New taxoids of general formula (I):

their preparation and pharmaceutical compositions containing them.

The new products of general formula (I) in which Z represents a radical of general formula (II):

display noteworthy antitumor and antileukaemic properties.
METHODS OF TREATING CELL LINES EXPRESSING MULTIDRUG RESISTANCE P-GLYCOPROTEIN

The present invention relates to new taxoids of general formula (I):

\[
\text{(I)}
\]

[0002] in which

[0003] \(Z\) represents a hydrogen atom or a radical of general formula (II):

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\text{(II)}
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[0004] in which:

[0005] \(R_1\) represents

[0006] a benzoyle radical optionally substituted with one or more identical or different atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms and trifluoromethyl radicals,

[0007] a phenyl or furyl radical or

[0008] a radical \(R_2\) —O—CO— in which \(R_2\) represents:

[0009] an alkyl radical containing 1 to 8 carbon atoms,

[0010] an alkenyl radical containing 2 to 8 carbon atoms,

[0011] an alkynyl radical containing 3 to 8 carbon atoms,

[0012] a cycloalkyl radical containing 3 to 6 carbon atoms,

[0013] a cycloalkenyl radical containing 4 to 6 carbon atoms or

[0014] a bicycloalkyl radical containing 7 to 10 carbon atoms,

[0015] these radicals being optionally substituted with one or more substituents selected from halogen atoms, hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino radicals, morpholino radicals, 1-piperazinyl radicals, said piperazinyl radicals being optionally substituted at position 4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, cycloalkyl radicals containing 3 to 6 carbon atoms, cycloalkenyl radicals containing 4 to 6 carbon atoms, phenyl radicals, said phenyl radicals being optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, and alkoxy radicals containing 1 to 4 carbon atoms, cyano radicals, carboxyl radicals and alkoxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

[0016] a phenyl or \(\alpha\) - or \(\beta\) -naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, and alkoxy radicals containing 1 to 4 carbon atoms,

[0017] a 5-membered aromatic heterocyclic radical preferably selected from furyl and thiophene radicals,

[0018] or a saturated heterocyclic radical containing 4 to 6 carbon atoms, optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

[0019] \(R_3\) represents

[0020] an unbranched or branched alkyl radical containing 1 to 8 carbon atoms,

[0021] an unbranched or branched alkenyl radical containing 2 to 8 carbon atoms,

[0022] an unbranched or branched alkynyl radical containing 2 to 8 carbon atoms,

[0023] a cycloalkyl radical containing 3 to 6 carbon atoms,

[0024] a phenyl or \(\alpha\) - or \(\beta\) -naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, alkoxyamino, alkoxyacylaminor, aminor, alkenyllamino, dialkylamino, aralkylamino, aralkylamino, alkoxycarbonyl, alkoxycarbonyl, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbambonyl, dialkylcarbambonyl, cyano, nitro and trifluoromethyl radicals,

[0025] or a 5-membered aromatic heterocycle containing one or more identical or different hetero atoms selected from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents selected from halogen atoms, alkyl, aryl, aminor, alkylaminor, dialkylamino, alkoxyaminor, acyl, aroyl-
carbonyl, cyano, carboxyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl and alkoxy carbonyl radicals,

[0026] with the understanding that, in the substituents of the phenyl, α- or β-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, the alkyl and alkenyl radicals contain 2 to 8 carbon atoms, and the aryl radicals are phenyl or α- or β-naphthyl radicals,

[0027] R₄ represents

[0028] an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain,

[0029] an alkenyloxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain,

[0030] an alkynylxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain,

[0031] a cycloalkyloxy radical containing 3 to 6 carbon atoms or

[0032] a cycloalkenyloxy radical containing 4 to 6 carbon atoms,

[0033] these radicals being optionally substituted with one or more substituents selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkylthio radical containing 1 to 4 carbon atoms, a carboxyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical and a N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms, or both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, said saturated 5- or 6-membered heterocyclic radical optionally being substituted with a substituent selected from an alkoxy radical containing 1 to 4 carbon atoms, a phenyl radical, and a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

[0034] R₄ represents

[0035] an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain,

[0036] an alkenyloxy radical containing 3 to 6 carbon atoms,

[0037] an alkynylxy radical containing 3 to 6 carbon atoms,

[0038] a cycloalkyloxy radical containing 3 to 6 carbon atoms or

[0039] a cycloalkenyloxy radical containing 3 to 6 carbon atoms,

[0040] these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxycarbonyl radical containing 1 to 4 carbon atoms, an alkylthio radical containing 2 to 4 carbon atoms, a carboxyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and a N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms, or, with the nitrogen atom to which it is linked, forms a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with a substituent selected from an alkoxy radical containing 1 to 4 carbon atoms, a phenyl radical and a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

[0041] Preferably, the aryl radicals which can be represented by R₃ are phenyl or α- or β-naphthyl radicals optionally substituted with one or more atoms or radicals selected from halogen atoms (fluorine, chlorine, bromine, iodine) alkyl, alkenyl, alkynyl, aryl, arylethyl, alkoxy, alkylthio, arylethoxycarbonyl, mercapto, formyl, acyl, acylamino, aroylamino, aroylcarbamoylaminoo, aminocarbonyl, aminosulphonyl, carbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals, on the understanding that the alkyl and alkyl radicals contain 2 to 8 carbon atoms and that the aryl radicals are phenyl or α- or β-naphthyl radicals.

[0042] Preferably, the heterocyclic radicals which can be represented by R₄ are 3-membered aromatic heterocyclic radicals containing one or more identical or different atoms selected from nitrogen, oxygen and sulphur atoms, optionally substituted with one or more identical or different substituents selected from halogen atoms (fluorine, chlorine, bromine, iodine), alkyl radicals containing 1 to 4 carbon atoms, ary1 radicals containing 6 or 10 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, ary1oxy radicals containing 6 or 10 carbon atoms, amido radicals, alkylamino radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, acylamino radicals in which the acyl portion contains 1 to 4 carbon atoms, alkoxy carbonylamino radicals containing 1 to 4 carbon atoms, acyl radicals containing 1 to 4 carbon atoms, ary1 carbamoyl radicals in which the ary1 portion contains 1 to 4 carbon atoms, carbamoyl radicals, carboxylic acid radicals, carbamoyl radicals, dialkylcarbamoyl radicals in which each alkyl portion contains 1 to 4 carbon atoms, and alkoxy carbonylamino radicals in which the alkyl portion contains 1 to 4 carbon atoms.

[0043] Preferably, the radicals R₅ and R₆, which may be identical or different, represent unbranched or branched alkoxy radicals containing 1 to 6 carbon atoms, optionally substituted with a methoxy, ethoxy, ethylthio, carboxyl, methoxycarbonyl, ethoxycarbonyl, cyano, carbamoyl, N-methylcarbamoyl, N-ethy1carbamoyl, N,N-dimethylcarbamoyl, N,N-diethy1carbamoyl, N-pyrrolidinocarbonyl or N-piperidinocarbonyl radical.

[0044] More particularly, the present invention relates to the products of general formula (I) in which Z represents a hydrogen atom or a radical of general formula (II) in which R₅ represents a benzoyl radical or a radical R₆—O—CO—
in which \( R_2 \) represents a tert-butyl radical and \( R_3 \) represents an alkyl radical containing 1 to 6 carbon atoms, an alkenyl radical containing 2 to 6 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a phenyl radical optionally substituted with one or more identical or different atoms or radicals selected from from halogen atoms (fluorine, chlorine), alkyl (methyl), alkoxy (methoxy), dialkylamino (dimethylamino), acylamino (acetylamino), alkoxyacyl group contained within a saturated 5- or 6-membered heterocycle, or by means of a derivative of this acid, to obtain an ester of general formula (V):

\[
\text{COCH}_3
\]

in which \( R_1, R_3, R_4, R_5, R_6 \), and \( R_7 \) are defined as above, followed by replacement of the protective groups represented by \( R_4 \) and/or \( R_5 \) by hydrogen atoms.

[0051] The esterification by means of an acid of general formula (IV) may be performed in the presence of a condensing agent (carbodiimide, reactive carbonate) and an activating agent (aminopyridines) in an organic solvent (ether, esters, ketones, nitrites, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons) at a temperature from −10 to 90°C.

[0052] The esterification may also be carried out using the acid of general formula (IV) in the form of the symmetrical anhydride, working in the presence of an activating agent (aminopyridines) in an organic solvent (ethers, esters, ketones, nitrites, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons) at a temperature of from 0 to 80°C.

[0053] The esterification may also be carried out using the acid of general formula (IV) in halide form or in the form of a mixed anhydride with an aliphatic or aromatic acid, optionally prepared in situ, in the presence of a base (tertiary aliphatic amine), working in an organic solvent (ethers, esters, ketones, nitrites, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons) at a temperature of from 0 to 80°C.

[0054] Preferably, \( R_6 \) represents a hydrogen atom and \( R_7 \) represents a group protecting the hydroxyl function, or alternatively \( R_6 \) and \( R_7 \) together form a saturated 5- or 6-membered heterocycle.

[0055] When \( R_6 \) represents a hydrogen atom, \( R_7 \) preferably represents a methoxymethyl, 1-ethoxethyl, benzylmethoxymethyl, trimethylsilyl, triethylsilyl, \( \beta \)-trimethylsilylithiethoxymethyl, benzoylcarbonyl or tetrahydropyranyl radical.

[0056] When \( R_6 \) and \( R_7 \) together form a heterocycle, the latter is preferably an oxazolidine ring optionally monosubstituted or gem-disubstituted at position 2.

[0057] Replacement of the protective groups \( R_2 \) and/or \( R_3 \) and \( R_4 \) by hydrogen atoms may be performed, depending on their nature, in the following manner:

[0058] 1) When \( R_1 \) represents a hydrogen atom and \( R_2 \) represents a group protecting the hydroxyl function, replacement of the protective groups by hydro-
gen atoms is performed by means of an inorganic acid (hydrochloric acid, sulphuric acid, hydrofluoric acid) or organic acid (acetic acid, methanesulphonic acid, trifluoromethanesulphonic acid, p-toluenesulphonic acid) used alone or mixed, working in an organic solvent chosen from alcohols, ethers, esters, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons or nitriles at a temperature of from -10 to 60 °C, or by means of a source of fluoride ions such as a hydrofluoric acid/triethylamine complex, or by catalytic hydrogenation,

[0059] 2) when R₆ and R₇ together form a saturated 5- or 6-membered heterocycle, and more especially an oxazolidine ring of general formula (VI):

![Diagram of oxazolidine ring](image)

[0060] in which R₁ is defined as above and R₆ and R₇, which may be identical or different, represent a hydrogen atom or an alkyl radical containing 1 to 4 carbon atoms, or an aralkyl radical in which the alkyl portion contains 1 to 4 carbon atoms and the aryl portion preferably represents a phenyl radical optionally substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms, or an aryloxy radical preferably representing a phenyl radical optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms, or alternatively R₆ represents an alkoxy radical containing 1 to 4 carbon atoms or a trihaloalkyl radical such as trichloromethyl or a phenyl radical substituted with a trihalomethyl radical such as trichloromethyl and R₇ represents a hydrogen atom, or alternatively R₆ and R₇, together with the carbon atom to which they are linked, form a 4- to 7-membered ring, replacement of the protective group formed by R₆ and R₇ by hydrogen atoms may be performed, depending on the meanings of R₁, R₆ and R₇, in the following manner:

[0061] a) when R₁ represents a tert-butoxycarbonyl radical and R₆ and R₇, which may be identical or different, represent an alkyl radical or an aralkyl (benzyl) or aryl (phenyl) radical, or alternatively R₆ and R₇, together with the carbon atom to which they are linked, form a 4- to 7-membered ring, treatment of the ester of general formula (V) with an inorganic or organic acid, where appropriate in an organic solvent such as an alcohol, yields the product of general formula (VII).

[0062] in which R₆ and R₇, which are defined as above, which is acylated by means of benzoyl chloride in which the phenyl ring is optionally substituted or by means of thienyl chloride, of furoyl chloride or of a product of general formula.

[0063] in which R₆ is defined as above and X represents a halogen atom (fluorine, chlorine) or a residue —O—R₇ or —O—CO—O—R₇, to obtain a product of general formula (I) in which Z represents a radical of general formula (II).

[0064] Preferably, the product of general formula (V) is treated with formic acid at a temperature in the region of 20°C to yield the product of general formula (VII).

[0065] Preferably, the acylation of the product of general formula (VII) by means of a benzoyl chloride in which the phenyl radical is optionally substituted or by means of thienyl chloride, of furoyl chloride or of a product of general formula (VIII) is performed in an inert organic solvent chosen from esters such as ethyl acetate, isopropyl acetate or n-butyl acetate and halogenated aliphatic hydrocarbons such as dichloromethane or 1,2-dichloroethane, in the presence of an inorganic base such as sodium bicarbonate or an organic base such as triethylamine. The reaction is performed at a temperature of from 0 to 50°C, and preferably at about 20°C.

[0066] b) when R₁ represents an optionally substituted benzoyl radical, a thienyl or furoyl radical or a radical R₆O—CO— in which R₆ is defined as above, R₆ represents a hydrogen atom or an alkoxy radical containing 1 to 4 carbon atoms or a phenyl radical substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms and R₇ represents a hydrogen atom, replacement of the protective group formed by R₆ and R₇ by hydrogen atoms is performed in the presence of an inorganic acid (hydrochloric acid, sulphuric acid) or organic acid (acetic acid, methanesulphonic acid, trifluoromethanesulphonic acid, p-toluenesulphonic acid) used alone or mixed in a stoichiometric or catalytic amount, working in an organic solvent chosen from alcohols, ethers, esters, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons and aromatic hydrocarbons at a temperature of from -10 to 60°C, and preferably from 15 to 30°C.

