

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 December 2003 (24.12.2003)

PCT

(10) International Publication Number
WO 2003/105756 A3

(51) International Patent Classification⁷: **C07C 319/00**,
41/09, 211/35, 211/36, C07D 207/12

(21) International Application Number:
PCT/US2003/018136

(22) International Filing Date: 10 June 2003 (10.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/389,418 14 June 2002 (14.06.2002) US

(71) Applicant (for all designated States except US): **JOHN-
SON MATTHEY PHARMACEUTICAL MATERI-
ALS, INC.** [US/US]; 25 Patton Road, Devens, MA 01432
(US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **JURAYI, Jurjus,
F.** [US/US]; 16C Strawberry Hill Road, #32, Acton, MA
01720 (US). **FARHAN, Emile** [US/US]; 140 Chickering
Road, Dedham, MA 02026 (US). **SHARMA, Pradeep, K.**
[CA/US]; 27 hosmer Street, Apt. #2, Marlborough, MA
01752 (US).

(74) Agents: **PIERCE, N., Scott** et al.; Hamilton, Brook, Smith
& Reynolds, P.C., 530 Virginia Road, P.O. Box 9133, Con-
cord, MA 01742-9133 (US).

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

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (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:
4 March 2004

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: STEREOSELECTIVE SYNTHESIS OF 1,2-DISUBSTITUTED CYCLOALKYLS

(57) Abstract: A stereoselectively method of preparing a 1,2-disubstituted cycloalkyl, such as aminocycloalkyl ether compounds, from a trans-1,2-disubstituted cycloalkyl or a cis-2- substituted cycloalkanol. For example, a stereoselective method of preparing 1R-(3R-hydroxypyrrolidin-1-yl)-2R-(2-phenylethoxy)-cyclohexane from 1R,2R-cyclohexanediol or from meso-cis-1,2-cyclohexanediol is described. Aminocycloalkyl ethers, such as 1R-(3R-hydroxypyrrolidin-1-yl)-2R-(2-phenylethoxy)-cyclohexane, can be used to treat cardiac disease.



WO 2003/105756 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/18136

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07C 319/00, 41/09, 211/35, 211/36; C07D 207/12
US CL : 568/57, 58, 606, 609; 548/541; 564/306, 453, 461, 462

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)
U.S. : 568/57, 58, 606, 609; 548/541; 564/306, 453, 461, 462

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)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99/50225 A1 (NORTON PHARMACEUTICALS INC.) 07 October 1999 (07.10.99), pages 32-35.	1-46
A	HARADA et al. Enantiodifferentiating Functionalization of cis-Cycloalkane-1,2-diols and cis-endo-5-Norbornen-2,3-ylenebis(methanol) via Chiral Spiroacetals Derived from l-Menthone. J. Org. Chem. May 1989, Vol. 54. No. 11, pages 2599-2605, especially pages 2601-2603.	1-46

☐ 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 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

24 November 2003 (24.11.2003)

Date of mailing of the international search report

19 DEC 2003

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

Rosalynd Keys

Telephone No. 703-308-1235

INTERNATIONAL SEARCH REPORT

PCT/US03/18136

Continuation of B. FIELDS SEARCHED Item 3:

CAS ONLINE, EAST

search terms: 1,2-disubstituted cycloalkyl, galactosidase, 1R-(3R-hydroxypyrrolidin-1-yl)-2R-(2-phenylethoxy)-cyclohexane