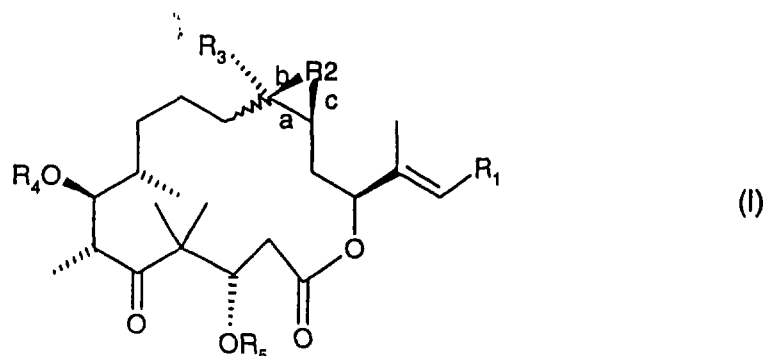


AbstractEpothilone Derivatives and their Synthesis and Use

The invention relates to epothilone analog represented by the formula I



wherein

(i) R_2 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 R_2 is oxygen then "b" and "c" are both a single bond and "a" is a single bond; if R_2 is absent then "b" and "c" are absent and "a" is a double bond; and if "a" is a double bond, then R_2 , "b" and "c" are absent;

R_3 is a radical selected from the group consisting of hydrogen; lower alkyl; $-\text{CH}=\text{CH}_2$; $-\text{C}\equiv\text{CH}$; $-\text{CH}_2\text{F}$; $-\text{CH}_2\text{Cl}$; $-\text{CH}_2\text{OH}$; $-\text{CH}_2\text{O}-(\text{C}_1\text{--C}_6\text{-alkyl})$; and $-\text{CH}_2\text{S}-(\text{C}_1\text{--C}_6\text{-alkyl})$;

R_4 and R_5 are independently selected from hydrogen, methyl or a protecting group; and

R_1 is as defined in the specification, or a salt of a compound of the 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.



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