2, 3 y 4; y

n se selecciona a partir de 0, 1, 2 y 3,

o sal de los mismos.

La presente invención se refiere al uso de compuestos de las fórmula I y IA como los definidos anteriormente en la presente así como a las sales de

los mismos. Las sales para uso en formulaciones farmacéuticas serán sales farmacéuticamente aceptables, pero otras sales podrían ser útiles en la producción de los compuestos de las fórmulas I y Ia.

Los ejemplos de sales farmacéuticamente aceptables pueden ser, pero no se limitan a clorhidrato, 4-aminobenzoato, antranilato, 4-aminosalicilato, 4-hidroxibenzoato, 3,4-dihidroxibenzoato, 3-hidroxi-2-naftoato, nitrato y trifluoroacetato. Otras sales farmacéuticamente aceptables y métodos para preparar estas sales se pueden encontrar en, por ejemplo, Remington's Pharmaceutical Sciences (18ª edición, Mack Publishing Co.).

Algunos compuestos de la fórmula I pueden tener centros quirales y/o centros isoméricos geométricos (isómeros E y Z), y se debe entender que la invención abarca a todos de dichos isómeros ópticos, diastereoisómeros e isómeros geométricos.

La invención se refiere a cualquiera y a todas las formas tautoméricas de los compuestos de la fórmula I.

La invención se refiere a los siguientes compuestos, los cuales se pueden utilizar como intermediarios en la preparación de un compuesto de la fórmula I:

Acido 6-metilpiridin-4-carboxílico,

1-ciano-3-etilbenceno,

Acido 3-etilbenzoico,

Acido 3-fluoro-5-metil-benzoico,

Acido 3-metoximetil-benzoico,

N-hidroxi-3-metoxi-benzamidina,

N-hidroxi-benzamidina,

N-hidroxi-3-metil-benzamidina,

5-clorometil-3-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-clorometil-3-fenil-[1,2,4]oxadiazol,

5-clorometil-3-m-tolil-[1,2,4]oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-(5-clorometil-[1,2,4]oxadiazol-3-il)-benzonitrilo,

3-clorometil-5-m-tolil-[1,2,4]oxadiazol,

3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina,

3-clorometil-5-(3-nitro-fenil)-[1,2,4]oxadiazol,

4-(3-clorometil-[1,2,4]oxadiazol-5-il)-2-metil-piridina,

3-clorometil-5-(3-etil-fenil)-[1,2,4]oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-

dimetil-amina,

3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-clorometil-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol,

5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol,

3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol,

3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-tiazol-4-il-[1,2,4]oxadiazol,

3-clorometil-5-(3-iodo-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]-oxadiazol,

5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-fenil-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-piridin-2-il-4*H*-[1,2,4]triazol-3-tiol,

5-(4-bencil-morfolin-2-il)-4-metil-4*H*-[1,2,4]-triazol-3-tiol,

5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-piridin-3-il-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-tiol,

5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-tiol,

Acido 5-cloro-tiofen-3-carboxílico,

Acido 3-metilsulfanil-benzoico,

Acido 3-ciclopropil-benzoico,

Acido 3-ter-butoxicarbonilamino-benzoico,

Acido 3-acetil-benzoico,

Hidrazida del ácido 2-metil-isonicotínico,

Hidrazida del ácido 5-cloro-2-fluoro-benzoico,

Hidrazida del ácido 3-ciano-benzoico,

Hidrazida del ácido 2-cloro-isonicotínico,

Hidrazida del ácido 2-fluoro-5-metil-benzoico,

Hidrazida del ácido pirimidin-4-carboxílico,

3-fluoro-N-hidroxi-benzamidina,

N-hidroxi-tiofen-3-carboxamidina,

2-cloro-N-hidroxi-propionamidina,

3,N-dihidroxi-benzamidina,

N-hidroxi-2-metil-benzamidina,

N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina,

3-cloro-N-hidroxi-benzamidina,

N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina,

2,5-difluoro-N-hidroxi-benzamidina,

4-metil-5-piridin-3-il-4H-[1,2,4)triazol-3-tiol,

4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol,

4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-

triazol-3-tiol,

5-tiofen-2-il-4-tiofen-2-ilmetil-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-furan-2-ilmetil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol,

4-etil-5-piridin-3-il-4H-[1,2,4]triazol-3-tiol,

4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-furan-2-ilmetil-5-piridin-3-il-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol,

5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol,

5-(2-cloro-6-metil-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]-

triazol-3-tiol,

4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(tetrahidro-furan-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

Ester metílico del ácido 4-etil-5-tioxo-4,5-dihidro-1H-[1,2,4]triazol-3-carboxílico,

5-(2-cloro-piridin-4-il)-4-etil-4H-[1,2,4]-triazol-3-tiol,

5-(2-cloro-6-metoxi-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]-triazol-3-tiol,

4-propil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol ,

4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]-triazol-3-tiol,

3-(5-mercapto-4-metil-4H-[1,2,4]triazol-3-il)-benzonitrilo,

5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-tiol,

5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-pirimidin-5-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-furan-3-il-2,4-dihidro-[1,2,4]-

triazol-3-tiona,

4-(tetrahidrofuran-2-ilmetil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

5-ciclopentil-4-etil-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(2-(4-metoxi-fenil)-etil]-2,4-dihidro-[1,2,4]triazol-3-tiona,

5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(3-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(4-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-nitrofenil)-4H-[1,2,4]triazol-3-tiol,

5-(2,5-difluorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(3-clorofenil)4-etil-4H-[1,2,4]triazol-3-tiol,

5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-metoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-metil-5-piridin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-alil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(4-metoxi-fenoximetil)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-fenoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-hidroximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(2-metoxi-etil)-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-metilsulfanilmetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

5-etoximetil-4-etil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

5-furan-3-il-4-metil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-metil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-piridazin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-piridin-4-ilmetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(6-hidroxi-piridin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(4-hidroxi-fenil)-2,4-dihidro-[1,2,4]-

triazol-3-tiona,

4-etil-5-p-toliloximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(6-metoxi-piridin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(2-metoxi-piridin-4-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-pirimidin-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(5-metoxi-pirimidin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol,

4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol,

4-ciclopropilmetil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol,

4-ciclopropil-5-tiofen-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

5-furan-2-il-4-(2-metoxi-etil)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-ciclopropil-5-furan-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

Ester metílico del ácido (3-tiofen-2-il-5-tioxo-1,5-dihidro-[1,2,4]triazol-4-il)-acético,

4-ciclopropilmetil-5-tiofen-2-il-2,4-dihidro-

[1,2,4]triazol-3-tiona,

4-(2-metoxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

Tiofen-2-il-4-(2,2,2-trifluoroetil)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-ciclopropil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-ciclopropil-5-piridin-3-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-tiol,

4-etil-3-metansulfonil-5-tiofen-2-il-4H-[1,2,4]-triazol,

4-(5-metansulfonil-4-metil-4H-[1,2,3]triazol-3-il)-piridina,

4-(2-hidroxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-(4,5-dimetil-4H-[1,2,4]triazol-3-il)-piridina,

Metil-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-il)-amina,

3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]-triazolo[4,3-a]pirimidina,

3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

4-etil-5-(6-metoxi-piridazin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(5-metoxi-piridin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

5-clorometil-3-fenil-[1,2,4]oxadiazol,

5-clorometil-3-(3-fluoro-fenil)-[1,2,4]-oxadiazol,

5-clorometil-3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

5-clorometil-3-tiofen-2-il-[1,2,4]oxadiazol,

5-clorometil-3-tiofenl-3-il-[1,2,4]oxadiazol,

3-(5-clorometil-[1,2,4]oxadiazol-3-il)-fenol,

5-clorometil-3-o-tolil-[1,2,4]oxadiazol,

5-clorometil-3-(3-clorofenil)-[1,2,4]oxadiazol,

5-clorometil-3-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo,

2-cloro-4-(3-clorometil-[1,2,4]oxadiazol-5-il)-piridina,

3-clorometil-5-(2,5-dimetil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(2,5-diclorofenil)-[1,2,4]-

oxadiazol,

3-clorometil-5-(2-fluoro-5-bromo-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(3-metil-fenil)-[I,2,4]oxadiazol,

3-clorometil-5-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(3-ciclopropil-fenil)-[1,2,4]-oxadiazol,

Ester ter-butílico del ácido 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-carbámico,

1-(3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-etanona,

5-(5-cloro-2-fluoro-fenil)-3-clorometil-[1,2,4]-oxadiazol,

2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-fenol,

3-clorometil-5-(2-cloro-5-metil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(2,5-dicloro-tiofen-3-il)-[1,2,4]-oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(2-metil-tiazol-4-il)-[1,2,4]-oxadiazol,

3-clorometil-5-(4-fluoro-fenil)-[1,2,4]oxadiazol,

5-(5-bromo-2-fluoro-fenil)-3-clorometil-[1,2,4]-oxadiazol,

3-clorometil-5-(4-metil-tiofen-2-il)-[1,2,4]-oxadiazol,

5-(3-clorometil-[1,2,4]oxadiazol-5-il)-tiofen-3-carbonitrilo,

2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-benzonitrilo,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-fluoro-benzonitrilo,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-fluoro-benzonitrilo,

4-cloro-2-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenol,

3-(1-cloro-etil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

3-(1-cloro-etil)-5-(3-fluoro-fenil)-[1,2,4]-oxadiazol,

3-(1-cloro-etil)-5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol,

[3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-metanol,

3-clorometil-5-[1-(toluen-4-sulfonil)-1H-pirrol-3-il]-[1,2,4]oxadiazol,

3-clorometil-5-furan-3-il-[1,2,4]oxadiazol,

3-clorometil-5-(5-cloro-tiofen-2-il)-[1,2,4]-oxadiazol,

1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etanol,

(5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-metanol,

1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etanol,

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanol,

2-clorometil-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol,

2-clorometil-5-(3-clorofenil)-[1,3,4]oxadiazol,

4-(5-clorometil-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

2-clorometil-5-m-tolil-[1,3,4]oxadiazol,

3-(5-clorometil-[1,3,4]oxadiazol-2-il)-benzonitrilo,

2-cloro-4-(5-clorometil-[1,3,4]oxadiazol-2-il)-piridina,

2-(5-cloro-2-fluoro-fenil)-5-clorometil-[1,3,4]-oxadiazol,

2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol,

2-(1-bromo-etil)-5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol,

4-[5-(1-bromo-etil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

2-(1-bromo-etil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol,

2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol,

3-(1-bromo-etil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

1-[5-(3-clorofenil)-isoxazol-3-il]-etanol,

1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etanol,

Ester metílico del ácido 5-(2-fluoro-5-metil-fenil)-isoxazol-3-carboxílico,

Ester metílico del ácido 5-tiofen-3-il-isoxazol-3-carboxílico,

Ester metílico del ácido 5-fenil-isoxazol-3-carboxílico,

Ester etílico del ácido 5-(3-clorofenil)-4-metil-isoxazol-3-carboxílico,

Ester metílico del ácido 5-(5-cloro-tiofen-3-il)-isoxazol-3-carboxílico,

[5-(3-clorofenil)-isoxazol-3-il]-metanol,

[2-(3-clorofenil)-oxazol-4-il]-metanol,

[3-(3-clorofenil)-isoxazol-5-il]-metanol,

5-(tiofen-3-il-isoxazol-3-il)metanol,

[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-metanol,

(5-fenil-isoxazol-3-il)-metanol,

[5-(3-clorofenil)-4-metil-isoxazol-3-il]-metanol,

[5-(5-cloro-tiofen-3-il)-isoxazol-3-il)]-metanol,

Ester 1-[5-(3-clorofenil)-isoxazol-3-il]-etílico del ácido metansulfónico,

Ester 2-(3-clorofenil)-oxazol-4-il-metílico del ácido metansulfónico,

Ester 3-(3-clorofenil)-isoazol-5-il-metílico del ácido metansulfónico,

Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester -fenil)-isoxazol-5-il]-etílico del ácido metansulfónico,

Ester 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(3-clorofenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-tiofen-3-il-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-fenil-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(3-clorofenil)-4-metil-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(5-cloro-tiofen-3-il)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico,

Ester 1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico,

Ester 4-cloro-5-(3-clorofenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Acido pirimidin-4-carboxílico,

Ester metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico,

2-bromometil-5-(3-clorofenil)-oxazol,

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico,

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico,

1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-

il]-etanol,

1-[3-(3-clorofenil)-isoxazol-5-il]-etanol,

[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-metanol,

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico,

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico,

Clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico,

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico,

Hidrazida del ácido (5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético,

Hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico,

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-3-metil-butírico,

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona,

3-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona,

3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]-oxadiazol,

1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-

3-ilmetoxi]-1H-benzotriazol,

(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-acetonitrilo,

Acido 2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-propiónico,

Acido 2-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanil)-propiónico,

3-(3-clorofenil)-5-(4-metil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol o

Ester ter-butílico del ácido {3-[3-(4-metil-5-tiofen-2-il-4H[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il-fenil}-carbámico.

Formulaciones farmacéuticas

De conformidad con un aspecto de la presente invención se provee una formulación farmacéutica que comprende un compuesto de la fórmula I, o sal del mismo, para ser utilizado en la prevención y/o tratamiento de trastornos mediados por el subtipo 5 del receptor de glutamato metabotrópico (mGluR5) y cualesquiera trastornos listados más adelante.

La composición puede estar en una forma apropiada para administración por vía oral, por ejemplo como una tableta, píldora, jarabe, polvo, gránulo o cápsula, para inyección parenteral (incluyendo

inyección intravenosa, subcutánea, intramuscular, intravascular, o infusión) como una solución, suspensión o emulsión estéril, para administración por vía tópica como un ungüento, parche o crema o para administración por vía rectal como un supositorio.

En general, las composiciones anteriores se pueden preparar en una manera convencional utilizando uno o más excipientes, diluyentes farmacéuticos y/o vehículos inertes convencionales. De conformidad con otro aspecto de la invención, se provee una formulación farmacéutica que comprende como ingrediente activo una cantidad terapéuticamente efectiva de un compuesto de la fórmula I en asociación con uno o más diluyentes, excipientes y/o vehículo inerte farmacéuticamente aceptables.

Las dosis apropiadas de los compuestos de la fórmula I en el tratamiento de un mamífero, incluyendo humanos, son de aproximadamente 0.01 a 250 mg/kg de peso corporal para administración por vía oral y de aproximadamente 0.001 hasta 250 mg/kg de peso corporal en la administración por vía parenteral. La dosis diaria típica de los ingredientes activos varía dentro de un intervalo amplio y depende de diversos factores tales como la indicación relevante, la vía de administración, la edad, peso y sexo del paciente

y puede ser determinada por un médico.

Uso médico

Se ha descubierto que los compuestos de conformidad con la presente invención, o sales de los mismos, presentan un alto grado de potencia y selectividad para subtipos individuales del receptor de glutamato metabotrópico (mGluR). En particular existen compuestos de conformidad con la presente invención que son potentes y selectivos para el receptor del Grupo I de mGluR y de manera más particular para mGluR5. Por consiguiente, se espera que los compuestos de la presente invención sean útiles en la prevención y/o tratamiento de condiciones asociadas con la activación excitadora de un receptor del Grupo I de mGluR y para inhibir el daño a las neuronas ocasionado por la activación excitadora de un receptor del Grupo I de mGluR, específicamente cuando el receptor del Grupo I de mGluR es mGluR5. Los compuestos se pueden utilizar para producir un efecto inhibidor del Grupo I de mGluR, en especial mGluR5, en mamíferos, incluyendo humanos.

mGluR5 está altamente expresado en el sistema nervioso central y periférico y en otros

tejidos. Por lo tanto, se espera que los compuestos de la invención sean bastante adecuados para la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5, tales como trastornos neurológicos y psiquiátricos agudos y crónicos y trastornos del dolor agudos y crónicos.

Trastornos adicionales son la demencia senil de la enfermedad de Alzheimer, demencia inducida por SIDA, enfermedad de Parkinson, esclerosis lateral amiotrófica, Corea de Huntington, migraña, epilepsia, esquizofrenia, depresión, ansiedad, ansiedad aguda, trastorno obsesivo-compulsivo, trastornos oftalmológicos tales como retinopatías, retinopatías diabéticas, glaucoma, trastornos auditivos neuropáticos tales como tinnitus, neuropatías inducidas por quimioterapia, neuralgia post-herpética, y neuralgia del trigémino, tolerancia, dependencia, adicción y trastornos del ansia (craving), trastornos del desarrollo neuronal incluyendo X frágil, autismo, retraso mental, esquizofrenia y síndrome de Down.

Los compuestos también son bastante adecuados para la prevención y/o tratamiento de dolor relacionado con migraña, dolor inflamatorio, trastornos de dolor neuropático tales como neuropatías diabéticas, artritis y enfermedades reumatoides, dolor de la zona

baja de la espalda, dolor post-operativo y dolor asociado con diversas condiciones incluyendo angina de pecho, cólicos renales o biliares, menstruación, migraña y gota.

Otros trastornos son apoplejía, trauma cefálico, daños anóxicos e isquémicos, hipoglucemia, enfermedades cardiovasculares y epilepsia.

La dosis requerida para el tratamiento terapéutico o preventivo de un trastorno particular necesariamente variará dependiendo del hospedero tratado, la vía de administración y la gravedad de la enfermedad que está siendo tratada.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para ser utilizados en terapia.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos neurológicos.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos psiquiátricos.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la

presente invención, para uso en la prevención y/o tratamiento de trastornos del dolor crónicos y agudos.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de demencia senil de la enfermedad de Alzheimer, demencia inducida por SIDA, enfermedad de Parkinson, esclerosis lateral amiotrófica, Corea de Huntington, migraña, epilepsia, esquizofrenia, depresión, ansiedad, ansiedad aguda, trastornos oftalmológicos tales como retinopatías, retinopatías diabéticas, glaucoma, trastornos neuropáticos auditivos tales como tinnitus, neuropatías inducidas por quimioterapia, neuralgia post-herpética y neuralgia del trigémino, tolerancia, dependencia, X frágil, autismo, retraso mental, esquizofrenia y síndrome de Down.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la

presente invención, para uso en la prevención y/o tratamiento de dolor relacionado con migraña, dolor inflamatorio, trastornos del dolor neuropáticos tales como neuropatías diabéticas, artritis y enfermedades reumatoides, dolor de la zona baja de la espalda, dolor post-operativo y dolor asociado con diversas condiciones incluyendo angina de pecho, cólicos renales o biliares, menstruación, migraña y gota.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de apoplejía, trauma cefálico, daños anóxicos e isquémicos, hipoglucemia, trastornos cardiovasculares y epilepsia.

La presente invención se refiere también al uso de un compuesto de la fórmula I como el definido anteriormente en la presente invención, en la fabricación de un medicamento para la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5 y cualquier trastorno antes listado.

La invención también provee un método de tratamiento y/o prevención de trastornos mediados por el receptor mGluR5 y cualquier trastorno antes listado, en un paciente que padece del mismo, o que está en riesgo de padecer dicha condición, que

comprende administrar al paciente una cantidad efectiva de un compuesto de la fórmula I, como el definido anteriormente en la presente invención.

En el contexto de la presente descripción, el término "terapia" incluye tratamiento así como prevención, a menos que existan indicaciones específicas de lo contrario. Los términos "terapéutico" y "terapéuticamente" se deben considerar en forma correspondiente.

En esta descripción, a menos que se indique lo contrario, el término "antagonista" significa un compuesto que mediante cualesquiera medios, bloquea parcial o completamente, la ruta de transducción que conduce a la producción de una respuesta por el ligando.

El término "trastorno", a menos que se indique lo contrario, significa cualquier condición y enfermedad asociada con la actividad del receptor de glutamato metabotrópico.

Uso no médico

Además de su uso en medicina terapéutica, los compuestos de la fórmula I o sal del mismo, también son útiles como herramientas farmacológicas en el desarrollo y normalización de sistemas de

evaluación *in vitro* e *in vivo* para la evaluación de los efectos de inhibidores de actividad relacionada con mGluR en animales de laboratorio tales como gatos, perros, conejos, monos, ratas y ratones, como parte de la búsqueda respecto a nuevos agentes terapéuticos.

Farmacología

Se pueden analizar las propiedades farmacológicas de los compuestos de la invención utilizando pruebas normales para actividad funcional. Los ejemplos de pruebas para el receptor de glutamato son bien conocidas en la técnica, como se describen por ejemplo en Aramori *et al.*, *Neuron* *8*:757 (1992), Tanabe *et al.*, *Neuron* *8*:169 (1992), Miller *et al.*, *J. Neuroscience* *15*:6103 (1995), Balazs, *et al.*, *J. Neurochemistry* *69*:151 (1997). La metodología descrita en estas publicaciones se incorpora en la presente invención para referencia. De manera conveniente, los compuestos de la invención se pueden estudiar por medio de una prueba que mida la movilización de calcio intracelular, $[Ca^{2+}]_i$ en células que expresen a mGluR5.

La movilización de calcio intracelular se mide detectando cambios en fluorescencia de células

cargadas con el indicador fluorescente fluo-3. Las señales fluorescentes se miden utilizando el sistema FLIPR (Molecular Devices). Se utiliza un experimento de dos adiciones que pueda detectar compuestos que activen o antagonicen al receptor.

Para el análisis FLIPR, se siembran células que expresen a mGluR5d de humano en placas de 96 cavidades de fondo claro revestidas con colágena, con lados negros y el análisis de la movilización de $[Ca^{2+}]_i$ se efectúa 24 horas después de la siembra.

Los experimentos de FLIPR se efectúan utilizando un ajuste de láser de 0.800 W y una velocidad de disparador de cámara CCD de 0.4 segundos. Cada experimento de FLIPR se inicia con 160 µL de solución reguladora presente en cada cavidad de la placa celular. Después de cada adición del compuesto, se muestrea la señal de fluorescencia 50 veces a intervalos de 1 segundo seguido por 3 muestras a intervalos de 5 segundos. Las respuestas se miden como la altura del pico de la respuesta dentro del intervalo de muestreo. Se efectúan determinaciones de CE_{50} y CI_{50} a partir de los datos obtenidos provenientes de curvas de concentración-respuesta de 8 puntos (CRC) efectuadas por duplicado. Se generan CRC agonistas escalando todas las

respuestas hasta la respuesta máxima observada para la placa. El bloqueo antagonista de la exposición a los agonistas se normaliza con la respuesta promedio de la exposición al agonista en 14 cavidades de control en la misma placa.

Se valida una prueba funcional secundaria para mGluR5d basada en el recambio de fosfato de inositol (IP_3). La acumulación de IP_3 se mide como un índice del recambio de fosfolipasa C mediada por receptor. Se incuban células GHEK que expresen de manera estable a los receptores mGluR5d de humano con [3H]-mioinositol durante la noche, se lavan tres veces en solución salina regulada con HEPES y se pre-incuban durante 10 minutos con LiCl 10 mM. Se agregan los compuestos (agonistas) y se incuba durante 30 minutos a 37°C. La actividad antagonista se determina pre-incubando los compuestos de prueba durante 15 minutos, incubando después en presencia de glutamato (80 µM) o DHPG (30 µM) durante 30 minutos. Las reacciones se terminan mediante la adición de ácido perclórico (al 5%). Se recolectan las muestras y se neutralizan, y se separan los fosfatos de inositol utilizando columnas de intercambio iónico alimentadas por la fuerza de gravedad.

Más adelante, en los ejemplos farmacéuticos,

se provee un protocolo detallado para la evaluación de los compuestos de la invención.

Abreviaturas

FLIPR	Lectora de placas por formación de imagen fluorométrica
CCD	dispositivo acoplado por carga
CRC	curva de concentración-respuesta
GHEK	Células de riñón embrionario de humano que expresan al transportador de glutamato
HEPES	Ácido 4-(2-hidroxietil)-1-piperazin-etansulfónico (solución reguladora)
IP_3	Trifosfato de inositol
DHPG	3,5-dihidroxifenilglicina
BSA	Seroalbúmina de bovino
EDTA	Acido etilendiamintetra-acético

Métodos de preparación

Otro aspecto de la presente invención provee un procedimiento para preparar un compuesto de la fórmula I o sal del mismo.

A través de la siguiente descripción de dichos procedimiento se entiende que, en casos en los que sea apropiado, se agregarán, y posteriormente se retirarán grupos protectores apropiados a los diversos reactivos e intermediarios en una manera que

será fácilmente entendida por el experto en la técnica de síntesis orgánica. Los procedimientos convencionales para utilizar dichos grupos protectores así como ejemplos de grupos protectores apropiados se describen, por ejemplo, en "Protective Groups in Organic Síntesis" T.W. Green, P.G.M. Wuts, Wiley-Interscience, New York, 1999.

A menos que se indique lo contrario, P Q, X^1, X^2, X^3, X^4, R, R^1, R^2, R^3, R^4, R^5, R^6, M^1, M^2, M y N, son como se definen en la fórmula I.

Todos los materiales de partida se pueden conseguir comercialmente o se describieron anteriormente en la literatura. Los espectros de RMN ^1H y ^{13}C se registran en espectrómetros ya sea Bruker 300, Bruker DPX400 o Varian +400 que funcionan a 300, 400 y 400 MHz para ^1H RMN respectivamente, utilizando TMS o la señal de solvente residual como patrón de referencia, en cloroformo deuterado como solvente a menos que se indique de otra manera. Todos los corrimientos químicos reportados están en ppm en la escala delta, y la división fina de las señales como aparecen en los registros (s: singulete, d: doblete, t: triplete, q: cuarteto, m: multiplete).

Las separaciones de cromatografía líquida en línea, analíticas seguidas por detecciones de

espectros de masa, se registran en un aparato Waters LCMS que consiste de un espectrómetro de masas Alliance 2795 (LC) y un ZQ de un solo cuadrupolo. El espectrómetro de masas está equipado con una fuente de iones para electroaspersión operada en un modo iónico positivo o negativo. El voltaje para aspersión de iones es ±3 kV y el espectrómetro de masas se barre desde *m/z* 100-700 a un tiempo de barrido de 0.8 segundos. A la columna X-Terra MS, Waters, C8, 2.1 x 50 mm, 3.5 µm, se aplica un gradiente lineal de 5% hasta 100% de acetonitrilo en acetato de amonio 10 mM (acuoso), o en TFA al 0.1% (acuoso). La cromatografía de fase inversa preparatoria se corre en un HPLC auto-preparativo de Wilson con un detector de arreglo de diodos utilizando una Xterra MS C8, 19x300 mm, 7 µm como columna.

La cromatografía de fase inversa preparativa inducida por MS se corre en un sistema LC-MS de autopurificación de Waters con un detector de arreglo de diodo y un detector de masas ZQ utilizando una XTerra MS C8, 19x100 mm, 5 µm como columna.

La purificación mediante un cromatotrón se efectúa en láminas de vidrio revestidas con gel de sílice/yeso giratorias (Merck, 60 PF-254 con sulfato

de calcio), con una capa de revestimiento de 1, 2, o 4 mm utilizando un cromatotrón TC Research 7924T.

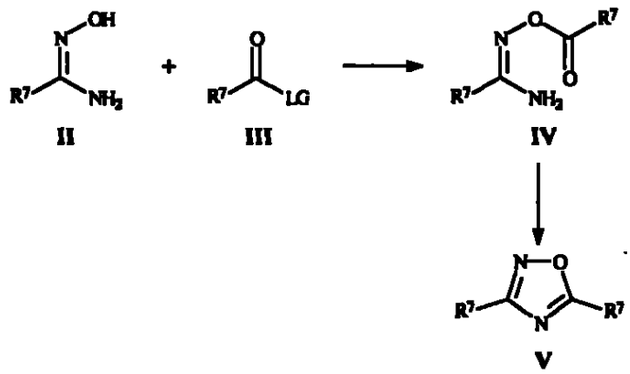
También se efectúa la purificación de los productos utilizando columnas para extracción Chem Elut (Varian, cat #1219-8002), Mega BE-SI (Bond Elut Silica) columnas de tipo SPE (Varian, cat # 12256018; 12256026; 12256034), o mediante cromatografía de vaporización instantánea en columnas de vidrio rellenadas con sílice. El calentamiento con microondas se efectúa en una cavidad de microondas de modo individual Smith Synthesizer que produce irradiación continua a 2,450 MHz (Personal Chemistry AB, Uppsala, Suecia).

Abreviaturas

DMF	N,N-dimetilformamida
BOPA	Peróxido de benzoilo
P-BEMP	2-ter-butilimino-2-dietilamino-1,3-dimetil-perhidro-1,3,2-diazafosforina unida a poliestireno
Deoxofluor	Trifluoruro de [Bis(2-metoxietil)amino]azufre
DAST	Trifluoruro de (dietilamino)azufre
EDCI	Clorhidrato de 1-(3-dimetilamino-propil)-3-etilcarbodiimida
HOBt	hidrato de 1-hidroxibenzotriazol
THF	tetrahidrofurano

TFA	Acido trifluoroacético
Et	etilo
Ac	acetilo
DIBAL	hidruro de di-isobutilaluminio
M, N	molar y normal
HBTU	hexafluorofosfato de O-benzotriazol-1-il-N,N,N',N'-tetrametiluronio
Boc	ter-butoxicarboniloxi
LDA	di-isopropilamina de litio
LHA	hidruro de litio y aluminio
MCPBA	ácido meta-cloroperoxibenzoico
SPE	extracción en fase sólida
Reactivo de Lawesson	[2,4-bis(4-metoxifenil)-1,3-ditia-2,4-difosfetan-2,4-disulfuro

Síntesis General de los compuestos de la fórmula V



Un compuesto de la fórmula V, en la cual R^7

se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)n-G$ en el cual G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, se puede preparar a través de ciclización de un compuesto de la fórmula IV formado a partir de un compuesto activado de manera apropiada de la fórmula III, en la cual LG es un grupo saliente, con un compuesto de la fórmula II. El compuesto de la fórmula II se puede preparar a partir de un nitrilo apropiado mediante adición de hidroxilamina en un solvente apropiado tal como metanol, etanol, agua o mezclas de los mismos, utilizando una base apropiada tal como hidróxido, carbonato o acetato.

El compuesto de la fórmula III se puede activar de la siguiente manera; i) como el cloruro de acilo formado a partir del ácido utilizando un reactivo apropiado tal como cloruro de oxalilo o cloruro de tionilo; ii) como un anhídrido o anhídrido mixto formado a partir del tratamiento con un reactivo tal como cloroformiato de alquilo; iii) utilizando métodos tradicionales para activar ácidos en reacciones de copulación de amida tales como EDCI con HOBt o sales de uronio tales como HBTU; iv) como

un éster de alquilo cuando se desprotona la hidroxiamidina utilizando una base fuerte tal como ter-butóxido; v) mediante cualquier otro método apropiado de activación para el substrato deseado.

La formación del éster se puede lograr utilizando un solvente aprótico apropiado tal como diclorometano, tetrahidrofurano, N,N-dimetilformamida o tolueno, opcionalmente con una base orgánica apropiada tal como trietilamina, di-isopropiletilamina y similares o una base inorgánica tal como bicarbonato de sodio o carbonato de potasio.

La ciclización del éster para formar un oxadiazol se puede efectuar en el éster crudo, con evaporación y reemplazo del solvente con un solvente de punto de ebullición más alto tal como DMF, o con extracción acuosa para proveer un material semi-purificado o con material purificado mediante métodos cromatográficos normales. La ciclización se puede lograr calentando de manera convencional o mediante irradiación de microondas (100-180°C), en un solvente apropiado tal como piridina o N,N-dimetilformamida o utilizando un método de temperatura más baja que emplee reactivos tales como fluoruro de tetrabutil-amonio en tetrahidrofurano o utilizando cualquier otro método apropiado conocido en la literatura.

También pueden estar presentes en los substratos otros grupos funcionales no reactivos, compatibles, protegidos de manera apropiada.

Los ejemplos adicionales de las reacciones antes descritas se pueden encontrar en Poulain et al., Tetrahedron Lett., (2001), 42, 1495-98, Ganglott et al., Tetrahedron Lett., (2001), 42, 1441-43, las cuales se incluyen en la presente invención como referencias.

Síntesis de nitrilos y ácidos para ser utilizados en la preparación de compuestos de las fórmulas II y III

Los nitrilos de arilo se pueden conseguir utilizando una variedad de métodos que incluyen cianuración de un halogenuro de arilo o triflato de arilo bajo catálisis con paladio o níquel utilizando una fuente de cianuro apropiada tal como cianuro de zinc en un solvente apropiado tal como N,N-dimetilformamida. El ácido correspondiente se puede conseguir a partir del nitrilo mediante hidrólisis ya sea bajo condiciones ácidas o básicas en un solvente apropiado tal como alcoholes acuosos. Los ácidos de arilo también se pueden conseguir a partir de una variedad de otras fuentes, incluyendo intercambio de

yodo- o bromo- litio seguido por entrampamiento con CO_2 para producir directamente el ácido.

El ácido se puede convertir a la amida primaria utilizando cualquier método compatible para activar al ácido, incluyendo a través del cloruro de acilo o anhídrido mixto, seguido por entrampamiento con cualquier fuente de amoniaco, incluyendo cloruro de amonio en presencia de una base apropiada, hidróxido de amonio, amoniaco metanólico o amoniaco en un solvente no prótico tal como dioxano. Este intermediario amida se puede convertir al nitrilo utilizando una variedad de reactivos para deshidratación tales como cloruro de oxalilo o cloruro de tionilo. También se puede aplicar esta secuencia de reacción para convertir un ácido en el nitrilo hasta ácidos no aromáticos, incluyendo derivados de aminoácido protegidos de manera apropiada. Un grupo protector apropiado para una amina, en un aminoácido o en una posición lejana de cualquier otro material de partida tipo ácido, puede ser cualquier grupo que remueva el carácter básico y las propiedades nucleofílicas del grupo funcional amina, incluyendo grupos protectores tipo carbamato tales como Boc.

Algunos ácidos se preparan más fácilmente tomando ventaja de análogos comercialmente disponibles.

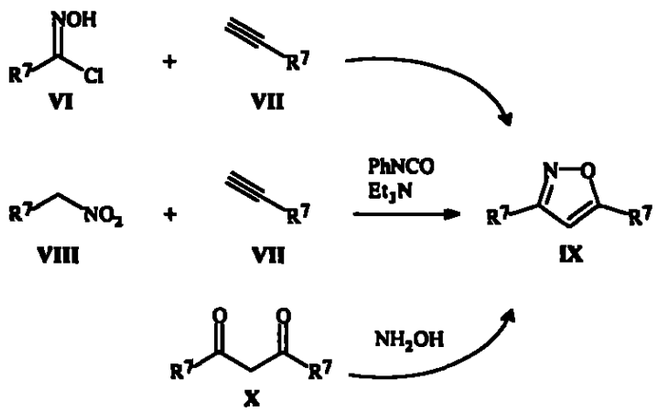
Por ejemplo el ácido 6-metilpiridin-4-carboxílico se prepara mediante eliminación de cloro del ácido 2-cloro-6-metilpiridin-4-carboxílico. Algunos tipos de fluoro-benzonitrilos y ácidos benzoicos sustituidos se pueden conseguir a partir de bromo-difluoro-benceno mediante desplazamiento de un grupo fluoro con un nucleófilo apropiado tal como imidazol en presencia de una base tal como carbonato de potasio en un solvente compatible tal como N,N-dimetil-formamida a temperaturas elevadas (80-120°C) durante intervalos prolongados de tiempo. El grupo bromo se puede convertir posteriormente en el ácido o nitrilo como se indicó anteriormente. Se pueden preparar ácidos benzoicos y benzonitrilos 1,3-disustituidos y 1,3,5-trisustituidos tomando ventaja de derivados de ácido isoftálico sustituidos fácilmente disponibles. La monohidrólisis del diéster permite la reacción selectiva del ácido con una variedad de reactivos, típicamente agentes activadores tales como cloruro de tionilo, cloruro de oxalilo o cloroformiato de isobutilo y similares. A partir del ácido activado, se puede conseguir un número de productos. Además de la amida primaria utilizada para formar el nitrilo mediante deshidratación como se mencionó anteriormente, se puede efectuar la reducción hasta el análogo

hidroximetilo en el anhidrido mixto o cloruro de acilo utilizando una variedad de agentes reductores tales como borohidruro de sodio en un solvente compatible tal como tetrahidrofurano. El derivado hidroximetilo se puede reducir posteriormente hasta el análogo metilo utilizando hidrogenación catalítica con una fuente apropiada de catalizador tal como paladio sobre carbón en un solvente apropiado tal como etanol. También se puede utilizar el grupo hidroximetilo en cualquier reacción apropiada para alcoholes bencílicos tales como acilación, alquilación, transformación hasta el halógeno y similares. También se pueden obtener ácidos halogenometilbenzoicos de este tipo a partir de la bromación del derivado metilo cuando no se pueda conseguir comercialmente. Los éteres obtenidos mediante alquilación de los derivados hidroximetilo también se pueden obtener a partir de los derivados halogenometilaril-benzoato mediante reacción con el alcohol apropiado utilizando una base apropiada tal como carbonato de potasio o hidróxido de sodio en un solvente apropiado tal como tetrahidrofurano o el alcohol. Cuando están presentes otros sustituyentes, éstos también se pueden utilizar en reacciones de transformación estándar. El tratamiento de una anilina con ácido y nitrito de sodio puede producir una sal de

diazonio, la cual se puede transformar en el halogenuro tal como fluoruro, utilizando ácido tetrafluorobórico.

Los fenoles reaccionan en presencia de una base apropiada tal como carbonato de potasio con agentes alquilantes para formar éteres aromáticos.

Formación de los compuestos de la fórmula IX



Se puede preparar un compuesto de la fórmula IX, en el cual R^7 se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)n-G$, en los cuales G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, mediante una cicloadición 1,3-dipolar entre compuestos de la fórmula VI y VII bajo condiciones básicas utilizando una base apropiada tal como bicarbonato de sodio o trietilamina a temperaturas apropiadas (0°C a

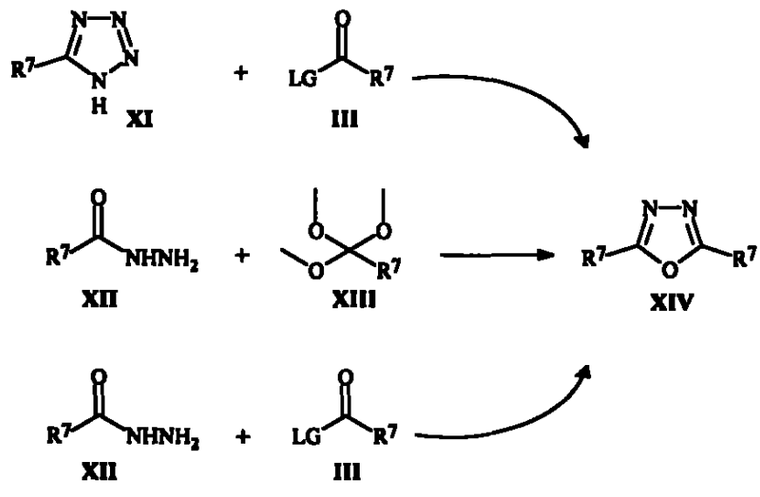
100°C) en solventes tales como tolueno. La síntesis de compuestos del tipo **VI** ha sido descrita previamente en la literatura, por ejemplo Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57, 6649-50. La cicloadición 1,3-dipolar con acetilenos del tipo **VII** también se puede efectuar utilizando nitrometanos sustituidos del tipo **VIII** mediante activación con un reactivo electrofílico tal como PhNCO en presencia de una base tal como trietilamina a temperaturas elevadas (50-100°C). Li, C-S.; Lacasse, E.; Tetrahedron Lett. (2002) 43; 3565-3568. Se pueden conseguir comercialmente varios compuestos del tipo **VII**, o éstos se pueden sintetizar utilizando métodos estándar como los conocidos por el experto en la técnica.

De manera alternativa, los compuestos de la fórmula **X**, los cuales se pueden conseguir a partir de la condensación de Claisen de una metilcetona y un éster utilizando condiciones básicas, empleando bases tales como hidruro de sodio o terbutóxido de potasio, pueden producir los compuestos de la fórmula **IX** mediante condensación y ciclización subsiguiente utilizando hidroxilamina, por ejemplo en forma de la sal clorhidrato, a temperaturas elevadas (60-120°C).

Se entiende que para ambos métodos, podrían

ser necesarias transformaciones de grupo funcional posteriores. En el caso de un grupo éster, estas transformaciones pueden incluir, pero no se limitan a, cualquiera de los siguientes tres procedimientos: a) reducción completa utilizando un agente reductor apropiado tal como LAH en solventes tales como THF. b) reducción parcial utilizando un agente reductor selectivo apropiado tal como DIBAL seguido por alquilación con un halogenuro de alquilo. c) alquilación utilizando un reactivo de tipo alquil-metal tal como un halogenuro de alquilmagnesio en solventes tales como tolueno o THF, seguido por reducción con, por ejemplo, borohidruro de sodio en metanol.

Formación de los compuestos de la fórmula **XIV**

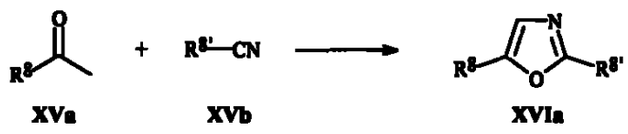


Se puede preparar un compuesto de la fórmula **XIV**, en el cual R^7 se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)_n-G$, en los cuales G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, a partir de compuestos de tetrazol del tipo **XI** mediante acilación utilizando un compuesto susceptible de aislamiento del tipo **III** tal como un cloruro o anhidrido de ácido, o un compuesto del tipo **III** en el cual LG se puede formar in situ, por ejemplo a partir de la activación de un ácido utilizando un reactivo tal como DCC o EDCI, seguido por transposición hasta el 1,3,4-oxadiazol. Jursic, B.S.; Zdravkovski, Z.; Synth. Común.; (1994) *24*; 1575-1582.

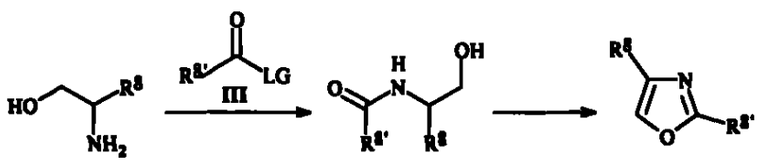
De manera alternativa, también se pueden preparar los compuestos de la fórmula **XIV** a partir de la hidrazida de acilo del tipo **XII** mediante calentamiento en presencia de compuestos de la fórmula **XIII** o **III**, en los cuales LG es un grupo saliente tal como cloruro o alcóxido, a temperaturas elevadas (60-130°C) en un sólo paso. La reacción de los compuestos de la fórmula **XIII** se puede efectuar en forma pura o utilizando un solvente no prótico apropiado tal como benceno o xileno, o un solvente prótico tal como etanol o n-

butanol, y se puede facilitar por la presencia de una base tal como KOtBu o un ácido tal como ácido para-toluensulfónico o ácido acético. Véase referencias: Saunders, J.; Cassidy, M.; Freedman, S. B.; Harley, E. A.; Iversen, L.L. J.Med.Chem.; (1990) 33; 1128-1138; Peet, N. P.; Sunder, S. J.Heterocycl.Chem.; (1984) 21; 1807-1816. Para los compuestos de la fórmula **III** se puede utilizar un agente deshidratante tal como pentóxido de fósforo para incrementar la ciclización del intermediario de reacción formado como se ha descrito previamente por ejemplo, por Kakefuda, Akio; et al.; Bioorg. Med. Chem. (2002), *10*; 1905-1912.

Formación de los compuestos de la fórmula **XVI**



XVa **XVb** **XVIa**



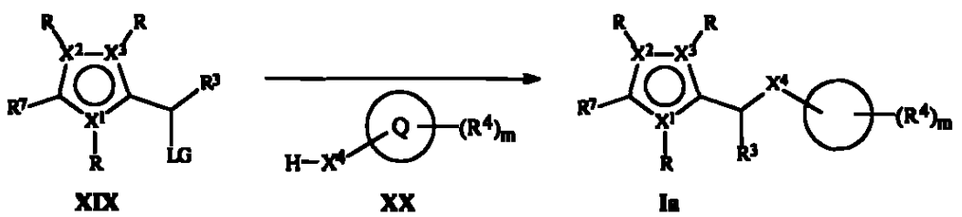
XVII **XVIII** **XVIb**

Se puede preparar un compuesto de la fórmula **XVI**, en el cual R^8 como el definido anteriormente, se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-$

$(R^4)_{m2}$, y $M^2-(R^3)_n-G$, en los cuales G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, haciendo reaccionar compuestos de la fórmula **XVa** y **XVb** en presencia de Tl(OTf)3 generado in situ bajo condiciones ácidas de conformidad con el procedimiento de Lee y Hong; Tetrahedron Lett., (1997), *38*, 8959-60.

De manera alternativa los compuestos de las fórmulas **III** y **XVII** se hacen reaccionar como se describió anteriormente para la fórmula **V** para obtener un intermediario de la fórmula **XVIII**. Dicho intermediario puede producir el oxazol requerido mediante ciclo-deshidratación con, para generar la oxazolina seguida por deshidrogenación, utilizando $BrCCl_3$ en el mismo recipiente de reacción. Phillips, A.J.; Uto, Y.; Wipf, P.; Reno, M.J. y Williams, D.R., Organic Letters, (2000) *2*, 1165-8.

<u>Formación del enlace entre X^4 y M^2 o Q y M^2 a través del desplazamiento nucleofílico de un grupo saliente</u>



XIX **XX** **Ia**

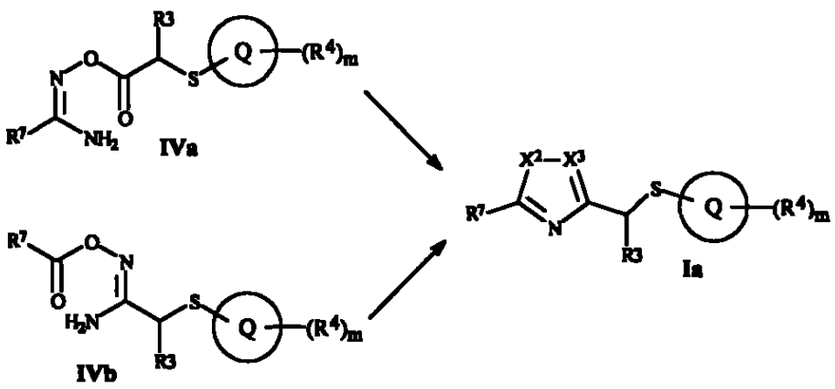
Se puede utilizar un compuesto de la fórmula **XX**, para desplazar el grupo saliente LG en los compuestos de la fórmula **XIX** (R^7 es M^1-$(R^2)_n$-P-$(R^1)_{m1}$). Cuando X^4 se representa mediante un heteroátomo tal como N y S, la reacción se efectúa en presencia de una base apropiada tal como carbonato de potasio, carbonato de cesio, hidruro de sodio, trietilamina o similares, lo cual puede facilitar la reacción mediante desprotonación del residuo X^4 y evitar la formación de cualquier ácido en exceso que pudiera ser generado por la reacción en ausencia de una base. La reacción se puede lograr utilizando cualquier solvente apropiado tal como acetonitrilo o DMF, y se puede efectuar a temperatura ambiente o a temperatura elevada (35-100°C) para acelerar la reacción.

Se pueden utilizar dichas condiciones con las modificaciones apropiadas, del equipo utilizado para la síntesis en paralelo, utilizando técnicas estándar conocidas por el experto en el campo.

De igual manera, estas condiciones de reacción se pueden efectuar para compuestos de la fórmula **XX** cuando X^4 = enlace y el anillo Q es un biciclo fusionado que contiene un heteroátomo tal como N como se definió anteriormente. En cualquiera del último o el primer descrito con X^4=N, se prefiere NaH en DMF

como se describe en las referencias de la literatura, por ejemplo, Murdoch, Robert; Tully, W. Roger; Westwood, Robert; J.Heterocycl.Chem.; (1986), *23*; 833-841.

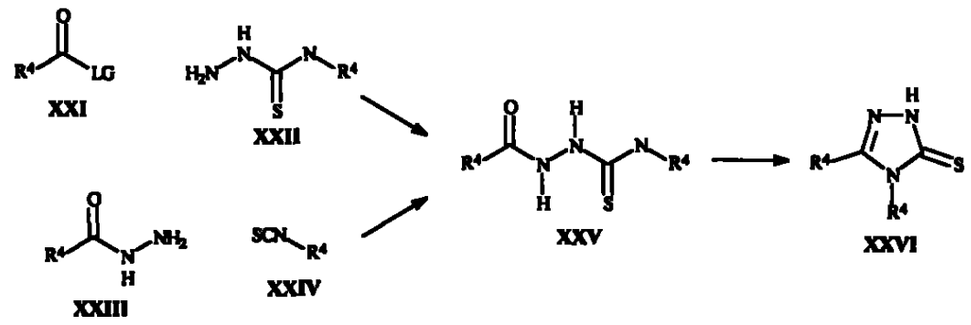
Para compuestos de la fórmula **XX** que contienen X^4=C, es necesario utilizar una base más fuerte para lograr la desprotonación, tal como por ejemplo LDA, n-butil-litio o cualquier otra base de tipo alquil-metal en solventes no próticos apropiados tales como THF, hexano o tolueno a temperaturas por lo general menores a las temperaturas ambientales, por ejemplo a -78°C ó 0°C.



Un procedimiento alternativo para la síntesis del tipo antes descrito de tiometil-oxadiazol es formar un éster aciclico **IVa** y **IVb** a partir de la combinación de una hidroxiamidina sustituida en forma apropiada y un compañero de copulación tipo ácido activado también sustituido en forma apropiada. El desplazamiento del cloruro utilizando el nucleófilo

tiol puede presentarse inmediatamente antes de la ciclización, utilizando uno de los métodos de formación de oxadiazol antes descritos. También se puede efectuar el desplazamiento en la clorometil-hidroxiamidina o en los materiales de partida de ácido de clorometilo, seguido por la esterificación y ciclización en dos pasos como se indicó anteriormente. Se pueden utilizar las condiciones descritas con modificaciones apropiadas del equipo utilizado para la síntesis en paralelo empleando técnicas estándar conocidas por el experto en el campo.

Formación de 4-alquiltriazol tioles/tionas



Se hace reaccionar cualquier agente acilante apropiado tal como un cloruro de acilo o un ácido activado o el ácido correspondiente bajo condiciones de copulación de amida como se indicó anteriormente, con una 4-alquil-3-tiosemicarbazida apropiada en presencia de una base tal como piridina o aminas no

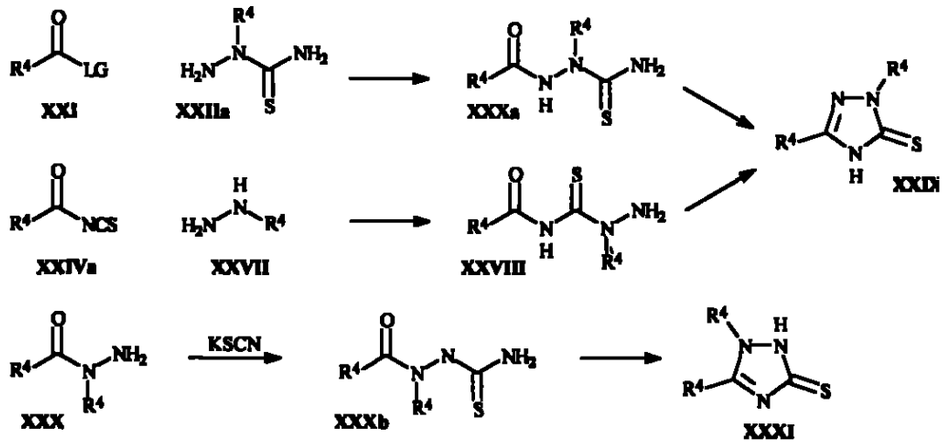
nucleofílicas para formar el compuesto intermediario no cíclico de la fórmula **XXV**, en el cual R^4 es como se definió anteriormente. También se puede conseguir el mismo intermediario a través de la reacción de una hidrazida de acilo con un isotiocianato de alquilo. La ciclización para obtener un compuesto de la fórmula **XXVI** se efectúa fácilmente mediante tratamiento con una base inorgánica apropiada tal como hidróxido o bicarbonato a temperatura elevada en un solvente apropiado tal como agua, agua-dioxano, un alcohol acuoso o mezclas de los mismos.

Se pueden utilizar dichas condiciones con las modificaciones apropiadas del equipo empleado cuando se utiliza una base en fase sólida en lugar de aquellas antes mencionadas, tales como por ejemplo P-BEMP para la síntesis en paralelo utilizando técnicas estándar conocidas por el experto en el campo.

El compuesto de la fórmula **XXV** reacciona a través de su forma tautomérica bajo las condiciones descritas anteriormente con los compuestos de la fórmula **XIX** para producir los compuestos de S-alquilación de la fórmula **Ia**.

Las triazol-tionas **XXIX** y **XXXI** alquiladas en los otros átomos de nitrógeno del anillo (1 y 2) se pueden conseguir a través de procedimientos similares.

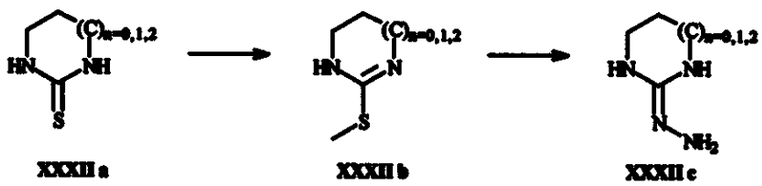
La 2-alquil-triazol-tiona **XXVIII** se puede obtener mediante tratamiento de un isotiocianato de aroílo con una hidrazina de alquilo en tolueno a temperaturas elevadas, por ejemplo 85°C, seguido por calentamiento con bicarbonato acuoso. También se puede obtener el mismo producto a través del tratamiento de la 2-alquil-3-tiosemicarbazida análoga con un ácido activado en presencia de una base apropiada tal como piridina o trietilamina seguido por el cierre de anillo en medio alcalino en una forma similar al cierre de anillo en medio alcalino que produce el compuesto **XXVI** anterior.



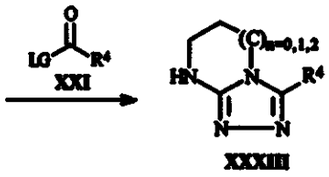
Las 1-alquil-triazol-tionas **XXXI** se pueden preparar mediante la reacción de una N-alquil-N-acilhidrazida apropiada con tiocianato de potasio en presencia de un ácido tal como HCl u otro ácido fuerte compatible mediante el intermediario 1-acil-1-

alquil-3-tiosemicarbazida la cual se somete a cierre del anillo en medio alcalino en una forma similar al cierre de anillo en medio alcalino que produce los compuestos de la fórmula **XXVI** anteriores.

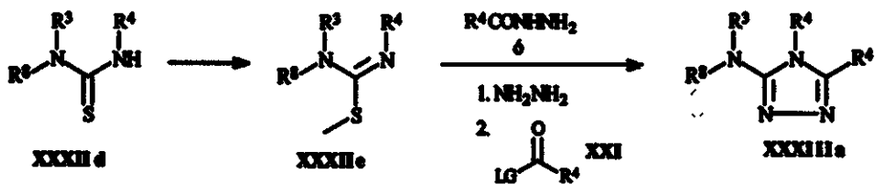
Formación de compuestos de la fórmula **XXXIII**



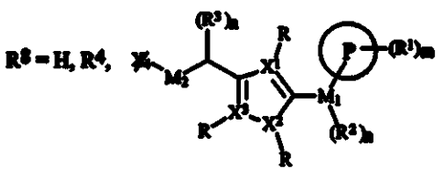
XXXIIa **XXXIIb** **XXXIIc**



XXXIII



XXXIId **XXXIIe** **XXXIIIa**



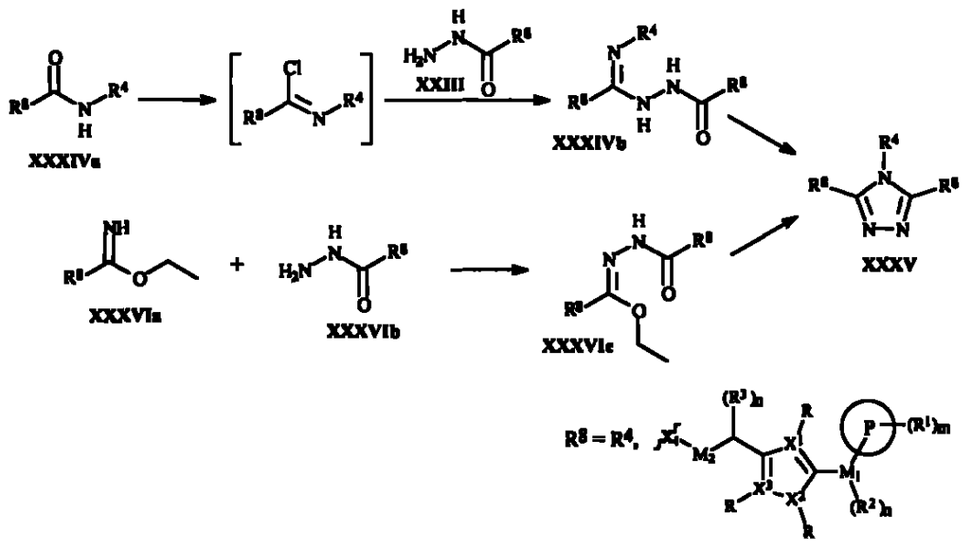
Se puede preparar un compuesto de la fórmula **XXXIII** mediante alquilación de tioureas cíclicas de la fórmula **XXXIIa**, en la cual n se define como 0, 1 o 2, lo que da como resultado el compuesto de la fórmula **XXXIIb**, por ejemplo, 2-metiltio-1,4,5,6-

tetrahidropirimidina en caso de n = 1. La alquilación con, por ejemplo, yoduro de metilo como el agente alquilante se puede efectuar en varios solventes (DMF, acetona, CH_2Cl_2, etc.) a temperatura ambiente o temperaturas elevadas y dará el producto como su sal yodohidrato como ácido descrito previamente por Kennedy, Kevin J.; Simandan, Tiberiu L.; Dix, Thomas A.; Synth.Commun.; (1998); *24*; 741-746. Las tioureas cíclicas se pueden conseguir fácilmente ya sea a través de síntesis como es sabido por el experto en la técnica, o a partir de fuentes comerciales. Los compuestos de la fórmula **XXXIIc** resultan de la hidrazinolisis de los compuestos correspondientes del tipo **XXXIIb**. La hidrazinolisis de preferencia se efectúa en EtOH bajo reflujo con hidrato de hidrazina como se describió previamente por Krezel, Izabella; Pharmazie; (1994); 94, 27-31. Por último, los triazoles fusionados de la fórmula **XXXIII** se pueden formar a través de la acilación térmica y reacción de condensación entre compuestos de la fórmula **XXI** en la cual LG es un grupo saliente tal como por ejemplo un halogenuro, y compuestos de la fórmula **XXXIIc**. Dichas reacciones se pueden efectuar en piridina o en EtOH o tolueno en presencia de una base. Se puede utilizar calentamiento normal o irradiación de microondas. De

igual manera, el compuesto XXXIII se puede preparar en presencia de una base, tal como metóxido de sodio en un solvente apropiado tal como metanol o etanol a temperaturas elevadas en las cuales XXI también puede ser un éster o ácido carboxílico.

También se pueden utilizar tioureas acíclicas de la fórmula **XXXIId**, en la cual R^8 es como se definió anteriormente en el esquema y R^3 y R^4 son como se definen en la fórmula I, empleando métodos similares para obtener los compuestos de la fórmula **XXXIIIa**, en la cual la introducción de la porción hidrazina se puede efectuar utilizando ya sea hidrazina seguido por acilación, o utilizando una hidrazina de acilo pre-formada.

Formación de los compuestos de la fórmula **XXXV**

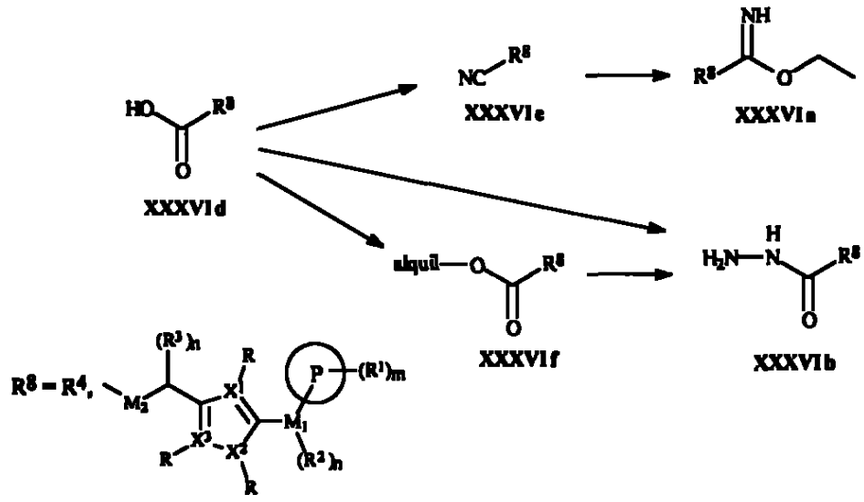


Se pueden preparar los compuestos de la fórmula **XXXIVb** utilizando métodos similares a los anteriores, por ejemplo mediante activación de **XXXIVa** para dar el cloruro de imidoilo correspondiente empleando cloruro de oxalilo o pentaclorofosfina en presencia opcional de una base tal como trietilamina. El intermediario se puede utilizar in situ o se puede aislar antes del entrampamiento por un compuesto de la fórmula **XXIII** como se utilizó anteriormente. El producto subsiguiente se puede ciclizar bajo condiciones ácidas o básicas en un solvente apropiado tal como DMF para producir los compuestos de la fórmula **XXXV**. El compuesto **XXXV** puede ser un intermediario utilizado en la formación de los compuestos de la fórmula **I**, o puede ser el compuesto bioactivo final de la fórmula **I**.

También se puede preparar un compuesto de la fórmula **XXXV**, en la cual R^8 se selecciona de manera independiente a partir de un grupo como los descritos anteriormente, a través de la reacción de compuestos de la fórmula **XXXVIa** (se muestra imidoato de etilo como ejemplo) y **XXXVIb** seguido por ciclización a temperaturas elevadas (40-80°C) en presencia de una amina, mientras que la amina de preferencia debe tener, pero no se limita a, un punto de ebullición bajo de manera tal que ésta se pueda utilizar en exceso y simplificar el procedimiento de

tratamiento. Los ejemplos para dichas aminas pueden ser, pero no se limitan a, metilamina o etilamina las cuales se pueden utilizar como soluciones en, por ejemplo, metanol, THF o diclorometano.

Formación de los compuestos de la fórmula **XXXVIa** y **XXXVIb**

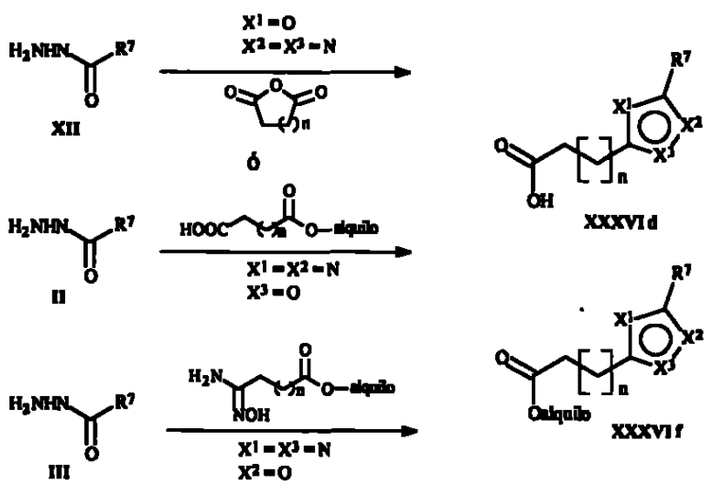


Se puede preparar un compuesto de la fórmula **XXXVIa**, en la cual R8 se selecciona de manera independiente a partir de un grupo como los descritos anteriormente, a través de la reacción de un nitrilo de la fórmula **XXXVIe** en un alcohol tal como etanol, en presencia de un ácido prótico, por ejemplo ácido clorhídrico. El nitrilo se puede obtener a partir de un ácido **XXXVId** como se describió anteriormente. Los compuestos de la fórmula **XXXVId** también se pueden

utilizar para preparar hidrazinas de acilo de la fórmula **XXXVIb**, en la cual R^8 se selecciona de manera independiente a partir de un grupo como los mostrados anteriormente. Este tipo de sustancia **XXXVIb** también se puede formar directamente a partir de un ácido. Podrían existir ventajas en hacer reaccionar un éster intermediario del tipo **XXXVIf** con cualquiera de hidrazina pura, sal de hidrazina en presencia de una base o hidrato de hidrazina para facilitar un tratamiento más sencillo. Sin embargo, la ruta directa a través del ácido utilizando la activación in situ podría ser conveniente en substratos sensibles al ataque nucleofílico y también producir el producto en una secuencia de pasos más corta.

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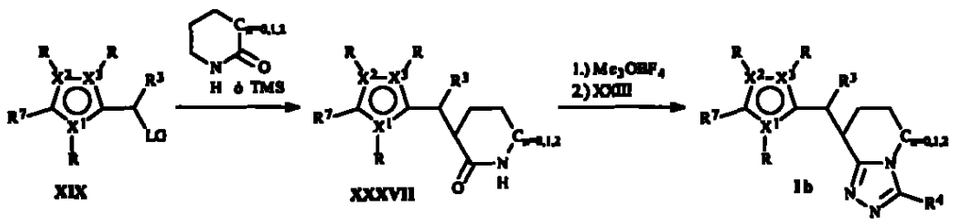
Formación de compuestos de las fórmulas **XXXVId y XXXVIf**



Se pueden preparar los compuestos de las fórmulas **XXXVId** y **XXXVIf**, en las cuales R^7 es un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, mediante cualquiera de los métodos no limitativos: a) reacción de compuestos de hidrazida de acilo de la fórmula XII con un anhídrido cíclico o diácido monoesterificado seguido por ciclización del intermediario formado lo que conduce a 1,3,4-oxadiazoles del tipo **XXXVId** y **XXXVIf** respectivamente (X^1= O, X^2 y X^3=N); b) se puede utilizar la reacción y ciclización de una hidroxiamidina de la fórmula II con un anhídrido cíclico o con el diácido monoesterificado para proveer los análogos 1,2,4-oxaziazol **XXXVId** y **XXXVIf** en las cuales X^1 y X^2 =N, X^3=O; c) se puede utilizar la reacción de un compuesto del tipo III con un compuesto de tipo hidroxamidina, con excepción del derivado succinilo, para proveer los análogos 1,2,4-oxaziazol **XXXVIf** en la cual X^1 y X^3 =N, X^2 =O.

Los compuestos **XXXVId** y **XXXVIf** se pueden convertir entre si, de manera independiente de la naturaleza de X^1, X^2 o X^3 como se describió anteriormente.

Formación de compuestos de la fórmula Ib

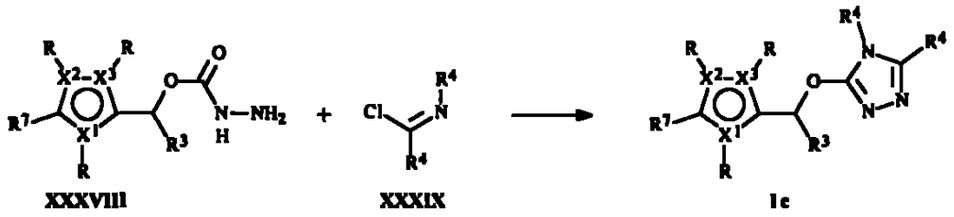


Se puede preparar un compuesto de la fórmula **Ib**, en la cual R^7 se selecciona a partir de un grupo $M^1-(R^2)_n-P-(R^1)_{m1}$, a partir de compuestos de la fórmula **XXXVII**, generados a partir de **XIV** como se describe más adelante, a través de la O-alquilación selectiva utilizando Me_3OBF_4 o sulfato de dimetilo (como se describe en los antecedentes en la literatura, por ejemplo: a) Shen, Jennline; Smith, Michael B.; Oeschger, Thomas R.; Satchell, Jacqueline; Org. Prep. Proced. Int.; (1992); *24*, 147-158; o b) Hutchinson, Ian S.; Matlin, Stephen A.; Mete, Antonio, Tetrahedron Lett.; (2001); *42*; 1773-1776). Después se puede desplazar el grupo metoxi con una hidrazida de acilo del tipo **XXIII**, seguido por una condensación de cierre de anillo para formar el heterociclo triazol. Esto se puede efectuar en etanol, tolueno, DMF o piridina bajo condiciones térmicas con calentamiento regular o irradiación de microondas, en la forma previamente descrita por, por ejemplo, Lawson, Edward

C.; Hoekstra, William J.; Addo, Michael F.; Andrade-Gordon, Patricia; Damiano, Bruce P.; Kauffman, Jack A.; Mitchell, John A.; Maryanoff, Bruce E.; Bioorg. Med. Chem. Lett.; (2001); *11*; 2619 - 2622.

Los compuestos del tipo **XXXVII** se pueden preparar mediante la reacción de amidas cíclicas, lactamas, las cuales se pueden alquilar fácilmente en la posición α con respecto al carbonilo mediante tratamiento sucesivo con dos equivalentes de una base fuerte, por ejemplo n-BuLi, para generar el dianión seguido por adición de un equivalente de los compuestos de la fórmula **XIX**, en un solvente no prótico tal como THF, como se ha descrito previamente por, por ejemplo, Grieco, Paul A.; Kaufman, Michael D.; J. Org. Chem.; (1999); *64*; 6041-6048). De manera alternativa, se puede utilizar una lactama N-protegida en la cual únicamente se necesita un equivalente de base, por ejemplo LDA, para generar el anión para la alquilación como ha sido descrito previamente por, por ejemplo Padwa, Albert; Beall, L. Scott; Heidelbaugh, Todd M.; Liu, Bing; Sheehan, Scout M.; J. Org. Chem.; (2000); 65; 2684 - 2695.

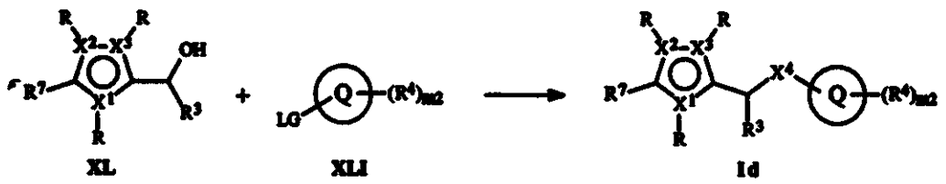
Síntesis general de compuestos de la fórmula Ic



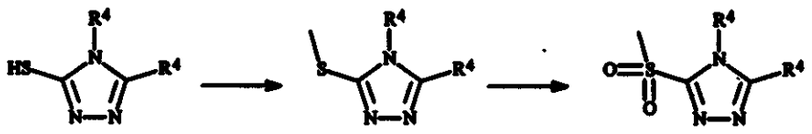
XXXVIII XXXIX Ic

Se puede preparar un compuesto de la fórmula Ic, en la cual R^7 consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, a través de la reacción con ciclización subsiguiente de compuestos de la fórmula **XXXVIII**, con un compuesto de la fórmula **XXXIX**. El compuesto de la fórmula **XIX** se puede preparar a partir de una amida secundaria apropiada utilizando cloruro de oxalilo o pentacloro-fosfina en presencia opcional de una base tal como trietilamina, y se puede utilizar ya sea in situ o como un material aislado como se describió anteriormente a partir de **XXXIVa**.

Los compuestos de la fórmula **XXXVIII**, se pueden preparar a partir del alcohol correspondiente haciendo reaccionar el alcohol con fosgeno o de preferencia un análogo de fosgeno tal como carbonil-di-imidazol seguido por copulación a hidrazina.



XL XLI Id



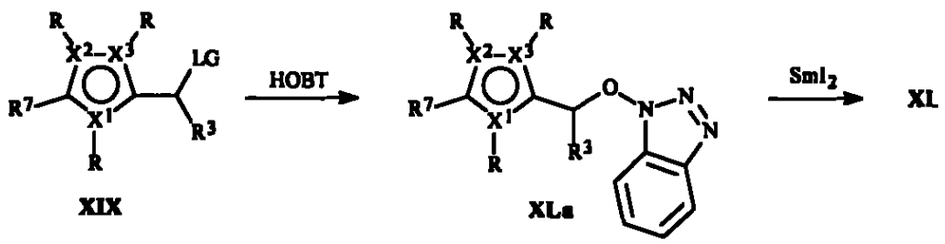
XXVI XLII XLIa

Otros medios para sintetizar un compuesto de la fórmula **Ic** o **Id**, en los cuales $X^4 = O$ y en los cuales R^7 es $M^1-(R^2)_n-P-(R^1)_{m1}$, puede ser mediante la O-alquilación de compuestos del tipo **XL** con compuestos del tipo **XLI** en los cuales el grupo saliente puede consistir de un grupo tosilo, mesilo, halógeno o cualquier otro grupo apropiado, en una base apropiada tal como carbonato de cesio o de potasio, hidruro de sodio en solventes tales como por ejemplo DMF o DMSO.

Los compuestos del tipo **XLI** se pueden sintetizar como se ejemplifica con el triazol **XXVI** mediante alquilación o arilación del grupo sulfuro utilizando un agente alquilante o arilante apropiado seguido por la doble oxidación del grupo tio hasta la sulfona correspondiente utilizando oxidantes tales como MCPBA, peróxido de hidrógeno en ácido acético o permanganato de potasio. Dicha secuencia ha sido

descrita previamente por ejemplo, por Åkerblom et al. *J. Med. Chem.* 16, 312 (1973). De manera alternativa, se pueden sintetizar los halogenuros de triazol como se describió previamente en la literatura, por ejemplo por Ashton, W. T. et al. *J. Med. Chem.* 36, 591 (1993).

Los alcoholes se pueden preparar ya sea directamente después de la síntesis del oxadiazol o parte de isoxazol como se describió anteriormente bajo la síntesis general de compuestos de la fórmula V. De manera alternativa, éstos se pueden preparar a partir de una unidad oxadiazol o isoxazol con un grupo saliente apropiado tal como un halogenuro, por ejemplo cloruro, utilizando una secuencia de tres pasos como la descrita por Palazzo et al. *J. Heterocycl. Chem.* (1979) 16: 1469, seguido por un protocolo de reducción normal del aldehído resultante (o hidrato del mismo) utilizando por ejemplo borohidruro de sodio en metanol.

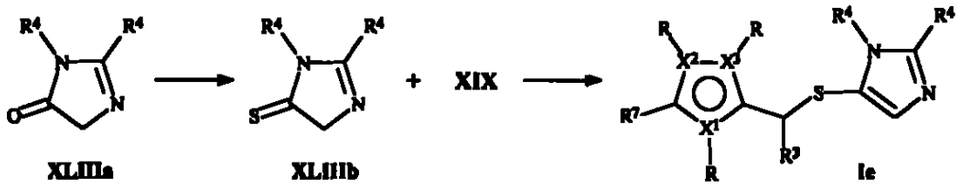


XIX XLa

Incluso otro método puede implicar la reacción de una unidad de un compuesto de la estructura **XIV** que contenga un grupo saliente apropiado tal como halogenuro, por ejemplo cloruro, con hidroxibenzotriazol en presencia de una base apropiada tal como carbonato de potasio o trietilamina en un solvente apropiado tal como DMSO, acetonitrilo, acetona, DMF, para producir los compuestos del tipo **XLa**. De manera alternativa, el compuesto **XLa** se puede obtener si está presente el hidroxibenzotriazol durante la ciclización hasta el oxadiazol, ya sea como un co-activador con EDCI, o como resultado de un subproducto proveniente de un reactivo de copulación tal como HBTU, como se describió anteriormente bajo la reacción de los compuestos de las fórmulas **II-V**. El compuesto **XLa** se puede convertir al alcohol mediante la adición de diyoduro de samario, de preferencia a través de un periodo prolongado de tiempo (5-360 minutos) en un solvente apropiado tal como tetrahidrofurano, metanol, agua o mezclas de los mismos, siendo THF un solvente preferido, a una temperatura apropiada (-75°C hasta +75°C). La ruptura del enlace N-O se puede efectuar de manera alternativa utilizando métodos de hidrogenación comúnmente empleados en presencia de un catalizador

apropiado tal como níquel Raney como es sabido por el experto en la técnica. En los compuestos de la fórmula **XLa** el grupo funcional oxobenzotriazol también puede servir como un grupo saliente. Por lo tanto, los compuestos **XLa** pueden reaccionar con compuestos **XX** como se describió anteriormente.

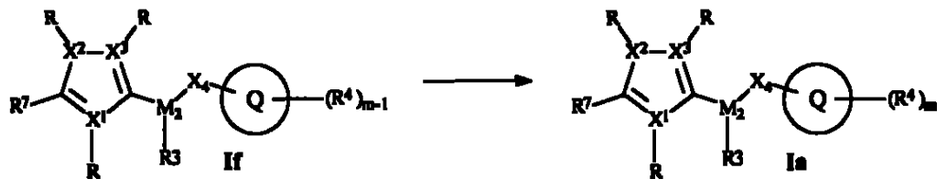
Formación de compuestos del tipo Ie



Se puede preparar un compuesto de la fórmula **Ie**, en el cual R^7 es $M^1-(R^2)_n-P-(R^1)_{m1}$, a través de sustitución nucleofílica de compuestos del tipo **XLIIIb** con compuestos del tipo **XIX** como se describió anteriormente. Los compuestos del tipo **XLIIIb** se pueden preparar mediante reacción de sus análogos oxo **XLIIIa** utilizando P_2S_{10} o reactivo de Lawesson bajo condiciones térmicas. La síntesis de los compuestos del tipo **XLIIIa** ha sido descrita por Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989); *45*; 6375-6386.

Introducción de sustitución en el anillo Q

Si se desea la sustitución en el anillo Q, se puede elegir un aril-tiol o heteroaril-tiol sustituido en forma apropiada para que se use en la reacción de desplazamiento. Lo mismo es válido para otros reactivos nucleofílicos diferentes a los aril-tioles o heteroaril-tioles sustituidos o no sustituidos que sirvan para sustituir al mismo en los compuestos finales. Si el residuo arilo o heteroarilo tiene una porción reactiva factible, ya sea introducida directamente o como resultado de una reacción de desprotección, incluyendo pero sin limitarse a un sitio NH libre como en la anilina, imidazol, bencimidazol, indol y similares, un compuesto de la fórmula If (R^7 es M^1-$(R^2)_n$-P-$(R^1)_{m1}$) se puede sustituir con R^4 utilizando una base apropiada tal como un alquil-litio o hidruro o hidróxido de metal alcalino para desprotonar al residuo NH, seguido por la adición de un reactivo electrofílico apropiado tal como halógenuros de alquilo, cloruros de acilo o anhídridos, cloroformiatos, cloruros de carbamoilo, cloruros de sulfonilo, isocianatos, isotiocianatos y similares para proveer el producto sustituido de la fórmula Ia.

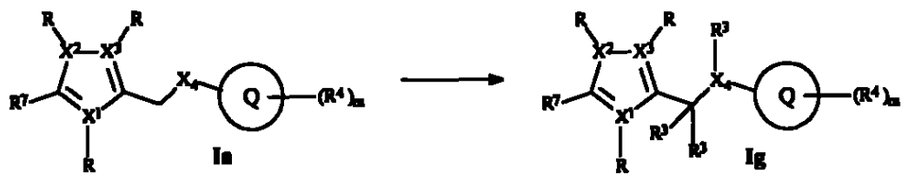


If Ia

Introducción del sustituyente o sustituyentes M^2 y del sustituyente o sustituyentes X^4

Cuando los protones más ácidos están posicionados en el átomo adyacente a X^4 o en X^4 mismo, se puede lograr la sustitución mediante desprotonación del compuesto de la fórmula Ia con una base fuerte tal como alquil-litio o un hidruro de metal alcalino en un solvente no prótico, no ácido apropiado tal como THF o éter dietílico seguido por entrampamiento del anión resultante con un electrófilo apropiado tal como los halogenuros de alquilo, cloruros de acilo o anhídridos, cloroformiatos, cloruros de carbamoilo, cloruros de sulfonilo, isocianatos, isotiocianatos y similares. Cuando se emplea un exceso de base y electrófilo y la reacción se deja durante tiempo suficiente, se pueden reemplazar dos átomos de hidrógeno con el electrófilo como se ilustra más adelante para la introducción de dos sustituyentes R^3 (M^2 se ejemplifica como carbono). También se podrían introducir dos o más sustituyentes,

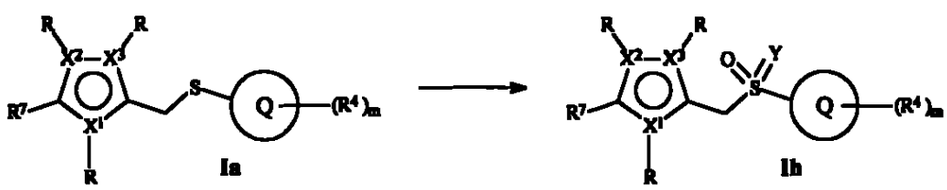
iguales o diferentes, en forma correspondiente mediante desprotonaciones y reacciones subsiguientes con electrófilos apropiados para producir los compuestos de la fórmula Ig.



Ia Ig

Oxidación del átomo S de la cadena (cuando X^4 sea S) o átomos N en los sustituyentes

Se puede lograr la oxidación del átomo de azufre para producir sulfonas (Y=O) y sulfóxidos (Y=":", es decir, un par solitario), mediante oxidación directa utilizando cualquier agente oxidante apropiado incluyendo peroxiácidos tales como MCPBA. En el caso de oxidación con MCPBA, es posible obtener una mezcla de productos a partir de una reacción individual y separarlos mediante cromatografía en columna normal o para obtener en forma selectiva el sulfóxido o sulfona controlando la estequiometría y temperatura de la reacción.



Ia Ih

Si uno de los sustituyentes, por ejemplo R^4 contiene uno o más átomos de nitrógeno, como por ejemplo una porción piridina o cualquier otro sustituyente como el definido anteriormente, la oxidación de este nitrógeno se puede presentar en la reacción anterior de **Ia** con un oxidante tal como MCPBA para dar el N-óxido correspondiente. El experto en la técnica entiende que dichos productos pueden obtenerse mediante separación utilizando cromatografía en columna normal o cualquier otro protocolo de purificación estándar incluso en el caso de mezclas que contengan por ejemplo **Ih** y el N-óxido. El experto en la técnica también entiende que la formación de N-óxidos se puede reducir mediante la elección de condiciones de reacción apropiadas tales como el uso de medios ácidos para proteger la amina básica.

Otras reacciones diversas

Cuando los compuestos intermediarios contienen un grupo funcional reactivo apropiado tal como un aril-halogenuro o triflato, se puede utilizar el grupo funcional para elaborar también al producto. Por ejemplo, cuando está presente 3-halógeno-fenilo en $P\text{-}(R^1)_{m1}$, es posible utilizar las condiciones estándar de Suzuki para copular un ácido aril-

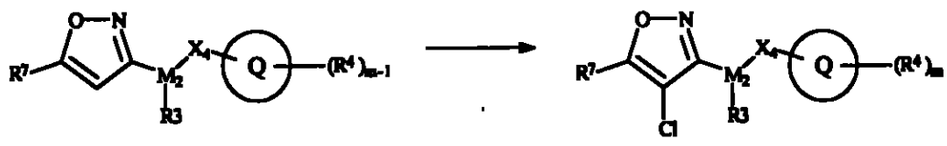
borónico para producir un producto de copulación tipo diarilo. Miyaura, N., Yanagi, T., Suzuki, A., Synth.Commun., (1981), 11; 7, 513-520.

Otros grupos funcionales tales como un alcohol alifático se pueden convertir, por ejemplo, a un grupo fluoro mediante el uso de un agente para fluoración tal como DAST u otros grupos halogenuro mediante el uso de por ejemplo trifenilfosfina y cualquiera de yodo, N-bromosuccinimida o N-cloro-succinimida. Estos halogenuros pueden servir como grupos salientes para la elaboración posterior o pueden permanecer como sustituyentes en compuestos activos de la fórmula **Ia**.

En una manera similar, los alcoholes los alcoholes se pueden transformar hasta grupos salientes tales como los ejemplos no limitativos mesilo o tosilo empleando el halogenuro de sulfonilo o anhídrido de sulfonilo apropiado, en presencia de una base no nucleofílica junto con el alcohol para obtener el derivado de éster sulfónico.

Otros grupos funcionales que también se pueden elaborar, se muestran en el siguiente ejemplo no limitativo (R^7 es M^1-$(R^2)_n$-P-$(R^1)_{m1}$), en el cual la halogenación se puede efectuar sobre un átomo de carbono de una unidad oxazol empleando un agente para

cloración tal como cloruro de sulfurilo.



EJEMPLOS

A continuación se ilustran modalidades apropiadas de la invención mediante los siguientes ejemplos no limitativos.

Las mediciones de RMN se efectúan en la escala delta (δ).

Los compuestos preparados de conformidad con los ejemplos 1 a 39 y 100 A 328 son intermediarios. Los compuestos preparados de conformidad con los ejemplos 40 a 99 y 329 a 794 son productos finales.

INTERMEDIARIOS

EJEMPLO 1

Acido 6-metilpiridin-4-carboxílico

Se une un globo lleno con hidrógeno a un matraz que contiene ácido 2-cloro-6-metilpiridin-4-carboxílico (2 g, 12.0 mmoles), paladio al 10% en peso sobre carbón activado (0.5 g), trietilamina (4.8

ml) y etanol (24 ml) y después se agita durante la noche a temperatura ambiente. La mezcla de reacción se filtra a través de celita, se lava con metanol y se concentra. El residuo se tritura con diclorometano y después se filtra para obtener ácido 6-metilpiridin-4-carboxílico como un sólido de color blanco; 1.05 g (66%).

^{1}H RMN (MeOD) δ (ppm): 8.62 (d, 1H), 7.68 (s, 1H), 7.60 (d, 1H), 2.55 (s, 3H).

EJEMPLO 2

1-ciano-3-etilbenceno

Se hace burbujear argón en una solución de 1-bromo-3-etilbenceno (2.5 g,13.5 mmoles) en DMF (37 ml) durante 10 minutos y después se agrega cianuro de zinc (1.75 g, 14.9 mmoles) y tetrakis(trifenil-fosfin)paladio(0) (1.56 g, 1.35 mmoles). Después de agitar a 80°C durante la noche la mezcla de reacción se diluye con acetato de etilo (35 ml) después se filtra a través de celita para remover el precipitado. El material filtrado se lava con agua (3x), salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. El producto se purifica mediante cromatografía de vaporización

instantánea utilizando acetato de etilo al 2% en hexano lo que permite obtener un líquido incoloro (1.42 g).

GC-mS (M+): 131.18.

EJEMPLO 3

Acido 3-etilbenzoico

Se agrega hidróxido de sodio 6M (25 ml) a 1-ciano-3-etilbenceno (1 g, 7.62 mmoles) en metanol (25 ml) y después se calienta hasta 100°C durante la noche. Después de concentrar la mezcla de reacción, la capa acuosa se lava con diclorometano (2x), después se acidula el pH hasta 3 aproximadamente con HCl 12M. El precipitado se extrae con acetato de etilo después se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener ácido 3-etilbenzoico como un aceite incoloro; 0.770 g (28% de rendimiento en los 2 pasos).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.76 (d, 2H), 7.43 (m, 2H), 2.67 (m, 2H),1.19 (t,3H).

EJEMPLO 4

Acido 3-fluoro-5-metil-benzoico

Se agrega HCl concentrado (30 ml) a una suspensión fría (-5°C) de 5-amino isoftalato de dimetilo (20 g, 95.6 mmoles) en agua (75 ml), seguido por la adición en porciones de $NaNO_2$ (7.5 g, 109 mmoles). La mezcla de reacción se agita después durante 15 minutos, después de lo cual se agrega HBF_4 (18 ml, 100 mmoles, solución acuosa al 48%). La mezcla resultante se agita a 0°C durante 30 minutos y el precipitado que se forma se recolecta mediante filtración y se lava con metanol frío (60 ml) y éter (60 ml). El residuo se descompone después mediante calentamiento en un baño de aceite (~110°C). La mezcla ya fría se diluye después con éter, se concentra sobre gel de sílice y se purifica mediante cromatografía de vaporización instantánea con acetato de etilo al 5% hexano como eluyente para obtener 9.0 g (44%) de producto como un sólido esponjoso de color blanco.

^1H RMN ($CDCl_3$), δ (ppm): 8.57 (s, 1H), 7.95 (d, 2H), 3.97 (s, 6H).

Se trata una suspensión del éster dimetílico

del ácido 5-fluoro-isoftálico (1.7 g, 8.0 mmoles) en metanol (41 ml) con hidróxido de sodio 1.0N (7.2 ml, 7.2 mmoles). La reacción se deja agitando durante toda la noche a temperatura ambiente. Después que se concentra la solución, el residuo se disuelve en agua y se transfiere a un embudo de separación. La capa acuosa se lava con diclorometano (3 veces) y después se acidula con HCl 1.0 N hasta pH 2. Se utiliza acetato de etilo para extraer el precipitado, el cual se lava después con salmuera y se seca con sulfato de sodio anhidro. Después de eliminar el solvente al vacío, se aísla un total de 1.3 g (83%) del éster monometílico del ácido 5-fluoro-isoftálico como un sólido de color blanco.

^{1}H RMN (DMSO), δ (ppm): 8.31 (t, 1H), 7.96 (m, 2H), 3.91 (s, 3H).

Se agregan trietilamina (2.2 ml, 16.0 mmoles) y cloroformiato de isobutilo (1.0 ml, 8.0 mmoles) a una solución helada de éster monometílico del ácido 5-fluoro-isoftálico (1.3 g, 6.7 mmoles) en diclorometano (20 ml) y después se calientan hasta temperatura ambiente. Después de agitar durante 2 h, la mezcla de reacción se filtra y se concentra. El residuo se vuelve a disolver en tetrahidrofurano (10

ml) y después se agrega, mediante goteo, borohidruro de sodio (1.1 g, 29.02 mmoles) en agua (3ml). Después de 1 hora, la reacción se extingue con metanol y después se diluye con acetato de etilo, se lava con agua y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. La cromatografía de vaporización instantánea en columna con gel de sílice utilizando acetato de etilo al 30% en hexanos permite obtener 667 mg (54%) del éster metílico del ácido 3-fluoro-5-hidroximetil-benzoico como un aceite incoloro.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.82 (s, 1H), 7.63 (d, 1H), 7.32 (d, 1H), 4.76 (s, 2H), 3.93 (s, 3H).

Se agrega etanol (2 ml) a un matraz de fondo redondo que contiene le éster metílico del ácido 3-fluoro-5-hidroximetil-benzoico (667 mg, 3.6 mmoles) y paladio (10% en peso sobre carbón activado, 300 mg) bajo argón. El matraz se evacua utilizando un aspirador de agua y después se llena con hidrógeno proveniente de un globo. Después de agitar durante 2 h, se retira el paladio sobre carbón mediante filtración a través de celita. El material filtrado se concentra después para obtener 520 mg (87%) del éster metílico del ácido 3-fluoro-5-metil-benzoico.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.65 (s, 1H), 7.51 (d, 1H), 7.08 (d, 1H), 3.91 (s, 3H), 2.40 (s, 3H).

Se agrega hidróxido de litio 0.5 N (7.4 ml, 3.7 mmoles) a una solución del éster metílico del ácido 3-fluoro-5-metil-benzoico (520 mg, 3.1 mmoles) en tetrahidrofurano (7.4 ml). La mezcla de reacción se agita a 75°C durante 2 h y después se elimina el solvente al vacío. El residuo se disuelve en una cantidad pequeña de agua y después se acidula (pH 2 aproximadamente) mediante la adición de HCl al 10% (acuoso). Después de extraer la capa acuosa con acetato de etilo, la capa orgánica se lava después con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener 469 mg (98%) de ácido 3-fluoro-5-metil-benzoico como un sólido de color blanco.

^{1}H RMN (DMSO), d (ppm): 7.62 (s, 1H), 7.45 (d, 1H), 7.32 (d, 1H), 2.38 (s, 3H).

EJEMPLO 5

Acido 3-metoximetil-benzoico

Se calienta una mezcla de éster metílico del ácido 3-bromometil-benzoico (556 mg, 2.4 mmoles) y

carbonato de potasio (670 mg, 4.9 mmoles) en metanol (10 ml) y tetrahidrofurano (10 ml) a 55°C durante 2 h. Después de enfriar, la mezcla de reacción se diluye con agua y después se extrae con acetato de etilo. La capa orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. Después de secar al vacío, se aísla el éster metílico del ácido 3-metoximetil-benzoico (436 mg, cuantitativo) como un sólido de color blanco.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.01 (s, 1H), 7.98 (d, 1H), 7.55 (d, 1H), 7.43 (t, 1H), 4.50 (s, 2H), 3.92 (s, 3H), 3.41 (s, 3H).

Se agrega hidróxido de sodio 1N (3.6 ml, 3.6 mmoles) a un éster metílico del ácido 3-metoximetil-benzoico (436 mg, 2.4 mmoles) en metanol (5 ml) y tetrahidrofurano (5 ml). La mezcla de reacción se agita a 70°C durante 30 minutos y después se elimina el solvente al vacío. El residuo se disuelve en una cantidad pequeña de agua y después se acidula (pH 2 aproximadamente) mediante la adición de HCl 1N (acuoso). Después de extraer la capa acuosa con acetato de etilo, la capa orgánica se lava después con agua y salmuera saturada, se seca con sulfato de

sodio anhidro, se filtra, y se concentra para obtener 395 mg (98%) de ácido 3-metoximetil-benzoico como un sólido de color blanco.

^{1}H RMN (DMSO), δ (ppm): 7.90 (s, 1H), 7.87 (d, 1H), 7.56 (d, 1H), 7.48 (t, 1H), 4.48 (s, 2H), 3.31 (s, 3H).

EJEMPLO 6

N-hidroxi-3-metoxi-benzamidina

Utilizando el procedimiento general de Shine et al., J. Heterocyclic Chem. (1989) 26:125-128, se agregan clorhidrato de hidroxilamina (22 ml, 5 M, 110 mmoles) e hidróxido de sodio (11 ml, 10 M, 110 mmoles) a una solución de 3-metoxibenzonitrilo (11.5 ml. 94 mmoles) en etanol (130 ml). La mezcla de reacción se calienta después a reflujo (80°C) durante 12 h. Después que se enfría la mezcla, se elimínala mayoría del solvente al vacío. El producto crudo se separa entre acetato de etilo y agua, se lava con salmuera saturada, se seca con sulfato de sodio anhidro y el solvente se elimina al vacío. La cromatografía de vaporización instantánea con gel de sílice utilizando acetato de etilo al 35-50% en hexano produce el compuesto del título (8.05 g, 52%).

Los ejemplos 7-9 se preparan en un método análogo el procedimiento indicado en el ejemplo 6.

EJEMPLO 7

***N*-hidroxi-benzamidina**

El compuesto *N*-hidroxi-benzamidina (4.83 g, 91%, sólido de color blanco) se obtiene a partir de benzonitrilo (4 g, 38.9 mmoles), clorhidrato de hidroxilamina (8.89 ml, 44.0 mmoles) e hidróxido de sodio (4.49 ml, 45.0 mmoles) en etanol (30 ml).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.81 (pico ancho, 1H), 7.63 (m, 2H), 7.39 (m, 3H), 4.91 (s, 2H).

EJEMPLO 8

***N*-hidroxi-3-metil-benzamidina**

El compuesto *N*-hidroxi-3-metil-benzamidina (3.65 g, 94%, sólido de color blanco) se obtiene a partir de m-tolunitrilo (3 g, 26.0 mmoles), clorhidrato de hidroxilamina (5.9 ml, 29.6 mmoles), e hidróxido de sodio (3.0 ml, 29.9 mmoles) en etanol (20 ml).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.25 (pico ancho, 1H), 7.36 (m, 2H), 7.25 (m, 2H), 4.88 (s, 2H), 2.38 (s, 3H).

EJEMPLO 9

3-ciano-*N*-hidroxi-benzamidina

El compuesto 3-ciano-*N*-hidroxi-benzamidina (1.32 g, 52%, sólido de color blanco) se obtiene a partir de isoftalonitrilo (2 g, 15.6 mmoles), clorhidrato de hidroxilamina (3.12 ml, 5 M, 15.6 mmoles) e hidróxido de sodio (15.6 ml, 1 M, 15.6 mmoles) en etanol (20 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 20-50% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 9.91 (s,1H), 8.06 (s, 1H), 8.01 (d, 1H), 7.85 (d, 1H), 7.59 (t, 1H), 6.01 (bs, 2H).

EJEMPLO 10

5-clorometil-3-(3-metoxi-fenil)-[1,2,4]oxadiazol

Se agregan cloruro de cloroacetilo (0.72 ml, 9.03 mmoles) y trietilamina (1.50 ml, 10.23 mmoles) a *N*-hidroxi-3-metoxi-benzamidina (1 g, 6.02 mmoles) en diclorometano (12.0 ml) a 0°C y la mezcla resultante se agita durante 20 min. Para efectuar la ciclización hasta oxadiazol, se concentra la solución y se agrega DMF (20 ml) al residuo y se calienta a 120°C durante

5 h. El producto se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 10-20% en hexano para obtener 0.90 g (66% de rendimiento en los 2 pasos) del compuesto del título (aceite de color amarillo).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.68 (m, 1M, 7.60 (d, 1H), 7.40 (t, 1H), 7.07 (m, 1H), 4.76 (s, 2H), 3.88 (s, 3H).

Los ejemplos 11-14 se preparan en un método análogo el procedimiento indicado en el ejemplo 10.

EJEMPLO 11

5-clorometil-3-fenil-[1,2,4]oxadiazol

El compuesto 5-clorometil-3-fenil-[1,2,4]-oxadiazol (1.62 g, 57% de rendimiento en los 2 pasos, aceite de color amarillo) se obtiene a partir de cloruro de cloroacetilo (1.76 ml, 22.05 mmoles) y trietilamina (3.32 ml, 24.99 mmoles) con *N*-hidroxi-benzamidina (2 g, 14.7mmoles) en diclorometano (29.3 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 10% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.08 (m, 2H), 7.51 (m, 3H), 4.76 (s, 2H).

EJEMPLO 12

5-clorometil-3-m-tolil-[1,2,4]oxadiazol

El compuesto 5-clorometil-3-m-tolil-[1,2,4]-oxadiazol (1.75 g, 62% de rendimiento en los 2 pasos, aceite de color amarillo) se obtiene a partir de cloruro de cloroacetilo (1.59 ml, 20.0 mmoles) y trietilamina (3.00 ml, 22.7 mmoles) con *N*-hidroxi-3-metil-benzamidina (2 g,13.3 mmoles) en diclorometano (26.6 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 10% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.87 (s, 1H), 7.36 (m, 2H), 4.75 (s, 2H), 2.34 (s, 3H).

EJEMPLO 13

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo

El compuesto 3-(3-clorometil-[1,2,4]-oxadiazol-5-il)-benzonitrilo (3.57 g, 43%) se obtiene a partir de 2-cloro-*N*-hidroxi-acetamidina (4.05 g, 37.4 mmoles) y cloruro de 3-cianobenzoilo (6.2 g, 37.4 mmoles) en diclorometano (60 ml) con trietilamina (6.5 ml, 46.7 mmoles). La purificación se efectúa cromatografía en gel de sílice.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.47 (bs, 1H), 8.41 (dd, 1H), 7.91 (dd, 1H), 7.72(t, 1H), 4.70 (s, 2H); GC-mS (M+): 219.

EJEMPLO 14

3-(5-clorometil-[1,2,4]oxadiazol-3-il)-benzonitrilo

El compuesto 3-(5-clorometil-[1,2,4]-oxadiazol-3-il)-benzonitrilo (1.2 g, 87%, sólido de color café claro): 3-ciano-*N*-hidroxi-benzamidina (1.0 g, 6.2 mmoles), trietilamina (1.5 ml, 10.6 mmoles) y cloruro de cloroacetilo (0.74 ml, 9.3 mmoles) en diclorometano (12 ml). La purificación se efectúa mediante decoloración con gel de sílice.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.40 (s, 1H, 8.32 (d, 1H), 7.82 (d, 1H), 7.64 (t, 1H), 4.77 (s, 2H).

EJEMPLO 15

3-clorometil-5-m-tolil-[1,2,4]oxadiazol

Se agrega cloruro de 3-metil-benzoilo (0.80 ml, 6.1 mmoles) a una solución de 2-cloro-*N*-hidroxi-acetamidina (440 mg, 4.1 mmoles) en diclorometano (10 ml) a temperatura ambiente y la mezcla resultante se agita durante 30 minutos. Después se agrega

trietilamina (0.62 ml, 4.5 mmoles) y la mezcla resultante se agita durante 30 minutos. El producto se separa en diclorometano y la capa orgánica se lava con agua y salmuera y se seca con sulfato de sodio. La evaporación del solvente y la cromatografía de vaporización instantánea en sílice (acetato de etilo al 10-20% en hexanos) producen el intermediario de éster acíclico (814 mg). Se calienta una solución de este intermediario en DMF (10 ml) a 135°C durante 4 h. El producto se divide en acetato de etilo y la capa orgánica se lava con agua y salmuera y se seca con sulfato de sodio. La evaporación del solvente y la cromatografía de vaporización instantánea en sílice (acetato de etilo al 5% en hexanos) produce 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (469 mg, 54% en los 2 pasos, sólido de color blanco).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.99 (s, 1H), 7.97 (m, 1H), 7.43 (d, 2H), 4.68 (s, 2H), 2.45 (s, 3H).

EJEMPLO 16

3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol

Se agrega DMF (10 ml) a una mezcla de ácido 3-fluorobenzoico (710 mg, 5.07 mmoles), clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodi-imida (EDCI)

(972 mg, 5.07 mmoles), hidrato de 1-hidroxi-benzotriazol (HOBt) (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) a temperatura ambiente y después se agita durante la noche. La mezcla de reacción se diluye con acetato de etilo, se lava con agua (3 veces) y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. Se agrega DMF (14 ml) al residuo y la solución resultante se calienta a 135°C durante 3.5 h para efectuar la ciclización hasta oxadiazol. Después de enfriar la mezcla de reacción se lava con agua (3 veces) y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. Se obtiene 3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol (383 mg, 35% de rendimiento en los 2 pasos, aceite de color amarillo) mediante cromatografía de vaporización instantánea en gel de sílice, utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.96 (d, 1H), 7.86 (m, 1H), 7.54 (m,1H), 7.33 (m, 1H), 4.68 (s, 2H).

Los ejemplos 17-30 se preparan en un método análogo el procedimiento indicado en el ejemplo 16.

EJEMPLO 17

3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol (197 mg, 20% de rendimiento en los 2 pasos, sólido de color blanco) a partir del ácido 3-tiofencarboxílico (700 mg, 4.96 mmoles), EDCI (950 mg, 4.96 mmoles), HOBt (670 mg, 4.96 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (538 mg, 5.46 mmoles) en DMF (10 ml). El producto acíclico se purifica mediante cromatografía de vaporización instantánea en columna eluyendo con diclorometano:hexano:acetato de etilo 2:1.2:0.8. El compuesto del título se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN (CDCl3), δ (ppm): 8.28 (s, 1H), 7.70 (d, 1H), 7.48 (m, 1H).

EJEMPLO 18

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina

Se obtiene 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina (25 mg, 4% de rendimiento en los 2 pasos) a partir de ácido 5-metilnicotínico (472

mg, 3.44 mmoles), EDCI (652 mg, 3.44 mmoles), HOBt (465 mg, 3.44 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (340 mg, 3.13 mmoles) en DMF (10 ml). El intermediario acíclico se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 100%; también se aíslan 200 mg (30%) del éster acíclico como producto secundario.

EJEMPLO 19

3-clorometil-5-(3-nitro-fenil)-[1,2,4] oxadiazol

Se obtiene 3-clorometil-5-(3-nitro-fenil)-[1,2,4]oxadiazol (335 mg, 30% de rendimiento en los 2 pasos, sólido de color amarillo) a partir de ácido 3-nitrobenzoico (847 mg, 5.07 mmoles), EDCI (972 mg, 5.07 mmoles), HOBt (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) en DMF (10 ml). El intermediario acíclico se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 100%. La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 15% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.03 (t, 1H), 8.50 (t, 2H), 7.79 (t, 1H), 4.71 (s, 2H)

EJEMPLO 20

4-(3-clorometil-[1,2,4]oxadiazol-5-il)-2-metil-piridina

Se obtiene 4-(3-clorometil-[1,2,4]oxadiazol-5-il)-2-metil-piridina (316 mg, 28% de rendimiento en los 2 pasos, aceite de color amarillo) a partir de ácido 6-metilpiridin-4-carboxílico (800 mg, 5.8 mmoles), EDCI (1.12 g, 5.8 mmoles), HOBt (788 mg, 5.8 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (575 mg, 5.3 mmoles) en DMF (10 ml) más trietilamina (536 mg, 5.3 mmoles). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 30% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.75 (d, 1H), 7.88 (s, 1H), 7.79 (d, 1H), 4.70 (s, 2H), 2.70 (s, 3H)

EJEMPLO 21

3-clorometil-5-(3-etil-fenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-etil-fenil)-[1,2,,4]oxadiazol (446 mg, 52% de rendimiento en los 2 pasos, aceite de color amarillo) a partir de ácido 3-etilbenzoico (770 mg, 3.81 mmoles), EDCI (803 mg, 4.19 mmoles), HOBt (566 mg, 4.19 mmoles) y 2-cloro-*N*-

hidroxi-acetamidina (454 mg, 4.19 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.96 (t, 2H), 7.42 (m, 2H), 4.68 (s, 2H), 2.74 (m, 2H), 1.28 (m, 3H).

EJEMPLO 22

3-(3-clorometil[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina

Se obtiene 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina (40 mg, 4% de rendimiento en los 2 pasos, sólido de color amarillo) a partir de ácido 3-(dimetilamino)benzoico (656 mg, 3.97 mmoles), EDCI (761 mg, 3.97 mmoles), HOBt (536 mg, 3.97 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 3.6 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.46 (t, 2H), 7.37 (t, 1H), 6.94 (d, 1H), 4.68 (s, 2H), 3.04 (s, 6H).

EJEMPLO 23

3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol (406 mg, 43% de rendimiento en los 2 pasos, sólido de color blanco) a partir de ácido 3-clorobenzoico (708 mg, 4.52 mmoles), EDCI (866 mg, 4.52 mmoles), HOBt (611 mg, 4.52 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (446 mg, 4.11 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.17 (t, 1H), 8.05 (d, 1H), 7.59 (t, 1H), 7.50 (t, 1H), 4.68 (s, 2H).

EJEMPLO 24

3-clorometil-5-(3-trifluorometoxi-fenil)-[1,2,4]-oxadiazol

Se obtiene 3-clorometil-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol (707 mg, 55% de rendimiento en los 2 pasos, aceite de color amarillo claro) a partir de ácido 3-trifluorometoxibenzoico (1.05 g, 5.07 mmoles), EDCI (972 mg, 5.07 mmoles), HOBt (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500

mg, 4.61 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

EJEMPLO 25

5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol

Se obtiene 5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol (707 mg, 55% de rendimiento en los 2 pasos, sólido de color blanco) a partir de ácido 3-bromobenzoico (1.05 g, 5.07 mmoles), EDCI (972 mg, 5.07 mmoles), HOBt (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$) δ (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

EJEMPLO 26

3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-tiofen-2-il-[1,2,4]-

oxadiazol (202 mg, 20%, sólido de color blanquecino) a partir de ácido tiofen-2-carboxílico (649 mg, 5.1 mmoles), 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.6 mmoles), EDCI (972 mg, 5.1 mmoles) y HOBt (684 mg, 5.1 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.00 (s,1H), 7.83 (d,1H), 7.19 (t, 1H), 4.13 (s, 2H).

EJEMPLO 27

3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol

Se obtiene 3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]oxadiazol (312 mg, 46%, aceite incoloro) a partir de ácido 3-fluoro-5-metil-benzoico (469 mg, 3.0 mmoles), 2-cloro-*N*-hidroxi-acetamidina (363 mg, 3.3 mmoles), EDCI (641 mg, 3.3 mmoles) y HOBt (452 mg, 3.3 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.79 (s, 1H), 7.65 (d,1H), 7.15 (d, 1H), 4.67 (s, 2H), 2.46 (s, 3H).

EJEMPLO 28

3-clorometil-5-tiazol-4-il-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-tiazol-4-il-[1,2,4]-oxadiazol (37 mg, 5%, sólido de color amarillo) a partir de ácido tiazol-4-carboxílico (500 mg, 3.9 mmoles), 2-cloro-*N*-hidroxi-acetamidina (462 mg, 4.3 mmoles), EDCI (817 mg, 4.3 mmoles) y HOBt (575 mg, 4.3 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 30% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.02 (d, 1H), 8.42 (d, 1H), 4.70 (s, 2H).

EJEMPLO 29

3-clorometil-5-(3-yodo-fenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-yodofenil)-[1,2,4]oxadiazol (2.9 g, 44%, sólido de color blanco) a partir de ácido 3-yodo-benzoico (5.0 g, 20.2 mmoles), 2-cloro-*N*-hidroxi-acetamidina (2.4 g, 22.2 mmoles), EDCI (4.3 g, 22.2 mmoles) y HOBt (3.0 g, 22.2 mmoles) en DMF (10 ml). El intermediario de éster acíclico se purifica mediante cromatografía de

vaporización instantánea utilizando acetato de etilo al 50-80% en hexanos. El compuesto del título se purifica mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.52 (s, 1H), 8.13 (d, 1H), 7.96 (d, 1H), 7.29 (t, 1H), 4.68 (s, 2H).

EJEMPLO 30

3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol (193 mg, 34%, aceite de color amarillo claro) a partir de ácido 3-metoximetil-benzoico (395 mg, 2.4 mmoles), 2-cloro-*N*-hidroxi-acetamidina (284 mg, 2.6 mmoles), EDCI (501 mg, 2.6 mmoles) y HOBt (353 mg, 2.6 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.14 (s, 1H), 8.08 (d, 1H), 7.61(d,1H), 7.53 (t, 1H), 4.68 (s, 2H), 4.54 (s, 2H), 3.44 (s, 3H).

EJEMPLO 31

5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-tiol

Se agrega cloruro de 2-furoilo (0.76 ml, 7.66 mmoles) mediante goteo, a una solución de 4-metil-3-tiosemicarbazida (732 mg, 6.96 mmoles) y piridina (7 ml) y la solución resultante se agita a temperatura ambiente durante 4 h. La mezcla de reacción se diluye con acetato de etilo (100 ml), se lava en forma sucesiva con agua (3x100 ml) y salmuera (100 ml). La fase orgánica se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo se suspende en bicarbonato de sodio (70 ml, 69.6 mmoles, 1 M en agua) y se deja agitando a 100°C durante la noche. La mezcla de reacción se enfría hasta 0°C, después se lleva a pH de aproximadamente 6 utilizando ácido clorhídrico (70 ml, 1 N en agua). El compuesto del título (298 mg) se recolecta mediante filtración como un sólido de color blanco.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.4 (bs,1H), 7.63 (d,1H), 7.02 (d, 1H), 6.60 (dd, 1H), 3.83 (s, 3H).

Los ejemplos 32-35 se preparan en un método análogo el procedimiento indicado en el ejemplo 31.

EJEMPLO 32

4-metil-5-fenil-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-fenil-4H-[1,2,4]-triazol-3-tiol (478 mg, sólido de color blanquecino) a partir de 4-metil-3-tiosemicarbazida (732 mg, 6.96 mmoles) y piridina (7 ml) con cloruro de benzoilo (0.89 ml, 7.66 mmoles). Después se agrega bicarbonato de sodio (70 ml, 69.6 mmoles, 1 M en agua) a 100°C durante la noche y el compuesto del título se recolecta mediante filtración.

^{1}H RMN ($CDCl_3$), δ (ppm): 12.3(bs, 1H), 7.55 (m, 5H), 3.65 (s, 3H).

EJEMPLO 33

4-metil-5-piridin-2-il-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-piridin-2-il-4H-[1,2,4]-triazol-3-tiol (44 mg, sólido de color verduzco) a partir de 4-metil-3-tiosemicarbazida (537 mg, 5.11 mmoles) y piridina (7 ml) con clorhidrato de cloruro de 2-piridincarbonilo (1.00 g, 5.62 mmoles). Después se agrega bicarbonato de sodio (51 ml, 1 M en agua) a 100°C durante la noche y el compuesto del título se recolecta utilizando extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.1 (bs, 1H), 8.70 (d, 1H), 8.02 (d, 1H), 7.84 (m, 1H), 7.41 (dd, 1H), 4.05 (s, 3H).

EJEMPLO 34

5-(4-bencil-morfolin-2-il)-4-metil-4H-[1,2,4]triazol-3-tiol

Se obtiene (83.3 mg, sólido de color amarillo sucio) a partir de 4-metil-3-tiosemicarbazida (346 mg, 3.29 mmoles) y piridina (7 ml) con clorhidrato de cloruro de 4 bencil-2-morfolincarbonilo (1.00 g, 3.62 mmoles). Después se agrega bicarbonato de sodio (33 ml, 1 M en agua) a 100°C durante la noche y el compuesto del título se recolecta utilizando extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.48 (bs, 1H), 7.25 (m, 5H), 4.68 (dd, 1H), 3.86 (dAb, 1H), 3.68 (tAB, 1H), 3.59-3.64 (m, 5H), 3.07 (d, 1H), 2.88 (d, 1H), 2.61 (t, 1H), 2.37 (dt, 1H).

EJEMPLO 35

5-ter-butil-4-metil-4H-[1,2,4]triazol-3-tiol

Se obtiene 5-ter-butil-4-metil-4H-[1,2,4]-

triazol-3-tiol (2.21 g, 83%, sólido de color blanquecino) a partir de 4-metil-3-tiosemicarbazida (1.80 g, 17.2 mmoles) y piridina (20 ml) con cloruro de trimetilacetilo (1.92 ml, 15.6 mmoles). Después se agrega hidróxido de sodio (200 ml, 5% en agua) y se deja agitando a 60°C durante la noche y el compuesto del título se recolecta mediante extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.7 (bs, 1H), 3.72 (s, 3H) 1.40 (s, 9H).

EJEMPLO 36

4-metil-5-piridin-3-il-4*H*-[1,2,4]triazol-3-tiol

Se agita una solución de 4-metil-3-tiosemicarbazida (902 mg, 8.58 mmoles), ácido nicotínico (960 mg, 7.80), EDCI (1.64 g, 8.58 mmoles), HOBt (1.16 g, 8.58 mmoles) en DMF (10 ml) a temperatura ambiente durante la noche. La mezcla de reacción se diluye con acetato de etilo (100 ml), se lava en forma sucesiva con ácido clorhídrico (50 ml, al 10% acuoso), agua (50 ml), carbonato de sodio saturado (50 ml, acuoso), agua (50 ml) y salmuera (50 ml). La fase orgánica se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo se agita en hidróxido de sodio (53.4 ml, 66.7 mmoles, 5%

acuoso) a 60°C durante la noche. La mezcla de reacción se enfría hasta temperatura ambiente, después se lleva cuidadosamente hasta pH de aproximadamente 6 utilizando ácido clorhídrico (1 N en agua). La fase acuosa se satura con cloruro de sodio sólido, después se extrae con acetato de etilo (4x50 ml). La fase orgánica combinada se lava con salmuera (100 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío (180 mg, sólido de color blanquecino).

^{1}H RMN ($CDCl_3$), δ (ppm): 11.6 (bs, 1H), 8.94 (s, 1H), 8.83 (dd, 1H), 7.98 (m, 1H), 7.51 (dd, 1H), 3.69 (s, 3H).

Los ejemplos 37-39 se preparan en un método análogo el procedimiento indicado en el ejemplo 36.

EJEMPLO 37

4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-tiol (693 mg, sólido de color blanco) a partir de 4-metil-3-tiosemicarbazida (902 mg, 8.58 mmoles), ácido 3-tiofencarboxílico (1 g, 7.80 mmoles), EDCI (1.64 g, 8.58 mmoles), HOBt (1.16 g, 8.58 mmoles) en DMF (10 ml). Después hidróxido de

sodio (88 ml, 110 mmoles, 5% acuoso) a 60°C durante la noche y el compuesto del título se recolecta extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.4 (bs, 1H), 7.77 (dd, 1H), 7.51 (dd, 1H), 7.42 (dd, 1H), 3.61 (s, 3H).

EJEMPLO 38

4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-tiazol-4-il-4*H*-[1,2,4]-triazol-3-tiol (71.2 mg, aceite de color amarillo pegajoso) a partir de 4-metil-3-tiosemicarbazida (902 mg, 8.58 mmoles), 4-carboxitiazol (1.01 g, 7.80), EDCI (1.64 g, 8.58 mmoles), HOBt (1.16 g, 8.58 mmoles) en DMF (10 ml). Después hidróxido de sodio (43 ml, 54 mmoles, 5% acuoso) a 60°C durante la noche y el compuesto del título se recolecta extracción y evaporación.

EJEMPLO 39

5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 5-ciclohexil-4-metil-4H-[1,2,4]-triazol-3-tiol (403 mg, sólido color beige) a partir de 4-metil-3-tiosemicarbazida (1.80 g,17.2 mmoles),

ácido ciclohexan-carboxílico (2 g,15.6 mmoles), EDCI (2.99 g, 17.2 mmoles) y HOBt (2.10 g, 17.2 mmoles) en DMF (20 ml); después hidróxido de sodio (195 ml, 244 mmoles, 5% acuoso) a 60°C durante la noche.

EJEMPLO 40

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol

Se agrega 1*H*-benzoimidazol-2-tiol (150 mg, 1 mmoles) a una solución del 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (30 mg, 0.13 mmoles) y carbonato de potasio (50 mg, 0.36 mmoles) en DMF (2 ml) a temperatura ambiente. El solvente se elimina al vacío y el producto se obtiene mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 20-100% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.71 (d, 1H), 7.62 (d, 1H), 7.53 (m, 2H), 7.42 (t, 1H), 7.18 (se traslapan, m, 3H), 4.52 (s, 2H), 3.87 (s, 3H).

Los ejemplos 41-92 se preparan en un método análogo el procedimiento indicado en el ejemplo 40.

EJEMPLO 41

5-(3-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

El compuesto del título se prepara a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (50 mg, 0.22 mmoles), carbonato de potasio (92.4 mg, 0.67 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (52.8 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 30-40% en hexanos lo que permite obtener 76 mg (90%) del compuesto del título como un sólido de color blanco.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.68 (d, 1H), 7.57 (t, 1H), 7.49 (m, 2H), 7.41 (t, 1H), 7.15 (m, 2H), 4.53 (s, 2H), 3.85 (s, 3H), 3.72 (s, 3H).

LC-MS $(M+1)^+$ 386.3.

EJEMPLO 42

3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo

Se obtiene 3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-

benzonitrilo (39 mg, 47%, sólido de color blanco) a partir de 3-clorometil-3-(5-clorometil-[1,2,4]-oxadiazol-3-il)-benzonitrilo (50 mg, 0.22 mmoles), carbonato de potasio (92.4 mg, 0.67 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (52.8 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.34 (s, 1H), 8.28 (d, 1H), 7.79 (d, 1H), 7.60 (t,1H), 7.53 (d, 1H), 7.49 (d, 1H), 7.19 (m, 1H), 4.70 (s, 2H), 3.74 (s, 3H).

LS-mS (ES+ barrido completo, $C_{17}H_{12}N_6OS_2$)M^+ calculado 380.05, encontrado $(M+1)^+$ 381.04.

EJEMPLO 43

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]traiazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]traiazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]-oxadiazol (41.2 mg, 44%, sólido de color blanquecino) a partir de 3-clorometil-5-fenil-[1,2,4]oxadiazol (50 mg, 0.26 mmoles), carbonato de potasio (106 mg, 0.77 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-

tiol (60.8 mg, 0.31 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.09 (m, 2H), 7.57 (m, 5H), 7.17 (dd,1H), 4.53 (s, 2H), 3.72 (s, 3H).

EJEMPLO 44

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-metil-1*H*-benzoimidazol

Se obtiene 2-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-5-metil-1*H*-benzoimidazol (75.5 mg, 70.5%, espuma de color blanco) a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (82 mg, 0.365 mmoles), carbonato de potasio (210 mg, 1.520 mmoles), 2-tiol-5-metil-1H-benzoimidazol (50 mg, 0.305 mmoles) en acetonitrilo (3 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de vaporización instantánea de SPE utilizando acetato de etilo al 50% en hexanos seguido por trituración con acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.95 (bs, 1H), 7.80 (d, 1H), 7.70 (s, 1H), 7.52 (m, 2H), 7.21 (dd, 2H), 7.17 (d, 1H), 4.40 (s, 2H), 3.95 (s, 3H), 2.50 (s, 3H).

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EJEMPLO 45

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (76 mg, 85%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99.4 mg, 0.72 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (56.7 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.50 (m, 2H), 7.40 (m, 2H), 7.18 (t, 1H), 4.52 (s, 2H), 3.71 (s, 3H), 2.41 (s, 3H).

EJEMPLO 46

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]-oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-trifluorometil-fenil)-

[1,2,4]oxadiazol (84 mg, 86%, sólido de color blanco) se obtiene a partir de 3-clorometil-5-(3-trifluorometil-fenil)-[1,2,4]oxadiazol (60 mg, 0.23 mmoles), carbonato de potasio (95 mg, 0.69 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (54 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-60% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.38 (s, 1H), 7.29 (d, 1H), 7.86 (d, 1H), 7.68 (t, 1H), 7.50 (t, 2H), 7.19 (m, 1H), 4.57 (s, 2H), 3.75 (s, 3H).

EJEMPLO 47

3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (74.3 mg, 88%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (53.3 mg, 0.27 mmoles), 5-clorometil-3-(3-metoxi-fenil)-[1,2,4]oxadiazol (50 mg, 0.22) mmoles), y carbonato de potasio (92.6 mg, 0.67 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La

purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.62 (d, 1H), 7.52 (d, 2H), 7.48 (d, 1H), 7.37 (t, 1H), 7.18 (t, 1H), 7.06 (m, 1H), 4.64 (s, 2H), 3.84 (s, 3H), 3.71 (s, 3H).

LC-mS (MH+): 386.06.

EJEMPLO 48

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol

Se obtiene 5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]-oxadiazol (79.9 mg, 87%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (86.8 mg, 0.44 mmoles), 5-clorometil-3-fenil-[1,2,4]oxadiazol (50 mg, 0.26 mmoles), y carbonato de potasio (152.0 mg, 1.1 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.02 (d, 2H), 7.47 (m, 5H), 7.18 (t, 1H).

EJEMPLO 49

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]oxadiazol

Se obtiene 5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]-oxadiazol (71.8 mg, 91%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (78.9 mg, 0.40 mmoles), 5-clorometil-3-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles) y carbonato de potasio (138.2 mg, 1.0 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 45-65% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.82 (d, 2H), 7.52 (d, 1H), 7.47 (d, 1H), 7.31 (m, 2H), 7.18 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H), 2.39 (s, 3H). LC-mS (MH^+): 370.06.

EJEMPLO 50

3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo

Se obtiene 3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-

il]-benzonitrilo (130 mg, 75%) a partir de 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo (100 mg, 0.45 mmoles) con K_2CO_3 (189 mg, 1.36 mmoles) y 4-metil-5-(2-tienil)1,2,4-triazol-3-tiol (110 mg, 0.54 mmoles) en acetonitrilo a temperatura ambiente. La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 50% en diclorometano.

^1H RMN($CDCl_3$), δ (ppm): 8.38 (bs,1H), 8.32 (d,1H), 7.88 (d,1H), 7.68 (t,1H), 7.51 (dd, 2H), 7.18 (dd,1H), 4.56 (s,2H), 3.75 (s,3H).

LC-mS $(M+H)^+$: 381.

EJEMPLO 51

3-[4-metil-5-(2-metil-tiazol-4-il)-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

3-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol (82.8 mg, 90%, sólido de color blanco) se obtiene a partir de 3-clorometil-5-m-tolil-[1,2,4]-oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]-triazol-3-tiol (61 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se

efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.96 (s, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.53 (s, 2H), 3.91 (s, 3H), 2.75 (s, 3H), 2.41 (s, 3H).

