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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 March 2006 (02.03.2006)

PCT

(10) International Publication Number
WO 2006/021885 A1

(51) International Patent Classification:
C12P 7/22 (2006.01) *C12P 41/00* (2006.01)
C07C 33/46 (2006.01)

(21) International Application Number:
PCT/IB2005/002839

(22) International Filing Date: 15 August 2005 (15.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/605,118 26 August 2004 (26.08.2004) US

(71) Applicant *(for all designated States except US)*: **PFIZER INC.** [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **KUNG, Pei-Pei** [US/US]; Pfizer Global Research and Development, 10770 Science Center Drive, San Diego, CA 92121 (US). **MARTINEZ, Carlos, Alberto** [CO/US]; Pfizer Global Research and Development, 10770 Science Center Drive, San Diego, CA 92121 (US). **TAO, Junhua** [CN/US]; Pfizer Global Research and Development, 10770 Science Center Drive, San Diego, CA 92121 (US).

(74) Agents: **FULLER, Grover, F., Jr.** et al.; Pfizer Inc., 201 Tabor Road, Morris Plains, NJ 07950 (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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, 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*

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.

WO 2006/021885 A1

(54) Title: ENANTIOSELECTIVE BIOTRANSFORMATION FOR PREPARATION OF PROTEIN TYROSINE KINASE INHIBITOR INTERMEDIATES

(57) Abstract: The invention relates to biocatalytic methods for preparing enantiomerically pure stereoisomers of 1-(2,6-dichloro-3-fluorophenyl)ethanol. Disclosed are methods of preparation of the desired (S)-enantiomer, which methods are based on a combination of enzymatic resolution, chemical esterification and chemical hydrolysis with inversion of 1-(2,6-dichloro-3-fluorophenyl)ethyl esters or stereoselective bio-reduction of 2,6-dichloro-3-fluoro-acetophenone with a biocatalyst such as an enzyme or a microorganism. The chiral (*S*)-enantiomer can be used in the synthesis of certain enantiomerically enriched, ether linked 2-aminopyridine compounds that potently inhibit auto-phosphorylation of human heptocyte growth factor receptor.