

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
11 October 2007 (11.10.2007)

PCT

(10) International Publication Number
WO 2007/113261 A1

(51) International Patent Classification:

C07D 401/04 (2006.01) C07D 413/04 (2006.01)
C07D 403/04 (2006.01) C07D 417/04 (2006.01)

(21) International Application Number:

PCT/EP2007/053118

(22) International Filing Date: 30 March 2007 (30.03.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0607899.2 3 April 2006 (03.04.2006) GB

(71) Applicant (for all designated States except US): **Glaxo Group Limited** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **BACCHI, Sergio** [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT).

(74) Agent: **GIDDINGS, Peter, John**; GlaxoSmithKline, Corporate Intellectual Property CN925.1, 980 Great West Road, Brentford Middlesex TW8 9GS (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, 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, 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, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

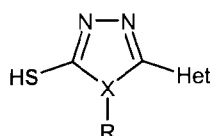
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, 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

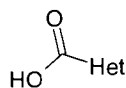
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PROCESS FOR PREPARING HETEROCYCLIC DERIVATIVES

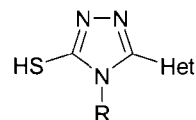
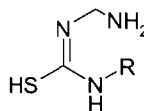
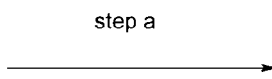


(I)

Scheme 1



(IIA)



(II)

(57) **Abstract:** The present invention relates to a novel process, useful for preparing key intermediates of formula (I) in the synthesis of various compounds, among them compounds which are potent and specific antagonists of D3 receptors, Formula (I) in which X may be Nitrogen or Sulfur; Het means aryl or heteroaryl; each of which may be substituted by 1 to 4 groups J selected from: halogen, C1 -C6 alkyl, C1 -C6 alkoxy, halo C1 -C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, halo C1 -C6 alkoxy, -C(O)R1, nitro, hydroxy, -NR2R3, cyano or a group Z; R1 is a C1 -C4 alkyl, -OR3 Or -NR3R4; R2 is hydrogen or C1 -C6 alkyl; R3 is hydrogen or C1 -C6 alkyl; R is H, C1 -C6 alkyl, aryl, benzyl; each of which may be substituted by 1 to 4 groups J; according to the following Scheme 1 : Scheme 1, in which step a means a reaction in basic conditions of compounds (NA) with 3- thiosemicarbazide derivatives, followed by a treatment with an inorganic base and n-propane phosphonic cyclic anhydride and final pH adjustment with inorganic acids to give compounds of formula (II).