

9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES

This application claims priority from U.S. Application No.60/713,112 filed August 31, 2005 the entire disclosure of which is incorporated herein by reference.

5 FIELD OF THE INVENTION

The present invention relates to 9-aminocarbonylsubstituted derivatives of glycylicyclines which are useful as antibiotic agents and exhibit antibacterial activity against a wide spectrum of organisms including organisms which are resistant to
10 tetracyclines and other antibiotics.

BACKGROUND OF THE INVENTION

Since 1947 a variety of tetracycline antibiotics have been synthesized and
15 described for the treatment of infectious diseases in man and animals. Tetracyclines inhibit protein synthesis by binding to the 30S subunit of the bacterial ribosome preventing binding of aminoacyl RNA (Chopra, Handbook of Experimental Pharmacology, Vol. 78, 317-392, Springer-Verlag, 1985). Resistance to tetracyclines has emerged among many clinically important microorganisms which limit the utility
20 of these antibiotics. There are two major mechanisms of bacterial resistance to tetracyclines: a) energy-dependent efflux of the antibiotic mediated by proteins located in the cytoplasmic membrane which prevents intracellular accumulation of tetracycline (S. B. Levy, et al., Antimicrob. Agents Chemotherapy 33, 1373-1374 (1989); and b) ribosomal protection mediated by a cytoplasmic protein which
25 interacts with the ribosome such that tetracycline no longer binds or inhibits protein synthesis (A. A. Salyers, B. S. Speers and N. B. Shoemaker, Mol. Microbiol, 4:151-156, 1990). The efflux mechanism of resistance is encoded by resistance determinants designated tetA-tetL. They are common in many Gram-negative bacteria (resistance genes Class A-E), such as Enterobacteriaceae, Pseudomonas,
30 Haemophilus and Aeromonas, and in Gram- positive bacteria (resistance genes Class K and L), such as Staphylococcus, Bacillus and Streptococcus. The ribosomal protection mechanism of resistance is encoded by resistance determinants designated TetM, N and O, and is common in Staphylococcus, Streptococcus,

Campylobacter, Gardnerella, Haemophilus and Mycoplasma (A. A. Salyers, B. S. Speers and N. B. Shoemaker, Mol. Microbiol, 4:151-156 1990).

A particularly useful tetracycline compound is 7-(dimethylamino)- 6-demethyl-6-deoxytetracycline, known as minocycline (see U.S. Pat. No. 3,148,212, U.S. Pat. No. RE 26,253 and U.S. Pat. No. 3,226,436 discussed below). However, strains
5 harboring the tetB (efflux in gram-negative bacteria) mechanism, but not tetK (efflux in Staphylococcus) are resistant to minocycline. Also, strains carrying tetM (ribosomal protection) are resistant to minocycline.

Duggar, U.S. Pat. No. 2,482,055, discloses the preparation of
10 Aureomycin.RTM. by fermentation which have antibacterial activity. Growich et al., U.S. Pat. No. 3,007,965, disclose improvements to the fermentation preparation. Beereboom et al., U.S. Pat. No. 3,043,875 discloses tetracycline derivatives Boothe et al., U.S. Pat. No. 3,148,212, reissued as U.S. Pat. No. RE 26,253, and Petisi et al., U.S. Pat. No. 3,226,436, discloses tetracycline derivatives which are useful for
15 treating bacterial infections. Blackwood et al., U.S. Pat. No. 3,200,149 discloses tetracycline derivatives which possess microbiological activity. Petisi et al., U.S. Pat. No. 3,338,963 discloses tetracycline compounds which have broad-spectrum antibacterial activity. Bitha et al., U.S. Pat. No. 3,341,585 discloses tetracycline compounds which have broad-spectrum antibacterial activity. Shu, U.S. Pat. No.
20 3,360,557 discloses 9- hydroxytetracyclines which have been found to possess antibacterial activity. Zambrano, U.S. Pat. No. 3,360,561 discloses a process for preparing 9-nitrotetracyclines. Martell et al., U.S. Pat. No. 3,518,306 discloses tetracyclines which possess in vivo antibacterial activity.

In U.S. Pat. No. 5,021,407 a method of overcoming the resistance of
25 tetracycline resistant bacteria is disclosed. The method involves utilizing a blocking agent compound in conjunction with a tetracycline type antibiotic. This patent does not disclose novel tetracycline compounds which themselves have activity against resistant organisms. Described in U.S. Pat. No. 5,494,903 are 7-substituted-9-substitutedamino-6-demethyl-6-deoxytetracyclines which have broad spectrum
30 antibacterial activity.

Despite the advances being made to overcome the resistance of tetracycline resistant bacteria, there remains a need for newer and better antibiotics to overcome

the increasing incidence of resistance. The present invention provides such antibiotics.

In summary, none of the above patents teach or suggest the novel derivatives of glycylicyclines of this application.

