9900977-7
IPOS

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 401/14, C07F 9/6558, C07H 19/04, C07D 401/04, A61K 31/435 — A1

(11) International Publication Number: WO 98/11098

(43) International Publication Date: 19 March 1998 (19.03.98)

(21) International Application Number: PCT/US97/15903

(22) International Filing Date: 11 September 1997 (11.09.97)

(30) Priority Data:
08/713,703 13 September 1996 (13.09.96) US

(71) Applicant: SCHERING CORPORATION [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033 (US).

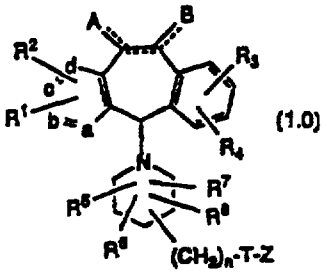
(72) Inventors: COOLER, Alan, B.; 23 Natalie Drive, West Caldwell, NJ 07006 (US). MALLANS, Alan, K.; 147 Kings Highway, Hackettstown, NJ 07840 (US). GIRIJAVALLABHAN, Viyyoor, M.; 10 Maplewood Drive, Parsippany, NJ 07054 (US). DOLL, Ronald, J.; 126 Union Avenue, Maplewood, NJ 07040 (US). TAVERAS, Arthur, G.; 43 Crestwood Road, Rockaway, NJ 07866 (US). NJOROGE, F., George; 2597 Juliat Place, Union, NJ 07083 (US). BALDWIN, John, J.; 621 Gypsy Hill Circle, Gwynedd Valley, PA 19437 (US). READER, John, C.; 112 Biscayne Court #8, Princeton, NJ 08540 (US).

(74) Agents: MAJKA, Joseph, T. et al.; Schering-Plough Corporation, Patent Dept. K-6-1 1990, 2000 Galloping Hill Road, Kenilworth, NJ 07033 (US).

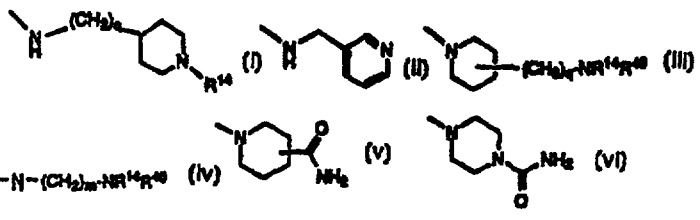
(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: NOVEL TRICYCLIC PIPERIDINYL COMPOUNDS USEFUL AS INHIBITORS OF FARNESYL-PROTEIN TRANSFERASE



(1.0)



(57) Abstract

Novel tricyclic compounds of formula (1.0) or a pharmaceutically acceptable salt or solvate thereof, wherein: one of a, b, c, and d represents N or NR^9, wherein R^9 is O-, $-CH_3$ or $-(CH_2)_nCO_2H$ wherein n is 1 to 3, and the remaining a, b, c and d groups represent CR^1 or CR^2; or each of a, b, c and d is independently selected from CR^1 or CR^2; each R^1 and each R^2 is independently selected from H, halo, $-CR_3$, $-OR^{10}$, $-COR^{10}$, $-SR^{10}$, $-S(O)_tR^{11}$ (wherein t is 0, 1 or 2), -SCN, $-N(R^{10})_2$, $-NR^{10}R^{11}$, $-NO_2$, $-OC(O)R^{10}$, $-CO_2R^{10}$, $-OCO_2R^{11}$, -CN, $-NHC(O)R^{10}$, $-NHSO_2R^{10}$, $-CONHR^{10}$, $-CONHCH_2CH_2OH$, $-NR^{10}COOR^{11}$, $-SR^{11}C(O)OR^{11}$, $-SR^{11}N(R^{75})^2$; n is 0 (zero), 1, 2, 3, 4, 5 or 6; T is -CO-; -SO-; $-SO_2$-; or $-CR^{30}R^{31}$-; Z represents alkyl, aryl, aralkyl, heteroalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, heterocycloalkylalkyl, $-OR^{40}$, $-SR^{40}$, $-CR^{40}R^{42}$, $-NR^{40}R^{42}$, formulae (i), (ii), (iii), (iv), (v) and (vi). Pharmaceutical compositions are disclosed which are inhibitors of the enzyme, farnesyl protein transferase. Also disclosed is a method of inhibiting Ras function and therefore inhibiting the abnormal growth of cells. The method comprises administering the novel tricyclic compound to a biological system. In particular, the method inhibits the abnormal growth of cells in a mammal such as a human.