2002041556

08 JUL 2002

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 July 2001 (19.07.2001)

PCT

(10) International Publication Number
WO 01/51477 A1

(51) International Patent Classification[7]: C07D 307/87

(21) International Application Number: PCT/DK00/00016

(22) International Filing Date: 14 January 2000 (14.01.2000)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant *(for all designated States except US)*: H. LUNDBECK A/S [DK/DK]; Ottiliavej 9, DK-2500 Valby-Copenhagen (DK).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: PETERSEN, Hans [DK/DK]; Guldagervej 11, DK-2720 Vanløse (DK).

(74) Common Representative: H. LUNDBECK A/S; Meidahl Peterson, John, Ottilavej 9, DK-2500 Valby-Copenhagen (DK).

(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, 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, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**
— *with international search report*

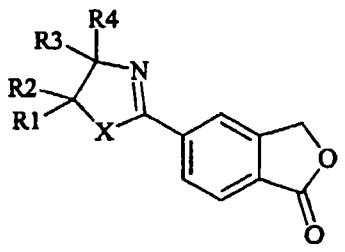
*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

*162162*

*ACTION*

(54) Title: METHOD FOR THE PREPARATION OF 5-CYANOPHTHALIDE

WO 01/51477 A1




(IV)

(57) Abstract: A method for the preparation of 5-cyanophthalide comprising treatment of a compound of formula (IV) wherein X is O or S; $R^1$-$R^2$ are each independently selected from hydrogen and $C_{1-6}$alkyl, or $R^1$ and $R^2$ together form a $C_{2-5}$alkylene chain thereby forming a spiro-ring; $R^3$ is selected from hydrogen and $C_{1-6}$alkyl, $R^4$ is selected from hydrogen, $C_{1-6}$alkyl, a carboxy group or a precursor group therefore, or $R^3$ and $R^4$ together form a $C_{2-5}$alkylene chain thereby forming a spiro-ring; with a dehydration agent or alternatively where X is S, thermally cleavage of the thiazoline ring or treatment with a radical initiator, such as peroxide or with light, to form 5-cyanophthalide, which is an important intermediate used in the preparation of the antidepressant drug citalopram.