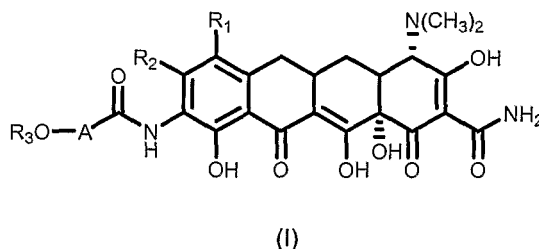
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SUMMARY OF THE INVENTION

This invention is concerned with 9-aminocarbonylsubstituted derivatives of glycylicyclines represented by Formula I which have antibacterial activity; with methods of treating infectious diseases in humans and other animals when administering these new compounds; with pharmaceutical preparations containing these compounds; and with novel processes for the production of compounds of Formula I.

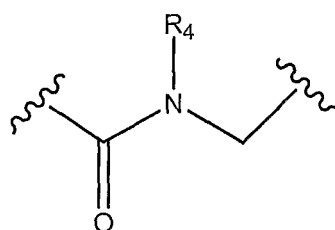
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In accordance with the present invention, there is provided compounds represented by Formula (I);



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wherein:



A is a moiety

or is absent;

25 R_1 is selected from hydrogen, -OH, amino, -NR₇R₈, halogen,

alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group phenyl, heteroaryl, halogen, amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, alkyl, hydroxyl, and alkoxy;

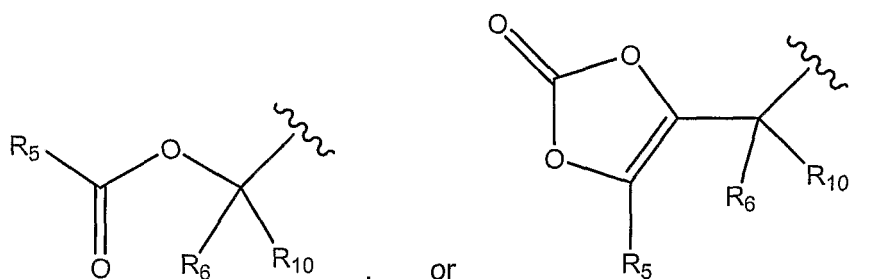
R₂ is selected from hydrogen, halogen, alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group phenyl, heteroaryl, halogen, amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl and aryl of N-(alkyl of 1 to 12

carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and

- 5 alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, alkyl, hydroxyl, and alkoxy;

R₃ is the moiety R₉,

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- R₄ is selected from hydrogen, alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group phenyl, heteroaryl, halogen, amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro,

cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, alkyl, hydroxyl, and alkoxy, aryl of 6, 10 or 14 carbon atoms said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, N-(alkyl of 1 to 12 carbon atoms)-aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl of 7 to 13 carbon atoms optionally substituted, SR³, heteroaryl optionally substituted and heteroaryl carbonyl optionally substituted;

R₅ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl of 6, 10 or 14 carbon atoms, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl, may be optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH₂(CO)OCH₂aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryloxy and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted, heteroaryl optionally substituted, aryl of 6, 10 or 14 carbon atoms

optionally substituted, alkynyl of 2 to 12 carbon atoms optionally substituted, cycloalkyl 3 to 6 ring atoms, aryl-CH=CH-, cycloalkyl-alkyl; and adamantyl;

5 R_6 is selected from hydrogen, alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl
10 of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and cycloalkyl of 3 to 6 carbon atoms;

15 R_7 and R_8 are each independently H or alkyl of 1 to 12 carbon atoms or R_7 and R_8 when optionally taken together with the nitrogen atom to which each is attached form a 3 to 8 membered heterocyclyl ring;

20 R_9 is aralkyl of 7 to 16 carbon atoms optionally substituted or alkyl of 1 to 12 carbon atoms;

R_{10} is H or alkyl of 1 to 12 carbon atoms;

or a pharmaceutically acceptable salt thereof.

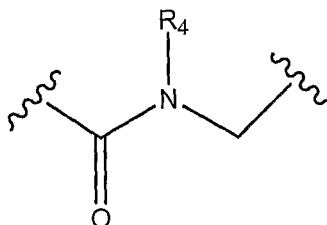
25 An embodiment of this invention provides compounds of Formula I wherein R_1 is -NR₇R₈, R_7 is hydrogen, R_8 is methyl, ethyl, n-propyl, n-butyl, 1-methylethyl, 1-methylpropyl, 2-methylpropyl or 1,1-dimethylethyl or a pharmaceutically acceptable salt thereof.

30 Another embodiment of this invention provides compounds of Formula I wherein R_1 is -NR₇R₈, R_7 is methyl or ethyl, R_8 is methyl, ethyl, n-propyl, 1-methylethyl, n-propyl, 1-methylpropyl, or 2-methylpropyl or a pharmaceutically acceptable salt thereof.

- A further embodiment of this invention provides compounds of Formula I wherein R_1 is $-NR_7R_8$, R_7 and R_8 are taken together with the nitrogen atom to which each is attached form a 3 to 8 membered heterocyclyl ring or a pharmaceutically acceptable salt thereof.

