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(54) Title: C10 CARBAMOYLOXY SUBSTITUTED TAXANES AS ANTITUMOR AGENTS

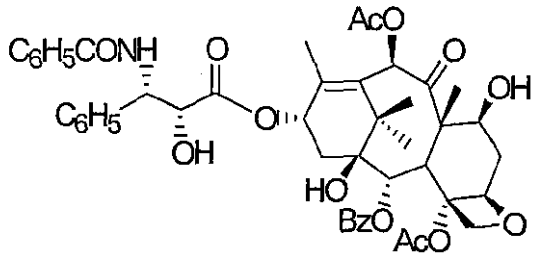
(57) Abstract: Taxanes having a carbamoyloxy substituent at C(10), a hydroxy substituent at C(7), and a range of C(2), C(9), C(14), and side chain substituents.

C10 CARBAMOYLOXY SUBSTITUTED TAXANES AS ANTITUMOR AGENTS

BACKGROUND OF THE INVENTION

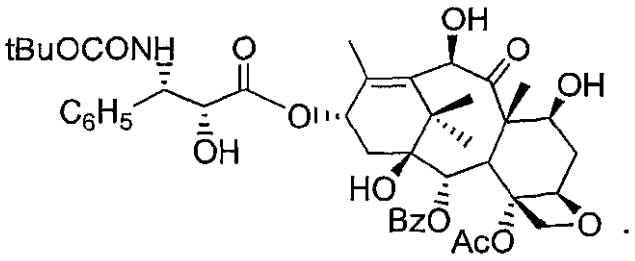
The present invention is directed to novel taxanes which have exceptional utility as antitumor agents.

The taxane family of terpenes, of which baccatin III and taxol are members, has been the subject of considerable interest in both the biological and chemical arts. Taxol itself is employed as a cancer chemotherapeutic agent and possesses a broad range of tumor-inhibiting activity. Taxol has a 2′R, 3′S configuration and the following structural formula:



wherein Ac is acetyl.

Colin et al. reported in U.S. Patent 4,814,470 that certain taxol analogs have an activity significantly greater than that of taxol. One of these analogs, commonly referred to as docetaxel, has the following structural formula:



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Although taxol and docetaxel are useful chemotherapeutic agents, there are limitations on their effectiveness, including limited efficacy against certain types of cancers and toxicity to subjects when administered at various doses. Accordingly, a need remains for additional chemotherapeutic agents with improved efficacy and less toxicity.

SUMMARY OF THE INVENTION

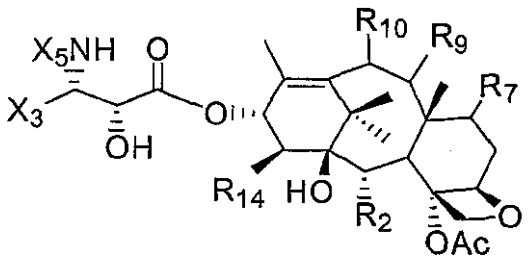
Among the objects of the present invention, therefore, is the provision of taxanes which compare favorably to taxol and docetaxel with respect to efficacy as anti-tumor agents and with respect to toxicity. In general, these taxanes possess a carbamoyloxy substituent at C-10, a hydroxy substituent at C-7 and a range of C-3' substituents.

Briefly, therefore, the present invention is directed to the taxane composition, per se, to pharmaceutical compositions comprising the taxane and a pharmaceutically acceptable carrier, and to methods of administration.

Other objects and features of this invention will be in part apparent and in part pointed out hereinafter.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In one embodiment of the present invention, the taxanes of the present invention correspond to structure (1):



(1)

wherein

R_2 is acyloxy;

R_7 is hydroxy;

R_9 is keto, hydroxy, or acyloxy;

R_{10} is carbamoyloxy;

R_{14} is hydrido or hydroxy;

X_3 is substituted or unsubstituted alkyl, alkenyl, alkynyl, phenyl or heterocyclo;

X_5 is $-COX_{10}$, $-COOX_{10}$, or $-CONHX_{10}$;

X_{10} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo;

Ac is acetyl; and

R_7, R_9, and R_{10} independently have the alpha or beta stereochemical configuration.

In one embodiment, R_2 is an ester ($R_{2a}C(O)O$-), a carbamate ($R_{2a}R_{2b}NC(O)O$-), a carbonate ($R_{2a}OC(O)O$-), or a thiocarbamate ($R_{2a}SC(O)O$-) wherein R_{2a} and R_{2b} are independently hydrogen, hydrocarbyl, substituted hydrocarbyl or heterocyclo. In a preferred embodiment, R_2 is an ester ($R_{2a}C(O)O$-), wherein R_{2a} is aryl or heteroaromatic. In another preferred embodiment, R_2 is an ester ($R_{2a}C(O)O$-), wherein R_{2a} is substituted or unsubstituted phenyl, furyl, thienyl, or pyridyl. In one particularly preferred embodiment, R_2 is benzoyloxy.

While R_9 is keto in one embodiment of the present invention, in other embodiments R_9 may have the alpha or beta stereochemical configuration, preferably the beta stereochemical configuration, and may be, for example, α- or β-hydroxy or α- or β-acyloxy. For example, when R_9 is acyloxy, it may be an ester ($R_{9a}C(O)O$-), a carbamate ($R_{9a}R_{9b}NC(O)O$-), a carbonate ($R_{9a}OC(O)O$-), or a thiocarbamate ($R_{9a}SC(O)O$-) wherein R_{9a} and R_{9b} are independently hydrogen, hydrocarbyl, substituted hydrocarbyl or heterocyclo. If R_9 is an ester ($R_{9a}C(O)O$-), R_{9a} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaromatic. Still more preferably, R_9 is an ester ($R_{9a}C(O)O$-), wherein R_{9a} is substituted or unsubstituted phenyl, substituted or unsubstituted furyl, substituted or unsubstituted thienyl, or substituted or unsubstituted pyridyl. In one embodiment R_9 is ($R_{9a}C(O)O$-) wherein R_{9a} is methyl, ethyl, propyl (straight, branched or cyclic), butyl (straight, branched or cyclic), pentyl, (straight, branched or cyclic), or hexyl (straight, branched or cyclic). In another embodiment R_9 is ($R_{9a}C(O)O$-) wherein R_{9a} is substituted methyl, substituted ethyl, substituted propyl (straight, branched or cyclic), substituted butyl (straight, branched or cyclic), substituted pentyl, (straight, branched or cyclic), or substituted hexyl (straight, branched or cyclic) wherein the substituent(s) is/are selected from the group consisting of heterocyclo, alkoxy, alkenoxy, alkynoxy, aryloxy, hydroxy, protected hydroxy, keto, acyloxy, nitro, amino, amido, thiol, ketal, acetal, ester and ether moieties, but not phosphorous containing moieties.

In one embodiment, R_{10} is $R_{10a}R_{10b}NCOO$- wherein R_{10a} and R_{10b} are independently hydrogen, hydrocarbyl, substituted hydrocarbyl, or heterocyclo. Exemplary preferred R_{10} substituents include $R_{10a}R_{10b}NCOO$- wherein (a) R_{10a} and R_{10b} are each hydrogen, (b) one of R_{10a} and R_{10b} is hydrogen and the other is (i) substituted or unsubstituted C_1 to C_8 alkyl such as methyl, ethyl, or straight, branched or cyclic propyl, butyl, pentyl, or hexyl; (ii) substituted or unsubstituted

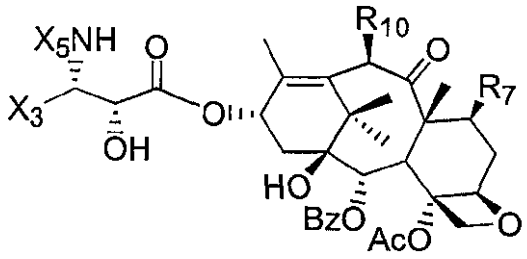
C_2 to C_8 alkenyl such as ethenyl or straight, branched or cyclic propenyl, butenyl, pentenyl or hexenyl; (iii) substituted or unsubstituted C_2 to C_8 alkynyl such as ethynyl or straight or branched propynyl, butynyl, pentynyl, or hexynyl; (iv) substituted or unsubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl, or (c) R_{10a} and R_{10b} are independently (i) substituted or unsubstituted C_1 to C_8 alkyl such as methyl, ethyl, or straight, branched or cyclic propyl, butyl, pentyl, or hexyl; (ii) substituted or unsubstituted C_2 to C_8 alkenyl such as ethenyl or straight, branched or cyclic propenyl, butenyl, pentenyl or hexenyl; (iii) substituted or unsubstituted C_2 to C_8 alkynyl such as ethynyl or straight or branched propynyl, butynyl, pentynyl, or hexynyl; (iv) substituted or unsubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl. The substituents may be those identified elsewhere herein for substituted hydrocarbyl. In one embodiment, preferred R_{10} substituents include $R_{10a}R_{10b}NCOO$- wherein one of R_{10a} and R_{10b} is hydrogen and the other is methyl, ethyl, or straight, branched or cyclic propyl.

Exemplary X_3 substituents include substituted or unsubstituted C_2 to C_8 alkyl, substituted or unsubstituted C_2 to C_8 alkenyl, substituted or unsubstituted C_2 to C_8 alkynyl, substituted or unsubstituted heteroaromatics containing 5 or 6 ring atoms, and substituted or unsubstituted phenyl. Exemplary preferred X_3 substituents include substituted or unsubstituted ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclohexyl, isobutenyl, furyl, thienyl, and pyridyl.

Exemplary X_5 substituents include $-COX_{10}$, $-COOX_{10}$ or $-CONHX_{10}$ wherein X_{10} is substituted or unsubstituted alkyl, alkenyl, phenyl or heteroaromatic. Exemplary preferred X_5 substituents include $-COX_{10}$, $-COOX_{10}$ or $-CONHX_{10}$ wherein X_{10} is (i) substituted or unsubstituted C_1 to C_8 alkyl such as substituted or unsubstituted methyl, ethyl, propyl (straight, branched or cyclic), butyl (straight, branched or cyclic), pentyl (straight, branched or cyclic), or hexyl (straight, branched or cyclic); (ii) substituted or unsubstituted C_2 to C_8 alkenyl such as substituted or unsubstituted ethenyl, propenyl (straight, branched or cyclic), butenyl (straight, branched or cyclic), pentenyl (straight, branched or cyclic) or hexenyl (straight, branched or cyclic); (iii) substituted or unsubstituted C_2 to C_8 alkynyl such as substituted or unsubstituted ethynyl, propynyl (straight or branched), butynyl (straight or branched), pentynyl (straight or branched), or hexynyl (straight or branched); (iv) substituted or unsubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl,

wherein the substituent(s) is/are selected from the group consisting of heterocyclo, alkoxy, alkenoxy, alkynoxy, aryloxy, hydroxy, protected hydroxy, keto, acyloxy, nitro, amino, amido, thiol, ketal, acetal, ester and ether moieties, but not phosphorous containing moieties.

In one embodiment of the present invention, the taxanes of the present invention correspond to structure (2):



(2)

wherein

R_7 is hydroxy;

R_{10} is carbamoyloxy;

X_3 is substituted or unsubstituted alkyl, alkenyl, alkynyl, or heterocyclo, wherein alkyl comprises at least two carbon atoms;

X_5 is $-COX_{10}$, $-COOX_{10}$, or $-CONHX_{10}$; and

X_{10} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo.

For example, in this preferred embodiment in which the taxane corresponds to structure (2), R_{10} may be $R_{10a}R_{10b}NCOO-$ wherein one of R_{10a} and R_{10b} is hydrogen and the other is (i) substituted or unsubstituted C_1 to C_8 alkyl such as methyl, ethyl, or straight, branched or cyclic propyl, butyl, pentyl, or hexyl; (ii) substituted or unsubstituted C_2 to C_8 alkenyl such as ethenyl or straight, branched or cyclic propenyl, butenyl, pentenyl or hexenyl; (iii) substituted or unsubstituted C_2 to C_8 alkynyl such as ethynyl or straight or branched propynyl, butynyl, pentynyl, or hexynyl; (iv) phenyl or substituted phenyl such as nitro, alkoxy or halosubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl. The substituents may be those identified elsewhere herein for substituted hydrocarbyl. In one embodiment, preferred R_{10} substituents include $R_{10a}R_{10b}NCOO-$ wherein one of R_{10a} and R_{10b} is hydrogen and the other is substituted or unsubstituted, preferably unsubstituted methyl, ethyl, or straight, branched or cyclic propyl. In another embodiment, preferred R_{10} substituents include $R_{10a}R_{10b}NCOO-$ wherein one of R_{10a} and R_{10b} is hydrogen and the other is substituted or unsubstituted phenyl or heterocyclo. While R_{10a} and R_{10b} are

selected from among these, in one embodiment X_3 is selected from substituted or unsubstituted alkyl, alkenyl, phenyl or heterocyclo, more preferably substituted or unsubstituted alkenyl, phenyl or heterocyclo, still more preferably substituted or unsubstituted phenyl or heterocyclo, and still more preferably heterocyclo such as furyl, thienyl or pyridyl. While R_{10a}, R_{10b}, and X_3 are selected from among these, in one embodiment X_5 is selected from $-COX_{10}$ wherein X_{10} is phenyl, alkyl or heterocyclo, more preferably phenyl. Alternatively, while R_{10a}, R_{10b}, and X_3 are selected from among these, in one embodiment X_5 is selected from $-COX_{10}$ wherein X_{10} is phenyl, alkyl or heterocyclo, more preferably phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is alkyl, preferably t-butyl. Among the more preferred embodiments, therefore, are taxanes corresponding to structure 2 in which (i) X_5 is $-COOX_{10}$ wherein X_{10} is tert-butyl or X_5 is $-COX_{10}$ wherein X_{10} is phenyl, (ii) X_3 is substituted or unsubstituted cycloalkyl, alkenyl, phenyl or heterocyclo, more preferably substituted or unsubstituted isobutenyl, phenyl, furyl, thienyl, or pyridyl, still more preferably unsubstituted isobutenyl, furyl, thienyl or pyridyl, and (iii) R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen and the other is substituted or unsubstituted substituted or unsubstituted C_1 to C_8 alkyl, phenyl or heterocyclo.

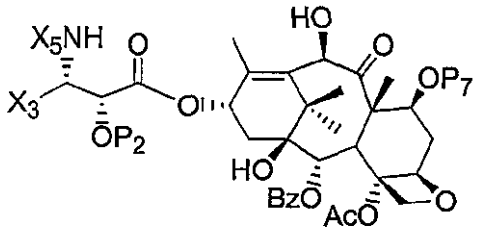
Among the preferred embodiments, therefore, are taxanes corresponding to structure 1 or 2 wherein R_{10} is $R_{10a}R_{10b}NCOO-$ wherein R_{10a} is methyl and R_{10b} is hydrido. In this embodiment, X_3 is preferably cycloalkyl, isobutenyl, phenyl, substituted phenyl such as p-nitrophenyl, or heterocyclo, more preferably heterocyclo, still more preferably furyl, thienyl or pyridyl; and X_5 is preferably benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl. In one alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is keto and R_{14} is hydrido. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is keto and R_{14} is hydrido. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is keto and R_{14} is hydroxy. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more

preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is hydroxy and R_{14} is hydroxy. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is hydroxy and R_{14} is hydrido. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is acyloxy and R_{14} is hydroxy. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is acyloxy and R_{14} is hydrido. In each of the alternatives of this embodiment when the taxane has structure 1, R_7 and R_{10} may each have the beta stereochemical configuration, R_7 and R_{10} may each have the alpha stereochemical configuration, R_7 may have the alpha stereochemical configuration while R_{10} has the beta stereochemical configuration or R_7 may have the beta stereochemical configuration while R_{10} has the alpha stereochemical configuration.

Also among the preferred embodiments are taxanes corresponding to structure 1 or 2 wherein R_{10} is $R_{10a}R_{10b}NCOO$- wherein R_{10a} is ethyl and R_{10b} is hydrido. In this embodiment, X_3 is preferably cycloalkyl, isobutenyl, phenyl, substituted phenyl such as p-nitrophenyl, or heterocyclo, more preferably heterocyclo, still more preferably furyl, thienyl or pyridyl; and X_5 is preferably benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl. In one alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is keto and R_{14} is hydrido. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is keto and R_{14} is hydrido. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is keto and R_{14} is hydroxy. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more

preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is hydroxy and R_{14} is hydroxy. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is hydroxy and R_{14} is hydrido. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is acyloxy and R_{14} is hydroxy. In another alternative of this embodiment, X_3 is heterocyclo; X_5 is benzoyl, alkoxycarbonyl, or heterocyclocarbonyl, more preferably benzoyl, t-butoxycarbonyl or t-amyloxycarbonyl, still more preferably t-butoxycarbonyl; R_2 is benzoyl, R_9 is acyloxy and R_{14} is hydrido. In each of the alternatives of this embodiment when the taxane has structure 1, R_7 and R_{10} may each have the beta stereochemical configuration, R_7 and R_{10} may each have the alpha stereochemical configuration, R_7 may have the alpha stereochemical configuration while R_{10} has the beta stereochemical configuration or R_7 may have the beta stereochemical configuration while R_{10} has the alpha stereochemical configuration.

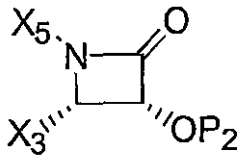
Taxanes having the general formula 1 may be obtained by carbamoylation of a suitably protected taxane intermediate having the structural formula:



wherein X_3 and X_5 are as previously defined, P_2 is a hydroxy protecting group, and P_7 is either hydrogen or a hydroxy protecting group, by reaction with an isocyanate or a carbamoyl chloride, followed by removal of the hydroxy protecting group(s).

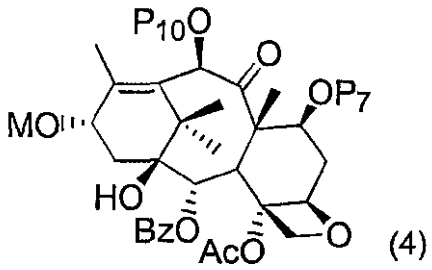
The intermediate taxane may be obtained by treatment of a β-lactam with an alkoxide having the taxane tetracyclic nucleus and a C-13 metallic oxide substituent to form compounds having a β-amido ester substituent at C-13 (as described more fully in Holton U.S. Patent 5,466,834), followed by removal of

either the C(10) protecting group, or both the C(10) and C(7) protecting groups. The β-lactam has the formula (3):



(3)

wherein P_2 is a hydroxy protecting group and X_3 and X_5 are as previously defined and the alkoxide has the formula (4):



(4)

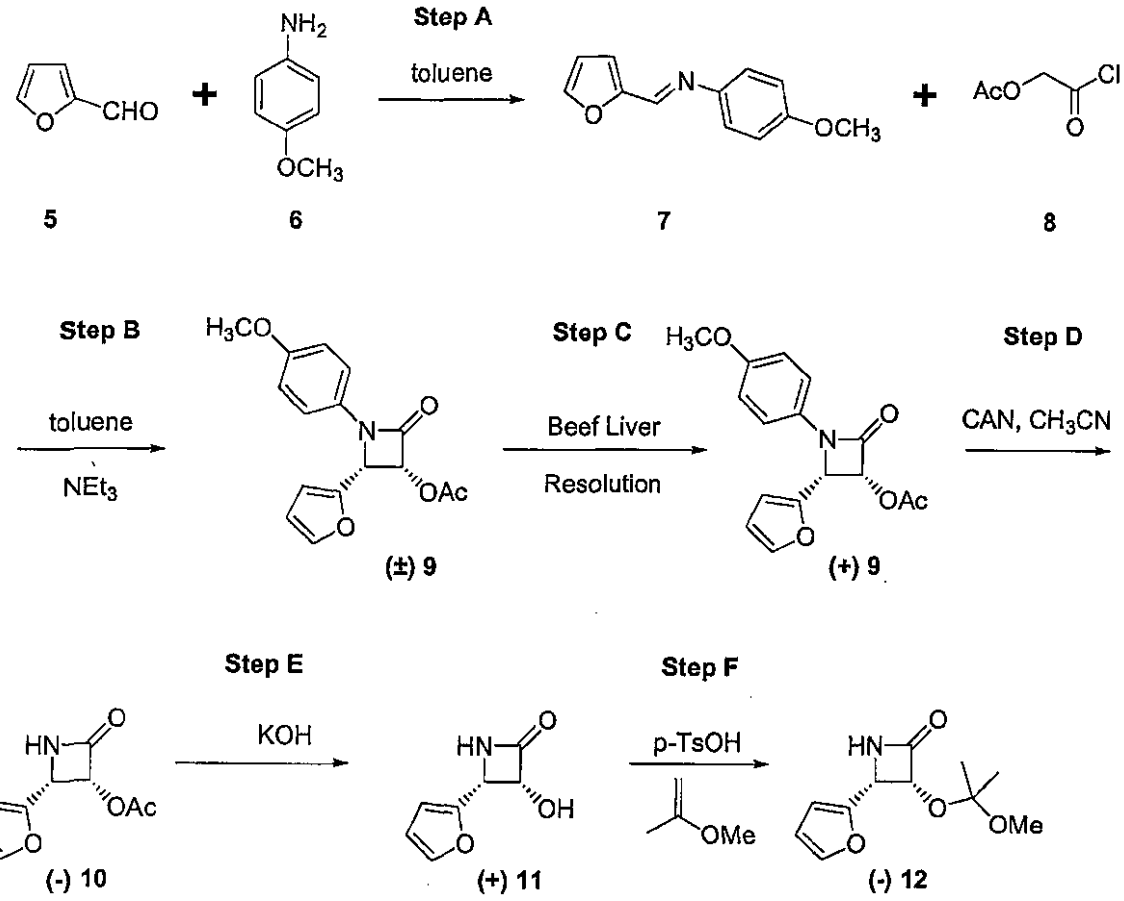
wherein M is a metal or ammonium, and P_7 and P_{10} are hydroxy protecting groups.

The alkoxide may be prepared from 10-deacetylbaccatin III by protection of the C-7 and C-10 hydroxyl groups (as described more fully in Holton et al., PCT Patent Application WO 99/09021) followed by treatment with a metallic amide.

Derivatives of 10-deacetylbaccatin III having alternative substituents at C(2), C(9) and C(14) and processes for their preparation are known in the art. Taxane derivatives having acyloxy substituents other than benzoyloxy at C(2) may be prepared, for example, as described in Holton et al., U.S. Patent No. 5,728,725 or Kingston et al., U.S. Patent No. 6,002,023. Taxanes having acyloxy or hydroxy substituents at C(9) in place of keto may be prepared, for example as described in Holton et al., U.S. Patent No. 6,011,056 or Gunawardana et al., U.S. Patent No. 5,352,806. Taxanes having a beta hydroxy substituent at C(14) may be prepared from naturally occurring 14-hydroxy-10-deacetylbaccatin III.

Processes for the preparation and resolution of the β-lactam starting material are generally well known. For example, the β-lactam may be prepared as described in Holton, U.S. Patent No. 5,430,160 and the resulting enatiomeric mixtures of β-lactams may be resolved by a stereoselective hydrolysis using a

lipase or enzyme as described, for example, in Patel, U.S. Patent No. 5,879,929 Patel U.S. Patent No. 5,567,614 or a liver homogenate as described, for example, in PCT Patent Application No. 00/41204. In a preferred embodiment in which the β-lactam is furyl substituted at the C(4) position, the β-lactam can be prepared as illustrated in the following reaction scheme:



wherein Ac is acetyl, NEt_3 is triethylamine, CAN is ceric ammonium nitrate, and p-TsOH is p-toluenesulfonic acid. The beef liver resolution may be carried out, for example, by combining the enatiomeric β-lactam mixture with a beef liver suspension (prepared, for example, by adding 20 g of frozen beef liver to a blender and then adding a pH 8 buffer to make a total volume of 1 L).

Compounds of formula 1 of the instant invention are useful for inhibiting tumor growth in mammals including humans and are preferably administered in the form of a pharmaceutical composition comprising an effective antitumor amount of a compound of the instant invention in combination with at least one

pharmaceutically or pharmacologically acceptable carrier. The carrier, also known in the art as an excipient, vehicle, auxiliary, adjuvant, or diluent, is any substance which is pharmaceutically inert, confers a suitable consistency or form to the composition, and does not diminish the therapeutic efficacy of the antitumor compounds. The carrier is "pharmaceutically or pharmacologically acceptable" if it does not produce an adverse, allergic or other untoward reaction when administered to a mammal or human, as appropriate.