EJEMPLO 52

3-[5-(2-metil-tiazol-4-il)-[1,3,4]oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[5-(2-metil-tiazol-4-il)-[1,3,4]-oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol (89 mg, 99%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(2-metil-triazol-4-il)-[1,3,4]oxadiazol-2-tiol (57.3 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.97 (s, 1H), 7.90 (m, 2H), 7.40 (m, 2H), 4.66 (s, 2H), 2.80 (s, 3H), 2.42 (s, 3H).

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EJEMPLO 53

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il- [1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]-oxadiazol (80 mg, 88%, sólido de color blanco) a partir de 3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol (50 mg, 0.25 mmoles), carbonato de potasio (103 mg, 0.75 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (59 mg, 0.30 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.65 (m, 1H), 7.51 (m, 2H), 7.19 (m, 2H), 4.50 (t, 2H), 3.74 (s, 3H).

EJEMPLO 54

3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-

[1,2,4]oxadiazol (54.2 mg, 57%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(2,4-dimetil-tiazol-5-il)-4-metil-4H-[1,2,4]triazol-3-tiol (65.1 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.39 (m, 2H), 4.57 (s, 2H), 3.49 (s, 3H), 2.73 (s, 3H), 2.43 (d, 6H).

EJEMPLO 55

3-[4-metil-5-(5-nitro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil- [1,2,4]oxadiazol

se obtiene 3-[4-metil-5-(5-nitro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol (77.9 mg, 81%, sólido de color amarillo) se obtiene a partir de 3-clorometil-5-m-tolil-[1,2,4]-oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 4-metil-5-(5-nitro-furan-2-il)-4H-[1,2,4]triazol-3-tiol (65.1 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel

de sílice utilizando acetato de etilo al 80% en.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (m, 2H), 7.46 (d, 1H), 7.40 (m, 2H), 7.33 (d, 1H), 4.59 (s, 2H), 3.91 (s, 3H), 2.42 (s, 3H).

EJEMPLO 56

4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 4-[4-metil-5-(5-m-tolil-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (66 mg, 75%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol (55.3 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.79 (dd, 2H), 7.89 (m, 2H), 7.63 (dd, 2H), 7.40 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.41 (s, 3H).

EJEMPLO 57

3-[5-(4-ter-butil-fenil)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol

Se obtiene 3-[5-(4-ter-butil-fenil)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol (100 mg, 99%, sólido ceroso de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]-oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(4-ter-butil-fenil)-4-metil-4*H*-[1,2,4]triazol-3-tiol (71.1 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.57 (m, 4H), 7.39 (d, 2H),4.55 (s, 2H), 3.61 (s, 3H), 2.40 (s, 3H), 1.35 (s, 9H).

EJEMPLO 58

2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (53.8 mg, 56%, sólido de color blanco)

a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(6-cloro-piridin-3-il)-4-metil-4H-[1,2,4]-triazol-3-tiol (65.2 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.67 (d, 1H), 8.02 (dd,1H), 7.88 (m, 2H), 7.49 (d, 1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.65 (s, 3H), 2.42 (s, 3H).

EJEMPLO 59

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-benzo-oxazol

Se obtiene 2-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-benzo-oxazol (138 mg, 62%) a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]-oxadiazol (225.9 mg, 1.11 mmoles), benzo-oxazol-2-tiol (167 mg, 1.00 mmoles), carbonato de potasio (180 mg, 1.3 mmoles) en DMF (4.5 ml) a temperatura ambiente durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 10-20% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.67 (d, 1H), 7.57 (m, 3H), 7.43 (t, 1H), 7.21 (m, 2H), 7.14 (m, 1H),

4.50 (s, 2H), 3.86 (s, 3H).

EJEMPLO 60

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]-oxa-diazol (73.6 mg, 73%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (61 mg, 0.31 mmoles), 3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol (50 mg, 0.28 mmoles), y carbonato de potasio (115 mg, 0.83 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.20 (d, 1H), 7.64 (d, 1H), 7,48 (m, 3H), 7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H).

EJEMPLO 61

3-(5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(5-furan-2-il-4-metil-4*H*-[1,2,4]-

triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (51.0 mg, 76%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40.0 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-tiol (41.7 mg, 0.23 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.58 (s, 1H), 7.40 (m, 2H), 7.10 (d, 1H), 6.58 (dd, 1H), 4.51 (s, 2H), 3.77 (s, 3H), 2.41 (s, 3H).

EJEMPLO 62

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (75.4 mg, 83%, sólido de color blanco) a partir de 4-metil-5-tiofen-il-4H-[1,2,4]triazol-3-tiol (51 mg, 0.26 mmoles), 3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol (50 mg, 0.24 mmoles) y carbonato de potasio (98 mg, 0.71 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización

instantánea) utilizando acetato de etilo al 55-60% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.78 (m, 1H), 7.51 (m, 3H), 7.32 (m, 1H), 7.18 (m, 1H), 4.55 (s, 2H), 3.74 (s, 3H)

EJEMPLO 63

2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-piridina

Se obtiene 2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-piridina (27.3 mg, 96.5%) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (20.8 mg, 0.1 mmoles) con piridin-2-tiol (12.2 mg, 0.11 mmoles) y carbonato de potasio en DMF (0.8 ml) a temperatura ambiente durante 15 h. La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo al 20% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.47 (dd, 1H), 7.94 (s, 1H), 7.90 (t, 1H), 7.51 (dt, 1H), 7.38 (d, 2H), 7.26 (dd, 1H), 7.02 (dd, 1H), 4.61 (s, 2H), 2.42 (s, 3H).

EJEMPLO 64

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-imidazo[4,5-b]piridina

Se obtiene 2-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-1*H*-imidazo[4,5-b]piridina (74.5 mg, 96%) a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (51.2 mg, 0.25 mmoles), 1H-imidazo[4,5-b]piridin-2-tiol (37.5 mg, 0.23 mmoles) y carbonato de potasio (80 mg, 0.58 mmoles) en DMF (1.5 ml) a temperatura ambiente durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 25-50% en diclorometano.

^{1}H-RMN (DMSO-d_6), δ (ppm): 8.24 (br s, 1H), 7.88 br s, 1H), 7.66 (d, 1H), 7.55 (m, 3H), 7.29 (d, 1H), 7.19 (m, 1H), 4.82 (s, 2H), 3.85 (s, 3H).

EJEMPLO 65

5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-[1,2,4]oxadiazol (58 mg, 68%, sólido de color blanco) a partir de 3-clorometil-5-(3-fluoro-5-metil-fenil)-

[1,2,4]oxadiazol (50 mg, 0.22 mmoles), carbonato de potasio (91.5 mg, 0.66 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (52.2 mg, 0.26 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-100% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.70 (s, 1H), 7.58 (d, 1H), 7.52 (m, 1H), 7.49 (m, 1H), 7.18 (m, 1H), 7.12 (d, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 2.42 (s, 3H).

EJEMPLO 66

3-metil-5-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

Se obtiene 3-metil-5-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxa-diazol-5-il]-piridina (19.0 mg, 43%, sólido de color amarillo claro) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol (26 mg, 0.13 mmoles), 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina (25 mg, 0.12 mmoles) y carbonato de potasio (50 mg, 0.36 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La

purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 100%.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.13 (s, 1H), 8.65 (s, 1H), 8.16 (s, 1H), 7.50 (m, 2H), 7.19 (t, 1H) 4.57 (s, 2H), 3.74 (s, 3H), 2.43 (s, 3H)

EJEMPLO 67

3-(4-metil-5-fenil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-fenil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (55.8 mg, 67%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (48.4 mg, 0.23 mmoles), carbonato de potasio (96 mg, 0.70 mmoles), 4-metil-5-fenil-4*H*-[1,2,4]triazol-3-tiol (44.4 mg, 0.23 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.64 (m, 2H), 7.50 (m, 3H), 7.39 (m, 2H), 4.56 (s, 2H), 3.61 (s, 3H), 2.41 (s, 3H).

EJEMPLO 68

2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 2-[4-metil-5-(5-m-tolil-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (42.8 mg, 51%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (48.4 mg, 0.23 mmoles), carbonato de potasio (96 mg, 0.70 mmoles), 4-metil-5-piridin-2-il-4*H*-[1,2,4]triazol-3-tiol (44.6 mg, 0.23 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.62 (d, 1H), 8.30 (d,1H), 7.85 (m, 3H), 7.36 (m, 3H), 4.59 (s, 2H), 4.02 (s, 3H), 2.40 (s, 3H).

EJEMPLO 69

4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-morfolina

Se obtiene 4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-morfolina (95.8 mg, 83%, aceite claro) a partir

de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (59.9 mg, 0.29 mmoles), carbonato de potasio (119 mg, 0.86 mmoles), 5-(4-bencil-morfolin-2-il)-4-metil-4*H*-[1,2,4]-triazol-3-tiol (83.3 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando metanol al 10% en acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.31 (m, 7H), 4.75 (dd, 1H), 4.47 (dd, 2H), 3.84 (m, 2H), 3.59 (bs, 5H), 3.20 (d, 1H), 2.72 (m, 2H), 2.43 (s, 3H), 2.30 (dt, 1H).

EJEMPLO 70

4-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol3-il-piridina

Se obtiene 4-[4-metil-5-(5-tiofen-3-il-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (24 mg, 34%, sólido de color blanco) a partir de 3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol (40 mg, 0.20 mmoles), carbonato de potasio (82.5 mg, 0.60 mmoles), 4-metil-5-piridin-4-il-4*H*-[1,2,4]triazol-3-tiol (38.3 mg, 0.20 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando metanol al 10% en acetato

de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.80 (bs, 2H), 8.20 (dd, 1H), 7.62 (m, 3H), 7.45 (dd, 1H), 4.59 (s, 2H), 3.70 (s, 3H).

EJEMPLO 71

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxa-diazol (44 mg, 67%, sólido de color blanco) a partir de 3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol (37 mg, 0.18 mmoles), carbonato de potasio (75.3 mg, 0.54 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (43 mg, 0.22 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-100% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 9.37 (d, 1H), 8.86 (d, 1H), 7.80 (d, 1H), 7.65 (d, 1H), 7.26 (t, 1H), 4.54 (s, 2H), 3.75 (s, 3H).

EJEMPLO 72

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil) -[1,2,4] oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,2,4]oxadiazol (21.1 mg, 13%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol (91 mg, 0.46 mmoles), 3-clorometil-5-(3-nitro-fenil)-[1,2,4]oxadiazol (100 mg, 0.42 mmoles) y carbonato de potasio (173 mg, 1.25 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 60% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.96 (s, 1H), 8.44 (t, 2H), 7.75 (t, 1H), 7.51 (m, 2H), 7.19 (t, 1H), 4.59 (s, 2H), 3.76 (s, 3H)

EJEMPLO 73

2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

Se obtiene 2-metil-4-[3-(4-metil-5-tiofen-2-

il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina (59.2 mg, 66%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (51 mg, 0.26 mmoles), 4-(3-cloro-metil-[1,2,4]oxadiazol-5-il)-2-metil-piridina (50 mg, 0.24 mmoles), y carbonato de potasio (100 mg, 0.72 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 100%.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.71 (d, 1H), 7.79 (s, 1H), 7.73 (d, 1H), 7.49 (m, 2H), 7.19 (t, 1H), 4.58 (s, 2H), 3.73 (s, 3H), 2.65 (s, 3H).

EJEMPLO 74

3-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 3-[4-metil-5-(5-m-tolil-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (30 mg, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 4-metil-5-piridin-3-il-4*H*-[1,2,4]triazol-3-tiol (46.1 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante

la noche. La purificación se efectúa en gel de sílice utilizando metanol al 5% en acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.90 (bs,1H), 8.76 (bs, 1H), 8.03 (m, 1H), 7.88 (m, 2H), 7.46 (dd,1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.66 (s, 3H), 2.42 (s, 3H).

EJEMPLO 75

3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (60 mg, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-tiol (47.3 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 40% en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.71 (dd, 1H), 7.48 (m, 2H), 7.38 (m, 2H), 4.52 (s, 2H), 3.67 (s, 3H), 2.41 (s, 3H).

EJEMPLO 76

3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (30 mg, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 4-metil-5-triazol-4-il-4*H*-[1,2,4]triazol-3-tiol (47.5 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 60% en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.89 (d, 1H), 8.22 (d, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.55 (s, 2H), 3.94 (s, 3H), 2.41 (s, 3H).

EJEMPLO 77

5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (725 mg, 97%, sólido de color blanco) a partir de 3-clorometil-5-(3-yodo-fenil)-[1,2,4]oxa-

diazol (500 mg, 1.56 mmoles), carbonato de potasio (647 mg, 4.68 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (369 mg, 1.87 mmoles) en acetonitrilo (10 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo al 40% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 8.06 (d, 1H), 7.93 (d, 1H), 7.51 (m, 2H), 7.26 (t, 1H), 7.19 (m, 1H), 4.54 (s, 2H), 3.73 (s, 3H).

EJEMPLO 78

5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (28.1 mg, 27%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (59 mg, 0.30 mmoles), 3-clorometil-5-(3-etil-fenil)-[1,2,4]oxadiazol (60 mg, 0.27 mmoles) y carbonato de potasio (111 mg, 0.80 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de

etilo al 50% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (t, 2H), 7.51 (m, 2H), 7.42 (t, 2H), 7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H), 2.70 (m, 2H), 1.26 (t, 3H)

EJEMPLO 79

2-[5-(2-metil-piridin-4-il)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(2-metil-piridin-4-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (46.0 mg, 59%, sólido de color blanco) a partir de 2-mercaptobencimidazol (41 mg, 0.27 mmoles), 4-(3-cloro-metil-[1,2,4]oxadiazol-5-il)-2-metil-piridina (50 mg, 0.24 mmoles), y carbonato de potasio (100 mg, 0.72 mmoles) en DMF (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 100% y se tritura con éter.

^{1}H RMN (DMSO-d_6), δ (ppm): 8.72 (d, 1H), 7.87 (s, 1H), 7.78 (d, 1H), 7.47 (t, 2H), 7.14 (m, 2H), 4.81 (s, 2H), 2.59 (s, 3H)

EJEMPLO 80

2-[5-(3-yodo-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(3-yodo-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (36 mg, 51%, sólido de color blanco) a partir de 3-cloro-metil-5-(3-yodo-fenil)-[1,2,4]oxadiazol (50 mg, 0.16 mmoles), carbonato de potasio (65 mg, 0.47 mmoles), 1*H*-benzoimidazol-2-tiol (23 mg, 0.16 mmoles) en DMF (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-100% en hexanos seguido por trituración con acetato de etilo.

^{1}H RMN (DMSO), δ (ppm): 12.73 (bs, 1H), 8.30 (s, 1H), 8.09 (d, 2H), 7.45 (m, 3H), 7.18 (m, 2H), 4.78 (s, 2H).

EJEMPLO 81

3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (54.3 mg, 80%, aceite claro) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40 mg, 0.19

mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 4-metil-5-triflurometil-4*H*-[1,2,4]triazol-3-tiol (35.1 mg, 0.19 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.41 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.43 (s, 3H).

EJEMPLO 82

2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]-triazol-3-il]-piridina (51.4 mg, 62%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 5-(2,6-dicloro-piridin-4-il)-4-metil-4*H*-[1,2,4]triazol-3-tiol (50.1 mg, 0.19 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.61 (s, 2H), 7.40 (m, 2H), 4.60 (s, 2H), 3.71 (s, 3H), 2.42 (s, 3H).

EJEMPLO 83

3-(4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-p-tolil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (57.8 mg, 81%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-tiol (39.4 mg, 0.19 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.53 (d, 2H), 7.39 (m, 2H), 7.30 (d, 2H), 4.55 (s, 2H), 3.59 (s, 3H), 2.42 (d, 6H).

EJEMPLO 84

Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil)-amina

Se obtiene Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil)-amina (28.0 mg, 85%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-

[1,2,4]triazol-3-tiol (18 mg, 0.093 mmoles), 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina (20 mg, 0.084 mmoles), y carbonato de potasio (35 mg, 0.25 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.49 (m, 2H), 7.36 (m, 3H), 7.17 (t, 1H), 6.91 (d, 1H), 4.51 (s, 2H), 3.72 (s, 3H), 3.00 (s, 6H)

EJEMPLO 85

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (76.8 mg, 90%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (47 mg, 0.24 mmoles), 3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol (50 mg, 0.22 mmoles), y carbonato de potasio (91 mg, 0.66 mmoles en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de

etilo al 70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.49 (m, 4H), 7.18 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

EJEMPLO 86

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol (144.0 mg, 91%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (78 mg, 0.39 mmoles), 3-cloro-metil-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol (100 mg, 0.36 mmoles) y carbonato de potasio (149 mg, 1.08 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 55% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.04 (d, 1H), 7.95 (s, 1H), 7.51 (m, 4H), 7.18 (m, 1H), 4.56 (s, 2H), 3.74 (s, 3H)

EJEMPLO 87

3-(5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(5-ciclohexil-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (10.5 mg, aceite claro) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (165 mg, 1.20 mmoles), 5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-tiol (94.6 mg, 0.48 mmoles) en acetonitrilo (3 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando amoniaco al 2% (2 N en metanol) en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.39 (m, 2H), 4.42 (s, 2H), 3.46 (s, 3H), 2.60 (m, 1H), 2.42 (d, 3H), 1.74 (m, 7H), 1.34 (m, 3H).

EJEMPLO 88

3-(5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(5-ter-butil-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (56.8 mg, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24

mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-tiol (41 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.40 (m, 2H), 4.46 (s, 2H), 3.63 (s, 3H), 2.43 (m, 3H), 1.45 (s, 9H).

EJEMPLO 89

5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (83.4 mg, 86%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (47 mg, 0.24 mmoles), 5-(3-bromo-fenil)-3-cloro-metil-[1,2,4]oxadiazol (60 mg, 0.22 mmoles), y carbonato de potasio (91 mg, 0.66 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 60% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.25 (t, 1H), 8.02 (d, 1H), 7.73 (d, 1H), 7.50 (m, 2H), 7.40 (t, 1H),

7.19 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

EJEMPLO 90

2-[5-(3-bromo-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(3-bromo-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (71.1 mg, 84%, sólido de color blanco) a partir de 2-mercaptobencimidazol (35 mg, 0.23 mmoles), 5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol (60 mg, 0.22 mmoles) y carbonato de potasio (91 mg, 0.66 mmoles) en DMF (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 35% en hexano y se tritura con éter.

^{1}H RMN (DMSO-d_6), δ (ppm): 12.78 (s ancho, 1H), 8.18 (s, 1H), 8.07 (d, 1H), 7.93 (d, 1H), 7.59 (t, 1H), 7.46 (s, 2H), 7.14 (m, 2H), 4.77 (s, 2H)

EJEMPLO 91

5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-metoximetil-fenil)-3-(4-

metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-[1,2,4]oxadiazol (76 mg, 90%, sólido de color blanco) a partir de 3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol (50 mg, 0.21 mmoles), carbonato de potasio (87 mg, 0.63 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (50 mg, 0.25 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.06 (s, 1H), 8.01 (d, 1H), 7.59 (d, 1H), 7.50 (m, 3H), 7.18 (t, 1H), 4.54 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H), 3.43 (s, 3H).

EJEMPLO 92

2-[5-(3-metoximetil-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(3-metoximetil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (62 mg, 84%, sólido de color blanco) a partir de 3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol (50 mg, 0.21 mmoles), carbonato de potasio (87 mg, 0.63 mmoles), 1*H*-benzoimidazol-2-tiol (32 mg, 0.21 mmoles) en DMF (2 ml) a temperatura ambiente. La purificación se efectúa

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mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-100% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 8.09 (d, 2H), 7.59 (m, 2H), 7.46 (bs, 2H), 7.14 (m, 2H), 4.77 (s, 2H), 4.51 (s, 2H), 3.35 (s, 3H).

EJEMPLO 93

4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

Se trata una solución de cloruro de isonicotinoilo (2.0 g, 11.2 mmoles) en diclorometano con 2-cloro-N-hidroxi-acetamidina (1.58 g, 14.6 mmoles), seguido por la adición de trietilamina (4.67 ml, 33.6 mmoles) mediante goteo. Después de agitar a temperatura ambiente 1 h, la extracción con acetato de etilo utilizando lavados con agua y salmuera permite obtener el intermediario oxi-arilo (que se utiliza sin purificación adicional, 150 mg, 0.7 mmoles). Se agita una solución el producto crudo en acetonitrilo (2 ml) y DMSO (2 ml) con K_2CO_3 (292 mg, 2.1 mmoles) y 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (140 mg, 0.7 mmoles) a temperatura ambiente durante 24 h seguido por 1.5 h a 120°C (tubo sellado). El tratamiento acuoso normal con acetato de

mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-100% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 8.09 (d, 2H), 7.59 (m, 2H), 7.46 (bs, 2H), 7.14 (m, 2H), 4.77 (s, 2H), 4.51 (s, 2H), 3.35 (s, 3H).

EJEMPLO 93

4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

Se trata una solución de cloruro de isonicotinoilo (2.0 g, 11.2 mmoles) en diclorometano con 2-cloro-N-hidroxi-acetamidina (1.58 g, 14.6 mmoles), seguido por la adición de trietilamina (4.67 ml, 33.6 mmoles) mediante goteo. Después de agitar a temperatura ambiente 1 h, la extracción con acetato de etilo utilizando lavados con agua y salmuera permite obtener el intermediario oxi-arilo (que se utiliza sin purificación adicional, 150 mg, 0.7 mmoles). Se agita una solución el producto crudo en acetonitrilo (2 ml) y DMSO (2 ml) con K_2CO_3 (292 mg, 2.1 mmoles) y 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (140 mg, 0.7 mmoles) a temperatura ambiente durante 24 h seguido por 1.5 h a 120°C (tubo sellado). El tratamiento acuoso normal con acetato de

etilo utilizando lavados con agua y salmuera seguido por cromatografía en gel de sílice permite obtener el compuesto del título (110 mg, 44%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.41 dd,2H), 7.92 dd,2H), 7.50 dd,1H), 7.47 dd,1H), 7.18 dd,1H), 4.58 (s,2H), 3.74 (s,3H)

LC-mS $(M+H)^+$: 357.

El ejemplo 94 se prepara en un método análogo al procedimiento dado en el ejemplo 93.

EJEMPLO 94

4[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina

Se obtiene 4-[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina (12 mg, 5%) a partir de *N*-hidroxi-isonicotinamidina (200 mg, 1.4 mmoles) con cloruro de cloroacetilo (0.11 ml, 1.4 mmoles) y trietilamina (0.5 ml, 3.5 mmoles); el tratamiento acuoso produce el intermediario (150 mg, 0.7 mmoles); se trata con K_2CO_3 (292 mg, 2.1 mmoles), y 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (140 mg, 0.7 mmoles). La purificación se efectúa mediante cromatografía en gel de sílice y recristalización.

^{1}H RMN($CDCl_3$), δ (ppm): 8.76 (dd,2H), 7.89 (dd,2H), 7.53 (dd,1H), 7.48 (dd,1H), 7.18 (dd,1H), 4.71 (s,2H), 3.73 (s,3H).

LC-MS (M+H)+: 357.

EJEMPLO 95

2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-1-metil-1*H*-imidazo[4,5-b]piridina

Y

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1-metil-1*H*-imidazo[4,5-b]piridina

Se agrega THF (3 ml) a una mezcla de hidruro de sodio (60%, 8 mg, 0.2 mmoles) y 2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-imidazo-[4,5-b]piridina (24.6 mg, 0.072 mmoles) y la mezcla resultante se agita a 0°C durante 15 minutos aproximadamente. Se agrega yoduro de metilo (20 µL, 0.32 mmoles) la mezcla resultante se agita a 0°C durante 2h. La reacción se extingue mediante la adición de diclorometano (10 ml) y agua (2 ml). Después de agitar vigorosamente, los extractos orgánicos (10 ml, más 3x5 ml) se eluyen a través de una Columna de extracción Chem Elut (Varian, cat #1219-8002). La purificación utilizando cromatografía

de SPE (5 g de sílice) empleando 25/25/50 a 50/25/25 acetato de etilo / diclorometano / hexano permite obtener dos productos. El primer producto en eluir es 2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etil-sulfanil}-1-metil-1H-imidazo[4,5-b]piridina (6 mg, 23%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.46 (d, 1H), 7.72 (d, 1H), 7.62 (d, 1H), 7.55 (d,1H), 7.42 (t,1H), 7.14 (m, 2H), 5.67 (q, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 2.01 (d, 3H).

El segundo producto en eluir es 2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1-metil-1H-imidazo[4,5-b]piridina (12 mg, 47%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 7.69 (d, 1H), 7.60 (d, 1H), 7.55 (d, 1H), 7.41 (t, 1H), 7.13 (m, 1H), 4.90 (s, 2H), 3.87 (s, 3H), 3.70 (s, 3H).

Los ejemplos 96-97 se preparan en un método análogo al procedimiento dado en el ejemplo 95.

EJEMPLO 96

3-[1-metil-1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[1-metil-1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]-oxadiazol (13 mg, 47%) a partir de 3-(4-metil-5-tiofen-2-

il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (25.5 mg, 0.069 mmoles) con 60% de hidruro de sodio (37 mg, 0.92 mmoles) y yoduro de metilo (0.10 ml, 1.6 mmoles) en THF (3 ml) a temperatura ambiente durante 2 h. El producto se extrae con acetato de etilo y se purifica mediante SPE con 20-40% de acetato de etilo en diclorometano : hexano 1:1.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.48 (d, 1H), 7.42 (d, 1H), 7.36 (m, 2H), 7.13 (m, 1H), 3.50 (s, 3H), 2.35 (s, 3H), 1.95 (s, 6H).

EJEMPLO 97

3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]-oxadiazol (6.1 mg, 17%) a partir de 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (33.8 mg, 0.091 mmoles) con 60% de hidruro de sodio (17 mg, 0.42 mmoles) y yoduro de metilo (20 µL, 0.32 mmoles) en THF (2.5 ml) a temperatura ambiente durante 1 hora. El producto se extrae con diclorometano y se purifica mediante SPE 25-40% acetato de etilo en cloroformo : hexano 1:1.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (br s, 2H), 7.50 (d, 1H), 7.46 (d, 1H), 7.38 (m, 2H), 7.16 (m, 1H), 4.89 (q, 1H), 3.64 (s, 3H), 2.37 (s, 3H), 1.90 (d, 3H).

EJEMPLO 98

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol y 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]-oxadiazol

Se agrega diclorometano (2.5 ml) a una mezcla de ácido 3-cloro-bencencarboperoxóico (57-85%, 49.5 mg, 0.16-0.25 mmoles) y 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (45 mg, 0.12 mmoles) y la mezcla resultante se agita a temperatura ambiente durante la noche. La reacción se extingue mediante la adición de diclorometano (10 ml) e hidróxido de sodio 1M (3 ml). Después de agitar vigorosamente, los extractos orgánicos (10 ml, más 3x5 ml) se eluyen a través de una Columna de extracción Chem Elut (Varian, cat #1219-8002). La purificación se efectúa mediante cromatografía de SPE (5 g de sílice) utilizando 10-30% acetato de etilo en diclorometano : hexano 1:1 lo que permite obtener dos productos. El primer producto en eluir es 3-(4-metil-

5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol (12.3 mg, 25%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.63 (d, 1H), 7.56 (d, 1H), 7.36 (m, 2H), 7.24 (m, 1H), 5.12 (s, 2H), 3.94 (s, 3H), 2.36 (d, 3H).

El segundo producto en eluir es 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]oxadiazol (33.2 mg, 71%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (br s, 2H), 7.59 (d, 1H), 7.54 (d, 1H), 7.38 (m, 2H), 7.22 (m, 1H), 5.05 (dAB), 1H), 4.90 (dAB, 1H), 4.03 (s, 3H), 2.39 (d, 3H).

EJEMPLO 99

5-(3-furan-3-il-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Al compuesto 5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (50 mg, 0.10 mmoles) en un frasco se agrega ácido 3-furanborónico (17 mg, 0.16 mmoles), tetrakis-(trifenilfosfin)paladio(0) (6 mg, 0.0052 mmoles), éter dimetílico de etilenglicol (1 ml) y carbonato de sodio 2M (1 ml). El frasco se sella después y se calienta a 90°C durante 1 hora con agitación

vigorosa. La reacción se enfría, se diluye con acetato de etilo, se lava con agua y salmuera saturada, se filtra y se concentra. El residuo se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 70% en hexanos. La purificación adicional mediante trituración con una mezcla de éter dietílico y hexanos y después filtración permite obtener el compuesto del título como un sólido color beige, 25 mg (57%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.18 (s, 1H), 7.98 (d, 1H), 7.79 (s, 1H), 7.71 (d, 1H), 7.51 (m, 4H), 7.17 (m, 1H), 6.74 (s, 1H), 4.55 (s, 2H), 3.73 (s, 3H).

INTERMEDIARIOS

EJEMPLO 100

Acido pirimidin-4-carboxílico

Se somete a reflujo 3-metil-pirimidina (9.41 g, 100 mmoles), permanganato de potasio (26.9 g) y carbonato de sodio (10.6 g) en agua (100 ml) durante 72 h seguido por filtración a través de celita. El material filtrado se lava con varias porciones de DCM y EtOAc antes de acidular con HCl concentrado. El precipitado formado se recolecta y se lava con con agua para producir 1.37 g del compuesto del título

como un sólido de color blanco.

^{1}H RMN (DMSO-d6) δ (ppm): 13.94 (br. s, 1H), 9.37 (d, 1H), 9.07 (d, 1H), 8.01 (dd, 1H).

EJEMPLO 101

Acido 5-cloro-tiofen-3-carboxílico

Se someten a reflujo ácido tiofen-3-carboxílico (17.51 g, 136.6 mmoles) y 1-cloro-pirrolidin-2,5-diona (23.7 g) en ácido acético (200 ml) durante 4 h bajo argón antes de verter en agua (700 ml). La extracción repetida con varias porciones pequeñas de DCM, seguido por extracción por retroceso a partir de las fases orgánicas combinadas con varias porciones pequeñas de hidróxido de sodio acuoso 2 M, produce una solución acuosa alcalina combinada que se lava con DCM antes de acidular con HCl concentrado para precipitar el material crudo. Este precipitado se vuelve a cristalizar con agua para producir 14.98 g del compuesto del título como un sólido de color gris contaminado con aproximadamente 20% molar de un subproducto diclorado según se juzga a partir de MS y ^{1}H-RMN.

^{1}H RMN (DMSO-d_6) d (ppm): 8.15 (d, 1H), 7.37 (d, 1H).

EJEMPLO 102

Acido 3-metilsulfanil-benzoico

Se agrega yoduro de metilo (0.972 ml) a una mezcla de ácido 3-mercapto-benzoico (601 mg, 3.9 mmoles) y carbonato de potasio (2.7 g, 19.5 mmoles) en DMF (8 ml) en un baño de hielo. Después que la reacción se calienta hasta temperatura ambiente y se agita durante 1 hora, la mezcla de reacción se diluye con acetato de etilo, se lava con agua (3X), se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener el éster metílico del ácido 3-metilsulfanil-benzoico (684 mg, 96%, aceite de color amarillo).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.80 (d, 1H), 7.44 (d, 1H), 7.35 (t, 1H), 3.92 (s, 3H), 2.53 (s, 3H).

Se calienta el éster metílico del ácido 3-metilsulfanil-benzoico (684-mg, 3.8 mmoles) y NaOH 1N (5.6 ml, 5.6 mmoles) en metanol (8 ml) y THF (8 ml) a 70°C durante 1 hora. La mezcla de reacción se concentra y después se diluye el residuo con agua. Después de acidular con HCl 1N hasta pH 2 aproximadamente, la capa acuosa se extrae con

acetato de etilo y después se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener el ácido 3-metilsulfanil-benzoico (616 mg, 97%, sólido de color blanco).

^{1}H RMN (DMSO), δ (ppm): 13.1 (bs, 1H), 7.76 (s, 1H), 7.70 (d, 1H), 7.51 (d, 1H), 7.44 (t, 1H), 2.52 (s, 3H).

EJEMPLO 103

Acido 3-ciclopropil-benzoico

Se agrega dietil-zinc 1.0 M en hexanos (27.3 ml, 27.3 mmoles) a una solución de 2,4,6-triclorofenol (5.4g, 27.3 mmoles) en diclorometano (100 ml) a -40°C. Después de agitar durante 15 minutos, se agrega diyodo-metano (2.2 ml, 27.3 mmoles) a -40°C y se agita durante 15 minutos adicionales. Después se agrega 1-bromo-3-vinilbenceno (2.5 g, 13.7 mmoles) a la mezcla de reacción, se deja calentar hasta temperatura ambiente, y se deja bajo agitación durante la noche. La mezcla de reacción se diluye con diclorometano, se lava con HCl 1N (2X), bicarbonato de sodio saturado (2X), sulfito de sodio saturado, hidróxido

de sodio 1N, y salmuera saturada, se seca con sulfato de magnesio, se filtra y se concentra. El análisis con GC-MS revela que la mezcla de reacción contiene 1-bromo-3-ciclopropil-benceno y 1-bromo-3-vinilbenceno. Para eliminar el bromo-3-vinil-benceno, la mezcla cruda se hace reaccionar con permanganato de potasio. Se agrega, mediante goteo, una solución de permanganato de potasio/agua (1.5 g/20 ml) a una solución de la mezcla cruda (aproximadamente 3.5 g) en THF (40 ml) a 0°C y después se deja calentar hasta temperatura ambiente. Después de 1 hora, la reacción se diluye con éter dietílico, se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. La purificación mediante cromatografía de vaporización instantánea eluyendo con 100 hexanos permite obtener 1-bromo-3-ciclopropil-benceno (2.20g, 81%).

Se agrega, mediante goteo, n-butil-litio 1.6 M en hexanos (3.2 ml, 5.1 mmoles) a una solución de 1-bromo-3-ciclopropil-benceno a -78°C y se agita durante 1 hora. Esta mezcla de reacción se transfiere después mediante cánula a un matraz de fondo redondo de 250 ml equipado con una barra de agitación, lleno aproximadamente hasta 1/4 de su

capacidad con dióxido de carbono sólido y se agita durante 1 hora. La mezcla de reacción se concentra y después se diluye el residuo con agua. La capa acuosa se lava con diclorometano (3X), se acidula con HCl 1N hasta pH 2 aproximadamente, y se extrae con acetato de etilo. La fase orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener ácido 3-ciclopropil-benzoico (356 mg, 43%, sólido de color blanco).

^{1}H RMN (DMSO), δ (ppm): 12.90 (bs, 1H), 7.71 (d, 1H), 7.64 (s, 1H), 7.34 (m, 2H), 2.01 (m, 1H), 0.99 (m, 2H), 0.70 (m, 2H).

EJEMPLO 104

ácido 3-ter-butoxicarbonilamino-benzoico

A un matraz que contiene etil-3-amino-benzoato (1 g, 6.05 mmoles) se agrega dicarbonato de di-*ter*-butilo (3.16 g, 14.5 mmoles), trietilamina (500 mg, 4.94 mmoles), y THF (10 ml) y se deja agitar a 60°C durante dos horas y después durante la noche a temperatura ambiente. El THF se elimina al vacío, y el éster crudo se separa entre acetato de etilo y agua, se lava con salmuera saturada, se seca

con sulfato de sodio anhidro y el solvente se elimina al vacío. El producto se purifica después mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 15% en hexano para obtener 2g del éster etílico del ácido 3-ter-butoxicarbonilamino-benzoico (suspensión espesa de color blanco).

Al éster etílico del ácido 3-ter-butoxi-carbonilaminobenzoico crudo (aproximadamente 2.0g, 0.00754 mmoles) se agrega THF (15 ml), y LiOH 0.5M (15 ml). La mezcla se calienta durante dos horas a 75°C y el THF se elimina al vacío después de enfriar. El precipitado se filtra a partir de la mezcla remanente y el material filtrado se transfiere a un embudo de separación. La capa acuosa se lava con diclorometano (3x) y se acidula hasta pH 5 aproximadamente utilizando HCl 1M. El producto se extrae después con acetato de etilo, se lava con agua, salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. Se aíslan 730 mg del ácido 3-ter-butoxi-carbonilamino-benzoico (sólido de color blanco).

^{1}H RMN (DMSO-d6) δ (ppm): 9.58 (s, 1H), 8.16 (s, 1H), 7.63 (d, 1H), 7.54 (d, 1H), 7.37 (t, 1H), 1.49 (s, 9H).

EJEMPLO 105

Acido 3-acetil-benzoico

Se agrega hidróxido de sodio 6M (25 ml) a 3-acetilbenzonitrilo (850 mg, 5.82 mmoles) en metanol (25 ml) y después se calienta a 90°C durante la noche. Después de concentrar la mezcla de reacción, la capa acuosa se lava con diclorometano (2x), después se acidula el pH hasta 3 aproximadamente con HCl 12M. El precipitado se extrae con acetato de etilo después se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener ácido 3-etilbenzoico como un aceite incoloro; 0.800g (92%).

^{1}H RMN ($CDCl_3$) δ (ppm): 8.70 (s, 2H), 8.33 (d, 2H), 8.24 (d, 2H), 7.64 (t, 1H), 2.70 (s, 3H).

EJEMPLO 106

Hidrazida del ácido 2-metil-isonicotínico

Se agrega diclorometano (10 ml) a la sal clorhidrato del ácido 2-metilnicotínico (1.1 g, 6.34 mmoles) y se agrega lentamente cloruro de oxalilo (6.95ml, 13.9mmoles) bajo argón mientras el matraz se enfría en hielo. Se agrega dimetilformamida (2

gotas) y la reacción se deja agitando durante la noche, tiempo durante el cual ésta se calienta hasta temperatura ambiente. Se concentra la reacción y se agrega al matraz THF (10 ml) y éste se coloca en un baño de hielo. Se agrega metanol (5 ml) y se deja que la reacción se agite durante una hora. Se concentra la reacción y el residuo se separa entre $NaHCO_3$ (saturado) y EtOAc. El producto se extrae con EtOAc tres veces. Las capas orgánicas combinadas se lavan con salmuera, se secan con Na_2SO_4, se filtran y se concentran. La purificación se efectúa mediante tubo de extracción en fase sólida (EtOAc al 20%/hexanos) lo cual permite obtener el compuesto del título como un aceite claro.

^1H RMN $CDCl_3$ δ (ppm): 8.51 (d, 1H), 7.57 (d, 1H), 7.51 (d, 1H), 3.82 (s, 3H), 2.50 (s, 3H).

Se disuelve el éster metílico del ácido 2-metil-isonicotínico (316.5 mg, 2.093 mmoles) en MeOH (7 ml) bajo argón y se agrega monohidrato de hidrazina al 98% (1 ml, 20.93 mmoles). La reacción se deja agitando bajo argón a temperatura ambiente durante 18 horas. La reacción se concentra para obtener el compuesto del título (271.9 mg, 86%) como un sólido de color blanco.

^{1}H RMN $CDCl_3$ δ (ppm): 8.59 (d, 1H), 7.50 (s, 1H), 7.38 (d, 1H), 3.09 (br. s, 3H), 2.60 (s, 3H).

EJEMPLO 107

Hidrazida del ácido 5-cloro-2-fluoro-benzoico

Paso 1

Ester metílico del ácido 5-cloro-2-fluoro-benzoico:

Se agrega metanol (20 ml) a una solución de cloruro de 5-cloro-2-fluorobenzoilo (1.2 g, 6.2 mmoles) en diclorometano (10 ml) en un baño de hielo. La mezcla de reacción se calienta hasta temperatura ambiente, se agita durante 3 horas y después se concentra para obtener el éster metílico del ácido 5-cloro-2-fluoro-benzoico (1.17 g, 100%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.93 (m, 1H), 7.48 (m, 1H), 7.12 (m, 1H), 3.96 (s, 3H).

Paso 2

Hidrazida del ácido 5-cloro-2-fluoro-benzoico:

Se agita a temperatura ambiente durante la noche una mezcla de éster metílico del ácido 5-cloro-2-fluoro-benzoico (1.17 g, 6.2 mmoles) y monohidrato de hidrazina (0.451 ml, 9.3 mmoles) en etanol (20

ml). La mezcla de reacción se concentra y después se tritura el residuo con éter dietílico para obtener la hidrazida del ácido 5-cloro-2-fluoro-benzoico (497 mg, 42%, sólido de color blanco).

^{1}H RMN (DMSO), δ (ppm): 9.66 (bs, 1H), 7.58 (m, 2H), 7.36 (m, 1H), 4.58 (bs, 2H).

El ejemplo 108 se prepara en una forma análoga a la del ejemplo 107.

EJEMPLO 108

Hidrazida del ácido 3-ciano-benzoico

Se agita cloruro de 3-ciano-benzoilo (3g, 18.12 mmoles) en diclorometano (5 ml) y metanol (20 ml) a temperatura ambiente y durante la noche. El solvente se elimina utilizando un evaporador giratorio para obtener un sólido de color blanco (3.76 g).

^{1}H RMN (DMSO) δ (ppm): 8.33 (m, 1H), 8.24 (m, 1H), 8.14 (m, 1H), 7.76 (m, 1H), 3.89 (d, 3H).

Se agita una mezcla del éster metílico del ácido 3-ciano-benzoico (2 g, 12 mmoles) y monohidrato de hidrazina (0.60 ml, 12 mmoles) en etanol (10 ml) a temperatura ambiente durante la noche. La mezcla de

reacción se concentra y el residuo se tritura después con éter dietílico para obtener la hidrazida del ácido 3-ciano-benzoico (1.02 g, 51%, sólido de color rosa).

^{1}H RMN (DMSO) δ (ppm): 10.31 (s, 1H), 8.21 (m, 1H), 8.11 (m, 1H), 7.99 (m, 1H), 7.70 (m, 1H), 4.50 (s, 1H).

EJEMPLO 109

Hidrazida del ácido 2-cloro-isonicotínico

Se agregan HOBt (823 mg, 6.09 mmoles), y EDCI (1.2 g, 6.09 mmoles) a una suspensión del ácido 2-cloro-isonicotínico (800 mg, 5.08 mmoles) en acetonitrilo (10.3 ml) a temperatura ambiente. Después de dos horas se agrega mediante goteo, a 0°C, una solución de monohidrato de hidrazina (0.493 ml, 10.2 mmoles) en acetonitrilo (5.0 ml). Después de 30 minutos, se elimina el solvente utilizando un evaporador giratorio y el residuo se diluye con acetato de etilo, se extingue con agua, se seca con sulfato de sodio, se filtra y se concentra para obtener la hidrazida del ácido 2-cloro-isonicotínico (493 mg, 57%, sólido de color amarillo).

^{1}H RMN (DMSO) d (ppm): 10.21 (bs, 1H), 8.55

(d, 1H), 7.82 (s, 1H), 7.75 (d, 1H), 4.69 (bs, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 109:

Ejemplo No.	Nombre
110	Hidrazida del ácido 2-fluoro-5-metil-benzoico
111	Hidrazida del ácido pirimidin-4-carboxílico

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 6:

Ejemplo No.	Nombre
112	3-fluoro-N-hidroxi-benzamidina
113	N-hidroxi-tiofen-3-carboxamidina
114	2-cloro-N.-hidroxi-propionamidina
115	3,N-hidroxi-benzamidina
116	N-hidroxi-2-metil-benzamidina
117	N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina
118	3-cloro-N-hidroxi-benzamidina
119	N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina
120	2,5-difluoro-N-hidroxi-benzamidina

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 31:

Ejemplo No.	Nombre
121	4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-tiol
122	4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
123	4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol
124	4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
125	4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol
126	5-tiofen-2-il-4-tiofen-2-ilmetil-4H-[1,2,4]-triazol-3-tiol
127	4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
128	4-furan-2-ilmetil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol
129	4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol
130	4-etil-5-piridin-3-il-4H-[1,2,4]triazol-3-tiol
131	4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
132	4-furan-2-ilmetil-5-piridin-3-il-4H-[1,2,4]-triazol-3-tiol
133	4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-tiol
134	4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol
135	4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol
136	5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol
137	4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol
138	4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol
139	5-(2-cloro-6-metil-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol
140	5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]-triazol-3-tiol
141	4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol
142	4-etil-5-(tetrahidro-furan-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona
143	Ester metílico del ácido 4-etil-5-tioxo-4,5-dihidro-1H-[1,2,4]triazol-3-carboxílico

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 36:

Ejemplo No.	Nombre
144	5-(2-cloro-piridin-4-il)-4-etil-4H-[1,2,4]-triazol-3-tiol
145	5-(2-cloro-6-metoxi-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol
146	4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-tiol
147	4-propil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol
148	4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-tiol
149	4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-tiol
150	3-(5-mercapto-4-metil-4H-[1,2,4]triazol-3-il)-benzonitrilo
151	5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol
152	5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol
153	5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol
154	5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol
155	5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-tiol
156	5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]-triazol-3-tiol
157	5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-tiol
158	5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-tiol
159	4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-tiol
160	5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]-triazol-3-tiol
161	5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]-triazol-3-tiol
162	5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol
163	5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]-triazol-3-tiol
164	4-etil-5-pirimidin-5-il-2,4-dihidro-[1,2,4]-triazol-3-tiona

Ejemplo No.	Nombre
165	4-etil-5-furan-3-il-2,4-dihidro-[1,2,4]triazol-3-tiona
166	4-(tetrahidrofuran-2-ilmetil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
167	5-ciclopentil-4-etil-2,4-dihidro-[1,2,4]-triazol-3-tiona
168	4-etil-5-[2-(4-metoxi-fenil)-etil]-2,4-dihidro-[1,2,4]triazol-3-tiona

EJEMPLO 169

5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol

Se mezcla ácido 3,5-dicloro-benzoico (382 mg, 2 mmoles) con trietilamina (606 mg, 3 mmoles) en THF (6 ml) a 10°C. Después se agrega, mediante goteo, cloroformiato de isobutilo (300 mg, 2.2 mmoles) y se agita durante durante 45 minutos. A la mezcla de reacción se agrega 4-metil-3-tiosemicarbazida (238.4 mg, 2 mmoles). Después que se agita a temperatura ambiente durante 10 minutos, la mezcla de reacción se calienta a 70°C durante la noche. Tratamiento estándar. El producto se purifica mediante cromatografía en columna con acetato de etilo al 25-30% en hexanos para obtener 46.4 mg (8.5 %) de 5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol.

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 169:

Ejemplo No.	Nombre
170	5-(3-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol
171	5-(4-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol
172	4-etil-5-(3-nitrofenil)-4H-[1,2,4]triazol-3-tiol
173	5-(2,5-difluorofenil)-4-etil-4H-[1,2,4]-triazol-3-tiol
174	5-(3-clorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol
175	5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol

EJEMPLO 176

4-etil-5-metoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona

Paso 1

N-etil-2-(metoxiacetil)hidrazincarbotioamida:

Se mezclan ácido metoxiacético (360 mg, 3.99 mmol), 4-etil-3-tiosemicarbazida (581 mg, 4.87 mmol), diisopropilcarbodi-imida (615 mg, 4.87 mmol) e hidroxi-benzotriazol (69.6 mg, 0.51 mmol) en dimetilformamida (10 ml) y se agitan bajo argón a temperaturas ambientales durante 19 h. Después de evaporar hasta sequedad el producto crudo se utiliza directamente en el siguiente paso.

MS (ESI) m/z 192 (M+1).

Paso 2

4-etil-5-metoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona:

Se suspenden N-etil-2-(metoxiacetil)hidrazin-carbotioamida (760 mg de producto crudo, 4 mmol) y bicarbonato de sodio (560 mg, 6.6 mmol) en agua (15 ml) y se refluja durante 5 h. Después de enfriar y filtrar, el filtrado se acidula con ácido clorhídrico concentrado, seguido por extraction con acetato de etilo. Después de evaporar hasta sequedad el producto crudo se recristaliza con acetato de etilo/heptano. La filtración y recristalización de la solución madre permite obtener un rendimiento combinado de 325 mg (47%) del compuesto del título.

. ^{1}H RMN ($CDCl_3$), δ (ppm): 4.47 (s, 2H), 4.13 (q, 2H), 3.37 (s, 3H), 1.38 (t, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 176:

Ejemplo No.	Nombre
177	4-metil-5-piridin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
178	4-alil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
179	4-etil-5-(4-metoxi-fenoximetil)-2,4-dihidro-[1,2,4]triazol-3-tiona
180	4-etil-5-fenoximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona

Ejemplo No.	Nombre
181	4-etil-5-hidroximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona
182	4-etil-5-(2-metoxi-etil)-2,4-dihidro-[1,2,4]-triazol-3-tiona
183	4-etil-5-metilsulfanilmetil-2,4-dihidro-[1,2,4]triazol-3-tiona
184	5-etoximetil-4-etil-2,4-dihidro-[1,2,4]triazol-3-tiona
185	5-furan-3-il-4-metil-2,4-dihidro-[1,2,4]-triazol-3-tiona
186	4-metil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
187	4-etil-5-piridazin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
188	4-etil-5-piridin-4-ilmetil-2,4-dihidro-[1,2,4]-triazol-3-tiona
189	4-etil-5-(6-hidroxi-piridin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona
190	4-etil-5-(4-hidroxi-fenil)-2,4-dihidro-[1,2,4]triazol-3-tiona
191	4-etil-5-p-toliloximetil-2,4-dihidro-[1,2,4]triazol-3-tiona
192	4-etil-5-(6-metoxipiridin-3-il)-2,4-dihidro[1,2,4]triazol-3-tiona
193	4-etil-5-(2-metoxi-piridin-4-il)-2,4-dihidro-[1,2,4]triazol-3-tiona
194	4-etil-5-pirimidin-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
195	4-etil-5-(5-metoxi-pirimidin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona

EJEMPLO 196

4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol

Se agrega una solución de hidrazida de ácido fórmico (439 mg, 7.809 mmol) en piridina (20 ml) a una solución de 2-isotiocianatometil-furano (1 g, 7.185 mmol) en piridina (20ml). La reacción toma

lugar a temperatura ambiente durante la noche, y se agrega etanol (20 ml) directamente a la reacción y se coloca en una baño a 80C durante la noche. Se evapora el solvente y el compuesto del título (1.09 g, 83%) se obtiene a partir de la purificación mediante cromatografía de SPE en gel de sílice con 500 ml al 20%, 250 ml al 25%, 250 ml al 30%, 250 ml al 35%, 250 ml al 40%, y 250 ml al 50% de acetato de etilo en hexanos.

^{1}H RMN (CD_3OD), δ (ppm): 14.0 (bs, 1H), 8.19 (s, 1H), 7.52 (q, 1H), 6.52 (m, 1H), 6.42 (m, 1H), 4.90 (s, 2H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 196:

Ejemplo No.	Nombre
197	4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol
198	4-ciclopropilmetil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol

EJEMPLO 199

4-ciclopropil-5-tiofen-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona

A una suspensión hidrazida de ácido tiofen-2-carboxílico (866 mg, 6.09 mmoles) en iPrOH (25 ml)

se agrega isotiocianato-ciclopropano (602 mg, 6.08 mmoles). La mezcla se agita a 70°C durante 72 h y después se enfría hasta temperatura ambiente. Se filtra el precipitado de color blanco y se suspende en una mezcla de MeOH:H_2O (9:1, 40 ml) junto con NaOH acuoso (2%, 5 ml). La mezcla de reacción se agita a 70°C durante la noche y después se enfría hasta temperatura ambiente. El pH se ajusta a 4 aproximadamente con HCl acuoso (1N). El precipitado de color blanco se filtra, se lava con agua y se seca al vacío (829 mg, 61%).

^{1}H RMN (CD_3OD), δ (ppm): 7.67 (dd, 1H), 7.63 (dd, 1H), 7.17 (dd, 1H), 3.15 (m, 1H), 1.14 (m, 2H), 0.86 (m, 2H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 199:

Ejemplo No.	Nombre
200	5-furan-2-il-4-(2-metoxi-etil)-2,4-dihidro-[1,2,4]triazol-3-tiona
201	4-ciclopropil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
202	Ester metílico del ácido (3-tiofen-2-il-5-tioxo-1,5-dihidro-[1,2,4]triazol-4-il)-acético
203	4-ciclopropilmetil-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
204	4-(2-metoxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
205	Tiofen-2-il-4-(2,2,2-trifluoroetil)-2,4-dihidro-[1,2,4]triazol-3-tiona

Ejemplo No.	Nombre
206	4-ciclopropil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]triazol-3-tiona
207	4-ciclopropil-5-piridin-3-il-2,4-dihidro-[1,2,4]triazol-3-tiona

EJEMPLO 208

4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-tiol

A una solución de 4-etil-3-tiosemicarbazida(2.38 g, 20 mmoles) y trietilamina (6.06 g, 60 mmoles) en THF (30 ml), se agrega anhídrido trifluoroacético (5.04 g, 24 mmoles). La mezcla de reacción se agita a temperatura ambiente durante una hora y se calienta a 60°C durante la noche. Tratamiento estándar, el producto se tritura con hexanos para obtener 564g de 4-etil-5-trifluorometil-4H-[1,2,4]-triazol-3-tiol como un sólido de color café pálido.

^{1}H-RMN($CDCl_3$) d(ppm): 12.64 (w, 1H), 4.22 (q, 2H) y 1.44 (t, 3H).

EJEMPLO 209

4-etil-3-metansulfonil-5-tiofen-2-il-4H-[1,2,4]triazol

El compuesto del título se sintetiza de conformidad con el método descrito en Åkerblom et al.

J. Med. Chem. 16, 312 (1973). Se disuelve 4-etil-3-metilsulfanil-5-tiofen-2-il-4H-[1,2,4]triazol (1.14 g, 5.06 mmoles) en ácido acético glacial (20 ml) seguido por la adición de peróxido de hidrógeno al 30% (5 ml). Después de agitar a temperaturas ambientales durante 16 horas se agrega peróxido de hidrógeno al 30% adicional (5 ml). La mezcla se agita durante 3 h a temperatura ambiente, después se calienta a 100°C durante 2.5 h. Después de enfriar en un baño de hielo/agua la reacción se neutraliza con hidróxido de sodio y se extrae dos veces con diclorometano. Las capas orgánicas se combinan, se evaporan hasta sequedad y se secan al vacío para producir el compuesto del título (0.78 g, 60%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.60 (d, 1H), 7.56 (d, 1H), 7.22 (m, 1H), 4.51 (q, 2H), 3.58 (s, 3H), 1.55 (t, 3H).

El siguiente compuesto se prepara de manera análoga la del ejemplo 209:

Ejemplo No.	Nombre
210	4-(5-metansulfonil-4-metil-4H-[1,2,4]triazol-3-il)-piridina

EJEMPLO 211

4-(2-hidroxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona

A una suspensión de LAH (38.1 mg, 1.00 mmoles) en THF anhidro (8 ml) se agrega mediante goteo ácido (3-tiofen-2-il-5-tioxo-1,5-dihidro-[1,2,4]-triazol-4-il)-acético (101 mg, 0.42 mmoles) en THF anhidro (4 ml). La mezcla se hace reaccionar durante 2 h y después se extingue con Na_2SO_4 acuoso saturado (10 ml). El THF se elimina a presión reducida y el residuo se acidula con HCl acuoso (3N) y se divide entre EtOAc y agua. La capa acuosa se extrae con EtOAc (3 x 20 ml). Las capas orgánicas combinadas se lavan con salmuera (15 ml), se secan ($MgSO_4$) y se concentran a presión reducida. El producto crudo se utiliza sin purificación en el siguiente paso.

^1H RMN (DMSO-d6), δ (ppm): 13.94 (s, 1H), 7.86 (d, 1H); 7.81 (d, 1H), 7.24 (dd, 1H), 5.09 (t, 1H), 4.16 (t, 2H), 3.76 (app. q, 2H).

EJEMPLO 212

4-(4,5-dimetil-4H-[1,2,4]triazol-3-il)-piridina

Se agregan lentamente 860 µl (10 mmoles) de

cloruro de oxalilo a una solución de 731 mg (10 mmoles) de N-metil-acetamida y 2.33 ml (20 mmoles) de 2,6-lutidina en 20 ml de CH_2Cl_2 a 0°C. Después de 15 minutos se agregan en una porción 1.37 g (10 mmoles) de hidrazida del ácido isonicotínico. La mezcla resultante se agita a temperatura ambiente durante 1 hora y después se neutraliza con $NaHCO_3$(sat). Se separan las fases, y la fase acuosa se extrae con CH_2Cl_2. Las fases orgánicas combinadas se secan y se concentran. El residuo se disuelve en 20 ml de ácido acético y se calienta a 120°C durante 2h. Después de enfriar, se elimina el solvente. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 10:1) permite obtener 765 mg (44%) de un sólido de color gris/blanco.

^{1}H RMN ($CDCl_3$), d (ppm): 2.52 (s, 3 H) 3.66 (s, 3 H) 7.58 (d, 2 H) 8.76 (d, 2 H).

EJEMPLO 213

Metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-amina

Se calienta con microondas, durante 5 minutos a 160°C, una mezcla de 1000 mg (4.35 mmoles) de yodhidrato de N-amino-N',N"-dimetil-guanidina (Henry; Smith; J.Amer.Chem.Soc.; 73; 1951; 1858) y

774 mg (4.35 mmoles) de clorhidrato de cloruro de isonicotinoilo en 3 ml de piridina. Se agrega K_2CO_3 (saturado) y la mezcla se extrae 4 veces con $CHCl_3$. La fase orgánica se seca y se concentra. La recristalización con etanol, agua y EtOAc produce 216 mg (26%) de un sólido de color blanco-amarillento.

^1H RMN (DMSO), d (ppm): 2.85 (d, 3 H) 3.45 (s, 3 H) 6.25 (d, 1 H) 7.65 (m, 2 H) 8.67 (m, 2 H).

EJEMPLO 214

3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina

Se calienta a 120°C, durante la noche, una solución de 750 mg (3.1 mmoles) de yodhidrato de (1,4,5,6-tetrahidro-pirimidin-2-il)-hidrazina (ref. Krezel, Izabella; Pharmazie; EN; 49; 1; 1994; 27-31) y 552 mg (3.1 mmoles) clorhidrato de cloruro de isonicotinoilo en 3 ml de piridina. La mezcla de reacción se enfría y se diluye con K_2CO_3 (saturado) y se extrae con 3 x 10 ml de cloroformo. Los extractos orgánicos combinados se secan y se concentran. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 10:1) permite obtener 83 mg (18%) de un sólido de color blanco.

^{1}H RMN ($CDCl_3$), d (ppm): 1.91 (m, 2 H) 3.24 (m, 2 H) 4.13 (m, 2 H) 7.67 (m, 2 H) 8.65 (m, 2 H).

El siguiente compuesto se prepara de manera análoga a la del ejemplo 214:

Ejemplo No.	Nombre
215	3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]-triazolo[4,3-a]pirimidina

EJEMPLO 216

4-etil-5-(6-metoxi-piridazin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona

Paso 1

Acido 6-cloro-piridazin-3-carboxílico:

A una solución de 3-cloro-6-metil-piridazina (1.2 g, 9.3 mmoles) en H_2SO_4 (10 ml), se agrega, en porciones, dicromato de potasio (3.3 g, 11.2 mmoles). Después de la adición, la mezcla se agita a 50°C. La reacción se vierte en hielo y la mezcla se extrae tres veces con éter dietílico. Las fases orgánicas combinadas se secan y se concentran para obtener el compuesto del título (840 mg, 57%).

LC-MS (M++1): 159 y 161 (3:1).

Paso 2

éster metílico del ácido 6-cloro-piridazin-3-carboxílico:

Se somete a reflujo, durante 3 horas, una solución de ácido 6-cloro-piridazìn-3-carboxílico (700 mg, 4.53-mmoles) en cloruro de tionilo (15 ml). La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega metóxido de sodio (244 mg, 4.53 mmoles) en MeOH (20 ml) al residuo y la solución se continúa agitando a temperatura ambiente (t. amb.). Se agrega H_2O y la mezcla se extrae tres veces con DCM. Las fases orgánicas combinadas se secan y se concentran. La cromatografía de vaporización instantánea (SiO_2, heptano/EtOAc 1:1) permite obtener 560 mg (72%) del compuesto del título.

^1H RMN ($CDCl_3$), δ (ppm): 4.09 (s, 3 H), 7.69 (d, 1 H), 8.18 (d, 1 H).

LC-MS (M++1): 173 y 175 (3:1).

Paso 3

Ester metílico del ácido 6-metoxi-piridazin-3-carboxílico:

Se somete a reflujo una solución del éster metílico del ácido 6-cloro-piridazin-3-carboxílico en NaOMe en MeOH (1 M, 10 ml). Se agrega H_2O y la mezcla

se extrae tres veces con DCM para obtener la fase orgánica I. Las fases orgánicas combinadas I se secan y se concentran para obtener el compuesto del título (40 mg, 10%). La fase acuosa se acidula con ácido clorhídrico concentrado y se extrae tres veces con DCM para obtener la fase orgánica II. Las fases orgánicas combinadas II se secan y se concentran para obtener ácido 6-metoxi-piridazin-3-carboxílico (LC-MS (M++1): 155) (230 mg, 65%). Se somete a reflujo una solución del ácido 6-metoxi-piridazin-3-carboxílico en cloruro de tionilo (6 ml) durante 3 h. La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega MeOH (10 ml) al residuo y la solución se continúa agitando a temperatura ambiente. Se agrega $NaHCO_3$ (acuoso) saturado y la mezcla se extrae tres veces con DCM. Las fases orgánicas combinadas se secan y se concentran para obtener el compuesto del título (253 mg, 100%).

LC-MS (M++1): 169.

Paso 4

4-etil-5-(6-metoxi-piridazin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona:

Se agrega NaOMe (86 mg, 1.6 mmoles) a una solución del éster metílico del ácido 6-metoxi-

piridazin-3-carboxílico (210 mg, 1.25 mmoles) y 4-etil-3-tiosemicarbazida (190 mg, 1.6 mmoles) en MeOH (6 ml) y la mezcla se calienta hasta 70°C a 72 h. La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega H_2O (10 ml) al residuo y la mezcla se acidula con ácido clorhídrico concentrado y el compuesto del título, 35 mg (12%), se recolecta mediante filtración.

LC-MS (M++1): 238.

EJEMPLO 217

4-etil-5-(5-metoxi-piridin-2-il)-2,4-dihidro-[1,2,4]-triazol-3-tiona

Paso 1

Ester metílico del ácido 5-metoxi-piridin-2-carboxílico:

Se disuelve 5-metoxi-2-metil-piridina (700 mg, 5.69 mmoles) en H_2O (20 ml) y se calienta a 80°C. Se agrega $KMnO_4$ (4 g, 25.3 mmoles) en porciones, a la solución en el transcurso de 1 hora. Después de agitar a 80°C durante 5 h se filtra la mezcla y el filtrado se lava con H_2O (60°C). Se concentra la fase acuosa combinada. Se agregan DMF (20 ml), K_2CO_3 (785 mg, 5.7 mmoles) seguido por MeI (540 ml, 8.6 mmoles)

al residuo remanente y la mezcla se calienta a 80°C. La reacción se enfría hasta temperatura ambiente y se agrega H_2O y la mezcla se extrae tres veces con tolueno. Las fases orgánicas combinadas se secan y se concentran. La cromatografía de vaporización instantánea (SiO_2, heptano/EtOAc 1:1) permite obtener 210 mg (22%) del compuesto del título.

^1H RMN (CDCl3):d ppm 3.93 (s, 3 H) 4.00 (s, 3 H) 7.23 (m, 1 H) 8.13 (d, 1 H) 8.40 (d, 1 H).

Paso 2

4-etil-5-(5-metoxi-piridin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona:

Se agrega NaOMe (4 ml, 4.0 mmol, 1M) a una solución de éster metílico del ácido 5-metoxi-piridin-2-carboxílico (200 mg, 1.2 mmoles), 4-etil-3-tiosemicarbazida (145 mg, 1.2 mmoles) en MeOH (10 ml) y la mezcla se calienta a 70°C. La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega H_2O (10 ml) al residuo y la mezcla se acidula con ácido clorhídrico concentrado y el compuesto del título 50 mg (18%) se recolecta mediante filtración.

LC-MS (M++1): 237.

Los siguientes compuestos se preparan en forma análoga a la del ejempo 10:

Ejemplo No.	Nombre
218	5-clorometil-3-fenil-[1,2,4]oxadiazol
219	5-clorometil-3-(3-fluoro-fenil)-[1,2,4]-oxadiazol
220	5-clorometil-3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol
221	5-clorometil-3-tiofen-2-il-[1,2,4]oxadiazol
222	5-clorometil-3-tiofen-3-il-[1,2,4]oxadiazol
223	3-(5-clorometil-[1,2,4]oxadiazol-3-il)-fenol
224	5-clorometil-3-o-tolil-[1,2,4]oxadiazol
225	5-clorometil-3-(3-clorofenil)-[1,2,4]oxadiazol
226	5-clorometil-3-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 16:

Ejemplo No.	Nombre
227	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo
228	2-cloro-4-(3-clorometil-[1,2,4]oxadiazol-5-il)-piridina
229	3-clorometil-5-(2,5-dimetil-fenil)-[1,2,4]-oxadiazol
230	3-clorometil-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol
231	3-clorometil-5-(2,5-diclorofenil)-[1,2,4]-oxadiazol
232	3-clorometil-5-(2-fluoro-5-bromo-fenil)-[1,2,4]oxadiazol
233	3-clorometil-5-(3-metil-fenil)-[1,2,4]oxadiazol

Ejemplo No.	Nombre
234	3-clorometil-5-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol
235	3-clorometil-5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol
236	3-clorometil-5-(3-ciclopropil-fenil)-[1,2,4]-oxadiazol
237	Ester metílico del ácido 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-carbámico
238	1-[3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-etanona
239	5-(5-cloro-2-fluoro-fenil)-3-clorometil-[1,2,4]oxadiazol
240	2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-fenol

EJEMPLO 241

3-clorometil-5-(2-cloro-5-metil-fenil)-[1,2,4]-oxadiazol

Se trata ácido 2-cloro-5-metil-benzoico (1 g, 5.8 mmoles) con 5 ml cloruro de tionilo a reflujo durante dos horas. Se elimina el exceso de cloruro de tionilo a presión reducida. El residuo se agrega a una suspensión de 2-cloro-N-hidroxi-acetamidina (638 mg, 5.8 mmoles) en diclorometano (10 ml) a temperatura ambiente. Después de agitar durante 30 minutos, se agrega trietilamina (2.04 ml, 14.6 mmoles) y se agita durante una hora adicional. La mezcla de reacción se diluye con acetato de etilo, se lava con agua y salmuera, se seca con sulfato de

sodio anhidro, se filtra y se concentra. La cromatografía de vaporización instantánea en columna utilizando acetato de etilo al 10-20% en hexanos permite obtener 460 mg del intermediario éster acíclico. Se agrega DMF a este intermediario y después se calienta hasta 135°C durante 4 h para efectuar la ciclización hasta oxadiazol. Después de enfriar la mezcla de reacción se lava con agua (3 veces) y salmuera, se seca con sulfato de sodio anhidro, se filtra, y se concentra. La purificación mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo al 5% en hexanos permite obtener el compuesto del título 160 mg (12% en los 2 pasos) como un sólido de color blanco.

m/z 244 (GCMS).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 241:

Ejemplo No.	Nombre
242	3-clorometil-5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadiazol
243	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo
244	3-clorometil-5-(3-fluoro-fenil)-[1,2,4]-oxadiazol
245	3-clorometil-5-(2-metil-tiazol-4-il)-[1,2,4]-oxadiazol

Ejemplo No.	Nombre
246	3-clorometil-5-(4-fluoro-fenil)-[1,2,4]-oxadiazol
247	5-(5-bromo-2-fluoro-fenil)-3-clorometil-[1,2,4]oxadiazol
248	3-clorometil-5-(4-metil-tiofen-2-il)-[1,2,4]-oxadiazol
249	5-(3-clorometil-[1,2,4]oxadiazol-5-il)-tiofen-3-carbonitrilo
250	2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-benzonitrilo
251	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-fluoro-benzonitrilo
252	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-fluoro-benzonitrilo
253	4-cloro-2-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenol
254	3-(1-cloro-etil)-5-(3-clorofenil)-[1,2,4]-oxadiazol
255	3-(1-cloro-etil)-5-(3-fluoro-fenil)-[1,2,4]-oxadiazol
256	3-(1-cloro-etil)-5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol

EJEMPLO 257

[3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-metanol

Se disuelven ácido 3-hidroximetilbenzoico, descrito en Reed, G. A.; Dimmel, D.R.; Malcolm, E. W. J. Org. Chem. 1993, 58 (23), 6372-6376, (175 mg, 1.15 mmoles), 2-cloro-N-hidroxi-acetamidina (125 mg, 1.15 mmoles) y HBTU en DMF anhidra (4 ml). Se agrega trietilamina (0.48 ml, 3.5 mmoles) y la reacción se agita a temperatura ambiente durante la noche. El

producto crudo se separa entre diclorometano y $NaHCO_3$ (acuoso), la fase orgánica se seca ($MgSO_4$) y el diclorometano se elimina al vacío. La solución en DMF resultante se calienta a 120°C durante la noche. La mezcla de reacción se concentra al vacío y el compuesto del título (64 mg, 25%) se aísla mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 25-50% en heptano.

^1H RMN ($CDCl_3$), δ (ppm): 8.15 (s, 1H), 8.06 (d, 1H), 7.62 (d, 1H), 7.53 (t, 1H); 4.80 (d, 2H), 4.66 (s, 1H); 1.99 (br. t, 1H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 257:

Ejemplo No.	Nombre
258	3-clorometil-5-[1-(toluen-4-sulfonil)-1H-pirrol-3-il]-[1,2,4]oxadiazol
259	3-clorometil-5-furan-3-il-[1,2,4]oxadiazol
260	3-clorometil-5-(5-cloro-tiofen-2-il)-[1,2,4]-oxadiazol

EJEMPLO 261

1-[5-(3-clorofenil)-[1,3,4] oxadiazol-2-il]-etanol

Paso 1

1-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-

il]-etoxi}-1H-benzotriazol:

Se disuelven 2-(1-cloro-etil)-5-(3-cloro-fenil)-[1,3,4]oxadiazol (109 mg, 0.45 mmoles), hidroxibenzotriazol (76.4 mg, 0.56 mmoles) y yoduro de potasio (23.0 mg, 0.14 mmoles) en DMF (2.5 ml), seguido por la adición de carbonato de potasio (74.0 mg, 0.53 mmoles). Después de agitar bajo argón a temperaturas ambientales durante 24 h la mezcla de reacción se diluye con acetato de etilo y se lava con solución de cloruro de amonio 2N. Después de volver a extraer la capa acuosa con acetato de etilo, las capas orgánicas combinadas se lavan con salmuera y se evaporan hasta sequedad. La cromatografía en columna en 12 g de sílice utilizando heptano / acetato de etilo = 4/1 permite obtener, después de secar al vacío, el compuesto del título (129 mg, 84%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.94 (d, 1 H), 7.82 (m, 1 H), 7.76 (m, 1 H), 7.46 (m, 1 H), 7.39-7.27 (m, 4 H), 5.98 (q, 1 H), 2.04 (d, 3 H).

Paso 2

1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etanol:

Se disuelve, bajo argón 1-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etoxi)-1H-benzotriazol

(58.4 mg, 0.17 mmoles) en THF seco (3 ml). A esta mezcla se agrega lentamente una solución 0.1 molar de diyoduro de samario en THF (5 ml, 0.5 mmoles) en el transcurso de 20 minutos. Después de agitar durante 80 minutos se agrega solución adicional de diyoduro de samario (4 ml, 0.4 mmoles) durante 5 minutos. La mezcla de reacción se extingue, después de 15 minutos adicionales de agitación, con $Na_2S_2O_3$ acuoso, se diluye con éter dietílico y se lava con ácido clorhídrico acuoso 1M, se seca con sulfato de sodio y se evapora hasta sequedad. Después de secar al vacío se obtiene el compuesto del título crudo (36.0 mg, 92%) el cual se utiliza en el siguiente paso sin purificación adicional.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.98-7.75 (m, 2 H), 7.50-7.38 (m, 2 H), 5.25 (q, 1 H), 1.74 (d, 3 H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 261:

Ejemplo No.	Nombre
262	[5-(5-cloro-2-fluoro-fenil)-[1,2,4]-oxadiazol-3-il]-metanol

EJEMPLO 263

1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etanol

A una solución de 3.19 g (30.6 mmoles) de 2,N-dihidroxi-propionamidina en 25 ml de piridina se agregan 4.3 ml (33.7 mmoles) de cloruro de 3-cloro-benzoilo a 0°C. Se retira el enfriamiento y la mezcla se agita a temperatura ambiente durante 25 minutos y a reflujo durante 25 minutos. Después de enfriar, la mezcla se vierte en agua y se extrae dos veces con CH_2Cl_2. La fase orgánica se seca y se concentra. La recristalización con heptano/EtOAc permite obtener 4.12 g (60%) de un sólido de color blanco.

^1H RMN ($CDCl_3$), d (ppm): 1.68 (d, 3 H) 2.67 (m, 1 H) 5.09 (m, 1 H) 7.46 (t, 1 H) 7.56 (d, 1 H) 8.01 (d, 1 H) 8.13 (s, 1 H).

EJEMPLO 264

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanol

Paso 1

N-{4-[(Z)-{[5-(3-clorofenil)-1,2,4-oxadiazol-3-il]metilen}(óxido)amino]fenil}-N,N-dimetilamina:

El compuesto del título se sintetiza de

conformidad con el método descrito en Palazzo et al. J. Heterocycl. Chem. (1979) 16:1469. Se disuelve cloruro de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metil]-piridinio (1.81 g, 5.87 mmoles) en agua (20 ml). A esta solución se agrega 4-nitroso-N,N-dimetilanilina (0.88 g, 5.86 mmoles) disuelta en etanol (50 ml), seguido por la adición lenta de hidróxido de sodio acuoso 1 molar (5.9 ml, 5.9 mmoles) en el transcurso de un intervalo de 3 minutos. Después de 1 hora, se filtra el precipitado formado, se lava con agua y se seca al aire para obtener el compuesto del título (2.08 g, húmedo) el cual se utiliza inmediatamente en el siguiente paso.

MS (ESI) m/z 344 (M+1).

Paso 2

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanodiol:

Se suspende N-{4-[(Z)-{[5-(3-clorofenil)-1,2,4-oxadiazol-3-il]metilen)(óxido)amino]fenil}-N,N-dimetilamina (2.08 g húmedo) en éter dietílico (30 ml), seguido por la adición de ácido clorhídrico acuoso 1 molar. La mezcla se agita vigorosamente durante 20 minutos, se transfiere a un embudo de separación y se diluye con éter dietílico y ácido

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clorhídrico acuoso 1 molar. Después de la extracción, la capa acuosa se extrae dos veces más con éter dietílico. La combinación de las capas orgánicas, secado con sulfato de magnesio, seguido por evaporación hasta sequedad y secado al vacío permite obtener el compuesto del título como producto crudo (0.56 g, 42% a partir de cloruro de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piridinio).

MS (ESI) m/z 227 (M+1).

Paso 3

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanol:

Se disuelve cloruro de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piridinio (99.3 mg, 0.44 mmoles) en metanol (4 ml) seguido por la adición de borohidruro de sodio (32 mg, 0.84 mmoles). Se agrega más borohidruro de sodio después de 2 horas y se deja que la reacción proceda durante la noche. La mezcla de reacción se diluye con diclorometano y cloruro de amonio acuoso y se agita vigorosamente. Después de separar las capas y lavar la capa orgánica con salmuera, seguido por evaporación hasta sequedad, se obtiene el producto crudo. Este se purifica mediante cromatografía de vaporización instantánea utilizando

heptano/acetato de etilo lo cual produce el compuesto del título (32.0 mg, 32%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.11 (s, 1H), 8.00 (d aparente, 1H), 7.56 (d aparente, 1H), 7.46 (t aparente, 1H), 4.87 (d, 2H), 2.91 (t, 1H).

EJEMPLO 265

2-clorometil-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol

Se calientan hidrazida de ácido 2-fluoro-5-metil-benzoico (320 mg, 1.9 mmoles) y 2-cloro-1,1,1-trietoxi-etano (1.9 ml) en un frasco sellado a 120°C durante 30 minutos. La mezcla de reacción se coloca directamente en una columna de vaporización instantánea (gel de sílice) y se purifica utilizando acetato de etilo al 0-5% en hexanos para obtener 2-clorometil-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol (284.5 mg, 66%).

^{1}H RMN ($CDCl_3$) d (ppm): 7.89 (q, 1H), 7.36 (m, 1H), 7.16 (t, 1H), 4.81 (s, 2H), 2.43 (s, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 265:

Ejemplo No.	Nombre
266	2-clorometil-5-(3-clorofenil)-[1,3,4]-oxadiazol
267	4-(5-clorometil-[1,3,4]oxadiazol-2-il)-2-metil-piridina
268	2-clorometil-5-m-tolil-[1,3,4]oxadiazol
269	3-(5-clorometil-[1,3,4]oxadiazol-2-il)-benzonitrilo
270	2-cloro-4-(5-clorometil-[1,3,4]oxadiazol-2-il)-piridina
271	2-(5-cloro-2-fluoro-fenil)-5-clorometil-[1,3,4]oxadiazol

EJEMPLO 272

2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]oxadiazol

Se calientan hidrazida de ácido 3-cloro-benzoico (170 mg, 1 mmoles) y 2-bromo-1,1,1-trietoxi-propano (1 ml) en un frasco sellado a 120°C durante 10 minutos. La mezcla de reacción se coloca directamente en una columna de vaporización instantánea (gel de sílice) y se purifica utilizando diclorometano al 0-5% en hexanos. El producto se vuelve a purificar mediante cromatografía de vaporización instantánea utilizando una mezcla de acetato de etilo:hexanos:diclorometano (1:19:20) para obtener 2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol (93 mg, 32%, aceite incoloro).

^{1}H RMN ($CDCl_3$) d (ppm): 8.09 (t, 1H), 7.99

(t, 1H), 7.55 (m, 3H), 5.30 (m, 1H), 2.21 (q, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 272:

Ejemplo No.	Nombre
273	2-(1-bromo-etil)-5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol
274	4-[5-(1-bromo-etil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina
275	2-(1-bromo-etil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol
276	2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol

EJEMPLO 277

3-(1-bromo-etil)-5-(3-clorofenil)-[1,2,4]oxadiazol

Se agrega mediante goteo una solución de 396 mg (2.22 mmoles) de N-bromosuccinimida en 2 ml de THF a una solución de 583 mg (2.22 mmoles) de trifenilfosfina en 2 ml de THF a 0°C. Después de agitar durante 20 minutos, se agregan 416 mg (1.85 mmoles) de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etanol en 2 ml de THF. Se continúa agitando durante la noche a temperatura ambiente antes de eliminar el solvente a presión reducida. La cromatografía de vaporización instantánea (heptano/EtOAc 6:1) permite obtener 168 mg (32%).

^{1}H RMN ($CDCl_3$), d (ppm): 2.12 (d, 3 H) 5.21 (q, 1 H) 7.47 (t, 1 H) 7.57 (m, 1 H) 8.03 (d, 1 H) 8.15 (s, 1 H).

EJEMPLO 278

1-[5-(3-clorofenil)-isoxazol-3-il]-etanol

Paso 1

Ester etílico del ácido 4-(3-clorofenil)-2,4-dioxo-butírico:

Se agrega en porciones, hidruro de sodio (dispersión en aceite al 60%, 1.24 g, 31.1 mmoles) a una solución de 3-cloroacetofenona (4.0 g, 25.9 mmoles) y oxalato de dietilo (4.54 g, 31.1 mmoles) en DMF (32 ml) a 0°C. La mezcla se agita a temperatura ambiente durante 1 hora y después se calientan hasta 80°C durante media hora. Después de enfriar, la mezcla se trata con HCl 3N y después se diluye con acetato de etilo. La capa orgánica se lava con agua (3X) y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. El residuo resultante se purifica después mediante cromatografía de vaporización instantánea en sílice utilizando acetato de etilo al 0-10% en hexanos para obtener el éster etílico del ácido 4-(3-clorofenil)-2,4-dioxo-

butírico (4.43g, 67%, sólido de color amarillo).

^{1}H RMN ($CDCl_3$) d (ppm): 15.12 (br s, 1H), 7.98 (s, 1H), 7.88 (d, 1H), 7.58 (d, 1H), 7.47 (t, 1H), 7.05 (s, 1H), 4.39 (m, 2H), 1.41 (m, 3H).

Paso 2

Ester etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico:

Se calienta a 80°C, durante 4 horas, una solución de éster etílico del ácido 4-(3-clorofenil)-2,4-dioxo-butírico (3.0 g, 11.8 mmoles) y clorhidrato de hidroxilamina (2.46 g, 35.4 mmoles) en metanol (60 ml). Después de enfriar, la mezcla se filtra y se lava con metanol frío para obtener el éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (2.0 g, 71 %, sólido de color blanco).

^{1}H RMN ($CDCl_3$) d (ppm): 7.82 (s, 1H), 7.72 (m, 1H), 7.47 (m, 2H), 4.03 (s, 3H). Mezcla de ambos ésteres metílico y etílico (principalmente metílico).

Paso 3

1-[5-(3-clorofenil)-isoxazol-3-il]-etanona:

En un frasco con capa roscada equipado con barra de agitación, se agrega yoduro de metilmagnesio (3M en éter dietílico) (0.79 ml, 2.38 mmoles),

tolueno (1 ml), tetrahidrofurano (0.39 ml, 4.77 mmoles) y trietilamina (1 ml, 7.15 mmoles). La solución se enfría hasta 0°C y a ésta se agrega solución de el éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (300 mg, 1.19 mmoles) en tolueno (5 ml). La mezcla resultante se deja agitando a 0°C durante 5 horas. La mezcla de reacción se extingue ácido clorhídrico 1N (acuoso, 6.5 ml, 6.5 mmoles), se diluye con tolueno (35 ml), se lava en forma secuencial con agua (50 ml), bicarbonato de sodio saturado (acuoso, 30 ml), agua (50 ml) y salmuera (30 ml). La fase orgánica se concentra al vacío. El residuo aislado se disuelve en metanol (8 ml) e hidróxido de potasio al 20% (acuoso, 1 ml). La mezcla se agita a 45°C durante 30 minutos. En este punto la mezcla se concentra al vacío. El residuo aislado se disuelve en tolueno (60 ml), se lava en forma secuencial con agua (50 ml), bicarbonato de sodio saturado (acuoso, 50 ml) y agua (50 ml). La fase orgánica se concentra al vacío. El residuo crudo se purifica en gel de sílice utilizando acetato de etilo al 2% en hexanos para aislar el compuesto deseado como un sólido de color blanco (156 mg, 60%).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.77 (m, 1H), 7.66

(m, 1H), 7.42 (m, 2H), 6.90 (s, 1H), 2.69 (s, 3H).

Paso 4

1-[5-(3-clorofenil)-isoxazol-3-il]-etanol:

En un frasco con tapa roscada equipado con barra de agitación se agrega 1-[5-(3-clorofenil)-isoxazol-3-il]-etanona (100 mg, 0.45 mmoles), borohidruro de sodio (34 mg, 0.90 mmoles) y metanol (3 ml). La mezcla resultante se deja agitando a temperatura ambiente durante 3 horas. La reacción se extingue con agua (30 ml) y salmuera (30 ml), se extrae con diclorometano (3 X 30 ml). La fase orgánica combinada se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar 1-[5-(3-clorofenil)-isoxazol-3-il]-etanol como un sólido de color blanco (110 mg).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.69 (m, 1H), 7.59 (m, 1H), 7.37 (m, 2H), 6.59 (s, 1H), 5.07 (q, 1H), 3.45 (bs, 1H), 1.58 (d, 3H).

El siguiente compuesto se prepara de manera análoga a la del ejemplo 278:

Ejemplo No.	Nombre
279	1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etanol

Los siguientes compuestos se preparan en forma análoga a la del éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (paso 2 en la síntesis del ejemplo 279):

Ejemplo No.	Nombre
280	Ester metílico del ácido 5-(2-fluoro-5-metil-fenil)-isoxazol-3-carboxílico
281	Ester metílico del ácido 5-tiofen-3-il-isoxazol-3-carboxílico
282	Ester metílico del ácido 5-fenil-isoxazol-3-carboxílico
283	Ester etílico del ácido 5-(3-clorofenil)-4-metil-isoxazol-3-carboxílico
284	Ester metílico del ácido 5-(5-cloro-tiofen-3-il)-isoxazol-3-carboxílico

EJEMPLO 285

[5-(3-clorofenil)-isoxazol-3-il]-metanol

Se agrega lentamente hidruro de litio y aluminio (320 mg, 8.4 mmoles) a una solución de éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (2.0 g, 8.4) en THF (100 ml) a temperatura ambiente. Después de 1 hora, la mezcla de reacción se extingue con agua y después se extrae con acetato de etilo. La capa orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra. El residuo resultante se purifica después mediante cromatografía

de vaporización instantánea utilizando acetato de etilo al 15-40% en hexano para obtener [5-(3-clorofenil)-isoxazol-3-il]-metanol (1.32g, 75%, sólido de color amarillo).

^{1}H RMN ($CDCl_3$) d (ppm): 7.78 (s, 1H), 7.68 (m, 1H), 7.43 (m, 2H), 6.63 (s, 1H), 4.84 (d, 2H), 2.23 (t, 1H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 285:

Ejemplo No.	Nombre
286	[2-(3-clorofenil)-oxazol-4-il]-metanol
287	[3-(3-clorofenil)-isoxazol-5-il]-metanol
288	5-(tiofen-3-il-isoxazol-3-il)metanol
289	[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-metanol
290	(5-fenil-isoxazol-3-il)-metanol
291	[5-(3-clorofenil)-4-metil-isoxazol-3-il]-metanol
292	[5-(5-cloro-tiofen-3-il)-isoxazol-3-il)]-metanol

EJEMPLO 293

Ester 1-[5-(3-clorofenil)-isoxazol-3-il]-etílico del ácido metansulfónico

En un frasco con tapa roscada equipado con

barra de agitación se agrega 1-[5-(3-clorofenil)-isoxazol-3-il]-etanol (110 mg, 0.49 mmoles), diclorometano (3 ml) y trietilamina (0.34 ml, 2.46 mmoles). La mezcla se enfría hasta 0°C y a ésta se agrega cloruro de metansulfonilo (0.08 ml, 0.98 mmoles). La mezcla de reacción se deja agitando a temperatura ambiente durante 30 minutos. La reacción se extingue con bicarbonato de sodio saturado (acuoso, 40 ml) y se extrae con diclorometano (3X30 ml). La fase orgánica combinada se lava con salmuera (40 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar el compuesto deseado como un aceite de color café.

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 293:

Ejemplo No.	Nombre
294	Ester 2-(3-clorofenil)-oxazol-4-ilmetílico del ácido metansulfónico
295	Ester 3-(3-clorofenil)-isoazol-5-ilmetílico del ácido metansulfónico
296	Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetílico del ácido metansulfónico
297	Ester -fenil)-isoxazol-5-il]-etílico del ácido metansulfónico
298	Ester 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetílico del ácido metansulfónico
299	Ester 5-(3-clorofenil)-isoxazol-3-ilmetílico del ácido metansulfónico
300	Ester 5-tiofen-3-il-isoxazol-3-ilmetílico del ácido metansulfónico

Ejemplo No.	Nombre
301	Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetílico del ácido metansulfónico
302	Ester 5-fenil-isoxazol-3-ilmetílico del ácido metansulfónico
303	Ester 5-(3-clorofenil)-4-metil-isoxazol-3-ilmetílico del ácido metansulfónico
304	Ester 5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetílico del ácido metansulfónico
305	Ester 1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico
306	Ester 1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico

EJEMPLO 307

Ester 4-cloro-5-(3-clorofenil)-isoxazol-3-ilmetílico del ácido metansulfónico

Se agrega cloruro de sulfurilo (1 ml) se al éster 5-(3-clorofenil)-isoxazol-3-ilmetílico del ácido metansulfónico (200 mg, 0.70 mmoles) y después se agita a 60°C durante la noche. La mezcla de reacción se diluye con diclorometano, se lava con bicarbonato de sodio saturado, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener éster 4-cloro-5-(3-clorofenil)-isoxazol-3-ilmetílico del ácido metansulfónico (219 mg„ 97%, sólido de color café claro).

^{1}H RMN ($CDCl_3$) d (ppm): 8.07 (m, 1H), 7.92 (m, 1H), 7.50 (m, 2H), 5.38 (s, 2H), 3.16 (s, 3H).

EJEMPLO 308

Ester metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico

Paso 1

3-cloro-N-hidroxi-benzamidina:

Se agrega una solución de 3-clorobenzaldehído (3.35 ml, 0.030 mmoles) en etanol (40 ml) a una solución de clorhidrato de hidroxilamina (2.47 g, 0.036 mmoles) e hidróxido de sodio (1.42 g, 0.036) en agua (20 ml) a temperatura ambiente y después se calienta a 90°C durante 24 horas. Después de enfriar, se concentra la mezcla de reacción, el residuo se diluye con agua y después el precipitado se filtra y se seca para obtener 3-cloro-N-hidroxi-benzamidina (1.13 g, 93 %).

^{1}H RMN ($CDCl_3$) d (ppm): 8.11 (s, 1H), 7.72 (s, 1H), 7.61 (m, 1H), 7.46 (m, 1H), 7.36 (m, 1H).

Paso 2

Cloruro de 3-cloro-N-hidroxi-benzimidoilo:

Se agrega N-clorosuccinimida (858 mg, 6.4 mmoles) a una solución de 3-cloro-N-hidroxi-benzamidina (1 g, 6.4 mmoles) a temperatura ambiente y se agita durante 1 hora. La mezcla de reacción se

diluye con éter dietílico y después se lava con agua (3X), se seca con sulfato de magnesio anhidro, se filtra, y se concentra para obtener el compuesto del título (1.13 g, 93 %). 1H RMN (CDCl3) d (ppm): 8.03 (s, 1H), 7.87 (m, 1H), 7.76 (m, 1H), 7.43 (m,1H).

Paso 3

Ester metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico:

Se agrega mediante goteo trietilamina (0.73 ml, 5.3 mmoles) a una solución de cloruro de 3-cloro-N-hidroxi-bencimidoilo (1.0 g, 5.3 mmoles) y propiolato de metilo (2.2 ml, 25.3 mmoles) en un baño de hielo. La mezcla de reacción se calienta hasta temperatura ambiente y se deja en agitación durante la noche. Después de diluir la reacción con diclorometano, la capa orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra. La purificación mediante cromatografía de vaporización instantánea eluyendo con hexanos al 50% en acetato de etilo y después la recristalización con metanol permite obtener el éster metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico (635 mg, 51%, sólido de color blanco).

^{1}H RMN ($CDCl_3$) d (ppm): 7.86 (m, 1H), 7.74 (m, 1H), 7.46 (2H), 7.2 (s, 1H), 4.05 (s, 3H).

EJEMPLO 309

2-bromometil-5-(3-clorofenil)-oxazol

Paso 1

5-(3-clorofenil)-2-metil-oxazol:

A una solución de Tl(OAc)3 (4.2 g, 11.1 mmoles) en acetonitrilo (80 ml), se agrega mediante goteo ácido trifluorometansulfúrico (5g, 33.3 mmoles) a temperatura ambiente y se agita durante 15 minutos. La mezcla de reacción se calienta después hasta 80°C y se agrega 1-(3-clorofenil)-etanona (1.14 g, 7.4 mmoles) en acetonitrilo (40 ml). Después de una hora, la reacción se extingue con diclorometano y bicarbonato de sodio saturado. La capa orgánica se seca, se purifica mediante cromatografía en columna con acetato de etilo al 5~19% en hexanos para obtener 1.2 (83.9 %) g de 5-(3-clorofenil)-2-metil-oxazol como un aceite de color amarillo.

^{1}H RMN($CDCl_3$) d(ppm): 7.60 (s, 1H), 7.48 (d, 1H), 7.29 (m, 2H), 7.23 (s, 1H) y 2.34 (s, 3H).

Paso 2

2-Bromometil-5-(3-clorofenil)-oxazol:

Se mezcla 5-(3-clorofenil)-2-metil-oxazol (580 mg, 3 mmoles) con NBS (531 mg, 3 mmoles) y BPOA (36.3 mg, 0.15 mmoles) en CCl_4 a temperatura ambiente. La mezcla de reacción se calienta a 75°C durante 2 horas y después se extingue con agua y diclorometano. La capa orgánica se seca, se concentra, se purifica mediante cromatografía en columna con acetato de etilo 2~5 % acetato de etilo en hexanos para obtener 562 mg (68.3 %) de 2-bromometil-5-(3-clorofenil)-oxazol como un aceite de color amarillo.

^{1}H-RMN($CDCl_3$) d(ppm): 7.67 (s, 1H), 7.54 (d, 1H), 7.35(m, 3H) y 4.56 (s, 2H).

EJEMPLO 310

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico

A una mezcla de ácido 3-clorobenzoico (5.0 g, 31.9 mmoles), clorhidrato de éster metílico de serina (6.1 g, 31.9 mmoles) y HOBt (4.31 g, 31.9 mmoles) en DMF (100 ml) se agrega N-metilmorfolina (NMM) (7.0 ml, 63.8 mmoles) y EDCI (4.97 g, 31.9

mmoles) a 0°C. La mezcla se deja calentar hasta temperatura ambiente y se agita durante 18 horas. La mezcla se diluye con acetato de etilo (300 ml) y después se lava con agua (3 x 250 ml) seguido por salmuera. El extracto orgánico se seca con Na_2SO_4 (anhidro) y después se concentra al vacío para obtener el éster metílico del ácido 2-(3-cloro-benzoilamino)-3-hidroxi-propiónico (7.2 g, 93%) de un sólido de color amarillo pálido.

^1H RMN ($CDCl_3$) d (ppm): 7.78 (s, 1 H), 7.66 (d, 1 H), 7.45, (dd, 1 H), 7.34 (t, 1 H), 7.25 (br, d, 1H), 4.82 (m, 1 H), 4.08 (m, 2 H), 3.79 (s, 3 H), 3.19 (br, t, 1H).

A una solución del éster metílico del ácido 2-(3-cloro-benzoilamino)-3-hidroxi-propiónico (7.2 g, 29.6 mmoles) en CH_2Cl_2 a -20°C se agrega, mediante goteo, "De-oxofluor" (7.2 g, 32.6 mmoles). Después de agitar a esta temperatura durante 30 minutos, se agrega $BrCCl_3$ (3.6 g, 18.1 mmoles), mediante goteo, seguido por DBU (2.798, 18.1 mmoles). La mezcla se agita después a 2-3°C durante 8 horas y después se extingue con $NaHCO_3$ saturado seguido por extracción con acetato de etilo. El extracto orgánico se lava después con salmuera y se seca con Na_2SO_4 (anhidro).

La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo en hexanos como eluyente para obtener el éster metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico (4.1 g, 59%) como un sólido de color amarillo.

^{1}H RMN ($CDCl_3$) d (ppm): 8.30 (s, 1 H), 8.12 (d, 1 H), 7.98 (dd, 1 H), 7.45 (m, 2 H), 3.96 (s, 3 H).

EJEMPLO 311

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico

A una mezcla de ácido 3-clorobenzoico (5.0 g, 31.9 mmoles), clorhidrato del éster metílico de serina (6.1 g, 31.9 mmoles) y HOBt (4.31 g, 31.9 mmoles) en DMF (100 ml) se agrega N-metilmorfolina (NMM) (7.0 ml, 63.8 mmoles) y EDCI (4.97 g, 31.9 mmoles) a 0°C. La mezcla se deja calentar hasta temperatura ambiente y se agita durante 18 horas. La mezcla se diluye con acetato de etilo (300 ml) y después se lava con agua (3 x 250 ml) seguido por salmuera. El extracto orgánico se seca con Na_2SO_4 (anhidro) y después se concentra al vacío para obtener el éster metílico del ácido 2-(3-cloro-

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benzoilamino)-3-hidroxi-propiónico (7.2 g, 93%) de un sólido de color amarillo pálido.

^{1}H RMN ($CDCl_3$) d (ppm): 7.78 (s, 1 H), 7.66 (d, 1 H), 7.45, (dd, 1 H), 7.34 (t, 1 H), 7.25 (br, d, 1H), 4.82 (m, 1 H), 4.08 (m, 2 H), 3.79 (s, 3 H), 3.19 (br, t, 1H).

A una solución del éster metílico del ácido 2-(3-cloro-benzoilamino)-3-hidroxi-propiónico (7.2 g, 29.6 mmoles) en CH_2Cl_2 a -20°C se agrega, mediante goteo, De-oxofluor (7.2 g, 32.6 mmoles). Después de agitar a esta temperatura durante 30 minutos, se agrega, mediante goteo, $BrCCl_3$ (3.6 g, 18.1 mmoles) seguido por DBU (2.79g, 18.1 mmoles). La mezcla se agita después a 2-3°C durante 8 horas y después se extingue con $NaHCO_3$ saturado seguido por extracción con acetato de etilo. El extracto orgánico se lava después con salmuera y se seca con Na_2SO_4 (anhidro). La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo en hexanos como eluyente para obtener el éster metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico (4.1g, 59%) como un sólido de color amarillo.

^{1}H RMN ($CDCl_3$) d (ppm): 8.30 (s, 1 H), 8.12

(d, 1 H), 7.98 (dd, 1 H), 7.45 (m, 2 H), 3.96 (s, 3 H).

EJEMPLO 312

1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etanol

Paso 1

5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carbaldehído:

En un matraz de fondo redondo de 50 ml equipado con barra de agitación y tubo para secado se agregan éster etílico del ácido 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carboxílico (0.78 g, 2.89 mmoles) y diclorometano (10 ml). La solución se enfría hasta -78°C y a esta solución agitada se agrega hidruro de diisobutilaluminio (1M en hexanos, 5.3 ml, 5.3 mmoles). La mezcla resultante se deja bajo agitación a -78°C durante 3 horas. La reacción se extingue utilizando sulfato de sodio decahidratado. La mezcla resultante se agita a 63°C durante 15 minutos después de lo cual ésta se filtra a través de una almohadilla de celita. El material filtrado se concentra al vacío para aislar un sólido de color blanquecino, el cual se tritura con hexanos para aislar el compuesto del título como un sólido de color blanco (0.558, 84%).

^{1}H RMN ($CDCl_3$), d (ppm): 10.2 (s, 1H),

7.99(m, 1H), 7.44 (m, 1H), 7.20 (m, 1H), 7.10 (d, 1H).

Paso 2

1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etanol:

En un matraz de fondo redondo de 50 ml equipado con barra de agitación se agrega 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carbaldehído (0.55 g, 2.42 mmoles) y tetrahidrofurano (6 ml). La mezcla se enfría hasta 0°C y a ésta se agrega yoduro de metilmagnesio (3M en éter dietílico, 3.23 ml, 9.67 mmoles). La mezcla resultante se deja agitando a 0°C durante 3 horas. La mezcla de reacción se extingue con ácido clorhídrico (1N, acuoso, 10 ml), se extrae con éter dietílico (3X50 ml). La fase orgánica combinada se lava con agua (50 ml), salmuera (50 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo crudo se purifica en gel de sílice utilizando acetato de etilo al 10% en hexanos para aislar el compuesto deseado como un aceite claro (179 mg, 31%).

EJEMPLO 313

1-[3-(3-clorofenil)-isoxazol-5-il]-etanol

Se suspende cloruro de 3-cloro-benzohidroximoilo (e.g. Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57(24), 6649-50) (2.84 g, 14.8 mmoles) en benceno (50 ml) y se enfría hasta 0°C. Se agregan 3-butin-2-ol (2.10 g, 29.9 mmoles) y trietilamina (1.89 ml, 26.7 mmoles). La mezcla se calienta a 60°C durante 1.5 horas, se enfría y se diluye con benceno y ácido clorhídrico acuoso 1N. Después de agitar, se evapora hasta sequedad la capa de benceno separada y el producto crudo se purifica mediante cromatografía de vaporización instantánea con sílice utilizando heptano/acetato de etilo = 5/1 para obtener, después de secar al vacío, el compuesto del título (0.49 g, 15%).

^{1}H RMN ($CDCl_3$), δ (ppm): 1.64 (d, 3 H), 5.07 (dq, 1 H), 6.50 (s, 1 H), 7.40 (m, 2 H), 7.68 (m, 1 H), 7.79 (m, 1 H)

EJEMPLO 314

[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-metanol

Paso 1

(5-cloro-2-fluoro-fenilethynyl)-trimetil-silano:

En un matraz de fondo redondo de 250 ml equipado con una barra de agitación y condensador de reflujo se agregan 4-cloro-2-bromo-1-fluoro-benceno (5 g, 23.9 mmoles), trifenilfosfina (250 mg, 0.10 mmoles), (trimetilsilil)acetileno (5.2 ml, 36.5 mmoles) y trietilamina (60 ml). La mezcla de reacción se purga con argón, seguido por adición de acetato de paladio (II) (108 mg, 0.05 mmoles). La mezcla resultante se deja agitando a reflujo bajo argón, durante la noche. La mezcla de reacción se filtra a través de una almohadilla de celita utilizando acetato de etilo y el material filtrado se concentra al vacío. El residuo aislado se absorbe en gel de sílice y se filtra utilizando hexanos. El material filtrado se concentra al vacío para aislar el compuesto del título como un aceite de color café (5.42 g).

Paso 2

4-cloro-2-etinil-1-fluoro-benceno: En un matraz de fondo redondo de 250 ml equipado con barra de agitación se agregan (5-cloro-2-fluoro-feniletinil)-trimetil-silano (5.42 g, 23.9 mmoles), carbonato de

potasio (16.5 g, 120 mmoles) y metanol (60 ml). La mezcla de reacción se deja agitando a temperatura ambiente durante 1 hora. La mezcla de reacción se diluye con hexanos (200 ml) y se lava con agua (250 ml). La fase acuosa se extrae con hexanos (2X100 ml). La fase orgánica combinada se lava con salmuera (200 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar el compuesto deseado como un aceite de color café (3.56 g).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.47 (dd, 1H), 7.30 (m, 1H), 7.05 (t, 1H), 3.36 (s, 1H).

Paso 3

Ester etílico del ácido cloro-hidroxi-imino-acético:

En un matraz de fondo redondo de 1 litro equipado con barra de agitación se agrega clorhidrato del éster etílico del ácido amino-acético (20 g, 143 mmoles) y agua (30 ml). La solución se enfría hasta 0°C seguido por la adición en secuencia de ácido clorhídrico concentrado (11.8 ml, 143 mmoles) y la adición mediante goteo de solución de nitrito de sodio (9.89 g, 143 mmoles) en agua (15 ml). Después de 10 minutos se agrega otro equivalente de cada un o de ácido clorhídrico concentrado y de solución de

nitrito de sodio en agua. La mezcla de reacción se deja agitando a 0°C durante 1 hora. La mezcla de reacción se extrae con éter (4X100 ml). La fase orgánica combinada se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar un sólido de color amarillo limón. El sólido se recristaliza con hexanos para aislar un sólido de color blanco (11 g, 51%).

^{1}H RMN ($CDCl_3$), d (ppm): 9.98 (bs, 1H), 4.40 (q, 2H), 1.38 (t, 3H).

Paso 4

Ester etílico del ácido 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carboxílico:

En un matraz de fondo redondo de 250 ml equipado con barra de agitación se agrega 4-cloro-2-etinil-1-fluoro-benceno (2 g, 12.9 mmoles), éster etílico del ácido cloro-hidroxi-imino-acético (3.92 g, 25.9 mmoles), bicarbonato de sodio (7.07 g, 84.1 mmoles) y tolueno (50 ml). La mezcla de reacción se deja agitando a temperatura ambiente durante 48 horas, después de lo cual ésta se concentra al vacío. El residuo se lleva a acetato de etilo (200 ml), se lava en forma secuencial con agua (150 ml), salmuera (150 ml), se seca (sulfato de sodio), se filtra y se

concentra al vacío. El residuo crudo se purifica en gel de sílice utilizando acetona al 3% en hexanos para aislar el compuesto del título como un sólido de color blanquecino (1.56 g).

^{1}H-RMN ($CDCl_3$), d (ppm): 8.00 (dd, 1H), 7.43 (m, 1H), 7.18 (m, 2H), 4.51 (q, 2H), 1.47 (t, 3H).

Paso 5

[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-metanol:

En un matraz de fondo redondo de 50 ml equipado con barra de agitación y tubo para secado se agregan éster etílico del ácido 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carboxílico (0.78 g, 2.89 mmoles) y tetrahidofurano (10 ml). A esta solución agitada se agrega solución de hidruro de litio y aluminio (0.12 g, 2.89 mmoles) en tetrahidrofurano(2 ml). La mezcla resultante se deja agitando a temperatura ambiente durante 1 hora. La reacción se extingue utilizando sulfato de sodio decahidratado. La mezcla resultante se agita a 63°C durante 15 minutos después de lo cual ésta se filtra a través de una almohadilla de celita. El material filtrado se concentra al vacío para aislar el compuesto del título como un sólido de color amarillo (0.65 g, 99%).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.73 (dd, 1H), 7.27 (m, 1H), 7.24 (t, 1H), 6.73 (d, 1H), 4.77 (s, 2H), 4.45 (bs, 1H).

EJEMPLO 315

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]-oxadiazol-2-il]-propiónico

Paso 1

Acido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico:

Se mezclan hidrazida del ácido 3-cloro-benzoico (3.4 g, 20 mmoles) y anhídrido succínico (2. g, 20 mmoles) en acetato de etilo (50 ml) a temperatura ambiente durante 15 minutos. La mezcla de reacción se diluye con éter y el precipitado se filtra para obtener 5.1 g de ácido 4-[N'-(3-cloro-benzoil)-hidrazino]-4-oxo-butírico.

^{1}H RMN($CDCl_3$ + DMSO-d_6) d(ppm): 10.01 (s, 1H), 9.53 (s, 1H), 7.68 (s, 1H), 7.55 (d, 1H), 7.21 (d, 1H), 7.12 (t, 1H) y 2.35 (m, 4H).

Este sólido se mezcla con H_2SO_4 concentrado y se agita a temperatura ambiente durante 45 minutos y la mezcla de reacción se agrega cuidadosamente a hielo triturado (400g). El precipitado se filtra para

obtener 4.07 g (80.6%) de ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico como un sólido de color blanco.

^{1}H-RMN(DMSO-d6) d(ppm): 12.4 (w, 1H), 7.96 (s, 1H), 7.91 (d, 1H), 7.71 (d, 1H), 7.63 (t, 1H), 3.15 (t, 2H) y 2.82 (t, 2H).

Paso 2

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico:

Se mezcla ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico (2.52 g, 10 mmoles) con yodometano (5.68 g, 40 mmoles) y K_2CO_3 (5.52 g, 40 mmoles) en DMF (25 ml) a temperatura ambiente durante la noche. La mezcla de reacción se diluye con acetato de etilo y se lava con agua 3 veces, se seca con $MgSO_4$ y se concentra para obtener 2.57 g del éster metílico del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico. El éster metílico (2.54 g, 9.52 mmoles) se mezcla con hidrato de hidrazina al 98% (4.76 g, 95.2 mmoles) en metanol (10 ml) durante una hora. La mezcla de reacción se concentra, se diluye con agua, se filtra para obtener 2.17 g (81.4 %) de hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico como un

sólido de color blanco.

^{1}H RMN($CDCl_3$ + DMSO-d_6) d(ppm): 8.75 (w, 1H), 7.91 (s, 1H), 7.82 (d, 1H), 7.42 (m, 2H), 3.45 (w, 2H), 3.19 (t, 2H) and 2.68 (t, 2H).

EJEMPLO 316

Hidrazida de ácido 3-[5-(3-clorofenil)-[1,3,4]-oxadiazol-2-il]-butírico

Paso 1

Ester dimetílico del ácido 2-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-malónico:

Se mezcla 2-(1-cloro-etil)-5-(3-clorofenil)-[1,3,4]oxadiazol (331 mg, 1.36 mmoles) con malonato de dimetilo (360 mg, 2/76 mmoles) y DBU (207 mg, 1.36 mmoles) en acetonitrilo (3 ml) a 70°C durante la noche. La mezcla de reacción se diluye con diclorometano y se lava con agua. La capa orgánica se seca y se concentra. El residuo se purifica con acetato de etilo al 5~20 % en hexanos para obtener 357 mg (74.3%) de éster dimetílico del ácido 2-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-malónico como un sólido de color blanco.

^{1}H-RMN($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.95 (d, 1H), 7.53 (d, 1H), 7.47 (t, 1H), 4.06 (d, 1H), 3.95

(m, 1H), 3.84 (s, 3H), 3.74 (s, 3H) y 1.51 (d, 3H).

Paso 2

Ester metílico del ácido 3-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-butírico:

Se mezcla el éster dimetílico del ácido 2-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-malónico (352.8 mg, 1.0 mmoles) con cloruro de sodio (76.3 mg, 1.3 mmoles) y una gota de agua en DMSO (1.5 ml) a 175°C durante una hora. La mezcla de reacción se diluye con agua y se extrae con diclorometano. La capa orgánica se lava con agua y se concentra. El residuo se purifica mediante cromatografía en columna con acetato de etilo al 10-20% en hexanos para obtener 215 mg (76.8%) del éster metílico del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico como un aceite claro.

^{1}H-RMN(CDCl3) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.45 (t, 1H), 3.73 (s, 3H), 3.67 (m, 1H), 3.05 (dd, 1H), 2.73 (dd, 1H) y 1.50 (d, 3H).

Paso 3

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico:

La hidrazida del ácido 3-[5-(3-clorofenil)-

[1,3,4]oxadiazol-2-il]-butírico (146 mg, %) se obtiene haciendo reaccionar el éster metílico del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico (215 mg, 0.766 mmoles) con hidrato de hidrazina (0.74 ml) en metanol (3 ml) a temperatura ambiente durante 2.5 horas.

^{1}H RMN($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.46 (t, 1H), 7.23 (w, 1H), 3.93 (w, 2H), 3.71 (m, 1H), 2.90 (dd, 1H), 2.57 (dd, 1H) y 1.50 (d, 3H).

EJEMPLO 317

Clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico

Paso 1

3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionamida:

Se hace reaccionar el ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico (1.6 g, 6.33 mmoles) con $SOCl_2$ (10 ml) a temperatura ambiente durante la noche. La mezcla de reacción se concentra al vacío. El residuo se mezcla con THF (20 ml) y se extingue con $NH_3 \cdot H_2O$ al 28% (5 ml) a 0°C. Después que se agita durante 2 horas, la mezcla de reacción se

diluye con diclorometano y se lava con agua y salmuera. La capa orgánica se seca, se concentra y se tritura con hexanos para obtener 1.21 g (76 %) de 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionamida.

^{1}H RMN(CDCl3) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.32 (t, 2H) y 2.87 (t, 2H).

Paso 2

3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionitrilo:

Se mezcla 3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-propionamida (1.2 g, 4.77 mmoles) con piridina (0.829 g, 10.5 mmoles) y anhídrido trifluoroacético (1.2 g, 5.72 mmoles) en diclorometano (25 ml) a temperatura ambiente durante 2 horas. La mezcla de reacción se diluye con diclorometano y se lava con agua y salmuera. La capa orgánica se seca para obtener 1.1 g (98%) de 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionitrilo como un aceite de color café pálido.

^{1}H-RMN($CDCl_3$) d(ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.35 (t, 2H) y 3.01 (t, 2H).

Paso 3

Clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico:

Se mezcla 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionitrilo (1.1 g, 4.71 mmoles) con HCl al 24% en etanol (8 ml) durante la noche. El precipitado se filtra y se lava con éter para obtener 0.99 g (66 %) de clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico como un sólido de color blanco.

^{1}H RMN(DMSO-d_6) d(ppm): 11.70 (w, 2H), 7.78 (m, 2H), 7.64 (m, 2H), 4.41 (q, 2H), 3.45 (t, 2H), 3.22 (t, 2H) y 1.28 (t, 3H).

EJEMPLO 318

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-propiónico

Paso 1

Acido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico:

Se calienta 3-cloro-N-hidroxi-benzamidina 4.52 g, 26.5 mmoles) con anhídridos succínico (2.65 mg, 26.5 mmoles) en DMF (5 ml) a 150°C durante una hora. La mezcla de reacción se enfría y se diluye con

acetato de etilo. La solución orgánica se lava con agua y salmuera, se concentra al vacío. El residuo se tritura con acetato de etilo al 20% en hexanos para obtener 4.0 g (60 %) del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico como un sólido de color blanco).

^{1}H RMN($CDCl_3$) d(ppm): 8.08 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.42 (t, 1H), 3.28 (t, 2H) y 3.04 (t, 2H).

Paso 2

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico:

Este ácido se hace reaccionar con yodoetano (1.6g, 10.5 mmoles) y K_2CO_3 (1.46 10.5 mmoles) en DMF (5 ml) durante 5 minutos para formar el éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico. El éster etílico se trata después con hidracina al 37% (2ml) en etanol (5 ml) a 80°C durante 2 horas para obtener 595 mg (65% en los 3 pasos) de la hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico como un sólido de color blanquecino.

^{1}H RMN($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.43 (t, 1H), 7.00 (w, 1H), 3.95

(w, 2H), 3.34 (t, 2H) and 2.79 (t, 2H).

EJEMPLO 319

Hidrazida del ácido [5-(3-clorofenil)-[1,2,4]-oxadiazol-3-il]-acético

Paso 1

Ester etílico del ácido (N-hidroxi-carbamimidoil)-acético:

A una solución en etanol de (40 ml) del éster etílico del ácido ciano-acético (9.9 g, 0.1 mol), se agrega la mezcla constituida por solución de hidróxido de sodio (4 g, 0.1 mol) en agua (40 ml) y clorhidrato de hidroxilamina 5M (20 ml) y la mezcla de reacción se agita a 50°C durante la noche. Después que se concentra, la mezcla de reacción se diluye con agua y se extrae con acetato de etilo. La capa orgánica se seca, se concentra de nuevo. El residuo se purifica mediante cromatografía en columna con acetato de etilo 30~70 % acetato de etilo en hexanos para obtener 3.32 g (22.7 %) del éster etílico del ácido (N-hidroxicarbamimidoil)-acético como un sólido de color blanco.

^{1}H-RMN($CDCl_3$) d(ppm): 5.04 (ws, 2H), 4.20 (q, 2H), 3.19 (s, 2H) y 1.30 (t, 3H).

Paso 2

Ester etílico del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético:

A una solución en diclorometano (10 ml) del éster etílico del ácido (N-hidroxicarbamimidoil)-acético (1.46 g, 10 mmoles) y trietilamina, se agrega lentamente, a 5°C, cloruro de 3-clorobenzoilo (1.75 g, 10 mmoles) y la mezcla de reacción se agita durante 10 minutos. Se agrega DMF (8 ml) a la mezcla de reacción, se calienta a 135°C durante 2 horas. Tratamiento estándar, el producto se hace pasar en la columna con diclorometano para obtener 1.2 g (45 %) del éster etílico del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético como un aceite de color amarillo pálido.

^{1}H-RMN($CDCl_3$) d(ppm): 8.168 (s, 1H), 8.04 (d, 1H), 7.59 (d, 1H), 7.49 (t, 1H), 4.26 (q, 2H), 3.91 (s, 2H) y 1.31 (t, 3H).

Paso 3

Hidrazida del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético:

Se mezcla el éster etílico del ácido 5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético (0.64 g, 2.4 mmoles) con hidrazina al 37% (1.6 ml) en etanol

(10 ml) a 80°C durante 4 horas. La mezcla de reacción se concentra y se diluye con agua. El precipitado se filtra, se lava con agua para obtener 0.51 g (83.3 %) de la hidrazida del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético.

EJEMPLO 320

Hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-butírico

Paso 1

Ester metílico del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico:

A una solución del ester 4-metílico del ácido (R)-2-metilsuccínico (2.2 g, 15 mmoles) y trietilamina (4.54 g, 45 mmoles) en THF (30 ml), se agrega, mediante goteo, isobutilcloroformiato (2.16 g, 15.8 mmoles) a 0°C. Después que se agita durante 30 minutos, se agrega la 3-cloro-N-hidroxi-benzamidina (2.56 g, 15 mmoles). La mezcla de reacción se agita a temperatura ambiente durante otros 30 minutos y después se calienta a 135°C con DMF durante 45 minutos. La mezcla de reacción se diluye con acetato de etilo y se lava con agua y salmuera. La capa orgánica se seca y se concentra

para obtener 4.0 g (95 %) del éster metílico del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico como un aceite de color amarillo pálido.

Paso 2

Hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico:

La hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico (430 mg, 77%) se obtiene haciendo reaccionar el éster metílico del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico (461.4 mg, 2.0 mmoles) con hidrato de hidrazina (2ml) en metanol (2 ml) a 65°C durante 1 hora.

^{1}H-RMN($CDCl_3$) d (ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.46 (m, 2H), 6.98 (w, 1H), 3.93 (w, 2H), 3.78 (m, 1H), 2.86 (dd, 1H), 2.55 (dd, 1H) y 1.59 (d, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 320:

Ejemplo No.	Nombre
321	Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-3-metil-butírico

EJEMPLO 322

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona

Se agregan 1.33 ml (3.32 mmoles) de n-BuLi (2.5 M en hexanos), mediante goteo, a una solución de 157 mg (1.58 mmoles) de d-valerolactona en 5,3 ml de THF a 0°C. Después de agitar durante 2 horas a 0°C, se agregan 400 mg (1.58 mmoles) de 3-clorometil-5-[3-clorofenil)-[1,2,4]oxadiazol en una porción y la agitación se continúa durante 3 horas. Se agrega NH_4Cl (saturado) para extinguir la reacción y la mezcla se extrae dos veces con CH_2Cl_2. Las fases orgánicas combinadas se secan y se concentran. La cromatografía de vaporización instantánea (SiO_2, heptano/EtOAc 1:8) permite obtener 113 mg (25%) de un sólido de color blanco amarillento.

^1H RMN ($CDCl_3$):d ppm 1.80 (m, 1 H) 1.89 (m, 1 H) 2.00 (m, 1 H) 2.91 (m, 1 H) 2.98 (m, 1 H) 3.35 (m, 1 H) 3.52 (m, 1 H) 5.83 (s, 1 H) 7.46 (t, 1 H) 7.55 (d, J=8.08 Hz, 1 H) 8.00 (d, 1 H) 8.11 (s, 1 H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 322:

Ejemplo No.	Nombre
323	3-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]-oxadiazol-3-ilmetil]-piperidin-2-ona

EJEMPLO 324

3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol y 1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol

Una solución de 2-cloro-N-hidroxi-acetamidina (781 mg, 7.2 mmoles), ácido 5-cloro-tiofen-3-carboxílico (1.4 g), HBTU (3.55 g) y DIPEA (1.3 g) en DMF (20 ml) se agita a temperatura ambiente durante 1 hora antes de calentar a 120°C durante 4 horas bajo argón. La remoción del solvente al vacío seguido por cromatografía en gel de sílice el residuo obtenido utilizando EtOAc al 0-20% en n-heptano produce 38.5 mg del compuesto que eluye más rápido 3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]-oxadiazol como un jarabe, seguido por 65 mg del compuesto que eluye más lento 1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol como un sólido de color blanco.

3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol:

^{1}H RMN ($CDCl_3$) d (ppm): 8.01 (d, 1H), 7.50 (d, 1H), 4.63 (s, 2H).

1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol:

^{1}H RMN ($CDCl_3$) d (ppm): 7.97 (m, 2H), 7.52 (dt, 1H), 7.44 (m, 2H), 7.34 (m, 1H), 5.70 (s, 2H).

EJEMPLO 325

(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-acetonitrilo

Se agitan juntos 4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-tiol (197 mg, 1.0 mmoles), cloroacetonitilo (95 ml, 1.5 mmoles), carbonato de sodio (424 mg, 4 mmoles) y yoduro de potasio (332mg, 2.0 mmoles) a 100°C durante 3 horas, agregando una cantidad adicional de cloroacetonitrilo (60 ml, 0.5 mmoles) después de 2 horas. La reacción se enfría, se diluye con acetato de etilo y se lava con agua. La solución orgánica se seca, se filtra y evapora. La cromatografía con gel de sílice (diclorometano:metanol 19:1) produce 150 mg del compuesto deseado.

EJEMPLO 326

Acido 2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-propiónico

Se diauelven ácido (R)-2-cloro-propiónico (500 mg, 4.6 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (1.09 g, 5.58 mmoles) y carbonato de potasio (1.94 g, 14.03 mmoles) en acetonitrilo (15 ml) a temperatura ambiente. La reacción continúa durante 2.5 horas y se separa entre acetato de etilo (350 ml) y agua 3 veces, se lava con HCl 1M, una vez con salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra al vacío. La reacción no es completa en esta etapa y el producto crudo se agita en DMF (10 ml) durante la noche. Se repite la extracción y la purificación se efectúa mediante cromatografía de SPE (extracción en fase sólida) en gel de sílice utilizando 300 ml de acetato de etilo, 100 ml 1%, y 100 ml de ácido fórmico al 3% en acetato de etilo, para obtener el compuesto del título (150.7 mg, 12%).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.52 (dd, 2H), 7.19 (m, 1H), 4.21 (q, 1H), 3.78 (s, 3H), 1.64 (d, 311).

Los siguientes compuestos se preparan en

forma análoga a la del ejemplo 326:

Ejemplo No.	Nombre
327	Acido 2-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanil)-propiónico

EJEMPLO 328

3-(3-clorofenil)-5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

El compuesto del título (2.08 g, 81.5 %) se obtiene a partir de 5-clorometil-3-(3-clorofenil)-[1,2,4]oxadiazol (1.9 g, 8.29 mmoles) que se hace reaccionar con 4-metil-4H-[1,2,4]triazol-3-tiol (1.0 g, 8.71 mmoles) y K_2CO_3 (4.58 g, 33.2 mmoles) en DMF (19 ml) a temperatura ambiente durante la noche.

^1H RMN($CDCl_3$) d (ppm): 8.21 (s, 1H), 8.05 (s, 1H), 7.94 (d, 1H), 7.49(d, 1H), 7.43 (t, 1H), 4.69 (s, 2H) y 3.64(s, 3H).

EJEMPLO 329

Ester ter-butílico del ácido {3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol-5-il-fenil)-carbámico

El compuesto del título se prepara a partir

de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (53 mg, 0.27 mmoles), éster ter-butílico del ácido 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-carbámico (75 mg, 0.24 mmoles), y carbonato de potasio (101 mg, 0.73 mmoles) en acetonitrilo (2.5 ml). El producto se purifica mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 65% en hexano (88.0 mg, 79%, sólido de color blanco).