[0067] According to the invention, the products of general formula (III), that is to say the products of general formula...
(I) in which Z represents a hydrogen atom and R₄ and R₅ are defined as above, may be obtained from 10-deacetylbaccatin III of formula (IX):

(IX)

(0068) It can be especially advantageous to protect the hydroxyl functions at the positions 7 and 13 selectively, for example in the form of a silyl diether which may be obtained by the action of a silyl halide of general formula:

(RO₃)₂Si—H₂Si(R₄)₂—Sil (X)

(0069) in which the symbols R, which may be identical or different, represent an alkyl radical containing 1 to 6 carbon atoms, optionally substituted with a phenyl radical, or a cycloalkyl radical containing 3 to 6 carbon atoms or a phenyl radical, on 10-deacetylbaccatin III, to obtain a product of general formula (XI):

(XI)

(0070) in which R is defined as above, followed by the action of a product of general formula:

R₂—X₂ (XII)

(0071) in which R₄ represents a radical such that R₄—O is identical to R₄ defined as above and X₁ represents a reactive ester residue such as a sulphonic or sulphonic ester residue or a halogen atom, to obtain a product of general formula (XIII):

(XIII)

(0072) in which R and R₄ are defined as above, the silyl protective groups of which are replaced by hydrogen atoms to obtain a product of general formula (XIV):

(XIV)

(0073) in which R₄ is defined as above, which is etherified selectively at position 7 by the action of a product of general formula:

R₂—X₂ (XV)

(0074) in which R₄ represents a radical such that R₄—O is identical to R₄ defined as above and X₂ represents a halogen atom or a reactive ester residue such as a sulphonic or sulphonic ester residue, to give the product of general formula (III).

(0075) Generally, the action of a silyl derivative of general formula (X) on 10-deacetylbaccatin III is performed in pyridine or triethylamine, where appropriate in the presence of an organic solvent such as an aromatic hydrocarbon, for instance benzene, toluene or xylene, at a temperature between 0° C. and the refluxing temperature of the reaction mixture.

(0076) Generally, the action of a product of general formula (XII) on a product of general formula (XI) is performed, after metatation of the hydroxyl function at position 10 by means of an alkali metal hydride, such as sodium hydride, an alkali metal amide, such as lithium amide, or an alkali metal alkylide, such as butyllithium, working in an organic solvent, such as dimethylformamide or tetrahydrofuran, at a temperature of from 0 to 50° C.

(0077) Generally, the replacement of the silyl protective groups of the product of general formula (XIII) by hydrogen atoms is performed by means of an acid such as hydrofluoric acid or trifluoroacetic acid in the presence of a base such as triethylamine or pyridine optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms, the base optionally being combined with an inert organic solvent such as a nitrile, for instance acetonitrile, or a halogenated aliphatic hydrocarbon, such as dichloromethane, at a temperature of from 0 to 80° C.

(0078) Generally, the action of a product of general formula (XV) on a product of general formula (XIV) is performed under the conditions described above for the action of a product of general formula (XII) on a product of general formula (XI).

(0079) According to the inventions the products of general formula (I) in which Z represents a radical of general formula (II), R₃ is defined as above and R₅ is defined as above may be obtained from a product of general formula (XVI):
[0080] In which R, R, R, and R, are defined as above, by silylation at position 7 by means of a product of general formula (X), to obtain a product of general formula (XVII):

\[
\text{(XVII)} \quad R \quad R \quad \text{O} \quad \text{O} \quad \text{Si}(R) \quad \text{O} \quad \text{N} \quad \text{O}
\]

[0083] Which, by the action of a product of general formula (XV), yields the product of general formula (V), the protective groups of which are replaced by hydrogen atoms to give a product of general formula (I) in which Z represents a radical of general formula (II).

[0084] The reactions used for silylation, functionalization and replacement of the protective groups by hydrogen atoms are performed under conditions similar to those described above.

[0085] The products of general formula (XVI) may be obtained under the conditions described in European Patent EP 0,336,841 and international Applications PCT WO 92/09589 and WO 94/07878, the disclosures of which are hereby incorporated by reference in their entirety, or from the products of general formula (XX):

\[
\text{(XX)}
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[0081] In which R, R, R, R, and R, are defined as above, which is functionalized at position 10 by means of a product of general formula (XII) to give a product of general formula (XVIII):

\[
\text{(XVIII)}
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[0086] In which R, and R, are defined as above, according to known methods for protecting the hydroxyl function of the side chain without affecting the remainder of the molecule.

[0087] According to the invention, the products of general formula (I) in which Z represents a hydrogen atom or a radical of general formula (II) may be obtained by the action of activated Raney nickel, in the presence of an aliphatic alcohol containing 1 to 3 carbon atoms or an ether such as tetrahydrofuran or dioxane, on a product of general formula (XXI).
in which \( R_4 \) is defined as above and \( R' \) and \( R'' \), which may be identical or different, represent a hydrogen atom or an alkyl radical containing 1 to 6 carbon atoms, an alkynyl radical containing 2 to 6 carbon atoms, an alkenyl radical containing 2 to 6 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms or a cycloalkenyl radical containing 3 to 6 carbon atoms, optionally substituted, or alternatively \( R' \) and \( R'' \), together with the carbon atom to which they are linked, form a cycloalkyl radical containing 3 to 6 carbon atoms or a cycloalkenyl radical containing 4 to 6 carbon atoms, and \( Z_1 \) represents a hydrogen atom or a radical of general formula (XXI):

\[
\text{(XXI)}
\]

in which \( R_2, R_3, R_5 \), and \( R_7 \) are defined as above, and, to obtain a product of general formula (XXIII):

\[
\text{(XXIII)}
\]

followed, when \( Z_2 \) represents a radical of general formula (XXII), that is to say when the product of general formula (XXIII) is identical to the product of general formula (V), by replacement of the protective groups represented by \( R_6 \) and/or \( R_8 \) and \( R_9 \) by hydrogen atoms under the conditions described above.

Generally, the action of activated Raney nickel in the presence of an aliphatic alcohol or an ether is performed at a temperature of from \(-10\) to \(60^\circ C\).

According to the invention, the product of general formula (XXI) in which \( Z_1 \) and \( R_4 \) are defined as above may be obtained by the action of a sulphoxide of general formula (XXIV):

\[
\text{(XXIV)}
\]

in which \( R' \) and \( R'' \) are defined as above, on a product of general formula (XIX).

Generally, the reaction of the sulphones of general formula (XXIV), preferably dimethyl sulphonie oxide, with the product of general formula (XIX) is performed in the presence of a mixture of acetic acid and acetic anhydride or a derivative of acetic acid such as a haloacetic acid at a temperature of from 0° to 50° C., and preferably at about 25° C.

The new products of general formula (I) obtained by carrying out the processes according to the invention may be purified according to known methods such as crystallization or chromatography.

The products of general formula (I) in which \( Z \) represents a radical of general formula (II) display noteworthy biological properties.

In vitro, measurement of the biological activity is performed on tubulin extracted from pig's brain by the method of M. L. Shelanski et al., Proc. Natl Acad. Sci. USA, 70, 765-768 (1973). Study of the depolymerization of microtubules to tubulin is performed according to the method of G. Chauvière et al., C.R. Acad. Sci., 293, series II, 501-503 (1981). In this study, the products of general formula (I) in which \( Z \) represents a radical of general formula (II) were shown to be at least as active as taxol and Taxotere.

In vivo, the products of general formula (I) in which \( Z \) represents a radical of general formula (II) were shown to be active in mice grafted with B16 melanoma at doses of from 1 to 30 mg/kg administered intraperitoneally, as well as on other liquid or solid tumours.

The new products have antitumour properties, and more especially activity against tumours which are resistant to Taxol® or to Taxotere®. Such tumours comprise colon tumours which have a high expression of the mdr 1 gene (multiple drug resistance gene). Multiple drug resistance is a customary term relating to the resistance of a tumour to different products having different structures and mechanisms of action. Taxoids are generally known to be strongly recognized by experimental tumours such as P388/DOX, a cell line selected for its resistance to doxorubicin (DOX) which expresses mdr 1.

The examples which follow illustrate the present invention.

**EXAMPLE 1**

126 mg of dicyclohexylcarbodiimide and then 14 mg of 4-(N,N-dimethylamino)pyridine were added succes-
sively at a temperature in the region of 20°C. To a suspension containing 217.8 mg of 4-acetoxy-2-c-benzoyloxy-5H,20-epoxy-11,13c-dihydroxy-7β,10β-dimethoxy-9-oxo-11-taxane, 200 mg of (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-
methoxyphenyl)-4-penyl-1,3-oxazolidine-5-carboxylic acid and 50 mg of powdered 4 Å molecular sieve in 2 cm³ of ethyl acetate. The suspension obtained was stirred at a temperature in the region of 20°C. under an argon atmosphere for 16 hours, and then concentrated to dryness under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. The residue obtained was purified by chromatography at atmospheric pressure on 50 g of silica (0.063-0.2 mm) contained in a column 2 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 10:90 to 40:60 by volume), collecting 10-cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C. For 2 hours, 271.8 mg of 4-acetoxy-2-c-benzoyloxy-5β,20-epoxy-11-
hydroxy-7β,10β-dimethoxy-9-oxo-11-taxon-13c-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-penyl-
1,3-oxazolidine-5-carboxylate were thereby obtained in the form of a white solid, the characteristics of which were as follows:

**[0102]** 1H NMR spectrum (400 MHz; CDCl₃), chemical shifts δ in ppm; coupling constants J in Hz: 1.02 (d, 3H, CH₃); 1.10 (s, 3H, CH₃); 1.17 (s, 3H, CH₃); 1.63 (s, 3H, CH₃); from 1.65 to 1.85 and 2.60 (2 mts, 1H each; CH₃ at position 6); 1.78 (unres. comp., 3H, CH₃); 2.02 and 2.15 (2 d, J=14 and 9, 1H each; CH₃ at position 14); 2.14 (s, 3H, CH₃); 3.22 and 3.35 (2 s, 3H each; OCH₃); 3.64 (d, J=7, 1H; at position 3); 3.75 (mt, 1H; at position 7); 3.76 (s, 3H, ArOCH₃); 4.06 and 4.16 (2 d, J=5.5, 1H each; CH₃ at position 20); 4.53 (d, J=5.5, 1H; at position 2); 4.67 (s, 1H; at position 10); 4.85 (broad br, J=10, 1H; at position 5); 5.36 (mt, 1H; at position 9); 5.52 (d, J=7, 1H; at position 2); 6.07 (mt, 1H; at position 13); 6.33 (unres. comp., 1H; at position 5); 6.88 (d, J=8, 2H; aromatic H at the ortho position with respect to OCH₃); from 7.25 to 7.40 (mt, 7H; aromatic H at position 3' and aromatic H at the meta position with respect to OCH₃); 7.43 (t, J=7.5, 2H; OCOCH₃,H at the meta position); 7.58 (t, J=7.5, 1H; OCOCH₃H at the para position); 7.96 (d, J=7.5, 2H; OCOCH₃H at the ortho position).

**[0103]** A solution of 446.3 mg of 4acetoxy-2-c-benzoyloxy-5β,20-epoxy-11-hydroxy-7β,10β-dimethoxy-9-oxo-11-taxon-13c-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-penyl-1,3-oxazolidine-5-carboxylate in 11.6 cm³ of a 0.1N solution of hydrogen chloride in ethanol was stirred constantly at a temperature in the region of 0°C. for 16 hours under an argon atmosphere. The reaction mixture was then diluted with 40 cm³ of dichloromethane and 5 cm³ of distilled water. After settling had taken place, the aqueous phase was separated and extracted with 5 cm³ of dichloromethane. The organic phases were combined, dried over magnesium sulphate, filtered through sintered glass and then concentrated to dryness under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 570 mg of a pale yellow solid were thereby obtained, which product was purified by preparative thin-layer chromatography [12 Marek preparative silica gel 60%25 Å plates, thickness 1 mm, application in solution in a methanol/dichloromethane (5:95 by volume) mixture, eluting with a methanol/dichloromethane (3:95 by volume) mixture]. After elution of the zone corresponding to the main product with a methanol/dichloromethane (15:85 by volume) mixture, filtration through sintered glass and evaporation of the solvents under reduced pressure (0.27 kPa) at a temperature in the region of 40°C., 126 mg of 4acetoxy-2-c-benzoyloxy-5β,20-epoxy-
11-hydroxy-7β,10β-dimethoxy-9-oxo-11-taxon-13c-yl (2R,3S)3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionic acid was obtained in the form of an ivory-coloured foam, the characteristics of which were as follows:

**[0104]** optical rotation [α]₂³⁰D = -32.9 (c=0.5; methanol)

**[0105]** 1H NMR spectrum (400 MHz; CDCl₃), chemical shifts δ in ppm; coupling constants J in Hz: 1.23 (3, 3H, CH₃); 1.25 (3, 3H, CH₃); 1.39 (3, 3H, CH₃); 1.70 (s, 1H; OH at position 1); 1.75 (s, 3H, CH₃); 1.82 and 2.72 (2 mts, 1H each; CH₃ at position 6); 1.91 (s, 3H, CH₃); 2.31 (limiting AB, 2H, CH at position 14); 2.39 (3, s, 3H, COCH₃); 3.33 and 3.48 (2 s, 3H each; OCH₃); 3.48 (mt, 1H; at position 2); 3.85 (d, J=7, 1H; H 3); 3.88 (dd, J=11 and 7, 1H; H 7); 4.20 and 4.33 (2 d, J=8.5, 1H each; CH₂ at position 20); 4.65 (mt, 1H; at position 2); 4.83 (s, 1H; at position 10); 5.00 (broad d, J=10, 1H; at position 5); 5.30 (broad br, J=10, 1H; at position 3); 5.47 (d, J=10, 1H; CONH); 5.66 (d, J=7, 1H; at position 2); 6.24 (broad t, J=9, 1H; at position 13); from 7.30 to 7.50 (mt, 5H aromatic H at position 3'); 7.52 (t, J=7.5, 2H; OCOCH₃H, H at the meta position); 7.63 (t, J=7.5, 1H; OCOCH₃H, H at the para position); 8.12 (d, J=7.5, 2H; OCOCH₃H, at the ortho position).

