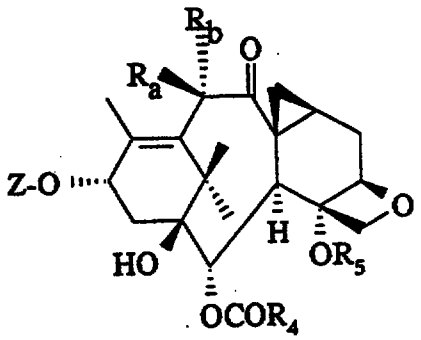
NEW TAXOIDS, THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

The present invention relates to new taxoids of general formula:

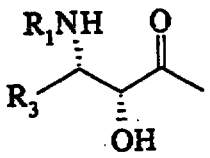


(I)

in which:

R_a represents a hydrogen atom or a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl portion contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, or alternatively R_a and R_b, together with the carbon atom to which they are attached, form a keto function,

Z represents a hydrogen atom or a radical of general formula:



(II)

in which:

R_1 represents a benzoyl radical optionally substituted with one or more identical or different atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms or trifluoromethyl radicals, a thenoyl or furoyl radical or 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 chosen from halogen atoms and hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino or 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 chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms),

cyano or carboxyl radicals or 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 atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms, or a 5-membered aromatic heterocyclic radical preferably chosen from furyl and thienyl radicals,

- 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 atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals, or a 5-membered aromatic heterocycle

containing one or more identical or different hetero atoms chosen from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical or different substituents chosen from halogen atoms and alkyl, aryl, amino, alkylamino, dialkylamino, alkoxycarbonylamino, acyl, arylcarbonyl, cyano, carboxyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl or alkoxycarbonyl radicals, on 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, and that the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms, and that the aryl radicals are phenyl or α- or β-naphthyl radicals, and

R_4 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 cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 11 carbon atoms, these radicals being optionally substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkyloxy radicals containing 1 to 4 carbon atoms, dialkyamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino or 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, optionally substituted phenyl radicals, cyano or carboxyl radicals or alkoxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

- or an aryl radical optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxylalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro, azido, trifluoromethyl or trifluoromethoxy radicals,

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

R^5 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 cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl

radical containing 7 to 11 carbon atoms, these radicals being optionally substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkyloxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino or 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, optionally substituted phenyl radicals, cyano or carboxyl radicals or alkyloxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

on the understanding that the cycloalkyl, cycloalkenyl or bicycloalkyl radicals may be optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms.

Preferably, the aryl radicals which can be represented by R_3 and/or R_4 are phenyl or α- or β-naphthyl radicals optionally substituted with one or more atoms or radicals chosen from halogen atoms (fluorine, chlorine, bromine, iodine) and alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino,

alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, dialkylcarbamoyl, cyano, nitro, azido, trifluoromethyl and trifluoromethoxy radicals, on the understanding that the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, that the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms and that the aryl radicals are phenyl or α- or β-naphthyl radicals.

Preferably, the heterocyclic radicals which can be represented by R_3 and/or R_4 are 5-membered aromatic heterocyclic radicals containing one or more identical or different atoms chosen from nitrogen, oxygen and sulphur atoms, optionally substituted with one or more identical or different substituents chosen from halogen atoms (fluorine, chlorine, bromine, iodine) and alkyl radicals containing 1 to 4 carbon atoms, aryl radicals containing 6 to 10 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, aryloxy radicals containing 6 to 10 carbon atoms, amino 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, alkoxycarbonylamino radicals containing 1 to 4 carbon atoms, acyl radicals containing 1 to 4 carbon atoms, arylcarbonyl radicals in which the aryl portion contains 6 to 10 carbon atoms, cyano, carboxyl

or carbamoyl radicals, alkylcarbamoyl radicals in which the alkyl portion contains 1 to 4 carbon atoms, dialkylcarbamoyl radicals in which each alkyl portion contains 1 to 4 carbon atoms or alkoxycarbonyl radicals in which the alkoxy portion contains 1 to 4 carbon atoms.

More especially, the present invention relates to the products of general formula (I) in which R_a represents a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl portion contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-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 chosen from halogen atoms (fluorine, chlorine) and alkyl (methyl), alkoxy (methoxy), dialkylamino (dimethylamino), acylamino (acetylamino), alkoxycarbonylamino (tert-butoxycarbonylamino) or trifluoromethyl radicals, or a 2- or 3-furyl, 2- or 3-thienyl or 2-, 4- or 5-thiazolyl radical, and R_4 represents a phenyl radical optionally

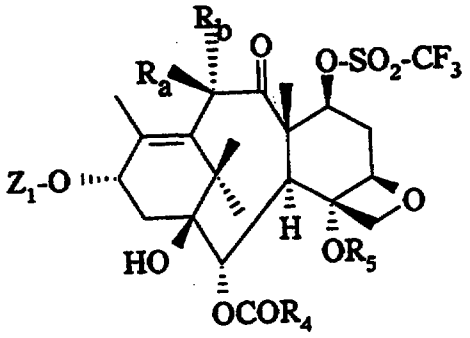
substituted with one or more identical or different atoms or radicals chosen from halogen atoms and alkyl, alkoxy, amino, alkylamino, dialkylamino, acylamino, alkoxycarbonylamino, azido, trifluoromethyl and trifluoromethoxy radicals, or a 2- or 3-thienyl or 2- or 3-furyl radical, and R_5 represents an optionally substituted alkyl radical containing 1 to 4 carbon atoms.

Still more especially, the present invention relates to the products of general formula (I) in which R_a represents a hydrogen atom or a hydroxyl or acetyloxy or methoxyacetoxy radical and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-O-CO- in which R_2 represents a tert-butyl radical and R_3 represents an isobutyl, isobutenyl, butenyl, cyclohexyl, phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl or 5-thiazolyl radical and R_4 represents a phenyl radical optionally substituted with a halogen atom and R_5 represents an alkyl radical containing 1 to 4 carbon atoms.

The products of general formula (I) in which Z represents a radical of general formula (II) display noteworthy antitumour and antileukaemic properties.

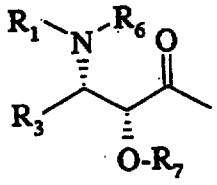
According to the present invention, the products of general formula (I) in which R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy

radical, R_b represents a hydrogen atom and R_4, R_5 and Z are defined as above may be obtained by the action of an alkali metal halide (sodium chloride, sodium iodide, potassium fluoride) or an alkali metal azide (sodium azide) or a quaternary ammonium salt or an alkali metal phosphate on a product of general formula:



(III)

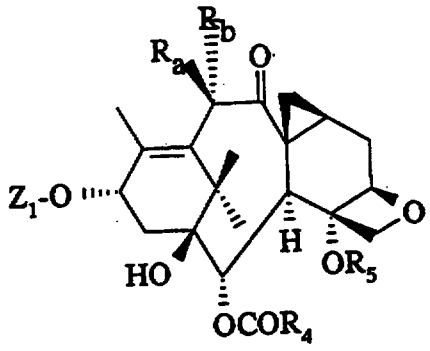
in which Z_1 represents a hydrogen atom or a radical of general formula (II) in which R_1 and R_3 are defined as above or a radical of general formula:



(IV)

in which R_1 and R_3 are defined as above, and either R_6 represents a hydrogen atom and R_7 represents a group protecting the hydroxyl function, or R_6 and R_7 together form a saturated 5- or 6-membered heterocycle, R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, preferably a 2,2,2-trichloroethoxycarbonyloxy radical, and R_b represents a

hydrogen atom, or alternatively R_a and R_b, together with the carbon atom to which they are attached, form a keto function, to obtain a product of general formula:



(V)

in which Z_1, R_4, R_5, R_a and R_b are defined as above, followed, if necessary, by replacement of the protective group borne by R_a or of the protective groups represented by R_7 and/or by R_6 and R_7 by the hydrogen atoms.

Generally, the reaction is performed in an organic solvent chosen from ethers (tetrahydrofuran, diisopropyl ether, methyl, tert-butyl ether) and nitriles (acetonitrile), alone or mixed, at a temperature between 20°C and the boiling point of the reaction mixture.

A product of general formula (V) in which Z_1 represents a hydrogen atom or a radical of general formula (II), R_a represents a hydrogen atom or a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl portion contains 1 to 4 carbon atoms and R_b

represents a hydrogen atom, or alternatively R_a and R_b, together with the carbon atom to which they are attached, form a keto function, is identical to a product of general formula (I).

In the general formula (V), when Z_1 represents a radical of general formula (IV) and when R_6 represents a hydrogen atom, R_7 preferably represents a methoxymethyl, 1-ethoxyethyl, benzyloxymethyl, trimethylsilyl, triethylsilyl, β-trimethylsilylethoxymethyl, benzyloxycarbonyl or tetrahydropyrranyl radical, or alternatively, 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.