The pharmaceutical compositions containing the antitumor compounds of the present invention may be formulated in any conventional manner. Proper formulation is dependent upon the route of administration chosen. The compositions of the invention can be formulated for any route of administration so long as the target tissue is available via that route. Suitable routes of administration include, but are not limited to, oral, parenteral (e.g., intravenous, intraarterial, subcutaneous, rectal, subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intraperitoneal, or intrasternal), topical (nasal, transdermal, intraocular), intravesical, intrathecal, enteral, pulmonary, intralymphatic, intracavital, vaginal, transurethral, intradermal, aural, intramammary, buccal, orthotopic, intratracheal, intralesional, percutaneous, endoscopical, transmucosal, sublingual and intestinal administration.

Pharmaceutically acceptable carriers for use in the compositions of the present invention are well known to those of ordinary skill in the art and are selected based upon a number of factors: the particular antitumor compound used, and its concentration, stability and intended bioavailability; the disease, disorder or condition being treated with the composition; the subject, its age, size and general condition; and the route of administration. Suitable carriers are readily determined by one of ordinary skill in the art (see, for example, J. G. Nairn, in: Remington's Pharmaceutical Science (A. Gennaro, ed.), Mack Publishing Co., Easton, Pa., (1985), pp. 1492-1517, the contents of which are incorporated herein by reference).

The compositions are preferably formulated as tablets, dispersible powders, pills, capsules, gelcaps, caplets, gels, liposomes, granules, solutions, suspensions, emulsions, syrups, elixirs, troches, dragees, lozenges, or any other dosage form which can be administered orally. Techniques and compositions for making oral dosage forms useful in the present invention are described in the following references: 7 Modern Pharmaceutics, Chapters 9 and 10 (Banker & Rhodes, Editors, 1979); Lieberman et al., Pharmaceutical Dosage Forms: Tablets

(1981); and Ansel, Introduction to Pharmaceutical Dosage Forms 2nd Edition (1976).

The compositions of the invention for oral administration comprise an effective antitumor amount of a compound of the invention in a pharmaceutically acceptable carrier. Suitable carriers for solid dosage forms include sugars, starches, and other conventional substances including lactose, talc, sucrose, gelatin, carboxymethylcellulose, agar, mannitol, sorbitol, calcium phosphate, calcium carbonate, sodium carbonate, kaolin, alginic acid, acacia, corn starch, potato starch, sodium saccharin, magnesium carbonate, tragacanth, microcrystalline cellulose, colloidal silicon dioxide, croscarmellose sodium, talc, magnesium stearate, and stearic acid. Further, such solid dosage forms may be uncoated or may be coated by known techniques; e.g., to delay disintegration and absorption.

The antitumor compounds of the present invention are also preferably formulated for parenteral administration, e.g., formulated for injection via intravenous, intraarterial, subcutaneous, rectal, subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intraperitoneal, or intrasternal routes. The compositions of the invention for parenteral administration comprise an effective antitumor amount of the antitumor compound in a pharmaceutically acceptable carrier. Dosage forms suitable for parenteral administration include solutions, suspensions, dispersions, emulsions or any other dosage form which can be administered parenterally. Techniques and compositions for making parenteral dosage forms are known in the art.

Suitable carriers used in formulating liquid dosage forms for oral or parenteral administration include nonaqueous, pharmaceutically-acceptable polar solvents such as oils, alcohols, amides, esters, ethers, ketones, hydrocarbons and mixtures thereof, as well as water, saline solutions, dextrose solutions (e.g., DW5), electrolyte solutions, or any other aqueous, pharmaceutically acceptable liquid.

Suitable nonaqueous, pharmaceutically-acceptable polar solvents include, but are not limited to, alcohols (e.g., α-glycerol formal, β-glycerol formal, 1, 3-butyleneglycol, aliphatic or aromatic alcohols having 2-30 carbon atoms such as methanol, ethanol, propanol, isopropanol, butanol, t-butanol, hexanol, octanol, amylene hydrate, benzyl alcohol, glycerin (glycerol), glycol, hexylene glycol, tetrahydrofurfuryl alcohol, lauryl alcohol, cetyl alcohol, or stearyl alcohol, fatty acid esters of fatty alcohols such as polyalkylene glycols (e.g., polypropylene glycol,

polyethylene glycol), sorbitan, sucrose and cholesterol); amides (e.g., dimethylacetamide (DMA), benzyl benzoate DMA, dimethylformamide, N-(β-hydroxyethyl)-lactamide, N, N-dimethylacetamide amides, 2-pyrrolidinone, 1-methyl-2-pyrrolidinone, or polyvinylpyrrolidone); esters (e.g., 1-methyl-2-pyrrolidinone, 2-pyrrolidinone, acetate esters such as monoacetin, diacetin, and triacetin, aliphatic or aromatic esters such as ethyl caprylate or octanoate, alkyl oleate, benzyl benzoate, benzyl acetate, dimethylsulfoxide (DMSO), esters of glycerin such as mono, di, or tri-glyceryl citrates or tartrates, ethyl benzoate, ethyl acetate, ethyl carbonate, ethyl lactate, ethyl oleate, fatty acid esters of sorbitan, fatty acid derived PEG esters, glyceryl monostearate, glyceride esters such as mono, di, or tri-glycerides, fatty acid esters such as isopropyl myristrate, fatty acid derived PEG esters such as PEG-hydroxyoleate and PEG-hydroxystearate, N-methyl pyrrolidinone, pluronic 60, polyoxyethylene sorbitol oleic polyesters such as poly(ethoxylated)$_{30-60}$ sorbitol poly(oleate)$_{2-4}$, poly(oxyethylene)$_{15-20}$ monooleate, poly(oxyethylene)$_{15-20}$ mono 12-hydroxystearate, and poly(oxyethylene)$_{15-20}$ mono ricinoleate, polyoxyethylene sorbitan esters such as polyoxyethylene-sorbitan monooleate, polyoxyethylene-sorbitan monopalmitate, polyoxyethylene-sorbitan monolaurate, polyoxyethylene-sorbitan monostearate, and Polysorbate® 20, 40, 60 or 80 from ICI Americas, Wilmington, DE, polyvinylpyrrolidone, alkyleneoxy modified fatty acid esters such as polyoxyl 40 hydrogenated castor oil and polyoxyethylated castor oils (e.g., Cremophor® EL solution or Cremophor® RH 40 solution), saccharide fatty acid esters (i.e., the condensation product of a monosaccharide (e.g., pentoses such as ribose, ribulose, arabinose, xylose, lyxose and xylulose, hexoses such as glucose, fructose, galactose, mannose and sorbose, trioses, tetroses, heptoses, and octoses), disaccharide (e.g., sucrose, maltose, lactose and trehalose) or oligosaccharide or mixture thereof with a C_4-C_{22} fatty acid(s)(e.g., saturated fatty acids such as caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid and stearic acid, and unsaturated fatty acids such as palmitoleic acid, oleic acid, elaidic acid, erucic acid and linoleic acid)), or steroidal esters); alkyl, aryl, or cyclic ethers having 2-30 carbon atoms (e.g., diethyl ether, tetrahydrofuran, dimethyl isosorbide, diethylene glycol monoethyl ether); glycofurol (tetrahydrofurfuryl alcohol polyethylene glycol ether); ketones having 3-30 carbon atoms (e.g., acetone, methyl ethyl ketone, methyl isobutyl ketone); aliphatic, cycloaliphatic or aromatic hydrocarbons having 4-30 carbon atoms (e.g., benzene, cyclohexane, dichloromethane, dioxolanes, hexane, n-decane, n-dodecane, n-hexane, sulfolane, tetramethylenesulfon,

tetramethylenesulfoxide, toluene, dimethylsulfoxide (DMSO), or tetramethylenesulfoxide); oils of mineral, vegetable, animal, essential or synthetic origin (e.g., mineral oils such as aliphatic or wax-based hydrocarbons, aromatic hydrocarbons, mixed aliphatic and aromatic based hydrocarbons, and refined paraffin oil, vegetable oils such as linseed, tung, safflower, soybean, castor, cottonseed, groundnut, rapeseed, coconut, palm, olive, corn, corn germ, sesame, persic and peanut oil and glycerides such as mono-, di- or triglycerides, animal oils such as fish, marine, sperm, cod-liver, haliver, squalene, squalane, and shark liver oil, oleic oils, and polyoxyethylated castor oil); alkyl or aryl halides having 1-30 carbon atoms and optionally more than one halogen substituent; methylene chloride; monoethanolamine; petroleum benzin; trolamine; omega-3 polyunsaturated fatty acids (e.g., alpha-linolenic acid, eicosapentaenoic acid, docosapentaenoic acid, or docosahexaenoic acid); polyglycol ester of 12-hydroxystearic acid and polyethylene glycol (Solutol® HS-15, from BASF, Ludwigshafen, Germany); polyoxyethylene glycerol; sodium laurate; sodium oleate; or sorbitan monooleate.

Other pharmaceutically acceptable solvents for use in the invention are well known to those of ordinary skill in the art, and are identified in The Chemotherapy Source Book (Williams & Wilkens Publishing), The Handbook of Pharmaceutical Excipients, (American Pharmaceutical Association, Washington, D.C., and The Pharmaceutical Society of Great Britain, London, England, 1968), Modern Pharmaceutics, (G. Banker et al., eds., 3d ed.)(Marcel Dekker, Inc., New York, New York, 1995), The Pharmacological Basis of Therapeutics, (Goodman & Gilman, McGraw Hill Publishing), Pharmaceutical Dosage Forms, (H. Lieberman et al., eds.,)(Marcel Dekker, Inc., New York, New York, 1980), Remington's Pharmaceutical Sciences (A. Gennaro, ed., 19th ed.)(Mack Publishing, Easton, PA, 1995), The United States Pharmacopeia 24, The National Formulary 19, (National Publishing, Philadelphia, PA, 2000), A.J. Spiegel et al., and Use of Nonaqueous Solvents in Parenteral Products, JOURNAL OF PHARMACEUTICAL SCIENCES, Vol. 52, No. 10, pp. 917-927 (1963).

Preferred solvents include those known to stabilize the antitumor compounds, such as oils rich in triglycerides, for example, safflower oil, soybean oil or mixtures thereof, and alkyleneoxy modified fatty acid esters such as polyoxyl 40 hydrogenated castor oil and polyoxyethylated castor oils (e.g., Cremophor® EL solution or Cremophor® RH 40 solution). Commercially available triglycerides include Intralipid® emulsified soybean oil (Kabi-Pharmacia

Inc., Stockholm, Sweden), Nutralipid ® emulsion (McGaw, Irvine, California), Liposyn® II 20% emulsion (a 20% fat emulsion solution containing 100 mg safflower oil, 100 mg soybean oil, 12 mg egg phosphatides, and 25 mg glycerin per ml of solution; Abbott Laboratories, Chicago, Illinois), Liposyn® III 2% emulsion (a 2% fat emulsion solution containing 100 mg safflower oil, 100 mg soybean oil, 12 mg egg phosphatides, and 25 mg glycerin per ml of solution; Abbott Laboratories, Chicago, Illinois), natural or synthetic glycerol derivatives containing the docosahexaenoyl group at levels between 25% and 100% by weight based on the total fatty acid content (Dhasco® (from Martek Biosciences Corp., Columbia, MD), DHA Maguro® (from Daito Enterprises, Los Angeles, CA), Soyacal®, and Travemulsion®. Ethanol is a preferred solvent for use in dissolving the antitumor compound to form solutions, emulsions, and the like.

Additional minor components can be included in the compositions of the invention for a variety of purposes well known in the pharmaceutical industry. These components will for the most part impart properties which enhance retention of the antitumor compound at the site of administration, protect the stability of the composition, control the pH, facilitate processing of the antitumor compound into pharmaceutical formulations, and the like. Preferably, each of these components is individually present in less than about 15 weight % of the total composition, more preferably less than about 5 weight %, and most preferably less than about 0.5 weight % of the total composition. Some components, such as fillers or diluents, can constitute up to 90 wt.% of the total composition, as is well known in the formulation art. Such additives include cryoprotective agents for preventing reprecipitation of the taxane, surface active, wetting or emulsifying agents (e.g., lecithin, polysorbate-80, Tween® 80, pluronic 60, polyoxyethylene stearate), preservatives (e.g., ethyl-p-hydroxybenzoate), microbial preservatives (e.g., benzyl alcohol, phenol, m-cresol, chlorobutanol, sorbic acid, thimerosal and paraben), agents for adjusting pH or buffering agents (e.g., acids, bases, sodium acetate, sorbitan monolaurate), agents for adjusting osmolarity (e.g., glycerin), thickeners (e.g., aluminum monostearate, stearic acid, cetyl alcohol, stearyl alcohol, guar gum, methyl cellulose, hydroxypropylcellulose, tristearin, cetyl wax esters, polyethylene glycol), colorants, dyes, flow aids, non-volatile silicones (e.g., cyclomethicone), clays (e.g., bentonites), adhesives, bulking agents, flavorings, sweeteners, adsorbents, fillers (e.g., sugars such as lactose, sucrose, mannitol, or sorbitol, cellulose, or calcium phosphate), diluents (e.g., water, saline, electrolyte solutions), binders (e.g., starches such as maize

starch, wheat starch, rice starch, or potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropyl methylcellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidone, sugars, polymers, acacia), disintegrating agents (e.g., starches such as maize starch, wheat starch, rice starch, potato starch, or carboxymethyl starch, cross-linked polyvinyl pyrrolidone, agar, alginic acid or a salt thereof such as sodium alginate, croscarmellose sodium or crospovidone), lubricants (e.g., silica, talc, stearic acid or salts thereof such as magnesium stearate, or polyethylene glycol), coating agents (e.g., concentrated sugar solutions including gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, or titanium dioxide), and antioxidants (e.g., sodium metabisulfite, sodium bisulfite, sodium sulfite, dextrose, phenols, and thiophenols).

In a preferred embodiment, a pharmaceutical composition of the invention comprises at least one nonaqueous, pharmaceutically acceptable solvent and an antitumor compound having a solubility in ethanol of at least about 100, 200, 300, 400, 500, 600, 700 or 800 mg/ml. While not being bound to a particular theory, it is believed that the ethanol solubility of the antitumor compound may be directly related to its efficacy. The antitumor compound can also be capable of being crystallized from a solution. In other words, a crystalline antitumor compound, such as compound 1393, can be dissolved in a solvent to form a solution and then recrystallized upon evaporation of the solvent without the formation of any amorphous antitumor compound. It is also preferred that the antitumor compound have an ID50 value (i.e, the drug concentration producing 50% inhibition of colony formation) of at least 4, 5, 6, 7, 8, 9, or 10 times less that of paclitaxel when measured according to the protocol set forth in the working examples.

Dosage form administration by these routes may be continuous or intermittent, depending, for example, upon the patient's physiological condition, whether the purpose of the administration is therapeutic or prophylactic, and other factors known to and assessable by a skilled practitioner.

Dosage and regimens for the administration of the pharmaceutical compositions of the invention can be readily determined by those with ordinary skill in treating cancer. It is understood that the dosage of the antitumor compounds will be dependent upon the age, sex, health, and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment, and the nature of the effect desired. For any mode of administration, the actual amount of antitumor compound delivered, as well as the dosing schedule necessary to

achieve the advantageous effects described herein, will also depend, in part, on such factors as the bioavailability of the antitumor compound, the disorder being treated, the desired therapeutic dose, and other factors that will be apparent to those of skill in the art. The dose administered to an animal, particularly a human, in the context of the present invention should be sufficient to effect the desired therapeutic response in the animal over a reasonable period of time. Preferably, an effective amount of the antitumor compound, whether administered orally or by another route, is any amount which would result in a desired therapeutic response when administered by that route. Preferably, the compositions for oral administration are prepared in such a way that a single dose in one or more oral preparations contains at least 20 mg of the antitumor compound per m^2 of patient body surface area, or at least 50, 100, 150, 200, 300, 400, or 500 mg of the antitumor compound per m^2 of patient body surface area, wherein the average body surface area for a human is 1.8 m^2. Preferably, a single dose of a composition for oral administration contains from about 20 to about 600 mg of the antitumor compound per m^2 of patient body surface area, more preferably from about 25 to about 400 mg/m^2, even more preferably, from about 40 to about 300 mg/m^2, and even more preferably from about 50 to about 200 mg/m^2. Preferably, the compositions for parenteral administration are prepared in such a way that a single dose contains at least 20 mg of the antitumor compound per m^2 of patient body surface area, or at least 40, 50, 100, 150, 200, 300, 400, or 500 mg of the antitumor compound per m^2 of patient body surface area. Preferably, a single dose in one or more parenteral preparations contains from about 20 to about 500 mg of the antitumor compound per m^2 of patient body surface area, more preferably from about 40 to about 400 mg/m^2, and even more preferably, from about 60 to about 350 mg/m^2. However, the dosage may vary depending on the dosing schedule which can be adjusted as necessary to achieve the desired therapeutic effect. It should be noted that the ranges of effective doses provided herein are not intended to limit the invention and represent preferred dose ranges. The most preferred dosage will be tailored to the individual subject, as is understood and determinable by one of ordinary skill in the art without undue experimentation.

The concentration of the antitumor compound in a liquid pharmaceutical composition is preferably between about 0.01 mg and about 10 mg per ml of the composition, more preferably between about 0.1 mg and about 7 mg per ml, even more preferably between about 0.5 mg and about 5 mg per ml, and most

preferably between about 1.5 mg and about 4 mg per ml. Relatively low concentrations are generally preferred because the antitumor compound is most soluble in the solution at low concentrations. The concentration of the antitumor compound in a solid pharmaceutical composition for oral administration is preferably between about 5 weight % and about 50 weight %, based on the total weight of the composition, more preferably between about 8 weight % and about 40 weight %, and most preferably between about 10 weight % and about 30 weight %.

In one embodiment, solutions for oral administration are prepared by dissolving an antitumor compound in any pharmaceutically acceptable solvent capable of dissolving the compound (e.g., ethanol or methylene chloride) to form a solution. An appropriate volume of a carrier which is a solution, such as Cremophor® EL solution, is added to the solution while stirring to form a pharmaceutically acceptable solution for oral administration to a patient. If desired, such solutions can be formulated to contain a minimal amount of, or to be free of, ethanol, which is known in the art to cause adverse physiological effects when administered at certain concentrations in oral formulations.

In another embodiment, powders or tablets for oral administration are prepared by dissolving an antitumor compound in any pharmaceutically acceptable solvent capable of dissolving the compound (e.g.,ethanol or methylene chloride) to form a solution. The solvent can optionally be capable of evaporating when the solution is dried under vacuum. An additional carrier can be added to the solution prior to drying, such as Cremophor® EL solution. The resulting solution is dried under vacuum to form a glass. The glass is then mixed with a binder to form a powder. The powder can be mixed with fillers or other conventional tabletting agents and processed to form a tablet for oral administration to a patient. The powder can also be added to any liquid carrier as described above to form a solution, emulsion, suspension or the like for oral administration.

Emulsions for parenteral administration can be prepared by dissolving an antitumor compound in any pharmaceutically acceptable solvent capable of dissolving the compound (e.g., ethanol or methylene chloride) to form a solution. An appropriate volume of a carrier which is an emulsion, such as Liposyn® II or Liposyn® III emulsion, is added to the solution while stirring to form a pharmaceutically acceptable emulsion for parenteral administration to a patient. If desired, such emulsions can be formulated to contain a minimal amount of, or to

be free of, ethanol or Cremophor® solution, which are known in the art to cause adverse physiological effects when administered at certain concentrations in parenteral formulations.

Solutions for parenteral administration can be prepared by dissolving an antitumor compound in any pharmaceutically acceptable solvent capable of dissolving the compound (e.g., ethanol or methylene chloride) to form a solution. An appropriate volume of a carrier which is a solution, such as Cremophor® solution, is added to the solution while stirring to form a pharmaceutically acceptable solution for parenteral administration to a patient. If desired, such solutions can be formulated to contain a minimal amount of, or to be free of, ethanol or Cremophor® solution, which are known in the art to cause adverse physiological effects when administered at certain concentrations in parenteral formulations.

If desired, the emulsions or solutions described above for oral or parenteral administration can be packaged in IV bags, vials or other conventional containers in concentrated form and diluted with any pharmaceutically acceptable liquid, such as saline, to form an acceptable taxane concentration prior to use as is known in the art.

Definitions

The terms "hydrocarbon" and "hydrocarbyl" as used herein describe organic compounds or radicals consisting exclusively of the elements carbon and hydrogen. These moieties include alkyl, alkenyl, alkynyl, and aryl moieties. These moieties also include alkyl, alkenyl, alkynyl, and aryl moieties substituted with other aliphatic or cyclic hydrocarbon groups, such as alkaryl, alkenaryl and alkynaryl. Unless otherwise indicated, these moieties preferably comprise 1 to 20 carbon atoms.

The "substituted hydrocarbyl" moieties described herein are hydrocarbyl moieties which are substituted with at least one atom other than carbon, including moieties in which a carbon chain atom is substituted with a hetero atom such as nitrogen, oxygen, silicon, phosphorous, boron, sulfur, or a halogen atom. These substituents include halogen, heterocyclo, alkoxy, alkenoxy, alkynoxy, aryloxy, hydroxy, protected hydroxy, keto, acyl, acyloxy, nitro, amino, amido, nitro, cyano, thiol, ketals, acetals, esters and ethers.

Unless otherwise indicated, the alkyl groups described herein are preferably lower alkyl containing from one to eight carbon atoms in the principal

chain and up to 20 carbon atoms. They may be straight or branched chain or cyclic and include methyl, ethyl, propyl, isopropyl, butyl, hexyl and the like.

Unless otherwise indicated, the alkenyl groups described herein are preferably lower alkenyl containing from two to eight carbon atoms in the principal chain and up to 20 carbon atoms. They may be straight or branched chain or cyclic and include ethenyl, propenyl, isopropenyl, butenyl, isobutenyl, hexenyl, and the like.

Unless otherwise indicated, the alkynyl groups described herein are preferably lower alkynyl containing from two to eight carbon atoms in the principal chain and up to 20 carbon atoms. They may be straight or branched chain and include ethynyl, propynyl, butynyl, isobutynyl, hexynyl, and the like.

The terms "aryl" or "ar" as used herein alone or as part of another group denote optionally substituted homocyclic aromatic groups, preferably monocyclic or bicyclic groups containing from 6 to 12 carbons in the ring portion, such as phenyl, biphenyl, naphthyl, substituted phenyl, substituted biphenyl or substituted naphthyl. Phenyl and substituted phenyl are the more preferred aryl.

The terms "halogen" or "halo" as used herein alone or as part of another group refer to chlorine, bromine, fluorine, and iodine.

The terms "heterocyclo" or "heterocyclic" as used herein alone or as part of another group denote optionally substituted, fully saturated or unsaturated, monocyclic or bicyclic, aromatic or nonaromatic groups having at least one heteroatom in at least one ring, and preferably 5 or 6 atoms in each ring. The heterocyclo group preferably has 1 or 2 oxygen atoms, 1 or 2 sulfur atoms, and/or 1 to 4 nitrogen atoms in the ring, and may be bonded to the remainder of the molecule through a carbon or heteroatom. Exemplary heterocyclo include heteroaromatics such as furyl, thienyl, pyridyl, oxazolyl, pyrrolyl, indolyl, quinolinyl, or isoquinolinyl and the like. Exemplary substituents include one or more of the following groups: hydrocarbyl, substituted hydrocarbyl, keto, hydroxy, protected hydroxy, acyl, acyloxy, alkoxy, alkenoxy, alkynoxy, aryloxy, halogen, amido, amino, nitro, cyano, thiol, ketals, acetals, esters and ethers.