**[0106]** 4acetoxy-2-c-benzoyloxy-5β,20-epoxy-11,13c-dihydroxy-7β,10β-dimethoxy-9-oxo-11-taxane (or 7β,10β-
dimethoxy-10-deacetoxybaccatin III) was prepared in the following manner:

**[0107]** 86 mg of sodium hydride at a concentration of 50% by weight in liquid paraffin were added portionwise to a solution, maintained under an argon atmosphere, at a temperature in the region of 0°C, of 500 mg of 4acetoxy-
2-c-benzoyloxy-5β,20-epoxy-11,13c-dihydroxy-7β,10β-dimethoxy-9-oxo-11-taxane in 5 cm³ of isodimethane and 0.5 cm³ of dimethylformamide. After 45 minutes at a temperature in the region of 0°C, the reaction mixture was diluted with 50 cm³ of ethyl acetate and 8 cm³ of distilled water. After settling had taken place, the organic phase was separated and washed with twice 8 cm³ of distilled water and then 8 cm³ of saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 280 mg of 4acetoxy-2-c-benzoyloxy-5β,20-epoxy-11,13c-dihydroxy-7β,10β-dimethoxy-9-oxo-11-taxane were thereby obtained in the form of a pale yellow solid, the characteristics of which were as follows:

**[0108]** 1H NMR spectrum (400 MHz; CDCl₃), with a few drops of CD₃OD-d₆, chemical shifts δ in ppm; coupling constants J in Hz: 1.03 (3, 3H, CH₃); 1.11 (3, 3H, CH₃); 1.65 (s, 3H, CH₃); 1.72 and 2.67 (2 mts, 1H each; CH₃ at position 6); 2.05 (3, 3H, CH₃); 2.21 (limiting AB, J=14 and 9, 2H; CH₂ at position 14); 2.25 (3, 3H, COCH₃); 3.26 and 3.40 (2
s, 3H each: OCH₃); 3.85 (d, J=7, 1H: H at position 3); 3.89 (dd, J=11 and 6.5, 1H: H at position 7); 4.12 and 4.25 (2 d, J=8.5, 1H each: CH₃: H at position 20); 2.97 (broad d, J=11, 1H: H at position 6); 7.39 (t, J=7.5, 1H: OCOC₃H₇ at the meta position); 7.63 (t, J=7.5, 1H: OCOC₃H₇ H at the para position); 8.12 (d, J=7.5, 2H: OCOC₃H₇ H at the ortho position).

[0109] 4α-Acetoxy-2α-benzoyloxy-5β,20-epoxy-1β,7β, 13α-trihydroxy-10β-methoxy-9-oxo-11-taxene (or 10β-methoxy-10-deacetoxybaccatin III) was prepared in the following manner:

[0110] 50 cm³ of hydrogen fluoride/triethylamine complex (3H:Et₃N) were added slowly to a solution, maintained under an argon atmosphere, at a temperature in the region of 0°C, of 3.62 g of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene in 10 cm³ of dichloromethane. After 48 hours at a temperature in the region of 20°C, the reaction mixture was poured into a suspension of 100 cm³ of super-saturated aqueous sodium hydrogen carbonate solution maintained at a temperature in the region of 0°C. After settling had taken place, the aqueous phase was separated and reextracted with three times 80 cm³ of dichloromethane and then twice 80 cm³ of ethyl acetate. The organic phases were combined, dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 3.45 g of a yellow foam were thereby obtained, which product was purified by chromatography at atmospheric pressure on 150 g of silica (0.063-0.2 mm) contained in a column 3.5 cm in diameter, eluting with a methanol/dichloromethane (5:95 by volume) mixture and collecting 35 cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 1.97 g of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β,7β, 13α-trihydroxy-10β-methoxy-9-oxo-11-taxene were thereby obtained in the form of a white solid, the characteristics of which were as follows:

[0111] 1H NMR spectrum (400 MHz; CDCl₃): chemical shifts δ in ppm; coupling constants J in Hz): 1.10 (s, 3H: CH₃); 1.19 (s, 3H: CH₃); 1.48 (d, J=8.5, 1H: OH at position 13); 1.70 (s, 3H: CH₃); 1.81 and 2.01 (2 mts, 1H each: CH₂ at position 6); 2.09 (d, J=5, 1H: OH at position 7); 2.11 (s, 3H: CH₃); 2.30 (s, 3H: COCH₃); 2.32 (d, J=9, 2H: CH₂ at position 20); 2.43 (mt, 1H: H at position 7); 4.93 (mt, 1H: H at position 13); 4.99 (s, 1H: H at position 10); 5.01 (broad d, J=10, 1H: H at position 5); 5.66 (d, J=7, 1H: H at position 2); 7.49 (t, J=7.5, 2H: OCOC₃H₇ at the meta position); 7.63 (t, J=7.5, 1H: OCOC₃H₇ H at the para position); 8.12 (d, J=7.5, 2H: OCOC₃H₇ H at the ortho position).

[0112] 4α-Acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene (or 10β-methoxy-10-deacetoxy-7,13-bis(triethylsilyl) baccatin III) was prepared in the following manner:

[0113] 375 mg of sodium hydride at a concentration of 50% by weight in liquid paraffin were added portwise to a solution, maintained under an argon atmosphere, at a temperature in the region of 0°C, of 5 g of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β,10β-dihydroxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene in 25 cm³ of isodamethane. The solution was stirred constantly for 45 minutes at a temperature in the region of 0°C, and then for 5 hours 30 minutes at a temperature in the region of 20°C. The reaction mixture was cooled again to a temperature in the region of 0°C, and 125 mg of sodium hydride at a concentration of 50% by weight in liquid paraffin were added portionwise. After 1 hour at 20°C and then 18 hours at 5°C, the reaction mixture was diluted by adding 50 cm³ of dichloromethane and poured into 50 cm³ of saturated aqueous ammonium chloride solution, and settling was allowed to take place. The aqueous phase was separated and extracted with twice 30 cm³ of dichloromethane, and the organic phases were then combined, washed with 10 cm³ of distilled water, dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 5.15 g of a yellow foam were thereby obtained, which product was purified by chromatography at atmospheric pressure on 300 g of silica (0.063-0.2 mm) contained in a column 5 cm in diameter (elution gradient: ethyl acetate/ dichloromethane from 0:100 to 90:10 by volume), collecting 30 cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 3.62 g of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene were thereby obtained in the form of a pale yellow foam, the characteristics of which were as follows:

[0114] 1H NMR spectrum (600 MHz; CDCl₃): chemical shifts δ in ppm; coupling constants J in Hz): 0.58 and 0.69 (2 mts, 6H each: ethyl CH₂); 0.97 and 1.04 (2, J=7.5, 9H each: ethyl CH₂); 1.15 (s, 3H: CH₃); 1.18 (s, 3H: CH₃); 1.58 (s, 1H: OH at position 1); 1.68 (s, 3H: CH₃); 1.89 and 2.48 (2 mts, 1H each: CH₂ at position 6); 2.04 (s, 3H: CH₃); 2.15 and 2.23 (2 dd, J=16 and 9, 1H each: CH₂ at position 14); 2.29 (s, 3H: COCH₃); 3.40 (s, 3H: CH₃); 3.83 (d, J=7, 1H: H at position 13); 4.15 and 4.30 (2 dd, J=6.5, 1H each: CH₂ at position 20); 4.43 (dd, J=11 and 7, 1H: H at position 7); 4.91 (s, 1H: H at position 10); 4.96 (broad d, J=10, 1H at position 5); 5.01 (broad t, J=9, 1H: H at position 13); 5.62 (d, J=7, 1H: H at position 2); 7.46 (t, J=7.5, 2H: OCOC₃H₇ H at the meta position); 7.60 (t, J=7.5, 1H: OCOC₃H₇ H at the para position); 8.09 (d, J=7.5, 2H: OCOC₃H₇ H at the ortho position).

[0115] 4α-Acetoxy-2α-benzoyloxy-5β,20-epoxy-1β,10β-dihydroxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene (or 10-deacetyl-7,13-bis(triethylsilyl) baccatin III) was prepared in the following manner:

[0116] 10.8 cm³ of triethylsilyl chloride were added to a solution, maintained under an argon atmosphere, at a temperature in the region of 20°C, of 14 g of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β,7β,10β,13α-tetrahydroxy-9-oxo-11-taxene (10-deacetyl baccatin III) in 50 cm³ of anhydrous pyridine. After 17 hours at a temperature in the region of 20°C, the reaction mixture was brought to a temperature in the region of 115°C and 10.8 cm³ of triethylsilyl chloride were then added. After 3 hours 15 minutes at a temperature in the region of 115°C, the reaction mixture was brought back to a temperature in the region of 20°C and diluted with 30 cm³ of ethyl acetate and 100 cm³ of distilled water. After settling took place, the
aqueous phase was separated and extracted with twice 50 cm of ethyl acetate. The organic phases were combined, washed with 50 cm of saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered through sintered glass and then concentrated to dryness under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 63.1 g of a brown oil were thereby obtained, which product was purified by chromatography on a column 7 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 0:100 to 5:95 by volume), collecting 60-cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 9.77 g of 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B,10B-dihydroxyster-9-oxo-7B,13a-bis(triethylsilyl)oxy)-11-taxene were thereby obtained in the form of a cream-coloured foam, the characteristics of which were as follows:

**[0117]** 1H NMR spectrum (400 MHz; CDCl₃); chemical shifts δ in ppm; coupling constants J in Hz): 0.55 and 0.68 (2 ms, 6H each: ethyl CH₂); 1.04 and 1.06 (2 t, 1J = 7.5, 9H each: ethyl CH₂); 1.08 (s, 3H: CH₃); 1.17 (s, 3H: CH₃); 1.58 (s, 1H: OH at position 1); 1.73 (s, 3H: CH₃); 1.91 and 2.57 (2 ms, 1H each: CH₂ at position 2); 2.04 (s, 3H: CH₃); 2.12 and 2.23 (2 dd, J = 16 and 9, 1H each: CH₃ at position 4); 2.30 (s, 3H: COCH₃); 3.88 (d, J = 7, 1H at position 3); 4.16 and 4.32 (2 d, J = 8.5, 1H each: CH₂ at position 20); 4.27 (d, J = 1, 1H: OH at position 10); 4.40 (dd, J = 11 and 7, 1H: H at position 7); 4.95 (broad d, J = 10, 1H: H at position 5); 4.95 (mt, 1H: H at position 13); 5.16 (d, J = 11, 1H: H at position 10); 5.60 (d, J = 7, 1H: H at position 2); 7.46 (t, J = 7.5, 2H: OCOCH₃ H at the meta position); 7.60 (t, J = 7.5, 1H: OCOCH₃ H at the para position); 8.09 (d, J = 7.5, 2H: OCOCH₃ H at the ortho position).