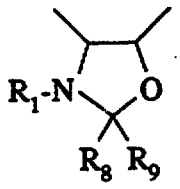
Replacement of the protective groups R_7 and/or R_6 and R_7 by hydrogen atoms, and where appropriate of R_a by a hydroxyl radical, may be performed, depending on their nature, in the following manner:

1) when R_6 represents a hydrogen atom and R_7 represents a group protecting the hydroxyl function, and R_a represents an alkoxy, acyloxy or alkoxyacetoxy radical, replacement of the protective groups by hydrogen 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 between -10 and 60°C,

2) when R_6 represents a hydrogen atom and R_7 represents a group protecting the hydroxyl function, and R_a represents a 2,2,2-trichloroethoxycarbonyloxy radical, replacement of the protective group R_7 is performed under the conditions described above under 1) and that of R_a by treatment with zinc, optionally in combination with copper, in the presence of acetic acid at a temperature of between 30 and 60°C, or by means of an inorganic or organic acid such as hydrochloric acid or acetic acid in solution in an aliphatic alcohol containing 1 to 3 carbon atoms (methanol, ethanol, propanol, isopropanol) or in an aliphatic ester (ethyl acetate, isopropyl acetate, n-butyl acetate) in the presence of zinc, optionally in combination with copper,

3) when R_6 and R_7 together form a 5- or 6-membered saturated heterocycle, and more especially an oxazolidine ring of general formula:



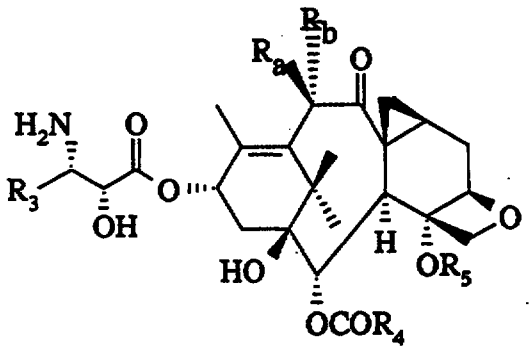
(VI)

in which R_1 is defined as above and R_8 and R_9, 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 aryl radical preferably representing a phenyl radical optionally substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms, or alternatively R_8 represents an alkoxy radical containing 1 to 4 carbon atoms or a trihalomethyl radical such as trichloromethyl or a phenyl radical substituted with a trihalomethyl radical such as trichloromethyl and R_9 represents a hydrogen atom, or alternatively R_8 and R_9, together with the carbon atom to which they are attached, form a 4- to 7-membered ring, and R_a represents an acyloxy or alkoxyacetoxy or 2,2,2-trichloroethoxycarbonyloxy radical, replacement of the protective group formed by R_6 and R_7 by hydrogen atoms and of R_a by a hydroxyl radical may be performed, depending on the meanings of R_a, R_1, R_8 and R_9, in the following manner:

a) when R_1 represents a tert-butoxycarbonyl radical and R_8 and R_9, which may be identical or different, represent an alkyl radical or an aralkyl (benzyl) or aryl (phenyl) radical, or alternatively R_8 represents a trihalomethyl radical or a phenyl radical substituted with a trihalomethyl radical and R_9 represents a hydrogen atom, or alternatively R_8 and R_9

together 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:

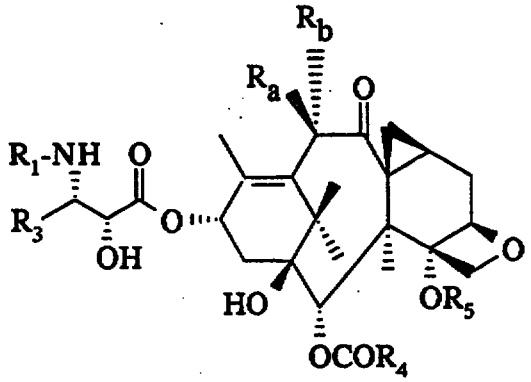


(VII)

in which R_a, R_b, R_3, R_4 and R_5 are defined as above, which is acylated by means of benzoyl chloride in which the phenyl ring is optionally substituted or by means of thenoyl chloride, of furoyl chloride or of a product of general formula:

$$R_2\text{-O-CO-X} \qquad \text{(VIII)}$$

in which R_2 is defined as above and X represents a halogen atom (fluorine, chlorine) or a residue -O-R_2 or -O-CO-O-R_2, to obtain a product of general formula:



(IX)

in which R_a, R_b, R_1, R_3, R_4 and R_5 are defined as above, in which the protective group R_a, when it represents a protected hydroxyl radical, is replaced, if necessary, by a hydroxyl radical.

Preferably the product of general formula (V) is treated with formic acid at a temperature in the region of 20°C.

Preferably, the acylation of the product of general formula (IX) by means of a benzoyl chloride in which the phenyl radical is optionally substituted or by means of thenoyl 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 between 0 and 50°C, and preferably in the region of 20°C.

Preferably, replacement of the protective group R_a, when it represents a 2,2,2-trichloroethoxycarbonyloxy radical, is performed under the conditions described above under 2).

b) when R_1 represents an optionally substituted benzoyl radical, a thenoyl or furoyl radical or a radical R_2O-CO- in which R_2 is defined as above, R_8 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 R_9 represents a hydrogen atom, replacement of the protective group formed by R_6 and R_7 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 between -10 and 60°C, and preferably between 15 and 30°C, and replacement of the protective group R_a, when it represents a 2,2,2-trichloroethoxycarbonyloxy radical, by a hydrogen atom is performed under the conditions described above under 2).

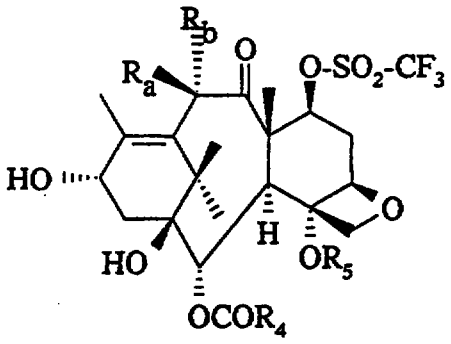
4) when R_a represents an alkoxyacetyl radical and R_6 and R_7 are defined as in point 1) above, replacement of the protective group R_7 by a hydrogen atom is first performed by working under the acid conditions described in point 1) above, and R_a is then replaced, where appropriate, by a hydroxyl radical by treatment in an alkaline medium or by the action of a zinc halide under conditions which do not affect the remainder of the molecule. Generally, the alkaline treatment is performed by the action of ammonia in an aqueous-

alcoholic medium or of hydrazine hydrate in an alcoholic medium at a temperature in the region of 20°C. Generally, the treatment with a zinc halide, preferably zinc iodide, is performed in methanol at a temperature in the region of 20°C.

5) when R_a represents an alkoxyacetoxy radical and R_6 and R_7 are defined as in point 3-a) above, replacement of the radical R_a by a hydroxyl radical is performed by treatment in an alkaline medium or by treatment with a zinc halide under the conditions described in point 4) above, and the product of general formula (VI) obtained is then treated under the deprotection and acylation conditions described in point 3-a) above.

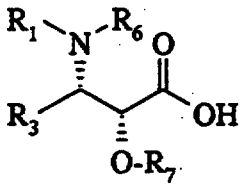
6) when R_a represents an alkoxyacetoxy radical and R_6 and R_7 are defined as in point 3-b) above, replacement of the radical R_a by a hydroxyl radical is performed by treatment in an alkali medium or by treatment with a zinc halide under the conditions described in point 4) above, and the product obtained is then treated under the conditions described in point 3-b) above.

The product of general formula (III) in which Z_1 represents a radical of general formula (II) or a radical of general formula (IV) may be obtained by esterification of a product of general formula:



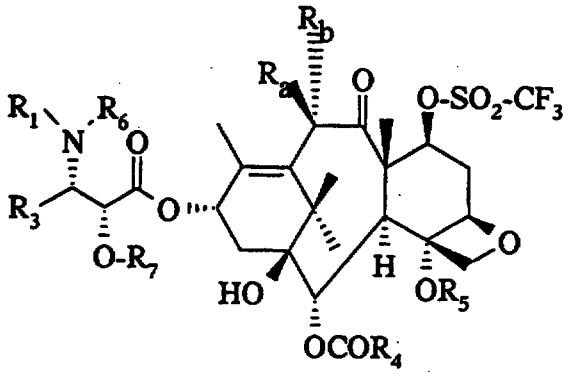
(X)

in which R_4 and R_5 are defined as above, and R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protective hydroxyl radical, and R_b represents a hydrogen atom, by means of an acid of general formula:



(XI)

in which R_1 and R_3 are defined as above, either R_6 represents a hydrogen atom and R_7 represents a group protecting the hydroxyl function, and or R_6 and R_7 together form a saturated 5- or 6-membered heterocycle, or a derivative of this acid, to obtain an ester of general formula:



(XII)

in which R_a, R_b, R_1, R_3, R_4, R_5, R_6 and R_7 are defined as above, followed, if necessary, by replacement of the protective groups represented by R_7 and/or R_6 and R_7 by hydrogen atoms, and, where appropriate, R_a when it represents an acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, by a hydroxyl radical, under the conditions described above for replacement of the protective groups of the product of general formula (V) in which Z_1 represents a radical of general formula (IV).

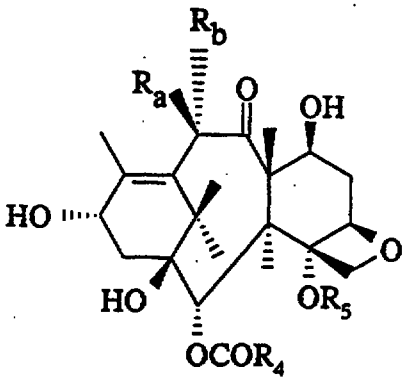
The esterification by means of an acid of general formula (XI) may be performed in the presence of a condensing agent (carbodiimide, reactive carbonate) and an activating agent (aminopyridines) in an organic solvent (ether, ester, ketones, nitriles, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons) at a temperature of between -10 and 90°C.

The esterification may also be carried out using the acid of general formula (XI) in an anhydride form, working in the presence of an activating agent

(aminopyridines) in an organic solvent (ethers, esters, ketones, nitriles, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons) at a temperature of between 0 and 90°C.

The esterification may also be carried out using the acid of general formula (XI) in halide form or in anhydride form 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, nitriles, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons) at a temperature of between 0 and 80°C.

According to the invention, the products of general formula (III) in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical, R_b represents a hydrogen atom and Z_1 represents a hydrogen atom may be obtained by the action of a trifluoromethanesulphonic acid derivative such as the anhydride or N-phenyltrifluoromethanesulphonimide on a product of general formula:

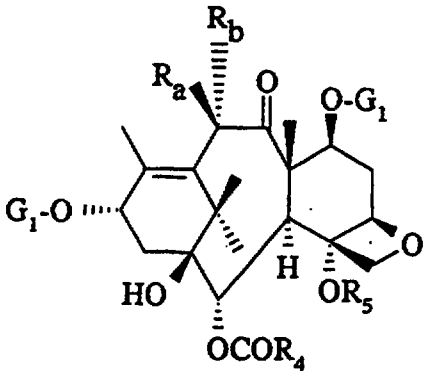


(XIII)

in which R_a, R_b, R_4 and R_5 are defined as above.