The term "heteroaromatic" as used herein alone or as part of another group denote optionally substituted aromatic groups having at least one heteroatom in at least one ring, and preferably 5 or 6 atoms in each ring. The heteroaromatic group preferably has 1 or 2 oxygen atoms, 1 or 2 sulfur atoms, and/or 1 to 4 nitrogen atoms in the ring, and may be bonded to the remainder of the molecule through a carbon or heteroatom. Exemplary heteroaromatics

include furyl, thienyl, pyridyl, oxazolyl, pyrrolyl, indolyl, quinolinyl, or isoquinolinyl and the like. Exemplary substituents include one or more of the following groups: hydrocarbyl, substituted hydrocarbyl, keto, hydroxy, protected hydroxy, acyl, acyloxy, alkoxy, alkenoxy, alkynoxy, aryloxy, halogen, amido, amino, nitro, cyano, thiol, ketals, acetals, esters and ethers.

The term "acyl," as used herein alone or as part of another group, denotes the moiety formed by removal of the hydroxyl group from the group --COOH of an organic carboxylic acid, e.g., RC(O)-, wherein R is R^1, R^1O-, R^1R^2N-, or R^1S-, R^1 is hydrocarbyl, heterosubstituted hydrocarbyl, or heterocyclo and R^2 is hydrogen, hydrocarbyl or substituted hydrocarbyl.

The term "acyloxy," as used herein alone or as part of another group, denotes an acyl group as described above bonded through an oxygen linkage (--O--), e.g., RC(O)O- wherein R is as defined in connection with the term "acyl."

Unless otherwise indicated, the alkoxycarbonyloxy moieties described herein comprise lower hydrocarbon or substituted hydrocarbon or substituted hydrocarbon moieties.

Unless otherwise indicated, the carbamoyloxy moieties described herein are derivatives of carbamic acid in which one or both of the amine hydrogens is optionally replaced by a hydrocarbyl, substituted hydrocarbyl or heterocyclo moiety.

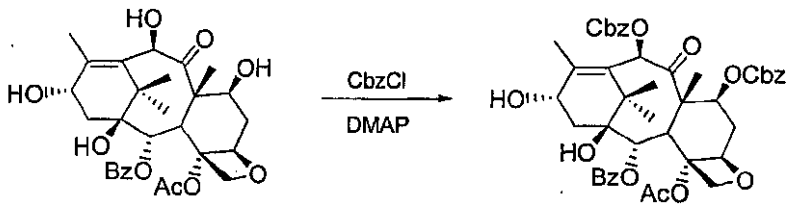
The terms "hydroxyl protecting group" and "hydroxy protecting group" as used herein denote a group capable of protecting a free hydroxyl group ("protected hydroxyl") which, subsequent to the reaction for which protection is employed, may be removed without disturbing the remainder of the molecule. A variety of protecting groups for the hydroxyl group and the synthesis thereof may be found in "Protective Groups in Organic Synthesis" by T. W. Greene, John Wiley and Sons, 1981, or Fieser & Fieser. Exemplary hydroxyl protecting groups include methoxymethyl, 1-ethoxyethyl, benzyloxymethyl, (.beta.-trimethylsilylethoxy)methyl, tetrahydropyranyl, 2,2,2-trichloroethoxycarbonyl, t-butyl(diphenyl)silyl, trialkylsilyl, trichloromethoxycarbonyl and 2,2,2-trichloroethoxymethyl.

As used herein, "Ac" means acetyl; "Bz" means benzoyl; "Et" means ethyl; "Me" means methyl; "Ph" means phenyl; "iPr" means isopropyl; "tBu" and "t-Bu" means tert-butyl; "R" means lower alkyl unless otherwise defined; "py" means pyridine or pyridyl; "TES" means triethylsilyl; "TMS" means trimethylsilyl; "LAH" means lithium aluminum hydride; "10-DAB" means 10-desacetylbaccatin III";

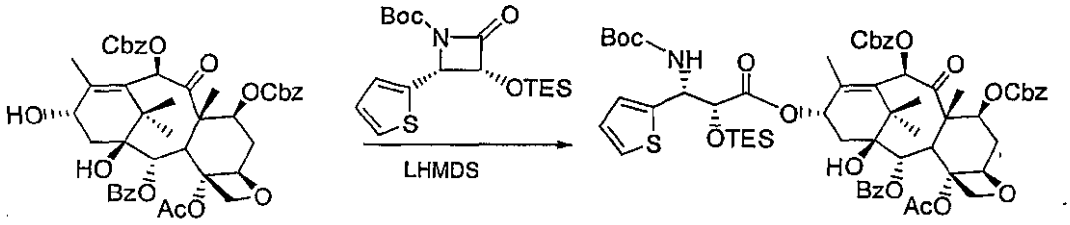
"amine protecting group" includes, but is not limited to, carbamates, for example, 2,2,2-trichloroethylcarbamate or tertbutylcarbamate; "protected hydroxy" means -OP wherein P is a hydroxy protecting group; "tBuOCO" and "Boc" mean tert-butoxycarbonyl; "tAmOCO" means tert-amyloxycarbonyl; "2-FuCO" means 2-furylcarbonyl; "2-ThCO" means 2-thienylcarbonyl; "2-PyCO" means 2-pyridylcarbonyl; "3-PyCO" means 3-pyridylcarbonyl; "4-PyCO" means 4-pyridylcarbonyl; "C_4H_7CO" means butenylcarbonyl; "EtOCO" means ethoxycarbonyl; "ibueCO" means isobutenylcarbonyl; "iBuCO" means isobutylcarbonyl; "iBuOCO" means isobutoxycarbonyl; "iPrOCO" means isopropyloxycarbonyl; "nPrOCO" means n-propyloxycarbonyl; "nPrCO" means n-propylcarbonyl; "ibue" means isobutenyl; "THF" means tetrahydrofuran; "DMAP" means 4-dimethylamino pyridine; "LHMDS" means Lithium HexamethylDiSilazanide.

The following examples illustrate the invention.

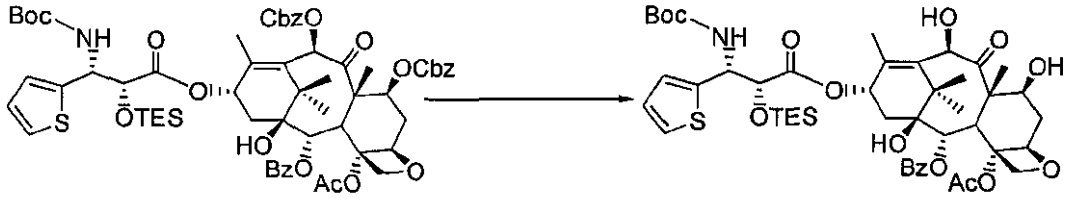
Example 1



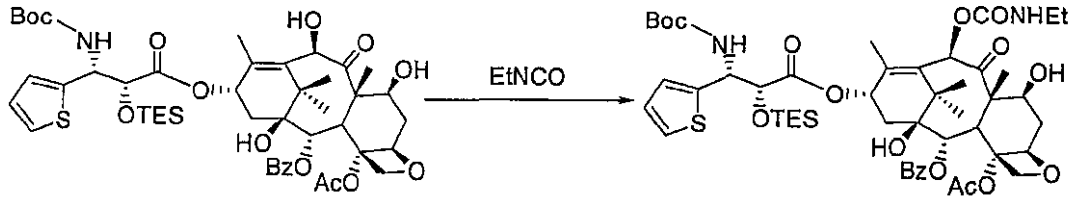
7,10-(*bis*)-carbobenzyloxy-10-deacetyl baccatin III. To a solution of 10-DAB (1.14 g, 2.11 mmol) in 20 mL of methylene chloride was added DMAP (6.20 g, 50.6 mmol) and benzyl chloroformate (1.8 mL, 12.7 mmol) slowly under a nitrogen atmosphere. The mixture was heated to 40-45 oC, kept at this temperature for 2 h, and an additional 1.8 mL (12.7 mmol) of benzyl chloroformate was added. Heating at 40-45 oC was continued for an additional 6 h, the mixture was diluted with 200 mL of CH_2Cl_2 and washed three times first with 1N HCl and then with saturated sodium bicarbonate solution. The combined washings were extracted three times with 30 mL of CH_2Cl_2, the organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Chromatography of the residue on silica gel eluting with CH_2Cl_2/EtOAc gave 1.48 g (86%) of 7,10-(*bis*)-carbobenzyloxy-10-deacetyl baccatin III.



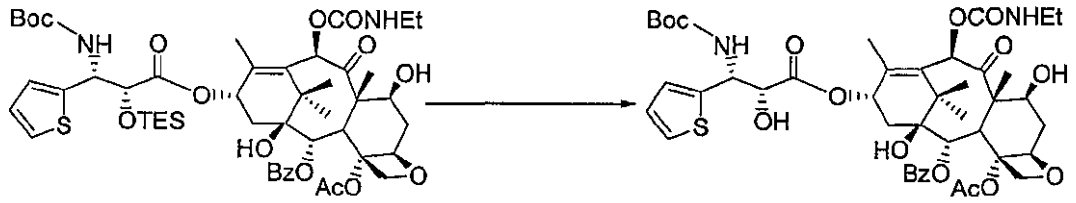
7,10-(*bis*)-carbobenzyloxy-3'-desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl docetaxel. To a solution of 425 mg (0.523 mmol) of 7,10-(*bis*)-carbobenzyloxy-10-deacetyl baccatin III in THF (4.5 mL) at -45 oC under a nitrogen atmosphere was added 0.80 mL of a solution of LHMDS (0.98 M) in THF dropwise. The mixture was kept at -45 oC for 1h prior to addition of a solution of 341 mg (0.889 mmol) of *cis*-N-*t*butoxycarbonyl-3-triethylsilyloxy-4-(2-thienyl) azetidin-2-one in 2 mL of THF. The mixture was allowed to warm to 0 °C, and after 2 h was poured into 20 mL of saturated ammonium chloride solution. The aqueous layer was extracted three times with 50 mL of EtOAc/Hexanes (1:1) and the organic layers were combined, washed with brine, dried over Na_2SO_4 and concentrated. Chromatography of the residue on silica gel eluting with EtOAc/Hexanes gave 576 mg (92%) of 7,10-(*bis*)-carbobenzyloxy-3'-desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl docetaxel.



3'-Desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl docetaxel. A suspension of 550 mg of 7,10-(*bis*)-carbobenzyloxy-3'-desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl docetaxel and 50 mg of 10% Pd/C in 30 mL of EtOH and 10 mL of EtOAc was stirred under a hydrogen atmosphere for 2 h at room temperature. The slurry was filtered through a pad of celite 545 which was then washed with EtOAc. The washings were concentrated and the residue was purified by column chromatography on silica gel using EtOAc/Hexanes as eluent to give 405 mg (95%) of 3'-desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl docetaxel.



3'-Desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl-10-N-ethylcarbamoyl docetaxel. To a slurry of 3'-desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl docetaxel (201 mg, 0.217 mmol) and CuCl (43.0 mg, 0.434 mmol) in THF (3.5 mL) at -15 oC under a nitrogen atmosphere was added a solution of 51.5 mL (0.651 mmol) of ethyl isocynate in 1.9 mL of THF. The mixture was warmed to 0 °C and after 1.4 h 5mL of saturated aqueous sodium bicarbonate solution and 20 mL of ethyl acetate were added. The water layer was extracted three times with 50 mL of EtOAc/Hexanes (1:1). The organic layers were combined, dried over Na_2SO_4 and evaporated to give 218 mg of a residue which was used directly without purification.

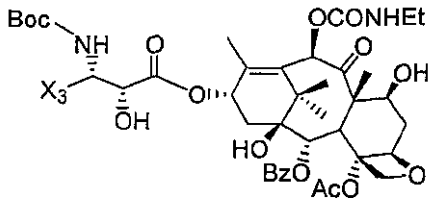


2722

3'-Desphenyl-3'-(2-thienyl)-10-N-ethylcarbamoyl docetaxel (2722). To a solution of the 218 mg of 3'-desphenyl-3'-(2-thienyl)-2'-O-triethylsilyl-10-N-ethylcarbamoyl docetaxel obtained above in 6 mL of pyridine and 12 mL of CH_3CN at 0 °C was added 1.0 mL of 49% aqueous HF. The mixture was warmed to room temperature and after 2.5 h 50 mL of EtOAc was added. The mixture was washed with saturated aqueous sodium bicarbonate solution and brine, dried over sodium sulfate, and concentrated under reduced pressure. Chromatography of the residue on silica gel using CH_2Cl_2/MeOH as eluent gave 169 mg (88% for 2 steps) of 3'-desphenyl-3'-(2-thienyl)-10-N-ethylcarbamoyl docetaxel (**2722**).

Example 2

The procedures described in Example 1 were repeated, but other suitably protected β-lactams and acylating agents were substituted for the β-lactam and acylating agent of Example 1 to prepare the series of compounds having the combination of substituents identified in the following table. The following table also includes characterization data for certain of these compounds, along with characterization data for the compound (**2722**) prepared in Example 1.

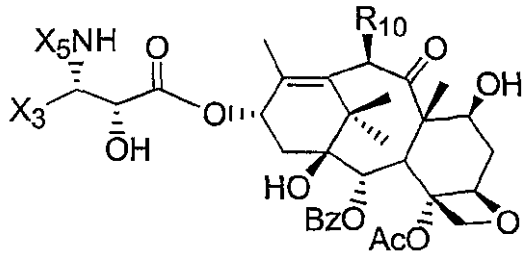


No.	X_3	m.p. (°C)	$[\alpha]_D(CHCl_3)$	Elemental Analysis
2600	2-pyridyl	173-175	-71.4 (c 0.22)	Found: C, 60.70; H, 6.69 (Calcd. for $C_{45}H_{57}N_3O_{15}.0.5H_2O$: C, 60.79; H, 6.58)
2616	3-pyridyl	183-185	-61.0 (c 0.20)	Found: C, 58.96; H, 6.51 (Calcd. for $C_{45}H_{57}N_3O_{15}.2H_2O$: C, 59.00; H, 6.69)
2622	3-thienyl	173-175	-68.1 (c 0.19)	Found: C, 58.40; H, 6.42 (Calcd. for $C_{44}H_{56}N_2O_{15}S.H_2O$: C, 58.47; H, 6.47)
2633	*i*-propyl	170-172	-75.7 (c 0.22)	Found: C, 60.10; H, 7.15 (Calcd. for $C_{43}H_{60}N_2O_{15}.H_2O$: C, 59.84; H, 7.24)
2686	*i*-butenyl	167-169	-106.7 (c 0.17)	Found: C, 61.12; H, 7.10 (Calcd. for $C_{44}H_{60}N_2O_{15}.0.5H_2O$: C, 61.02; H, 7.10)
2692	4-pyridyl	203-205	-69.7 (c 0.18)	Found: C, 60.19; H, 6.61 (Calcd. for $C_{45}H_{57}N_3O_{15}.H_2O$: C, 60.13; H, 6.62)
2700	2-furyl	169-171	-73.6 (c 0.22)	Found: C, 60.59; H, 6.58 (Calcd. for $C_{44}H_{56}N_2O_{16}$: C, 60.82; H, 6.50)
2717	3-furyl	165-167	-53.8 (c 0.23)	Found: C, 60.07; H, 6.48 (Calcd. for $C_{44}H_{56}N_2O_{16}.0.5H_2O$: C, 60.14; H, 6.54)

2722	2-thienyl	166-168	-52.2 (c 0.25)	Found: C, 58.28; H, 6.32 (Calcd. for $C_{44}H_{56}N_2O_{15}S.H_2O$: C, 58.47; H, 6.47)
2733	cyclobutyl	168-170	-73.9 (c 0.23)	Found: C, 60.96; H, 7.02 (Calcd. for $C_{44}H_{60}N_2O_{15}.0.5H_2O$: C, 61.02; H, 7.10)
2757	cyclopropyl	168-170	-91.7 (c 0.23)	Found: C, 60.07; H, 6.86 (Calcd. for $C_{43}H_{58}N_2O_{15}.H_2O$: C, 59.98; H, 7.02)

Example 3

The procedures described in Example 1 were repeated, but other suitably protected β-lactams and were substituted for the *cis*-N-*t*butoxycarbonyl-3-triethylsilyloxy-4-(2-thienyl) azetidin-2-one of Example 1 to prepare the series of compounds corresponding to structure 14 and having the combination of substituents identified in the following table.

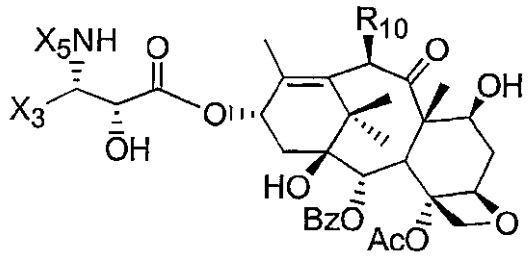


(14)

Compound	X_5	X_3	R_{10}
2640	tBuOCO-	phenyl	EtNHCOO-
2743	tBuOCO-	p-nitrophenyl	EtNHCOO-
6015	tC_3H_5CO-	2-furyl	3,4diFPhNHCOO-
6024	tC_3H_5CO-	2-furyl	PhNHCOO-
6072	tC_3H_5CO-	2-furyl	EtNHCOO-

Example 4

Following the processes described in Example 1 and elsewhere herein, the following specific taxanes having structural formula 14 and the combinations of substituents identified in the following table may be prepared, wherein R_{10} is as previously defined including wherein R_{10} is $R_{10a}R_{10b}NCOO$- and (a) R_{10a} and R_{10b} are each hydrogen, (b) one of R_{10a} and R_{10b} is hydrogen and the other is (i) substituted or unsubstituted C_1 to C_8 alkyl such as methyl, ethyl, or straight, branched or cyclic propyl, butyl, pentyl, or hexyl; (ii) substituted or unsubstituted C_3 to C_8 alkenyl such as ethenyl or straight, branched or cyclic propenyl, butenyl, pentenyl or hexenyl; (iii) substituted or unsubstituted C_3 to C_8 alkynyl such as ethynyl or straight or branched propynyl, butynyl, pentynyl, or hexynyl; (iv) substituted or unsubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl, or (c) R_{10a} and R_{10b} are independently (i) substituted or unsubstituted C_1 to C_8 alkyl such as methyl, ethyl, or straight, branched or cyclic propyl, butyl, pentyl, or hexyl; (ii) substituted or unsubstituted C_2 to C_8 alkenyl such as ethenyl or straight, branched or cyclic propenyl, butenyl, pentenyl or hexenyl; (iii) substituted or unsubstituted C_2 to C_8 alkynyl such as ethynyl or straight or branched propynyl, butynyl, pentynyl, or hexynyl; (iv) substituted or unsubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl. For example, R_{10} may be $R_{10a}R_{10b}NCOO$- wherein one of R_{10a} and R_{10b} is hydrogen and the other is methyl, ethyl, or straight, branched or cyclic propyl. The substituents may be those identified elsewhere herein for substituted hydrocarbyl.



(14)

X_5	X_3	R_{10}
tBuOCO	2-furyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	3-furyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	2-thienyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	3-thienyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	2-pyridyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	3-pyridyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	4-pyridyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	isobutenyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	isopropyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	cyclopropyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	cyclobutyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	cyclopentyl	$R_{10a}R_{10b}NCOO$-
tBuOCO	phenyl	$R_{10a}R_{10b}NCOO$-
benzoyl	2-furyl	$R_{10a}R_{10b}NCOO$-
benzoyl	3-furyl	$R_{10a}R_{10b}NCOO$-
benzoyl	2-thienyl	$R_{10a}R_{10b}NCOO$-
benzoyl	3-thienyl	$R_{10a}R_{10b}NCOO$-
benzoyl	2-pyridyl	$R_{10a}R_{10b}NCOO$-
benzoyl	3-pyridyl	$R_{10a}R_{10b}NCOO$-
benzoyl	4-pyridyl	$R_{10a}R_{10b}NCOO$-
benzoyl	isobutenyl	$R_{10a}R_{10b}NCOO$-
benzoyl	isopropyl	$R_{10a}R_{10b}NCOO$-

benzoyl	cyclopropyl	$R_{10a}R_{10b}NCOO$--
benzoyl	cyclobutyl	$R_{10a}R_{10b}NCOO$-
benzoyl	cyclopentyl	$R_{10a}R_{10b}NCOO$-
benzoyl	phenyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	2-furyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	isobutenyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	isopropyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	cyclobutyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
2-FuCO-	phenyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	2-furyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	isobutenyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	isopropyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	cyclobutyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
2-ThCO-	phenyl	$R_{10a}R_{10b}NCOO$-
2-PyCO-	2-furyl	$R_{10a}R_{10b}NCOO$-

2-PyCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
2-PyCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
2-PyCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
2-PyCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
2-PyCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
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3-PyCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
3-PyCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
3-PyCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
3-PyCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
3-PyCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
3-PyCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
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3-PyCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
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4-PyCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
4-PyCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
4-PyCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-

4-PyCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
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4-PyCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
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4-PyCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
4-PyCO-	phenyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	2-furyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	3-furyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	isobutenyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	isopropyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	cyclobutyl	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
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EtOCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
EtOCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
EtOCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
EtOCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
EtOCO-	isobutenyl	$R_{10a}R_{10b}NCOO$-
EtOCO-	isopropyl	$R_{10a}R_{10b}NCOO$-
EtOCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
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EtOCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
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ibueCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
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ibueCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	isobutenyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	isopropyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	cyclobutyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
ibueCO-	phenyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	2-furyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	isobutenyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	isopropyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	cyclopropyl	$R_{10a}R_{10b}NCOO$-
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iBuCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
iBuCO-	phenyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	2-furyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-

iBuOCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
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iBuOCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
iBuOCO-	phenyl	$R_{10a}R_{10b}NCOO$-
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iPrOCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
iPrOCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
iPrOCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
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iPrOCO-	cyclopentyl	$R_{10a}R_{10b}NCOO$-
iPrOCO-	phenyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	2-furyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	3-furyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	2-thienyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	3-thienyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	2-pyridyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	3-pyridyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	4-pyridyl	$R_{10a}R_{10b}NCOO$-
nPrOCO-	isobutenyl	$R_{10a}R_{10b}NCOO$-

nPrOCO-	isopropyl	$R_{10a}R_{10b}NCOO-$
nPrOCO-	cyclopropyl	$R_{10a}R_{10b}NCOO-$
nPrOCO-	cyclobutyl	$R_{10a}R_{10b}NCOO-$
nPrOCO-	cyclopentyl	$R_{10a}R_{10b}NCOO-$
nPrOCO-	phenyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	2-furyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	3-furyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	2-thienyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	3-thienyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	2-pyridyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	3-pyridyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	4-pyridyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	isobutenyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	isopropyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	cyclopropyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	cyclobutyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	cyclopentyl	$R_{10a}R_{10b}NCOO-$
nPrCO-	phenyl	$R_{10a}R_{10b}NCOO-$

Example 5

Following the processes described in Example 1 and elsewhere herein, the following specific taxanes having structural formula 15 may be prepared, wherein R_7 is hydroxy and R_{10} in each of the series (that is, each of series "A" through "K") is as previously defined, including wherein R_{10} is $R_{10a}R_{10b}NCOO-$ and one of R_{10a} and R_{10b} is hydrogen and the other is (i) substituted or unsubstituted C_1 to C_8 alkyl such as methyl, ethyl, or straight, branched or cyclic propyl, butyl, pentyl, or hexyl; (ii) substituted or unsubstituted C_2 to C_8 alkenyl such as ethenyl or straight, branched or cyclic propenyl, butenyl, pentenyl or hexenyl; (iii) substituted or unsubstituted C_2 to C_8 alkynyl such as ethynyl or straight or branched propynyl, butynyl, pentynyl, or hexynyl; (iv) phenyl or substituted phenyl such as nitro, alkoxy or halosubstituted phenyl, or (v) substituted or unsubstituted heteroaromatic such as furyl, thienyl, or pyridyl. The substituents may be those

identified elsewhere herein for substituted hydrocarbyl. In one embodiment, preferred R_{10} substituents include $R_{10a}R_{10b}NCOO$- wherein one of R_{10a} and R_{10b} is hydrogen and the other is methyl, ethyl, or straight, branched or cyclic propyl. In another embodiment, preferred R_{10} substituents include $R_{10a}R_{10b}NCOO$- wherein one of R_{10a} and R_{10b} is hydrogen and the other is substituted methyl, ethyl, or straight, branched or cyclic propyl.

In the "A" series of compounds, X_{10} is as otherwise as defined herein. Preferably, heterocyclo is substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), and R_7 and R_{10} each have the beta stereochemical configuration.

In the "B" series of compounds, X_{10} and R_{2a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7 and R_{10} each have the beta stereochemical configuration.

