

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 February 2006 (16.02.2006)

PCT

(10) International Publication Number
WO 2006/016237 A3

(51) International Patent Classification:
C07D 413/10 (2006.01) **A61K 31/497** (2006.01)
A61K 31/4523 (2006.01) **A61P 29/00** (2006.01)

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(21) International Application Number:
PCT/IB2005/002292

(22) International Filing Date: 2 August 2005 (02.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/598,621 4 August 2004 (04.08.2004) US

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

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

Published:

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

(88) Date of publication of the international search report:
26 May 2006

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: HETEROCYCLIC DERIVATIVES AS ANTI-INFLAMMATORY AGENTS

(57) Abstract: The present invention relates to some heterocyclic derivatives having the structure of formula (Ia) wherein Ar₁, Ar₂, W, Q, Z, X, R₁, R₂, m, p, r and t are as defined in the description as anti-inflammatory agents. The compounds of this invention can be useful, for inhibition and/or prevention of inflammation and associated pathologies including inflammatory and autoimmune diseases such as sepsis, rheumatoid arthritis, inflammatory bowel disease, type-1 diabetes, asthma, chronic obstructive pulmonary disorder, organ transplant rejection and psoriasis. This invention also relates to pharmacological compositions containing the compounds disclosed herein and the methods of treating and/or preventing sepsis, rheumatoid arthritis, inflammatory bowel disease, type-1 diabetes, asthma, chronic obstructive pulmonary disorder, organ transplant rejection and psoriasis, and other inflammatory and/or autoimmune disorders, using the compounds.

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2005/002292

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D413/10 A61K31/4523 A61K31/497 A61P29/00

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)

C07D A61K A61P

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, EMBASE, MEDLINE, BIOSIS, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/64676 A (SCIOS, INC) 7 September 2001 (2001-09-07) cited in the application claims 9-13; compounds 90,93,184,185,216	1-16
Y	WO 00/12074 A (SCIOS INC; GOEHRING, R., RICHARD; LUEDTKE, GREGORY, R; MAVUNKEL, BABU,) 9 March 2000 (2000-03-09) cited in the application page 23 - page 24; claims 1,16,26,28; compounds 90,93	1-16
X	WO 02/26720 A (COR THERAPEUTICS, INC; ZHU, BING-YAN; JIA, ZHAOZHONG, JON; ZHANG, PENG) 4 April 2002 (2002-04-04) page 91 - page 92; claims 1-3,13; examples 533,539,541	1
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Further documents are listed in the continuation of Box C.



See patent family 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.

Z document member of the same patent family

Date of the actual completion of the international search

24 March 2006

Date of mailing of the international search report

03/04/2006

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2005/002292

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/46590 A (TAKEDA CHEMICAL INDUSTRIES, LTD; ISHIHARA, YUJI; FUJISAWA, YUKIO; FURU) 22 October 1998 (1998-10-22) page 326 - page 327; claims 16-31, 44; examples 261, 262 -----	1
X	DE 44 07 134 A1 (DR. KARL THOMAE GMBH, 88400 BIBERACH, DE) 7 September 1995 (1995-09-07) claims 1-6; example 1 -----	1
X	TAO, BIN ET AL: "Novel bisbenzamidines and bisbenzimidazolines as noncompetitive NMDA receptor antagonists" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , 9(9), 1299-1304 CODEN: BMCLE8; ISSN: 0960-894X, 1999, XP004163962 page 1302; table I; compound 1 -----	1
X	SPYCHALA, JAROSLAW: "A general synthesis of diaryl cyclic diamidines" TETRAHEDRON LETTERS , 40(14), 2841-2844 CODEN: TELEAY; ISSN: 0040-4039, 1999, XP004159452 page 2842; table I; compound 3E -----	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2005/002292

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

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

1. ☒ Claims Nos.: 8-11
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 8-11 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. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2005/002292

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