Generally, the reaction is performed in an inert organic solvent (aliphatic hydrocarbons, optionally halogenated, aromatic hydrocarbons) in the presence of an organic base such as a tertiary aliphatic amine (triethylamine) or pyridine at a temperature of between -50 and +20°C.

The products of general formula (XIII) in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical and R_b represents a hydrogen atom may be obtained by the action of hydrofluoric acid or trifluoroacetic acid in a basic organic solvent such as pyridine optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms, or triethylamine optionally in combination with an inert organic solvent such as methylene chloride or acetonitrile or tetrahydrofuran, at a temperature of between 20 and 80°C, on a product of general formula:



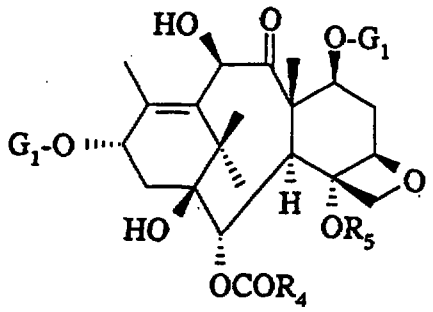
(XIV)

in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, R_b represents a hydrogen atom and the symbols G_1, which are identical, represent a trialkylsilyl radical.

The product of general formula (XIV) in which R_a represents an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical and R_b represents a hydrogen atom may be obtained by the action of a product of general formula:

R-Y (XV)

in which R represents an alkyl, alkanoyl or alkoxyacetyl radical or a group protecting the hydroxyl function and Y represents a halogen atom, on a product of general formula:



(XVI)

in which R_4, R_5 and G_1 are defined as above.

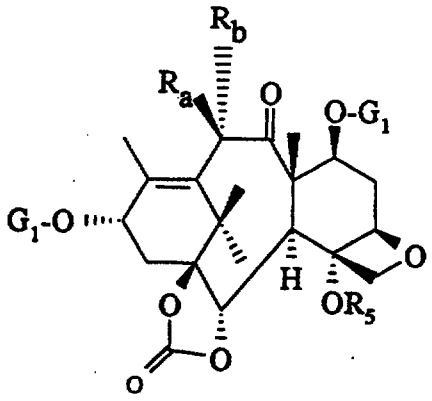
When R represents an alkanoyl or alkoxyacetyl radical, it is especially advantageous to work in a basic organic solvent such as pyridine or in an inert organic solvent such as methylene chloride, chloroform or 1,2-dichloroethane, in the presence of a tertiary amine such as triethylamine or pyridine at a temperature in the region of 0°C.

When R represents an alkyl radical, it is especially advantageous to metalate the hydroxyl function on a secondary carbon atom beforehand by means of an alkali metal hydride (sodium hydride) or a metal alkyl (butyllithium).

The product of general formula (XVI), and where appropriate the product of general formula (XIV), may be obtained by the action of an organometallic derivative of general formula:

$$R_4\text{-}M \qquad \text{(XVII)}$$

in which R_4 is defined as above and M represents a metal atom, preferably a lithium or magnesium atom, on a product of general formula:

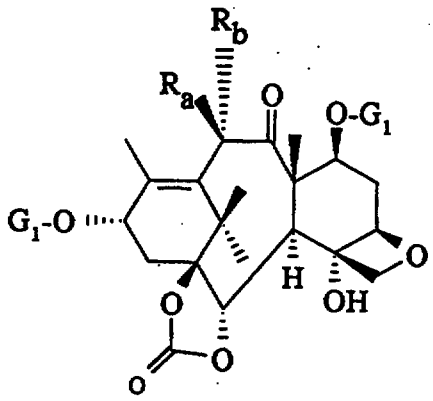


(XVIII)

in which R_a, R_b, R_5 and G_1 are defined as above.

Generally, the reaction is performed in an organic solvent such as an ether (tetrahydrofuran) at a temperature below -50°C, preferably in the region of -78°C.

The product of general formula (XVIII) may be obtained by etherification of a product of general formula:



(XIX)

in which R_a, R_b and G_1 are defined as above, by means of a halide of general formula:

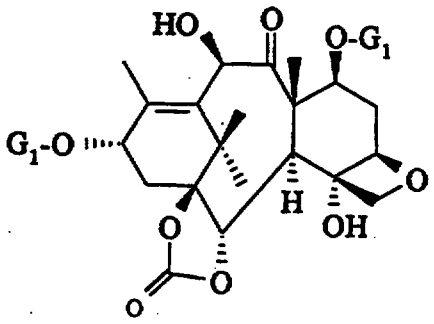
$$R_5\text{-Hal} \qquad \text{(XX)}$$

in which R_5 is defined as above and Hal represents a halogen atom.

It is especially advantageous to metalate the tertiary hydroxyl function of the product of general formula (XIX) by the action of an alkali metal hydride or amide such as sodium hydride of lithium diisopropylamide prior to the action of the product of general formula (XX).

Generally, the reaction is performed in a polar organic solvent such as dimethylformamide at a temperature of between 0 and 50°C.

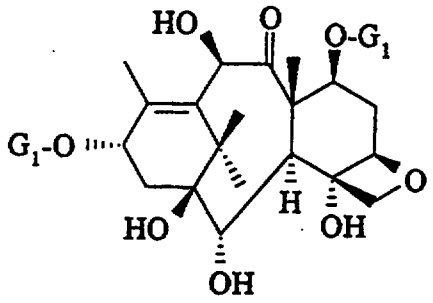
The product of general formula (XIX) may be obtained by the action of a product of general formula (XV) on a product of general formula:



(XXI)

in which G_1 is defined as above, under the conditions described above for the action of a product of general formula (XV) on a product of general formula (XVI).

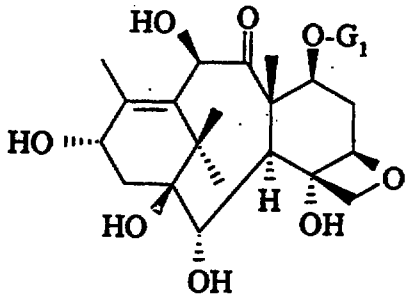
The product of general formula (XXI) may be prepared by the action of phosgene or one of its derivatives, such as triphosgene, on a product of general formula:



(XXII)

in which G_1 is defined as above, working in a basic organic solvent such as pyridine at a temperature below -50°C, preferably in the region of -78°C.

The product of general formula (XXII) may be prepared by the action of a halotrialkylsilane on a product of general formula:



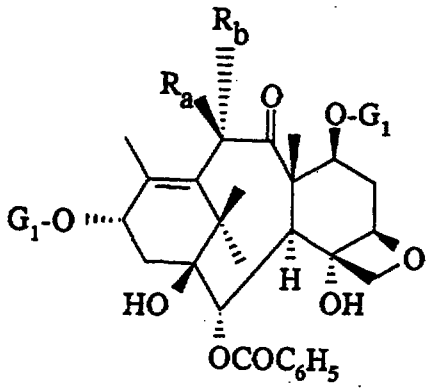
(XXIII)

in which G_1 is defined as above, working in a basic organic solvent.

The product of general formula (XXIII) may be prepared under the conditions described by D.G.I. Kingston et al., Journal of Nat. Prod., 56, 884 (1993).

The products of general formula (XIV) in which R_4 represents a phenyl radical, R_5 is defined as above, R_a represents a hydrogen atom or a hydroxyl, alkoxy, acyloxy or alkoxyacetoxy radical or a protected

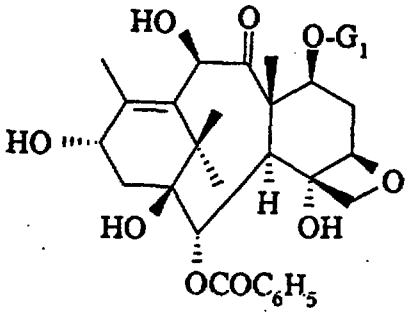
hydroxyl radical and R_b represents a hydrogen atom may be obtained by the action of a product of general formula (XX) on a product of general formula:



(XXIV)

in which R_a and R_b are defined as above and G_1 is defined as above, under the conditions described above for the action of a product of general formula (XX) on a product of general formula (XIX).

The products of general formula (XXIV) in which R_a represents a group protecting the hydroxyl function which is identical to G_1 and R_b represents a hydrogen atom may be obtained by the action of a halotrialkylsilane on a product of general formula:



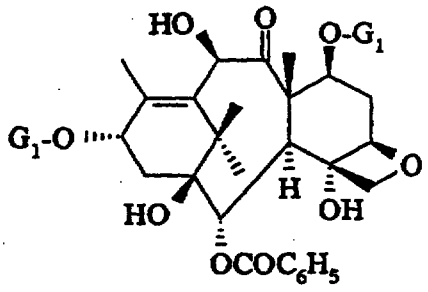
(XXV)

in which G_1 is defined as above.

The reaction is preferably performed in an organic solvent such as dimethylformamide in the

presence of imidazole.

The products of general formula (XXIV) in which R_a represents an alkoxy, acyloxy or alkoxyacetoxy radical, R_b represents a hydrogen atom and G_1 is defined as above may be obtained by the action of a product of general formula (XV) on a product of general formula:



(XXVI)

in which G_1 is as defined above, under the conditions described above for the action of a product of general formula (XV) on a product of general formula (XVI).

The products of general formula (XXVI) may be obtained by the action of a halotrialkylsilane on a product of general formula (XXV) under the conditions described above for the action of a halotrialkylsilane of a product of general formula (XXIII).

The products of general formula (XXV) may be obtained under the conditions described by D.G.I. Kingston et al., Tetrahedron Letters, 35, 6839 (1992).