In the "C" series of compounds, X_{10} and R_{9a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{9a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7, R_9 and R_{10} each have the beta stereochemical configuration.

In the "D" and "E" series of compounds, X_{10} is as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), and R_7, R_9 (series D only) and R_{10} each have the beta stereochemical configuration.

In the "F" series of compounds, X_{10}, R_{2a} and R_{9a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7, R_9 and R_{10} each have the beta stereochemical configuration.

In the "G" series of compounds, X_{10} and R_{2a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl,

pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7, R_9 and R_{10} each have the beta stereochemical configuration.

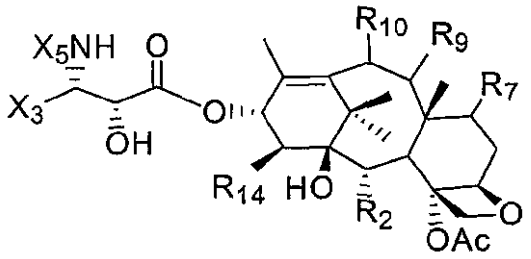
In the "H" series of compounds, X_{10} is as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7 and R_{10} each have the beta stereochemical configuration.

In the "I" series of compounds, X_{10} and R_{2a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7 and R_{10} each have the beta stereochemical configuration.

In the "J" series of compounds, X_{10} and R_{2a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7, R_9 and R_{10} each have the beta stereochemical configuration.

In the "K" series of compounds, X_{10}, R_{2a} and R_{9a} are as otherwise as defined herein. Preferably, heterocyclo is preferably substituted or unsubstitued furyl, thienyl, or pyridyl, X_{10} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl (e.g., tert-butyl), R_{2a} is preferably substituted or unsubstitued furyl, thienyl, pyridyl, phenyl, or lower alkyl, and R_7, R_9 and R_{10} each have the beta stereochemical configuration.

Any substituents of each of X_3, X_5, R_2, R_7, and R_9 may be hydrocarbyl or any of the heteroatom containing substituents selected from the group consisting of heterocyclo, alkoxy, alkenoxy, alkynoxy, aryloxy, hydroxy, protected hydroxy, keto, acyloxy, nitro, amino, amido, thiol, ketal, acetal, ester and ether moieties, but not phosphorous containing moieties.



(15)

Series	X_5	X_3	R_{10}	R_2	R_9	R_{14}
A1	-$COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A2	-COX_{10}	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A3	-$CONHX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A4	-$COOX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A5	-COX_{10}	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A6	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A7	-$COOX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A8	-COX_{10}	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A9	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A10	-$COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H

A11	$-COX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	O	H
A12	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	O	H
B1	$-COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B2	$-COX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B3	$-CONHX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B4	$-COOX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B5	$-COX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B6	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B7	$-COOX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B8	$-COX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B9	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B10	$-COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B11	$-COX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H

B12	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
C1	$-COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C2	$-COX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C3	$-CONHX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C4	$-COOX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C5	$-COX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C6	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C7	$-COOX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C8	$-COX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C9	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C10	$-COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C11	$-COX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
C12	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	$R_{9a}COO-$	H
D1	$-COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	OH	H
D2	$-COX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	OH	H

D3	-CONHX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D4	-COOX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D5	-COX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D6	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D7	-COOX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D8	-COX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D9	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D10	-COOX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D11	-COX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D12	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
E1	-COOX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E2	-COX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E3	-CONHX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E4	-COOX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E5	-COX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH

E6	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E7	-COOX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E8	-COX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E9	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E10	-COOX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E11	-COX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E12	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
F1	-COOX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H
F2	-COX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H
F3	-CONHX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H
F4	-COOX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H
F5	-COX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H
F6	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H
F7	-COOX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	H

F8	$-COX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F9	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F10	$-COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F11	$-COX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F12	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
G1	$-COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G2	$-COX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G3	$-CONHX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G4	$-COOX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G5	$-COX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G6	$-CONHX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G7	$-COOX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G8	$-COX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H

G9	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
G10	-COOX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
G11	-COX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
G12	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
H1	-COOX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H2	-COX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H3	-CONHX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H4	-COOX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H5	-COX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H6	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H7	-COOX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H8	-COX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H9	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH

H10	-$COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H11	-COX_{10}	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H12	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
I1	-$COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I2	-COX_{10}	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I3	-$CONHX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I4	-$COOX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I5	-COX_{10}	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I6	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I7	-$COOX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I8	-COX_{10}	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I9	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I10	-$COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH

I11	-COX_{10}	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
I12	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	OH
J1	-$COOX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J2	-COX_{10}	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J3	-$CONHX_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J4	-$COOX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J5	-COX_{10}	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J6	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J7	-$COOX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J8	-COX_{10}	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J9	-$CONHX_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J10	-$COOX_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
J11	-COX_{10}	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH

J12	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
K1	-COOX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K2	-COX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K3	-CONHX$_{10}$	heterocyclo	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K4	-COOX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K5	-COX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K6	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K7	-COOX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K8	-COX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K9	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkenyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K10	-COOX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K11	-COX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K12	-CONHX$_{10}$	optionally substituted C_2 to C_8 alkynyl	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH

Example 6

In Vitro cytotoxicity measured by the cell colony formation assay

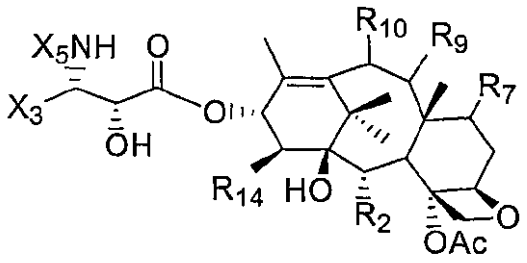
Four hundred cells (HCT116) were plated in 60 mm Petri dishes containing 2.7 mL of medium (modified McCoy's 5a medium containing 10% fetal bovine serum and 100 units/mL penicillin and 100 g/mL streptomycin). The cells were incubated in a CO_2 incubator at 37 °C for 5 h for attachment to the bottom of Petri dishes. The compounds identified in Example 2 were made up fresh in medium at ten times the final concentration, and then 0.3 mL of this stock solution was added to the 2.7 mL of medium in the dish. The cells were then incubated with drugs for 72 h at 37 ° C. At the end of incubation the drug-containing media were decanted, the dishes were rinsed with 4 mL of Hank's Balance Salt Solution (HBSS), 5 mL of fresh medium was added, and the dishes were returned to the incubator for colony formation. The cell colonies were counted using a colony counter after incubation for 7 days. Cell survival was calculated and the values of ID50 (the drug concentration producing 50% inhibition of colony formation) were determined for each tested compound.

Compound	IN VITRO ID 50 (nm) HCT116
taxol	2.1
docetaxel	0.6
2600	<1
2616	27
2622	<1
2633	<10
2686	<1
2692	<1
2700	<1
2717	<1
2722	<1
2733	<10
2757	<1

2640	<1
2743	<1
6015	<10
6024	<1
6072	<1

Claims

1. A taxane having the formula:



wherein

R_2 is acyloxy;

R_7 is hydroxy;

R_9 is keto, hydroxy, or acyloxy;

R_{10} is carbamoyloxy;

R_{14} is hydrido or hydroxy;

X_3 is substituted or unsubstituted alkyl, alkenyl, alkynyl, phenyl or heterocyclo, wherein alkyl comprises at least two carbon atoms;

X_5 is $-COX_{10}$, $-COOX_{10}$, or $-CONHX_{10}$;

X_{10} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo; and

Ac is acetyl.

2. The taxane of claim 1 wherein R_{10} is $R_{10a}R_{10b}NCOO-$ and R_{10a} and R_{10b} are independently hydrogen, hydrocarbyl, substituted hydrocarbyl, or heterocyclo.

3. The taxane of claim 2 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

4. The taxane of claim 2 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

5. The taxane of claim 2 wherein X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

6. The taxane of claim 2 wherein R_{14} is hydrido.

7. The taxane of claim 6 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

8. The taxane of claim 6 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

9. The taxane of claim 6 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

10. The taxane of claim 2 wherein R_2 is benzoyloxy.

11. The taxane of claim 10 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

12. The taxane of claim 10 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

13. The taxane of claim 10 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

14. The taxane of claim 2 wherein R_{14} is hydrido and R_9 is keto.

15. The taxane of claim 14 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

16. The taxane of claim 14 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

17. The taxane of claim 14 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

18. The taxane of claim 2 wherein R_2 is benzoyloxy and R_9 is keto.

19. The taxane of claim 18 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

20. The taxane of claim 18 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

21. The taxane of claim 18 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

22. The taxane of claim 2 wherein R_{14} is hydrido and R_2 is benzoyloxy.

23. The taxane of claim 22 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

24. The taxane of claim 22 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

25. The taxane of claim 22 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

26. The taxane of claim 2 wherein R_{14} is hydrido, R_9 is keto, and R_2 is benzoyloxy.

27. The taxane of claim 26 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

28. The taxane of claim 26 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

29. The taxane of claim 26 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

30. The taxane of claim 1 wherein R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen and the other is hydrocarbyl, substituted hydrocarbyl, or heterocyclo.

31. The taxane of claim 30 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

32. The taxane of claim 30 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

33. The taxane of claim 30 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

34. The taxane of claim 30 wherein R_{14} is hydrido.

35. The taxane of claim 34 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

36. The taxane of claim 34 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

37. The taxane of claim 34 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

38. The taxane of claim 30 wherein R_2 is benzoyloxy.

39. The taxane of claim 38 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

40. The taxane of claim 38 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

41. The taxane of claim 38 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

42. The taxane of claim 30 wherein R_{14} is hydrido and R_9 is keto.

43. The taxane of claim 42 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

44. The taxane of claim 42 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

45. The taxane of claim 42 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

46. The taxane of claim 30 wherein R_2 is benzoyloxy and R_9 is keto.

47. The taxane of claim 46 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

48. The taxane of claim 46 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

49. The taxane of claim 46 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

50. The taxane of claim 30 wherein R_{14} is hydrido and R_2 is benzoyloxy.

51. The taxane of claim 50 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

52. The taxane of claim 50 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

53. The taxane of claim 50 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

54. The taxane of claim 30 wherein R_{14} is hydrido, R_9 is keto, and R_2 is benzoyloxy.

55. The taxane of claim 54 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

56. The taxane of claim 54 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

57. The taxane of claim 54 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

58. The taxane of claim 1 wherein R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen and the other is substituted or unsubstituted C_1 - C_8 alkyl, phenyl, furyl, thienyl or pyridyl.

59. The taxane of claim 58 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

60. The taxane of claim 58 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

61. The taxane of claim 58 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

62. The taxane of claim 58 wherein R_{14} is hydrido.

63. The taxane of claim 62 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

64. The taxane of claim 62 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

65. The taxane of claim 62 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

66. The taxane of claim 58 wherein R_2 is benzoyloxy.

67. The taxane of claim 66 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

68. The taxane of claim 66 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

69. The taxane of claim 66 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

70. The taxane of claim 58 wherein R_{14} is hydrido and R_9 is keto.

71. The taxane of claim 70 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

72. The taxane of claim 70 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

73. The taxane of claim 70 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

74. The taxane of claim 58 wherein R_2 is benzoyloxy and R_9 is keto.

75. The taxane of claim 74 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

76. The taxane of claim 74 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

77. The taxane of claim 74 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

78. The taxane of claim 58 wherein R_{14} is hydrido and R_2 is benzoyloxy.

79. The taxane of claim 78 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

80. The taxane of claim 78 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

81. The taxane of claim 78 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

82. The taxane of claim 58 wherein R_{14} is hydrido, R_9 is keto, and R_2 is benzoyloxy.

83. The taxane of claim 82 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

84. The taxane of claim 82 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

85. The taxane of claim 82 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

86. The taxane of claim 82 wherein X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

87. The taxane of claim 86 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

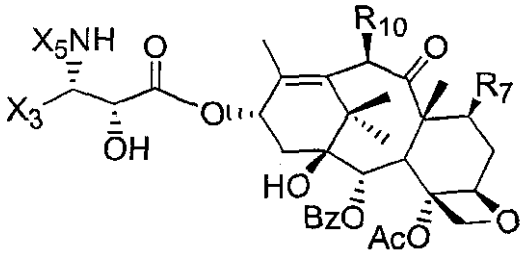
88. The taxane of claim 86 wherein X_3 is furyl or thienyl.

89. The taxane of claim 86 wherein X_3 is 2-furyl.

90. The taxane of claim 86 wherein X_3 is 2- thienyl.

91. The taxane of claim 86 wherein X_3 is cycloalkyl.

92. A taxane having the formula:



R_7 is hydroxy;

R_{10} is carbamoyloxy;

X_3 is substituted or unsubstituted alkyl, alkenyl, alkynyl, or heterocyclo, wherein alkyl comprises at least two carbon atoms;

X_5 is $-COX_{10}$, $-COOX_{10}$, or $-CONHX_{10}$;

X_{10} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo,

Ac is acetyl, and

Bz is benzoyl.

93. The taxane of claim 92 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

94. The taxane of claim 93 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

95. The taxane of claim 93 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

96. The taxane of claim 92 wherein X_3 is furyl or thienyl.

97. The taxane of claim 96 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

98. The taxane of claim 96 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

99. The taxane of claim 93 wherein X_3 is cycloalkyl.

100. The taxane of claim 99 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

101. The taxane of claim 99 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

102. The taxane of claim 93 wherein X_3 is isobutenyl.

103. The taxane of claim 102 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

104. The taxane of claim 102 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

105. The taxane of claim 92 wherein R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen and the other is C_1 - C_8 alkyl, phenyl or heterocyclo.

106. The taxane of claim 105 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

107. The taxane of claim 106 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

108. The taxane of claim 106 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

109. The taxane of claim 105 wherein X_3 is furyl or thienyl.

110. The taxane of claim 109 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

111. The taxane of claim 109 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

112. The taxane of claim 105 wherein X_3 is cycloalkyl.

113. The taxane of claim 112 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

114. The taxane of claim 112 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

115. The taxane of claim 105 wherein X_3 is isobutenyl.

116. The taxane of claim 115 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

117. The taxane of claim 115 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

118. The taxane of claim 92 wherein X_3 is furyl or thienyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is C_1 - C_8 alkyl, phenyl, or heterocyclo, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

119. The taxane of claim 92 wherein X_3 is substituted or unsubstituted furyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is methyl, ethyl, or straight, branched or cyclic propyl, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

120. The taxane of claim 92 wherein X_3 is substituted or unsubstituted furyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted phenyl or heterocyclo, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

121. The taxane of claim 92 wherein X_3 is substituted or unsubstituted thienyl, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is methyl, ethyl, or straight, branched or cyclic propyl, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

122. The taxane of claim 92 wherein X_3 is substituted or unsubstituted thienyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted phenyl or heterocyclo, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

123. The taxane of claim 92 wherein X_3 is substituted or unsubstituted phenyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a}

and R_{10b} is methyl, ethyl, or straight, branched or cyclic propyl, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

124. The taxane of claim 92 wherein X_3 is substituted or unsubstituted phenyl, R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted phenyl or heterocyclo, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

125. The taxane of claim 92 wherein X_3 is isobutenyl, one of R_{10a} and R_{10b} is hydrogen, R_{10} is $R_{10a}R_{10b}NCOO-$, the other of R_{10a} and R_{10b} is methyl, ethyl, or straight, branched or cyclic propyl, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

126. The taxane of claim 92 wherein X_3 is alkyl, R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is methyl, ethyl, or straight, branched or cyclic propyl, and X_5 is $-COX_{10}$ wherein X_{10} is phenyl, or X_5 is $-COOX_{10}$ wherein X_{10} is t-butyl.

127. The taxane of claim 92 wherein X_3 is 2-furyl or 2-thienyl, R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is methyl, ethyl, or straight, branched or cyclic propyl, X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

128. The taxane of claim 92 wherein X_3 is 2-furyl or 2-thienyl, R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted phenyl or heterocyclo, X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

129. The taxane of claim 92 wherein X_3 is cycloalkyl, R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted phenyl or heterocyclo, X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

130. A pharmaceutical composition comprising the taxane of claim 1 and at least one pharmaceutically acceptable carrier.

131. The pharmaceutical composition of claim 130 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

132. The pharmaceutical composition of claim 131 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

133. The pharmaceutical composition of claim 131 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

134. The pharmaceutical composition of claim 130 wherein R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted C_1 - C_8 alkyl, phenyl or heterocyclo.

135. The pharmaceutical composition of claim 134 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

136. The pharmaceutical composition of claim 135 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

137. The pharmaceutical composition of claim 135 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

138. The pharmaceutical composition of claim 131 wherein X_3 is furyl or thienyl, R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is C_1 - C_8 alkyl, phenyl or heterocyclo, and X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

139. The pharmaceutical composition of claim 131 wherein X_3 is cycloalkyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is C_1 - C_8 alkyl, phenyl or heterocyclo, and X_5 is -COX_{10} wherein X_{10} is phenyl, or X_5 is -$COOX_{10}$ wherein X_{10} is t-butyl.

140. The pharmaceutical composition of claim 131 wherein X_3 is substituted or unsubstituted phenyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is C_1 - C_8 alkyl, phenyl or heterocyclo, and X_5 is -COX_{10} wherein X_{10} is phenyl, or X_5 is -$COOX_{10}$ wherein X_{10} is t-butyl.

141. The pharmaceutical composition of claim 131 wherein X_3 is isobutenyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is C_1 - C_8 alkyl, phenyl or heterocyclo, and X_5 is -COX_{10} wherein X_{10} is phenyl, or X_5 is -$COOX_{10}$.

142. The pharmaceutical composition of claim 131 wherein X_3 is alkyl, R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is C_1 - C_8 alkyl, phenyl or heterocyclo, and X_5 is -COX_{10} wherein X_{10} is phenyl, or X_5 is -$COOX_{10}$ wherein X_{10} is t-butyl.

143. A pharmaceutical composition comprising the taxane of claim 92 and at least one pharmaceutically acceptable carrier.

144. A pharmaceutical composition comprising the taxane of claim 96 and at least one pharmaceutically acceptable carrier.

145. A composition for oral administration comprising the taxane of claim 1 and at least one pharmaceutically acceptable carrier.

146. The composition of claim 145 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

147. The composition of claim 146 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is

-$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

148. The composition of claim 146 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

149. The composition of claim 145 wherein R_{10} is $R_{10a}R_{10b}NCOO$-, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted C_1 - C_8 alkyl, phenyl or heterocyclo.

150. The composition of claim 149 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

151. The composition of claim 150 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

152. The composition of claim 150 wherein X_5 is -COX_{10} and X_{10} is phenyl, or X_5 is -$COOX_{10}$ and X_{10} is t-butyl.

153. A composition for oral administration comprising the taxane of claim 92 and at least one pharmaceutically acceptable carrier.

154. A composition for oral administration comprising the taxane of claim 96 and at least one pharmaceutically acceptable carrier.

155. A method of inhibiting tumor growth in a mammal, said method comprising orally administering a therapeutically effective amount of a pharmaceutical composition comprising the taxane of claim 1 and at least one pharmaceutically acceptable carrier.

156. The method of claim 155 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

157. The method of claim 156 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

158. The method of claim 156 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

159. The method of claim 155 wherein R_{10} is $R_{10a}R_{10b}NCOO-$, one of R_{10a} and R_{10b} is hydrogen, the other of R_{10a} and R_{10b} is substituted or unsubstituted C_1 - C_8 alkyl, phenyl or heterocyclo.

160. The method of claim 159 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

161. The method of claim 160 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

162. The method of claim 160 wherein X_5 is $-COX_{10}$ and X_{10} is phenyl, or X_5 is $-COOX_{10}$ and X_{10} is t-butyl.

163. A method of inhibiting tumor growth in a mammal, said method comprising orally administering a therapeutically effective amount of a pharmaceutical composition comprising the taxane of claim 92 and at least one pharmaceutically acceptable carrier.

164. A method of inhibiting tumor growth in a mammal, said method comprising orally administering a therapeutically effective amount of a pharmaceutical composition comprising the taxane of claim 96 and at least one pharmaceutically acceptable carrier.

INTERNATIONAL SEARCH REPORT

	Ir onal Application No PCT/US 01/03633

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D409/12 A61K31/335 A61P35/00 C07D407/12 C07D305/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 53592 A (ASAHI KASEI KOGYO KABUSHIKI KAISHA) 14 September 2000 (2000-09-14) claims 1-33	1-164
X	WO 97 32578 A (THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK) 12 September 1997 (1997-09-12) claims 1-11	1-164
X	WO 96 13495 A (THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK) 9 May 1996 (1996-05-09) claims 1-11	1-164
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[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

° Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
31 May 2001	11/06/2001

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Int ›nal Application No
PCT/US 01/03633

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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[19]中华人民共和国国家知识产权局

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C07D407/12 C07D305/14

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代理人 程金山

权利要求书16页 说明书47页 附图页数0页

[54]发明名称 C10氨基甲酰氧基取代的紫衫烷抗肿瘤剂

[57]摘要

具有C(10)位氨基甲酰氧基取代基,C(7)位羟基取代基和一些C(2),C(9),C(14)位和侧链取代基的紫衫烷。

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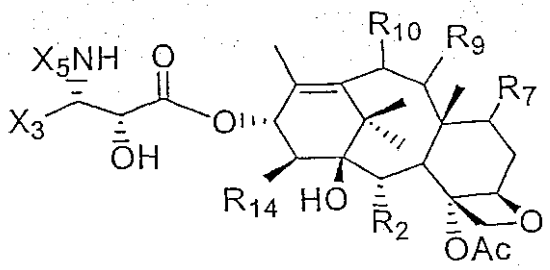
权 利 要 求 书

1、具有下列结构式的紫杉烷：



其中

R_2是酰氧基；

R_7是羟基；

R_9是酮基，羟基或酰氧基；

R_{10}是氨基甲酰氧基；

R_{14}是氢或羟基；

X_3是取代的或未取代的烷基，链烯基，炔基，苯基或杂环基；其中烷基包含至少两个碳原子；

X_5是$-COX_{10}$，$-COOX_{10}$或$-CONHX_{10}$；

X_{10}是烃基，取代的烃基或杂环基；并且

Ac是乙酰基。

2、权利要求1的紫杉烷，其中R_{10}为$R_{10a}R_{10b}NCOO-$并且R_{10a}和R_{10b}独立地为氢，烃基，取代的烃基或杂环基。

3、权利要求2的紫杉烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

4、权利要求2的紫杉烷，其中X_5为$-COX_{10}$并且X_{10}为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

5、权利要求2的紫杉烷，其中X_5为$-COX_{10}$，其中X_{10}为苯基，或者X_5

为-$COOX_{10}$，其中 X_{10} 为叔丁基。

6、权利要求 2 的紫衫烷，其中 R_{14} 为氢。

7、权利要求 6 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

8、权利要求 6 的紫衫烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

9、权利要求 6 的紫衫烷，其中 X_5 为-COX_{10} 并且 X_{10} 为苯基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为叔丁基。

10、权利要求 2 的紫衫烷，其中 R_2 为苯甲酰氧基。

11、权利要求 10 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

12、权利要求 10 的紫衫烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

13、权利要求 10 的紫衫烷，其中 X_5 为-COX_{10} 并且 X_{10} 为苯基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为叔丁基。

14、权利要求 2 的紫衫烷，其中 R_{14} 为氢并且 R_9 为酮基。

15、权利要求 14 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

16、权利要求 14 的紫衫烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

17、权利要求 14 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

18、权利要求 2 的紫杉烷，其中 R_2 为苯甲酰氧基并且 R_9 为酮基。

19、权利要求 18 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

20、权利要求 18 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

21、权利要求 18 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

22、权利要求 2 的紫杉烷，其中 R_{14} 为氢并且 R_2 为苯甲酰氧基。

23、权利要求 22 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

24、权利要求 22 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

25、权利要求 22 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

26、权利要求 2 的紫杉烷，其中 R_{14} 为氢，R_9 为酮基，并且 R_2 为苯甲酰氧基。

27、权利要求 26 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

28、权利要求 26 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-

吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

29、权利要求26的紫衫烷，其中X_5为$-COX_{10}$并且X_{10}为苯基，或者X_5为$-COOX_{10}$并且X_{10}为叔丁基。

30、权利要求1的紫衫烷，其中R_{10}为$R_{10a}R_{10b}NCOO-$，R_{10a}和R_{10b}中的一个为氢，另一个为烃基，取代的烃基或杂环基。

