

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
13 July 2006 (13.07.2006)

PCT

(10) International Publication Number  
**WO 2006/074269 A3**

(51) International Patent Classification:  
*C07D 401/06* (2006.01)

(21) International Application Number:  
PCT/US2006/000261

(22) International Filing Date: 5 January 2006 (05.01.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/641,910 6 January 2005 (06.01.2005) US

(71) Applicant (for all designated States except US): **SCHERING CORPORATION** [US/US]; 2000 Galloping Hill Road, Kenilworth, New Jersey 07033-0530 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **WU, Wenxue** [US/US]; 53 Zaitz Farm Road, Princeton Junction, New Jersey 08550 (US). **TRAN, Loc, Thanh** [CA/US]; 235 Vasser Drive, Parsippany, New Jersey 08854 (US). **D'SA, Bosco** [IN/US]; 5 Leland Road, Edison, New Jersey 08817 (US). **LIANG, Feng** [US/US]; 28 Potomac Road, Monmouth Junction, New Jersey 08852 (US). **LEONG, William** [US/US]; 342 Edgewood Avenue, Westfield, New Jersey 07090 (US). **LEE, Hong-Chang** [US/US]; 56 Lee Road, Livingston, New Jersey 07039 (US). **KLOPFER, Kevin** [US/US]; 235 Old Farm Road, Flemington, New Jersey 08822 (US). **SABESEN, Vijay** [IN/US]; 320 Vallejo Drive, Apt. 21, Millbrae, California 94030 (US).

(74) Agent: **KALYANARAMAN, Palaiyur, S.**; Schering-plough Corporation, 2000 Galloping Hill Road, Mail Stop K-6-1 1990, Kenilworth, New Jersey 07033-0530 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, 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, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (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:  
14 September 2006

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

(54) Title: PREPARATION OF PHARMACEUTICAL SALTS OF PIPERAZINE COMPOUNDS

(57) Abstract: The present invention is generally directed to a process to directly prepare pharmaceutically acceptable salts enriched with respect to selected rotameric salts of a basic compound, by creative choice of an acid and a solvent medium. The process is particularly useful in preparing specific rotamers of pharmaceutically useful salts in desired preponderance of a rotamer.



WO 2006/074269 A3

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/000261

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. C07D401/06

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, BEILSTEIN Data, PAJ, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/048153 A (SCHERING CORPORATION) 12 June 2003 (2003-06-12)  the whole document	1-13, 17, 18, 20, 32, 34-36, 52-54
Y	US 2003/139446 A1 (CHEN MINZHANG ET AL) 24 July 2003 (2003-07-24) cited in the application the whole document	1-64
Y	WO 03/066593 A (SCHERING CORPORATION) 14 August 2003 (2003-08-14) the whole document	1-64
	-/--	

Further documents are listed in the continuation of Box C.       See patent family annex.

\* Special categories of cited documents :

<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>* &amp; * document member of the same patent family</p>
--	--

Date of the actual completion of the international search  <b>28 June 2006</b>	Date of mailing of the international search report  <b>06/07/2006</b>
--	---

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2260 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  <b>Zellner, A</b>
---	---

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/000261

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 2003/008877 A1 ((SCHERING-PLOUGH CORPORATION) 9 January 2003 (2003-01-09) cited in the application the whole document -----	1-64
A	US 6 270 325 B1 (HSIEH HSIN-MAO) 7 August 2001 (2001-08-07) cited in the application the whole document -----	1-64
A	WO 02/079194 A (SCHERING CORPORATION) 10 October 2002 (2002-10-10) the whole document -----	1-64
A	WO 00/66558 A (SCHERING CORPORATION; BAROUDY, BAHIGE, M; CLADER, JOHN, W; JOSIEN, HUB) 9 November 2000 (2000-11-09) the whole document -----	1-64

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/000261

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
WO 03048153	A	12-06-2003	AU 2002346569 A1	17-06-2003
			CA 2468525 A1	12-06-2003
			CN 1596254 A	16-03-2005
			EP 1451174 A2	01-09-2004
			JP 2005511693 T	28-04-2005
			MX PA04005210 A	19-08-2004
			-----	
US 2003139446	A1	24-07-2003	NONE	
-----				
WO 03066593	A	14-08-2003	AU 2002365439 A1	02-09-2003
			CA 2467555 A1	14-08-2003
			CN 1599610 A	23-03-2005
			EP 1448528 A2	25-08-2004
			JP 2005518424 T	23-06-2005
			MX PA04005155 A	11-08-2004
			-----	
US 2003008877	A1	09-01-2003	US 2004157854 A1	12-08-2004
-----				
US 6270325	B1	07-08-2001	NONE	
-----				
WO 02079194	A	10-10-2002	AT 299139 T	15-07-2005
			BR 0208398 A	15-06-2004
			CA 2442227 A1	10-10-2002
			CN 1547580 A	17-11-2004
			CZ 20032636 A3	17-12-2003
			DE 60204951 D1	11-08-2005
			DE 60204951 T2	11-05-2006
			DK 1373256 T3	10-10-2005
			EP 1373256 A1	02-01-2004
			ES 2242856 T3	16-11-2005
			HK 1057363 A1	25-11-2005
			HU 0400349 A2	28-12-2004
			JP 2004525157 T	19-08-2004
			MX PA03008853 A	04-12-2003
			NO 20034311 A	26-11-2003
			NZ 527768 A	24-03-2005
			PL 364560 A1	13-12-2004
			PT 1373256 T	30-11-2005
SK 11962003 A3	02-03-2004			
ZA 200307474 A	24-12-2004			
-----				
WO 0066558	A	09-11-2000	AU 780888 B2	21-04-2005
			AU 4500900 A	17-11-2000
			AU 2005202357 A1	23-06-2005
			BR 0010304 A	13-02-2002
			CA 2371583 A1	09-11-2000
			CZ 20013940 A3	17-04-2002
			EP 1175401 A1	30-01-2002
			HU 0202867 A2	28-01-2003
			JP 3722700 B2	30-11-2005
			JP 2002543185 T	17-12-2002
			NO 20015366 A	03-01-2002
			PL 351388 A1	07-04-2003
			SK 15692001 A3	02-07-2002
			TR 200103214 T2	21-03-2002
			ZA 200108868 A	27-01-2003