The products of general formula (I) in which R_a and R_b each represent a hydrogen atom may be obtained by electrolytic reduction of a product of general formula (I) in which R_a represents a hydroxyl radical

or an acyloxy or alkoxyacetoxy radical, or under the conditions described in International Application PCT WO 93/06093.

The products of general formula (I) in which R_a and R_b, together with the carbon atom to which they are attached, form a keto function may be obtained by oxidation of a product of general formula (I) in which R_a represents a hydroxyl radical and R_b represents a hydrogen atom, by means, for example, of pyridinium chlorochromate, pyridinium dichromate, potassium dichromate, ammonium dichromate or manganese dioxide.

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 between 1 and 10 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 overexpresses mdr 1.

The examples which follow illustrate the present invention.

EXAMPLE 1

A solution of 40 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 450 µl of a 0.1N solution of hydrogen

chloride in ethanol is kept stirring at a temperature in the region of 0°C for 3 hours. The reaction mixture is concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. The crude product obtained is dissolved in 10 cm^3 of dichloromethane and 10 cm^3 of saturated aqueous sodium bicarbonate solution. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 59 mg of a product are obtained, which product is purified by preparative chromatography on a silica plate 0.5 mm thick, eluting with a cyclohexane/ethyl acetate (60:40 by volume) mixture. 12 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz); 1.20 (s, 6H : CH_3); 1.35 (s, 9H : $C(CH_3)_3$; from 1.35 to 1.60 (mt, 1H : H at position 7); 1.73 (s, 1H : OH at position 1); 1.81 and 2.27 (2 mts, 1H each : CH_2 at position 19); 1.90 (s, 3H : CH_3); 2.07 and 2.26 (2 mts, 1H each : CH_2 at position 6); 2.35 and 2.87 (2 mts, 1H each : CH_2 at position 14); 3.24 (mt, 1H : OH at position 2'); 3.46 (s, 3H :

OCH_3); 3.70 (d, J = 7, 1H : H at position 3); 3.97 and 4.39 (2 d, J = 9, 1H each : CH_2 at position 20); 4.24 (broad s, 1H : OH at position 10); 4.62 (mt, 1H : H at position 2'); 4.90 (broad d, J = 4, 1H : H at position 5); 4.98 (s, 1H : H at position 10); 5.36 (mt, 1H : H at position 3'); 5.48 (d, J = 10, 1H : CONH); 5.69 (d, J = 7, 1H : H at position 2); 6.24 (mt, 1H : H at position 13); from 7.25 to 7.50 (mt, 5H : aromatic H at position 3'); 7.49 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.57 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.12 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate may be prepared in the following manner:

100 mg of powdered 4Å molecular sieves and 100 mg of sodium azide are added successively to a solution of 112 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-9-ox-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 1 cm^3 of acetonitrile and 0.1 cm^3 of tetrahydrofuran. The reaction mixture is kept stirring at a temperature in the region of 75°C for 3 hours, and 50 cm^3 of dichloromethane and 50 cm^3 of saturated aqueous sodium

chloride solution are then added at a temperature in the region of 20°C. The organic phase is separated after settling has taken place, washed with 2 times 40 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 77 mg of a product are obtained, which product is purified by preparative chromatography on a silica plate 2 mm thick, eluting with a dichloromethane/methanol (90:10 by volume) mixture. 45 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13-yl (2R,4S,5R)-3-tert-butyoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; at a temperature of 330°K; δ in ppm; coupling constants J in Hz) : 1.10 (s, 9H : $C(CH_3)_3$); 1.20 (s, 3H : CH_3); 1.22 (s, 3H : CH_3); 1.29 (mt, 1H : H at position 7); 1.68 (s, 3H : CH_3); 1.78 and from 2.25 to 2.35 (2 mts, 1H each : CH_2 at position 19); 1.99 and 2.24 (dt and broad d, respectively, J = 17 and 4 and J = 17, 1H each : CH_2 at position 6); from 2.25 to 2.35 and 2.56 (mt and dd, respectively (J = 15 and 7), 1H each : CH_2 at position 14); 3.06 (s, 3H : OCH_3); 3.67 (d, J = 7, 1H : H at position 3); 3.80 (s, 3H : $ArOCH_3$); 3.96 and 4.26 (2d, J = 9, 1H each : CH_2 at position 20); 4.17 (broad s,

1H : OH at position 10); 4.66 (d, J = 5, 1H : H at position 2'); 4.78 (broad d, J = 4, 1H : H at position 5); 4.92 (broad s, 1H : H at position 10); 5.48 (mt, 1H : H at position 3'); 5.66 (d, J = 7, 1H : H at position 2); 6.05 (mt, 1H : H at position 13); 6.38 (s, 1H : H at position 5'); 6.91 (d, J = 8.5, 2H: aromatic H at the ortho position with respect to OCH_3); from 7.30 to 7.50 (mt, 7H : aromatic H at position 3' and $OCOC_6H_5$ H at the meta position); 7.41 (d, J = 8.5, 2H : aromatic H at the meta position with respect to OCH_3); 7.58 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 7.96 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate may be prepared in the following manner:

70 mg of (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid, 50 mg of dicyclohexylcarbodiimide and 6 mg of 4-(methylamino)pyridine are added successively at a temperature in the region of 20°C to a solution of 100 mg of 2α-benzoyloxy-5β,20-epoxy-4α-methoxy-9-oxo-7β-trifluoromethanesulphonyloxy-1β,10β,13α-trihydroxy-11-taxene in 4 cm^3 of anhydrous ethyl acetate. The reaction mixture is stirred for 3 hours 30 minutes under an argon atmosphere at a temperature in the region of 20°C. 30 cm^3 of ethyl acetate and 20 cm^3 of

saturated aqueous ammonium chloride solution are added. The organic phase is separated after settling has taken place, washed with 2 times 20 cm^3 of water and then dried over magnesium sulphate. After filtration and concentration to dryness under reduced pressure (2.7 kPa) at 40°C, 200 mg of a product are obtained, which product is purified by chromatography on 15 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with a cyclohexane/ethyl acetate (80:20 by volume) mixture, collecting 8-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 112 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-methoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; at a temperature of 333°K; δ in ppm; coupling constants J in Hz) : 1.10 (s, 9H : $C(CH_3)_3$); 1.13 (s, 3H : CH_3); 1.18 (s, 3H : CH_3); 1.77 (s, 3H: CH_3); 1.87 (s, 3H : CH_3); 2.33 and 2.76 (2 dd, J = 15 and 11 Hz and J = 15 and 7, 1H each : CH_2 at position 14); 2.36 and 2.68 (2 mts, 1H each : CH_2 at position 6); 3.19 (s, 3H : OCH_3); 3.44 (d, J = 6, 1H : H at position 3); 3.83 (s, 3H : $ArOCH_3$); 3.95 (broad s, 1H : OH at position 10); 4.19 and 4.34

(2d, J = 9, 1H each : CH_2 at position 20); 4.66 (d, J = 5.5, 1H : H at position 2'); from 4.85 to 4.95 (mt, 2H : H at position 7 and H at position 5); 5.32 (broad s, 1H : H at position 10); 5.49 (d, J = 5.5, 1H : H at position 3'); 5.60 (d, J = 6, 1H : H at position 2); 5.95 (mt, 1H: H at position 13); 6.38 (s, 1H : H at position 5'); 6.94 (d, J = 8.5, 2H : aromatic H at the ortho position with respect to OCH_3); from 7.30 to 7.50 (mt, 7H : aromatic H at position 3' and $OCOC_6H_5$ H at the meta position); 7.40 (d, J = 8.5, 2H : aromatic H at the meta position with respect to OCH_3); 7.60 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 7.97 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-5β,20-epoxy-4α-methoxy-9-oxo-7β-trifluoromethanesulphonyloxy-1β,10β,13α-trihydroxy-11-taxene may be prepared in the following manner:

25 µl of triflic anhydride are added at a temperature in the region of 0°C to a solution of 51.6 mg of 2α-benzoyloxy-5β,20-epoxy-4α-methoxy-9-oxo-1β,7β,10β,13α-tetrahydroxy-11-taxene in 0.5 cm^3 of dichloromethane and 24 µl of pyridine. The reaction mixture is stirred for 20 minutes at a temperature in the region of 0°C, and 15 cm^3 of dichloromethane and 3 cm^3 of water are then added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous ammonium chloride solution, then dried over magnesium sulphate. After filtration and concentration to dryness under reduced

pressure (2.7 kPa) at 20°C, 72 mg of a product are obtained, which product is purified by chromatography on a silica plate 2 mm thick, eluting with a dichloromethane/methanol (90:10 by volume) mixture.