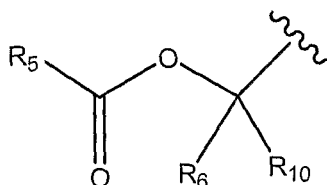
Another embodiment of this invention provides compounds of Formula I wherein R_2 is H or a pharmaceutically acceptable salt thereof.

- 10 Another embodiment of this invention provides compounds of Formula I wherein A is a moiety



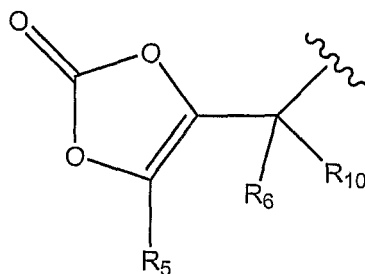
- or a pharmaceutically acceptable salt thereof.
- 15 A further embodiment of this invention provides compounds of Formula I wherein A is absent or a pharmaceutically acceptable salt thereof.

- A further embodiment of this invention provides compounds of Formula I wherein R_3 is a moiety
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- 25 or a pharmaceutically acceptable salt thereof.

A further additional embodiment of this invention provides compounds of Formula I wherein R_3 is a moiety

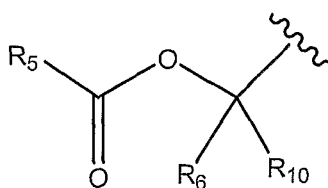


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or a pharmaceutically acceptable salt thereof.

An embodiment of this invention provides compounds of Formula I wherein R_3 is a moiety

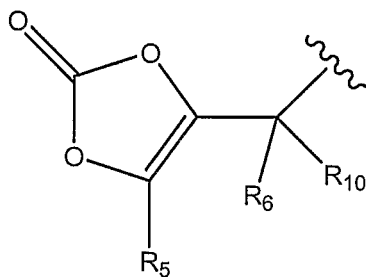
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15 and R_6 and R_{10} are H or a pharmaceutically acceptable salt thereof.

An additional embodiment of this invention provides compounds of Formula I wherein R_3 is a moiety

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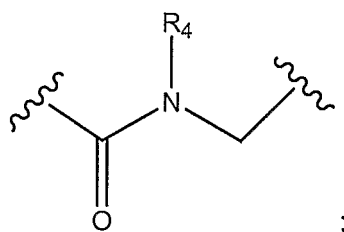


and R_6 and R_{10} are H or a pharmaceutically acceptable salt thereof.

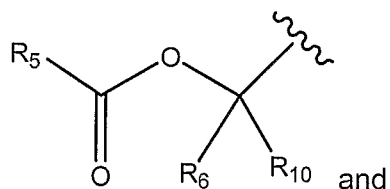
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A further embodiment of this invention provides compounds of Formula I wherein R_3 is R_9 or a pharmaceutically acceptable salt thereof.

- 10 An additional embodiment of this invention provides compounds of Formula I wherein A is the moiety,



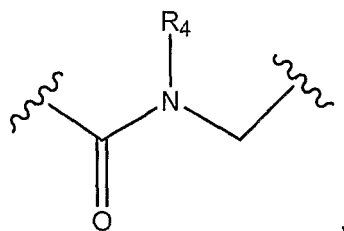
- 15 R_3 is the moiety



R_5 is aryl of 6 carbon atoms or a pharmaceutically acceptable salt thereof.

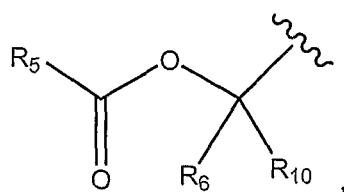
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A further embodiment of this invention provides compounds of Formula I wherein A is the moiety



R₃ is the moiety ,

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10 R₄ is 1,1-dimethylethyl and

R₅ is aryl of 6 carbon atoms or a pharmaceutically acceptable salt thereof.

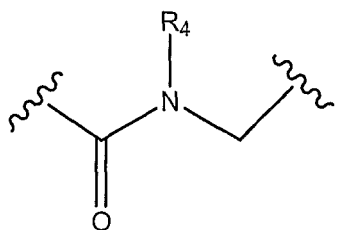
An additional embodiment of this invention provides compounds of Formula I

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wherein:

A is a moiety

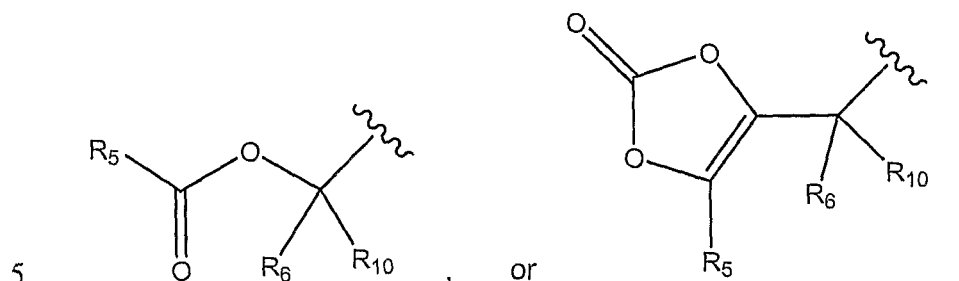
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R₁ is -NR₇R₈;

