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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 September 2010 (02.09.2010)

PCT

(10) International Publication Number
WO 2010/097802 A3

(51) International Patent Classification:
C07D 207/20 (2006.01) *C07D 213/61* (2006.01)
C07D 211/70 (2006.01)

(21) International Application Number:
PCT/IN2010/000045

(22) International Filing Date:
25 January 2010 (25.01.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
441/MUM/2009 27 February 2009 (27.02.2009) IN

(71) Applicant *(for all designated States except US)*: **CADILA HEALTHCARE LIMITED** [IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad 380 015, Gujarat (IN).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **PANDEY, Bipin** [IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad 380 015, Gujarat (IN). **DAVE, Mayank Ghanshyambhai** [IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad 380 015, Gujarat (IN). **SHAH, Mitesh** [IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad 380 015, Gujarat (IN).

(74) Agents: **SUBRAMANIAM, Hariharan** et al.; Nataraj & Associates, E-556, Greater Kailash-II, New Delhi 110 048 (IN).

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

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

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

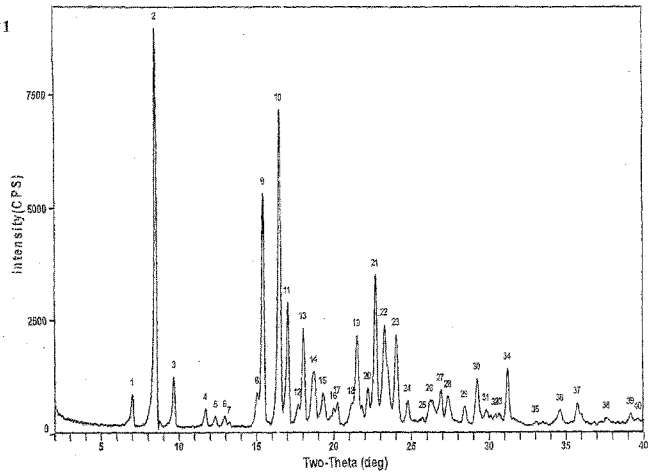
— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:
23 December 2010

(54) Title: A PROCESS FOR THE PREPARATION OF ETORICOXIB

Fig. 1



(57) Abstract: The present invention provides a improved process for preparing Etoricoxib using substituted β-chlorovinaniidinium salts containing a cyclic group, optionally containing a heteroatom. The present invention also provides a process for the preparation of the intermediate β-chlorovinamidinium salts. In one of the embodiments is provided a process for the purification of Etoricoxib as well as the intermediates.

WO 2010/097802 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2010/000045

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D207/20 C07D211/70 C07D213/61
ADD.

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DAVIES I W ET AL: "A PRACTICAL SYNTHESIS OF A COX-2-SPECIFIC INHIBITOR" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON.; US LNKD-DOI:10.1021/J0000870Z, vol. 65, 1 January 2000 (2000-01-01), pages 8415-8420, XP002326845 ISSN: 0022-3263	1-8,20, 26-30
A	page 8419, from left column line 16 through right column line 8; scheme 4; page 8420 right column lines 22-47	21-25

-/--

[X] Further documents are listed in the continuation of Box C.

[X] 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.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 October 2010	08/11/2010

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, Fax: (+31-70) 340-3016	Matés Valdivielso, J

2

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2010/000045

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DAVIES, IAN W. ET AL: "Preparation and Novel Reduction Reactions of Vinamidinium Salts" JOURNAL OF ORGANIC CHEMISTRY , 66(1), 251-255 CODEN: JOCEAH; ISSN: 0022-3263, 2001, XP002592388 compounds 1,5a, 7 the synthesis of compound 5a in the second paragraph of the experimental section (page 254, left column)	9-19,30
X	JP 2003 160563 A (SANKYO CHEMICAL CO., LTD., JAPAN) 3 June 2003 (2003-06-03) paragraphs [0034] - [0038]; compounds 1-22	9,12-15

2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2010/000045

Box No. 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.:
because they relate to subject matter not required to be searched by this Authority, namely:

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 No. 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:

see additional sheet

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 fees, this Authority did not invite payment of additional fees.

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 and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20, 26-30

The process for the preparation of Etoricoxib via the intermediate compound of formula (IIIb) (claims 1-8), the process for the preparation of intermediate compound (IIIb) (claims 9-19), intermediate compound (IIIc) (claim 20), the polymorphic forms of 2-chloro-1,3-(bis piperidinyl)-trimethinium hexafluorophosphate (claims 26-29) and Etoricoxib prepared according to the process of the invention (claim 30).

---

2. claims: 21-25

The process for the purification of Etoricoxib of claims 21-25.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IN2010/000045

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 2003160563 A	03-06-2003	NONE	