^{1}H RMN (CDCl3) d (ppm): 8.06 (s, 1H), 7.73 (d, 1H), 7.66 (d, 1H), 7.51 (t, 2H), 7.42 (t, 1H), 7.18 (m, 1H), 6.68 (s, 1H), 4.51 (s, 2H), 3.73 (s, 3H), 1.53 (s, 9H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 41:

Ejemplo No.	Nombre	1H RMN	MS
330	4-(4-ciclopropil-5-(1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.88 (d, 2H), 7.81 (m,1H), 7.75 (m, 2H), 7.22(m, 2H), 5.42 (q, 1H), 3.22 (m, 1H), 1.98 (d,3H), 1.17 (m, 2H), 0.79(m, 2H)	
331	4-(5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.69 (m, 2H), 7.6 (m,1H), 7.52 (m, 3H), 7.35 (t, 1H), 7.04 (m, 1H), 4.93 (q, 1H), 3.78 (t,3H), 3.55 (s, 3H), 1.86(d, 3H)	

Ejemplo No.	Nombre	1H RMN	MS
332	4-{4-metil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.71 (m, 2H), 7.82 (m,2H) 7.53 (m, 2H), 7.32(m, 2H), 4.94 (q, 1H), 3.54 (s, 3H), 2.33 (s,3H), 1.87 (d, 3H)	
333	5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-3-o-tolil-[1,2,4]oxadiazol	2.58 (s, 3H) 3.70 (s, 3H) 4.65 (s, 2H) 7.17 (s, 1H) 7.29 (s, 2H) 7.36 (s, 1H) 7.46 (s, 1H) 7.51 (s, 1H) 7.90 (s, 1H)	370.0
334	5-(3-cloro-fenil)-3-(4-ciclopropil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	0.87 (m, 2H) 1.18 (m, 2H) 3.47 (ddd, J=6.95, 3.41, 3.28 Hz, 1H) 4.70(s, 2H) 7.23 (m, 1H) 7.67 (m, 2H) 7.77 (m, 2H) 8.04 (d, 2H)	415.9
335	2-{3-[5-(2-Fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-etanol	2.36 (s, 3H) 4.03 (t, 2H) 4.30 (t, 2H) 4.57 (s,2H) 7.11 (m, 2H) 7.35(s, 1H) 7.47 (d, 1H) 7.64 (d, 1H) 7.81 (d, 1H)	417.9
336	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-pirimidina	1.38(t, 3 H) 2.34 (s, 3H) 4.66 (m, 4 H) 7.19(m, 1H) 7.47 (m, 1H)7.83 (d, 1 H) 8.23 (d, 1H) 8.94 (d, 1H) 9.28 (s,1H)	398.0

Ejemplo No.	Nombre	1H RMN	MS
337	3-(4-etil-5-furan-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	1.34 (t, 3H) 2.37 (s, 3H) 4.06 (q, 2H) 4.61 (s,2H) 6.82 (s, 1H) 7.12 (m, 1H) 7.36 (ddd, 1H)7.55 (s, 1H) 7.85 (d, 2H).	386.0
338	Ester metílico del ácido {3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-acético	2.36 (s, 3H) 3.70 (s, 3H) 4.46 (s, 2H) 5.10 (s,2H) 7.21 (m, 2H) 7.47 (m, 2H) 7.73 (d, 1H) 7.86 (m, 1H)	445.9
339	5-(2-fluoro-5-metil-fenil)-3-[5-furan-2-il-4-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	2.26 (s, 3H) 3.16 (s, 3H) 3.57 (t, 2H) 4.42 (t,2H) 4.44 (s, 2H) 6.60 (s, 1H) 7.10 (m, 2H) 7.37 (m, 1H) 7.70 (s, 1H) 7.73 (d,1H)	416.0
340	3-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	0.87 (m, 2H) 1.14 (m,2H) 2.35(s,3H) 3.39(dt,1H) 4.71 (s, 2H) 6.72(s, 1H) 7.09 (d, 1H) 7.39 (m, 1H) 7.56 (m, 1H) 7.87 (d, 1H) 7.93 (s,1H)	398.0
341	3-(5-cloro-2-fluoro-fenil)-5-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	0.32 (m,2H) 0.56 (m,2H) 1.14 (d,1H) 4.00 (d,2H) 4.76 (s, 2H) 7.16(ddd, 2H) 7.43 (m, 1H) 7.50 (t,2H) 7.99 (dd, 1H)	448.1

Ejemplo No.	Nombre	1H RMN	MS
342	4-(5-[3-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina	1.40 (t, 3H) 4.63 (q, 2H) 4.72 (s, 2H) 7.20 (m,1H) 7.53 (m, 1H) 8.06 (dd, 1H) 8.29 (d, 1H) 8.86 (d, 1H) 9.26 (s, 1H).	417.8
343	3-(5-ciclopentil-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	1.29 (t, 3H) 1.66 (m, 3H) 1.87 (m, 2H) 2.02 (m,3H) 2.42 (s,3H) 3.01 (s, 2H) 3.90 (d, 2H) 4.52 (s, 2H) 7.39 (d,2H) 7.90(d,2H)	370.2
344	3-(3-cloro-fenil)-5-{4-etil-5-[2-(4-metoxi-fenil)-etil]-4H-[1,2,4]triazol-3-ilsulfanilmetil}-[1,2,4]oxadiazol	1.18 (t, 3H) 2.95 (t, 2H) 3.09 (t, 2H) 3.72 (q, 2H) 3.76 (s,3H) 4.66 (s, 2H) 6.81 (d, 2H) 7.09 (d, 2H) 7.40 (t, 1H) 7.47 (m, 1H) 7.92 (d, 1H) 8.03 (s, 1H)	456.1
345	5-(3-cloro-fenil)-3-(4-etil-5-p-toliloximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.23 (t, 3 H) 2.22 (s, 3H) 4.02 (d, 2H) 4.60 (s,2H) 5.22 (s, 2H) 6.92(d, 2H) 7.09 (d, 2H)7.65 (t, 1H) 7.79 (d, 1H) 8.04 (m, 2H)	442.1

Ejemplo No.	Nombre	1H RMN	MS
346	5-(3-cloro-fenil)-3-[4-(2-metoxi-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	3.14 (s, 3 H) 3.57 (t, 2H) 4.30 (t, 2 H) 4.58 (s,2 H) 7.23 (m, 1H) 7.64(m, 2 H) 7.78 (m, 2 H)8.03 (d, 2 H)	433.9
347	3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.98 (m, 1H), 7.43 (m,1H), 7.16 (t aparente,1H), 4.73 (s, 2H), 4.62(s, 2H), 4.01 (q, 2H),3.33 (s, 3H), 1.34 (t,3H).	384.9
348	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.05 (m, 1H), 7.53 (m,1H), 7.21 (t aparente,1H); 4.62 (s, 2H), 4.61(s, 2H), 4.02 (q, 2H),3.34 (s, 3H), 1.32 (t,	384.9
349	5-(3-cloro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.07 (s aparente , IH),7.97 (m, 1H), 7.55 (m,1H), 7.45 (t aparente,1H), 4.62 (s, 2H), 4.59(s, 2H), 4.01 (q, 2H),3.34 (s, 3H), 1.32 (t,3H).	366.9
350	3-(3-cloro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.02 (m, 1H), 7.92 (m,1H) , 7.46 (m, 1H), 7.39(t aparente, 1H), 4.71 (s,2H), 4.62 (s, 2H), 4.01(q, 2H), 3.34 (s, 3H),1.34 (t, 3H).	366.9

Ejemplo No.	Nombre	1H RMN	MS
351	4-(5-{1-[3-(3-cloro-fenil)-isoxazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	1.82 (d, 3 H), 3.46 (s, 3H), 4.93 (q, 1 H), 6.33(s, 1 H), 7.23-7.31 (m, 2H), 7.44 (d, 2 H), 7.49(m, 1 H), 7.61 (s, 1 H),8.63 (d, 2 H).	399.1
352	3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	4.6 (s, 2 H), 4.8 (d, 2 H),5.0 (d, 1 H), 5.2 (d, 1H) 5.9 (m, 1 H), 6.5 (m,1 H), 7.1 (d, 1 H), 7.4 (t,1 H), 7.5 (m, 2 H), 8.0(d, 1 H), 8.1 (s, 1 H)	399.95
353	3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	4.5 (s, 2 H) 4.8 (d, 2 H)5.0 (d, 1 H) 5.2 (d, 1 H)5.9 (m, 1 H) 6.5 (m, 1H) 7.0 (d, 1 H) 7.4 (m, 1H)7.5(s,1H)7.6(d,1 H) 8.2 (m, 1 H)	371.98
354	5-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-furan-2-il-[1,2,4]oxadiazol	4.7(s,2H)4.8(m,2 H)5.0 (d, 1 H) 5.2 (d, 1 H)5.9 (m, 1 H) 6.5 (dt, 2H) 7.1 (dd, 2 H) 7.6 (dd,2 H)	356.01
355	5-(3-cloro-fenil)-3-[4-etil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.4 (t, 3 H) 3.7 (s, 3 H)4.1 (q, 2 H) 4.6 (s, 2 H)5.2 (s, 2 H) 6.8 (d, 2 H)6.9 (d, 2 H) 7.4 (t, 1 H)7.6 (d, 1 H) 8.0 (d, 1 H)8.1 (s, 1 H)	457.91

Ejemplo No.	Nombre	1H RMN	MS
356	3-(3-cloro-fenil)-5-[4-etil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.4(t,3H)3.7(s,3H)4.1 (q, 2 H) 4.8 (s, 2 H)5.2 (s, 2 H) 6.8 (d, 2 H)6.9 (d, 2 H) 7.4 (t, 1 H)7.5 (m, 1 H) 7.9 (d, 1 H)8.0 (s, 1 H)	457.97
357	(5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-metanol	1.4 (t, 3 H) 4.2 (d, 2 H)4.7 (s, 2 H) 4.9 (s, 2 H)7.4 (t, 1 H) 7.5 (m, 1 H)7.9 (d, 1 H) 8.0 (s, 1 H)	352.09
358	3-(3-cloro-fenil)-5-[4-etil-5-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.3 (t, 3 H) 3.0 (t, 2 H)3.3 (s, 3 H) 3.8 (t, 2 H)3.9 (q, 2 H) 4.7 (s, 2 H)7.4 (t, 1 H) 7.5 (ddd, 1H) 7.9 (dt, 1 H) 8.0 (t, 1H)	380.12
359	3-(3-cloro-fenil)-5-(4-etil-5-metilsulfanilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.4 (t, 3 H) 2.1 (s, 3 H)3.8 (s, 2 H) 4.0 (q, 2 H)4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (ddd, 1 H) 7.9 (dt, 1H) 8.0 (t, 1 H)	382.07
360	3-(3-cloro-fenil)-5-(5-etoximetil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	.2 (t, 3 H) 1.3 (t, 3 H)3.5 (q, 2 H) 4.0 (q, 2 H)4.7 (s, 2 H) 4.7 (s, 2 H)7.4 (t, 1 H) 7.5 (ddd, 1H) 7.9 (dt, 1 H) 8.0 (t, 1H)	379.13
361	5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-carboxilico ácido metil ester		

Ejemplo No.	Nombre	1H RMN	MS
362	2-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	1.4(t,3 H)4.2(q, 2H)4.7(s,2 H)6.6(dd,1H)7.1(d,1H)7.2(m,1H)7. 5 (ddd, 1 H) 7.6 (d, 1H) 8.0 (dd, 1 H)	406.07
363	2-(3-cloro-fenil)-5-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	0.9 (m, 2 H) 1.2 (m, 2H) 3.2 (m, 1 H) 4.8 (s, 2H) 6.6 (m, 1 H) 7.0 (d, 1H) 7.4 (t, 1 H) 7.5 (m, 1H) 7.6 (m, 1 H) 7.9 (m,1H)8.0(m,1H)	399.86
364	5-(3-cloro-fenil)-3-{1-[4-etil-5-(tetrahidro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol	1.3(t,3H)1.9(d,3 H)2.0 (m, 1 H) 2.1 (m, 1H) 2.3 (m,1 H) 2.8 (m,1 H) 3.8 (m, 2 H) 4.0(m, 1 H) 4.1 (m, 1 H)5.0 (m, 1 H) 5.1 (m, 1H) 7.4 (t, 1 H) 7.6 (m, 1 H) 8.0 (m, 1 H) 8.1 (s, 1H)	406.04
365	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridazina	1.4 (t, 3 H) 1.9 (d, 3 H)4.1 (m, 2 H) 5.2 (q, 1 H)7.4 (t, 1 H) 7.5 (m, 1 H)7.8 (m, 1 H) 8.0 (m, 1H) 8.1 (m, 1 H) 9.4 (m,1 H) 9.5 (s, 1 H)	414.12
366	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-ilmetil)-piridina	1.0 (t, 3 H) 1.9 (d, 3 H)3.7 (m, 2 H) 4.2 (m, 2H) 5.0 (q, 1 H) 7.1 (m, 2H) 7.4 (t, 1 H) 7.5 (m, 1H) 7.9 (d, 1 H) 8.1 (s, 1H) 8.5 (m, 2 H)	427.06

Ejemplo No.	Nombre	1H RMN	MS
367	5-(5-[1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol	1.3 (t, 3 H) 1.9 (d, 3 H).3.9 (m, 2 H) 5.1 (q, 1 H)6.7(d,1H) 7.5(t, 1H)7.6 (m, 1 H) 7.7 (m, 1H) 7.7 (s, 1 H) 8.0 (d, 1H) 8.1 (s, 1 H) 13.1 (s, 1H)	429.1
368	4-(5-(1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-fenol	1.2(t,3H)1.9(d,3 H)3.9 (q, 2 H) 5.1 (q, 1 H)6.9 (d, 2 H) 7.3 (d, 2 H)7.4 (t, 1 H) 7.5 (m, 1 H)7.9 (m, 1 H) 8.1 (m, 1H) 10.2 (s, 1 H)	428.08
369	5-(3-cloro-fenil)-3-[5-(4-metoxi-fenoximetil)-4-(tetrahidro-furan-2-ilmetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.54 (m, 1 H) 1.86 (m, 2H) 2.02 (m, 1 H) 3.71(m, 4 H) 3.79 (m, 1 H) 4.13 (m, 3 H) 4.60 (m, 2 H) 5.30 (s, 2 H) 6.82 (m,2H) 6.92(m,2H) 7.44 (t,1H) 7.55 (d,1H) 7.95 (d, 1 H) 8.07 (s, 1H)	
370	5-(3-cloro-fenil)-3-[4-ciclopropil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.14 (m, 4 H) 3.10 (s, 1H) 3.75 (s, 3 H) 4.70 (s,2 H) 5.21 (s, 2 H) 6.82(d, 2 H) 6.95 (d, 2 H)7.45 (t, 1 H) 7.56 (m, 1H) 7.99 (d, 1H) 8.10 (s,1 H)	

Ejemplo No.	Nombre	1H RMN	MS
371	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.38 (t, 3 H) 4.27 (q, 2H) 4.64 (s, 2 H) 6.58 (m,1 H) 7.21 (m, 2 H) 7.53(m, 1 H) 7.59 (m, 1 H)8.06 (m, 1H)	
372	3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol.	1.29 (t, 3 H) 2.40 (s, 3H) 3.31 (s, 3 H) 3.99 (m,2 H) 4.56 (s, 2 H) 4.60(s, 2 H) 7.37 (m, 2 H)7.87 (m, 2 H)	346
373	3-[4-etil-5-(tetrahidro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol	1.30 (t, 3 H) 1.97 (m, 1H) 2.10 (m, 1 H) 2.24(m, 1 H) 2.39 (s, 3 H)2.80 (m, 1 H) 3.79 (m, 1H) 3.86 (m, 1 H) 3.99(m, 1 H) 4.08 (m, 1 H)4.54 (m, 2 H) 4.98 (m, 1H)7.36(m,2H)7.86(m, 1 H) 7.88 (s, 1 H)	372
374	2-(3-cloro-fenil)-5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	1.18 (m, 3 H) 1.95 (d, 3H) 3.81 (s, 3 H) 3.90 (q,2 H) 5.15 (q, 1 H) 6.94(m, 2 H) 7.35 (m, 1 H)7.45 (m, 3 H) 7.81 (m, 1H) 7.92 (m, 1 H)	
375	4-{5-[3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina	1.43 (t, 3 H), 4.64 (q, 2H), 4.87 (s, 2 H), 7.18(m , 2 H), 7.72 (m, 1 H),8.29 (dd, 1 H), 8.89 (d, 1H), 9.30 (d, 1	402.1

Ejemplo No.	Nombre	1H RMN	MS
376	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina	4.12 (s, 3 H), 4.64 (s, 2H), 7.21 (t, 1 H), 7.57(m, 1 H), 8.06 (dd, 1 H),8.28 (dd, 1 H), 8.92 (d, 1H), 9.30 (d, 1	404.1
377	3-(3-cloro-fenil)-5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.03 (s 1H), 7.92 (d,1H), 7.53 (d, 1H), 7.48(m, 2H), 7.40 (t, 1H),7.18 (t, 1H), 4.87 (s,2H), 3.72 (s,	390.96
378	5-(3-metilsulfanil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.92 (s, 1H), 7.84 (d,1H), 7.53 (m, 2H), 7.43(m, 2H), 7.18 (m, 1H),4.53 (s, 2H), 3.73 (s,3H), 2.52 (s,	
379	2-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilrnetilsulfanil]-1H-benzoimidazole		
380	5-(2,5-dimetil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.87 (s, 1H), 7.49 (m, 2H), 7.22 (m, 3H), 4.56(d, 2H), 3.74 (s, 3H),2.61 (s, 3H), 2.37	
381	5-(2-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.83 (dd, 1H), 7.49 (m,2H), 7.35 (m, 1H), 7.16(m, 2H), 4.53 (s, 2H),3.73 (s,	388.10
382	5-(3-ciclopropil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.87 (d, 1H), 7.79 (s,1H), 7.51 (m, 2H), 7.40,(t 1H), 7.30 (m, 1H),7.20 (m, 1H), 4.53 (s,2H), 3.73 (s, 3H), 1.96(m, 1H), 1.04 (m,	

Ejemplo No.	Nombre	1H RMN	MS
383	4-{5-[2-(3-cloro-fenil)-oxazol-4-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (d, 2H), 8.02 (dd,1H), 7.88 (dd, 1H), 7.80(s, 1H), 7.60 (d, 2H),7.42 (m, 2H), 4.51 (s,2H), 3.64 (s, 3H).	
384	4-[4-metil-5-(5-tiofen-2-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (bs, 2H), 7.90 (m,1H), 7.66 (m, 3H), 7.22(m, 1H), 4.58 (s, 2H),3.73 (s, 3H).	
385	4-{4-metil-5-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.81 (m, 2H), 7.95 (s,1H), 7.86 (m, 1H), 7.64(m, 2H), 7.45 (m, 2H),4.63 (s, 2H), 3.72 (s,3H), 2.55 (s,3H).	
386	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (d, 2H), 8.11 (s, 1H), 8.00 (d, 1H), 7.64(m, 2H), 7.60 (m, 1H),7.49 (t, 1H), 4.64 (s,2H), 3.73 (s, 3H).	I -
387	2-metil-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.82 (d, 2H), 8.74 (d,1H), 7.82 (s, 1H), 7.76(d,1H),7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s,3H), 2.68 (s, 3H).	
388	1-{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-etanona	8.67 (s, 1H), 8.29 (d,1H) 8.20 (d, 1H), 7.68(t, 1H), 7.52 (m, 2H),7.20 (m, 1H), 4.58 (s,2H), 3.76 (s, 3H), 2.68(s, 3H).	

Ejemplo No.	Nombre	1H MNR	MS
389	4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (dd, 2H), 7.86 (d,1H), 7.64 (m, 2H), 7.39(m, 1H), 7.14 (dd, 1H),4.63 (s, 2H), 3.73 (s,3H), 2.39 (s, 3H).	383.09
390	2-metil-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.68 (dd, 1H),7.92 (m,2H), 7.52 (bs, 1H), 7.4(m, 3H), 4.61 (s, 2H),3.7 (s, 3H), 2.67 (s, 3H),2.44 (s, 3913H).	
391	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-5-tiofen-2-il-4H-[1,2,4]triazol	7.76 (s, 1H), 7.68 (m,1H) , 7.54 (m, 1H), 7.48(m, 1H), 7.40 (m 2H),7.20(m,1H),6 .76 (s,1H), 4.56 (s, 2H), 3.70(s, 3H).	
392	4-(5-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (m, 2H), 7.76 (m,1H), 7.65 (m, 3H), 7.41(m, 2H), 6.77 (s, 1H),4.61 (s, 2H), 3.69 (s,3H).	
393	3-(4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.07 (s, 1H), 7.95 (dd,1H), 7.48 (m, 4H), 7.17(dd, 1H), 4.59 (s, 2H),4.05 (t, 2H), 1.67 (m,2H), 1.30 (m, 2H), 0.88(t, 3H).	
394	5-(3-cloro-fenil)-3-[4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.01 (d, 1H), 7.91 (dd,1H), 7.48 (m, 4H), 7.12(m, 1H), 4.51 (s, 2H),4.17 (t, 2H), 3.34 (t,2H), 3.18 (s, 3H), 1.90(m, 2H).	

Ejemplo No.	Nombre	1H RMN	MS
395	3-(4-benzil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.09 (s, 1H), 7.97 (dd,1H), 7.57 (m, 1H), 7.47(m, 2H), 7.24 (m, 4H),7.06 (m, 3H), 5.37 (s,2H), 4.57 (s, 2H).	
396	5-(3-cloro-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.10 (d, 1H), 8.03 (dd, 1H),7.55 (m, 4H), 7.38(s, 1H), 7.20 (dd,1H),6.32 (m, 2H), 5.30 (s,2H), 4.60 (s, 2H).	457.02
397	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.93 (m, 1H),8.78 (m,1H), 8.03 (m, 3H), 7.59(m, 1H), 7.51 (m, 2H),4.63 (s, 2H), 3.69 (s, 3H).	
398	5-(3-cloro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (m, 1H), 8.05 (m,1H), 7.74 (m, 1H), 7.59(m, 1H), 7.51 (m, 3H),4.57 (s, 2H), 3.71 (s,3H).	
399	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-2-metil-piridina	8.69 (d, 1H), 8.10 (s,1H), 8.00 (m, 1H), 7.49(m, 4H), 4.63 (s, 2H),3.71 (s, 3H), 2.67 (s,3H).	
400	5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.08 (m, 1H), 7.51 (m,1H) 7.21 (m, 1H), 4.59(s, 2H), 3.77 (s, 3H).	409.00
401	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 8.08 (m,1H) 8.29 (d, 1H), 7.64(d, 2H), 7.56 (m,1H) ,7.24 (t, 1H), 4.66 (s,2H), 3.75 (s, 3H).	404.07

Ejemplo No.	Nombre	1H RMN	MS
402	3-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (s, 1H), 8.76 (d,1H), 8.07 (d, 1H), 7.87(d, 1H), 7.36 (m, 3H),4.59 (s, 2H), 3.69 (s,3H), 2.39 (s, 3H)	
403	5-(3-cloro-fenil)-3-(5-tiofen-2-il-4-tiofen-2-ilmetil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	(CD30D como solvente):8.05 (m, 1H), 8.00 (dd,1H), 7.75 (dd, 1H), 7.58(m, 1H), 7.54 (m, 1H),7.53 (m, 1H), 7.26 (m,1H), 7.22 (m, 1H), 6.86(m,	
404	5-(3-cloro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	(CD30D como solvente):8.08 (m, 1H),8.07 (dd, 1H), 7.75 (m,1H), 7.67 (m, 1H), 7.60(m, 2H), 7.28 (dd, 1H),4.57 (s, 2H), 4.27 (m,2H), 1.29 (m, 3H).	405.10
405	3-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.90 (m, 1H), 8.77 (dd,1H), 8.03 (m, 1H), 7.78(m, 1H), 7.48 (m, 1H),7.28 (m, 1H), 7.12 (m,1H), 4.73 (s, 2H), 3.68(s, 3H), 2.36 (s,	
406	4-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (m, 2H), 7.77 (m,1H), 7.62 (m, 2H), 7.31(m, 1H), 7.11 (dd, 1H),4.75 (s, 2H), 3.72 (s,3H), 2.37 (s, 3H)	
407	4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (m, 2H), 8.23 (m,1H), 7.71 (m, 2H), 7.65(m, 1H), 7.18 (d, 1H),4.66 (s, 2H), 3.75	448.02

Ejemplo No.	Nombre	1H RMN	MS
408	3-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (m, 1H), 8.76 (m,1H), 8.22 (m, 1H), 8.05(m, 1H), 7.50 (m, 1H),7.48 (m, 1H), 7.17 (dd,1H), 4.63 (s, 2H), 3.70(s, 3H).	
409	5-(5-bromo-2-fluoró-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.23 (dd, 1H), 7.70 (m,1H), 7.52 (m, 2H), 7.19(m, 2H), 4.49 (s, 2H),3.77 (s, 3H)	452.90
410	5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol	8.06 (d, 2H) 7.34 (d,1H), 7.51 (m, 5H), 4.68(s, 2H), 3.68 (s, 3H).	
411	3-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (s, 1H), 8.78 (d,1H) 8.05 (d, 1H), 7.93(d, 1H), 7.91 (d, 1H),7.50 (m, 2H), 7.28 (t,1H), 4.64 (s, 2H), 3.70(s, 3H).	
412	4-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 7.93 (d,1H) 7.90 (d, 1H), 7.64(d, 2H), 7.52 (m, 1H),7.33 (m, 1H), 4.64 (s,2H), 3.73 (s, 3H).	
413	5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.90 (d, 1H) 7.82 (d,1H), 7.74 (d, 1H), 7.51(m, 3H), 4.58 (s, 2H),3.71 (s, 3H).	
414	3-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.91 (s, 1H), 8.78 (d,1H) 8.23 (d, 1H), 8.04(d, 1H), 7.66 (d, 1H),7.49 (m, 2H), 4.60 (s,2H), 3.69 (s, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
415	3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.22 (d, 1H) 7.74 (d,1H), 7.63 (d, 1H), 7.49(m 3H), 4.54 (s, 2H),3.70 (s, 3H).	
416	2-cloro-4-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.92 (s, 1H), 8.78 (d,1H) 8.65 (d, 1H), 8.04(t, 2H), 7.89 (d, 1H),7.51 (m, 1H), 4.69 (s,2H), 3.71 (s, 3H).	
417	2-cloro-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.82 (d, 2H), 8.65 (d,1H) 8.02 (s, 1H), 7.89(d,1H),7.64 (d, 2H),4.70 (s, 2H), 3.74 (s,3H).	
418	2-cloro-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.64 (d, 1H) 8.01 (s,1H), 7.88 (d, 1H), 7.75,(d,1H),7.52 (m, 2H),4.62 (s, 2H), 3.72 (s,3H).	
419	4-[4-metil-5-(5-fenil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (d, 2H), 8.12 (d,2H) 7.63 (m, 3H), 7.55(m, 2H), 4.63 (s, 2H),3.72 (s, 3H).	
420	3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol	8.11 (d, 2H) 7.74 (d,1H), 7.57 (m, 1H), 7.52(m, 4H), 4.56 (s, 2H),3.70 (s, 3H).	
421	5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-3il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(CD30D como solvente):8.21 (m, 1H),8.02 (m, 1H), 7.82 (m,1H), 7.68 (m, 1H), 7.56(m, 1H), 7.33 (t, 1H),4.50 (s, 2H), 3.82 (s,3H).	

Ejemplo No.	Nombre	1H RMN	MS
422	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol	(CD30D como solvente): 7.84 (s, 1H), 7.75 (m,2H), 7.60 (m, 1H) 7.50(m, 2H), 7.27 (m, 1H),6.92 (s, 1H), 4.51 (s,2H), 4.23 (q,	404.05
423	2-cloro-4-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.64 (d, 1H), 8.01 (s,1H) 7.98 (d, 1H), 7.54(d, 1H), 7.50 (d, 1H),7.20 (m, 1H), 4.61 (s,2H), 3.76 (s, 3H).	392.00
424	4-{5-[3-(3-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (d, 2H), 7.85 (d,1H) 7.78 (d, 1H), 7.62(d, 2H), 7.46 (m, 1H),7.22 (m, 1H), 4.76 (s,2H), 3.72 (s, 3H).	
425	3-(3-fluoro-fenil)-5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.84 (d, 1H) 7.74 (m,1H), 7.51 (m, 3H), 7.24(m, 1H), 4.70 (s, 2H),3.70 (s, 3H).	
426	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	(CD30D como solvente):7.89 (m, 2H),7.76 (m, 1H), 7.60 (m,1H), 7.47 (m, 2H), 7.27(m, 1H), 4.55 (s, 2H),4.25 (q, 2H), 2.41 (s,3H), 1.32 (s, 3H)	384.13
427	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fuoro-5-metil-fenil)-[1,2,4]oxadiazol	(CD30D como solvente):7.85 (m, 1H),7.75 (m, 1H), 7.60 (m,1H), 7.55 (m, 1H), 7.27(m, 1H), 7.22 (m, IH),4.57 (s, 2H), 4.27 (q,2H), 2.36 (s,	402.09

Ejemplo No.	Nombre	1H RMN	MS
428	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente):8.75 (m, 2H),8.04 (m, 2H), 7.78 (m,2H), 7.66 (m, 1H), 7.60(m, 1H), 7.37 (m, 1H),6.30 (m, 2H), 5.42 (s,2H), 4.56 (s, 2H).	452.10
429	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (m, 2H), 8.09 (m,1H), 7.98 (m, 1H), 7.58(m, 3H), 7.50 (dd, 1H),4.69 (s, 2H), 4.12 (m,2H), 1.36 (m, 3H).	
430	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente):8.87 (s, 1H),8.77 (d, 1H), 8.07 (m,3H), 7.67 (m, 2H), 7.61(dd, 1H), 4.62 (s, 2H),4.13 (m, 2H), 1.26 (m,3H).	400.12
431	5-(3-cloro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(CD30D como solvente):7.79 (m, 3H),7.67 (m, 2H), 7.51 (m,2H), 4.56 (s, 2H), 4.22(q,	405.07
432	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente):8.86 (s, 1H),8.76 (d, 1H), 8.07 (m, 1H), 8.01 (m, 2H), 7.64(m, 3H), 7.36 (s, 1H),6.29 (s, 2H), 5.37	452.12
433	3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	(CD30D como solvente) :7.87 (m, 2H),7.73 (m,1H),7.63 (m,1H),7.45(m,3H),7.25 (m,1H),6.31 (m,2H), 5.42(s,2H),4.49(	436.16

Ejemplo No.	Nombre	1H RMN	MS
434	5-(5-fluoro-2-metil-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(CD30D como solvente):7.75 (dd, 1H),7.69 (m, 1H), 7.66 (m,1H), 7.41 (m, 1H), 7.38(m, 1H), 7.25 (m, 2H),6.32 (s, 2H), 5.44 (s,2H), 4.51 (s, 2H), 2.36(s, 3H).	454.12
435	5-(3-cloro-fenil)-3-(4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.23 (s, 1H), 8.09 (m,1H), 7.97 (m, 1H), 7.48(m, 1H), 7.45 (m, 1H),7.37 (s, 1H), 6.39 (m,1H), 6.34 (m, 1H), 5.12(s, 2H), 4.55 (s,	375.09
436	3-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.92 (s, 1H), 8.78 (d,1H) 8.43 (s, 1H), 8.35(d,1H), 8.05(d,1H), 7.91(d,1H),7.72 (t,1H),7.52(m,1H),4.67(s,2H),3.7 1 (s,3H).	376.20
437	3-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.82 (d, 2H), 8.43 (s,1H) 8.35 (d, 1H), 7.90(t, 1H), 7.64 (d, 2H),4.68 (s, 2H), 3.74 (s,3H).	376.10
438	3-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.42 (s, 1H), 8.35 (d,1H) 7.89 (d, 1H), 7.72(m, 2H), 7.52 (s, 1H),4.61 (s, 2H), 3.73 (s,3H).	
439	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.08 (m, 1H), 7.54 (m,2H), 7.48 (d, 1H), 7.20(m, 2H), 4.69 (s, 2H),4.18 (m, 2H), 1.39 (t,3H).	423.12

Ejemplo No.	Nombre	1H RMN	MS
440	2-cloro-4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.64 (d, 1H), 8.02 (s,1H), 7.89 (d, 1H), 7.53(d, 1H), 7.48 (d, 1H),7.20 (t, 1H), 4.69 (s,2H), 4.17 (m, 2H), 1.40(t, 3H).	406.00
441	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.23 (s, 1H), 7.66 (d,1H), 7.53 (d, 1H), 7.48(m, 2H), 7.19 (t, 1H),4.63 (s, 2H), 4.17 (m,2H), 1.40 (t, 3H)	376.10
442	3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	7.93 (m, 2H), 7.71 (m,1H), 7.49 (m, 2H), 7.42(m, 2H), 4.63 (s, 2H),4.10 (q, 2H), 2.43 (s,3H), 1.36 (t, 3H)	384.10
443	4-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.80 (m, 2H), 7.91 (m,2H), 7.60 (m, 2H), 7.41(m, 2H), 4.68 (s, 2H),4.09 (m, 2H), 2.43 (s,3H), 1.29 (s,	379.20 I
444	3-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	(CD30D como solvente):8.87 (s, 1H),8.77 (d, 1H), 8.02 (m,1H), 7.92 (m, 2H), 7.49(m, 1H), 7.42 (m, 2H),4.67 (s, 2H), 4.05 (q,2H), 2.43 (s, 3H), 1.35(t, 3H).	379.20
445	3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	7.88 (dd, 1H), 7.71 (m,1H), 7.49 (m, 2H), 7.28(m, 1H), 7.14 (dd, 1H),4.66 (s, 2H), 4.11 (q,2H), 2.39 (s,	

Ejemplo No.	Nombre	1H RMN	MS
446	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.80 (m, 2H), 7.86 (m,1H), 7.60 (m, 2H), 7.38(m, 1H), 7.14 (dd, 1H),4.70 (s, 2H), 4.11 (q,2H), 2.39 (s, 3H), 1.36(t, 3H).	398.20
447	3-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.87 (s, 1H), 8.76 (d,1H), 8.01 (m, 1H), 7.88(m, 1H), 7.49 (m, IH),7.28 (m, 1H), 7.14 (dd,1H), 4.69 (s, 2H), 4.07(q, 2H), 2.39 (q,	
448	3-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina	(DMSO-D6 como solvente):8.75 (dd, 2H), 8.05 (m,4H), 7.79 (m, 1H), 7.66(dd, 1H), 6.33 (s, 2H),4.65 (s, 2H).	387.05
449	4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (dd, 2H), 8.24 (m,IH), 7.71 (m, 1H), 7.61(m, 2H), 7.18 (dd, 1H),4.72 (s, 2H), 4.13 (m,2H), 1.29 (m,	464.02
450	5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol	7.75 (m, 2H), 7.51 (m,3H), 7.16 (m, 1H), 4.64(s, 2H), 3.70 (s, 3H).	
451	3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.42 (s, 1H), 8.35 (d,1H), 7.89 (d, IH), 7.71(t 1H) 7.54 (d, 1H),7.48 (d, 1H), 7.20 (t,1H), 4.68 (s, 2H),4.16(m, 2H), 1.40 (t, 3H).	395.10

Ejemplo No.	Nombre	1H RMN	MS
452	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol	8.13 (d, 2H), 7.49 (brm, 5H), 7.20 (m, 1H),4.65 (s, 2H), 4.16 (m,2H), 1.40 (t, 3H)	370.09
453	4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metoxi-piridina	8.36 (d, 1H), 7.51 (brm, 3H), 7.42 (s, 1H),7.19 (m, 1H), 4.68 (s,2H), 4.16 (m, 2H), 1.42(t, 3H)	
454	3-(3-cloro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (s, 1H), 7.95 (d,1H), 7.54 (m, 1H), 7.49(m, 1H),7.42 (m, 2H),7.20 (m, 1H), 4.78 (s,2H), 4.17 (q, 2H), 1.41(t,	
455	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-Piridina	8.82 (m, 2H), 7.76 (m,1H) 7.66 (m, 1H), 7.60(m, 2H), 7.41 (m, 2H),6.78 (s, 1H), 4.65 (s,2H), 4.07 (q, 2H), 1.40(t,	399.10
456	2-metil-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.73 (d, 1H), 7.81 (s,, 1H).7.75(s, 2H), 7.51(m,2H) 4.60(s, 2H),3.71(s,3H)2.68(s,3H).	
457	4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.73 (d, 1H), 7.82 (s,1H), 7.76 (d, 1H), 7.54(d, 1H), 7.48 (d, 1H),7.29 (m, 1H), 4.68 (s,2H), 4.16 (m, 2H), 2.68(s, 3H), 1.41 (t,	
458	5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol	7.78 (d, 1H), 7.53 (t,2H), 7.48 (d, 1H), 7.18(m, 2H),376.00 4.74 (s, 2H),4.17 (m, 2H), 1.41	

Ejemplo No.	Nombre	1H RMN	MS
459	4{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 8.09 (m,1H), 7.58 (m, 3H), 7.24(m, 1 H), 4.73 (s, 2H),4.13 (m, 2H), 1.41 (t,3H).	418.10
460	4-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.82 (d, 2H), 8.75 (d,1H), 7.84 (s, 1H), 7.76(d, 1H), 7.60 (d, 2H),4.74 (s, 2H), 4.13 (m,2H), 1.41 (t,
461	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-benzonitrilo	8.11 (s, 1H), 7.97 (m,3H), 7.83 (d, 1H),7.63(m, 3H), 7.50 (t,1H), 4.63 (s, 2H) y 3.68 (s, 3H)	
462	5-(3-cloro-fenil)-3-[5-(3-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d,1H), 7.67(m, 1H), 7.50(m, 5H), 4.61 (s, 2H) y 3.66 (s, 3H).	
463	5-(3-cloro-fenil)-3-[5-(4-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H), 7.55 (m, 6H), 4.61(s, 2H) y 3.64 (s, 3H).	
464	4-{5-[5-(2,5-dicloro-fenil) [1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H),8.05 (m,1H), 7.59 (m,2H), 7.47(s, 2H),4.73 (s, 2H),4.11 (m, 2H), 1.32 (m,3H).	
465	5-(2,5-dicloro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (dd, 1H), 7.50 (m,4H), 7.19 (dd, 1H), 4.68(s, 2H), 4.17 (q, 2H),1.39 (t, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
466	5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.80 (dd, 2H), 7.79 (m,1H), 7.60 (m, 2H), 7.28(m, 1H), 4.68 (s, 2H),4.11 (q, 2H), 1.39 (t, 3H).	406.10
467	4-{5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	7.80 (m, 1H), 7.52 (m,1H), 7.48 (m,1H), 7.20(m, 4H), 4.68 (s, 2H),4.17 (m, 2H), 1.40 (t,3H).	
468	5-(2,5-dicloro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.07 (dd, 1H), 7.71 (dd,, 1H),7.49 (m, 4H), 4.69(s, 2H), 4.12 (m, 2H),1.38 (t, 3H).	
469	5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.80 (m, 1H), 7.72 (m,1H), 7.49 (m, 2H), 7.28(m, 2H), 4.68 (s, 2H),4.12 (q, 2H), 1.37 (t,3H).	406.10
470	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 8.11 (m,1H), 7.99 (m, 1H), 7.57(m, 3H), 7.48 (t, 1H),4.70 (s, 2H), 3.99 (q,2H), 1.72 (m, 2H), 0.91(t, 3H).	
471	4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 7.87 (dd,1H), 7.58 (m, 2H), 7.39(m, 1H), 7.15 (q, 1H),4.70 (s, 2H), 4.01 (m,2H), 2.40 (s, 3H), 1.70(m, 2H), 0.87 (t,	

Ejemplo No.	Nombre	1H RMN	MS
472	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol	7.91 (d, 1H), 7.67 (d,1H), 7.52 (d, 1H), 7.48(d, 1H), 7.20 (m, 2H),4.62 (s, 2H), 4.18 (m, 2H), 1.38 (t,	376.10
473	3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol	7.90 (s, 1H), 7.74 (d,1H), 7.67 (d, 1H), 7.52(m, 2H), 7.21 (m, 1H),4.60 (s, 2H), 3.71 (s,3H) 2.68 (s, 3H).	
474	4-[4-metil-5-(3-tiofen-3-il-[1,2,4]oxadiazol-5-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (d, 2H), 8.05 (s,1H), 7.61 (m, 3H), 7.44(m, 1H), 4.73 (s, 2H),3.70 (s, 3H)	
475	5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol	8.05 (s, 1H), 7.73 (d,1H), 7.62 (d, 1H), 7.51(s, 2H), 7.44 (m, 1H),4.66 (s, 2H), 3.68 (s,3H).	
476	5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol	8.05 (d, 1H), 7.62 (d,1H), 7.53 (d, 1H), 7.47(d, 1H), 7.44 (m, 1H),7.19 (m, 1H), 4.75 (s,2H), 4.15 (m, 2H), 1.40(t, 3H).	376.10
477	5-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-tiofen-3-carbonitrilo	8.18 (d, 1H), 8.03 (d,1H), 7.51 (m, 1H), 7.46(m, 1H), 7.18 (m, 1H),4.63 (s, 2H), 4.16 (q,2H), 1.40 (t, 3H).	401.00

Ejemplo No.	Nombre	1H RMN	MS
478	5-(3-cloro-fenil)-3-[5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d,1H), 7.52(m, 4H), 7.34(t, 1H), 7.27 (m, 1H),4.63 (s, 2H) y 3.54 (s,3H).	
479	5-(3-cloro-fenil)-3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s 1H), 8.00 (d,1H), 7.52(m, 5H), 7.27(m, 1H), 4.62 (s, 2H)y 3.66 (s, 3H).	403.00
480	5-(3-cloro-fenil)-3-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d,1H),7.59(m,4H),7.49(t,1H), 7.22 (m, H),4.61 (s, 2H) y 3.64 (s,3H).	403.10
481	3-(5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H) , 7.87(m, 2H), 7.72(s, 1H), 7.58 (d, 1H),7.45 (m, 3H), 4.60 (s,2H) y 3.85 (s, 3H).	
482	5-(3-cloro-fenil)-3-[5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.59(dd, 1H), 7.49(t, 1H), 7.44 (t, 1H), 7.2(m, 2H), 7.05 (dd, 1H),4.60 (s, 2H), 3.88 (s,3H) y 3.65 (s, 3H).	
483	5-(3-cloro-fenil)-3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s 1H), 8.01 (d,1H), 7.59(m, 3H), 7.49(t, 1H), 7.03 (d, 2H),4.59 (s, 2H), 3.89 (s,3H) y 3.63 (s,3H).	415.00

Ejemplo No.	Nombre	1H RMN	MS
484	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	7.86 (dd, 1H), 7.59 (m,1H), 7.37 (m, 1H), 7.14(m, 2H), 6.58 (q, 1H),4.63 (s, 2H), 4.26 (q,2H), 2.39 (s, 3H), 1.37(t, 3H).	386.10
485	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	7.91 (m, 2H), 7.59 (m,1H), 7.40 (m, 2H), 7.10(q, 1H), 6.58 (q, 1H),4.61 (s, 2H), 4.24 (q,2H), 2.43 (s, 3H), 1.36(t, 3H).	368.20
486	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fuoro-5-metil-fenil)-[1,2,4]oxadiazol	7.97 (m, 1H), 7.47 (m, 1H),7.16 (t,1H), 4.72(d, 2H), 4.16 (m,2H),2.41 (d, 3H),1.37(m,3H).	
487	3-[5-(2-fuoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina	(CD30D como solvente):8.72 (m, 2H),8.17 (m, 2H), 7.86 (dd,1H), 7.49 (m, 1H), 7.23(dd, 1H), 4.59 (s, 2H),2.35 (s, 3H).	
488	3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-ilamina	(CD30D como solvente):8.05 (s, 1H),7.84 (dd, 1H), 7.69 (m,1H), 7.47 (m, 1H), 7.22(m, 2H), 4.52 (s, 2H),2.33 (s, 3H).	
489	3-piridin-4-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina	(CD30D como solvente):8.73 (dd, 2H),8.17 (dd, 2H), 7.89 (m,2H), 7.46 (m, 2H), 4.58(s, 2H), 2.389 (s, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
490	3-tiofen-2-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina	(CD30D como solvente):8.05(dd,1H),7.87(d,2H),7.70(dd,1H),7.45 (m,2H),7.23(q,1H),4.50 (s,2H),2.39(s,	
491	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.23 (m, 1H), 7.66 (m,1H), 7.60 (m, 1H), 7.47(m, 1H), 7.11 (m, 1H),6.60 (m, 1H), 4.61 (s,2H), 4.26 (q, 2H), 1.38(t, 3H).	360.10
492	5-(3-cloro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (m, 1H), 8.00 (m,1H), 7.59 (m, 2H), 7.51(t, 1H), 7.12 (m, 1H),6.60 (m, 1H), 4.63 (s,2H), 4.26 (q, 2H), 1.38(t, 3H).	389.00
493	4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.73 (d, 1H), 7.82 (s,1H), 7.75 (m, 1H), 7.60(m, 1H), 7.12 (m, 1H),6.60 (m, 1H), 4.65 (s,2H), 4.26 (q, 2H), 2.68(s, 3H), 1.39 (t,	
494	5-(2,5-difluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.80 (m, 1H), 7.61 (m,1H), 7.29 (m, 2H), 7.12(m, 1H), 6.60 (m, 1H),4.65 (s, 2H), 4.28 (q,2H), 1.39 (t,	390.09
495	4-[4-etil-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (m, 2H), 7.63 (m,1H), 7.59 (m, 2H), 7.41(m, 2H), 6.58 (s, 1H),4.63 (s, 2H), 4.06 (q,2H), 1.38 (t,	371.00

Ejemplo No.	Nombre	1H RMN	MS
496	4-etil-3-furan-2-il-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol	7.77 (m, 1H), 7.60 (m,1H) 7.40 (m, 2H), 7.10(m, 1H), 6.60 (m, 1H),6.55 (s, 1H), 4.58 (s,2H), 4.21 (q, 2H), 1.38(t, 3H).	359.10
497	5-(3-cloro-fenil)-3-[5-(3,5-dicloro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.60(d, 1H), 7.54(s, 3H), 7.47 (t, 1H),4.69 (s, 2H),4.06 (q, 2H) y 1.36 (t, 3H).	
498	5-(3-cloro-fenil)-3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01(d,1H), 7.53(m, 4H), 7.20(d, 2H), 4.68 (s, 2H),4.03 (q, 3H), 2.45(s,1H) y 1.32 (t, 3H).	
499	5-(3-cloro-fenil)-3-(4-etil-5-m-tolil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d,1H), 7.58(d, 1H), 7.297.50(m, 5H), 4.66 (s,2H), 4.02 (q, 2H), 2.45(s, 1H) y 1.32 (t, 3H).	
500	5-(3-cloro-fenil)-3-[4-etil-5-(3-nitro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.52 (s, 1H), 8.40 (d,1H), 8.12 (s, 1H), 8.05(dd, 2H), 7.76(t,1H)(t, ,7.60 (d, 1H), 7.50(t,1H), 4.72 (s, 2H),4.10 (q, 2H) y 1.41 (t,3H).	
501	4-{5-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	7.80 (m, 2H), 7.78 (m,1H), 7.65 (m, 1H), 7.59(m, 2H), 7.40 (m, 2H), 6.65 (s, 1H), 4.67 (s,2H), 3.64 (s, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
502	5-(3-cloro-fenil)-3-[5-(2,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-isulfanilmetil]-[1,2,4]oxadiazol	8.14 (s, 1H), 8.02 (d,1H), 7.60(d, 1H), 7.52(t, 1H), 7.32 (m, 1H),7.23 (m, 2H), 4.70 (s,2H), 3.96 (q, 2H) y 1.27 (t, 3H).	
503	5-(3-cloro-fenil)-3-[5-(3-cloro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.06 (d,1H), 7.63(s, 1H), 7.58(d, 1H), 7.49 (m, 4H),7.23 (m, 2H), 4.68 (s,2H), 4.04 (q, 2H) y 1.34 (t, 3H).	
504	5-(3-cloro-fenil)-3-[5-(4-cloro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d,1H), 7.3(m,6H), 4.68 (s,2H),4.03 (q, 2H) y 1.34 (t, 3H).	
505	4-{5-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.78 (d, 2H), 7.55 (m,3H), 7.44(m, 1H), 7.29(m, 3H), 4.69 (s, 2H),4.04 (q, 2H) y 1.34 (t,3H).	
506	3-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol	7.55 (s, 1H), 7.50 (d,1H), 7.44(m, 2H), 7.28(m, 3H), 7.18 (dd, 1H),4.64 (s, 2H), 4.10 (q,2H) 7.58 (s, 1H),	404.00
507	3-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.53 (s,1H), 7.40 (m, 1H), 7.27(m, 3H), 7.10 (d, 1H),6.68 (d, 1H), 4.62 (s,2H), 4.19 (q, 2H) y 1.33 (t,	388.00

Ejemplo No.	Nombre	1H RMN	MS
508	5-(2-cloro-5-metil-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.83 (s, 1H), 7.53 (d,1H), 7.44 (m, 2H), 7.32(d, 1H), 7.18 (t, 2H),4.63 (s, 2H), 4.17 (q,2H), 2.37 (s, 3H), 1.38(t, 3H).	
509	4-{5-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-etil-4H)-[1,2,4]triazol-3-il}-piridina	8.80 (m, 2H), 7.78 (m,1H), 7.66 (m, 1H), 7.57(m, 2H), 7.41 (2H),6.67 (s, 1H).4.71(s,2H), 4.03 (q,2H), 1.36(t, 3H).	
510	3-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol	7.78 (s, 1H), 7.64 (m,1H) 7.52 (m, 1H), 7.41(m, 3H), 7.18 (m, 1H),6.65 (s, 1H), 4.66 (s,2H), 4.08 (q, 2H), 1.36(t, 3H).	404.00
511	3-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.77 (s,1H),7.64 (d,1H), 7.59 (m, 1H), 7.39(m, 2H), 7.10 (m, 1H),6.62 (s, 1H), 6.59 (m,1H), 4.65 (s, 2H), 4.17(q, 2H), 1.35 (t, 3H).	388.10
512	4-{5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina		

596

Ejemplo No.	Nombre	1H RMN	MS
513	5-(2,5-dicloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(DMSO-d6 como solvente):7.82(d d, 1H), 7.65 (d,1H), 7.58 (m,1H), 7.25(m, 1H), 4.60 (s, 2H),4.16 (q, 2H), 1.24 (t,3H).	
514	4-{5-[5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.78(d, 2H), 7.71 (d,2H), 7.68 (m,1H), 4.67(s, 2H), 4.10 (q, 2H),1.21 (t, 3H).	
515	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.81 (m, 2H), 7.73 (m,1H), 7.60 (m, 2H), 7.21(m, 1H), 7.07 (m, 1H),6.76 (m, 1H), 4.63 (s,2H), 4.02 (q, 2H), 2.40(s, 3H), 1.38 (t,	
516	4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-tiofen-2-il-4H-[1,2,4]triazol	7.71 (d, 1H), 7.53 (m,1H), 7.47 (m, 1H), 7.46(m, 2H), 7.07 (m, 1H),6.77 (d, 1H), 4.63 (s,2H), 4.12 (q, 2H), 2.40(s, 3H), 1.39 (t,	
517	4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-furan-2-il-4H-[1,2,4]triazol	7.72 (d, 1H), 7.60 (m,1H), 7.10 (m, 1H), 7.05(m, 2H), 6.77 (d, 1H),6.60 (m, 1H), 4.61 (s,2H), 4.21 (q, 2H), 2.39(s, 3H), 1.38 (t,	
518	5-(3-cloro-fenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H), 7.60 (d, 1H), 7.50(t, 1H), 4.72(s, 2H), 4.12(q, 2H) y 1.42 (t, 3H).	391.00

Ejemplo No.	Nombre	1H RMN	MS
519	3-(3-cloro-fenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.05 (s, 1 H), 7.94 (d,1H) , 7.50 (d,1H), 7.43(t, 1H), 4.83(s, 2H), 4.13(q, 2H) y 1.44 (t, 3H)	
520	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.23 (s, 1H), 7,65 (d,1H), 7.48 (m, 1H), 4.69 (s, 2H), 4.12 (q, 2H) y 1.41 (t, 3H).	
521	5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-isulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol	8.05 (s, 1H), 7,61 (d,1H), 7.43 (m, 1H), 4.81(s, 2H), 4.12 (q, 2H) y 1.43 (t, 3H).	
522	5-(3-cloro-fenil)-3-[4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (d, 1H), 8.00 (d,1H), 7.52 (m, 4H), 7.25(m, 2H), 4.67 (s, 2H),4.06 (q, 2H), 1.31 (t,3H).	
523	5-(3-cloro-fenil)-3-[4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.10 (s, 1H), 7.99 (d,1H), 7.59 (m, 4H), 7.48(t, 1H), 7.22 (d, 1H),4.67 (s, 2H), 4.01 (q,2H), 1.30 (t, 3H)	
524	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol	7.91 (s, 1H), 7,68 (d,1H), 7.21 (m, 1H), 4.67(s, 2H), 4.13 (q, 2H) y 1,41 (t, 3H).	
525	3-{3-[5-(3-cloro-tiofen-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-benzonitrilo	8.35(m, 2H), 7.89 (d,1H), 7.87 (t, 1H), 7.58(d,1H), 7.09 (d,1H),4.70 (s, 2H), 4.00 (q, 2H), 1.27 (t, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
526	4-[5-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 8.01 (d,1H), 9.93 (m, 1H), 7.59(m, 2H), 7.52 (m, 1H),7.47 (m, 1H), 4.83 (s,2H), 4.11 (q, 2H), 1.40(t, 3H).	400.10
527	2-(3-cloro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.00 (s, 1H), 7.89 (d,1H), 7.60 (m, 1H), 7.50(m, 1H), 7.44 (m, 1H),7.13 (m, 1H), 6.60 (m,1H), 4.76 (s, 2H), 4.25(q, 2H), 1.38 (t, 3H).	389.00
528	5-(3-cloro-fenil)-3-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.57 (m, 3H), 7.51(t, 1H), 7.05 (d, 2H),4.67 (s, 2H), 4.02 (q,2H), 3.89 (s, 3H), 1.31(t, 3H).	
529	5-(3-cloro-fenil)-3-[5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.02 (d,1H), 7.58 (d, 1H), 7.52(d, 1H), 7.35 (d, 2H),7.23 (s, 1H), 7.22 (d,1H), 6.19 (s, 1H), 6.04(s, 1H), 5.13 (s, 2H),4.61 (s, 2H), 2.37	
530	4-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.74 (d, 1H), 7,81 (s,1H), 7.74 (d, 1H), 4.74(s, 2H), 4.12 (q, 2H)2.69 (s,1H) y 1.42 (t, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
531	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol	7.70 (d, 1H), 7,60 (s,1H), 7.44 (t, 1H), 7.16(d, 1H), 4.70 (s, 2H),4.12 (q, 2H), 3.90 (s,3H) y 1.41 (t, 3H).	
532	5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-metoxi-fenil)-[1,2,4]oxadiazol	7.63 (d, 1H), 7,56 (s,1H), 7.39 (t, 1H), 7.07(d, 1H), 4.82 (s, 2H),4.12 (q, 2H) y 1.42 (t,3H).	
533	5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol	7.77 (s, 1H), 7,52 (d,1H), 7.16 (m, 1H), 4.79(s, 2H), 4.13 (q, 2H) y 1.42 (t, 3H).	
534	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	8.07 (dd, 1H), 7.56 (m,1H), 7.24 (dd, 1H), 4.73(s, 2H), 4.13 (q, 2H) y 1.42 (t, 3H).	
535	3-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.40 (s, 1H), 8.34 (d, 1H),7.91(d,1H),7.01(t, 1H), 4.73 (s, 2H),4.12 (q, 2H) y 1.42 (t,3H).	381.10
536	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol	7.75 (s, 1H), 7.63 (m,1H), 7.40 (m, 2H), 6.73(s, 1H), 4.65 (s, 2H),4.07 (q, 2H) y 1.40 (t,3H).	
537	3-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol	7.58 (s, 1H), 7.46 (d,1H), 7.32 (d, 3H), 4.74(s, 2H), 4.09 (q, 2H) y 1.39 (t, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
538	4-etil-3-(5-tiofen-3-il-isoxazol-3-ihnetilsulfanil)-5-trifluorometil-4H-[1,2,4]triazol	7.78 (s, 1H), 7.39 (m,1H), 6.53 (d, 1H), 4.63(s' 2H), 4.07 (q, 2H) y 1.39 (t, 3H).	
539	4-{3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il} -2-metil-piridina	8.73 (d, 1H), 7.83 (s,1H), 7.76 (d, 1H), 7.47(m, 3H), 7.27 (s, -1H),4.65 (s, 2H), 3.67 (s,3H), 2.69 (s,	
540	4-{3-[5-(3-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il} -2-metil-piridina	8.74 (d, 1H), 7.82 (s,1H), 7.67 (d, 1H), 7.56(d, 1H), 7.51 (m, 1H),7.48 (m, -1H), 7.46 (s,1H), 4.65 (s, 2H), 3.67(s, 3H), 2.69 (s,	
541	4-{3-[5-(4-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il} -2-metil-piridina	8.73 (d, 1 H), 7.82 (s,1H), 7.75 (d, 1H), 7.63(d , 2H), 7.51 (d, -2H),4.65 (s, 2H), 3.65 (s,3H), 2.69 (s,	
542	4-{3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}- 2-metil-piridina	8.73 (d, 1H), 7.83 (s,1H), 7.45 (d, 1H), 7.61(d, 2H), 7.04 (d, 2H),4.62 (s, 2H), 3.89 (s,3H), 3.64 (s, 3H), 2.69(s, 3H).	
543	4-[3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.74 (d, 1H), 7.85 (s,1H), 7.77 (d, 1H), 7.51(d, 2H), 7.32 (d, 2H) 4.70 (s, 2H), 4.03 (q,2H), 2.70 (s, 3H), 2.45(s, 3H), 1.31 (t, 3H).,	

Ejemplo No.	Nombre	1H RMN	MS
544	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-fluoro-fenil)-[1,2,4]oxadiazol	(DMSO-d6 como solvente):7.93(m, 1H), 7.86 (m,2H), 7.80 (m,1H), 7.67(m, 2H), 7.25 (m,1H),4.61 (s, 2T, 4.16 (q,2H), 1.24 (t, 3H).	I 388.10
545	4-(4-etil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3 -ilmetilsulfanil]-4H-[1,2,4]triazol-3-il)-piridina	8.78(bs, 2H), 7.92 (m,2H), 7.71 (d, 2H), 7.68(4.70 m,1H), 7.27 (m,1H),(s, 2H), 4.10 (q,2H), 1.39 (t, 3H).	383.10
546	5-(3-cloro-fenil)-3-[5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H), 7.58 (d, 1H), 7.50(t, 1H), 7.21 (m, 2H),7.00 (t, 1H), 4.68 (s,2H), 4.07 (q, 2H), 1.35(t, 3H).	
547	5-(3-cloro-fenil)-3-[5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.02 (d,1H), 7.59 (m, 2H), 7.52(d, 1H), 7.41 (d, 1H),7.04 (d, 1H), 4.73 (s,2H), 4.21 (q, 2H), 1.42(t, 3H).	
548	2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol	9.89 s 1H 7.70 s,1H) 7.56 (d, 1H), 7.54(d' 1H), 7.30 (m, 1H),7.18 (m, 1H), 6.98 (d,1H), 4.66 (s, 21-1), 4.12(q, 2H), 2.34 (s, 3H),1.37 (t, 3H).	399.90

Ejemplo No.	Nombre	1H RMN	MS
549	3-(1-[5-(3-cloro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.73 (bs, 1H), 7.59 (m,2H), 7.41 (m, 2H), 7.10(dd, 1H), 6.59 (m, 2H),5.05 (q, 1H), 4.13 (q,2H), 1.91 (d, 3H), 1.27(t, 3H).	401.10
550	4-(5-{1-[5-(3-cloro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.8 (dd, 2H), 7.74 (bs,1H), 7.63 (m, 1H), 7.57(dd, 2H), 7.40 (m, 2H),6.62 (s, 2H), 5.15 (q,1H), 4.05 (q, 2H), 1.95(d, 3H), 1.34 (t,	
551	3-[5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.58 (d, 1H), 7.52, 2H), 7.49 (d, 1 H),7 (d.01 (d, 2H), 4.69 (s,2H), 4.02 (q, 4H), 1.82(m, 2H), 1.51 (q, 2H),1.32 (t, 3H), 1.01 (t,3H).	
552	3-(5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.12 (s, 1H), 8.00 (d,1H), 7.58 (d, 1H), 7.51(d, 1H), 7.09 (d, 2H),6.96 (s, 1H), 6.08 (s,2H), 4.67 (s, 2H), 4.02(q, 2H), 1.31 (t,	
553	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-metil-tiazol-4-il)-[1,2,4]oxadiazol	8.11 (s, 1H), 7.48 (m,2H), 7.16 (t, 1H), 4.63(s, 2H), 4.13 (q, 2H), 2.82 (s, 3H), 1.37 (t,3H).	391.90

Ejemplo No.	Nombre	1H RMN	MS
554	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-fluoro-fenil)-[1,2,4]oxadiazol	(DMSO-d6 como solvente):8.21 (m, 2H), 7.51 (m,2H), 7.21 (m,3H), 4.63(s, 2H), 4.16 (q, 2H),1.38 (t, 3H).	
555	4-etil-3-{1-[5-(2-fluoro-5-metil- 1H)-etilsulfanil}-5-furan-2-il-4H-[1,2,4]triazole	7.71 (dd, 1H), 7.59 (dd,, 7.26 (m, 1H), 7.06(m, 2H) 6.(d, 1H) ,61H),58 (dd,, 1H)66, 5(q,4 .13 (q, 2H),.06 2.39(s, 3H), 1.91 (d, 3H),1.28 (t, 3H).	
556	4-(4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 7.71 (dd,1H) , 7.59 (dd, 2H), 7.23(m, 1 H) , 7 (m, 1 H),6.64 (d, 1H).06, 5.15 (q,1H), 4.01 (q, 2H), 2.39(s, 3H), 1.94 (d, 3H),1.30 (t, 3H).	410.10
557	5-(3-cloro-fenil)-3-[4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d,1H), 7.66 (s, 1H), 7.58(d, 1H), 7.52 (t, 1H),7.37 (s, 1H), 4.69 (s,2H), 4.09 (q, 2H), 3.93(s, 3H), 1.37 (t,	
558	5-(3-cloro-fenil)-3-[4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.57 (d, 1H), 7.51(t, 1H), 7.17 (s, 1H),7.04 (s, 1H), 4.69 (s, 2H), 4.56 (q, 2H), 4.12(s, 3H), 1.40 (t, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
559	5-(3-cloro-fenil)-3-[4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.65 (s, 1H), 7.57(d, 1H), 7.48 (d, 2H),4.60 (s, 2H), 4.50 (q,2H), 3.79 (s, 3H), 1.36(t, 3H).	
560	4-{5-[5-(3-cloro-fenil)-4-metil-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (bs, 2H), 7.70 (m,1H), 7.61 (m, 3H), 7.44(m, 2H), 4.65 (s, 2H),4.09 (q, 2H), 2.31 [illegible]	
561	3-[5-(3-cloro-fenil)-4-metil-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.70 (s, 1H), 7.60 (m,2H), 7.43 (m, 2H), 7.10(m, 1H), 6.59 (m, 1H),4.59 (s, 2H), 4.23 (q,2H), 2.28 (s, 3H), 1.38(t,31-1).	
562	3-(4-etil-5-tiofen-2-il-4H [1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil=tiofen-2-il)-[1,2,4]oxadiazol	7.61(d, 1H), 7.49 (m,2H), 7.22 (m,2H), 4.59(s, 2H), 4.16 (q,2H),2.32 (s,3H), 1.38 (t,3H).	
563	5-(3-cloro-fenil)-3-[4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d,1H), 7.58 (d, 1H), 7.52(d, 1H), 7.45 (d, 1H),7.02 (d, 1H), 4.69 (s,2H), 3.97 (q, 2H), 2.32(s, 3H), 1.28 (t,	
564	15-(3-cloro-fenil)-3-[4-etil-5- I(5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d, (5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil] - [1,2,4]oxadiazol	

Ejemplo No.	Nombre	1H RMN	MS
565	4-{5-[4-cloro-5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (d, 2H), 7.99 (m,1H), 7.90 (m, 1H), 7.60(m, 2H), 7.48 (m, 2H),4.65 (s, 2H), 4.10 (q,2H), 1.39 (t, 3H).	
566	3-[4-cloro-5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.99 (s, 1H), 7.90 (m,1H), 7.60 (m, 1H), 7.47(m, 2H), 7.12 (m, 1H),6.60 (m, 1H), 4.59 (s,2H), 4.25 (q, 2H), 1.38(t, 3H).	
567	2-cloro-4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metil-piridina	8.11 (s, 1H), 8.00 (d,1H), 7.58 (d, 1H), 7.52(d, 1H), 7.40 (d, 2H),4.71 (s, 2H), 4.10 (q,2H), 2.64 (s, 31-1), 1.40(t, 3H).	
568	3-[5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.11 (s, 1H), 7.99 (d,1H), 7.58 (d, 1H), 7.51(t, 1H), 7.07 (d, 1H),6.52 (d, 1H), 4.64 (s,2H), 4.23 (q, 2H), 1.40(t, 3H).	
569	2-cloro-4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il} -piridina	8.59 (d, 1H), 8.10 (s,1H), 8.00 (d, 1H), 7.66(s, 1H), 7.59 (d, 1H), 7.54 (d, 1H), 7.50 (d,1H), 4.72 (s, 2H), 4.11(q, 2H), 1.42 (t, 3H).	

Ejemplo No.	Nombre	1H RMN	MS
570	2-cloro-4- {5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il} -6-metoxi-piridina	8.11 (s, 1H), 8.00 (d,1H), 7.58 (d, 1H), 7.50(t, 1H), 7.24 (s, 1H),6.91 (s, 1H), 4.70 (s,2H), 4.08 (q, 2H), 4.02(s, 3H), 1.39 (t,	464.10
571	2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-benzonitrilo	8.02 (s, 1H), 7.76 (d,2H), 7.47 (m,3H), 7.17(t, 1H), 4.68 (s, 2H),4.19 (q, 2H), 2.51 (s,3H), 1.39 (t,	
572	5-(3-cloro-fenil)-3-[4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.14 (s, IH), 8.03 (d,1H), 7.58 (d, 1H), 7.50(d, 1H), 7.44 (d, 1H),6.94 (1H), 4.67 (s, 2H),4.03 (q, 2H), 3.88 (s,3H), 1.29 (t,	
573	3-[5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.61 (m, 1H), 7.52 (d,1H), 7.21 (d, 1H), 7.11(m, 1H), 7.61 (m, 1H),6.55 (s, 1H), 4.57 (s,2H), 4.21 (q, 2H), 1.38(t, 3H).	393.10
574	3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-5-fluoro-benzonitrilo	8.21(m, 1 H), 8.04 (dd,1H), 7.59 (m, 2H), 7.10(dd4.64 ,1H),6.59(dd,1H) ,(s, 2H), 4.25 (q,2H), 1.38 (t, 3H).	
575	4-etil-3-(5-fenil isoxazol-3-ilmetilsulfanil)-5-tiofen-2-il-4H-[1,2,4]triazol	7.77 (m, 2H), 7.53 (d,1H), 7.47 (m, 4H), 7.19(dd, 1H), 6.71 (s, 1H),4.61 (s, 2H), 4.12 (q,2H) and 1.39 (t,	

Ejemplo No.	Nombre	1H NMR	MS
576	4-metil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-3-il-4H-[1,2,4]triazol	7.77 (m, 3H), 7.50 (m,5H), 6.69 (s, 1H), 4.56(s, 2H) y 3.67 (s, 3H)	
577	4-etil-3-furan-2-il-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol	7.77 (m, 2H), 7.61 (s,1H) , 7.46 (m, 3H), 7.14(d, 1H), 6.69 (s, 1H),6.60 (d, 1H), 4.60 (s,2H), 4.22 (q, 2H) y 1.38 (t, 3H).	
578	4-[4-etil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (w, 2H), 7.77 (m,2H), 7.61 (d, 2H), 7.45(m, 3H), 6.71 (s, 1H),4.65 (s, 2H), 4.06 (q,2H) y 1.39 (t, 3H).	
579	4-[4-metil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (w, 2H), 7.77 (m,2H), 7.63 (d, 2H), 7.46(m, 3H), 6.70 (s, 1H),4.60 (s, 2H) y 3.68 (s,3H).	
580	2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,3,4]oxadiazol	7.80 (m, 2H), 7.70 (m,1H), 7.35(m, 2H), 7.13(m, 2H), 6.60 (m, 1H),4.74 (s, 2H), 4.23 (q,2H), 2.40 (s, 3H), 1.36(t, 3H).	368.10
581	4-[4-metil-5-(5-m-tolil-[1,3,4]oxadiazol-2-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (m, 2H), 7.80 (m, 2H), 7.61 (d, 2H), 7.39(m, 2H), 4.74 (s, 2H),3.71 (s, 3H), 2.4 (s, 3H).	365.10

Ejemplo No.	Nombre	1H RMN	MS
582	4-[4-etil-5-(5-m-tolil-[1,3,4]oxadiazol-2-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (d, 2H), 7.81 (m,2H), 7.58 (m, 2H), 7.37(m, 2H), 4.81 (s, 2H),4.41 (q, 2H), 2.42 (s,3H), 1.33 (t,	379.10
583	4-{5-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-	8.80 (d, 2H), 7.98 (m,1H), 7.58 (d, 2H), 7.46(d ,1H), ,1H), 4.66 (s, 2H),4.10 (q, 2H), 1.38(t,3H).	405.90
584	3-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo	8.79 (bs, 2H), 8.46 (m,1H) , 7.91 (m, 1H), 7.59(4,.74 2H),, 7(t, 1H),(s2H).43 , 4 .12 (q,2H), 1.41 (t,3H).	
585	3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo	8.45(dd, 1H), 7.91 (m,1H), 7.59 (d, 1H), 7.43(t, 1H), 7.10 (d, 1H),6.58 (dd,1H), 4.65 (s,2H), 4.27 (q, 2H), 1.39(t, 3H).	397.10
586	3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo	8.45 (dd, 1H), 7.90 (m,1H), 7.47 (m,3H), 7.18(t, 1H), 4.68 (s, 2H),4.17 (q, 2H), 1.41 (t,3H).	
587	3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.41 (m, 2H), 7.89 (d,1H), 7.69 (d, 1H), 7.13(m, 1H), 6.60 (m, 1H),4.65 (s, 2H), 4.27 (q,2H), 1.40 (t, 3H).	379.10

Ejemplo No.	Nombre	1H RMN	MS
588	3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo	8.36 (m, 2H), 7.80 (t,1H), 7.62 (m, 2H), 7.15(m, 1H), 6.61 (m, 1H),4.78 (s, 2H), 4.2 (q, 2H),1.40 (t,	379.10
589	3-[3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.41 (m, 2H), 7.90 (m,1 H), 7.72 (t, 1H), 4.68(s, 2H), 3.73 (s, 3H).	
590	5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	8.08 (m, 1H), 7.58 (m,1H), 7.25 (m, 1H), 4.67(s, 2H), 3.74 (s, 3H).	394.90
591	2-cloro-4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.63 (m, 1H), 8.02 (m,1H), 7.89 (m, 1H), 7.61(m, 1H), 7.14 (m, 1H),6.61 (m, 1H), 4.67 (s,2H), 4.27 (q, 2H), 1.40(t, 3H).	390.00
592	2-cloro-4-[3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.63 (d, 1H), 8.00 (d,1H), 7.88 (m, 1H), 7.62(d, 1 H), 7.14 (d, 1 H),6.61 (m, 1H), 4.60 (s,2H),	
593	2-(3-cloro-fenil)-5-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	7.98 (m, 2H), 7.89 (d,1H), 7.49 (m, 1H), 7.44(m, 1H), 4.69 (s, 2H),3.92 (s, 3H), 2.77 (s, 3H).	
594	2-(3-cloro-fenil)-5-(4-metil-5-tiazol-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.91 (s, 1H), 8.24 (s,1H), 7.98 (s, 1H), 7.91(d, 1H), 7.49 (m, 1H),7.43 (m, 1H), 4.72 (s,2H), 3.96 (s,	

Ejemplo No.	Nombre	1H RMN	MS
595	2-(3-cloro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.00 (s, 1H), 7.89 (d,1H), 7.60 (s, 1H), 7.53(m, 1H), 7.43 (m, 1H),7.12 (d, 1H), 6.60 (d de d, 1H), 4.68 (s, 2H),3.80 (s, 3H).	
596	2-(3-cloro-fenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.00 (s, 1H), 7.90 (d,1H), 7.52 (m, 2H), 4.86(s, 2H), 4.13 (q, 2H),1.42 (t, 3H).	
597	4-{4-etil-5-[5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 7.68 (s,(m4,, 1H).59 72H), 7.23.101H), 4(d,.63 (s, 2H),(q, 2H), 2.32(d,3H), 1.37 (t,3H).	
598	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol	7.67 (d, 1H), 7.59 (m,1H), 7.2 (s, 1H), 7.09 (d,1H), 6.58 (dd,1H), 4.56(s, 2H), 4.24 (q, 2H),2.32 (s, 3H), 1.36 (t,3H).	374.00
599	3-(3-cloro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.02 (m, 1 H), 7.91 (m,1H), 7.57 (d, 1H), 7.35(m, 2H), 7.08 (d, 1H),6.56 (dd,1H), 4.72 (s, 2H), 4.22 (q, 2H), 2.32(s, 3H), 1.36 (t, 3H)	
600	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfa il]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (dd, 2H), 8.02(m,1H), 7.92 (m, 1H),7.57 (dd, 2H), 7.42(m,2H), 4.80 (s, 2H),4.08 (q, 2H), 1.38(t,3H).	

Ejemplo No.	Nombre	1H RMN	MS
601	4-{4-etil-5-[5-(3-nitro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.87 (m, 3H), 8.42 (m,2H), 7.75 (t, 1H), 7.66(d° 2H), 4.88 (s, 2H),4.15 (q, 2H), 1.45 (t,3H).	
602	2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,3,4]oxadiazol	8.87 (t, 1H), 8.39 (m,2H), 7.73 (t, 1H), 7.61(m, 1H), 7.15 (m, 1H),6.61 (m, 1H), 4.28 (q,2H), 1.78 (s, 2H), 1.41(t, 3H).	
603	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 7.78 (m,3H) , 7.66 (m, 1H), 7.39(m, 2H), 6.84 (s, 1T,4.69 (s, 2H), 3.27 (m,1H), 1.20 (q, 2H), 0.83(m, 2H).	411.00
604	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol	7.77 (m, 1H), 7.65 (m,1H), 7.56 (m, 2H), 7.41(m, 2H), 7.04 (m, 2H),6.79 (s, 1H), 4.61 (s,2H), 3.97 (q, 2H), 3.89(s, 3H), 1.32 (t,	428.20
605	5-(3-cloro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol	8.08 (rn, 1H), 7.96 (dd,1H), 7.45 (m, 4H), 7.17(m, 1H), 4.93 (q , 1H),3.67 (s, 3H), 1.91(d,3H).	404.92
606	5-(3-cloro-fenil)-3-[1-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol	8.1(d, 1H), 7.98 (d, 1H),7.51 (m,4H), 7.17 (t,1H), 5.11 (q, 1H), 4.11(q, 2H), 1.93 (d,3H),1.34 (t, 3H).	418.90

Ejemplo No.	Nombre	1H RMN	MS
607	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.08(m,1H), 7.98 (dd, 1H),7.59 (m, 3H), 7.46 (t,1H), 5.05 (q, 1H), 3.66(s, 3H), 1.94 (d, 3H).	400.07
608	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.1 Q(m, 1H), 7.99 (dd, 1H),7.58 (m, 3H), 7.47 (t,1H), 5.20 (q, 1H), 4.06(q, 2H), 1.96 (d, 3H),1.33 (t,3H).	414.05
609	3-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo	8.84 (s, 2H),8.30 (m,2H), 7.85 (m, 1H), 7.66(m, 3H), 4.84 (s, 2H),4.14 (q, 2H), 1.43 (t,3H).	
610	3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo	8.27 (m, 2H), 7.82 (m,1H), 7.62 (m, 2H), 7.18(t, 1H), 6.62 (m, 1H),4.79 (s, 2H), 4.27 (q,2H), 1.40 (t, 3H)	
611	3-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo	8.83(d,21-1),8.31(m,2H), 7.84 (m, 4H), 4.81(s, 2H), 3.77 (s, 3H).	
612	3-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil-mil]-etil)-[1,3,4]oxadiazol-2-il-benzonitrilo	8.82 (s, 2H), 8.33 (m,2H), 7.86 (t, 3H), 7.67(t, 1 H), 4.91 (d, 2H),1.24 (m, 3H), 0.88 (m,2H).	402.20

Ejemplo No.	Nombre	1H RMN	MS
613	4-{5-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente 8.80 (s (br), 2H), 7.96(m, 2H), 7.81(d,2H),7.61 (m, 2H), 4.73 (s,2H), 3.84 (s, 3H).	
614	4-{5-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente):8.75 (d, 2H), 8.02 (s,1H), 7.96 (d, 1H), 7.89(d , 2H), 7.60 (m, 2H),4.89 (s, 2H), 3.59 (m,1H), 1.21 (m, 2H), 0.84(m, 2H).	412.16
615	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	7.80 (m, 2H), 8.04 (m,1H), 7.77 (d, 2H), 7.51(m, 1H), 7.21 (t, 1H),4.92 (s, 2H), 3.32 (m,1H), 1.21 (m, 2H), 0.85(m, 2H).	430.11
616	2-(5-cloro-2-fluoro-fenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	8.02 (m, 1H), 7.52 (m,3H), 7.20 (t, 1H), 7.04(m, 2H), 4.81 (s, 2H),4.03 (q, 2H), 3.89 (s,3H), 1.33 (t, 3H).	

617	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (d, 2H), 8.03 (m,1H), 7.65 (m, 2H), 7.51(m, 1H), 7.20 (t, 1H), 4.78 (s, 2H), 3.75 (s,3H).	
618	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (bs, 2H), 8.02 (m,1H), 7.61 (m, 2H), 7.51 (m, 1H), 7.20 (t, 1H), 4.85 (s, 2H), 4.13 (q,2H), 1.41 (t, 3H).	
619	2-(3-cloro-fenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	8.01 (d of d collapsed,1H), 7.85 (d, 1H), 7.51 (m, 4H), 7.00 (d,2H), 4.79 (s, 2H), 4.00(q, 2H), 3.88 (s, 3H), 1.30 (t, 3H).	
620	2-(3-cloro-fenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol	7.97 (s, 1H), 7.84 (d,1H), 7.58 (d, 1H), 7.49 (m, 1H), 7.40 (m, 1H), 7.12 (d, 1H), 6.59 (d de d, 1H), 5.16 (q, 1H), 4.17 (q, 2H), 2.02 (d,3H), 1.28 (t, 3H).	
621	5-(5-cloro-2-fluoro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol	8.06 (m, 1H), 7.54 (m, 3H), 7.23 (m, 2H), 4.93 (q, 1H), 3.72 (s, 3H),1.91 (d,3H).	
622	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.07 (dd,1H), 7.62 (dd, 2H), 7.54 (m, 1H), 7.21 (t, 1H), 5.07 (q, 1H), 3.69 (s, 3H), 1.95 (d, 3H).	418.10

623	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.08 (m,1H), 7.57 (m, 3H), 7.22 (t, 1H), 5.21 (q, 1H), 4.08 (q, 2H), 1.97 (d, 3H), 1.35 (t,3H).	
624	2-cloro-4-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.83 (m, 2H), 8.65 (m, 1H), 8.05 (t, 1H), 7.92(t, 1H), 7.76 (t, 2H), 4.82 (2H), 3.31 (m, 1H), 1.23 (m, 2H), 0.86 (m,2H).	
625	4-{5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (t, 2H), 7.82 (m, 1H), 7.63 (m, 2H), 7.32 (m, 1H), 7.10 (m, 1H), 4.75 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H), 1.61 _ (d, 1H).	
626	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 7.82 (m,1H), 7.59 (t, 2H), 7.33(m, 1H), 7.11 (m, IH),4.82 (s, 2H), 4.10 (m,2H), 2.39 (s, 3H), 1.38(t, 3H).	397.08
627	4-{4-Ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.80 (s, 2H), 7.84 (m,1H), 7.76 (d, 2H), 7.32(m, 1H), 7.12 (q, 1H),4.91 (s, 2H), 3.31 (m,1H), 2.39 (d, 3H),1.21(m, 2H), 0.84 (m, 2H).	409.15

628	2-(4-etil-5-füran-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol	7.77 (m, 1H), 7.61 (m,1H), 7.32 (d, 1H), 7.12(m, 2H), 6.61 (m, 1H),4.76 (s, 2H), 4.26 (q,2H), 2.37 (d, 3H), 1.23(t, 3H).	
629	2-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol	7.81 (m, 1H), 7.54 (m,2H), 7.32 (d, 1H), 7.11(m, 1H), 7.03 (m, 2H),4.79 (s, 2H), 4.02 (q,2H), 3.89 (s, 3H), 2.37(d, 3H), 1.31 (t, 3H).	426.15
630	4-(5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.82 (dd, 2H), 7.91 (dd,1H), 7.60 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H),6.86 (d, 1H), 4.67 (s,2H), 4.05 (q, 2H), 1.37(t, 3H).	417.02
631	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.81 (dd, 2H), 7.91 (dd,1H), 7.59 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H),6.74 (d, 1H), 5.20 (q,1H), 4.05 (q, 2H), 1.95(d, 3H), 1.34 (t, 3H).	431.10
632	4-(5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.82 (dd, 2H), 7.91 (dd,1H), 7.63 (dd, 2H), 7.39(m, 1H), 7.15 (m, 1H),6.85 (d, 1H), 4.62 (s,2H), 3.69 (s, 3H).	403.10

633	4-{5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (dd, 2H), 7.91 (dd,1H), 7.60 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H), 6.72 (d, 1H), 5.06 (q,1H), 3.64 (s, 3H), 1.93(d, 3H).	417.10
634	4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 7.92 (dd,1H), 7.76 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H),6.95 (d, 1H), 4.71 (s,2H), 3.27 (m, 1H), 1.18(m, 2H), 0.82 (m, 2H).	429.10
635	4-{5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (dd, 2H), 7.92 (dd,1H) 7.76 (dd, 2H), 7.38m, 1H), 7.15 (m, 1H),6. (85 (d, 1H), 5.40 (q,1H), 3.24 (m, 1H),1.98(d, 3H), 1.88 (m, 2H),0.80 (m, 2H).	443.20
636	3-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.90 (dd, 1H), 7.60 (dd,1H), 7.39 (m, 1H), 7.11(m, 2H), 6.85 (d, 1H),6.59 (dd, 1H), 4.62 (s,2H), 4.20 (q, 2H), 1.38(t, 3H).	

637	3-(1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil)-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.88 (dd,1H), 7.59 (dd,1H), 7.39 (m, 1H), 7.11(m, 2H), 6.74 (d, 1H),6.58 (dd, 1H), 5.08 (q,1H), 4.20 (q, 2H), 1.92(d, 311),134 (t, 3H).	
638	4-(5-(1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-4-metil-4H-[1,2,4]triázol-3-il)-piridina	1.96 (d, 3 H) 3.61 (s, 3H) 5.10 (q, 1 H) 7.38 (t,1 H) 7.47 (m, 1 H) 7.54(m, 2 H) 7.84 (m, 1 H)7.93 (m, 1 H) 8.74 (d, 2H)	
639	4-(5-(1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.80 (bs, 2H), 7.99 (m,1H), 7.90 (m, 1H), 7.58(d, 2H), 7.51 (m, 1H),7.46 (t, 1H), 5.31 (q,1H), 4.06 (q, 2H), 2.04(d, 3H), 1.31 (t, 3H).	414.10
640	4-(5-(1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (bs, 2H), 8.03 (m,1H), 7.94 (d, 1H), 7.76(d, 2H), 7.51 (m, 1H),7.45 (t, 1H), 7.54 (q,1H), 3.25 (m, 1H), 2.06(d, 3H), 1.19 (m, 2H),0.81 (m, 2H).	426.07
641	5-(5-cloro-2-fluoro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (dd, 1H), 7.60 (d,1H), 7.55 (m, 1H), 7.22(4 1H), 7.09 (d, 1H),6.58 (m,1H), 4.55 (s,2H), 3.81 (s, 3H).	

642	5-(5-cloro-2-fluoro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (dd, 1H), 7.89 (d,1H), 7.55 (m, 2H), 7.22(t, 1H), 6.88 (dd,1H),4.55 (s, 2H), 3.67 (s,3H).
643	4-cloro-2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol	10.08(s,1H), 7.88(d,1H), 7.47 (m, 3H), 7.17(t,1H), 7.06 (d, 1H),4.68 (s, 2H), 4.14 (q,2H), 1.38 (t, 3H).
644	2-cloro-4[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-[1,3,4]oxadiazol-2-il]-piridina piridina	s.83 (á! 2H), s.6o (m,1H)m,, 71H), (4.82 11~,.94 7 (.m, 62 (m, 2I.85 ~;(s, 2H), 3.75 (s,3H).
645	2-cloro-4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina	8.82 (d, 2H), 8.60 (m,1H), 7.94 (m, 1H), 7.86(m, 1H), 7.59 (m, 2H),4.87 (s, 2H), 4.12 (q,2H), 1.43 (t, 3H).
646	2-cloro-4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il1-piridina	8.81 (d, 2H), 8.60 (m,1H), 7.96 (m, 1H), 7.86(m, 1H), 7.75 (m, 2H),4.92 (s, 2H), 3.32 (m,1H), 1.21 (m, 2H), 0.87(q, 2H).

647	2-cloro-4-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina	8.57 (m, 1H), 7.92 (m,1H), 7.81 (m, 1H), 7.61(m, 1H), 7.12 (m, 1H),6.61 (m, 1H), 4.79 (s,2H), 4.26 (q, 2H), 1.40(t, 3H).
648	2-cloro-4-{5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol-2-il}-piridina	8.59 (m, 1H), 7.94 (m,1H), 7.84 (m, 1H), 7.55(m, 2H), 7.05 (m, 2H),4.g3 (s, 2H), 4.02 (q,2H), 1.34 (t, 3H).
649	2-(3-cloro-fenil)-5-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	8.00 (m, 1H), 7.87 (d,1H), 7.53 (m, 3H), 7.42(t, 1H), 7.01 (m, 2H),5.07 (q, 1H), 3.88 (s,3H), 3.54 (s, 3H),2.00(d, 3H).
650	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.81 (bs, 2H), 8.01 (m,1H), 7.63 (d, 2H), 7.50m, 1H), 7.18 (m, 1H),5. (17 (q, 1H), 3.69 (s,3H), 2.02 (d, 3H).
651	5-(5-Bromo-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.20 (m, 1H), 7.65 (m,1H)' 7.60 (s, 1H), 7.13(m, 2H), 6.56 (m, 1H),4.64 (s, 2H), 4.25 (q,2H), 1.38 (t, 3H).

652	2-(3-cloro-fenil)-5-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	8.02 (d, 1H), 7.90 (d,1H), 7.50 (m, 4H), 7.03(d, 2H), 4.71 (s, 2H),3.88 (s, 3H), 3.61 (s,3H).	
653	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 8.09 (t,1H), 7.97 (m, 1H), 7.76(d, 2H), 7.45 (m, 2H),4.89 (s, 2H), 3.30 (m,1H), 1.22 (m, 2H), 0.86(m, 2H).	412.07
654	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.78 (s, 2H), 8.14 (m,1H), 8.04 (m, 1H), 7.77(t, 2H), 7.54 (m, 2H),4.79 (s, 2H), 3.29 (m,1H), 1.21 (m, 2H), 0.85(d, 2H).	
655	4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (s, 2H), 7.79 (t,11H), 7.61 (t, 2H), 7.33(m, 1H), 7.08 (m, 1H),5.09 (m, 1H), 3.65 (s,3H), 2.37 (s, 311), 2.02(d, 3H).	
656	4-{4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.81 (m, 2H), 8.23 (m,1H), 7.79 (d, 2H), 7.32(m, 1H), 7.09 (m, 1H),5.28 (m, 1H), 4.07 (m,2H), 2.37 (s, 3H), 2.04(d, 3H), 1.24 (m, 3H).	

657	4-(4-Ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.78 (m, 2H), 7.82 (d,1H), 7.74 (d, 2H), 7.31(m, 1H), 7.11 (m, 1H),5.51 (m, 1H), 3.23 (m,1H), 238 (s, 3H), 2.06(d, 3H), 1.16 (m, 2H),0.78 (m, 2H).
658	4-(4-Ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.83 (m, 2H), 7.78 (m,1H), 7.59 (m, 2H), 7.33m, 1H), 7.10 (m, 1H),5. (26(m, 1 H), 3.90 (m,2H) 2.37 s 3 2.03(d, 3H), 0.92 (m, 1H),0.48 (m, 2H), 0.21 (m,2H).
659	2-(2-fluoro-5-metil-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	7.98 (s, 1H), 7.75 (m,1H), 7.31 (m, 1H), 7.08(m, 1H), 5.03 (q, 1H),3.85 (s, 3H), 2.75 (s,3H), 2.35 (s, 3H), 1.98(d, 3H).
660	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.80 (m, 2H), 8.01 (m,1H), 7.58 (m, 2H), 7.49(m, 1H), 7.19 (m, 1H),5.32 (q, 1H), 4.08 (q,2H), 2.04 (d, 3H), 1.35(t, 3H).
661	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (d, 2H), 8.03 (m,1H), 7.75 (m, 2H), 7.50(m, 1H), 7.20 (m, 1H),5.55 (q, 1H), 3.26 (s,1H), 2.06 (d, 311), 1.18(m, 2H), 0.81 (m, 2H).

662	2-(5-cloro-2-fluoro-fenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]pxadiazol	8.97 (m, 1H), 7.59 (m,1H), 7.47 (m, 1H), 7.17(m, 1H), 7.12 (m, I H),6.59 (m, 1H), 5.18 (q,1H), 4.21 (q, 2H), 2.00(d, 3H), 1.33 (t, 3H).
663	2-(5-cloro-2-fluoro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	7.99 (s, 1H), 7.96 (m,1H), 7.48 (m, 1H), 7.17(t, 1H), 7.06 (q, 1H),3.86 (s, 3H), 2.75 (s,311),1.98 (d, 3H).
664	4-(4-Ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.78 (dd, 2H), 7.71 (dd,1H), 7.58 (dd, 2H), 7.25(m, 1H), 7.08 (m, 1H),6.62 (d, 1H), 5.12 (q,1H), 3.87 (dd, 2H), 2.40(s, 3H), 1.94 (d, 3H), 0.90 (m, 1H), 0.49 (m,2H), 0.19 (m, 2H).
665	4-(5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (bs, 211), 7.92 (d,1H), 7.80 (dd, 1H), 7.60(d, 2H), 7.50 (m,1H),7.25 (m, 1H), 5.05 (q,2H), 3.65 (s, 3H), 1.94(d, 3H).

666	4-(4-Ciclopropil-5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.76 (d, 2H), 7.95 (d,1H), 7.85 (dd, 1H), 7.75(d , 2H), 7.50 (m,1H),7.25 (m, 1H), 5.45 (q,2H), 3.20 (m, 1H), 1.98(d, 3H) 1.22 (m, 2H),0.88 (m, 2H).
667	4-(5-{1-[5-(4-Metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.65 (d, 1H), 7.71 (s,1H), 7.63 (d, 1H), 7.54(d, 2H), 7.00 (d, 2H),5.10 (q, 1H), 3.87 (s,3H), 3.53 (s, 3H), 2.58(s, 31-1),2.00 (d, 3H).
668	4-(5- { 1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metYl-	8.65 (d, 1H), 7.71 (s,1H), 7.63 (d, 1H), 7.49(d, 2H), 7.01 (d, 2H),5.26 (q, 1H), 3.96 (q,2H), 3.88 (s, 3H), 2.62(s, (s, 3H), 2.02 (d, 3H),1.24 (t, 3H).
669	4-(5-[1 -(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina	879 (d, 2H), 8.67 (d,1H)' 7.73 (s, 1H), 7.65(d5.33 , 1H), 7.55 (d, 2H),(q, 1H), 4.08 (q,2H), 2.64 (s, 3H), 2.03(d, 3H), 1.30 (t, 3H).

670	4-{5-[1-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina	8.77 (d, 2H), 8.68 (d,1H), 7.72 (m, 4H), 5.55(q, 1H), 3.24 (m, 1H),2.64 (s, 3H), 2.04 (d,3H), 1.16 (m, 2H), 0.81(m, 2H).
671	4-{5-[1-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina	8.61 (d, 1H), 7.57 (m,3H), 7.08 (d, 1H), 6.57(d' 1H), 5.02 (q, 1H),3.70 (s, 3H), 1.96 (d,3H).
672	2-(3-cloro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	7.99 (s, 1H), 7.94(m,1H), 7.86 (m, 1H),7.48 (m, 1H), 7.39 (m,1H), 5.03 (q, 1H), 3.82(t, 3H), 2.73 (d, 3H),1.98 (d, 3H).
673	3-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.88 (s, 1H), 8.76 (d,1H), 8.00 (m, 2H), 7.90(d, 1H), 7.48 (m, 3H),5.14 (q, 1H), 3.60 (s,3H), 2.02 (d, 3H)
674	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-2-metil-piridina	8.66 (d, 1H), 7.99 (m,, 1H)88 7. m, 1H), 7. 51(m, 1H), 7(.43 (m, 2H),7.34 (d, 1H), 5.13 (q,1H), 3.61 (s, 3H), 2.63(s, 3H), 2.00 (d, 3H).

675	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.68 (dd, 2H), 8.05 (d,1H), 7.92 (d, 1H), 7.67(dd, 2H), 7.51 (d, 1H),7.37 (t, 1H) 5.37 (q,1H), 3.18 (m, 1H),.1.90(d, 3H), 1.08 (m, 2H),0.74 (m, 2H).
676	5-(3-cloro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-rnetil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol	8.01 (s, 1H), 7.90 (d,1H), 7.50 (m, 3H), 7.38(t, 1H), 6.92 (d, 2H),4.88 (q, 1H) 3.78 (s,3H), 3.47 (s, 3H), 1.83(d, 3H).
677	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.70 (dd, 2H), 8.05 (m,1H), 7.67 (m, 2H), 7.46(m, 1H), 7.18 (m, 1H),5.41 (q, 1H), 3.18 (m,1H), 1.90 (d, 3H), 1.08(m, 2H), 0.74 (m, 2H).
678	5-(5-cloro-2-fluoro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol	8.05 (m, 1H), 7.56 (m,,3H).21 7 (t, 111), 7 .00(m,3m, 3H), , 5. 1H),.85 (s, 3H), 3(q, .56 (s,3H), 1.90 (d, 3H)
679	4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina	8.79 (d, 2H), 8.67 (d,1H), 7.75 (s, 1H), 7.67(d, 1H), 7.56 (d, 2H),4.82 (s, 2H), 4.10 (q,2H), 2.64 (s, 3H), 1.39(t, 3H).

680	4-[5-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il1-2-metil-piridina	8.78 (d, 3H), 8.68 (d,1H), 7.74 (m, 4H), 4.90(s, 2H), 3.30 (m, IH),2.65 (s, 3H), 1.21 (m,2H), 0.84 (m, 2H).
681	4-{5-[5-(5-cloro-2-fuoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 8.12 (m,1H), 7.76 (m, 2H), 7.57(m, 1H), 7.25 (m, 1H),4.81 (s, 2H), 3.31 (m,1H), 1.20 (m, 2H), 0.85(m, 2H).
682	4-[5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina	8.66 (d, 1H), 7.72(s,1H), 7.65 (d, 1H), 7.60(d, 1H), 7.11 (d, 1H),6.60(d of d, 1H), 4.70 (s,2H), 3.80 (s, 3H), 2.64(s, 3H).
683	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-4-ciclopropilmetil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (bs, 2H), 7.98 (m,1H)' 7.88 (m, 1H), 7.51(m, 4H), 5.30 (q, 1H),3 .90 (m, 2H), 2.05 (t,3H), 0.94 (ms, 1H), 0.50(m, 2H), 0.19 (m, 2H).
684	4-(5-{1-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.66 (d, 1H), 7.72 (s,1H), 7.60 (m, 3H), 7.17(m' 3H), 5.13 (q, 1H),3.57 (s, 3H), 2.63 (s,3H), 2.00 (d, 3H).

685	4-(5-(1-[5-(3-fluoro-fenil)-4-metil-4H-[1;2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.65 (d, 1H), 7.72 (s,7.,20 1H)66 7(.m, (d, 1H), 7. 48 4H), 5.15 (q,1H), 3.60 (s, 3H), 2.63(s, 3H), 2.01 (d, 3H).
686	3-[3-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrile	8.77 (dd, 2H), 8.49(dd,1H), 7.90 (m, 1H),7.74 (dd, 2H), 7.43 (t,1H), 4.81 (s, 2H), 3.31(m, 1H), 1.21 (m, 2H),0.83 (m, 2H).
687	4-cloro-2-[3-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol	10.15 (bs, 1H), 8.77 (dd,2H), 7.89 (d,1H), 7.75(dd, 2H), 7.45 (dd, 1H),7.06 (d, 1H), 4.79 (s,2H), 3.29 (m, 1H), 1.21(m, 2H), 0.83 (m, 2H).
688	4-(4-Ciclopropil-5-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.77 (dd, 2H), 7.72 (m,3H), 7.62 (dd, 1H), 7.43(t, 1H), 7.14 (m, 1H),4.77 (s, 2H), 3.88 (s,3H), 3.28 (m, 1H), 1.17(m, 2H), 0.84 (m, 2H).
689	4-(4-Ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.7 (q, 2H), 7.81 (d,1H), 7.7 (q, 2H), 7.29(m, 1H), 7.1 (t, 1H),4.71 (s, 2H), 3.23 (m,1H), 2.32 (s, 3H), 1.11(m, 2H), 0.76 (m, 2H)

690	4-{4-Ciclopropil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.67 (m, 2H), 7.82 (m, 1H), 7.72 (m, 1H), 7.66(m, 1H), 7.42 (m, 1H),7.21 (m, 1H), 4.68 (s,1H), 3.23 (m, 1H), 1.11(m, 2H), 0.75 (m, 2H)
691	4-[4-Ciclopropil-5-(S-m-tolil-[1,2,4]oxadiazol-3-Ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.69 (q, 2H), 7.85 (m,2H), 7.67 (q, 2H), 7.32(m, 2H), 4.69 (s, 2H),3.2 (m, 1H), 2.35 (s,3H), 1.11 (m, 2H), 0.76(m, 2H)
692	3-[3-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.71 (b s, 2H), 8.36 (m,1H), 8.28 (d, 1H), 7.83(d d, 1H), 7.67 (m, 3H), 4.72 (s, 2H), 3.23 (m,1H), 1.14 (m, 2H), 0.77(m, 2H)
693	4-{4-Ciclopropil-5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.75 (t, 2H), 7.79 (m,2H), 7.26 (m, 2H), 4.78(s, 2H), 3.28 (m, 1H),1.14 (m, 2H), 0.82 (m,2H)
694	4-{4-Ciclopropil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.67 (d d, 2H), 7.87 (m,2H), 7.67 (d d, 2H), 7.33(m, 2H), 5.36 (q, 1H), 3.15 (m, 1H), 2.36 (s,3H), 1.92 (d, 3H), 1.07(m, 2H), 0.72 (m, 2H)

695	4-(4-Ciclopropil-5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina.	8.69 (m, 2H), 7.6 (m,3H), 7.52 (m, 1H), 7.35(t, 1H), 7.04 (d d, 1H),5.35(q, 1H), 3.81 (s,3H), 3.15 (m, 1H), 1.91(d, 3H), 1.11 (m, 2H),0.7(m, 2H)
696	4-{5-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-	8.69 (d, 2H), 7.78 (m,1H), 7.67 (m, 2H), 7.35(d, 1H), 7.24 (m, 1H),

Ejemplo No.	4H-[1,2,4]triazol-3-il}-piridina	4.72 (s, 2H), 3.22 (m, 1H), 2.31 (s, 3H), 1 (m, 2H), 0.76 (m, 2H)
697	2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol	9.89 (s, 1H), 8.7 (m, 2H), 7.68 (m, 3H), 7.2 (m, 1H), 6.92 (d, 1H), 4.72 (s, 2H), 3.22 (m, 1H), 2.26 (s, 3H), 1.01 (m, 2H), 0.74 (m, 2H)

698	4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.69 (d d, 2H), 7.8 (q, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.22 (m, 1H), 5.4 (q, 1H), 3.16 (m, 1H), 2.32 (s, 3H), 1.93 (d, 3H), 1.09 (m, 2H), 0.73 (m, 2H)

EJEMPLO 699

{3-[3-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-metanol

Se disuelve [3-(3-clorometil-[1,2,4]-oxadiazol-5-il)-fenil]-metanol (32 mg, 0.14 mmoles), 4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-tiol (41 mg, 0.21 mmoles) y carbonato de potasio (29 mg, 0.21 mmoles) en acetonitrilo anhidro y se somete a reflujo bajo atmósfera de nitrógeno durante 1 hora. El solvente se elimina al vacío y el residuo se disuelve en $NaHCO_3$ (acuoso) y se extrae con diclorometano ('3). La fase orgánica se seca ($MgSO_4$), se filtra y se concentra. El compuesto del título se aísla como un aceite incoloro (43 mg, 80%) mediante

cromatografía de vaporización instantánea utilizando metanol al 3% en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.07 (s, 1H), 7.98 (d, 1H), 7.60 (d, 1H) 7.52-7.45 (m, 3H), 7.16 (dd, 1H), 5.29 (s, 2H), 4.75 (s, 2H), 4.50 (s, 2H), 3.71 (s, 1H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 699:

Ejemplo No.	Nombre	1H RMN	MS
700	3-[5-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-fenol		
701	5-(3-cloro-fenil)-3-[4-(tetrahidro-furan-2-ilmetil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.5 (m, 1H) 1.8 (m, 2H) 2.0 (m, 1H) 3.7 (m, 1H) 3.8 (m, 1H) 4.1 (s,m, 3H)) 4.5 (dd, 2H) 7.1 (dd, 1H) 7.4 (t, 2H) 7.5 (m, 2H) 7.9 (dd, 1H) 8.0(m,1H	460.00

702	(2-cloro-fenil)-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-isobutil-4H-[1,2,4]triazol-3-il}-metanol	0.8 (2 d, 6 H) 2.0 (m, 1H) 3.5 (dd, 1H) 3.6 (dd, 1H) 4.5 (s, 2H) 6.3 (d, 1H) 7.3 (m, 3H)) 7.5 (triplete aparente, 1H) 7.6 (m, 2H) 8.0 (d aparente, 1H) 8.1 (m, 1H)	490
703	5-(2-fluoro-5-metil-fenil)-3-[5-tiofen-2-il-4-(2,2,2-trifluoro-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	2.4 (s, 3H)) 4.6 (s, 2H) 4.8 (q, J=7.7 Hz, 2H) 7.1 (m, 1H) 7.2 (m, 1H) 7.4 (m, 1H) 7.5 (m, 1H) 7.6 (m, 1H) 7.8 (m, 1H)	455.9

EJEMPLO 704

3-(2,5-difluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se disuelve 5-clorometil-3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol (23 mg, 0.10 mmoles) y 4-etil-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona (23 mg, 0.11 mmoles) en DMF anhidra (1 ml) y se agrega carbonato de potasio (21 mg, 0.15 mmoles). Después de agitar durante 22 horas se agrega acetato

de etilo, la mezcla resultante se lava dos veces con agua y una vez con salmuera, se seca con $MgSO_4$ y se evapora. La cromatografía de vaporización instantánea utilizando heptano:acetato de etilo 1:1 permite obtener el compuesto del título (20 mg, 50%).

^1H RMN ($CDCl_3$) d (ppm): 7.64 (m, 1H), 7.45 (d, 1H), 7.39 (d, 1H), 7.10 (m, 3H), 4.70 (s, 2H), 4.08 (q, 2H), 1.32 (t, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplos 704:

Ejemplo No.	Nombre	1H RMN	MS
705	5-furan-3-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.71 (s, 3H) 4.51 (s, 2H) 6.88 (dd, 1H) 7.17 (dd, 1H) 7.48 (dd, 1H) 7.51 (dd, 1H) 7.54 (t, 1H) 8.18 (m, 1H)	345.92
706	3-(3-cloro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.78 (s, 3H)) 4.64 (s, 2H) 6.57 (dd, 1H) 7.09 (d, 1H) 7.38 (t, 1H) 7.46 (m, 1H) 7.58 (d, 1H) 7.91 (d, 1H) 8.01 (m, 1H)	373.96

707	3-(3-cloro-fenil)-5-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.63 (s, 3H)) 4.64 (s, 2H) 6.85 (d, 1H) 7.39 (t,1H) 7.47 (dt, 1H) 7.56 (t, 1H) 7.87 (br. s, 1H) 7.91 (dt, 1H) 8.01 (t, 1H)	373.96
708	5-(3-cloro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.77 (s, 3H)) 4.50 (s, 2H) 6.55 (dd, 1H) 7.07 (d, 1H) 7.43 (t, 1H) 7.55 (m, 2H) 7.95 (dt, 1H) 8.05 (t, 1H) 13.63 (s, 3H))	373.96
709	5-(3-cloro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	4.49 (s, 2H) 6.84 (br. s, 1H) 7.43 (t, 1H) 7.54 (m, 2H) 7.87 (s, 1H) 7.94 (d, 1H) 8.04 (m, 1H)	373.97
710	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina	4.06 (s, 3H)) 4.63 (s, 2H) 7.43 (t, 1H) 7.53 (m,1H) 7.95 (d, 1H) 8.05 (t, 1H) 8.27 (dd, 1H) 8.85 (d, 1H) 9.25 (d, 1H)	385.97
711	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina	4.06 (s, 3H)) 4.75 (s, 2H) 7.35 (t, 1H) 7.42 (ddd, 1H) 7.88 (dt, 1H) 7.97 (t, 1H) 8.24 (dd, 1H) 8.84 (d, 1H) 9.23 (d, 1H)	385.97

712	3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.29(t, 3H)) 4.07 (q, 2) 4.68 (s, 2H) 7.08 (m, 2H) 7.35 (m, 2H) 7.44 (dd, 1H) 7.87 (dd, 1H)	421.99
713	3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.32(t,3H)4.18(q, 2H) 4.71 (s, 2H) 6.51 (dd, 1H) 7.02 (dd, 1H) 7.10 (dd, 1H) 7.37 (ddd, 1H) 7.53 (dd, 1H) 7.91 (dd, 1H)	406.02
714	5-(5-cloro-tiofen-2-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.30(t,3H)4.09(q, 2H) 4.47 (s, 2H) 6.96 (d, 1H) 7.11 (dd, 1H) 7.40 (dd, 1H) 7.47 (dd, 1H) 7.60 (d, 1H)	409.92
715	5-(5-cloro-tiofen-2-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.33(t,3H)4.21(q,2H) 4.52 (s, 2H) 6.54 (dd, 1H) 6.98 (d, 1H) 7.05 (dd, 1H) 7.55 (dd, 1H) 7.62 (d, 1H)	393.96
716	5-(5-cloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.36(t,3H)4.12(q,2H) 4.58 (s, 2H) 7.15(dd, 1H) 7.43 (m, 2H)7.48 (dd, 1H) 7.94 (d, 1	409.92
717	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}-fenol	1.30(43H)4.02(q, 2H) 4.51 (s, 2H) 5.07 (s,2H) 6.72 (m, 4 H) 7.39(t, 1H) 7.49 (m, 1H)7.89 (m, 1H) 7.99 (t, 1H)	443.9

718	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}-fenol	1.33(t,3H)4.05(q,2H) 4.70 (s, 2H) 5.11 (s,2H) 6.74 (m, 4 H)7.13(t, 1H) 7.44 (m, 1H)7.93 (dd, 1H)	461.9
719	3-(2,5-difluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.75 (m, 1H), 7.64 (d,1H), 7.23 (m, 2H), 7.16(d, 1H), 6.63 (dd,1H),4.80 (s, 2H), 4.29 (q,2H), 1.43 (t, 3H)	389.9
720	3-(2,5-difluoro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.17 (dd, 1H), 7.87 (m,1H), 7.74 (m, 2H), 7.33(dd, 1H),6.95 (dd, 1H),5.01 (s, 2H), 3.96 (s,3H)	375.8
721	4-(5-{1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.74 (d, 2H), 7.97 (s, 1H), 7.87 (m, 1H), 7.56(d, 2H), 7.44 (m, 1H),7.36 (apparent t, 1H),5.06 (q, 1H), 3.58 (s, 3H), 1.96 (d, 3H)).	400
722	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-yhnetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-pirimidina	0.90 (m, 2H), 1.22 (m,2H), 3.49 (m, 1H),4.81 (s, 2H), 7.26 (t, 1H), 7.53 (m, 1H), 8.11(m, 2H), 8.88 (d, 1H)9.33(s,1H)	430.1

723	2-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-pirimidina	1.32 (t, 3H)), 1.94 (d, 31-1), 4.00 (s, 3H), 4.50(m, 2H), 5.20 (q, 1H),7.46 (t, 1H), 7.56 (m, 1H), 7.99 (d, 1H), 8.10(t, 1H), 8.56 (d, 2H).	444.1
724	2-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina	1.34 (t, 3H)), 1.94 (d, 3H), 4.50 (m, 2H), 5.26 (q, 1H), 7.36 (t, 1H), 7.46 (t, 1H), 7.57 (d, 1H), 7.99 (m, 1H), 8.10 (m,1H), 8.92 (d, 2H).	414
725	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina	1.32 (t, 3H)), 1.97 (d, 3H), 3.99 (s, 3H), 4.06 (m,2H), 5.19 (q, 1H),6.98 (bs, 1H), 7.16 (m,1H), 7.47 (t, 1H), 7.58(m, 1H), 7.98 (dt, 1H),8.10 (m, 1H) 8.31 (d, 1H).	443.1
726	5-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina	1.30 (t, 3 11), 1.96 (d, 3 H), 3.99(m, 2H), 4.00 (s,3H)), 5.16 (q, 1H), 6.87 (d, 1H), 7.47 (t, 1H),7.58 (m, 1H), 7.86 (dd,1H), 8.00 (d, 1H), 8.11(t, 1H) 8.40 (d, 1H).	443

727	2-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-piridina	1.30 (t, 3H)), 1.93 (d, 3H)' 3.92 (s, 3H)), 4.52(m, 2H), 5.13 (q, 11-1),7.32 (dd, 1H), 7.46 (t, 1H), 7.56 (m, 1H), 7.99(dt, 1H), 8.10 (t, 11-1),8.25 (d, 1H) 8.30 (d, 1	443.1
728	3-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridazina	1.38 (t, 3 11), 1.96 (d, 3H), 4.20 (s, 3H)), 4.61(m, 2H), 5.20 (q, 11-»,7.12 (d, 1H),444 7.46 (t, 1H), 7.56 (t, 1H), 8.00(d, 1H), 8.10 (s, 1H),8.40 (d, 1H)	
729	3-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	0.77 (m, 2H), 1.14 (m,2H)' 1.99 (d,3H)), 3.22(m, 1H), 5.44 (q, 1H),7.45 (m, 2H), 7.58 (d, 1H), 8.02 (d, 1H), 8.15(m, 2H), 8.72 (d, 1H)9.05 (s, 1H).	
730	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	3.69 (s, 3H)) 4.73 (s, 2 1H) 7.39 (t, 1H) 7.47 (m,1H) 7.60384.91 (m, 2H) 7.92(m, 1H) 8.02 (t, 1H)8.79 (m, 2H)	

EJEMPLO 731

5-(3-cloro-fenil)-3-(5-furan-2-il-4-isobutil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

El compuesto del título se sintetiza de conformidad con el método descrito por Graybill et al. Tetrahedron lett. 2002 43, 5305-5309 a partir de la hidrazida del ácido furan-2-carboxílico (55.2 mg, 0.44 mmoles), 1-isotiocianato-2-metil-propano (47 ml, 0.38 mmoles) y 3-clorometil-5-(3-cloro-fenil)-[1,2,4]oxadiazol (45.0 mg, 0.20 mmoles) con P-bEMP (136 mg, 0.30 mmoles) como base. La purificación mediante cromatografía de vaporización instantánea (33-66% EtOAc en heptano) permite obtener el producto como un aceite (12.7 mg, 15.6%).

^{1}H RMN ($CDCl_3$) d (ppm): 8.08 (s, 1H), 7.97 (d, 1H), 7.55 (d, 2H), 7.45 (t, 1H), 7.10 (d, 1H), 6.56 (d, 1H), 4.62 (s, 2H), 4.01 (d, 2H), 2.03 (m, 1H), 0.86 (d, 6H).

General

Se disuelven tiofen-2-carbohidrazida (1.5 equiv) y un isotiocianato (1.3 equiv) en DMF (1 ml). Se agrega 2-ter-butilimino-2-dietilamino-1,3-dimetil-perhidro-1,3,2-diazafosforina (1 equiv) en poliestireno y las reacciones se agitan en un mini bloque de Bohdan a temperatura ambiente durante 1 hora y después durante una hora adicional a 45°C. La

resina se lava con dioxano:agua 1:1 varias veces. El cierre del anillo se efectúa a 85°C durante 48 horas en dioxano:agua 1:1 en el mini bloque. La resina se lava con acetonitrilo (2'2 ml). Se agrega el 3-(clorometil)-5-(3-clorofenil)-1,2,4-oxadiazol a la reacción y se agitan en acetonitrilo a 50°C durante 2 horas. El producto se filtra y purifica en HPLC preparativa dirigida con MS, gradiente 0-100% de acetonitrilo en un lapso de 15 minutos.

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 731:

Ejemplo No.	Nombre	1H RMN	MS
732	5-(3-cloro-fenil)-3-[4-(-metilsulfanil-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		464.0
733	5-(3-cloro-fenil)-3-(4-hexil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		460.0
734	5-(3-cloro-fenil)-3-(4 ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		430.0

735	5-(3-cloro-fenil)-3-[4-(3-fluoro-benzil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	484.0
736	5-(3-cloro-fenil)-3-[4-(3-metil-benzil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	480.0
737	5-(3-cloro-fenil)-3-[4-(2-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	446.0
738	5-(3-cloro-fenil)-3-[4-(3-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	446.0
739	5-(3-cloro-fenil)-3-[4-(2-fluoro-benzil)-5-thiophen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	484.0

EJEMPLO 740

5-(3-cloro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-iloximetil)-[1,2,4]oxadiazol

5

se disuelven [5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-metanol (28.0 mg, 0.13 mmoles), 4-etil-3-metansulfonil-5-tiofen-2-il-4H-[1,2,4]triazol (35.2 mg, 0.13 mmoles) y carbonato de cesio (130 mg) en dimetilformamida y se agita bajo argón a temperaturas ambientales durante 46 horas. Después de evaporar hasta sequedad, el producto crudo se somete a cromatografía en 12 g de sílice, heptano/acetato de etilo 4/1 a 2/1. La recolección de las fracciones apropiadas permite obtener, después de evaporar a sequedad y secar al vacío, el compuesto del título (17.0 mg, 33%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.13 (m, 1H), 8.02 (m, 1H), 7.58 (m, 1H), 7.47 (m, 2H), 7.40 (dd, 1H), 7.14 (dd, 1H), 5.74 (s, 2H), 4.04 (q, 2H), 1.38 (t, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 740:

Ejemplo	Nombre	1H RMN	M5
741	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetoxi]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (s broad, 2H), 8.12(d aparented, 1H), 7.78(s, 1H), 7.56 (s broad, 2H), 7.25 (apparent t, 1H), 5.79 (s, 2H), 3.66(s, 3H)).	388

742	4-(5-t1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etoxi)-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.82 (s broad, 2H),8.07-7.94 (m, 2H), 7.69(s broad, 2H), 7.47 (m,2H), 6.47 (q, 1H), 3.63(s, 3H)), 2.02 (d, 3H)).	384.1
743	4-(5-{1-[3-(3-cloro-fenil)-isoxazol-5-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	1.92 (d, 3H), 3.57 (s, 3H)' 6.36 (q, 1H), 6.74 (s, 1H), 7.39 (m, 2H),7.60 (m, 2H), 7.66 (m,1H), 7.78 (m, 1H), 8.75(m, 2H)	383.1
744	3-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etoxi}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina		

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 740 excepto que se utiliza hidruro de sodio como la base y la reacción se calienta a 80°C:

745	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-yhnetoxi]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.77 (d, 211), 8.17 (s,1H), 8.05 (d, 1H), 7.79(d, 2H), 7.62 (dd, 1H),7.52 (t, 1H), 5.79 (s,2H), 3.25 (m, 1H), 1.14(d, 2H), 0.89 (m, 2H)
746	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetoxi]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.77 (d, 2H), 7.79 (m,3H) , 7.7 (m, 1H), 7.44(m, 2H), 6.84 (s, 1H),5.71 (s, 2H), 3.21 (m,1H), 1.13 (d, 2H), 0.82(m, 2H)

EJEMPLO 747

5-(2-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se agregan HBTU (171 mg, 0.45 mmoles) y HOBT (8 mg, 0.06 mmoles) a una solución de ácido 2-metoxi benzoico (68 mg, 0.45 mmoles) y DIPEA (192 ml, 1.11 mmoles) en DMF (3 ml). Después de 10 minutos, se agrega N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4}triazol-3-ilsulfanil)-acetamidina (100 mg, 0.37 mmoles). La mezcla de reacción se agita a temperatura ambiente durante 7 horas y después a

110°C durante la noche. Después de enfriar, la mezcla de reacción se diluye con agua y se extrae con CH_2Cl_2. la fase orgánica se seca y concentra. La cromatografía de vaporización instantánea (heptano/EtOAc 1:2) permite obtener 1.9 mg (11%) del producto deseado.

^1H RMN ($CDCl_3$), d (ppm): 7.99 (m, 1H), 7.53 (m, 1H), 7.50 (m, 1H), 7.47 (m, 1H), 7.16 (m, 1H), 7.04 (m, 2H), 4.52 (s, 2H), 3.94 (s, 3H), 3.71 (s, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 747:

Ejemplo No.	Nombre	1H RMN	MS
748	5-furan-2-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.72 (s, 3H)) 4.52 (s, 2H) 6.61 (dd, 1H) 7.16(dd, 1H) 7.30 (dd,345.92 1H)7.47 (dd, 11-1) 7.50 (dd,1H) 7.67 (dd, 1H)	
749	3-[3-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilxnetil)-[1,2,4]oxadiazol-5-il]-benzoic acid metil ester		414.0

750	5-(2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	374.0
751	5-(2,5-difluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	392.0
752	3-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-S-(3-vinil-fenil)-[1,2,4]oxadiazol	382.1
753	5-(3-difluorometoxi-fenil)-3-(4-metil-S-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	422.0
754	5-(4-metoxi-tiofen-3-il)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	392.0
755	5-(2-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	390.0
756	5-(4-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	374.0

EJEMPLO 757

3-(3-cloro-fenil)-5-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol

Se agrega DMF a una mezcla de ácido 2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-propiónico (50 mg, 0.186 mmoles), clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodi-imida (EDCI) (35.7 mg, 0.186 mmoles), hidrato de 1-hidroxibenzotriazol (HOBT) (28.5 mg, 0.186 mmoles) y 3-cloro-N-hidroxi-benzamidina (29.3 mg, 0.172 mmoles) a temperatura ambiente y se agita durante toda la noche. La mezcla de reacción se diluye con acetato de etilo (75 ml), se lava con agua 3 veces, una vez con HCl 1.0 M (30 ml), $NaHCO_3$ saturado (30 ml) y salmuera saturada (30 ml), se seca con sulfato de sodio anhidro, se filtra y se concentra al vacío. Se agrega DMF (1 ml) al residuo y la solución resultante se calienta a 135°C durante 3 horas para efectuar la ciclización hasta el oxadiazol. Después de enfriar, la mezcla de reacción se diluye con acetato de etilo (75 ml), se lava con agua 3 veces, una vez con HCl 1.0 M (30 ml), $NaHCO_3$ saturado (30 ml) y salmuera saturada (30 ml), se seca con sulfato de sodio anhidro, se filtra y se concentra al vacío. El

compuesto del título (46.5 mg, 66.9%) se purifica mediante cromatografía de SPE en gel de sílice utilizando 50 ml al 40%, 150 ml al 50% de acetato de etilo en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.03 (s, 1H), 7.92 (m, 1H), 7.47 (m, 4H), 7.18 (dd, 1H), 4.99 (q, 1H), 3.64 (s, 3H), 1.97 (d, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 757:

Ejemplo No.	Nombre	1H RMN	MS
758	3-(5-{1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil)-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.88 (d, 1H), 8.76 (dd, 1H), 8.03 (m, 2H), 7.93 (d, 1H), 7.74 (m, 3H), 5.09 (m, 1H), 3.58 (s, 3H), 2.00 (d, 3H)	

Los siguientes compuestos se preparan de manera análoga a la del ejemplo10:

Ejemplo No.	Nombre
759	5-(1-cloro-etil)-3-(3-cloro-fenil)-[1,2,4]oxadiazol
760	3-(1-cloro-etil)-5-m-tolil-[1,2,4]oxadiazol
761	3-(1-cloro-etil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol

762	3-(1-cloro-etil)-5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol
763	3-(1-cloro-etil)-5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol
764	3-(1-cloro-etil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol
765	3-[3-(1-cloro-etil)-[1,2,4]oxadiazol-5-il]-benzonitrilo

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 40:

Ejemplo No.	Nombre	1H RMN	MS
766	4-(5-{1-[5-(2-cloro-5-metil-phenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.74 (d, 2H), 7.79 (s,1H), 7.57 (d d, 2H),7.38 (d, 1H), 7.25._..., (d,1H), 5 (q, 1H), 3.62 (s,3H), 2.33 (s, 3H), 1.92(d, 3H)	
767	4-(5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4}triazol-3-il)-piridina	8.67 (d, 2H), 7.7 (m,1H), 7.57 (d d, 2H), 7.2(m, 2H), 5 (q, 1H), 3.61(s, 3H), 1.87 (d, 3H)	
768	4-(5-{1-[5-(2-fluoro-5-metil-phenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.77 (d, 2H), 7.85 (m,1H), 7.61 (m, 2H), 7.38(m, 1H), 7.06 (t, 1H)5.02~ (q, 1H), 3.66 (s,311),237 (s, 3H), 1.94(d, 311)	

769	-(4-ciclopropil-5-{1-[5-(2-fluoro-1 5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.75 (d, 2H), 7.9 (m, 1H), 7.74 (m, 2H), 7.38(m, 1H), 7.13 (m, 1H),5.45 (q, 1H), 3.24 (m,1H), 2.39 (s, 3H), 2 (d,311),1.15 (m, 2H), 0.79(m, 2H)
770	3-{3-[1-(4-metil5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrile	8.76 (d d, 21D, 8.4 (s,1H), 8.32 (d, 1H), 7.87(d, 1H), 7.65 (t, 1H),7.59 (m, 2H), 5.07 (q,1H), 3.67 (s, 3H), 2.59(s, 2H), 1.91 (d, 3H)
771	3-{3-[1-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrile	8.77 (m, 2H), 8.42 (d,1H), 8.38 (m, 1H), 7.9(m, 1H), 7.71 (m, 3H),5.49 (q, 1H), 3.25 (m,1H), 2 (d, 3H), 1.17 (m,2H), 0.81 (m, 2H)
772	3-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-5-piridin-4-il-[1,2,4]triazol-4-ilamina	8.77 (br s, 2H), 8.18 (d,2H), 7.98 (s, 1H), 7.87(d,1H), 7.52 (d, 1H),7.44 (t, 1H),5.66 (s,2H), 4.88 (q, 1H), 1.98(d, 3H)

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 316:

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Ejemplo No.	Nombre
773	3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-metil-propiónico acidkydrazide
774	Rac-3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-butyric acidydrazide

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 318:

Ejemplo	Nombre
775	-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropanecarboxílico

EJEMPLO 776

hidrazida de ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico

Se calienta 3,3-dimetil-dihidro-furan-2,5-diona (6.4 g) a 50°C en etanol (150 ml) durante la noche. El solvente se elimina al vacío y el residuo se tritura con hexano para producir el éster 4-etílico del ácido 2,2-dimetil-succínico (4.668) el cual se utiliza sin purificación adicional. Se agrega t-butanol (7.5 ml) a una mezcla de éster 4-etílico del ácido 2,2-dimetil-succínico (2.74 g, 15.7 mmoles) en diclorometano (62 ml) que contiene sulfato de magnesio (7.5 g) y ácido sulfúrico concentrado (0.85 ml) y la mezcla se agita a temperatura ambiente

durante la noche. Se agrega solución saturada de bicarbonato de sodio y el producto se extrae con diclorometano, se lava con solución de salmuera, se seca y se concentra para obtener el diéster (diested) como un aceite incoloro (1.89 g). El éster etílico se hidroliza tratando la muestra cruda con hidróxido de potasio (2.75g) en una mezcla de etanol (50 ml) y agua (25 ml) a temperatura ambiente durante 2 horas. La reacción se acidula utilizando HCl 1N (acuoso) y se extrae con éter, se seca y se concentra para obtener el éster 1-ter-butílico del ácido 2,2-dimetil-succínico (1.4g). Este ácido se trata bajo las condiciones del ejemplo 320 (paso 1) para obtener el éster t-butílico del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico (1.9g). Este éster t-bu se desprotege utilizando ácido fórmico (19 ml) a 50°C durante 20 minutos. El producto crudo se concentra y se tritura con una mezcla de éter y hexano para obtener el ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico (1.12g). A una solución de ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico (561 mg, 2 mmoles) y trietilamina (1.1 ml, 8 mmoles) en THF (9 ml), se agrega, mediante goteo, cloroformiato de isobutilo (0.31 ml, 2.4 mmoles) a -

78°C. Después que se agita durante 1 hora, se agrega hidrato de hidracina (1 ml, 11 mmoles). La mezcla de reacción se agita a temperatura ambiente durante 1 hora y se concentra. Se agrega una pequeña cantidad de hielo para extinguir cualquier reactivo en exceso y precipitar el producto, el cual se recolecta mediante filtración para obtener 482 mg del compuesto del título.