**EXAMPLE 2**

340 mg of 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B-hydroxy-7B,10B-dimethoxy-9-oxo-11-taxen-13c-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate were dissolved in 8 cm of a 0.1N ethanol solution of hydrochloric acid containing 1% of water. The solution thereby obtained was stirred for 13 hours at a temperature in the region of 20°C and then for 80 hours at 40°C, and 20 cm³ of dichloromethane were added. The organic phase was separated after settling had taken place and washed successively with 3 times 5 cm³ of saturated aqueous sodium hydrogen carbonate solution, dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 300 mg of a white foam were obtained, which product was purified by chromatography on silica gel coated on plates [gel 1 mm thick, plates 20x20 cm, eluent: dichloromethane/ethyl acetate (90:10 by volume)] in 80 mg fractions (4 plates). After localization with UV rays of the zone corresponding to the adsorbed desired product, this zone was scraped off, and the silica collected was washed on sintered glass with 10 times 5 cm³ of ethyl acetate. The filtrates were combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. A white foam was obtained, which was repurified according to the same technique [3 plates: 20x20 cm; eluent: dichloromethane/ethyl acetate (90:10 by volume)]. 205 mg of 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B-hydroxy-7B,10B-dimethoxy-9-oxo-11-taxen-13c-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate were thereby obtained in the form of a white foam, the characteristics of which were as follows:

**[0119]** optical rotation: [α]20D = -33 (c=0.5, methanol).

**[0120]** 1H NMR spectrum (400 MHz; CDCl₃); chemical shifts δ in ppm; coupling constants J in Hz): 1.23 (s, 3H: —CH₃); 1.25 (s, 3H: —CH₃); 1.39 [s, 9H: —CH(CH₃)₂]; 1.70 (s, 1H: —OH at position 1); 1.75 (s, 3H: —CH₃); 1.82 and 2.72 (2 ms, 1H each: —CH₂ at position 6); 1.91 (s, 3H: —CH₃); 2.31 (limiting AB, 2H: —CH₂ at position 14); 2.39 (s, 3H: —COCH₃); 3.33 and 3.48 (2 s, 3H each: —OCH₃); 3.48 (mt, 1H: OH at position 2); 3.85 (d, J = 7, 1H: —H at position 3); 3.88 (dd, J = 11 and 7, 1H: —H at position 7); 4.20 and 4.33 (2 dd, J = 8.5, 1H each: —CH₂ at position 20); 4.65 (mt, 1H: —H at position 2); 4.83 (s, 1H: —H at position 10); 5.00 (broad d, J = 10, 1H: —H at position 5); 5.30 (broad d, J = 10, 1H: —H at position 3); 5.47 (d, J = 10, 1H: —CONH—); 5.66 (d, J = 7, 1H: —H at position 2); 6.24 (broad t, J = 9, 1H: —H at position 13); from 7.30 to 7.50 (mt, 5H: —C₆H₅ at position 3); 7.52 [t, J = 7.5, 2H: —OCCOCH₃H (—H at position 3 and H at position 5)]; 7.63 [t, J = 7.5, 1H: —OCCOCH₃H (—H at position 2 and H at position 6)]; 8.12 [d, J = 7.5, 2H: —OCCOCH₃H (—H at position 2 and H at position 6)].

**[0121]** 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B-hydroxy-7B,10B-dimethoxy-9-oxo-11-taxen-13c-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate was prepared in the following manner:

**[0122]** 100 cm³ of an ethanolic suspension of activated nickel according to Raney (obtained from 80 cm³ of the approximately 50% commercial aqueous suspension by successive washing, to a pH in the region of 7, with 15 times 100 cm³ of distilled water and with 5 times 100 cm³ of ethanol) were added at a temperature in the region of 20°C to a solution, maintained under an argon atmosphere and kept stirring, of 1 g of 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B-hydroxy-7B,10B-bis(methylthiomethylthio) oxy-oxo-11-taxen-13c-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 100 cm³ of anhydrous ethanol. The reaction medium was kept stirring for 24 hours at a temperature in the region of 20°C and then filtered through sintered glass, the sintered glass was washed with 4 times 80 cm³ of ethanol, and the filtrates were combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 710 mg of a yellow foam were obtained, which product was purified by chromatography on silica gel coated on plates [gel 1 mm thick, plates 20x20 cm, eluent: dichloromethane/ethyl acetate (90:10 by volume)], collecting 6-cm³ fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 350 mg of 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B-hydroxy-7B,10B-dimethoxy-9-oxo-11-taxen-13c-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate were thereby obtained in the form of a white foam.

**[0123]** 4-acetoxy-2a-benzoyloxy-5B,20-epoxy-1B-hydroxy-7B,10B-bis(methylthiomethylthio)oxy-oxo-11-taxen-13c-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate was prepared in the following manner:
2.3 cm³ of acetic acid and 7.55 cm³ of acetic anhydride were added at a temperature in the region of 20°C. to a solution, maintained under an argon atmosphere and kept stirring, of 3.1 g of 4-acetoxy-2-benzoxazolyl-5β,20-epoxy-1β-hydroxy-9-oxo-7β,10β-bis(2,2,2-trichloroethoxy-carbonyl)-11-taxon-13α-y1 (2R,4S,5R)-3-tet-butoxy-carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid and 7.55 cm³ of acetic anhydride. The mixture reaction was kept stirring for 7 days at a temperature in the region of 20°C, and then poured into a mixture of 500 cm³ of distilled water and 250 cm³ of dichloromethane. 30 cm³ of saturated aqueous potassium carbonate solution were then added with efficient stirring to a pH in the region of 7. After 10 minutes of stirring, the organic phase was separated after settling had taken place and the aqueous phase was extracted with twice 250 cm³ of dichloromethane. The organic phases were combined, washed with 250 cm³ of distilled water, dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 5.2 g of a pale yellow oil were obtained, which product was purified by chromatography on 200 g of silica (0.063-0.4 mm) contained in a column 3 cm in diameter (elucent: dichloromethane:methanol 99:1 by volume), collecting 50-cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.25 g of 4-acetoxy-2-benzoxazolyl-5β,20-epoxy-1β-hydroxy-7β,10β-bis(methylthioether)-9-oxo-11-taxon-13α-y1 (2R,4S,5R)-3-tet-butoxy-carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid were thereby obtained in the form of a white foam.

A solution of 5.1 g of 4-acetoxy-2-benzoxazolyl-5β,20-epoxy-1β-hydroxy-9-oxo-7β,10β-bis(2,2,2-trichloroethoxy-carbonyl)-11-taxon-13α-y1 (2R,4S,5R)-3-tet-butoxy-carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid in a mixture of 100 cm³ of methanol and 100 cm³ of acetic acid was heated, with stirring and under an argon atmosphere, to a temperature in the region of 60°C., and 10 g of powdered zinc were then added. The reaction mixture was then stirred for 15 minutes at 60°C., thereafter cooled to a temperature in the region of 20°C. and passed through a filtered glass lined with Celite. The filtered glass was washed with twice 15 cm³ of methanol. The filtrate was concentrated to dryness under reduced pressure (2.7 kPa) at a temperature in the region of 40°C. 50 cm³ of ethyl acetate and 25 cm³ of saturated aqueous sodium hydrogen carbonate solution were added to the residue. The organic phase was separated after settling had taken place and washed successively with 25 cm³ of saturated aqueous sodium hydrogen carbonate solution and with 25 cm³ of distilled water, then dried over magnesium sulphate, filtered through the glass and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 3.1 g of 4-acetoxy-2-benzoxazolyl-5β,20-epoxy-1β-hydroxy-9-oxo-7β,10β-bis(methylthioether)-11-taxon-13α-y1 (2R,4S,5R)-3-tet-butoxy-carbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid were thereby obtained in the form of a white foam.
A solution of 48 mg of 4-ace-acetoxyc-2a-benzoyloxy-5f,20-epoxy-10β-ethoxy-11-hydroxy-7β-methoxy-9-oxo-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxy carbonyl-2-(4-methoxyphethyl)-phenyl-1,3-oxazolidine-5-carboxylate in 0.5 cm³ of ethyl acetate and 0.004 cm³ of 37% hydrochloric acid was kept stirring at a temperature in the region of 20°C for 1.5 hours under an argon atmosphere. The reaction mixture was then purified by preparative thin-layer chromatography: application of the crude reaction mixture to 5 Merck preparative silica gel 60F254 plates, thickness 0.5 mm, eluting with a methanol/dichloromethane (4:96 by volume) mixture. After elution of the zone corresponding to the main product with a methanol/dichloromethane (15:85 by volume) mixture, filtration through cotton wool and then evaporation of the solvents under reduced pressure (2.7 kPa) at a temperature in the region of 40°C, 2.65 mg of 4-ace-acetoxyc-2a-benzoyloxy-5f,20-epoxy-10β-ethoxy-1β-hydroxy-7β-methoxy-9-oxo-11-taxen-13α-yl (2R,3S)-3-tert-butoxy carbonylamino-2-hydroxy-3-phenyl propanoate were obtained in the form of an ivory-coloured foam, the characteristics of which were as follows:

**1H NMR spectrum (400 MHz; CDCl3, chemical shifts δ in ppm; coupling constants J in Hz):**
- 1.22 (s, 3H, CH3)
- 1.25 (s, 3H, CH3)
- 1.32 (s, J=7.3H, ethyl CH2)
- 1.38 (s, 9H, C(CH3)3)
- 1.64 (s, 1H, OH at position 1)
- 1.73 (s, 3H, CH3)
- 1.60 and 2.70 (2 mts, 1H each: CH2 at position 6)
- 1.88 (s, 3H, CH3)
- 2.30 (mt, 2H, CH2 at position 14)
- 2.38 (s, 3H, COCH3)
- 3.31 (s, 3H, OCH3)
- 3.44 (unres. comp., 1H: OH at position 2)
- 3.50 and 3.70 (2 mts, 1H each: ethyl OCH2)
- 3.64 (d, J=7.5, 1H at position 3)
- 3.67 (dd, J=11 and 6.5, 1H: H at position 7)
- 4.18 and 4.32 (2 d, J=6.5, 1H each: CH3 at position 20)
- 4.64 (mt, 1H: H at position 2)
- 4.90 (s, 1H, H at position 10)
- 4.98 (broad d, J=10, 1H, H at position 5)
- 5.28 (broad d, J=10, 1H, H at position 3)
- 5.42 (d, J=10, 1H, CONH)
- 5.64 (d, J=7.5, 1H: H at position 2)
- 6.22 (broad t, J=9, 1H: H at position 13)
- From 7.25 to 7.45 (mt, 5H aromatic H at position 3)
- 7.50 (d, J=7.5, 2H, OCOCH3, H at the meta position)
- 7.62 (t, J=7.5, 1H, OCOCH3, H at the para position)
- 8.12 (d, J=7.5, 2H, OCOCH3, H at the ortho position).

**32C NMR spectrum:**
- 43 mg of sodium hydride at a concentration of 50% by weight in liquid paraffin were added portionwise to a solution, maintained under an argon atmosphere, at a temperature in the region of 6°C, of 235 mg of 4-ace-acetoxyc-2a-benzoyloxy-5f,20-epoxy-10β-ethoxy-1β,13α-dihydroxy-7β-methoxy-9-oxo-11-taxene (or 10β-ethoxy-7β-methoxy-9-oxo-11-taxene) in 6 cm³ of dimethyl formamide. After 30 minutes at a temperature in the region of 0°C, the reaction mixture was diluted with 40 cm³ of ethyl acetate, 6 cm³ of distilled water and 8 cm³ of saturated aqueous ammonium chloride solution. After settling had taken place, the organic phase was separated and washed with three times 8 cm³ of distilled water and then 8 cm³ of saturated aqueous NaCl solution, dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (2.7 kPa) at a temperature in the region of 40°C. 268 mg of a yellow solid were thereby obtained, which product was purified by chromatography at atmospheric pressure on 50 g of silica (0.063–0.2 mm) contained in a column 2.5 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 0:100 to 15:85 by volume), collecting 10 cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 380 mg of 4-ace-acetoxyc-2a-benzoyloxy-5f,20-epoxy-10β-ethoxy-1β,13α-dihydroxy-7β-methoxy-9-oxo-11-taxene were thereby obtained in the form of a white powder, the characteristics of which were as follows:

**13C NMR spectrum (300 MHz; CDCl3, with the addition of a few drops of CD3OD-d8, chemical shifts δ in ppm, coupling constants J in Hz):**
- 1.09 (s, 3H, CH3)
- 1.22 (t, J=7, 3H, ethyl CH2)
- 1.62 (s, 3H, CH3)
- 1.68 and 2.66 (2 mts, 1H each: CH2)
- 2.03 (s, 3H, CH3)
- 2.13 and 2.22 (2 dd, J=16 and 9, 1H each: CH2 at position 14)
- 2.23 (s, 3H, COCH3)
- 3.23 (s, 3H, OCH3)
- From 3.40 to 3.65 (mt, 2H, ethyl CH2)
- 3.84 (d, J=7.5, 1H: H at position 3)
- 3.88 (dd, J=10 and 6.5, 1H: H at position 7)
- 4.10 and 4.23 (2 d, J=8.5, 1H each: CH2)
- 4.75 (broad t, J=9, 1H: H at position 13)
- 5.67 (s, 1H: H at position 10)
- 6.39 (d, J=10, 1H, H at position 5)
- 5.41 (d, J=7.5, 1H: H at position 2)
- 7.45 (d, J=7.5, 2H, OCOCH2, H at the meta position)
- 7.43 (d, J=7.5, 1H: OCOCH2, H at the ortho position).