8 mg of 2α-benzoyloxy-5β,20-epoxy-4α-methoxy-1β,10β,13α-trihydroxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : 1.06 (s, 3H :CH_3); 1.10 (s, 3H : CH_3); 1.86 (s, 3H : CH_3); 2.13 (s, 3H : CH_3); 2.41 and 2.74 (2 mts, 1H each : CH_2 at position 6); 2.47 and 2.59 (2 dd, J = 16 and 10 and J = 16 and 4, 1H each: CH_2 at position 14); 2.96 (broad d, J = 10, 1H : OH at position 13); 3.66 (s, 3H : OCH_3); 3.79 (d, J = 6, 1H : H at position 3); 3.95 (broad s, 1H : OH at position 10); 4.30 and 4.49 (2d, J = 9, 1H each : CH_2 at position 20); 4.57 (mt, 1H : H at position 13); 4.98 (dd, J = 12 and 6, 1H : H at position 7); 5.04 (dd, J = 10 and 3, 1H : H at position 5); 5.42 (broad s, 1H : H at position 10); 5.61 (d, J = 6, 1H : H at position 2); 7.59 (t, J = 7.5, 2H : $OCOC_6H_5$ at the meta position); 7.63 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.00 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-5β,20-epoxy-4α-methoxy-9-oxo-1β,7β,10β,13α-tetrahydroxy-11-taxene may be prepared in the following manner:

7.5 cm^3 of triethylamine-hydrofluoric acid complex are added at a temperature in the region of 20°C to a solution of 338 mg of 2α-benzoyloxy-1β,10β,-dihydroxy-7β,13α-ditriethylsilyloxy-5β,20-epoxy-4α-methoxy-9-oxo-11-taxene in 5 cm^3 of trichloromethane. The reaction mixture is stirred for 2 hours at a temperature in the region of 20°C and 50 cm^3 of dichloromethane and 50 cm^3 of saturated aqueous sodium hydrogen carbonate solution are then added. The organic phase is separated after settling has taken place, washed with 2 times 50 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate. After filtration and concentration to dryness under reduced pressure (2.7 kPa) at 40°C, 420 mg of a product are obtained, which product is purified by chromatography on 60 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with a dichloromethane/methanol (95:5 by volume) mixture, collecting 10-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 184 mg of 2α-benzoyloxy-5β,20-epoxy-4α-methoxy-9-oxo-1β,7β,10β,13α-tetrahydroxy-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constances J in Hz): 1.05 (s, 3H : CH_3); 1.10 (s, 3H : CH_3); 1.72 (s, 3H : CH_3); 1.99 and from 2.40 to

2.55 (2 mts, 1H each : CH_2 at position 6); 2.09 (s, 3H : CH_3); 2.48 and 2.69 (2 dd, J = 16 and 10 and J = 16 and 4, 1H each : CH_2 at position 14); 3.15 (broad d, J = 11, 1H : OH at position 13); 3.65 (s, 3H : OCH_3); 3.74 (d, J = 6, 1H : H at position 3); 3.78 (dd, J = 12 and 6, 1H : H at position 7); 4.13 (broad s, 1H : OH at position 10); 4.31 and 4.45 (2 d, J = 9.5, 1H each : CH_2 at position 20); 4.54 (mt, 1H : H at position 13); 5.00 (dd, J = 10 and 3, 1H : H at position 5); 5.27 (broad s, 1H : H at position 10); 5.61 (d, J = 6, 1H : H at position 2); 7.48 (t, J = 7.5, 2H : $OCOC_6H$ H at the meta position); 7.62 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.03 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-1β,10β-dihydroxy-7β,13α-ditriethylsilyloxy-5β,20-epoxy-4α-methoxy-9-oxo-11-taxene may be prepared in the following manner:

2.22 cm^3 of a 1M solution of phenyllithium in tetrahydrofuran are added at a temperature in the region of -78°C to a solution of 940 mg of 1β,2α-carbonato-7β,13α-ditriethylsilyloxy-5β,20-epoxy-4α-methoxy-10β-methoxyacetoxy-9-oxo-11-taxene in 45 cm^3 of anhydride tetrahydrofuran. The reaction mixture is stirred for 2 hours 30 minutes at a temperature in the region of -78°C, and 20 cm^3 of saturated aqueous ammonium chloride solution are then added. At a temperature in the region of 20°C, 50 cm^3 of water and 100 cm^3 of ethyl acetate are added. The organic phase

is separated after settling has taken place, washed with 2 times 50 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate. After filtration and concentration to dryness under reduced pressure (2.7 kPa) at 40°C, 1.2 mg of a product are obtained, which product is purified by chromatography on 100 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter, eluting with an ethyl acetate/cyclohexane (15:85 by volume) mixture, collecting 10-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 734 mg of 2α-benzoyloxy-1β,10β-dihydroxy-7β,13α-ditriethylsilyloxy-5β,20-epoxy-4α-methoxy-9-oxo-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constances J in Hz): 0.55 (mt, 6 H : ethyl CH_2); 0.70 (q, J = 7.5, 6 H : ethyl CH_2); 0.93 (t, J = 7.5, 9H : ethyl CH_3); 1.05 (t, J = 7.5, 9H : ethyl CH_3); 1.09 (s, 3H : CH_3); 1.14 (s, 3H : CH_3); 1.55 (s, 1H : OH at position 1); 1.71 (s, 3H : CH_3); 2.02 and 2.33 (2 mts, 1H each : CH_2 at position 6); 2.07 (s, 3H : CH_3); 2.12 and 2.74 (2 dd, J = 15 and 9 Hz and J = 15 and 7.5, 1H each: CH_2 at position 14); 3.43 (s, 3H : OCH_3); 3.47 (d, J = 7, 1H : H at position 3); 3.85 (dd, J = 11 and 6, 1H : H7); 4.17 and 4.29 (2 d, J = 8.5, 1H

each : CH_2 20); 4.27 (d, J = 2, 1H : OH at position 10); 4.95 (mt, 1H : H at position 13); 5.00 (dd, J = 10 and 3, 1H : H at position 5); 5.14 (d, J = 2, 1H : H at position 10); 5.59 (d, J = 7, 1H : H at position 2); 7.45 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.57 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.07 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

1β,2α-Carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-methoxy-10β-methoxyacetoxy-9-oxo-11-taxene may be prepared in the following manner:

0.3 g of 4A molecular sieves, 12 cm^2 of methyl iodide and 90 mg of sodium hydride are added at a temperature in the region of 20°C and under an argon atmosphere to a solution of 510 mg of 1β,2α-carbonato-7β,13α-ditriethylsilyloxy-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene in 6 cm^3 of dimethylformamide. The reaction medium is stirred at a temperature in the region of 20°C for 3 hours. 10 cm^3 of saturated aqueous ammonium chloride solution and 30 cm^3 of dichloromethane are added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate. After filtration and concentration to dryness under reduced pressure (2.7 kPa) at 40°C, 715 mg of a product are obtained, which product is purified by chromatography on 50 g of silica (0.063:0.2 mm) contained in a column 1 cm in diameter, eluting with an

ethyl acetate/cyclohexane (25:75 by volume) mixture, collecting 10-cm^3 fractions. Fractions containing only the desired produced are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C.

494 mg of 1β,2α-carbonato-7β,13α-ditriethylsilyloxy-5β,20-epoxy-4α-methoxy-10β-methoxyacetoxy-9-oxo-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : 0.60 (q, J = 7.5, 6 H : ethyl CH_2); 0.68 (q, J = 7.5, 6 H : ethyl CH_2); 0.92 (t, J = 7.5, 9H : ethyl CH_3); 1.03 (t, J = 7.5, 9H : ethyl CH_3); 1.19 (s, 3H : CH_3); 1.23 (s, 3H : CH_3); 1.44 (s, 1H : OH at position 1); 1.71 (s, 3H : CH_3); 1.99 and 2.47 (2 mts, 1H each : CH_2 at position 6); 2.15 (s, 3H : CH_3); 2.32 and 2.93 (2 dd, J = 15 and 9 and J = 15 and 6.5, 1H each : CH_2 at position 14); 2.89 (d, J = 5, 1H : H at position 3); 3.45 and 3.51 (2 s, 3H each : OCH_3); 4.10 (dd, J = 10.5 and 7, 1H : H at position 7); 4.17 (limiting AB, J = 16, 2H : $OCOCH_2O$); 4.41 (d, J = 5, 1H : H at position 2); 4.43 and 4.79 (2 d, J = 10, 1H each: CH_2 at position 20); 4.93 (mt, 1H : H at position 13); 5.10 (broad d, J = 10, 1H : H at position 5); 6.51 (s, 1H : H at position 10).

EXAMPLE 2

15 mg of powdered 4Å molecular sieves and

27 mg of sodium chloride are added successively to a solution of 18 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonate-11-taxene-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate in 233 µl of acetonitrile and 23 µl of tetrahydrofuran. The reaction medium is kept stirring at a temperature in the region of 75°C for 3 hours, and 15 cm^3 of dichloromethane and 15 cm^3 of saturated aqueous sodium chloride solution are then added at a temperature in the region of 20°C. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 22 mg of a product are obtained, which product is purified by preparative chromatography on a silica place 0.25 mm thick, eluting with a dichloromethane/methanol (95:5 by volume) mixture. 10 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,10-epoxy-4α-ethoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 Mhz; $CDCl_3$; δ in ppm; coupling constants J in Hz): 1.21 (s, 3H : CH_3); 1.28 (s, 3H : CH_3); 1.37 (s, 9H : $C(CH_3)_3$); 1.35 (mt, 1H :

H7); 1.47 (t, J = 7, 3H : CH_3 of C_2H_5 at position 4); 1.72 (s, 1H : OH at position 1); 1.84 and 2.32 (t and dd, respectively, J = 6 and J = 10 and 6, 1H each : CH_2 at position 19); 1.89 (s, 3H : CH_3); 2.03 and 2.22 (dt and broad d, respectively, J = 16 and 4 and J = 16, 1H each : CH_2 at position 6); 2.20 and 2.90 (dd and broad dd, respectively, J = 16 and 9, 1H each; CH_2 at position 14); 3.22 (unres.comp., 1H : OH at position 2'); 3.47 and 3.68 (2 mts, 1H each : CH_2 of C_2H_5 at position 4); 3.65 (d, J = 7, 1H : H at position 3); 4.02 and 4.39 (2 d, J = 9, 1H each : CH_2 at position 20); 4.26 (broad s, 1H : OH at position 10); 4.61 (mt, 1H : H at position 2'); 4.87 (mt, 1H : H at position 5); 4.95 (broad s, 1H : H at position 10); 5.33 (broad d, J = 10, 1H : H at position 3'); 5.42 (d, J = 10, 1H : CONH); 5.67 (d, J = 7, 1H : H at position 2); 6.28 (broad t, J = 9, 1H : H at position 13); from 7.30 to 7.45 (mt, 5H : aromatic H at position 3'); 7.49 (t, J = 7.5, 2H : $OCOC_6H_5$ at the meta position); 7.60 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.11 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate may be prepared in the following manner:

A solution of 66 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-

trifluoromethanesulphonyloxy-11-taxene-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 1.5 ml of a 0.1N solution of hydrogen chloride in ethanol is kept stirring at a temperature in the region of 0°C for 19 hours. The reaction mixture is concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. 82 mg of a product are obtained, which product is purified by preparative chromatography on a silica plate 0.25 mm thick, eluting with a dichloromethane/methanol (95:5 by volume) mixture. 20 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (600 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz): 1.13 (s, 3H : CH_3); 1.25 (s, 3H : CH_3); 1.40 (s, 9H : $C(CH_3)_3$); 1.47 (t, J = 7, 3H : CH_3 of C_2H_5 at position 4); 1.58 (s, 1H : OH at position 1); 1.90 and 2.25 (mt and dd respectively, J = 16 and 9, 1H each : CH_2 at position 14); 1.92 (s, 3H : CH_3); 1.94 (s, 3H : CH_3); 2.40 and 2.70 (2 mts, 1H each: CH_2 at position 6); 3.18 (broad s, 1H : OH at position 2'); 3.43 (d, J = 6.5, 1H : H at position 3); 3.75 and 3.82 (2 mts, 1H each : CH_2 of C_2H_5 at position 4); 4.05 (broad s, 1H : OH at position 10); 4.28 and 4.46 (2 d, J = 9, 1H each : CH_2 at position 20); 4.63

(mt, 1H : H at position 2'); 4.92 (dd, J = 11 and 7, 1H : H at position 7); 5.03 (dd, J = 10 and 2, 1H : H at position 5); 5.32 (mt, 1H : H at position 3'); 5.33 (broad s, 1H : H at position 10); 5.45 (d, J = 10, 1H : CONH); 5.65 (d, J = 6.5, 1H : H at position 2); 6.20 (broad t, J = 9, 1H : H at position 13); from 7.30 to 7.55 (mt, 5H : aromatic H at position 3'); 7.49 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.61 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.02 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonate-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate may be prepared in the following manner:

60 mg of (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid, 42 mg of dicyclohexylcarbodiimide and 5 mg of 4-(dimethylamino)pyridine are added successively at a temperature in the region of 20°C to a solution of 90 mg of 2α-benzoyloxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonyloxy-1β,10β,13α-trihydroxy-11-taxene in 4 cm^3 of anhydrous ethyl acetate. The reaction mixture is stirred for 6 hours under an argon atmosphere at a temperature in the region of 20°C. 30 cm^3 of ethyl acetate and 20 cm^3 of saturated aqueous ammonium chloride solution are added. The organic phase is separated after settling

has taken place, washed with 2 times 20 cm^3 of water, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 140 mg of a product are obtained, which product is purified by chromatography on 30 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with a cyclohexane/ethyl acetate (70:30 by volume) mixture collecting 8-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 110 mg of 2α-benzoyloxy-1β,10β-dihydroxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : 1.10 (s, 15H : $C(CH_3)_3$ - CH_3 and CH_3 of C_2H_5 at position 4); 1.19 (s, 3H : CH_3); 1.51 (s, 1H : OH at position 1); 1.64 (s, 3H : CH_3); 1.85 (s, 3H : CH_3); from 2.25 to 2.40 and 2.66 (2 mts, 1H each : CH_2 at position 6); from 2.25 to 2.40 and 2.88 (mt and dd respectively, J = 16 and 8, 1H each : CH_2 at position 14); 3.35 (d, J = 6.5, 1H : H at position 3); 3.52 and 3.62 (2 mts, 1H each : CH_2 of C_2H_5 at position 4); 3.84 (s, 3H : $ArOCH_3$); 4.01 (d, J = 1, 1H : OH at position 10); 4.20 and 4.34 (2d, J = 9, 1H

each : CH_2 at position 20); 4.64 (d, J = 4, 1H : H at position 2'); 4.85 (dd, J = 11.5 and 6.5, 1H : H at position 7); 4.92 (broad d, J = 10.5, 1H : H at position 5); 5.26 (d, J = 1, 1H : H at position 10); 5.55 (spread unres. comp. 1H : H at position 3'); 5.59 (d, J = 6.5, 1H : H at position 2); 5.91 (mt, 1H : H at position 13); 6.40 (spread unres. comp. 1H : H at position 5'); 6.94 (d, J = 8.5, 2H : H at the ortho position with respect to OCH_3); from 7.30 to 7.50 (mt, 9H : aromatic H at position 3', H at the meta position with respect to OCH_3 and $OCOC_6H_5$ H at the meta position); 7.63 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 7.95 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-5β,20-epoxy-4α-ethoxy-9-oxo-7β-trifluoromethanesulphonyloxy-1β,10β,13α-trihydroxy-11-taxene are prepared in the following manner:

200 µl of triflic anhydride are added at a temperature in the region of 0°C to a solution of 260 mg of 2α-benzoyloxy-5β,20-epoxy-4α-ethoxy-9-oxo-1β,7β,10β,13α-tetrahydroxy-11-taxene in 10 cm^3 of dichloromethane and 145 µl of pyridine. The reaction mixture is stirred for 45 minutes at a temperature in the region of 0°C, and 15 cm^3 of dichloromethane and 10 cm^3 of water are then added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium hydrogen carbonate solution, then dried over magnesium sulphate,

filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. 308 mg of a product are obtained, which product is purified by chromatography on 60 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with an ethyl acetate/cyclohexane (40:60 by volume) mixture and collecting 10-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 90 mg of 2α-benzoyloxy-5β,20-epoxy-4α-ethoxy-1β,10β,13α-trihydroxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (300 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : 1.07 (s, 3H : CH_3); 1.12 (s, 3H : CH_3); 1.47 (t, J = 7, 3H : CH_3 from C_2H_5 at position 4); 1.87 (s, 3H : CH_3); 2.05 (s, 1H : OH at position 1); 2.15 (s, 3H : CH_3); 2.38 and 2.75 (2 mts, 1H each : CH_2 at position 6); 2.49 and 2.65 (2 dd, J = 16 and 9 and J = 16 and 3.5, respectively, 1H each : CH_2 at position 14); 2.89 (d, J = 10, 1H : OH at position 13); 3.72 (d, J = 6.5, 1H : H at position 3); from 3.80 to 3.95 (mt, 2H : CH_2 from C_2H_5 at position 4); 3.97 (d, J = 1, 1H : OH at position 10); 4.30 and 4.48 (2d, J = 9, 1H each : CH_2 at position 20); 4.57 (broad t, J = 10, 1H : H at position 13); from 4.95 to 5.15 (mt, 2H : H at position 5 and H at position 7);

5.42 (d, J = 1, 1H : H at position 10); 5.63 (d, J = 6.5, 1H : H at position 2); 7.48 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.63 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.00 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-5β,20-epoxy-4α-ethoxy-9-oxo-1β,7β,10β,13α-tetrahydroxy-11-taxene may be prepared in the following manner:

10 cm^3 of triethylamine-hydrofluoric acid complex are added at a temperature in the region of 20°C to a solution of 524 mg of 2α-benzoyloxy-5β,20-epoxy-4α-ethoxy-1β-hydroxy-9-oxo-7β,10β,13α-tris-(triethylsilyloxy)-11-taxene in 8 cm^3 of dichloromethane. The reaction mixture is stirred for 7 hours at a temperature in the region of 20°C, and 100 cm^3 of dichloromethane and 200 cm^3 of saturated aqueous sodium hydrogen carbonate solution are then added. The organic phase is separated after settling has taken place, washed with 2 times 50 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 260 mg of 2α-benzoyloxy-5β,20-epoxy-4α-ethoxy-9-oxo-1β,7β,10β,13α-tetrahydroxy-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : 1.06 (s, 3H : CH_3); 1.12

(s, 3H : CH_3); 1.46 (t, J = 7, 3H : CH_3 of C_2H_5 at position 4); 1.72 (s, 3H : CH_3); 1.99 and 2.50 (2 mts, 1H each : CH_2 at position 6); 2.04 (s, 1H : OH at position 1); 2.10 (s, 3H : CH_3); from 2.45 to 2.55 (mt, 1H : OH at position 7); 2.50 and 2.65 (mt and dd, respectively, J = 16 and 3.5, 1H each : CH_2 at position 14); 3.06 (d, J = 11, 1H : OH at position 13); 3.70 (d, J = 6.5, 1H : H at position 3); 3.84 (mt, 1H : H at position 7); 3.89 and 3.96 (2 mts, 1H each : CH_2 of C_2H_5 at position 4); 4.15 (broad s, 1H : OH at position 10); 4.31 and 4.44 (2d, J = 9 Hz, 1H each : CH_2 at position 20); 4.54 (broad t, J = 10; 1H : H 13); 4.93 (dd, J = 10 and 3.5, 1H : H at position 5); 5.28 (s, 1H : H at position 10); 5.63 (d, J = 6.5, 1H : H 2) 7.48 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.61 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.02 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

2α-Benzoyloxy-5β,20-epoxy-4α-ethoxy-1β-hydroxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene may be prepared according to one of the following methods:

1) 320 µl of a 1M solution of phenyllithium in tetrahydrofuran are added at a temperature in the region of -78°C to a solution of 253 mg of 1β,2α-carbonate-5β,20-epoxy-4α-ethoxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene in 13 cm^3 of anhydrous tetrahydrofuran. The reaction mixture is stirred for 1 hour 30 minutes at a temperature in the region of

-78°C, and 10 cm^3 of saturated aqueous ammonium chloride solution are then added. At a temperature in the region of 20°C, 10 cm^3 of water and 50 cm^3 of ethyl acetate are added. The organic phase is separated after settling has taken place, washed with 2 times 20 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 500 mg of a product are obtained, which product is purified by chromatography on 50 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter, eluting with an ethyl acetate/cyclohexane (15:85 by volume) mixture, collecting 10-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 260 mg of 2α-benzoyloxy-5β,20-epoxy-4α-ethoxy-1β-hydroxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : from 0.55 to 0.75 (mt, 18H : CH_2 of C_2H_5); from 0.90 to 1.10 (mt, 27H : CH_3 of C_2H_5); 1.15 (s, 3H : CH_3); 1.22 (s, 3H : CH_3); 1.38 (t, J = 7, 3H : CH_3 of C_2H_5 in position 4); 1.50 (s, 1H : OH at position 1); 1.65 (s, 3H : CH_3); 2.00 and 2.39 (2 mts, 1H each : CH_2 at position 6); 2.02 (s, 3H : CH_3); 2.05 and 2.85 (2 dd, J = 16 and 9 and J = 16 and