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 320:

Ejemplo No.	Nombre
777	(S)-(1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-hydrazinocarbonil-etil)-carbamic acid tert-butil ester

EJEMPLO 778

3-(3-cloro-fenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol

Paso 1

(Etoxi-tiofen-2-il-metilen)-hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico:

Se mezcla hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico (266.69 mg, 1 mmoles) con éster etílico del ácido tiofen-2-

carboximídico (191.6 mg, 1 mmol) en etanol (6 ml) y se agita a temperatura ambiente durante la noche. La reacción se extingue con agua, se extrae con acetato de etilo, se seca y se concentra al vacío. El producto crudo se tritura con hexano para obtener (etoxi-tiofen-2-il-metilen)-hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico como un sólido de color blanco (305 mg, 75%).

^{1}H-RMN($CDCl_3$) d(ppm): 8.99 (ws, 1H), 8.09 (s, 1H), 7.98 (d, 1H), 7.41(m, 4H), 7.08 (dd, 1H), 4.27 (q, 2H), 3.34 (m, 4H) y 1.41 (t, 3H).

Paso 2

3-(3-cloro-fenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol:

Se mezcla la (etoxi-tiofen-2-il-metilen)-hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico (81 mg, 0.2 mmoles) con metilamina 2M (0.3 ml en THF) en etanol (2 ml) a 70~80°C durante la noche. La mezcla de reacción se concentra con gel de sílice y se purifica mediante cromatografía en columna con 0.5~2.0% de metanol en acetato de etilo para obtener 54 mg (72.5 %) de 3-(3-cloro-fenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol.

^{1}H RMN($CDCl_3$) d (ppm): 8.08 (s, 1H), 7.97 (d, 1H), 7.41 (m, 4H), 7.20 (dd, 1H), 3.80 (s, 3H), 3.68 (dd, 2H), 3.38 (dd, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 778:

Ejemplo No.	Nombre	1H RMN	MS
779	3-(3-cloro-fenil)-5-[2-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-yl)-etil]-[1,2,4]oxadiazol	8.08 (s, 1H), 7.97 (d,1H), 7.47(m, 4H), 7.20(dd, 1H), 4.20 (q, 2H),3.72 (dd, 2H), 3.38 (dd,2H) and 1.47 (t, 3H)	
780	5-(3-cloro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilmetil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H)' 7.61(s, 1H), 7.58(d, 1H), 7.48 (t, 1H),7.11 (d, 1H), 6.59 (m,1H), 4.48 (s, 2H) and 3.92 (s, 3H)	
781	2-(3-cloro-fenil)-5-[2-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol	8.04 (s, 1H), 7.93 (d,1H)' 7.60(s, 1H), 7.52(d, 1H), 7.46 (t, 1H),7.06 (d, 1H), 6.59 (m,1H), 3.87 (s, 3H), 3.65(t, 2H) and 3.3 8 (t, 2H)	

		8.05 (s, 1H), 7.94 (d,1H), 7.60(s, 1H), 7.52(d, 1H),			
782	2-(3-cloro-fenil)-5-[2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol	7.47 (t, 1H),7.10 (d, 1H), (m,1H), (q, 3.67(t, 3.39 (t, and 1.43 (t, 3H)	2H), 2H) 2H)	6.59 4.30	
783	2-(3-cloro-fenil)-5-[2-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol	8.05 (s, 1H), 7.94 (d,1H), 7.63 (s, 1H), 7.52(d, 1H), 7.46 (t, 1H),7.01 (d, 1H), (m,1H), (dd, 3.51(t, 3.33 (m, 1.25 (m, and 0.93(m,	2H), 2H) 1H) 2H) 2H)	6.58	383.12

EJEMPLO 784

4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina

Paso 1

{4-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-etoxi-butiliden}-hidrazida del ácido isonicotínico:

Se mezcla clorhidrato del éster del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propionimídico (473.3, 1.5 mmoles) con hidrazida del

ácido isonicotínico (205.7 mg, 1.5 mmoles) en etanol (8 ml) a 60°C durante una hora y después a temperatura ambiente durante 2 horas. La mezcla de reacción se diluye con diclorometano y se lava con agua. La capa orgánica se seca, se concentra con vacío y el residuo se tritura con éter para obtener 490 mg (78.9 %) de {4-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-etoxi-butiliden}-hidrazida del ácido isonicotínico como un sólido de color blanco.

Paso 2

Se obtiene 4-(5-{2-[3(3-cloro-fenil)-[1,2,4]oxadiazol-5-il}-etil)-4-metil-4H-[1,2,4]-triazol-3-il)-piridina (47.1 mg, 82 %) como un sólido de color blanco a partir de {4-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-etoxi-butiliden)-hidrazida del ácido isonicotínico (60 mg, 0.15 mmoles) que se hace reaccionar con metilamina 2M (0.45 ml, 0.9 mmoles) en etanol (1 ml) a 60 °C durante la noche.

^{1}H RMN($CDCl_3$) d(ppm): 8.77 (d, 2H), 8.02 (s, 1H), 7.91 (d, 1H), 7.58(d, 2H), 7.42 (m, 2H), 3.76 (s, 3H), 3.66 (t, 2H) and 3.38 (t, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 784:

Ejemplo No.	Nombre	1H RMN	MS
785	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (d, 2H), 8.05 (s,IH), 7.94 (d, 1H),7.58(d, 2H), 7.43 (m,2H), 4.16 (q, 2H), 3.72(t, 2H), 3.40 (t, 2H) and 1.44 (t, 3H)	
786	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.77 (d, 2H), 8.05 (s,1H), 7.93 (d, 1H),7.73(d, 2H), 7.44 (m,2H), 3.72(t, 3H), 3.51(t, 2H), 3.38 (m, 1H),1.23 (m, 2H) and 0.79(m, 2H)	

EJEMPLO 787

4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina

Paso 1

N-ciclopropil-isonicotinamida:

Se mezcla ester etílico del ácido isonicotínico (3.0 g, 20 mmoles) con ciclopropilamina

(2 ml) a 120°C en un frasco sellado durante 40 horas. La mezcla de reacción se tritura con éter para obtener 1.62 g (50 %) de N-ciclopropil-isonicotinamida como un sólido blanquecino.

^{1}H RMN($CDCl_3$) d (ppm): 8.73 (d, 2H), 7.60 (d, 2H) and 6.55 (w, 1H), 2.92 (m, 1H), 0.90 (m, 2H) and 0.66 (m, 2H).

Paso 2

clorhidrato de cloruro de N-ciclopropil-isonicotinimidoilo:

Se hace reaccionar N-ciclopropil-isonicotinamida (1.62 g, 10 mmoles) con $SOCl_2$ (12 g, 100 mol) a 80°C durante la noche. La mezcla de reacción se concentra y se tritura con diclorometano para obtener 1.3 g (64%) de clorhidrato de cloruro de N-ciclopropil-isonicotinimidoilo como un sólido de color amarillo.

Paso 3

4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina:

se mezcla hidrazida del ácido (R)-3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]- butírico (56 mg,

Ejemplo No.	Nombre	1H RMN	MS
788	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.74 (d, 2H), 8.04 (s,1H), 7.94 (d, 1H), 7.67(d, 2H), 7.43 (m, 2H),3.48(s, 2H), 3.09 (m,1H), 1.75 (s, 6H), 1.16(m, 2H) and 0.68 (m,2H)	
789	4-(5-{2-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.76 (w, 2H), 8.03 (s,1H), 7.92 (d, 1H),7.72(d, 2H), 7.44 (m,2H), 4.13(m, 1H), 3.72(dd, 1H), 3.43 (m, 1H),3.27 (dd, 1H), 1.66 (d,3H), 1.25 (m, 2H) and 0.79 (m, 2H)	
790	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (d, 2H), 8.01 (s,1H), 7.91 (d, 1H), 7.73(d, 2H), 7.49 (d, 1H),7.42 (t, 1H), 3.99 (m,1H), 3.83 (dd, 1H), 3.48(m, 1H), 3.39 (m, 1H),1.61 (d, 3H), 1.25 (m,2H), 0.98 (m, 1H), 0.74(m, 1H)	

0.2 mmoles) con clorhidrato de cloruro de N-ciclopropil-isonicotinimidoilo (40.6 mg, 0.2 mmoles) y K_2CO_3 (60 mg, 0.43 mmoles) en DMF (1 ml) a 100°C durante 3 horas. La mezcla de reacción se diluye con diclorometano y después se lava con agua. La capa orgánica se concentra y purifica con 5~6% de metanol en acetato de etilo para obtener 32 mg (39%) del compuesto del título.

^{1}H-RMN($CDCl_3$) d (ppm): 8.78 (d, 2H), 8.05 (s, 1H), 7.96(d, 1H), 7.73(d, 2H), 7.45(m, 2H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.68 (d, 3H), 1.25 (m, 2H) y 0.79 (m, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 787: se debe indicar que algunas reacciones proveen productos de ciclización de 1,3,4-oxadiazol con pérdida del grupo metilamino o ciclopropilamino en lugar de, o también como, el producto triazol.

791	cis-4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.73 (d, 2H), 7.88 (s,1H), 7.78 (d, 1H), 7.65(d, 2H), 7.41 (d, 1H),7.34 (t, 1H), 3.20 (m,1H), 2.89 (m, 2H), 2.54(dd, 1H), 2.00 (td, 1H),1.20 (m, 211), 0.83 (m,2H)
792	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina	8.82 (m, 2H), 7.98 (s,1H), 7.90 (m, 3H), 7.47(d, 1H), 7.39 (t, 1H),3.51 (s, 2H), 1.70 (s,6H)
793	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-[1,3,4]oxadiazol-2-il)-piridina	8.76 (d, 2H), 8.07 (s,1H), 7.97 (d, 1H), 7.77(d, 2H), 7.49 (dd, 1H),7.43 (t, 1H), 3.53 (s,2H), 1.69 (s, 6H)
794	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-[1,3,4]oxadiazol-2-il)-piridina	8.82 (d, 2H), 8.05 (m,1H), 7.95 (d, 1H), 7.91(d, 2H), 7.50 (dd, 1H),7.42 (t, 1H), 3.94 (dd,1H), 3.67 (dd, 1H), 3.41(dd, 1H), 1.66 (d, 3H)

795	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-[1,3,4]oxadiazol-2-y1)-piridina	8.77 (d, 2H), 7.81 (m,4H), 7.42 (d, 1H), 7.32(t, 1H), 3.07 (q, 1H),2.99 (q, 1H), 2.41 (q,1H), 2.08 (td, 1H)
796	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.76 (d, 2H), 7.85 (m,1H), 7.77 (d, 1H), 7.55(d, 2H), 7.44 (dd, 1H),7.34 (t, 1H), 3.70 (s,3H), 2.89 (m, 1H), 2.72(m, 1H), 2.51 (q, 1H),2.02 (dt, 1H)
797	4-(5-{2-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (d, 2H), 8.02 (s,1H), 7.93 (d, 1H), 7.59(d, 2H), 7.53 (d, 1H),7.46 (t, 1H), 4.03 (m,1H), 3.80 (s, 3H), 3.52(m, 1H), 3.23 (dd, 1H),1.66 (d, 3H)
798	4-(5-{2-[3-(3-cloro-pheriyl)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina	8.81 (d, 2H), 8.07 (s,1H), 7.97 (d, 1H), 7.87(d, 2H), 7.50 (d, 1H),7.43 (t, 1H), 3.91 (q,1H), 3.66 (dd, 1H), 3.44(dd, 1H), 1.65 (d, 3H)

799	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.80 (d, 2H), 8.05 (s,1H), 7.95 (d, 1H), 7.61(d, 2H), 7.51 (d, 1H),7.45 (t, 1H), 4.07 (q,1H), 3.75 (s, 3H), 3.48(dd, 1H), 3.23 (dd, 1H),1.68 (d, 3H)
800	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (d, 2H), 8.05 (s,1H), 7.96 (d, 1H), 7.74(d, 2H), 7.50 (dd, 1H),7.46 (t, 1H), 4.15 (q,1H), 3.64 (dd, 1H), 3.31(m, 2H), 1.67 (d, 3H),1.25 (m, 2H), 0.81 (m,2H)
801	(S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbamicacid tert-butil ester	

EJEMPLO 802

(S)-1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H[1,2,4]triazol-3-il)-etilamina

Se mezcla éster ter-butilico del ácido (S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico (135 mg) con ácido fórmico al 96% (1.3 ml) y se calienta a 50°C durante 1 hora. La mezcla de reacción se concentra al vacío. El residuo se extingue con bicarbonato de sodio saturado y se extrae con acetato de etilo. La capa orgánica se seca con sulfato de sodio y se concentra. La purificación se efectúa mediante cromatografía de vaporización instantánea en columna con gel de sílice con 2-3% (amoniaco 2 M en metanol) en diclorometano para obtener 106 mg del compuesto del título como un sólido blanquecino.

^{1}H RMN ($CDCl_3$):d ppm 8.73 (d, 2H), 8.03 (s, 1H), 7.93 (d, 1H), 7.69 (d, 2H), 7.46 (d, M), 7.42 (t, 1H), 5.02 (dd, 1H), 3.61 (dd, I H), 3.49 (dd, 1H), 3.35 (m, 1B), 2.47 (br s, 2H), 1.20 (m, 2H), 0.75 (m, 2H)

EJEMPLO 803

(S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-dimetil-amina

Se agrega cianoborohidruro de sodio (0.1 ml, 1M en THF) a una solución de (S)-1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etilamina (30 mg) en metanol (0.8 ml) que contiene ácido fórmico al 96% (0.1 ml) y solución de formalina al 37% (0.1 ml). El residuo se extingue con agua y se extrae con acetato de etilo. La capa orgánica se seca con sulfato de sodio y se concentra. La purificación se efectúa mediante cromatografía de vaporización instantánea en columna con gel de sílice con 3% (amoniaco 2M en metanol) en diclorometano para obtener 22 mg del compuesto del título.

^{1}H RMN ($CDCl_3$):d ppm. 8.76 (d, 2H), 8.06 (s, 1H), 7.97 (d, 1H), 7.73 (d, 2H), 7.47 (d, I H), 7.45 (t, 1H), 5.00 (dd, I H), 3.76 (dd, 1H), 3.51 (dd, 1H), 3.42 (m, I H), 2.45 (br s, 6H), 1.26 (m, 2H), 0.88 (m, 1H), 0.79 (m, 1H).

EJEMPLO 804

8-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]piridina

Se agregan 37 mg (0.25 mmoles) de Me_3OBF_4 a una solución de 60 mg (0.21 mmoles) de 3-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona en 2 ml de CH_2Cl_2. La mezcla se agita durante la noche a temperatura ambiente. La mezcla de reacción se diluye con CH_2Cl_2, se lava con $NaHCO_3$ (saturado), se seca y se concentra. El residuo se disuelve en 3 ml de EtOH y se agregan 22 mg (0.16 mmoles) de hidrazida isonicotínica. La solución se calienta con microondas a 120°C durante 10 minutos. La mezcla de reacción se enfría y se eliminan los volátiles a presión reducida. El producto crudo se purifica mediante HPLC preparativa para obtener 17 mg (20%) del producto deseado.

^1H RMN ($CDCl_3$):d ppm 1.75 (m, 1H) 1.99 (m, 1H) 2.21 (m, 2H) 3.16 (dd, 1H) 3.73 (m, 1H) 3.85 (dd, 1H) 4.07 (m, 1H) 4.19 (m, 1H) 7.47 (t, 1H) 7.56 (m, 1H) 7.67 (m, 2H) 8.01 (m, 1H) 8.11 m, 1H) 8.76 (d, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 804:

Ejemplo No.	Nombre	1H RMN	MS
805	8-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-tiofen-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]piridina	1.69 (m, 1H) 1.99 (m, 1 H)2.18(m,2H)3.11 (m, 1H) 3.67 (m, 1H) 3.87 (m, 1H) 4.02 (m, 1 H) 4.24 (m, 1H) 7.15 (m, 1H) 7.47 (m, 3H)) 7.56 (m, 1H) 8.01 (d, J=7.83H)z, 1H) 8.12 (d, J=1.77 Hz, 1H)	
806	8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmethyl]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]piridina	1.76 (m, 1H) 2.00 (m, 1 1-1) 2.21 (m, 2H) 3.22 (dd, , 1H) 3.74 (m, 1H) 3.87 (dd, 1H) 4.09 (m, 11-1) 4.19 (m, 1H) 7.23 (m, 1H) 7.53 (m, 1H) 7.68 (m, 2H) 8.10 (dd, 1H) 8.77 (m, 2H)	

EJEMPLO 807

5-(5-bromo-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-cloro-fenil)-[1,2,4]oxadiazol

Se mezcla 3-(3-cloro-fenil)-5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol con 30 ml de cloroformo/piridina (25/1) a temperatura

ambiente. Después se agrega, mediante goteo, bromo en cloroformo (0.5 ml) y la mezcla de reacción se calienta a 70°C durante la noche. La mezcla de reacción se diluye con cloroformo y se lava con NH4Cl saturado dos veces y la capa orgánica se seca con sulfato de sodio, se concentra, el residuo se tritura con éter dietílico para obtener el compuesto del título (1.5 g, 57.5%, sóido de color amarillo).

^{1}H RMN($CDCl_3$) d(ppm): 8.05 (s, 1H), 7.94 (d, 1H), 7.47(d, 1H), 7.43 (t, 1H), 4.66 (s, 2H) and 3.59 (s, 3H).

EJEMPLO 808

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina

Se agrega TFA (1.5 ml) al éster ter-butilico del ácido {3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)[1,2,4]oxadiazol-5-il-fenil)-carbámico (88.0 mg, 0.19 mmoles) en diclorometano (3 ml) a 0°C y se deja agitar durante 1 hora. La mezcla de reacción se calienta hasta temperatura ambiente y el solvente se elimina al vacío. Se agrega dichlorometano al residuo resultante y la mezcla se enfría hasta 0°C y se agrega

bicarbonato de sodio saturado a la solución en agitación hasta que se torna básica (pH ~ 8). La mezcla se transfiere después a un embudo de separación y el producto se extrae con diclorometano, se seca utilizando sulfato de sodio anhidro, y se concentra al vacío. El residuo resultante se tritura con éter y se aíslan 61.1 mg (87%) de 3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina (sólido de color amarillo claro).

^{1}H RMN (DMSO-d_6) d (ppm): 7.81 (d, 1H), 7.64 (d, 1H), 7.23 (m, 4H), 6.84 (d, 1H), 5.57 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 98:

Ejemplo No.	Nombre	1H RMN	MS
809	5-(3-cloro-ph6nil)-3-(4-metil-5 tiofen-2-il-4H-[1,2,4]triazol-3-sulfonilmetil)-[1,2,4]oxadiazole		423.01
810	5-(3-cloro-fenil)-3-(4-metil-5 tiofen-2-il-4H-[1,2,4]triazol-3 sulfinilmetil)-[1,2,4]oxadiazole		

Los siguientes compuestos se preparan de manera análoga a la del ejemplo93:

Ejemplo No.	Nombre	1H RMN MS
811	2-metil6-[3-(4-metil-5 tiofen-2-il-4H-[1,2,4]triazol-3 ilsulfanilmetil)-[1,2,4]oxadiazol 5-il]-piridina	

EJEMPLO 812

4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol

Se agregan HBr (1 ml) y HOAc (1 ml) a 4-(5-{1-[5-(3-cloro-fenil)[1,2,4]oxadiazol-3-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina (9 mg, 0.02 mmoles) y la reacción se agita a 80°C. Se agrega $NaHCO_3$ saturado (acuoso) a la reacción y la mezcla se extrae tres veces con diclorometano. Las fases orgánicas combinadas se secan y se concentran para obtener el compuesto del título (8.5 mg, 99%).

^1H RMN ($CDCl_3$), δ (ppm): 1.37 (t, 3H)), 1.96 (d, 3H)), 4.10 (q, 2H), 5.23 (q, 1H), 6.80 (m, 2H), 7.49 (t, 2H), 7.59 (m, 1H), 7.99 (d, 1H), 8.11 (s, 1H).

EJEMPLO 813

4-(5-(2-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-propil)-4-metil-4H-[1,2,4]triazol-3-il)-piridina

se agregan, mediante goteo 84 microl (0.21 mmoles, 2.5 M) de n-BuLi a una solución de 37 mg (0.21 mmoles) de 4-(4,5-dimetil-4H-[1,2,4]triazol-3-il)-piridina en 2.1 ml de THF a 0°C. Después de 20 minutos se agrega, mediante goteo, una solución de 60 mg (0.21 mmoles) de 3-(1-bromo-etil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol. Se deja que la mezcla de reacción llegué a temperatura ambiente y se agita durante la noche. Se agrega NH_4Cl (saturado) y la mezcla se extrae dos veces con EtOAc. La fase orgánica se seca y se concentra. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 20:1) permite obtener 7.7 mg (10%) del producto deseado.

^1H RMN ($CDCl_3$), d (ppm): 1.57 (d, 3H)) 3.16 (m, 1H) 3.38 (m, 1H) 3.71 (s, 3H)) 3.84 (d, 1H) 7.46 (t, 1H) 7.55 (m, 1H) 7.58 (m, 2H) 7.98 (m, 1H) 8.10 (t, 1H) 8.77 (d, 2H).

EJEMPLO 814

[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-amina

Se agregan 10 mg (0.4 mmoles) de NaH a una solución de 38 mg (0.2 mmoles) de metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-amina en 3 ml de DMF bajo una atmósfera de nitrógeno. Después de 10 minutos, se agrega una solución de 50 mg (0.22 mmoles) de 3-clorometil-5-(3-cloro-fenil)-[1,2,4] oxadiazol en 2 ml de DMF. Después de agitar durante 45 minutos, se agrega NH_4Cl (saturado) y la mezcla se extrae dos veces con $CHCl_3$. La fase orgánica se seca y se concentra. La cromatografía de vaporización instantánea(CH_2Cl_2/MeOH 20:1) permite obtener 41 mg (54%) del producto deseado.

^1H RMN ($CDCl_3$), d (ppm): 3.07 (s, 3H)) 3.71 (s, 3H)) 4.56 (s, 2H) 7.45 (m, 1H) 7.55 (m, 1H) 7.62 (d, 2H) 7.98 (d, 1H) 8.09 (m, 1H) 8.73 (d, 2H).

EJEMPLO 815

8-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina

Se agregan 32 mg (1.31 mmoles) de NaH a una solución de 193 mg (0.96 mmoles) de 3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina en 10 ml de DMF a temperatura ambiente. Después de 10 minutos, se agregan 200 mg (0.87mmol) 5-(3-cloro-fenil)-3-clorometil-[1,2,4]oxadiazol a la mezcla de reacción. La mezcla de reacción se agita a temperatura ambiente durante la noche. La mezcla de reacción se diluye con NH_4Cl (saturado) y se extrae dos veces con EtOAc. Las fases orgánicas combinadas se lavan con agua, se secan y se concentran. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 20:1) permite obtener 111 mg (32%) de un sólido de color blanco.

^1H RMN ($CDCl_3$), d (ppm): 2.24 (m, 2H) 3.57 (m, 2H) 4.15 (m, 2H) 5.01 (s, 2H) 7.46 (t, 1H) 7.56 (d, 1H) 7.62 (d, 2H) 7.99 (d, 1H) 8.10 (s, 1H) 8.70 (d, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 815:

Ejemplo No.	Nombre	1H RMN	MS
816	8-[5-(5-cloro-2-fluoro-fenil) [1,2,4]oxadiazol-3-ilmetil]-3 piridin-4-il-5,6,7,8-tetrahydro [1,2,4]triazolo[4,3-a]pirimidina		
817	8-[5-(3-cloro-fenil) [1,3,4]oxadiazol-2-ilrnetil]-3 piridin-4-il-5,6,7,8-tetrahydro [1,2,4]triazolo[4,3-a]pirimidina		
818	8-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etil}-3-piridin-4-il-5,6,7, 8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina	1.81(d,3H)2.19(m,2 11) 3.47 (m, 2H) 4.12 (m, 2H) 6.07 (q, 1H) 7.42 (m, 1H) 7.49 (m, 1 H) 7.61 (m, 2H) 7.91 (m, 1H) 8.00 (m, 1H) 8.70 (m, 2H)	
819	8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina	2.23 (m, 2H) 3.50 (m, 2 H) 4.20 (m, 2H) 4.97 (s, 2H) 6.49 (m, 1H) 6.89 (d, 1H) 7.19 (t, 1H) 7.48 (m, 1H) 7.51 /m, 1 H) 8.06 (m, 1H)	

820	8-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina	1.74 (d, 3H)) 2.17 (m, 2H) 3.45 (m, 2H) 4.10 (m, 2H) 5.96 (m, 1H) 7.44 (t, 1H) 7.53 (m, 1H) 7.59 (m, 2H) 7.97 (m, 1H) 8.08 (m, 1H) 8.67 (d, 2H)

EJEMPLO 821

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(1H-pirrol-3-il)-[1,2,4]oxadiazol

Se calientan 3-clorometil-5-[1-(toluen-4-sulfonil)-1H-pirrol-3-il]-[1,2,4]oxadiazol (50 mg) e hidróxido de potasio (50 mg) durante dos horas en metanol (5 ml). La mezcla se diluye con acetato de etilo (10 ml), se lava con agua y salmuera, se seca con $MgSO_4$, se filtra y se concentra. El compuesto del título se aísla con 57% de rendimiento mediante cromatografía de vaporización instantánea en gel de sílice utilizando 40% de acetato de etilo en heptano.

^1H RMN ($CDCl_3$) d (ppm): 9.8 (s, 1H), 7.5 (m, 2H), 7.4 (d, 1H), 7.2 (dd, 1H), 6.8 (m, 1H), 6.7 (d, 1H), 4.5 (s, 2H), 4.1 (q, 2H), 1.4 (t, 3H).

EJEMPLO 822

1-óxido de 4-[5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina

Se disuelven 4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]-triazol-3-il}-piridina y MCPBA al 57%-86% húmedo (52.4 mg, 0.20-0.30 mmoles)en diclorometano (4 ml) y se agita durante 16 horas. La mezcla de reacción se purifica mediante cromatografía líquida preparativa de fase invertida para obtener el compuesto del título (7.5 mg, 8%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.33 (d, 2H), 8.06 (m, 1H), 7.96 (m, 1H), 7.67 (d, 2H), 7.57 (m, 1H), 7.46 (apparent t, 1H), 4.60 (s, 2H), 3.71 (s, 3H)).

EJEMPLO 823

5-(3-cloro-fenil)-3-(2-furan-2-il-3-metil-3H-imidazol-4-ilsulfanilmetil)-[1,2,4]oxadiazol

Se disuelve 2-furan-2-il-3-metil-3,5-dihidro-imidazol-4-ona (descrita en Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989) 6375-6386) (50 mg, 0.30 mmoles) en dioxano (3 ml) y se

agrega reactivo de Lawesson (136 mg, 0.34 mmoles). La mezcla de reacción se calienta a reflujo durante la noche y después se deja que llegue a temperatura ambiente momento en el cual se agregan DIPEA (212 ml, 1.22 mmoles) y 3-clorometil-5-(3-cloro-fenil)-[1,2,4]oxadiazol (140 mg, 0.61 mmoles). La mezcla resultante se calienta a reflujo durante 5 horas y después se mantiene a temperatura ambiente durante la noche. Se agrega acetato de etilo y la mezcla de reacción se lava con agua seguido por salmuera. La fase orgánica se seca con $MgSO_4$ y se evapora. El compuesto del título (13 mg, 11%) se obtiene mediante cromatografía de vaporización instantánea utilizando 1% de metanol en cloroformo.

^1H RMN (CD_3OD) d (ppm): 7.96 (m, 1 H), 7.90 (m, 1H), 7.60 (dd, 1H), 7.57 (ddd,1H), 7.46 (t, 1H), 7.09 (s, 1H), 6.86 (dd, 1H), 6.52 (dd, 1H), 3.95 (s, 2H), 3.74 (s, 3H).

EJEMPLO 824

5-(5-cloro-2-fluoro-fenil)-3-[4-(2-fluoro-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol

A una solución fría (-15 °C) de 2-{3-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-etanol (46 mg, 0.11 mmoles) en THF anhidro (15 ml) se agrega mediante goteo DAST (32 ml, 0.24 mmoles). La mezcla se agita a temperatura ambiente durante 1.5 horas y después se extingue con MeOH (1 ml). El solvente se elimina a presión reducida y el residuo se divide entre salmuera y EtOAc. La capa acuosa se extrae con EtOAc (2 x 20 ml). Las capas orgánicas combinadas se lavan con salmuera (10 ml), se secan ($MgSO_4$) y se concentran a presión reducida. La purificación mediante cromatografía de vaporización instantánea (EtOAc:heptano 2:1) y HPLC preparativa permite obtener el compuesto del título como un sólido de color blanco (11 mg, 22%).

^1H RMN ($CDCl_3$) d (ppm): 8.05 (dd, 1H), 7.52 (m, 3H), 7.20 (m, 1H), 7.16 (m, 1H), 4.75 (t, 1H), 4.63 (m, 3H), 4.45 (m, 2H).

EJEMPLO 825

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4] oxadiazol

El compuesto del título se prepara de conformidad con el método para 2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1H-benzoimidazol, con la excepción que se utiliza el equivalente molar de carbonato de cesio en lugar de carbonato de potasio como la base, a partir de 1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol (32.3 mg, 0.097 mmoles) y 4-etil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona (23 mg) utilizando 50% de EtOAc en n-heptano como el eluyente para cromatografía para obtener 21 mg.

^{1}H RMN ($CDCl_3$) d (ppm): 7.95 (d, 1H), 7.57 (dd, 1H), 7.44 (d, 1H), 7.07 (dd, 1H), 6.56 (dd, 1H), 4.56 (s, 2H), 4.22 (q, 2H), 1.35 (t, 3H).

EJEMPLO 826

3-[3-(4-Ethil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-hidroxi-benzonitrilo

El compuesto del título se prepara utilizando el procedimiento general de Rogers et al., Tetrahedron Letters (2002) 43: 3585-3587. A una solución en agitación de 3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-

[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo (20mg, 0.050 mmoles), 2-(metilsulfonil-etanol) (9.38 mg, 0.075 mmoles), y DMF (0.05 M) a 0°C se agrega NaH (5.8 mg, 0.150 mmoles). Se agita durante 20 minutos y se retira el baño de hielo. Se agita 20 minutos adicionales mientras se calienta hasta temperatura ambiente. La mezcla de reacción se extingue con solución de HCl 1N y se divide entre acetato de etilo y salmuera. La capa orgánica se seca (Na_2SO_4), se filtra y se concentra hasta sequedad. Los materiales orgánicos crudos se purifican mediante cromatografía de vaporización instantánea en columna utilizando acetato de etilo seguido por 5% de metanol en acetato de etilo para obtener el compuesto del título (8.1 mg, 41%, sólido de color blanco).

^1H RMN ($CDCl_3$), δ (ppm): 8.25 (m, 1H), 7.75 (m, 1H), 7.60 (s, 1H), 7.18 (m, 2H), 6.60 (m, 1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).

Ejemplos farmacéuticos

Prueba FLIPR de actividad antagonista del receptor del grupo I

Para el análisis FLIPR, se siembran células en placas de 96 cavidades de fondo transparente revestidas con colágena con lados oscuros y se

efectúa el análisis de movilización de $[Ca^{2+}]_i$ 24 horas después de la siembran.

Los cultivos de células en las placas de 96 cavidades se cargan con una solución 4 µM de la forma de éster acetoximetílico del indicador fluorescente de calcio fluor-3 (Molecular Probes, Eugene, Oregon) en Pluronic al 0.01%. Todas las pruebas se efectúan en una solución reguladora que contiene 127 mM de NaCl, 5 mM de KCI, 2 mM de $MgCl_2$, 0.7 mM de NaH_2PO_4, 2 mM de $CaCl_2$, 0.422 mg/ml de $NaHCO_3$, 2.4 mg/ml de HEPES, 1.8 mg/ml de glucosa y 1 mg/ml de fracción IV de BSA (pH 7.4).

Los experimentos FLIPR se efectúan utilizando un ajuste de láser de 0.800 W y una velocidad de obturador de cámara CCD de 0.4 segundos con longitudes de onda de excitación y emisión de 488 nm y 562 nm, respectivamente. Cada experimento FLIPR se inicia con 160 µL de solución reguladora presente en cada cavidad de la placa de células. Una adición de 40 µL proveniente de la placa de antagonista es seguida por una adición de 50 µl proveniente de la placa de agonista. Después de cada adición, se muestrea la señal de fluorescencia 50 veces a intervalos de 1 segundo seguido por tres muestras a intervalos de 5 segundos. Las respuestas se miden

como la altura del pico de la respuesta dentro del periodo de la muestra.

Las determinaciones de CE_{50}/CI_{50} se efectúan a partir de datos obtenidos de curvas de concentración-respuesta de 8 puntos (CRC por sus siglas en inglés) efectuadas por duplicado. Las CRC del agonista se generan escalando todas las respuestas hasta la respuesta máxima observada para la placa. El bloque de antagonista de la exposición al agonista se normaliza con la respuesta promedio de la exposición al agonista en 14 cavidades de control en la misma placa.

Medición del recambio de fosfato de inositol en células enteras intactas

Se siembran células GHEK expresan en forma estable al receptor mGluR5d de humano en placas de 24 cavidades revestidas con poli-L-lisina a 40 x 10^4 células/cavidad en medio que contiene 1 µCi/ cavidad de [3H] mio-inositol. Las células se incuban durante la noche (16 horas), después se lavan tres veces y se incuban durante 1 hora a 37°C en solución salina regulada con HEPES (146 mM de NaCl, 4.2 mM de KCl, 0.5 mM de $MgCl_2$, 0.1% de glucosa, 20 mM de HEPES, pH 7.4) complementado con 1 unidad/ml de glutamato

piruvato transaminasa y 2 mM de piruvato. Las células se lavan una vez en solución salina regulada con HEPES y se pre-incuban durante 10 minutos en solución salina regulada con HEPES que contiene 10 mM de LiCl. Se agregan los compuestos (agonistas) y se incuban a 37°C durante 30 minutos. La actividad antagonista se determina pre-incubando los compuestos de prueba durante 15 minutos, incubando después en presencia de glutamato (80 µM) o DHPG (30 µM) durante 30 minutos. La reacción se determina mediante adición de 0.5 ml de ácido perclórico (5%) en hielo, con incubación a 4°C durante por lo menos 30 minutos. Las muestras se recolectan en tubos Falcon de 15 ml y los fosfatos de inositol se separan utilizando columnas Dowex como se describe más adelante.

Prueba para fosfatos de inositol utilizando columnas de intercambio iónico alimentadas por la fuerza de gravedad

a) preparación de las columnas de intercambio iónico

Se lava tres veces la resina para intercambio iónico (forma de formato Dowex AG1-X8, malla 200-400, BIORAD) con agua destilada y se

almacenan a 4°C. Se agregan 1.6 ml de resina a cada columna y se lavan con 3 ml de HEPES 2.5 mM, 0.5 mM de EDTA, pH 7.4.

b) tratamiento de la muestra

las muestras se recolectan en tubos Falcon de 15 ml y se neutralizan con HEPES 0.375 M, 0.75 M de KOH. Se agregan 4 ml de HEPES/EDTA (2.5/0.5 mM, pH 7.4) para precipitar el perclorato de potasio. Se agrega el sobrenadante a las columnas Dowex preparadas.

c) separación del fosfato de inositol

Se eluyen los glicero fosfatidil inositoles con 8 ml de formiato de amonio 30 mM.

Se eluyen los fosfatos de inositol con 8 ml de formiato de amonio 700 mM/ácido fórmico 100 mM y se recolecta el eluato en frascos para cintigrafía. Se efectúa el conteo en el eluato con 8 ml de reactivo para cintigrafía.

Resultados

Los valores de CI_{50} típicos, según se mide en las pruebas antes descritas, son 10 µm o menores. En un aspecto de la invención el CI_{50} es menor de 2

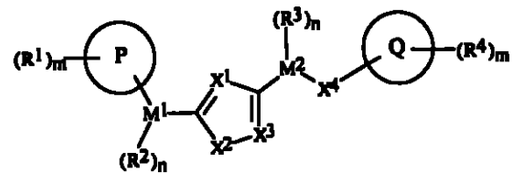
µM. En otro aspecto de la invención el CI_{50} es menor de 0.2 µM. En otro aspecto adicional de la invención el CI_{50} es menor de 0.05 µM.

NOVEDAD DE LA INVENCION

Habiendo descrito el presente invento se considera como novedad y por lo tanto se reclama como propiedad lo contenido en las siguientes:

REIVINDICACIONES

1.-Un compuesto que tiene la fórmula Ia:



(I)

caracterizado porque:

P se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{3-7} o un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro,

halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})-arilo, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, alquil(C_{1-6})OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})$(CO)R^5$, O-alquil(C_{1-6})$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-$(CO)NR^5R^6$, O-alquil(C_{1-6})$(CO)NR^5R^6$, alquil(C_{0-6})NR^5-$(CO)R^6$, O-alquil(C_{2-6})$NR^5(CO)R^6$, alquil(C_{0-6})$NR^5(CO)$-NR^5R^6, alquil(C_{0-6})SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})-$(SO)R^5$, O-alquil(C_{2-6})$(SO)R^5$, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})$(SO_2)NR^5R^6$, O-alquil(C_{2-6})-$(SO_2)NR^5R^6$, alquil-(C_{0-6})$NR^5(SO_2)R^6$, O-alquil(C_{2-6})NR^5-$(SO_2)R^6$, alquil(C_{0-6})-$NR^5(SO_2)NR^5R^6$, O-alquil(C_{2-6})NR^5-$(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})-$NR^5(CO)OR^6$, O-alquil-(C_{2-6})$NR^5(CO)OR^6$, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, en el cual dicho anillo puede estar sustituido con uno o más A;

M^1 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquenilo de

C_{2-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-3})(CO)NR^5-alquilo de C_{0-3}, alquil(C_{0-4})NR^5, alquil(C_{0-3})-S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)-alquilo de C_{0-3} o alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^2 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^1, X^2 y X^3 se seleccionan de manera independiente a partir del grupo que consiste de CR, CO, N, NR, O y S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5, alquil(C_{0-3})NR^5R^6 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, cicloalquilo de C_{3-7}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil-(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5; alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})-

(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, =NR^5, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5, alquil(C_{0-4})(NR^5R^6), alquil(C_{0-4})-(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halogenoalquilo de C_{1-4}, C, O, SO, SO_2 y S;

Q es un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S y cuyo anillo fusionado puede estar sustituido con uno o más A;

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, =NR^5, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo,

O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, en el cual dicho anillo puede estar sustituido con uno o más A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno, hidroxi, alquilo de C_{1-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, y en el cual R^5 y R^6 pueden formar juntos un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

en el cual cualquier alquilo de C_{1-6}, alquenilo de C_{2-6}, alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo y alquil(C_{0-6})-heteroarilo definido bajo R^1, R^2, R^3, R^4, R^5 y R^6 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, oxo, halógeno, nitro,

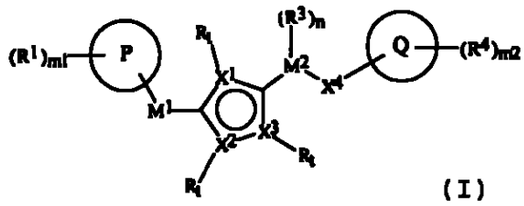
alquil(C_{0-6})ciano, alquilo de C_{1-4}, alquil(C_{0-4})cicloalquilo de C_{3-6}, halogenoalquilo de C_{1-6}, O-halógenoalquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquilo de C_{1-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, alquil(C_{0-6})-NR^5R^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})-NR^5(CO)NR^5R^6, O(CO)NR^5R^6, NR^5(CO)OR^6, alquil(C_{0-6})(SO_2)-NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)-NR^5R^6, O-alquil(C_{2-6})(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m se selecciona a partir de 0, 1, 2, 3 y 4; y

n se selecciona a partir de 0, 1, 2 y 3,

o sal del mismo.

2.- Un compuesto de la fórmula I



(I)

caracterizado porque:

P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5;

R^1 está unido a P a través de un átomo de carbono en el anillo P y se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})-(CO)R^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, alquil(C_{0-6})NR^5(CO)R^6, O-

alquil(C_{2-6})$NR^5(CO)R^6$, alquil(C_{0-6})$NR^5(CO)NR^5R^6$, alquil(C_{0-6})-SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})$(SO)R^5$, O-alquil(C_{2-6})-$(SO)R^5$, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})-$(SO_2)NR^5R^6$, O-alquil(C_{2-6})$(SO_2)NR^5R^6$, alquil(C_{0-6})NR^5-$(SO_2)R^6$, O-alquil(C_{2-6})$NR^5(SO_2)R^6$, alquil(C_{0-6})$NR^5(SO_2)$-NR^5R^6, O-alquil(C_{2-6})$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})$NR^5(CO)OR^6$, O-alquil(C_{2-6})$NR^5(CO)$-OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

M^1 es un enlace;

X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S;

X^2 se selecciona a partir del grupo que consiste de C, N, O y S;

X^3 es i) seleccionada a partir del grupo que consiste de N, O y S, o

ii) se selecciona a partir de N, O, S, y C cuando X^2 se selecciona a partir de N, O, o S, y cuando X^3 es C, el sustituyente R en X^3 es H;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})$(CO)OR^5$ y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que

consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)-alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo;

Q es i) seleccionada a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en los cuales cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y cualquier átomo de carbono apropiado está opcionalmente sustituido

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con R^4; y

R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})-(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})N-(alquilo de C_{1-4})$_2$ y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N

y O, y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A; o

ii) se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo; y

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A;

R^5 y R^6 se seleccionan de manera independiente

a partir del grupo que consiste de hidrógeno y alquilo de C_{1-6};

en el cual cualquier alquilo de C_{1-6} definido bajo R^1, R^2 y R^4 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})-NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)-NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5-(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m1 se selecciona a partir de 0, 1, 2, 3 y 4;

m2 se selecciona a partir de 0, 1, 2 y 3;

n se selecciona a partir de 0, 1 y 2; y

t es 0 o 1,

y sales de los mismos,

con la condición que el compuesto no sea 5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol, 1,2-di{2-(3-amino-fenil)-[1,3,4]-oxadiazol-il)etano, 1,2-di{5-[5-(4-nitrofenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-bromo-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-cloro-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano y 1,2-di{5-[5-(2,4-dibromofenil)furan-2-il]-[1,3,4]-oxadiazol-il)etano.

** 3. Un compuesto de conformidad con la reivindicación 2, caracterizado porque P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo o fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5 y R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})cicloalquilo de C_{3-6}, alquil(C_{1-6})OR^5, alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})CO_2R^5, alquil(C_{0-6})-ciano, alquil(C_{0-6})NR^5R^6, alquil(C_{0-6})SR^5 y un anillo

de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

4.- Un compuesto de conformidad con la reivindicación 3, caracterizado porque P es fenilo sustituido en la posición 3 o disustituido en las posiciones 2 y 5.

5.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque X^1 es N y uno de X^2 y X^3 es O y el otro es N.

6.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque el anillo que contiene a X^1, X^2 y X^3 forma un oxadiazol, isoxazol, oxazol, cloro-isoxazol o un metil-isoxazol.

7.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque M^2 es un enlace o alquilo de C_{1-3} y R^3 es hidrógeno, metilo o dimetilo.

8.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque X^4 se selecciona a partir del grupo que consiste de alquil$(C_{0-4})R^5R^6$, cicloalquilo de C_{3-7}, NR^5, O, SO, SO_2 y S y R^5 y R^6 se seleccionan de manera independiente a partir de hidrógeno y alquilo de C_{1-6}.

9.- Un compuesto de conformidad con la

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reivindicación 8, caracterizado porque X^4 se selecciona a partir del grupo que consiste de CH_2, $CHCH_3$, $CH(CH_3)_2$ y NR^5.

10.- Un compuesto de conformidad con la reivindicación 8, caracterizado porque X^4 es S.

11.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno, y cualquier átomo de carbono apropiado está sustituido opcionalmente con R^4 y R^4 se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-

heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

12. Un compuesto de conformidad con cualquiera de las reivindicaciones 2 u 11, caracterizado porque Q se selecciona a partir del grupo que consiste de triazolilo y tiadiazolilo.

13.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo y R^4 es hidrógeno o alquilo de C_{1-6}.

14.- Un compuesto de conformidad con

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cualquiera de las reivindicaciones 2 o 13, caracterizado porque Q se selecciona a partir del grupo que consiste de piridonilo, tetrahidrotriazolopiridilo y tetrahidrotriazolo-pirimidinilo.

15.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque R^4 se selecciona a partir del grupo que consiste de benzo[b]tiofenilo, benzodioxolilo, bromo, bromofurilo, butoxifenilo, clorometoxipiridilo, clorofenilo, clorofenilmetanol, cloropiridilo, clorotiofeno, cianofenilo, ciclohexilo, ciclopentilo, diclorofenilo, dicloropiridilo, difluorofenilo, dimetiltiazolilo, etanol, etoximetilo, fluorometilfenilo, fluorofenilo, éster metílico del ácido fórmico, furilo, hidrógeno, hidroxifenoximetilo, hidroxifenilo, imidazolilo, metoxietilo, metoximetilo, metoxifenoximetilo, metoxifenilo, metoxifeniletilo, metoxipiridazinilo, metoxipiridilo, metoxipirimidinilo, metoxitiofeno, metilimidazolilo, metilpiridilo, metilsulfanilmetilo, metiltiazolilo, metiltiofeno, nitrofurilo, nitrofenilo, fenilo, p-toliloximetilo, piridazinilo, piridin-oxidilo, bencilmorfolinilo, piridinolilo, piridilo, piridilmetilo, pirimidinilo, ter-

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butilfenilo, tetrahidrofurilo, tiazolilo, tiofeno, tolilo, trifluorometilo, éster metílico del ácido acético, alilo, amino, bencilo, ciclopropilmetilo, etilo, fluorobencilo, fluoroetilo, furilmetilo, hidroxietilo, isobutilo, metilo, metilbencilo, metilbutilo, metilsulfanilpropilo, n-butilo, n-hexilo, n-propilo, tetrahidrofurilmetilo, tiofenilmetilo y trifluoroetilo.

16.- Un compuesto caracterizado porque se selecciona a partir del grupo que consiste de:

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

5-(3-metoxifenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-metil-1*H*-benzoimidazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]-oxadiazol,

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3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[4-metil-5-(2-metil-tiazol-4-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-[5-(2-metil-tiazol-4-il)-[1,3,4]oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

3-[4-metil-5-(5-nitro-furan-2-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-[5-(4-ter-butilfenil)-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-benzo-oxazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)piridina,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-imidazo[4,5-b]piridina,

5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

3-metil-5-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-metil-5-fenil-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxa-diazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-morfolina,

4-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,2,4]oxadiazol,

2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(2-metilpiridin-4-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

2-[5-(3-yodofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil}-amina,

5-(3-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-trifluorometoxi-fenil)[1,2,4]-oxadiazol,

3-(5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-bromo-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-benzoimidazol,

5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-[5-(3-metoximetil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

4-[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina,

2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-1-metil-1*H*-imidazo[4,5-b]piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1-metil-1*H*-imidazo[4,5-b],

3-[1-metil-1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]oxadiazol, o

5-(3-furan-3-il-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

o sal de los mismos.

17.- Un compuesto caracterizado porque se selecciona a partir del grupo que consiste de

4-(4-ciclopropil-5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-

piridina,

4-{4-metil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-o-tolil-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-{3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]-triazol-4-il}-etanol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxa-diazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(4-etil-5-furan-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

Ester metílico del ácido {3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-acético,

5-(2-fluoro-5-metil-fenil)-3-[5-furan-2-il-4-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-

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oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-{5-[3-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-ciclopentil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-{4-etil-5-[2-(4-metoxi-fenil)-etil]-4H-[1,2,4]triazol-3-ilsulfanilmetil}-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-toliloximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metoxi-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metoximetil-4H-

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[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etil-sulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-furan-2-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenoxi-metil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

3-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenoxi-metil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-metanol,

3-(3-clorofenil)-5-[4-etil-5-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metilsulfanilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-etoximetil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]-

triazol-3-carboxílico,

2-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-{1-[4-etil-5-(tetrahidrofuran-2-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridazina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-ilmetil)-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-fenol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenoximetil)-4-(tetrahidrofuran-2-ilmetil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-ciclopropil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-il-

sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-[4-etil-5-(tetrahidrofuran-2-il)-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-{5-[3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(3-clorofenil)-5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-metilsulfanil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1H-benzoimidazol,

5-(2,5-dimetil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-ciclopropil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[2-(3-clorofenil)-oxazol-4-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-metil-5-(5-tiofen-2-il-[1,2,4]oxadiazol-3-

ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{4-metil-5-[5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

2-metil-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

1-{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-etanona,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-metil-5-tiofen-2-il-4H-[1,2,4]triazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-2-metil-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-tiofen-2-il-4-tiofen-2-il-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxa-diazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

3-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[4-metil-5-(5-fenil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

2-cloro-4-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[3-(3-fluoro-fenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(3-fluoro-fenil)-5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-iI}-piridina,

5-(3-clorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(5-fluoro-2-metil-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]-

triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

4-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metoxi-piridina,

3-(3-clorofenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-benzo-nitrilo,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

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5-(3-clorofenil)-3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(2,5-diclorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4)oxadiazol,

4-{5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4)triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

4-[4-metil-5-(3-tiofen-3-il-[1,2,4]oxadiazol-5-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-tiofen-3-carbonitrilo,

5-(3-clorofenil)-3-[5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-[5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-ilamina,

3-piridin-4-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-tiofen-2-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(2,5-difluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[4-etil-5-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-etil-3-furan-2-il-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-tolil-4H-[1,2,4]-

triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-m-tolil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-nitro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-[5-(2,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

5-(2-cloro-5-metil-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-{5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-dicloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-tiofen-2-il-4H-[1,2,4]triazol,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-furan-2-il-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-{3-[5-(3-cloro-tiofen-2-il)-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-{4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-trifluoro-

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metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

4-etil-3-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-5-trifluorometil-4H-[1,2,4]triazol,

4-{3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-[3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

4-{4-etil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-

3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol,

3-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-(5-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-metil-tiazol-4-il)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(4-fluoro-fenil)-[1,2,4]oxadiazol,

4-etil-3-{1-(5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-5-furan-2-il-4H-[1,2,4]triazol,

4-(4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-(4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[4-cloro-5-(3-clorofenil)-isoxazol-3-ilm-etilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[4-cloro-5-(3-clorofenil)-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metil-

piridina,

3-[5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metoxi-piridina,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-benzonitrilo,

5-(3-clorofenil)-3-[4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-[5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-5-fluorobenzonitrilo,

4-etil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-2-il-4H-[1,2,4]triazol,

4-metil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-3-il-4H-[1,2,4]triazol,

4-etil-3-furan-2-il-5-(5-fenil-isoxazol-3-il-metilsulfanil)-4H-[1,2,4]triazol,

4-[4-etil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

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4-[4-metil-5-(5-fenil-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,3,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-[4-etil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{5-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-[3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tri-

fluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-cloro-4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-(3-clorofenil)-5-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-metil-5-tiazol-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

4-{4-etil-5-[5-(4-metiltiofen-2-il)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(3-nitro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-5-(3-nitro-fenil)-[1,3,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[1-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-

piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-(5-cloro-2-fluorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-

piridina,

2-cloro-4-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-(5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4)triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol,

2-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-(1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-

il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4(5-(1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-cloro-2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]tri-

azol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

2-cloro-4-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-furan-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-{5-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol-2-il}-piridina,

2-(3-clorofenil)-5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-(5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4)triazol-3-il}-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-etil-5-{1-[5-(2-fluoro-5-metilfenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

2-(2-fluoro-5-metil-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

2-(5-cloro-2-fluoro-fenil)-5-[1-(4-etil-5-furan-

2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

2-(5-cloro-2-fluoro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(3-fluorofenil)-[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-{5-[1-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-{5-[1-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

4-{5-[1-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

2-(3-clorofenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

3-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol,

4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-(1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-[5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropilmetil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

4-cloro-2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

4-{4-ciclopropil-5-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-

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piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(3-fluoro-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-ciclopropil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il)-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

4-{4-ciclopropil-5-[5-(2,5-difluorofenil)[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[1-(5-m-tolil-[1,2,4]oxadi-azol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-(4-ciclopropil-5-{1-[5-(3-metoxifenil)[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]tri-azol-3-ilsulfanilmetil)(1,2,4]oxadiazol-5-il]-4-metilfenol,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-metanol,

3-[5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-fenol,

5-(3-clorofenil)-3-[4-(tetrahidro-furan-2-il-metil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

(2-clorofenil)-{5-[5-(3-clorofenil)-(1,2,4]oxadiazol-3-ilmetilsulfanil]-4-isobutil-4H-[1,2,4]triazol-3-il}-metanol,

5-(2-fluoro-5-metil-fenil)-3-[5-tiofen-2-il-4-(2,2,2-trifluoro-etil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-3-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-

[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(5-furan-2-il-4-metil-

4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridazina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-furan-2-il-4-isobutil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metilsulfanil-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-hexil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-iloximetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadi-

azol-3-ilmetoxi]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(2-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-2-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzoico,

5-(2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-vinil-fenil)-[1,2,4]oxadiazol,

5-(3-difluorometoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metoxi-tiofen-3-il)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-

[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(3-clorofenil)-5-[2-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[2-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-tiofen-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]piridina,

5-(5-bromo-4-metil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-(3-clorofenil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfonilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfinilmetil)-[1,2,4]oxadiazol,

2-metil-6-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{2-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-

propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)amina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(1H-pirrol-3-il)-[1,2,4]oxadiazol,

1-óxido de 4-{5-[5-(3-clorofenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-

piridina,

5-(3-clorofenil)-3-(2-furan-2-il-3-metil-3H-imidazol-4-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[4-(2-fluoro-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-hidroxi-benzonitrilo,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina, o

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etoxi}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil--4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

3-{3-[1-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-{3-[1-(4-ciclopropil-5-piridin4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

3-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

cis-4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il)-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

Ester ter-butílico del ácido (S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico,

(S)-1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-

(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil-amina,

(S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-dimetil-amina,

o sal de los mismos.

18.- Una formulación farmacéutica caracterizada porque comprende como ingrediente activo una cantidad terapéuticamente efectiva de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 17 en asociación con uno o más diluyentes, excipientes y/o vehículo inerte farmacéuticamente aceptables.

19.- La formulación farmacéutica de conformidad con la reivindicación 18, para uso en la prevención y/o tratamiento de trastornos mediados por el receptor mG1uR5.

20.- Un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 17 para uso en terapia.

21.- El compuesto de conformidad con la reivindicación 20, para uso en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

22.- El compuesto de conformidad con la

reivindicación 20, para uso en la prevención y/o tratamiento de trastornos neurológicos.

23.- El compuesto de conformidad con la reivindicación 20, para uso en la prevención y/o tratamiento de trastornos psiquiátricos.

24.- El compuesto de conformidad con la reivindicación 20, para uso en la prevención y/o tratamiento de trastornos del dolor crónico y agudo.

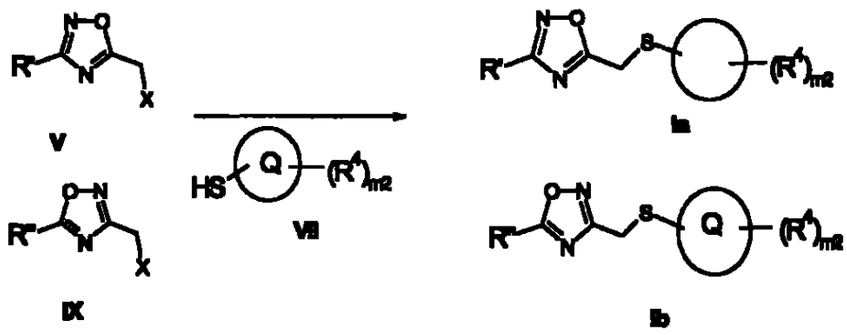
25.- El uso de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 17 en la fabricación de un medicamento para uso en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

26.- Un método de prevención y/o tratamiento de trastornos mediados por el receptor mGluR5, caracterizado porque comprende administrar a un mamífero, incluyendo humanos, en necesidad de dicha prevención y/o tratamiento, una cantidad terapéuticamente efectiva de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 17.

27.- Un método para inhibir la activación de los receptores mGluR5, caracterizado porque comprende tratar una célula que contiene a dicho receptor con una cantidad efectiva de un compuesto de conformidad

con cualquiera de las reivindicaciones 1 a 17.

28.- Procedimientos para la preparación de un compuesto de conformidad con la reivindicación 2, que comprenden:



caracterizados porque R' y R" contiene ya sea un grupo representado en la fórmula I mediante $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$ o un grupo saliente tal como $(CH_2)_nX$, en el cual X es cualquier grupo saliente apropiado tal como cloro o mesilato o un grupo que se pueda transformar posteriormente en un grupo saliente y Q, X^4, R^3, R^4, M^2, m y n son como se definen en la reivindicación 1.

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RESUMEN DE LA INVENCIÓN

La presente invención se refiere a compuestos novedosos de la fórmula I, (I) un procedimiento para su preparación e intermediarios novedosos preparados en el mismo, formulaciones farmacéuticas que contienen a dichos compuestos y al uso de dichos compuestos en terapia.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BENT, Stephen A.
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, D.C. 20007-5143
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	08.11.2004

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
085747-0270	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 03/24846	08.08.2003	09.08.2002

Applicant
ASTRAZENECA AB et al.

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 application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary 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.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Ambroa, J.R. Tel. +49 89 2399-8012

Form PCT/IPEA/416 (January 2004)

ATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 085747-0270	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US 03/24848	International filing date *(day/month/year)* 08.08.2003	Priority date *(day/month/year)* 09.08.2002
International Patent Classification (IPC) or both national classification and IPC C07D413/12		
Applicant ASTRAZENECA AB et al.		

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 5 sheets, including this cover sheet.

   ☒ 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 44 sheets.

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

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) 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
04.03.2004	08.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Seymour, L Telephone No. +49 89 2399-8694

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT International application No. PCT/US 03/24846

I. Basis of the report

1. With regard to the **elements** of the international application *(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))*:

Description, Pages

1-273 as originally filed

Claims, Numbers

1-27 received on 19.03.2004 with letter of 18.03.2004

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 the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 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 written 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. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

~~PCT~~

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/24846

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

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

   ☐ the entire international application,

   ☒ claims Nos. 1-27 (all partially); 25 and 26 with respect to industrial applicability

   because:

   ☒ the said international application, or the said claims Nos. 25 and 26 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

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

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

   ☒ no international search report has been established for the said claims Nos. 1-27 (all partially)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-27
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-24,27
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Claims 25 and 26 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

For reasoning with regards to unsearched subject-matter, see Form PCT/ISA/210 of the International Search Report. No international Preliminary Examination will be carried out with respect to subject-matter which is not covered by the search report (Rule 66.1(e) PCT).

Re Item V

1. Reference is made to the following documents:
   D1: WO-A-99 26927 D2: EP-A-0 397 365 D3: US-A-5 140 034
   D4: EP-A-0 422 369 D5: WO-A-00 35913
   D6: Eur. J. Med. Chem. vol. 35, no. 2, 2000, pages 267-271
   D7: Il Farmaco, vol. 54, 1999, pages 826-831
   D8: Eur. J. Med. Chem. vol. 9, no. 4, 1974, pages 445-448
   D9: Beilstein [Online], Database accession no. 4885431 (BRN), XP002264298
   D10: Beilstein [Online], Database accession no. 4208871 (BRN), XP002264299

2. Novelty (Article 33(2) PCT)

   The subject-matter of the present claims is not new (see search report and Form PCT/ISA/210).

3. Inventive step (Article 33(3) PCT)

   Document D1 discloses metabotropic glutamate receptor antagonists. The general formula disclosed in claim 1 overlaps with that of present claim 1, and compound 5 of Figure 1 in D1 falls within the present scope claimed.

Documents D2 and D3 disclose compounds falling within the scope of present claims. These compounds are useful in the treatment of diseases falling within the scope of present claims 24-26 (e.g. anxiety, pain and schizophrenia).

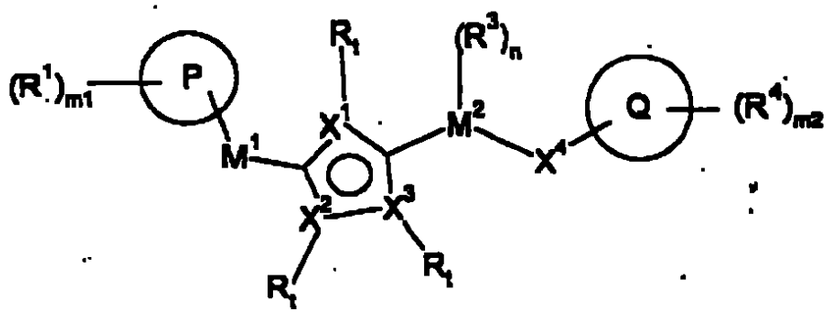
In view of the above, the present compounds cannot be viewed as an inventive solution to the problem of providing further compounds useful in the treatment of diseases associated with mGluR5 modulation.

4. Industrial applicability (Article 33(4) PCT)

For the assessment of the present claims 25 and 26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

CLAIMS

1. A compound having the formula I



(I)

wherein:

P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

M^1 is a bond;

X^1 selected from the group consisting of C, CO, N, O and S;

X^2 is selected from the group consisting of C, N, O and S;

X^3 is i) selected from the group consisting of N, O and S, or

ii) selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H. ;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$ and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl$(NR^5R^6)=N$, NR^5C_{0-4}alkyl$(NR^5R^6)=N$, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and any suitable carbon atom is optionally substituted with R^4; and

R^4 is selected from the group consisting of C_{0-6}alkylcyano, $=NC_{1-4}$alkyl, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl, C_{0-6}alkyl$Oaryl$, C_{0-6}alkyl$Oheteroaryl$, C_{0-6}alkyl$Naryl$, C_{0-6}alkyl$Nheteroaryl$, OC_{0-6}alkyl$Oaryl$, OC_{0-6}alkyl$Oheteroaryl$, OC_{0-6}alkyl$Naryl$, OC_{0-6}alkyl$Nheteroaryl$, NC_{0-6}alkyl$Oaryl$, NC_{0-6}alkyl$Oheteroaryl$, NC_{0-6}alkyl$Naryl$, NC_{0-6}alkyl$Nheteroaryl$, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}$alkyl$)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl,

imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-6}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m1 is selected from 0, 1, 2, 3 and 4;

m2 is selected from 0, 1, 2 and 3;

n is selected from 0, 1 and 2; and

t is 0 or 1,

and salts thereof,

with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole, 1,2-di{2-(3-amino-phenyl)-[1,3,4]oxadiazole-yl)ethane, 1,2-di{5-[5-(4-nitro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-bromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-chloro-phenyl)furan-2-yl]-

[1,3,4]oxadiazol-yl)ethane and 1,2-di{5-[5-(2,4-dibromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane.

2. A compound according to claim 1, wherein P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl or phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5 and R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

3. A compound according to claim 2, wherein P is phenyl substituted on position 3 or disubstituted on positions 2 and 5.

4. A compound according to claim 1, wherein X^1 is N and one of X^2 and X^3 is O and the other is N.

5. A compound according to claim 1, wherein the ring containing X^1, X^2 and X^3 forms an oxadiazole, isoxazole, oxazole, chloro-isoxazole or a methyl-isoxazole.

6. A compound according to claim 1, wherein M^2 is a bond or C_{1-3}alkyl and R^3 is hydrogen, methyl or dimethyl.

7. A compound according to claim 1, wherein X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, NR^5, O, SO, SO_2 and S and R^5 and R^6 are independently selected from hydrogen and C_{1-6}alkyl.

8. A compound according to claim 7, wherein X^4 is selected from the group consisting of CH_2, $CHCH_3$, $CH(CH_3)_2$ and NR^5.

9. A compound according to claim 7, wherein X^4 is S.

10. A compound according to claim 1, wherein Q is selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^6 on such nitrogen atom, and any suitable carbon atom is optionally substituted with R^6 and R^4 is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

11. A compound according to any one of claims 1 or 10, wherein Q is selected from the group consisting of triazolyl and thiadiazolyl.

12. A compound according to claim 1, wherein Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl and R^4 is hydrogen or C_{1-6}alkyl.

13. A compound according to any one of claims 1 or 12, wherein Q is selected from the group consisting of pyridonyl, tetrahydrotriazolopyridyl and tetrahydrotriazolopyrimidinyl.

14. A compound according to claim 1, wherein R^4 is selected from the group consisting of benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl,

dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl, trifluoromethyl, acetic acid methylester, allyl, amino, benzyl, cyclopropylmethyl, ethyl, fluorobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

15. A compound which is selected from the group consisting of

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole,

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine,

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine,

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

Dimethyl-(3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl)-amine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole,

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

4-[5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine,

2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b],

3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole and

5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

or salt thereof.

17. A compound which is selected from the group consisting of

4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester,

2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole,

5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine,

3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole,

4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole,

4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine,

3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile,

4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole,

4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine,

2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol,

3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol,

5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester,

5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole,

5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole,

2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,3;4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide,

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine, or

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester,

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine,

or salt thereof.

17. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 16 in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

18. The pharmaceutical formulation according to claim 17, for use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

19. A compound according to any one of claims 1 to 16 for use in therapy.

20. The compound according to claim 19, for use in prevention and/or treatment of mGluR5 receptor-mediated disorders.

21. The compound according to claim 19, for use in prevention and/or treatment of neurological disorders.

22. The compound according to claim 19, for use in prevention and/or treatment of psychiatric disorders.

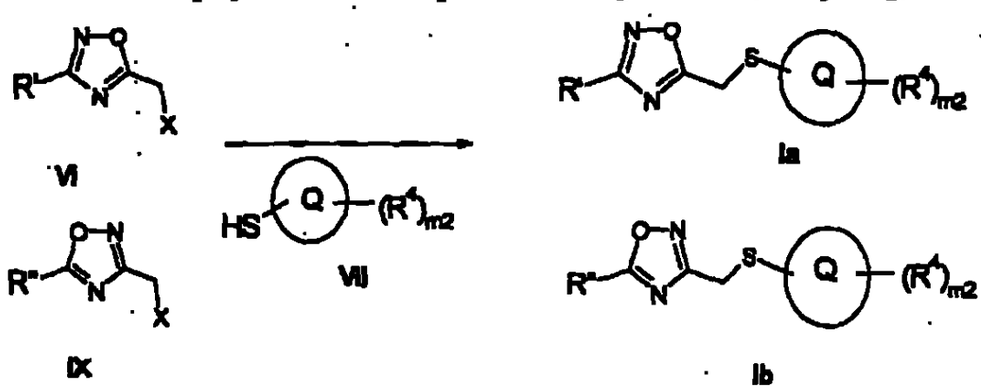
23. The compound according to claim 19, for use in prevention and/or treatment of chronic and acute pain disorders.

24. The use of a compound according to any one of claims 1 to 16 in the manufacture of a medicament for the use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

25. A method of prevention and/or treatment of mGluR5 receptor-mediated disorders, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound according to any one of claims 1 to 16.

26. A method for inhibiting activation of mGluR5 receptors, comprising treating a cell containing said receptor with an effective amount of a compound according to any one of claims 1 to 16.

27. Processes for the preparation of a compound according to claim 2, comprising;



wherein R' and R'' contains either a group represented in Formula I by M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$ or a leaving group such as $(CH_2)_nX$, wherein X is any suitable leaving group such as chloro or mesylate or a group which may subsequently be transformed into a leaving group and Q, X^4, R^3 R^4, M^2, m2 and n are as defined in claim 1.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BENT, Stephen A.
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, D.C. 20007-5143
ETATS-UNIS D'AMERIQUE

PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	28.04.2004
Applicant's or agent's file reference: 085747-0270	REPLY DUE: within 3 month(s) from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 03/24846	08.08.2003	09.08.2002

International Patent Classification (IPC) or both national classification and IPC
C07D413/12, C07D413/12

Applicant
ASTRAZENECA AB et al.

1. This written opinion is the **second** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) 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

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 09.12.2004

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer
Seymour, L.

Formalities officer (incl. extension of time limits)
Siefert, A
Telephone No. +49 89 2399-2469

I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-273 as originally filed

Claims, Numbers

1-27 received on 19.03.2004 with letter of 18.03.2004

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 the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 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 written 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. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

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

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

☐ the entire international application,

☒ claims Nos. 1-27 (all partially); 25 and 26 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 25 and 26 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

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

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

☒ no international search report has been established for the said claims Nos. 1-27 (all partially)

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

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

1. Statement

Novelty (N)	Claims	1-27 (no)
Inventive step (IS)	Claims	1-27 (no)
Industrial applicability (IA)	Claims	1-24,27(yes)

2. Citations and explanations

see separate sheet

8 13

Re Item I

Should amendments be filed in response to this written opinion, these will only be taken into account when the applicant identifies clearly all amendments made (e.g. by submitting one set of originally filed pages with hand-written amendments) and indicates on which passages of the original application these amendments are based (Rule 66.8 PCT).

Re Item III

Claims 25 and 26 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For reasoning with regards to unsearched subject-matter, see Form PCT/ISA/210 of the International Search Report. No international Preliminary Examination will be carried out with respect to subject-matter which is not covered by the search report (Rule 66.1(e) PCT).

Re Item V

1. Reference is made to the following documents:

   D1: WO-A-99 26927 D2: EP-A-0 397 365 D3: US-A-5 140 034
   D4: EP-A-0 422 369 D5: WO-A-00 35913
   D6: Eur. J. Med. Chem. vol. 35, no. 2, 2000, pages 267-271
   D7: Il Farmaco, vol. 54, 1999, pages 826-831
   D8: Eur. J. Med. Chem. vol. 9, no. 4, 1974, pages 445-448
   D9: Beilstein [Online], Database accession no. 4885431 (BRN), XP002264298
   D10: Beilstein [Online], Database accession no. 4208871 (BRN), XP002264299

2. Novelty (Article 33(2) PCT)

   The subject-matter of the present claims is not new (see search report and Form PCT/ISA/210).

3. Inventive step (Article 33(3) PCT)

Document D1 discloses metabotropic glutamate receptor antagonists. The general formula disclosed in claim 1 overlaps with that of present claim 1, and compound 5 of Figure 1 in D1 falls within the present scope claimed.

Documents D2 and D3 disclose compounds falling within the scope of present claims. These compounds are useful in the treatment of diseases falling within the scope of present claims 24-26 (e.g. anxiety, pain and schizophrenia).

In view of the above, the present compounds cannot be viewed as an inventive solution to the problem of providing further compounds useful in the treatment of diseases associated with mGluR5 modulation.

4. Industrial applicability (Article 33(4) PCT)

For the assessment of the present claims 25 and 26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

IN THE INTERNATIONAL BUREAU of WIPO

Applicant:	AstraZeneca AB
Title:	*1,2,4-Oxadiazoles as Modulators of Metabotropic Glutamate Receptor-5*
Appl. No.:	PCT/US03/24846
International Filing Date:	August 8, 2003
File Reference:	85747-270

AMENDMENT UNDER PCT ARTICLE 19

International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Sir:

Prior to preliminary examination of the present international application, Applicant respectfully requests that the claims of the application be amended as set forth in the appended set of replacement sheets 274-317.

Original claim 1 is cancelled. Thus original claims 2-28 are renumbered as claims 1-27.

Respectfully submitted,

Date March 18, 2004

By Reg No. 34,717

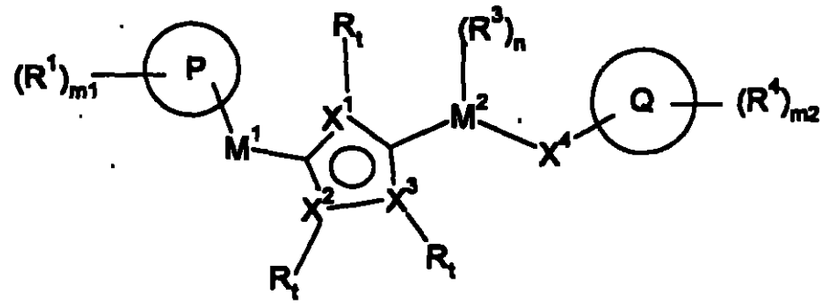
FOLEY & LARDNER LLP
Telephone: (202) 672-5404
Facsimile: (202) 672-5399

Stephen A. Bent
Attorney for Applicant
Registration No. 29,768

cc: International Preliminary Examining Authority (EPO)

CLAIMS

1. A compound having the formula I



(I)

wherein:

P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

M^1 is a bond;

X^1 selected from the group consisting of C, CO, N, O and S;

X^2 is selected from the group consisting of C, N, O and S;

X^3 is i) selected from the group consisting of N, O and S, or

ii) selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H. ;

R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl$(CO)OR^5$ and C_{0-3}alkylaryl;

M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl$(CO)C_{0-4}$alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl$(CO)NR^5$, C_{0-4}alkylNR^5, C_{0-3}alkyl$(SO)C_{0-3}$alkyl and C_{0-3}alkyl$(SO_2)C_{0-3}$alkyl;

R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, $O(CO)C_{1-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and any suitable carbon atom is optionally substituted with R^4; and

R^4 is selected from the group consisting of C_{0-6}alkylcyano, $=NC_{1-4}$alkyl, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}$alkyl$)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl,

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imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl(SO_2)NR^5R^6, OC_{2-6}alkyl(SO_2)NR^5R^6, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO_2)R^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

m1 is selected from 0, 1, 2, 3 and 4;

m2 is selected from 0, 1, 2 and 3;

n is selected from 0, 1 and 2; and

t is 0 or 1,

and salts thereof,

with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole, 1,2-di{2-(3-amino-phenyl)-[1,3,4]oxadiazole-yl)ethane, 1,2-di{5-[5-(4-nitro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-bromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-chloro-phenyl)furan-2-yl]-

[1,3,4]oxadiazol-yl)ethane and 1,2-di{5-[5-(2,4-dibromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane.

2. A compound according to claim 1, wherein P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl or phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5 and R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

3. A compound according to claim 2, wherein P is phenyl substituted on position 3 or disubstituted on positions 2 and 5.

4. A compound according to claim 1, wherein X^1 is N and one of X^2 and X^3 is O and the other is N.

5. A compound according to claim 1, wherein the ring containing X^1, X^2 and X^3 forms an oxadiazole, isoxazole, oxazole, chloro-isoxazole or a methyl-isoxazole.

6. A compound according to claim 1, wherein M^2 is a bond or C_{1-3}alkyl and R^3 is hydrogen, methyl or dimethyl.

7. A compound according to claim 1, wherein X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, NR^5, O, SO, SO_2 and S and R^5 and R^6 are independently selected from hydrogen and C_{1-6}alkyl.

8. A compound according to claim 7, wherein X^4 is selected from the group consisting of CH_2, $CHCH_3$, $CH(CH_3)_2$ and NR^5.

9. A compound according to claim 7, wherein X^4 is S.

10. A compound according to claim 1, wherein Q is selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom, and any suitable carbon atom is optionally substituted with R^4 and R^4 is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

11. A compound according to any one of claims 1 or 10, wherein Q is selected from the group consisting of triazolyl and thiadiazolyl.

12. A compound according to claim 1, wherein Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl and R^4 is hydrogen or C_{1-6}alkyl.

13. A compound according to any one of claims 1 or 12, wherein Q is selected from the group consisting of pyridonyl, tetrahydrotriazolopyridyl and tetrahydrotriazolopyrimidinyl.

14. A compound according to claim 1, wherein R^4 is selected from the group consisting of benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl,

dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl, trifluoromethyl, acetic acid methylester, allyl, amino, benzyl, cyclopropylmethyl, ethyl, fluorobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

15. A compound which is selected from the group consisting of

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole,

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine,

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine,

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2,6-Dichloro-4-[4-methyl-5-(5-*m*-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole,

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

4-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine,

2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b],

3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole and

5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

or salt thereof.

17. A compound which is selected from the group consisting of

4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol,

3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester,

2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole,

5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2;4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine,

3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

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3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole,

4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole,

4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

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2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2;4]triazol-3-yl}-6-methyl-pyridine,

3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2;4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile,

4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole,

4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2;4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine,

2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol,

3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol,

5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester,

5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole,

5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole,

2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide,

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine, or

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester,

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine,

or salt thereof.

17. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 16 in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

18. The pharmaceutical formulation according to claim 17, for use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

19. A compound according to any one of claims 1 to 16 for use in therapy.

20. The compound according to claim 19, for use in prevention and/or treatment of mGluR5 receptor-mediated disorders.

21. The compound according to claim 19, for use in prevention and/or treatment of neurological disorders.

22. The compound according to claim 19, for use in prevention and/or treatment of psychiatric disorders.

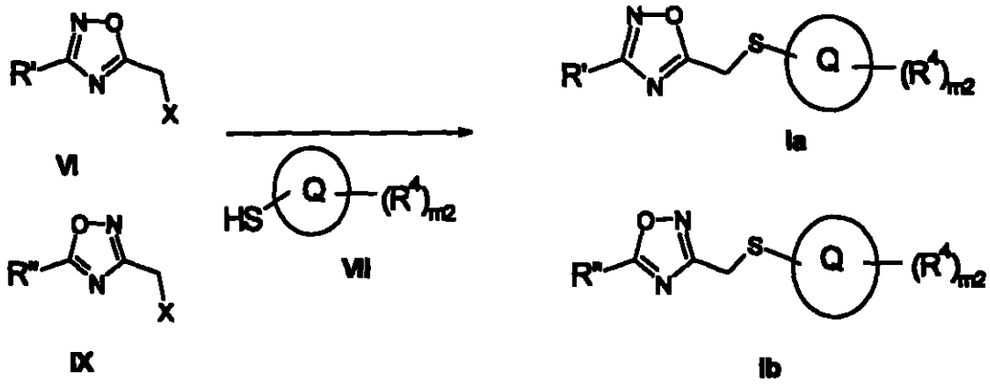
23. The compound according to claim 19, for use in prevention and/or treatment of chronic and acute pain disorders.

24. The use of a compound according to any one of claims 1 to 16 in the manufacture of a medicament for the use in the prevention and/or treatment of mGluR5 receptor-mediated disorders.

25. A method of prevention and/or treatment of mGluR5 receptor-mediated disorders, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound according to any one of claims 1 to 16.

26. A method for inhibiting activation of mGluR5 receptors, comprising treating a cell containing said receptor with an effective amount of a compound according to any one of claims 1 to 16.

27. Processes for the preparation of a compound according to claim 2, comprising;



wherein R' and R" contains either a group represented in Formula I by M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$ or a leaving group such as $(CH_2)_nX$, wherein X is any suitable leaving group such as chloro or mesylate or a group which may subsequently be transformed into a leaving group and Q, X^4, R^3 R^4, M^2, m2 and n are as defined in claim 1.

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Title

Compounds exhibiting activity as metabotropic glutamate receptors

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"1,2,4" OXADIAZOLES COMO MODULADORES DE RECEPTOR-5 METABOTROPICO DE GLUTAMATO

CAMPO DE LA INVENCION

La presente invención se refiere a una clase novedosa de compuestos, a formulaciones farmacéuticas que contienen a dichos compuestos y al uso de dichos compuestos en terapia. La presente invención también se refiere al procedimiento para la preparación de dichos compuestos y a los intermediarios nuevos preparados en el mismo.

ANTECEDENTES DE LA INVENCION

El glutamato es el principal neurotransmisor excitador en el sistema nervioso central de mamífero (SNC). El glutamato produce su efecto en las neuronas centrales uniéndose a, y por lo tanto activando, los receptores de la superficie celular. Estos receptores se han dividido en dos clases principales, los receptores de glutamato ionotrópicos y los metabotrópicos, tomando como base las características estructurales de las proteínas del receptor, los medios mediante los cuales los receptores transducen

las señales al interior de la célula, y los perfiles farmacológicos.

Los receptores de glutamato metabotrópicos (mGluR) son receptores acoplados a proteína G que activan una variedad de sistemas de segundos mensajeros intracelulares después de la unión del glutamato. La activación de los mGluR en neuronas de mamífero intactas induce una o más de las siguientes respuestas: activación de fosfolipasa C; incremento en la hidrólisis de fosfoinositido (PI); liberación de calcio intracelular; activación de fosfolipasa D; activación o inhibición de adenil ciclasa; incremento o reducción en la formación de monofosfato cíclico de adenosina (cAMP); activación de guanilil ciclasa; incremento en la formación de monofosfato cíclico de guanosina (cGMP); activación de fosfolipasa A_2; incremento en la liberación de ácido araquidónico; e incremento o reducción en la actividad de canales iónicos regulados por voltaje y por ligando. *Schoepp et al., Trends Pharmacol. Sci. 14*:13 (1993), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al., Neuropharmacology 34*:1 (1995), Bordi y Ugolini, *Prog. Neurobiol. 59*:55 (1999).

La clonación molecular ha identificado ocho subtipos distintos de mGluR, denominados mGluR1 a

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mGluR8. Nakanishi, *Neuron 13*:1031 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995). La diversidad de receptor adicional se presenta a través de la expresión de formas empalmadas en forma alternada de algunos subtipos de mGluR. Pin *et al.*, *PNAS 89*:10331 (1992), Minakami *et al.*, *BBRC 199*:1136 (1994), Joly *et al.*, *J. Neurosci. 15*:3970 (1995).

Los subtipos de receptor de glutamato metabotrópicos se pueden subdividir en tres grupos, mGluR de grupo I, grupo II y grupo III, tomando como base la homología de secuencia de aminoácidos, los sistemas de segundos mensajeros utilizados por los receptores, y sus características farmacológicas. El mGluR del grupo I comprende mGluR1, mGluR5 y sus variantes empalmadas en forma alternada. La unión de agonistas a estos receptores da como resultado la activación de fosfolipasa C y la movilización subsiguiente de calcio intracelular.

Los intentos para esclarecer los papeles fisiológicos de los mGluR del grupo I sugieren que la activación de estos receptores induce la excitación neuronal. Varios estudios han demostrado que los agonistas de mGluR del grupo I pueden producir excitación post-sináptica después de aplicación a las

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neuronas en el hipocampo, corteza cerebral, cerebelo, hipotálamo, así como en otras regiones del sistema nervioso central. Las evidencias indican que esta excitación se debe a la activación directa de los mGluR post-sinápticos, pero también se ha sugerido que se presenta la activación de los mGluR pre-sinápticos, lo que da como resultado una liberación incrementada de neurotransmisor. Baskys, *Trends Pharmacol. Sci. 15*:92 (1992), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al., Neuropharmacology 34*:1 (1995), Watkins *et al., Trends Pharmacol. Sci. 15*:33 (1994).

Los receptores de glutamato metabotrópicos se han implicado en un número de procesos normales en el SNC de mamífero. Se ha demostrado que es necesaria la activación de los mGluR para la inducción de potenciación a largo plazo del hipocampo y para la depresión a largo plazo del cerebelo. Bashir *et al., Nature 363*:347 (1993), Bortolotto *et al., Nature 368*:740 (1994), Aiba *et al., Cell 79*:365 81994), Aiba *et al., Cell 79*:377 (1994). También se ha demostrado un papel para la activación de mGluR en la nocicepción y analgesia, Meller *et al., Neuroreport 4*:879 (1993), Bordi y Ugolini, *Brain Res. 871*:223 (1999). Además, se ha sugerido que la activación de

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mGluR desempeña un papel modulador en una variedad de otros procesos normales incluyendo transmisión sináptica, desarrollo neuronal, muerte neuronal apoptótica, plasticidad sináptica, aprendizaje espacial, memoria olfatoria, control central de la actividad cardiaca, vigilia, control motor y control del reflejo vestíbulo-ocular. Nakanishi, *Neuron 13*:1031 (1994), Pin *et al.*, *Neuropharmacology 34*:1, Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995).

Asimismo, se ha sugerido que los receptores de glutamato metabotrópico del grupo I y en particular mGluR5, participan en una variedad de procesos y trastornos fisiopatológicos que afectan al SNC. Estos incluyen apoplejía, trauma cefálico, daños anóxicos e isquémicos, hipoglucemia, epilepsia, trastornos neurodegenerativos tales como la enfermedad de Alzheimer, y dolor. Shoepp *et al.*, *Trends Pharmacol. Sci. 14*:13 (1993), Cunningham *et al.*, *Life Sci. 54*:135 (1994), Hollman *et al.*, *Ann. Rev. Neurosci. 17*:31 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995), Spooren *et al.*, *Trends Pharmacol. Sci. 22*:331 (2001), Gasparini *et al. Curr. Opin. Pharmacol. 2*: 43 (2002), Neugebauer *Pain 98*:1 (2002). Se piensa que mucha de la patología en estas

condiciones es ocasionada por una excitación excesiva de las neuronas del SNC inducida por glutamato. Debido a que los mGluR del grupo I parecen incrementar la excitación neuronal mediada por glutamato a través de mecanismos post-sinápticos y de la liberación incrementada de glutamato pre-sináptica, su activación probablemente contribuya a la patología. Por consiguiente, los antagonistas selectivos de los receptores de mGluR del grupo I podrían ser terapéuticamente benéficos, en específico como agentes neuroprotectores, analgésicos o anti-convulsivos.

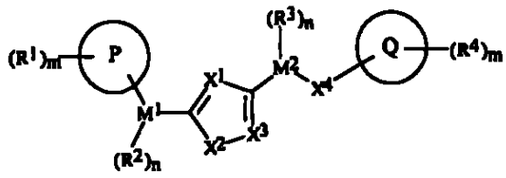
Los avances recientes en el esclarecimiento de los papeles neurofisiológicos de los receptores de glutamato metabotrópicos en general, y en particular del grupo I, han establecido a estos receptores como blancos para fármaco promisorios en la terapia de trastornos neurológicos y psiquiátricos agudos y crónicos, y en trastornos de dolor crónico y agudo. Debido a su significación fisiológica y fisiopatológica, existe la necesidad respecto a nuevos agonistas y antagonistas potentes de mGluR que presenten una alta selectividad para los subtipos de mGluR, en particular el subtipo de receptor del grupo I, de manera más particular el subtipo mGluR5.

El objetivo de la presente invención es

proveer compuestos que presenten una actividad en los receptores de glutamato metabotrópicos (mGluRs), en especial en el receptor mGluR5.

BREVE DESCRIPCIÓN DE LA INVENCION

La presente invención provee un compuesto de la fórmula Ia:



(Ia)

en la cual:

P se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{3-7} o un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6},

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alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})-arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})(CO)R^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, alquil(C_{0-6})NR^5-(CO)R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)-NR^5R^6, alquil(C_{0-6})SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})-(SO)R^5, O-alquil(C_{2-6})(SO)R^5, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)NR^5R^6, alquil-(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5-(SO_2)R^6, alquil(C_{0-6})-NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})NR^5-(SO_2)NR^5R^6, (CO)NR^5R^6, O(CO)NR^5R^6, NR^5OR^6, alquil(C_{0-6})-NR^5(CO)OR^6, O-alquil-(C_{2-6})NR^5(CO)OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, en el cual dicho anillo puede estar sustituido con uno o más A;

M^1 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4},

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alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-3})(CO)NR^5-alquilo de C_{0-3}, alquil(C_{0-4})NR^5, alquil(C_{0-3})-S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)-alquilo de C_{0-3} o alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^2 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^1, X^2 y X^3 se seleccionan de manera independiente a partir del grupo que consiste de CR, CO, N, NR, O y S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5, alquil(C_{0-3})NR^5R^6 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, cicloalquilo de C_{3-7}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil-(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5; alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})-(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

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R^3 se selecciona a partir de un grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, =NR^5, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5, alquil(C_{0-4})(NR^5R^6), alquil(C_{0-4})-(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halogenoalquilo de C_{1-4}, C, O, SO, SO_2 y S;

Q es un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S y cuyo anillo fusionado puede estar sustituido con uno o más A;

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, NR^5, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4},

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alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, en el cual dicho anillo puede estar sustituido con uno o más A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno, hidroxi, alquilo de C_{1-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, y en el cual R^5 y R^6 pueden formar juntos un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

en el cual cualquier alquilo de C_{1-6}, alquenilo de C_{2-6}, alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo y alquil(C_{0-6})-heteroarilo definido bajo R^1, R^2, R^3, R^4, R^5 y R^6 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, oxo, halógeno, nitro, alquil(C_{0-6})ciano, alquilo de C_{1-4}, alquil(C_{0-4})ciclo-

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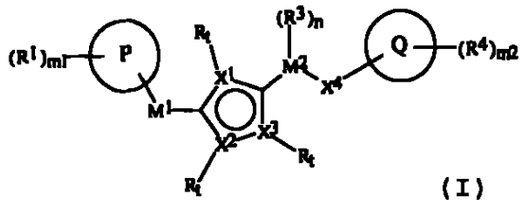
alquilo de C_{3-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquilo de C_{1-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, alquil(C_{0-6})-NR^5R^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})-NR^5(CO)NR^5R^6, O(CO)NR^5R^6, NR^5(CO)OR^6, alquil(C_{0-6})(SO_2)-NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)-NR^5R^6, O-alquil(C_{2-6})(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m se selecciona a partir de 0, 1, 2, 3 y 4; y

n se selecciona a partir de 0, 1, 2 y 3,

o sal del mismo.

La presente invención provee un compuesto de la fórmula I



(I)

en la cual:

P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5;

R^1 está unido a P a través de un átomo de carbono en el anillo P y se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})-(CO)R^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-

$(CO)NR^5R^6$, O-alquil$(C_{1-6})(CO)NR^5R^6$, alquil$(C_{0-6})NR^5(CO)R^6$, O-alquil$(C_{2-6})NR^5(CO)R^6$, alquil$(C_{0-6})NR^5(CO)NR^5R^6$, alquil(C_{0-6})-SR^5, O-alquil$(C_{2-6})SR^5$, alquil$(C_{0-6})(SO)R^5$, O-alquil(C_{2-6})-$(SO)R^5$, alquil$(C_{0-6})SO_2R^5$, O-alquil$(C_{2-6})SO_2R^5$, alquil(C_{0-6})-$(SO_2)NR^5R^6$, O-alquil$(C_{2-6})(SO_2)NR^5R^6$, alquil$(C_{0-6})NR^5$-$(SO_2)R^6$, O-alquil$(C_{2-6})NR^5(SO_2)R^6$, alquil$(C_{0-6})NR^5(SO_2)$-NR^5R^6, O-alquil$(C_{2-6})NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil$(C_{0-6})NR^5(CO)OR^6$, O-alquil$(C_{2-6})NR^5(CO)$-OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

M^1 es un enlace;

X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S;

X^2 se selecciona a partir del grupo que consiste de C, N, O y S;

X^3 i) se selecciona a partir del grupo que consiste de N, O y S, o

ii) se selecciona a partir de N, O, S, y C cuando X^2 se selecciona a partir de N, O, o S, y cuando X^3 es C, el sustituyente R en X^3 es H;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil$(C_{0-3})OR^5$, alquil$(C_{0-3})NR^5R^6$, alquil$(C_{0-3})(CO)OR^5$ y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)-alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo;

Q es i) seleccionado a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en los cuales cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y cualquier átomo

de carbono apropiado está opcionalmente sustituido con R^4; y

R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})-(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})N-(alquilo de C_{1-4})$_2$ y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera

independiente a partir del grupo que consiste de C, N y O, y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A; o

ii) se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo; y

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno y alquilo de C_{1-6};

en el cual cualquier alquilo de C_{1-6} definido bajo R^1, R^2 y R^4 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})-NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)-NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5-(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m1 se selecciona a partir de 0, 1, 2, 3 y 4;

m2 se selecciona a partir de 0, 1, 2 y 3;

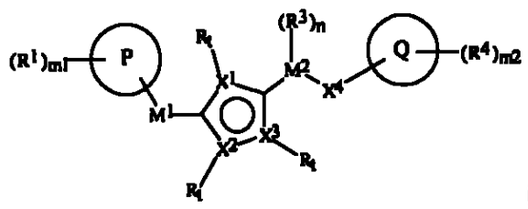
n se selecciona a partir de 0, 1 y 2; y

t es 0 o 1,

y sales de los mismos,

con la condición que el compuesto no sea 5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol, 1,2-di{2-(3-amino-fenil)-[1,3,4]-oxadiazol-il)etano, 1,2-di{5-[5-(4-nitrofenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-bromo-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-cloro-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano y 1,2-di{5-[5-(2,4-dibromofenil)furan-2-il]-[1,3,4]-oxadiazol-il)etano.

La presente invención provee un compuesto de la fórmula Ib



(Ib)

en la cual:

P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5;

R^1 está unido a P a través de un átomo de

carbono en el anillo P y se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})-(CO)R^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, alquil(C_{0-6})NR^5-(CO)R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)-NR^5R^6, alquil(C_{0-6})SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})-(SO)R^5, O-alquil(C_{2-6})(SO)R^5, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5-(SO_2)R^6, alquil(C_{0-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})NR^5-(SO_2)NR^5R^6, (CO)NR^5R^6, O(CO)NR^5R^6, NR^5OR^6, alquil(C_{0-6})-NR^5(CO)OR^6, O-alquil(C_{2-6})NR^5(CO)OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

M^1 es un enlace;

X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S;

X^2 se selecciona a partir del grupo que consiste de C, N, O y S;

X^3 se selecciona a partir del grupo que consiste de N, O y S, o X^3 es CH cuando X^2 es N, O ó S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)-alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-

alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo ;

Q es i) seleccionado a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno; y

R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})-heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})-heteroarilo, alquil(C_{0-6})O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-

alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})N(alquilo de C_{1-4})$_2$ y un anillo no aromático de 3 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A; o

ii) se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetra-hidrotriazolopiridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolo-piridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo; y

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de

5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno y alquilo de C_{1-6};

en el cual cualquier alquilo de C_{1-6} definido bajo R^1, R^2 y R^4 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})ciano, O-alquil(C_{1-6})CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{1-6})(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{0-6})-(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5-(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)-

NR^5R^6, alquil$(C_{0-6})NR^5(SO_2)R^6$, O-alquil$(C_{2-6})NR^5(SO_2)R^6$, SO_3R^5, alquil$(C_{1-6})NR^5(SO_2)NR^5R^6$, O-alquil$(C_{2-6})(SO_2)R^5$, alquil$(C_{0-6})(SO_2)R^5$, alquil$(C_{0-6})(SO)R^5$, O-alquil$(C_{2-6})(SO)R^5$ y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m1 se selecciona a partir de 0, 1, 2, 3 y 4;

m2 se selecciona a partir de 0, 1, 2 y 3;

n se selecciona a partir de 0, 1 y 2; y

t es 0 o 1,

y sales de los mismos,

con la condición que el compuesto no sea 5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol.

En un aspecto adicional de la invención, se proveen formulaciones farmacéuticas que comprenden una cantidad terapéuticamente efectiva de un compuesto de la fórmula I y un vehículo farmacéuticamente aceptable.

En un aspecto adicional de la invención se provee una formulación farmacéutica que incluye un compuesto de la fórmula I para ser utilizada en el tratamiento de trastornos mediados por el receptor mGluR5, y en particular trastornos neurológicos,

trastornos psiquiátricos, dolor agudo y crónico.

Incluso en una aspecto adicional de la invención, se provee un compuesto de la fórmula I para ser utilizado en terapia para el tratamiento de trastornos mediados por el receptor mGluR5, y en particular trastornos neurológicos, trastornos psiquiátricos, dolor agudo y crónico.

En otro aspecto de la invención se provee un procedimiento para la preparación de compuestos de la fórmula I, y los intermediarios provistos en el mismo.

Estos y otros aspectos de la presente invención se describen con mayor detalle en la misma a continuación.

DESCRIPCION DETALLADA DE LA INVENCION

A continuación se listan las definiciones de diversos términos utilizados en la descripción y reivindicaciones para describir la presente invención.

Con el fin de evitar dudas, se debe entender que en casos en los que en esta descripción se califique a un grupo con "definido anteriormente en la presente invención", "antes definido en la presente invención" o "definido anteriormente" dicho grupo abarca la definición más amplia y que ocurra primero

así como todas y cada una de las otras definiciones para dicho grupo.

Con el fin de evitar dudas, se debe entender que en esta descripción "C_{1-6}" significa un grupo de carbono que tiene 1, 2, 3, 4, 5 o 6 átomos de carbono.

En esta descripción "C" significa un átomo de carbono.

En esta descripción, a menos que se indique lo contrario, el término "alquilo" incluye grupos alquilo de cadena tanto recta como ramificada y puede ser metilo, etilo, n-propilo, i-propilo, n-butilo, i-butilo, s-butilo, t-butilo, n-pentilo, i-pentilo, t-pentilo, neo-pentilo, n-hexilo o i-hexilo, t-hexilo. El término "alquilo de C_{1-3}" se refiere a un grupo alquilo que tiene 1, 2 o 3 átomos de carbono, y puede ser metilo, etilo, n-propilo e i-propilo.

En esta descripción, a menos que se indique lo contrario, el término "cicloalquilo" se refiere a un sistema de anillo de hidrocarburo cíclico, saturado, opcionalmente sustituido. El término "cicloalquilo de C_{3-7}" puede ser ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo y cicloheptilo.

En esta descripción, a menos que se indique lo contrario, el término "alquenilo" incluye grupos

alquenilo de cadena tanto recta como ramificada. El término "alquenilo de C_{2-6}" se refiere a un grupo alquenilo que tiene 2 a 6 átomos de carbono y uno o dos dobles enlaces, y puede ser, pero no se limita a vinilo, alilo, propenilo, i-propenilo, butenilo, i-butenilo, crotilo, pentenilo, i-pentenilo y hexenilo.

En esta descripción, a menos que se indique lo contrario, el término "alquinilo" incluye grupos alquinilo de cadena tanto recta como ramificada. El término "alquinilo de C_{2-6}" tiene de 2 a 6 átomos de carbono y uno o dos triples enlaces, y puede ser, pero no se limita a etinilo, propargilo, butinilo, i-butinilo, pentinilo, i-pentinilo y hexinilo.

El término "arilo" se refiere a un sistema de anillo de hidrocarburo monocíclico o bicíclico, opcionalmente sustituido, que contiene por lo menos un anillo aromático insaturado. Los ejemplos y valores apropiados del término "arilo" son fenilo, naftilo, 1,2,3,4-tetrahidronaftilo, indilo e indenilo.

En esta descripción, a menos que se indique lo contrario, el término "heteroarilo" se refiere a un sistema de anillo aromático, monocíclico o bicíclico, insaturado, opcionalmente sustituido que contiene por lo menos un heteroátomo que se selecciona de manera independiente a partir de N, O ó S. Los

ejemplos de "heteroarilo" pueden ser, pero no se limitan a tiofeno, tienilo, piridilo, tiazolilo, furilo, pirrolilo, triazolilo, imidazolilo, oxadiazolilo, oxazolilo, isoxazolilo, pirazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolo-pirimidinilo, benzofurilo, indolilo, isoindolilo, piridonilo, piridazinilo, pirimidinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, piridilo, imidazo-piridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo.

En esta descripción, a menos que se indique lo contrario, los términos "alquilarilo", "alquil-heteroarilo" y "alquilcicloalquilo" se refieren a un sustituyente que está unido mediante el grupo alquilo a un grupo arilo, heteroarilo y cicloalquilo.

En esta descripción, a menos que se indique lo contrario, un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, incluye anillos aromáticos y heteroaromáticos así como anillos carbocíclicos y heterocíclicos los cuales pueden ser saturados o insaturados. Los ejemplos de dichos anillos pueden ser, pero no se limitan a furilo,

isoxazolilo, isotiazolilo, oxazolilo, pirazinilo, pirazolilo, piridazinilo, piridilo, pirimidilo, pirrolilo, tiazolilo, tienilo, imidazolilo, imidazolidinilo, imidazolinilo, triazolilo, morfolinilo, piperazinilo, piperidilo, piperidonilo, pirazolidinilo, pirazolinilo, pirrolidinilo, pirrolinilo, tetrahidropiranilo, tiomorfolinilo, fenilo, ciclohexilo, ciclopentilo y ciclohexenilo.

En esta descripción, a menos que se indique lo contrario, un anillo de 3 a 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, incluye anillos aromáticos y heteroaromáticos así como anillos carbocíclicos y heterocíclicos los cuales pueden ser saturados o insaturados. Los ejemplos de dichos anillos pueden ser, pero no se limitan a imidazolidinilo, imidazolinilo, morfolinilo, piperazinilo, piperidilo, piperidonilo, pirazolidinilo, pirazolinilo, pirrolidinilo, pirrolinilo, tetrahidropiranilo o tiomorfolinilo, tetrahidrotiopiranilo, furilo, pirrolilo, isoxazolilo, isotiazolilo, oxazolilo, oxazolidinonilo, pirazinilo, pirazolilo, piridazinilo, piridilo, pirimidilo, pirrolilo, tiazolilo, tienilo, imidazolilo, triazolilo, fenilo, ciclopropilo, aziridinilo, ciclobutilo, azetidinilo, ciclopentilo, ciclopentenilo,

ciclohexilo, ciclohexenilo, cicloheptilo, cicloheptenilo, ciclo-octilo y ciclo-octenilo.

En esta descripción, a menos que se indique lo contrario, un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O ó S, incluye anillos aromáticos y heteroaromáticos así como anillos carbocíclicos y heterocíclicos los cuales pueden ser saturados o insaturados. Los ejemplos de dichos anillos pueden ser, pero no se limitan a naftilo, norcarilo, cromilo, isocromilo, indanilo, benzoimidazol o tetralinilo, benzo-oxazolilo, benzotiazolilo, benzofurilo, benzotienilo, benzotriazolilo, indolilo, azaindolilo, indazolilo, indolinilo, isoindolinilo, bencimidazolilo, oxadiazolilo, tiadiazolilo, quinolinilo, quinoxalinilo y benzotriazolilo.

En esta descripción, a menos que se indique lo contrario, los términos "$=NR^5$" y "$=NOR^5$" incluyen grupos imino y oximo que portan un sustituyente R^5 y pueden ser, o ser parte de, grupos que incluyen, pero sin limitarse a, iminoalquilo, iminohidroxi, iminoalcoxi,

amidina, hidroxiamidina y alcoxiamidina.

En el caso en el cual un subíndice es el número entero 0 (cero) el grupo al cual se refiere el subíndice, indica que el grupo está ausente, es decir que existe un enlace directo entre los grupos.

En esta descripción, a menos que se indique lo contrario, el término "enlace" es un enlace saturado.

En esta descripción, a menos que se indique lo contrario, el término "halógeno" puede ser fluoro, cloro, bromo, o yodo.

En esta descripción, a menos que se indique lo contrario, el término "halogenoalquilo" significa un grupo alquilo como el definido anteriormente, sustituido con uno o más halógenos. El término "halogenoalquilo de C_{1-6}" puede incluir, pero no se limita a fluorometilo, difluorometilo, trifluorometilo, fluoroetilo, difluoroetilo y bromopropilo. El término "O-halogenoalquilo de C_{1-6}" puede incluir, pero no se limita a fluorometoxi, difluorometoxi, trifluorometoxi, fluoroetoxi y difluoroetoxi.

En una modalidad de la invención P puede ser hidrógeno o alquilo de C_{3-7} o P puede ser un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan a partir C, N, O ó S, dicho anillo puede

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estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene 1 o más átomos que se seleccionan de manera independiente a partir de C, N, O, o S. En una modalidad preferida de la invención P se selecciona a partir de anillos aromáticos y hetero-aromáticos de 5 y 6 miembros. En una modalidad preferida adicional, P se selecciona a partir de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5. Incluso en una modalidad preferida de la invención, P es fenilo sustituido en la posición 3 o disustituido en las posiciones 2 y 5.

P está opcionalmente sustituido mediante un átomo de carbono, con 0, 1, 2, 3 o 4 grupos R^1, en el cual el número de sustituyentes R^1 en el anillo P se designa con el término *m1*. En modalidades preferidas de la invención *m1* es 1 o 2. En modalidades preferidas adicionales de la invención, *m1* es 1.

En modalidades apropiadas de la invención R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-

cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})(CO)R^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{0-6})CO_2R^5, O-alquil(C_{1-6})CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, alquil(C_{0-6})NR^5(CO)R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})-NR^5(CO)NR^5R^6, alquil(C_{0-6})SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5, alquil(C_{0-6})-SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})-NR^5(SO_2)R^6, alquil(C_{0-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})NR^5-(SO_2)NR^5R^6, (CO)NR^5R^6, O(CO)NR^5R^6, NR^5OR^6, alquil(C_{0-6})-NR^5(CO)OR^6, O-alquil(C_{2-6})NR^5(CO)OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S.

En una modalidad más apropiada de la invención R^1 se selecciona a partir de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{1-6})-OR^5, alquil(C_{1-6})-(CO)R^5, alquil(C_{0-6})-CO_2R^5, alquil(C_{0-6})ciano, alquil(C_{0-6})-NR^5R^6, alquil(C_{0-6})-

SR^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

Cualquier alquilo de C_{1-6} definido bajo R^1 puede estar sustituido con uno o más A. En una modalidad de la invención R^1 es etilo y A es hidroxilo.

En una modalidad apropiada adicional de la invención R^1 se selecciona a partir de hidrógeno, metilo, etilo, ciclopropilo, hidroxi, metoxi, ciano, fluoro, cloro, bromo, iodo, trifluorometilo, difluorometoxi, trifluorometoxi, amino, nitro, dimetilamino, metilsulfanilo, vinilo, acetilo, éster metílico del ácido fórmico, metoximetilo, etanol y furilo.

En una modalidad más apropiada de la invención P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo o fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5 y R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halógeno-alquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{1-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, alquil(C_{0-6})-ciano, alquil(C_{0-6})-NR^5R^6, alquil(C_{0-6})SR^5 y un anillo de 5

miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

En una modalidad apropiada adicional de la invención P es fenilo sustituido en la posición 3 o disustituido en las posiciones 2 y 5 y R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{1-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, alquil(C_{0-6})-ciano, alquil(C_{0-6})-NR^5R^6, alquil(C_{0-6})SR^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

De conformidad con otro aspecto de la invención, el anillo P se conecta al anillo central mediante M^1, en el cual M^1 puede ser un enlace que une directamente a P al anillo central. M^1 también puede ser un enlazador de alquilo de C_{1-3}.

En una modalidad preferida de la invención M^1 es un enlace.

Cuando M^1 no sea un enlace directo, M^1 puede estar sustituido también con 0, 1, 2 o 3 sustituyentes

R^2, en el cual el número de sustituyentes R^2 se designa con el término *n*. Los sustituyentes R^2 se pueden seleccionar a partir de hidrógeno, hidroxi, oxo, halogenoalquilo de C_{1-4}, halógeno y alquilo de C_{1-4}. En una modalidad preferida de la invención *n* es 0.

En otro aspecto de la invención, se proveen compuestos de la fórmula I en la cual X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S. En un aspecto adicional de la invención, X^2 se selecciona a partir del grupo que consiste de C, N, O y S. Incluso en un aspecto adicional de la invención, X^3 se selecciona a partir del grupo que consiste de N, O, y S, o X^3 se selecciona a partir de N, O, S, y C cuando X^2 se seleccione a partir de N, O, o S, y cuando X^3 es C, el sustituyente R en X^3 es H.

X^1, X^2 y X^3 también pueden estar sustituidos con 0, 1 o 2 sustituyentes R en el cual el número de sustituyentes R se designa con el término t. El sustituyente R se puede seleccionar a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil$(C_{0-3})OR^5$, alquil$(C_{0-3})NR^5R^6$, alquil(C_{0-3})-$(CO)OR^5$, alquil$(C_{0-3})NR^5R^6$ y alquil(C_{0-3})arilo. En una modalidad de la invención R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3} y halógeno.

En una modalidad preferida de la invención X^1 es C, N, u O y R se selecciona a partir de hidrógeno, alquilo de C_{0-3} y halógeno. En una modalidad R se selecciona a partir de hidrógeno, cloro o metilo.

En otra modalidad preferida de la invención X^1 es N.

En una modalidad apropiada X^2 se selecciona a partir de N, O y S, y R es hidrógeno. En otra modalidad de la invención X^3 es N, O ó S. En una modalidad preferida adicional de la invención X^1 es O y uno de X^2 y X^3 es O y el otro es N. Incluso en una modalidad preferida adicional de la invención X^1 es N y uno de X^2 y X^3 es O y el otro es N. Incluso en otra modalidad preferida de la invención X^1 es C o CR y uno de X^2 y X^3 es O y el otro es N.

En otra modalidad preferida de la invención X^2 es O y X^3 es N, e incluso en otra modalidad preferida de la invención X^2 es N y X^3 es O.

En una modalidad preferida adicional de la invención X^1 es O y X^2 y X^3 son N.

En otra modalidad apropiada de la invención el anillo que contiene a X^1, X^2 y X^3 forma un oxadiazol, isoxazol, oxazol, cloroisoxazol o un metil-isoxazol.

En una modalidad preferida de la invención

el anillo que contiene a X^1, X^2 y X^3 forma un oxadiazol. En otra modalidad preferida de la invención el anillo que contiene a X^1, X^2 y X^3 forma un isoxazol.

El anillo que contiene a X^1, X^2 y X^3 no debe estar anillado adicionalmente en cualquier otro anillo. En una modalidad apropiada de la invención M^2 puede ser un enlace directo desde el anillo central hacia la variable X^4 o M^2 se puede seleccionar a partir del grupo que consiste de enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})-(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3}.

En modalidades preferidas de la invención M^2 es un enlace o alquilo de C_{1-3}. En modalidades preferidas adicionales de la invención M^2 es alquilo de C_{1-3}, de preferencia metilo o etilo.

Cuando M^2 no sea un enlace directo M^2 puede estar también sustituido con 0, 1 o 2 grupos R^3 en el cual el número de sustituyentes R^3 se designa con el término *n*. En una modalidad de la invención *n* es 1 o 2. En otra modalidad de la invención *n* es 0.

En una modalidad apropiada de la invención R^3 se selecciona a partir del grupo que consiste de R^3 se selecciona a partir de un grupo que consiste de

hidroxi, alquil(C_{0-6})-ciano, oxo, =NR^5, =NOR^5, halógeno-alquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)-alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6.

En una modalidad preferida R^3 se selecciona a partir de hidrógeno y alquilo de C_{1-4}, de preferencia metilo o dimetilo.

En otra modalidad preferida M^2 se puede seleccionar a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})-(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3} y R^3 se selecciona a partir de hidrógeno y alquilo de C_{1-4}.

Incluso en otras modalidades preferidas de la invención M^2 es un enlace o alquilo de C_{1-3} y R^3 es hidrógeno, metilo o dimetilo.

En una modalidad preferida adicional M^2 se puede seleccionar a partir del grupo que consiste de un enlace, metilo y etilo y R^3 es hidrógeno, metilo o dimetilo.

En una modalidad adicional de la invención

M^2 es nitrógeno. Incluso en una modalidad adicional de la invención M^2 es oxígeno.

De conformidad con otro aspecto de la invención X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo.

En una modalidad preferida de la invención X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, NR^5, O, SO, SO_2 y S y R^5 y R^6 se seleccionan de manera independiente a partir de hidrógeno y alquilo de C_{1-6}.

En una modalidad preferida adicional de la invención X^4 se selecciona a partir del grupo que consiste de CH_2, $CHCH_3$, $CH(CH_3)_2$ y NR^5. En una modalidad preferida adicional de la invención X^4 es NR^5 y R^5 se selecciona a partir de hidrógeno y alquilo de C_{1-6}. En una modalidad preferida de la invención R^5 es metilo o hidrógeno y R^6 es hidrógeno.

Incluso en otra modalidad preferida adicional de la invención X^4 es O. Incluso en otra modalidad preferida de la invención X^4 es S.

Se debe entender que el enlace entre M^2 y X^4

512
903

es un enlace sencillo en todas las formas tautoméricas.

Las modalidades de la presente invención incluyen aquellas en las cuales Q es un anillo de 5 o 6 miembros. Cuando Q es un anillo de 5 miembros, Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en el cual cualquier átomo de nitrógeno susceptible de sustitución en el anillo está sustituido con R^4 en dicho átomo de nitrógeno.

En una modalidad, el anillo de 5 miembros Q se selecciona a partir del grupo que consiste de triazolilo y tiadiazolilo. En otra modalidad, el anillo de 5 miembros Q se selecciona a partir del grupo que consiste de tetrazolilo y oxadiazolilo. En una modalidad adicional, el anillo de 5 miembros Q es imidazolilo.

Cuando Q es un anillo de 6 miembros, Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxaxolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo.

En una modalidad preferida de la invención

el anillo de 6 miembros Q se selecciona a partir del grupo que consiste de piridonilo, tetrahidrotriazolopiridilo y tetrahidrotriazolopirimidinilo. En otra modalidad el anillo de 6 miembros Q es piridazinilo. En una modalidad adicional el anillo de 6 miembros Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo e imidazopiridilo.

Q también puede estar sustituido con 0, 1, 2 o 3 sustituyentes R^4, en el cual el número de sustituyentes R^4 se designa con el término *m2*. En una modalidad preferida *m2* es 1 ó 2.

Cuando Q es un anillo de 5 miembros el sustituyente R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})-heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})-heteroarilo, alquil(C_{0-6})O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-

alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)-alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})-N(alquilo de C_{1-4})$_2$ y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En una modalidad adicional de la invención R^4 en el anillo de 5 miembros Q se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-

arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En una modalidad de la invención Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y R^4 se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo, O-alquil(C_{0-6})-arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})O-arilo, alquil(C_{0-6})-O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-

heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En otra modalidad de la invención Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y R^4 se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo,

N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

Cuando Q es un anillo de 6 miembros el sustituyente R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})-arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})-(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo

de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

En una modalidad apropiada de la invención R^4 en el anillo Q de 6 miembros se selecciona a partir de hidrógeno y alquilo de C_{1-6}. En una modalidad adicional de la invención R^4 es hidrógeno, metilo, etilo, propilo, butilo o hexilo.

En una modalidad preferida de la invención Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolo-piridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo y R^4 es hidrógeno o alquilo de C_{1-6}.

En otra modalidad preferida de la invención Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolo-

piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo y imidazopiridilo, y R^4 es hidrógeno o alquilo de C_{1-6}.

En una modalidad apropiada de la invención R^4 se selecciona a partir del grupo que consiste de benzo[b]tiofenilo, benzodioxolilo, bromo, bromofurilo, butoxifenilo, clorometoxipiridilo, clorofenilo, clorofenilmetanol, cloropiridilo, clorotiofeno, cianofenilo, ciclohexilo, ciclopentilo, diclorofenilo, dicloropiridilo, difluorofenilo, dimetiltiazolilo, etanol, etoximetilo, fluorometilfenilo, fluorofenilo, éster metílico del ácido fórmico, furilo, hidrógeno, hidroxifenoximetilo, hidroxifenilo, imidazolilo, metoxietilo, metoximetilo, metoxifenoximetilo, metoxifenilo, metoxifeniletilo, metoxipiridazinilo, metoxipiridilo, metoxipirimidinilo, metoxitiofeno, metilimidazolilo, metilpiridilo, metilsulfanilmetilo, metiltiazolilo, metiltiofeno, nitrofurilo, nitrofenilo, fenilo, p-toliloximetilo, piridazinilo, piridinoxidilo, bencilmorfolinilo, piridinolilo, piridilo, piridilmetilo, pirimidinilo, ter-butilfenilo, tetrahidrofurilo, tiazolilo, tiofeno, tolilo, trifluorometilo, éster metílico del ácido acético, alilo, amino, bencilo, ciclopropilmetilo, etilo, fluorobencilo, fluoroetilo, furilmetilo, hidroxietilo, isobutilo,

metilo, metilbencilo, metilbutilo, metilsulfanilpropilo, n-butilo, n-hexilo, n-propilo, tetrahidrofurilmetilo, tiofenilmetilo y trifluoroetilo.

El anillo Q puede estar sustituido con uno o más R^4 en un átomo de carbono y/o un átomo de nitrógeno en el anillo. Cuando Q está sustituido en el átomo de carbono, R^4 se selecciona a partir de benzo[b]tiofenilo, benzodioxolilo, bromo, bromofurilo, butoxifenilo, clorometoxipiridilo, clorofenilo, clorofenilmetanol, cloropiridilo, clorotiofeno, cianofenilo, ciclohexilo, ciclopentilo, diclorofenilo, dicloropiridilo, difluorofenilo, dimetiltiazolilo, etanol, etoximetilo, fluorometilfenilo, fluorofenilo, éster metílico del ácido fórmico, furilo, hidrógeno, hidroxifenoximetilo, hidroxifenilo, imidazolilo, metoxietilo, metoximetilo, metoxifenoximetilo, metoxifenilo, metoxifeniletilo, metoxipiridazinilo, metoxipiridilo, metoxipirimidinilo, metoxitiofeno, metilimidazolilo, metilpiridilo, metilsulfanilmetilo, metiltiazolilo, metiltiofeno, nitrofurilo, nitrofenilo, fenilo, p-toliloximetilo, piridazinilo, piridinoxidilo, bencilmorfolinilo, piridinolilo, piridilo, piridilmetilo, pirimidinilo, ter-butilfenilo, tetrahidrofurilo, tiazolilo, tiofeno, tolilo y trifluorometilo.

Cuando Q está sustituido en el átomo de

nitrógeno, R^4 se selecciona a partir de éster metílico del ácido acético, alilo, amino, bencilo, ciclopropilo, ciclopropilmetilo, etilo, fluorobencilo, fluoroetilo, furilmetilo, hidroxietilo, isobutilo, metoxietilo, metilo, metilbencilo, metilbutilo, metilsulfanilpropilo, *n*-butilo, *n*-hexilo, *n*-propilo, tetrahidrofurilmetilo, tiofenilmetilo y trifluoroetilo.

Cuando R^4 es un anillo R^4 puede estar sustituido con uno o más sustituyentes A, en el cual A se selecciona a partir de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})-cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})ciano, O-alquil(C_{1-6})CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{1-6})(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})-NR^5(CO)NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})-NR^5(SO_2)R^6, SO_3R^5, alquil(C_{1-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})-(SO_2)R^5, alquil(C_{0-6})(SO_2)R^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de

manera independiente a partir del grupo que consiste de C, N, O y S.

En una modalidad preferida A se selecciona a partir de hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})-arilo, alquil(C_{0-6})OR^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

Las modalidades específicas de la invención incluyen:

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

5-(3-metoxifenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-metil-1*H*-benzoimidazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]-

oxadiazol,

3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[4-metil-5-(2-metil-tiazol-4-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-[5-(2-metil-tiazol-4-il)-[1,3,4]oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

3-[4-metil-5-(5-nitro-furan-2-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-[5-(4-ter-butilfenil)-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-

3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-benzo-oxazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)piridina,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-imidazo[4,5-b]piridina,

5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

3-metil-5-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-metil-5-fenil-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxa-diazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-

morfolina,

4-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,2,4]oxadiazol,

2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(2-metilpiridin-4-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

2-[5-(3-yodofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-

3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil}-amina,

5-(3-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-trifluorometoxi-fenil)[1,2,4]-oxadiazol,

3-(5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-bromo-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-benzoimidazol,

5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-[5-(3-metoximetil-fenil)-[1,2,4]oxadiazol-

3-ilmetilsulfanil]-1*H*-benzoimidazol,

4-[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina,

2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-1-metil-1*H*-imidazo[4,5-b]piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1-metil-1*H*-imidazo[4,5-b],

3-[1-metil-1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]oxadiazol, o

5-(3-furan-3-il-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

o sal de los mismos.

Las modalidades específicas adicionales de la invención incluyen:

4-(4-ciclopropil-5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-

3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{4-metil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-o-tolil-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-{3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]-triazol-4-il}-etanol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxa-diazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(4-etil-5-furan-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

Ester metílico del ácido {3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-acético,

5-(2-fluoro-5-metil-fenil)-3-[5-furan-2-il-4-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-

3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-{5-[3-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-ciclopentil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-{4-etil-5-[2-(4-metoxi-fenil)-etil]-4H-[1,2,4]triazol-3-ilsulfanilmetil}-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-toliloximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metoxi-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etil-sulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-furan-2-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenoxi-metil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

3-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenoxi-metil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxa-diazol,

{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-metanol,

3-(3-clorofenil)-5-[4-etil-5-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metilsulfanilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-etoximetil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 5-[3-(3-clorofenil)-

[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]-triazol-3-carboxílico,

2-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-{1-[4-etil-5-(tetrahidro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridazina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-ilmetil)-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-fenol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenoximetil)-4-(tetrahidrofuran-2-ilmetil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-ciclopropil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-[4-etil-5-(tetrahidrofuran-2-il)-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-{5-[3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(3-clorofenil)-5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-metilsulfanil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1H-benzoimidazol,

5-(2,5-dimetil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-ciclopropil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[2-(3-clorofenil)-oxazol-4-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

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4-[4-metil-5-(5-tiofen-2-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{4-metil-5-[5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

2-metil-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

1-{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-etanona,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-metil-5-tiofen-2-il-4H-[1,2,4]triazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-

sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-2-metil-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-tiofen-2-il-4-tiofen-2-il-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxa-diazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-

piridina,

4-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

3-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]-

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triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[4-metil-5-(5-fenil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

2-cloro-4-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[3-(3-fluoro-fenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(3-fluoro-fenil)-5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-

piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(5-fluoro-2-metil-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

4-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadi-azol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metoxi-piridina,

3-(3-clorofenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-benzonitrilo,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-metil-4H-

[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(2,5-diclorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4)oxadiazol,

4-{5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4)triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

4-[4-metil-5-(3-tiofen-3-il-[1,2,4]oxadiazol-5-

ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-tiofen-3-carbonitrilo,

5-(3-clorofenil)-3-[5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-[5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-ilamina,

3-piridin-4-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-tiofen-2-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(2,5-difluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[4-etil-5-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-etil-3-furan-2-il-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-tolil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-m-tolil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-nitro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-[5-(2,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

5-(2-cloro-5-metil-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-

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4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-{5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-dicloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-tiofen-2-il-4H-[1,2,4]triazol,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-furan-2-il-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-fluoro-fenil)-4H-

[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-{3-[5-(3-cloro-tiofen-2-il)-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-trifluoro-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxa-diazol,

3-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

4-etil-3-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-5-trifluorometil-4H-[1,2,4]triazol,

4-{3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-[3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

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4-{4-etil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol,

3-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-(5-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-metil-tiazol-4-il)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(4-fluoro-fenil)-[1,2,4]oxadiazol,

4-etil-3-{1-(5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-5-furan-2-il-4H-[1,2,4]triazol,

4-(4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-

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piridina,

5-(3-clorofenil)-3-(4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[4-cloro-5-(3-clorofenil)-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[4-cloro-5-(3-clorofenil)-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-

3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metil-piridina,

3-[5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metoxi-piridina,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-benzonitrilo,

5-(3-clorofenil)-3-[4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-[5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-5-fluorobenzonitrilo,

4-etil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-2-il-4H-[1,2,4]triazol,

4-metil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-3-il-4H-[1,2,4]triazol,

4-etil-3-furan-2-il-5-(5-fenil-isoxazol-3-il-metilsulfanil)-4H-[1,2,4]triazol,

4-[4-etil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-

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4H-[1,2,4]triazol-3-il]-piridina,

4-[4-metil-5-(5-fenil-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,3,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-[4-etil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{5-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-[3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-cloro-4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-(3-clorofenil)-5-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-metil-5-tiazol-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

4-{4-etil-5-[5-(4-metiltiofen-2-il)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(3-nitro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

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2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,3,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[1-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-

metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-(5-cloro-2-fluorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-

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diazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

2-cloro-4-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4)triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol,

2-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4(5-(1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-cloro-2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

2-cloro-4-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-furan-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-{5-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol-2-il}-piridina,

2-(3-clorofenil)-5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-

piridina,

4-{5-(5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4)triazol-3-il}-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-etil-5-{1-[5-(2-fluoro-5-metilfenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-4H-[1,2,4]-triazol-3-il)-piridina,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

2-(2-fluoro-5-metil-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

2-(5-cloro-2-fluoro-fenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

2-(5-cloro-2-fluoro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(3-fluorofenil)-[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-{5-[1-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

4-{5-[1-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-

piridina,

4-{5-[1-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

2-(3-clorofenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

3-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol,

4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-(1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-[5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropilmetil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

4-cloro-2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

4-{4-ciclopropil-5-[5-(3-metoxi-fenil)-[1,2,4]-

oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(3-fluoro-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-ciclopropil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il)-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

4-{4-ciclopropil-5-[5-(2,5-difluorofenil)[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-(4-ciclopropil-5-{1-[5-(3-metoxifenil)[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]tri-

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azol-3-ilsulfanilmetil)(1,2,4]oxadiazol-5-il]-4-metilfenol,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-metanol,

3-[5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-fenol,

5-(3-clorofenil)-3-[4-(tetrahidro-furan-2-il-metil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

(2-clorofenil)-{5-[5-(3-clorofenil)-(1,2,4]oxadiazol-3-ilmetilsulfanil]-4-isobutil-4H-[1,2,4]triazol-3-il}-metanol,

5-(2-fluoro-5-metil-fenil)-3-[5-tiofen-2-il-4-(2,2,2-trifluoro-etil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-3-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridazina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-

etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-furan-2-il-4-isobutil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metilsulfanil-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-hexil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-iloximetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetoxi]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(2-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-2-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzoico,

5-(2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-vinil-fenil)-[1,2,4]oxadiazol,

5-(3-difluorometoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metoxi-tiofen-3-il)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(3-clorofenil)-5-[2-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[2-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-

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2-metil-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-tiofen-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]piridina,

5-(5-bromo-4-metil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-(3-clorofenil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfonilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfinilmetil)-[1,2,4]oxadiazol,

2-metil-6-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{2-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)amina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(1H-pirrol-3-il)-[1,2,4]oxadiazol,

1-óxido de 4-{5-[5-(3-clorofenil)-[1,2,4]oxa-

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diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(2-furan-2-il-3-metil-3H-imidazol-4-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[4-(2-fluoro-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-hidroxi-benzonitrilo,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina, o

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-

etoxi}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil--4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

3-{3-[1-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-{3-[1-(4-ciclopropil-5-piridin4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

3-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil)-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

cis-4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il)-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

Ester ter-butílico del ácido (S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico,

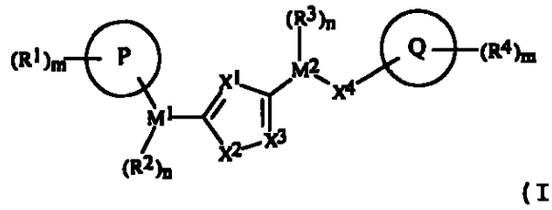
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(S)-1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil-amina,

(S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-dimetil-amina,

o sal de los mismos.