**1H NMR (400 MHz, CDCl3, δ in ppm):**
- 9 cm³ of hydrogen fluoride/triethylamine complex (3HF:Et3N) were added to a solution, maintained under an argon atmosphere, at a temperature in the region of 20°C, of 591 mg of 4-ace-acetoxyc-2a-benzoyloxy-5f,20-epoxy-1β,13α-dihydroxy-10β-ethoxy-9-oxo-11-taxene (or 10β-ethoxy-10-deacetoxyc-baccatin III) was prepared in the following manner:

**13C NMR:** 230.2 mg of 4-ace-acetoxyc-2a-benzoyloxy-5f,20-epoxy-1β,13α-dihydroxy-10β-ethoxy-9-oxo-11-taxene were thereby obtained in the form of a white solid, the characteristics of which were as follows:
\[0137\] 1H NMR spectrum (400 MHz; CDCl₃; chemical shifts δ in ppm, coupling constants J in Hz): 1.08 (s, 3H: CH₃); 1.19 (s, 3H: CH₃); 1.29 (t, J=7.5, 3H: ethyl CH₂); 1.38 (d, J=9, 1H: OH at position 7); 1.59 (s, 1H: OH at position 1); 1.69 (s, 3H: CH₃); 1.82 and 2.62 (2 mts, each: CH₂ at position 6); 2.02 (d, J=5, 1H: OH at position 13); 2.08 (s, 3H: CH₃); 2.30 (s, 3H: COCl₂); 2.32 (d, J=9, 2H: CH₂ at position 14); 3.56 and 3.67 (2 mts, each: ethyl OCH₂); 3.98 (d, J=7, 1H: H at position 3); 4.18 and 4.33 (2 d, J=8.5 Hz, 1H each: CH₂); 4.30 (mt, 1H: H at position 10); 4.50 (mt, 1H: H at position 2); 4.79 (t, J=7.5, 2H: OCOCH₂-H at the meta position); 7.63 (t, J=7.5, 1H: OCOCH₂-H at the para position); 8.12 (d, J=7.5, 2H: OCOCH₂H H at the ortho position).

\[0139\] 93 mg of sodium hydride at a concentration of 50% by weight of liquid paraffin were added portionwise to a solution, maintained under argon atmosphere, at a temperature in the region of 20°C, of 1 g of 4-acetoxy-2a-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-ethoxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxane (or 10β-ethoxy-16-deacetoxy-7,13-bis(triethylsilyl)-baccatin III) was prepared in the following manner: 3.59 g of sodium hydride at a concentration of 50% by weight in liquid paraffin was then added portionwise. After 50 minutes at a temperature in the region of 20°C, the reaction mixture was diluted with 100 cm³ of ethyl acetate and 10 cm³ of saturated aqueous ammonium chloride solution. The organic phase was separated after settling had taken place and washed with six 10 cm³ portions of distilled water. The aqueous phase was then dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (2.7 kPa) at a temperature in the region of 40°C. 1.2 g of a yellow foam were thereby obtained, which product was purified by chromatography at atmospheric pressure on 150 g of silica (0.06-0.2 mm) contained in a column 3.5 cm in diameter, eluting with an ethyl acetate/dichloromethane (2:98) fraction of volume) mixture and collecting 15 cm³ fractions. Fractions containing only the desired compound were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C. 379.2 mg of 4-acetoxy-2a-benzoyloxy-5β,20-epoxy-1β,10β-dihydroxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxane were thereby obtained in the form of a pale yellow foam and 430 mg of 4-acetoxy-2a-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-ethoxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxane were obtained in the form of a white foam, the characteristics of which are as follows:

\[0140\] 1H NMR spectrum (400 MHz; CDCl₃; chemical shifts δ in ppm, coupling constants J in Hz): 0.57 and 0.70 (2 mts, 6H each; ethyl CH₂); 0.97 and 1.03 (2, J=7.5, 9H each: ethyl CH₂; 1.13 (s, 3H: CH₃); 1.20 (s, 3H: CH₃); 1.29 (t, J=7.5, 3H: CH₃ of ethoxy at position 10); 1.58 (s, 1H: OH at position 1); 1.66 (s, 3H: CH₃); 1.89 and 2.58 (2 mts, 1H each: CH₂ at position 2); 2.03 (s, 3H: CH₃); 2.13 and 2.23 (2 dd, J=16 and 9, 1H each: CH₂ at position 14); 2.30 (s, 3H: COCl₂); 3.53 (mt, 2H: CH₂ of ethoxy at position 10); 3.64 (d, J=7, 1H: H at position 3); 4.15 and 4.50 (2 d, J=8.5, 1H each: CH₂ at position 20); 4.43 (dd, J=11 and 6.5, 1H: H at position 7); from 4.90 to 5.00 (mt, 2H: H at position 13 and H at position 5); 5.01 (s, 1H: H at position 10); 5.61 (d, J=7, 1H: H at position 2); 7.48 (t, J=7.5, 2H: OCOCH₂H H at the meta position); 7.61 (t, J=7.5, 1H: OCOCH₂H H at the para position); 8.10 (d, J=7.5, 2H: OCOCH₂H H at the ortho position).

\[0141\] 65 mg of dicyclohexylcarbodiimide and then 7 mg of 4-(N,N-dimethylamino)pyridine were added successively at a temperature in the region of 20°C, to a suspension containing 115 mg of 4-acetoxy-2a-benzoyloxy-5β,20-epoxy-1β-(1-propyloxy)-1,13α-dihydroxy-7β-methoxy-9-oxo-11-taxene and 100 mg of (2R,4S,5R)-3-tert-butyloxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid in 1 cm³ of anhydrous toluene. The suspension obtained was stirred at a temperature in the region of 20°C under an argon atmosphere for 1 hour, and then purified by direct application to a column for chromatography at atmospheric pressure on 30 g of silica (0.063-0.2 mm) contained in a column 2.5 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 2:98 to 10:90 by volume), collecting 10 cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 2 hours. 276.2 mg of a white solid were thereby obtained, which product was purified by preparative thin-layer chromatography: 10 Merck preparative silica gel 60F₂₅₄ plates, thickness 0.5 mm, application in solution in dichloromethane, eluting with a methanol/dichloromethane (3:97 by volume) mixture. After elution of the zones corresponding to the main products with a methanol/methanol (15:85 by volume) mixture, filtration through cotton wool and then evaporation of the solvents under reduced pressure (2.7 kPa) at a temperature in the region of 40°C, 84.8 mg of 4-acetoxy-2a-benzoyloxy-5β,20-epoxy-1β-(1-propyloxy)-1,13α-dihydroxy-7β-methoxy-9-oxo-11-taxene (2R,4S,5R)-3-tert-butyloxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid were obtained in the form of a white foam, the characteristics of which were as follows:

\[0142\] 1H NMR spectrum (300 MHz; CDCl₃; chemical shifts δ in ppm, coupling constants J in Hz): 0.97 (t, J=7, 3H: propyl CH₃); 1.07 (s, 9H: (CH₃)₃Si); 1.19 (s, 6H: CH₃); from 1.50 to 1.80 (mt, 3H: OH at position 1 and central CH₂ of propyl); 1.60 (s, 3H: CH₃); 1.70 (s, 3H: CH₃); 1.78 and 2.63 (2 mts, 1H each: CH₂ at position 6); 1.82 (unres. comp. 3H: COCH₂); 2.07 and 2.19 (2 dd, J=16 and 9, 1H each: CH₂ at position 14); 3.26 (s, 3H: OCH₃); 3.30 and 3.58 (2 mts, 1H each: propyl OCH₂); 3.73 (d, J=7.5, 1H: H at position 3); 3.81 (s, 3H: ArOCH₂); 3.81 (mt, 1H: H at position 7); 4.09 and 4.23 (2 d, J=8.5, 1H each: CH₂ at position 20); 4.57 (d, J=4.5, 1H: H at position 2); 4.79 (s, 1H: H at position 10); 4.90 (broad d, J=10, 1H: H at position 5); 5.40 (unres. comp. 1H: H at position 3); 5.58 (d, J=7, 5H: H at position 2); 6.13 (broad d, J=9, 1H: H at position 13); 6.40 ( spreading unres. comp 1H: H at position 7); 6.92 (d, J=8.5, 2H: aromatic H at the ortho position with respect to OCH₂); from 7.30 to 7.60 (mt, 9H, 1H at position 3,—aromatic H at the meta position with respect to OCH₂ and OCOCH₂H meta H); 7.63 (t, J=7.5, 1H: OCOCH₂H H at the para position); 8.03 (d, J=7.5, 2H: OCOCH₂H H at the ortho position).
[0143] 4α-Acetoxy-2α-benzoyloxy-5β,20-epoxy-10β-(1-propyl)oxy-1β,11-deoxy-7β-methoxy-9-oxo-11-taxen-3β-yl (2R,3S)-3tert-butylobenzoylamino-2-hydroxy-3-pheny1propanoate was prepared in the following manner:

[0144] A solution of 84 mg of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-10β-(1-propyl)oxy-1β,11-deoxy-7β-methoxy-9-oxo-11-taxen-3β-yl (2R,3S)-3-tert-butylobenzoylamino-2-hydroxy-3-pheny1propanoate was prepared in the following manner:

[0145] After settling had taken place, the organic phase was separated and washed with three times 7 cm of distilled water and then 7 cm³ of saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (2.7 kPa) at a temperature in the region of 40° C. 224 mg of the yellow solid were thereby obtained, which product was purified by chromatography at atmospheric pressure on 20 g of silica (0.063-0.2 mm) contained in a column 2.5 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 0:100 to 15:65 by volume), collecting 10 cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40° C. 2 hours. 117.5 mg of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-10β-(1-propyl)oxy-1β,13α-dihydroxy-7β-methoxy-9-oxo-11-taxene were thereby obtained in the form of a white foam, the characteristics of which were as follows:

[0148] 1H NMR spectrum (300 MHz; CDCl₃; chemical shifts δ in ppm, coupling constants J in Hz): 0.98 (t, J=7.3, 3H; propyl CH₃); 1.22 (s, 3H; CH₃); 1.25 (s, 3H; CH₃); 1.38 (s, 9H; CH(CH₃)₂); 1.64 (s, 1H; OH at position 1); 1.69 (mt, 2H; central CH₂ of propyl); 1.73 (s, 3H; CH₃); 1.80 and 2.70 (2 mts, 1H each; CH₂ at position 6); 1.88 (s, 3H; CH₃); 2.30 (mt, 2H; CH₂ at position 14); 2.38 (s, 3H; COCH₃); 3.31 (s, 3H; OCH₃); 3.36 and 3.64 (2 mts, 1H each; propyl OCH₃); 3.44 (unres. comp. 1H; OH at position 2); 3.84 (d, J=7.3, 1H; H at position 3); 3.87 (dd, J=11 and 6.5, 1H; H at position 7); 4.18 and 4.30 (2 d, J=8.5, 1H each; CH at position 20); 4.64 (mt, 1H; H at position 2); 4.89 (s, 1H; H at position 10); 4.98 (broad d, J=10, 1H; H at position 5); 5.28 (broad d, J=10, 1H; H at position 3); 5.42 (d, J=10, 1H; CONH); 5.64 (d, J=7.5, 1H; H at position 2); 6.22 (broad t, J=9, 1H; H at position 13); from 7.25 to 7.45 (mt, 5H; aromatic H at position 3); 7.50 (d, J=7.5, 2H; OCOCH₃ H at the meta position); 7.61 (t, J=7.5, 1H; OCOCH₃ H at the para position); 8.12 (d, J=7.5, 2H; OCOCH₃ H at the ortho position).

[0149] 4α-Acetoxy-2α-benzoyloxy-5β,20-epoxy-10β-(1-propyl)oxy-9-oxo-11-taxene (or 10β-(1-propyl)oxy-9-oxo-11-deoxyacetoxycembrin III) was prepared in the following manner:

[0150] 8.75 cm³ of hydrogen fluoride/triethylamine complex (5H:Et₃N) were added to a solution, maintained under an argon atmosphere, at a temperature in the region of 20° C. of 585 mg of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-10β-(1-propyl)oxy-9-oxo-11-taxene in 6 cm³ of dichloromethane. After 24 hours at a temperature in the region of 20° C., the reaction mixture was diluted with 30 cm³ of dichloromethane and poured into a suspension of 30 cm³ of supersaturated aqueous hydrogen carbonate solution maintained at a temperature in the region of 0° C. After dilution with 10 cm³ of distilled water and settling had taken place, the aqueous phase was separated and re-extracted with twice 20 cm³ of diethyl ether. The organic phases were combined, washed with 20 cm³ of distilled water and 20 cm³ of saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered through magnesium sulphate and concentrated to dryness under reduced pressure (2.7 kPa) at a temperature in the region of 40° C. 500 mg of a pale yellow foam were thereby obtained, which product was purified by chromatography at atmospheric pressure on 40 g of silica (0.063-0.2 mm) contained in a column 2.5 cm in diameter, eluting with a methanol/dichloromethane (2:98 by volume) mixture and collecting 15 cm³ fractions. Fractions containing only the desired product were pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40° C for 2 hours. 373.8 mg of 4α-acetoxy-2α-benzoyloxy-5β,
20-epoxy-1β,7β,13α-trihydroxy-10β-(1-propyl)oxy-9-oxo-11-taxene were thereby obtained in the form of a white solid, the characteristics of which were as follows:

**[0151]** 1H NMR spectrum (300 MHz, CDCl₃; chemical shifts δ in ppm, coupling constants J in Hz): 0.95 (t, J=7.9, 3H: propyl CH₃); 1.06 (s, 3H: CH₃); 1.22 (s, 3H: CH₃); 1.45 (d, J=7.5, 1H: OH at position 7); from 1.60 to 1.80 (mt, 2H: central CH of propyl); 1.67 (s, 3H: CH₃); 1.83 and 2.62 (2 mts, 1H each: CH₂ at position 6); 2.05 (s, 3H: CH₃); 2.05 (mt, 1H: OH at position 13); 2.27 (limiting AB, 2H: CH₂ at position 4); 2.28 (s, 3H: COCH₃); 3.40 and 3.57 (2 mts, 1H each: propyl OCH₂); 3.97 (d, J=7.5, 1H: H at position 3); 4.15 and 4.30 (2 d, J=8.5, 1H each: CH₁ at position 6); 4.28 (mt, 1H: H at position 7); 4.90 (mt, 1H: H at position 13); 4.98 (broad d, J=10, 1H H at position 5); 5.03 (s, 1H: H at position 10); 5.65 (d, J=7.5, 1H: H at position 2); 7.50 (t, J=7.5, 2H: COC₆H₅, H at the para position); 7.60 (t, J=7.5, 1H: COC₆H₅, H at the meta position); 8.00 (d, J=7.5, 2H: COC₆H₅, H at the ortho position).

