



(43) International Publication Date
1 November 2012 (01.11.2012)

(10) International Publication Number
WO 2012/147103 A3

- (51) **International Patent Classification:**
C07C 227/06 (2006.01) *C07C 229/30* (2006.01)
- (21) **International Application Number:**
PCT/IN2012/000302
- (22) **International Filing Date:**
25 April 2012 (25.04.2012)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
1205/DEL/2011 25 April 2011 (25.04.2011) IN
0598/DEL/2012 2 March 2012 (02.03.2012) IN
- (71) **Applicant (for all designated States except US):** COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH [IN/IN]; Anusandhan Bhawan, Rafi Marg, New Delhi 110 001 (IN).
- (72) **Inventors; and**
- (75) **Inventors/Applicants (for US only):** KULKARNI, Amol, Arvind [IN/IN]; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411 008, Maharashtra (IN). JOSHI, Ramesh, Anna [IN/IN]; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411 008, Maharashtra (IN). JOSHI, Rohini, Ramesh [IN/IN]; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411 008, Maharashtra (IN).
- (74) **Agent:** KOUL, Sunaina; Patent Agent, Lall Lahiri & Salhotra, Plot No. B-28, Sector-32, Institutional Area, Gurgaon-122001 Haryana (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, QA, RO, RS, RU, RW, 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, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, 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, RS, 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))
- of inventorship (Rule 4.17(iv))

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:**
20 December 2012

(54) **Title:** PROCESS FOR CONTINUOUS FLOW SYNTHESIS OF β -AMINO CROTONATE

(57) **Abstract:** Beta aminocrotonates are important intermediates for the synthesis of Ca channel blockers. The processes available in the art are batch processes with yields about 85%. There are no continuous processes available for the synthesis of such compounds. This gap in the art is addressed by the invention by disclosing a continuous process resulting in high yields of beta amino crotonates.



WO 2012/147103 A3

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference LLS 246	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/IN2012/000302	International filing date (<i>day/month/year</i>) 25/04/2012	(Earliest) Priority Date (<i>day/month/year</i>) 25/04/2011
Applicant COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH		

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 3 sheets.

☒ 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
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant
- ☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
- ☐ as suggested by the applicant
- ☐ as selected by this Authority, because the applicant failed to suggest a figure
- ☐ as selected by this Authority, because this figure better characterizes the invention
- b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2012/000302

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C227/06 C07C229/30
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)
C07C

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

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

EPO-Internal, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 423 866 B1 (BRAUN MAX [DE] ET AL) 23 July 2002 (2002-07-23)	1,3,5,6, 8,9,11
Y	column 4, line 9 - line 22; example 5 -----	2,4,7,10
X	US 2005/106689 A1 (BRAUN MAX [DE] ET AL) 19 May 2005 (2005-05-19) page 3 - paragraph 39; claims 1,3,9-11; examples 1,3 ----- -/--	1,3,5,6, 8,9,11



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 application or patent 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

10 October 2012

Date of mailing of the international search report

23/10/2012

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Voyiazoglou, D

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2012/000302

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	C.A. BRANDT ET AL: "Efficient synthetic method for beta-enaminoesters using ultrasound", SYNTHESIS., no. 10, 2004, pages 1557-1559, XP002684435, DEGEORG THIEME VERLAG, STUTTGART. ISSN: 0039-7881	2,7
A	Scheme 1; table 1	1,5,6,9, 11
Y	----- P.C.ANDERSON ET AL: "2-Aryl-3-acetyl-4(IH)-quinolones", JOURNAL OF ORGANIC CHEMISTRY., vol. 30, 1965, pages 3033-3037, XP002684436, USAMERICAN CHEMICAL SOCIETY, WASHINGTON, DC. ISSN: 0022-3263	4,10
A	page 3034, right-hand column, line 7 - line 16; table II	1-3,5,6, 8,11
A	----- GB 2 219 294 A (EGYT GYOGYSZERVEGYESZETI GYAR [HU]) 6 December 1989 (1989-12-06) page 4, last paragraph; claims 1-7	1-11
A	----- E. TOJA ET AL: "Pyrrolidine analogs of Nalidixic acid. 2. Pyrrolo(3,4-b)pyridines", JOURNAL OF HETEROCYCLIC CHEMISTRY, vol. 23, 1986, pages 1561-1564, XP002684437, Wiley-Blackwell Publishing, Inc. ISSN: 0022-152X page 1562, last paragraph	1,2,4-6, 8,11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IN2012/000302

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6423866	B1	23-07-2002	AT 221517 T 15-08-2002
		DE 19849918 A1	20-05-1999
		EP 1028938 A1	23-08-2000
		IN 189969 A1	24-05-2003
		JP 2001522825 A	20-11-2001
		US 6423866 B1	23-07-2002
		WO 9924390 A1	20-05-1999

US 2005106689	A1	19-05-2005	NONE

GB 2219294	A	06-12-1989	DE 3918122 A1 14-12-1989
		FR 2632303 A1	08-12-1989
		GB 2219294 A	06-12-1989
		HU 202474 B	28-03-1991
		IT 1230856 B	08-11-1991
		JP 2085237 A	26-03-1990
		NL 8901409 A	02-01-1990
		SU 1836334 A3	23-08-1993