Los ejemplos adicionales factibles de compuestos de la fórmula I son provistos por compuestos de la fórmula Ia



(Ia)

en la cual:

P se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{3-7} y un anillo de 3 a 8 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del

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grupo que consiste de C, N, O y S;

R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})-arilo, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, alquil(C_{1-6})OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})(CO)R^5, O-alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})-ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})(CO)-NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, alquil(C_{0-6})NR^5(CO)R^6, O-alquil(C_{2-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)NR^5R^6, alquil(C_{0-6})SR^5 O-alquil(C_{2-6})SR^5, alquil(C_{0-6})(SO)R^5, O-alquil(C_{2-6})(SO)R^5, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})-SO_2R^5, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})(SO_2)NR^5R^6, alquil(C_{0-6})NR^5(SO_2)R^6, O-alquil(C_{2-6})NR^5(SO_2)R^6, alquil(C_{0-6})NR^5(SO_2)NR^5R^6, O-alquil(C_{2-6})NR^5(SO_2)NR^5R^6, (CO)NR^5R^6, O(CO)NR^5R^6, NR^5OR^6, alquil(C_{0-6})NR^5(CO)OR^6, O-alquil(C_{2-6})NR^5(CO)OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S, en el cual dicho

anillo puede estar sustituido con uno o más A;

M^1 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, alquenilo de C_{2-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-3})(CO)NR^5 alquilo de C_{0-3}, alquil(C_{0-4})NR^5, alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^2 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^1, X^2 y X^3 se seleccionan de manera independiente a partir del grupo que consiste de CR, CO, N, NR, O y S;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5, alquil(C_{0-3})NR^5R^6 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir del grupo que consiste de un enlace, alquilo de C_{1-3}, cicloalquilo de C_{3-7}, alquenilo de C_{2-3}, alquinilo de C_{2-3},

alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})-(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})S-alquilo de C_{0-3}, alquil(C_{0-3})(SO)alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)-alquilo de C_{0-3};

R^3 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})-(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5, alquil(C_{0-4})(NR^5R^6), alquil(C_{0-4})-(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halogenoalquilo de C_{1-4}, C, O, SO, SO_2 y S;

Q es un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo grupo puede estar fusionado opcionalmente con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S y cuyo anillo fusionado puede estar sustituido con uno o más A;

R^4 se selecciona a partir del grupo que

consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, oxo, =NR^5, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})-arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, en el cual dicho anillo puede estar sustituido con uno o más A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno, hidroxi, alquilo de C_{1-6}, alquil(C_{0-6})cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})heteroarilo y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, y en el cual R^5 y R^6 pueden formar juntos un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S;

en el cual cualquier alquilo de C_{1-6} alquenilo de C_{2-6}, alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo y alquil(C_{0-6})-heteroarilo definido bajo R^1, R^2, R^3, R^4, R^5 y R^6

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puede estar sustituido con uno o más A; y

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, oxo, halógeno, nitro, alquil(C_{0-6})-ciano, alquilo de C_{1-4}, alquil(C_{0-4})-cicloalquilo de C_{3-6}, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquenilo de C_{2-6}, O-alquilo de C_{1-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})OR^5, alquil(C_{1-6})SR^5 O-alquil(C_{2-6})SR^5, $(CO)R^5$, $O(CO)R^5$, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, $O(CO)OR^5$, O-alquil(C_{1-6})-$(CO)R^5$, alquil(C_{1-6})-$(CO)R^5$, NR^5OR^6, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, $NR^5(CO)OR^6$, alquil(C_{0-6})$(SO_2)NR^5R^6$, O-alquil(C_{2-6})(SO_2)-NR^5R^6, alquil(C_{0-6})$NR^5(SO_2)R^6$, O-alquil(C_{2-6})$NR^5(SO_2)R^6$, SO_3R^5, alquil(C_{1-6})$NR^5(SO_2)NR^5R^6$, O-alquil(C_{2-6})$(SO_2)R^5$, alquil(C_{0-6})$(SO_2)R^5$, alquil(C_{0-6})$(SO)R^5$, O-alquil(C_{2-6})-$(SO)R^5$ y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S;

m se selecciona a partir de 0, 1, 2, 3 y 4; y

n se selecciona a partir de 0, 1, 2 y 3,

o sal de los mismos.

La presente invención se refiere al uso de compuestos de las fórmula I y IA como los definidos

anteriormente en la presente así como a las sales de los mismos. Las sales para uso en formulaciones farmacéuticas serán sales farmacéuticamente aceptables, pero otras sales podrían ser útiles en la producción de los compuestos de las fórmulas I y Ia.

Los ejemplos de sales farmacéuticamente aceptables pueden ser, pero no se limitan a clorhidrato, 4-aminobenzoato, antranilato, 4-aminosalicilato, 4-hidroxibenzoato, 3,4-dihidroxibenzoato, 3-hidroxi-2-naftoato, nitrato y trifluoroacetato. Otras sales farmacéuticamente aceptables y métodos para preparar estas sales se pueden encontrar en, por ejemplo, Remington's Pharmaceutical Sciences (18ª edición, Mack Publishing Co.).

Algunos compuestos de la fórmula I pueden tener centros quirales y/o centros isoméricos geométricos (isómeros E y Z), y se debe entender que la invención abarca a todos de dichos isómeros ópticos, diastereoisómeros e isómeros geométricos.

La invención se refiere a cualquiera y a todas las formas tautoméricas de los compuestos de la fórmula I.

La invención se refiere a los siguientes compuestos, los cuales se pueden utilizar como intermediarios en la preparación de un compuesto de

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la fórmula I:

Acido 6-metilpiridin-4-carboxílico,

1-ciano-3-etilbenceno,

Acido 3-etilbenzoico,

Acido 3-fluoro-5-metil-benzoico,

Acido 3-metoximetil-benzoico,

N-hidroxi-3-metoxi-benzamidina,

N-hidroxi-benzamidina,

N-hidroxi-3-metil-benzamidina,

5-clorometil-3-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-clorometil-3-fenil-[1,2,4]oxadiazol,

5-clorometil-3-m-tolil-[1,2,4]oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-(5-clorometil-[1,2,4]oxadiazol-3-il)-benzonitrilo,

3-clorometil-5-m-tolil-[1,2,4]oxadiazol,

3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina,

3-clorometil-5-(3-nitro-fenil)-[1,2,4]oxadiazol,

4-(3-clorometil-[1,2,4]oxadiazol-5-il)-2-metil-piridina,

3-clorometil-5-(3-etil-fenil)-[1,2,4]oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina,

3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-clorometil-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol,

5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol,

3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol,

3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-tiazol-4-il-[1,2,4]oxadiazol,

3-clorometil-5-(3-iodo-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]-oxadiazol,

5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-fenil-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-piridin-2-il-4*H*-[1,2,4]triazol-3-tiol,

5-(4-bencil-morfolin-2-il)-4-metil-4*H*-[1,2,4]-triazol-3-tiol,

5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-piridin-3-il-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-tiol,

4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-tiol,

5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-tiol,

Acido 5-cloro-tiofen-3-carboxílico,

Acido 3-metilsulfanil-benzoico,

Acido 3-ciclopropil-benzoico,

Acido 3-ter-butoxicarbonilamino-benzoico,

Acido 3-acetil-benzoico,

Hidrazida del ácido 2-metil-isonicotínico,

Hidrazida del ácido 5-cloro-2-fluoro-benzoico,

Hidrazida del ácido 3-ciano-benzoico,

Hidrazida del ácido 2-cloro-isonicotínico,

Hidrazida del ácido 2-fluoro-5-metil-benzoico,

Hidrazida del ácido pirimidin-4-carboxílico,

3-fluoro-N-hidroxi-benzamidina,

N-hidroxi-tiofen-3-carboxamidina,

2-cloro-N-hidroxi-propionamidina,

3,N-dihidroxi-benzamidina,

N-hidroxi-2-metil-benzamidina,

N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina,

3-cloro-N-hidroxi-benzamidina,

N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina,

2,5-difluoro-N-hidroxi-benzamidina,

4-metil-5-piridin-3-il-4H-[1,2,4)triazol-3-tiol,

4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol,

4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol,

5-tiofen-2-il-4-tiofen-2-ilmetil-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-furan-2-ilmetil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol,

4-etil-5-piridin-3-il-4H-[1,2,4]triazol-3-tiol,

4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol,

4-furan-2-ilmetil-5-piridin-3-il-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol,

5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol,

5-(2-cloro-6-metil-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(tetrahidro-furan-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

Ester metílico del ácido 4-etil-5-tioxo-4,5-dihidro-1H-[1,2,4]triazol-3-carboxílico,

5-(2-cloro-piridin-4-il)-4-etil-4H-[1,2,4]-triazol-3-tiol,

5-(2-cloro-6-metoxi-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]-triazol-3-tiol,

4-propil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol ,

4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]-triazol-3-tiol,

4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]-triazol-3-tiol,

3-(5-mercapto-4-metil-4H-[1,2,4]triazol-3-il)-benzonitrilo,

5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-

3-tiol,

5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-tiol,

5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-pirimidin-5-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-furan-3-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-(tetrahidrofuran-2-ilmetil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

5-ciclopentil-4-etil-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(2-(4-metoxi-fenil)-etil]-2,4-dihidro-[1,2,4]triazol-3-tiona,

5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(3-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(4-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-(3-nitrofenil)-4H-[1,2,4]triazol-3-tiol,

5-(2,5-difluorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

5-(3-clorofenil)4-etil-4H-[1,2,4]triazol-3-tiol,

5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol,

4-etil-5-metoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-metil-5-piridin-4-il-2,4-dihidro-[1,2,4]-

triazol-3-tiona,

4-alil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(4-metoxi-fenoximetil)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-fenoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-hidroximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(2-metoxi-etil)-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-metilsulfanilmetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

5-etoximetil-4-etil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

5-furan-3-il-4-metil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-metil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-piridazin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-piridin-4-ilmetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(6-hidroxi-piridin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(4-hidroxi-fenil)-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-p-toliloximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(6-metoxi-piridin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(2-metoxi-piridin-4-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-pirimidin-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

4-etil-5-(5-metoxi-pirimidin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol,

4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol,

4-ciclopropilmetil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol,

4-ciclopropil-5-tiofen-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

5-furan-2-il-4-(2-metoxi-etil)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-ciclopropil-5-furan-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona,

Ester metílico del ácido (3-tiofen-2-il-5-tioxo-1,5-dihidro-[1,2,4]triazol-4-il)-acético,

4-ciclopropilmetil-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-(2-metoxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

Tiofen-2-il-4-(2,2,2-trifluoroetil)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-ciclopropil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-ciclopropil-5-piridin-3-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-tiol,

4-etil-3-metansulfonil-5-tiofen-2-il-4H-[1,2,4]-triazol,

4-(5-metansulfonil-4-metil-4H-[1,2,3]triazol-3-il)-piridina,

4-(2-hidroxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-(4,5-dimetil-4H-[1,2,4]triazol-3-il)-piridina,

Metil-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-il)-amina,

3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]-triazolo[4,3-a]pirimidina,

3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-

[4,3-a]pirimidina,

4-etil-5-(6-metoxi-piridazin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

4-etil-5-(5-metoxi-piridin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona,

5-clorometil-3-fenil-[1,2,4]oxadiazol,

5-clorometil-3-(3-fluoro-fenil)-[1,2,4]-oxadiazol,

5-clorometil-3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

5-clorometil-3-tiofen-2-il-[1,2,4]oxadiazol,

5-clorometil-3-tiofenl-3-il-[1,2,4]oxadiazol,

3-(5-clorometil-[1,2,4]oxadiazol-3-il)-fenol,

5-clorometil-3-o-tolil-[1,2,4]oxadiazol,

5-clorometil-3-(3-clorofenil)-[1,2,4]oxadiazol,

5-clorometil-3-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo,

2-cloro-4-(3-clorometil-[1,2,4]oxadiazol-5-il)-piridina,

3-clorometil-5-(2,5-dimetil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(2,5-diclorofenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(2-fluoro-5-bromo-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(3-metil-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(3-ciclopropil-fenil)-[1,2,4]-oxadiazol,

Ester ter-butílico del ácido 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-carbámico,

1-(3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-etanona,

5-(5-cloro-2-fluoro-fenil)-3-clorometil-[1,2,4]-oxadiazol,

2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-fenol,

3-clorometil-5-(2-cloro-5-metil-fenil)-[1,2,4]-oxadiazol,

3-clorometil-5-(2,5-dicloro-tiofen-3-il)-[1,2,4]-oxadiazol,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

3-clorometil-5-(2-metil-tiazol-4-il)-[1,2,4]-oxadiazol,

3-clorometil-5-(4-fluoro-fenil)-[1,2,4]oxadiazol,

5-(5-bromo-2-fluoro-fenil)-3-clorometil-[1,2,4]-oxadiazol,

3-clorometil-5-(4-metil-tiofen-2-il)-[1,2,4]-oxadiazol,

5-(3-clorometil-[1,2,4]oxadiazol-5-il)-tiofen-3-carbonitrilo,

2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-benzonitrilo,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-fluoro-benzonitrilo,

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-fluoro-benzonitrilo,

4-cloro-2-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenol,

3-(1-cloro-etil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

3-(1-cloro-etil)-5-(3-fluoro-fenil)-[1,2,4]-oxadiazol,

3-(1-cloro-etil)-5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol,

[3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-

metanol,

3-clorometil-5-[1-(toluen-4-sulfonil)-1H-pirrol-3-il]-[1,2,4]oxadiazol,

3-clorometil-5-furan-3-il-[1,2,4]oxadiazol,

3-clorometil-5-(5-cloro-tiofen-2-il)-[1,2,4]-oxadiazol,

1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etanol,

(5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-metanol,

1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etanol,

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanol,

2-clorometil-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol,

2-clorometil-5-(3-clorofenil)-[1,3,4]oxadiazol,

4-(5-clorometil-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

2-clorometil-5-m-tolil-[1,3,4]oxadiazol,

3-(5-clorometil-[1,3,4]oxadiazol-2-il)-benzonitrilo,

2-cloro-4-(5-clorometil-[1,3,4]oxadiazol-2-il)-piridina,

2-(5-cloro-2-fluoro-fenil)-5-clorometil-[1,3,4]-

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oxadiazol,

2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol,

2-(1-bromo-etil)-5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol,

4-[5-(1-bromo-etil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

2-(1-bromo-etil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol,

2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol,

3-(1-bromo-etil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

1-[5-(3-clorofenil)-isoxazol-3-il]-etanol,

1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etanol,

Ester metílico del ácido 5-(2-fluoro-5-metil-fenil)-isoxazol-3-carboxílico,

Ester metílico del ácido 5-tiofen-3-il-isoxazol-3-carboxílico,

Ester metílico del ácido 5-fenil-isoxazol-3-carboxílico,

Ester etílico del ácido 5-(3-clorofenil)-4-metil-isoxazol-3-carboxílico,

Ester metílico del ácido 5-(5-cloro-tiofen-

3-il)-isoxazol-3-carboxílico,

[5-(3-clorofenil)-isoxazol-3-il]-metanol,

[2-(3-clorofenil)-oxazol-4-il]-metanol,

[3-(3-clorofenil)-isoxazol-5-il]-metanol,

5-(tiofen-3-il-isoxazol-3-il)metanol,

[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-metanol,

(5-fenil-isoxazol-3-il)-metanol,

[5-(3-clorofenil)-4-metil-isoxazol-3-il]-metanol,

[5-(5-cloro-tiofen-3-il)-isoxazol-3-il)]-metanol,

Ester 1-[5-(3-clorofenil)-isoxazol-3-il]-etílico del ácido metansulfónico,

Ester 2-(3-clorofenil)-oxazol-4-il-metílico del ácido metansulfónico,

Ester 3-(3-clorofenil)-isoazol-5-il-metílico del ácido metansulfónico,

Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester -fenil)-isoxazol-5-il]-etílico del ácido metansulfónico,

Ester 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(3-clorofenil)-isoxazol-3-il-metílico

del ácido metansulfónico,

Ester 5-tiofen-3-il-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-fenil-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(3-clorofenil)-4-metil-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 5-(5-cloro-tiofen-3-il)-isoxazol-3-il-metílico del ácido metansulfónico,

Ester 1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico,

Ester 1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico,

Ester 4-cloro-5-(3-clorofenil)-isoxazol-3-il-metílico del ácido metansulfónico,

Acido pirimidin-4-carboxílico,

Ester metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico,

2-bromometil-5-(3-clorofenil)-oxazol,

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico,

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico,

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1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etanol,

1-[3-(3-clorofenil)-isoxazol-5-il]-etanol,

[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-metanol,

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico,

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico,

Clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico,

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico,

Hidrazida del ácido (5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético,

Hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico,

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-3-metil-butírico,

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona,

3-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona,

3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]-oxadiazol,

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1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol,

(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-acetonitrilo,

Acido 2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-propiónico,

Acido 2-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanil)-propiónico,

3-(3-clorofenil)-5-(4-metil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol o

Ester ter-butílico del ácido {3-[3-(4-metil-5-tiofen-2—il-4H[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il-fenil}-carbámico.

Formulaciones farmacéuticas

De conformidad con un aspecto de la presente invención se provee una formulación farmacéutica que comprende un compuesto de la fórmula I, o sal del mismo, para ser utilizado en la prevención y/o tratamiento de trastornos mediados por el subtipo 5 del receptor de glutamato metabotrópico (mGluR5) y cualesquiera trastornos listados más adelante.

La composición puede estar en una forma apropiada para administración por vía oral, por ejemplo como una tableta, píldora, jarabe, polvo,

gránulo o cápsula, para inyección parenteral (incluyendo inyección intravenosa, subcutánea, intramuscular, intravascular, o infusión) como una solución, suspensión o emulsión estéril, para administración por vía tópica como un ungüento, parche o crema o para administración por vía rectal como un supositorio.

En general, las composiciones anteriores se pueden preparar en una manera convencional utilizando uno o más excipientes, diluyentes farmacéuticos y/o vehículos inertes convencionales. De conformidad con otro aspecto de la invención, se provee una formulación farmacéutica que comprende como ingrediente activo una cantidad terapéuticamente efectiva de un compuesto de la fórmula I en asociación con uno o más diluyentes, excipientes y/o vehículo inerte farmacéuticamente aceptables.

Las dosis apropiadas de los compuestos de la fórmula I en el tratamiento de un mamífero, incluyendo humanos, son de aproximadamente 0.01 a 250 mg/kg de peso corporal para administración por vía oral y de aproximadamente 0.001 hasta 250 mg/kg de peso corporal en la administración por vía parenteral. La dosis diaria típica de los ingredientes activos varía dentro de un intervalo amplio y depende de diversos factores tales como la indicación relevante, la vía

de administración, la edad, peso y sexo del paciente y puede ser determinada por un médico.

Uso médico

Se ha descubierto que los compuestos de conformidad con la presente invención, o sales de los mismos, presentan un alto grado de potencia y selectividad para subtipos individuales del receptor de glutamato metabotrópico (mGluR). En particular existen compuestos de conformidad con la presente invención que son potentes y selectivos para el receptor del Grupo I de mGluR y de manera más particular para mGluR5. Por consiguiente, se espera que los compuestos de la presente invención sean útiles en la prevención y/o tratamiento de condiciones asociadas con la activación excitadora de un receptor del Grupo I de mGluR y para inhibir el daño a las neuronas ocasionado por la activación excitadora de un receptor del Grupo I de mGluR, específicamente cuando el receptor del Grupo I de mGluR es mGluR5. Los compuestos se pueden utilizar para producir un efecto inhibidor del Grupo I de mGluR, en especial mGluR5, en mamíferos, incluyendo humanos.

mGluR5 está altamente expresado en el

sistema nervioso central y periférico y en otros tejidos. Por lo tanto, se espera que los compuestos de la invención sean bastante adecuados para la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5, tales como trastornos neurológicos y psiquiátricos agudos y crónicos y trastornos del dolor agudos y crónicos.

Trastornos adicionales son la demencia senil de la enfermedad de Alzheimer, demencia inducida por SIDA, enfermedad de Parkinson, esclerosis lateral amiotrófica, Corea de Huntington, migraña, epilepsia, esquizofrenia, depresión, ansiedad, ansiedad aguda, trastorno obsesivo-compulsivo, trastornos oftalmológicos tales como retinopatías, retinopatías diabéticas, glaucoma, trastornos auditivos neuropáticos tales como tinnitus, neuropatías inducidas por quimioterapia, neuralgia post-herpética, y neuralgia del trigémino, tolerancia, dependencia, adicción y trastornos del ansia (craving), trastornos del desarrollo neuronal incluyendo X frágil, autismo, retraso mental, esquizofrenia y síndrome de Down.

Los compuestos también son bastante adecuados para la prevención y/o tratamiento de dolor relacionado con migraña, dolor inflamatorio, trastornos de dolor neuropático tales como neuropatías diabéticas,

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artritis y enfermedades reumatoides, dolor de la zona baja de la espalda, dolor post-operativo y dolor asociado con diversas condiciones incluyendo angina de pecho, cólicos renales o biliares, menstruación, migraña y gota.

Otros trastornos son apoplejía, trauma cefálico, daños anóxicos e isquémicos, hipoglucemia, enfermedades cardiovasculares y epilepsia.

La dosis requerida para el tratamiento terapéutico o preventivo de un trastorno particular necesariamente variará dependiendo del hospedero tratado, la vía de administración y la gravedad de la enfermedad que está siendo tratada.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para ser utilizados en terapia.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos neurológicos.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos psiquiátricos.

La invención se refiere a compuestos de la

fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos del dolor crónicos y agudos.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de demencia senil de la enfermedad de Alzheimer, demencia inducida por SIDA, enfermedad de Parkinson, esclerosis lateral amiotrófica, Corea de Huntington, migraña, epilepsia, esquizofrenia, depresión, ansiedad, ansiedad aguda, trastornos oftalmológicos tales como retinopatías, retinopatías diabéticas, glaucoma, trastornos neuropáticos auditivos tales como tinnitus, neuropatías inducidas por quimioterapia, neuralgia post-herpética y neuralgia del trigémino, tolerancia, dependencia, X frágil, autismo, retraso mental, esquizofrenia y síndrome de Down.

La invención se refiere a compuestos de la

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fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de dolor relacionado con migraña, dolor inflamatorio, trastornos del dolor neuropáticos tales como neuropatías diabéticas, artritis y enfermedades reumatoides, dolor de la zona baja de la espalda, dolor post-operativo y dolor asociado con diversas condiciones incluyendo angina de pecho, cólicos renales o biliares, menstruación, migraña y gota.

La invención se refiere a compuestos de la fórmula I como los definidos anteriormente en la presente invención, para uso en la prevención y/o tratamiento de apoplejía, trauma cefálico, daños anóxicos e isquémicos, hipoglucemia, trastornos cardiovasculares y epilepsia.

La presente invención se refiere también al uso de un compuesto de la fórmula I como el definido anteriormente en la presente invención,. en la fabricación de un medicamento para la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5 y cualquier trastorno antes listado.

La invención también provee un método de tratamiento y/o prevención de trastornos mediados por el receptor mGluR5 y cualquier trastorno antes listado, en un paciente que padece del mismo, o que

está en riesgo de padecer dicha condición, que comprende administrar al paciente una cantidad efectiva de un compuesto de la fórmula I, como el definido anteriormente en la presente invención.

En el contexto de la presente descripción, el término "terapia" incluye tratamiento así como prevención, a menos que existan indicaciones específicas de lo contrario. Los términos "terapéutico" y "terapéuticamente" se deben considerar en forma correspondiente.

En esta descripción, a menos que se indique lo contrario, el término "antagonista" significa un compuesto que mediante cualesquiera medios, bloquea parcial o completamente, la ruta de transducción que conduce a la producción de una respuesta por el ligando.

El término "trastorno", a menos que se indique lo contrario, significa cualquier condición y enfermedad asociada con la actividad del receptor de glutamato metabotrópico.

Uso no médico

Además de su uso en medicina terapéutica, los compuestos de la fórmula I o sal del mismo, también son útiles como herramientas farmacológicas

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en el desarrollo y normalización de sistemas de evaluación *in vitro* e *in vivo* para la evaluación de los efectos de inhibidores de actividad relacionada con mGluR en animales de laboratorio tales como gatos, perros, conejos, monos, ratas y ratones, como parte de la búsqueda respecto a nuevos agentes terapéuticos.

Farmacología

Se pueden analizar las propiedades farmacológicas de los compuestos de la invención utilizando pruebas normales para actividad funcional. Los ejemplos de pruebas para el receptor de glutamato son bien conocidas en la técnica, como se describen por ejemplo en Aramori *et al.*, *Neuron* *8*:757 (1992), Tanabe *et al.*, *Neuron* *8*:169 (1992), Miller *et al.*, *J. Neuroscience* *15*:6103 (1995), Balazs, *et al.*, *J. Neurochemistry* *69*:151 (1997). La metodología descrita en estas publicaciones se incorpora en la presente invención para referencia. De manera conveniente, los compuestos de la invención se pueden estudiar por medio de una prueba que mida la movilización de calcio intracelular, $[Ca^{2+}]_i$ en células que expresen a mGluR5.

La movilización de calcio intracelular se

mide detectando cambios en fluorescencia de células cargadas con el indicador fluorescente fluo-3. Las señales fluorescentes se miden utilizando el sistema FLIPR (Molecular Devices). Se utiliza un experimento de dos adiciones que pueda detectar compuestos que activen o antagonicen al receptor.

Para el análisis FLIPR, se siembran células que expresen a mGluR5d de humano en placas de 96 cavidades de fondo claro revestidas con colágena, con lados negros y el análisis de la movilización de $[Ca^{2+}]_i$ se efectúa 24 horas después de la siembra.

Los experimentos de FLIPR se efectúan utilizando un ajuste de láser de 0.800 W y una velocidad de disparador de cámara CCD de 0.4 segundos. Cada experimento de FLIPR se inicia con 160 µL de solución reguladora presente en cada cavidad de la placa celular. Después de cada adición del compuesto, se muestrea la señal de fluorescencia 50 veces a intervalos de 1 segundo seguido por 3 muestras a intervalos de 5 segundos. Las respuestas se miden como la altura del pico de la respuesta dentro del intervalo de muestreo. Se efectúan determinaciones de CE_{50} y CI_{50} a partir de los datos obtenidos provenientes de curvas de concentración-respuesta de 8 puntos (CRC) efectuadas por duplicado.

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Se generan CRC agonistas escalando todas las respuestas hasta la respuesta máxima observada para la placa. El bloqueo antagonista de la exposición a los agonistas se normaliza con la respuesta promedio de la exposición al agonista en 14 cavidades de control en la misma placa.

Se valida una prueba funcional secundaria para mGluR5d basada en el recambio de fosfato de inositol (IP_3). La acumulación de IP_3 se mide como un índice del recambio de fosfolipasa C mediada por receptor. Se incuban células GHEK que expresen de manera estable a los receptores mGluR5d de humano con [3H]-mioinositol durante la noche, se lavan tres veces en solución salina regulada con HEPES y se pre-incuban durante 10 minutos con LiCl 10 mM. Se agregan los compuestos (agonistas) y se incuba durante 30 minutos a 37°C. La actividad antagonista se determina pre-incubando los compuestos de prueba durante 15 minutos, incubando después en presencia de glutamato (80 µM) o DHPG (30 µM) durante 30 minutos. Las reacciones se terminan mediante la adición de ácido perclórico (al 5%). Se recolectan las muestras y se neutralizan, y se separan los fosfatos de inositol utilizando columnas de intercambio iónico alimentadas por la fuerza de gravedad.

Más adelante, en los ejemplos farmacéuticos, se provee un protocolo detallado para la evaluación de los compuestos de la invención.

Abreviaturas

FLIPR	Lectora de placas por formación de imagen fluorométrica
CCD	dispositivo acoplado por carga
CRC	curva de concentración-respuesta
GHEK	Células de riñón embrionario de humano que expresan al transportador de glutamato
HEPES	Ácido 4-(2-hidroxietil)-1-piperazin-etansulfónico (solución reguladora)
IP_3	Trifosfato de inositol
DHPG	3,5-dihidroxifenilglicina
BSA	Seroalbúmina de bovino
EDTA	Acido etilendiamintetra-acético

Métodos de preparación

Otro aspecto de la presente invención provee un procedimiento para preparar un compuesto de la fórmula I o sal del mismo.

A través de la siguiente descripción de dichos procedimiento se entiende que, en casos en los que sea apropiado, se agregarán, y posteriormente se retirarán grupos protectores apropiados a los

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diversos reactivos e intermediarios en una manera que será fácilmente entendida por el experto en la técnica de síntesis orgánica. Los procedimientos convencionales para utilizar dichos grupos protectores así como ejemplos de grupos protectores apropiados se describen, por ejemplo, en "Protective Groups in Organic Síntesis" T.W. Green, P.G.M. Wuts, Wiley-Interscience, New York, 1999.

A menos que se indique lo contrario, P Q, X^1, X^2, X^3, X^4, R, R^1, R^2, R^3, R^4, R^5, R^6, M^1, M^2, M y N, son como se definen en la fórmula I.

Todos los materiales de partida se pueden conseguir comercialmente o se describieron anteriormente en la literatura. Los espectros de RMN ^1H y ^{13}C se registran en espectrómetros ya sea Bruker 300, Bruker DPX400 o Varian +400 que funcionan a 300, 400 y 400 MHz para ^1H RMN respectivamente, utilizando TMS o la señal de solvente residual como patrón de referencia, en cloroformo deuterado como solvente a menos que se indique de otra manera. Todos los corrimientos químicos reportados están en ppm en la escala delta, y la división fina de las señales como aparecen en los registros (s: singulete, d: doblete, t: triplete, q: cuarteto, m: multiplete).

Las separaciones de cromatografía líquida

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en línea, analíticas seguidas por detecciones de espectros de masa, se registran en un aparato Waters LCMS que consiste de un espectrómetro de masas Alliance 2795 (LC) y un ZQ de un solo cuadrupolo. El espectrómetro de masas está equipado con una fuente de iones para electroaspersión operada en un modo iónico positivo o negativo. El voltaje para aspersión de iones es ±3 kV y el espectrómetro de masas se barre desde *m/z* 100-700 a un tiempo de barrido de 0.8 segundos. A la columna X-Terra MS, Waters, C8, 2.1 x 50 mm, 3.5 µm, se aplica un gradiente lineal de 5% hasta 100% de acetonitrilo en acetato de amonio 10 mM (acuoso), o en TFA al 0.1% (acuoso). La cromatografía de fase inversa preparatoria se corre en un HPLC auto-preparativo de Wilson con un detector de arreglo de diodos utilizando una Xterra MS C8, 19x300 mm, 7 µm como columna.

La cromatografía de fase inversa preparativa inducida por MS se corre en un sistema LC-MS de autopurificación de Waters con un detector de arreglo de diodo y un detector de masas ZQ utilizando una XTerra MS C8, 19x100 mm, 5 µm como columna.

La purificación mediante un cromatotrón se efectúa en láminas de vidrio revestidas con gel de

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sílice/yeso giratorias (Merck, 60 PF-254 con sulfato de calcio), con una capa de revestimiento de 1, 2, o 4 mm utilizando un cromatotrón TC Research 7924T.

También se efectúa la purificación de los productos utilizando columnas para extracción Chem Elut (Varian, cat #1219-8002), Mega BE-SI (Bond Elut Silica) columnas de tipo SPE (Varian, cat # 12256018; 12256026; 12256034), o mediante cromatografía de vaporización instantánea en columnas de vidrio rellenadas con sílice. El calentamiento con microondas se efectúa en una cavidad de microondas de modo individual Smith Synthesizer que produce irradiación continua a 2,450 MHz (Personal Chemistry AB, Uppsala, Suecia).

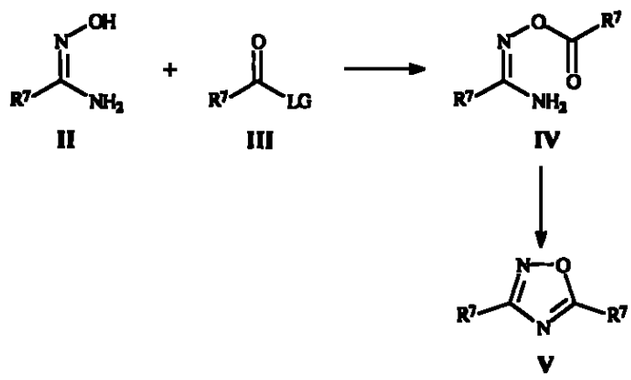
Abreviaturas

DMF	N,N-dimetilformamida
BOPA	Peróxido de benzoilo
P-BEMP	2-ter-butilimino-2-dietilamino-1,3-dimetil-perhidro-1,3,2-diazafosforina unida a poliestireno
Deoxofluor	Trifluoruro de [Bis(2-metoxietil)amino]azufre
DAST	Trifluoruro de (dietilamino)azufre
EDCI	Clorhidrato de 1-(3-dimetilamino-propil)-3-etilcarbodi-imida
HOBt	hidrato de 1-hidroxibenzotriazol
THF	tetrahidrofurano

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TFA	Acido trifluoroacético
Et	etilo
Ac	acetilo
DIBAL	hidruro de di-isobutilaluminio
M, N	molar y normal
HBTU	hexafluorofosfato de O-benzotriazol-1-il-N,N,N',N'-tetrametiluronio
Boc	ter-butoxicarboniloxi
LDA	di-isopropilamina de litio
LHA	hidruro de litio y aluminio
MCPBA	ácido meta-cloroperoxibenzoico
SPE	extracción en fase sólida
Reactivo de Lawesson	[2,4-bis(4-metoxifenil)-1,3-ditia-2,4-difosfetan-2,4-disulfuro

Síntesis General de los compuestos de la fórmula V



Un compuesto de la fórmula V, en la cual R^7 se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)n-G$ en el cual G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, se puede preparar a través de ciclización de un compuesto de la fórmula IV formado a partir de un compuesto activado de manera apropiada de la fórmula III, en la cual LG es un grupo saliente, con un compuesto de la fórmula II. El compuesto de la fórmula II se puede preparar a partir de un nitrilo apropiado mediante adición de hidroxilamina en un solvente apropiado tal como metanol, etanol, agua o mezclas de los mismos, utilizando una base apropiada tal como hidróxido, carbonato o acetato.

El compuesto de la fórmula III se puede activar de la siguiente manera; i) como el cloruro de acilo formado a partir del ácido utilizando un reactivo apropiado tal como cloruro de oxalilo o cloruro de tionilo; ii) como un anhídrido o anhídrido mixto formado a partir del tratamiento con un reactivo tal como cloroformiato de alquilo; iii) utilizando métodos tradicionales para activar ácidos en reacciones de copulación de amida tales como EDCI

con HOBt o sales de uronio tales como HBTU; iv) como un éster de alquilo cuando se desprotona la hidroxiamidina utilizando una base fuerte tal como ter-butóxido; v) mediante cualquier otro método apropiado de activación para el substrato deseado.

La formación del éster se puede lograr utilizando un solvente aprótico apropiado tal como diclorometano, tetrahidrofurano, N,N-dimetilformamida o tolueno, opcionalmente con una base orgánica apropiada tal como trietilamina, di-isopropiletilamina y similares o una base inorgánica tal como bicarbonato de sodio o carbonato de potasio.

La ciclización del éster para formar un oxadiazol se puede efectuar en el éster crudo, con evaporación y reemplazo del solvente con un solvente de punto de ebullición más alto tal como DMF, o con extracción acuosa para proveer un material semi-purificado o con material purificado mediante métodos cromatográficos normales. La ciclización se puede lograr calentando de manera convencional o mediante irradiación de microondas (100-180°C), en un solvente apropiado tal como piridina o N,N-dimetilformamida o utilizando un método de temperatura más baja que emplee reactivos tales como fluoruro de tetrabutil-amonio en tetrahidrofurano o utilizando cualquier

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otro método apropiado conocido en la literatura.

También pueden estar presentes en los substratos otros grupos funcionales no reactivos, compatibles, protegidos de manera apropiada.

Los ejemplos adicionales de las reacciones antes descritas se pueden encontrar en Poulain et al., Tetrahedron Lett., (2001), 42, 1495-98, Ganglott et al., Tetrahedron Lett., (2001), 42, 1441-43, las cuales se incluyen en la presente invención como referencias.

Síntesis de nitrilos y ácidos para ser utilizados en la preparación de compuestos de las fórmulas II y III

Los nitrilos de arilo se pueden obtener utilizando una variedad de métodos que incluyen cianuración de un halogenuro de arilo o triflato de arilo bajo catálisis con paladio o níquel utilizando una fuente de cianuro apropiada tal como cianuro de zinc en un solvente apropiado tal como N,N-dimetilformamida. El ácido correspondiente se puede obtener a partir del nitrilo mediante hidrólisis ya sea bajo condiciones ácidas o básicas en un solvente apropiado tal como alcoholes acuosos. Los ácidos de arilo también se pueden obtener a partir de una

variedad de otras fuentes, incluyendo intercambio de yodo- o bromo- litio seguido por entrampamiento con CO_2 para producir directamente el ácido.

El ácido se puede convertir a la amida primaria utilizando cualquier método compatible para activar al ácido, incluyendo a través del cloruro de acilo o anhídrido mixto, seguido por entrampamiento con cualquier fuente de amoniaco, incluyendo cloruro de amonio en presencia de una base apropiada, hidróxido de amonio, amoniaco metanólico o amoniaco en un solvente no prótico tal como dioxano. Este intermediario amida se puede convertir al nitrilo utilizando una variedad de reactivos para deshidratación tales como cloruro de oxalilo o cloruro de tionilo. También se puede aplicar esta secuencia de reacción para convertir un ácido en el nitrilo hasta ácidos no aromáticos, incluyendo derivados de aminoácido protegidos de manera apropiada. Un grupo protector apropiado para una amina, en un aminoácido o en una posición lejana de cualquier otro material de partida tipo ácido, puede ser cualquier grupo que remueva el carácter básico y las propiedades nucleofílicas del grupo funcional amina, incluyendo grupos protectores tipo carbamato tales como Boc.

Algunos ácidos se preparan más fácilmente

tomando ventaja de análogos comercialmente disponibles. Por ejemplo el ácido 6-metilpiridin-4-carboxílico se prepara mediante eliminación de cloro del ácido 2-cloro-6-metilpiridin-4-carboxílico. Algunos tipos de fluoro-benzonitrilos y ácidos benzoicos sustituidos se pueden obtener a partir de bromo-difluoro-benceno mediante desplazamiento de un grupo fluoro con un nucleófilo apropiado tal como imidazol en presencia de una base tal como carbonato de potasio en un solvente compatible tal como N,N-dimetil-formamida a temperaturas elevadas (80-120°C) durante intervalos prolongados de tiempo. El grupo bromo se puede convertir posteriormente en el ácido o nitrilo como se indicó anteriormente. Se pueden preparar ácidos benzoicos y benzonitrilos 1,3-disustituidos y 1,3,5-trisustituidos tomando ventaja de derivados de ácido isoftálico sustituidos fácilmente disponibles. La monohidrólisis del diéster permite la reacción selectiva del ácido con una variedad de reactivos, típicamente agentes activadores tales como cloruro de tionilo, cloruro de oxalilo o cloroformiato de isobutilo y similares. A partir del ácido activado, se puede obtener un número de productos. Además de la amida primaria utilizada para formar el nitrilo mediante deshidratación como se mencionó anteriormente,

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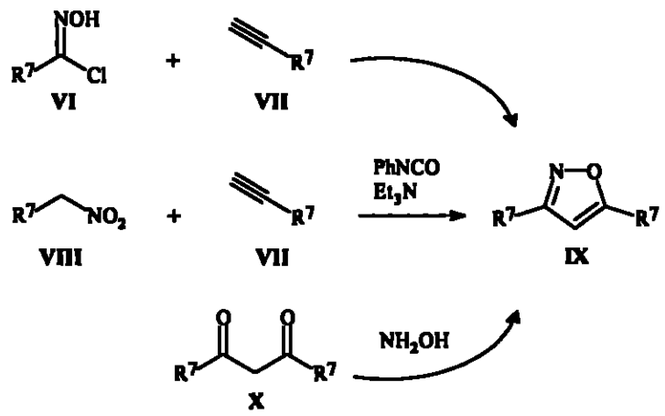
se puede efectuar la reducción hasta el análogo hidroximetilo en el anhídrido mixto o cloruro de acilo utilizando una variedad de agentes reductores tales como borohidruro de sodio en un solvente compatible tal como tetrahidrofurano. El derivado hidroximetilo se puede reducir posteriormente hasta el análogo metilo utilizando hidrogenación catalítica con una fuente apropiada de catalizador tal como paladio sobre carbón en un solvente apropiado tal como etanol. También se puede utilizar el grupo hidroximetilo en cualquier reacción apropiada para alcoholes bencílicos tales como acilación, alquilación, transformación hasta el halógeno y similares. También se pueden obtener ácidos halogenometilbenzoicos de este tipo a partir de la bromación del derivado metilo cuando no se pueda conseguir comercialmente. Los éteres obtenidos mediante alquilación de los derivados hidroximetilo también se pueden obtener a partir de los derivados halogenometilaril-benzoato mediante reacción con el alcohol apropiado utilizando una base apropiada tal como carbonato de potasio o hidróxido de sodio en un solvente apropiado tal como tetrahidrofurano o el alcohol. Cuando están presentes otros sustituyentes, éstos también se pueden utilizar en reacciones de transformación estándar. El tratamiento de una anilina

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con ácido y nitrito de sodio puede producir una sal de diazonio, la cual se puede transformar en el halogenuro tal como fluoruro, utilizando ácido tetrafluorobórico.

Los fenoles reaccionan en presencia de una base apropiada tal como carbonato de potasio con agentes alquilantes para formar éteres aromáticos.

Formación de los compuestos de la fórmula IX



Se puede preparar un compuesto de la fórmula IX, en el cual R^7 se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)n-G$, en los cuales G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, mediante una cicloadición 1,3-dipolar entre compuestos de la fórmula VI y VII bajo condiciones básicas utilizando una base apropiada tal como bicarbonato de

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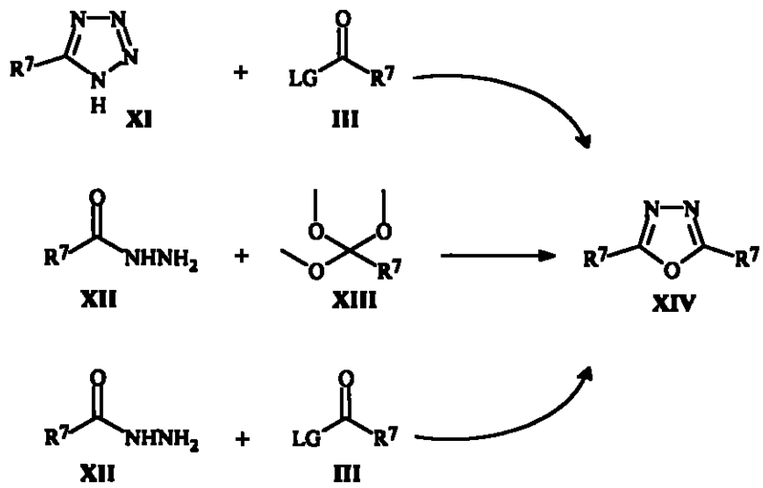
sodio o trietilamina a temperaturas apropiadas (0°C a 100°C) en solventes tales como tolueno. La síntesis de compuestos del tipo **VI** ha sido descrita previamente en la literatura, por ejemplo Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57, 6649-50. La cicloadición 1,3-dipolar con acetilenos del tipo **VII** también se puede efectuar utilizando nitrometanos sustituidos del tipo **VIII** mediante activación con un reactivo electrofílico tal como PhNCO en presencia de una base tal como trietilamina a temperaturas elevadas (50-100°C). Li, C-S.; Lacasse, E.; Tetrahedron Lett. (2002) 43; 3565-3568. Se pueden conseguir comercialmente varios compuestos del tipo **VII**, o éstos se pueden sintetizar utilizando métodos estándar como los conocidos por el experto en la técnica.

De manera alternativa, los compuestos de la fórmula **X**, los cuales se pueden obtener a partir de la condensación de Claisen de una metilcetona y un éster utilizando condiciones básicas, empleando bases tales como hidruro de sodio o terbutóxido de potasio, pueden producir los compuestos de la fórmula **IX** mediante condensación y ciclización subsiguiente utilizando hidroxilamina, por ejemplo en forma de la sal clorhidrato, a temperaturas elevadas (60-120°C).

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Se entiende que para ambos métodos, podrían ser necesarias transformaciones de grupo funcional posteriores. En el caso de un grupo éster, estas transformaciones pueden incluir, pero no se limitan a, cualquiera de los siguientes tres procedimientos: a) reducción completa utilizando un agente reductor apropiado tal como LAH en solventes tales como THF. b) reducción parcial utilizando un agente reductor selectivo apropiado tal como DIBAL seguido por alquilación con un halogenuro de alquilo. c) alquilación utilizando un reactivo de tipo alquil-metal tal como un halogenuro de alquilmagnesio en solventes tales como tolueno o THF, seguido por reducción con, por ejemplo, borohidruro de sodio en metanol.

Formación de los compuestos de la fórmula **XIV**



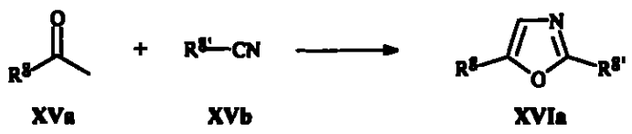
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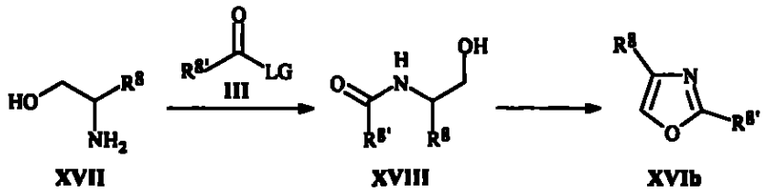
Se puede preparar un compuesto de la fórmula **XIV**, en el cual R^7 se selecciona de manera independiente a partir de un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)_n-G$, en los cuales G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, a partir de compuestos de tetrazol del tipo **XI** mediante acilación utilizando un compuesto susceptible de aislamiento del tipo **III** tal como un cloruro o anhídrido de ácido, o un compuesto del tipo **III** en el cual LG se puede formar in situ, por ejemplo a partir de la activación de un ácido utilizando un reactivo tal como DCC o EDCI, seguido por transposición hasta el 1,3,4-oxadiazol. Jursic, B.S.; Zdravkovski, Z.; Synth. Común.; (1994) *24*; 1575-1582.

De manera alternativa, también se pueden preparar los compuestos de la fórmula **XIV** a partir de la hidrazida de acilo del tipo **XII** mediante calentamiento en presencia de compuestos de la fórmula **XIII** o **III**, en los cuales LG es un grupo saliente tal como cloruro o alcóxido, a temperaturas elevadas (60-130°C) en un sólo paso. La reacción de los compuestos de la fórmula **XIII** se puede efectuar en forma pura o utilizando un solvente no prótico apropiado tal como benceno o

xileno, o un solvente prótico tal como etanol o n-butanol, y se puede facilitar por la presencia de una base tal como KOtBu o un ácido tal como ácido para-toluensulfónico o ácido acético. Véase referencias: Saunders, J.; Cassidy, M.; Freedman, S. B.; Harley, E. A.; Iversen, L.L. J.Med.Chem.; (1990) 33; 1128-1138; Peet, N. P.; Sunder, S. J.Heterocycl.Chem.; (1984) 21; 1807-1816. Para los compuestos de la fórmula III se puede utilizar un agente deshidratante tal como pentóxido de fósforo para incrementar la ciclización del intermediario de reacción formado como se ha descrito previamente por ejemplo, por Kakefuda, Akio; et al.; Bioorg. Med. Chem. (2002), *10*; 1905-1912.

Formación de los compuestos de la fórmula **XVI**





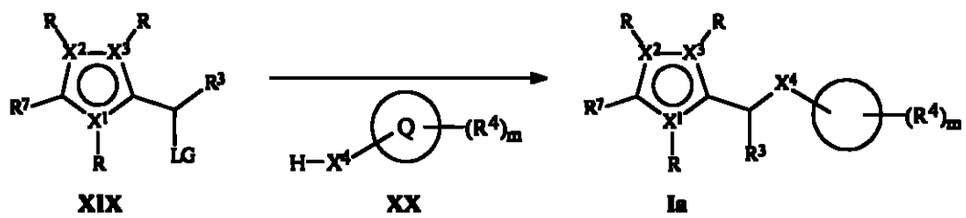
Se puede preparar un compuesto de la fórmula **XVI**, en el cual R^8 como el definido anteriormente, se selecciona de manera independiente a partir de un

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grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$, y $M^2-(R^3)_n-G$, en los cuales G es un grupo saliente o un grupo que se pueda transformar posteriormente en un grupo saliente, haciendo reaccionar compuestos de la fórmula **XVa** y **XVb** en presencia de Tl(OTf)3 generado in situ bajo condiciones ácidas de conformidad con el procedimiento de Lee y Hong; Tetrahedron Lett., (1997), *38*, 8959-60.

De manera alternativa los compuestos de las fórmulas **III** y **XVII** se hacen reaccionar como se describió anteriormente para la fórmula **V** para obtener un intermediario de la fórmula **XVIII**. Dicho intermediario puede producir el oxazol requerido mediante ciclo-deshidratación con, para generar la oxazolina seguida por deshidrogenación, utilizando $BrCCl_3$ en el mismo recipiente de reacción. Phillips, A.J.; Uto, Y.; Wipf, P.; Reno, M.J. y Williams, D.R., Organic Letters, (2000) *2*, 1165-8.

<u>Formación del enlace entre X^4 y M^2 o Q y M^2 a través del desplazamiento nucleofílico de un grupo saliente</u>



XIX **XX** **Ia**

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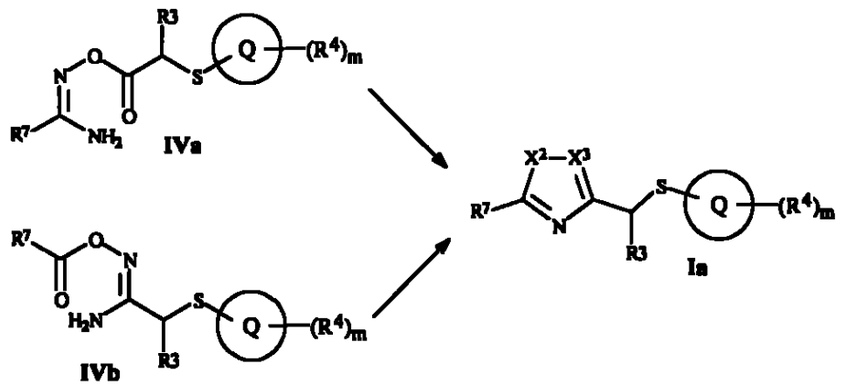
Se puede utilizar un compuesto de la fórmula **XX**, para desplazar el grupo saliente LG en los compuestos de la fórmula **XIX** (R^7 es M^1-$(R^2)_n$-P-$(R^1)_{m1}$). Cuando X^4 se representa mediante un heteroátomo tal como N y S, la reacción se efectúa en presencia de una base apropiada tal como carbonato de potasio, carbonato de cesio, hidruro de sodio, trietilamina o similares, lo cual puede facilitar la reacción mediante desprotonación del residuo X^4 y evitar la formación de cualquier ácido en exceso que pudiera ser generado por la reacción en ausencia de una base. La reacción se puede lograr utilizando cualquier solvente apropiado tal como acetonitrilo o DMF, y se puede efectuar a temperatura ambiente o a temperatura elevada (35-100°C) para acelerar la reacción.

Se pueden utilizar dichas condiciones con las modificaciones apropiadas, del equipo utilizado para la síntesis en paralelo, utilizando técnicas estándar conocidas por el experto en el campo.

De igual manera, estas condiciones de reacción se pueden efectuar para compuestos de la fórmula **XX** cuando X^4 = enlace y el anillo Q es un biciclo fusionado que contiene un heteroátomo tal como N como se definió anteriormente. En cualquiera del último o

el primer caso descritos con X^4=N, se prefiere NaH en DMF como se describe en las referencias de la literatura, por ejemplo, Murdoch, Robert; Tully, W. Roger; Westwood, Robert; J.Heterocycl.Chem.; (1986), *23*; 833-841.

Para compuestos de la fórmula **XX** que contienen X^4=C, es necesario utilizar una base más fuerte para lograr la desprotonación, tal como por ejemplo LDA, n-butil-litio o cualquier otra base de tipo alquil-metal en solventes no próticos apropiados tales como THF, hexano o tolueno a temperaturas por lo general menores a las temperaturas ambientales, por ejemplo a -78°C ó 0°C.

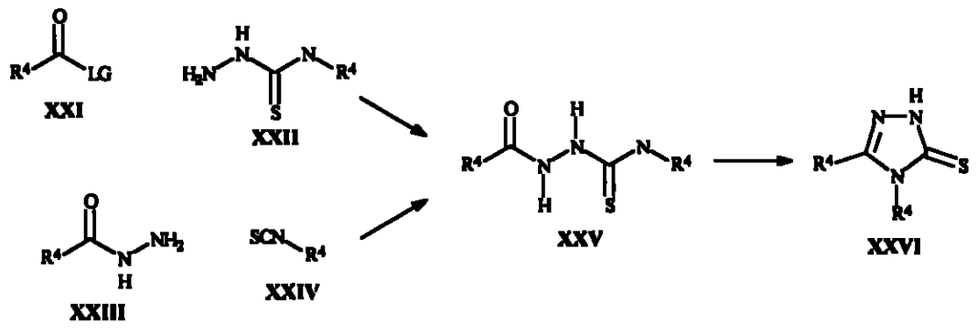


Un procedimiento alternativo para la síntesis del tipo antes descrito de tiometil-oxadiazol es formar un éster acíclico **IVa** y **IVb** a partir de la combinación de una hidroxiamidina sustituida en forma apropiada y un compañero de copulación tipo ácido activado también sustituido en forma apropiada. El

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desplazamiento del cloruro utilizando el nucleófilo tiol puede presentarse inmediatamente antes de la ciclización, utilizando uno de los métodos de formación de oxadiazol antes descritos. También se puede efectuar el desplazamiento en la clorometil-hidroxiamidina o en los materiales de partida de ácido de clorometilo, seguido por la esterificación y ciclización en dos pasos como se indicó anteriormente. Se pueden utilizar las condiciones descritas con modificaciones apropiadas del equipo utilizado para la síntesis en paralelo empleando técnicas estándar conocidas por el experto en el campo.

Formación de 4-alquiltriazol tioles/tionas



Se hace reaccionar cualquier agente para acilación apropiado tal como un cloruro de acilo o un ácido activado o el ácido correspondiente bajo condiciones de copulación de amida como se indicó anteriormente, con una 4-alquil-3-tiosemicarbazida

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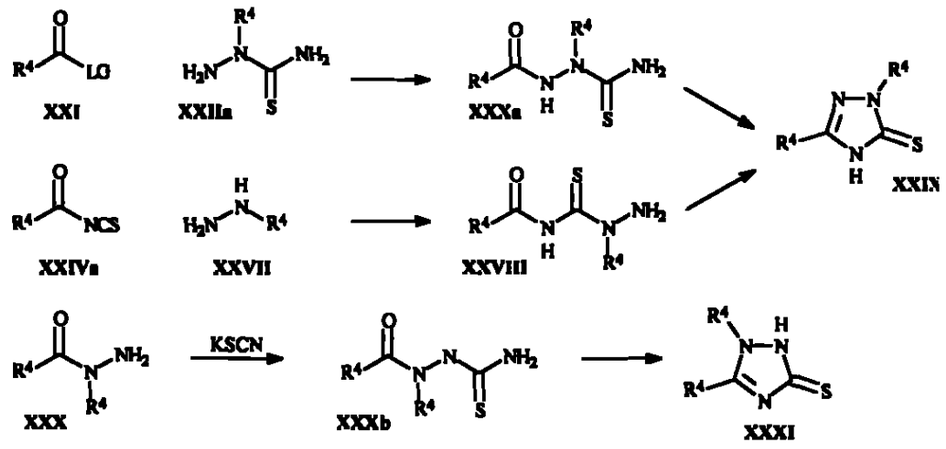
apropiada en presencia de una base tal como piridina o aminas no nucleofílicas para formar el compuesto intermediario no cíclico de la fórmula **XXV**, en el cual R^4 es como se definió anteriormente. También se puede conseguir el mismo intermediario a través de la reacción de una hidrazida de acilo con un isotiocianato de alquilo. La ciclización para obtener un compuesto de la fórmula **XXVI** se efectúa fácilmente mediante tratamiento con una base inorgánica apropiada tal como hidróxido o bicarbonato a temperatura elevada en un solvente apropiado tal como agua, agua-dioxano, un alcohol acuoso o mezclas de los mismos.

Se pueden utilizar dichas condiciones con las modificaciones apropiadas del equipo empleado cuando se utiliza una base en fase sólida en lugar de aquellas antes mencionadas, tales como por ejemplo P-BEMP para la síntesis en paralelo utilizando técnicas estándar conocidas por el experto en el campo.

El compuesto de la fórmula **XXV** reacciona a través de su forma tautomérica bajo las condiciones descritas anteriormente con los compuestos de la fórmula **XIX** para producir los compuestos de S-alquilación de la fórmula **Ia**.

Las triazol-tionas **XXIX** y **XXXI** alquiladas en los otros átomos de nitrógeno del anillo (1 y 2) se

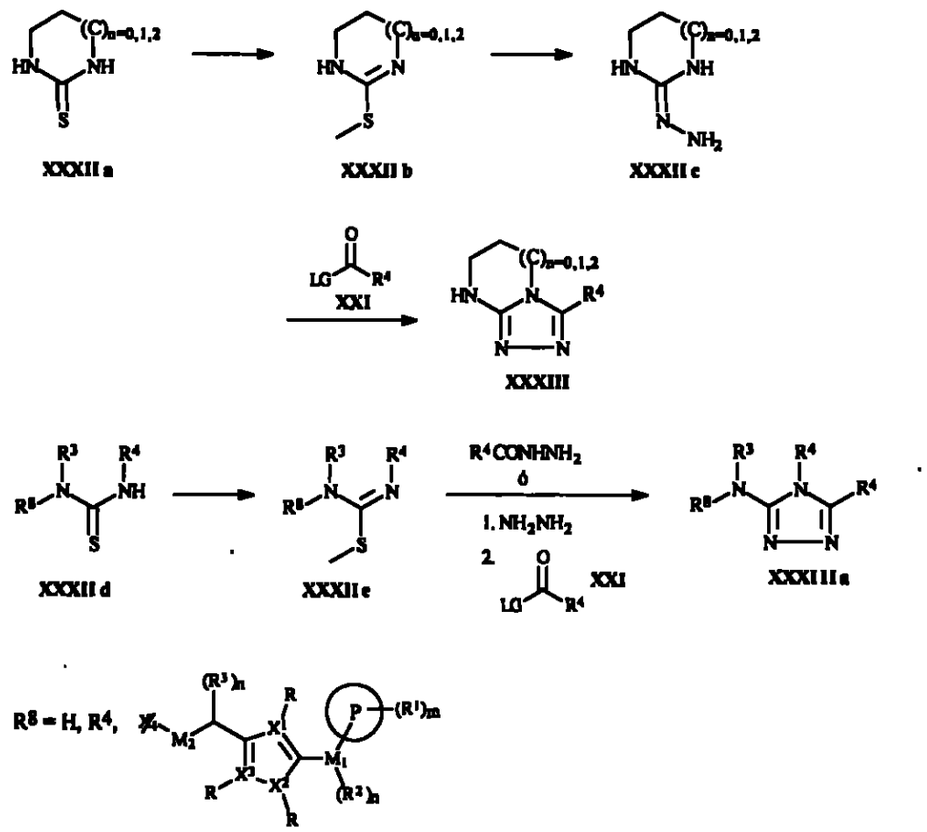
pueden conseguir a través de procedimientos similares. La 2-alquil-triazol-tiona **XXVIII** se puede obtener mediante tratamiento de un isotiocianato de aroilo con una hidrazina de alquilo en tolueno a temperaturas elevadas, por ejemplo 85°C, seguido por calentamiento con bicarbonato acuoso. También se puede obtener el mismo producto a través del tratamiento de la 2-alquil-3-tiosemicarbazida análoga con un ácido activado en presencia de una base apropiada tal como piridina o trietilamina seguido por el cierre de anillo en medio alcalino en una forma similar al cierre de anillo en medio alcalino que produce el compuesto **XXVI** anterior.



Las 1-alquil-triazol-tionas **XXXI** se pueden preparar mediante la reacción de una N-alquil-N-acilhidrazida apropiada con tiocianato de potasio en presencia de un ácido tal como HCl u otro ácido

fuerte compatible mediante el intermediario 1-acil-1-alquil-3-tiosemicarbazida la cual se somete a cierre del anillo en medio alcalino en una forma similar al cierre de anillo en medio alcalino que produce los compuestos de la fórmula **XXVI** anteriores.

Formación de compuestos de la fórmula **XXXIII**



Se puede preparar un compuesto de la fórmula **XXXIII** mediante alquilación de tioureas cíclicas de la fórmula **XXXIIa**, en la cual n se define como 0, 1 o 2, lo que da como resultado el compuesto de la

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fórmula **XXXIIb**, por ejemplo, 2-metiltio-1,4,5,6-tetrahidropirimidina en caso de n = 1. La alquilación con, por ejemplo, yoduro de metilo como el agente alquilante se puede efectuar en varios solventes (DMF, acetona, CH_2Cl_2, etc.) a temperatura ambiente o temperaturas elevadas y dará el producto como su sal yodohidrato como ácido descrito previamente por Kennedy, Kevin J.; Simandan, Tiberiu L.; Dix, Thomas A.; Synth.Commun.; (1998); *24*; 741-746. Las tioureas cíclicas se pueden conseguir fácilmente ya sea a través de síntesis como es sabido por el experto en la técnica, o a partir de fuentes comerciales. Los compuestos de la fórmula **XXXIIc** resultan de la hidrazinolisis de los compuestos correspondientes del tipo **XXXIIb**. La hidrazinolisis de preferencia se efectúa en EtOH bajo reflujo con hidrato de hidrazina como se describió previamente por Krezel, Izabella; Pharmazie; (1994); 94, 27-31. Por último, los triazoles fusionados de la fórmula **XXXIII** se pueden formar a través de la acilación térmica y reacción de condensación entre compuestos de la fórmula **XXI** en la cual LG es un grupo saliente tal como por ejemplo un halogenuro, y compuestos de la fórmula **XXXIIc**. Dichas reacciones se pueden efectuar en piridina o en EtOH o tolueno en presencia de una base. Se puede utilizar

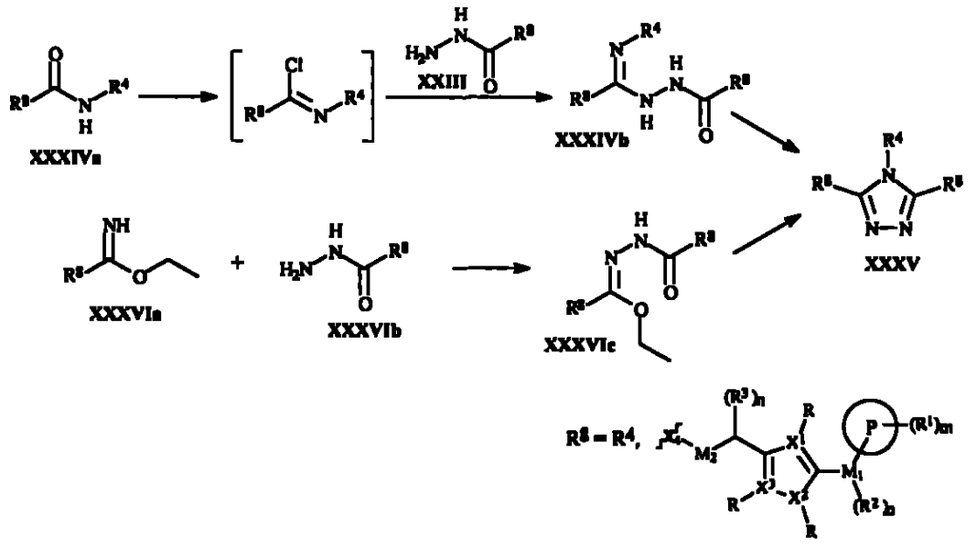
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calentamiento normal o irradiación de microondas. De igual manera, el compuesto XXXIII se puede preparar en presencia de una base, tal como metóxido de sodio en un solvente apropiado tal como metanol o etanol a temperaturas elevadas en las cuales XXI también puede ser un éster o ácido carboxílico.

También se pueden utilizar tioureas acíclicas de la fórmula **XXXIId**, en la cual R^8 es como se definió anteriormente en el esquema y R^3 y R^4 son como se definen en la fórmula I, empleando métodos similares para obtener los compuestos de la fórmula **XXXIIIa**, en la cual la introducción de la porción hidrazina se puede efectuar utilizando ya sea hidrazina seguido por acilación, o utilizando una hidrazina de acilo pre-formada.

Formación de los compuestos de la fórmula **XXXV**



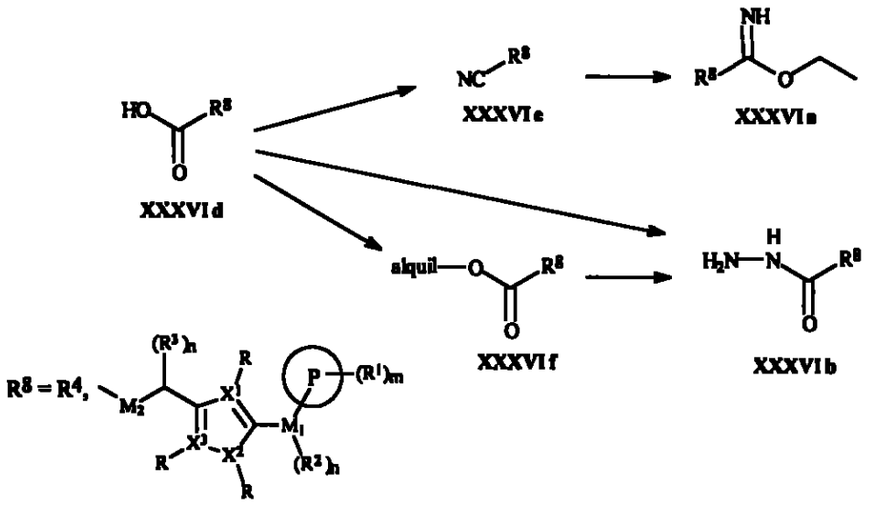
Se pueden preparar los compuestos de la fórmula **XXXIVb** utilizando métodos similares a los anteriores, por ejemplo mediante activación de **XXXIVa** para dar el cloruro de imidoilo correspondiente empleando cloruro de oxalilo o pentaclorofosfina en presencia opcional de una base tal como trietilamina. El intermediario se puede utilizar in situ o se puede aislar antes del entrampamiento por un compuesto de la fórmula **XXIII** como se utilizó anteriormente. El producto subsiguiente se puede ciclizar bajo condiciones ácidas o básicas en un solvente apropiado tal como DMF para producir los compuestos de la fórmula **XXXV**. El compuesto **XXXV** puede ser un intermediario utilizado en la formación de los compuestos de la fórmula **I**, o puede ser el compuesto bioactivo final de la fórmula **I**.

También se puede preparar un compuesto de la fórmula **XXXV**, en la cual R^8 se selecciona de manera independiente a partir de un grupo como los descritos anteriormente, a través de la reacción de compuestos de la fórmula **XXXVIa** (se muestra imidoato de etilo como ejemplo) y **XXXVIb** seguido por ciclización a temperaturas elevadas (40-80°C) en presencia de una amina, mientras que la amina de preferencia debe tener, pero no se limita a, un punto de ebullición bajo de manera tal que ésta se pueda

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utilizar en exceso y simplificar el procedimiento de tratamiento. Los ejemplos para dichas aminas pueden ser, pero no se limitan a, metilamina o etilamina las cuales se pueden utilizar como soluciones en, por ejemplo, metanol, THF o diclorometano.

Formación de los compuestos de la fórmula **XXXVIa y XXXVIb**

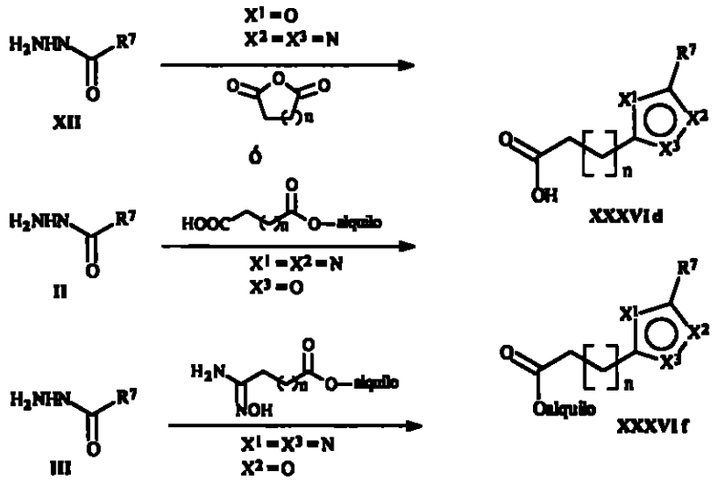


Se puede preparar un compuesto de la fórmula **XXXVIa**, en la cual R^8 se selecciona de manera independiente a partir de un grupo como los descritos anteriormente, a través de la reacción de un nitrilo de la fórmula **XXXVIe** en un alcohol tal como etanol, en presencia de un ácido prótico, por ejemplo ácido clorhídrico. El nitrilo se puede obtener a partir de un ácido **XXXVId** como se describió anteriormente. Los

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compuestos de la fórmula **XXXVId** también se pueden utilizar para preparar hidrazinas de acilo de la fórmula **XXXVIb**, en la cual R^8 se selecciona de manera independiente a partir de un grupo como los mostrados anteriormente. Este tipo de sustancia **XXXVIb** también se puede formar directamente a partir de un ácido. Podrían existir ventajas en hacer reaccionar un éster intermediario del tipo **XXXVIf** con cualquiera de hidrazina pura, sal de hidrazina en presencia de una base o hidrato de hidrazina para facilitar un tratamiento más sencillo. Sin embargo, la ruta directa a través del ácido utilizando la activación in situ podría ser conveniente en substratos sensibles al ataque nucleofílico y también producir el producto en una secuencia de pasos más corta.

Formación de compuestos de las fórmulas **XXXVId y XXXVIf**

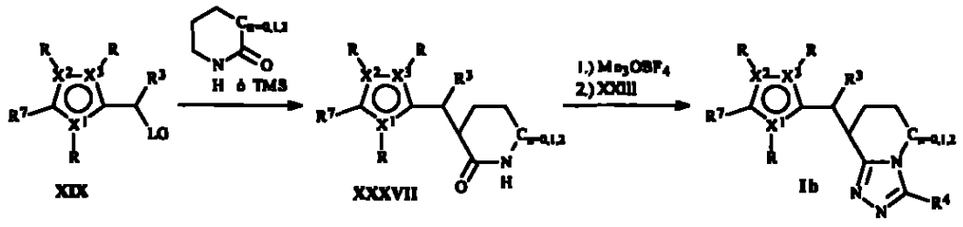


Se pueden preparar los compuestos de las fórmulas **XXXVId** y **XXXVIf**, en las cuales R^7 es un grupo que consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, mediante cualquiera de los métodos no limitativos: a) reacción de compuestos de hidrazida de acilo de la fórmula XII con un anhídrido cíclico o diácido monoesterificado seguido por ciclización del intermediario formado lo que conduce a 1,3,4-oxadiazoles del tipo **XXXVId** y **XXXVIf** respectivamente (X^1= O, X^2 y X^3=N); b) se puede utilizar la reacción y ciclización de una hidroxiamidina de la fórmula II con un anhídrido cíclico o con el diácido monoesterificado para proveer los análogos 1,2,4-oxaziazol **XXXVId** y **XXXVIf** en las cuales X^1 y X^2 =N, X^3=O; c) se puede utilizar la reacción de un compuesto del tipo III con un compuesto de tipo hidroxamidina, con excepción del derivado succinilo, para proveer los análogos 1,2,4-oxaziazol **XXXVIf** en la cual X^1 y X^3 =N, X^2 =O.

Los compuestos **XXXVId** y **XXXVIf** se pueden convertir entre sí, de manera independiente de la naturaleza de X^1, X^2 o X^3 como se describió anteriormente.

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Formación de compuestos de la fórmula Ib



Se puede preparar un compuesto de la fórmula **Ib**, en la cual R^7 se selecciona a partir de un grupo $M^1-(R^2)_n-P-(R^1)_{m1}$, a partir de compuestos de la fórmula **XXXVII**, generados a partir de **XIV** como se describe más adelante, a través de la O-alquilación selectiva utilizando Me_3OBF_4 o sulfato de dimetilo (como se describe en los antecedentes en la literatura, por ejemplo: a) Shen, Jennline; Smith, Michael B.; Oeschger, Thomas R.; Satchell, Jacqueline; Org. Prep. Proced. Int.; (1992); *24*, 147-158; o b) Hutchinson, Ian S.; Matlin, Stephen A.; Mete, Antonio, Tetrahedron Lett.; (2001); *42*; 1773-1776). Después se puede desplazar el grupo metoxi con una hidrazida de acilo del tipo **XXIII**, seguido por una condensación de cierre de anillo para formar el heterociclo triazol. Esto se puede efectuar en etanol, tolueno, DMF o piridina bajo condiciones térmicas con calentamiento regular o irradiación de microondas, en la forma

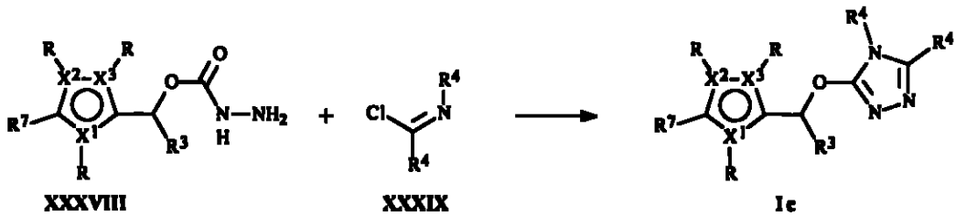
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previamente descrita por, por ejemplo, Lawson, Edward C.; Hoekstra, William J.; Addo, Michael F.; Andrade-Gordon, Patricia; Damiano, Bruce P.; Kauffman, Jack A.; Mitchell, John A.; Maryanoff, Bruce E.; Bioorg. Med. Chem. Lett.; (2001); *11*; 2619 - 2622.

Los compuestos del tipo **XXXVII** se pueden preparar mediante la reacción de amidas cíclicas, lactamas, las cuales se pueden alquilar fácilmente en la posición α con respecto al carbonilo mediante tratamiento sucesivo con dos equivalentes de una base fuerte, por ejemplo n-BuLi, para generar el dianión seguido por adición de un equivalente de los compuestos de la fórmula **XIX**, en un solvente no prótico tal como THF, como se ha descrito previamente por, por ejemplo, Grieco, Paul A.; Kaufman, Michael D.; J. Org. Chem.; (1999); *64*; 6041-6048). De manera alternativa, se puede utilizar una lactama N-protegida en la cual únicamente se necesita un equivalente de base, por ejemplo LDA, para generar el anión para la alquilación como ha sido descrito previamente por, por ejemplo Padwa, Albert; Beall, L. Scott; Heidelbaugh, Todd M.; Liu, Bing; Sheehan, Scout M.; J. Org. Chem.; (2000); 65; 2684 - 2695.

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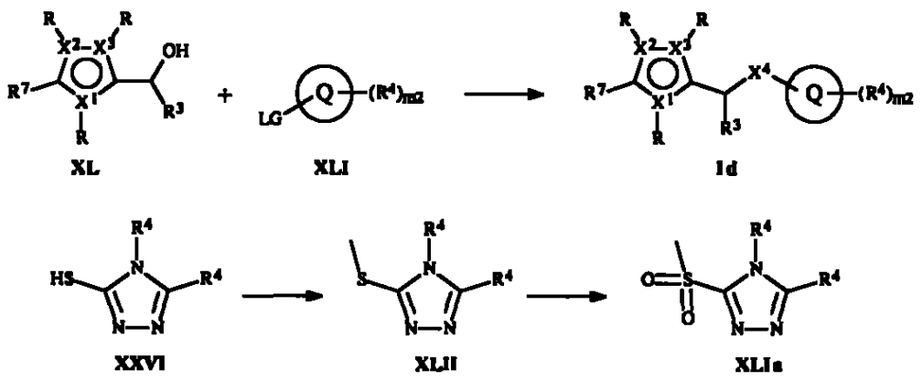
Síntesis general de compuestos de la fórmula Ic



XXXVIII XXXIX Ic

Se puede preparar un compuesto de la fórmula Ic, en la cual R^7 consiste de $M^1-(R^2)_n-P-(R^1)_{m1}$, a través de la reacción con ciclización subsiguiente de compuestos de la fórmula **XXXVIII**, con un compuesto de la fórmula **XXXIX**. El compuesto de la fórmula **XIX** se puede preparar a partir de una amida secundaria apropiada utilizando cloruro de oxalilo o pentacloro-fosfina en presencia opcional de una base tal como trietilamina, y se puede utilizar ya sea in situ o como un material aislado como se describió anteriormente a partir de **XXXIVa**.

Los compuestos de la fórmula **XXXVIII**, se pueden preparar a partir del alcohol correspondiente haciendo reaccionar el alcohol con fosgeno o de preferencia un análogo de fosgeno tal como carbonil-di-imidazol seguido por copulación a hidrazina.



XL XLI Id

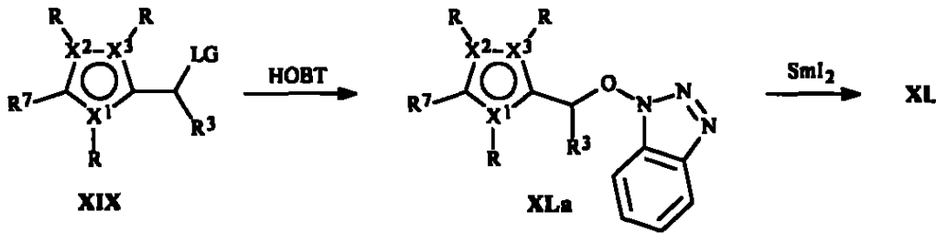
XXVI XLII XLIa

Otros medios para sintetizar un compuesto de la fórmula **Ic** o **Id**, en los cuales X^4 = O y en los cuales R^7 es $M^1-(R^2)_n-P-(R^1)_{m1}$, puede ser mediante la O-alquilación de compuestos del tipo **XL** con compuestos del tipo **XLI** en los cuales el grupo saliente puede consistir de un grupo tosilo, mesilo, halógeno o cualquier otro grupo apropiado, en una base apropiada tal como carbonato de cesio o de potasio, hidruro de sodio en solventes tales como por ejemplo DMF o DMSO.

Los compuestos del tipo **XLI** se pueden sintetizar como se ejemplifica con el triazol **XXVI** mediante alquilación o arilación del grupo sulfuro utilizando un agente alquilante o arilante apropiado seguido por la doble oxidación del grupo tio hasta la sulfona correspondiente utilizando oxidantes tales como MCPBA, peróxido de hidrógeno en ácido acético o

permanganato de potasio. Dicha secuencia ha sido descrita previamente por ejemplo, por Åkerblom et al. *J. Med. Chem.* 16, 312 (1973). De manera alternativa, se pueden sintetizar los halogenuros de triazol como se describió previamente en la literatura, por ejemplo por Ashton, W. T. et al. *J. Med. Chem.* 36, 591 (1993).

Los alcoholes se pueden preparar ya sea directamente después de la síntesis del oxadiazol o parte de isoxazol como se describió anteriormente bajo la síntesis general de compuestos de la fórmula V. De manera alternativa, éstos se pueden preparar a partir de una unidad oxadiazol o isoxazol con un grupo saliente apropiado tal como un halogenuro, por ejemplo cloruro, utilizando una secuencia de tres pasos como la descrita por Palazzo et al. *J. Heterocycl. Chem.* (1979) 16: 1469, seguido por un protocolo de reducción normal del aldehído resultante (o hidrato del mismo) utilizando por ejemplo borohidruro de sodio en metanol.



XIX XLa

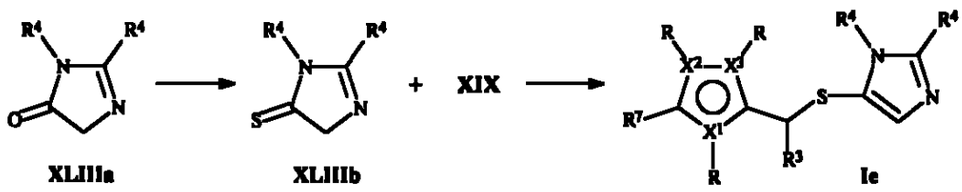
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Incluso otro método puede implicar la reacción de una unidad de un compuesto de la estructura **XIV** que contenga un grupo saliente apropiado tal como halogenuro, por ejemplo cloruro, con hidroxibenzotriazol en presencia de una base apropiada tal como carbonato de potasio o trietilamina en un solvente apropiado tal como DMSO, acetonitrilo, acetona, DMF, para producir los compuestos del tipo **XLa**. De manera alternativa, el compuesto **XLa** se puede obtener si está presente el hidroxibenzotriazol durante la ciclización hasta el oxadiazol, ya sea como un co-activador con EDCI, o como resultado de un subproducto proveniente de un reactivo de copulación tal como HBTU, como se describió anteriormente bajo la reacción de los compuestos de las fórmulas **II-V**. El compuesto **XLa** se puede convertir al alcohol mediante la adición de diyoduro de samario, de preferencia a través de un periodo prolongado de tiempo (5-360 minutos) en un solvente apropiado tal como tetrahidrofurano, metanol, agua o mezclas de los mismos, siendo THF un solvente preferido, a una temperatura apropiada (-75°C hasta +75°C). La ruptura del enlace N-O se puede efectuar de manera alternativa utilizando métodos de hidrogenación

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comúnmente empleados en presencia de un catalizador apropiado tal como níquel Raney como es sabido por el experto en la técnica. En los compuestos de la fórmula **XLa** el grupo funcional oxobenzotriazol también puede servir como un grupo saliente. Por lo tanto, los compuestos **XLa** pueden reaccionar con compuestos **XX** como se describió anteriormente.

Formación de compuestos del tipo **Ie**



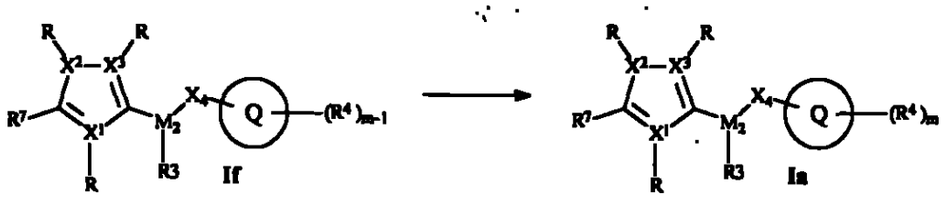
Se puede preparar un compuesto de la fórmula **Ie**, en el cual R^7 es $M^1-(R^2)_n-P-(R^1)_{m1}$, a través de sustitución nucleofílica de compuestos del tipo **XLIIIb** con compuestos del tipo **XIX** como se describió anteriormente. Los compuestos del tipo **XLIIIb** se pueden preparar mediante reacción de sus análogos oxo **XLIIIa** utilizando P_2S_{10} o reactivo de Lawesson bajo condiciones térmicas. La síntesis de los compuestos del tipo **XLIIIa** ha sido descrita por Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989); *45*; 6375-6386.

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Introducción de sustitución en el anillo Q

Si se desea la sustitución en el anillo Q, se puede elegir un aril-tiol o heteroaril-tiol sustituido en forma apropiada para que se use en la reacción de desplazamiento. Lo mismo es válido para otros reactivos nucleofílicos diferentes a los aril-tioles o heteroaril-tioles sustituidos o no sustituidos que sirvan para sustituir al mismo en los compuestos finales. Si el residuo arilo o heteroarilo tiene una porción reactiva factible, ya sea introducida directamente o como resultado de una reacción de desprotección, incluyendo pero sin limitarse a un sitio NH libre como en la anilina, imidazol, bencimidazol, indol y similares, un compuesto de la fórmula If (R^7 es M^1-$(R^2)_n$-P-$(R^1)_{m1}$) se puede sustituir con R^4 utilizando una base apropiada tal como un alquil-litio o hidruro o hidróxido de metal alcalino para desprotonar al residuo NH, seguido por la adición de un reactivo electrofílico apropiado tal como halogenuros de alquilo, cloruros de acilo o anhidridos, cloroformiatos, cloruros de carbamoilo, cloruros de sulfonilo, isocianatos, isotiocianatos y similares para proveer el producto sustituido de la fórmula Ia.

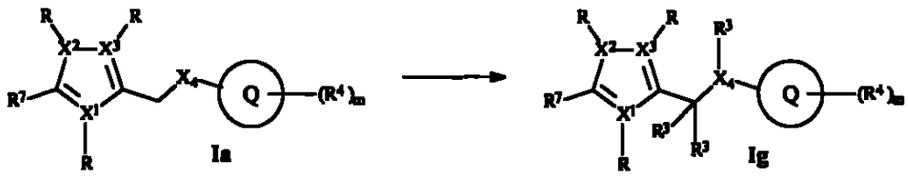


If Ia

Introducción del sustituyente o sustituyentes M^2 y del sustituyente o sustituyentes X^4

Cuando los protones más ácidos están posicionados en el átomo adyacente a X^4 o en X^4 mismo, se puede lograr la sustitución mediante desprotonación del compuesto de la fórmula Ia con una base fuerte tal como alquil-litio o un hidruro de metal alcalino en un solvente no prótico, no ácido apropiado tal como THF o éter dietílico seguido por entrampamiento del anión resultante con un electrófilo apropiado tal como los halogenuros de alquilo, cloruros de acilo o anhídridos, cloroformiatos, cloruros de carbamoilo, cloruros de sulfonilo, isocianatos, isotiocianatos y similares. Cuando se emplea un exceso de base y electrófilo y la reacción se deja durante tiempo suficiente, se pueden reemplazar dos átomos de hidrógeno con el electrófilo como se ilustra más adelante para la introducción de dos sustituyentes R^3 (M^2 se ejemplifica como carbono).

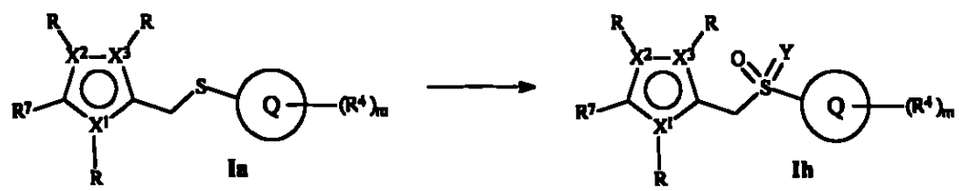
También se podrían introducir dos o más sustituyentes, iguales o diferentes, en forma correspondiente mediante desprotonaciones y reacciones subsiguientes con electrófilos apropiados para producir los compuestos de la fórmula Ig.



Ia Ig

Oxidación del átomo S de la cadena (cuando X^4 sea S) o átomos N en los sustituyentes

Se puede lograr la oxidación del átomo de azufre para producir sulfonas (Y=O) y sulfóxidos (Y=":", es decir, un par solitario), mediante oxidación directa utilizando cualquier agente oxidante apropiado incluyendo peroxiácidos tales como MCPBA. En el caso de oxidación con MCPBA, es posible obtener una mezcla de productos a partir de una reacción individual y separarlos mediante cromatografía en columna normal o para obtener en forma selectiva el sulfóxido o sulfona controlando la estequiometría y temperatura de la reacción.



Ia Ih

Si uno de los sustituyentes, por ejemplo R^4 contiene uno o más átomos de nitrógeno, como por ejemplo una porción piridina o cualquier otro sustituyente como el definido anteriormente, la oxidación de este nitrógeno se puede presentar en la reacción anterior de **Ia** con un oxidante tal como MCPBA para dar el N-óxido correspondiente. El experto en la técnica entiende que dichos productos pueden obtenerse mediante separación utilizando cromatografía en columna normal o cualquier otro protocolo de purificación estándar incluso en el caso de mezclas que contengan por ejemplo **Ih** y el N-óxido. El experto en la técnica también entiende que la formación de N-óxidos se puede reducir mediante la elección de condiciones de reacción apropiadas tales como el uso de medios ácidos para proteger la amina básica.

Otras reacciones diversas

Cuando los compuestos intermediarios contienen un grupo funcional reactivo apropiado tal como un aril-halogenuro o triflato, se puede utilizar el grupo funcional para elaborar también al producto. Por ejemplo, cuando está presente 3-halógeno-fenilo en $P\text{-}(R^1)_{m1}$, es posible utilizar las condiciones

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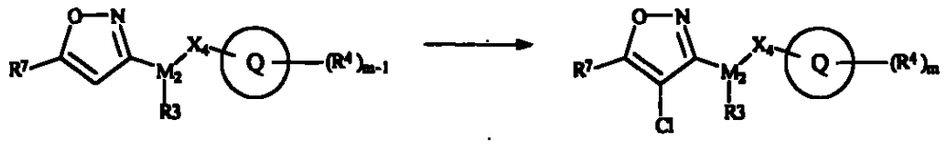
estándar de Suzuki para copular un ácido aril-borónico para producir un producto de copulación tipo diarilo. Miyaura, N., Yanagi, T., Suzuki, A., Synth.Commun., (1981), 11; 7, 513-520.

Otros grupos funcionales tales como un alcohol alifático se pueden convertir, por ejemplo, a un grupo fluoro mediante el uso de un agente para fluoración tal como DAST u otros grupos halogenuro mediante el uso de por ejemplo trifenilfosfina y cualquiera de yodo, N-bromosuccinimida o N-cloro-succinimida. Estos halogenuros pueden servir como grupos salientes para la elaboración posterior o pueden permanecer como sustituyentes en compuestos activos de la fórmula Ia.

En una manera similar, los alcoholes los alcoholes se pueden transformar hasta grupos salientes tales como los ejemplos no limitativos mesilo o tosilo empleando el halogenuro de sulfonilo o anhídrido de sulfonilo apropiado, en presencia de una base no nucleofílica junto con el alcohol para obtener el derivado de éster sulfónico.

Otros grupos funcionales que también se pueden elaborar, se muestran en el siguiente ejemplo no limitativo (R^7 es M^1-$(R^2)_n$-P-$(R^1)_{m1}$), en el cual la halogenación se puede efectuar sobre un átomo de

carbono de una unidad oxazol empleando un agente para cloración tal como cloruro de sulfurilo.



EJEMPLOS

A continuación se ilustran modalidades apropiadas de la invención mediante los siguientes ejemplos no limitativos.

Las mediciones de RMN se efectúan en la escala delta (δ).

Los compuestos preparados de conformidad con los ejemplos 1 a 39 y 100 A 328 son intermediarios. Los compuestos preparados de conformidad con los ejemplos 40 a 99 y 329 a 794 son productos finales.

INTERMEDIARIOS

EJEMPLO 1

Acido 6-metilpiridin-4-carboxílico

Se une un globo lleno con hidrógeno a un matraz que contiene ácido 2-cloro-6-metilpiridin-4-carboxílico (2 g, 12.0 mmoles), paladio al 10% en

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peso sobre carbón activado (0.5 g), trietilamina (4.8 ml) y etanol (24 ml) y después se agita durante la noche a temperatura ambiente. La mezcla de reacción se filtra a través de celita, se lava con metanol y se concentra. El residuo se tritura con diclorometano y después se filtra para obtener ácido 6-metilpiridin-4-carboxílico como un sólido de color blanco; 1.05 g (66%).

^{1}H RMN (MeOD) δ (ppm): 8.62 (d, 1H), 7.68 (s, 1H), 7.60 (d, 1H), 2.55 (s, 3H).

EJEMPLO 2

1-ciano-3-etilbenceno

Se hace burbujear argón en una solución de 1-bromo-3-etilbenceno (2.5 g,13.5 mmoles) en DMF (37 ml) durante 10 minutos y después se agrega cianuro de zinc (1.75 g, 14.9 mmoles) y tetrakis(trifenil-fosfin)paladio(0) (1.56 g, 1.35 mmoles). Después de agitar a 80°C durante la noche la mezcla de reacción se diluye con acetato de etilo (35 ml) después se filtra a través de celita para remover el precipitado. El material filtrado se lava con agua (3x), salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. El producto se

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purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 2% en hexano lo que permite obtener un líquido incoloro (1.42 g).

GC-mS (M+): 131.18.

EJEMPLO 3

Acido 3-etilbenzoico

Se agrega hidróxido de sodio 6M (25 ml) a 1-ciano-3-etilbenceno (1 g, 7.62 mmoles) en metanol (25 ml) y después se calienta hasta 100°C durante la noche. Después de concentrar la mezcla de reacción, la capa acuosa se lava con diclorometano (2x), después se acidula el pH hasta 3 aproximadamente con HCl 12M. El precipitado se extrae con acetato de etilo después se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener ácido 3-etilbenzoico como un aceite incoloro; 0.770 g (28% de rendimiento en los 2 pasos).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.76 (d, 2H), 7.43 (m, 2H), 2.67 (m, 2H),1.19 (t,3H).

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EJEMPLO 4

Acido 3-fluoro-5-metil-benzoico

Se agrega HCl concentrado (30 ml) a una suspensión fría (-5°C) de 5-amino isoftalato de dimetilo (20 g, 95.6 mmoles) en agua (75 ml), seguido por la adición en porciones de $NaNO_2$ (7.5 g, 109 mmoles). La mezcla de reacción se agita después durante 15 minutos, después de lo cual se agrega HBF_4 (18 ml, 100 mmoles, solución acuosa al 48%). La mezcla resultante se agita a 0°C durante 30 minutos y el precipitado que se forma se recolecta mediante filtración y se lava con metanol frío (60 ml) y éter (60 ml). El residuo se descompone después mediante calentamiento en un baño de aceite (~110°C). La mezcla ya fría se diluye después con éter, se concentra sobre gel de sílice y se purifica mediante cromatografía de vaporización instantánea con acetato de etilo al 5% hexano como eluyente para obtener 9.0 g (44%) de producto como un sólido esponjoso de color blanco.

^1H RMN ($CDCl_3$), δ (ppm): 8.57 (s, 1H), 7.95 (d, 2H), 3.97 (s, 6H).

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Se trata una suspensión del éster dimetílico del ácido 5-fluoro-isoftálico (1.7 g, 8.0 mmoles) en metanol (41 ml) con hidróxido de sodio 1.0N (7.2 ml, 7.2 mmoles). La reacción se deja agitando durante toda la noche a temperatura ambiente. Después que se concentra la solución, el residuo se disuelve en agua y se transfiere a un embudo de separación. La capa acuosa se lava con diclorometano (3 veces) y después se acidula con HCl 1.0 N hasta pH 2. Se utiliza acetato de etilo para extraer el precipitado, el cual se lava después con salmuera y se seca con sulfato de sodio anhidro. Después de eliminar el solvente al vacío, se aísla un total de 1.3 g (83%) del éster monometílico del ácido 5-fluoro-isoftálico como un sólido de color blanco.

^{1}H RMN (DMSO), δ (ppm): 8.31 (t, 1H), 7.96 (m, 2H), 3.91 (s, 3H).

Se agregan trietilamina (2.2 ml, 16.0 mmoles) y cloroformiato de isobutilo (1.0 ml, 8.0 mmoles) a una solución helada de éster monometílico del ácido 5-fluoro-isoftálico (1.3 g, 6.7 mmoles) en diclorometano (20 ml) y después se calientan hasta temperatura ambiente. Después de agitar durante 2 h, la mezcla de reacción se filtra y se concentra. El

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residuo se vuelve a disolver en tetrahidrofurano (10 ml) y después se agrega, mediante goteo, borohidruro de sodio (1.1 g, 29.02 mmoles) en agua (3ml). Después de 1 hora, la reacción se extingue con metanol y después se diluye con acetato de etilo, se lava con agua y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. La cromatografía de vaporización instantánea en columna con gel de sílice utilizando acetato de etilo al 30% en hexanos permite obtener 667 mg (54%) del éster metílico del ácido 3-fluoro-5-hidroximetil-benzoico como un aceite incoloro.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.82 (s, 1H), 7.63 (d, 1H), 7.32 (d, 1H), 4.76 (s, 2H), 3.93 (s, 3H).

Se agrega etanol (2 ml) a un matraz de fondo redondo que contiene le éster metílico del ácido 3-fluoro-5-hidroximetil-benzoico (667 mg, 3.6 mmoles) y paladio (10% en peso sobre carbón activado, 300 mg) bajo argón. El matraz se evacua utilizando un aspirador de agua y después se llena con hidrógeno proveniente de un globo. Después de agitar durante 2 h, se retira el paladio sobre carbón mediante filtración a través de celita. El material filtrado se concentra después para obtener 520 mg (87%) del

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éster metílico del ácido 3-fluoro-5-metil-benzoico.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.65 (s, 1H), 7.51 (d, 1H), 7.08 (d, 1H), 3.91 (s, 3H), 2.40 (s, 3H).

Se agrega hidróxido de litio 0.5 N (7.4 ml, 3.7 mmoles) a una solución del éster metílico del ácido 3-fluoro-5-metil-benzoico (520 mg, 3.1 mmoles) en tetrahidrofurano (7.4 ml). La mezcla de reacción se agita a 75°C durante 2 h y después se elimina el solvente al vacío. El residuo se disuelve en una cantidad pequeña de agua y después se acidula (pH 2 aproximadamente) mediante la adición de HCl al 10% (acuoso). Después de extraer la capa acuosa con acetato de etilo, la capa orgánica se lava después con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener 469 mg (98%) de ácido 3-fluoro-5-metil-benzoico como un sólido de color blanco.

^{1}H RMN (DMSO), d (ppm): 7.62 (s, 1H), 7.45 (d, 1H), 7.32 (d, 1H), 2.38 (s, 3H).

EJEMPLO 5

Acido 3-metoximetil-benzoico

Se calienta una mezcla de éster metílico del

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ácido 3-bromometil-benzoico (556 mg, 2.4 mmoles) y carbonato de potasio (670 mg, 4.9 mmoles) en metanol (10 ml) y tetrahidrofurano (10 ml) a 55°C durante 2 h. Después de enfriar, la mezcla de reacción se diluye con agua y después se extrae con acetato de etilo. La capa orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. Después de secar al vacío, se aísla el éster metílico del ácido 3-metoximetil-benzoico (436 mg, cuantitativo) como un sólido de color blanco.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.01 (s, 1H), 7.98 (d, 1H), 7.55 (d, 1H), 7.43 (t, 1H), 4.50 (s, 2H), 3.92 (s, 3H), 3.41 (s, 3H).

Se agrega hidróxido de sodio 1N (3.6 ml, 3.6 mmoles) a un éster metílico del ácido 3-metoximetil-benzoico (436 mg, 2.4 mmoles) en metanol (5 ml) y tetrahidrofurano (5 ml). La mezcla de reacción se agita a 70°C durante 30 minutos y después se elimina el solvente al vacío. El residuo se disuelve en una cantidad pequeña de agua y después se acidula (pH 2 aproximadamente) mediante la adición de HCl 1N (acuoso). Después de extraer la capa acuosa con acetato de etilo, la capa orgánica se lava después

con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener 395 mg (98%) de ácido 3-metoximetil-benzoico como un sólido de color blanco.

^{1}H RMN (DMSO), δ (ppm): 7.90 (s, 1H), 7.87 (d, 1H), 7.56 (d, 1H), 7.48 (t, 1H), 4.48 (s, 2H), 3.31 (s, 3H).

EJEMPLO 6

N-hidroxi-3-metoxi-benzamidina

Utilizando el procedimiento general de Shine et al., J. Heterocyclic Chem. (1989) 26:125-128, se agregan clorhidrato de hidroxilamina (22 ml, 5 M, 110 mmoles) e hidróxido de sodio (11 ml, 10 M, 110 mmoles) a una solución de 3-metoxibenzonitrilo (11.5 ml. 94 mmoles) en etanol (130 ml). La mezcla de reacción se calienta después a reflujo (80°C) durante 12 h. Después que se enfría la mezcla, se elimínala mayoría del solvente al vacío. El producto crudo se separa entre acetato de etilo y agua, se lava con salmuera saturada, se seca con sulfato de sodio anhidro y el solvente se elimina al vacío. La cromatografía de vaporización instantánea con gel de sílice utilizando acetato de etilo al 35-50% en

hexano produce el compuesto del título (8.05 g, 52%). Los ejemplos 7-9 se preparan en un método análogo el procedimiento indicado en el ejemplo 6.

EJEMPLO 7

***N*-hidroxi-benzamidina**

El compuesto *N*-hidroxi-benzamidina (4.83 g, 91%, sólido de color blanco) se obtiene a partir de benzonitrilo (4 g, 38.9 mmoles), clorhidrato de hidroxilamina (8.89 ml, 44.0 mmoles) e hidróxido de sodio (4.49 ml, 45.0 mmoles) en etanol (30 ml).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.81 (pico ancho, 1H), 7.63 (m, 2H), 7.39 (m, 3H), 4.91 (s, 2H).

EJEMPLO 8

***N*-hidroxi-3-metil-benzamidina**

El compuesto *N*-hidroxi-3-metil-benzamidina (3.65 g, 94%, sólido de color blanco) se obtiene a partir de m-tolunitrilo (3 g, 26.0 mmoles), clorhidrato de hidroxilamina (5.9 ml, 29.6 mmoles), e hidróxido de sodio (3.0 ml, 29.9 mmoles) en etanol (20 ml).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.25 (pico ancho, 1H), 7.36 (m, 2H), 7.25 (m, 2H), 4.88 (s, 2H), 2.38

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(s, 3H).

EJEMPLO 9

3-ciano-*N*-hidroxi-benzamidina

El compuesto 3-ciano-*N*-hidroxi-benzamidina (1.32 g, 52%, sólido de color blanco) se obtiene a partir de isoftalonitrilo (2 g, 15.6 mmoles), clorhidrato de hidroxilamina (3.12 ml, 5 M, 15.6 mmoles) e hidróxido de sodio (15.6 ml, 1 M, 15.6 mmoles) en etanol (20 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 20-50% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 9.91 (s,1H), 8.06 (s, 1H), 8.01 (d, 1H), 7.85 (d, 1H), 7.59 (t, 1H), 6.01 (bs, 2H).

EJEMPLO 10

5-clorometil-3-(3-metoxi-fenil)-[1,2,4]oxadiazol

Se agregan cloruro de cloroacetilo (0.72 ml, 9.03 mmoles) y trietilamina (1.50 ml, 10.23 mmoles) a *N*-hidroxi-3-metoxi-benzamidina (1 g, 6.02 mmoles) en diclorometano (12.0 ml) a 0°C y la mezcla resultante se agita durante 20 min. Para efectuar la ciclización hasta oxadiazol, se concentra la solución y se agrega

DMF (20 ml) al residuo y se calienta a 120°C durante 5 h. El producto se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 10-20% en hexano para obtener 0.90 g (66% de rendimiento en los 2 pasos) del compuesto del título (aceite de color amarillo).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.68 (m, 1M, 7.60 (d, 1H), 7.40 (t, 1H), 7.07 (m, 1H), 4.76 (s, 2H), 3.88 (s, 3H).

Los ejemplos 11-14 se preparan en un método análogo el procedimiento indicado en el ejemplo 10.

EJEMPLO 11

5-clorometil-3-fenil-[1,2,4]oxadiazol

El compuesto 5-clorometil-3-fenil-[1,2,4]-oxadiazol (1.62 g, 57% de rendimiento en los 2 pasos, aceite de color amarillo) se obtiene a partir de cloruro de cloroacetilo (1.76 ml, 22.05 mmoles) y trietilamina (3.32 ml, 24.99 mmoles) con *N*-hidroxi-benzamidina (2 g, 14.7mmoles) en diclorometano (29.3 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 10% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.08 (m, 2H), 7.51

(m, 3H), 4.76 (s, 2H).

EJEMPLO 12

5-clorometil-3-m-tolil-[1,2,4]oxadiazol

El compuesto 5-clorometil-3-m-tolil-[1,2,4]-oxadiazol (1.75 g, 62% de rendimiento en los 2 pasos, aceite de color amarillo) se obtiene a partir de cloruro de cloroacetilo (1.59 ml, 20.0 mmoles) y trietilamina (3.00 ml, 22.7 mmoles) con *N*-hidroxi-3-metil-benzamidina (2 g,13.3 mmoles) en diclorometano (26.6 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 10% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.87 (s, 1H), 7.36 (m, 2H), 4.75 (s, 2H), 2.34 (s, 3H).

EJEMPLO 13

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo

El compuesto 3-(3-clorometil-[1,2,4]-oxadiazol-5-il)-benzonitrilo (3.57 g, 43%) se obtiene a partir de 2-cloro-*N*-hidroxi-acetamidina (4.05 g, 37.4 mmoles) y cloruro de 3-cianobenzoilo (6.2 g, 37.4 mmoles) en diclorometano (60 ml) con trietilamina (6.5 ml, 46.7 mmoles). La purificación

se efectúa cromatografía en gel de sílice.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.47 (bs, 1H), 8.41 (dd, 1H), 7.91 (dd, 1H), 7.72(t, 1H), 4.70 (s, 2H);

GC-MS (M+): 219.

EJEMPLO 14

3-(5-clorometil-[1,2,4]oxadiazol-3-il)-benzonitrilo

El compuesto 3-(5-clorometil-[1,2,4]-oxadiazol-3-il)-benzonitrilo (1.2 g, 87%, sólido de color café claro): 3-ciano-*N*-hidroxi-benzamidina (1.0 g, 6.2 mmoles), trietilamina (1.5 ml, 10.6 mmoles) y cloruro de cloroacetilo (0.74 ml, 9.3 mmoles) en diclorometano (12 ml). La purificación se efectúa mediante decoloración con gel de sílice.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.40 (s, 1H, 8.32 (d, 1H), 7.82 (d, 1H), 7.64 (t, 1H), 4.77 (s, 2H).

EJEMPLO 15

3-clorometil-5-m-tolil-[1,2,4]oxadiazol

Se agrega cloruro de 3-metil-benzoilo (0.80 ml, 6.1 mmoles) a una solución de 2-cloro-*N*-hidroxi-acetamidina (440 mg, 4.1 mmoles) en diclorometano (10 ml) a temperatura ambiente y la mezcla resultante se

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agita durante 30 minutos. Después se agrega trietilamina (0.62 ml, 4.5 mmoles) y la mezcla resultante se agita durante 30 minutos. El producto se separa en diclorometano y la capa orgánica se lava con agua y salmuera y se seca con sulfato de sodio. La evaporación del solvente y la cromatografía de vaporización instantánea en sílice (acetato de etilo al 10-20% en hexanos) producen el intermediario de éster acíclico (814 mg). Se calienta una solución de este intermediario en DMF (10 ml) a 135°C durante 4 h. El producto se divide en acetato de etilo y la capa orgánica se lava con agua y salmuera y se seca con sulfato de sodio. La evaporación del solvente y la cromatografía de vaporización instantánea en sílice (acetato de etilo al 5% en hexanos) produce 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (469 mg, 54% en los 2 pasos, sólido de color blanco).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.99 (s, 1H), 7.97 (m, 1H), 7.43 (d, 2H), 4.68 (s, 2H), 2.45 (s, 3H).

EJEMPLO 16

3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol

Se agrega DMF (10 ml) a una mezcla de ácido 3-fluorobenzoico (710 mg, 5.07 mmoles), clorhidrato

de 1-(3-dimetilaminopropil)-3-etilcarbodi-imida (EDCI) (972 mg, 5.07 mmoles), hidrato de 1-hidroxi-benzotriazol (HOBt) (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) a temperatura ambiente y después se agita durante la noche. La mezcla de reacción se diluye con acetato de etilo, se lava con agua (3 veces) y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. Se agrega DMF (14 ml) al residuo y la solución resultante se calienta a 135°C durante 3.5 h para efectuar la ciclización hasta oxadiazol. Después de enfriar la mezcla de reacción se lava con agua (3 veces) y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. Se obtiene 3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol (383 mg, 35% de rendimiento en los 2 pasos, aceite de color amarillo) mediante cromatografía de vaporización instantánea en gel de sílice, utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.96 (d, 1H), 7.86 (m, 1H), 7.54 (m,1H), 7.33 (m, 1H), 4.68 (s, 2H).

Los ejemplos 17-30 se preparan en un método análogo el procedimiento indicado en el ejemplo 16.

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EJEMPLO 17

3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol (197 mg, 20% de rendimiento en los 2 pasos, sólido de color blanco) a partir del ácido 3-tiofencarboxílico (700 mg, 4.96 mmoles), EDCI (950 mg, 4.96 mmoles), HOBt (670 mg, 4.96 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (538 mg, 5.46 mmoles) en DMF (10 ml). El producto acíclico se purifica mediante cromatografía de vaporización instantánea en columna eluyendo con diclorometano:hexano:acetato de etilo 2:1.2:0.8. El compuesto del título se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.28 (s, 1H), 7.70 (d, 1H), 7.48 (m, 1H).

EJEMPLO 18

3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina

Se obtiene 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina (25 mg, 4% de rendimiento en

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los 2 pasos) a partir de ácido 5-metilnicotínico (472 mg, 3.44 mmoles), EDCI (652 mg, 3.44 mmoles), HOBt (465 mg, 3.44 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (340 mg, 3.13 mmoles) en DMF (10 ml). El intermediario acíclico se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 100%; también se aíslan 200 mg (30%) del éster acíclico como producto secundario.

EJEMPLO 19

3-clorometil-5-(3-nitro-fenil)-[1,2,4] oxadiazol

Se obtiene 3-clorometil-5-(3-nitro-fenil)-[1,2,4]oxadiazol (335 mg, 30% de rendimiento en los 2 pasos, sólido de color amarillo) a partir de ácido 3-nitrobenzoico (847 mg, 5.07 mmoles), EDCI (972 mg, 5.07 mmoles), HOBt (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) en DMF (10 ml). El intermediario acíclico se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 100%. La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 15% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.03 (t, 1H), 8.50 (t, 2H), 7.79 (t, 1H), 4.71 (s, 2H)

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EJEMPLO 20

4-(3-clorometil-[1,2,4]oxadiazol-5-il)-2-metil-piridina

Se obtiene 4-(3-clorometil-[1,2,4]oxadiazol-5-il)-2-metil-piridina (316 mg, 28% de rendimiento en los 2 pasos, aceite de color amarillo) a partir de ácido 6-metilpiridin-4-carboxílico (800 mg, 5.8 mmoles), EDCI (1.12 g, 5.8 mmoles), HOBt (788 mg, 5.8 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (575 mg, 5.3 mmoles) en DMF (10 ml) más trietilamina (536 mg, 5.3 mmoles). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 30% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.75 (d, 1H), 7.88 (s, 1H), 7.79 (d, 1H), 4.70 (s, 2H), 2.70 (s, 3H)

EJEMPLO 21

3-clorometil-5-(3-etil-fenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-etil-fenil)-[1,2,,4]oxadiazol (446 mg, 52% de rendimiento en los 2 pasos, aceite de color amarillo) a partir de ácido 3-etilbenzoico (770 mg, 3.81 mmoles), EDCI (803 mg,

4.19 mmoles), HOBt (566 mg, 4.19 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (454 mg, 4.19 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.96 (t, 2H), 7.42 (m, 2H), 4.68 (s, 2H), 2.74 (m, 2H), 1.28 (m, 3H).

EJEMPLO 22

3-(3-clorometil[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina

Se obtiene 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina (40 mg, 4% de rendimiento en los 2 pasos, sólido de color amarillo) a partir de ácido 3-(dimetilamino)benzoico (656 mg, 3.97 mmoles), EDCI (761 mg, 3.97 mmoles), HOBt (536 mg, 3.97 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 3.6 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.46 (t, 2H), 7.37 (t, 1H), 6.94 (d, 1H), 4.68 (s, 2H), 3.04 (s, 6H).

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EJEMPLO 23

3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol (406 mg, 43% de rendimiento en los 2 pasos, sólido de color blanco) a partir de ácido 3-clorobenzoico (708 mg, 4.52 mmoles), EDCI (866 mg, 4.52 mmoles), HOBt (611 mg, 4.52 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (446 mg, 4.11 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.17 (t, 1H), 8.05 (d, 1H), 7.59 (t, 1H), 7.50 (t, 1H), 4.68 (s, 2H).

EJEMPLO 24

3-clorometil-5-(3-trifluorometoxi-fenil)-[1,2,4]-oxadiazol

Se obtiene 3-clorometil-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol (707 mg, 55% de rendimiento en los 2 pasos, aceite de color amarillo claro) a partir de ácido 3-trifluorometoxibenzoico (1.05 g, 5.07 mmoles), EDCI (972 mg, 5.07 mmoles), HOBt (685

mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

EJEMPLO 25

5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol

Se obtiene 5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol (707 mg, 55% de rendimiento en los 2 pasos, sólido de color blanco) a partir de ácido 3-bromobenzoico (1.05 g, 5.07 mmoles), EDCI (972 mg, 5.07 mmoles), HOBt (685 mg, 5.07 mmoles) y 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.61 mmoles) en DMF (10 ml). La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 5% en hexano.

^{1}H RMN ($CDCl_3$) δ (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

EJEMPLO 26

3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-tiofen-2-il-[1,2,4]-oxadiazol (202 mg, 20%, sólido de color blanquecino) a partir de ácido tiofen-2-carboxílico (649 mg, 5.1 mmoles), 2-cloro-*N*-hidroxi-acetamidina (500 mg, 4.6 mmoles), EDCI (972 mg, 5.1 mmoles) y HOBt (684 mg, 5.1 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.00 (s,1H), 7.83 (d,1H), 7.19 (t, 1H), 4.13 (s, 2H).

EJEMPLO 27

3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol

Se obtiene 3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]oxadiazol (312 mg, 46%, aceite incoloro) a partir de ácido 3-fluoro-5-metil-benzoico (469 mg, 3.0 mmoles), 2-cloro-*N*-hidroxi-acetamidina (363 mg, 3.3 mmoles), EDCI (641 mg, 3.3 mmoles) y HOBt (452 mg, 3.3 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.79 (s, 1H), 7.65

(d,1H), 7.15 (d, 1H), 4.67 (s, 2H), 2.46 (s, 3H).

EJEMPLO 28

3-clorometil-5-tiazol-4-il-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-tiazol-4-il-[1,2,4]-oxadiazol (37 mg, 5%, sólido de color amarillo) a partir de ácido tiazol-4-carboxílico (500 mg, 3.9 mmoles), 2-cloro-*N*-hidroxi-acetamidina (462 mg, 4.3 mmoles), EDCI (817 mg, 4.3 mmoles) y HOBt (575 mg, 4.3 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 30% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.02 (d, 1H), 8.42 (d, 1H), 4.70 (s, 2H).

EJEMPLO 29

3-clorometil-5-(3-yodo-fenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-yodofenil)-[1,2,4]oxadiazol (2.9 g, 44%, sólido de color blanco) a partir de ácido 3-yodo-benzoico (5.0 g, 20.2 mmoles), 2-cloro-*N*-hidroxi-acetamidina (2.4 g, 22.2 mmoles), EDCI (4.3 g, 22.2 mmoles) y HOBt (3.0 g, 22.2 mmoles) en DMF (10 ml). El intermediario de

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éster acíclico se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 50-80% en hexanos. El compuesto del título se purifica mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.52 (s, 1H), 8.13 (d, 1H), 7.96 (d, 1H), 7.29 (t, 1H), 4.68 (s, 2H).

EJEMPLO 30

3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol

Se obtiene 3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol (193 mg, 34%, aceite de color amarillo claro) a partir de ácido 3-metoximetil-benzoico (395 mg, 2.4 mmoles), 2-cloro-*N*-hidroxi-acetamidina (284 mg, 2.6 mmoles), EDCI (501 mg, 2.6 mmoles) y HOBt (353 mg, 2.6 mmoles) en DMF (5 ml). La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 5% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.14 (s, 1H), 8.08 (d, 1H), 7.61(d,1H), 7.53 (t, 1H), 4.68 (s, 2H), 4.54 (s, 2H), 3.44 (s, 3H).

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EJEMPLO 31

5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-tiol

Se agrega cloruro de 2-furoilo (0.76 ml, 7.66 mmoles) mediante goteo, a una solución de 4-metil-3-tiosemicarbazida (732 mg, 6.96 mmoles) y piridina (7 ml) y la solución resultante se agita a temperatura ambiente durante 4 h. La mezcla de reacción se diluye con acetato de etilo (100 ml), se lava en forma sucesiva con agua (3x100 ml) y salmuera (100 ml). La fase orgánica se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo se suspende en bicarbonato de sodio (70 ml, 69.6 mmoles, 1 M en agua) y se deja agitando a 100°C durante la noche. La mezcla de reacción se enfría hasta 0°C, después se lleva a pH de aproximadamente 6 utilizando ácido clorhídrico (70 ml, 1 N en agua). El compuesto del título (298 mg) se recolecta mediante filtración como un sólido de color blanco.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.4 (bs,1H), 7.63 (d,1H), 7.02 (d, 1H), 6.60 (dd, 1H), 3.83 (s, 3H).

Los ejemplos 32-35 se preparan en un método análogo el procedimiento indicado en el ejemplo 31.

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EJEMPLO 32

4-metil-5-fenil-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-fenil-4H-[1,2,4]-triazol-3-tiol (478 mg, sólido de color blanquecino) a partir de 4-metil-3-tiosemicarbazida (732 mg, 6.96 mmoles) y piridina (7 ml) con cloruro de benzoilo (0.89 ml, 7.66 mmoles). Después se agrega bicarbonato de sodio (70 ml, 69.6 mmoles, 1 M en agua) a 100°C durante la noche y el compuesto del título se recolecta mediante filtración.

^{1}H RMN ($CDCl_3$), δ (ppm): 12.3(bs, 1H), 7.55 (m, 5H), 3.65 (s, 3H).

EJEMPLO 33

4-metil-5-piridin-2-il-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-piridin-2-il-4H-[1,2,4]-triazol-3-tiol (44 mg, sólido de color verduzco) a partir de 4-metil-3-tiosemicarbazida (537 mg, 5.11 mmoles) y piridina (7 ml) con clorhidrato de cloruro de 2-piridincarbonilo (1.00 g, 5.62 mmoles). Después se agrega bicarbonato de sodio (51 ml, 1 M en agua) a 100°C durante la noche y el compuesto del título se

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recolecta utilizando extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.1 (bs, 1H), 8.70 (d, 1H), 8.02 (d, 1H), 7.84 (m, 1H), 7.41 (dd, 1H), 4.05 (s, 3H).

EJEMPLO 34

5-(4-bencil-morfolin-2-il)-4-metil-4H-[1,2,4]triazol-3-tiol

Se obtiene (83.3 mg, sólido de color amarillo sucio) a partir de 4-metil-3-tiosemicarbazida (346 mg, 3.29 mmoles) y piridina (7 ml) con clorhidrato de cloruro de 4-bencil-2-morfolincarbonilo (1.00 g, 3.62 mmoles). Después se agrega bicarbonato de sodio (33 ml, 1 M en agua) a 100°C durante la noche y el compuesto del título se recolecta utilizando extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.48 (bs, 1H), 7.25 (m, 5H), 4.68 (dd, 1H), 3.86 (dAb, 1H), 3.68 (tAB, 1H), 3.59-3.64 (m, 5H), 3.07 (d, 1H), 2.88 (d, 1H), 2.61 (t, 1H), 2.37 (dt, 1H).

EJEMPLO 35

5-ter-butil-4-metil-4H-[1,2,4]triazol-3-tiol

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Se obtiene 5-ter-butil-4-metil-4H-[1,2,4]-triazol-3-tiol (2.21 g, 83%, sólido de color blanquecino) a partir de 4-metil-3-tiosemicarbazida (1.80 g, 17.2 mmoles) y piridina (20 ml) con cloruro de trimetilacetilo (1.92 ml, 15.6 mmoles). Después se agrega hidróxido de sodio (200 ml, 5% en agua) y se deja agitando a 60°C durante la noche y el compuesto del título se recolecta mediante extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.7 (bs, 1H), 3.72 (s, 3H) 1.40 (s, 9H).

EJEMPLO 36

4-metil-5-piridin-3-il-4*H*-[1,2,4]triazol-3-tiol

Se agita una solución de 4-metil-3-tiosemicarbazida (902 mg, 8.58 mmoles), ácido nicotínico (960 mg, 7.80), EDCI (1.64 g, 8.58 mmoles), HOBt (1.16 g, 8.58 mmoles) en DMF (10 ml) a temperatura ambiente durante la noche. La mezcla de reacción se diluye con acetato de etilo (100 ml), se lava en forma sucesiva con ácido clorhídrico (50 ml, al 10% acuoso), agua (50 ml), carbonato de sodio saturado (50 ml, acuoso), agua (50 ml) y salmuera (50 ml). La fase orgánica se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo se agita

en hidróxido de sodio (53.4 ml, 66.7 mmoles, 5% acuoso) a 60°C durante la noche. La mezcla de reacción se enfría hasta temperatura ambiente, después se lleva cuidadosamente hasta pH de aproximadamente 6 utilizando ácido clorhídrico (1 N en agua). La fase acuosa se satura con cloruro de sodio sólido, después se extrae con acetato de etilo (4x50 ml). La fase orgánica combinada se lava con salmuera (100 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío (180 mg, sólido de color blanquecino).