8.5, respectively, 1H each : CH_2 at position 14); 3.43 (d, J = 6.5, 1H : H 3); 3.44 and 3.90 (2 mts, 1H each : CH_2 of C_2H_5 at position 4); 3.91 (mt, 1H : H at position 7); 4.20 and 4.30 (2d, J = 9, 1H each : CH_2 at position 20); 4.93 (dd, J = 10 and 3.5, 1H : H at position 5); 4.97 (broad t, J = 9, 1H : H at position 13); 5.17 (s, 1H : H at position 10); 5.60 (d, J = 6.5, 1H : H 2); 7.45 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.57 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.06 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

1β,2α-Carbonato-5β,20-epoxy-4α-ethoxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene may be prepared in the following manner:

0.3 of 4Å molecular sieves, 4.2 cm^3 of ethyl iodide and 68 mg of 80% sodium hydride are added at a temperature in the region of 20°C and under an argon atmosphere to a solution of 353 mg of 1β,2α-carbonato-5β,20-epoxy-4α-hydroxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene in 2.1 cm^3 of dimethylformamide. The reaction mixture is stirred at a temperature in the region of 20°C for 1 hour. 10 cm^3 of saturated aqueous ammonium chloride solution and 30 cm^3 of dichloromethane are added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 500 mg of a product are obtained,

which product is purified by chromatography on 25 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with an ethyl acetate/cyclohexane (10:90 by volume) mixture, collecting 10-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 253 mg of 1β,2α-carbonato-5β,20-epoxy-4α-ethoxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : from 0.55 to 0.75 (mt, 18H : CH_2 of C_2H_5); from 0.90 to 1.10 (mt, 27H : CH_3 of C_2H_5); 1.17 (s, 3H : CH_3); 1.25 (s, 3H : CH_3); 1.25 (t, J = 7, 3H : CH_3 of C_2H_5 at position 4); 1.68 (s, 3H : CH_3); 1.98 and 2.47 (2 mts, 1H each : CH_2 at position 6); 1.98 (s, 3H : CH_3); 2.26 and 3.07 (2 dd, J = 16 and 9 and J = 16 and 7, respectively, 1H each : CH_2 at position 14); 2.87 (d, J = 5 Hz, 1H : H at position 3); 3.71 and 3.82 (2 mts, 1H each : CH_2 of C_2H_5 at position 4); 4.05 (dd, J = 10 and 7, 1H : H at position 7); 4.39 (d, J = 5, 1H : H at position 2); 4.45 and 4.77 (2d, J = 9, 1H each: CH_2 at position 20); 4.97 (mt, 1H : H at position 13); 5.03 (broad d, J = 10, 1H : H at position 5); 5.15 (s, 1H : H at position 10).

1β,2α-Carbonato-5β,20-epoxy-4α-hydroxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene may be

prepared in the following manner:

51 mg of imidazole and 50 µL of triethylsilane chloride are added at a temperature in the region of 20°C and under an argon atmosphere to a solution of 98 mg of 7β,13α-bis(triethylsilyloxy)-1β,2α-carbonato-4α,10β-dihydroxy-5β,20-epoxy-9-oxo-11-taxene in 1 cm^3 of dimethylformamide. The reaction mixture is stirred at a temperature in the region of 20°C for 72 hours. 10 cm^3 of water and 20 cm^3 of ethyl acetate are added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 190 mg of a product are obtained, which product is purified by preparative chromatography on a thin layer 2 mm thick, eluting with a cyclohexane/ethyl acetate (75:25 by volume) mixture. 58 mg of 1β,2α-carbonyldioxy-5β,20-epoxy-4α-hydroxy-9-oxo-7β,10β,13α-tris-(triethylsilyloxy)-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : from 0.50 to 0.70 and 0.74 (2 mts, 12H and 6H, respectively : CH_2 of C_2H_5); from 0.90 to 1.10 (mt, 27H : CH_3 of C_2H_5); 1.14 (s, 3H : CH_3); 1.19 (s, 3H : CH_3); 1.63 (s, 3H : CH_3); 1.98 and 2.50 (2 mts, 1H each: CH_2 at position 6); 1.98 (s, 3H :

CH_3); 2.55 and 2.67 (J = 16 and 9 and J = 16 and 3.5, respectively, 1H each : CH_2 at position 14); 3.00 (s, 1H : OH at position 4); 3.11 (d, J = 5, 1H : H at position 3); 4.14 (dd, J = 10 and 7, 1H : H at position 7), 4.33 (d, J = 5, 1H : H 2); 4.54 (limiting AB, J = 9, 2H : CH_2 at position 20); 4.73 (broad d, J = 9, 1H : H at position 13); 4.77 (broad d, J = 10, 1H : H at position 5); 5.23 (s, 1H : H at position 10).

7β,13α-Bis(triethylsilyloxy)-1β,2α-carbonato-4α,10β-dihydroxy-5β,20-epoxy-9-oxo-11-taxene may be prepared in the following manner:

0.3 g of 4Å molecular sieves and 470 mg of zinc iodide are added at a temperature in the region of 20°C and under an argon atmosphere to a solution of 108 mg of 7β,13α-bis(triethylsilyloxy)-1β,2α-carbonato-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene in 3.5 cm^3 of methanol. The reaction mixture is stirred at a temperature in the region of 20°C for 72 hours. 10 cm^3 of water and 20 cm^3 of ethyl acetate are added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 90 mg of a product are obtained, which product is purified by preparative chromatography on a thin layer 2 mm thick, eluting with a cyclohexane/ethyl acetate (75:25 by volume) mixture. 56 mg of 7β,13α-bis(triethylsilyloxy)-

1β,2α-carbonato-4α,10β-dihydroxy-5β,20-epoxy-9-oxo-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (400 MHz; $CDCl_3$,; δ in ppm; coupling constants J in Hz) : 0.54 and 0.74 (2 mts, 6H each : CH_2 of C_2H_5); 0.91 and 1.03 (2 t, J = 7.5 Hz, 9H each : CH_3 of C_2H_5); 1.12 (s, 3H : CH_3); 1.20 (s, 3H : CH_3); 1.72 (s, 3H : CH_3); 1.98 and 2.46 (2 mts, 1H each : CH_2 at position 6); 2.04 (s, 3H : CH_3); 2.55 and 2.67 (2 dd, J = 16 and 9 and J = 16 and 3.5, respectively, 1H each : CH_2 at position 14); 3.00 (s, 1H : OH at position 4); 3.14 (d, J = 5, 1H : H at position 3); 4.07 (d, J = 10 and 7, 1H : H at position 7); 4.19 (d, J = 2, 1H : OH at position 10); 4.33 (d, J = 5, 1H : H at position 2); 4.54 (limiting AB, J = 10, 2H : CH_2 at position 20); 4.76 (broad d, J = 9, 1H : H at position 13); 4.82 (broad d, J = 10, 1H : H at position 5); 5.18 (d, J = 2, 1H : H at position 10).

2) 0.3 g of 4Å molecular sieves, 1 cm^3 of ethyl iodide and 34 mg of 50% sodium hydride are added at a temperature in the region of 20°C and under an argon atmosphere to a solution of 200 mg of 2α-benzoyloxy-1β,4α-dihydroxy-5β,20-epoxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene in 6 cm^3 of dimethylformamide. The reaction mixture is stirred at a temperature in the region of 20°C for 1 hour. 10 cm^3 of saturated aqueous ammonium chloride solution and 30 cm^3

of ethyl acetate are added. The organic phase is separated after settling has taken place, washed with 2 times 10 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 320 mg are obtained, the product being purified by chromatography on 100 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with an ethyl acetate/cyclohexane (10:90 by volume) mixture, collecting 10-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 38 mg of 2α-benzoyloxy-4α-ethoxy-5β,20-epoxy-1β-hydroxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene are obtained in the form of a white foam, the physical characteristics of which are identical to those of the product obtained above.

2α-Benzoyloxy-1β,4α-dihydroxy-5β,20-epoxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene may be prepared in the following manner:

4.6 g of imidazole and 2.35 g of triethylsilane chloride are added at a temperature in the region of 20°C and under an argon atmosphere to a solution of 4.2 g of 2α-benzoyloxy-5β,20-epoxy-9-oxo-1β,4α,10β,13α-tetrahydroxy-7β-triethylsilyloxy-11-taxene, prepared according to D.G. Kingston et. al. Tetrahedron Letters.35, 6839 (1994), in 50 cm^3 of dimethylformamide. The reaction mixture is stirred at a

temperature in the region of 20°C for 72 hours. 30 cm^3 of water and 100 cm^3 of ethyl acetate are added. The organic phase is separated after settling has taken place, washed with 2 times 30 cm^3 of saturated aqueous sodium chloride solution, then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 12 g of a product are obtained, which product is purified by chromatography on 100 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter, eluting with an ethyl acetate/cyclohexane (10:90 by volume) mixture, collecting 20-cm^3 fractions. Fractions containing only the desired product are pooled and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 3.6 g of 2α-benzoyloxy-1β,4α-dihydroxy-5β,20-epoxy-9-oxo-7β,10β,13α-tris(triethylsilyloxy)-11-taxene are thereby obtained in the form of a white foam, the physical characteristics of which are as follows:

- proton NMR spectrum (300 MHz; $CDCl_3$; δ in ppm; coupling constants J in Hz) : 0.57 and from 0.60 to 0.85 (2 mts, 6H and 12H, respectively : CH_2 of C_2H_5); from 0.90 to 1.10 (mt, 30H : CH_3 of C_2H_5 and CH_3); 1.21 (s, 3H : CH_3); 1.53 (s, 3H : CH_3); 1.63 (s, 1H : OH at position 1); 1.96 (s, 3H : CH_3); 1.97 and 2.45 (2 mts, 1H each : CH_2 at position 6); 2.32 and 2.60 (2 dd, J = 16 and 9 and J = 16 and 2.5, respectively, 1H each : CH_2 at position 14); 3.61 (d, J = 6, 1H : H at position 3); 3.80 (broad s, 1H : OH at position 4);

4.05 (dd, J = 11.5 and 6, 1H : H at position 7); 4.23 and 4.27 (limiting AB, J = 9, 2H : CH_2 at position 20); 4.64 (broad d, J = 9, 1H : H at position 13); 4.71 (dd, J = 10 and 4, 1H : H at position 5); 5.25 (s, 1H : H at position 10); 5.54 (d, J = 6, 1H : H at position 2); 7.42 (t, J = 7.5, 2H : $OCOC_6H_5$ H at the meta position); 7.55 (t, J = 7.5, 1H : $OCOC_6H_5$ H at the para position); 8.11 (d, J = 7.5, 2H : $OCOC_6H_5$ H at the ortho position).