**[0152]** 4α-Acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-(1-propyl)oxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene (or 10β-(1-propyl)oxy-10-deacetoxy-7,13-bis(triethylsilyloxy)acacetin III) was prepared in the following manner:

**[0153]** 93 mg of sodium hydride at a concentration of 50% by weight in liquid paraffin were added portionwise to a solution, maintained under an argon atmosphere, at a temperature in the region of 20°C, of 1 g of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene in 100 ml of isooctane and 4 cm³ of dimethylformamide. The solution was kept stirring for 19 hours at a temperature in the region of 20°C, and 93 mg of sodium hydride at a concentration of 50% by weight in liquid paraffin were then added portionwise. After 3 hours at a temperature in the region of 20°C, the reaction mixture was diluted with 100 ml of ethyl acetate and 10 cm³ of saturated aqueous ammonium chloride solution. The organic phase was separated after settling had taken place, and washed with six times 10 cm³ of distilled water and then 10 cm³ of saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered through sintered glass and concentrated to dryness under reduced pressure (2.7 kPa) at a temperature in the region of 40°C. 1.32 g of a pale yellow foam were thereby obtained, which product was purified by chromatography at atmospheric pressure on 150 g of silica (0.06-0.2 mm) contained in a column 3.5 cm in diameter, eluting with an ethyl acetate/dichloromethane (2:98, then 5:95 by volume) mixture and collecting 15 cm³ fractions. Fractions containing only the desired products were pooled and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 376.3 mg of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene were thereby obtained in the form of a pale yellow foam and 395.3 mg of 4α-acetoxy-2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-(1-propyl)oxy-9-oxo-7β,13α-bis(triethylsilyloxy)-11-taxene were thereby obtained in the form of a pale yellow foam, the characteristics of which were as follows:

**[0154]** 1H NMR spectrum (400 MHz; CDCl₃; chemical shifts δ in ppm, coupling constants J in Hz): 0.42 and 0.70 (2 mts, 6H each: ethyl CH₃); 0.94 and 1.03 (2 t, J=7.5, 9H each: ethyl CH₂); 0.94 (t, J=7.5, 3H: propyl CH₃); 1.14 (s, 3H: CH₃); 1.21 (s, 3H: CH₃); 1.67 (s, 3H: CH₃); 1.69 (mt, 2H: central CH of propyl); 1.88 and 2.48 (2 mts, 1H each: CH₂ at position 6); 2.03 (s, 3H: CH₃); 2.13 and 2.23 (2 d, J=16 and 9, 1H each: CH₂ at position 14); 2.30 (s, 3H: COCH₃); 3.40 (mt, 2H: propyl OCH₂); 3.84 (d, J=7.5, 1H: H at position 3); 4.16 and 4.30 (2 d, J=8.5, 1H each: CH₂ at position 20); 4.44 (dd, J=11 and 6.5, 1H: H at position 7); 4.96 (broad d, J=10 Hz, 1H: H-S); 4.97 (s, 1H: H-10); 4.99 (broad t, J=9Hz, 1H: H at position 13); 5.62 (d, J=7.5, 1H: H at position 2); 7.48 (t, J=7.5, 2H: COOC₆H₅, H at the meta position); 7.60 (t, J=7.5, 1H: COOC₆H₅, H at the para position); 8.00 (d, J=7.5, 2H: COOC₆H₅, H at the ortho position).

**[0155]** The new products of general formula (I) in which Z represents a radical of general formula (II) manifest significant inhibitory activity with respect to abnormal cell proliferation, and possess therapeutic properties permitting the treatment of patients having pathological conditions associated with abnormal cell proliferation. The pathological conditions include the abnormal cell proliferation of malignant or non-malignant cells of various tissues and/or organs, comprising, without implied limitation, muscle, bone or connective tissue, the skin, brain, lungs, sex organs, the lymphatic or renal systems, mammary or blood cells, liver, the digestive system, pancreas and thyroid or adren al glands. These pathological conditions can also include psoriasis, solid tumours, cancers of the ovary, breast, brain, prostate, colon, stomach, kidney or testis, Kaposi’s sarcoma, cholangiocarcinoma, choriocarcinoma, neuroblastoma, Wilms’ tumour, Hodgkin’s disease, melanoma, multiple myeloma, chronic lymphocytic leukaemia and acute or chronic granulocytic leymphoma.

**[0156]** The new products according to the invention are especially useful for the treatment of cancer of the ovary. The products according to the invention may be used to prevent or delay the appearance or reappearance of the pathological conditions, or to treat these pathological conditions.

**[0157]** The products according to the invention may be administered to a patient according to different dosage forms suited to the chosen administration route, which is preferably the parenteral route. Parenteral administration comprises intravenous, intraperitoneal, intramuscular or subcutaneous administration. Intraperitoneal or intravenous administration is more especially preferred.

**[0158]** The present invention also comprises pharmaceutical compositions containing at least one product of general formula (I), in a sufficient amount suitable for use in human or veterinary therapy. The compositions may be prepared according to the customary methods, using one or more pharmaceutically acceptable adjuvants, vehicles or excipients. Suitable vehicles include diluents, sterile aqueous media and various non-toxic solvents. Preferably, the compositions take the form of aqueous solutions or suspensions, injectable solutions which can contain emulsifying agents, colourings, preservatives or stabilizers. However, the compositions can also take the form of tablets, pills, powders or granules which can be administered orally.

**[0159]** The choice of adjuvants or excipients may be determined by the solubility and the chemical properties of the product, the particular mode of administration and good pharmaceutical practice.

**[0160]** For parenteral administration, sterile, aqueous or non-aqueous solutions or suspensions are used. For the preparation of non-aqueous solutions or suspensions, natural vegetable oils such as olive oil, sesame oil or liquid petroluem, or injectable organic esters such as ethyl oleate, may
be used. The sterile aqueous solutions can consist of a solution of a pharmaceutically acceptable salt dissolved in water. The aqueous solutions are suitable for intravenous administration provided the pH is appropriately adjusted and the solution is made isotonic, for example with a sufficient amount of sodium chloride or glucose. The sterilization may be carried out by heating or by any other means which does not adversely affect the composition.

[0161] It is clearly understood that all the products participating in the compositions according to the invention must be pure and non-toxic in the amounts used.

[0162] The compositions can contain at least 0.01% of therapeutically active product. The amount of active product in a composition is such that a suitable dosage can be prescribed. Preferably, the compositions are prepared in such a way that a single dose contains from 0.01 to 1000 mg approximately of active product for parenteral administration.

[0163] The therapeutic treatment may be performed concurrently with other therapeutic treatments including anticancer drugs, monoclonal antibodies, immunotherapy or radiotherapy or biological response modifiers. The response modifiers include, without implied limitation, lymphokines and cytokines such as interleukins, interferons (α, β or δ) and TNF.

[0164] Other chemotherapeutic agents which are useful in the treatment of disorders due to abnormal cell proliferation include, without implied limitation, alkylating agents, for instance nitrogen mustards such as mechloethamine, cyclophosphamide, melphalan and chlorambucil, alkyl sulfonates such as busulfan, nitrosoureas such as carmustine, lomustine, semustine and streptozocin, triazines such as dacarbazine, antimetabolites such as folic acid analogues, for instance methotrexate, pyrimidine analogues such as fluorouracil and cytarabine, purine analogues such as mercaptopurine and thioguanine, natural products, for instance vinca alkaloids such as vinblastine, vincristine and vindesine, epipodophyllotoxins such as etoposide and teniposide, antibiotics such as dactinomycin, daunorubicin, doxorubicin, bleomycin, plicamycin and mitomycin, enzymes such as L-asparaginase, various agents such as coordination complexes of platinum, for instance cisplatin, substituted ureas such as hydroxyurea, methylhydrazine derivatives such as procarbazine, adrenocortical suppressants such as milotane and aminoglutethimide, hormones and antagonists such as adrenocorticosteroids such as prednisone, progestins such as hydroxyprogesterone caproate, methoxyprogesterone acetate and megestrol acetate, oestrogens such as diethylstilboestrol and ethynylestradiol, anticestrogens such as tamoxifen, and androgens such as testosterone propionate and fluoxymesterone.

[0165] The doses used for carrying out the methods according to the invention are those which permit a prophylactic treatment or a maximum therapeutic response. The doses vary according to the administration form, the particular product selected and features distinctive to the subject to be treated. In general, the doses are those which are therapeutically effective for the treatment of disorders due to abnormal cell proliferation.

[0166] The products according to the invention may be administered as often as necessary to obtain the desired therapeutic effect. Some patients may respond rapidly to relatively high or low doses, and then require low or zero maintenance doses. Generally, low doses will be used at the beginning of the treatment and, if necessary, increasingly stronger doses will be administered until an optimum effect is obtained.

[0167] For other patients, it may be necessary to administer maintenance doses 1 to 8 times a day, and preferably 1 to 4 times, according to the physiological requirements of the patient in question. It is also possible that some patients may require the use of only one to two daily administrations.

[0168] In man, the doses generally range from 0.01 to 200 mg/kg. For intraperitoneal administration, the doses will generally range from 0.1 to 100 mg/kg, preferably from 0.5 to 50 mg/kg and still more specifically from 1 to 10 mg/kg. For intravenous administration, the doses generally range from 0.1 to 50 mg/kg, preferably from 0.1 to 5 mg/kg and still more specifically from 1 to 2 mg/kg. It is understood that, in order to choose the most suitable dosage, account should be taken of the administration route, the patient’s weight, general state of health and age and all factors which may influence the efficacy of the treatment.

[0169] The example which follows illustrates a composition according to the invention.

EXAMPLE

[0170] 40 mg of the product obtained in Example 1 are dissolved in 1 cm³ of Emulphor EL 620 and 1 cm³ of ethanol, and the solution is then diluted by adding 18 cm³ of physiological saline. The composition is administered by perfusion over 1 hour by introduction in physiological solution.

We claim:

1. A taxoid of the formula (I):

\[
\text{R}_1 \text{NH}_2
\]

in which:

Z represents a hydrogen atom or a radical of formula (II).

\[
\text{R}_1 \text{NH}_2
\]

in which:

R₁ represents a benzoyl radical optionally substituted with one or more identical or different atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4
carbon atoms, trifluoromethyl radicals, a thienyl radical, a furanyl radical, and a radical R_2—O—CO— in which R_2 represents:

an alkyl radical containing 1 to 8 carbon atoms, an alkenyl radical containing 2 to a carbon atom, an alkylnyl radical containing 3 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkynyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 10 carbon atoms, these radicals being optionally substituted with one or more substituents selected from halogen atoms, hydroxyl radicals, alkoxyl radicals containing 1 to 4 carbon atoms; dialkylaminol radicals in which each alkyl portion contains 1 to 4 carbon atoms; piperidino radicals; morpholino radicals; 1-piperazinyl radicals optionally substituted at position 4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms; cycloalkyl radicals containing 3 to 6 carbon atoms; cycloalkynyl radicals containing 4 to 6 carbon atoms; phenyl radicals optionally substituted with one or more radicals or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms and alkoxyl radicals containing 1 to 4 carbon atoms; cyano radicals; carboxyl radicals; and alkoxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

a phenyl or α- or β-naphthyl radical optionally substituted with one or more radicals or radicals selected from halogen atoms; alkyl radicals containing 1 to 4 carbon atoms; and alkoxyl radicals containing 1 to 4 carbon atoms,

or a 5-membered aromatic heterocyclic radical,

or a saturated heterocyclic radical containing 4 to 6 carbon atoms, optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

R_3 represents an unbranched or branched alkyl radical containing 1 to 8 carbon atoms, an unbranched or branched alkenyl radical containing 2 to 8 carbon atoms, an unbranched or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a phenyl or α- or β-naphthyl radical optionally substituted with one or more radicals or radicals selected from halogen atoms, alkyl, alkenyl, alkylnyl, aryl, aralkyl, alkoxy, alkythio, aryloxy, arythio, hydroxyl, hydroxalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxyacylamino, aminoo, alkylamino, dialkylamino, carboxyl, alkoxyacetyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoroethyl radicals,

or a 5-membered aromatic heterocyclic containing one or more identical or different hetero atoms selected from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents selected from halogen atoms, alkyl, aryl, aminoo, dialkylamino, carboxylamino, acyl, arylacetyl, carbamoyl, cyano, aryl, alkylcarbamoyl, dialkylcarbamoyl and alkoxyacetyl radicals,

with the proviso that, in the substituents of the phenyl, α- or β-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, and the alkoxyl and alkylnyl radicals contain 2 to 8 carbon atoms, and the aryl radicals are phenyl or α- or β-naphthyl radicals,

R_4 represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain, an alkoxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkoxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkyl radical containing 3 to 6 carbon atoms or a cycloalkyl radical containing 7 to 10 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkoxy radical containing 1 to 4 carbon atoms, a carboxyl radical, a carboxyloxy radical, in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms,

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkoxy radical containing 1 to 4 carbon atoms, a phenyl or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

R_5 represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain optionally substituted with an alkoxy radical containing 1 to 4 carbon atoms, an alkoxy radical containing 3 to 6 carbon atoms, an alkoxy radical containing 3 to 6 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms or a cycloalkyl radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkoxy radical containing 1 to 4 carbon atoms, a carboxyl radical, a carboxyloxy radical, in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms,

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkoxy radical containing 1 to 4 carbon atoms, a phenyl or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

2. A taxoid according to claim 1, wherein Z represents a hydrogen atom or a radical of formula (II) in which

R_4 represents a benzylic radical or a radical R_2—O—CO— in which R_2 represents a tert-butyl radical,

R_3 represents an alkyl radical containing 1 to 6 carbon atoms; an alkenyl radical containing 2 to 6 carbon atoms; a cycloalkyl radical containing 3 to 6 carbon atoms; or a phenyl radical optionally substituted with one
or more identical or different atoms or radicals selected from halogen atoms, alkyl, alkoxy, dialkylamino, acylamino, alkoxy carbonylamino and trifluoromethyl radicals; or a 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl, or 5-thiazolyl radical, and

R₄ and R₅, which may be identical or different, each represent an unbranched or branched alkoxy radical containing 1 to 6 carbon atoms.