31、权利要求30的紫衫烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

32、权利要求30的紫衫烷，其中X_5为$-COX_{10}$并且X_{10}为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

33、权利要求30的紫衫烷，其中X_5为$-COX_{10}$并且X_{10}为苯基，或者X_5为$-COOX_{10}$并且X_{10}为叔丁基。

34、权利要求30的紫衫烷，其中R_{14}为氢。

35、权利要求34的紫衫烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

36、权利要求34的紫衫烷，其中X_5为$-COX_{10}$并且X_{10}为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

37、权利要求34的紫衫烷，其中X_5为$-COX_{10}$并且X_{10}为苯基，或者X_5为$-COOX_{10}$并且X_{10}为叔丁基。

38、权利要求30的紫衫烷，其中R_2为苯甲酰氧基。

39、权利要求38的紫衫烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

40、权利要求 38 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

41、权利要求 38 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

42、权利要求 30 的紫衫烷，其中 R_{14} 为氢并且 R_9 为酮基。

43、权利要求 42 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

44、权利要求 42 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

45、权利要求 42 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

46、权利要求 30 的紫衫烷，其中 R_2 为苯甲酰氧基并且 R_9 为酮基。

47、权利要求 46 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

48、权利要求 46 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

49、权利要求 46 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

50、权利要求 30 的紫衫烷，其中 R_{14} 为氢并且 R_2 为苯甲酰氧基。

51、权利要求 50 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯

基或 C_2-C_8 炔基。

52、权利要求 50 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

53、权利要求 50 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

54、权利要求 30 的紫衫烷，其中 R_{14} 为氢，R_9 为酮基并且 R_2 为苯甲酰氧基。

55、权利要求 54 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

56、权利要求 54 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

57、权利要求 54 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

58、权利要求 1 的紫衫烷，其中 R_{10} 为 $R_{10a}R_{10b}NCOO-$ 并且 R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的 C_1-C_8 烷基，苯基，呋喃基，噻吩基或吡啶基。

59、权利要求 58 的紫衫烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

60、权利要求 58 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

61、权利要求 58 的紫衫烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5

为$-COOX_{10}$并且X_{10}为叔丁基。

62、权利要求58的紫杉烷，其中R_{14}为氢。

63、权利要求62的紫杉烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

64、权利要求62的紫杉烷，其中X_5为$-COX_{10}$并且X_{10}为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

65、权利要求62的紫杉烷，其中X_5为$-COX_{10}$，其中X_{10}为苯基，或者X_5为$-COOX_{10}$，其中X_{10}为叔丁基。

66、权利要求58的紫杉烷，其中R_2为苯甲酰氧基。

67、权利要求66的紫杉烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

68、权利要求66的紫杉烷，其中X_5为$-COX_{10}$并且X_{10}为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

69、权利要求66的紫杉烷，其中X_5为$-COX_{10}$并且X_{10}为苯基，或者X_5为$-COOX_{10}$并且X_{10}为叔丁基。

70、权利要求58的紫杉烷，其中R_{14}为氢并且R_9为酮基。

71、权利要求70的紫杉烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

72、权利要求70的紫杉烷，其中X_5为$-COX_{10}$并且X_{10}为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

73、权利要求 70 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

74、权利要求 58 的紫杉烷，其中 R_2 为苯甲酰氧基并且 R_9 为酮基。

75、权利要求 74 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

76、权利要求 74 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

77、权利要求 74 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

78、权利要求 58 的紫杉烷，其中 R_{14} 为氢并且 R_2 为苯甲酰氧基。

79、权利要求 78 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

80、权利要求 78 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

81、权利要求 78 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

82、权利要求 58 的紫杉烷，其中 R_{14} 为氢，R_9 为酮基并且 R_2 为苯甲酰氧基。

83、权利要求 82 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

84、权利要求 82 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-

吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基，或者X_5为$-COOX_{10}$并且X_{10}为取代的或未取代的C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

85、权利要求82的紫杉烷，其中X_5为$-COX_{10}$并且X_{10}为苯基，或者X_5为$-COOX_{10}$并且X_{10}为叔丁基。

86、权利要求82的紫杉烷，其中X_5为$-COOX_{10}$并且X_{10}为叔丁基。

87、权利要求86的紫杉烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8烷基，C_2-C_8链烯基或C_2-C_8炔基。

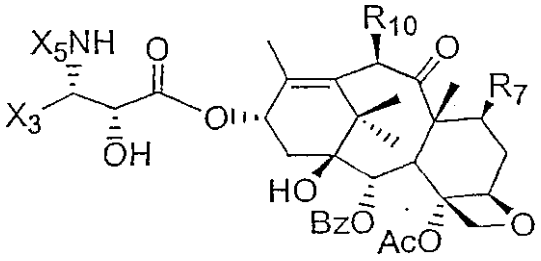
88、权利要求86的紫杉烷，其中X_3为呋喃基或噻吩基。

89、权利要求86的紫杉烷，其中X_3为2-呋喃基。

90、权利要求86的紫杉烷，其中X_3为2-噻吩基。

91、权利要求86的紫杉烷，其中X_3为环烷基。

92、具有下列结构式的紫杉烷：



其中

R_7是羟基；

R_{10}是氨基甲酰氧基；

X_3是取代的或未取代的烷基，链烯基，炔基，或杂环基；其中烷基包含至少两个碳原子；

X_5是$-COX_{10}$，$-COOX_{10}$或$-CONHX_{10}$；

X_{10}是烃基，取代的烃基或杂环基；

Ac是乙酰基，并且

Bz是苯甲酰基。

93、权利要求92的紫杉烷，其中X_3为2-呋喃基，3-呋喃基，2-噻吩

基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

94、权利要求 93 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

95、权利要求 93 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为苯基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为叔丁基。

96、权利要求 92 的紫杉烷，其中 X_3 为呋喃基或噻吩基。

97、权利要求 96 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

98、权利要求 96 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为苯基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为叔丁基。

99、权利要求 93 的紫杉烷，其中 X_3 为环烷基。

100、权利要求 99 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

101、权利要求 99 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为苯基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为叔丁基。

102、权利要求 93 的紫杉烷，其中 X_3 为异丁烯基。

103、权利要求 102 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

104、权利要求 102 的紫杉烷，其中 X_5 为-COX_{10} 并且 X_{10} 为苯基，或者 X_5 为-$COOX_{10}$ 并且 X_{10} 为叔丁基。

105、权利要求 92 的紫杉烷，其中 R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基。

106、权利要求 105 的紫杉烷，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

107、权利要求 106 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

108、权利要求 106 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

109、权利要求 105 的紫杉烷，其中 X_3 为呋喃基或噻吩基。

110、权利要求 109 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

111、权利要求 109 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

112、权利要求 105 的紫杉烷，其中 X_3 为环烷基。

113、权利要求 112 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

114、权利要求 112 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

115、权利要求 105 的紫杉烷，其中 X_3 为异丁烯基。

116、权利要求 115 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$

并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

117、权利要求 115 的紫杉烷，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

118、权利要求 92 的紫杉烷，其中 X_3 为呋喃基或噻吩基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

119、权利要求 92 的紫杉烷，其中 X_3 为取代的或未取代的呋喃基，R_{10} 为 $R_{10a}R_{10b}NCOO-$ 并且 R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基或直链，支链或环状丙基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

120、权利要求 92 的紫杉烷，其中 X_3 为取代的或未取代的呋喃基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的苯基或杂环基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

121、权利要求 92 的紫杉烷，其中 X_3 为取代的或未取代的噻吩基，R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基或直链，支链或环状丙基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

122、权利要求 92 的紫杉烷，其中 X_3 为取代的或未取代的噻吩基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的苯基或杂环基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

123、权利要求 92 的紫杉烷，其中 X_3 为取代的或未取代的苯基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基或直链，支链或环状丙基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

124、权利要求 92 的紫杉烷，其中 X_3 为取代的或未取代的苯基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的苯基或杂环基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其

中 X_{10} 为叔丁基。

125、权利要求 92 的紫杉烷，其中 X_3 为异丁烯基，R_{10a} 和 R_{10b} 中的一个为氢，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的另一个为甲基，乙基或直链，支链或环状丙基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

126、权利要求 92 的紫杉烷，其中 X_3 为烷基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基或直链，支链或环状丙基，并且 X_5 为 $-COX_{10}$，其中 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

127、权利要求 92 的紫杉烷，其中 X_3 为 2-呋喃基或 2-噻吩基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基或直链，支链或环状丙基，X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

128、权利要求 92 的紫杉烷，其中 X_3 为 2-呋喃基或 2-噻吩基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的苯基或杂环基，X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

129、权利要求 92 的紫杉烷，其中 X_3 为环烷基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的苯基或杂环基，并且 X_5 为 $-COOX_{10}$，其中 X_{10} 为叔丁基。

130、一种药物组合物，它包含权利要求 1 的紫杉烷和至少一种可药用载体。

131、权利要求 130 的药物组合物，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

132、权利要求 131 的药物组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

133、权利要求 131 的药物组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

134、权利要求 130 的药物组合物，其中 R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的 C_1-C_8 烷基，苯基或杂环基。

135、权利要求 134 的药物组合物，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

136、权利要求 135 的药物组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

137、权利要求 135 的药物组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

138、权利要求 131 的药物组合物，其中 X_3 为呋喃基或噻吩基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基，X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

139、权利要求 131 的药物组合物，其中 X_3 为环烷基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基，X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

140、权利要求 131 的药物组合物，其中 X_3 为取代的或未取代的苯基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基，并且 X_5 为 $-COX_{10}$ 其中 X_{10} 为苯基或者 X_5 为 $-COOX_{10}$ 其中 X_{10} 为叔丁基。

141、权利要求 131 的药物组合物，其中 X_3 为异丁烯基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基，X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基或者 X_5 为 $-COOX_{10}$。

142、权利要求 131 的药物组合物，其中 X_3 为烷基，R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为 C_1-C_8 烷基，苯基或杂环基，并且 X_5 为 $-COX_{10}$ 其中 X_{10} 为苯基或者 X_5 为 $-COOX_{10}$ 其中 X_{10} 为叔丁基。

143、一种药物组合物，它包含权利要求 92 的紫杉烷和至少一种可药用载体。

144、一种药物组合物，它包含权利要求 96 的紫杉烷和至少一种可药用载体。

145、一种口服给药的组合物，它包含权利要求 1 的紫杉烷和至少一种可药用载体。

146、权利要求 145 的组合物，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

147、权利要求 146 的组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

148、权利要求 146 的组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

149、权利要求 145 的组合物，其中 R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的 C_1-C_8 烷基，苯基或杂环基。

150、权利要求 149 的组合物，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

151、权利要求 150 的组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

152、权利要求 150 的组合物，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

153、一种口服给药的组合物，它包含权利要求 92 的紫杉烷和至少一种可药用载体。

154、一种口服给药的组合物，它包含权利要求 96 的紫杉烷和至少一种可药用载体。

155、一种抑制哺乳动物肿瘤生长的方法，所述方法包括口服给予治疗有效量包含权利要求 1 的紫杉烷和至少一种可药用载体的药物组合物。

156、权利要求 155 的方法，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩

基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

157、权利要求 156 的方法，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

158、权利要求 156 的方法，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

159、权利要求 155 的方法，其中 R_{10} 为 $R_{10a}R_{10b}NCOO-$，R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的 C_1-C_8 烷基，苯基或杂环基。

160、权利要求 159 的方法，其中 X_3 为 2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

161、权利要求 160 的方法，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为取代的或未取代的苯基，2-呋喃基，3-呋喃基，2-噻吩基，3-噻吩基，2-吡啶基，3-吡啶基，4-吡啶基，C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为取代的或未取代的 C_1-C_8 烷基，C_2-C_8 链烯基或 C_2-C_8 炔基。

162、权利要求 160 的方法，其中 X_5 为 $-COX_{10}$ 并且 X_{10} 为苯基，或者 X_5 为 $-COOX_{10}$ 并且 X_{10} 为叔丁基。

163、一种抑制哺乳动物肿瘤生长的方法，所述方法包括口服给予治疗有效量包含权利要求 92 的紫杉烷和至少一种可药用载体的药物组合物。

164、一种抑制哺乳动物肿瘤生长的方法，所述方法包括口服给予治疗有效量包含权利要求 96 的紫杉烷和至少一种可药用载体的药物组合物。

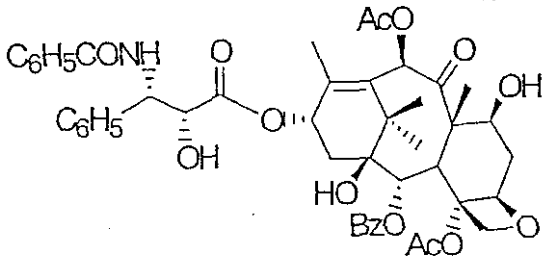
说　明　书

C10 氨基甲酰氧基取代的紫杉烷抗肿瘤剂

本发明背景

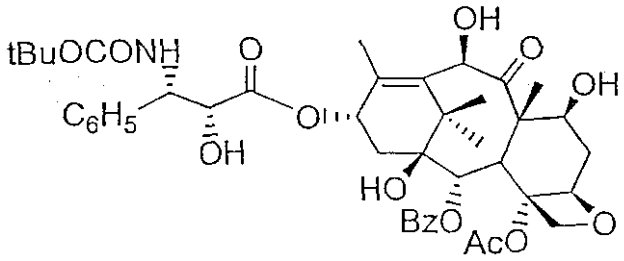
本发明提供新的紫杉烷(taxanes)，它作为抗肿瘤剂具有特别的效用。

以浆果赤霉素 II 和紫杉酚为成员的紫杉烷族萜烯已成为在生物学和化学领域具有重要意义的研究对象。紫杉酚本身用作癌化学治疗剂并且具有广泛的肿瘤抑制活性。紫杉酚具有 2'R, 3'S 构型和下列结构式:



其中 Ac 为乙酰基。

Colin 等人在美国专利 4,814,470 中报道，某些紫杉酚类似物具有比紫杉酚明显大的活性。这些类似物中的一种通常称作 docetaxel 并且具有下列结构式:



尽管紫杉酚和 docetaxel 是有效的化学治疗剂，但是其功效是有限的，包括有限的抗某种癌症功效并且当以各种剂量给予时，对受试体有毒性。因此，需要开发其他具有改进功效和低毒性的化学治疗剂。

本发明简述

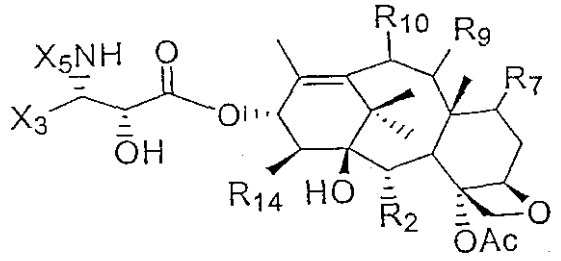
因此，本发明目的之一是提供抗肿瘤剂功效和毒性与紫杉酚和docetaxel 相比改进的紫杉烷。通常，这些紫杉烷具有 C-10 位氨基甲酰氧基取代基，C-7 位羟基取代基和一些 C-3' 取代基。

因此简单地说，本发明提供紫杉烷组合物本身，包含紫杉烷和可药用载体的药物组合物及其给药方法。

本发明的其他目的和特征部分是显而易见的并且部分在下文中指出。

优选实施方案的详述

在本发明一个实施方案中，本发明紫杉烷具有(1)结构：



(1)

其中

R_2是酰氧基；

R_7是羟基；

R_9是酮基，羟基或酰氧基；

R_{10}是氨基甲酰氧基；

R_{14}是氢或羟基；

X_3是取代的或未取代的烷基，链烯基，炔基，苯基或杂环基；

X_5是$-COX_{10}$，$-COOX_{10}$或$-CONHX_{10}$；

X_{10}是烃基，取代的烃基或杂环基；

Ac 是乙酰基；并且

R_7，R_9和R_{10}独立地具有α或β立体化学构型。

在一个实施方案中，R_2是酯($R_{2a}C(O)O-$)，氨基甲酸酯($R_{2a}R_{2b}NC(O)O-$)，碳酸酯($R_{2a}OC(O)O-$)，或硫代氨基甲酸酯($R_{2a}SC(O)O-$)，其中 R_{2a}和 R_{2b}独

立地为氢，烃基，取代的烃基或杂环基。在优选的实施方案中，R_2 是酯($R_{2a}C(O)O-$)，其中 R_{2a} 是芳基或杂芳香基，在另一优选的实施方案中，R_2 是酯($R_{2a}C(O)O-$)，其中 R_{2a} 是取代的或未取代的苯基，呋喃基，噻吩基或吡啶基。在一个特别优选的实施方案中，R_2 是苯甲酰氧基。

尽管在本发明一个实施方案中，R_9 是酮基，但在其他实施方案中，R_9 可能具有α或β立体化学构型，优选β立体化学构型，并且例如，可以是α-或β-羟基或者α-或β-酰氧基。例如，当 R_9 是酰氧基时，它可以是酯($R_{9a}C(O)O-$)，氨基甲酸酯($R_{9a}R_{9b}NC(O)O-$)，碳酸酯($R_{9a}OC(O)O-$)，或硫代氨基甲酸酯($R_{9a}SC(O)O-$)，其中 R_{9a} 和 R_{9b} 独立地为氢，烃基，取代的烃基或杂环基。如果 R_9 是酯($R_{9a}C(O)O-$)，那么 R_{9a} 是取代的或未取代的烷基，取代的或未取代的链烯基，取代的或未取代的芳基或取代的或未取代的杂芳香基。进一步更优选地，R_9 是酯($R_{9a}C(O)O-$)，其中 R_{9a} 是取代的或未取代的苯基，取代的或未取代的呋喃基，取代的或未取代的噻吩基或取代的或未取代的吡啶基。在一个实施方案中，R_9 是($R_{9a}C(O)O-$)，其中 R_{9a} 是甲基，乙基，丙基(直链、支链或环状的)，丁基(直链、支链或环状的)，戊基(直链、支链或环状的)，或己基(直链、支链或环状的)。在另一实施方案中，R_9 是($R_{9a}C(O)O-$)，其中 R_{9a} 是取代的甲基，取代的乙基，取代的丙基(直链、支链或环状的)，取代的丁基(直链、支链或环状的)，取代的戊基(直链、支链或环状的)，或取代的己基(直链、支链或环状的)，其中所述取代基选自杂环基，烷氧基，链烯氧基，炔氧基，芳氧基，羟基，保护的羟基，酮基，酰氧基，硝基，氨基，酰氨基，巯基，缩酮，缩醛，酯和醚部分，但不是含磷部分。

在一个实施方案中，R_{10} 是 $R_{10a}R_{10b}NCOO-$，其中 R_{10a} 和 R_{10b} 独立地为氢，烃基，取代的烃基或杂环基。优选的 R_{10} 取代基的实例包括 $R_{10a}R_{10b}NCOO-$，其中(a)、R_{10a} 和 R_{10b} 各为氢，(b)、R_{10a} 和 R_{10b} 中的一个为氢，另一个为(i)、取代的或未取代 C_1-C_8 烷基如甲基，乙基，或者直链、支链或环状丙基，丁基，戊基或己基；(ii)、取代的或未取代 C_2-C_8 链烯基如乙烯基，或者直链、支链或环状丙烯基，丁烯基，戊烯基或己烯基；(iii)、取代的或未取代 C_2-C_8 炔基如乙炔基，或者直链或支链丙炔基，丁炔基，戊炔基或

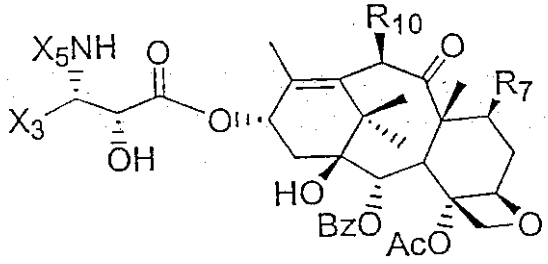
己炔基；（iv）、取代的或未取代的苯基，或(V)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基，或者(c)、R_{10a}和 R_{10b}独立地为(i)、取代的或未取代 C_1-C_8烷基如甲基，乙基，或者直链、支链或环状丙基，丁基，戊基或己基；（ii）、取代的或未取代 C_2-C_8链烯基如乙烯基，或者直链、支链或环状丙烯基，丁烯基，戊烯基或己烯基；（iii）、取代的或未取代 C_2-C_8炔基如乙炔基，或者直链或支链丙炔基，丁炔基，戊炔基或己炔基；（iv）、取代的或未取代的苯基，或(V)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基。所述取代基可以是本文在关于取代的烃基中所确定的那些基团。在一个实施方案中，优选的 R_{10}取代基包括 $R_{10a}R_{10b}NCOO$-，其中 R_{10a}和 R_{10b}中的一个为氢，另一个为甲基，乙基，或者直链、支链或环状的丙基。

X_3取代基的实例包括取代的或未取代 C_2-C_8烷基，取代的或未取代 C_2-C_8链烯基，取代的或未取代 C_2-C_8炔基，取代的或未取代的包含 5 或 6 个环原子的杂芳香基和取代的或未取代的苯基。优选的 X_3取代基的实例包括取代的或未取代的乙基，丙基，丁基，环丙基，环丁基，环己基，异丁烯基，呋喃基，噻吩基，和吡啶基。

X_5取代基的实例包括-COX_{10}，-$COOX_{10}$或-$CONHX_{10}$，其中 X_{10}是取代的或未取代的烷基，链烯基，苯基或杂芳香基。优选的 X_5取代基的实例包括-COX_{10}，-$COOX_{10}$或-$CONHX_{10}$，其中 X_{10}是(i)、取代的或未取代 C_1-C_8烷基如取代的或未取代的甲基，乙基，丙基(直链、支链或环状的)，丁基(直链、支链或环状的)，戊基(直链、支链或环状的)或己基(直链、支链或环状的)；（ii）、取代的或未取代 C_2-C_8链烯基如取代的或未取代的乙烯基，丙烯基(直链、支链或环状的)，丁烯基(直链、支链或环状的)，戊烯基(直链、支链或环状的)或己烯基(直链、支链或环状的)；（iii）、取代的或未取代 C_2-C_8炔基如取代的或未取代的乙炔基，丙炔基(直链、或支链)，丁炔基(直链、或支链)，戊炔基(直链、或支链)或己炔基(直链、或支链)；(iv)、取代的或未取代的苯基，或(V)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基，其中所述取代基选自杂环基，烷氧基，链烯氧基，炔氧基，芳氧基，羟基，保护的羟基，酮基，酰氧基，硝基，氨

基，酰氨基，巯基，缩酮，缩醛，酯和醚部分，但不是含磷部分。

在本发明一个实施方案中，本发明紫杉烷具有(2)结构：



(2)

其中

R_7是羟基；

R_{10}是氨基甲酰氧基；

X_3是取代的或未取代的烷基，链烯基，炔基，或杂环基，其中烷基包含至少两个碳原子；

X_5是$-COX_{10}$，$-COOX_{10}$或$-CONHX_{10}$；并且

X_{10}是烃基，取代的烃基或杂环基。

例如，在其中紫杉烷具有结构式(2)结构的优选实施方案中，R_{10}可以是$R_{10a}R_{10b}NCOO-$，其中R_{10a}和R_{10b}中的一个为氢，另一个为(i)、取代的或未取代C_1-C_8烷基如甲基，乙基，或者直链、支链或环状丙基，丁基，戊基或己基；(ii)、取代的或未取代C_2-C_8链烯基如乙烯基，或者直链、支链或环状丙烯基，丁烯基，戊烯基或己烯基；(iii)、取代的或未取代C_2-C_8炔基如乙炔基，或者直链或支链丙炔基，丁炔基，戊炔基或己炔基；(iv)、苯基或取代的苯基如硝基，烷氧基或卤素取代的苯基，或(v)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基。所述取代基可以是本文在关于取代的烃基中所确定的那些基团。在一个实施方案中，优选的R_{10}取代基包括$R_{10a}R_{10b}NCOO-$，其中R_{10a}和R_{10b}中的一个为氢，另一个为取代的或未取代的，优选未取代的甲基，乙基，或者直链、支链或环状的丙基。在另一实施方案中，优选的R_{10}取代基包括$R_{10a}R_{10b}NCOO-$，其中R_{10a}和R_{10b}中的一个为氢，另一个为取代的或未取代的苯基或杂环基。在一个实施方案中，当R_{10a}和R_{10b}选自这些基团时，X_3选自取代的或未取代烷基，