R₂ is hydrogen;

R₃ is the moiety



R₄ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, and aryloxy wherein said aryl and aryloxy is optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryloxy and phenyl;

15

R₅ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl of 6, 10 or 14 carbon atoms, and aryloxy wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl, may be optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH₂(CO)OCH₂aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryloxy and

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phenyl, heteroaryl optionally substituted, aryl of 6, 10 or 14 carbon atoms optionally substituted, cycloalkyl 3 to 6 ring atoms, aryl-CH=CH-, cycloalkyl-alkyl; and adamantyl;

5 R₆ is hydrogen;

R₇ and R₈ are each independently H or alkyl of 1 to 12 carbon atoms;

10 R₉ is aralkyl of 7 to 16 carbon atoms optionally substituted or alkyl of 1 to 12 carbon atoms;

R₁₀ is H;

or a pharmaceutically acceptable salt thereof.

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Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

20 {{{(2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 2-methylpropanoate,

25 {{{(2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate,

30 {{{(2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate,

- {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate,
- 5 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 4-methylbenzoate,
- 10 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate,
- 15 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl cyclobutanecarboxylate,
- 20 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate,
- 25 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl pivalate,
- 30 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 2-methylpropanoate,
- 30 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl phenylacetate,

- (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl phenylacetate,
- 5 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl pivalate,
- 10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl heptanoate,
- 15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl cyclobutanecarboxylate,
- 20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl heptanoate,
- 25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate,
- 30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,
- (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate,

($\{([2-((5R,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino]-2-oxoethyl)(propyl)amino]carbonyl\}oxy)methyl\ 1,1'-biphenyl-4-carboxylate,$

5

{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate.

10 ({[(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(propyl)amino]carbonyl]oxy)methyl 4-tert-butylbenzoate,

15 1-({[(2-{{(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino)-2-oxoethyl)(butyl)amino]carbonyloxy}ethyl acetate,

20 ({{(2-((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(propyl)amino}carbonyloxy)methyl cyclohexanecarboxylate,

(2-((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(butyl)amino]carbonyl]oxymethyl cyclohexanecarboxylate,

25

{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate,

30 {{{2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate,

- (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate,
- 5 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl cyclopentylacetate,
- 10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate,
- 15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl cyclopentylacetate,
- 20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate,
- 25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate,
- 30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate,
- 30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 2-methylpropanoate,

5 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl cyclopentanecarboxylate,

10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-methylbenzoate,

15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl heptanoate, and

20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-methoxybenzoate.

Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

25 benzyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(propyl)carbamate,

30 ethyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(propyl)carbamate, and

isobutyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate.

- 5 Additional further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

10 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl thiophene-2-carboxylate,

15 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl thiophene-2-carboxylate,

20 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl thiophene-3-carboxylate,

25 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl thiophene-3-carboxylate,

30 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 2-furoate, and

35 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 2-furoate.

Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

- 5
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl propionate,
- 10
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate,
- 15
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate,
- 20
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate,
- 25
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3-methylbutanoate,
- 30
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl cyclopentylacetate,
- 35
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-(trifluoromethyl)benzoate,
- 40
 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl cyclopropanecarboxylate,

- ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate,
- 5 butyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(tert-butyl)carbamate,
- isobutyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-
- 10 1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(tert-butyl)carbamate,
- methyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-
- 15 oxoethyl(tert-butyl)carbamate,
- ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl pentanoate,
- 20 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclobutanecarboxylate,
- 25 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-cyclohexylpropanoate,
- 30 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl (4-fluorophenoxy)acetate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclohexylacetate,

5 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,6-dimethylbenzoate,

10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl phenylacetate,

15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl pivalate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,

20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-naphthoate,

25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-naphthoate,

30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,6-difluorobenzoate,

- {{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2-fluorobenzoate,
- 5 {{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2-(trifluoromethyl)benzoate,
- 10 {{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-2-carboxylate,
- 15 {{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2,4,6-trimethylbenzoate,
- 20 {{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-isopropoxybenzoate,
- 25 {{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3,4,5-trimethoxybenzoate,
- 30 {{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl (2E)-3-phenylprop-2-enoate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl [3,5-bis(trifluoromethyl)phenyl]acetate,

5

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-(heptyloxy)benzoate,

10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 2-(2-phenylethyl)benzoate,

15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-(dodecyloxy)benzoate,

20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-(acetylamino)benzoate,

25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl anthracene-9-carboxylate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-benzoylbenzoate, and

30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl diphenylacetate.