3. A taxoid according to claim 1, wherein Z represents a hydrogen atom or a radical of formula (II) in which

R₁ represents a benzoyl radical or a radical —O—CO— in which R₂ represents a tert-butyl radical,

R₃ represents an isobutyl, isobutyl, butyl, cyclohexyl, phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl or 5-thiazolyl radical, and

R₄ and R₅, which may be identical or different, each represent a methoxy, ethoxy or propoxy radical.

4. A taxoid according to claim 1, wherein when R₅ represents a 5-membered aromatic heterocyclic radical, said radical is a furyl or thieryl radical.

5. A process for preparing the taxoid according to claim 1, wherein Z represents a radical of formula (II), said process comprising esterifying a product of formula (III):

with an acid of formula (IV):

in which R₄ and R₅ are defined as in claim 1

with an acid of formula (IV):

in which R₂ and R₃ are defined as above, and either R₄ represents a hydrogen atom and R₅ represents a group protecting the hydroxyl function, or R₄ and R₅ together form a saturated 5- or 6-membered heterocycle, or

with a derivative of said acid, to obtain an ester of formula (V):

in which R₁, R₂, R₃, R₄, R₅ and R₆ are defined as above, and

replacing the protective group(s) of said ester of formula (V), represented by R₇ or R₈ and R₉, by hydrogen atoms.

6. A process according to claim 5, wherein said esterifying step is performed with an acid of formula (IV) in the presence of a condensing agent and an activating agent in an organic solvent at a temperature of from -10 to 90°C.

7. A process according to claim 5, wherein said esterifying step is performed with an acid of formula (IV) in the form of the symmetrical anhydride thereof, in the presence of an activating agent in an organic solvent at a temperature of from 0 to 90°C.

8. A process according to claim 5, wherein said esterifying step is performed with the acid of formula (IV) in halide form or in the form of a mixed anhydride with an aliphatic or aromatic acid, optionally prepared in situ, in the presence of a base, in an organic solvent at a temperature of from 0 to 80°C.

9. A process according to claim 5, further comprising replacing the protective group(s) R₇, R₈ and R₉ by hydrogen atoms, wherein:

1) when R₇ represents a hydrogen atom and R₈ represents a group protecting the hydroxyl function, said replacing the protective groups by hydrogen atoms is accomplished

with at least one inorganic or organic acid in an organic solvent selected from alcohols, ethers, esters, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons and nitriles at a temperature from -10 to 60°C, or

with a source of fluoride ions, or

with catalytic hydrogenation,

2) when R₇ and R₈ together form a saturated 5- or 6-membered heterocycle of formula (VI):
in which R is defined as above and Rs and Ro, which may be identical or different,
represent a hydrogen atom or an alkyl radical containing 1 to 4 carbon atoms, or an aralkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, or an aryl radical, or
alternatively Rs represents an alkoxy radical containing 1 to 4 carbon atoms or a trihalomethyl radical or a phenyl radical substituted with a trihalomethyl radical and Ro represents a hydrogen atom, or
alternatively Rs and Ro, together with the carbon atom to which they are linked, form a 4- to 7-membered ring,
wherein when:
a) R1 represents a tert-butoxycarbonyl radical and Rs and Ro, which may be identical or different, represent an alkyl radical or an aralkyl or aryl radical, or
alternatively Rs represents a trihalomethyl radical or a phenyl radical substituted with a trihalomethyl radical and Ro represents a hydrogen atom, or
alternatively Rs and Ro together form a 4- to 7-membered ring,
the ester of formula (V) is treated with an inorganic or organic acid, and where appropriate, in an organic solvent, to obtain the product of formula (VII):

\[
\text{R}_1 \text{N} \quad \begin{array}{c}
\text{OCOCH}_3 \\
\text{HO}
\end{array}
\]

(VI)

in which R1 is defined as above and R1, and R0, which may be identical or different,

b) when R1 represents an optionally substituted benzylic radical, a thienyl or furanyl radical or a radical R2O—CO— in which R2 is defined as above, R1 represents a hydrogen atom or an alkyl radical containing 1 to 4 carbon atoms or a phenyl radical substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms and R0 represents a hydrogen atom,
the protective group formed by Rs and Ro is replaced by hydrogen atoms in the presence of at least one inorganic or organic acid in a stoichiometric or catalytic amount, and in an organic solvent selected from alcohols, ethers, esters, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons and aromatic hydrocarbons
at a temperature of from -10 to 60°C.

10. A process according to claim 9, wherein when Rs and Ro together form a saturated 5- or 6-membered heterocycle of formula (VI), and Rs and Ro, which may be identical or different, represent an alanyl radical in which the alkyl portion contains 1 to 4 carbon atoms, the aryl portion of said aralkyl radical represents a phenyl radical optionally substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms.

11. A process according to claim 9, wherein when Rs and Ro together form a saturated 5- or 6-membered heterocycle of formula (VI), and Rs and Ro, which may be identical or different, represent an aryl radical, said aryl radical is a phenyl radical optionally substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms.

12. A process according to claim 9, wherein said temperature ranges from 15 to 30°C.

13. A process for preparing a new taxoid according to claim 1, wherein Z represents a hydrogen atom and Rs and R0 are defined as in claim 1, said process comprising:
treating 10-deacetylbaccatin III of formula (IX):

\[
\begin{array}{c}
\text{HO} \\
\text{OCOC}_6\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

(IX)
in which R2, Rs, and Ro are defined as above, and
said product of formula (VII) is acylated with
benzoyl chloride in which the phenyl ring is optionally substituted or thienyl chloride, or furanyl chloride or a product of formula (VIII):

\[
\text{R}_1 \text{O—CO—X}
\]

(VIII)
radical, a cycloalkyl radical containing 3 to 6 carbon atoms or a phenyl radical, to obtain a product of formula (XI):

\[ \text{(XI)} \]

\[
\begin{array}{c}
\text{(R)}_3\text{Si} - \text{O} = \text{Si}(\text{R})_3 \\
\text{HO} \\
\text{OCOC}_4\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

in which \( R \) is defined as above,

treating said product of formula (XI) with a product of formula:

\[ \text{R}_2 - \text{X}_1 \quad \text{(XII)} \]

in which \( \text{R}_2 \) represents a radical such that \( \text{R}_2 - \text{O} \) is identical to \( \text{R}_1 \) defined as in claim 1 and \( \text{X}_1 \) represents a halogen atom or a reactive ester residue, to obtain a product of formula (XIII):

\[ \text{(XIII)} \]

\[
\begin{array}{c}
\text{(R)}_3\text{Si} - \text{O} = \text{Si}(\text{R})_3 \\
\text{HO} \\
\text{OCOC}_4\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

in which \( \text{R} \) and \( \text{R}_1 \) are defined as above,

replacing the silyl protective groups of said product of formula (XIII) by hydrogen atoms to obtain a product of formula (XIV):

\[ \text{(XIV)} \]

\[
\begin{array}{c}
\text{R}_4 \\
\text{HO} \\
\text{OCOC}_4\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

in which \( \text{R}_4 \) is defined as above, and

etherifying said compound of formula (XIV) selectively at position 7 with a product of formula (XV):

\[ \text{R}_2' - \text{X}_2 \quad \text{(XV)} \]

in which \( \text{R}_2' \) represents a radical such that \( \text{R}_2' - \text{O} \) is identical to \( \text{R}_1 \) defined as in claim 1 and \( \text{X}_2 \) represents a reactive ester residue or a halogen atom, to give the product of formula (I) in which \( \text{Z} \) represents a hydrogen atom.

14. A process for preparing a product according to claim 1, wherein \( \text{Z} \) represents a radical of formula (II) and \( \text{R}_1 \) and \( \text{R}_2 \) are defined as in claim 1, said process comprising:
treating a product of formula (XVI):

\[ \text{(XVI)} \]

\[
\begin{array}{c}
\text{R}_1 \text{N} - \text{R}_2 \\
\text{O} = \text{R}_7 \\
\text{OCOC}_4\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

in which \( \text{R}_1, \text{R}_3, \text{R}_4 \) and \( \text{R}_2 \) are defined as in claim 1, with a product of formula (X):

\[ \text{(X)} \]

\[
\begin{array}{c}
\text{(R)}_3\text{Si} - \text{Hal} \\
\text{HO} \\
\text{OCOC}_4\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

in which the symbols \( \text{R} \), which may be identical or different, represent an alkyl radical containing 1 to 6 carbon atoms, optionally substituted with a phenyl radical, or a cycloalkyl radical containing 3 to 6 carbon atoms or a phenyl radical, to obtain a product of formula (XVII):

\[ \text{(XVII)} \]

\[
\begin{array}{c}
\text{R}_1 \text{N} - \text{R}_2 \\
\text{O} = \text{R}_7 \\
\text{OCOC}_4\text{H}_5 \\
\text{OCOCH}_3
\end{array}
\]

in which \( \text{R}, \text{R}_1, \text{R}_3, \text{R}_4 \) and \( \text{R}_2 \) are defined as above,

functionalizing said compound of formula (XVII) at position 10 with a product of formula:

\[ \text{R}_2' - \text{X}_1 \quad \text{(XII)} \]

in which \( \text{R}_2' \) represents a radical such that \( \text{R}_2' - \text{O} \) is identical to \( \text{R}_1 \) defined as in claim 1 and \( \text{X} \) represents a halogen atom or a reactive ester residue, to give a product of formula (XVIII):
in which R, R', R', R', R' and R' are defined as above, replacing the silyl protective group of said product of formula (XVIII) by a hydrogen atom to give a product of formula (XIX):

(XIX)

which, when reacted with a product of formula (XV), yields the product of formula (V), and replacing the protective groups of formula (V) with hydrogen atoms to give a product of formula (I) in which Z represents a radical of formula (II).

15. A process for preparing a product according to claim 1, comprising reacting activated Raney nickel, in the presence of an aliphatic alcohol containing 1 to 3 carbon atoms or an ether, with a product of formula (XXI):

(XXI)

followed, when Z, represents a radical of formula (XXII), by replacing the protective group(s) represented by R, or R and R, by hydrogen atoms under the conditions of claim 9.

16. A preparation process according to claim 15, wherein said process is carried out at a temperature of from -10 to 60°C.
20. A pharmaceutical composition comprising at least one product according to claim 1 wherein Z represents a radical of formula (II), in combination with one or more pharmaceutically acceptable diluents or adjuvants and optionally one or more compatible and pharmacologically active compounds.

21. A pharmaceutical composition comprising at least the product according to claim 17 in combination with one or more pharmaceutically acceptable diluents or adjuvants and optionally one or more compatible and pharmacologically active compounds.

22. A pharmaceutical composition comprising at least the product according to claim 18 in combination with one or more pharmaceutically acceptable diluents or adjuvants and optionally one or more compatible and pharmacologically active compounds.

23. A pharmaceutical composition comprising at least the product according to claim 19 in combination with one or more pharmaceutically acceptable diluents or adjuvants and optionally one or more compatible and pharmacologically active compounds.

24. An ester of the formula (V):

\[
\text{(V)}
\]

wherein 

\( R_1 \) represents a benzyol radical optionally substituted with one or more identical or different atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, triluoromethyl radicals, a phenyl radical, a furanoyl radical, and a radical \( R_2 - O - CO \) in which \( R_2 \) represents:

- an alkyl radical containing 1 to 8 carbon atoms, an alkenyl radical containing 2 to 8 carbon atoms, an alkyloxyl radical containing 3 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 10 carbon atoms, these radicals being optionally substituted with one or more substituents selected from halogen atoms, hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, a piperidino radical, morpholino radicals, 1-piperazinyl radicals optionally substituted at position 4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alky portion contains 1 to 4 carbon atoms; cycloalkyl radicals containing 3 to 6 carbon atoms; cycloalkenyl radicals containing 4 to 6 carbon atoms, phenyl radicals optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms and alkoxy radicals containing 1 to 4 carbon atoms, cyano radicals; carboxyl radicals; and alkoxy carbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms, a phenyl or \( \alpha \)- or \( \beta \)-naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms; alkyl radicals containing 1 to 4 carbon atoms; and alkoxy radicals containing 1 to 4 carbon atoms.

or a 5-membered aromatic heterocyclic radical, or a saturated heterocyclic radical containing 4 to 6 carbon atoms, optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms, a 5-membered aromatic heterocyclic radical containing 1 to 8 carbon atoms, an unbranched or branched alkynyl radical containing 2 to 8 carbon atoms, a cyanoalkyl radical containing 3 to 6 carbon atoms, a phenyl or \( \alpha \)- or \( \beta \)-naphthyl radical optionally substituted with one or more radicals selected from halogen atoms, alkyl, alkenyl, aryl, aralkyl, alkoxy, alkythio, aryloxy, arylthio, hydroxy, hydroxalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxy carbonylamino, amine, alkyalamino, dialkylamino, carbonyl, alkoxy carbonyl, carbamoyl, alkyl carbamoyl, dialkyl carbamoyl, cyano, nitro and triluoromethyl radicals, or a 5-membered aromatic heterocyclic containing one or more identical or different hetero atoms selected from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents selected from halogen atoms, alkyl, aryl, aminoo, alkylamino, dialkylamino, alkoxy carbonylamino, acyl, arylcarboxyl, cyano, carbomoyl, alky carbamoyl, dialkyl carbamoyl and alkoxy carbonyl radicals,

with the proviso that, in the substituents of the phenyl, \( \alpha \)- or \( \beta \)-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkylo portions of the other radicals contain 1 to 4 carbon atoms, and the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms, and the aryl radicals are phenyl or \( \alpha \)- or \( \beta \)-naphthyl radicals,

\( R_4 \) represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain, an alkenyloxyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkyloxyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkenyl radical containing 3 to 6 carbon atoms or a cycloalkenyl radical containing 4 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkythio radical containing 1 to 4 carbon atoms, a carbonyl radical, an alkylcarboxyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carboxamidoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkyl carbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms.
or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical, or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, and

either R₄ represents a hydrogen atom and R₅ represents a group protecting the hydroxyl function, or R₄ and R₅ together form a saturated 5- or 6-membered heterocycle.

