

**(19) World Intellectual Property Organization
International Bureau**



162162

(43) International Publication Date
30 May 2002 (30.05.2002)

(10) International Publication Number
WO 02/42258 A1

PCT

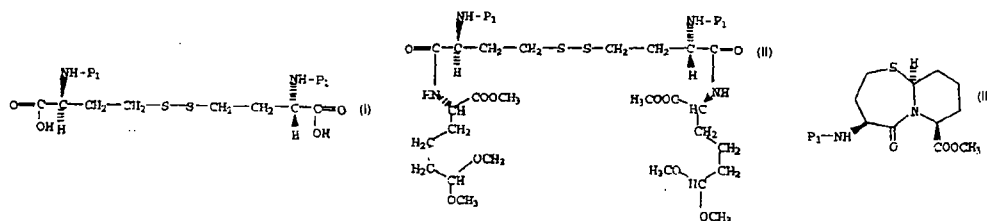
- (51) **International Patent Classification⁷:** C07C 261/00, 229/04, 229/22, C07D 281/02
- (21) **International Application Number:** PCT/US99/15380
- (22) **International Filing Date:** 29 July 1999 (29.07.1999)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (71) **Applicant:** BRISTOL-MYERS SQUIBB COMPANY [US/US]; P.O. Box 4000, Princeton, NJ 08543-4000 (US).
- (72) **Inventors:** MONIOT, Jerome, L.; 139 South Road, Chester, NJ 07930 (US). RAMIG, Keith; 389 Lawn Ridge Road, Orange, NJ 07050 (US). JASS, Paul, A.; 315 East Pleasant Grove Road, Jackson, NJ 08527 (US). DILLON, John, L., Jr.; 7309 Snowball Run, East Syracuse, NY 13057 (US). RACHA, Saibaba; 408 Summerhaven Drive, East Syracuse, NY 13057 (US). SHRIVASTAVA, Sushil, K.; 9 Kayann Drive, Dayton, NJ 08810 (US). WINTER, William, J.; 160 Union Street, Montgomery, NY 12549 (US). VENIT, John, J.; 260 Dawes Road, North Brunswick, NJ 08902 (US). SWAMINATHAN, Shankar; 8 Albury Way, North Brunswick, NJ 08902 (US). SIMPSON, James; 8 Apple Hill Road, Belle Mead, NJ 08502-3812 (US). CHEN, Chien-Kuang; 58 Robertsville Road, Marlboro, NJ 07746 (US). PACK, Shawn, K.; 3509 Quail Ridge Drive, Plainsboro, NJ 08536 (US). SCHWINDEN, Mark, D.; 1907 Hopkins Court, Holland, PA 18966 (US).
- (74) **Agents:** DAVIS, Stephen, B. et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543-4000 (US).
- (81) **Designated States (national):** AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, 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, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SI, 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:**
— 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.*

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:** PREPARATION OF [4S-(4 α ,7 α ,10A β)]-4-AMINO-OCTAHYDRO-5-OXO-7H-PYRIDO[2,1-B][1,3]THIAZEPINE-7-CARBOXYLIC ACID, METHYL ESTER AND SALTS THEREOF VIA NOVEL DISULFIDES



- (S7) Abstract:** N-protected-L-homocysteine disulfide of the formula (I) or an activated form thereof is reacted with (S)-2-amino-6,6-dimethoxyhexanoic acid, methyl ester to give the disulfide intermediate of the formula (II). The disulfide intermediate of formula (II) is reacted to cleave the disulfide bond and the resulting monomer is subjected to an acid catalyzed cyclization reaction to give the N-protected lactam of the formula (III). Removal of the N-protecting group gives [4S-(4 α ,7 α ,10 α)]-4-aminooctahydro-5-oxo-7H-pyrido[2,1-b][1,3]thiazepine-7-carboxylic acid, methyl ester which along with its salt is useful as an intermediate in the preparation of the dual inhibitor [4S-(4 α (R*),7 α ,10 α)]-octahydro-4-[(2-mercapto-1-oxo-3-phenylpropyl)amino]-5-oxo-7H-pyrido-[2,1-b][1,3]thiazepine-7-carboxylic acid.



G00002

WO 02/42258 A1