



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 493/00	A2	(11) International Publication Number: WO 99/67252 (43) International Publication Date: 29 December 1999 (29.12.99)
(21) International Application Number: PCT/EP99/04287 (22) International Filing Date: 21 June 1999 (21.06.99) (30) Priority Data: 09/102,602 22 June 1998 (22.06.98) US (71) Applicant (for all designated States except AT US): NOVARTIS AG [CH/CH]; Schwarzwaldallee 215, CH-4058 Basel (CH). (71) Applicant (for AT only): NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT MBH [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT). (71) Applicant (for all designated States except US): THE SCRIPPS RESEARCH INSTITUTE [US/US]; 10550 North Torrey Pines Road, La Jolla, CA 92037 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): NICOLAOU, Kyriacos, Costa [US/US]; 9625 Blackgold Road, La Jolla, CA 92037 (US). KING, Nigel, Paul [GB/US]; 3550 Lebon Drive, No. 6219, San Diego, CA 92122 (US). FINLAY, Maurice, Raymond, Verschoyle [GB/US]; 3550 Nobel Drive, No. 6219, San Diego, CA 92122 (US). HE, Yun [CN/US];		3950 Mahaila Avenue, No. J-36, San Diego, CA 92122 (US). ROSCHANGAR, Frank [DE/US]; 5101 Copper Ridge Drive, No. 303, Durham, NC 27707 (US). VOURLOUMIS, Dionisios [GR/US]; 4249 Nobel Drive, No. 39, San Diego, CA 92122 (US). VALLBERG, Hans [SE/SE]; Mangårdsvägen 10, S-141 51 Huddinge (SE). BIGOT, Antony [FR/US]; 3969 Nobel Drive, No. 273, San Diego, CA 92122 (US). (74) Agent: BECKER, Konrad; Novartis AG, Corporate Intellectual Property, Patent & Trademark Dept., CH-4002 Basel (CH). (81) Designated States: AE, 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, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published Without international search report and to be republished upon receipt of that report.
(54) Title: EPOTHILONE DERIVATIVES AND THEIR SYNTHESIS AND USE (I) (57) Abstract The invention relates to epothilone analog represented by formula (I) wherein (i) R₂ is absent or oxygen; "a" can be either a single or double bond; "b" can be either absent or a single bond; and "c" can be either absent or a single bond, with the proviso that if R₂ is oxygen then "b" and "c" are both a single bond and "a" is a single bond; if R₂ is absent then "b" and "c" are absent and "a" is a double bond; and if "a" is a double bond, then R₂, "b" and "c" are absent; R₃ is a radical selected from the group consisting of hydrogen; lower alkyl; -CH=CH₂; -C≡CH; -CH₂F; -CH₂Cl; -CH₂-OH; -CH₂-O-(C₁-C₆-alkyl); and -CH₂-S-(C₁-C₆-alkyl); R₄ and R₅ are independently selected from hydrogen, methyl or a protecting group; and R₁ is as defined in the specification, or a salt of a compound of formula (I) where a salt-forming group is present. A further aspect of the invention is related to the synthesis of epothilone E. These compounds have inter alia microtubuli depolymerisation inhibiting activity and are e.g. useful against proliferative diseases.		