链烯基，苯基或杂环基，更优选取代的或未取代的链烯基，苯基或杂环基，进一步更优选取代的或未取代的苯基或杂环基，并且进一步更优选杂环基如呋喃基，噻吩基或吡啶基。在一个实施方案中，当 R_{10a}，R_{10b} 和 X_3 选自这些基团时，X_5 选自 $-COX_{10}$，其中 X_{10} 是苯基，烷基或杂环基，更优选苯基。或者，在一个实施方案中，当 R_{10a}，R_{10b} 和 X_3 选自这些基团时，X_5 选自 $-COX_{10}$，其中 X_{10} 是苯基，烷基或杂环基，更优选苯基，或者 X_5 是 $-COOX_{10}$，其中 X_{10} 是烷基，优选叔丁基。因此，更优选的实施方案是具有结构式 2 结构的紫衫烷，其中(i)、X_5 是 $-COOX_{10}$，其中 X_{10} 是叔丁基或者 X_5 是 $-COX_{10}$，其中 X_{10} 是苯基，(ii)、X_3 是取代的或未取代的环烷基，链烯基，苯基或杂环基，更优选取代的或未取代的异丁烯基，苯基，呋喃基，噻吩基或吡啶基，进一步更优选未取代的异丁烯基，呋喃基，噻吩基或吡啶基，并且(iii)、R_{10} 是 $R_{10a}R_{10b}NCOO-$，其中 R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的或未取代的 C_1-C_8 烷基，苯基或杂环基。

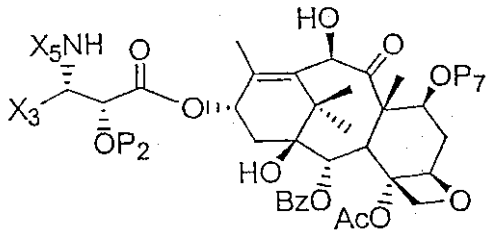
因此，优选的实施方案是具有结构式 1 或 2 结构的紫衫烷，其中 R_{10} 是 $R_{10a}R_{10b}NCOO-$，其中 R_{10a} 是甲基并且 R_{10b} 是氢。在该实施方案中，X_3 优选环烷基，异丁烯基，苯基，取代的苯基如对-硝基苯基，或杂环基，更优选杂环基，进一步更优选呋喃基，噻吩基或吡啶基；并且 X_5 优选苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基。在此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酮基并且 R_{14} 是氢。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酮基并且 R_{14} 是氢。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酮基并且 R_{14} 是羟基。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰

基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是羟基并且 R_{14} 是羟基。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是羟基并且 R_{14} 是氢。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酰氧基并且 R_{14} 是羟基。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酰氧基并且 R_{14} 是氢。在各此实施方案的备选方案中，当紫杉烷具有结构式 1 结构时，R_7 和 R_{10} 可以各具有β立体化学构型，R_7 和 R_{10} 可以各具有α立体化学构型，R_7 可以具有α立体化学构型，同时 R_{10} 具有β立体化学构型，或者 R_7 可以具有β立体化学构型，同时 R_{10} 具有α立体化学构型。

优选的实施方案也包括具有结构式 1 或 2 结构的紫杉烷，其中 R_{10} 是 $R_{10a}R_{10b}NCOO-$，其中 R_{10a} 是乙基并且 R_{10b} 是氢。在该实施方案中，X_3 优选环烷基，异丁烯基，苯基，取代的苯基如对-硝基苯基，或杂环基，更优选杂环基，进一步更优选呋喃基，噻吩基或吡啶基；并且 X_5 优选苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基。在此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酮基并且 R_{14} 是氢。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酮基并且 R_{14} 是氢。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2 是苯甲酰基，R_9 是酮基并且 R_{14} 是羟基。在另一此实施方案的备选方案中，X_3 是杂环基；X_5 是苯甲酰基，烷氧

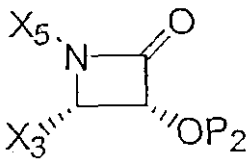
基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2是苯甲酰基，R_9是羟基并且R_{14}是羟基。在另一此实施方案的备选方案中，X_3是杂环基；X_5是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2是苯甲酰基，R_9是羟基并且R_{14}是氢。在另一此实施方案的备选方案中，X_3是杂环基；X_5是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2是苯甲酰基，R_9是酰氧基并且R_{14}是羟基。在另一此实施方案的备选方案中，X_3是杂环基；X_5是苯甲酰基，烷氧基羰基，或杂环基羰基，更优选苯甲酰基，叔丁氧基羰基或叔戊氧基羰基，进一步更优选叔丁氧基羰基；R_2是苯甲酰基，R_9是酰氧基并且R_{14}是氢。在各此实施方案的备选方案中，当紫杉烷具有结构式 1 结构时，R_7和R_{10}可以各具有β立体化学构型，R_7和R_{10}可以各具有α立体化学构型，R_7可以具有α立体化学构型，同时R_{10}具有β立体化学构型，或者R_7可以具有β立体化学构型，同时R_{10}具有α立体化学构型。

具有通式 1 结构的紫杉烷可通过将具有下列结构式并适当保护的紫杉烷中间体与异氰酸酯或氨基甲酰基氯反应，然后除掉羟基保护基进行氨基甲酰化获得:



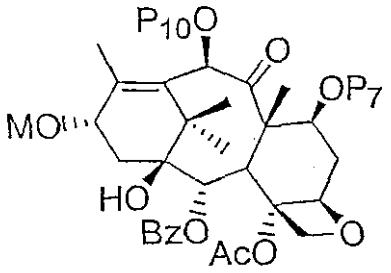
其中X_3和X_5如先前的定义，P_2是羟基保护基，并且P_7是氢或羟基保护基。

中间体紫杉烷可通过用具有紫杉烷四环核和 C-13 金属氧化物取代基的醇盐处理β-内酰胺形成在 C-13 上具有β-酰氨酯取代基的化合物（如 Holton U. S. Patent 5,466,834 中详述），然后除掉 C(10)保护基或 C(10)和 C(7)保护基获得。β-内酰胺具有式(3)结构:



(3)

其中 P_2 是羟基保护基并且 X_3 和 X_5 如先前的定义，并且醇盐具有式(4)结构：



(4)

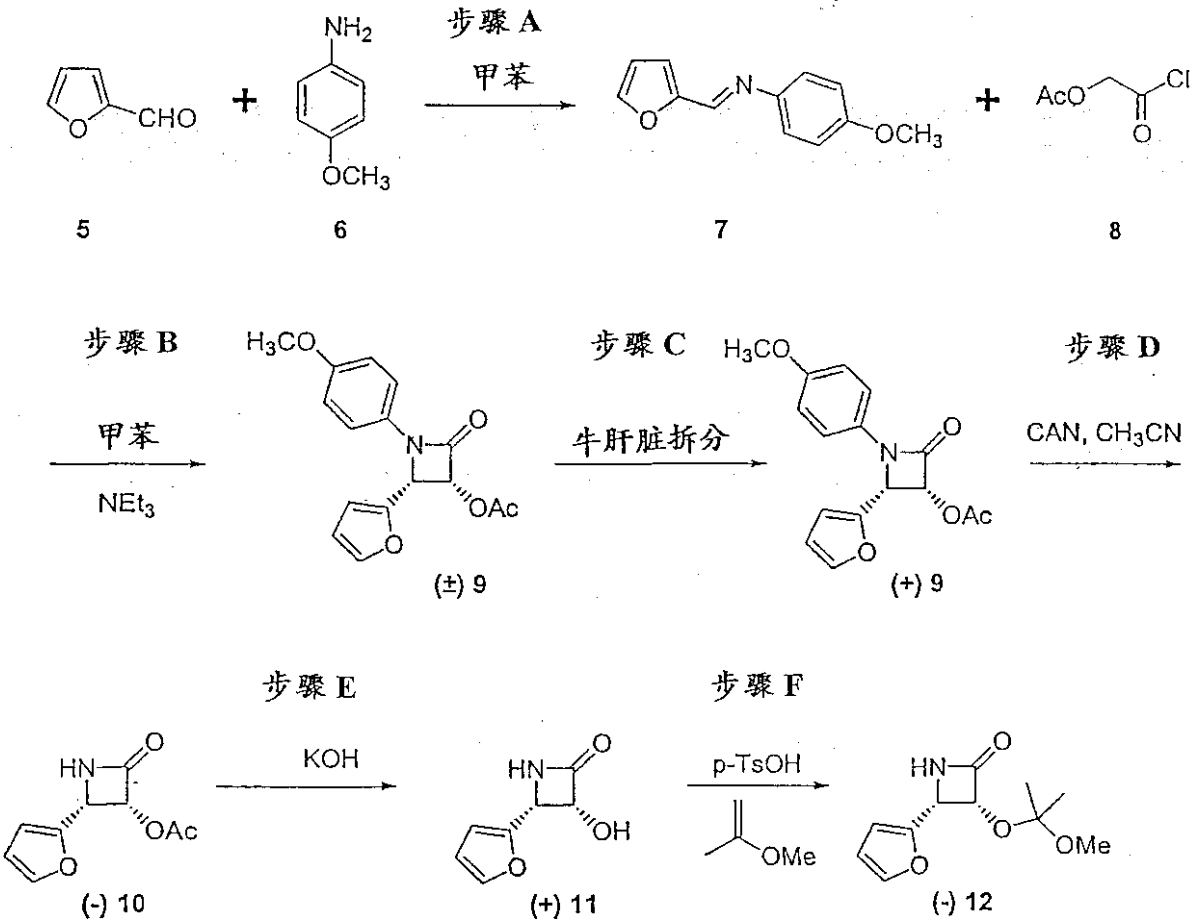
其中 M 是金属或铵，并且 P_7 和 P_{10} 是羟基保护基。

醇盐可通过将 10-脱乙酰基浆果赤霉素 III 的 C-7 和 C-10 羟基进行保护(如 Holton et al., PCT Patent Application WO 99/09021 详述)，然后用金属氨化物（metallic amide）处理制备。

在 C(2), C(9)和 C(14)位具有其他取代基的 10-脱乙酰基浆果赤霉素 III 的衍生物及其制备方法是本领域已知的。例如，在 C(2)位具有不同于苯甲酰氧基的酰氧基取代基的紫杉烷衍生物可如 Holton et al., U. S. Patent No. 5,728,725 或 Kingston et al., U. S. Patent No. 6,002,023 所述制备。例如，在 C(9)位代替酮基具有酰氧基或羟基取代基的紫杉烷可如 Holton et al., U. S. Patent No. 6,011,056 或 Gunawardana et al., U. S. Patent No. 5,352,806 所述制备。在 C(14)位具有β羟基取代基的紫杉烷可由天然存在的 14-羟基-10-10-脱乙酰基浆果赤霉素 III 制备。

β-内酰胺起始物质的制备和拆分方法通常是公知的。例如，β-内酰胺可如 Holton , U. S. Patent No. 5,430,160 所述制备并且所得到的β-内酰胺对映异构体混合物可通过用脂肪酶或例如在 Patel, U. S. Patent No. 5,879,929 ,或 Patel, U. S. Patent No. 5,567,614 中所描述的酶或例如在 PCT Patent Application No. 00/41204 中所描述的肝组织匀浆进行立体选择性水解拆分。在其中β-内酰胺为在 C(4)位呋喃取代的

优选实施方案中，β-内酰胺可如下列反应方案所述制备:



其中 Ac 为乙烯基，NEt_3 为三乙胺，CAN 为硝酸高铈铵，并且 p-TsOH 为对甲苯磺酸。例如，牛肝脏拆分可通过将β-内酰胺对映异构体混合物与牛肝脏悬浮液(例如通过将 20g 冷冻牛肝脏加到捣碎器中，然后加入 pH8 的缓冲液至总体积 1L 制备)组合进行。

本发明式 1 化合物用于抑制哺乳动物包括人肿瘤生长并且优选地以药物组合物形式给予，所述药物组合物包含有效抗肿瘤剂量本发明化合物和至少一种可药用或生理上适宜的载体。本领域也已知为赋形剂，媒介物，辅助物，助剂或稀释剂的载体是药学惰性、提供适宜的稠度或形成组合物并且不会降低抗肿瘤剂化合物治疗功效的任何物质。当给予哺乳动物或人时，如果所述载体不产生不良反应、变态反应或其他事与愿违的反应，那么，该载体是“可药用的或生理上适宜的”。

包含本发明抗肿瘤剂化合物药物组合物可以以任何常规方式配制。适

宜的制剂依赖于所选择的给药途径。本发明组合物可配制成适用于任何给药途径的制剂，只要通过所述给药途径可到达靶组织即可。适宜的给药途径包括但不限制于口服给药，非肠道(例如静脉内，动脉内，皮下，直肠，肌肉内，皮下，眼眶内，囊内，脊柱内，腹膜内或胸骨内)给药，局部(鼻，透皮，眼内)给药，膀胱内给药，鞘内给药，肠内给药，肺内给药，淋巴管内给药，腔内给药， 阴道内给药，经尿道给药，真皮内给药，耳内给药，乳房内给药，口腔给药，orthotopic 给药，气管内给药，伤口内(intralesional)给药，经皮给药，经内窥镜(endoscopical)给药，经粘膜给药，舌下给药和肠道给药。

在本发明组合物中所使用的可药用载体是本领域普通技术人员公知的并且可根据许多因素选择，所述因素包括：所使用的特定抗肿瘤剂化合物，及其浓度，稳定性和预期的生物利用度；用所述组合物治疗的疾病，病症和状况；受试体，其年龄，大小和一般状况；和给药途径。适宜的载体是本领域普通技术人员容易确定的(例如，参见 J. G. Nairn, in: Remington's Pharmaceutical Science (A. Gennaro, ed.), Mack Publishing Co., Easton, Pa., (1985), pp. 1492-1517, 其内容引入本文供参考)。

优选地，所述组合物配制成片剂，可分散粉剂，丸剂，胶囊剂，gelcaps，caplets，凝胶，脂质体，颗粒剂，溶液剂，悬浮液，乳剂，糖浆剂，酏剂，锭剂，糖衣丸，糖锭或任何其他可通过口服给药的剂型。在下列参考中描述了制备本发明所使用口服剂型的技术和成分：7 Modern Pharmaceutics, Chapters 9 and 10 (Banker & Rhodes, Editors, 1979); Lieberman et al., Pharmaceutical Dosage Forms: Tablets(1981); and Ansel, Introduction to Pharmaceutical Dosage Forms 2nd Edition (1976)。

本发明口服给药组合物在可药用载体中包含有效抗肿瘤剂量的本发明化合物。适宜的固体剂型载体包括糖，淀粉和其他常规物质包括乳糖，滑石粉，蔗糖，明胶，羧甲基纤维素，琼脂，甘露糖醇，山梨糖醇，磷酸钙，碳酸钙，碳酸钠，高岭土，藻酸，阿拉伯胶，玉米淀粉，马铃薯

淀粉，糖精钠，碳酸镁，西黄耆胶，微晶纤维素，胶态二氧化硅，羧甲基纤维素钠，滑石粉，硬脂酸镁和硬脂酸。此外，所述固体剂型可以是未包衣的或者，例如为了延迟崩解和吸收，可以通过已知的技术包衣。

优选地，本发明抗肿瘤剂化合物也配制成用于非肠道给药的制剂，例如配制成通过静脉内，动脉内，皮下，直肠，肌肉内，眼眶内，囊内，脊柱内，腹膜内或肠道途径给药的制剂。本发明非肠道给药组合物在可药用载体中包含有效抗肿瘤剂量抗肿瘤剂化合物。适用于非肠道给药的剂型包括溶液剂，悬浮液，可分散体，乳剂或任何其他可通过非肠道给药的剂型。制备非肠道给药剂型的技术和成分是本领域已知的。

在配制口服或非肠道给药液体剂型中所使用的适宜的载体包括非水性可药用极性溶剂如油，醇，酰胺，醚，酮，烃及其混合物，以及水，盐溶液，葡萄糖溶液(例如 DW5)，电解质溶液，或其他水性可药用液体。

适宜的非水性可药用极性溶剂包括，但不限制于醇，(例如α-环亚甲基甘油醚，β-环亚甲基甘油醚，1,3-丁二醇，具有 2-30 个碳原子的脂肪族或芳族醇如甲醇，乙醇，丙醇，异丙醇，丁醇，叔丁醇，己醇，辛醇，水合戊烯，苯甲醇，丙三醇(甘油)，乙二醇，己二醇，四氢糠醇，月桂醇，鲸蜡醇或硬脂醇，脂肪醇的脂肪酸酯如聚亚烷基二醇(例如聚丙二醇，聚乙二醇)，山梨糖醇，蔗糖和胆固醇)；酰胺(例如二甲基乙酰胺(DMA)，苯甲酸苄酯 DMA，二甲基甲酰胺，N-(β-羟乙基)-乳酰胺，N,N-二甲基乙酰胺，2-吡咯烷酮，1-甲基-2-吡咯烷酮或聚乙烯吡咯烷酮)；酯(例如 1-甲基-2-吡咯烷酮，2-吡咯烷酮，乙酸酯如甘油一乙酸酯，甘油二乙酸酯和甘油三乙酸酯，脂肪族或芳族酯如辛酸乙酯，油酸烷基酯，苯甲酸苄酯，乙酸苄酯，二甲基亚砜(DMSO)，甘油酯如甘油一、二或三柠檬酸酯或酒石酸酯，苯甲酸乙酯，乙酸乙酯，碳酸乙酯，乳酸乙酯，油酸乙酯，山梨糖醇的脂肪酸酯，脂肪酸衍生的 PEG 酯，甘油一硬脂酸酯，甘油酯如一、二或三甘油酯，脂肪酸酯如肉豆蔻酸异丙酯，脂肪酸衍生的 PEG 酯如 PEG-羟基油酸酯和 PEG-羟基硬脂酸酯，N-甲基吡咯烷酮，pluronic 60，聚氧乙烯山梨糖醇油酸聚酯如聚(乙氧基化)$_{30-60}$ 山梨糖醇聚(油酸酯)$_{2-4}$，聚(氧乙烯)$_{15-20}$ 一油酸酯，聚(氧乙烯)15_{-20} 一 12-羟基硬脂酸酯

和聚(氧乙烯)$_{15-20}$一蓖麻油酸酯，聚氧乙烯山梨糖醇酯如聚氧乙烯-山梨糖醇一油酸酯，聚氧乙烯-山梨糖醇一棕榈酸酯，聚氧乙烯-山梨糖醇酯一月桂酸酯，聚氧乙烯-山梨糖醇一硬脂酸酯，和 ICI Americas, Wilmington, DE 的聚山梨酯®20, 40, 60 或 80，聚乙烯吡咯烷酮，烯化氧修饰的脂肪酸酯如聚氧乙烯 40 氢化的蓖麻油和聚氧乙基化蓖麻油(例如 Cremophor® EL 溶液或 Cremophor® RH 40 溶液)，糖类的脂肪酸酯(即单糖 (例如戊糖如核糖，核酮糖，阿拉伯糖，木糖，来苏糖和木酮糖，己糖如葡萄糖，果糖，半乳糖，甘露糖和山梨糖，丙糖，丁糖，庚糖和辛糖)，二糖(例如蔗糖，麦芽糖，乳糖和海藻糖)或低聚糖或其混合物与 C_4-C_{22} 脂肪酸(例如饱和脂肪酸如辛酸，癸酸，月桂酸，肉豆蔻酸，棕榈酸和硬脂酸，和不饱和脂肪酸如棕榈烯酸，油酸，反油酸，芥酸，亚油酸)的缩合产物)，或甾族酯)；具有 2-30 个碳原子的烷醚，芳醚或环醚(例如乙醚，四氢呋喃，二甲基异山梨醇醚，二甘醇一乙醚)；glycofurol(四氢糠醇聚乙二醇醚)；具有 3-30 个碳原子的酮(例如丙酮，甲乙酮，甲基异丁基酮)；具有 4-30 个碳原子的脂族烃、环状脂族烃或芳烃(例如苯，环己烷，二氯甲烷，二氧噁烷，己烷，正癸烷，正十二烷，正己烷，环丁砜，四氢噻吩砜，四甲基砜，四甲基亚砜，甲苯，二甲基亚砜(DMSO)，或四甲基亚砜)；天然的或合成的矿物油，植物油，动物油(例如矿物油如脂族烃或蜡烃，芳族烃，混合的脂族烃和芳族烃，和精制石蜡油，植物油如亚麻子油，桐油，红花油，豆油，蓖麻油，棉子油，花生油，菜子油，椰子油，棕榈油，橄榄油，玉米油，玉米胚油，芝麻油，桃仁油和花生油，和甘油酯一、二或三甘油酯，动物油如鱼油，海生动物油，鲸油， 鳕鱼肝油，鲆鱼肝油，角鲨烯，角鲨烷，和鲨鱼肝油，油酸油，和聚氧乙烯蓖麻油)；具有 1-30 个碳原子并且可有可无地具有 1 个以上卤素取代基的烷基或芳基卤；二氯甲烷；一乙醇胺；石油醚；trolamine；ω-3 多不饱和脂肪酸(例如α-亚麻酸，二十碳五烯酸，鲱油酸或二十二碳六烯酸)；12-羟基硬脂酸的聚乙二醇酯和聚乙二醇(来自 BASF, Ludwigshafen, Germany 的 Solutol®HS-15,)；聚氧化乙二醇；月桂酸钠；油酸钠；或脱水山梨糖醇一油酸酯。

本发明中所使用的其他可药用溶剂是本领域普通技术人员公知的，并且参见 The Chemotherapy Source BooK (Williams & Wilkens Publishing), The Handbook of Pharmaceutical Excipients, (American Pharmaceutical Association, Washington, D. C., and The Pharmaceutical Society of Great Britain, London, England, 1968), Modern Pharmaceutics, (G. Banker et al., eds., 3d ed.) (Marcel Dekker, Inc., New York, New York, 1995), The Pharmacological Basis of Therapeutics, (Goodman & Gilman, McGraw Hill Publishing), Pharmaceutical Dosage Forms, (H. Lieberman et al., eds.,) (Marcel Dekker, Inc., New York, New York, 1980), Remington's Pharmaceutical Sciences (A. Gennaro, ed., 19th ed.) (Mack Publishing, Easton, PA, 1995), The United States Pharmacopeia 24, The National Formulary 19, (National Publishing, Philadelphia, PA, 2000), A. J. Spiegel 等人，和 Use of Nonaqueous Solvents in Parenteral Products, JOURNAL OF PHARMACEUTICAL SCIENCES, Vol. 52, No. 10, pp. 917-927 (1963)。

优选的溶剂包括已知用于稳定抗肿瘤剂化合物的溶剂，如富含甘油三酯的油，例如红花油，豆油或其混合物，和烯化氧基修饰的脂肪酸酯如聚氧乙烯 40 氢化的蓖麻油和聚氧乙基化蓖麻油(例如 Cremophor® EL 溶液或 Cremophor® RH 40 溶液)。通过商业渠道获得的甘油三酯包括 Intralipid®乳化豆油 (Kabi-Pharmacia Inc., Stockholm, Sweden), Nutralipid®乳剂 (McGqw, Irvine, California), Liposyn®II 20%乳剂 (20%的脂肪乳溶液，其中每 ml 溶液包含 100mg 红花油，100mg 豆油，12mg 卵磷脂和 25mg 甘油; Abbott Laboratories, Chicago, Illinois), Liposyn®III 2%乳剂 (2%的脂肪乳溶液，其中每 ml 溶液包含 100mg 红花油，100mg豆油，12mg卵磷脂和25mg甘油; Abbott Laboratories, Chicago, Illinois)，天然或合成的包含基于总脂肪酸重量 25%-100%二十二碳六烯酰基的甘油衍生物 (Dhasco®(来自 Martek Biosciences Corp., Columbia, MD), DHA Maguro®(来自 Daito Enterprises, Los Angeles,

