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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 July 2013 (11.07.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/102935 A3

(51) International Patent Classification:
C07D 307/88 (2006.01)

(21) International Application Number:
PCT/IN2013/000005

(22) International Filing Date:
3 January 2013 (03.01.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0011/DEL/2012 3 January 2012 (03.01.2012) IN

(71) Applicant: **COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH** [IN/IN]; Anusandhan Bhawan, 2 Rafi Marg, New Delhi 110 001 (IN).

(72) Inventors: **REDDY, Santhosh, Rekula**; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, Maharashtra 411008 (IN). **PRAGATI, Kishore, Prasad**; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, Maharashtra 411008 (IN). **NAGA, Kiran, Chaithanya, Indukuru**; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, Maharashtra 411008 (IN). **SUDALAI, Arumugam**; National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, Maharashtra 411008 (IN).

(74) Agents: **CHOPRA, Priyanka** et al.; K & S Partners, Intellectual Property Attorneys, 109, Sector 44, Gurgaon, National Capital Region 122003 (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, BN, 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, PA, 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, 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:

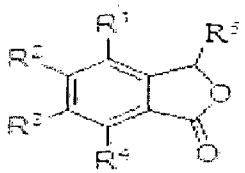
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

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

(88) Date of publication of the international search report:
3 October 2013

(54) Title: Cu-MEDIATED ANNULATION FOR THE EFFECTIVE SYNTHESIS OF 3-SUBSTITUTED PHTHALIDES



Formula I

(57) Abstract: The present invention disclosed herein is a novel commercially feasible, one pot synthesis of library of 3-substituted phthalides of formula I via CuCN mediated oxidative cyclization in high yield. Formula I

WO 2013/102935 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2013/000005

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D307/88
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 practicable, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DIEM H. T. PHAN ET AL: "Phthalides by Rhodium-Catalyzed Ketone Hydroacylation", JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 131, no. 43, 4 November 2009 (2009-11-04), pages 15608-15609, XP055055590, ISSN: 0002-7863, DOI: 10.1021/ja907711a cited in the application table 3	1-8

-/--

[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 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	Date of mailing of the international search report
11 March 2013	11/07/2013

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	Brandstetter, T

2

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

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KAZUHIRO KOBAYASHI ET AL: "An Efficient Synthesis of 3-Substituted 3H-Isobenzofuran-1-ylidenamines by the Reaction of 2-Cyanobenzaldehydes with Organolithiums and Their Conversion into Isobenzofuran-1(3H)-ones", HETEROCYCLES.INTERNATIONAL JOURNAL FOR REVIEWS AND COMMUNICATIONS IN HETEROCYCLIC CHEMISTRY, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 83, no. 1, 1 January 2011 (2011-01-01), pages 99-106, XP009167763, ISSN: 0385-5414, DOI: 10.3987/COM-10-12071 cited in the application scheme 1 page 100; table 1	1-8

A	GUANGLEI LV ET AL: "Rhodium or palladium-catalyzed cascade aryl addition/intramolecular lactonization of phthalaldehydonitrile to access 3-aryl and 3-alkenyl phthalides", TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 67, no. 26, 29 April 2011 (2011-04-29), pages 4879-4886, XP028227655, ISSN: 0040-4020, DOI: 10.1016/J.TET.2011.04.100 [retrieved on 2011-05-06] cited in the application page 4883; table 3	1-8

Y	FOA M ET AL: "Cobalt-catalysed carbonylation of aryl halides", JOURNAL OF ORGANOMETALLIC CHEMISTRY, ELSEVIER-SEQUOIA S.A. LAUSANNE, CH, vol. 285, no. 1-3, 16 April 1985 (1985-04-16), pages 293-303, XP026619794, ISSN: 0022-328X, DOI: 10.1016/0022-328X(85)87375-7 [retrieved on 1985-04-16] table 5	1-8

	-/--	

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KATIE A. KEATON ET AL: "A Cyclopropanol-Based Strategy for Subunit Coupling: Total Synthesis of (+)-Spirolaxine Methyl Ether", ORGANIC LETTERS, vol. 9, no. 14, 1 July 2007 (2007-07-01), pages 2717-2719, XP055055790, ISSN: 1523-7060, DOI: 10.1021/ol0710111 scheme 3; page 2719	1-8
Y	HUA-MING MIAO ET AL: "Exquisite Synthesis of a Designed PAR-1 Antagonist", HELVETICA CHIMICA ACTA, vol. 94, no. 11, 1 November 2011 (2011-11-01), pages 1981-1993, XP055055516, ISSN: 0018-019X, DOI: 10.1002/hlca.201100128 page 1993, line 8 - line 28 scheme 5; page 1987	1-3,5-8
Y	S. ATTALURI ET AL: "DNA adducts of aristolochic acid II: total synthesis and site-specific mutagenesis studies in mammalian cells", NUCLEIC ACIDS RESEARCH, vol. 38, no. 1, 1 January 2010 (2010-01-01), pages 339-352, XP055055519, ISSN: 0305-1048, DOI: 10.1093/nar/gkp815 step A in figure 3; page 347 2nd paragraph; page 341, column 2	1-3,5-8
Y	WO 2010/129379 A1 (MERCK SHARP & DOHME [US]; PASTERNAK ALEXANDER [US]; SHAHRIPOUR AURASH) 11 November 2010 (2010-11-11) step C; page 36 step C; page 45	1-3,5-8
Y	XIANG-HUI TAN ET AL: "Novel carbonyl allylation mediated by SnCl2/Cu in water", TETRAHEDRON LETTERS, vol. 43, no. 51, 1 December 2002 (2002-12-01), pages 9373-9376, XP055055807, ISSN: 0040-4039, DOI: 10.1016/S0040-4039(02)02370-5 scheme 2 entries 5-6 of table 1	4

2 -/--

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KOZO SHISHIDO ET AL: "An efficient total synthesis of ( )-decaline and ( )-vertaline", TETRAHEDRON LETTERS, vol. 24, no. 27, 1 January 1983 (1983-01-01), pages 2783-2786, XP055055798, ISSN: 0040-4039, DOI: 10.1016/S0040-4039(00)88022-3 step a; page 2785	4
T	JACOPO ZANON ET AL: "Copper-Catalyzed Domino Halide Exchange-Cyanation of Aryl Bromides", JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 125, no. 10, 1 March 2003 (2003-03-01), pages 2890-2891, XP055055809, ISSN: 0002-7863, DOI: 10.1021/ja0299708 page 2890, lines 1-3	8

2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2013/000005

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.:

1-8

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IN2013/000005

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010129379 A1	11-11-2010	AR 076836 A1	13-07-2011
		AU 2010246269 A1	24-11-2011
		CA 2759399 A1	11-11-2010
		CN 102459216 A	16-05-2012
		CO 6460758 A2	15-06-2012
		CR 20110578 A	09-01-2012
		EA 201171361 A1	30-05-2012
		EC SP11011444 A	30-12-2011
		EP 2427444 A1	14-03-2012
		JP 5092068 B2	05-12-2012
		JP 2012526118 A	25-10-2012
		JP 2013014607 A	24-01-2013
		KR 20120011069 A	06-02-2012
		MA 33342 B1	01-06-2012
		PE 03462012 A1	06-05-2012
		SG 175841 A1	29-12-2011
		TW 201043615 A	16-12-2010
		US 2010286123 A1	11-11-2010
		WO 2010129379 A1	11-11-2010

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-8

   processes for the preparation of compounds of formula I

   ---

2. claim: 9

   compounds according to claim 9