Additional further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

5 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 4-fluorobenzoate,

10 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 3,5-dimethylbenzoate,

15 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl pivalate,

20 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 3,3-dimethylbutanoate,

25 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 2,2-dimethylbutanoate,

30 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 2-ethylbutanoate,

35 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl thiophene-2-carboxylate,

[[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl cyclopentylacetate, and

- 5 [[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 4-tert-butylbenzoate.

Further embodiments of the invention are the following specifically preferred
10 compounds of Formula I or pharmaceutically acceptable salts thereof:

{[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1H-indole-2-carboxylate,

15

{[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl nicotinate,

20 {[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl isonicotinate,

25 {[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-pyrrolidin-1-ylbenzoate,

30 {[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3-methyl-1-benzofuran-2-carboxylate,

- {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-indole-3-carboxylate,
 5 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl quinoline-2-carboxylate,
 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-benzofuran-2-carboxylate, and
 10 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-pyrrole-2-carboxylate.

Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

- 20 (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-[[[(7S,10aR)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate,
 (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(butyl)carbamate,
 25 (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl 2-[[[(7R,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate,

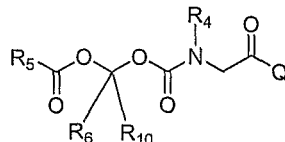
[5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate,

- 5 (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate and

- 10 [5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate.

An additional embodiment of this invention are compounds represented by Formula (II):

15



20

(II)

wherein:

- 25 R₄ is selected from hydrogen, alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents
- 30 independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl,

- alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl,
 alkenyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents
 independently selected from the group phenyl, heteroaryl, halogen, amino, cyano,
 5 alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl,
 wherein said aryl and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be
 substituted with 1 to 3 substituents independently selected from halogen, nitro,
 cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino,
 carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl
 10 and phenyl, alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3
 substituents independently selected from the group halogen, amino, cyano, alkyl,
 hydroxyl, and alkoxy, aryl of 6, 10 or 14 carbon atoms said aryl optionally substituted
 with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl,
 hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl,
 15 alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl,
 N-(alkyl of 1 to 12 carbon atoms)-aryl, said aryl optionally substituted with 1 to 3
 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl,
 alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl,
 aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16
 20 carbon atoms optionally substituted, aroyl of 7 to 13 carbon atoms optionally
 substituted, SR³, heteroaryl optionally substituted and heteroarylcarbonyl optionally
 substituted;
- 25 R₅ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3
 substituents independently selected from the group halogen, amino, cyano, cycloalkyl
 of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to
 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon
 atoms, heterocyclyl of 3 to 8 ring atoms, aryl of 6, 10 or 14 carbon atoms, aryloxy and
 30 N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of
 1 to 12 carbon atoms)-aryl, may be optionally substituted with 1 to 3 substituents
 independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl,
 alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-

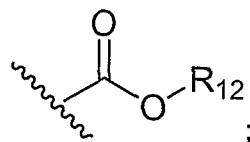
C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH₂(CO)OCH₂aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryloxy and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted, heteroaryl optionally substituted, aryl of 6, 10 or 14 carbon atoms optionally substituted, alkynyl of 2 to 12 carbon atoms optionally substituted, cycloalkyl 3 to 6 ring atoms, aryl-CH=CH-, cycloalkyl-alkyl; and adamantyl;

10 R₆ is selected from hydrogen, alkyl of 1 to 12 carbon atoms optionally substituted
with 1 to 3 substituents independently selected from the group halogen, amino,
cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl,
hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-
cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and
15 N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl
of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents
independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl,
alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-
C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and cycloalkyl of 3 to 6 carbon
20 atoms;

R₁₀ is H or alkyl of 1 to 12 carbon atoms;

Q is $-OR_{11}$, Cl, Br or I;

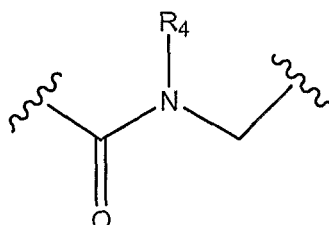
R₁₁ is H, benzyl optionally substituted with nitro or a moiety of the formula



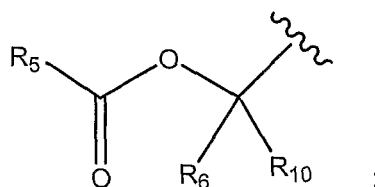
R₁₂ is alkyl of 1 to 6 carbon atoms.

The compounds having Formula II are useful as chemical intermediates for making the compounds having formula I and the pharmaceutically acceptable salt thereof wherein: A is a moiety

5



and R₃ is the moiety



10 where R₄ and R₅ are as defined above.

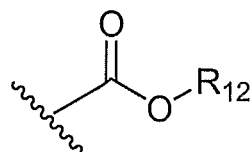
An embodiment of the invention provides compounds of Formula II wherein R₄ is t-butyl, R₅ is alkyl of 1 to 6 carbon atoms, and R₁₁ is benzyl optionally substituted with
15 nitro.