^{1}H RMN ($CDCl_3$), δ (ppm): 11.6 (bs, 1H), 8.94 (s, 1H), 8.83 (dd, 1H), 7.98 (m, 1H), 7.51 (dd, 1H), 3.69 (s, 3H).

Los ejemplos 37-39 se preparan en un método análogo el procedimiento indicado en el ejemplo 36.

EJEMPLO 37

4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-tiol (693 mg, sólido de color blanco) a partir de 4-metil-3-tiosemicarbazida (902 mg, 8.58 mmoles), ácido 3-tiofencarboxílico (1 g, 7.80

mmoles), EDCI (1.64 g, 8.58 mmoles), HOBt (1.16 g, 8.58 mmoles) en DMF (10 ml). Después hidróxido de sodio (88 ml, 110 mmoles, 5% acuoso) a 60°C durante la noche y el compuesto del título se recolecta extracción y evaporación.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.4 (bs, 1H), 7.77 (dd, 1H), 7.51 (dd, 1H), 7.42 (dd, 1H), 3.61 (s, 3H).

EJEMPLO 38

4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 4-metil-5-tiazol-4-il-4*H*-[1,2,4]-triazol-3-tiol (71.2 mg, aceite de color amarillo pegajoso) a partir de 4-metil-3-tiosemicarbazida (902 mg, 8.58 mmoles), 4-carboxitiazol (1.01 g, 7.80), EDCI (1.64 g, 8.58 mmoles), HOBt (1.16 g, 8.58 mmoles) en DMF (10 ml). Después hidróxido de sodio (43 ml, 54 mmoles, 5% acuoso) a 60°C durante la noche y el compuesto del título se recolecta extracción y evaporación.

EJEMPLO 39

5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-tiol

Se obtiene 5-ciclohexil-4-metil-4H-[1,2,4]-

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triazol-3-tiol (403 mg, sólido color beige) a partir de 4-metil-3-tiosemicarbazida (1.80 g,17.2 mmoles), ácido ciclohexan-carboxílico (2 g,15.6 mmoles), EDCI (2.99 g, 17.2 mmoles) y HOBt (2.10 g, 17.2 mmoles) en DMF (20 ml); después hidróxido de sodio (195 ml, 244 mmoles, 5% acuoso) a 60°C durante la noche.

EJEMPLO 40

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol

Se agrega 1*H*-benzoimidazol-2-tiol (150 mg, 1 mmoles) a una solución del 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (30 mg, 0.13 mmoles) y carbonato de potasio (50 mg, 0.36 mmoles) en DMF (2 ml) a temperatura ambiente. El solvente se elimina al vacío y el producto se obtiene mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 20-100% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.71 (d, 1H), 7.62 (d, 1H), 7.53 (m, 2H), 7.42 (t, 1H), 7.18 (se traslapan, m, 3H), 4.52 (s, 2H), 3.87 (s, 3H).

Los ejemplos 41-92 se preparan en un método análogo el procedimiento indicado en el ejemplo 40.

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EJEMPLO 41

5-(3-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

El compuesto del título se prepara a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (50 mg, 0.22 mmoles), carbonato de potasio (92.4 mg, 0.67 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (52.8 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 30-40% en hexanos lo que permite obtener 76 mg (90%) del compuesto del título como un sólido de color blanco.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.68 (d, 1H), 7.57 (t, 1H), 7.49 (m, 2H), 7.41 (t, 1H), 7.15 (m, 2H), 4.53 (s, 2H), 3.85 (s, 3H), 3.72 (s, 3H).

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EJEMPLO 42

3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo

Se obtiene 3-[5-(1-metil-5-tiofen-2-il-1*H*-

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imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo (39 mg, 47%, sólido de color blanco) a partir de 3-clorometil-3-(5-clorometil-[1,2,4]-oxadiazol-3-il)-benzonitrilo (50 mg, 0.22 mmoles), carbonato de potasio (92.4 mg, 0.67 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (52.8 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.34 (s, 1H), 8.28 (d, 1H), 7.79 (d, 1H), 7.60 (t,1H), 7.53 (d, 1H), 7.49 (d, 1H), 7.19 (m, 1H), 4.70 (s, 2H), 3.74 (s, 3H).

LS-MS (ES+ barrido completo, $C_{17}H_{12}N_6OS_2$)M^+ calculado 380.05, encontrado $(M+1)^+$ 381.04.

EJEMPLO 43

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]traiazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]traiazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]-oxadiazol (41.2 mg, 44%, sólido de color blanquecino) a partir de 3-clorometil-5-fenil-[1,2,4]oxadiazol (50 mg, 0.26 mmoles), carbonato de potasio (106 mg, 0.77

mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (60.8 mg, 0.31 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.09 (m, 2H), 7.57 (m, 5H), 7.17 (dd,1H), 4.53 (s, 2H), 3.72 (s, 3H).

EJEMPLO 44

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-metil-1*H*-benzoimidazol

Se obtiene 2-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-5-metil-1*H*-benzoimidazol (75.5 mg, 70.5%, espuma de color blanco) a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (82 mg, 0.365 mmoles), carbonato de potasio (210 mg, 1.520 mmoles), 2-tiol-5-metil-1H-benzoimidazol (50 mg, 0.305 mmoles) en acetonitrilo (3 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de vaporización instantánea de SPE utilizando acetato de etilo al 50% en hexanos seguido por trituración con acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 11.95 (bs, 1H), 7.80 (d, 1H), 7.70 (s, 1H), 7.52 (m, 2H), 7.21 (dd, 2H),

7.17 (d, 1H), 4.40 (s, 2H), 3.95 (s, 3H), 2.50 (s, 3H).

EJEMPLO 45

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (76 mg, 85%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99.4 mg, 0.72 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (56.7 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.50 (m, 2H), 7.40 (m, 2H), 7.18 (t, 1H), 4.52 (s, 2H), 3.71 (s, 3H), 2.41 (s, 3H).

EJEMPLO 46

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]-oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-

triazol-3-ilsulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]oxadiazol (84 mg, 86%, sólido de color blanco) a partir de 3-clorometil-5-(3-trifluoro-metil-fenil)-[1,2,4]oxadiazol (60 mg, 0.23 mmoles), carbonato de potasio (95 mg, 0.69 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (54 mg, 0.27 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-60% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.38 (s, 1H), 7.29 (d, 1H), 7.86 (d, 1H), 7.68 (t, 1H), 7.50 (t, 2H), 7.19 (m, 1H), 4.57 (s, 2H), 3.75 (s, 3H).

EJEMPLO 47

3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (74.3 mg, 88%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (53.3 mg, 0.27 mmoles), 5-clorometil-3-(3-metoxi-fenil)-[1,2,4]oxadiazol (50 mg, 0.22) mmoles), y carbonato de potasio (92.6 mg, 0.67 mmoles) en

acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.62 (d, 1H), 7.52 (d, 2H), 7.48 (d, 1H), 7.37 (t, 1H), 7.18 (t, 1H), 7.06 (m, 1H), 4.64 (s, 2H), 3.84 (s, 3H), 3.71 (s, 3H).

LC-MS (MH+): 386.06.

EJEMPLO 48

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol

Se obtiene 5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]-oxadiazol (79.9 mg, 87%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (86.8 mg, 0.44 mmoles), 5-clorometil-3-fenil-[1,2,4]oxadiazol (50 mg, 0.26 mmoles), y carbonato de potasio (152.0 mg, 1.1 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.02 (d, 2H), 7.47 (m, 5H), 7.18 (t, 1H).

EJEMPLO 49

5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]oxadiazol

Se obtiene 5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]-oxadiazol (71.8 mg, 91%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (78.9 mg, 0.40 mmoles), 5-clorometil-3-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles) y carbonato de potasio (138.2 mg, 1.0 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 45-65% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.82 (d, 2H), 7.52 (d, 1H), 7.47 (d, 1H), 7.31 (m, 2H), 7.18 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H), 2.39 (s, 3H).

LC-MS (MH^+): 370.06.

EJEMPLO 50

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo

Se obtiene 3-[3-(4-metil-5-tiofen-2-il-4*H*-

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[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo (130 mg, 75%) a partir de 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo (100 mg, 0.45 mmoles) con K_2CO_3 (189 mg, 1.36 mmoles) y 4-metil-5-(2-tienil)1,2,4-triazol-3-tiol (110 mg, 0.54 mmoles) en acetonitrilo a temperatura ambiente. La purificación se efectúa mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 50% en diclorometano.

^1H RMN($CDCl_3$), δ (ppm): 8.38 (bs, 1H), 8.32 (d, 1H), 7.88 (d, 1H), 7.68 (t, 1H), 7.51 (dd, 2H), 7.18 (dd, 1H), 4.56 (s, 2H), 3.75 (s, 3H).

LC-MS $(M+H)^+$: 381.

EJEMPLO 51

3-[4-metil-5-(2-metil-tiazol-4-il)-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol (82.8 mg, 90%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]-oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]-triazol-3-tiol (61 mg, 0.29 mmoles) en acetonitrilo

(2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.96 (s, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.53 (s, 2H), 3.91 (s, 3H), 2.75 (s, 3H), 2.41 (s, 3H).

EJEMPLO 52

3-[5-(2-metil-tiazol-4-il)-[1,3,4]oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[5-(2-metil-tiazol-4-il)-[1,3,4]-oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol (89 mg, 99%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(2-metil-triazol-4-il)-[1,3,4]oxadiazol-2-tiol (57.3 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.97 (s, 1H), 7.90 (m, 2H), 7.40 (m, 2H), 4.66 (s, 2H), 2.80 (s, 3H), 2.42 (s, 3H).

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EJEMPLO 53

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il- [1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]-oxadiazol (80 mg, 88%, sólido de color blanco) a partir de 3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol (50 mg, 0.25 mmoles), carbonato de potasio (103 mg, 0.75 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (59 mg, 0.30 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.65 (m, 1H), 7.51 (m, 2H), 7.19 (m, 2H), 4.50 (t, 2H), 3.74 (s, 3H).

EJEMPLO 54

3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[5-(2,4-dimetil-tiazol-5-il)-4-

metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol (54.2 mg, 57%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(2,4-dimetil-tiazol-5-il)-4-metil-4H-[1,2,4]triazol-3-tiol (65.1 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.39 (m, 2H), 4.57 (s, 2H), 3.49 (s, 3H), 2.73 (s, 3H), 2.43 (d, 6H).

EJEMPLO 55

3-[4-metil-5-(5-nitro-furan-2-il)-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[4-metil-5-(5-nitro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol (77.9 mg, 81%, sólido de color amarillo) a partir de 3-clorometil-5-m-tolil-[1,2,4]-oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 4-metil-5-(5-nitro-furan-2-il)-4H-[1,2,4]triazol-3-tiol (65.1 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La

purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (m, 2H), 7.46 (d, 1H), 7.40 (m, 2H), 7.33 (d, 1H), 4.59 (s, 2H), 3.91 (s, 3H), 2.42 (s, 3H).

EJEMPLO 56

4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 4-[4-metil-5-(5-m-tolil-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (66 mg, 75%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol (55.3 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.79 (dd, 2H), 7.89 (m, 2H), 7.63 (dd, 2H), 7.40 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.41 (s, 3H).

EJEMPLO 57

3-[5-(4-ter-butil-fenil)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol

Se obtiene 3-[5-(4-ter-butil-fenil)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol (100 mg, 99%, sólido ceroso de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]-oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(4-ter-butil-fenil)-4-metil-4*H*-[1,2,4]triazol-3-tiol (71.1 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.57 (m, 4H), 7.39 (d, 2H),4.55 (s, 2H), 3.61 (s, 3H), 2.40 (s, 3H), 1.35 (s, 9H).

EJEMPLO 58

2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-

3-il]-piridina (53.8 mg, 56%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (99 mg, 0.72 mmoles), 5-(6-cloro-piridin-3-il)-4-metil-4H-[1,2,4]-triazol-3-tiol (65.2 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.67 (d, 1H), 8.02 (dd,1H), 7.88 (m, 2H), 7.49 (d, 1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.65 (s, 3H), 2.42 (s, 3H).

EJEMPLO 59

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-benzo-oxazol

Se obtiene 2-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-benzo-oxazol (138 mg, 62%) a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]-oxadiazol (225.9 mg, 1.11 mmoles), benzo-oxazol-2-tiol (167 mg, 1.00 mmoles), carbonato de potasio (180 mg, 1.3 mmoles) en DMF (4.5 ml) a temperatura ambiente durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 10-20% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.67 (d, 1H), 7.57

(m, 3H), 7.43 (t, 1H), 7.21 (m, 2H), 7.14 (m, 1H), 4.50 (s, 2H), 3.86 (s, 3H).

EJEMPLO 60

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]-oxa-diazol (73.6 mg, 73%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (61 mg, 0.31 mmoles), 3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol (50 mg, 0.28 mmoles), y carbonato de potasio (115 mg, 0.83 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.20 (d, 1H), 7.64 (d, 1H), 7,48 (m, 3H), 7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H).

EJEMPLO 61

3-(5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(5-furan-2-il-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (51.0 mg, 76%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40.0 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-tiol (41.7 mg, 0.23 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.58 (s, 1H), 7.40 (m, 2H), 7.10 (d, 1H), 6.58 (dd, 1H), 4.51 (s, 2H), 3.77 (s, 3H), 2.41 (s, 3H).

EJEMPLO 62

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (75.4 mg, 83%, sólido de color blanco) a partir de 4-metil-5-tiofen-il-4H-[1,2,4]triazol-3-tiol (51 mg, 0.26 mmoles), 3-clorometil-5-(3-fluoro-fenil)-[1,2,4]oxadiazol (50 mg, 0.24 mmoles) y carbonato de potasio (98 mg, 0.71 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa

mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 55-60% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.78 (m, 1H), 7.51 (m, 3H), 7.32 (m, 1H), 7.18 (m, 1H), 4.55 (s, 2H), 3.74 (s, 3H)

EJEMPLO 63

2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-piridina

Se obtiene 2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-piridina (27.3 mg, 96.5%) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (20.8 mg, 0.1 mmoles) con piridin-2-tiol (12.2 mg, 0.11 mmoles) y carbonato de potasio en DMF (0.8 ml) a temperatura ambiente durante 15 h. La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo al 20% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.47 (dd, 1H), 7.94 (s, 1H), 7.90 (t, 1H), 7.51 (dt, 1H), 7.38 (d, 2H), 7.26 (dd, 1H), 7.02 (dd, 1H), 4.61 (s, 2H), 2.42 (s, 3H).

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EJEMPLO 64

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-imidazo[4,5-b]piridina

Se obtiene 2-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-1*H*-imidazo[4,5-b]piridina (74.5 mg, 96%) a partir de 3-clorometil-5-(3-metoxi-fenil)-[1,2,4]oxadiazol (51.2 mg, 0.25 mmoles), 1H-imidazo[4,5-b]piridin-2-tiol (37.5 mg, 0.23 mmoles) y carbonato de potasio (80 mg, 0.58 mmoles) en DMF (1.5 ml) a temperatura ambiente durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 25-50% en diclorometano.

^{1}H-RMN (DMSO-d_6), δ (ppm): 8.24 (br s, 1H), 7.88 br s, 1H), 7.66 (d, 1H), 7.55 (m, 3H), 7.29 (d, 1H), 7.19 (m, 1H), 4.82 (s, 2H), 3.85 (s, 3H).

EJEMPLO 65

5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-[1,2,4]oxadiazol (58 mg, 68%, sólido de color blanco)

a partir de 3-clorometil-5-(3-fluoro-5-metil-fenil)-[1,2,4]oxadiazol (50 mg, 0.22 mmoles), carbonato de potasio (91.5 mg, 0.66 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (52.2 mg, 0.26 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-100% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.70 (s, 1H), 7.58 (d, 1H), 7.52 (m, 1H), 7.49 (m, 1H), 7.18 (m, 1H), 7.12 (d, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 2.42 (s, 3H).

EJEMPLO 66

3-metil-5-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

Se obtiene 3-metil-5-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxa-diazol-5-il]-piridina (19.0 mg, 43%, sólido de color amarillo claro) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol (26 mg, 0.13 mmoles), 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-metil-piridina (25 mg, 0.12 mmoles) y carbonato de potasio (50 mg, 0.36 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La

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purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 100%.

^{1}H RMN ($CDCl_3$), δ (ppm): 9.13 (s, 1H), 8.65 (s, 1H), 8.16 (s, 1H), 7.50 (m, 2H), 7.19 (t, 1H) 4.57 (s, 2H), 3.74 (s, 3H), 2.43 (s, 3H)

EJEMPLO 67

3-(4-metil-5-fenil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-fenil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (55.8 mg, 67%, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (48.4 mg, 0.23 mmoles), carbonato de potasio (96 mg, 0.70 mmoles), 4-metil-5-fenil-4*H*-[1,2,4]triazol-3-tiol (44.4 mg, 0.23 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.64 (m, 2H), 7.50 (m, 3H), 7.39 (m, 2H), 4.56 (s, 2H), 3.61 (s, 3H), 2.41 (s, 3H).

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EJEMPLO 68

2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 2-[4-metil-5-(5-m-tolil-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (42.8 mg, 51%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (48.4 mg, 0.23 mmoles), carbonato de potasio (96 mg, 0.70 mmoles), 4-metil-5-piridin-2-il-4*H*-[1,2,4]triazol-3-tiol (44.6 mg, 0.23 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.62 (d, 1H), 8.30 (d,1H), 7.85 (m, 3H), 7.36 (m, 3H), 4.59 (s, 2H), 4.02 (s, 3H), 2.40 (s, 3H).

EJEMPLO 69

4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-morfolina

Se obtiene 4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-

3-il]-morfolina (95.8 mg, 83%, aceite claro) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (59.9 mg, 0.29 mmoles), carbonato de potasio (119 mg, 0.86 mmoles), 5-(4-bencil-morfolin-2-il)-4-metil-4*H*-[1,2,4]-triazol-3-tiol (83.3 mg, 0.29 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando metanol al 10% en acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.31 (m, 7H), 4.75 (dd, 1H), 4.47 (dd, 2H), 3.84 (m, 2H), 3.59 (bs, 5H), 3.20 (d, 1H), 2.72 (m, 2H), 2.43 (s, 3H), 2.30 (dt, 1H).

EJEMPLO 70

4-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol3-il-piridina

Se obtiene 4-[4-metil-5-(5-tiofen-3-il-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (24 mg, 34%, sólido de color blanco) a partir de 3-clorometil-5-tiofen-3-il-[1,2,4]oxadiazol (40 mg, 0.20 mmoles), carbonato de potasio (82.5 mg, 0.60 mmoles), 4-metil-5-piridin-4-il-4*H*-[1,2,4]triazol-3-tiol (38.3 mg, 0.20 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa

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en gel de sílice utilizando metanol al 10% en acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.80 (bs, 2H), 8.20 (dd, 1H), 7.62 (m, 3H), 7.45 (dd, 1H), 4.59 (s, 2H), 3.70 (s, 3H).

EJEMPLO 71

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxa-diazol (44 mg, 67%, sólido de color blanco) a partir de 3-clorometil-5-tiofen-2-il-[1,2,4]oxadiazol (37 mg, 0.18 mmoles), carbonato de potasio (75.3 mg, 0.54 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (43 mg, 0.22 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-100% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 9.37 (d, 1H), 8.86 (d, 1H), 7.80 (d, 1H), 7.65 (d, 1H), 7.26 (t, 1H), 4.54 (s, 2H), 3.75 (s, 3H).

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EJEMPLO 72

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil) -[1,2,4] oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,2,4]oxadiazol (21.1 mg, 13%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol (91 mg, 0.46 mmoles), 3-clorometil-5-(3-nitro-fenil)-[1,2,4]oxadiazol (100 mg, 0.42 mmoles) y carbonato de potasio (173 mg, 1.25 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 60% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.96 (s, 1H), 8.44 (t, 2H), 7.75 (t, 1H), 7.51 (m, 2H), 7.19 (t, 1H), 4.59 (s, 2H), 3.76 (s, 3H)

EJEMPLO 73

2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

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Se obtiene 2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina (59.2 mg, 66%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (51 mg, 0.26 mmoles), 4-(3-cloro-metil-[1,2,4]oxadiazol-5-il)-2-metil-piridina (50 mg, 0.24 mmoles), y carbonato de potasio (100 mg, 0.72 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 100%.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.71 (d, 1H), 7.79 (s, 1H), 7.73 (d, 1H), 7.49 (m, 2H), 7.19 (t, 1H), 4.58 (s, 2H), 3.73 (s, 3H), 2.65 (s, 3H).

EJEMPLO 74

3-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 3-[4-metil-5-(5-m-tolil-[1,2,4]-oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina (30 mg, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 4-metil-5-piridin-3-il-4*H*-[1,2,4]triazol-3-tiol (46.1

mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando metanol al 5% en acetato de etilo.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.90 (bs,1H), 8.76 (bs, 1H), 8.03 (m, 1H), 7.88 (m, 2H), 7.46 (dd,1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.66 (s, 3H), 2.42 (s, 3H).

EJEMPLO 75

3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (60 mg, sólido de color blanco) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-tiol (47.3 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 40% en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.71 (dd, 1H), 7.48 (m, 2H), 7.38 (m, 2H), 4.52 (s, 2H), 3.67 (s, 3H), 2.41 (s, 3H).

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EJEMPLO 76

3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (30 mg, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 4-metil-5-triazol-4-il-4*H*-[1,2,4]triazol-3-tiol (47.5 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 60% en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.89 (d, 1H), 8.22 (d, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.55 (s, 2H), 3.94 (s, 3H), 2.41 (s, 3H).

EJEMPLO 77

5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (725 mg, 97%, sólido de color blanco) a

partir de 3-clorometil-5-(3-yodo-fenil)-[1,2,4]oxadiazol (500 mg, 1.56 mmoles), carbonato de potasio (647 mg, 4.68 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (369 mg, 1.87 mmoles) en acetonitrilo (10 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo al 40% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 8.06 (d, 1H), 7.93 (d, 1H), 7.51 (m, 2H), 7.26 (t, 1H), 7.19 (m, 1H), 4.54 (s, 2H), 3.73 (s, 3H).

EJEMPLO 78

5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (28.1 mg, 27%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (59 mg, 0.30 mmoles), 3-clorometil-5-(3-etil-fenil)-[1,2,4]oxadiazol (60 mg, 0.27 mmoles) y carbonato de potasio (111 mg, 0.80 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE

(vaporización instantánea) utilizando acetato de etilo al 50% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (t, 2H), 7.51 (m, 2H), 7.42 (t, 2H), 7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H), 2.70 (m, 2H), 1.26 (t, 3H)

EJEMPLO 79

2-[5-(2-metil-piridin-4-il)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(2-metil-piridin-4-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (46.0 mg, 59%, sólido de color blanco) a partir de 2-mercaptobencimidazol (41 mg, 0.27 mmoles), 4-(3-cloro-metil-[1,2,4]oxadiazol-5-il)-2-metil-piridina (50 mg, 0.24 mmoles), y carbonato de potasio (100 mg, 0.72 mmoles) en DMF (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 100% y se tritura con éter.

^{1}H RMN (DMSO-d_6), δ (ppm): 8.72 (d, 1H), 7.87 (s, 1H), 7.78 (d, 1H), 7.47 (t, 2H), 7.14 (m, 2H), 4.81 (s, 2H), 2.59 (s, 3H)

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EJEMPLO 80

2-[5-(3-yodo-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(3-yodo-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (36 mg, 51%, sólido de color blanco) a partir de 3-cloro-metil-5-(3-yodo-fenil)-[1,2,4]oxadiazol (50 mg, 0.16 mmoles), carbonato de potasio (65 mg, 0.47 mmoles), 1*H*-benzoimidazol-2-tiol (23 mg, 0.16 mmoles) en DMF (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 50-100% en hexanos seguido por trituración con acetato de etilo.

^{1}H RMN (DMSO), δ (ppm): 12.73 (bs, 1H), 8.30 (s, 1H), 8.09 (d, 2H), 7.45 (m, 3H), 7.18 (m, 2H), 4.78 (s, 2H).

EJEMPLO 81

3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-

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oxadiazol (54.3 mg, 80%, aceite claro) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-tiol (35.1 mg, 0.19 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 50% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.41 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.43 (s, 3H).

EJEMPLO 82

2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina

Se obtiene 2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]-triazol-3-il]-piridina (51.4 mg, 62%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 5-(2,6-dicloro-piridin-4-il)-4-metil-4*H*-[1,2,4]triazol-3-tiol (50.1 mg, 0.19 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.61

(s, 2H), 7.40 (m, 2H), 4.60 (s, 2H), 3.71 (s, 3H), 2.42 (s, 3H).

EJEMPLO 83

3-(4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-p-tolil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (57.8 mg, 81%, sólido de color blanquecino) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (40 mg, 0.19 mmoles), carbonato de potasio (79 mg, 0.58 mmoles), 4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-tiol (39.4 mg, 0.19 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.53 (d, 2H), 7.39 (m, 2H), 7.30 (d, 2H), 4.55 (s, 2H), 3.59 (s, 3H), 2.42 (d, 6H).

EJEMPLO 84

Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil)-amina

Se obtiene dimetil-{3-[3-(4-metil-5-tiofen-

2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil)-amina (28.0 mg, 85%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (18 mg, 0.093 mmoles), 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-dimetil-amina (20 mg, 0.084 mmoles), y carbonato de potasio (35 mg, 0.25 mmoles) en acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.49 (m, 2H), 7.36 (m, 3H), 7.17 (t, 1H), 6.91 (d, 1H), 4.51 (s, 2H), 3.72 (s, 3H), 3.00 (s, 6H)

EJEMPLO 85

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (76.8 mg, 90%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (47 mg, 0.24 mmoles), 3-clorometil-5-(3-clorofenil)-[1,2,4]oxadiazol (50 mg, 0.22 mmoles), y carbonato de potasio (91 mg, 0.66 mmoles en

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acetonitrilo (1 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 70% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.49 (m, 4H), 7.18 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

EJEMPLO 86

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol

Se obtiene 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol (144.0 mg, 91%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-tiol (78 mg, 0.39 mmoles), 3-cloro-metil-5-(3-trifluorometoxi-fenil)-[1,2,4]oxadiazol (100 mg, 0.36 mmoles) y carbonato de potasio (149 mg, 1.08 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 55% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.04 (d, 1H), 7.95 (s, 1H), 7.51 (m, 4H), 7.18 (m, 1H), 4.56 (s, 2H),

3.74 (s, 3H)

EJEMPLO 87

3-(5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(5-ciclohexil-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (10.5 mg, aceite claro) a partir de 3-clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (165 mg, 1.20 mmoles), 5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-tiol (94.6 mg, 0.48 mmoles) en acetonitrilo (3 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando amoniaco al 2% (2 N en metanol) en diclorometano.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.39 (m, 2H), 4.42 (s, 2H), 3.46 (s, 3H), 2.60 (m, 1H), 2.42 (d, 3H), 1.74 (m, 7H), 1.34 (m, 3H).

EJEMPLO 88

3-(5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-(5-ter-butil-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (56.8 mg, sólido de color blanco) a partir de 3-

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clorometil-5-m-tolil-[1,2,4]oxadiazol (50 mg, 0.24 mmoles), carbonato de potasio (100 mg, 0.72 mmoles), 5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-tiol (41 mg, 0.24 mmoles) en acetonitrilo (2 ml) a 60°C durante la noche. La purificación se efectúa en gel de sílice utilizando acetato de etilo al 80% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.40 (m, 2H), 4.46 (s, 2H), 3.63 (s, 3H), 2.43 (m, 3H), 1.45 (s, 9H).

EJEMPLO 89

5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (83.4 mg, 86%, sólido de color blanco) a partir de 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (47 mg, 0.24 mmoles), 5-(3-bromo-fenil)-3-cloro-metil-[1,2,4]oxadiazol (60 mg, 0.22 mmoles), y carbonato de potasio (91 mg, 0.66 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 60% en hexano.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.25 (t, 1H), 8.02

(d, 1H), 7.73 (d, 1H), 7.50 (m, 2H), 7.40 (t, 1H), 7.19 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

EJEMPLO 90

2-[5-(3-bromo-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(3-bromo-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (71.1 mg, 84%, sólido de color blanco) a partir de 2-mercaptobencimidazol (35 mg, 0.23 mmoles), 5-(3-bromo-fenil)-3-clorometil-[1,2,4]oxadiazol (60 mg, 0.22 mmoles) y carbonato de potasio (91 mg, 0.66 mmoles) en DMF (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 35% en hexano y se tritura con éter.

^{1}H RMN (DMSO-d_6), δ (ppm): 12.78 (s ancho, 1H), 8.18 (s, 1H), 8.07 (d, 1H), 7.93 (d, 1H), 7.59 (t, 1H), 7.46 (s, 2H), 7.14 (m, 2H), 4.77 (s, 2H)

EJEMPLO 91

5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se obtiene 5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil-metil)-[1,2,4]oxadiazol (76 mg, 90%, sólido de color blanco) a partir de 3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol (50 mg, 0.21 mmoles), carbonato de potasio (87 mg, 0.63 mmoles), 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (50 mg, 0.25 mmoles) en acetonitrilo (2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-70% en hexanos.

^{1}H RMN ($CDCl_3$), δ (ppm): 8.06 (s, 1H), 8.01 (d, 1H), 7.59 (d, 1H), 7.50 (m, 3H), 7.18 (t, 1H), 4.54 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H), 3.43 (s, 3H).

EJEMPLO 92

2-[5-(3-metoximetil-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol

Se obtiene 2-[5-(3-metoximetil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol (62 mg, 84%, sólido de color blanco) a partir de 3-clorometil-5-(3-metoximetil-fenil)-[1,2,4]oxadiazol (50 mg, 0.21 mmoles), carbonato de potasio (87 mg, 0.63 mmoles), 1*H*-benzoimidazol-2-tiol (32 mg, 0.21 mmoles) en DMF

(2 ml) a temperatura ambiente. La purificación se efectúa mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 40-100% en hexanos.

^{1}H RMN (DMSO), δ (ppm): 8.09 (d, 2H), 7.59 (m, 2H), 7.46 (bs, 2H), 7.14 (m, 2H), 4.77 (s, 2H), 4.51 (s, 2H), 3.35 (s, 3H).

EJEMPLO 93

4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina

Se trata una solución de cloruro de isonicotinoilo (2.0 g, 11.2 mmoles) en diclorometano con 2-cloro-N-hidroxi-acetamidina (1.58 g, 14.6 mmoles), seguido por la adición de trietilamina (4.67 ml, 33.6 mmoles) mediante goteo. Después de agitar a temperatura ambiente 1 h, la extracción con acetato de etilo utilizando lavados con agua y salmuera permite obtener el intermediario oxi-arilo (que se utiliza sin purificación adicional, 150 mg, 0.7 mmoles). Se agita una solución el producto crudo en acetonitrilo (2 ml) y DMSO (2 ml) con K_2CO_3 (292 mg, 2.1 mmoles) y 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (140 mg, 0.7 mmoles) a temperatura ambiente durante 24 h seguido por 1.5 h a 120°C (tubo

sellado). El tratamiento acuoso normal con acetato de etilo utilizando lavados con agua y salmuera seguido por cromatografía en gel de sílice permite obtener el compuesto del título (110 mg, 44%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.41 dd,2H), 7.92 dd,2H), 7.50 dd,1H), 7.47 dd,1H), 7.18 dd,1H), 4.58 (s,2H), 3.74 (s,3H)

LC-MS $(M+H)^+$: 357.

El ejemplo 94 se prepara en un método análogo al procedimiento dado en el ejemplo 93.

EJEMPLO 94

4[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina

Se obtiene 4-[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina (12 mg, 5%) a partir de *N*-hidroxi-isonicotinamidina (200 mg, 1.4 mmoles) con cloruro de cloroacetilo (0.11 ml, 1.4 mmoles) y trietilamina (0.5 ml, 3.5 mmoles); el tratamiento acuoso produce el intermediario (150 mg, 0.7 mmoles); se trata con K_2CO_3 (292 mg, 2.1 mmoles), y 4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-tiol (140 mg, 0.7 mmoles). La

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purificación se efectúa mediante cromatografía en gel de sílice y recristalización.

^{1}H RMN($CDCl_3$), δ (ppm): 8.76 (dd, 2H), 7.89 (dd, 2H), 7.53 (dd, 1H), 7.48 (dd, 1H), 7.18 (dd, 1H), 4.71 (s, 2H), 3.73 (s, 3H).

LC-MS (M+H)+: 357.

EJEMPLO 95

2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-1-metil-1*H*-imidazo[4,5-b]piridina

Y

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1-metil-1*H*-imidazo[4,5-b]piridina

Se agrega THF (3 ml) a una mezcla de hidruro de sodio (60%, 8 mg, 0.2 mmoles) y 2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-imidazo-[4,5-b]piridina (24.6 mg, 0.072 mmoles) y la mezcla resultante se agita a 0°C durante 15 minutos aproximadamente. Se agrega yoduro de metilo (20 µl, 0.32 mmoles) la mezcla resultante se agita a 0°C durante 2h. La reacción se extingue mediante adición de diclorometano (10 ml) y agua (2 ml). Después de agitar vigorosamente, los extractos orgánicos (10 ml, más 3x5 ml) se eluyen a través de una columna de

extracción Chem Elut (Varian, cat #1219-8002). La purificación utilizando cromatografía de SPE (5 g de sílice) empleando 25/25/50 a 50/25/25 de acetato de etilo/diclorometano/hexano permite obtener dos productos. El primer producto en eluir es 2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etil-sulfanil}-1-metil-1H-imidazo[4,5-b]piridina (6 mg, 23%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.46 (d, 1H), 7.72 (d, 1H), 7.62 (d, 1H), 7.55 (d, 1H), 7.42 (t, 1H), 7.14 (m, 2H), 5.67 (q, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 2.01 (d, 3H).

El segundo producto en eluir es 2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1-metil-1H-imidazo[4,5-b]piridina (12 mg, 47%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 7.69 (d, 1H), 7.60 (d, 1H), 7.55 (d, 1H), 7.41 (t, 1H), 7.13 (m, 1H), 4.90 (s, 2H), 3.87 (s, 3H), 3.70 (s, 3H).

Los ejemplos 96-97 se preparan en un método análogo al procedimiento dado en el ejemplo 95.

EJEMPLO 96

3-[1-metil-1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[1-metil-1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]-oxadiazol (13 mg, 47%) a partir de 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (25.5 mg, 0.069 mmoles) con 60% de hidruro de sodio (37 mg, 0.92 mmoles) y yoduro de metilo (0.10 ml, 1.6 mmoles) en THF (3 ml) a temperatura ambiente durante 2 horas. El producto se extrae con acetato de etilo y se purifica mediante SPE con 20-40% de acetato de etilo en diclorometano:hexano 1:1.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.48 (d, 1H), 7.42 (d, 1H), 7.36 (m, 2H), 7.13 (m, 1H), 3.50 (s, 3H), 2.35 (s, 3H), 1.95 (s, 6H).

EJEMPLO 97

3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol

Se obtiene 3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]-oxadiazol (6.1 mg, 17%) a partir de 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol (33.8 mg, 0.091 mmoles) con 60% de hidruro de sodio (17 mg, 0.42 mmoles) y yoduro de metilo (20 µl, 0.32 mmoles) en THF (2.5 ml) a

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temperatura ambiente durante 1 hora. El producto se extrae con diclorometano y se purifica mediante SPE 25-40% acetato de etilo en cloroformo : hexano 1:1.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.89 (br s, 2H), 7.50 (d, 1H), 7.46 (d, 1H), 7.38 (m, 2H), 7.16 (m, 1H), 4.89 (q, 1H), 3.64 (s, 3H), 2.37 (s, 3H), 1.90 (d, 3H).

EJEMPLO 98

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol y 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]-oxadiazol

Se agrega diclorometano (2.5 ml) a una mezcla de ácido 3-cloro-bencencarboperoxóico (57-85%, 49.5 mg, 0.16-0.25 mmoles) y 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]-oxadiazol (45 mg, 0.12 mmoles) y la mezcla resultante se agita a temperatura ambiente durante la noche. La reacción se extingue mediante adición de diclorometano (10 ml) e hidróxido de sodio 1M (3 ml). Después de agitar vigorosamente, los extractos orgánicos (10 ml, más 3x5 ml) se eluyen a través de una columna de extracción Chem Elut (Varian, cat #1219-8002). La purificación se efectúa mediante cromatografía de SPE

(5 g de sílice) utilizando 10-30% acetato de etilo en diclorometano:hexano 1:1 lo que permite obtener dos productos. El primer producto en eluir es 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol (12.3 mg, 25%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.63 (d, 1H), 7.56 (d, 1H), 7.36 (m, 2H), 7.24 (m, 1H), 5.12 (s, 2H), 3.94 (s, 3H), 2.36 (d, 3H).

El segundo producto en eluir es 3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]oxadiazol (33.2 mg, 71%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.87 (br s, 2H), 7.59 (d, 1H), 7.54 (d, 1H), 7.38 (m, 2H), 7.22 (m, 1H), 5.05 (d_{AB}, 1H), 4.90 (d_{AB}, 1H), 4.03 (s, 3H), 2.39 (d, 3H).

EJEMPLO 99

5-(3-furan-3-il-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Al compuesto 5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol (50 mg, 0.10 mmoles) en un frasco se agrega ácido 3-furanborónico (17 mg, 0.16 mmoles), tetrakis-(trifenilfosfin)paladio(0) (6 mg, 0.0052 mmoles),

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éter dimetílico de etilenglicol (1 ml) y carbonato de sodio 2M (1 ml). El frasco se sella después y se calienta a 90°C durante 1 hora con agitación vigorosa. La reacción se enfría, se diluye con acetato de etilo, se lava con agua y salmuera saturada, se filtra y se concentra. El residuo se purifica mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 70% en hexanos. La purificación adicional mediante trituración con una mezcla de éter dietílico y hexanos y después filtración permite obtener el compuesto del título como un sólido color beige, 25 mg (57%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.18 (s, 1H), 7.98 (d, 1H), 7.79 (s, 1H), 7.71 (d, 1H), 7.51 (m, 4H), 7.17 (m, 1H), 6.74 (s, 1H), 4.55 (s, 2H), 3.73 (s, 3H).

INTERMEDIARIOS

EJEMPLO 100

Acido pirimidin-4-carboxílico

Se somete a reflujo 3-metil-pirimidina (9.41 g, 100 mmoles), permanganato de potasio (26.9 g) y carbonato de sodio (10.6 g) en agua (100 ml) durante 72 horas seguido por filtración a través de celita. El material filtrado se lava con varias porciones de

DCM y EtOAc antes de acidular con HCl concentrado. El precipitado formado se recolecta y se lava con agua para producir 1.37 g del compuesto del título como un sólido de color blanco.

^{1}H RMN (DMSO-d6) δ (ppm): 13.94 (br. s, 1H), 9.37 (d, 1H), 9.07 (d, 1H), 8.01 (dd, 1H).

EJEMPLO 101

Acido 5-cloro-tiofen-3-carboxílico

Se someten a reflujo ácido tiofen-3-carboxílico (17.51 g, 136.6 mmoles) y 1-cloro-pirrolidin-2,5-diona (23.7 g) en ácido acético (200 ml) durante 4 h bajo argón antes de verter en agua (700 ml). La extracción repetida con varias porciones pequeñas de DCM, seguido por extracción por retroceso a partir de las fases orgánicas combinadas con varias porciones pequeñas de hidróxido de sodio acuoso 2 M, produce una solución acuosa alcalina combinada que se lava con DCM antes de acidular con HCl concentrado para precipitar el material crudo. Este precipitado se vuelve a cristalizar con agua para producir 14.98 g del compuesto del título como un sólido de color gris contaminado con aproximadamente 20% molar de un subproducto diclorado según se juzga a partir de MS y

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^{1}H-RMN.

^{1}H RMN (DMSO-d_6) d (ppm): 8.15 (d, 1H), 7.37 (d, 1H).

EJEMPLO 102

Acido 3-metilsulfanil-benzoico

Se agrega yoduro de metilo (0.972 ml) a una mezcla de ácido 3-mercapto-benzoico (601 mg, 3.9 mmoles) y carbonato de potasio (2.7 g, 19.5 mmoles) en DMF (8 ml) en un baño de hielo. Después que la reacción se calienta hasta temperatura ambiente y se agita durante 1 hora, la mezcla de reacción se diluye con acetato de etilo, se lava con agua (3X), se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener el éster metílico del ácido 3-metilsulfanil-benzoico (684 mg, 96%, aceite de color amarillo).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.80 (d, 1H), 7.44 (d, 1H), 7.35 (t, 1H), 3.92 (s, 3H), 2.53 (s, 3H).

Se calienta el éster metílico del ácido 3-metilsulfanil-benzoico (684-mg, 3.8 mmoles) y NaOH 1N (5.6 ml, 5.6 mmoles) en metanol (8 ml) y THF (8

ml) a 70°C durante 1 hora. La mezcla de reacción se concentra y el residuo se diluye después con agua. Después de acidular con HCl 1N hasta pH 2 aproximadamente, la capa acuosa se extrae con acetato de etilo y después se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra para obtener el ácido 3-metilsulfanil-benzoico (616 mg, 97%, sólido de color blanco).

^{1}H RMN (DMSO), δ (ppm): 13.1 (bs, 1H), 7.76 (s, 1H), 7.70 (d, 1H), 7.51 (d, 1H), 7.44 (t, 1H), 2.52 (s, 3H).

EJEMPLO 103

Acido 3-ciclopropil-benzoico

Se agrega dietil-zinc 1.0 M en hexanos (27.3 ml, 27.3 mmoles) a una solución de 2,4,6-triclorofenol (5.4g, 27.3 mmoles) en diclorometano (100 ml) a -40°C. Después de agitar durante 15 minutos, se agrega diyodo-metano (2.2 ml, 27.3 mmoles) a -40°C y se agita durante 15 minutos adicionales. Después se agrega 1-bromo-3-vinilbenceno (2.5 g, 13.7 mmoles) a la mezcla de reacción, se deja calentar hasta temperatura

ambiente, y se deja bajo agitación durante la noche. La mezcla de reacción se diluye con diclorometano, se lava con HCl 1N (2X), bicarbonato de sodio saturado (2X), sulfito de sodio saturado, hidróxido de sodio 1N, y salmuera saturada, se seca con sulfato de magnesio, se filtra y se concentra. El análisis con GC-MS revela que la mezcla de reacción contiene 1-bromo-3-ciclopropil-benceno y 1-bromo-3-vinilbenceno. Para eliminar el bromo-3-vinil-benceno, la mezcla cruda se hace reaccionar con permanganato de potasio. Se agrega, mediante goteo, una solución de permanganato de potasio/agua (1.5 g/20 ml) a una solución de la mezcla cruda (aproximadamente 3.5 g) en THF (40 ml) a 0°C y después se deja calentar hasta temperatura ambiente. Después de 1 hora, la reacción se diluye con éter dietílico, se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. La purificación mediante cromatografía de vaporización instantánea eluyendo con 100 hexanos permite obtener 1-bromo-3-ciclopropil-benceno (2.20g, 81%).

Se agrega, mediante goteo, n-butil-litio 1.6 M en hexanos (3.2 ml, 5.1 mmoles) a una solución de 1-bromo-3-ciclopropil-benceno a -78°C y se agita

durante 1 hora. Esta mezcla de reacción se transfiere después mediante cánula a un matraz de fondo redondo de 250 ml equipado con una barra de agitación, lleno aproximadamente hasta 1/4 de su capacidad con dióxido de carbono sólido y se agita durante 1 hora. La mezcla de reacción se concentra y el residuo se diluye después con agua. La capa acuosa se lava con diclorometano (3X), se acidula con HCl 1N hasta pH 2 aproximadamente, y se extrae con acetato de etilo. La fase orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener ácido 3-ciclopropil-benzoico (356 mg, 43%, sólido de color blanco).

^{1}H RMN (DMSO), δ (ppm): 12.90 (bs, 1H), 7.71 (d, 1H), 7.64 (s, 1H), 7.34 (m, 2H), 2.01 (m, 1H), 0.99 (m, 2H), 0.70 (m, 2H).

EJEMPLO 104

Acido 3-ter-butoxicarbonilamino-benzoico

A un matraz que contiene etil-3-amino-benzoato (1 g, 6.05 mmoles) se agrega dicarbonato de di-*ter*-butilo (3.16 g, 14.5 mmoles), trietilamina (500 mg, 4.94 mmoles), y THF (10 ml) y se deja

agitar a 60°C durante dos horas y después durante la noche a temperatura ambiente. El THF se elimina al vacío, y el éster crudo se divide entre acetato de etilo y agua, se lava con salmuera saturada, se seca con sulfato de sodio anhidro y el solvente se elimina al vacío. El producto se purifica después mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 15% en hexano para obtener 2g del éster etílico del ácido 3-ter-butoxicarbonilamino-benzoico (suspensión espesa de color blanco).

Al éster etílico del ácido 3-ter-butoxi-carbonilaminobenzoico crudo (aproximadamente 2.0g, 0.00754 mmoles) se agrega THF (15 ml), y LiOH 0.5M (15 ml). La mezcla se calienta durante dos horas a 75°C y el THF se elimina al vacío después de enfriar. El precipitado se filtra a partir de la mezcla remanente y el material filtrado se transfiere a un embudo de separación. La capa acuosa se lava con diclorometano (3x) y se acidula hasta pH 5 aproximadamente utilizando HCl 1M. El producto se extrae después con acetato de etilo, se lava con agua, salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. Se aíslan 730 mg del ácido 3-ter-butoxi-carbonilamino-benzoico

(sólido de color blanco).

^{1}H RMN (DMSO-d6) δ (ppm): 9.58 (s, 1H), 8.16 (s, 1H), 7.63 (d, 1H), 7.54 (d, 1H), 7.37 (t, 1H), 1.49 (s, 9H).

EJEMPLO 105

Acido 3-acetil-benzoico

Se agrega hidróxido de sodio 6M (25 ml) a 3-acetilbenzonitrilo (850 mg, 5.82 mmoles) en metanol (25 ml) y después se calienta a 90°C durante la noche. Después de concentrar la mezcla de reacción, la capa acuosa se lava con diclorometano (2x), después se acidula hasta pH 3 aproximadamente con HCl 12M. El precipitado se extrae con acetato de etilo después se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener ácido 3-etilbenzoico como un aceite incoloro; 0.800 g (92%).

^{1}H RMN ($CDCl_3$) δ (ppm): 8.70 (s, 2H), 8.33 (d, 2H), 8.24 (d, 2H), 7.64 (t, 1H), 2.70 (s, 3H).

EJEMPLO 106

Hidrazida del ácido 2-metil-isonicotínico

Se agrega diclorometano (10 ml) a la sal clorhidrato del ácido 2-metilnicotínico (1.1 g, 6.34 mmoles) y se agrega lentamente cloruro de oxalilo (6.95 ml, 13.9 mmoles) bajo argón mientras el matraz se enfría en hielo. Se agrega dimetilformamida (2 gotas) y la reacción se deja agitando durante la noche, tiempo durante el cual ésta se calienta hasta temperatura ambiente. Se concentra la reacción y se agrega THF (10 ml) al matraz y éste se coloca en un baño de hielo. Se agrega metanol (5 ml) y se deja que la reacción se agite durante una hora. Se concentra la reacción y el residuo se divide entre $NaHCO_3$ (saturado) y EtOAc. El producto se extrae con EtOAc tres veces. Las capas orgánicas combinadas se lavan con salmuera, se secan con Na_2SO_4, se filtran y se concentran. La purificación se efectúa mediante tubo de extracción en fase sólida (EtOAc al 20%/hexanos) lo cual permite obtener el compuesto del título como un aceite claro.

^1H RMN $CDCl_3$ δ (ppm): 8.51 (d, 1H), 7.57 (d, 1H), 7.51 (d, 1H), 3.82 (s, 3H), 2.50 (s, 3H).

Se disuelve el éster metílico del ácido 2-metil-isonicotínico (316.5 mg, 2.093 mmoles) en MeOH (7 ml) bajo argón y se agrega monohidrato de

hidrazina al 98% (1 ml, 20.93 mmoles). La reacción se deja agitando bajo argón a temperatura ambiente durante 18 horas. La reacción se concentra para obtener el compuesto del título (271.9 mg, 86%) como un sólido de color blanco.

^{1}H RMN $CDCl_3$ δ (ppm): 8.59 (d, 1H), 7.50 (s, 1H), 7.38 (d, 1H), 3.09 (br. s, 3H), 2.60 (s, 3H).

EJEMPLO 107

Hidrazida del ácido 5-cloro-2-fluoro-benzoico

Paso 1

Ester metílico del ácido 5-cloro-2-fluoro-benzoico:

Se agrega metanol (20 ml) a una solución de cloruro de 5-cloro-2-fluorobenzoilo (1.2 g, 6.2 mmoles) en diclorometano (10 ml) en un baño de hielo. La mezcla de reacción se calienta hasta temperatura ambiente, se agita durante 3 horas y después se concentra para obtener el éster metílico del ácido 5-cloro-2-fluoro-benzoico (1.17 g, 100%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.93 (m, 1H), 7.48 (m, 1H), 7.12 (m, 1H), 3.96 (s, 3H).

Paso 2

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Hidrazida del ácido 5-cloro-2-fluoro-benzoico:

Se agita a temperatura ambiente durante la noche una mezcla de éster metílico del ácido 5-cloro-2-fluoro-benzoico (1.17 g, 6.2 mmoles) y monohidrato de hidrazina (0.451 ml, 9.3 mmoles) en etanol (20 ml). La mezcla de reacción se concentra y después se tritura el residuo con éter dietílico para obtener la hidrazida del ácido 5-cloro-2-fluoro-benzoico (497 mg, 42%, sólido de color blanco).

^{1}H RMN (DMSO), δ (ppm): 9.66 (bs, 1H), 7.58 (m, 2H), 7.36 (m, 1H), 4.58 (bs, 2H).

El ejemplo 108 se prepara en una forma análoga a la del ejemplo 107.

EJEMPLO 108

Hidrazida del ácido 3-ciano-benzoico

Se agita cloruro de 3-ciano-benzoilo (3 g, 18.12 mmoles) en diclorometano (5 ml) y metanol (20 ml) a temperatura ambiente y durante la noche. El solvente se elimina utilizando un evaporador giratorio para obtener un sólido de color blanco (3.76 g).

^{1}H RMN (DMSO) δ (ppm): 8.33 (m, 1H), 8.24 (m, 1H), 8.14 (m, 1H), 7.76 (m, 1H), 3.89 (d, 3H).

1129

Se agita una mezcla del éster metílico del ácido 3-ciano-benzoico (2 g, 12 mmoles) y monohidrato de hidrazina (0.60 ml, 12 mmoles) en etanol (10 ml) a temperatura ambiente durante la noche. Se concentra la mezcla de reacción y el residuo se tritura después con éter dietílico para obtener la hidrazida del ácido 3-ciano-benzoico (1.02 g, 51%, sólido de color rosa).

^{1}H RMN (DMSO) δ (ppm): 10.31 (s, 1H), 8.21 (m, 1H), 8.11 (m, 1H), 7.99 (m, 1H), 7.70 (m, 1H), 4.50 (s, 1H).

EJEMPLO 109

Hidrazida del ácido 2-cloro-isonicotínico

Se agregan HOBt (823 mg, 6.09 mmoles), y EDCI (1.2 g, 6.09 mmoles) a una suspensión del ácido 2-cloro-isonicotínico (800 mg, 5.08 mmoles) en acetonitrilo (10.3 ml) a temperatura ambiente. Después de dos horas se agrega mediante goteo, a 0°C, una solución de monohidrato de hidrazina (0.493 ml, 10.2 mmoles) en acetonitrilo (5.0 ml). Después de 30 minutos, se elimina el solvente utilizando un evaporador giratorio y el residuo se diluye con

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acetato de etilo, se extingue con agua, se seca con sulfato de sodio, se filtra y se concentra para obtener la hidrazida del ácido 2-cloro-isonicotínico (493 mg, 57%, sólido de color amarillo).

^{1}H RMN (DMSO) d (ppm): 10.21 (bs, 1H), 8.55 (d, 1H), 7.82 (s, 1H), 7.75 (d, 1H), 4.69 (bs, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 109:

Ejemplo No.	Nombre
110	Hidrazida del ácido 2-fluoro-5-metil-benzoico
111	Hidrazida del ácido pirimidin-4-carboxílico

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 6:

Ejemplo No.	Nombre
112	3-fluoro-N-hidroxi-benzamidina
113	N-hidroxi-tiofen-3-carboxamidina
114	2-cloro-N.-hidroxi-propionamidina
115	3,N-hidroxi-benzamidina
116	N-hidroxi-2-metil-benzamidina
117	N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina
118	3-cloro-N-hidroxi-benzamidina
119	N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanil)-acetamidina
120	2,5-difluoro-N-hidroxi-benzamidina

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 31:

Ejemplo No.	Nombre
121	4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-tiol
122	4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
123	4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol
124	4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
125	4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-tiol
126	5-tiofen-2-il-4-tiofen-2-ilmetil-4H-[1,2,4]-triazol-3-tiol
127	4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
128	4-furan-2-ilmetil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol
129	4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol
130	4-etil-5-piridin-3-il-4H-[1,2,4]triazol-3-tiol
131	4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol
132	4-furan-2-ilmetil-5-piridin-3-il-4H-[1,2,4]-triazol-3-tiol
133	4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-tiol
134	4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol
135	4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-tiol
136	5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol
137	4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol
138	4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol
139	5-(2-cloro-6-metil-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol
140	5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]-triazol-3-tiol
141	4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]-triazol-3-tiol

Ejemplo No.	Nombre
142	4-etil-5-(tetrahidro-furan-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona
143	Ester metílico del ácido 4-etil-5-tioxo-4,5-dihidro-1H-[1,2,4]triazol-3-carboxílico

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 36:

Ejemplo No.	Nombre
144	5-(2-cloro-piridin-4-il)-4-etil-4H-[1,2,4]-triazol-3-tiol
145	5-(2-cloro-6-metoxi-piridin-4-il)-4-etil-4H-[1,2,4]triazol-3-tiol
146	4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-tiol
147	4-propil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol
148	4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-tiol
149	4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-tiol
150	3-(5-mercapto-4-metil-4H-[1,2,4]triazol-3-il)-benzonitrilo
151	5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol
152	5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-tiol
153	5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol
154	5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-tiol
155	5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-tiol
156	5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]-triazol-3-tiol
157	5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-tiol
158	5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-tiol
159	4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-tiol
160	5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]-triazol-3-tiol

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Ejemplo No.	Nombre
161	5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]-triazol-3-tiol
162	5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-tiol
163	5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]-triazol-3-tiol
164	4-etil-5-pirimidin-5-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
165	4-etil-5-furan-3-il-2,4-dihidro-[1,2,4]triazol-3-tiona
166	4-(tetrahidrofuran-2-ilmetil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
167	5-ciclopentil-4-etil-2,4-dihidro-[1,2,4]-triazol-3-tiona
168	4-etil-5-[2-(4-metoxi-fenil)-etil]-2,4-dihidro-[1,2,4]triazol-3-tiona

EJEMPLO 169

5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol

Se mezcla ácido 3,5-dicloro-benzoico (382 mg, 2 mmoles) con trietilamina (606 mg, 3 mmoles) en THF (6 ml) a 10°C. Después se agrega, mediante goteo, cloroformiato de isobutilo (300 mg, 2.2 mmoles) y se agita durante 45 minutos. A la mezcla de reacción se agrega 4-metil-3-tiosemicarbazida (238.4 mg, 2 mmoles). Después que se agita a temperatura ambiente durante 10 minutos, la mezcla de reacción se calienta a 70°C durante la noche. Tratamiento estándar. El producto se purifica mediante cromatografía en

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columna con acetato de etilo al 25-30% en hexanos para obtener 46.4 mg (8.5%) de 5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol.

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 169:

Ejemplo No.	Nombre
170	5-(3-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol
171	5-(4-metilfenil)-4-etil-4H-[1,2,4]triazol-3-tiol
172	4-etil-5-(3-nitrofenil)-4H-[1,2,4]triazol-3-tiol
173	5-(2,5-difluorofenil)-4-etil-4H-[1,2,4]-triazol-3-tiol
174	5-(3-clorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol
175	5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-tiol

EJEMPLO 176

4-etil-5-metoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona

Paso 1

N-etil-2-(metoxiacetil)hidrazincarbotioamida:

Se mezclan ácido metoxiacético (360 mg, 3.99 mmoles), 4-etil-3-tiosemicarbazida (581 mg, 4.87 mmoles), diisopropilcarbodi-imida (615 mg, 4.87 mmoles) e hidroxi-benzotriazol (69.6 mg, 0.51 mmoles) en dimetil-formamida (10 ml) y se agitan bajo argón a temperaturas ambientales durante 19 horas. Después de evaporar hasta

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sequedad el producto crudo se utiliza directamente en el siguiente paso.

MS (ESI) m/z 192 (M+1).

Paso 2

4-etil-5-metoximetil-2,4-dihidro-[1,2,4]triazol-3-tiona:

Se suspenden N-etil-2-(metoxiacetil)hidrazincarbotioamida (760 mg de producto crudo, 4 mmoles) y bicarbonato de sodio (560 mg, 6.6 mmolwa) en agua (15 ml) y se someten a reflujo durante 5 horas. Después de enfriar y filtrar, el filtrado se acidula con ácido clorhídrico concentrado, seguido por extracción con acetato de etilo. Después de evaporar hasta sequedad el producto crudo se recristaliza con acetato de etilo/heptano. La filtración y recristalización de la solución madre permite obtener un rendimiento combinado de 325 mg (47%) del compuesto del título.

^{1}H RMN ($CDCl_3$), δ (ppm): 4.47 (s, 2H), 4.13 (q, 2H), 3.37 (s, 3H), 1.38 (t, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 176:

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Ejemplo No.	Nombre
177	4-metil-5-piridin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
178	4-alil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
179	4-etil-5-(4-metoxi-fenoximetil)-2,4-dihidro-[1,2,4]triazol-3-tiona
180	4-etil-5-fenoximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona
181	4-etil-5-hidroximetil-2,4-dihidro-[1,2,4]-triazol-3-tiona
182	4-etil-5-(2-metoxi-etil)-2,4-dihidro-[1,2,4]-triazol-3-tiona
183	4-etil-5-metilsulfanilmetil-2,4-dihidro-[1,2,4]triazol-3-tiona
184	5-etoximetil-4-etil-2,4-dihidro-[1,2,4]triazol-3-tiona
185	5-furan-3-il-4-metil-2,4-dihidro-[1,2,4]-triazol-3-tiona
186	4-metil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
187	4-etil-5-piridazin-4-il-2,4-dihidro-[1,2,4]-triazol-3-tiona
188	4-etil-5-piridin-4-ilmetil-2,4-dihidro-[1,2,4]-triazol-3-tiona
189	4-etil-5-(6-hidroxi-piridin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona
190	4-etil-5-(4-hidroxi-fenil)-2,4-dihidro-[1,2,4]triazol-3-tiona
191	4-etil-5-p-toliloximetil-2,4-dihidro-[1,2,4]triazol-3-tiona
192	4-etil-5-(6-metoxipiridin-3-il)-2,4-dihidro[1,2,4]triazol-3-tiona
193	4-etil-5-(2-metoxi-piridin-4-il)-2,4-dihidro-[1,2,4]triazol-3-tiona
194	4-etil-5-pirimidin-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
195	4-etil-5-(5-metoxi-pirimidin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona

EJEMPLO 196

4-furan-2-ilmetil-4H-[1,2,4]triazol-3-tiol

Se agrega una solución de hidrazida de ácido fórmico (439 mg, 7.809 mmoles) en piridina (20 ml) a una solución de 2-isotiocianatometil-furano (1 g, 7.185 mmoles) en piridina (20 ml). La reacción toma lugar a temperatura ambiente durante la noche, y se agrega etanol (20 ml) directamente a la reacción y se coloca en una baño a 80C durante la noche. Se evapora el solvente y el compuesto del título (1.09 g, 83%) se obtiene a partir de la purificación mediante cromatografía de SPE en gel de sílice con 500 ml al 20%, 250 ml al 25%, 250 ml al 30%, 250 ml al 35%, 250 ml al 40%, y 250 ml al 50% de acetato de etilo en hexanos.

^{1}H RMN (CD_3OD), δ (ppm): 14.0 (bs, 1H), 8.19 (s, 1H), 7.52 (q, 1H), 6.52 (m, 1H), 6.42 (m, 1H), 4.90 (s, 2H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 196:

Ejemplo No.	Nombre
197	4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-tiol
198	4-ciclopropilmetil-5-piridin-4-il-4H-[1,2,4]triazol-3-tiol

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EJEMPLO 199

4-ciclopropil-5-tiofen-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona

A una suspensión de hidrazida de ácido tiofen-2-carboxílico (866 mg, 6.09 mmoles) en iPrOH (25 ml) se agrega isotiocianato-ciclopropano (602 mg, 6.08 mmoles). La mezcla se agita a 70°C durante 72 horas y después se enfría hasta temperatura ambiente. Se filtra el precipitado de color blanco y se suspende en una mezcla de MeOH:H_2O (9:1, 40 ml) junto con NaOH acuoso (2%, 5 ml). La mezcla de reacción se agita a 70°C durante la noche y después se enfría hasta temperatura ambiente. El pH se ajusta a 4 aproximadamente con HCl acuoso (1N). El precipitado de color blanco se filtra, se lava con agua y se seca al vacío (829 mg, 61%).

^{1}H RMN (CD_3OD), δ (ppm): 7.67 (dd, 1H), 7.63 (dd, 1H), 7.17 (dd, 1H), 3.15 (m, 1H), 1.14 (m, 2H), 0.86 (m, 2H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 199:

Ejemplo No.	Nombre
200	5-furan-2-il-4-(2-metoxi-etil)-2,4-dihidro-[1,2,4]triazol-3-tiona
201	4-ciclopropil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
202	Ester metílico del ácido (3-tiofen-2-il-5-tioxo-1,5-dihidro-[1,2,4]triazol-4-il)-acético
203	4-ciclopropilmetil-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
204	4-(2-metoxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona
205	Tiofen-2-il-4-(2,2,2-trifluoroetil)-2,4-dihidro-[1,2,4]triazol-3-tiona
206	4-ciclopropil-5-pirimidin-4-il-2,4-dihidro-[1,2,4]triazol-3-tiona
207	4-ciclopropil-5-piridin-3-il-2,4-dihidro-[1,2,4]triazol-3-tiona

EJEMPLO 208

4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-tiol

A una solución de 4-etil-3-tiosemicarbazida (2.38 g, 20 mmoles) y trietilamina (6.06 g, 60 mmoles) en THF (30 ml), se agrega anhídrido trifluoro-acético (5.04 g, 24 mmoles). La mezcla de reacción se agita a temperatura ambiente durante una hora y se calienta a 60°C durante la noche. Tratamiento estándar, el producto se tritura con hexanos para obtener 564 g de 4-etil-5-trifluorometil-4H-[1,2,4]-triazol-3-tiol como un sólido de color café pálido.

^{1}H-RMN ($CDCl_3$) d(ppm): 12.64 (w, 1H), 4.22

(q, 2H) y 1.44 (t, 3H).

EJEMPLO 209

4-etil-3-metansulfonil-5-tiofen-2-il-4H-[1,2,4]triazol

El compuesto del título se sintetiza de conformidad con el método descrito en Åkerblom et al. J. Med. Chem. 16, 312 (1973). Se disuelve 4-etil-3-metilsulfanil-5-tiofen-2-il-4H-[1,2,4]triazol (1.14 g, 5.06 mmoles) en ácido acético glacial (20 ml) seguido por la adición de peróxido de hidrógeno al 30% (5 ml). Después de agitar a temperaturas ambientales durante 16 horas se agrega peróxido de hidrógeno al 30% adicional (5 ml). La mezcla se agita durante 3 horas a temperatura ambiente, después se calienta a 100°C durante 2.5 horas. Después de enfriar en un baño de hielo/agua la reacción se neutraliza con hidróxido de sodio y se extrae dos veces con diclorometano. Las capas orgánicas se combinan, se evaporan hasta sequedad y se secan al vacío para producir el compuesto del título (0.78 g, 60%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.60 (d, 1H), 7.56 (d, 1H), 7.22 (m, 1H), 4.51 (q, 2H), 3.58 (s, 3H), 1.55 (t, 3H).

El siguiente compuesto se prepara de manera

análoga la del ejemplo 209:

Ejemplo No.	Nombre
210	4-(5-metansulfonil-4-metil-4H-[1,2,4]triazol-3-il)-piridina

EJEMPLO 211

4-(2-hidroxi-etil)-5-tiofen-2-il-2,4-dihidro-[1,2,4]-triazol-3-tiona

A una suspensión de LAH (38.1 mg, 1.00 mmoles) en THF anhidro (8 ml) se agrega, mediante goteo, ácido (3-tiofen-2-il-5-tioxo-1,5-dihidro-[1,2,4]-triazol-4-il)-acético (101 mg, 0.42 mmoles) en THF anhidro (4 ml). La mezcla se hace reaccionar durante 2 horas y después se extingue con Na_2SO_4 acuoso saturado (10 ml). El THF se elimina a presión reducida y el residuo se acidula con HCl acuoso (3N) y se divide entre EtOAc y agua. La capa acuosa se extrae con EtOAc (3 x 20 ml). Las capas orgánicas combinadas se lavan con salmuera (15 ml), se secan ($MgSO_4$) y se concentran a presión reducida. El producto crudo se utiliza sin purificación en el siguiente paso.

^{1}H RMN (DMSO-d6), δ (ppm): 13.94 (s, 1H), 7.86 (d, 1H); 7.81 (d, 1H), 7.24 (dd, 1H), 5.09 (t,

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1H), 4.16 (t, 2H), 3.76 (q aparente, 2H).

EJEMPLO 212

4-(4,5-dimetil-4H-[1,2,4]triazol-3-il)-piridina

Se agregan lentamente 860 µl (10 mmoles) de cloruro de oxalilo a una solución de 731 mg (10 mmoles) de N-metil-acetamida y 2.33 ml (20 mmoles) de 2,6-lutidina en 20 ml de CH_2Cl_2 a 0°C. Después de 15 minutos se agregan, en una porción, 1.37 g (10 mmoles) de hidrazida del ácido isonicotínico. La mezcla resultante se agita a temperatura ambiente durante 1 hora y después se neutraliza con $NaHCO_3$ (sat). Se separan las fases, y la fase acuosa se extrae con CH_2Cl_2. Las fases orgánicas combinadas se secan y se concentran. El residuo se disuelve en 20 ml de ácido acético y se calienta a 120°C durante 2h. Después de enfriar, se elimina el solvente. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 10:1) permite obtener 765 mg (44%) de un sólido de color gris/blanco.

^1H RMN ($CDCl_3$), d (ppm): 2.52 (s, 3H) 3.66 (s, 3H) 7.58 (d, 2H) 8.76 (d, 2H).

EJEMPLO 213

Metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-amina

Se calienta con microondas, durante 5 minutos a 160°C, una mezcla de 1000 mg (4.35 mmoles) de yodhidrato de N-amino-N',N''-dimetil-guanidina (Henry; Smith; J.Amer.Chem.Soc.; 73; 1951; 1858) y 774 mg (4.35 mmoles) de clorhidrato de cloruro de isonicotinoilo en 3 ml de piridina. Se agrega K_2CO_3 (saturado) y la mezcla se extrae 4 veces con $CHCl_3$. La fase orgánica se seca y se concentra. La recristalización con etanol, agua y EtOAc produce 216 mg (26%) de un sólido de color blanco-amarillento.

^1H RMN (DMSO), d (ppm): 2.85 (d, 3H) 3.45 (s, 3H) 6.25 (d, 1H) 7.65 (m, 2H) 8.67 (m, 2H).

EJEMPLO 214

3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina

Se calienta a 120°C, durante la noche, una solución de 750 mg (3.1 mmoles) de yodhidrato de (1,4,5,6-tetrahidro-pirimidin-2-il)-hidrazina (ref. Krezel, Izabella; Pharmazie; EN; 49; 1; 1994; 27-31) y 552 mg (3.1 mmoles) clorhidrato de cloruro de isonicotinoilo en 3 ml de piridina. La mezcla de reacción se enfría y se diluye con K_2CO_3 (saturado) y se extrae con 3 x 10 ml de cloroformo. Los extractos

orgánicos combinados se secan y se concentran. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 10:1) permite obtener 83 mg (18%) de un sólido de color blanco.

^1H RMN ($CDCl_3$), d (ppm): 1.91 (m, 2H) 3.24 (m, 2H) 4.13 (m, 2H) 7.67 (m, 2H) 8.65 (m, 2H).

El siguiente compuesto se prepara de manera análoga a la del ejemplo 214:

Ejemplo No.	Nombre
215	3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]-triazolo[4,3-a]pirimidina

EJEMPLO 216

4-etil-5-(6-metoxi-piridazin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona

Paso 1

Acido 6-cloro-piridazin-3-carboxílico:

A una solución de 3-cloro-6-metil-piridazina (1.2 g, 9.3 mmoles) en H_2SO_4 (10 ml), se agrega, en porciones, dicromato de potasio (3.3 g, 11.2 mmoles). Después de la adición, la mezcla se agita a 50°C. La reacción se vierte en hielo y la mezcla se extrae tres veces con éter dietílico. Las fases orgánicas

combinadas se secan y se concentran para obtener el compuesto del título (840 mg, 57%).

LC-MS (M++1): 159 y 161 (3:1).

Paso 2

Ester metílico del ácido 6-cloro-piridazin-3-carboxílico:

Se somete a reflujo, durante 3 horas, una solución de ácido 6-cloro-piridazin-3-carboxílico (700 mg, 4.53 mmoles) en cloruro de tionilo (15 ml). La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega metóxido de sodio (244 mg, 4.53 mmoles) en MeOH (20 ml) al residuo y la solución se continúa agitando a temperatura ambiente (t. amb.). Se agrega H_2O y la mezcla se extrae tres veces con DCM. Las fases orgánicas combinadas se secan y se concentran. La cromatografía de vaporización instantánea (SiO_2, heptano/EtOAc 1:1) permite obtener 560 mg (72%) del compuesto del título.

^1H RMN ($CDCl_3$), δ (ppm): 4.09 (s, 3H), 7.69 (d, 1H), 8.18 (d, 1H).

LC-MS (M++1): 173 y 175 (3:1).

Paso 3

Ester metílico del ácido 6-metoxi-piridazin-

3-carboxílico:

Se somete a reflujo una solución del éster metílico del ácido 6-cloro-piridazin-3-carboxílico en NaOMe, en MeOH (1 M, 10 ml). Se agrega H_2O y la mezcla se extrae tres veces con DCM para obtener la fase orgánica I. Las fases orgánicas combinadas I se secan y se concentran para obtener el compuesto del título (40 mg, 10%). La fase acuosa se acidula con ácido clorhídrico concentrado y se extrae tres veces con DCM para obtener la fase orgánica II. Las fases orgánicas combinadas II se secan y se concentran para obtener ácido 6-metoxi-piridazin-3-carboxílico (LC-MS (M++1): 155) (230 mg, 65%). Se somete a reflujo una solución del ácido 6-metoxi-piridazin-3-carboxílico en cloruro de tionilo (6 ml) durante 3 h. La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega MeOH (10 ml) al residuo y la solución se continúa agitando a temperatura ambiente. Se agrega $NaHCO_3$ (acuoso) saturado y la mezcla se extrae tres veces con DCM. Las fases orgánicas combinadas se secan y se concentran para obtener el compuesto del título (253 mg, 100%).

LC-MS (M++1): 169.

<u>Paso 4</u>

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4-etil-5-(6-metoxi-piridazin-3-il)-2,4-dihidro-[1,2,4]triazol-3-tiona:

Se agrega NaOMe (86 mg, 1.6 mmoles) a una solución del éster metílico del ácido 6-metoxi-piridazin-3-carboxílico (210 mg, 1.25 mmoles) y 4-etil-3-tiosemicarbazida (190 mg, 1.6 mmoles) en MeOH (6 ml) y la mezcla se calienta hasta 70°C a 72 h. La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega H_2O (10 ml) al residuo y la mezcla se acidula con ácido clorhídrico concentrado y el compuesto del título, 35 mg (12%), se recolecta mediante filtración.

LC-MS (M++1): 238.

EJEMPLO 217

4-etil-5-(5-metoxi-piridin-2-il)-2,4-dihidro-[1,2,4]-triazol-3-tiona

Paso 1

Ester metílico del ácido 5-metoxi-piridin-2-carboxílico:

Se disuelve 5-metoxi-2-metil-piridina (700 mg, 5.69 mmoles) en H_2O (20 ml) y se calienta a 80°C. Se agrega a la solución $KMnO_4$ (4 g, 25.3 mmoles) en porciones, en el transcurso de 1 hora. Después de

agitar a 80°C durante 5 horas, la mezcla se filtra y el filtrado se lava con H_2O (60°C). Se concentra la fase acuosa combinada. Se agregan DMF (20 ml), K_2CO_3 (785 mg, 5.7 mmoles) seguido por MeI (540 ml, 8.6 mmoles) al residuo remanente y la mezcla se calienta a 80°C. La reacción se enfría hasta temperatura ambiente y se agrega H_2O y la mezcla se extrae tres veces con tolueno. Las fases orgánicas combinadas se secan y se concentran. La cromatografía de vaporización instantánea (SiO_2, heptano/EtOAc 1:1) permite obtener 210 mg (22%) del compuesto del título.

^1H RMN ($CDCl_3$):d ppm 3.93 (s, 3H) 4.00 (s, 3H) 7.23 (m, 1H) 8.13 (d, 1H) 8.40 (d, 1H).

Paso 2

4-etil-5-(5-metoxi-piridin-2-il)-2,4-dihidro-[1,2,4]triazol-3-tiona:

Se agrega NaOMe (4 ml, 4.0 mmoles, 1M) a una solución de éster metílico del ácido 5-metoxi-piridin-2-carboxílico (200 mg, 1.2 mmoles), 4-etil-3-tiosemicarbazida (145 mg, 1.2 mmoles) en MeOH (10 ml) y la mezcla se calienta a 70°C. La reacción se enfría hasta temperatura ambiente y se evapora hasta sequedad. Se agrega H_2O (10 ml) al residuo y la

mezcla se acidula con ácido clorhídrico concentrado y el compuesto del título 50 mg (18%) se recolecta mediante filtración.

LC-MS (M++1): 237.

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 10:

Ejemplo No.	Nombre
218	5-clorometil-3-fenil-[1,2,4]oxadiazol
219	5-clorometil-3-(3-fluoro-fenil)-[1,2,4]-oxadiazol
220	5-clorometil-3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol
221	5-clorometil-3-tiofen-2-il-[1,2,4]oxadiazol
222	5-clorometil-3-tiofen-3-il-[1,2,4]oxadiazol
223	3-(5-clorometil-[1,2,4]oxadiazol-3-il)-fenol
224	5-clorometil-3-o-tolil-[1,2,4]oxadiazol
225	5-clorometil-3-(3-clorofenil)-[1,2,4]oxadiazol
226	5-clorometil-3-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 16:

Ejemplo No.	Nombre
227	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo
228	2-cloro-4-(3-clorometil-[1,2,4]oxadiazol-5-il)-piridina
229	3-clorometil-5-(2,5-dimetil-fenil)-[1,2,4]-oxadiazol

Ejemplo No.	Nombre
230	3-clorometil-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol
231	3-clorometil-5-(2,5-diclorofenil)-[1,2,4]-oxadiazol
232	3-clorometil-5-(2-fluoro-5-bromo-fenil)-[1,2,4]oxadiazol
233	3-clorometil-5-(3-metil-fenil)-[1,2,4]oxadiazol
234	3-clorometil-5-(2,5-difluoro-fenil)-[1,2,4]-oxadiazol
235	3-clorometil-5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol
236	3-clorometil-5-(3-ciclopropil-fenil)-[1,2,4]-oxadiazol
237	Ester metílico del ácido 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-carbámico
238	1-[3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-etanona
239	5-(5-cloro-2-fluoro-fenil)-3-clorometil-[1,2,4]oxadiazol
240	2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-fenol

EJEMPLO 241

3-clorometil-5-(2-cloro-5-metil-fenil)-[1,2,4]-oxadiazol

Se trata ácido 2-cloro-5-metil-benzoico (1 g, 5.8 mmoles) con 5 ml cloruro de tionilo a reflujo durante dos horas. Se elimina el exceso de cloruro de tionilo a presión reducida. El residuo se agrega a una suspensión de 2-cloro-N-hidroxi-acetamidina (638 mg, 5.8 mmoles) en diclorometano (10 ml) a temperatura

ambiente. Después de agitar durante 30 minutos, se agrega trietilamina (2.04 ml, 14.6 mmoles) y se agita durante una hora adicional. La mezcla de reacción se diluye con acetato de etilo, se lava con agua y salmuera, se seca con sulfato de sodio anhidro, se filtra y se concentra. La cromatografía de vaporización instantánea en columna utilizando acetato de etilo al 10-20% en hexanos permite obtener 460 mg del intermediario éster acíclico. Se agrega DMF a este intermediario y después se calienta hasta 135°C durante 4 horas para efectuar la ciclización hasta oxadiazol. Después de enfriar, la mezcla de reacción se lava con agua (3 veces) y salmuera, se seca con sulfato de sodio anhidro, se filtra, y se concentra. La purificación mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo al 5% en hexanos permite obtener el compuesto del título, 160 mg (12% en los 2 pasos) como un sólido de color blanco.

m/z 244 (GCMS).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 241:

Ejemplo No.	Nombre
242	3-clorometil-5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadiazol
243	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-benzonitrilo

Ejemplo No.	Nombre
244	3-clorometil-5-(3-fluoro-fenil)-[1,2,4]-oxadiazol
245	3-clorometil-5-(2-metil-tiazol-4-il)-[1,2,4]-oxadiazol
246	3-clorometil-5-(4-fluoro-fenil)-[1,2,4]-oxadiazol
247	5-(5-bromo-2-fluoro-fenil)-3-clorometil-[1,2,4]oxadiazol
248	3-clorometil-5-(4-metil-tiofen-2-il)-[1,2,4]-oxadiazol
249	5-(3-clorometil-[1,2,4]oxadiazol-5-il)-tiofen-3-carbonitrilo
250	2-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-metil-benzonitrilo
251	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-5-fluoro-benzonitrilo
252	3-(3-clorometil-[1,2,4]oxadiazol-5-il)-4-fluoro-benzonitrilo
253	4-cloro-2-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenol
254	3-(1-cloro-etil)-5-(3-clorofenil)-[1,2,4]-oxadiazol
255	3-(1-cloro-etil)-5-(3-fluoro-fenil)-[1,2,4]-oxadiazol
256	3-(1-cloro-etil)-5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol

EJEMPLO 257

[3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-metanol

Se disuelven ácido 3-hidroximetilbenzoico, descrito en Reed, G. A.; Dimmel, D.R.; Malcolm, E. W. J. Org. Chem. 1993, 58 (23), 6372-6376, (175 mg, 1.15 mmoles), 2-cloro-N-hidroxi-acetamidina (125 mg, 1.15 mmoles) y HBTU en DMF anhidra (4 ml). Se agrega

trietilamina (0.48 ml, 3.5 mmoles) y la reacción se agita a temperatura ambiente durante la noche. El producto crudo se separa entre diclorometano y $NaHCO_3$ (acuoso), la fase orgánica se seca ($MgSO_4$) y el diclorometano se elimina al vacío. La solución en DMF resultante se calienta a 120°C durante la noche. La mezcla de reacción se concentra al vacío y el compuesto del título (64 mg, 25%) se aísla mediante cromatografía de vaporización instantánea utilizando acetato de etilo al 25-50% en heptano.

^1H RMN ($CDCl_3$), δ (ppm): 8.15 (s, 1H), 8.06 (d, 1H), 7.62 (d, 1H), 7.53 (t, 1H); 4.80 (d, 2H), 4.66 (s, 1H); 1.99 (br. t, 1H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 257:

Ejemplo No.	Nombre
258	3-clorometil-5-[1-(toluen-4-sulfonil)-1H-pirrol-3-il]-[1,2,4]oxadiazol
259	3-clorometil-5-furan-3-il-[1,2,4]oxadiazol
260	3-clorometil-5-(5-cloro-tiofen-2-il)-[1,2,4]-oxadiazol

EJEMPLO 261

1-[5-(3-clorofenil)-[1,3,4] oxadiazol-2-il]-etanol

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Paso 1

1-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etoxi}-1H-benzotriazol:

Se disuelven 2-(1-cloro-etil)-5-(3-cloro-fenil)-[1,3,4]oxadiazol (109 mg, 0.45 mmoles), hidroxibenzotriazol (76.4 mg, 0.56 mmoles) y yoduro de potasio (23.0 mg, 0.14 mmoles) en DMF (2.5 ml), seguido por la adición de carbonato de potasio (74.0 mg, 0.53 mmoles). Después de agitar bajo argón a temperaturas ambientales durante 24 horas la mezcla de reacción se diluye con acetato de etilo y se lava con solución de cloruro de amonio 2N. Después de volver a extraer la capa acuosa con acetato de etilo, las capas orgánicas combinadas se lavan con salmuera y se evaporan hasta sequedad. La cromatografía en columna en 12 g de sílice utilizando heptano/acetato de etilo = 4/1 permite obtener, después de secar al vacío, el compuesto del título (129 mg, 84%).

^{1}H RMN ($CDCl_3$), δ (ppm): 7.94 (d, 1H), 7.82 (m, 1H), 7.76 (m, 1H), 7.46 (m, 1H), 7.39-7.27 (m, 4 H), 5.98 (q, 1H), 2.04 (d, 3H).

Paso 2

1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etanol:

Se disuelve, bajo argón 1-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etoxi)-1H-benzotriazol (58.4 mg, 0.17 mmoles) en THF seco (3 ml). A esta mezcla se agrega lentamente una solución 0.1 molar de diyoduro de samario en THF (5 ml, 0.5 mmoles) en el transcurso de 20 minutos. Después de agitar durante 80 minutos se agrega solución adicional de diyoduro de samario (4 ml, 0.4 mmoles) durante 5 minutos. La mezcla de reacción se extingue, después de 15 minutos adicionales de agitación, con $Na_2S_2O_3$ acuoso, se diluye con éter dietílico y se lava con ácido clorhídrico acuoso 1M, se seca con sulfato de sodio y se evapora hasta sequedad. Después de secar al vacío se obtiene el compuesto del título crudo (36.0 mg, 92%) el cual se utiliza en el siguiente paso sin purificación adicional.

^{1}H RMN ($CDCl_3$), δ (ppm): 7.98-7.75 (m, 2H), 7.50-7.38 (m, 2H), 5.25 (q, 1H), 1.74 (d, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 261:

Ejemplo No.	Nombre
262	[5-(5-cloro-2-fluoro-fenil)-[1,2,4]-oxadiazol-3-il]-metanol

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EJEMPLO 263

1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etanol

A una solución de 3.19 g (30.6 mmoles) de 2,N-dihidroxi-propionamidina en 25 ml de piridina se agregan 4.3 ml (33.7 mmoles) de cloruro de 3-cloro-benzoilo a 0°C. Se retira el enfriamiento y la mezcla se agita a temperatura ambiente durante 25 minutos y a reflujo durante 25 minutos. Después de enfriar, la mezcla se vierte en agua y se extrae dos veces con CH_2Cl_2. La fase orgánica se seca y se concentra. La recristalización con heptano/EtOAc permite obtener 4.12 g (60%) de un sólido de color blanco.

^1H RMN ($CDCl_3$), d (ppm): 1.68 (d, 3H) 2.67 (m, 1H) 5.09 (m, 1H) 7.46 (t, 1H) 7.56 (d, 1H) 8.01 (d, 1H) 8.13 (s, 1H).

EJEMPLO 264

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanol

Paso 1

N-{4-[(Z)-{[5-(3-clorofenil)-1,2,4-oxadiazol-3-il]metilen}(óxido)amino]fenil}-N,N-dimetilamina:

El compuesto del título se sintetiza de

conformidad con el método descrito en Palazzo et al. J. Heterocycl. Chem. (1979) 16:1469. Se disuelve cloruro de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metil]-piridinio (1.81 g, 5.87 mmoles) en agua (20 ml). A esta solución se agrega 4-nitroso-N,N-dimetilanilina (0.88 g, 5.86 mmoles) disuelta en etanol (50 ml), seguido por la adición lenta de hidróxido de sodio acuoso 1 molar (5.9 ml, 5.9 mmoles) en el transcurso de un periodo de 3 minutos. Después de 1 hora, se filtra el precipitado formado, se lava con agua y se seca al aire para obtener el compuesto del título (2.08 g, húmedo) el cual se utiliza inmediatamente en el siguiente paso.

MS (ESI) m/z 344 (M+1).

Paso 2

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanodiol:

Se suspende N-{4-[(Z)-{[5-(3-clorofenil)-1,2,4-oxadiazol-3-il]metilen)(óxido)amino]fenil}-N,N-dimetilamina (2.08 g húmedo) en éter dietílico (30 ml), seguido por la adición de ácido clorhídrico acuoso 1 molar. La mezcla se agita vigorosamente durante 20 minutos, se transfiere a un embudo de separación y se diluye con éter dietílico y ácido

clorhídrico acuoso 1 molar. Después de la extracción, la capa acuosa se extrae dos veces más con éter dietílico. La combinación de las capas orgánicas, secado con sulfato de magnesio, seguido por evaporación hasta sequedad y secado al vacío permite obtener el compuesto del título como producto crudo (0.56 g, 42% a partir de cloruro de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piridinio).

MS (ESI) m/z 227 (M+1).

Paso 3

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-metanol:

Se disuelve cloruro de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piridinio (99.3 mg, 0.44 mmoles) en metanol (4 ml) seguido por la adición de borohidruro de sodio (32 mg, 0.84 mmoles). Se agrega más borohidruro de sodio después de 2 horas y se deja que la reacción proceda durante la noche. La mezcla de reacción se diluye con diclorometano y cloruro de amonio acuoso y se agita vigorosamente. Después de separar las capas y lavar la capa orgánica con salmuera, seguido por evaporación hasta sequedad, se obtiene el producto crudo. Este se purifica mediante cromatografía de vaporización instantánea utilizando

heptano/acetato de etilo lo cual produce el compuesto del título (32.0 mg, 32%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.11 (s, 1H), 8.00 (d aparente, 1H), 7.56 (d aparente, 1H), 7.46 (t aparente, 1H), 4.87 (d, 2H), 2.91 (t, 1H).

EJEMPLO 265

2-clorometil-5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol

Se calientan a 120°C hidrazida de ácido 2-fluoro-5-metil-benzoico (320 mg, 1.9 mmoles) y 2-cloro-1,1,1-trietoxi-etano (1.9 ml) en un frasco sellado durante 30 minutos. La mezcla de reacción se coloca directamente en una columna de vaporización instantánea (gel de sílice) y se purifica utilizando acetato de etilo al 0-5% en hexanos para obtener 2-clorometil-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol (284.5 mg, 66%).

^{1}H RMN ($CDCl_3$) d (ppm): 7.89 (q, 1H), 7.36 (m, 1H), 7.16 (t, 1H), 4.81 (s, 2H), 2.43 (s, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 265:

Ejemplo No.	Nombre
266	2-clorometil-5-(3-clorofenil)-[1,3,4]-oxadiazol

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Ejemplo No.	Nombre
267	4-(5-clorometil-[1,3,4]oxadiazol-2-il)-2-metil-piridina
268	2-clorometil-5-m-tolil-[1,3,4]oxadiazol
269	3-(5-clorometil-[1,3,4]oxadiazol-2-il)-benzonitrilo
270	2-cloro-4-(5-clorometil-[1,3,4]oxadiazol-2-il)-piridina
271	2-(5-cloro-2-fluoro-fenil)-5-clorometil-[1,3,4]oxadiazol

EJEMPLO 272

2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]oxadiazol

Se calientan a 120°C hidrazida de ácido 3-cloro-benzoico (170 mg, 1 mmoles) y 2-bromo-1,1,1-trietoxi-propano (1 ml) en un frasco sellado durante 10 minutos. La mezcla de reacción se coloca directamente en una columna de vaporización instantánea (gel de sílice) y se purifica utilizando diclorometano al 0-5% en hexanos. El producto se vuelve a purificar mediante cromatografía de vaporización instantánea utilizando una mezcla de acetato de etilo:hexanos: diclorometano (1:19:20) para obtener 2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol (93 mg, 32%, aceite incoloro).

^{1}H RMN ($CDCl_3$) d (ppm): 8.09 (t, 1H), 7.99

(t, 1H), 7.55 (m, 3H), 5.30 (m, 1H), 2.21 (q, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 272:

Ejemplo No.	Nombre
273	2-(1-bromo-etil)-5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol
274	4-[5-(1-bromo-etil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina
275	2-(1-bromo-etil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol
276	2-(1-bromo-etil)-5-(3-clorofenil)-[1,3,4]-oxadiazol

EJEMPLO 277

3-(1-bromo-etil)-5-(3-clorofenil)-[1,2,4]oxadiazol

Se agrega mediante goteo una solución de 396 mg (2.22 mmoles) de N-bromosuccinimida en 2 ml de THF a una solución de 583 mg (2.22 mmoles) de trifenilfosfina en 2 ml de THF a 0°C. Después de agitar durante 20 minutos, se agregan 416 mg (1.85 mmoles) de 1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etanol en 2 ml de THF. Se continúa agitando durante la noche a temperatura ambiente antes de eliminar el solvente a presión reducida. La cromatografía de vaporización instantánea (heptano/EtOAc 6:1) permite obtener 168 mg (32%).

^{1}H RMN ($CDCl_3$), d (ppm): 2.12 (d, 3H) 5.21

(q, 1H) 7.47 (t, 1H) 7.57 (m, 1H) 8.03 (d, 1H) 8.15 (s, 1H).

EJEMPLO 278

1-[5-(3-clorofenil)-isoxazol-3-il]-etanol

Paso 1

Ester etílico del ácido 4-(3-clorofenil)-2,4-dioxo-butírico:

Se agrega en porciones, hidruro de sodio (dispersión en aceite al 60%, 1.24 g, 31.1 mmoles) a una solución de 3-cloroacetofenona (4.0 g, 25.9 mmoles) y oxalato de dietilo (4.54 g, 31.1 mmoles) en DMF (32 ml) a 0°C. La mezcla se agita a temperatura ambiente durante 1 hora y después se calienta hasta 80°C durante media hora. Después de enfriar, la mezcla se trata con HCl 3N y después se diluye con acetato de etilo. La capa orgánica se lava con agua (3X) y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra. El residuo resultante se purifica después mediante cromatografía de vaporización instantánea en sílice utilizando acetato de etilo al 0-10% en hexanos para obtener el éster etílico del ácido 4-(3-clorofenil)-2,4-dioxo-butírico (4.43g, 67%, sólido de color amarillo).

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^{1}H RMN ($CDCl_3$) d (ppm): 15.12 (br s, 1H), 7.98 (s, 1H), 7.88 (d, 1H), 7.58 (d, 1H), 7.47 (t, 1H), 7.05 (s, 1H), 4.39 (m, 2H), 1.41 (m, 3H).

Paso 2

Ester etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico:

Se calienta a 80°C, durante 4 horas, una solución de éster etílico del ácido 4-(3-clorofenil)-2,4-dioxo-butírico (3.0 g, 11.8 mmoles) y clorhidrato de hidroxilamina (2.46 g, 35.4 mmoles) en metanol (60 ml). Después de enfriar, la mezcla se filtra y se lava con metanol frío para obtener el éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (2.0 g, 71%, sólido de color blanco).

^{1}H RMN ($CDCl_3$) d (ppm): 7.82 (s, 1H), 7.72 (m, 1H), 7.47 (m, 2H), 4.03 (s, 3H). Mezcla de ambos ésteres metílico y etílico (principalmente metílico).

Paso 3

1-[5-(3-clorofenil)-isoxazol-3-il]-etanona:

En un frasco con tapa roscada equipado con barra de agitación, se agrega yoduro de metilmagnesio (3M en éter dietílico) (0.79 ml, 2.38 mmoles), tolueno (1 ml), tetrahidrofurano (0.39 ml, 4.77 mmoles) y

trietilamina (1 ml, 7.15 mmoles). La solución se enfría hasta 0°C y a ésta se agrega solución de éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (300 mg, 1.19 mmoles) en tolueno (5 ml). La mezcla resultante se deja agitando a 0°C durante 5 horas. La mezcla de reacción se extingue con ácido clorhídrico 1N (acuoso, 6.5 ml, 6.5 mmoles), se diluye con tolueno (35 ml), se lava en forma secuencial con agua (50 ml), bicarbonato de sodio saturado (acuoso, 30 ml), agua (50 ml) y salmuera (30 ml). La fase orgánica se concentra al vacío. El residuo aislado se disuelve en metanol (8 ml) e hidróxido de potasio al 20% (acuoso, 1 ml). La mezcla se agita a 45°C durante 30 minutos. En este punto la mezcla se concentra al vacío. El residuo aislado se disuelve en tolueno (60 ml), se lava en forma secuencial con agua (50 ml), bicarbonato de sodio saturado (acuoso, 50 ml) y agua (50 ml). La fase orgánica se concentra al vacío. El residuo crudo se purifica en gel de sílice utilizando acetato de etilo al 2% en hexanos para aislar el compuesto deseado como un sólido de color blanco (156 mg, 60%).

^{1}H RMN ($CDCl_3$), d (ppm): 7.77 (m, 1H), 7.66 (m, 1H), 7.42 (m, 2H), 6.90 (s, 1H), 2.69 (s, 3H).

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Paso 4

1-[5-(3-clorofenil)-isoxazol-3-il]-etanol:

En un frasco con tapa roscada equipado con barra de agitación se agrega 1-[5-(3-clorofenil)-isoxazol-3-il]-etanona (100 mg, 0.45 mmoles), borohidruro de sodio (34 mg, 0.90 mmoles) y metanol (3 ml). La mezcla resultante se deja agitando a temperatura ambiente durante 3 horas. La reacción se extingue con agua (30 ml) y salmuera (30 ml), se extrae con diclorometano (3 X 30 ml). La fase orgánica combinada se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar 1-[5-(3-clorofenil)-isoxazol-3-il]-etanol como un sólido de color blanco (110 mg).

^{1}H RMN ($CDCl_3$), d (ppm): 7.69 (m, 1H), 7.59 (m, 1H), 7.37 (m, 2H), 6.59 (s, 1H), 5.07 (q, 1H), 3.45 (bs, 1H), 1.58 (d, 3H).

El siguiente compuesto se prepara de manera análoga a la del ejemplo 278:

Ejemplo No.	Nombre
279	1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etanol

Los siguientes compuestos se preparan en

forma análoga a la del éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (paso 2 en la síntesis del ejemplo 279):

Ejemplo No.	Nombre
280	Ester metílico del ácido 5-(2-fluoro-5-metil-fenil)-isoxazol-3-carboxílico
281	Ester metílico del ácido 5-tiofen-3-il-isoxazol-3-carboxílico
282	Ester metílico del ácido 5-fenil-isoxazol-3-carboxílico
283	Ester etílico del ácido 5-(3-clorofenil)-4-metil-isoxazol-3-carboxílico
284	Ester metílico del ácido 5-(5-cloro-tiofen-3-il)-isoxazol-3-carboxílico

EJEMPLO 285

[5-(3-clorofenil)-isoxazol-3-il]-metanol

Se agrega lentamente hidruro de litio y aluminio (320 mg, 8.4 mmoles) a una solución de éster etílico del ácido 5-(3-clorofenil)-isoxazol-3-carboxílico (2.0 g, 8.4 mmoles) en THF (100 ml) a temperatura ambiente. Después de 1 hora, la mezcla de reacción se extingue con agua y después se extrae con acetato de etilo. La capa orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra. El residuo resultante se purifica después mediante cromatografía de vaporización instantánea utilizando acetato de

etilo al 15-40% en hexano para obtener [5-(3-clorofenil)-isoxazol-3-il]-metanol (1.32 g, 75%, sólido de color amarillo).

^{1}H RMN ($CDCl_3$) d (ppm): 7.78 (s, 1H), 7.68 (m, 1H), 7.43 (m, 2H), 6.63 (s, 1H), 4.84 (d, 2H), 2.23 (t, 1H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 285:

Ejemplo No.	Nombre
286	[2-(3-clorofenil)-oxazol-4-il]-metanol
287	[3-(3-clorofenil)-isoxazol-5-il]-metanol
288	5-(tiofen-3-il-isoxazol-3-il)metanol
289	[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-metanol
290	(5-fenil-isoxazol-3-il)-metanol
291	[5-(3-clorofenil)-4-metil-isoxazol-3-il]-metanol
292	[5-(5-cloro-tiofen-3-il)-isoxazol-3-il)]-metanol

EJEMPLO 293

Ester 1-[5-(3-clorofenil)-isoxazol-3-il]-etílico del ácido metansulfónico

En un frasco con tapa roscada equipado con barra de agitación se agrega 1-[5-(3-clorofenil)-

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isoxazol-3-il]-etanol (110 mg, 0.49 mmoles), diclorometano (3 ml) y trietilamina (0.34 ml, 2.46 mmoles). La mezcla se enfría hasta 0°C y a ésta se agrega cloruro de metansulfonilo (0.08 ml, 0.98 mmoles). La mezcla de reacción se deja agitando a temperatura ambiente durante 30 minutos. La reacción se extingue con bicarbonato de sodio saturado (acuoso, 40 ml) y se extrae con diclorometano (3X30 ml). La fase orgánica combinada se lava con salmuera (40 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar el compuesto deseado como un aceite de color café.

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 293:

Ejemplo No.	Nombre
294	Ester 2-(3-clorofenil)-oxazol-4-ilmetílico del ácido metansulfónico
295	Ester 3-(3-clorofenil)-isoazol-5-ilmetílico del ácido metansulfónico
296	Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetílico del ácido metansulfónico
297	Ester -fenil)-isoxazol-5-il]-etílico del ácido metansulfónico
298	Ester 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetílico del ácido metansulfónico
299	Ester 5-(3-clorofenil)-isoxazol-3-ilmetílico del ácido metansulfónico
300	Ester 5-tiofen-3-il-isoxazol-3-ilmetílico del ácido metansulfónico
301	Ester 5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetílico del ácido metansulfónico
302	Ester 5-fenil-isoxazol-3-ilmetílico del ácido metansulfónico

Ejemplo No.	Nombre
303	Ester 5-(3-clorofenil)-4-metil-isoxazol-3-ilmetílico del ácido metansulfónico
304	Ester 5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetílico del ácido metansulfónico
305	Ester 1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico
306	Ester 1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etílico del ácido metansulfónico

EJEMPLO 307

Ester 4-cloro-5-(3-clorofenil)-isoxazol-3-ilmetílico del ácido metansulfónico

Se agrega cloruro de sulfurilo (1 ml) al éster 5-(3-clorofenil)-isoxazol-3-il-metílico del ácido metansulfónico (200 mg, 0.70 mmoles) y después se agita a 60°C durante la noche. La mezcla de reacción se diluye con diclorometano, se lava con bicarbonato de sodio saturado, se seca con sulfato de sodio anhidro, se filtra y se concentra para obtener éster 4-cloro-5-(3-clorofenil)-isoxazol-3-il-metílico del ácido metansulfónico (219 mg„ 97%, sólido de color café claro).

^{1}H RMN ($CDCl_3$) d (ppm): 8.07 (m, 1H), 7.92 (m, 1H), 7.50 (m, 2H), 5.38 (s, 2H), 3.16 (s, 3H).

EJEMPLO 308

Ester metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico

Paso 1

3-cloro-N-hidroxi-benzamidina:

Se agrega una solución de 3-cloro-benzaldehído (3.35 ml, 0.030 mmoles) en etanol (40 ml) a una solución de clorhidrato de hidroxilamina (2.47 g, 0.036 mmoles) e hidróxido de sodio (1.42 g, 0.036 mmoles) en agua (20 ml) a temperatura ambiente y después se calienta a 90°C durante 24 horas. Después de enfriar, se concentra la mezcla de reacción, el residuo se diluye con agua y después el precipitado se filtra y se seca para obtener 3-cloro-N-hidroxi-benzamidina (1.13 g, 93%).

^{1}H RMN ($CDCl_3$) d (ppm): 8.11 (s, 1H), 7.72 (s, 1H), 7.61 (m, 1H), 7.46 (m, 1H), 7.36 (m, 1H).

Paso 2

Cloruro de 3-cloro-N-hidroxi-benzimidoilo:

Se agrega N-clorosuccinimida (858 mg, 6.4 mmoles) a una solución de 3-cloro-N-hidroxi-benzamidina (1 g, 6.4 mmoles) a temperatura ambiente

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y se agita durante 1 hora. La mezcla de reacción se diluye con éter dietílico y después se lava con agua (3X), se seca con sulfato de magnesio anhidro, se filtra, y se concentra para obtener el compuesto del título (1.13 g, 93%).

^{1}H RMN ($CDCl_3$) d (ppm): 8.03 (s, 1H), 7.87 (m, 1H), 7.76 (m, 1H), 7.43 (m,1H).

Paso 3

Ester metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico:

Se agrega mediante goteo trietilamina (0.73 ml, 5.3 mmoles) a una solución de cloruro de 3-cloro-N-hidroxi-bencimidoilo (1.0 g, 5.3 mmoles) y propiolato de metilo (2.2 ml, 25.3 mmoles) en un baño de hielo. La mezcla de reacción se calienta hasta temperatura ambiente y se deja en agitación durante la noche. Después de diluir la reacción con diclorometano, la capa orgánica se lava con agua y salmuera saturada, se seca con sulfato de sodio anhidro, se filtra, y se concentra. La purificación mediante cromatografía de vaporización instantánea eluyendo con hexanos al 50% en acetato de etilo y después la recristalización con metanol permite obtener el éster metílico del ácido 3-(3-clorofenil)-isoxazol-5-carboxílico (635 mg, 51%,

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sólido de color blanco).

^{1}H RMN ($CDCl_3$) d (ppm): 7.86 (m, 1H), 7.74 (m, 1H), 7.46 (2H), 7.2 (s, 1H), 4.05 (s, 3H).

EJEMPLO 309

2-bromometil-5-(3-clorofenil)-oxazol

Paso 1

5-(3-clorofenil)-2-metil-oxazol:

A una solución de Tl(OAc)3 (4.2 g, 11.1 mmoles) en acetonitrilo (80 ml), se agrega mediante goteo ácido trifluorometansulfúrico (5 g, 33.3 mmoles) a temperatura ambiente y se agita durante 15 minutos. La mezcla de reacción se calienta después hasta 80°C y se agrega 1-(3-clorofenil)-etanona (1.14 g, 7.4 mmoles) en acetonitrilo (40 ml). Después de una hora, la reacción se extingue con diclorometano y bicarbonato de sodio saturado. La capa orgánica se seca, se purifica mediante cromatografía en columna con acetato de etilo al 5~19% en hexanos para obtener 1.2 g (83.9%) de 5-(3-clorofenil)-2-metil-oxazol como un aceite de color amarillo.

^{1}H RMN($CDCl_3$) d(ppm): 7.60 (s, 1H), 7.48 (d, 1H), 7.29 (m, 2H), 7.23 (s, 1H) y 2.34 (s, 3H).

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Paso 2

2-Bromometil-5-(3-clorofenil)-oxazol:

Se mezcla 5-(3-clorofenil)-2-metil-oxazol (580 mg, 3 mmoles) con NBS (531 mg, 3 mmoles) y BPOA (36.3 mg, 0.15 mmoles) en CCl_4 a temperatura ambiente. La mezcla de reacción se calienta a 75°C durante 2 horas y después se extingue con agua y diclorometano. La capa orgánica se seca, se concentra, se purifica mediante cromatografía en columna con acetato de etilo al 2~5% en hexanos para obtener 562 mg (68.3%) de 2-bromometil-5-(3-clorofenil)-oxazol como un aceite de color amarillo.

^{1}H RMN($CDCl_3$) d(ppm): 7.67 (s, 1H), 7.54 (d, 1H), 7.35(m, 3H) y 4.56 (s, 2H).

EJEMPLO 310

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico

A una mezcla de ácido 3-clorobenzoico (5.0 g, 31.9 mmoles), clorhidrato de éster metílico de serina (6.1 g, 31.9 mmoles) y HOBt (4.31 g, 31.9 mmoles) en DMF (100 ml) se agrega N-metilmorfolina (NMM) (7.0 ml, 63.8 mmoles) y EDCI (4.97 g, 31.9

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mmoles) a 0°C. La mezcla se deja calentar hasta temperatura ambiente y se agita durante 18 horas. La mezcla se diluye con acetato de etilo (300 ml) y después se lava con agua (3 x 250 ml) seguido por salmuera. El extracto orgánico se seca con Na_2SO_4 (anhidro) y después se concentra al vacío para obtener el éster metílico del ácido 2-(3-cloro-benzoilamino)-3-hidroxi-propiónico, (7.2 g, 93%) de un sólido de color amarillo pálido.

^1H RMN ($CDCl_3$) d (ppm): 7.78 (s, 1H), 7.66 (d, 1H), 7.45, (dd, 1H), 7.34 (t, 1H), 7.25 (br, d, 1H), 4.82 (m, 1H), 4.08 (m, 2H), 3.79 (s, 3H), 3.19 (br, t, 1H).

A una solución del éster metílico del ácido 2-(3-cloro-benzoilamino)-3-hidroxi-propiónico (7.2 g, 29.6 mmoles) en CH_2Cl_2 a -20°C se agrega, mediante goteo, "De-oxofluor" (7.2 g, 32.6 mmoles). Después de agitar a esta temperatura durante 30 minutos, se agrega $BrCCl_3$ (3.6 g, 18.1 mmoles), mediante goteo, seguido por DBU (2.798, 18.1 mmoles). La mezcla se agita después a 2-3°C durante 8 horas y después se extingue con $NaHCO_3$ saturado seguido por extracción con acetato de etilo. El extracto orgánico se lava después con salmuera y se seca con Na_2SO_4 (anhidro).

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La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo en hexanos como eluyente para obtener el éster metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico (4.1 g, 59%) como un sólido de color amarillo.

^{1}H RMN ($CDCl_3$) d (ppm): 8.30 (s, 1H), 8.12 (d, 1H), 7.98 (dd, 1H), 7.45 (m, 2H), 3.96 (s, 3H).

EJEMPLO 311

Ester metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico

A una mezcla de ácido 3-clorobenzoico (5.0 g, 31.9 mmoles), clorhidrato del éster metílico de serina (6.1 g, 31.9 mmoles) y HOBt (4.31 g, 31.9 mmoles) en DMF (100 ml) se agrega N-metilmorfolina (NMM) (7.0 ml, 63.8 mmoles) y EDCI (4.97 g, 31.9 mmoles) a 0°C. La mezcla se deja calentar hasta temperatura ambiente y se agita durante 18 horas. La mezcla se diluye con acetato de etilo (300 ml) y después se lava con agua (3 x 250 ml) seguido por salmuera. El extracto orgánico se seca con Na_2SO_4 (anhidro) y después se concentra al vacío para obtener el éster metílico del ácido 2-(3-cloro-

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benzoilamino)-3-hidroxi-propiónico (7.2 g, 93%) de un sólido de color amarillo pálido.

^{1}H RMN ($CDCl_3$) d (ppm): 7.78 (s, 1H), 7.66 (d, 1H), 7.45, (dd, 1H), 7.34 (t, 1H), 7.25 (br, d, 1H), 4.82 (m, 1H), 4.08 (m, 2H), 3.79 (s, 3H), 3.19 (br, t, 1H).

A una solución del éster metílico del ácido 2-(3-cloro-benzoilamino)-3-hidroxi-propiónico (7.2 g, 29.6 mmoles) en CH_2Cl_2 a -20°C se agrega, mediante goteo, De-oxofluor (7.2 g, 32.6 mmoles). Después de agitar a esta temperatura durante 30 minutos, se agrega, mediante goteo, $BrCCl_3$ (3.6 g, 18.1 mmoles) seguido por DBU (2.79g, 18.1 mmoles). La mezcla se agita después a 2-3°C durante 8 horas y después se extingue con $NaHCO_3$ saturado seguido por extracción con acetato de etilo. El extracto orgánico se lava después con salmuera y se seca con Na_2SO_4 (anhidro). La purificación se efectúa mediante cromatografía de vaporización instantánea en gel de sílice utilizando acetato de etilo en hexanos como eluyente para obtener el éster metílico del ácido 2-(3-clorofenil)-oxazol-4-carboxílico (4.1 g, 59%) como un sólido de color amarillo.

^{1}H RMN ($CDCl_3$) d (ppm): 8.30 (s, 1H), 8.12

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(d, 1H), 7.98 (dd, 1H), 7.45 (m, 2H), 3.96 (s, 3H).

EJEMPLO 312

1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etanol

Paso 1

5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carbaldehído:

En un matraz de fondo redondo de 50 ml equipado con barra de agitación y tubo para secado se agregan éster etílico del ácido 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carboxílico (0.78 g, 2.89 mmoles) y diclorometano (10 ml). La solución se enfría hasta -78°C y a esta solución agitada se agrega hidruro de diisobutilaluminio (1M en hexanos, 5.3 ml, 5.3 mmoles). La mezcla resultante se deja bajo agitación a -78°C durante 3 horas. La reacción se extingue utilizando sulfato de sodio decahidratado. La mezcla resultante se agita a 63°C durante 15 minutos después de lo cual ésta se filtra a través de una almohadilla de celita. El material filtrado se concentra al vacío para aislar un sólido de color blanquecino, el cual se tritura con hexanos para aislar el compuesto del título como un sólido de color blanco (0.558, 84%).

^{1}H RMN ($CDCl_3$), d (ppm): 10.2 (s, 1H), 7.99(m, 1H), 7.44 (m, 1H), 7.20 (m, 1H), 7.10 (d, 1H).

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Paso 2

1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etanol:

En un matraz de fondo redondo de 50 ml equipado con barra de agitación se agrega 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carbaldehído (0.55 g, 2.42 mmoles) y tetrahidrofurano (6 ml). La mezcla se enfría hasta 0°C y a ésta se agrega yoduro de metilmagnesio (3M en éter dietílico, 3.23 ml, 9.67 mmoles). La mezcla resultante se deja agitando a 0°C durante 3 horas. La mezcla de reacción se extingue con ácido clorhídrico (1N, acuoso, 10 ml), se extrae con éter dietílico (3X50 ml). La fase orgánica combinada se lava con agua (50 ml), salmuera (50 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo crudo se purifica en gel de sílice utilizando acetato de etilo al 10% en hexanos para aislar el compuesto deseado como un aceite claro (179 mg, 31%).

EJEMPLO 313

1-[3-(3-clorofenil)-isoxazol-5-il]-etanol

Se suspende cloruro de 3-cloro-benzo-

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hidroximoilo (por ejemplo, Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57(24), 6649-50) (2.84 g, 14.8 mmoles) en benceno (50 ml) y se enfría hasta 0°C. Se agregan 3-butin-2-ol (2.10 g, 29.9 mmoles) y trietilamina (1.89 ml, 26.7 mmoles). La mezcla se calienta a 60°C durante 1.5 horas, se enfría y se diluye con benceno y ácido clorhídrico acuoso 1N. Después de agitar, se evapora hasta sequedad la capa de benceno separada y el producto crudo se purifica mediante cromatografía de vaporización instantánea con sílice utilizando heptano/acetato de etilo = 5/1 para obtener, después de secar al vacío, el compuesto del título (0.49 g, 15%).

^{1}H RMN ($CDCl_3$), δ (ppm): 1.64 (d, 3H), 5.07 (dq, 1H), 6.50 (s, 1H), 7.40 (m, 2H), 7.68 (m, 1H), 7.79 (m, 1H).

EJEMPLO 314

[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-metanol

Paso 1

(5-cloro-2-fluoro-feniletinil)-trimetil-silano:

En un matraz de fondo redondo de 250 ml equipado con una barra de agitación y condensador de

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reflujo se agregan 4-cloro-2-bromo-1-fluoro-benceno (5 g, 23.9 mmoles), trifenilfosfina (250 mg, 0.10 mmoles), (trimetilsilil)acetileno (5.2 ml, 36.5 mmoles) y trietilamina (60 ml). La mezcla de reacción se purga con argón, seguido por adición de acetato de paladio (II) (108 mg, 0.05 mmoles). La mezcla resultante se deja agitando a reflujo bajo argón, durante la noche. La mezcla de reacción se filtra a través de una almohadilla de celita utilizando acetato de etilo y el material filtrado se concentra al vacío. El residuo aislado se absorbe en gel de sílice y se filtra utilizando hexanos. El material filtrado se concentra al vacío para aislar el compuesto del título como un aceite de color café (5.42 g).

Paso 2

4-cloro-2-etinil-1-fluoro-benceno:

En un matraz de fondo redondo de 250 ml equipado con barra de agitación se agregan (5-cloro-2-fluoro-feniletinil)-trimetil-silano (5.42 g, 23.9 mmoles), carbonato de potasio (16.5 g, 120 mmoles) y metanol (60 ml). La mezcla de reacción se deja agitando a temperatura ambiente durante 1 hora. La mezcla de reacción se diluye con hexanos (200 ml) y

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se lava con agua (250 ml). La fase acuosa se extrae con hexanos (2X100 ml). La fase orgánica combinada se lava con salmuera (200 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar el compuesto deseado como un aceite de color café (3.56 g).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.47 (dd, 1H), 7.30 (m, 1H), 7.05 (t, 1H), 3.36 (s, 1H).

Paso 3

Ester etílico del ácido cloro-hidroxi-imino-acético:

En un matraz de fondo redondo de 1 litro equipado con barra de agitación se agrega clorhidrato de éster etílico del ácido amino-acético (20 g, 143 mmoles) y agua (30 ml). La solución se enfría hasta 0°C seguido por la adición en secuencia de ácido clorhídrico concentrado (11.8 ml, 143 mmoles) y la adición mediante goteo de solución de nitrito de sodio (9.89 g, 143 mmoles) en agua (15 ml). Después de 10 minutos se agrega otro equivalente de cada uno de ácido clorhídrico concentrado y de solución de nitrito de sodio en agua. La mezcla de reacción se deja agitando a 0°C durante 1 hora. La mezcla de reacción se extrae con éter (4X100 ml). La fase

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orgánica combinada se seca (sulfato de sodio), se filtra y se concentra al vacío para aislar un sólido de color amarillo limón. El sólido se recristaliza con hexanos para aislar un sólido de color blanco (11 g, 51%).

^{1}H RMN ($CDCl_3$), d (ppm): 9.98 (bs, 1H), 4.40 (q, 2H), 1.38 (t, 3H).

Paso 4

Ester etílico del ácido 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carboxílico:

En un matraz de fondo redondo de 250 ml equipado con barra de agitación se agrega 4-cloro-2-etinil-1-fluoro-benceno (2 g, 12.9 mmoles), éster etílico del ácido cloro-hidroxi-imino-acético (3.92 g, 25.9 mmoles), bicarbonato de sodio (7.07 g, 84.1 mmoles) y tolueno (50 ml). La mezcla de reacción se deja agitando a temperatura ambiente durante 48 horas, después de lo cual ésta se concentra al vacío. El residuo se lleva a acetato de etilo (200 ml), se lava en forma secuencial con agua (150 ml), salmuera (150 ml), se seca (sulfato de sodio), se filtra y se concentra al vacío. El residuo crudo se purifica en gel de sílice utilizando acetona al 3% en hexanos para aislar el compuesto del título como un sólido de

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color blanquecino (1.56 g).

^{1}H-RMN ($CDCl_3$), d (ppm): 8.00 (dd, 1H), 7.43 (m, 1H), 7.18 (m, 2H), 4.51 (q, 2H), 1.47 (t, 3H).

Paso 5

[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-metanol:

En un matraz de fondo redondo de 50 ml equipado con barra de agitación y tubo para secado se agregan éster etílico del ácido 5-(5-cloro-2-fluoro-fenil)-isoxazol-3-carboxílico (0.78 g, 2.89 mmoles) y tetrahidrofurano (10 ml). A esta solución agitada se agrega solución de hidruro de litio y aluminio (0.12 g, 2.89 mmoles) en tetrahidrofurano(2 ml). La mezcla resultante se deja agitando a temperatura ambiente durante 1 hora. La reacción se extingue utilizando sulfato de sodio decahidratado. La mezcla resultante se agita a 63°C durante 15 minutos después de lo cual ésta se filtra a través de una almohadilla de celita. El material filtrado se concentra al vacío para aislar el compuesto del título como un sólido de color amarillo (0.65 g, 99%).

^{1}H-RMN ($CDCl_3$), d (ppm): 7.73 (dd, 1H), 7.27 (m, 1H), 7.24 (t, 1H), 6.73 (d, 1H), 4.77 (s, 2H), 4.45 (bs, 1H).

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EJEMPLO 315

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]-oxadiazol-2-il]-propiónico

Paso 1

Acido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico:

Se mezclan hidrazida del ácido 3-cloro-benzoico (3.4 g, 20 mmoles) y anhídrido succínico (2. g, 20 mmoles) en acetato de etilo (50 ml) a temperatura ambiente durante 15 minutos. La mezcla de reacción se diluye con éter y el precipitado se filtra para obtener 5.1 g de ácido 4-[N'-(3-cloro-benzoil)-hidrazino]-4-oxo-butírico.

^{1}H RMN($CDCl_3$ + DMSO-d_6) d(ppm): 10.01 (s, 1H), 9.53 (s, 1H), 7.68 (s, 1H), 7.55 (d, 1H), 7.21 (d, 1H), 7.12 (t, 1H) y 2.35 (m, 4H).

Este sólido se mezcla con H_2SO_4 concentrado y se agita a temperatura ambiente durante 45 minutos y la mezcla de reacción se agrega cuidadosamente a hielo triturado (400g). El precipitado se filtra para obtener 4.07 g (80.6%) de ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico como un sólido de color blanco.

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^{1}H RMN(DMSO-d6) d(ppm): 12.4 (w, 1H), 7.96 (s, 1H), 7.91 (d, 1H), 7.71 (d, 1H), 7.63 (t, 1H), 3.15 (t, 2H) y 2.82 (t, 2H).

Paso 2

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico:

Se mezcla ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico (2.52 g, 10 mmoles) con yodometano (5.68 g, 40 mmoles) y K_2CO_3 (5.52 g, 40 mmoles) en DMF (25 ml) a temperatura ambiente durante la noche. La mezcla de reacción se diluye con acetato de etilo y se lava con agua 3 veces, se seca con $MgSO_4$ y se concentra para obtener 2.57 g del éster metílico del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico. El éster metílico (2.54 g, 9.52 mmoles) se mezcla con hidrato de hidrazina al 98% (4.76 g, 95.2 mmoles) en metanol (10 ml) durante una hora. La mezcla de reacción se concentra, se diluye con agua, se filtra para obtener 2.17 g (81.4%) de hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propiónico como un sólido de color blanco.

^{1}H RMN($CDCl_3$ + DMSO-d_6) d(ppm): 8.75 (w, 1H), 7.91 (s, 1H), 7.82 (d, 1H), 7.42 (m, 2H), 3.45 (w,

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2H), 3.19 (t, 2H) and 2.68 (t, 2H).

EJEMPLO 316

Hidrazida de ácido 3-[5-(3-clorofenil)-[1,3,4]-oxadiazol-2-il]-butírico

Paso 1

Ester dimetílico del ácido 2-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-malónico:

Se mezcla 2-(1-cloro-etil)-5-(3-clorofenil)-[1,3,4]oxadiazol (331 mg, 1.36 mmoles) con malonato de dimetilo (360 mg, 2/76 mmoles) y DBU (207 mg, 1.36 mmoles) en acetonitrilo (3 ml) a 70°C durante la noche. La mezcla de reacción se diluye con diclorometano y se lava con agua. La capa orgánica se seca y se concentra. El residuo se purifica con acetato de etilo al 5~20% en hexanos para obtener 357 mg (74.3%) de éster dimetílico del ácido 2-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-malónico como un sólido de color blanco.

^{1}H RMN ($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.95 (d, 1H), 7.53 (d, 1H), 7.47 (t, 1H), 4.06 (d, 1H), 3.95 (m, 1H), 3.84 (s, 3H), 3.74 (s, 3H) y 1.51 (d, 3H).

Paso 2

Ester metílico del ácido 3-[5-(3-cloro-

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fenil)-[1,3,4]oxadiazol-2-il]-butírico:

Se mezcla el éster dimetílico del ácido 2-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-malónico (352.8 mg, 1.0 mmoles) con cloruro de sodio (76.3 mg, 1.3 mmoles) y una gota de agua en DMSO (1.5 ml) a 175°C durante una hora. La mezcla de reacción se diluye con agua y se extrae con diclorometano. La capa orgánica se lava con agua y se concentra. El residuo se purifica mediante cromatografía en columna con acetato de etilo al 10~20% en hexanos para obtener 215 mg (76.8%) del éster metílico del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico como un aceite claro.

^{1}H RMN ($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.45 (t, 1H), 3.73 (s, 3H), 3.67 (m, 1H), 3.05 (dd, 1H), 2.73 (dd, 1H) y 1.50 (d, 3H).

Paso 3

Hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico:

La hidrazida del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico (146 mg,%) se obtiene haciendo reaccionar el éster metílico del ácido 3-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-butírico (215 mg, 0.766 mmoles) con hidrato de hidrazina (0.74 ml)

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en metanol (3 ml) a temperatura ambiente durante 2.5 horas.

^{1}H RMN ($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.46 (t, 1H), 7.23 (w, 1H), 3.93 (w, 2H), 3.71 (m, 1H), 2.90 (dd, 1H), 2.57 (dd, 1H) y 1.50 (d, 3H).

EJEMPLO 317

Clorhidrato de éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico

Paso 1

3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionamida:

Se hace reaccionar el ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico (1.6 g, 6.33 mmoles) con $SOCl_2$ (10 ml) a temperatura ambiente durante la noche. La mezcla de reacción se concentra al vacío. El residuo se mezcla con THF (20 ml) y se extingue con $NH_3 \cdot H_2O$ al 28% (5 ml) a 0°C. Después que se agita durante 2 horas, la mezcla de reacción se diluye con diclorometano y se lava con agua y salmuera. La capa orgánica se seca, se concentra y se tritura con hexanos para obtener 1.21 g (76%) de 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionamida.

^{1}H RMN ($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.32 (t, 2H) y 2.87 (t, 2H).

Paso 2

3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionitrilo:

Se mezcla 3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-propionamida (1.2 g, 4.77 mmoles) con piridina (0.829 g, 10.5 mmoles) y anhídrido trifluoro-acético (1.2 g, 5.72 mmoles) en diclorometano (25 ml) a temperatura ambiente durante 2 horas. La mezcla de reacción se diluye con diclorometano y se lava con agua y salmuera. La capa orgánica se seca para obtener 1.1 g (98%) de 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionitrilo como un aceite de color café pálido.

^{1}H RMN ($CDCl_3$) d(ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.35 (t, 2H) y 3.01 (t, 2H).

Paso 3

Clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico:

Se mezcla 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-

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5-il]-propionitrilo (1.1 g, 4.71 mmoles) con HCl al 24% en etanol (8 ml) durante la noche. El precipitado se filtra y se lava con éter para obtener 0.99 g (66%) de clorhidrato del éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propionimídico como un sólido de color blanco.

^{1}H RMN (DMSO-d_6) d(ppm): 11.70 (w, 2H), 7.78 (m, 2H), 7.64 (m, 2H), 4.41 (q, 2H), 3.45 (t, 2H), 3.22 (t, 2H) y 1.28 (t, 3H).

EJEMPLO 318

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-propiónico

Paso 1

Acido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico:

Se calienta 3-cloro-N-hidroxi-benzamidina 4.52 g, 26.5 mmoles) con anhídrido succínico (2.65 mg, 26.5 mmoles) en DMF (5 ml) a 150°C durante una hora. La mezcla de reacción se enfría y se diluye con acetato de etilo. La solución orgánica se lava con agua y salmuera, se concentra al vacío. El residuo se tritura con acetato de etilo al 20% en hexanos para obtener 4.0 g (60%) del ácido 3-[3-(3-clorofenil)-

[1,2,4]oxadiazol-5-il]-propiónico como un sólido de color blanco).

