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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 June 2001 (28.06.2001)

PCT

(10) International Publication Number
WO 01/45483 A2

(51) International Patent Classification: Not classified

(21) International Application Number: PCT/DK01/00147

(22) International Filing Date: 7 March 2001 (07.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 2000 01929 22 December 2000 (22.12.2000) DK

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

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: VILLA, Marco [IT/IT]; Via Riello 7A, I-35123 Padova (IT). SBROGIO, Federico [IT/IT]; Via Passo Pordoi, 9, I-30030 Favaro Veneto (IT). DANCER, Robert [AU/DK]; J.M. Thielesvej 8, st. th., DK-1961 Frederiksberg C (DK).

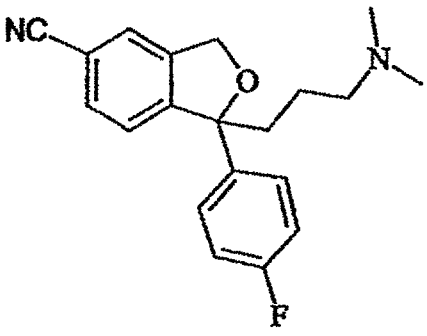
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AT (utility model), AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ (utility model), DE, DE (utility model), DK, DK (utility model), DM, DZ, EE, EE (utility model), ES, FI, FI (utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (utility model), 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, MZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

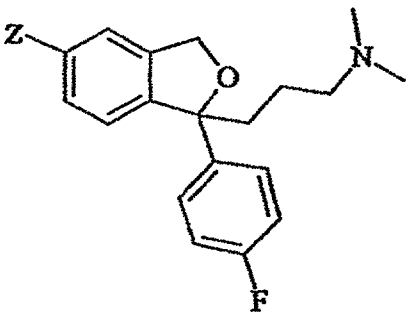
Published:
- — *Upon request of the applicant, before the expiration of the time limit referred to in Article 21(2)(a).*
- — *Without international search report and to be republished upon receipt of that report.*
- — *Without classification; title and abstract not checked by the International Searching Authority.*

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: METHOD FOR THE PREPARATION OF PURE CITALOPRAM



(I)



(II)

(57) Abstract: The present invention relates to a process for the preparation and purification of citalopram (I) in which a compound of Formula (II) wherein Z is iodo, bromo, chloro or CF_3-$(CF_2)_n$-SO_2-O-, n being 0, 1, 2, 3, 4, 5, 6, 7 or 8, is subjected to a cyanide exchange reaction with a cyanide source; the resultant crude citalopram product is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent; the reaction mixture is then subjected to an acid/base wash and/or crystallisation and recrystallisation of citalopram in order to remove the amides formed from the crude citalopram mixture; and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt thereof.

WO 01/45483 A2