Another embodiment of the invention provides compounds of Formula II wherein R₄ is alkyl of 1 to 6 carbon atoms, R₅ is phenyl optionally substituted and R₁₁ is benzyl optionally substituted with nitro.

20

An embodiment of the invention provides compounds of Formula II wherein R₅ is alkyl of 1 to 6 carbon atoms, R₄ is t-butyl and R₁₁ is H.

A further embodiment of the invention provides compounds of Formula II wherein R₅ is alkyl of 1 to 6 carbon atoms, R₄ is t-butyl, Q is -OR₁₁, R₁₁ is
25



and R₁₂ is alkyl of 1 to 6 carbon atoms.

Another embodiment of the invention provides compounds of Formula II wherein R₆
 5 and R₁₀ are H.

Further embodiments of the invention provides the following specifically preferred compounds of Formula II or pharmaceutically acceptable salts thereof.

10 ([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate,

{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate,

15 {[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-methylpropanoate,

{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl
 20 cyclopentanecarboxylate,

{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate,

{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl heptanoate,

25 {[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl propionate,

{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl
 cyclohexanecarboxylate,

30

- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3,5-dimethylbenzoate,
- 5 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 4-fluorobenzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3-methylbutanoate,
- 10 benzyl N-(tert-butyl)-N-([[(cyclopentylacetyl)oxy]methoxy]carbonyl)glycinate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 4-(trifluoromethyl)benzoate,
- 15 ([[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclopropanecarboxylate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl adamantane-1-carboxylate,
- 20 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl pentanoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclobutanecarboxylate,
- 25 ([[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3-cyclohexylpropanoate,
- benzyl N-(tert-butyl)-N-([[(4-fluorophenoxy)acetyl]oxy]methoxy)carbonyl]glycinate,
- 30 benzyl N-(tert-butyl)-N-([[(cyclohexylacetyl)oxy]methoxy]carbonyl)glycinate,
- ([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 2,6-dimethylbenzoate,

- benzyl N-(tert-butyl)-N-({[(phenylacetyl)oxy]methoxy}carbonyl)glycinate,
- 5 {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl pivalate,
- {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-benzofuran-2-carboxylate,
- 10 {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-pyrrole-2-carboxylate,
- {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,
- 15 {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate,
- {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1H-indole-2-carboxylate,
- 20 benzyl N-(tert-butyl)-N-({[(diphenylacetyl)oxy]methoxy}carbonyl)glycinate,
- {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-naphthoate,
- 25 {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-naphthoate,
- {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-indole-3-carboxylate,
- 30 {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl quinoline-2-carboxylate,
- {[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl nicotinate,

- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl isonicotinate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,6-
5 difluorobenzoate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-fluorobenzoate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-
10 (trifluoromethyl)benzoate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(1H-pyrrol-1-
yl)benzoate,
- 15 {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-2-
carboxylate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,4,6-
trimethylbenzoate,
20
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-
isopropoxybenzoate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,4,5-
25 trimethoxybenzoate,
- {{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-
dimethoxybenzoate,
- 30 3-phenyl-acrylic acid (benzyloxycarbonylmethyl-tert-butyl-carbamoyloxy)-methyl
ester,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-methyl-1-benzofuran-2-carboxylate,

5 benzyl N-({[[3,5-bis(trifluoromethyl)phenyl]acetyl]oxy)methoxy}carbonyl)-N-(tert-butyl)glycinate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(heptyloxy)benzoate,

10 ({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-(2-phenylethyl)benzoate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(dodecyloxy)benzoate,

15 ({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(acetylamino)benzoate,

20 ({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl anthracene-9-carboxylate and

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-benzoylbenzoate.

25 Additional embodiments of the invention are the following specifically preferred compounds of Formula II or pharmaceutically acceptable salts thereof.

N-(tert-butyl)-N-({[(4-tert-butylbenzoyl)oxy]methoxy}carbonyl)glycine,

30 N-(tert-butyl)-N-({[(isobutyryloxy)methoxy]carbonyl}glycine,

N-(tert-butyl)-N-({[(cyclopentylcarbonyl)oxy]methoxy}carbonyl)glycine,

- N-(tert-butyl)-N-({[(4-methylbenzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(heptanoyloxy)methoxy]carbonyl}glycine,
- 5 N-(tert-butyl)-N-({[(propionyloxy)methoxy]carbonyl}glycine,
- N-(tert-butyl)-N-({[(cyclohexylcarbonyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(3,5-dimethylbenzoyl)oxy]methoxy}carbonyl)glycine,
- 10 N-(tert-butyl)-N-({[(4-fluorobenzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(3-methylbutanoyl)oxy]methoxy}carbonyl)glycine,
- 15 N-(tert-butyl)-N-({[(cyclopentylacetyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(4-(trifluoromethyl)benzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(cyclopropylcarbonyl)oxy]methoxy}carbonyl)glycine,
- 20 N-({[(1-adamantylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
- N-(tert-butyl)-N-({[(pentanoyloxy)methoxy]carbonyl}glycine,
- 25 N-(tert-butyl)-N-({[(cyclobutylcarbonyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(3-cyclohexylpropanoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(4-fluorophenoxy)acetyl]oxy}methoxy}carbonyl]glycine
- 30 N-(tert-butyl)-N-({[(cyclohexylacetyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(2,6-dimethylbenzoyl)oxy]methoxy}carbonyl)glycine,