CA)，Soyacal®,和 Travemulsion®)。乙醇是溶解抗肿瘤剂化合物以便形成溶液剂，乳剂等优选的溶剂。

为了制药工业中公知的各种各样的目的，本发明组合物可包含其他次要成分。这些成分在极大程度上提供下列性质：增加抗肿瘤剂化合物在给药部位的停留时间，保护组合物的稳定性，控制 pH，有利于将抗肿瘤剂化合物加工成药物制剂等。优选地，这些成分中的每一种各自以低于总组合物重量大约 15%，更优选低于大约 5%，并且最优选低于总组合物重量大约 0.5% 的量存在。如制剂领域公知的，某些成分如填充剂或稀释剂可以占总组合物重量的高达 90%。所述添加剂包括用于防止紫衫烷再沉淀的低温防护剂，表面活性剂，润湿剂或乳化剂(例如卵磷脂，聚山梨醇酯-80，吐温®80，pluronic 60，聚氧乙烯硬脂酸酯)，防腐剂(例如对羟基苯甲酸乙酯)，防微生物剂(例如苯甲醇，苯酚，间甲苯酚，三氯叔丁醇，山梨酸，硫汞撒和 paraben)，pH 调节剂或缓冲剂(例如酸，碱，醋酸钠，脱水山梨醇一月桂酸酯)，克分渗透压浓度调节剂(例如甘油)，增稠剂(一硬脂酸铝，硬脂酸，鲸蜡醇，硬脂醇，瓜尔胶，甲基纤维素，羟丙基纤维素，三硬脂酸甘油酯，鲸蜡酯，聚乙二醇)，着色剂，染料，助流剂，非挥发性硅氧烷(例如 cyclomethicone)，粘土(例如膨润土)，粘合剂，膨胀剂，增香剂，甜味剂，吸收剂，填充剂(例如，糖如乳糖，蔗糖，甘露糖醇或山梨糖醇，纤维素或磷酸钙)，稀释剂(例如水，盐水，电解质溶液)，结合剂(例如，淀粉如玉米淀粉)，小麦淀粉，或马铃薯淀粉，明胶，西黄著胶，甲基纤维素，羟丙基甲基纤维素，羧甲基纤维素钠，聚乙烯吡咯烷酮，糖，聚合物，阿拉伯胶)，崩解剂(例如淀粉如玉米淀粉，小麦淀粉，大米淀粉，马铃薯淀粉或羧甲基淀粉，交联聚乙烯吡咯烷酮，琼脂，藻酸或其盐如藻酸钠，交联羧甲基纤维素钠或交联聚乙烯吡咯酮)，润滑剂(例如二氧化硅，滑石粉，硬脂酸或其盐如硬脂酸镁，或聚乙二醇)，包衣剂(例如浓糖溶液包括阿拉伯胶，滑石粉，聚乙烯吡咯烷酮，carbopol gel，聚乙二醇或二氧化钛)，和抗氧化剂(例如焦亚硫酸钠，亚硫酸氢钠，亚硫酸钠，葡萄糖，苯酚和硫苯酚)。

在优选的实施方案中，本发明药物组合物包含至少一种非水性可药用

溶剂和一种在乙醇中的溶解度至少大约为 100，200，300，400，500，600，700 或 800mg/ml 的抗肿瘤剂化合物。尽管不受特定理论的限制，但相信，抗肿瘤剂化合物在乙醇中的溶解度可能与其功效直接有关。抗肿瘤剂化合物也可能从溶液中结晶出来。换言之，抗肿瘤剂化合物结晶如化合物 1393 可能溶解在溶剂中形成溶液，并且当溶剂蒸发时又结晶出来而不会形成任何非晶形抗肿瘤剂化合物。也优选当按照工作实施例中所阐述的方法测定时 ID50 值(即产生 50% 抑制集落形成作用时药物的浓度)至少比 paclitaxel 低 4，5，6，7，8，9 或 10 倍的抗肿瘤剂化合物。

例如，可以根据患者的生理状况，给药的目的是治疗还是预防和其他已知因素，连续地或间歇地通过这些途径给药并且由熟练的医师确定。

给予本发明药物组合物的剂量和方案可以很容易地由治疗癌症的普通技术人员确定。可以理解，抗肿瘤剂化合物的剂量将依赖于受试体的年龄，性别，健康状况和体重，以及联合治疗方式(如果有的话)和治疗频率以及预期作用的性质。对于任何给药方式，所释放的抗肿瘤剂化合物实际量以及获得本文所述有利作用必需的给药表也将部分依赖于下列因素，如抗肿瘤剂化合物的生物利用度，所治疗的疾病，预期的治疗剂量和其他本领域技术人员显而易见的因素。在本发明上下文中，给予动物特别是人的剂量应该在合理的一段时间足以实现所述动物预期的治疗效应。优选地，无论通过口服或其他途径给药，抗肿瘤剂化合物的有效量是当通过所述途径给药时产生预期的治疗效应的任何量。优选地，制备口服给药组合物，使得一种或多种口服制剂的单次量为每 m^2 患者体表包含至少 20mg 抗肿瘤剂化合物，或每 m^2 患者体表包含至少 50，100，150，200，300，400 或 500mg 抗肿瘤剂化合物，其中人的平均体表为 1.8m^2。优选地，口服给药组合物的单次量为每 m^2 患者体表包含大约 20-600 mg 抗肿瘤剂化合物，更优选大约 25-400 mg/m^2，甚至更优选大约 40-300 mg/m^2，并且甚至更优选 50-200 mg/m^2。优选地，制备非肠道给药组合物，使得单次量为每 m^2 患者体表包含至少 20mg 抗肿瘤剂化合物，或每 m^2 患者体表包含至少 40，50，100，150，200，300，400 或 500mg 抗肿瘤剂化合物。优选地，一种或多种非肠道制剂的单次量为每 m^2 患者体表包含大约

20-500 mg 抗肿瘤剂化合物，更优选大约 40-400 mg/m^2，并且甚至更优选 60-350 mg/m^2。然而，当需要达到预期的治疗效应时，可进行调整的所述剂量可根据给药表改变。应该注意到，本文所提供的有效剂量的范围不意味着限制本发明，而是代表优选的剂量范围。正如本领域任一没有不当经验的普通技术人员可以理解和确定的那样，最优选的剂量是对于各受试体来说是特制的剂量。

优选地，在液体药物组合物中抗肿瘤剂化合物的浓度为每 ml 组合物大约 0.01mg-10mg，更优选每 ml 大约 0.1mg-7mg，甚至更优选每 ml 大约 0.5mg-5mg，并且最优选每 ml 大约 1.5mg-4mg。相对低的浓度通常是优选的，因为抗肿瘤剂化合物在低浓度时几乎全部溶解在溶液中。优选地，在口服给药固体药物组合物中的抗肿瘤剂化合物的浓度为总组合物重量的大约 5%-50%，更优选大约 8%-40%，并且最优选大约 10%-30%。

在一个实施方案中，可通过将抗肿瘤剂化合物溶解在任何能够溶解所述化合物形成溶液的可药用溶剂(例如乙醇或二氯甲烷)中来制备口服给药的溶液剂。将适宜体积的载体溶液，如 Cremophor®EL 溶液在搅拌下加到所述溶液中形成用于口服给予患者的可药用溶液剂。如果需要，所述溶液剂可配制成含最小量或不含乙醇的制剂，本领域已知，当给予包含某一浓度乙醇的口服制剂时，它引起不良的生理作用。

在另一实施方案中，可通过将将抗肿瘤剂化合物溶解在任何能够溶解所述化合物形成溶液的可药用溶剂(例如乙醇或二氯甲烷)中来制备口服给药的粉剂和片剂。当溶液真空干燥时，所述溶剂可以是能够蒸发的或不能蒸发的。在干燥前，可将其他载体如 Cremophor®EL 溶液加入到该溶液中。所得到的溶液真空干燥形成玻璃样物质。然后，将该玻璃样物质与粘合剂混合形成粉剂，该粉剂可与填充剂或其他常规压片剂混合并压片形成用于口服给予患者的片剂。所述粉剂也可以加到如上所述任何液体载体中形成用于口服给药的溶液剂，乳剂，悬浮液等。

可通过将抗肿瘤剂化合物溶解在任何能够溶解所述化合物形成溶液的可药用溶剂(例如乙醇或二氯甲烷)中来制备非肠道给药的乳剂。将适宜体积的载体乳剂，如 Liposyn®II 或 Liposyn®III 乳剂在搅拌下加到所述

溶液中形成用于非肠道给予患者的可药用乳剂。如果需要，所述乳剂可配制成含最小量或不含乙醇或 Cremophor®溶液的制剂，本领域已知，当给予包含某一浓度乙醇或 Cremophor®溶液的非肠道制剂时，它引起不良的生理作用。

可通过将抗肿瘤剂化合物溶解在任何能够溶解所述化合物形成溶液的可药用溶剂(例如乙醇或二氯甲烷)中来制备非肠道给药的溶液剂。将适宜体积的载体溶液，如 Cremophor®溶液在搅拌下加到所述溶液中形成用于口服给予患者的可药用溶液剂。如果需要，所述溶液剂可配制成含最小量或不含乙醇或 Cremophor®溶液的制剂，本领域已知，当给予包含某一浓度乙醇或 Cremophor®溶液的非肠道制剂时，它引起不良的生理作用。

如果需要，上述口服或非肠道给药的乳剂或溶液剂可以以浓缩形式包装在 IV 袋、小瓶或其他常规容器中并如本领域已知的，在使用前用任何可药用液体如盐水稀释形成适宜的紫杉烷浓度。

定义

本文所使用的术语“烃”或“烃基”描述的是只包含元素碳和氢的有机化合物或基团。这些部分包括烷基，链烯基，炔基，和芳基部分。这些部分也包括用其他脂肪烃基或环烃基取代的烷基，链烯基，炔基，和芳基部分，如烷芳基，链烯芳基和炔芳基。除非另外说明，优选地，这一部分包含 1-20 个碳原子。

本文所描述的”取代的烃基“部分是被至少一个非碳原子取代的烃基部分，包括其中碳链原子被杂原子如氮，氧，硅，磷，硼，硫或卤原子取代的烃基部分。这些取代基包括卤素，杂环，烷氧基，链烯氧基，炔氧基，芳氧基，羟基，保护的羟基，酮基，酰基，酰氧基，硝基，氨基，酰氨基，硝基，氰基，巯基，缩酮，缩醛，酯和醚。

除非另外说明，优选地，本文所描述的烷基是主链包含 1-8 个碳原子并且最高达 20 个碳原子的低级烷基。它们可以是直链的或支链的或环状的并且包括甲基，乙基，丙基，异丙基，丁基，己基等。

除非另外说明，优选地，本文所描述的链烯基是直链包含 2-8 个碳原

子并且最高达 20 个碳原子的低级链烯基。它们可以是直链的或支链的或环状的并且包括乙烯基，丙烯基，异丙烯基，丁烯基，异丁烯基，己烯基等。

除非另外说明，优选地，本文所描述的炔基是直链包含 2-8 个碳原子并且最高达 20 个碳原子的低级炔基。它们可以是直链的或支链的并且包括乙炔基，丙炔基，丁炔基，异丁炔基，己炔基等。

本文单独使用或作为另一基团部分的术语“芳基”或“芳”是指未取代的或取代的碳环芳基，优选环上包含 6-12 个碳原子的单环或二环基团，如苯基，二苯基，萘基，取代的苯基，取代的二苯基或取代的萘基。苯基和取代的苯基是更优选的芳基。

本文单独使用或作为另一基团部分的术语“卤素”或“卤”是指氯，溴，氟和碘。

本文单独使用或作为另一基团部分的术语“杂环”或“杂环的”是指未取代的或取代的、全饱和或不饱和的、单环或二环的、芳族或非芳族的、在至少一个环上具有至少一个杂原子，并且各环优选具有 5 或 6 个原子的基团。优选地，杂环基在环上具有 1 或 2 个氧原子，1 或 2 个硫原子，和/或 1-4 个氮原子，并且可以通过碳或杂原子与分子的残余部分结合。杂环基的实例包括杂芳基如呋喃基，噻吩基，吡啶基，噁唑基，吡咯基，吲哚基，喹啉基或异喹啉基等。取代基的实例包括一个或多个下列基团：烃基，取代的烃基，酮基，羟基，保护的羟基，酰基，酰氧基，烷氧基，链烯氧基，炔氧基，芳氧基，卤素，酰氨基，氨基，硝基，氰基，巯基，缩酮，缩醛，酯和醚。

本文单独使用或作为另一基团部分的术语“杂芳基”是指未取代的或取代的、在至少一个环上具有至少一个杂原子，并且各环优选具有 5 或 6 个原子的芳族基团。优选地，杂芳基在环上具有 1 或 2 个氧原子，1 或 2 个硫原子，和/或 1-4 个氮原子，并且可以通过碳或杂原子与分子的残余部分结合。杂芳基的实例包括呋喃基，噻吩基，吡啶基，噁唑基，吡咯基，吲哚基，喹啉基或异喹啉基等。取代基的实例包括一个或多个下列基团：烃基，取代的烃基，酮基，羟基，保护的羟基，酰基，酰氧基，

烷氧基，链烯氧基，炔氧基，芳氧基，卤素，酰氨基，氨基，硝基，氰基，巯基，缩酮，缩醛，酯和醚。

本文单独使用或作为另一基团部分的术语“酰基”是指通过除掉有机羧酸的-COOH 基团的羟基得到的部分，例如 RC(O)-，其中 R 为 R^1，R^1O-，R^1R^2N-或 R^1S-，R^1 是烃基，杂取代的烃基，或杂环并且 R^2 是氢，烃基或取代的烃基。

本文单独使用或作为另一基团部分的术语“酰氧基”是指通过氧键(-O-)连接的上述酰基，例如 RC(O)O-，其中 R 如术语“酰基”中的定义。

除非另外说明，本文所描述的烷氧基羰基氧基部分包括低级烃或取代烃或取代烃部分。

除非另外说明，本文所描述的氨基甲酰基氧基部分是其中一个或两个胺氢任选地被烃基，取代的烃基或杂环部分取代的氨基甲酸衍生物。

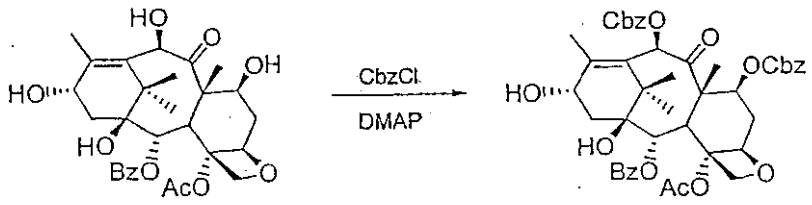
本文所使用的术语“羟基保护基”和“羟保护基”是指能够保护游离羟基的基团(“保护的羟基”)，该保护基可在利用保护进行反应之后除掉而不影响分子的残余部分。各种各样的羟基保护基及其合成可在“有机合成中的保护基” by T. W. Greene, John Wiley and Sons, 1981, or Fieser & Fieser 中找到。羟基保护基的实例包括甲氧基甲基，1-乙氧基乙基，苄氧基甲基，(β-三甲硅烷基乙氧基)甲基，四氢吡喃基，2,2,2-三氯乙氧基羰基，叔丁基(二苯基)甲硅烷基，三烷基甲硅烷基，三氯甲氧基羰基和 2,2,2-三氯乙氧基甲基。

本文所使用的"Ac"是指乙酰基；“Bz”是指苯甲酰基；“Et”是指乙基；“Me”是指甲基；“Ph”是指苯基；“iPr”是指异丙基；“tBu”和“t-Bu”是指叔丁基；“R”是指低级烷基，除非另外定义；“Py”是指吡啶或吡啶基；“TES”是指三乙基甲硅烷基“TMS”是指三甲硅烷基；“LAH”是指氢化锂铝；“10-DAB”是指 10-去乙酰浆果赤霉素 III；“胺保护基”包括但不限制于氨基甲酸酯，例如 2,2,2-三氯乙基氨基甲酸酯或氨基甲酸叔丁酯；“保护的羟基”是指 OP，其中 P 为羟基保护基；“tBuOCO”和“Boc”是指叔丁氧基羰基；“tAmOCO”是指叔戊氧基羰基；“2-FuCO”是指 2-呋喃基羰基，“2-ThCO”是指 2-噻吩基羰基；“2-PyCO”是指 2-吡啶基羰基；

“3-PyCO”是指3-吡啶基羰基；“4-PyCO”是指4-吡啶基羰基；“C_4H_7CO”是指丁烯基羰基；“EtOCO”是指乙氧基羰基；“ibueCO”是指异丁烯基羰基；“iBuCO”是指异丁基羰基；“iBuOCO”是指异丁氧基羰基“iPrOCO”是指异丙氧基羰基；“nPrOCO”是指正丙氧基羰基“nPrCO”是指正丙基羰基；“ibue”是指异丁烯基；“THF”是指四氢呋喃；“DMAP”是指4-二甲基氨基吡啶；“LHMDS”是指六甲基二硅氮化锂。

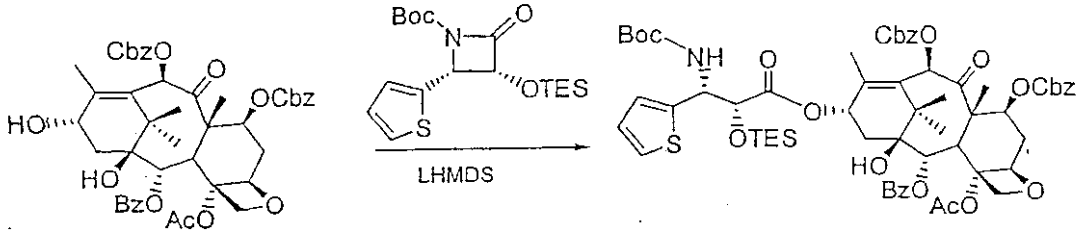
下列实施例用于说明本发明。

实施例1



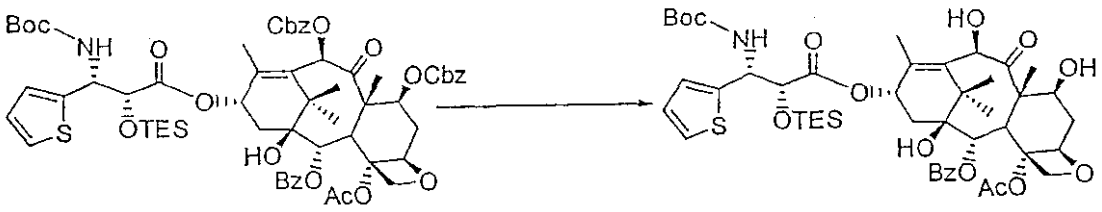
7,10-(二)-苄氧羰基-10-脱乙酰浆果赤霉素III

在氮环境下，向10-DAB(1.14g，2.11mmol)在20ml二氯甲烷的溶液中缓慢地加入DMAP(6.20g，50.6mmol)和氯甲酸苄酯(1.8ml，12.7mmol)。将该混合物加热至40-45℃，在该温度下保持2h，并再加入1.8ml(12.7mmol)氯甲酸苄酯。在40-45℃下继续再加热6h后，将该混合物用200mlCH_2Cl_2稀释并先用1N HCl洗涤，然后用饱和碳酸氢钠溶液洗涤。合并的洗涤液用30ml CH_2Cl_2提取3次，合并有机层，用盐水洗涤，用Na_2SO_4干燥，并减压浓缩。残渣在硅胶上色谱层析，用CH_2Cl_2/EtOAc洗脱，得到1.48g(86%)7,10-(二)-苄氧羰基(carbobenzyoxy)-10-脱乙酰浆果赤霉素III。



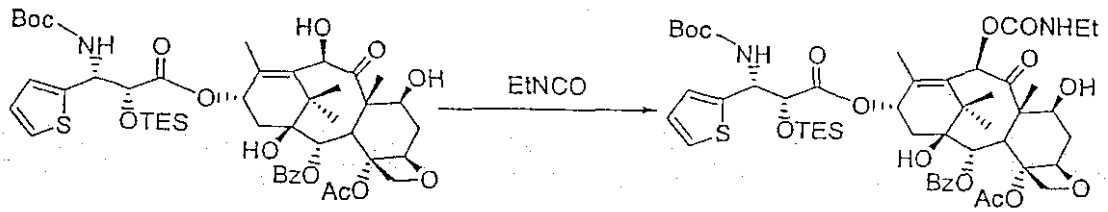
7,10-(二)-苄氧羰基-3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基 docetaxel

在-45℃氮环境下，向 425mg(0.523mmol)7,10-(二)-苄氧羰基-10-脱乙酰浆果赤霉素 III 的 THF(4.5ml)溶液中滴加 0.80ml LHMDS(0.98M)的 THF 溶液。在加入 341mg(0.889mmol)顺式-N-叔丁氧基羰基-3-三乙硅烷氧基-4-(2-噻吩基)氮杂环丁-酮的 THF(2ml)溶液之前，将该混合物在-45℃下保持 1h。容许该混合物温热至 0℃，并且在 2h 后，倾入 20ml 饱和氯化铵溶液中。水层用 50ml EtOAc/己烷(1:1)提取 3 次，合并有机层，用盐水洗涤，用 Na_2SO_4 干燥并减缩。残渣在硅胶上色谱层析，用 EtOAc/己烷洗脱，得到 576mg(92%)7,10-(二)-苄氧羰基-3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基（triethylsilyl）docetaxel。



3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基 docetaxel

在室温氢环境下，将 550mg7,10-(二)-苄氧羰基-3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基 docetaxel 和 50mg10%Pd/C 的 EtOH(30ml)和 EtOAc(10ml)悬浮液搅拌 2h。将该淤浆通过硅藻土 545 垫板过滤，然后用 EtOAc 洗涤。浓缩洗涤液，残渣通过在硅胶上色谱层析纯化，用 EtOAc/己烷作为洗脱剂，得到 405mg(95%)3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基 docetaxel。



3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基-10-N-乙基氨基甲酰基 docetaxel

在-15℃氮环境下，向 3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基 docetaxel(201mg, 0.217mmol)和CuCl(43.0mg, 0.434mmol)的 THF(3.5ml)淤浆中加入 51.5ml(0.651mmol)异氰酸乙酯的 THF(1.9ml)溶液。将该混合物温热至 0℃并在 1.4h 后加入 5ml 饱和碳酸氢钠溶液和 20ml 乙酸乙酯。水层用 50ml EtOAc/己烷(1:1)提取 3 次。合并有机层，用 Na_2SO_4 干燥并蒸发，得到 218mg 不必纯化即可直接使用的残渣。

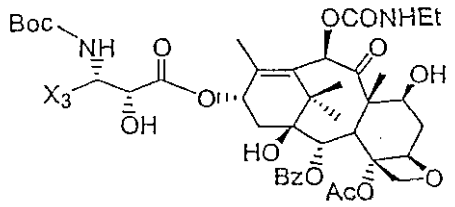
2722

3'-脱苯基-3'-(2-噻吩基)-10-N-乙基氨基甲酰基 docetaxel(2722)

在 0℃下，向 218mg 上述得到的 3'-脱苯基-3'-(2-噻吩基)-2'-O-三乙硅烷基-10-N-乙基氨基甲酰基 docetaxel 的吡啶(6ml)和 CH_3CN (12ml)溶液中加入 1.0ml 49%HF 水溶液。将该混合物温热至室温并在 2.5h 后加入 50ml EtOAc。该混合物用饱和碳酸氢钠水溶液和盐水洗涤，用硫酸钠干燥，并减压浓缩。残渣在硅胶上色谱层析，用 CH_2Cl_2/MeOH 作为洗脱剂，得到 169mg(两步共 88%)3'-脱苯基-3'-(2-噻吩基)-10-N-乙基氨基甲酰基 docetaxel(2722)。

实施例 2

重复实施例 1 所描述的方法，但用其他适宜保护的β-内酰胺和酰化剂代替实施例 1 的β-内酰胺和酰化剂，制备一系列具有下表所列出取代基组合的化合物。下表也包括这些化合物中某些化合物的特性数据与实施例 1 制备化合物 (2722) 化合物的特性数据。