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 adrenal glands. These pathological conditions can also include psoriasis, solid tumours, cancers of the ovary, breast, brain, prostate, colon, stomach, kidney or testicles, Kaposi's sarcoma, cholangiocarcinoma, choriocarcinoma, neuroblastoma, Wilms' tumour, Hodgkin's disease, melanoma, multiple myeloma, chronic lymphocytic leukaemia and acute or chronic granulocytic

lymphoma. 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.

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.

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.

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.

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 petroleum, 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.

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.

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.

The therapeutic treatment may be performed concurrently with other therapeutic treatments including antineoplastic 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. 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 mechloretamine, cyclophosphamide, melphalan and chlorambucil, alkyl sulphonates such as busulfan, nitrosoureas such as carmustine, lomustine, semustine and streptozocin, triazenes 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 vendesine, 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 mitotane and aminoglutethymide, hormones and antagonists such as adrenocorticosteroids such as prednisone, progestins such as hydroxyprogesterone caproate, methoxyprogesterone acetate and megestrol acetate, oestrogens such as diethylstilboestrol and ethynyloestradiol, antioestrogens such as tamoxifen, and androgens such as testosterone propionate and fluoxymesterone.

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. 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. 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.

In man, the doses are generally between 0.01 and 200 mg/kg. For intraperitoneal administration, the doses will generally be between 0.1 and 100 mg/kg, preferably between 0.5 and 50 mg/kg and still more specifically between 1 and 10 mg/kg. For intravenous administration, the doses are generally between 0.1 and 50 mg/kg, preferably between 0.1 and 5 mg/kg and still more specifically between 1 and 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.

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

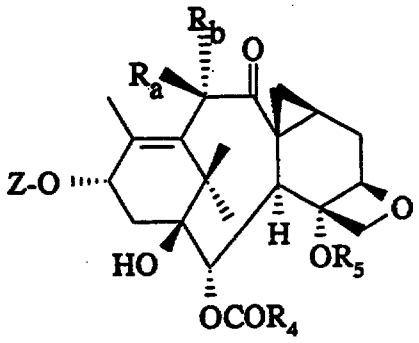
EXAMPLE

40 mg of the product obtained in Example 1 are dissolved in 1 cm^3 of Emulphor EL 620 and 1 cm^3 of ethanol, and the solution is then diluted by adding 18 cm^3 of physiological saline.

The composition is administered by infusion over 1 hour by introduction in physiological solution.

CLAIMS

1. New taxoids of general formula:

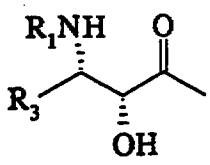


(I)

in which:

R_a represents a hydrogen atom or a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl portion contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, or alternatively R_a and R_b, together with the carbon atom to which they are attached, form a keto function,

Z represents a hydrogen atom or a radical of general formula:



(II)

in which:

R_1 represents a benzoyl radical optionally substituted with one or more identical or different atoms or radicals chosen from halogen atoms and alkyl

radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms or trifluoromethyl radicals, a thenoyl or furoyl radical or 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 chosen from halogen atoms and hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino or 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 chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms), cyano or carboxyl radicals or alkoxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

* C L M S *

- a phenyl or α- or β-naphthyl radical optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms, or a 5-membered aromatic heterocyclic radical preferably chosen from furyl and thienyl radicals,

- 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 atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals, or a 5-membered aromatic heterocycle containing one or more identical or different hetero atoms chosen from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more identical

* C L M S *

or different substituents chosen from halogen atoms and alkyl, aryl, amino, alkylamino, dialkylamino, alkoxycarbonylamino, acyl, arylcarbonyl, cyano, carboxyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl or alkoxycarbonyl radicals, on 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, and that the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms, and that the aryl radicals are phenyl or α- or β-naphthyl radicals, and

R_4 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 cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 11 carbon atoms, these radicals being optionally substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkyloxy radicals containing 1 to 4 carbon atoms, dialkyamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino or 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, optionally substituted phenyl radicals, cyano or carboxyl radicals or alkoxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

- or an aryl radical optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxylalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro, azido, trifluoromethyl or trifluoromethoxy radicals,

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

R^5 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 cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 11 carbon atoms, these radicals being optionally substituted with one or more substituents chosen from halogen atoms and hydroxyl

radicals, alkyloxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl portion contains 1 to 4 carbon atoms, piperidino or 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, optionally substituted phenyl radicals, cyano or carboxyl radicals or alkyloxycarbonyl radicals in which the alkyl portion contains 1 to 4 carbon atoms,

on the understanding that the cycloalkyl, cycloalkenyl or bicycloalkyl radicals may be optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms.

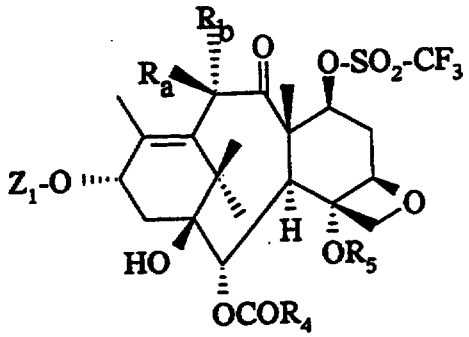
2. New taxoids according to claim 1 for which R_a represents a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl portion contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-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 chosen from halogen atoms (fluorine, chlorine) and alkyl, alkoxy, dialkylamino, acylamino, alkoxycarbonylamino or trifluoromethyl radicals, or a 2- or 3-furyl, 2- or 3-thienyl or 2-, 4- or 5-thiazolyl radical, and R_4 represents a phenyl radical optionally substituted with one or more identical or different atoms or radicals chosen from halogen atoms and alkyl, alkoxy, amino, alkylamino, dialkylamino, acylamino, alkoxycarbonylamino, azido, trifluoromethyl and trifluoromethoxy radicals, or a 2- or 3-thienyl or 2- or 3-furyl radical, and R_5 represents an optionally substituted alkyl radical containing 1 to 4 carbon atoms.

3. New taxoids according to claim 1 for which R_a represents a hydrogen atom or a hydroxyl or acetyloxy or methoxyacetoxy radical and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-O-CO- in which R_2 represents a tert-butyl radical and R_3 represents an isobutyl, isobutenyl, butenyl, cyclohexyl, phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl or 5-thiazolyl radical and R_4 represents a phenyl radical optionally substituted with a halogen atom and R_5 represents an alkyl radical containing 1 to

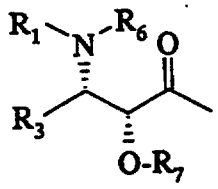
4 carbon atoms.

4. Process for preparing a product according to one of claims 1, 2 or 3, characterized in that a product of general formula:



(III)

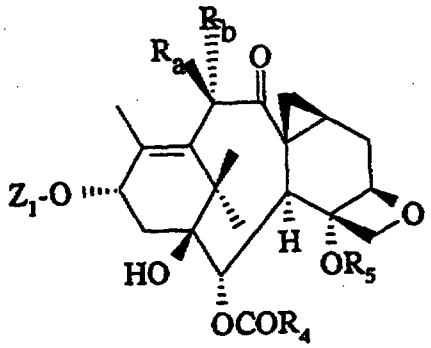
in which Z_1 represents a hydrogen atom or a radical of general formula (II) in which R_1 and R_3 are defined as above or a radical of general formula:



(IV)

in which R_1 and R_3 are defined as above, and either R_6 represents a hydrogen atom and R_7 represents a group protecting the hydroxyl function, or R_6 and R_7 together form a saturated 5- or 6-membered heterocycle, R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, preferably a 2,2,2-trichloroethoxycarbonyloxy radical, and R_b represents a hydrogen atom, or alternatively R_a and R_b, together with the nitrogen atom to which they are attached, form a

keto function, is treated with an alkali metal halide or an alkali metal azide or a quaternary ammonium salt or an alkali metal phosphate to obtain a product of general formula:



(V)

in which Z_1, R_4, R_5, R_a and R_b are defined as above, followed, if necessary, by replacement of the protective group borne by R_a or of the protective groups represented by R_7 and/or by R_6 and R_7 by the hydrogen atoms.

5. Process for preparing a product according to one of claims 1 to 3 for which R_4 and R_5 are defined as in one of claims 1 to 3 and R_a and R_b each represent a hydrogen atom, characterized in that a product according to one of claims 1 to 3 for which R_a represents a hydroxyl, acyloxy or alkoxyacetoxy radical is reduced electrolytically.

6. Process for preparing a product according to one of claims 1 to 3 for which R_4 and R_5 are defined as in one of claims 1 to 3 and R_a and R_b, together with the carbon atom to which they are attached, form a keto function, characterized in that a

product according to one of claims 1 to 3, for which R_a represents a hydroxyl radical and R_b represents a hydrogen atom is oxidized.

7. Pharmaceutical composition, characterized in that it contains at least one product according to one of claims 1 to 3 for which Z represents a radical of general formula (II), in combination with one or more pharmaceutically acceptable products which may be inert or pharmacologically active.