^{1}H RMN ($CDCl_3$) d(ppm): 8.08 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.42 (t, 1H), 3.28 (t, 2H) y 3.04 (t, 2H).

Paso 2

Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico:

Este ácido se hace reaccionar con yodoetano (1.6 g, 10.5 mmoles) y K_2CO_3 (1.46 10.5 mmoles) en DMF (5 ml) durante 5 minutos para formar el éster etílico del ácido 3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-propiónico. El éster etílico se trata después con hidrazina al 37% (2 ml) en etanol (5 ml) a 80°C durante 2 horas para obtener 595 mg (65% en los 3 pasos) de la hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propiónico como un sólido de color blanquecino.

^{1}H RMN ($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.43 (t, 1H), 7.00 (w, 1H), 3.95 (w, 2H), 3.34 (t, 2H) and 2.79 (t, 2H).

EJEMPLO 319

Hidrazida del ácido [5-(3-clorofenil)-[1,2,4]-

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oxadiazol-3-il]-acético

Paso 1

Ester etílico del ácido (N-hidroxi-carbamimidoil)-acético:

A una solución en etanol (40 ml) del éster etílico del ácido ciano-acético (9.9 g, 0.1 moles), se agrega la mezcla constituida por solución de hidróxido de sodio (4 g, 0.1 moles) en agua (40 ml) y clorhidrato de hidroxilamina 5M (20 ml) y la mezcla de reacción se agita a 50°C durante la noche. Después que se concentra, la mezcla de reacción se diluye con agua y se extrae con acetato de etilo. La capa orgánica se seca, se concentra de nuevo. El residuo se purifica mediante cromatografía en columna con acetato de etilo 30~70% acetato de etilo en hexanos para obtener 3.32 g (22.7%) del éster etílico del ácido (N-hidroxicarbamimidoil)-acético como un sólido de color blanco.

^{1}H-RMN ($CDCl_3$) d(ppm): 5.04 (ws, 2H), 4.20 (q, 2H), 3.19 (s, 2H) y 1.30 (t, 3H).

Paso 2

Ester etílico del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético:

A una solución en diclorometano (10 ml) del

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éster etílico del ácido (N-hidroxicarbamimidoil)-acético (1.46 g, 10 mmoles) y trietilamina, se agrega lentamente, a 5°C, cloruro de 3-clorobenzoilo (1.75 g, 10 mmoles) y la mezcla de reacción se agita durante 10 minutos. Se agrega DMF (8 ml) a la mezcla de reacción, se calienta a 135°C durante 2 horas. Tratamiento estándar, el producto se hace pasar en la columna con diclorometano para obtener 1.2 g (45%) del éster etílico del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético como un aceite de color amarillo pálido.

^{1}H RMN ($CDCl_3$) d(ppm): 8.168 (s, 1H), 8.04 (d, 1H), 7.59 (d, 1H), 7.49 (t, 1H), 4.26 (q, 2H), 3.91 (s, 2H) y 1.31 (t, 3H).

Paso 3

Hidrazida del ácido [5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético:

Se mezcla el éster etílico del ácido 5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-acético (0.64 g, 2.4 mmoles) con hidrazina al 37% (1.6 ml) en etanol (10 ml) a 80°C durante 4 horas. La mezcla de reacción se concentra y se diluye con agua. El precipitado se filtra, se lava con agua para obtener 0.51 g (83.3%) de la hidrazida del ácido [5-(3-clorofenil)-

[1,2,4]oxadiazol-3-il]-acético.

EJEMPLO 320

Hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]-oxadiazol-5-il]-butírico

Paso 1

Ester metílico del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico:

A una solución del éster 4-metílico del ácido (R)-2-metilsuccínico (2.2 g, 15 mmoles) y trietilamina (4.54 g, 45 mmoles) en THF (30 ml), se agrega, mediante goteo, isobutilcloroformiato (2.16 g, 15.8 mmoles) a 0°C. Después que se agita durante 30 minutos, se agrega 3-cloro-N-hidroxi-benzamidina (2.56 g, 15 mmoles). La mezcla de reacción se agita a temperatura ambiente durante otros 30 minutos y después se calienta a 135°C con DMF durante 45 minutos. La mezcla de reacción se diluye con acetato de etilo y se lava con agua y salmuera. La capa orgánica se seca y se concentra para obtener 4.0 g (95%) del éster metílico del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico como un aceite de color amarillo pálido.

Paso 2

1284
1195

Hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico:

La hidrazida del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico (430 mg, 77%) se obtiene haciendo reaccionar el éster metílico del ácido (R)-3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-butírico (461.4 mg, 2.0 mmoles) con hidrato de hidrazina (2 ml) en metanol (2 ml) a 65°C durante 1 hora.

^{1}H RMN($CDCl_3$) d (ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.46 (m, 2H), 6.98 (w, 1H), 3.93 (w, 2H), 3.78 (m, 1H), 2.86 (dd, 1H), 2.55 (dd, 1H) y 1.59 (d, 3H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 320:

Ejemplo No.	Nombre
321	Hidrazida del ácido 3-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-3-metil-butírico

EJEMPLO 322

3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona

Se agregan 1.33 ml (3.32 mmoles) de n-BuLi

225
1196

(2.5 M en hexanos), mediante goteo, a una solución de 157 mg (1.58 mmoles) de d-valerolactona en 5,3 ml de THF a 0°C. Después de agitar durante 2 horas a 0°C, se agregan 400 mg (1.58 mmoles) de 3-clorometil-5-[3-clorofenil)-[1,2,4]oxadiazol en una porción y la agitación se continúa durante 3 horas. Se agrega NH_4Cl (saturado) para extinguir la reacción y la mezcla se extrae dos veces con CH_2Cl_2. Las fases orgánicas combinadas se secan y se concentran. La cromatografía de vaporización instantánea (SiO_2, heptano/EtOAc 1:8) permite obtener 113 mg (25%) de un sólido de color blanco amarillento.

^1H RMN ($CDCl_3$):d ppm 1.80 (m, 1H) 1.89 (m, 1H) 2.00 (m, 1H) 2.91 (m, 1H) 2.98 (m, 1H) 3.35 (m, 1H) 3.52 (m, 1H) 5.83 (s, 1H) 7.46 (t, 1H) 7.55 (d, J=8.08 Hz, 1H) 8.00 (d, 1H) 8.11 (s, 1H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 322:

Ejemplo No.	Nombre
323	3-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]-oxadiazol-3-ilmetil]-piperidin-2-ona

1197

EJEMPLO 324

3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol

Y

1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol

Se agita una solución de 2-cloro-N-hidroxi-acetamidina (781 mg, 7.2 mmoles), ácido 5-cloro-tiofen-3-carboxílico (1.4 g), HBTU (3.55 g) y DIPEA (1.3 g) en DMF (20 ml) a temperatura ambiente durante 1 hora antes de calentar a 120°C durante 4 horas bajo argón. La remoción del solvente al vacío seguido por cromatografía en gel de sílice del residuo obtenido utilizando EtOAc al 0-20% en n-heptano produce 38.5 mg del compuesto que eluye más rápido 3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]-oxadiazol como un jarabe, seguido por 65 mg del compuesto que eluye más lento 1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol como un sólido de color blanco.

3-clorometil-5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol:

^{1}H RMN ($CDCl_3$) d (ppm): 8.01 (d, 1H), 7.50 (d, 1H), 4.63 (s, 2H).

1198

1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol:

^{1}H RMN ($CDCl_3$) d (ppm): 7.97 (m, 2H), 7.52 (dt, 1H), 7.44 (m, 2H), 7.34 (m, 1H), 5.70 (s, 2H).

EJEMPLO 325

(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-acetonitrilo

Se agitan juntos 4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-tiol (197 mg, 1.0 mmoles), cloro-acetonitrilo (95 ml, 1.5 mmoles), carbonato de sodio (424 mg, 4 mmoles) y yoduro de potasio (332 mg, 2.0 mmoles) a 100°C durante 3 horas, agregando una cantidad adicional de cloroacetonitrilo (60 ml, 0.5 mmoles) después de 2 horas. La reacción se enfría, se diluye con acetato de etilo y se lava con agua. La solución orgánica se seca, se filtra y evapora. La cromatografía con gel de sílice (diclorometano: metanol 19:1) produce 150 mg del compuesto deseado.

EJEMPLO 326

Acido 2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-propiónico

1199

Se disuelven ácido (R)-2-cloro-propiónico (500 mg, 4.6 mmoles), 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (1.09 g, 5.58 mmoles) y carbonato de potasio (1.94 g, 14.03 mmoles) en acetonitrilo (15 ml) a temperatura ambiente. La reacción continúa durante 2.5 horas y se divide entre acetato de etilo (350 ml) y agua 3 veces, se lava con HCl 1M, una vez con salmuera saturada, se seca con sulfato de sodio anhidro, se filtra y se concentra al vacío. La reacción no es completa en esta etapa y el producto crudo se agita en DMF (10 ml) durante la noche. Se repite la extracción, y la purificación se efectúa mediante cromatografía de SPE (extracción en fase sólida) en gel de sílice utilizando 300 ml de acetato de etilo, 100 ml al 1%, y 100 ml al 3% de ácido fórmico en acetato de etilo, para obtener el compuesto del título (150.7 mg, 12%).

^{1}H RMN ($CDCl_3$), d (ppm): 7.52 (dd, 2H), 7.19 (m, 1H), 4.21 (q, 1H), 3.78 (s, 3H), 1.64 (d, 311).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 326:

Ejemplo No.	Nombre
327	Acido 2-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanil)-propiónico

1200

EJEMPLO 328

3-(3-clorofenil)-5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

El compuesto del título (2.08 g, 81.5%) se obtiene a partir de 5-clorometil-3-(3-clorofenil)-[1,2,4]oxadiazol (1.9 g, 8.29 mmoles) que se hace reaccionar con 4-metil-4H-[1,2,4]triazol-3-tiol (1.0 g, 8.71 mmoles) y K_2CO_3 (4.58 g, 33.2 mmoles) en DMF (19 ml) a temperatura ambiente durante la noche.

^1H RMN ($CDCl_3$) d (ppm): 8.21 (s, 1H), 8.05 (s, 1H), 7.94 (d, 1H), 7.49(d, 1H), 7.43 (t, 1H), 4.69 (s, 2H) y 3.64 (s, 3H).

EJEMPLO 329

Ester ter-butílico del ácido {3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol-5-il-fenil}-carbámico

El compuesto del título se prepara a partir de 4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-tiol (53 mg, 0.27 mmoles), éster ter-butílico del ácido 3-(3-clorometil-[1,2,4]oxadiazol-5-il)-fenil]-carbámico (75 mg, 0.24 mmoles), y carbonato de potasio (101 mg,

0.73 mmoles) en acetonitrilo (2.5 ml). El producto se purifica mediante cromatografía de SPE (vaporización instantánea) utilizando acetato de etilo al 65% en hexano (88.0 mg, 79%, sólido de color blanco).

^{1}H RMN ($CDCl_3$) d (ppm): 8.06 (s, 1H), 7.73 (d, 1H), 7.66 (d, 1H), 7.51 (t, 2H), 7.42 (t, 1H), 7.18 (m, 1H), 6.68 (s, 1H), 4.51 (s, 2H), 3.73 (s, 3H), 1.53 (s, 9H).

Los siguientes compuestos se preparan en forma análoga a la del ejemplo 41:

Ejemplo No.	Nombre	^{1}H RMN	MS
330	4-(4-ciclopropil-5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etil-sulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.88 (d, 2H), 7.81 (m, 1H), 7.75 (m, 2H), 7.22 (m, 2H), 5.42 (q, 1H), 3.22 (m, 1H), 1.98 (d, 3H), 1.17 (m, 2H), 0.79 (m, 2H)	370.00
331	4-(5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.69 (m, 2H), 7.6 (m, 1H), 7.52 (m, 3H), 7.35 (t, 1H), 7.04 (m, 1H), 4.93 (q, 1H), 3.78 (t, 3H), 3.55 (s, 3H), 1.86 (d, 3H)	
332	4-{4-metil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.71 (m, 2H), 7.82 (m, 2H) 7.53 (m, 2H), 7.32 (m, 2H), 4.94 (q, 1H), 3.54 (s, 3H), 2.33 (s, 3H), 1.87 (d, 3H)	
333	5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-o-tolil-[1,2,4]oxadiazol	2.58 (s, 3H) 3.70 (s, 3H) 4.65 (s, 2H) 7.17 (s, 1H) 7.29 (s, 2H) 7.36 (s, 1H) 7.46 (s, 1H) 7.51 (s, 1H) 7.90 (s, 1H)	370.0

Ejemplo No.	Nombre	^{1}H RMN	MS
334	5-(3-cloro-fenil)-3-(4-ciclopropil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	0.87 (m, 2H) 1.18 (m, 2H) 3.47 (ddd, J=6.95, 3.41, 3.28 Hz, 1H) 4.70 (s, 2H) 7.23 (m, 1H) 7.67 (m, 2H) 7.77 (m, 2H) 8.04 (d, 2H)	415.9
335	2-{3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-etanol	2.36 (s, 3H) 4.03 (t, 2H) 4.30 (t, 2H) 4.57 (s, 2H) 7.11 (m, 2H) 7.35 (s, 1H) 7.47 (d, 1H) 7.64 (d, 1H) 7.81 (d, 1H)	417.9
336	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-pirimidina	1.38 (t, 3H) 2.34 (s, 3H) 4.66 (m, 4 H) 7.19 (m, 1H) 7.47 (m, 1H) 7.83 (d, 1H) 8.23 (d, 1H) 8.94 (d, 1H) 9.28 (s, 1H)	398.0
337	3-(4-etil-5-furan-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	1.34 (t, 3H) 2.37 (s, 3H) 4.06 (q, 2H) 4.61 (s, 2H) 6.82 (s, 1H) 7.12 (m, 1H) 7.36 (ddd, 1H) 7.55 (s, 1H) 7.85 (d, 2H).	386.0
338	Ester metílico del ácido {3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-acético	2.36 (s, 3H) 3.70 (s, 3H) 4.46 (s, 2H) 5.10 (s, 2H) 7.21 (m, 2H) 7.47 (m, 2H) 7.73 (d, 1H) 7.86 (m, 1H)	445.9
339	5-(2-fluoro-5-metil-fenil)-3-[5-furan-2-il-4-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	2.26 (s, 3H) 3.16 (s, 3H) 3.57 (t, 2H) 4.42 (t, 2H) 4.44 (s, 2H) 6.60 (s, 1H) 7.10 (m, 2H) 7.37 (m, 1H) 7.70 (s, 1H) 7.73 (d, 1H)	416.0

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Ejemplo No.	Nombre	^{1}H RMN	MS
340	3-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	0.87 (m, 2H) 1.14 (m, 2H) 2.35 (s,3H) 3.39 (dt, 1H) 4.71 (s, 2H) 6.72 (s, 1H) 7.09 (d, 1H) 7.39 (m, 1H) 7.56 (m, 1H) 7.87 (d, 1H) 7.93 (s, 1H)	398.0
341	3-(5-cloro-2-fluoro-fenil)-5-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	0.32 (m, 2H) 0.56 (m, 2H) 1.14 (d, 1H) 4.00 (d, 2H) 4.76 (s, 2H) 7.16 (ddd, 2H) 7.43 (m, 1H) 7.50 (t, 2H) 7.99 (dd, 1H)	448.1
342	4-{5-[3-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina	1.40 (t, 3H) 4.63 (q, 2H) 4.72 (s, 2H) 7.20 (m, 1H) 7.53 (m, 1H) 8.06 (dd, 1H) 8.29 (d, 1H) 8.86 (d, 1H) 9.26 (s, 1H).	417.8
343	3-(5-ciclopentil-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	1.29 (t, 3H) 1.66 (m, 3H) 1.87 (m, 2H) 2.02 (m, 3H) 2.42 (s, 3H) 3.01 (s, 2H) 3.90 (d, 2H) 4.52 (s, 2H) 7.39 (d, 2H) 7.90(d, 2H)	370.2
344	3-(3-cloro-fenil)-5-{4-etil-5-[2-(4-metoxi-fenil)-etil]-4H-[1,2,4]triazol-3-ilsulfanilmetil}-[1,2,4]oxadiazol	1.18 (t, 3H) 2.95 (t, 2H) 3.09 (t, 2H) 3.72 (q, 2H) 3.76 (s, 3H) 4.66 (s, 2H) 6.81 (d, 2H) 7.09 (d, 2H) 7.40 (t, 1H) 7.47 (m, 1H) 7.92 (d, 1H) 8.03 (s, 1H)	456.1
345	5-(3-cloro-fenil)-3-(4-etil-5-p-toliloximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.23 (t, 3H) 2.22 (s, 3H) 4.02 (d, 2H) 4.60 (s, 2H) 5.22 (s, 2H) 6.92 (d, 2H) 7.09 (d, 2H) 7.65 (t, 1H) 7.79 (d, 1H) 8.04 (m, 2H)	442.1

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Ejemplo No.	Nombre	^{1}H RMN	MS
346	5-(3-cloro-fenil)-3-[4-(2-metoxi-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	3.14 (s, 3H) 3.57 (t, 2H) 4.30 (t, 2H) 4.58 (s, 2H) 7.23 (m, 1H) 7.64 (m, 2H) 7.78 (m, 2H) 8.03 (d, 2H)	433.9
347	3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.98 (m, 1H), 7.43 (m,1H), 7.16 (t aparente, 1H), 4.73 (s, 2H), 4.62 (s, 2H), 4.01 (q, 2H), 3.33 (s, 3H), 1.34 (t, 3H).	384.9
348	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.05 (m, 1H), 7.53 (m, 1H), 7.21 (t aparente, 1H); 4.62 (s, 2H), 4.61 (s, 2H), 4.02 (q, 2H), 3.34 (s, 3H), 1.32 (t, 3H).	384.9
349	5-(3-cloro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.07 (s aparente, 1H), 7.97 (m, 1H), 7.55 (m, 1H), 7.45 (t aparente, 1H), 4.62 (s, 2H), 4.59 (s, 2H), 4.01 (q, 2H),3.34 (s, 3H), 1.32 (t, 3H).	366.9
350	3-(3-cloro-fenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.02 (m, 1H), 7.92 (m, 1H), 7.46 (m, 1H), 7.39 (t aparente, 1H), 4.71 (s, 2H), 4.62 (s, 2H), 4.01 (q, 2H), 3.34 (s, 3H),1.34 (t, 3H).	366.9
351	4-(5-{1-[3-(3-cloro-fenil)-isoxazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	1.82 (d, 3H), 3.46 (s, 3H), 4.93 (q, 1H), 6.33 (s, 1H), 7.23-7.31 (m, 2H), 7.44 (d, 2H), 7.49 (m, 1H), 7.61 (s, 1H), 8.63 (d, 2H).	399.1

Ejemplo No.	Nombre	^{1}H RMN	MS
352	3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	4.6 (s, 2H), 4.8 (d, 2H), 5.0 (d, 1H), 5.2 (d, 1H) 5.9 (m, 1H), 6.5 (m, 1H), 7.1 (d, 1H), 7.4 (t, 1H), 7.5 (m, 2H), 8.0 (d, 1H), 8.1 (s, 1H)	399.95
353	3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	4.5 (s, 2H) 4.8 (d, 2H) 5.0 (d, 1H) 5.2 (d, 1H) 5.9 (m, 1H) 6.5 (m, 1H) 7.0 (d, 1H) 7.4 (m, 1H) 7.5 (s, 1H) 7.6 (d, 1H) 8.2 (m, 1H)	371.98
354	5-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-furan-2-il-[1,2,4]oxadiazol	4.7 (s, 2H) 4.8 (m, 2H) 5.0 (d, 1H) 5.2 (d, 1H) 5.9 (m, 1H) 6.5 (dt, 2H) 7.1 (dd, 2H) 7.6 (dd, 2H)	356.01
355	5-(3-cloro-fenil)-3-[4-etil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.4 (t, 3H) 3.7 (s, 3H) 4.1 (q, 2H) 4.6 (s, 2H) 5.2 (s, 2H) 6.8 (d, 2H) 6.9 (d, 2H) 7.4 (t, 1H) 7.6 (d, 1H) 8.0 (d, 1H) 8.1 (s, 1H)	457.91
356	3-(3-cloro-fenil)-5-[4-etil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-isulfanilmetil]-[1,2,4]oxadiazol	1.4 (t, 3H) 3.7 (s, 3H) 4.1 (q, 2H) 4.8 (s, 2H) 5.2 (s, 2H) 6.8 (d, 2H) 6.9 (d, 2H) 7.4 (t, 1H) 7.5 (m, 1H) 7.9 (d, 1H) 8.0 (s, 1H)	457.97
357	{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il-metil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-metanol	1.4 (t, 3H) 4.2 (d, 2H) 4.7 (s, 2H) 4.9 (s, 2H) 7.4 (t, 1H) 7.5 (m, 1H) 7.9 (d, 1H) 8.0 (s, 1H)	352.09

Ejemplo No.	Nombre	^{1}H RMN	MS
358	3-(3-cloro-fenil)-5-[4-etil-5-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.3 (t, 3H) 3.0 (t, 2H) 3.3 (s, 3H) 3.8 (t, 2H) 3.9 (q, 2H) 4.7 (s, 2H) 7.4 (t, 1H) 7.5 (ddd, 1H) 7.9 (dt, 1H) 8.0 (t, 1H)	380.12
359	3-(3-cloro-fenil)-5-(4-etil-5-metilsulfanilmetil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	1.4 (t, 3H) 2.1 (s, 3H) 3.8 (s, 2H) 4.0 (q, 2H) 4.7 (s, 2H) 7.4 (t, 1H) 7.5 (ddd, 1H) 7.9 (dt, 1H) 8.0 (t, 1H)	382.07
360	3-(3-cloro-fenil)-5-(5-etoximetil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	.2 (t, 3H) 1.3 (t, 3H) 3.5 (q, 2H) 4.0 (q, 2H) 4.7 (s, 2H) 4.7 (s, 2H) 7.4 (t, 1H) 7.5 (ddd, 1H) 7.9 (dt, 1H) 8.0 (t, 1H)	379.13
361	Ester metílico del ácido 5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-carboxílico		
362	2-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	1.4 (t, 3H) 4.2 (q, 2H) 4.7 (s, 2H) 6.6 (dd, 1H) 7.1 (d, 1H) 7.2 (m, 1H) 7.5 (ddd, 1H) 7.6 (d, 1H) 8.0 (dd, 1H)	406.07
363	2-(3-cloro-fenil)-5-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	0.9 (m, 2H) 1.2 (m, 2H) 3.2 (m, 1H) 4.8 (s, 2H) 6.6 (m, 1H) 7.0 (d, 1H) 7.4 (t, 1H) 7.5 (m, 1H) 7.6 (m, 1H) 7.9 (m,1H) 8.0 (m, 1H)	399.86

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Ejemplo No.	Nombre	^{1}H RMN	MS
364	5-(3-cloro-fenil)-3-{1-[4-etil-5-(tetrahidro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol	1.3 (t, 3H) 1.9 (d, 3H) 2.0 (m, 1H) 2.1 (m, 1H) 2.3 (m, 1H) 2.8 (m, 1H) 3.8 (m, 2H) 4.0(m, 1H) 4.1 (m, 1H) 5.0 (m, 1H) 5.1 (m, 1H) 7.4 (t, 1H) 7.6 (m, 1H) 8.0 (m, 1H) 8.1 (s, 1H)	406.04
365	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridazina	1.4 (t, 3H) 1.9 (d, 3H) 4.1 (m, 2H) 5.2 (q, 1H) 7.4 (t, 1H) 7.5 (m, 1H) 7.8 (m, 1H) 8.0 (m, 1H) 8.1 (m, 1H) 9.4 (m,1H) 9.5 (s, 1H)	414.12
366	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-ilmetil)-piridina	1.0 (t, 3H) 1.9 (d, 3H) 3.7 (m, 2H) 4.2 (m, 2H) 5.0 (q, 1H) 7.1 (m, 2H) 7.4 (t, 1H) 7.5 (m, 1H) 7.9 (d, 1H) 8.1 (s, 1H) 8.5 (m, 2H)	427.06
367	5-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol	1.3 (t, 3H) 1.9 (d, 3H) 3.9 (m, 2H) 5.1 (q, 1H) 6.7 (d, 1H) 7.5 (t, 1H) 7.6 (m, 1H) 7.7 (m, 1H) 7.7 (s, 1H) 8.0 (d, 1H) 8.1 (s, 1H) 13.1 (s, 1H)	429.1
368	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-fenol	1.2 (t, 3H) 1.9 (d, 3H) 3.9 (q, 2H) 5.1 (q, 1H) 6.9 (d, 2H) 7.3 (d, 2H) 7.4 (t, 1H) 7.5 (m, 1H) 7.9 (m, 1H) 8.1 (m, 1H) 10.2 (s, 1H)	428.08

Ejemplo No.	Nombre	^{1}H RMN	MS
369	5-(3-cloro-fenil)-3-[5-(4-metoxi-fenoximetil)-4-(tetrahidro-furan-2-ilmetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.54 (m, 1H) 1.86 (m, 2H) 2.02 (m, 1H) 3.71 (m, 4 H) 3.79 (m, 1H) 4.13 (m, 3H) 4.60 (m, 2H) 5.30 (s, 2H) 6.82 (m, 2H) 6.92 (m, 2H) 7.44 (t, 1H) 7.55 (d, 1H) 7.95 (d, 1H) 8.07 (s, 1H)	
370	5-(3-cloro-fenil)-3-[4-ciclopropil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.14 (m, 4 H) 3.10 (s; 1H) 3.75 (s, 3H) 4.70 (s,2H) 5.21 (s, 2H) 6.82 (d, 2H) 6.95 (d, 2H) 7.45 (t, 1H) 7.56 (m, 1H) 7.99 (d, 1H) 8.10 (s,1H)	
371	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.38 (t, 3H) 4.27 (q, 2H) 4.64 (s, 2H) 6.58 (m, 1H) 7.21 (m, 2H) 7.53 (m, 1H) 7.59 (m, 1H) 8.06 (m, 1H)	
372	3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	1.29 (t, 3H) 2.40 (s, 3H) 3.31 (s, 3H) 3.99 (m, 2H) 4.56 (s, 2H) 4.60 (s, 2H) 7.37 (m, 2H) 7.87 (m, 2H)	346
373	3-[4-etil-5-(tetrahidro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol	1.30 (t, 3H) 1.97 (m, 1H) 2.10 (m, 1H) 2.24 (m, 1H) 2.39 (s, 3H) 2.80 (m, 1H) 3.79 (m, 1H) 3.86 (m, 1H) 3.99 (m, 1H) 4.08 (m, 1H) 4.54 (m, 2H) 4.98 (m, 1H) 7.36 (m, 2H) 7.86 (m, 1H) 7.88 (s, 1H)	372

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Ejemplo No.	Nombre	^{1}H RMN	MS
374	2-(3-cloro-fenil)-5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	1.18 (m, 3H) 1.95 (d, 3H) 3.81 (s, 3H) 3.90 (q, 2H) 5.15 (q, 1H) 6.94 (m, 2H) 7.35 (m, 1H) 7.45 (m, 3H) 7.81 (m, 1H) 7.92 (m, 1H)	
375	4-{5-[3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]-triazol-3-il}-pirimidina	1.43 (t, 3H), 4.64 (q, 2H), 4.87 (s, 2H), 7.18 (m , 2H), 7.72 (m, 1H), 8.29 (dd, 1H), 8.89 (d, 1H), 9.30 (d, 1H)	402.1
376	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-4-metil-4H-[1,2,4]-triazol-3-il}-pirimidina	4.12 (s, 3H), 4.64 (s, 2H), 7.21 (t, 1H), 7.57 (m, 1H), 8.06 (dd, 1H), 8.28 (dd, 1H), 8.92 (d, 1H), 9.30 (d, 1H)	404.1
377	3-(3-cloro-fenil)-5-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.03 (s 1H), 7.92 (d, 1H), 7.53 (d, 1H), 7.48 (m, 2H), 7.40 (t, 1H), 7.18 (t, 1H), 4.87 (s, 2H), 3.72 (s, 3H).	390.96
378	5-(3-metilsulfanil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol	7.92 (s, 1H), 7.84 (d, 1H), 7.53 (m, 2H), 7.43 (m, 2H), 7.18 (m, 1H),4.53 (s, 2H), 3.73 (s, 3H), 2.52 (s, 3H)	
379	2-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1H-benzoimidazol		

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Ejemplo No.	Nombre	^{1}H RMN	MS
380	5-(2,5-dimetil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.87 (s, 1H), 7.49 (m, 2H), 7.22 (m, 3H), 4.56 (d, 2H), 3.74 (s, 3H), 2.61 (s, 3H), 2.37 (s, 3H).	
381	5-(2-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.83 (dd, 1H), 7.49 (m, 2H), 7.35 (m, 1H), 7.16 (m, 2H), 4.53 (s, 2H), 3.73 (s, 3H), 2.35 (s,3H).	388.10
382	5-(3-ciclopropil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.87 (d, 1H), 7.79 (s, 1H), 7.51 (m, 2H), 7.40,(t 1H), 7.30 (m, 1H),7.20 (m, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 1.96 (m, 1H), 1.04 (m, 2H),0.77 (m, 2H).	
383	4-{5-[2-(3-cloro-fenil)-oxazol-4-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (d, 2H), 8.02 (dd, 1H), 7.88 (dd, 1H), 7.80 (s, 1H), 7.60 (d, 2H),7.42 (m, 2H), 4.51 (s, 2H), 3.64 (s, 3H).	
384	4-[4-metil-5-(5-tiofen-2-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (bs, 2H), 7.90 (m, 1H), 7.66 (m, 3H), 7.22 (m, 1H), 4.58 (s, 2H),3.73 (s, 3H).	
385	4-{4-metil-5-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.81 (m, 2H), 7.95 (s,1H), 7.86 (m, 1H), 7.64(m, 2H), 7.45 (m, 2H),4.63 (s, 2H), 3.72 (s,3H), 2.55 (3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
386	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (d, 2H), 8.11 (s, 1H), 8.00 (d, 1H), 7.64 (m, 2H), 7.60 (m, 1H),7.49 (t, 1H), 4.64 (s, 2H), 3.73 (s, 3H).	
387	2-metil-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.82 (d, 2H), 8.74 (d, 1H), 7.82 (s, 1H), 7.76 (d, 1H), 7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s, 3H), 2.68 (s, 3H).	
388	1-{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-etanona	8.67 (s, 1H), 8.29 (d, 1H) 8.20 (d, 1H), 7.68 (t, 1H), 7.52 (m, 2H), 7.20 (m, 1H), 4.58 (s, 2H), 3.76 (s, 3H), 2.68 (s, 3H).	
389	4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (dd, 2H), 7.86 (d, 1H), 7.64 (m, 2H), 7.39(m, 1H), 7.14 (dd, 1H),4.63 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H).	383.09
390	2-metil-4-{4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.68 (dd, 1H),7.92 (m, 2H), 7.52 (bs, 1H), 7.4 (m, 3H), 4.61 (s, 2H), 3.7 (s, 3H), 2.67 (s, 3H), 2.44 (s, 3913H).	
391	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-5-tiofen-2-il-4H-[1,2,4]triazol	7.76 (s, 1H), 7.68 (m, 1H), 7.54 (m, 1H), 7.48 (m, 1H), 7.40 (m 2H), 7.20 (m, 1H), 6.76 (s, 1H), 4.56 (s, 2H), 3.70 (s, 3H).	

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Ejemplo No.	Nombre	^{1}H RMN	MS
392	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (m, 2H), 7.76 (m, 1H), 7.65 (m, 3H), 7.41 (m, 2H), 6.77 (s, 1H),4.61 (s, 2H), 3.69 (s, 3H).	
393	3-(4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.07 (s, 1H), 7.95 (dd, 1H), 7.48 (m, 4H), 7.17 (dd, 1H), 4.59 (s, 2H),4.05 (t, 2H), 1.67 (m, 2H), 1.30 (m, 2H), 0.88 (t, 3H).	
394	5-(3-cloro-fenil)-3-[4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.01 (d, 1H), 7.91 (dd, 1H), 7.48 (m, 4H), 7.12 (m, 1H), 4.51 (s, 2H), 4.17 (t, 2H), 3.34 (t, 2H), 3.18 (s, 3H), 1.90 (m, 2H).	
395	3-(4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.09 (s, 1H), 7.97 (dd, 1H), 7.57 (m, 1H), 7.47 (m, 2H), 7.24 (m, 4H),7.06 (m, 3H), 5.37 (s, 2H), 4.57 (s, 2H).	
396	5-(3-cloro-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.10 (d, 1H), 8.03 (dd, 1H),7.55 (m, 4H), 7.38 (s, 1H), 7.20 (dd, 1H),6.32 (m, 2H), 5.30 (s, 2H), 4.60 (s, 2H).	457.02
397	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.93 (m, 1H),8.78 (m, 1H), 8.03 (m, 3H), 7.59 (m, 1H), 7.51 (m, 2H),4.63 (s, 2H), 3.69 (s, 3H).	
398	5-(3-cloro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (m, 1H), 8.05 (m, 1H), 7.74 (m, 1H), 7.59 (m, 1H), 7.51 (m, 3H),4.57 (s, 2H), 3.71 (s, 3H).	

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Ejemplo No.	Nombre	^{1}H RMN	MS
399	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-2-metil-piridina	8.69 (d, 1H), 8.10 (s, 1H), 8.00 (m, 1H), 7.49 (m, 4H), 4.63 (s, 2H), 3.71 (s, 3H), 2.67 (s, 3H).	
400	5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	8.08 (m, 1H), 7.51 (m, 1H) 7.21 (m, 1H), 4.59 (s, 2H), 3.77 (s, 3H).	409.00
401	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 8.08 (m, 1H) 8.29 (d, 1H), 7.64 (d, 2H), 7.56, (m, 1H), 7.24 (t, 1H), 4.66 (s, 2H), 3.75 (s, 3H).	404.07
402	3-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (s, 1H), 8.76 (d, 1H), 8.07 (d, 1H), 7.87 (d, 1H), 7.36 (m, 3H),4.59 (s, 2H), 3.69 (s, 3H), 2.39 (s, 3H).	
403	5-(3-cloro-fenil)-3-(5-tiofen-2-il-4-tiofen-2-ilmetil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	(CD_3OD como solvente):8.05 (m, 1H), 8.00 (dd, 1H), 7.75 (dd, 1H), 7.58 (m, 1H), 7.54 (m, 1H), 7.53 (m, 1H), 7.26 (m, 1H), 7.22 (m, 1H), 6.86 (m, 2H), 5.63 (s, 2H),4.51 (s, 2H).	
404	5-(3-cloro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	(CD_3OD como solvente): 8.08 (m, 1H), 8.07 (dd, 1H), 7.75 (m, 1H), 7.67 (m, 1H), 7.60(m, 2H), 7.28 (dd, 1H), 4.57 (s, 2H), 4.27 (m, 2H), 1.29 (m, 3H).	405.10

Ejemplo No.	Nombre	^{1}H RMN	MS
405	3-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.90 (m, 1H), 8.77 (dd, 1H), 8.03 (m, 1H), 7.78 (m, 1H), 7.48 (m, 1H), 7.28 (m, 1H), 7.12 (m, 1H), 4.73 (s, 2H), 3.68 (s, 3H), 2.36 (s, 3H).	
406	4-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (m, 2H), 7.77 (m, 1H), 7.62 (m, 2H), 7.31 (m, 1H), 7.11 (dd, 1H),4.75 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H).	
407	4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (m, 2H), 8.23 (m, 1H), 7.71 (m, 2H), 7.65(m, 1H), 7.18 (d, 1H), 4.66 (s, 2H), 3.75 (s, 3H).	448.02
408	3-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (m, 1H), 8.76 (m, 1H), 8.22 (m, 1H), 8.05 (m, 1H), 7.50 (m, 1H), 7.48 (m, 1H), 7.17 (dd, 1H), 4.63 (s, 2H), 3.70 (s, 3H).	
409	5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.23 (dd, 1H), 7.70 (m, 1H), 7.52 (m, 2H), 7.19 (m, 2H), 4.49 (s, 2H), 3.77 (s, 3H).	452.90
410	5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol	8.06 (d, 2H) 7.34 (d, 1H), 7.51 (m, 5H), 4.68 (s, 2H), 3.68 (s, 3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
411	3-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (s, 1H), 8.78 (d, 1H) 8.05 (d, 1H), 7.93 (d, 1H), 7.91 (d, 1H), 7.50 (m, 2H), 7.28 (t, 1H), 4.64 (s, 2H), 3.70 (s, 3H).	
412	4-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 7.93 (d, 1H) 7.90 (d, 1H), 7.64 (d, 2H), 7.52 (m, 1H), 7.33 (m, 1H), 4.64 (s, 2H), 3.73 (s, 3H).	
413	5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.90 (d, 1H) 7.82 (d, 1H), 7.74 (d, 1H), 7.51 (m, 3H), 4.58 (s, 2H), 3.71 (s, 3H).	
414	3-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.91 (s, 1H), 8.78 (d, 1H) 8.23 (d, 1H), 8.04 (d, 1H), 7.66 (d, 1H), 7.49 (m, 2H), 4.60 (s,2H), 3.69 (s, 3H).	
415	3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.22 (d, 1H) 7.74 (d, 1H), 7.63 (d, 1H), 7.49 (m, 3H), 4.54 (s, 2H), 3.70 (s, 3H).	
416	2-cloro-4-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.92 (s, 1H), 8.78 (d, 1H) 8.65 (d, 1H), 8.04 (t, 2H), 7.89 (d, 1H), 7.51 (m, 1H), 4.69 (s, 2H), 3.71 (s, 3H).	
417	2-cloro-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.82 (d, 2H), 8.65 (d, 1H) 8.02 (s, 1H), 7.89 (d, 1H), 7.64 (d, 2H),4.70 (s, 2H), 3.74 (s,3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
418	2-cloro-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.64 (d, 1H) 8.01 (s, 1H), 7.88 (d, 1H), 7.75, (d, 1H),7.52 (m, 2H), 4.62 (s, 2H), 3.72 (s, 3H).	
419	4-[4-metil-5-(5-fenil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (d, 2H), 8.12 (d, 2H) 7.63 (m, 3H), 7.55 (m, 2H), 4.63 (s, 2H),3.72 (s, 3H).	
420	3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol	8.11 (d, 2H) 7.74 (d, 1H), 7.57 (m, 1H), 7.52 (m, 4H), 4.56 (s, 2H), 3.70 (s, 3H).	
421	5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-3il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(CD_3OD como solvente): 8.21 (m, 1H), 8.02 (m, 1H), 7.82 (m, 1H), 7.68 (m, 1H), 7.56 (m, 1H), 7.33 (t, 1H), 4.50 (s, 2H), 3.82 (s,3H).	
422	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol	(CD_3OD como solvente): 7.84 (s, 1H), 7.75 (m, 2H), 7.60 (m, 1H) 7.50 (m, 2H), 7.27 (m, 1H), 6.92 (s, 1H), 4.51 (s, 2H), 4.23 (q, 2H), 1.33 (t, 3H).	404.05
423	2-cloro-4-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.64 (d, 1H), 8.01 (s, 1H) 7.98 (d, 1H), 7.54 (d, 1H), 7.50 (d, 1H), 7.20 (m, 1H), 4.61 (s, 2H), 3.76 (s, 3H).	392.00

Ejemplo No.	Nombre	^{1}H RMN	MS
424	4-{5-[3-(3-fluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (d, 2H), 7.85 (d, 1H) 7.78 (d, 1H), 7.62 (d, 2H), 7.46 (m, 1H),7.22 (m, 1H), 4.76 (s, 2H), 3.72 (s, 3H).	
425	3-(3-fluoro-fenil)-5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.84 (d, 1H) 7.74 (m, 1H), 7.51 (m, 3H), 7.24 (m, 1H), 4.70 (s, 2H), 3.70 (s, 3H).	
426	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	(CD_3OD como solvente): 7.89 (m, 2H),7.76 (m, 1H), 7.60 (m, 1H), 7.47 (m, 2H), 7.27 (m, 1H), 4.55 (s, 2H), 4.25 (q, 2H), 2.41 (s, 3H), 1.32 (s, 3H)	384.13
427	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	(CD_3OD como solvente): 7.85 (m, 1H), 7.75 (m, 1H), 7.60 (m, 1H), 7.55 (m, 1H), 7.27 (m, 1H), 7.22 (m, 1H), 4.57 (s, 2H), 4.27 (q, 2H), 2.36 (s, 3H), 1.33 (s, 3H).	402.09
428	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina	(CD_3OD como solvente): 8.75 (m, 2H), 8.04 (m, 2H), 7.78 (m, 2H), 7.66 (m, 1H), 7.60 (m, 1H), 7.37 (m, 1H), 6.30 (m, 2H), 5.42 (s, 2H), 4.56 (s, 2H).	452.10
429	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (m, 2H), 8.09 (m, 1H), 7.98 (m, 1H), 7.58 (m, 3H), 7.50 (dd, 1H), 4.69 (s, 2H), 4.12 (m, 2H), 1.36 (m, 3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
430	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	(CD_3OD como solvente): 8.87 (s, 1H), 8.77 (d, 1H), 8.07 (m, 3H), 7.67 (m, 2H), 7.61 (dd, 1H), 4.62 (s, 2H), 4.13 (m, 2H), 1.26 (m, 3H).	400.12
431	5-(3-cloro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(CD_3OD como solvente): 7.79 (m, 3H),7.67 (m, 2H), 7.51 (m, 2H), 4.56 (s, 2H), 4.22 (q, 2H), 1.30 (t, 3H).	405.07
432	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-4-furan-2-ilmetil-4H-[1,2,4]-triazol-3-il}-piridina	(CD_3OD como solvente): 8.86 (s, 1H), 8.76 (d, 1H), 8.07 (m, 1H), 8.01 (m, 2H), 7.64 (m, 3H), 7.36 (s, 1H),6.29 (s, 2H), 5.37 (s, 2H), 4.55 (s, 2H).	452.12
433	3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	(CD_3OD como solvente) :7.87 (m, 2H), 7.73 (m, 1H), 7.63 (m, 1H), 7.45 (m, 3H), 7.25 (m, 1H), 6.31 (m, 2H), 5.42 (s, 2H), 4.49 (s, 2H),2.40 (s, 3H).	436.16
434	5-(5-fluoro-2-metil-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(CD_3OD como solvente): 7.75 (dd, 1H), 7.69 (m, 1H), 7.66 (m, 1H), 7.41 (m, 1H), 7.38 (m, 1H), 7.25 (m, 2H), 6.32 (s, 2H), 5.44 (s, 2H), 4.51 (s, 2H), 2.36 (s, 3H).	454.12

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Ejemplo No.	Nombre	^{1}H RMN	MS
435	5-(3-cloro-fenil)-3-(4-furan-2-ilmetil-4H-[1,2,4]-triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol	8.23 (s, 1H), 8.09 (m, 1H), 7.97 (m, 1H), 7.48 (m, 1H), 7.45 (m, 1H),7.37 (s, 1H), 6.39 (m, 1H), 6.34 (m, 1H), 5.12 (s, 2H), 4.55 (s, 2H).	375.09
436	3-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.92 (s, 1H), 8.78 (d, 1H) 8.43 (s, 1H), 8.35 (d, 1H), 8.05 (d, 1H), 7.91 (d, 1H), 7.72 (t, 1H), 7.52 (m, 1H), 4.67 (s, 2H),3.71 (s, 3H).	376.20
437	3-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.82 (d, 2H), 8.43 (s, 1H) 8.35 (d, 1H), 7.90 (t, 1H), 7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s, 3H).	376.10
438	3-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.42 (s, 1H), 8.35 (d, 1H) 7.89 (d, 1H), 7.72 (m, 2H), 7.52 (s, 1H), 4.61 (s, 2H), 3.73 (s, 3H).	
439	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.08 (m, 1H), 7.54 (m, 2H), 7.48 (d, 1H), 7.20 (m, 2H), 4.69 (s, 2H),4.18 (m, 2H), 1.39 (t, 3H).	423.12
440	2-cloro-4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.64 (d, 1H), 8.02 (s, 1H), 7.89 (d, 1H), 7.53 (d, 1H), 7.48 (d, 1H), 7.20 (t, 1H), 4.69 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	406.00
441	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.23 (s, 1H), 7.66 (d, 1H), 7.53 (d, 1H), 7.48 (m, 2H), 7.19 (t, 1H), 4.63 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	376.10

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Ejemplo No.	Nombre	^{1}H RMN	MS
442	3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	7.93 (m, 2H), 7.71 (m, 1H), 7.49 (m, 2H), 7.42 (m, 2H), 4.63 (s, 2H),4.10 (q, 2H), 2.43 (s, 3H), 1.36 (t, 3H).	384.10
443	4-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.80 (m, 2H), 7.91 (m, 2H), 7.60 (m, 2H), 7.41 (m, 2H), 4.68 (s, 2H), 4.09 (m, 2H), 2.43 (s, 3H), 1.29 (s, 3H).	379.20
444	3-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	(CD_3OD como solvente): 8.87 (s, 1H), 8.77 (d, 1H), 8.02 (m, 1H), 7.92 (m, 2H), 7.49(m, 1H), 7.42 (m, 2H), 4.67 (s, 2H), 4.05 (q, 2H), 2.43 (s, 3H), 1.35 (t, 3H).	379.20
445	3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	7.88 (dd, 1H), 7.71 (m, 1H), 7.49 (m, 2H), 7.28 (m, 1H), 7.14 (dd, 1H), 4.66 (s, 2H), 4.11 (q, 2H), 2.39 (s, 3H), 1.34 (t, 3H).	
446	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.80 (m, 2H), 7.86 (m, 1H), 7.60 (m, 2H), 7.38 (m, 1H), 7.14 (dd, 1H), 4.70 (s, 2H), 4.11 (q, 2H), 2.39 (s, 3H), 1.36 (t, 3H).	398.20
447	3-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.87 (s, 1H), 8.76 (d, 1H), 8.01 (m, 1H), 7.88 (m, 1H), 7.49 (m, 1H), 7.28 (m, 1H), 7.14 (dd, 1H), 4.69 (s, 2H), 4.07 (q, 2H), 2.39 (q, 2H), 1.35 (t, 3H).	

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Ejemplo No.	Nombre	^{1}H RMN	MS
448	3-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina	(DMSO-D6 como solvente): 8.75 (dd, 2H), 8.05 (m, 4H), 7.79 (m, 1H), 7.66 (dd, 1H), 6.33 (s, 2H), 4.65 (s, 2H).	387.05
449	4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (dd, 2H), 8.24 (m, 1H), 7.71 (m, 1H), 7.61 (m, 2H), 7.18 (dd, 1H), 4.72 (s, 2H), 4.13 (m, 2H), 1.29 (m, 3H).	464.02
450	5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol	7.75 (m, 2H), 7.51 (m, 3H), 7.16 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H).	
451	3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.42 (s, 1H), 8.35 (d, 1H), 7.89 (d, 1H), 7.71 (t, 1H) 7.54 (d, 1H), 7.48 (d, 1H), 7.20 (t, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 1.40 (t, 3H).	395.10
452	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol	8.13 (d, 2H), 7.49 (br m, 5H), 7.20 (m, 1H), 4.65 (s, 2H), 4.16 (m, 2H), 1.40 (t, 3H).	370.09
453	4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metoxi-piridina	8.36 (d, 1H), 7.51 (br m, 3H), 7.42 (s, 1H), 7.19 (m, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 1.42 (t, 3H).	

1222

Ejemplo No.	Nombre	^{1}H RMN	MS
454	3-(3-cloro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (s, 1H), 7.95 (d, 1H), 7.54 (m, 1H), 7.49 (m, 1H),7.42 (m, 2H),7.20 (m, 1H), 4.78 (s,2H), 4.17 (q, 2H), 1.41 (t, 3H).	
455	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (m, 2H), 7.76 (m, 1H) 7.66 (m, 1H), 7.60 (m, 2H), 7.41 (m, 2H), 6.78 (s, 1H), 4.65 (s, 2H), 4.07 (q, 2H), 1.40 (t, 3H).	399.10
456	2-metil-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.73 (d, 1H), 7.81 (s, 1H), 7.75 (s, 2H), 7.51 (m, 2H) 4.60 (s, 2H), 3.71 (s, 3H) 2.68 (s, 3H).	
457	4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.73 (d, 1H), 7.82 (s, 1H), 7.76 (d, 1H), 7.54 (d, 1H), 7.48 (d, 1H), 7.29 (m, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 2.68 (s, 3H), 1.41 (t, 3H).	
458	5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol	7.78 (d, 1H), 7.53 (t, 2H), 7.48 (d, 1H), 7.18 (m, 2H), 4.74 (s, 2H),4.17 (m, 2H), 1.41 (t, 3H).	376.00
459	4{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 8.09 (m, 1H), 7.58 (m, 3H), 7.24 (m, 1H), 4.73 (s, 2H), 4.13 (m, 2H), 1.41 (t, 3H).	418.10

1223

Ejemplo No.	Nombre	^{1}H RMN	MS
460	4-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.82 (d, 2H), 8.75 (d, 1H), 7.84 (s, 1H), 7.76 (d, 1H), 7.60 (d, 2H),4.74 (s, 2H), 4.13 (m,2H), 1.41 (t, 3H).	
461	3-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-benzonitrilo	8.11 (s, 1H), 7.97 (m, 3H), 7.83 (d, 1H), 7.63(m, 3H), 7.50 (t, 1H), 4.63 (s, 2H) y 3.68 (s, 3H)	
462	5-(3-cloro-fenil)-3-[5-(3-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d, 1H), 7.67 (m, 1H), 7.50 (m, 5H), 4.61 (s, 2H) y 3.66 (s, 3H).	
463	5-(3-cloro-fenil)-3-[5-(4-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d, 1H), 7.55 (m, 6H), 4.61 (s, 2H) y 3.64 (s, 3H).	
464	4-{5-[5-(2,5-dicloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 8.05 (m, 1H), 7.59 (m, 2H), 7.47(s, 2H), 4.73 (s, 2H), 4.11 (m, 2H), 1.32 (m, 3H).	
465	5-(2,5-dicloro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (dd, 1H), 7.50 (m, 4H), 7.19 (dd, 1H), 4.68 (s, 2H), 4.17 (q, 2H), 1.39 (t, 3H).	
466	5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.80 (dd, 2H), 7.79 (m, 1H), 7.60 (m, 2H), 7.28 (m, 1H), 4.68 (s, 2H), 4.11 (q, 2H), 1.39 (t, 3H).	406.10

1224

Ejemplo No.	Nombre	^{1}H RMN	MS
467	4-{5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	7.80 (m, 1H), 7.52 (m, 1H), 7.48 (m, 1H), 7.20 (m, 4H), 4.68 (s, 2H),4.17 (m, 2H), 1.40 (t, 3H).	
468	5-(2,5-dicloro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.07 (dd, 1H), 7.71 (dd,, 1H),7.49 (m, 4H), 4.69 (s, 2H), 4.12 (m, 2H), 1.38 (t, 3H).	
469	5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.80 (m, 1H), 7.72 (m, 1H), 7.49 (m, 2H), 7.28 (m, 2H), 4.68 (s, 2H), 4.12 (q, 2H), 1.37 (t, 3H).	406.10
470	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 8.11 (m, 1H), 7.99 (m, 1H), 7.57 (m, 3H), 7.48 (t, 1H), 4.70 (s, 2H), 3.99 (q, 2H), 1.72 (m, 2H), 0.91 (t, 3H).	
471	4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 7.87 (dd, 1H), 7.58 (m, 2H), 7.39 (m, 1H), 7.15 (q, 1H), 4.70 (s, 2H), 4.01 (m, 2H), 2.40 (s, 3H), 1.70 (m, 2H), 0.87 (t, 3H).	
472	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol	7.91 (d, 1H), 7.67 (d, 1H), 7.52 (d, 1H), 7.48 (d, 1H), 7.20 (m, 2H), 4.62 (s, 2H), 4.18 (m, 2H), 1.38 (t, 3H).	
473	3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol	7.90 (s, 1H), 7.74 (d, 1H), 7.67 (d, 1H), 7.52 (m, 2H), 7.21 (m, 1H), 4.60 (s, 2H), 3.71 (s, 3H) 2.68 (s, 3H).	

1225

Ejemplo No.	Nombre	^{1}H RMN	MS
474	4-[4-metil-5-(3-tiofen-3-il-[1,2,4]oxadiazol-5-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.82 (d, 2H), 8.05 (s, 1H), 7.61 (m, 3H), 7.44 (m, 1H), 4.73 (s, 2H), 3.70 (s, 3H).	
475	5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol	8.05 (s, 1H), 7.73 (d, 1H), 7.62 (d, 1H), 7.51 (s, 2H), 7.44 (m, 1H), 4.66 (s, 2H), 3.68 (s, 3H).	
476	5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol	8.05 (d, 1H), 7.62 (d, 1H), 7.53 (d, 1H), 7.47 (d, 1H), 7.44 (m, 1H), 7.19 (m, 1H), 4.75 (s, 2H), 4.15 (m, 2H), 1.40 (t, 3H).	376.10
477	5-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-tiofen-3-carbonitrilo	8.18 (d, 1H), 8.03 (d, 1H), 7.51 (m, 1H), 7.46 (m, 1H), 7.18 (m, 1H), 4.63 (s, 2H), 4.16 (q, 2H), 1.40 (t, 3H).	401.00
478	5-(3-cloro-fenil)-3-[5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-isulfanilmetil]-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d, 1H), 7.52 (m, 4H), 7.34 (t, 1H), 7.27 (m, 1H), 4.63 (s, 2H) y 3.54 (s,3H).	
479	5-(3-cloro-fenil)-3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s 1H), 8.00 (d, 1H), 7.52 (m, 5H), 7.27 (m, 1H), 4.62 (s, 2H) y 3.66 (s, 3H).	403.00
480	5-(3-cloro-fenil)-3-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d, 1H), 7.59 (m, 4H), 7.49 (t, 1H), 7.22 (m, H), 4.61 (s, 2H) y 3.64 (s, 3H).	403.10

1226

Ejemplo No.	Nombre	^{1}H RMN	MS
481	3-(5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d, 1H), 7.87 (m, 2H), 7.72 (s, 1H), 7.58 (d, 1H), 7.45 (m, 3H), 4.60 (s, 2H) y 3.85 (s, 3H).	
482	5-(3-cloro-fenil)-3-[5-(3-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d, 1H), 7.59 (dd, 1H), 7.49 (t, 1H), 7.44 (t, 1H), 7.2 (m, 2H), 7.05 (dd, 1H), 4.60 (s, 2H), 3.88 (s, 3H) y 3.65 (s, 3H).	
483	5-(3-cloro-fenil)-3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s 1H), 8.01 (d, 1H), 7.59 (m, 3H), 7.49 (t, 1H), 7.03 (d, 2H), 4.59 (s, 2H), 3.89 (s, 3H) y 3.63 (s, 3H).	415.00
484	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol	7.86 (dd, 1H), 7.59 (m, 1H), 7.37 (m, 1H), 7.14 (m, 2H), 6.58 (q, 1H), 4.63 (s, 2H), 4.26 (q, 2H), 2.39 (s, 3H), 1.37 (t, 3H).	386.10
485	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol	7.91 (m, 2H), 7.59 (m, 1H), 7.40 (m, 2H), 7.10 (q, 1H), 6.58 (q, 1H), 4.61 (s, 2H), 4.24 (q, 2H), 2.43 (s, 3H), 1.36 (t, 3H).	368.20
486	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fuoro-5-metil-fenil)-[1,2,4]oxadiazol	7.97 (m, 1H), 7.47 (m, 1H),7.16 (t, 1H), 4.72 (d, 2H), 4.16 (m, 2H), 2.41 (d, 3H), 1.37 (m, 3H).	

1227

Ejemplo No.	Nombre	^{1}H RMN	MS
487	3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina	(CD_3OD como solvente): 8.72 (m, 2H), 8.17 (m, 2H), 7.86 (dd, 1H), 7.49 (m, 1H), 7.23 (dd, 1H), 4.59 (s, 2H), 2.35 (s, 3H).	
488	3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-ilamina	(CD_3OD como solvente): 8.05 (s, 1H), 7.84 (dd, 1H), 7.69 (m, 1H), 7.47 (m, 1H), 7.22 (m, 2H), 4.52 (s, 2H), 2.33 (s, 3H).	
489	3-piridin-4-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)-[1,2,4]-triazol-4-ilamina	(CD_3OD como solvente): 8.73 (dd, 2H), 8.17 (dd, 2H), 7.89 (m, 2H), 7.46 (m, 2H), 4.58(s, 2H), 2.389 (s, 3H).	
490	3-tiofen-2-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina	(C CD_3OD como solvente): 8.05 (dd, 1H), 7.87 (d, 2H), 7.70 (dd, 1H), 7.45 (m, 2H), 7.23 (q, 1H), 4.50 (s, 2H), 2.39 (s, 3H)	
491	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.23 (m, 1H), 7.66 (m, 1H), 7.60 (m, 1H), 7.47 (m, 1H), 7.11 (m, 1H), 6.60 (m, 1H), 4.61 (s, 2H), 4.26 (q, 2H), 1.38 (t, 3H).	360.10
492	5-(3-cloro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (m, 1H), 8.00 (m, 1H), 7.59 (m, 2H), 7.51 (t, 1H), 7.12 (m, 1H), 6.60 (m, 1H), 4.63 (s, 2H), 4.26 (q, 2H), 1.38 (t, 3H).	389.00

1227
1228

Ejemplo No.	Nombre	^{1}H RMN	MS
493	4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.73 (d, 1H), 7.82 (s, 1H), 7.75 (m, 1H), 7.60 (m, 1H), 7.12 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.26 (q, 2H), 2.68 (s, 3H), 1.39 (t, 3H).	
494	5-(2,5-difluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.80 (m, 1H), 7.61 (m, 1H), 7.29 (m, 2H), 7.12 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.28 (q,2H), 1.39 (t, 3H).	390.09
495	4-[4-etil-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (m, 2H), 7.63 (m, 1H), 7.59 (m, 2H), 7.41 (m, 2H), 6.58 (s, 1H), 4.63 (s, 2H), 4.06 (q, 2H), 1.38 (t, 3H).	371.00
496	4-etil-3-furan-2-il-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol	7.77 (m, 1H), 7.60 (m, 1H) 7.40 (m, 2H), 7.10 (m, 1H), 6.60 (m, 1H), 6.55 (s, 1H), 4.58 (s, 2H), 4.21 (q, 2H), 1.38 (t, 3H).	359.10
497	5-(3-cloro-fenil)-3-[5-(3,5-dicloro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d, 1H), 7.60 (d, 1H), 7.54 (s, 3H), 7.47 (t, 1H), 4.69 (s, 2H), 4.06 (q, 2H) y 1.36 (t, 3H).	
498	5-(3-cloro-fenil)-3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d, 1H), 7.53 (m, 4H), 7.20 (d, 2H), 4.68 (s, 2H), 4.03 (q, 3H), 2.45 (s, 1H) y 1.32 (t, 3H).	
499	5-(3-cloro-fenil)-3-(4-etil-5-m-tolil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d, 1H), 7.58(d, 1H), 7.29-7.50(m, 5H), 4.66 (s, 2H), 4.02 (q, 2H), 2.45(s, 1H) y 1.32 (t, 3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
500	5-(3-cloro-fenil)-3-[4-etil-5-(3-nitro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.52 (s, 1H), 8.40 (d, 1H), 8.12 (s, 1H), 8.05 (dd, 2H), 7.76 (t, 1H), 7.60 (d, 1H), 7.50 (t,1H), 4.72 (s, 2H), 4.10 (q, 2H) y 1.41 (t,3H).	
501	4-{5-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	7.80 (m, 2H), 7.78 (m, 1H), 7.65 (m, 1H), 7.59 (m, 2H), 7.40 (m, 2H), 6.65 (s, 1H), 4.67 (s, 2H), 3.64 (s, 3H).	
502	5-(3-cloro-fenil)-3-{5-(2,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.14 (s, 1H), 8.02 (d, 1H), 7.60 (d, 1H), 7.52 (t, 1H), 7.32 (m, 1H), 7.23 (m, 2H), 4.70 (s, 2H), 3.96 (q, 2H) y 1.27 (t, 3H).	
503	5-(3-cloro-fenil)-3-[5-(3-cloro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.06 (d, 1H), 7.63 (s, 1H), 7.58 (d, 1H), 7.49 (m, 4H), 7.23 (m, 2H), 4.68 (s, 2H), 4.04 (q, 2H) y 1.34 (t, 3H).	
504	5-(3-cloro-fenil)-3-[5-(4-cloro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d, 1H), 7.3 (m, 6H), 4.68 (s, 2H), 4.03 (q, 2H) y 1.34 (t, 3H).	
505	4-{5-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.78 (d, 2H), 7.55 (m,3H), 7.44 (m, 1H), 7.29 (m, 3H), 4.69 (s, 2H), 4.04 (q, 2H) y 1.34 (t, 3H).	
506	3-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol	7.55 (s, 1H), 7.50 (d, 1H), 7.44 (m, 2H), 7.28 (m, 3H), 7.18 (dd, 1H), 4.64 (s, 2H), 4.10 (q, 2H) y 1.35 (t, 3H).	404.00

Ejemplo No.	Nombre	^{1}H RMN	MS
507	3-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.58 (s, 1H), 7.53 (s, 1H), 7.40 (m, 1H), 7.27 (m, 3H), 7.10 (d, 1H), 6.68 (d, 1H), 4.62 (s, 2H), 4.19 (q, 2H) y 1.33 (t, 3H).	388.00
508	5-(2-cloro-5-metil-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.83 (s, 1H), 7.53 (d, 1H), 7.44 (m, 2H), 7.32 (d, 1H), 7.18 (t, 2H), 4.63 (s, 2H), 4.17 (q, 2H), 2.37 (s, 3H), 1.38 (t, 3H).	
509	4-{5-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-etil-4H)-[1,2,4]triazol-3-il}-piridina	8.80 (m, 2H), 7.78 (m, 1H), 7.66 (m, 1H), 7.57 (m, 2H), 7.41 (m, 2H),6.67 (s, 1H).4.71 (s, 2H), 4.03 (q, 2H), 1.36 (t, 3H).	
510	3-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol	7.78 (s, 1H), 7.64 (m, 1H) 7.52 (m, 1H), 7.41 (m, 3H), 7.18 (m, 1H), 6.65 (s, 1H), 4.66 (s, 2H), 4.08 (q, 2H), 1.36 (t, 3H).	
511	3-[3-(3-cloro-fenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.77 (s,1H),7.64 (d, 1H), 7.59 (m, 1H), 7.39 (m, 2H), 7.10 (m, 1H), 6.62 (s, 1H), 6.59 (m, 1H), 4.65 (s, 2H), 4.17 (q, 2H), 1.35 (t, 3H).	388.10
512	4-{5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina		

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Ejemplo No.	Nombre	1H RMN	MS
513	5-(2,5-dicloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	(DMSO-d6 como solvente): 7.82(dd, 1H), 7.65 (d, 1H), 7.58 (m, 1H), 7.25 (m, 1H), 4.60 (s, 2H), 4.16 (q, 2H), 1.24 (t,3H).	
514	4-{5-[5-(2,5-dicloro-tiofen-3-il)-[1,2,4]-oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]-triazol-3-il}-piridina	8.78 (d, 2H), 7.71 (d, 2H), 7.68 (m, 1H), 4.67 (s, 2H), 4.10 (q, 2H),1.21 (t, 3H).	
515	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.81 (m, 2H), 7.73 (m, 1H), 7.60 (m, 2H), 7.21 (m, 1H), 7.07 (m, 1H),6.76 (m, 1H), 4.63 (s, 2H), 4.02 (q, 2H), 2.40 (s, 3H), 1.38 (t, 3H).	
516	4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-tiofen-2-il-4H-[1,2,4]triazol	7.71 (d, 1H), 7.53 (m,1H), 7.47 (m, 1H), 7.46(m, 2H), 7.07 (m, 1H),6.77 (d, 1H), 4.63 (s,2H), 4.12 (q, 2H), 2.40(s, 3H), 1.39 (t, 3H).	
517	4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-furan-2-il-4H-[1,2,4]triazol	7.72 (d, 1H), 7.60 (m,1H), 7.10 (m, 1H), 7.05(m, 2H), 6.77 (d, 1H),6.60 (m, 1H), 4.61 (s,2H), 4.21 (q, 2H), 2.39(s, 3H), 1.38 (t, 3H).	
518	5-(3-cloro-fenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H), 7.60 (d, 1H), 7.50(t, 1H), 4.72(s, 2H), 4.12(q, 2H) y 1.42 (t, 3H).	391.00

1232

Ejemplo No.	Nombre	1H RMN	MS
519	3-(3-cloro-fenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.05 (s, 1H), 7.94 (d,1H) , 7.50 (d,1H), 7.43(t, 1H), 4.83(s, 2H), 4.13(q, 2H) y 1.44 (t, 3H).	
520	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol	8.23 (s, 1H), 7,65 (d,1H), 7.48 (m, 1H), 4.69 (s, 2H), 4.12 (q, 2H) y 1.41 (t, 3H).	
521	5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-isulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol	8.05 (s, 1H), 7,61 (d,1H), 7.43 (m, 1H), 4.81(s, 2H), 4.12 (q, 2H) y 1.43 (t, 3H).	
522	5-(3-cloro-fenil)-3-[4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (d, 1H), 8.00 (d,1H), 7.52 (m, 4H), 7.25(m, 2H), 4.67 (s, 2H),4.06 (q, 2H), 1.31 (t,3H).	
523	5-(3-cloro-fenil)-3-[4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.10 (s, 1H), 7.99 (d,1H), 7.59 (m, 4H), 7.48(t, 1H), 7.22 (d, 1H),4.67 (s, 2H), 4.01 (q,2H), 1.30 (t, 3H).	
524	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol	7.91 (s, 1H), 7,68 (d,1H), 7.21 (m, 1H), 4.67(s, 2H), 4.13 (q, 2H) y 1,41 (t, 3H).	
525	3-{3-[5-(3-cloro-tiofen-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-benzonitrilo	8.35(m, 2H), 7.89 (d,1H), 7.87 (t, 1H), 7.58(d,1H), 7.09 (d,1H),4.70 (s, 2H), 4.00 (q, 2H), 1.27 (t, 3H).	

1233

Ejemplo No.	Nombre	1H RMN	MS
526	4-(5-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.82 (d, 2H), 8.01 (d,1H), 9.93 (m, 1H), 7.59(m, 2H), 7.52 (m, 1H),7.47 (m, 1H), 4.83 (s,2H), 4.11 (q, 2H), 1.40(t, 3H).	400.10
527	2-(3-cloro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.00 (s, 1H), 7.89 (d,1H), 7.60 (m, 1H), 7.50(m, 1H), 7.44 (m, 1H),7.13 (m, 1H), 6.60 (m,1H), 4.76 (s, 2H), 4.25(q, 2H), 1.38 (t, 3H).	389.00
528	5-(3-cloro-fenil)-3-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.57 (m, 3H), 7.51(t, 1H), 7.05 (d, 2H),4.67 (s, 2H), 4.02 (q,2H), 3.89 (s, 3H), 1.31(t, 3H).	
529	5-(3-cloro-fenil)-3-[5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.02 (d,1H), 7.58 (d, 1H), 7.52(d, 1H), 7.35 (d, 2H),7.23 (s, 1H), 7.22 (d,1H), 6.19 (s, 1H), 6.04(s, 1H), 5.13 (s, 2H),4.61 (s, 2H), 2.37 (s,3H).	
530	4-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.74 (d, 1H), 7,81 (s,1H), 7.74 (d, 1H), 4.74(s, 2H), 4.12 (q, 2H)2.69 (s,1H) y 1.42 (t, 3H).	

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Ejemplo No.	Nombre	1H RMN	MS
531	3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol	7.70 (d, 1H), 7,60 (s,1H), 7.44 (t, 1H), 7.16(d, 1H), 4.70 (s, 2H),4.12 (q, 2H), 3.90 (s,3H) y 1.41 (t, 3H).	
532	5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-metoxi-fenil)-[1,2,4]oxadiazol	7.63 (d, 1H), 7,56 (s,1H), 7.39 (t, 1H), 7.07(d, 1H), 4.82 (s, 2H),4.12 (q, 2H) y 1.42 (t,3H).	
533	5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol	7.77 (s, 1H), 7,52 (d,1H), 7.16 (m, 1H), 4.79(s, 2H), 4.13 (q, 2H) y 1.42 (t, 3H).	
534	5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	8.07 (dd, 1H), 7.56 (m,1H), 7.24 (dd, 1H), 4.73(s, 2H), 4.13 (q, 2H) y 1.42 (t, 3H).	
535	3-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.40 (s, 1H), 8.34 (d, 1H),7.91(d,1H),7.01(t, 1H), 4.73 (s, 2H),4.12 (q, 2H) y 1.42 (t,3H).	381.10
536	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol	7.75 (s, 1H), 7.63 (m,1H), 7.40 (m, 2H), 6.73(s, 1H), 4.65 (s, 2H),4.07 (q, 2H) y 1.40 (t,3H).	
537	3-[5-(3-cloro-fenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol	7.58 (s, 1H), 7.46 (d,1H), 7.32 (d, 3H), 4.74(s, 2H), 4.09 (q, 2H) y 1.39 (t, 3H).	

1235

Ejemplo No.	Nombre	1H RMN	MS
538	4-etil-3-(5-tiofen-3-il-isoxazol-3-ihnetilsulfanil)-5-trifluorometil-4H-[1,2,4]triazol	7.78 (s, 1H), 7.39 (m,1H), 6.53 (d, 1H), 4.63(s' 2H), 4.07 (q, 2H) y 1.39 (t, 3H).	
539	4-{3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina	8.73 (d, 1H), 7.83 (s,1H), 7.76 (d, 1H), 7.47(m, 3H), 7.27 (s, 1H),4.65 (s, 2H), 3.67 (s,3H), 2.69 (s, 3H).	
540	4-{3-[5-(3-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina	8.74 (d, 1H), 7.82 (s,1H), 7.67 (d, 1H), 7.56(d, 1H), 7.51 (m, 1H),7.48 (m, 1H), 7.46 (s,1H), 4.65 (s, 2H), 3.67(s, 3H), 2.69 (s, 3H).	
541	4-{3-[5-(4-cloro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina	8.73 (d, 1H), 7.82 (s,1H), 7.75 (d, 1H), 7.63(d , 2H), 7.51 (d, 2H),4.65 (s, 2H), 3.65 (s,3H), 2.69 (s, 3H).	
542	4-{3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina	8.73 (d, 1H), 7.83 (s,1H), 7.45 (d, 1H), 7.61(d, 2H), 7.04 (d, 2H),4.62 (s, 2H), 3.89 (s,3H), 3.64 (s, 3H), 2.69(s, 3H).	
543	4-[3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina	8.74 (d, 1H), 7.85 (s,1H), 7.77 (d, 1H), 7.51(d, 2H), 7.32 (d, 2H) 4.70 (s, 2H), 4.03 (q,2H), 2.70 (s, 3H), 2.45(s, 3H), 1.31 (t, 3H).,	

1236

Ejemplo No.	Nombre	1H RMN	MS
544	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-fluoro-fenil)-[1,2,4]oxadiazol	(DMSO-d6 como solvente):7.93(m, 1H), 7.86 (m,2H), 7.80 (m,1H), 7.67(m, 2H), 7.25 (m,1H),4.61 (s, 2T, 4.16 (q,2H), 1.24 (t, 3H).	388.10
545	4-{4-etil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3 -ilmetilsulfanil}-4H-[1,2,4]triazol-3-iI}-piridina	8.78(bs, 2H), 7.92 (m, 2H), 7.71 (d, 2H), 7.68 (4.70 m, 1H), 7.27 (m, 1H), 4.70 (s, 2H), 4.10 (q, 2H), 1.39 (t, 3H).	383.10
546	5-(3-cloro-fenil)-3-[5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H), 7.58 (d, 1H), 7.50(t, 1H), 7.21 (m, 2H),7.00 (t, 1H), 4.68 (s,2H), 4.07 (q, 2H), 1.35(t, 3H).	
547	5-(3-cloro-fenil)-3-[5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.02 (d,1H), 7.59 (m, 2H), 7.52(d, 1H), 7.41 (d, 1H),7.04 (d, 1H), 4.73 (s,2H), 4.21 (q, 2H), 1.42(t, 3H).	
548	2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol	9.89 s 1H 7.70 s,1H) 7.56 (d, 1H), 7.54(d' 1H), 7.30 (m, 1H),7.18 (m, 1H), 6.98 (d,1H), 4.66 (s, 21-1), 4.12(q, 2H), 2.34 (s, 3H),1.37 (t, 3H).	399.90

1237

Ejemplo No.	Nombre	1H RMN	MS
549	3-{ 1-[5-(3-cloro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.73 (bs, 1H), 7.59 (m,2H), 7.41 (m, 2H), 7. 10(dd, 1H), 6.59 (m, 2H),5.05 (q, 1H), 4.13 (q,2H), 1.91 (d, 3H), 1.27(t, 3H).	401.10
550	4-(5-{1-[5-(3-cloro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.8 (dd, 2H), 7.74 (bs,1H), 7.63 (m, 1H), 7.57(dd, 2H), 7.40 (m, 2H),6.62 (s, 2H), 5.15 (q,1H), 4.05 (q, 2H), 1.95(d, 3H), 1.34 (t, 3H).	
551	3-[5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.52 (d, 2H), 7.49 (d, 1H),7.01 (d, 2H), 4.69 (s, 2H), 4.02 (q, 4H), 1.82 (m, 2H), 1.51 (q, 2H), 1.32 (t, 3H), 1.01 (t,3H).	
552	3-(5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.12 (s, 1H), 8.00 (d,1H), 7.58 (d, 1H), 7.51(d, 1H), 7.09 (d, 2H),6.96 (s, 1H), 6.08 (s,2H), 4.67 (s, 2H), 4.02(q, 2H), 1.31 (t, 3H).	
553	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-metil-tiazol-4-il)-[1,2,4]oxadiazol	8.11 (s, 1H), 7.48 (m,2H), 7.16 (t, 1H), 4.63(s, 2H), 4.13 (q, 2H), 2.82 (s, 3H), 1.37 (t,3H).	391.90

Ejemplo No.	Nombre	1H RMN	MS
554	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-fluoro-fenil)-[1,2,4]oxadiazol	(DMSO-d6 como solvente):8.21 (m, 2H), 7.51 (m,2H), 7.21 (m,3H), 4.63(s, 2H), 4.16 (q, 2H),1.38 (t, 3H).	
555	4-etil-3-(1-[5-(2-fluoro-5-metil- 1H)-etilsulfanil}-5-furan-2-il-4H-[1,2,4]triazole	7.71 (dd, 1H), 7.59 (dd,, 7.26 (m, 1H), 7.06(m, 2H) 6.(d, 1H),61H),58 (dd,, 1H)66, 5(q,4 .13 (q, 2H),.06 2.39(s, 3H), 1.91 (d, 3H),1.28 (t, 3H).	
556	4-(4-etil-5-(1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 7.71 (dd,1H) , 7.59 (dd, 2H), 7.23(m, 1H) , 7 (m, 1H),6.64 (d, 1H).06, 5.15 (q,1H), 4.01 (q, 2H), 2.39(s, 3H), 1.94 (d, 3H),1.30 (t, 3H).	410.10
557	5-(3-cloro-fenil)-3-[4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.00 (d,1H), 7.66 (s, 1H), 7.58(d, 1H), 7.52 (t, 1H),7.37 (s, 1H), 4.69 (s,2H), 4.09 (q, 2H), 3.93(s, 3H), 1.37 (t, 3H).	
558	5-(3-cloro-fenil)-3-[4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.57 (d, 1H), 7.51(t, 1H), 7.17 (s, 1H),7.04 (s, 1H), 4.69 (s, 2H), 4.56 (q, 2H), 4.12(s, 3H), 1.40 (t, 3H).	

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Ejemplo No.	Nombre	1H RMN	MS
559	5-(3-cloro-fenil)-3-[4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-isulfanilmetil]-[1,2,4]oxadiazol	8.12 (s, 1H), 8.01 (d,1H), 7.65 (s, 1H), 7.57(d, 1H), 7.48 (d, 2H),4.60 (s, 2H), 4.50 (q,2H), 3.79 (s, 3H), 1.36(t, 3H).	
560	4-{5-[5-(3-cloro-fenil)-4-metil-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (bs, 2H), 7.70 (m,1H), 7.61 (m, 3H), 7.44(m, 2H), 4.65 (s, 2H),4.09 (q, 2H), 2.31 (s,3H), 1.40 (t, 3H).	
561	3-[5-(3-cloro-fenil)-4-metil-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.70 (s, 1H), 7.60 (m,2H), 7.43 (m, 2H), 7.10(m, 1H), 6.59 (m, 1H),4.59 (s, 2H), 4.23 (q,2H), 2.28 (s, 3H), 1.38(t,31-1).	
562	3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil=tiofen-2-il)-[1,2,4]oxadiazol	7.61(d, 1H), 7.49 (m,2H), 7.22 (m,2H), 4.59(s, 2H), 4.16 (q,2H),2.32 (s,3H), 1.38 (t,3H).	
563	5-(3-cloro-fenil)-3-[4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.13 (s, 1H), 8.01 (d,1H), 7.58 (d, 1H), 7.52(d, 1H), 7.45 (d, 1H),7.02 (d, 1H), 4.69 (s,2H), 3.97 (q, 2H), 2.32(s, 3H), 1.28 (t, 3H).	
564	15-(3-cloro-fenil)-3-[4-etil-5- I(5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d, (5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-. [1,2,4]oxadiazol	

1240

Ejemplo No.	Nombre	1H RMN	MS
565	4-{5-[4-cloro-5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.81 (d, 2H), 7.99 (m,1H), 7.90 (m, 1H), 7.60(m, 2H), 7.48 (m, 2H),4.65 (s, 2H), 4.10 (q,2H), 1.39 (t, 3H).	
566	3-[4-cloro-5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.99 (s, 1H), 7.90 (m,1H), 7.60 (m, 1H), 7.47(m, 2H), 7.12 (m, 1H),6.60 (m, 1H), 4.59 (s,2H), 4.25 (q, 2H), 1.38(t, 3H).	
567	2-cloro-4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metil-piridina	8.11 (s, 1H), 8.00 (d,1H), 7.58 (d, 1H), 7.52(d, 1H), 7.40 (d, 2H),4.71 (s, 2H), 4.10 (q,2H), 2.64 (s, 31-1), 1.40(t, 3H).	
568	3-[5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-cloro-fenil)-[1,2,4]oxadiazol	8.11 (s, 1H), 7.99 (d,1H), 7.58 (d, 1H), 7.51(t, 1H), 7.07 (d, 1H),6.52 (d, 1H), 4.64 (s,2H), 4.23 (q, 2H), 1.40(t, 3H).	
569	2-cloro-4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il} -piridina	8.59 (d, 1H), 8.10 (s,1H), 8.00 (d, 1H), 7.66(s, 1H), 7.59 (d, 1H), 7.54 (d, 1H), 7.50 (d,1H), 4.72 (s, 2H), 4.11(q, 2H), 1.42 (t, 3H).	

1241

Ejemplo No.	Nombre	1H RMN	MS
570	2-cloro-4- {5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il} -6-metoxi-piridina	8.11 (s, 1H), 8.00 (d,1H), 7.58 (d, 1H), 7.50(t, 1H), 7.24 (s, 1H),6.91 (s, 1H), 4.70 (s,2H), 4.08 (q, 2H), 4.02(s, 3H), 1.39 (t, 3H).	464.10
571	2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-benzonitrilo	8.02 (s, 1H), 7.76 (d,2H), 7.47 (m,3H), 7.17(t, 1H), 4.68 (s, 2H),4.19 (q, 2H), 2.51 (s,3H), 1.39 (t, 3H).	
572	5-(3-cloro-fenil)-3-[4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	8.14 (s, IH), 8.03 (d,1H), 7.58 (d, 1H), 7.50(d, 1H), 7.44 (d, 1H),6.94 (1H), 4.67 (s, 2H),4.03 (q, 2H), 3.88 (s,3H), 1.29 (t, 3H).	
573	3-[5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.61 (m, 1H), 7.52 (d,1H), 7.21 (d, 1H), 7.11(m, 1H), 7.61 (m, 1H),6.55 (s, 1H), 4.57 (s,2H), 4.21 (q, 2H), 1.38(t, 3H).	393.10
574	3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-5-fluoro-benzonitrilo	8.21(m, 1H), 8.04 (dd,1H), 7.59 (m, 2H), 7.10(dd4.64 ,1H),6.59(dd,1H),(s, 2H), 4.25 (q,2H), 1.38 (t, 3H).	
575	4-etil-3-(5-fenil isoxazol-3-ilmetilsulfanil)-5-tiofen-2-il-4H-[1,2,4]triazol	7.77 (m, 2H), 7.53 (d,1H), 7.47 (m, 4H), 7.19(dd, 1H), 6.71 (s, 1H),4.61 (s, 2H), 4.12 (q,2H) and 1.39 (t, 3H).	

125
1242

Ejemplo No.	Nombre	^{1}H RMN	MS
576	4-metil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-3-il-4H-[1,2,4]triazol	7.77 (m, 3H), 7.50 (m,5H), 6.69 (s, 1H), 4.56(s, 2H) y 3.67 (s, 3H)	
577	4-etil-3-furan-2-il-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol	7.77 (m, 2H), 7.61 (s,1H) , 7.46 (m, 3H), 7.14(d, 1H), 6.69 (s, 1H),6.60 (d, 1H), 4.60 (s,2H), 4.22 (q, 2H) y 1.38 (t, 3H).	
578	4-[4-etil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il1-piridina	8.82 (w, 2H), 7.77 (m,2H), 7.61 (d, 2H), 7.45(m, 3H), 6.71 (s, 1H),4.65 (s, 2H), 4.06 (q,2H) y 1.39 (t, 3H).	
579	4-[4-metil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (w, 2H), 7.77 (m,2H), 7.63 (d, 2H), 7.46(m, 3H), 6.70 (s, 1H),4.60 (s, 2H) y 3.68 (s,3H).	
580	2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,3,4]oxadiazol	7.80 (m, 2H), 7.70 (m,1H), 7.35(m, 2H), 7.13(m, 2H), 6.60 (m, 1H),4.74 (s, 2H), 4.23 (q,2H), 2.40 (s, 3H), 1.36(t, 3H).	368.10
581	4-[4-metil-5-(5-m-tolil-[1,3,4]oxadiazol-2-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (m, 2H), 7.80 (m, 2H), 7.61 (d, 2H), 7.39(m, 2H), 4.74 (s, 2H),3.71 (s, 3H), 2.4 (s, 3H).	365.10

1243

Ejemplo No.	Nombre	1H RMN	MS
582	4-[4-etil-5-(5-m-tolil-[1,3,4]oxadiazol-2-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.81 (d, 2H), 7.81 (m,2H), 7.58 (m, 2H), 7.37(m, 2H), 4.81 (s, 2H),4.41 (q, 2H), 2.42 (s,3H), 1.33 (t, 3H).	379.10
583	4-{5-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-	8.80 (d, 2H), 7.98 (m,1H), 7.58 (d, 2H), 7.46(d ,1H), ,1H), 4.66 (s, 2H),4.10 (q, 2H), 1.38(t,3H).	405.90
584	3-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo	8.79 (bs, 2H), 8.46 (m,1H) , 7.91 (m, 1H), 7.59(4,.74 2H),, 7(t, 1H),(s2H).43 , 4 .12 (q,2H), 1.41 (t,3H).	
585	3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo	8.45(dd, 1H), 7.91 (m,1H), 7.59 (d, 1H), 7.43(t, 1H), 7.10 (d, 1H),6.58 (dd,1H), 4.65 (s,2H), 4.27 (q, 2H), 1.39(t, 3H).	397.10
586	3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo	8.45 (dd, 1H), 7.90 (m,1H), 7.47 (m,3H), 7.18(t, 1H), 4.68 (s, 2H),4.17 (q, 2H), 1.41 (t,3H).	
587	3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.41 (m, 2H), 7.89 (d,1H), 7.69 (d, 1H), 7.13(m, 1H), 6.60 (m, 1H),4.65 (s, 2H), 4.27 (q,2H), 1.40 (t, 3H).	379.10

1294

Ejemplo No.	Nombre	1H RMN	MS
588	3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo	8.36 (m, 2H), 7.80 (t,1H), 7.62 (m, 2H), 7.15(m, 1H), 6.61 (m, 1H),4.78 (s, 2H), 4.2 (q, 2H),1.40 (t, 3H).	379.10
589	3-[3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.41 (m, 2H), 7.90 (m,1H), 7.72 (t, 1H), 4.68(s, 2H), 3.73 (s, 3H).	
590	5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,2,4]oxadiazol	8.08 (m, 1H), 7.58 (m,1H), 7.25 (m, 1H), 4.67(s, 2H), 3.74 (s, 3H).	394.90
591	2-cloro-4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.63 (m, 1H), 8.02 (m,1H), 7.89 (m, 1H), 7.61(m, 1H), 7.14 (m, 1H),6.61 (m, 1H), 4.67 (s,2H), 4.27 (q, 2H), 1.40(t, 3H).	390.00
592	2-cloro-4-[3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.63 (d, 1H), 8.00 (d,1H), 7.88 (m, 1H), 7.62(d, 1H), 7.14 (d, 1H),6.61 (m, 1H), 4.60 (s,2H), 3.82 (s,	
593	2-(3-cloro-fenil)-5-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	7.98 (m, 2H), 7.89 (d,1H), 7.49 (m, 1H), 7.44(m, 1H), 4.69 (s, 2H),3.92 (s, 3H), 2.77 (s, 3H).	
594	2-(3-cloro-fenil)-5-(4-metil-5-tiazol-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.91 (s, 1H), 8.24 (s,1H), 7.98 (s, 1H), 7.91(d, 1H), 7.49 (m, 1H),7.43 (m, 1H), 4.72 (s,2H), 3.96 (s, 3H).	

1245

Ejemplo No.	Nombre	1H RMN	MS
595	2-(3-cloro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.00 (s, 1H), 7.89 (d,1H), 7.60 (s, 1H), 7.53(m, 1H), 7.43 (m, 1H),7.12 (d, 1H), 6.60 (d de d, 1H), 4.68 (s, 2H),3.80 (s, 3H).	
596	2-(3-cloro-fenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol	8.00 (s, 1H), 7.90 (d,1H), 7.52 (m, 2H), 4.86(s, 2H), 4.13 (q, 2H),1.42 (t, 3H).	
597	4-{4-etil-5-[5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 7.68 (s,(m4,, 1H).59 72H), 7.23.101H), 4(d,.63 (s, 2H),(q, 2H), 2.32(d,3H), 1.37 (t,3H).	
598	3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol	7.67 (d, 1H), 7.59 (m,1H), 7.2 (s, 1H), 7.09 (d,1H), 6.58 (dd,1H), 4.56(s, 2H), 4.24 (q, 2H),2.32 (s, 3H), 1.36 (t,3H).	374.00
599	3-(3-cloro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.02 (m, 1H), 7.91 (m,1H), 7.57 (d, 1H), 7.35(m, 2H), 7.08 (d, 1H),6.56 (dd,1H), 4.72 (s, 2H), 4.22 (q, 2H), 2.32(s, 3H), 1.36 (t, 3H).	
600	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfa il]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (dd, 2H), 8.02(m,1H), 7.92 (m, 1H),7.57 (dd, 2H), 7.42(m,2H), 4.80 (s, 2H),4.08 (q, 2H), 1.38(t,3H).	

1296

Ejemplo No.	Nombre	1H RMN	MS
601	4-{4-etil-5-[5-(3-nitro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.87 (m, 3H), 8.42 (m,2H), 7.75 (t, 1H), 7.66(d° 2H), 4.88 (s, 2H),4.15 (q, 2H), 1.45 (t,3H).	
602	2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,3,4]oxadiazol	8.87 (t, 1H), 8.39 (m,2H), 7.73 (t, 1H), 7.61(m, 1H), 7.15 (m, 1H),6.61 (m, 1H), 4.28 (q,2H), 1.78 (s, 2H), 1.41(t, 3H).	
603	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 7.78 (m,3H) , 7.66 (m, 1H), 7.39(m, 2H), 6.84 (s, 1T,4.69 (s, 2H), 3.27 (m,1H), 1.20 (q, 2H), 0.83(m, 2H).	411.00
604	3-[5-(3-cloro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol	7.77 (m, 1H), 7.65 (m,1H), 7.56 (m, 2H), 7.41(m, 2H), 7.04 (m, 2H),6.79 (s, 1H), 4.61 (s,2H), 3.97 (q, 2H), 3.89(s, 3H), 1.32 (t, 3H).	428.20
605	5-(3-cloro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol	8.08 (rn, 1H), 7.96 (dd,1H), 7.45 (m, 4H), 7.17(m, 1H), 4.93 (q , 1H),3.67 (s, 3H), 1.91(d,3H).	404.92
606	5-(3-cloro-fenil)-3-[1-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol	8.1(d, 1H), 7.98 (d, 1H),7.51 (m,4H), 7.17 (t,1H), 5.11 (q, 1H), 4.11(q, 2H), 1.93 (d,3H),1.34 (t, 3H).	418.90

1247

Ejemplo No.	Nombre	1H RMN	MS
607	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.08(m,1H), 7.98 (dd, 1H),7.59 (m, 3H), 7.46 (t,1H), 5.05 (q, 1H), 3.66(s, 3H), 1.94 (d, 3H).	400.07
608	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.1 Q(m, 1H), 7.99 (dd, 1H),7.58 (m, 3H), 7.47 (t,1H), 5.20 (q, 1H), 4.06(q, 2H), 1.96 (d, 3H),1.33 (t,3H).	414.05
609	3-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo	8.84 (s, 2H),8.30 (m,2H), 7.85 (m, 1H), 7.66(m, 3H), 4.84 (s, 2H),4.14 (q, 2H), 1.43 (t,3H).	
610	3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo	8.27 (m, 2H), 7.82 (m,1H), 7.62 (m, 2H), 7.18(t, 1H), 6.62 (m, 1H),4.79 (s, 2H), 4.27 (q,2H), 1.40 (t, 3H).	
611	3-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-isulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo	8.83(d,21-1),8.31(m,2H), 7.84 (m, 4H), 4.81(s, 2H), 3.77 (s, 3H).	
612	3-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil-mil]-etil)-[1,3,4]oxadiazol-2-il-benzonitrilo	8.82 (s, 2H), 8.33 (m,2H), 7.86 (t, 3H), 7.67(t, 1H), 4.91 (d, 2H),1.24 (m, 3H), 0.88 (m,2H).	402.20

1298

Ejemplo No.	Nombre	1H RMN	MS
613	4-{5-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente 8.80 (s (br), 2H), 7.96(m, 2H), 7.81(d,2H),7.61 (m, 2H), 4.73 (s,2H), 3.84 (s, 3H).	
614	4-{5-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	(CD30D como solvente):8.75 (d, 2H), 8.02 (s,1H), 7.96 (d, 1H), 7.89(d , 2H), 7.60 (m, 2H),4.89 (s, 2H), 3.59 (m,1H), 1.21 (m, 2H), 0.84(m, 2H).	412.16
615	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	7.80 (m, 2H), 8.04 (m,1H), 7.77 (d, 2H), 7.51(m, 1H), 7.21 (t, 1H),4.92 (s, 2H), 3.32 (m,1H), 1.21 (m, 2H), 0.85(m, 2H).	430.11
616	2-(5-cloro-2-fluoro-fenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	8.02 (m, 1H), 7.52 (m,3H), 7.20 (t, 1H), 7.04(m, 2H), 4.81 (s, 2H),4.03 (q, 2H), 3.89 (s,3H), 1.33 (t, 3H).	
617	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (d, 2H), 8.03 (m,1H), 7.65 (m, 2H), 7.51(m, 1H), 7.20 (t, 1H), 4.78 (s, 2H), 3.75 (s,3H).	
618	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (bs, 2H), 8.02 (m,1H), 7.61 (m, 2H), 7.51 (m, 1H), 7.20 (t, 1H), 4.85 (s, 2H), 4.13 (q,2H), 1.41 (t, 3H).	

1239

1249

Ejemplo No.	Nombre	^{1}H RMN	MS
619	2-(3-cloro-fenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	8.01 (d of d aplastado, 1H), 7.85 (d, 1H), 7.51 (m, 4H), 7.00 (d,2H), 4.79 (s, 2H), 4.00 (q, 2H), 3.88 (s, 3H), 1.30 (t, 3H).	
620	2-(3-cloro-fenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol	7.97 (s, 1H), 7.84 (d, 1H), 7.58 (d, 1H), 7.49 (m, 1H), 7.40 (m, 1H), 7.12 (d, 1H), 6.59 (d de d, 1H), 5.16 (q, 1H), 4.17 (q, 2H), 2.02 (d,3H), 1.28 (t, 3H).	
621	5-(5-cloro-2-fluoro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol	8.06 (m, 1H), 7.54 (m, 3H), 7.23 (m, 2H), 4.93 (q, 1H), 3.72 (s, 3H),1.91 (d,3H).	
622	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.07 (dd,1H), 7.62 (dd, 2H), 7.54 (m, 1H), 7.21 (t, 1H), 5.07 (q, 1H), 3.69 (s, 3H), 1.95 (d, 3H).	418.10
623	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (dd, 2H), 8.08 (m, 1H), 7.57 (m, 3H), 7.22 (t, 1H), 5.21 (q, 1H), 4.08 (q, 2H), 1.97 (d, 3H), 1.35 (t,3H).	
624	2-cloro-4-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina	8.83 (m, 2H), 8.65 (m, 1H), 8.05 (t, 1H), 7.92 (t, 1H), 7.76 (t, 2H), 4.82 (2H), 3.31 (m, 1H), 1.23 (m, 2H), 0.86 (m,2H).	

1250

Ejemplo No.	Nombre	^{1}H RMN	MS
625	4-{5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.83 (t, 2H), 7.82 (m, 1H), 7.63 (m, 2H), 7.32 (m, 1H), 7.10 (m, 1H), 4.75 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H), 1.61 (d, 1H).	
626	4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.82 (d, 2H), 7.82 (m,1H), 7.59 (t, 2H), 7.33(m, 1H), 7.11 (m, 1H),4.82 (s, 2H), 4.10 (m,2H), 2.39 (s, 3H), 1.38(t, 3H).	397.08
627	4-{4-Ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.80 (s, 2H), 7.84 (m,1H), 7.76 (d, 2H), 7.32(m, 1H), 7.12 (q, 1H),4.91 (s, 2H), 3.31 (m,1H), 2.39 (d, 3H),1.21(m, 2H), 0.84 (m, 2H).	409.15
628	2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol	7.77 (m, 1H), 7.61 (m,1H), 7.32 (d, 1H), 7.12(m, 2H), 6.61 (m, 1H),4.76 (s, 2H), 4.26 (q,2H), 2.37 (d, 3H), 1.23(t, 3H).	
629	2-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol	7.81 (m, 1H), 7.54 (m,2H), 7.32 (d, 1H), 7.11(m, 1H), 7.03 (m, 2H),4.79 (s, 2H), 4.02 (q,2H), 3.89 (s, 3H), 2.37(d, 3H), 1.31 (t, 3H).	426.15

1251

Ejemplo No.	Nombre	^{1}H RMN	MS
630	4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (dd, 2H), 7.91 (dd,1H), 7.60 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H),6.86 (d, 1H), 4.67 (s,2H), 4.05 (q, 2H), 1.37(t, 3H).	417.02
631	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.81 (dd, 2H), 7.91 (dd, 1H), 7.59 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H),6.74 (d, 1H), 5.20 (q,1H), 4.05 (q, 2H), 1.95(d, 3H), 1.34 (t, 3H).	431.10
632	4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.82 (dd, 2H), 7.91 (dd,1H), 7.63 (dd, 2H), 7.39(m, 1H), 7.15 (m, 1H),6.85 (d, 1H), 4.62 (s,2H), 3.69 (s, 3H).	403.10
633	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.81 (dd, 2H), 7.91 (dd,1H), 7.60 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H), 6.72 (d, 1H), 5.06 (q,1H), 3.64 (s, 3H), 1.93(d, 3H).	417.10
634	4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.80 (dd, 2H), 7.92 (dd,1H), 7.76 (dd, 2H), 7.38(m, 1H), 7.15 (m, 1H),6.95 (d, 1H), 4.71 (s,2H), 3.27 (m, 1H), 1.18(m, 2H), 0.82 (m, 2H).	429.10

1252

Ejemplo No.	Nombre	^{1}H RMN	MS
635	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (dd, 2H), 7.92 (dd,1H) 7.76 (dd, 2H), 7.38m, 1H), 7.15 (m, 1H),6. (85 (d, 1H), 5.40 (q,1H), 3.24 (m, 1H),1.98(d, 3H), 1.88 (m, 2H),0.80 (m, 2H).	443.20
636	3-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.90 (dd, 1H), 7.60 (dd,1H), 7.39 (m, 1H), 7.11(m, 2H), 6.85 (d, 1H),6.59 (dd, 1H), 4.62 (s,2H), 4.20 (q, 2H), 1.38(t, 3H).	
637	3-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol	7.88 (dd,1H), 7.59 (dd,1H), 7.39 (m, 1H), 7.11(m, 2H), 6.74 (d, 1H),6.58 (dd, 1H), 5.08 (q,1H), 4.20 (q, 2H), 1.92(d, 311),134 (t, 3H).	
638	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triázol-3-il)-piridina	1.96 (d, 3H) 3.61 (s, 3H) 5.10 (q, 1H) 7.38 (t,1H) 7.47 (m, 1H) 7.54(m, 2H) 7.84 (m, 1H)7.93 (m, 1H) 8.74 (d, 2H)	
639	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.80 (bs, 2H), 7.99 (m,1H), 7.90 (m, 1H), 7.58(d, 2H), 7.51 (m, 1H),7.46 (t, 1H), 5.31 (q,1H), 4.06 (q, 2H), 2.04(d, 3H), 1.31 (t, 3H).	414.10

1262
1253

Ejemplo No.	Nombre	^{1}H RMN	MS
640	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (bs, 2H), 8.03 (m, 1H), 7.94 (d, 1H), 7.76 (d, 2H), 7.51 (m, 1H), 7.45 (t, 1H), 7.54 (q, 1H), 3.25 (m, 1H), 2.06 (d, 3H), 1.19 (m, 2H), 0.81 (m, 2H).	426.07
641	5-(5-cloro-2-fluoro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (dd, 1H), 7.60 (d,1H), 7.55 (m, 1H), 7.22(4 1H), 7.09 (d, 1H),6.58 (m,1H), 4.55 (s,2H), 3.81 (s, 3H).	
642	5-(5-cloro-2-fluoro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.06 (dd, 1H), 7.89 (d, 1H), 7.55 (m, 2H), 7.22 (t, 1H), 6.88 (dd, 1H), 4.55 (s, 2H), 3.67 (s, 3H).	
643	4-cloro-2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol	10.08 (s,1H), 7.88 (d, 1H), 7.47 (m, 3H), 7.17 (t,1H), 7.06 (d, 1H), 4.68 (s, 2H), 4.14 (q, 2H), 1.38 (t, 3H).	
644	2-cloro-4[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-[1,3,4]oxadiazol-2-il]-piridina piridina	s.83 (á! 2H), s.6o (m,1H)m,, 71H), (4.82 11~,.94 7 (.m, 62 (m, 2I.85 ~;(s, 2H), 3.75 (s,3H).	
645	2-cloro-4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina	8.82 (d, 2H), 8.60 (m, 1H), 7.94 (m, 1H), 7.86 (m, 1H), 7.59 (m, 2H), 4.87 (s, 2H), 4.12 (q, 2H), 1.43 (t, 3H).	

1254

Ejemplo No.	Nombre	^{1}H RMN	MS
646	2-cloro-4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il1-piridina	8.81 (d, 2H), 8.60 (m,1H), 7.96 (m, 1H), 7.86(m, 1H), 7.75 (m, 2H),4.92 (s, 2H), 3.32 (m,1H), 1.21 (m, 2H), 0.87(q, 2H).	
647	2-cloro-4-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina	8.57 (m, 1H), 7.92 (m,1H), 7.81 (m, 1H), 7.61(m, 1H), 7.12 (m, 1H),6.61 (m, 1H), 4.79 (s,2H), 4.26 (q, 2H), 1.40(t, 3H).	
648	2-cloro-4-{5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol-2-il}-piridina	8.59 (m, 1H), 7.94 (m,1H), 7.84 (m, 1H), 7.55(m, 2H), 7.05 (m, 2H),4.g3 (s, 2H), 4.02 (q,2H), 1.34 (t, 3H).	
649	2-(3-cloro-fenil)-5-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	8.00 (m, 1H), 7.87 (d, 1H), 7.53 (m, 3H), 7.42 (t, 1H), 7.01 (m, 2H),5.07 (q, 1H), 3.88 (s, 3H), 3.54 (s, 3H), 2.00(d, 3H).	
650	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.81 (bs, 2H), 8.01 (m, 1H), 7.63 (d, 2H), 7.50 (m, 1H), 7.18 (m, 1H),5.17 (q, 1H), 3.69 (s, 3H), 2.02 (d, 3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
651	5-(5-Bromo-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.20 (m, 1H), 7.65 (m, 1H) 7.60 (s, 1H), 7.13 (m, 2H), 6.56 (m, 1H),4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	
652	2-(3-cloro-fenil)-5-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol	8.02 (d, 1H), 7.90 (d,1H), 7.50 (m, 4H), 7.03(d, 2H), 4.71 (s, 2H),3.88 (s, 3H), 3.61 (s,3H).	
653	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 8.09 (t,1H), 7.97 (m, 1H), 7.76(d, 2H), 7.45 (m, 2H),4.89 (s, 2H), 3.30 (m,1H), 1.22 (m, 2H), 0.86(m, 2H).	412.07
654	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.78 (s, 2H), 8.14 (m,1H), 8.04 (m, 1H), 7.77(t, 2H), 7.54 (m, 2H),4.79 (s, 2H), 3.29 (m,1H), 1.21 (m, 2H), 0.85(d, 2H).	
655	4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (s, 2H), 7.79 (t,11H), 7.61 (t, 2H), 7.33(m, 1H), 7.08 (m, 1H),5.09 (m, 1H), 3.65 (s,3H), 2.37 (s, 311), 2.02(d, 3H).	

1256

Ejemplo No.	Nombre	^{1}H RMN	MS
656	4-(4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.81 (m, 2H), 8.23 (m,1H), 7.79 (d, 2H), 7.32(m, 1H), 7.09 (m, 1H),5.28 (m, 1H), 4.07 (m,2H), 2.37 (s, 3H), 2.04(d, 3H), 1.24 (m, 3H).	
657	4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.78 (m, 2H), 7.82 (d, 1H), 7.74 (d, 2H), 7.31(m, 1H), 7.11 (m, 1H),5.51 (m, 1H), 3.23 (m, 1H), 238 (s, 3H), 2.06 (d, 3H), 1.16 (m, 2H),0.78 (m, 2H).	
658	4-(4-Ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.83 (m, 2H), 7.78 (m, 1H), 7.59 (m, 2H), 7.33 (m, 1H), 7.10 (m, 1H), 5.26 (m, 1H), 3.90 (m,2H) 2.37 (s, 3H) 2.03(d, 3H), 0.92 (m, 1H), 0.48 (m, 2H), 0.21 (m, 2H).	
659	2-(2-fluoro-5-metil-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	7.98 (s, 1H), 7.75 (m, 1H), 7.31 (m, 1H), 7.08(m, 1H), 5.03 (q, 1H),3.85 (s, 3H), 2.75 (s, 3H), 2.35 (s, 3H), 1.98 (d, 3H).	
660	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.80 (m, 2H), 8.01 (m, 1H), 7.58 (m, 2H), 7.49 (m, 1H), 7.19 (m, 1H), 5.32 (q, 1H), 4.08 (q, 2H), 2.04 (d, 3H), 1.35 (t, 3H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
661	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (d, 2H), 8.03 (m, 1H), 7.75 (m, 2H), 7.50 (m, 1H), 7.20 (m, 1H), 5.55 (q, 1H), 3.26 (s, 1H), 2.06 (d, 311), 1.18 (m, 2H), 0.81 (m, 2H).	
662	2-(5-cloro-2-fluoro-fenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol	8.97 (m, 1H), 7.59 (m, 1H), 7.47 (m, 1H), 7.17 (m, 1H), 7.12 (m, 1H),6.59 (m, 1H), 5.18 (q, 1H), 4.21 (q, 2H), 2.00 (d, 3H), 1.33 (t, 3H).	
663	2-(5-cloro-2-fluoro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	7.99 (s, 1H), 7.96 (m, 1H), 7.48 (m, 1H), 7.17 (t, 1H), 7.06 (q, 1H),3.86 (s, 3H), 2.75 (s, 3H), 1.98 (d, 3H).	
664	4-(4-Ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.78 (dd, 2H), 7.71 (dd, 1H), 7.58 (dd, 2H), 7.25 (m, 1H), 7.08 (m, 1H),6.62 (d, 1H), 5.12 (q, 1H), 3.87 (dd, 2H), 2.40 (s, 3H), 1.94 (d, 3H), 0.90 (m, 1H), 0.49 (m, 2H), 0.19 (m, 2H).	
665	4-(5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (bs, 211), 7.92 (d, 1H), 7.80 (dd, 1H), 7.60 (d, 2H), 7.50 (m,1H),7.25 (m, 1H), 5.05 (q, 2H), 3.65 (s, 3H), 1.94 (d, 3H).	

1258

Ejemplo No.	Nombre	^{1}H RMN	MS
666	4-(4-Ciclopropil-5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.76 (d, 2H), 7.95 (d, 1H), 7.85 (dd, 1H), 7.75 (d, 2H), 7.50 (m, 1H), 7.25 (m, 1H), 5.45 (q, 2H), 3.20 (m, 1H), 1.98 (d, 3H) 1.22 (m, 2H),0.88 (m, 2H).	
667	4-(5-{1-[5-(4-Metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.65 (d, 1H), 7.71 (s, 1H), 7.63 (d, 1H), 7.54 (d, 2H), 7.00 (d, 2H),5.10 (q, 1H), 3.87 (s, 3H), 3.53 (s, 3H), 2.58 (s, 3H),2.00 (d, 3H).	
668	4-(5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.65 (d, 1H), 7.71 (s, 1H), 7.63 (d, 1H), 7.49 (d, 2H), 7.01 (d, 2H), 5.26 (q, 1H), 3.96 (q, 2H), 3.88 (s, 3H), 2.62 (s, 3H), 2.02 (d, 3H),1.24 (t, 3H).	
669	4-{5-[1-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina	8.79 (d, 2H), 8.67 (d, 1H) 7.73 (s, 1H), 7.65 (d, 1H), 7.55 (d, 2H), 5.33 (q, 1H), 4.08 (q, 2H), 2.64 (s, 3H), 2.03 (d, 3H), 1.30 (t, 3H).	
670	4-{5-[1-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina	8.77 (d, 2H), 8.68 (d, 1H), 7.72 (m, 4H), 5.55 (q, 1H), 3.24 (m, 1H),2.64 (s, 3H), 2.04 (d, 3H), 1.16 (m, 2H), 0.81 (m, 2H).	

Ejemplo No.	Nombre	^{1}H RMN	MS
671	4-{5-[1-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina	8.61 (d, 1H), 7.57 (m, 3H), 7.08 (d, 1H), 6.57(d, 1H), 5.02 (q, 1H),3.70 (s, 3H), 1.96 (d,3H).	
672	2-(3-cloro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol	7.99 (s, 1H), 7.94 (m, 1H), 7.86 (m, 1H), 7.48 (m, 1H), 7.39 (m, 1H), 5.03 (q, 1H), 3.82 (t, 3H), 2.73 (d, 3H), 1.98 (d, 3H).	
673	3-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.88 (s, 1H), 8.76 (d, 1H), 8.00 (m, 2H), 7.90 (d, 1H), 7.48 (m, 3H), 5.14 (q, 1H), 3.60 (s, 3H), 2.02 (d, 3H)	
674	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-2-metil-piridina	8.66 (d, 1H), 7.99 (m,, 1H) 7.88 (m, 1H), 7.51 (m, 1H), 7.43 (m, 2H), 7.34 (d, 1H), 5.13 (q, 1H), 3.61 (s, 3H), 2.63 (s, 3H), 2.00 (d, 3H).	
675	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.68 (dd, 2H), 8.05 (d, 1H), 7.92 (d, 1H), 7.67 (dd, 2H), 7.51 (d, 1H),7.37 (t, 1H) 5.37 (q, 1H), 3.18 (m, 1H), 1.90 (d, 3H), 1.08 (m, 2H),0.74 (m, 2H).	

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Ejemplo No.	Nombre	^{1}H RMN	MS
676	5-(3-cloro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol	8.01 (s, 1H), 7.90 (d, 1H), 7.50 (m, 3H), 7.38 (t, 1H), 6.92 (d, 2H), 4.88 (q, 1H) 3.78 (s,3H), 3.47 (s, 3H), 1.83 (d, 3H).	
677	4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.70 (dd, 2H), 8.05 (m, 1H), 7.67 (m, 2H), 7.46 (m, 1H), 7.18 (m, 1H),5.41 (q, 1H), 3.18 (m, 1H), 1.90 (d, 3H), 1.08 (m, 2H), 0.74 (m, 2H).	
678	5-(5-cloro-2-fluoro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol	8.05 (m, 1H), 7.56 (m, 3H) 7.21 (t, 1H), 7.00 (m, 3H), , 5.01 (q, 1H), 3.85 (s, 3H), 3.56 (s, 3H), 1.90 (d, 3H)	
679	4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina	8.79 (d, 2H), 8.67 (d, 1H), 7.75 (s, 1H), 7.67 (d, 1H), 7.56 (d, 2H), 4.82 (s, 2H), 4.10 (q, 2H), 2.64 (s, 3H), 1.39 (t, 3H).	
680	4-[5-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina	8.78 (d, 3H), 8.68 (d, 1H), 7.74 (m, 4H), 4.90 (s, 2H), 3.30 (m, 1H),2.65 (s, 3H), 1.21 (m, 2H), 0.84 (m, 2H).	

1261

Ejemplo No.	Nombre	^{1}H RMN	MS
681	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.79 (d, 2H), 8.12 (m, 1H), 7.76 (m, 2H), 7.57 (m, 1H), 7.25 (m, 1H), 4.81 (s, 2H), 3.31 (m, 1H), 1.20 (m, 2H), 0.85(m, 2H).	
682	4-[5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina	8.66 (d, 1H), 7.72 (s,1H), 7.65 (d, 1H), 7.60 (d, 1H), 7.11 (d, 1H), 6.60(d de d, 1H), 4.70 (s, 2H), 3.80 (s, 3H), 2.64 (s, 3H).	
683	4-(5-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropilmetil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (bs, 2H), 7.98 (m, 1H), 7.88 (m, 1H), 7.51 (m, 4H), 5.30 (q, 1H), 3.90 (m, 2H), 2.05 (t, 3H), 0.94 (ms, 1H), 0.50 (m, 2H), 0.19 (m, 2H).	
684	4-(5-{1-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.66 (d, 1H), 7.72 (s, 1H), 7.60 (m, 3H), 7.17 (m, 3H), 5.13 (q, 1H), 3.57 (s, 3H), 2.63 (s, 3H), 2.00 (d, 3H).	
685	4-(5-{1-[5-(3-fluoro-fenil)-4-metil-4H-[1;2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina	8.65 (d, 1H), 7.72 (s, 1H), 7.66 (d, 1H), 7.48-7.20 (m, 4H), 5.15 (q,1H), 3.60 (s, 3H), 2.63 (s, 3H), 2.01 (d, 3H).	

1262

Ejemplo No.	Nombre	^{1}H RMN	MS
686	3-[3-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrile	8.77 (dd, 2H), 8.49(dd,1H), 7.90 (m, 1H),7.74 (dd, 2H), 7.43 (t,1H), 4.81 (s, 2H), 3.31(m, 1H), 1.21 (m, 2H),0.83 (m, 2H).	
687	4-cloro-2-[3-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol	10.15 (bs, 1H), 8.77 (dd,2H), 7.89 (d, 1H), 7.75 (dd, 2H), 7.45 (dd, 1H),7.06 (d, 1H), 4.79 (s, 2H), 3.29 (m, 1H), 1.21 (m, 2H), 0.83 (m, 2H).	
688	4-{4-Ciclopropil-5-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.77 (dd, 2H), 7.72 (m, 3H), 7.62 (dd, 1H), 7.43 (t, 1H), 7.14 (m, 1H),4.77 (s, 2H), 3.88 (s, 3H), 3.28 (m, 1H), 1.17 (m, 2H), 0.84 (m, 2H).	
689	4-{4-Ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.7 (q, 2H), 7.81 (d, 1H), 7.7 (q, 2H), 7.29(m, 1H), 7.1 (t, 1H), 4.71 (s, 2H), 3.23 (m, 1H), 2.32 (s, 3H), 1.11 (m, 2H), 0.76 (m, 2H)	
690	4-{4-Ciclopropil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.67 (m, 2H), 7.82 (m, 1H), 7.72 (m, 1H), 7.66 (m, 1H), 7.42 (m, 1H), 7.21 (m, 1H), 4.68 (s, 1H), 3.23 (m, 1H), 1.11 (m, 2H), 0.75 (m, 2H)	

1263

Ejemplo No.	Nombre	^{1}H RMN	MS
691	4-[4-Ciclopropil-5-(S-m-tolil-[1,2,4]oxadiazol-3-Ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina	8.69 (q, 2H), 7.85 (m, 2H), 7.67 (q, 2H), 7.32 (m, 2H), 4.69 (s, 2H),3.2 (m, 1H), 2.35 (s,3H), 1.11 (m, 2H), 0.76 (m, 2H)	
692	3-[3-(4-Ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo	8.71 (b s, 2H), 8.36 (m, 1H), 8.28 (d, 1H), 7.83 (d d, 1H), 7.67 (m, 3H), 4.72 (s, 2H), 3.23 (m, 1H), 1.14 (m, 2H), 0.77 (m, 2H)	
693	4-{4-Ciclopropil-5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.75 (t, 2H), 7.79 (m, 2H), 7.26 (m, 2H), 4.78 (s, 2H), 3.28 (m, 1H), 1.14 (m, 2H), 0.82 (m,2H)	
694	4-{4-Ciclopropil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina	8.67 (d d, 2H), 7.87 (m, 2H), 7.67 (d d, 2H), 7.33 (m, 2H), 5.36 (q, 1H), 3.15 (m, 1H), 2.36 (s, 3H), 1.92 (d, 3H), 1.07 (m, 2H), 0.72 (m, 2H)	
695	4-(4-Ciclopropil-5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina.	8.69 (m, 2H), 7.6 (m, 3H), 7.52 (m, 1H), 7.35 (t, 1H), 7.04 (d d, 1H), 5.35 (q, 1H), 3.81 (s, 3H), 3.15 (m, 1H), 1.91 (d, 3H), 1.11 (m, 2H), 0.7(m, 2H)	

1264

Ejemplo No.	Nombre	^{1}H RMN	MS
696	4-{5-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.69 (d, 2H), 7.78 (m, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.24 (m, 1H), 4.72 (s, 2H), 3.22 (m, 1H), 2.31 (s, 3H), 1 (m, 2H), 0.76 (m, 2H)	
697	2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol	9.89 (s, 1H), 8.7 (m, 2H), 7.68 (m, 3H), 7.2 (m, 1H), 6.92 (d, 1H), 4.72 (s, 2H), 3.22 (m, 1H), 2.26 (s, 3H), 1.01 (m, 2H), 0.74 (m, 2H)	
698	4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.69 (d d, 2H), 7.8 (q, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.22 (m, 1H), 5.4 (q, 1H), 3.16 (m, 1H), 2.32 (s, 3H), 1.93 (d, 3H), 1.09 (m, 2H), 0.73 (m, 2H)	

EJEMPLO 699

{3-[3-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-metanol

1265

Se disuelve [3-(3-clorometil-[1,2,4]-oxadiazol-5-il)-fenil]-metanol (32 mg, 0.14 mmoles), 4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-tiol (41 mg, 0.21 mmoles) y carbonato de potasio (29 mg, 0.21 mmoles) en acetonitrilo anhidro y se somete a reflujo bajo atmósfera de nitrógeno durante 1 hora. El solvente se elimina al vacío y el residuo se disuelve en $NaHCO_3$ (acuoso) y se extrae con diclorometano ('3). La fase orgánica se seca ($MgSO_4$), se filtra y se concentra. El compuesto del título se aísla como un aceite incoloro (43 mg, 80%) mediante cromatografía de vaporización instantánea utilizando metanol al 3% en diclorometano.

^1H RMN ($CDCl_3$), δ (ppm): 8.07 (s, 1H), 7.98 (d, 1H), 7.60 (d, 1H) 7.52-7.45 (m, 3H), 7.16 (dd, 1H), 5.29 (s, 2H), 4.75 (s, 2H), 4.50 (s, 2H), 3.71 (s, 1H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 699:

Ejemplo No.	Nombre	^1H RMN	MS
700	3-[5-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-fenol		

1235
1266

Ejemplo No.	Nombre	^{1}H RMN	MS
701	5-(3-cloro-fenil)-3-[4-(tetrahidro-furan-2-ilmetil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	1.5 (m, 1H) 1.8 (m, 2H) 2.0 (m, 1H) 3.7 (m, 1H) 3.8 (m, 1H) 4.1 (s,m, 3H)) 4.5 (dd, 2H) 7.1 (dd, 1H) 7.4 (t, 2H) 7.5 (m, 2H) 7.9 (dd, 1H) 8.0(m,1H	460.00
702	(2-cloro-fenil)-(5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-isobutil-4H-[1,2,4]triazol-3-il)-metanol	0.8 (2 d, 6 H) 2.0 (m, 1H) 3.5 (dd, 1H) 3.6 (dd, 1H) 4.5 (s, 2H) 6.3 (d, 1H) 7.3 (m, 3H)) 7.5 (triplete aparente, 1H) 7.6 (m, 2H) 8.0 (d aparente, 1H) 8.1 (m, 1H)	490
703	5-(2-fluoro-5-metil-fenil)-3-[5-tiofen-2-il-4-(2,2,2-trifluoro-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol	2.4 (s, 3H)) 4.6 (s, 2H) 4.8 (q, J=7.7 Hz, 2H) 7.1 (m, 1H) 7.2 (m, 1H) 7.4 (m, 1H) 7.5 (m, 1H) 7.6 (m, 1H) 7.8 (m, 1H)	455.9

EJEMPLO 704

3-(2,5-difluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se disuelve 5-clorometil-3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol (23 mg, 0.10 mmoles) y 4-etil-5-tiofen-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona

(23 mg, 0.11 mmoles) en DMF anhidra (1 ml) y se agrega carbonato de potasio (21 mg, 0.15 mmoles). Después de agitar durante 22 horas se agrega acetato de etilo, la mezcla resultante se lava dos veces con agua y una vez con salmuera, se seca con $MgSO_4$ y se evapora. La cromatografía de vaporización instantánea utilizando heptano:acetato de etilo 1:1 permite obtener el compuesto del título (20 mg, 50%).

^1H RMN ($CDCl_3$) d (ppm): 7.64 (m, 1H), 7.45 (d, 1H), 7.39 (d, 1H), 7.10 (m, 3H), 4.70 (s, 2H), 4.08 (q, 2H), 1.32 (t, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplos 704:

Ejemplo No.	Nombre	^1H RMN	MS
705	5-furan-3-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.71 (s, 3H) 4.51 (s, 2H) 6.88 (dd, 1H) 7.17 (dd, 1H) 7.48 (dd, 1H) 7.51 (dd, 1H) 7.54 (t, 1H) 8.18 (m, 1H)	345.92
706	3-(3-cloro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.78 (s, 3H)) 4.64 (s, 2H) 6.57 (dd, 1H) 7.09 (d, 1H) 7.38 (t, 1H) 7.46 (m, 1H) 7.58 (d, 1H) 7.91 (d, 1H) 8.01 (m, 1H)	373.96

Ejemplo No.	Nombre	^{1}H RMN	MS
707	3-(3-cloro-fenil)-5-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.63 (s, 3H)) 4.64 (s, 2H) 6.85 (d, 1H) 7.39 (t,1H) 7.47 (dt, 1H) 7.56 (t, 1H) 7.87 (br. s, 1H) 7.91 (dt, 1H) 8.01 (t, 1H)	373.96
708	5-(3-cloro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.77 (s, 3H)) 4.50 (s, 2H) 6.55 (dd, 1H) 7.07 (d, 1H) 7.43 (t, 1H) 7.55 (m, 2H) 7.95 (dt, 1H) 8.05 (t, 1H)	373.96
709	5-(3-cloro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	13.63 (s, 3H)) 4.49 (s, 2H) 6.84 (br. s, 1H) 7.43 (t, 1H) 7.54 (m, 2H) 7.87 (s, 1H) 7.94 (d, 1H) 8.04 (m, 1H)	373.97
710	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina	4.06 (s, 3H)) 4.63 (s, 2H) 7.43 (t, 1H) 7.53 (m,1H) 7.95 (d, 1H) 8.05 (t, 1H) 8.27 (dd, 1H) 8.85 (d, 1H) 9.25 (d, 1H)	385.97
711	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina	4.06 (s, 3H)) 4.75 (s, 2H) 7.35 (t, 1H) 7.42 (ddd, 1H) 7.88 (dt, 1H) 7.97 (t, 1H) 8.24 (dd, 1H) 8.84 (d, 1H) 9.23 (d, 1H)	385.97
712	3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.29(t, 3H)) 4.07 (q, 2) 4.68 (s, 2H) 7.08 (m, 2H) 7.35 (m, 2H) 7.44 (dd, 1H) 7.87 (dd, 1H)	421.99

1269

Ejemplo No.	Nombre	^{1}H RMN	MS
713	3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.32(t,3H)4.18(q, 2H) 4.71 (s, 2H) 6.51 (dd, 1H) 7.02 (dd, 1H) 7.10 (dd, 1H) 7.37 (ddd, 1H) 7.53 (dd, 1H) 7.91 (dd, 1H)	406.02
714	5-(5-cloro-tiofen-2-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.30(t,3H)4.09(q, 2H) 4.47 (s, 2H) 6.96 (d, 1H) 7.11 (dd, 1H) 7.40 (dd, 1H) 7.47 (dd, 1H) 7.60 (d, 1H)	409.92
715	5-(5-cloro-tiofen-2-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.33(t,3H)4.21(q,2H) 4.52 (s, 2H) 6.54 (dd, 1H) 6.98 (d, 1H) 7.05 (dd, 1H) 7.55 (dd, 1H) 7.62 (d, 1H)	393.96
716	5-(5-cloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	1.36(t,3H)4.12(q,2H) 4.58 (s, 2H) 7.15(dd, 1H) 7.43 (m, 2H)7.48 (dd, 1H) 7.94 (d, 1	409.92
717	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}-fenol	1.30(43H)4.02(q,2H) 4.51 (s, 2H) 5.07 (s,2H) 6.72 (m, 4 H) 7.39(t, 1H) 7.49 (m, 1H)7.89 (m, 1H) 7.99 (t, 1H)	443.9
718	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}-fenol	1.33(t,3H)4.05(q,2H) 4.70 (s, 2H) 5.11 (s,2H) 6.74 (m, 4 H) 7.13(t, 1H) 7.44 (m, 1H)7.93 (dd, 1H)	461.9

Ejemplo No.	Nombre	^{1}H RMN	MS
719	3-(2,5-difluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	7.75 (m, 1H), 7.64 (d,1H), 7.23 (m, 2H), 7.16(d, 1H), 6.63 (dd, 1H),4.80 (s, 2H), 4.29 (q,2H), 1.43 (t, 3H)	389.9
720	3-(2,5-difluoro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	8.17 (dd, 1H), 7.87 (m,1H), 7.74 (m, 2H), 7.33(dd, 1H), 6.95 (dd, 1H),5.01 (s, 2H), 3.96 (s,3H)	375.8
721	4-(5-{1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.74 (d, 2H), 7.97 (s, 1H), 7.87 (m, 1H), 7.56(d, 2H), 7.44 (m, 1H),7.36 (apparent t, 1H),5.06 (q, 1H), 3.58 (s, 3H), 1.96 (d, 3H)).	400
722	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-pirimidina	0.90 (m, 2H), 1.22 (m,2H), 3.49 (m, 1H),4.81 (s, 2H), 7.26 (t, 1H), 7.53 (m, 1H), 8.11(m, 2H), 8.88 (d, 1H)9.33(s,1H)	430.1
723	2-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-pirimidina	1.32 (t, 3H)), 1.94 (d, 31-1), 4.00 (s, 3H), 4.50(m, 2H), 5.20 (q, 1H),7.46 (t, 1H), 7.56 (m, 1H), 7.99 (d, 1H), 8.10(t, 1H), 8.56 (d, 2H).	444.1

Ejemplo No.	Nombre	^{1}H RMN	MS
724	2-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina	1.34 (t, 3H)), 1.94 (d, 3H), 4.50 (m, 2H), 5.26 (q, 1H), 7.36 (t, 1H), 7.46 (t, 1H), 7.57 (d, 1H), 7.99 (m, 1H), 8.10 (m,1H), 8.92 (d, 2H).	414
725	4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina	1.32 (t, 3H)), 1.97 (d, 3H), 3.99 (s, 3H), 4.06 (m,2H), 5.19 (q, 1H),6.98 (bs, 1H), 7.16 (m,1H), 7.47 (t, 1H), 7.58(m, 1H), 7.98 (dt, 1H),8.10 (m, 1H) 8.31 (d, 1H).	443.1
726	5-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina	1.30 (t, 3 11), 1.96 (d, 3H), 3.99(m, 2H), 4.00 (s,3H)), 5.16 (q, 1H), 6.87 (d, 1H), 7.47 (t, 1H),7.58 (m, 1H), 7.86 (dd,1H), 8.00 (d, 1H), 8.11(t, 1H) 8.40 (d, 1H).	443
727	2-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-piridina	1.30 (t, 3H)), 1.93 (d, 3H)' 3.92 (s, 3H)), 4.52(m, 2H), 5.13 (q, 11-1),7.32 (dd, 1H), 7.46 (t, 1H), 7.56 (m, 1H), 7.99(dt, 1H), 8.10 (t, 11-1),8.25 (d, 1H) 8.30 (d, 1	443.1

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Ejemplo No.	Nombre	^{1}H RMN	MS
728	3-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridazina	1.38 (t, 3 H), 1.96 (d, 3H), 4.20 (s, 3H), 4.61(m, 2H), 5.20 (q, 1H), 7.12 (d, 1H), 7.46 (t, 1H), 7.56 (t, 1H), 8.00 (d, 1H), 8.10 (s, 1H),8.40 (d, 1H)	444
729	3-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	0.77 (m, 2H), 1.14 (m, 2H), 1.99 (d, 3H)), 3.22 (m, 1H), 5.44 (q, 1H), 7.45 (m, 2H), 7.58 (d, 1H), 8.02 (d, 1H), 8.15 (m, 2H), 8.72 (d, 1H) 9.05 (s, 1H).	
730	4-{5-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	3.69 (s, 3H)) 4.73 (s, 2 1H) 7.39 (t, 1H) 7.47 (m,1H) 7.60 (m, 2H) 7.92(m, 1H) 8.02 (t, 1H)8.79 (m, 2H)	384.91

EJEMPLO 731

5-(3-cloro-fenil)-3-(5-furan-2-il-4-isobutil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

El compuesto del título se sintetiza de conformidad con el método descrito por Graybill et al. Tetrahedron lett. 2002 43, 5305-5309 a partir de

la hidrazida del ácido furan-2-carboxílico (55.2 mg, 0.44 mmoles), 1-isotiocianato-2-metil-propano (47 ml, 0.38 mmoles) y 3-clorometil-5-(3-cloro-fenil)-[1,2,4]oxadiazol (45.0 mg, 0.20 mmoles) con P-bEMP (136 mg, 0.30 mmoles) como base. La purificación mediante cromatografía de vaporización instantánea (33-66% EtOAc en heptano) permite obtener el producto como un aceite (12.7 mg, 15.6%).