- N-(tert-butyl)-N-({[(phenylacetyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(2,2-dimethylpropanoyl)oxy]methoxy}carbonyl)glycine,
- 5 N-({[(1-benzofuran-2-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
- N-(tert-butyl)-N-({[(1-methyl-1H-pyrrol-2-yl)carbonyl]oxy}methoxy)carbonyl]glycine,
- 10 N-({[(1,1'-biphenyl-4-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
- N-(tert-butyl)-N-({[(4-methoxybenzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(1H-indol-2-ylcarbonyl)oxy]methoxy}carbonyl)glycine,
- 15 N-(tert-butyl)-N-({[(diphenylacetyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(1-naphthoyloxy)methoxy]carbonyl}glycine,
- 20 N-(tert-butyl)-N-({[(2-naphthoyloxy)methoxy]carbonyl}glycine,
- N-(tert-butyl)-N-({[(1-methyl-1H-indol-3-yl)carbonyl]oxy}methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-({[(quinolin-2-ylcarbonyl)oxy]methoxy}carbonyl)glycine,
- 25 N-(tert-butyl)-N-({[(pyridin-3-ylcarbonyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(isonicotinoyloxy)methoxy]carbonyl}glycine,
- 30 N-(tert-butyl)-N-({[(2,6-difluorobenzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(2-fluorobenzoyl)oxy]methoxy}carbonyl)glycine,

- N-(tert-butyl)-N-([2-(trifluoromethyl)benzoyl]oxy)methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-([4-pyrrolidin-1-ylbenzoyl]oxy)methoxy)carbonyl]glycine,
- 5 N-([1,1'-biphenyl-2-ylcarbonyl]oxy)methoxy)carbonyl)-N-(tert-butyl)glycine,
- N-(tert-butyl)-N-([mesitylcarbonyl]oxy)methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-([4-isopropoxybenzoyl]oxy)methoxy)carbonyl]glycine,
- 10 N-(tert-butyl)-N-([3,4,5-trimethoxybenzoyl]oxy)methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-([3,5-dimethoxybenzoyl]oxy)methoxy)carbonyl]glycine,
- 15 N-(tert-butyl)-N-([(2E)-3-phenylprop-2-enoyl]oxy)methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-([3-methyl-1-benzofuran-2-yl]carbonyl]oxy)methoxy)carbonyl]glycine,
- 20 N-([3,5-bis(trifluoromethyl)phenyl]acetyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine,
- N-(tert-butyl)-N-([4-(heptyloxy)benzoyl]oxy)methoxy)carbonyl]glycine,
- 25 N-(tert-butyl)-N-([2-(2-phenylethyl)benzoyl]oxy)methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-([4-(dodecyloxy)benzoyl]oxy)methoxy)carbonyl]glycine,
- N-([4-(acetilamino)benzoyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine,
- 30 N-([9-anthrylcarbonyl]oxy)methoxy)carbonyl)-N-(tert-butyl)glycine and
- N-([4-benzoylbenzoyl]oxy)methoxy)carbonyl)-N-(tert-butyl)glycine

A further embodiment of the invention is the following specifically preferred compound of Formula II or pharmaceutically acceptable salts thereof.

- 5 3,3-Dimethyl-butyric acid [tert-butyl-(2-isobutoxycarbonyloxy-2-oxo-ethyl)-carbamoyloxy)-methyl ester.

Definitions

For the compounds of the invention defined above and referred to herein, unless
5 otherwise noted, the following terms are defined:

The term alkyl means a straight or branched alkyl moiety of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon
10 atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl,
15 alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl. In some embodiments of the invention alkyl is a moiety of 1 to 6 carbon atoms. In other embodiments of the invention alkyl is a moiety of 1 to 3 carbon atoms. In other embodiments of the invention alkyl is 1,1-dimethylethyl also termed t-butyl. In some
20 embodiments of the invention when alkyl is a methyl group wherein optional substitution is two independent phenyl rings. Non-limiting examples of alkyl are methyl, ethyl, n-propyl, 1-methylethyl, n-butyl, 1-methylpropyl, 2-methylpropyl and 1,1-dimethylethyl.

25 The term alkenyl means a straight or branched carbon chain of 2 to 12 carbon atoms having at least one site of unsaturation optionally independently substituted with 1 to 3 substituents selected from the group optionally independently substituted with 1 to 3 substituents selected from the group phenyl, heteroaryl, halogen, amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl,
30 wherein said aryl and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl

and phenyl. In some embodiments of the invention alkenyl is a vinyl moiety $\text{CH}_2=\text{CH}-$.