25. An ester of formula (VII):

![Chemical Structure](image)

wherein

R₄ represents an unbranched or branched alkyl radical containing 1 to 8 carbon atoms, an unbranched or branched alkenyl radical containing 2 to 8 carbon atoms, an unbranched or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a phenyl or α- or β-naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl, alkenyl, alkylnyl, aryl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, arylamino, alkoxyacarbonylamino, amino, alkylamino, dialkylamino, carbonyl, alkoxyacarbonyl, carbamoyl, alkoxy carbamoyl, dialkyl carbamoyl, cyano, nitro and trifluoromethyl radicals, or a 5-membered aromatic heterocycle containing one or more identical or different hetero atoms selected from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents selected from halogen atoms, alkyl, aryl, amino, alkylamino, dialkylamino, alkoxy carbamoylamino, acyl, arylcarbonyl, cyano, carbonyl, carbamoyl, alkyl carbamoyl, dialkyl carbamoyl and alkoxy carbonyl radicals,

with the proviso that, in the substituents of the phenyl, α- or β-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, and the alkyl and alkoxy radicals contain 2 to 8 carbon atoms, and the aryl radicals are phenyl or α- or β-naphthyl radicals, R₅ represents an alkyl radical containing 1 to 6 carbon atoms in an unbranched or branched chain, an alkenyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkynyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkoxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkylcarbonyl radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkyl radical containing 1 to 4 carbon atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkylthio radical containing 1 to 4 carbon atoms, a carbonyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkyl carbamoyl radical, and an N,N-dialkyl carbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms.

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, and

R₅ represents an alkyl radical containing 1 to 6 carbon atoms in an unbranched or branched chain optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, an alkoxy radical containing 3 to 6 carbon atoms, an alkoxy carbonyl radical containing 3 to 6 carbon atoms, an alkynyl radical containing 3 to 6 carbon atoms, a cycloalkylcarbonyl radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkyl radical containing 1 to 4 carbon atoms, an alkoxy radical containing 1 to 4 carbon atoms, a carbonyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkyl carbamoyl radical, and an N,N-dialkyl carbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms.

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, and
bered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical, or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms.

26. A method comprising the step of etherifying selectively at position 7 a compound of the formula (XIV):

\[
\begin{align*}
\text{(XIV)}
\end{align*}
\]

wherein \(R_1\) represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain, an alkenyloxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkynylloxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkyloxy radical containing 3 to 6 carbon atoms or a cycloalkenyloxy radical containing 4 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkylthio radical containing 1 to 4 carbon atoms, a carboxyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms.

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical, or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, with a compound of the formula (XV):

\[
\begin{align*}
R'_1 & = X_2
\end{align*}
\]

wherein \(R'_1\) represents a radical such that \(R'_1-O\) represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, an alkenyloxy radical containing 3 to 6 carbon atoms, an alkynylloxy radical containing 3 to 6 carbon atoms, a cycloalkyloxy radical containing 3 to 6 carbon atoms or a cycloalkenyloxy radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkylthio radical containing 2 to 4 carbon atoms, a carboxyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms.

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical, or a phenylalkyl radical in which the alkyl
portion contains 1 to 4 carbon atoms, and $X_2$ represents a reactive ester residue or a halogen atom, with a compound of the formula (XIX):

\[ (XIX) \]

wherein $R_1$ represents a benzoyl radical optionally substituted with one or more identical or different atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, trifluoromethyl radicals, a phenyl radical, a furyl radical, and a radical $R_2-O-$CO— in which $R_2$ represents:

an alkyl radical containing 1 to 8 carbon atoms, an alkenyl radical containing 2 to 8 carbon atoms, an alkynyl radical containing 3 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 10 carbon atoms, these radicals being optionally substituted with one or more substituents selected from halogen atoms; hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms; dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms; piperidino radicals; morpholino radicals; 1-piperazinyl radicals optionally substituted at position 4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms; cycloalkyl radicals containing 3 to 6 carbon atoms; cycloalkenyl radicals containing 4 to 6 carbon atoms; phenyl radicals optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms and alkoxy radicals containing 1 to 4 carbon atoms; cyano radicals; carboxyl radicals; and alkoxy carbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

a phenyl or $\alpha$- or $\beta$-naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms; alkyl radicals containing 1 to 4 carbon atoms; and alkoxy radicals containing 1 to 4 carbon atoms,

a 5-membered aromatic heterocyclic radical,

or a saturated heterocyclic radical containing 4 to 6 carbon atoms, optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

$R_3$ represents an unbranched or branched alkyl radical containing 1 to 8 carbon atoms, an unbranched or branched alkenyl radical containing 2 to 8 carbon atoms, an unbranched or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a phenyl or $\alpha$- or $\beta$-naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxy carbonylamino, amino, alkylation, dialkylamino, carboxyl, alkoxy carbonyl, carbamoyl, alky carbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals,

or a 5-membered aromatic heterocyclic containing one or more identical or different hetero atoms selected from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents selected from halogen atoms, alkyl, aryl, amino, alkylation, dialkylamino, alkoxy carbonylamino, acyl, aroylcarboxyl, cyano, carboxyl, carbamoyl, alkyl carbamoyl, dialkyl carbamoyl and alkoxy carbonyl radicals,

with the proviso that, in the substituents of the phenyl, $\alpha$- or $\beta$-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, and the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms, and the aryl radicals are phenyl or $\alpha$- or $\beta$-naphthyl radicals,

$R_4$ represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain, an alkenyloxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkynyoxy radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkyloxy radical containing 3 to 6 carbon atoms or a cycloalkynyoxy radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxy radical containing 1 to 4 carbon atoms, an alkylthio radical containing 1 to 4 carbon atoms, a carboxyl radical, an alkoxy carbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkyl carbamoyl radical, and an N,N-dialkyl carbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms,

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

either $R_5$ represents a hydrogen atom and $R_2$ represents a group protecting the hydroxyl function, or $R_3$ and $R_4$ together form a saturated 5- or 6-membered heterocycle,

to form a compound of the formula (V):
wherein Rs represents an alkoxy radical containing 1 to 6 carbon atoms in an unbranched or branched chain optionally substituted with an alkoxy radical containing 1 to 4 carbon atoms, an alkynylxylo radical containing 3 to 6 carbon atoms, an alkynylxylo radical containing 3 to 6 carbon atoms, a cyrcloalkyloxy radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkyl radical containing 1 to 4 carbon atoms, an alkylthio radical containing 2 to 4 carbon atoms, a carboxyl radical, an alkylxyloxyxylo radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical, or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, and R1, R3, R4, R6 and Rs are as defined above.

28. A method comprising the step of replacing with hydrogen atom(s) group(s) Rs and Rr in a compound of the formula (V):

wherein:

Rs represents a benzoyl radical optionally substituted with one or more identical or different atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, trifluoromethyl radicals, a phenyl radical, a furyl radical, and a radical R2—O—CO— in which R2 represents:

an alkyl radical containing 1 to 8 carbon atoms, an alkyl radical containing 2 to 8 carbon atoms, an alkyl radical containing 3 to 8 carbon atoms, a cyrcloalkyloxy radical containing 3 to 6 carbon atoms, a cyrcloalkyloxy radical containing 4 to 6 carbon atoms or a bicycloalkyloxy radical containing 7 to 10 carbon atoms, these radicals being optionally substituted with one or more substituents selected from halogen atoms; hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms; dialkylaminio radicals in which each alkyl portion contains 1 to 4 carbon atoms; piperidino radicals; morpholino radicals; 1-piperazinyl radicals optionally substituted at position 4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms; cyrcloalkyloxy radicals containing 3 to 6 carbon atoms; cyrcloalkyloxy radicals containing 4 to 6 carbon atoms; phenyl radicals optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl radicals containing 1 to 4 carbon atoms and alkoxy radicals containing 1 to 4 carbon atoms; cyano radicals; carboxyl radicals; and alkoxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms, a phenyl or a- or β-naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms; alkyl radicals containing 1 to 4 carbon atoms, and alkoxy radicals containing 1 to 4 carbon atoms, a 5-membered aromatic heterocyclic radical,
or a saturated heterocyclic radical containing 4 to 6 carbon atoms, optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms, Rr represents an unbranched or branched alkyl radical containing 1 to 8 carbon atoms, an unbranched or branched alkenyloxy radical containing 2 to 8 carbon atoms, an unbranched or branched alkynyl radical containing 2 to 8 carbon atoms, a cyrcloalkyloxy radical containing 3 to 6 carbon atoms, a phenyl or a- or β-naphthyl radical optionally substituted with one or more atoms or radicals selected from halogen atoms, alkyl, alkenyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylaminio, aroylamino, aroyloxycarbonylaminio, amino, aroylamino, dialkylamino, carbamoyl, alkoxycarbonyl, carboxamido, dialkylcarbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals, or a 5-membered aromatic heterocyclic containing one or more identical or different hetero atoms selected from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents selected from halogen atoms, alkyl, aryl, amino, alkyaminio, dialkylaminio, aroyloxycarbonylaminio, acyl, aroylacetyl, cyano, carboxyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl and alkoxycarbonyl radicals, with the proviso that, in the substituents of the phenyl, a- or β-naphthyl and aromatic heterocyclic radicals, the...
alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, and the alkenyl and alkynyl radicals contain 2 to 5 carbon atoms, and the aryl radicals are phenyl or α- or β-naphthyl radicals, 

R₁ represents an alkoxyl radical containing 1 to 6 carbon atoms in an unbranched or branched chain, an alkenyloxyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, an alkynylloxyl radical containing 3 to 6 carbon atoms in an unbranched or branched chain, a cycloalkyloxyl radical containing 3 to 6 carbon atoms or a cycloalkenylloxyl radical containing 4 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxyl radical containing 1 to 4 carbon atoms, an alkylthio radical containing 1 to 4 carbon atoms, a carboxyl radical, an alkoxycarbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alkylcarbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms 

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms,

R₂ represents an alkoxyl radical containing 1 to 6 carbon atoms in an unbranched or branched chain optionally substituted with an alkoxyl radical containing 1 to 4 carbon atoms, an alkenyloxyl radical containing 3 to 6 carbon atoms, an alkenyloxyl radical containing 3 to 6 carbon atoms, a cycloalkyloxyl radical containing 3 to 6 carbon atoms or a cycloalkenylloxyl radical containing 3 to 6 carbon atoms, these radicals being optionally substituted with at least one substituent selected from halogen atoms, an alkoxyl radical containing 1 to 4 carbon atoms, an alkylthio radical containing 2 to 4 carbon atoms, a carboxyl radical, an alkoxycarbonyl radical in which the alkyl portion contains 1 to 4 carbon atoms, a cyano radical, a carbamoyl radical, an N-alky-carbamoyl radical, and an N,N-dialkylcarbamoyl radical in which each alkyl portion contains 1 to 4 carbon atoms 

or, both alkyl portions, together with the nitrogen atom to which they are linked, form a saturated 5- or 6-membered heterocyclic radical optionally containing a second hetero atom selected from oxygen, sulphur and nitrogen atoms, optionally substituted with an alkyl radical containing 1 to 4 carbon atoms, a phenyl radical or a phenylalkyl radical in which the alkyl portion contains 1 to 4 carbon atoms, and 

either R₃ represents a hydrogen atom and R₄ represents a group protecting the hydroxyl function, or R₃ and R₄ together form a saturated 5- or 6-membered heterocycle, 

by treating the compound of formula (V) with an organic or inorganic acid, where appropriate in an organic solvent to obtain a compound of the formula (VII):

![Chemical structure](image)

wherein R₁, R₂, and R₃ are as defined above. 

29. A process according to claim 9, wherein said source of fluoride ions is a hydrofluoric acid/triethylamine complex. 

30. A process according to claim 9, wherein said triethylmethyl radical is trichloromethyl. 

31. A process according to claim 9, wherein when said ester of formula (V) is treated in an organic solvent, said organic solvent is an alcohol.

* * * * *