^{1}H RMN ($CDCl_3$) d (ppm): 8.08 (s, 1H), 7.97 (d, 1H), 7.55 (d, 2H), 7.45 (t, 1H), 7.10 (d, 1H), 6.56 (d, 1H), 4.62 (s, 2H), 4.01 (d, 2H), 2.03 (m, 1H), 0.86 (d, 6H).

General

Se disuelven tiofen-2-carbohidrazida (1.5 equiv) y un isotiocianato (1.3 equiv) en DMF (1 ml). Se agrega 2-ter-butilimino-2-dietilamino-1,3-dimetil-perhidro-1,3,2-diazafosforina (1 equiv) en poliestireno y las reacciones se agitan en un mini bloque de Bohdan a temperatura ambiente durante 1 hora y después durante una hora adicional a 45°C. La resina se lava con dioxano:agua 1:1 varias veces. El cierre del anillo se efectúa a 85°C durante 48 horas en dioxano:agua 1:1 en el mini bloque. La resina se lava con acetonitrilo (2'2 ml). Se agrega el 3-

(clorometil)-5-(3-clorofenil)-1,2,4-oxadiazol a la reacción y se agitan en acetonitrilo a 50°C durante 2 horas. El producto se filtra y purifica en HPLC preparativa dirigida con MS, gradiente 0-100% de acetonitrilo en un lapso de 15 minutos.

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 731:

Ejemplo No.	Nombre	^{1}H RMN	MS
732	5-(3-cloro-fenil)-3-[4-(-metilsulfanil-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		464.0
733	5-(3-cloro-fenil)-3-(4-hexil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		460.0
734	5-(3-cloro-fenil)-3-(4 ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		430.0
735	5-(3-cloro-fenil)-3-[4-(3-fluoro-benzil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		484.0

Ejemplo No.	Nombre	^{1}H RMN	MS
736	5-(3-cloro-fenil)-3-[4-(3-metil-benzil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		480.0
737	5-(3-cloro-fenil)-3-[4-(2-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		446.0
738	5-(3-cloro-fenil)-3-[4-(3-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		446.0
739	5-(3-cloro-fenil)-3-[4-(2-fluoro-benzil)-5-thiophen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol		484.0

EJEMPLO 740

5-(3-cloro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-iloximetil)-[1,2,4]oxadiazol

Se disuelven [5-(3-cloro-fenil)-[1,2,4]-oxadiazol-3-il]-metanol (28.0 mg, 0.13 mmoles), 4-etil-3-metansulfonil-5-tiofen-2-il-4H-[1,2,4]triazol (35.2 mg, 0.13 mmoles) y carbonato de cesio (130 mg) en dimetilformamida y se agita bajo argón a temperaturas ambientales durante 46 horas. Después de evaporar hasta sequedad, el producto crudo se somete a cromatografía en 12 g de silice, heptano/acetato de etilo 4/1 a 2/1. La recolección de las fracciones apropiadas permite obtener, después de evaporar a sequedad y secar al vacío, el compuesto del título (17.0 mg, 33%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.13 (m, 1H), 8.02 (m, 1H), 7.58 (m, 1H), 7.47 (m, 2H), 7.40 (dd, 1H), 7.14 (dd, 1H), 5.74 (s, 2H), 4.04 (q, 2H), 1.38 (t, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 740:

Ejemplo No.	Nombre	^{1}H RMN	MS
741	4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetoxi]-4-metil-4H-[1,2,4]triazol-3-il}-piridina	8.92 (s broad, 2H), 8.12 (d aparente, 1H), 7.78 (s, 1H), 7.56 (s ancho, 2H), 7.25 (t aparente, 1H), 5.79 (s, 2H), 3.66 (s, 3H)).	388
742	4-(5-t1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etoxi)-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.82 (s ancho, 2H), 8.07-7.94 (m, 2H), 7.69(s ancho, 2H), 7.47 (m, 2H), 6.47 (q, 1H), 3.63 (s, 3H), 2.02 (d, 3H)).	384.1

Ejemplo No.	Nombre	^{1}H RMN	MS
743	4-(5-{1-[3-(3-cloro-fenil)-isoxazol-5-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	1.92 (d, 3H), 3.57 (s, 3H)' 6.36 (q, 1H), 6.74 (s, 1H), 7.39 (m, 2H),7 .60 (m, 2H), 7.66 (m, 1H), 7.78 (m, 1H), 8.75(m, 2H)	383.1
744	3-(5-{1-[5-(3-cloro-fenil)-[1;2,4]oxadiazol-3-il]-etoxi}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina		

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 740 excepto que se utiliza hidruro de sodio como la base y la reacción se calienta a 80°C:

Ejemplo No.	Nombre	^{1}H RMN	MS
745	4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetoxi]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.77 (d, 2H), 8.17 (s, 1H), 8.05 (d, 1H), 7.79 (d, 2H), 7.62 (dd, 1H), 7.52 (t, 1H), 5.79 (s, 2H), 3.25 (m, 1H), 1.14 (d, 2H), 0.89 (m, 2H)	
746	4-{5-[5-(3-cloro-fenil)-isoxazol-3-ilmetoxi]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina	8.77 (d, 2H), 7.79 (m, 3H), 7.7 (m, 1H), 7.44 (m, 2H), 6.84 (s, 1H),5.71 (s, 2H), 3.21 (m,1H), 1.13 (d, 2H), 0.82 (m, 2H)	

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EJEMPLO 747

5-(2-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol

Se agregan HBTU (171 mg, 0.45 mmoles) y HOBT (8 mg, 0.06 mmoles) a una solución de ácido 2-metoxi benzoico (68 mg, 0.45 mmoles) y DIPEA (192 ml, 1.11 mmoles) en DMF (3 ml). Después de 10 minutos, se agrega N-hidroxi-2-(4-metil-5-tiofen-2-il-4H-[1,2,4)-triazol-3-ilsulfanil)-acetamidina (100 mg, 0.37 mmoles). La mezcla de reacción se agita a temperatura ambiente durante 7 horas y después a 110°C durante la noche. Después de enfriar, la mezcla de reacción se diluye con agua y se extrae con CH_2Cl_2. la fase orgánica se seca y concentra. La cromatografía de vaporización instantánea (heptano/EtOAc 1:2) permite obtener 1.9 mg (11%) del producto deseado.

^1H RMN ($CDCl_3$), d (ppm): 7.99 (m, 1H), 7.53 (m, 1H), 7.50 (m, 1H), 7.47 (m, 1H), 7.16 (m, 1H), 7.04 (m, 2H), 4.52 (s, 2H), 3.94 (s, 3H), 3.71 (s, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 747:

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Ejemplo No.	Nombre	^{1}H RMN	MS
748	5-furan-2-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol	3.72 (s, 3H)) 4.52 (s, 2H) 6.61 (dd, 1H) 7.16 (dd, 1H) 7.30 (dd, 1H) 7.47 (dd, 1H) 7.50 (dd, 1H) 7.67 (dd, 1H)	345.92
749	Ester metílico del ácido3-[3-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilxnetil)-[1,2,4]oxadiazol-5-il]-benzoico		414.0
750	5-(2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		374.0
751	5-(2,5-difluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		392.0
752	3-(4-metil5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-S-(3-vinil-fenil)-[1,2,4]oxadiazol		382.1
753	5-(3-difluorometoxi-fenil)-3-(4-metil-S-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		422.0

Ejemplo No.	Nombre	^{1}H RMN	MS
754	5-(4-metoxi-tiofen-3-il)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		392.0
755	5-(2-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		390.0
756	5-(4-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol		374.0

EJEMPLO 757

3-(3-cloro-fenil)-5-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol

Se agrega DMF a una mezcla de ácido 2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-propiónico (50 mg, 0.186 mmoles), clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodi-imida (EDCI) (35.7 mg, 0.186 mmoles), hidrato de 1-hidroxi-benzotriazol (HOBT) (28.5 mg, 0.186 mmoles) y 3-

cloro-N-hidroxi-benzamidina (29.3 mg, 0.172 mmoles) a temperatura ambiente y se agita durante toda la noche. La mezcla de reacción se diluye con acetato de etilo (75 ml), se lava con agua 3 veces, una vez con HCl 1.0 M (30 ml), $NaHCO_3$ saturado (30 ml) y salmuera saturada (30 ml), se seca con sulfato de sodio anhidro, se filtra y se concentra al vacío. Se agrega DMF (1 ml) al residuo y la solución resultante se calienta a 135°C durante 3 horas para efectuar la ciclización hasta el oxadiazol. Después de enfriar, la mezcla de reacción se diluye con acetato de etilo (75 ml), se lava con agua 3 veces, una vez con HCl 1.0 M (30 ml), $NaHCO_3$ saturado (30 ml) y salmuera saturada (30 ml), se seca con sulfato de sodio anhidro, se filtra y se concentra al vacío. El compuesto del título (46.5 mg, 66.9%) se purifica mediante cromatografía de SPE en gel de sílice utilizando 50 ml al 40%, 150 ml al 50% de acetato de etilo en hexanos.

^1H RMN ($CDCl_3$), δ (ppm): 8.03 (s, 1H), 7.92 (m, 1H), 7.47 (m, 4H), 7.18 (dd, 1H), 4.99 (q, 1H), 3.64 (s, 3H), 1.97 (d, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 757:

1282

Ejemplo No.	Nombre	^{1}H RMN	MS
758	3-(5-{1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil)-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.88 (d, 1H), 8.76 (dd,1H), 8.03 (m, 2H), 7.93(d, 1H), 7.74 (m, 3H),5.09 (m, 1H), 3.58 (s,3H), 2.00 (d, 3H)	

Los siguientes compuestos se preparan de manera análoga a la del ejemplo10:

Ejemplo No.	Nombre
759	5-(1-cloro-etil)-3-(3-cloro-fenil)-[1,2,4]oxadiazol
760	3-(1-cloro-etil)-5-m-tolil-[1,2,4]oxadiazol
761	3-(1-cloro-etil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol
762	3-(1-cloro-etil)-5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol
763	3-(1-cloro-etil)-5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol
764	3-(1-cloro-etil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol
765	3-[3-(1-cloro-etil)-[1,2,4]oxadiazol-5-il]-benzonitrilo

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 40:

1283

Ejemplo No.	Nombre	^{1}H RMN	MS
766	4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.74 (d, 2H), 7.79 (s,1H), 7.57 (d d, 2H),7.38 (d, 1H), 7.25 (d,1H), 5 (q, 1H), 3.62 (s, 3H), 2.33 (s, 3H), 1.92 (d, 3H)	
767	4-(5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4}triazol-3-il)-piridina	8.67 (d, 2H), 7.7 (m, 1H), 7.57 (d d, 2H), 7.2(m, 2H), 5 (q, 1H), 3.61 (s, 3H), 1.87 (d, 3H)	
768	4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.77 (d, 2H), 7.85 (m, 1H), 7.61 (m, 2H), 7.38 (m, 1H), 7.06 (t, 1H) 5.02 (q, 1H), 3.66 (s,3H),237 (s, 3H), 1.94(d, 3H)	
769	4-(4-ciclopropil-5-{1-[5-(2-fluoro-1-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina	8.75 (d, 2H), 7.9 (m, 1H), 7.74 (m, 2H), 7.38(m, 1H), 7.13 (m, 1H),5.45 (q, 1H), 3.24 (m,1H), 2.39 (s, 3H), 2 (d, 3H),1.15 (m, 2H), 0.79(m, 2H)	
770	3-{3-[1-(4-metil5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrilo	8.76 (d d, 2H), 8.4 (s, 1H), 8.32 (d, 1H), 7.87 (d, 1H), 7.65 (t, 1H), 7.59 (m, 2H), 5.07 (q, 1H), 3.67 (s, 3H), 2.59 (s, 2H), 1.91 (d, 3H)	

1284

Ejemplo No.	Nombre	^{1}H RMN	MS
771	3-{3-[1-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il}-benzonitrilo	8.77 (m, 2H), 8.42 (d, 1H), 8.38 (m, 1H), 7.9 (m, 1H), 7.71 (m, 3H),5.49 (q, 1H), 3.25 (m, 1H), 2 (d, 3H), 1.17 (m, 2H), 0.81 (m, 2H)	
772	3-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-5-piridin-4-il-[1,2,4]triazol-4-ilamina	8.77 (br s, 2H), 8.18 (d, 2H), 7.98 (s, 1H), 7.87(d,1H), 7.52 (d, 1H),7.44 (t, 1H),5.66 (s,2H), 4.88 (q, 1H), 1.98 (d, 3H)	

Los siguientes compuestos se preparan de manera análoga a la del ejemplo316:

Ejemplo No.	Nombre
773	Hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-metil-propiónico
774	Hidrazida del ácido Rac-3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-butírico

Los siguientes compuestos se preparan de manera análoga a la del ejemplo318:

Ejemplo No.	Nombre
775	Hidrazida del ácido 2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropan-carboxílico

1285

EJEMPLO 776

Hidrazida de ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico

Se calienta 3,3-dimetil-dihidro-furan-2,5-diona (6.4 g) a 50°C en etanol (150 ml) durante la noche. El solvente se elimina al vacío y el residuo se tritura con hexano para producir el éster 4-etílico del ácido 2,2-dimetil-succínico (4.668) el cual se utiliza sin purificación adicional. Se agrega t-butanol (7.5 ml) a una mezcla de éster 4-etílico del ácido 2,2-dimetil-succínico (2.74 g, 15.7 mmoles) en diclorometano (62 ml) que contiene sulfato de magnesio (7.5 g) y ácido sulfúrico concentrado (0.85 ml) y la mezcla se agita a temperatura ambiente durante la noche. Se agrega solución saturada de bicarbonato de sodio y el producto se extrae con diclorometano, se lava con solución de salmuera, se seca y se concentra para obtener el diéster (diested) como un aceite incoloro (1.89 g). El éster etílico se hidroliza tratando la muestra cruda con hidróxido de potasio (2.75g) en una mezcla de etanol (50 ml) y agua (25 ml) a temperatura ambiente durante 2 horas.

La reacción se acidula utilizando HCl 1N (acuoso) y se extrae con éter, se seca y se concentra para obtener el éster 1-ter-butílico del ácido 2,2-dimetil-succínico (1.4g). Este ácido se trata bajo las condiciones del ejemplo 320 (paso 1) para obtener el éster t-butílico del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico (1.9g). Este éster t-bu se desprotege utilizando ácido fórmico (19 ml) a 50°C durante 20 minutos. El producto crudo se concentra y se tritura con una mezcla de éter y hexano para obtener el ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico (1.12g). A una solución de ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2,2-dimetil-propiónico (561 mg, 2 mmoles) y trietilamina (1.1 ml, 8 mmoles) en THF (9 ml), se agrega, mediante goteo, cloroformiato de isobutilo (0.31 ml, 2.4 mmoles) a -78°C. Después que se agita durante 1 hora, se agrega hidrato de hidrazina (1 ml, 11 mmoles). La mezcla de reacción se agita a temperatura ambiente durante 1 hora y se concentra. Se agrega una pequeña cantidad de hielo para extinguir cualquier reactivo en exceso y precipitar el producto, el cual se recolecta mediante filtración para obtener 482 mg del compuesto del título.

1287

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 320:

Ejemplo No.	Nombre
777	Ester ter-butílico del ácido (S)-(1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-hidrazinocarbonil-etil)-carbámico

EJEMPLO 778

3-(3-cloro-fenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol

Paso 1

(Etoxi-tiofen-2-il-metilen)-hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico:

Se mezcla hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico (266.69 mg, 1 mmoles) con éster etílico del ácido tiofen-2-carboximídico (191.6 mg, 1 mmol) en etanol (6 ml) y se agita a temperatura ambiente durante la noche. La reacción se extingue con agua, se extrae con acetato de etilo, se seca y se concentra al vacío. El producto crudo se tritura con hexano para obtener (etoxi-tiofen-2-il-metilen)-hidrazida del ácido 3-[3-

(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propiónico como un sólido de color blanco (305 mg, 75%).

^{1}H-RMN($CDCl_3$) d(ppm): 8.99 (ws, 1H), 8.09 (s, 1H), 7.98 (d, 1H), 7.41(m, 4H), 7.08 (dd, 1H), 4.27 (q, 2H), 3.34 (m, 4H) y 1.41 (t, 3H).

Paso 2

3-(3-cloro-fenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol:

Se mezcla la (etoxi-tiofen-2-il-metilen)-hidrazida del ácido 3-[3-(3-cloro-fenil)-[1,2,4]-oxadiazol-5-il]-propiónico (81 mg, 0.2 mmoles) con metilamina 2M (0.3 ml en THF) en etanol (2 ml) a 70~80°C durante la noche. La mezcla de reacción se concentra con gel de sílice y se purifica mediante cromatografía en columna con 0.5~2.0% de metanol en acetato de etilo para obtener 54 mg (72.5%) de 3-(3-cloro-fenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol.

^{1}H RMN($CDCl_3$) d (ppm): 8.08 (s, 1H), 7.97 (d, 1H), 7.41 (m, 4H), 7.20 (dd, 1H), 3.80 (s, 3H), 3.68 (dd, 2H), 3.38 (dd, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 778:

1289

Ejemplo No.	Nombre	^{1}H RMN	MS
779	3-(3-cloro-fenil)-5-[2-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol	8.08 (s, 1H), 7.97 (d,1H), 7.47(m, 4H), 7.20 (dd, 1H), 4.20 (q, 2H),3.72 (dd, 2H), 3.38 (dd,2H) y 1.47 (t, 3H)	
780	5-(3-cloro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilmetil)-[1,2,4]oxadiazol	8.11 (s, 1H), 8.01 (d,1H)' 7.61(s, 1H), 7.58(d, 1H), 7.48 (t, 1H),7.11 (d, 1H), 6.59 (m,1H), 4.48 (s, 2H) y 3.92 (s, 3H)	
781	2-(3-cloro-fenil)-5-[2-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol	8.04 (s, 1H), 7.93 (d, 1H), 7.60(s, 1H), 7.52 (d, 1H), 7.46 (t, 1H),7.06 (d, 1H), 6.59 (m, 1H), 3.87 (s, 3H), 3.65(t, 2H) y 3.3 8 (t, 2H)	
782	2-(3-cloro-fenil)-5-[2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol	8.05 (s, 1H), 7.94 (d, 1H), 7.60(s, 1H), 7.52 (d, 1H), 7.47 (t, 1H),7.10 (d, 1H), 6.59 (m, 1H), 4.30 (q, 2H), 3.67 (t, 2H), 3.39 (t, 2H) y 1.43 (t, 3H)	
783	2-(3-cloro-fenil)-5-[2-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol	8.05 (s, 1H), 7.94 (d, 1H), 7.63 (s, 1H), 7.52 (d, 1H), 7.46 (t, 1H), 7.01 (d, 1H), 6.58 (m, 1H), 3.67 (dd, 2H), 3.51 (t, 2H), 3.33 (m, 1H) 1.25 (m, 2H) y 0.93(m, 2H)	383.12

1290

EJEMPLO 784

4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina

Paso 1

{4-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-etoxi-butiliden}-hidrazida del ácido isonicotínico:

Se mezcla clorhidrato del éster del ácido 3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propionimídico (473.3, 1.5 mmoles) con hidrazida del ácido isonicotínico (205.7 mg, 1.5 mmoles) en etanol (8 ml) a 60°C durante una hora y después a temperatura ambiente durante 2 horas. La mezcla de reacción se diluye con diclorometano y se lava con agua. La capa orgánica se seca, se concentra con vacío y el residuo se tritura con éter para obtener 490 mg (78.9%) de {4-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-etoxi-butiliden}-hidrazida del ácido isonicotínico como un sólido de color blanco.

Paso 2

Se obtiene 4-(5-{2-[3(3-cloro-fenil)-[1,2,4]-oxadiazol-5-il]-etil)-4-metil-4H-[1,2,4]-triazol-3-il)-piridina (47.1 mg, 82%) como un sólido de color blanco a partir de {4-[3-(3-cloro-fenil)-

[1,2,4]oxadiazol-5-il]-1-etoxi-butiliden)-hidrazida del ácido isonicotínico (60 mg, 0.15 mmoles) que se hace reaccionar con metilamina 2M (0.45 ml, 0.9 mmoles) en etanol (1 ml) a 60 °C durante la noche.

^{1}H RMN($CDCl_3$) d(ppm): 8.77 (d, 2H), 8.02 (s, 1H), 7.91 (d, 1H), 7.58(d, 2H), 7.42 (m, 2H), 3.76 (s, 3H), 3.66 (t, 2H) and 3.38 (t, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo784:

Ejemplo No.	Nombre	^{1}H RMN	MS
785	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (d, 2H), 8.05 (s, 1H), 7.94 (d, 1H),7.58(d, 2H), 7.43 (m,2H), 4.16 (q, 2H), 3.72(t, 2H), 3.40 (t, 2H) y 1.44 (t, 3H)	
786	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.77 (d, 2H), 8.05 (s, 1H), 7.93 (d, 1H),7.73(d, 2H), 7.44 (m,2H), 3.72(t, 3H), 3.51 (t, 2H), 3.38 (m, 1H),1.23 (m, 2H) y 0.79(m, 2H)	

EJEMPLO 787

4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina

1292

Paso 1

N-ciclopropil-isonicotinamida:

Se mezcla éster etílico del ácido isonicotínico (3.0 g, 20 mmoles) con ciclopropilamina (2 ml) a 120°C en un frasco sellado durante 40 horas. La mezcla de reacción se tritura con éter para obtener 1.62 g (50%) de N-ciclopropil-isonicotinamida como un sólido blanquecino.

^{1}H RMN($CDCl_3$) d (ppm): 8.73 (d, 2H), 7.60 (d, 2H) and 6.55 (w, 1H), 2.92 (m, 1H), 0.90 (m, 2H) and 0.66 (m, 2H).

Paso 2

Clorhidrato de cloruro de N-ciclopropil-isonicotinimidoilo:

Se hace reaccionar N-ciclopropil-isonicotinamida (1.62 g, 10 mmoles) con $SOCl_2$ (12 g, 100 mol) a 80°C durante la noche. La mezcla de reacción se concentra y se tritura con diclorometano para obtener 1.3 g (64%) de clorhidrato de cloruro de N-ciclopropil-isonicotinimidoilo como un sólido de color amarillo.

Paso 3

4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-

5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina:

Se mezcla hidrazida del ácido (R)-3-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]- butírico (56 mg, 0.2 mmoles) con clorhidrato de cloruro de N-ciclopropil-isonicotinimidoilo (40.6 mg, 0.2 mmoles) y K_2CO_3 (60 mg, 0.43 mmoles) en DMF (1 ml) a 100°C durante 3 horas. La mezcla de reacción se diluye con diclorometano y después se lava con agua. La capa orgánica se concentra y purifica con 5~6% de metanol en acetato de etilo para obtener 32 mg (39%) del compuesto del título.

^{1}H-RMN($CDCl_3$) d (ppm): 8.78 (d, 2H), 8.05 (s, 1H), 7.96(d, 1H), 7.73(d, 2H), 7.45(m, 2H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.68 (d, 3H), 1.25 (m, 2H) y 0.79 (m, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 787: se debe indicar que algunas reacciones proveen productos de ciclización de 1,3,4-oxadiazol con pérdida del grupo metilamino o ciclopropilamino en lugar de, o también como, el producto triazol.

Ejemplo No.	Nombre	^{1}H RMN	MS
788	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.74 (d, 2H), 8.04 (s,1H), 7.94 (d, 1H), 7.67(d, 2H), 7.43 (m, 2H),3.48(s, 2H), 3.09 (m,1H), 1.75 (s, 6H), 1.16(m, 2H) y 0.68 (m,2H)	
789	4-(5-{2-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.76 (w, 2H), 8.03 (s,1H), 7.92 (d, 1H),7.72(d, 2H), 7.44 (m,2H), 4.13(m, 1H), 3.72(dd, 1H), 3.43 (m, 1H),3.27 (dd, 1H), 1.66 (d,3H), 1.25 (m, 2H) y 0.79 (m, 2H)	
790	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (d, 2H), 8.01 (s, 1H), 7.91 (d, 1H), 7.73 (d, 2H), 7.49 (d, 1H),7.42 (t, 1H), 3.99 (m, 1H), 3.83 (dd, 1H), 3.48 (m, 1H), 3.39 (m, 1H), 1.61 (d, 3H), 1.25 (m,2H), 0.98 (m, 1H), 0.74 (m, 1H)	
791	cis-4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.73 (d, 2H), 7.88 (s,1H), 7.78 (d, 1H), 7.65(d, 2H), 7.41 (d, 1H),7.34 (t, 1H), 3.20 (m,1H), 2.89 (m, 2H), 2.54(dd, 1H), 2.00 (td, 1H),1.20 (m, 2H), 0.83 (m,2H)	

Ejemplo No.	Nombre	^{1}H RMN	MS
792	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina	8.82 (m, 2H), 7.98 (s,1H), 7.90 (m, 3H), 7.47(d, 1H), 7.39 (t, 1H),3.51 (s, 2H), 1.70 (s,6H)	
793	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-[1,3,4]oxadiazol-2-il)-piridina	8.76 (d, 2H), 8.07 (s,1H), 7.97 (d, 1H), 7.77(d, 2H), 7.49 (dd, 1H),7.43 (t, 1H), 3.53 (s,2H), 1.69 (s, 6H)	
794	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-[1,3,4]oxadiazol-2-il)-piridina	8.82 (d, 2H), 8.05 (m,1H), 7.95 (d, 1H), 7.91(d, 2H), 7.50 (dd, 1H),7.42 (t, 1H), 3.94 (dd,1H), 3.67 (dd, 1H), 3.41(dd, 1H), 1.66 (d, 3H)	
795	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-[1,3,4]oxadiazol-2-il)-piridina	8.77 (d, 2H), 7.81 (m,4H), 7.42 (d, 1H), 7.32(t, 1H), 3.07 (q, 1H),2.99 (q, 1H), 2.41 (q,1H), 2.08 (td, 1H)	
796	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.76 (d, 2H), 7.85 (m,1H), 7.77 (d, 1H), 7.55(d, 2H), 7.44 (dd, 1H),7.34 (t, 1H), 3.70 (s,3H), 2.89 (m, 1H), 2.72(m, 1H), 2.51 (q, 1H),2.02 (dt, 1H)	

Ejemplo No.	Nombre	^{1}H RMN	MS
797	4-(5-{2-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.79 (d, 2H), 8.02 (s, 1H), 7.93 (d, 1H), 7.59 (d, 2H), 7.53 (d, 1H), 7.46 (t, 1H), 4.03 (m, 1H), 3.80 (s, 3H), 3.52 (m, 1H), 3.23 (dd, 1H), 1.66 (d, 3H)	
798	4-(5-{2-[3-(3-cloro-pheriyl)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina	8.81 (d, 2H), 8.07 (s, 1H), 7.97 (d, 1H), 7.87 (d, 2H), 7.50 (d, 1H), 7.43 (t, 1H), 3.91 (q, 1H), 3.66 (dd, 1H), 3.44 (dd, 1H), 1.65 (d, 3H)	
799	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina	8.80 (d, 2H), 8.05 (s, 1H), 7.95 (d, 1H), 7.61 (d, 2H), 7.51 (d, 1H), 7.45 (t, 1H), 4.07 (q, 1H), 3.75 (s, 3H), 3.48 (dd, 1H), 3.23 (dd, 1H), 1.68 (d, 3H)	
800	4-(5-{2-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina	8.78 (d, 2H), 8.05 (s, 1H), 7.96 (d, 1H), 7.74 (d, 2H), 7.50 (dd, 1H), 7.46 (t, 1H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.67 (d, 3H), 1.25 (m, 2H), 0.81 (m,2H)	
801	Ester t-butílico del ácido (S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico		

1356

1297

EJEMPLO 802

(S)-1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H[1,2,4]triazol-3-il)-etilamina

Se mezcla éster ter-butílico del ácido (S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico (135 mg) con ácido fórmico al 96% (1.3 ml) y se calienta a 50°C durante 1 hora. La mezcla de reacción se concentra al vacío. El residuo se extingue con bicarbonato de sodio saturado y se extrae con acetato de etilo. La capa orgánica se seca con sulfato de sodio y se concentra. La purificación se efectúa mediante cromatografía de vaporización instantánea en columna con gel de sílice con 2-3% (amoniaco 2 M en metanol) en diclorometano para obtener 106 mg del compuesto del título como un sólido blanquecino.

^{1}H RMN ($CDCl_3$):d ppm 8.73 (d, 2H), 8.03 (s, 1H), 7.93 (d, 1H), 7.69 (d, 2H), 7.46 (d, M), 7.42 (t, 1H), 5.02 (dd, 1H), 3.61 (dd, I H), 3.49 (dd, 1H), 3.35 (m, 1B), 2.47 (br s, 2H), 1.20 (m, 2H), 0.75 (m, 2H)

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EJEMPLO 803

(S)-[1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-dimetil-amina

Se agrega cianoborohidruro de sodio (0.1 ml, 1M en THF) a una solución de (S)-1-[3-(3-cloro-fenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etilamina (30 mg) en metanol (0.8 ml) que contiene ácido fórmico al 96% (0.1 ml) y solución de formalina al 37% (0.1 ml). El residuo se extingue con agua y se extrae con acetato de etilo. La capa orgánica se seca con sulfato de sodio y se concentra. La purificación se efectúa mediante cromatografía de vaporización instantánea en columna con gel de sílice con 3% (amoniaco 2M en metanol) en diclorometano para obtener 22 mg del compuesto del título.

^{1}H RMN ($CDCl_3$):d ppm. 8.76 (d, 2H), 8.06 (s, 1H), 7.97 (d, 1H), 7.73 (d, 2H), 7.47 (d, I H), 7.45 (t, 1H), 5.00 (dd, I H), 3.76 (dd, 1H), 3.51 (dd, 1H), 3.42 (m, I H), 2.45 (br s, 6H), 1.26 (m, 2H), 0.88 (m, 1H), 0.79 (m, 1H).

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EJEMPLO 804

8-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina

Se agregan 37 mg (0.25 mmoles) de Me_3OBF_4 a una solución de 60 mg (0.21 mmoles) de 3-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-piperidin-2-ona en 2 ml de CH_2Cl_2. La mezcla se agita durante la noche a temperatura ambiente. La mezcla de reacción se diluye con CH_2Cl_2, se lava con $NaHCO_3$ (saturado), se seca y se concentra. El residuo se disuelve en 3 ml de EtOH y se agregan 22 mg (0.16 mmoles) de hidrazida isonicotínica. La solución se calienta con microondas a 120°C durante 10 minutos. La mezcla de reacción se enfría y se eliminan los volátiles a presión reducida. El producto crudo se purifica mediante HPLC preparativa para obtener 17 mg (20%) del producto deseado.

^1H RMN ($CDCl_3$):d ppm 1.75 (m, 1H) 1.99 (m, 1H) 2.21 (m, 2H) 3.16 (dd, 1H) 3.73 (m, 1H) 3.85 (dd, 1H) 4.07 (m, 1H) 4.19 (m, 1H) 7.47 (t, 1H) 7.56 (m, 1H) 7.67 (m, 2H) 8.01 (m, 1H) 8.11 m, 1H) 8.76 (d, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 804:

Ejemplo No.	Nombre	^{1}H RMN	MS
805	8-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-tiofen-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]piridina	1.69 (m, 1H) 1.99 (m, 1H) 2.18 (m,2H)3.11 (m, 1H) 3.67 (m, 1H) 3.87 (m, 1H) 4.02 (m, 1H) 4.24 (m, 1H) 7.15 (m, 1H) 7.47 (m, 3H)) 7.56 (m, 1H) 8.01 (d, J=7.83H)z, 1H) 8.12 (d, J=1.77 Hz, 1H)	
806	8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]piridina	1.76 (m, 1H) 2.00 (m, 1H) 2.21 (m, 2H) 3.22 (dd, 1H) 3.74 (m, 1H) 3.87 (dd, 1H) 4.09 (m, 1H) 4.19 (m, 1H) 7.23 (m, 1H) 7.53 (m, 1H) 7.68 (m, 2H) 8.10 (dd, 1H) 8.77 (m, 2H)	

EJEMPLO 807

5-(5-bromo-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-cloro-fenil)-[1,2,4]oxadiazol

Se mezcla 3-(3-cloro-fenil)-5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol con 30 ml de cloroformo/piridina (25/1) a temperatura ambiente. Después se agrega, mediante goteo, bromo en

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cloroformo (0.5 ml) y la mezcla de reacción se calienta a 70°C durante la noche. La mezcla de reacción se diluye con cloroformo y se lava con NH4Cl saturado dos veces y la capa orgánica se seca con sulfato de sodio, se concentra, el residuo se tritura con éter dietílico para obtener el compuesto del título (1.5 g, 57.5%, sólido de color amarillo).

^{1}H RMN($CDCl_3$) d(ppm): 8.05 (s, 1H), 7.94 (d, 1H), 7.47(d, 1H), 7.43 (t, 1H), 4.66 (s, 2H) and 3.59 (s, 3H).

EJEMPLO 808

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina

Se agrega TFA (1.5 ml) al éster ter-butílico del ácido (3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)[1,2,4]oxadiazol-5-il-fenil)-carbámico (88.0 mg, 0.19 mmoles) en diclorometano (3 ml) a 0°C y se deja agitar durante 1 hora. La mezcla de reacción se calienta hasta temperatura ambiente y el solvente se elimina al vacío. Se agrega diclorometano al residuo resultante y la mezcla se enfría hasta 0°C y se agrega bicarbonato de sodio saturado a la solución en

agitación hasta que se torna básica (pH ~ 8). La mezcla se transfiere después a un embudo de separación y el producto se extrae con diclorometano, se seca utilizando sulfato de sodio anhidro, y se concentra al vacío. El residuo resultante se tritura con éter y se aíslan 61.1 mg (87%) de 3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina (sólido de color amarillo claro).

^{1}H RMN (DMSO-d_6) d (ppm): 7.81 (d, 1H), 7.64 (d, 1H), 7.23 (m, 4H), 6.84 (d, 1H), 5.57 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 98:

Ejemplo No.	Nombre	^{1}H RMN	MS
809	5-(3-cloro-ph6nil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-sulfonil-metil)-[1,2,4]-oxadiazol		423.01
810	5-(3-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-sulfinil-metil)-[1,2,4]-oxadiazol		

Los siguientes compuestos se preparan de manera análoga a la del ejemplo93:

Ejemplo No.	Nombre	^{1}H RMN	MS
811	2-metil6-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina		

EJEMPLO 812

4-(5-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol

Se agregan HBr (1 ml) y HOAc (1 ml) a 4-(5-{1-[5-(3-cloro-fenil)[1,2,4]oxadiazol-3-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina (9 mg, 0.02 mmoles) y la reacción se agita a 80°C. Se agrega $NaHCO_3$ saturado (acuoso) a la reacción y la mezcla se extrae tres veces con diclorometano. Las fases orgánicas combinadas se secan y se concentran para obtener el compuesto del título (8.5 mg, 99%).

^{1}H RMN ($CDCl_3$), δ (ppm): 1.37 (t, 3H)), 1.96 (d, 3H)), 4.10 (q, 2H), 5.23 (q, 1H), 6.80 (m, 2H),

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7.49 (t, 2H), 7.59 (m, 1H), 7.99 (d, 1H), 8.11 (s, 1H).

EJEMPLO 813

4-(5-(2-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-propil)-4-metil-4H-[1,2,4]triazol-3-il)-piridina

Se agregan, mediante goteo 84 microl (0.21 mmoles, 2.5 M) de n-BuLi a una solución de 37 mg (0.21 mmoles) de 4-(4,5-dimetil-4H-[1,2,4]triazol-3-il)-piridina en 2.1 ml de THF a 0°C. Después de 20 minutos se agrega, mediante goteo, una solución de 60 mg (0.21 mmoles) de 3-(1-bromo-etil)-5-(3-cloro-fenil)-[1,2,4]oxadiazol. Se deja que la mezcla de reacción llegué a temperatura ambiente y se agita durante la noche. Se agrega NH_4Cl (saturado) y la mezcla se extrae dos veces con EtOAc. La fase orgánica se seca y se concentra. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 20:1) permite obtener 7.7 mg (10%) del producto deseado.

^1H RMN ($CDCl_3$), d (ppm): 1.57 (d, 3H)) 3.16 (m, 1H) 3.38 (m, 1H) 3.71 (s, 3H)) 3.84 (d, 1H) 7.46 (t, 1H) 7.55 (m, 1H) 7.58 (m, 2H) 7.98 (m, 1H) 8.10 (t, 1H) 8.77 (d, 2H).

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EJEMPLO 814

[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-amina

Se agregan 10 mg (0.4 mmoles) de NaH a una solución de 38 mg (0.2 mmoles) de metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-amina en 3 ml de DMF bajo una atmósfera de nitrógeno. Después de 10 minutos, se agrega una solución de 50 mg (0.22 mmoles) de 3-clorometil-5-(3-cloro-fenil)-[1,2,4] oxadiazol en 2 ml de DMF. Después de agitar durante 45 minutos, se agrega NH_4Cl (saturado) y la mezcla se extrae dos veces con $CHCl_3$. La fase orgánica se seca y se concentra. La cromatografía de vaporización instantánea(CH_2Cl_2/MeOH 20:1) permite obtener 41 mg (54%) del producto deseado.

^1H RMN ($CDCl_3$), d (ppm): 3.07 (s, 3H)) 3.71 (s, 3H)) 4.56 (s, 2H) 7.45 (m, 1H) 7.55 (m, 1H) 7.62 (d, 2H) 7.98 (d, 1H) 8.09 (m, 1H) 8.73 (d, 2H).

EJEMPLO 815

8-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina

Se agregan 32 mg (1.31 mmoles) de NaH a una solución de 193 mg (0.96 mmoles) de 3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirimidina en 10 ml de DMF a temperatura ambiente. Después de 10 minutos, se agregan 200 mg (0.87mmol) 5-(3-cloro-fenil)-3-clorometil-[1,2,4]oxadiazol a la mezcla de reacción. La mezcla de reacción se agita a temperatura ambiente durante la noche. La mezcla de reacción se diluye con NH_4Cl (saturado) y se extrae dos veces con EtOAc. Las fases orgánicas combinadas se lavan con agua, se secan y se concentran. La cromatografía de vaporización instantánea (CH_2Cl_2/MeOH 20:1) permite obtener 111 mg (32%) de un sólido de color blanco.

^1H RMN ($CDCl_3$), d (ppm): 2.24 (m, 2H) 3.57 (m, 2H) 4.15 (m, 2H) 5.01 (s, 2H) 7.46 (t, 1H) 7.56 (d, 1H) 7.62 (d, 2H) 7.99 (d, 1H) 8.10 (s, 1H) 8.70 (d, 2H).

Los siguientes compuestos se preparan de manera análoga a la del ejemplo 815:

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Ejemplo No.	Nombre	^{1}H RMN	MS
816	8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro[1,2,4]-triazolo[4,3-a]-pirimidina		
817	8-[5-(3-cloro-fenil)[1,3,4]oxadiazol-2-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro[1,2,4]-triazolo[4,3-a]-pirimidina		
818	8-{1-[5-(3-cloro-fenil)-[1,3,4]oxadiazol-2-il]-etil}-3-piridin-4-il-5,6,7, 8-tetrahidro[1,2,4]-triazolo[4,3-a]-pirimidina	1.81(d,3H)2.19(m,2H) 3.47 (m, 2H) 4.12 (m, 2H) 6.07 (q, 1H) 7.42 (m, 1H) 7.49 (m, 1H) 7.61 (m, 2H) 7.91 (m, 1H) 8.00 (m, 1H) 8.70 (m, 2H)	
819	8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina	2.23 (m, 2H) 3.50 (m, 2H) 4.20 (m, 2H) 4.97 (s, 2H) 6.49 (m, 1H) 6.89 (d, 1H) 7.19 (t, 1H) 7.48 (m, 1H) 7.51 /m, 1H) 8.06 (m, 1H)	
820	8-{1-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]-triazolo[4,3-a]pirimidina	1.74 (d, 3H)) 2.17 (m, 2H) 3.45 (m, 2H) 4.10 (m, 2H) 5.96 (m, 1H) 7.44 (t, 1H) 7.53 (m, 1H) 7.59 (m, 2H) 7.97 (m, 1H) 8.08 (m, 1H) 8.67 (d, 2H)	

EJEMPLO 821

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(1H-pirrol-3-il)-[1,2,4]oxadiazol

Se calientan 3-clorometil-5-[1-(toluen-4-sulfonil)-1H-pirrol-3-il]-[1,2,4]oxadiazol (50 mg) e hidróxido de potasio (50 mg) durante dos horas en metanol (5 ml). La mezcla se diluye con acetato de etilo (10 ml), se lava con agua y salmuera, se seca con $MgSO_4$, se filtra y se concentra. El compuesto del título se aísla con 57% de rendimiento mediante cromatografía de vaporización instantánea en gel de sílice utilizando 40% de acetato de etilo en heptano.

^1H RMN ($CDCl_3$) d (ppm): 9.8 (s, 1H), 7.5 (m, 2H), 7.4 (d, 1H), 7.2 (dd, 1H), 6.8 (m, 1H), 6.7 (d, 1H), 4.5 (s, 2H), 4.1 (q, 2H), 1.4 (t, 3H).

EJEMPLO 822

1-óxido de 4-[5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina

Se disuelven 4-{5-[5-(3-cloro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]-triazol-3-il}-piridina y MCPBA al 57%-86%

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húmedo (52.4 mg, 0.20-0.30 mmoles)en diclorometano (4 ml) y se agita durante 16 horas. La mezcla de reacción se purifica mediante cromatografía líquida preparativa de fase invertida para obtener el compuesto del título (7.5 mg, 8%).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.33 (d, 2H), 8.06 (m, 1H), 7.96 (m, 1H), 7.67 (d, 2H), 7.57 (m, 1H), 7.46 (apparent t, 1H), 4.60 (s, 2H), 3.71 (s, 3H)).

EJEMPLO 823

5-(3-cloro-fenil)-3-(2-furan-2-il-3-metil-3H-imidazol-4-ilsulfanilmetil)-[1,2,4]oxadiazol

Se disuelve 2-furan-2-il-3-metil-3,5-dihidro-imidazol-4-ona (descrita en Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989) 6375-6386) (50 mg, 0.30 mmoles) en dioxano (3 ml) y se agrega reactivo de Lawesson (136 mg, 0.34 mmoles). La mezcla de reacción se calienta a reflujo durante la noche y después se deja que llegue a temperatura ambiente momento en el cual se agregan DIPEA (212 ml, 1.22 mmoles) y 3-clorometil-5-(3-cloro-fenil)-[1,2,4]oxadiazol (140 mg, 0.61 mmoles). La mezcla resultante se calienta a reflujo durante 5 horas y después se mantiene a temperatura ambiente durante la

noche. Se agrega acetato de etilo y la mezcla de reacción se lava con agua seguido por salmuera. La fase orgánica se seca con $MgSO_4$ y se evapora. El compuesto del título (13 mg, 11%) se obtiene mediante cromatografía de vaporización instantánea utilizando 1% de metanol en cloroformo.

^1H RMN (CD_3OD) d (ppm): 7.96 (m, 1 H), 7.90 (m, 1H), 7.60 (dd, 1H), 7.57 (ddd,1H), 7.46 (t, 1H), 7.09 (s, 1H), 6.86 (dd, 1H), 6.52 (dd, 1H), 3.95 (s, 2H), 3.74 (s, 3H).

EJEMPLO 824

5-(5-cloro-2-fluoro-fenil)-3-[4-(2-fluoro-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol

A una solución fría (-15 °C) de 2-{3-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-etanol (46 mg, 0.11 mmoles) en THF anhidro (15 ml) se agrega mediante goteo DAST (32 ml, 0.24 mmoles). La mezcla se agita a temperatura ambiente durante 1.5 horas y después se extingue con MeOH (1 ml). El solvente se elimina a presión reducida y el residuo se divide entre salmuera y EtOAc. La capa acuosa se

extrae con EtOAc (2 x 20 ml). Las capas orgánicas combinadas se lavan con salmuera (10 ml), se secan ($MgSO_4$) y se concentran a presión reducida. La purificación mediante cromatografía de vaporización instantánea (EtOAc:heptano 2:1) y HPLC preparativa permite obtener el compuesto del título como un sólido de color blanco (11 mg, 22%).

^1H RMN ($CDCl_3$) d (ppm): 8.05 (dd, 1H), 7.52 (m, 3H), 7.20 (m, 1H), 7.16 (m, 1H), 4.75 (t, 1H), 4.63 (m, 3H), 4.45 (m, 2H).

EJEMPLO 825

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4] oxadiazol

El compuesto del título se prepara de conformidad con el método para 2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1H-benzoimidazol, con la excepción que se utiliza el equivalente molar de carbonato de cesio en lugar de carbonato de potasio como la base, a partir de 1-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetoxi]-1H-benzotriazol (32.3 mg, 0.097 mmoles) y 4-etil-5-furan-2-il-2,4-dihidro-[1,2,4]triazol-3-tiona (23 mg)

utilizando 50% de EtOAc en n-heptano como el eluyente para cromatografía para obtener 21 mg.

^{1}H RMN ($CDCl_3$) d (ppm): 7.95 (d, 1H), 7.57 (dd, 1H), 7.44 (d, 1H), 7.07 (dd, 1H), 6.56 (dd, 1H), 4.56 (s, 2H), 4.22 (q, 2H), 1.35 (t, 3H).

EJEMPLO 826

3-[3-(4-Ethil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-hidroxi-benzonitrilo

El compuesto del título se prepara utilizando el procedimiento general de Rogers et al., Tetrahedron Letters (2002) 43: 3585-3587. A una solución en agitación de 3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo (20mg, 0.050 mmoles), 2-(metilsulfonil-etanol) (9.38 mg, 0.075 mmoles), y DMF (0.05 M) a 0°C se agrega NaH (5.8 mg, 0.150 mmoles). Se agita durante 20 minutos y se retira el baño de hielo. Se agita 20 minutos adicionales mientras se calienta hasta temperatura ambiente. La mezcla de reacción se extingue con solución de HCl 1N y se divide entre acetato de etilo y salmuera. La capa orgánica se seca (Na_2SO_4), se

filtra y se concentra hasta sequedad. Los materiales orgánicos crudos se purifican mediante cromatografía de vaporización instantánea en columna utilizando acetato de etilo seguido por 5% de metanol en acetato de etilo para obtener el compuesto del título (8.1 mg, 41%, sólido de color blanco).

^{1}H RMN ($CDCl_3$), δ (ppm): 8.25 (m, 1H), 7.75 (m, 1H), 7.60 (s, 1H), 7.18 (m, 2H), 6.60 (m, 1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).

Ejemplos farmacéuticos

Prueba FLIPR de actividad antagonista del receptor del grupo I

Para el análisis FLIPR, se siembran células en placas de 96 cavidades de fondo transparente revestidas con colágena con lados oscuros y se efectúa el análisis de movilización de $[Ca^{2+}]_i$ 24 horas después de la siembran.

Los cultivos de células en las placas de 96 cavidades se cargan con una solución 4 μM de la forma de éster acetoximetílico del indicador fluorescente de calcio fluor-3 (Molecular Probes, Eugene, Oregon) en Pluronic al 0.01%. Todas las pruebas se efectúan en una solución reguladora que contiene 127 mM de NaCl, 5 mM de KCI, 2 mM de $MgCl_2$, 0.7 mM de NaH_2PO_4, 2

mM de $CaCl_2$, 0.422 mg/ml de $NaHCO_3$, 2.4 mg/ml de HEPES, 1.8 mg/ml de glucosa y 1 mg/ml de fracción IV de BSA (pH 7.4).

Los experimentos FLIPR se efectúan utilizando un ajuste de láser de 0.800 W y una velocidad de obturador de cámara CCD de 0.4 segundos con longitudes de onda de excitación y emisión de 488 nm y 562 nm, respectivamente. Cada experimento FLIPR se inicia con 160 µL de solución reguladora presente en cada cavidad de la placa de células. Una adición de 40 µL proveniente de la placa de antagonista es seguida por una adición de 50 µl proveniente de la placa de agonista. Después de cada adición, se muestrea la señal de fluorescencia 50 veces a intervalos de 1 segundo seguido por tres muestras a intervalos de 5 segundos. Las respuestas se miden como la altura del pico de la respuesta dentro del periodo de la muestra.

Las determinaciones de CE_{50}/CI_{50} se efectúan a partir de datos obtenidos de curvas de concentración-respuesta de 8 puntos (CRC por sus siglas en inglés) efectuadas por duplicado. Las CRC del agonista se generan escalando todas las respuestas hasta la respuesta máxima observada para la placa. El bloque de antagonista de la exposición

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al agonista se normaliza con la respuesta promedio de la exposición al agonista en 14 cavidades de control en la misma placa.

Medición del recambio de fosfato de inositol en células enteras intactas

Se siembran células GHEK expresan en forma estable al receptor mGluR5d de humano en placas de 24 cavidades revestidas con poli-L-lisina a 40 x 10^4 células/cavidad en medio que contiene 1 µCi/ cavidad de [3H] mio-inositol. Las células se incuban durante la noche (16 horas), después se lavan tres veces y se incuban durante 1 hora a 37°C en solución salina regulada con HEPES (146 mM de NaCl, 4.2 mM de KCl, 0.5 mM de $MgCl_2$, 0.1% de glucosa, 20 mM de HEPES, pH 7.4) complementado con 1 unidad/ml de glutamato piruvato transaminasa y 2 mM de piruvato. Las células se lavan una vez en solución salina regulada con HEPES y se pre-incuban durante 10 minutos en solución salina regulada con HEPES que contiene 10 mM de LiCl. Se agregan los compuestos (agonistas) y se incuban a 37°C durante 30 minutos. La actividad antagonista se determina pre-incubando los compuestos de prueba durante 15 minutos, incubando después en presencia de glutamato (80 µM) o DHPG (30 µM) durante 30 minutos.

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La reacción se determina mediante adición de 0.5 ml de ácido perclórico (5%) en hielo, con incubación a 4°C durante por lo menos 30 minutos. Las muestras se recolectan en tubos Falcon de 15 ml y los fosfatos de inositol se separan utilizando columnas Dowex como se describe más adelante.

Prueba para fosfatos de inositol utilizando columnas de intercambio iónico alimentadas por la fuerza de gravedad

a) preparación de las columnas de intercambio iónico

Se lava tres veces la resina para intercambio iónico (forma de formato Dowex AG1-X8, malla 200-400, BIORAD) con agua destilada y se almacenan a 4°C. Se agregan 1.6 ml de resina a cada columna y se lavan con 3 ml de HEPES 2.5 mM, 0.5 mM de EDTA, pH 7.4.

b) tratamiento de la muestra

las muestras se recolectan en tubos Falcon de 15 ml y se neutralizan con HEPES 0.375 M, 0.75 M de KOH. Se agregan 4 ml de HEPES/EDTA (2.5/0.5 mM, pH 7.4) para precipitar el perclorato de potasio. Se

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agrega el sobrenadante a las columnas Dowex preparadas.

c) separación del fosfato de inositol

Se eluyen los glicero fosfatidil inositoles con 8 ml de formiato de amonio 30 mM.

Se eluyen los fosfatos de inositol con 8 ml de formiato de amonio 700 mM/ácido fórmico 100 mM y se recolecta el eluato en frascos para cintigrafía. Se efectúa el conteo en el eluato con 8 ml de reactivo para cintigrafía.

Resultados

Los valores de CI_{50} típicos, según se mide en las pruebas antes descritas, son 10 µm o menores. En un aspecto de la invención el CI_{50} es menor de 2 µM. En otro aspecto de la invención el CI_{50} es menor de 0.2 µM. En otro aspecto adicional de la invención el CI_{50} es menor de 0.05 µM.

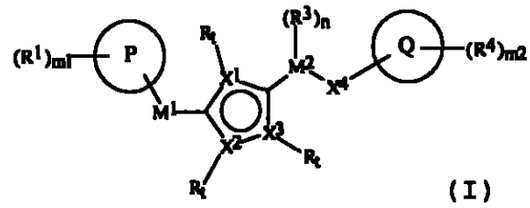
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NOVEDAD DE LA INVENCION

Habiendo descrito el presente invento se considera como novedad y por lo tanto se reclama como propiedad lo contenido en las siguientes:

REIVINDICACIONES

1.- Un compuesto de la fórmula I



(I)

caracterizado porque:

P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo y fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5;

R^1 está unido a P a través de un átomo de carbono en el anillo P y se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de

C_{2-6}, O-alquenilo de C_{2-6}, alquinilo de C_{2-6}, O-alquinilo de C_{2-6}, alquil(C_{0-6})-cicloalquilo de C_{3-6}, O-alquil(C_{0-6})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, O-alquil(C_{0-6})arilo, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, alquil(C_{1-6})-OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})-$(CO)R^5$, O-alquil(C_{1-6})$(CO)R^5$, alquil(C_{0-6})-CO_2R^5, O-alquil(C_{1-6})-CO_2R^5, alquil(C_{0-6})ciano, O-alquil(C_{2-6})-ciano, alquil(C_{0-6})NR^5R^6, O-alquil(C_{2-6})NR^5R^6, alquil(C_{1-6})-$(CO)NR^5R^6$, O-alquil(C_{1-6})$(CO)NR^5R^6$, alquil(C_{0-6})$NR^5(CO)R^6$, O-alquil(C_{2-6})$NR^5(CO)R^6$, alquil(C_{0-6})$NR^5(CO)NR^5R^6$, alquil(C_{0-6})-SR^5, O-alquil(C_{2-6})SR^5, alquil(C_{0-6})$(SO)R^5$, O-alquil(C_{2-6})-$(SO)R^5$, alquil(C_{0-6})SO_2R^5, O-alquil(C_{2-6})SO_2R^5, alquil(C_{0-6})-$(SO_2)NR^5R^6$, O-alquil(C_{2-6})$(SO_2)NR^5R^6$, alquil(C_{0-6})NR^5-$(SO_2)R^6$, O-alquil(C_{2-6})$NR^5(SO_2)R^6$, alquil(C_{0-6})$NR^5(SO_2)$-NR^5R^6, O-alquil(C_{2-6})$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, alquil(C_{0-6})$NR^5(CO)OR^6$, O-alquil(C_{2-6})$NR^5(CO)$-OR^6, SO_3R^5 y un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

M^1 es un enlace;

X^1 se selecciona a partir del grupo que consiste de C, CO, N, O y S;

X^2 se selecciona a partir del grupo que consiste de C, N, O y S;

X^3 es i) seleccionado a partir del grupo que

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consiste de N, O y S, o

ii) se selecciona a partir de N, O, S, y C cuando X^2 se selecciona a partir de N, O, o S, y cuando X^3 es C, el sustituyente R en X^3 es H;

R se selecciona a partir del grupo que consiste de hidrógeno, alquilo de C_{0-3}, halógeno, alquil(C_{0-3})OR^5, alquil(C_{0-3})NR^5R^6, alquil(C_{0-3})(CO)OR^5 y alquil(C_{0-3})arilo;

M^2 se selecciona a partir de un grupo que consiste de un enlace, alquilo de C_{1-3}, alquinilo de C_{2-3}, alquil(C_{0-4})(CO)alquilo de C_{0-4}, alquil(C_{0-3})O-alquilo de C_{0-3}, alquil(C_{0-3})NR^5-alquilo de C_{1-3}, alquil(C_{0-3})(CO)NR^5, alquil(C_{0-4})NR^5, alquil(C_{0-3})(SO)-alquilo de C_{0-3} y alquil(C_{0-3})(SO_2)alquilo de C_{0-3};

R^3 se selecciona a partir de un grupo que consiste de hidroxi, alquil(C_{0-6})-ciano, oxo, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-4}, O(CO)alquilo de C_{1-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, O-alquilo de C_{1-4}, alquil(C_{1-4})OR^5 y alquil(C_{0-4})NR^5R^6;

X^4 se selecciona a partir del grupo que consiste de alquil(C_{0-4})R^5R^6, cicloalquilo de C_{3-7}, alquil(C_{1-4})(NR^5R^6), NR^5, alquil(C_{0-4})(NR^5R^6)=N, NR^5-alquil(C_{0-4})(NR^5R^6)=N, NO-alquilo de C_{0-4}, halógeno-

alquilo de C_{1-4}, O, SO, SO_2 y S, y en el cual el enlace entre M^2 y X^4 es un enlace sencillo;

Q es i) seleccionado a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en los cuales cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno y cualquier átomo de carbono apropiado está opcionalmente sustituido con R^4; y

R^4 se selecciona a partir del grupo que consiste de alquil(C_{0-6})-ciano, =N-alquilo de C_{1-4}, =NOR^5, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, alquenilo de C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})-(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4},

alquil(C_{1-4})(SO_2)alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})N-(alquilo de C_{1-4})$_2$ y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O, y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A; o

ii) se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolopiridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo; y

R^4 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, alquil(C_{0-6})-ciano, $=NR^5$, $=NOR^5$, halogenoalquilo de C_{1-4}, halógeno, alquilo de C_{1-6}, O-alquilo de C_{1-4}, O-alquil(C_{0-6})arilo, O(CO)alquilo de C_{1-4}, alquil(C_{0-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})(SO)alquilo de C_{0-4}, alquil(C_{1-4})(SO_2)-alquilo de C_{0-4}, (SO)alquilo de C_{0-4}, (SO_2)alquilo de C_{0-4}, alquil(C_{1-4})OR^5, alquil(C_{0-4})NR^5R^6 y un anillo de

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5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 o 6 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A;

R^5 y R^6 se seleccionan de manera independiente a partir del grupo que consiste de hidrógeno y alquilo de C_{1-6};

en el cual cualquier alquilo de C_{1-6} definido bajo R^1, R^2 y R^4 puede estar sustituido con uno o más A;

A se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, oxo, alquil(C_{0-6})-ciano, alquil(C_{0-4})cicloalquilo de C_{3-6}, alquilo de C_{1-6}, halogenoalquilo de C_{1-6}, O-halógeno-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-3})arilo, alquil(C_{0-6})OR^5, O-alquil(C_{2-6})-OR^5, alquil(C_{1-6})SR^5, O-alquil(C_{2-6})SR^5, (CO)R^5, O(CO)R^5, O-alquil(C_{2-6})-ciano, O-alquil(C_{1-6})-CO_2R^5, O(CO)OR^5, O-alquil(C_{1-6})-(CO)R^5, alquil(C_{1-6})-(CO)R^5, NR^5OR^6, O-alquil(C_{2-6})-NR^5R^6, alquil(C_{0-6})(CO)NR^5R^6, O-alquil(C_{1-6})(CO)NR^5R^6, O-alquil(C_{2-6})-NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)R^6, alquil(C_{0-6})NR^5(CO)-NR^5R^6, O(CO)NR^5R^6, alquil(C_{0-6})(SO_2)NR^5R^6, O-alquil(C_{2-6})-

$(SO_2)NR^5R^6$, alquil$(C_{0-6})NR^5(SO_2)R^6$, O-alquil$(C_{2-6})NR^5$-$(SO_2)R^6$, SO_3R^5, alquil$(C_{1-6})NR^5(SO_2)NR^5R^6$, O-alquil$(C_{2-6})$-$(SO_2)R^5$, alquil$(C_{0-6})(SO_2)R^5$, alquil$(C_{0-6})(SO)R^5$, O-alquil$(C_{2-6})(SO)R^5$ y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N, O y S;

m1 se selecciona a partir de 0, 1, 2, 3 y 4;

m2 se selecciona a partir de 0, 1, 2 y 3;

n se selecciona a partir de 0, 1 y 2; y

t es 0 o 1,

y sales de los mismos,

con la condición que el compuesto no sea 5-(4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol, 1,2-di{2-(3-amino-fenil)-[1,3,4]-oxadiazol-il)etano, 1,2-di{5-[5-(4-nitrofenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-bromo-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano, 1,2-di{5-[5-(4-cloro-fenil)furan-2-il]-[1,3,4]oxadiazol-il)etano y 1,2-di{5-[5-(2,4-dibromofenil)furan-2-il]-[1,3,4]-oxadiazol-il)etano.

2.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque P se selecciona a partir del grupo que consiste de tiofeno, piridilo, tiazolilo, furilo, pirrolilo o

fenilo, en el cual el anillo fenilo está sustituido en la posición 3 o disustituido en las posiciones 2 y 5 y R^1 se selecciona a partir del grupo que consiste de hidrógeno, hidroxi, halógeno, nitro, halogenoalquilo de C_{1-6}, O-halogenoalquilo de C_{1-6}, alquilo de C_{1-6}, O-alquilo de C_{1-6}, alquenilo de C_{2-6}, alquil(C_{0-6})cicloalquilo de C_{3-6}, alquil(C_{1-6})OR^5, alquil(C_{1-6})(CO)R^5, alquil(C_{0-6})CO_2R^5, alquil(C_{0-6})-ciano, alquil(C_{0-6})NR^5R^6, alquil(C_{0-6})SR^5 y un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C y O.

3.- Un compuesto de conformidad con la reivindicación 2, caracterizado porque P es fenilo sustituido en la posición 3 o disustituido en las posiciones 2 y 5.

4.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque X^1 es N y uno de X^2 y X^3 es O y el otro es N.

5.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque el anillo que contiene a X^1, X^2 y X^3 forma un oxadiazol, isoxazol, oxazol, cloro-isoxazol o un metil-isoxazol.

6.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque M^2 es un

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enlace o alquilo de C_{1-3} y R^3 es hidrógeno, metilo o dimetilo.

7.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque X^4 se selecciona a partir del grupo que consiste de alquil$(C_{0-4})R^5R^6$, cicloalquilo de C_{3-7}, NR^5, O, SO, SO_2 y S y R^5 y R^6 se seleccionan de manera independiente a partir de hidrógeno y alquilo de C_{1-6}.

8.- Un compuesto de conformidad con la reivindicación 7, caracterizado porque X^4 se selecciona a partir del grupo que consiste de CH_2, $CHCH_3$, $CH(CH_3)_2$ y NR^5.

9.- Un compuesto de conformidad con la reivindicación 7, caracterizado porque X^4 es S.

10.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque Q se selecciona a partir del grupo que consiste de triazolilo, imidazolilo, oxadiazolilo, imidazolonilo, oxazolonilo, tiazolonilo, tetrazolilo y tiadiazolilo, y en la cual cualquier átomo de nitrógeno sustituible en el anillo está sustituido con R^4 en dicho átomo de nitrógeno, y cualquier átomo de carbono apropiado está sustituido opcionalmente con R^4 y R^4 se selecciona a partir del grupo que consiste de halogenoalquilo de C_{1-4}, alquilo de C_{1-6}, alquenilo de

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C_{2-4}, alquil(C_{0-2})-cicloalquilo de C_{3-6}, alquil(C_{0-6})arilo, alquil(C_{0-6})-heteroarilo, O-alquil(C_{0-6})arilo, O-alquil(C_{0-6})heteroarilo, N-alquil(C_{0-6})arilo, N-alquil(C_{0-6})heteroarilo, alquil(C_{0-6})-O-arilo, alquil(C_{0-6})O-heteroarilo, alquil(C_{0-6})N-arilo, alquil(C_{0-6})N-heteroarilo, O-alquil(C_{0-6})O-arilo, O-alquil(C_{0-6})O-heteroarilo, O-alquil(C_{0-6})N-arilo, O-alquil(C_{0-6})N-heteroarilo, N-alquil(C_{0-6})O-arilo, N-alquil(C_{0-6})O-heteroarilo, N-alquil(C_{0-6})N-arilo, N-alquil(C_{0-6})N-heteroarilo, alquil(C_{0-4})(CO)O-alquilo de C_{1-4}, alquil(C_{1-4})(S)alquilo de C_{0-4}, alquil(C_{1-4})OR^5 y un anillo de 3 o 6 miembros no aromático que contiene uno o más átomos que se seleccionan de manera independiente a partir de C, N, O y S, cuyo anillo puede estar opcionalmente fusionado con un anillo de 5 miembros que contiene uno o más átomos que se seleccionan de manera independiente a partir del grupo que consiste de C, N y O y en el cual dicho anillo y dicho anillo fusionado pueden estar sustituidos con uno o dos A.

11.- Un compuesto de conformidad con cualquiera de las reivindicaciones 1 o 10, caracterizado porque Q se selecciona a partir del grupo que consiste de triazolilo y tiadiazolilo.

12.- Un compuesto de conformidad con la

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reivindicación 1, caracterizado porque Q se selecciona a partir del grupo que consiste de benzoimidazolilo, benzo-oxazolilo, tetrahidrotriazolo-piridilo, tetrahidrotriazolopirimidinilo, piridonilo, piridazinilo, imidazopiridilo, oxazolopiridilo, tiazolopiridilo, imidazopiridazinilo, oxazolopiridazinilo, tiazolopiridazinilo y purinilo y R^4 es hidrógeno o alquilo de C_{1-6}.

13.- Un compuesto de conformidad con cualquiera de las reivindicaciones 1 o 12, caracterizado porque Q se selecciona a partir del grupo que consiste de piridonilo, tetrahidro-triazolopiridilo y tetrahidrotriazolo-pirimidinilo.

14.- Un compuesto de conformidad con la reivindicación 1, caracterizado porque R^4 se selecciona a partir del grupo que consiste de benzo[b]tiofenilo, benzodioxolilo, bromo, bromofurilo, butoxifenilo, clorometoxipiridilo, clorofenilo, clorofenilmetanol, cloropiridilo, clorotiofeno, cianofenilo, ciclohexilo, ciclopentilo, diclorofenilo, dicloropiridilo, difluorofenilo, dimetiltiazolilo, etanol, etoximetilo, fluorometilfenilo, fluorofenilo, éster metílico del ácido fórmico, furilo, hidrógeno, hidroxifenoxi-metilo, hidroxifenilo, imidazolilo, metoxietilo,

metoximetilo, metoxifenoximetilo, metoxifenilo, metoxifeniletilo, metoxipiridazinilo, metoxipiridilo, metoxipirimidinilo, metoxitiofeno, metilimidazolilo, metilpiridilo, metilsulfanilmetilo, metiltiazolilo, metiltiofeno, nitrofurilo, nitrofenilo, fenilo, p-toliloximetilo, piridazinilo, piridin-oxidilo, bencilmorfolinilo, piridinolilo, piridilo, piridilmetilo, pirimidinilo, ter-butilfenilo, tetrahidrofurilo, tiazolilo, tiofeno, tolilo, trifluorometilo, éster metílico del ácido acético, alilo, amino, bencilo, ciclopropilmetilo, etilo, fluorobencilo, fluoroetilo, furilmetilo, hidroxietilo, isobutilo, metilo, metilbencilo, metilbutilo, metilsulfanilpropilo, n-butilo, n-hexilo, n-propilo, tetrahidrofurilmetilo, tiofenilmetilo y trifluoroetilo.

15.- Un compuesto caracterizado porque se selecciona a partir del grupo que consiste de

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

5-(3-metoxifenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(1-metil-5-tiofen-2-il-1*H*-imidazol-2-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-

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3-ilsulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-metil-1*H*-benzoimidazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-trifluorometil-fenil)-[1,2,4]-oxadiazol,

3-(3-metoxi-fenil)-5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-3-m-tolil-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[4-metil-5-(2-metil-tiazol-4-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-[5-(2-metil-tiazol-4-il)-[1,3,4]oxadiazol-2-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-[5-(2,4-dimetil-tiazol-5-il)-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

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3-[4-metil-5-(5-nitro-furan-2-il)-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-[5-(4-ter-butilfenil)-4-metil-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]-oxadiazol,

2-cloro-5-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-benzo-oxazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(5-furan-2-il-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)piridina,

2-[5-(3-metoxifenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-imidazo[4,5-b]piridina,

5-(3-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

3-metil-5-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-

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piridina,

3-(4-metil-5-fenil-4*H*-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

4-bencil-2-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-morfolina,

4-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiazol-4-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,2,4]oxadiazol,

2-metil-4-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiazol-4-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-yodo-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

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5-(3-etil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(2-metilpiridin-4-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

2-[5-(3-yodofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-1*H*-benzoimidazol,

3-(4-metil-5-trifluorometil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

2,6-dicloro-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4*H*-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-p-tolil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

Dimetil-{3-[3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]fenil}-amina,

5-(3-cloro-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-trifluorometoxi-fenil)[1,2,4]-oxadiazol,

3-(5-ciclohexil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(5-ter-butil-4-metil-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(3-bromo-fenil)-3-(4-metil-5-tiofen-2-il-

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4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-bromo-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1*H*-benzoimidazol,

5-(3-metoximetil-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-[5-(3-metoximetil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1*H*-benzoimidazol,

4-[5-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-piridina,

2-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-1-metil-1*H*-imidazo[4,5-b]piridina,

2-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-1-metil-1*H*-imidazo[4,5-b],

3-[1-metil-1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]-triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-[1-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanil)-etil]-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfonilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-sulfinilmetil)-5-m-tolil-[1,2,4]oxadiazol, o

5-(3-furan-3-il-fenil)-3-(4-metil-5-tiofen-2-il-4*H*-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

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o sal de los mismos.

16.- Un compuesto que se selecciona a partir del grupo caracterizado porque consiste de

4-(4-ciclopropil-5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-metoxi-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{4-metil-5-[1-(5-m-tolil-[1,2,4]oxadiazol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-o-tolil-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-{3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]-triazol-4-il}-etanol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxa-diazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(4-etil-5-furan-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

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Ester metílico del ácido {3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-il}-acético,

5-(2-fluoro-5-metil-fenil)-3-[5-furan-2-il-4-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-{5-[3-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-ciclopentil-4-etil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-{4-etil-5-[2-(4-metoxi-fenil)-etil]-4H-[1,2,4]triazol-3-ilsulfanilmetil}-[1,2,4]oxa-diazol,

5-(3-clorofenil)-3-(4-etil-5-p-toliloximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metoxi-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-metoxi-

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metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-alil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-furan-2-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

3-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-metanol,

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3-(3-clorofenil)-5-[4-etil-5-(2-metoxi-etil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-metilsulfanilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-etoximetil-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]-triazol-3-carboxílico,

2-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-{1-[4-etil-5-(tetrahidro-furan-2-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-{5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridazina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-ilmetil)-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil)-4-etil-4H-[1,2,4]triazol-3-il)-fenol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenoximetil)-4-

(tetrahidrofuran-2-ilmetil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-ciclopropil-5-(4-metoxi-fenoximetil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-metoximetil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-[4-etil-5-(tetrahidrofuran-2-il)-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-5-m-tolil-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-{1-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-{5-[3-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(3-clorofenil)-5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-metilsulfanil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-[5-(3-metilsulfanil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-1H-benzoimidazol,

5-(2,5-dimetil-fenil)-3-(4-metil-5-tiofen-2-il-

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4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-fluoro-5-metil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-ciclopropil-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[2-(3-clorofenil)-oxazol-4-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-metil-5-(5-tiofen-2-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{4-metil-5-[5-(3-metilsulfanil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

2-metil-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

1-{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-etanona,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[4-metil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-metil-5-tiofen-2-il-4H-[1,2,4]triazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-butil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metoxi-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-bencil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-clorofenil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-2-metil-piridina,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxa-diazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

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5-(3-clorofenil)-3-(5-tiofen-2-il-4-tiofen-2-il-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[3-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-5-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-fenil-[1,2,4]oxadiazol,

3-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

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5-(3-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[4-metil-5-(5-tiofen-3-il-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[4-metil-5-(5-fenil-[1,2,4]oxadiazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

5-(5-bromo-2-fluoro-fenil)-3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

2-cloro-4-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[3-(3-fluoro-fenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

3-(3-fluoro-fenil)-5-(4-metil-5-tiofen-3-il-4H-

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[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

5-(5-fluoro-2-metil-fenil)-3-(4-furan-2-ilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-furan-2-ilmetil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-piridin-3-il-4H-[1,2,4]triazol-3-

ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-cloro-4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

4-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-[4-etil-5-(5-m-tolil-[1,2,4]oxadiazol-3-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

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3-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil-sulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

4-{5-[5-(5-bromo-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-fenil-[1,2,4]oxadiazol,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metoxi-piridina,

3-(3-clorofenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-metil-4-[3-(4-metil-5-tiofen-3-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-

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piridina,

4-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-benzonitrilo,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(2,5-diclorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4)oxadiazol,

4-{5-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4)triazol-3-il}-piridina,

5-(2,5-diclorofenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-etil-5-tiofen-3-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadi-

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azol-3-ilmetilsulfanil]-4-propil-4H-[1,2,4]triazol-3-il)-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

4-[4-metil-5-(3-tiofen-3-il-[1,2,4]oxadiazol-5-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

5-(4-metil-5-tiofen-3-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-tiofen-3-carbonitrilo,

5-(3-clorofenil)-3-[5-(2-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(5-benzo[b]tiofen-2-il-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-[5-(3-metoxi-fenil)-4-metil-

4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-m-tolil-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-5-tiofen-2-il-[1,2,4]triazol-4-ilamina,

3-piridin-4-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-tiofen-2-il-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-[1,2,4]triazol-4-ilamina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

5-(2,5-difluoro-fenil)-3-(4-etil-5-furan-2-il-4H-

[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-[4-etil-5-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-etil-3-furan-2-il-5-(5-tiofen-3-il-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[5-(3,5-diclorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-p-tolil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-m-tolil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-nitro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-[5-(2,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(3-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(4-clorofenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

5-(2-cloro-5-metil-fenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-isoxazol-5-ilmetil-sulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-tiofen-2-il-4H-[1,2,4]triazol,

3-[3-(3-clorofenil)-isoxazol-5-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-{5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(2,5-dicloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(2,5-dicloro-tiofen-3-il)-[1,2,4]oxadi-azol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-tiofen-2-il-4H-[1,2,4]triazol,

4-etil-3-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-ilmetilsulfanil]-5-furan-2-il-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-3-il-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-3-il-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-fluoro-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-tiofen-2-il-[1,2,4]oxadiazol,

3-{3-[5-(3-cloro-tiofen-2-il)-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2-fluoro-5-metil-fenil)-4-furan-2-ilmetil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-

3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-(3-metoxi-fenil)-[1,2,4]oxadiazol,

5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-3-tiofen-2-il-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

3-[5-(3-clorofenil)-oxazol-2-ilmetilsulfanil]-4-etil-5-trifluorometil-4H-[1,2,4]triazol,

4-etil-3-(5-tiofen-3-il-isoxazol-3-ilmetil-sulfanil)-5-trifluorometil-4H-[1,2,4]triazol,

4-{3-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(3-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-{3-[5-(4-clorofenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

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4-{3-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol-5-il}-2-metil-piridina,

4-[3-(4-etil-5-p-tolil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-2-metil-piridina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(3-fluoro-fenil)-[1,2,4]oxadiazol,

4-(4-etil-5-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-(3,5-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[5-(2,6-difluoro-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-fenol,

3-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4-(5-{1-[5-(3-clorofenil)-isoxazol-3-il]-etil-sulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-butoxi-fenil)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

3-(5-benzo[1,3]dioxol-5-il-4-etil-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-5-(3-clorofenil)-[1,2,4]-oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-

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sulfanilmetil)-5-(2-metil-tiazol-4-il)-[1,2,4]oxadiazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(4-fluoro-fenil)-[1,2,4]oxadiazol,

4-etil-3-{1-(5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-5-furan-2-il-4H-[1,2,4]triazol,

4-(4-etil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-(4-etil-5-(3-metil-3H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(1-metil-1H-imidazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-4-metil-isoxazol-3-il-metilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(3-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-etil-5-(5-metil-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

4-{5-[4-cloro-5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[4-cloro-5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-6-metil-piridina,

3-[5-(5-bromo-furan-2-il)-4-etil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(3-clorofenil)-[1,2,4]oxadiazol,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-cloro-4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridina,

2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-metil-benzonitrilo,

5-(3-clorofenil)-3-[4-etil-5-(3-metoxi-tiofen-2-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

3-[5-(5-cloro-tiofen-3-il)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-[1,2,4]oxadiazol-5-il]-5-fluorobenzonitrilo,

4-etil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-2-il-4H-[1,2,4]triazol,

4-metil-3-(5-fenil-isoxazol-3-ilmetilsulfanil)-5-tiofen-3-il-4H-[1,2,4]triazol,

4-etil-3-furan-2-il-5-(5-fenil-isoxazol-3-il-metilsulfanil)-4H-[1,2,4]triazol,

4-[4-etil-5-(5-fenil-isoxazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-[4-metil-5-(5-fenil-isoxazol-3-ilmetil-sulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-m-tolil-[1,3,4]oxadiazol,

4-[4-metil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-[4-etil-5-(5-m-tolil-[1,3,4]oxadiazol-2-il-metilsulfanil)-4H-[1,2,4]triazol-3-il]-piridina,

4-{5-[5-(5-cloro-tiofen-3-il)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

3-[3-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

3-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-

benzonitrilo,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-benzonitrilo,

3-[3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

5-(5-cloro-2-fluoro-fenil)-3-(4-metil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

2-cloro-4-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-cloro-4-[3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

2-(3-clorofenil)-5-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-metil-5-tiazol-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-(4-etil-5-trifluorometil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol,

4-{4-etil-5-[5-(4-metiltiofen-2-il)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-

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sulfanilmetil)-5-(4-metil-tiofen-2-il)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(3-nitro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(3-nitro-fenil)-[1,3,4]oxadiazol,

4-{5-[5-(3-clorofenil)-isoxazol-3-ilmetil-sulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

3-[5-(3-clorofenil)-isoxazol-3-ilmetilsulfanil]-4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol,

5-(3-clorofenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[1-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

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3-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-benzonitrilo,

3-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]benzonitrilo,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-(5-cloro-2-fluorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]-oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

2-(3-clorofenil)-5-[4-etil-5-(4-metoxi-fenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

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5-(5-cloro-2-fluoro-fenil)-3-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

2-cloro-4-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-{5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-etil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]-oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4)triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il)-piridina,

2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il-sulfanilmetil)-5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol,

2-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-5-(2-fluoro-5-metil-fenil)-[1,3,4]-

oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

3-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-ilmetil-sulfanil]-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

3-{1-[5-(5-cloro-2-fluoro-fenil)-isoxazol-3-il]-etilsulfanil}-4-etil-5-furan-2-il-4H-[1,2,4]triazol,

4(5-(1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]-oxadiazol,

4-cloro-2-[3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

2-cloro-4-[5-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-[5-(4-etil-5-furan-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-piridina,

2-cloro-4-{5-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol-2-il}-piridina,

2-(3-clorofenil)-5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-

piridina,

5-(5-bromo-2-fluoro-fenil)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,3,4]oxadiazol,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-{5-(5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-ciclopropil-4H-{1,2,4)triazol-3-il}-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-etil-5-{1-[5-(2-fluoro-5-metilfenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

2-(2-fluoro-5-metil-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-

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[1,3,4]oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

2-(5-cloro-2-fluoro-fenil)-5-[1-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol,

2-(5-cloro-2-fluoro-fenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol,

4-(4-ciclopropilmetil-5-{1-[5-(2-fluoro-5-metil-fenil)-isoxazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(3-fluorofenil)-[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-metoxifenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[4-etil-5-(4-metoxifenil)-4H-[1,2,4]-

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triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-{5-[1-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

4-{5-[1-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

4-{5-[1-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,3,4]oxadiazol-2-il}-2-metil-piridina,

2-(3-clorofenil)-5-{1-[4-metil-5-(2-metil-tiazol-4-il)-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,3,4]-oxadiazol,

3-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(3-clorofenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]-oxadiazol,

4-(5-{1-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

5-(5-cloro-2-fluoro-fenil)-3-{1-[5-(4-metoxi-fenil)-4-metil-4H-[1,2,4]triazol-3-ilsulfanil]-etil}-[1,2,4]oxadiazol,

4-[5-(4-etil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-[5-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-(1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

4-[5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,3,4]oxadiazol-2-il]-2-metil-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-4-ciclopropilmetil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(4-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

4-(5-{1-[5-(3-fluoro-fenil)-4-metil-4H-[1,2,4]-triazol-3-ilsulfanil]-etil}-[1,3,4]oxadiazol-2-il)-2-metil-piridina,

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3-{3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-fluoro-benzonitrilo,

4-cloro-2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenol,

4-{4-ciclopropil-5-[5-(3-metoxi-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[5-(3-fluoro-fenil)-[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-[4-ciclopropil-5-(5-m-tolil-[1,2,4]oxadiazol-3-ilmetilsulfanil)-4H-[1,2,4]triazol-3-il)-piridina,

3-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzonitrilo,

4-{4-ciclopropil-5-[5-(2,5-difluorofenil)[1,2,4]-oxadiazol-3-ilmetilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-{4-ciclopropil-5-[1-(5-m-tolil-[1,2,4]oxadi-azol-3-il)-etilsulfanil]-4H-[1,2,4]triazol-3-il}-piridina,

4-(4-ciclopropil-5-{1-[5-(3-metoxifenil)[1,2,4]-oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-piridina,

2-[3-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)(1,2,4]oxadiazol-5-il]-4-metilfenol,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

{3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenil}-metanol,

3-[5-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-3-il]-fenol,

5-(3-clorofenil)-3-[4-(tetrahidro-furan-2-il-metil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

(2-clorofenil)-{5-[5-(3-clorofenil)-(1,2,4]oxadiazol-3-ilmetilsulfanil]-4-isobutil-4H-[1,2,4]triazol-3-il}-metanol,

5-(2-fluoro-5-metil-fenil)-3-[5-tiofen-2-il-4-(2,2,2-trifluoro-etil)-4H-[1,2,4]triazol-3-ilsulfanil-metil]-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-tiofen-2-il-

4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-3-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-3-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-pirimidina,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(5-cloro-2-fluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-2-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il-metilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,3,4]oxadiazol-2-ilmetilsulfanil]-4-etil-4H-[1,2,4]triazol-3-ilmetoxi}fenol,

3-(2,5-difluoro-fenil)-5-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(2,5-difluoro-fenil)-5-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

4-(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-ciclopropil-4H-[1,2,4]triazol-3-il}-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-pirimidina,

2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-pirimidina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

5-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-2-metoxi-piridina,

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2-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}4-etil-4H-[1,2,4]triazol-3-il)-5-metoxi-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-6-metoxi-piridazina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-{5-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il-metilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(5-furan-2-il-4-isobutil-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metilsulfanil-propil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(3-clorofenil)-3-(4-hexil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-ciclopropilmetil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-metil-butil)-5-tiofen-2-

il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(3-metil-butil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-[4-(2-fluoro-bencil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-iloximetil)-[1,2,4]oxadiazol,

4-{5-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetoxi]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[3-(3-clorofenil)-isoxazol-5-il]-etoxi}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

5-(2-metoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-furan-2-il-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

Ester metílico del ácido 3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-benzoico,

5-(2-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2,5-difluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il-

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sulfanilmetil)-5-(3-vinil-fenil)-[1,2,4]oxadiazol,

5-(3-difluorometoxi-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-metoxi-tiofen-3-il)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(2-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(4-fluoro-fenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-(3-clorofenil)-5-[1-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol,

(5-{1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

3-(3-clorofenil)-5-[2-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-ilmetil)-[1,2,4]oxadiazol,

2-(3-clorofenil)-5-[2-(5-furan-2-il-4-metil-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

2-(3-clorofenil)-5-[2-(4-ciclopropil-5-furan-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,3,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

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4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-etil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-tiofen-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-piridina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]piridina,

5-(5-bromo-4-metil-4H-[1,2,4]triazol-3-il-sulfanilmetil)-3-(3-clorofenil)-[1,2,4]oxadiazol,

3-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-fenilamina,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-

[1,2,4]triazol-3-sulfonilmetil)-[1,2,4]oxadiazol,

5-(3-clorofenil)-3-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-sulfinilmetil)-[1,2,4]oxadiazol,

2-metil-6-[3-(4-metil-5-tiofen-2-il-4H-[1,2,4]-triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-piridina,

4-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-etil-4H-[1,2,4]triazol-3-il)-piridin-2-ol,

4-(5-{2-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-metil-(4-metil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)amina,

8-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-ilmetil]-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]-pirimidina,

8-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

8-[5-(5-cloro-2-fluoro-fenil)-[1,2,4]oxadiazol-3-ilmetil]-3-furan-2-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-

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[4,3-a]pirimidina,

8-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etil}-3-piridin-4-il-5,6,7,8-tetrahidro-[1,2,4]triazolo-[4,3-a]pirimidina,

3-(4-etil-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-5-(1H-pirrol-3-il)-[1,2,4]oxadiazol,

1-óxido de 4-{5-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-ilmetilsulfanil]-4-metil-4H-[1,2,4]triazol-3-il}-piridina,

5-(3-clorofenil)-3-(2-furan-2-il-3-metil-3H-imidazol-4-ilsulfanilmetil)-[1,2,4]oxadiazol,

5-(5-cloro-2-fluoro-fenil)-3-[4-(2-fluoro-etil)-5-tiofen-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil]-[1,2,4]-oxadiazol,

5-(5-cloro-tiofen-3-il)-3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol,

3-[3-(4-etil-5-furan-2-il-4H-[1,2,4]triazol-3-ilsulfanilmetil)-[1,2,4]oxadiazol-5-il]-4-hidroxi-benzonitrilo,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-

piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina, o

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

3-(5-{1-[5-(3-clorofenil)-[1,2,4]oxadiazol-3-il]-etoxi}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-cloro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2,5-difluoro-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4-metil--4H-[1,2,4]triazol-3-il)-piridina,

4-(4-ciclopropil-5-{1-[5-(2-fluoro-5-metil-fenil)-[1,2,4]oxadiazol-3-il]-etilsulfanil}-4H-[1,2,4]-triazol-3-il)-piridina,

3-{3-[1-(4-metil-5-piridin-4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il)-benzonitrilo,

3-{3-[1-(4-ciclopropil-5-piridin4-il-4H-[1,2,4]-triazol-3-ilsulfanil)-etil]-[1,2,4]oxadiazol-5-il)-

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benzonitrilo,

3-{1-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il]-etilsulfanil}-5-piridin-4-il-[1,2,4]triazol-4-ilamina,

3-(3-clorofenil)-5-[2-(4-metil-5-tiofen-2-il-4H-[1,2,4]triazol-3-il)-etil]-[1,2,4]oxadiazol,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

cis-4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1,1-dimetil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-metil-propil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-1-metil-etil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-[1,3,4]oxadiazol-2-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-ciclopropil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[5-(3-clorofenil)-[1,3,4]oxadiazol-2-il)-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-[1,3,4]oxadiazol-2-il)-piridina,

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4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-metil-4H-[1,2,4]triazol-3-il)-piridina,

4-(5-{2-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-propil}-4-ciclopropil-4H-[1,2,4]triazol-3-il)-piridina,

Ester ter-butílico del ácido (S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-carbámico,

(S)-1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil-amina,

(S)-[1-[3-(3-clorofenil)-[1,2,4]oxadiazol-5-il]-2-(4-ciclopropil-5-piridin-4-il-4H-[1,2,4]triazol-3-il)-etil]-dimetil-amina,

o sal de los mismos.

17.- Una formulación farmacéutica caracterizada porque comprende como ingrediente activo una cantidad terapéuticamente efectiva de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 16 en asociación con uno o más diluyentes, excipientes y/o vehículo inerte farmacéuticamente aceptables.

18.- La formulación farmacéutica de conformidad con la reivindicación 17, caracterizada porque se usa en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

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19.- Un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 16 caracterizada porque se usa en terapia.

20.- El compuesto de conformidad con la reivindicación 19, caracterizada porque se usa en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

21.- El compuesto de conformidad con la reivindicación 19, caracterizada porque se usa en la prevención y/o tratamiento de trastornos neurológicos.

22.- El compuesto de conformidad con la reivindicación 19, caracterizada porque se usa en la prevención y/o tratamiento de trastornos psiquiátricos.

23.- El compuesto de conformidad con la reivindicación 19, caracterizada porque se usa en la prevención y/o tratamiento de trastornos del dolor crónico y agudo.

24.- El uso de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 16 en la fabricación de un medicamento para uso en la prevención y/o tratamiento de trastornos mediados por el receptor mGluR5.

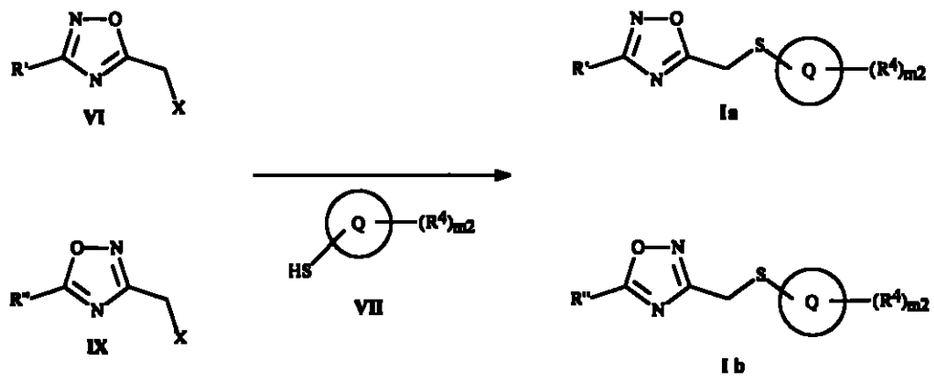
25.- Un método de prevención y/o tratamiento

(31)
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de trastornos mediados por el receptor mGluR5, caracterizado porque comprende administrar a un mamífero, incluyendo humanos, en necesidad de dicha prevención y/o tratamiento, una cantidad terapéuticamente efectiva de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 16.

26.- Un método para inhibir la activación de los receptores mGluR5, caracterizada porque comprende tratar una célula que contiene a dicho receptor con una cantidad efectiva de un compuesto de conformidad con cualquiera de las reivindicaciones 1 a 16.

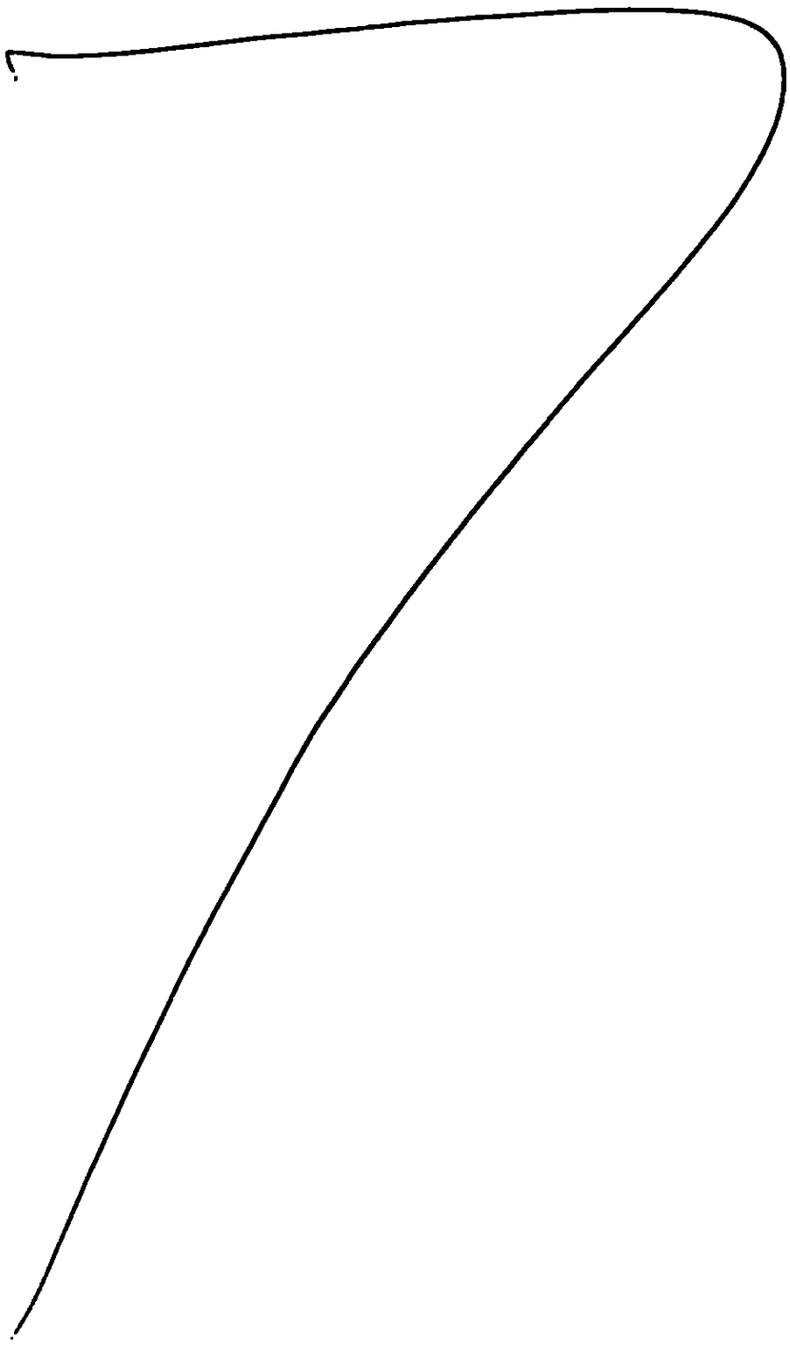
27.- Procedimientos para la preparación de un compuesto de conformidad con la reivindicación 2, que comprende:



caracterizados porque R' y R'' contienen ya sea un grupo representado en la fórmula I mediante $M^2-(R^3)_n-X^4-Q-(R^4)_{m2}$ o un grupo saliente tal como $(CH_2)_nX$, en

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el cual X es cualquier grupo saliente apropiado tal como cloro o mesilato o un grupo que se pueda transformar posteriormente en un grupo saliente y Q, X^4, R^3, R^4, M^2, m y n son como se definen en la reivindicación 1.



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RESUMEN DE LA INVENCIÓN

La presente invención se refiere a compuestos novedosos de la fórmula I, un procedimiento para su preparación y nuevos intermediarios preparados con el mismo, formulaciones farmacéuticas que contienen a los compuestos y el uso de los compuestos en terapias. En particular, de acuerdo a la presente invención existen compuestos potentes y selectivos para el receptor de mGluR de grupo I y más particularmente para mGluR5. De esta manera, se espera que los compuestos de la invención sean muy adecuados para la prevención y/o tratamiento de transtornos mediados por el receptor mGluR5, tales como trastornos neurológicos y psiquiátricos agudos y crónicos y transtornos de dolor agudos y crónicos.

1385 BSK

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To:
BENT, Stephen A.
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W. Suite 500
Washington, D.C. 20007-5143
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 19/03/2004

Applicant's or agent's file reference
085747-0270

REPLY DUE
within 2 / 00 months/days
from the above date of mailing

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US03/24846	08/08/2003	09/08/2002

International Patent Classification (IPC) or both national classification and IPC
C07D413/12

Applicant
ASTRAZENECA AB et al.

1. This written opinion is the first drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I [X] Basis of the opinion
- II [ ] Priority
- III [X] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV [ ] Lack of unity of invention
- V [X] Reasoned statement under Rule 66.2(a)(ii) 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

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 09/12/2004

Name and mailing address of the IPEA/
European Patent Office
D-80298 Munich
Tel. (+49-89) 2399-0, Tx: 523656 epmu d
Fax: (+49-89) 2399-4465

Authorized officer
Examiner

Formalities officer
(incl. extension of time limits)
Tel. (+49-89) 2399 2828

Europäisches Patentamt · European Patent Office · Office européen des brevets

WRITTEN OPINION International application No. PCT/US03/24846

I. Basis of the opinion

The basis of this written opinion is the application as originally filed.

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

The question of whether the claimed invention appears to be novel, to involve an inventive step, or to be industrially applicable has not been and will not be the subject of the international preliminary examination in respect of the claims which have not been searched (Article 17(2)(a) or (3) and Rule 66.1(e) PCT; see also international search report).

V. *Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability*

1. To the extent that the international preliminary examination has been carried out (see item III above), the following is pointed out:

2. In light of the documents cited in the international search report, it is considered that the invention as defined in at least some of the claims, which have been the subject of an international search report, does not appear to meet the criteria mentioned in Article 33(1) PCT, i.e. does not appear to be novel and/or to involve an inventive step (see international search report, in particular the documents cited X and/or Y and corresponding claim references).

3. If amendments are filed, the applicant should comply with the requirements of Rule 66.8 PCT and indicate the basis of the amendments in the documents of the application as originally filed (Article 34 (2) (b) PCT) otherwise these amendments may not be taken into consideration for the establishment of the international preliminary examination report. The attention of the applicant is drawn to the fact that if the application contains an unnecessary plurality of independent claims, no examination of any of the claims will be carried out.

NB: Should the applicant decide to request detailed substantive examination, then an international preliminary examination report will normally be established directly. Exceptionally the examiner may draw up a second written opinion, should this be explicitly requested.

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The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation.

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND

Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference 085747-0270
International application No. PCT/US03/24846	International filing date *(day/month/year)* 08 August 2003 (08/08/2003)	(Earliest) Priority date *(day/month/year)* 09 August 2002 (09/08/2002)

Title of invention
1, 2, 4 - OXADIAZOLES AS MODULATORS OF METABOTROPIC GLUTAMATE RECEPTOR-5

Box No. II APPLICANT(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*	Telephone No.:
AstraZeneca AB S-151 85 Södertälje SWEDEN	Facsimile No.:
	Teleprinter No.:
	Applicant's registration No. with the Office:

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

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.)*
NPS Pharmaceuticals, Inc.
420 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES OF AMERICA

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*
WENSBO, David
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

☒ Further applicants are indicated on a continuation sheet.

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1388

International application No.
PCT/US03/24846

Continuation of Box No. II APPLICANT(S)

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

XIN, Tao
10 Cornoq Avenue
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STEFANAC, Tomislav
4483 Bennett Road
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CA	CA

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Mississauga, Ontario L5H 3S6
CANADA

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

☒ Further applicants are indicated on another continuation sheet.

International application No. PCT/US03/24846 1389

Continuation of Box No. II APPLICANT(S)

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

ISAAC, Methvin
2101 Islington Avenue Apt #2105
Etobicoke, Ontario M9P 3R2
CANADA

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

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.)*

SLASSI, Abdelmalik
4780 Fulwell Road
Mississauga, Ontario L5M 7J7
CANADA

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

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.)*

STORMANN, Thomas M.
1327 Harrison Avenue
Salt Lake City, Utah 84105
UNITED STATES OF AMERICA

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

MCLEOD, Donald A.
7740 South Newport Way
Salt Lake City, Utah 84121
UNITED STATES OF AMERICA

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

☒ Further applicants are indicated on another continuation sheet.

International application No.
PCT/US03/24846

Continuation of Box No. II APPLICANT(S)

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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.)*

KERS, Annika
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

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.)*

MALMBERG, Johan
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

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.)*

OSCARSSON, Karin
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

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.)*

GYBACK, Helena
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

☒ Further applicants are indicated on another continuation sheet.

Sheet No. . . . 5

International application No.
PCT/US03/24846

Continuation of Box No. II APPLICANT(S)

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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.)*

JOHANSSON, Martin
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

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.)*

MINIDIS, Alexander
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

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.)*

WALDMAN, Magnus
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

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.)*

YNGVE, Ulrika
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

☒ Further applicants are indicated on another continuation sheet.

Sheet No. . . . 6

International application No.
PCT/US03/24846

Continuation of Box No. II APPLICANT(S)

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

OSTERWALL, Christoffer
c/o AstraZeneca AB
S-151 85 Södertälje
SWEDEN

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

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

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

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

☐ Further applicants are indicated on another continuation sheet.

International application No.
PCT/US03/24846

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

The following person is ☒ agent ☐ common representative

and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.

☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Stephen A. Bent
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5143

Telephone No.:
(202) 672-5404

Facsimile No.:
(202) 672-5399

Teleprinter No.:

Agent's registration No. with the Office:
29,768

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description ☒ as originally filed
☐ as amended under Article 34

the claims ☒ as originally filed
☐ as amended under Article 19 (together with any accompanying statement)
☐ as amended under Article 34

the drawings ☐ as originally filed
☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of the applicable time limit under Rule 69.1(d).

4. ☐ The applicant wishes the international preliminary examination to start earlier than at the expiration of the applicable time limit under Rule 54*bis*.1(a).

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: .....

☒ which is the language in which the international application was filed.
☐ which is the language of a translation furnished for the purposes of international search.
☐ which is the language of publication of the international application.
☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The filing of this demand constitutes the election of all Contracting States which are designated and are bound by Chapter II of the PCT.

Sheet No. ... 8

International application No.
PCT/US03/24846

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:			For International Preliminary Examining Authority use only: received	not received
1. translation of international application	:	sheets	☐	☐
2. amendments under Article 34	:	sheets	☐	☐
3. copy (or, where required, translation) of amendments under Article 19	:	sheets	☐	☐
4. copy (or, where required, translation) of statement under Article 19	:	sheets	☐	☐
5. letter	:	sheets	☐	☐
6. other *(specify)*:	:	sheets	☐	☐

The demand is also accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ original separate power of attorney
3. ☐ original general power of attorney
4. ☐ copy of general power of attorney; reference number, if any:
5. ☐ statement explaining lack of signature
6. ☐ sequence listing in computer readable form
7. ☐ tables in computer readable form related to a sequence listing
8. ☒ other *(specify)*: *Transmittal, Fax Cover*

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

S. A. Bent

Stephen A. Bent
Reg. No. 29,768

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.
   ☐ The applicant has been informed accordingly.
4. ☐ The date of receipt of the demand is WITHIN the time limit of 19 months from the priority date as extended by virtue of Rule 80.5.
5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.
6. ☐ The date of receipt of the demand is AFTER the expiration of the time limit under Rule 54*bis*.1(a) and item 7 or 8, below, does not apply.
7. ☐ The date of receipt of the demand is WITHIN the time limit under Rule 54*bis*.1(a) as extended by virtue of Rule 80.5.
8. ☐ Although the date of receipt of the demand is after the expiration of the time limit under Rule 54*bis*.1(a), the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

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)* 085747-0270

Box No. I TITLE OF INVENTION *NEW COMPOUNDS*

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.)*

AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

Telephone No.

Facsimile No.

Teleprinter No.

Applicant's registration No. with the Office

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

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

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.)*

NPS Pharmaceuticals, Inc.
420 Chipeta Way
Salt Lake City, UT 84108
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: US

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

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.)*

BENT, Stephen A.
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C., 20007-5101
UNITED STATES OF AMERICA

Telephone No.
(202) 672-5404

Facsimile No.
(202) 672-5399

Teleprinter No.

Agent's registration No. with the Office
29,768

☐ 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.

1396

Continuation of Box. 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.)*

WENSBO, David
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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.)*

XIN, Tao
10 Comoq Avenue
Woodbridge, Ontario L4H 2B1
CANADA

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: CA

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

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.)*

STEFANAC, Tomislav
4483 Bennett Road
Burlington, Ontario L7L 1Y5
CANADA

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: CA

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

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.)*

ARORA, Jalaj
34 Alana Avenue
Cambridge, Ontario N3C 3Y5
CANADA

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: CA

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

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. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Continuation of Box. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

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EDWARDS, Louise
871 Chippenham Drive
Mississauga, Ontario L5H 3S6
CANADA

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: CA

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

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

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ISAAC, Methvin
2101 Islington Avenue Apt #2105
Etobicoke, Ontario M9P 3R2
CANADA

This person is:
☐ applicant only
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SLASSI, Abdelmalik
4780 Fulwell Road
Mississauga, Ontario L5M 7J7
CANADA

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STORMANN, Thomas M.
1327 Harrison Avenue
Salt Lake City, Utah 84105
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: US

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

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.

1398

Continuation of Box. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

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MCLEOD, Donald A.
7740 South Newport Way
Salt Lake City, Utah 84121
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: US

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

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

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KERS, Annika
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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.)*

MALMBERG, Johan
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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

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

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

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OSCARSSON, Karin
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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☒ 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: SE

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

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

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1399

Continuation of Box. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

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GYBACK, Helena
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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

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JOHANSSON, Martin
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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

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MINIDIS, Alexander
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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☐ 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: SE

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

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.)*

WALDMAN, Magnus
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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.

1400

Continuation of Box. 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.)*

YNGVE, Ulrika
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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.)*

OSTERWALL, Christoffer
c/o AstraZeneca AB
S-151 85 Sodertalje
SWEDEN

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: SE

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

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

1401

Box No. V *DESIGNATION OF STATES*

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 Kazakstan, 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, HU Hungary, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, RO Romania, SE Sweden, SI Slovenia, 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	☒	HR	Croatia	☒	OM	Oman
☒	AG	Antigua and Barbuda	☒	HU	Hungary	☒	PG	Papua New Guinea
☒	AL	Albania	☒	ID	Indonesia	☒	PH	Philippines
☒	AM	Armenia	☒	IL	Israel	☒	PL	Poland
☒	AT	Austria	☒	IN	India	☒	PT	Portugal
☒	AU	Australia	☒	IS	Iceland	☒	RO	Romania
☒	AZ	Azerbaijan	☒	JP	Japan	☒	RU	Russian Federation
☒	BA	Bosnia and Herzegovina	☒	KE	Kenya			
☒	BB	Barbados	☒	KG	Kyrgyzstan	☒	SC	Seychelles
☒	BG	Bulgaria	☒	KP	Democratic People's Republic of Korea	☒	SD	Sudan
☒	BR	Brazil				☒	SE	Sweden
☒	BY	Belarus	☒	KR	Republic of Korea	☒	SG	Singapore
☒	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			
☒	DE	Germany	☒	MA	Morocco	☒	TZ	United Republic of Tanzania
☒	DK	Denmark	☒	MD	Republic of Moldova	☒	UA	Ukraine
☒	DM	Dominica				☒	UG	Uganda
☒	DZ	Algeria	☒	MG	Madagascar	☒	US	United States of America
☒	EC	Ecuador	☒	MK	The former Yugoslav Republic of Macedonia			
☒	EE	Estonia				☒	UZ	Uzbekistan
☒	ES	Spain	☒	MN	Mongolia	☒	VC	Saint Vincent and the Grenadines
☒	FI	Finland	☒	MW	Malawi			
☒	GB	United Kingdom	☒	MX	Mexico	☒	VN	Viet Nam
☒	GD	Grenada	☒	MZ	Mozambique	☒	YU	Serbia and Montenegro
☒	GE	Georgia	☒	NI	Nicaragua	☒	ZA	South Africa
☒	GH	Ghana	☒	NO	Norway	☒	ZM	Zambia
☒	GM	Gambia	☒	NZ	New Zealand	☒	ZW	Zimbabwe

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

☒ SY Syrian Arab Republic ..... ☐ ..... ☐ .....

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 fee) must reach the receiving Office within the 15-month time limit.)*

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Supplemental Box *If the Supplemental Box is not used, this sheet should not be included in the request.*

1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

(i) If more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. 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;

(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;

(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;

(iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;

(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;

(vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;

(vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

Continuation of Box IV
GEORGE C. BECK
STEPHEN A. BENT
BETH A. BURROUS
ALAN I. CANTOR
WILLIAM T. ELLIS
JOHN J. FELDHAUS
MICHAEL D. KAMINSKI
MARY MICHELLE KILE
KENNETH E. KROSIN
GLENN LAW
PETER G. MACK
STEPHEN B. MAEBIUS
BRIAN J. MC NAMARA
RICHARD C. PEET
GEORGE E. QUILLIN
ANDREW E. RAWLINS
BERNHARD D. SAXE
CHARLES F. SCHILL
RICHARD L. SCHWAAB
MICHELE M. SIMKIN
HAROLD C. WEGNER

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 or Member of WTO	Where earlier application is: regional application:* regional Office	Where earlier application is: international application: receiving Office
item (1) 09 August 2002 (09/08/02)	60/402,040	US		
item (2)				
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 the present 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, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

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/EP

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	:

1404 1405

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains:

a) In paper form, the following number of sheets:

Request (including declaration sheets)	:	10
Description (excluding sequence listings and/or tables related thereto)	:	273
claims:	:	44
abstract	:	1
drawings	:	
Sub-total number of sheets	:	328
Sequence listings	:	
tables related thereto	:	
(for both, actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (c) below)		
Total number of sheets	:	328

b) ☐ only in computer readable form (Section 801(a)(i))
- (i) ☐ sequence listings
- (ii) ☐ tables related thereto

c) ☐ also in computer readable form (Section 801(a)(ii))
- (i) ☐ sequence listings
- (ii) ☐ tables related thereto

Type and number of carriers (diskette, CD-ROM, CD-R or other) on which are contained the
- ☐ sequence listings:
- ☐ tables related thereto

(additional copies to be indicated under items 9(ii) and/or 10(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:	:
7. ☐ 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 listings in computer readable form *(indicate type and number of carriers)*	
(i) ☐ copy submitted for the purposes of international search under Rule 13ter only (and not as part of the international application)	:
(ii) ☐ *(only where check-box (b)(i) or (c)(i) is marked in left column)* additional copies including, where applicable, the copy for the purposes of international search under Rule 13ter	:
(iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listings mentioned in left column	:
10. ☐ tables in computer readable form related to sequence listings *(indicate type and number of carriers)*	
(i) ☐ copy submitted for the purposes of international search under Section 802(b-quarter) only (and not as part of the international Application)	:
(ii) ☐ *(only where check-box (b)(ii) or (c)(ii) is marked in left column)* additional copies including, where applicable, the copy for the purposes of international search under Section 802(b-quarter)	
(iii) ☐ together with relevant statement as to the identity of the copy or copies with the tables mentioned in left column	:
11. ☒ other *(specify)*: Transmittal Letter, Postcard & Check	:3

Figure of the drawings which should accompany the abstract: n/a

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

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).

S. A. Bent

Stephen A. Bent (Reg. No. 29,768)

For International Bureau 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:

UNITED STATES PATENT AND TRADEMARK OFFICE

DECEMBER 12, 2002

PTAS

Under Secretary of Commerce For Intellectual Property and
Director of the United States Patent and Trademark Office
Washington, DC 20231
www.uspto.gov

FOLEY & LARDNER
STEPHEN A. BENT
WASHINGTON HARBOUR
3000 K STREET, N.W., SUITE 500
WASHINGTON, D.C. 20007-5143

102227506A

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 09/13/2002

REEL/FRAME: 013290/0873
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
WENSBO, DAVID — DOC DATE: 09/02/2002

ASSIGNOR:
XIN, TAO — DOC DATE: 08/22/2002

ASSIGNOR:
STEFANAC, TOMISLAV — DOC DATE: 08/22/2002

ASSIGNOR:
ARORA, JALAJ — DOC DATE: 08/22/2002

ASSIGNOR:
EDWARDS, LOUISE — DOC DATE: 08/27/2002

ASSIGNOR:
ISAAC, METHVIN — DOC DATE: 08/22/2002

ASSIGNOR:
SLASSI, ABDELMALIK — DOC DATE: 08/22/2002

ASSIGNOR:
MCLEOD, DONALD A. DOC. DATE: 08/27/2002

ASSIGNOR:
STORMANN, THOMAS M. DOC DATE: 08/27/2002

ASSIGNEE:
NPS PHARMACEUTICALS
420 CHIPETA WAY
SALT LAKE CITY, UTAH

ASSIGNEE:
ASTRAZENECA
S-151 85 SODERTALJE, SWEDEN

SERIAL NUMBER: 60402040 FILING DATE: 08/09/2002
PATENT NUMBER: ISSUE DATE:

LAZENA MARTIN, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

1407

Atty. Dkt. No. 085747-0237

FORM PTO-1595 (modified)
(Rev 6-93)

RECORDATION FORM COVER SHEET

09-19-2002

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

102227506

To the Director of the United States Patent and Trademark Office: Please record the attached original documents or copies thereof.

1. Name of conveying party(ies):

David WENSBO - 09/02/02
Tao XIN - 08/22/02
Tomislav STEFANAC - 08/22/02
Jalaj ARORA - 08/22/02
Louise EDWARDS - 08/27/02
Methvin ISAAC - 08/22/02
Abdelmalik SLASSI - 08/22/02
Donald A. MCLEOD - 08/27/02
Thomas M. STORMANN - 08/27/02

Additional conveying party(ies) NO

2. Name and address of receiving party(ies):

NPS PHARMACEUTICALS
420 Chipeta Way
Salt Lake City, UTAH

and

ASTRAZENECA
S-151 85 Södertälje
SWEDEN

Additional name(s) & address(es) attached? NO

3. Nature of conveyance:

ASSIGNMENT

Execution Date: See Above

4. Application number(s) or patent number(s):

If this is being filed together with a new application, the execution date of the application is:

A. Patent Application Number(s):

60/402,040

B. Patent Number(s):

Additional numbers attached? NO

5. Name and address of party to whom correspondence concerning document should be mailed:

Stephen A. Bent
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5143

6. Total number of applications/patents involved: 1

7. Total fee (37 C.F.R. § 3.41): $40.00

X Check Enclosed

Charge to deposit account

8. Deposit account number: 19-0741

DO NOT USE THIS SPACE

9. Statement and signature:

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document. The Commissioner is hereby authorized to charge any additional recordation fees which may be required in this matter to the above-identified deposit account.

Stephen A. Bent		September 13, 2002
Name of person signing	Signature	Date

Total number of pages including cover sheet, attachments, and document: 3

09/19/2002 EBTESE 00000129 08402040
01 FC:581 40.00 OP

002.690189.1

F&L: 85747/0237
NPS: N-322
AZ: 100737

1408

ASSIGNMENT - WORLDWIDE

For good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, each undersigned inventor has sold and assigned, and by these presents hereby sells and assigns, unto

NPS PHARMACEUTICALS	**and**	**ASTRAZENECA**
420 Chipeta Way		**S-151 85 Södertälje**
Salt Lake City, UTAH		**SWEDEN**

its successors and assigns, the entire right, title and interest, so far as concerns the United States and the Territories and Possessions thereof and all foreign countries in and to the invention in

COMPOUNDS EXHIBITING ACTIVITY AS METABOTROPIC GLUTAMATE RECEPTORS

as set forth in this United States Patent Application

__ executed concurrently herewith
__ executed on _____
X Serial No. 60/402,040 filed August 9, 2002

said application for United States Letters Patent, including all divisional, renewal, substitute, continuation and Convention applications based in whole or in part upon said inventions or upon said applications, and any and all Letters Patent and reissues and extensions of Letters Patent granted for said inventions or upon said applications and every priority right that is or may be predicated upon or arise from said inventions, said applications, and said Letters Patent; said Assignee being hereby authorized to file patent applications in any or all countries on any or all said inventions in the name of the undersigned or in the name of said Assignee or otherwise as said Assignee may deem advisable, under the International Convention or otherwise; the Commissioner of Patents and Trademarks of the United States of America being hereby authorized to issue or transfer all said Letters Patent to said Assignee in accordance herewith; this assignment being under covenant, not only that full power to make the same is had by the undersigned, but also that such assigned right is not encumbered by any grant, license, or other right theretofore given, and that the undersigned will do all acts reasonably serving to ensure that the said inventions, patent applications and Letters Patent shall be held and enjoyed by said Assignee as fully and entirely as the same could have been held and enjoyed by the undersigned if this assignment had not been made, and particularly to execute and deliver to said Assignee all lawful documents including petitions, specifications, oaths, assignments, invention disclaimers, and lawful affidavits in form and substance which may be requested by said Assignee, to furnish said Assignee with all facts relating to said inventions or the history thereof and any and all documents, photographs, models, samples or other physical exhibits which may be of said inventions, and to testify in any proceedings relating to said inventions, patent applications and Letters Patent.

1409

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
FOLEY & LARDNER
Attn. Bent, Stephen A.
Washington Harbour
3000 K Street N.W., Suite 500
Washington, D.C. 20007-5101
UNITED STATES OF AMERICA

	Date of mailing *(day/month/year)* 16/04/2004
Applicant's or agent's file reference 085747-0270	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US 03/24846	International filing date *(day/month/year)* 08/08/2003
Applicant ASTRAZENECA AB	

1. [x] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

   When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

   Where? Directly to the International Bureau of WIPO
   34, chemin des Colombettes
   1211 Geneva 20, Switzerland
   Facsimile No.: (41-22) 740.14.35

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

   Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

   Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kerstin G^tz

Form PCT/ISA/220 (July 1998)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 16, 18 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

BNSDOCID: <WISA220NOENP4 1 >

1412

PATENT COOPERATION TREATY

From the RECEIVING OFFICE

To:
STEPHEN A. BENT
FOLEY & LARDNER
WASHINGTON HARBOUR
3000 K STREET, N.W., SUITE 500
WASHINGTONG, DISTRICT OF COLUMBIA
20007-5101

PCT

NOTIFICATION OF THE INTERNATIONAL APPLICATION NUMBER AND OF THE INTERNATIONAL FILING DATE

(PCT Rule 20.5(c))

Date of mailing *(day/month/year)*	16 Sep 2003
Applicant's or agent's file reference: 085747-0270	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US03/24848	08 Aug 2003	09 Aug 2002

Applicant: ASTRAZENECA AB

Title of the invention: NEW COMPOUNDS

1. *The applicant is hereby notified that the international application has been accorded the international application number and the international filing date indicated above.*

2. The applicant is further notified that the record copy of the international application:

[X] was transmitted to the International Bureau on 16 Sep 2003

[ ] has not yet been transmitted to the International Bureau for the reason indicated below and a copy of this notification has been sent to the International Bureau*:

[ ] because the necessary national security clearance has not yet been obtained.

[ ] because *(reason to be specified)*:

* The International Bureau monitors the transmittal of the record copy by the receiving Office and will notify the applicant (with Form PCT/IB/301) of its receipt. Should the record copy not have been received by the expiration of 14 months from the priority date, the International Bureau will notify the applicant (Rule 22.1(c)).

3. FOREIGN TRANSMITTAL LICENSE INFORMATION — Completed by: LR

[ ] Additional license for foreign transmittal not required. This subject matter is covered by a license already granted or the equivalent U.S. national application. Refer to that license for information concerning its scope.

[ ] License for foreign transmittal not required. 37 CFR 5.11(e)(1) or 37 CFR 5.11(e)(2). However, a license may be required for additional subject matter. See 37 CFR 5.15(b).

[X] Foreign transmittal license granted. 35 U.S.C. 184; 37 CFR 5.11 on 11 Sep 2003 (date):

[ ] 37 CFR 5.15(a) [X] 37 CFR 5.15(b)

Name and mailing address of the receiving Office	Authorized officer
Mail Stop PCT, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450	Latrice Russell
Facsimile No. 703-305-3230	Telephone No. 703-308-5829

Form PCT/RO/105 (July 1992)

1413

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCIÓN / MODELO DE UTILIDAD	( )	( )
- Indicación de que se solicita la concesión de una patente.	( )	( )
- Datos de identificación del solicitante o de la persona que se presenta la solicitud.	( )	( )
- Descripción de la invención.	( )	( )
- Dibujos de ser estos pertinentes.	( )	( )
- Comprobante de Pago de las tasas establecidas.		
COMPLETA ( )	INCOMPLETA ( )	( )
DISEÑO INDUSTRIAL ( )		
- Indicación de que se solicita el registro de Diseño Industrial	( )	( )
- Datos de identificación del solicitante o de la persona que presenta	( )	( )
- la solicitud.		
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño.	( )	( )
Comprobante de pago de las tasas establecidas	( )	( )
COMPLETA ( )	INCOMPLETA ( )	( )
ESQUEMA DE TRAZADO ( )		
- Indicación de que solicita el registro de un Esquema de trazado.	( )	( )
- Datos de identificación del solicitante o de la persona que presenta La solicitud.	( )	( )
Representación gráfica del esquema de trazado	( )	( )
Comprobante de pago de las tasas establecidas.	( )	( )
COMPLETA ( )	INCOMPLETA ( )	( )

Firma Responsable:

Fecha:

SUPERINDUSTRIA Y COMERCIO
Radicación : 93021462 00000000 Folios: 1004
Fecha (AMD): 2003-03-06 16:48:25
Tramite : 911 PCI-PRIMI S/I FASE ORAL 411 PRESENTAC
Dependencia: 0400 DIVISION DE NUEVAS CREACIONES

Industria y Comercio
SUPERINTENDENCIA

Folio 1414

2020
Bogotá, D.C.,

Doctor(a)
DILIA RODRIGUEZ D'ALEMAN

Oficio Nº. 17973

ASUNTO:

Radicación Nº	05-21462
Solicitud internacional	PCT/US2003/024846
Fecha inicio fase nacional	09/03/2003
Trámite	011
Evento	379
Actuación	430
Folios	001

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

- Se deben presentar los poderes debidamente otorgados por las sociedades solicitantes, 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.

- La solicitud no contiene la copia del documento en que consta la cesión del derecho a la patente de los inventores a los solicitantes o a sus causantes. (Art. 26-k) Decisión 486/00.

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 Nº 10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha, 29 ABR 2005.

Carrera 13 No. 27-00 Pisos 5, 7 y 10
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Bogotá, D.C., Colombia