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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 July 2003 (03.07.2003)

PCT

(10) International Publication Number
WO 03/053435 A1

(51) International Patent Classification[7]: A61K 31/4178, A61P 31/18, C07D 231/12, 277/42, 263/32, 513/04, 233/54, 233/88, 493/04, 277/40, 417/14, 417/12, A61K 31/506, 31/427, 31/425

(21) International Application Number: PCT/EP02/14839

(22) International Filing Date:
20 December 2002 (20.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
01205115.7 21 December 2001 (21.12.2001) EP

(71) Applicant *(for all designated States except US)*: **TIBOTEC PHARMACEUTICALS LTD.** [IE/IE]; Unit 4, Block 4B, Blanchardstown Corporate Park, Blanchardstown, 15 Dublin (IE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **VENDEVILLE, Sandrine, Marie, Helene** [FR/BE]; Square Marguerite, 14 - Boîte 18, B-1000 Brussels (BE). **VERSCHUEREN, Wim, Gaston** [BE/BE]; De Wittestraat 5, B-2600 Berchem (BE). **TAHRI, Abdellah** [MA/BE]; Rue Maurice Albert Raskin, 30, B-1070 Anderlecht (BE). **MOORS, Samuel, Leo, Christiaan** [BE/BE]; Kerkweg 8, B-3212 Pellenberg (BE). **ERRA SOLÀ, Montserrat** [ES/ES]; C/Mare de Déu de la Salut, 2, 08500 Vic (ES).

(74) Agent: **DAELEMANS, Frank**; Tibotec-Virco Comm. VA, Generaal De Wittelaan L11 b3, B-2800 Mechelen (BE).

(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, 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.

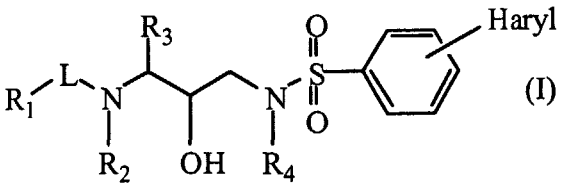
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG,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

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv)) for US only*

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: BROADSPECTRUM HETEROCYCLIC SUBSTITUTED PHENYL CONTAINING SULFONAMIDE HIV PROTEASE INHIBITORS



(57) Abstract: The present invention concerns the compounds having the formula (I), *N*-oxides, salts, stereoisomeric forms, racemic mixtures, prodrugs, esters and metabolites thereof, wherein Haryl is an aromatic monocyclic, bicyclic or tricyclic heterocycle having 3 to 14 ring members which contains one or more heteroatom ring members selected from nitrogen, oxygen and sulfur and which may optionally be substituted on (i) one or more carbon atoms by C_{1-6}alkyl, halogen, hydroxy, optionally mono- or disubstituted amino, nitro, cyano, haloC_{1-6}alkyl, carboxyl, C_{3-7}cycloalkyl, optionally mono- or disubstituted aminocarbonyl, methylthio, methylsulfonyl, aryl, -$(R_{7a})_n$-M-R_{7b}, Het^1 and Het^2; whereby the optional substituents on any amino function are independently selected from R_5 and -A-R_6; and on (ii) a nitrogen atom if present by hydroxy or -A-R_6. It further relates to their use as broadspectrum HIV protease inhibitors, processes for their preparation as well as pharmaceutical compositions and diagnostic kits comprising them. It also concerns combinations thereof with another anti-retroviral agent, and to their use in assays as reference compounds or as reagents.

WO 03/053435 A1