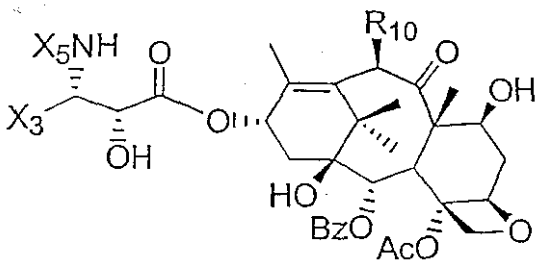


No.	X_3	m.p. (°C)	$[\alpha]_D(CHCl_3)$	元素分析
2600	2-吡啶基	173-175	-71.4 (c 0.22)	实测值: C, 60.70; H, 6.69 计算值 $C_{45}H_{57}N_3O_{15}.0.5H_2O$: C, 60.79; H, 6.58)
2616	3-吡啶基	183-185	-61.0 (c 0.20)	实测值: C, 58.96; H, 6.51 计算值 $C_{45}H_{57}N_3O_{15}.2H_2O$: C, 59.00; H, 6.69)
2622	3-噻吩基	173-175	-68.1 (c 0.19)	实测值: C, 58.40; H, 6.42 计算值 $C_{44}H_{56}N_2O_{15}S.H_2O$: C, 58.47; H, 6.47)
2633	i-丙基	170-172	-75.7 (c 0.22)	实测值: C, 60.10; H, 7.15 计算值 $C_{43}H_{60}N_2O_{15}.H_2O$: C, 59.84; H, 7.24)
2686	i-丁烯基	167-169	-106.7 (c 0.17)	实测值: C, 61.12; H, 7.10 计算值 $C_{44}H_{60}N_2O_{15}.0.5H_2O$: C, 61.02; H, 7.10)
2692	4-吡啶基	203-205	-69.7 (c 0.18)	实测值: C, 60.19; H, 6.61 计算值 $C_{45}H_{57}N_3O_{15}.H_2O$: C, 60.13; H, 6.62)
2700	2-呋喃基	169-171	-73.6 (c 0.22)	实测值: C, 60.59; H, 6.58 计算值 $C_{44}H_{56}N_2O_{16}$: C, 60.82; H, 6.50)
2717	3-呋喃基	165-167	-53.8 (c 0.23)	实测值: C, 60.07; H, 6.48 计算值 $C_{44}H_{56}N_2O_{16}.0.5H_2O$: C, 60.14; H, 6.54)

2722	2-噻吩基	166-168	-52.2 (c 0.25)	实测值：C, 58.28; H, 6.32 计算值 $C_{44}H_{56}N_2O_{15}S.H_2O$: C, 58.47; H, 6.47)
2733	环丁基	168-170	-73.9 (c 0.23)	实测值：C, 60.96; H, 7.02 计算值 $C_{44}H_{60}N_2O_{15}.0.5H_2O$: C, 61.02; H, 7.10)
2757	环丙基	168-170	-91.7 (c 0.23)	实测值：C, 60.07; H, 6.86 计算值 $C_{43}H_{58}N_2O_{15}.H_2O$: C, 59.98; H, 7.02)

实施例 3

重复实施例 1 所描述的方法，但用其他适宜保护的β-内酰胺代替实施例 1 的顺式-N-叔丁氧基羰基-3-三乙硅烷氧基-4-(2-噻吩基)氮杂环丁-2-酮，制备一系列与结构 14 一致并且具有下表所列出取代基组合的化合物。

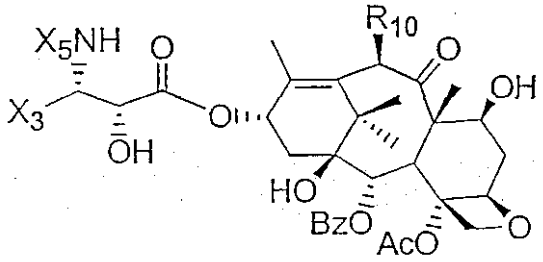


(14)

化合物	X_5	X_3	R_{10}
2640	tBuOCO-	苯基	EtNHCOO-
2743	tBuOCO-	对硝基苯基	EtNHCOO-
6015	tC_3H_5CO-	2-呋喃基	3,4diFPhNHCOO-
6024	tC_3H_5CO-	2-呋喃基	PhNHCOO-
6072	tC_3H_5CO-	2-呋喃基	EtNHCOO-

实施例 4

可按照实施例 1 和本文别处所描述的方法制备下列具有结构式 14 和下表所列出取代基组合的特定紫衫烷，其中 R_{10} 如前面的定义，包括其中 R_{10} 为 $R_{10a}R_{10b}NCOO$-和(a)、R_{10a} 和 R_{10b} 各独立地为氢，(b)、R_{10a} 和 R_{10b} 中的一个为氢，另一个为(i)、取代的或未取代 C_1-C_8 烷基如甲基，乙基，或者直链、支链或环状丙基，丁基，戊基或己基；(ii)、取代的或未取代 C_2-C_8 链烯基如乙烯基，或者直链、支链或环状丙烯基，丁烯基，戊烯基或己烯基；(iii)、取代的或未取代 C_3-C_8 炔基如乙炔基，或者直链或支链丙炔基，丁炔基，戊炔基或己炔基；(iv)、取代的或未取代的苯基，或(V)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基，或者(c)、R_{10a} 和 R_{10b} 独立地为(i)、取代的或未取代 C_1-C_8 烷基如甲基，乙基，或者直链、支链或环状丙基，丁基，戊基或己基；(ii)、取代的或未取代 C_2-C_8 链烯基如乙烯基，或者直链、支链或环状丙烯基，丁烯基，戊烯基或己烯基；(iii)、取代的或未取代 C_2-C_8 炔基如乙炔基，或者直链或支链丙炔基，丁炔基，戊炔基或己炔基；(iv)、取代的或未取代的苯基，或(V)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基。例如，R_{10} 可以是 $R_{10a}R_{10b}NCOO$-，其中 R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基，或者直链、支链或环状的丙基。所述取代基可以是本文在关于取代的烃基中所确定的那些基团。



(14)

X_5	X_3	R_{10}
tBuOCO	2-呋喃基	$R_{10a}R_{10b}NCOO-$
tBuOCO	3-呋喃基	$R_{10a}R_{10b}NCOO-$
tBuOCO	2-噻吩基	$R_{10a}R_{10b}NCOO-$
tBuOCO	3-噻吩基	$R_{10a}R_{10b}NCOO-$
tBuOCO	2-吡啶基	$R_{10a}R_{10b}NCOO-$
tBuOCO	3-吡啶基	$R_{10a}R_{10b}NCOO-$
tBuOCO	4-吡啶基	$R_{10a}R_{10b}NCOO-$
tBuOCO	异丁烯基	$R_{10a}R_{10b}NCOO-$
tBuOCO	异丙基	$R_{10a}R_{10b}NCOO-$
tBuOCO	环丙基	$R_{10a}R_{10b}NCOO-$
tBuOCO	环丁基	$R_{10a}R_{10b}NCOO-$
tBuOCO	环戊基	$R_{10a}R_{10b}NCOO-$
tBuOCO	苯基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	2-呋喃基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	3-呋喃基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	2-噻吩基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	3-噻吩基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	2-吡啶基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	3-吡啶基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	4-吡啶基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	异丁烯基	$R_{10a}R_{10b}NCOO-$
苯甲酰基	异丙基	$R_{10a}R_{10b}NCOO-$

苯甲酰基	环丙基	$R_{10a}R_{10b}NCOO$–
苯甲酰基	环丁基	$R_{10a}R_{10b}NCOO$-
苯甲酰基	环戊基	$R_{10a}R_{10b}NCOO$-
苯甲酰基	苯基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	异丙基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	环丙基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	环丁基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	环戊基	$R_{10a}R_{10b}NCOO$-
2-FuCO-	苯基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	异丙基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	环丙基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	环丁基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	环戊基	$R_{10a}R_{10b}NCOO$-
2-ThCO-	苯基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-

2-PyCO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	异丙基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	环丙基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	环丁基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	环戊基	$R_{10a}R_{10b}NCOO$-
2-PyCO-	苯基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	异丙基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	环丙基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	环丁基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	环戊基	$R_{10a}R_{10b}NCOO$-
3-PyCO-	苯基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-

4-PyCO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	异丙基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	环丙基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	环丁基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	环戊基	$R_{10a}R_{10b}NCOO$-
4-PyCO-	苯基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	异丙基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	环丙基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	环丁基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	环戊基	$R_{10a}R_{10b}NCOO$-
C_4H_7CO-	苯基	$R_{10a}R_{10b}NCOO$-
EtOCO-	2-呋喃基	$R_{10a}R_{10b}NCOO$-
EtOCO-	3-呋喃基	$R_{10a}R_{10b}NCOO$-
EtOCO-	2-噻吩基	$R_{10a}R_{10b}NCOO$-
EtOCO-	3-噻吩基	$R_{10a}R_{10b}NCOO$-
EtOCO-	2-吡啶基	$R_{10a}R_{10b}NCOO$-
EtOCO-	3-吡啶基	$R_{10a}R_{10b}NCOO$-
EtOCO-	4-吡啶基	$R_{10a}R_{10b}NCOO$-
EtOCO-	异丁烯基	$R_{10a}R_{10b}NCOO$-
EtOCO-	异丙基	$R_{10a}R_{10b}NCOO$-
EtOCO-	环丙基	$R_{10a}R_{10b}NCOO$-
EtOCO-	环丁基	$R_{10a}R_{10b}NCOO$-

EtOCO-	环戊基	$R_{10a}R_{10b}NCOO-$
EtOCO-	苯基	$R_{10a}R_{10b}NCOO-$
ibueCO-	2-呋喃基	$R_{10a}R_{10b}NCOO-$
ibueCO-	3-呋喃基	$R_{10a}R_{10b}NCOO-$
ibueCO-	2-噻吩基	$R_{10a}R_{10b}NCOO-$
ibueCO-	3-噻吩基	$R_{10a}R_{10b}NCOO-$
ibueCO-	2-吡啶基	$R_{10a}R_{10b}NCOO-$
ibueCO-	3-吡啶基	$R_{10a}R_{10b}NCOO-$
ibueCO-	4-吡啶基	$R_{10a}R_{10b}NCOO-$
ibueCO-	异丁烯基	$R_{10a}R_{10b}NCOO-$
ibueCO-	异丙基	$R_{10a}R_{10b}NCOO-$
ibueCO-	环丙基	$R_{10a}R_{10b}NCOO-$
ibueCO-	环丁基	$R_{10a}R_{10b}NCOO-$
ibueCO-	环戊基	$R_{10a}R_{10b}NCOO-$
ibueCO-	苯基	$R_{10a}R_{10b}NCOO-$
iBuCO-	2-呋喃基	$R_{10a}R_{10b}NCOO-$
iBuCO-	3-呋喃基	$R_{10a}R_{10b}NCOO-$
iBuCO-	2-噻吩基	$R_{10a}R_{10b}NCOO-$
iBuCO-	3-噻吩基	$R_{10a}R_{10b}NCOO-$
iBuCO-	2-吡啶基	$R_{10a}R_{10b}NCOO-$
iBuCO-	3-吡啶基	$R_{10a}R_{10b}NCOO-$
iBuCO-	4-吡啶基	$R_{10a}R_{10b}NCOO-$
iBuCO-	异丁烯基	$R_{10a}R_{10b}NCOO-$
iBuCO-	异丙基	$R_{10a}R_{10b}NCOO-$
iBuCO-	环丙基	$R_{10a}R_{10b}NCOO-$
iBuCO-	环丁基	$R_{10a}R_{10b}NCOO-$
iBuCO-	环戊基	$R_{10a}R_{10b}NCOO-$
iBuCO-	苯基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	2-呋喃基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	3-呋喃基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	2-噻吩基	$R_{10a}R_{10b}NCOO-$

iBuOCO-	3-噻吩基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	2-吡啶基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	3-吡啶基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	4-吡啶基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	异丁烯基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	异丙基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	环丙基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	环丁基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	环戊基	$R_{10a}R_{10b}NCOO-$
iBuOCO-	苯基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	2-呋喃基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	3-呋喃基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	2-噻吩基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	3-噻吩基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	2-吡啶基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	3-吡啶基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	4-吡啶基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	异丁烯基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	异丙基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	环丙基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	环丁基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	环戊基	$R_{10a}R_{10b}NCOO-$
iPrOCO-	苯基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	2-呋喃基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	3-呋喃基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	2-噻吩基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	3-噻吩基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	2-吡啶基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	3-吡啶基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	4-吡啶基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	异丁烯基	$R_{10a}R_{10b}NCOO-$

nPrOCO-	异丙基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	环丙基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	环丁基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	环戊基	$R_{10a}R_{10b}NCOO-$
nPrOCO-	苯基	$R_{10a}R_{10b}NCOO-$
nPrCO-	2-呋喃基	$R_{10a}R_{10b}NCOO-$
nPrCO-	3-呋喃基	$R_{10a}R_{10b}NCOO-$
nPrCO-	2-噻吩基	$R_{10a}R_{10b}NCOO-$
nPrCO-	3-噻吩基	$R_{10a}R_{10b}NCOO-$
nPrCO-	2-吡啶基	$R_{10a}R_{10b}NCOO-$
nPrCO-	3-吡啶基	$R_{10a}R_{10b}NCOO-$
nPrCO-	4-吡啶基	$R_{10a}R_{10b}NCOO-$
nPrCO-	异丁烯基	$R_{10a}R_{10b}NCOO-$
nPrCO-	异丙基	$R_{10a}R_{10b}NCOO-$
nPrCO-	环丙基	$R_{10a}R_{10b}NCOO-$
nPrCO-	环丁基	$R_{10a}R_{10b}NCOO-$
nPrCO-	环戊基	$R_{10a}R_{10b}NCOO-$
nPrCO-	苯基	$R_{10a}R_{10b}NCOO-$

实施例 5

可按照实施例 1 和本文别处所描述的方法制备下列具有结构式 15 的特定紫杉烷，其中 R_7 为羟基并且在各组(即“A” - “K”的各组)中的 R_{10} 如前面的定义，包括其中 R_{10} 为 $R_{10a}R_{10b}NCOO-$ 并且 R_{10a} 和 R_{10b} 中的一个为氢，另一个为(i)、取代的或未取代 C_1-C_8 烷基如甲基，乙基，或者直链、支链或环状丙基，丁基，戊基或己基；(ii)、取代的或未取代 C_2-C_8 链烯基如乙烯基，或者直链、支链或环状丙烯基，丁烯基，戊烯基或己烯基；(iii)、取代的或未取代 C_2-C_8 炔基如乙炔基，或者直链或支链丙炔基，丁炔基，戊炔基或己炔基；(iv)、苯基或取代的苯基如硝基，烷氧基或卤代苯基，或(V)、取代的或未取代的杂芳香基如呋喃基，噻吩基，或吡啶基。所述取代基可以是本文在关于取代的烃基中所确定的那些基团。在一个实施方案中，优选的 R_{10} 取代基包括 $R_{10a}R_{10b}NCOO-$，其中 R_{10a} 和 R_{10b} 中的一个为氢，另一个为甲基，乙基，或者直链、支链或环状的丙基。在另一实施方案中，优选的 R_{10} 取代基包括 $R_{10a}R_{10b}NCOO-$，其中 R_{10a} 和 R_{10b} 中的一个为氢，另一个为取代的甲基，乙基，或者直链、支链或环状的丙基。

在“A”组化合物中，X_{10} 如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，X_{10} 是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)并且 R_7 和 R_{10} 各具有β立体化学构型。

在“B”组化合物中，X_{10} 和 R_{2a} 如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10} 是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选地，R_{2a} 是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基，或低级烷基，并且 R_7 和 R_{10} 各具有β立体化学构型。

在“C”组化合物中，X_{10} 和 R_{9a} 如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10} 是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选

地，R_{9a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基并且R_7，R_9和R_{10}各具有β立体化学构型。

在“D”和“E”组化合物中，X_{10}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，并且R_7，R_9(只有D组)和R_{10}各具有β立体化学构型。

在“F”组化合物中，X_{10}，R_{2a}和R_{9a}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选地，R_{2a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基，并且R_7，R_9和R_{10}各具有β立体化学构型。

在“G”组化合物中，X_{10}和R_{2a}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选地，R_{2a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基并且R_7，R_9和R_{10}各具有β立体化学构型。

在“H”组化合物中，X_{10}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选地，R_{2a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基并且R_7和R_{10}各具有β立体化学构型。

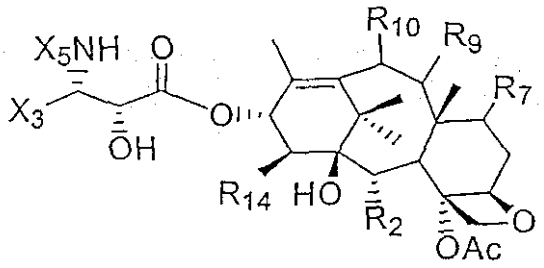
在“I”组化合物中，X_{10}和R_{2a}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选地，R_{2a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基并且R_7和R_{10}各具有β立体化学构型。

在“J”组化合物中，X_{10}和R_{2a}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选

地，R_{2a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基并且R_7，R_9和R_{10}各具有β立体化学构型。

在“K”组化合物中，X_{10}，R_{2a}和R_{9a}如本文在别处的定义。优选地，杂环是取代的或未取代的呋喃基，噻吩基或吡啶基，优选地，X_{10}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基(例如叔丁基)，优选地，R_{2a}是取代的或未取代的呋喃基，噻吩基，吡啶基，苯基或低级烷基并且R_7，R_9和R_{10}各具有β立体化学构型。

X_3，X_5，R_2，R_7和R_9中每一个的任何取代基都可以是烃基或任何包含杂原子的取代基的，选自杂环，烷氧基，链烯氧基，炔氧基，芳氧基，羟基，保护的羟基，酮基，酰氧基，硝基，氨基，酰氨基，巯基，缩酮，缩醛，酯和醚部分，不是含磷部分。



(15)

组	X_5	X_3	R_{10}	R_2	R_9	R_{14}
A1	-$COOX_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A2	-COX_{10}	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A3	-$CONHX_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A4	-$COOX_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A5	-COX_{10}	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A6	-$CONHX_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A7	-$COOX_{10}$	任选地取代的 C_2-C_8 链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A8	-COX_{10}	任选地取代的 C_2-C_8 链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A9	-$CONHX_{10}$	任选地取代的 C_2-C_8 链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H
A10	-$COOX_{10}$	任选地取代的 C_2-C_8 炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	H

A11	$-COX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	O	H
A12	$-CONHX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	O	H
B1	$-COOX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B2	$-COX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B3	$-CONHX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B4	$-COOX_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B5	$-COX_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B6	$-CONHX_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B7	$-COOX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B8	$-COX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B9	$-CONHX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B10	$-COOX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H
B11	$-COX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	H

B12	-CONHX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	O	H
C1	-COOX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C2	-COX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C3	-CONHX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C4	-COOX$_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C5	-COX$_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C6	-CONHX$_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C7	-COOX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C8	-COX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C9	-CONHX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C10	-COOX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C11	-COX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
C12	-CONHX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	$R_{9a}COO$-	H
D1	-COOX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D2	-COX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H

D3	-CONHX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D4	-COOX$_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D5	-COX$_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D6	-CONHX$_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D7	-COOX$_{10}$	任选地取代的 C_2-C_8 链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D8	-COX$_{10}$	任选地取代的 C_2-C_8 链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D9	-CONHX$_{10}$	任选地取代的 C_2-C_8 链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D10	-COOX$_{10}$	任选地取代的 C_2-C_8 炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D11	-COX$_{10}$	任选地取代的 C_2-C_8 炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
D12	-CONHX$_{10}$	任选地取代的 C_2-C_8 炔基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	H
E1	-COOX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E2	-COX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E3	-CONHX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E4	-COOX$_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH
E5	-COX$_{10}$	任选地取代的 C_2-C_8 烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	O	OH

E6	-CONHX$_{10}$	任选地取代的C$_2$-C$_8$烷基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
E7	-COOX$_{10}$	任选地取代的C$_2$-C$_8$链烯基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
E8	-COX$_{10}$	任选地取代的C$_2$-C$_8$链烯基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
E9	-CONHX$_{10}$	任选地取代的C$_2$-C$_8$链烯基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
E10	-COOX$_{10}$	任选地取代的C$_2$-C$_8$炔基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
E11	-COX$_{10}$	任选地取代的C$_2$-C$_8$炔基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
E12	-CONHX$_{10}$	任选地取代的C$_2$-C$_8$炔基	R$_{10a}$R$_{10b}$NCOO-	C$_6$H$_5$COO-	O	OH
F1	-COOX$_{10}$	杂环	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H
F2	-COX$_{10}$	杂环	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H
F3	-CONHX$_{10}$	杂环	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H
F4	-COOX$_{10}$	任选地取代的C$_2$-C$_8$烷基	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H
F5	-COX$_{10}$	任选地取代的C$_2$-C$_8$烷基	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H
F6	-CONHX$_{10}$	任选地取代的C$_2$-C$_8$烷基	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H
F7	-COOX$_{10}$	任选地取代的C$_2$-C$_8$链烯基	R$_{10a}$R$_{10b}$NCOO-	R$_{2a}$COO-	R$_{9a}$COO-	H

F8	$-COX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F9	$-CONHX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F10	$-COOX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F11	$-COX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
F12	$-CONHX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	$R_{9a}COO-$	H
G1	$-COOX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G2	$-COX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G3	$-CONHX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G4	$-COOX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G5	$-COX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G6	$-CONHX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G7	$-COOX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H
G8	$-COX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	H

G9	-CONHX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
G10	-COOX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
G11	-COX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
G12	-CONHX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	H
H1	-COOX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H2	-COX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H3	-CONHX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H4	-COOX$_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H5	-COX$_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H6	-CONHX$_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H7	-COOX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H8	-COX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH
H9	-CONHX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	C_6H_5COO-	OH	OH

H10	$-COOX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	OH	OH
H11	$-COX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	OH	OH
H12	$-CONHX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	C_6H_5COO-	OH	OH
I1	$-COOX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I2	$-COX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I3	$-CONHX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I4	$-COOX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I5	$-COX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I6	$-CONHX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I7	$-COOX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I8	$-COX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I9	$-CONHX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I10	$-COOX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH

I11	$-COX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
I12	$-CONHX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	O	OH
J1	$-COOX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J2	$-COX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J3	$-CONHX_{10}$	杂环	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J4	$-COOX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J5	$-COX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J6	$-CONHX_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J7	$-COOX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J8	$-COX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J9	$-CONHX_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J10	$-COOX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH
J11	$-COX_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO-$	$R_{2a}COO-$	OH	OH

J12	-CONHX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	OH	OH
K1	-COOX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K2	-COX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K3	-CONHX$_{10}$	杂环	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K4	-COOX$_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K5	-COX$_{10}$	任选地取代的 C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K6	-CONHX$_{10}$	任选地取代的C_2-C_8烷基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K7	-COOX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K8	-COX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K9	-CONHX$_{10}$	任选地取代的C_2-C_8链烯基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K10	-COOX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K11	-COX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH
K12	-CONHX$_{10}$	任选地取代的C_2-C_8炔基	$R_{10a}R_{10b}NCOO$-	$R_{2a}COO$-	$R_{9a}COO$-	OH

实施例 6

通过细胞集落形成分析测定的体外细胞毒性

将 400 个细胞(HCT116)放在含 2.7ml 培养基(包含 10%胎牛血清和 100 单位/ml 青霉素和 100g/ml 链霉素的改进的 McCoy's 5a 培养基)的 60mm 陪替氏培养皿中。将细胞在 37℃下的 CO_2 细菌培养器培养 5h，使之附着在陪替氏培养皿底部。将实施例 2 确定的化合物用培养基新配制成最终使用浓度 10 倍的储备溶液，然后，将 0.3ml 该储备溶液加到培养皿中的 2.7ml 培养基中。然后，将细胞与药物一起在 37℃下培养 72h。培养结束后，轻轻倒出含药物的培养基，培养皿用 4ml 汉氏平衡盐溶液(HBSS)轻洗，加入 5ml 新鲜培养基，并将培养皿放回细菌培养器中以便集落形成。培养 7 天后，用集落计数器计数细胞集落。计算细胞存活率并测定各试验化合物的 ID50(产生 50%抑制集落形成作用时的药物浓度)。

化合物	体外 ID 50 (nm) HCT116
紫衫酚	2.1
docetaxel	0.6
2600	<1
2616	27
2622	<1
2633	<10
2686	<1
2692	<1
2700	<1
2717	<1
2722	<1
2733	<10
2757	<1
2640	<1
2743	<1
6015	<10
6024	<1
6072	<1