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C07D 489/08 (2006.01) C07D 489/12 (2006.01)
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- (71) **Applicant (for all designated States except US):** **JOHNSON MATTHEY PLC** [GB/GB]; 5th Floor, 25 Farringdon Street, London EC4A 4AB (GB).
- (72) **Inventors; and**
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- (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).
- 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:**
7 November 2013



WO 2013/050748 A3

(54) **Title:** PROCESS FOR PREPARING BUPRENORPHINE

(57) **Abstract:** An improved process for preparing buprenorphine and a method for increasing the yield of buprenorphine or a derivative thereof.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2012/052423

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D489/08 C07D489/12
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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2010/039220 A1 (MALLINCKRODT INC [US]; ALLEN BRENDA E [US]; JARVI ESA T [US]; KALOTA D) 8 April 2010 (2010-04-08) paragraphs [0008] - [0066]; examples 1-13	1
A	& US 2010/087647 A1 (ALLEN BRENDA E [US] ET AL) 8 April 2010 (2010-04-08) cited in the application	1
A	GB 2 313 596 A (DONG KOOK PHARM CO LTD [KR]) 3 December 1997 (1997-12-03) pages 6-9; examples 1-3,5-8	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 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 22 August 2013	Date of mailing of the international search report 03/09/2013
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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 Hass, Christian
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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2012/052423

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 474 101 A (BENTLEY KENNETH WALTER) 21 October 1969 (1969-10-21) figure 2	1
Y	----- SCHÜTZ J ET AL: "Synthesis and pharmacological evaluation of 18,19-dehydrobuprenorphine", HETEROCYCLES.INTERNATIONAL JOURNAL FOR REVIEWS AND COMMUNICATIONS IN HETEROCYCLIC CHEMISTRY, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 54, no. 2 Sp. Issue, 2001, pages 989-998, XP008159157, ISSN: 0385-5414, DOI: 10.3987/COM-00-S(I)46 page 996, lines 14-32	19-27
A	-----	1
A	A. COOP ET AL.: "Structural Determinants of Opioid Activity in the Orvinols and Related Structures: Ethers of Orvinol and Isoorvinol", JOURNAL OF MEDICINAL CHEMISTRY, vol. 43, no. 9, 2000, pages 1852-1857, XP002691700, page 1853, left-hand column, chemical formulae and paragraph "Synthesis"; page 1855, figure 1 and left-hand column, paragraph "General Procedure B"; page 1856, left-hand column, preparation of compounds (5b), (5c) and (5d)	1
A	----- WU ET AL: "Functionalization of the 6,14-bridge of the orvinols. Part 3: Preparation and pharmacological evaluation of 18- and 19-hydroxyl substituted orvinols", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 17, no. 17, 4 August 2007 (2007-08-04), pages 4829-4831, XP022184917, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2007.06.050 page 4830, scheme 1; page 4831, left-hand column, first paragraph of text	1
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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2012/052423

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2009/122436 A2 (SUN PHARMACEUTICAL IND LTD [IN]; PATEL NILESHKUMAR SURESHBHAI [IN]; KI) 8 October 2009 (2009-10-08) pages 1, 2, formulae; page 4, scheme 1; page 30, lines 10-24 example 2	19-31
Y	XIN-REN HUANG ET AL.: "A Facile Synthesis and Structural Verification of Etorphine and Dihydroetorphine from Codeine", JOURNAL OF THE CHINESE CHEMICAL SOCIETY, vol. 58, no. 1, February 2011 (2011-02), pages 101-107, XP002711679, ISSN: 0009-4536 page 102, scheme 1; page 106, paragraph "Synthesis of dihydroetorphine 13"	19-26
Y	US 2009/005563 A1 (CARROLL ROBERT JAMES [CA] ET AL) 1 January 2009 (2009-01-01) pages 3, 4, reaction scheme; page 5, reaction scheme	28-31
Y	WO 2008/070462 A2 (PROGENICS PHARM INC [US]; PEREZ JULIO [US]; HAN AMI QI [US]; KUMARAN G) 12 June 2008 (2008-06-12) page 91, reaction scheme; page 98, reaction scheme; page 134, reaction scheme; page 138, reaction scheme	28,29
Y	WO 2009/067275 A1 (PROGENICS PHARM INC [US]; PEREZ JULIO [US]; HAN AMY QI [US]; ROTSHTEYN) 28 May 2009 (2009-05-28) page 92, reaction scheme; page 96, reaction scheme; page 100, reaction scheme; page 107, reaction scheme; page 109, reaction scheme; page 126, reaction scheme; page 137, reaction scheme	28,29
A,P	GERTA CAMI-KOBECE ET AL: "Structural Determinants of Opioid and NOP Receptor Activity in Derivatives of Buprenorphine", JOURNAL OF MEDICINAL CHEMISTRY, vol. 54, no. 19, 13 October 2011 (2011-10-13), pages 6531-6537, XP055035005, ISSN: 0022-2623, DOI: 10.1021/jm2003238 page 6532, scheme 1; page 6535, right-hand column, paragraph "General Procedure C: 3-O-Demethylation"	19-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2012/052423

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: 1-18

Process for the preparation of buprenorphine in a multi-step synthesis, starting from thebaine

2. claims: 19-31

Process for O-demethylation of the aryl-bound methoxy group in opiate alkaloids of formulae (Ia), (IIa) or (IIIa) to a hydroxy group

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2012/052423

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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