5

As used herein the term alkoxy refers to alkyl-O- wherein alkyl is hereinbefore defined. Non limiting examples include: methoxy and ethoxy.

- 10 As used herein the term aryl means an aromatic moiety having 6, 10 or 14 carbon atoms preferably 6 to 10 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, $\text{CH}_3\text{-C(O)-NH-}$, aralkyl, aryloxy, heterocyclyl and phenyl. In particular, aryl is phenyl or
- 15 naphthyl optionally substituted with 1 to 3 substituents.

The term aralkyl as used herein of 7 to 16 carbon atoms means an alkyl substituted with an aryl group in which the aryl and alkyl group are as defined herein. Non-limiting exemplary aralkyl groups include benzyl and phenethyl and the like.

20

Perhaloalkyl as used herein means an alkyl moiety of 1 to 6 carbon atoms in which each hydrogen atom is substituted with a halogen atom, an exemplary example is trifluoromethyl.

- 25 Phenyl as used herein refers to a 6-membered carbon aromatic ring.

- As used herein the term alkynyl includes both straight chain and branched moieties containing 2 to 12 carbon atoms having at least one carbon to carbon triple bond optionally substituted with 1 to 3 substituents independently selected from the group
- 30 halogen, amino, cyano, alkyl of 1 to 12 carbon atoms, hydroxyl, and alkoxy of 1 to 12 carbon atoms.

As used herein the term halogen or halo means F, Cl, Br or I.

As used herein the term cycloalkyl means a saturated monocyclic ring having from 3 to 6 carbon atoms. Exemplary cycloalkyl rings include but are not limited to cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. In an embodiment of the invention cycloalkyl is a moiety of 5 or 6 carbon atoms.

The term aroyl means an aryl-C(O)- group in which the aryl group is as previously defined. Non-limiting examples include benzoyl and naphthoyl.

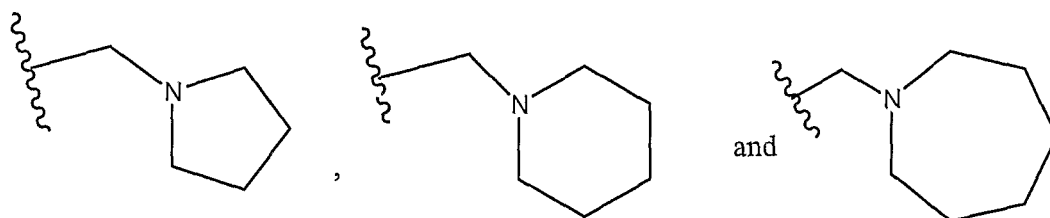
10 The term heteroaryl means an aromatic heterocyclic, monocyclic ring of 5 or 6 ring atoms containing 1 to 4 heteroatoms independently selected from O, N and S or bicyclic aromatic rings of 8 to 20 ring atoms containing 1 to 4 heteroatoms independently selected from O, N and S. Heteroaryl rings may optionally be substituted with 1 to 3 substituents independently selected from the group alkyl, 15 halogen, cyano, nitro, hydroxy, amino, alkylamino, dialkylamino, alkoxy, aryloxy, -CH₂OCOCH₃ and carboxy. Non-limiting heteroaryl moieties optionally substituted include: furanyl, benzofuranyl, benzothienyl, thienyl, pyridinyl, quinolinyl, tetrazolyl, imidazo, thiazolyl and the like.

20 Where terms are used in combination, the definition for each individual part of the combination applies unless defined otherwise. For instance, aralkyl refers to an aryl group, and alkyl refers to the alkyl group as defined above. Also, aryloxy refers to a arylO- group.

25 The term heteroarylcarbonyl means a heteroaryl-C(O)- group in which the heteroaryl group is as previously defined.

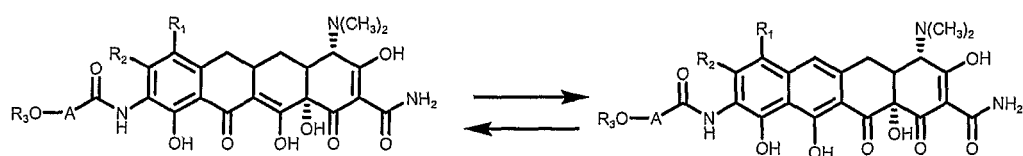
The term heterocyclyl as used herein represents a saturated ring of 3 to 8 ring atoms containing 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur. In some 30 embodiments of the invention a saturated ring of 5 or 6 ring atoms is preferred. Representative examples are pyrrolidyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl, aziridinyl, tetrahydrofuranyl and the like.

The term alkylheterocyclyl means an alkyl-heterocyclyl group in which the alkyl and heterocyclyl group are independently previously defined. Non-limiting exemplary alkylheterocyclyl groups include moieties of the formulae:



Some of the compounds of Formula (I) may also exist in their tautomeric forms. Such forms although not explicitly indicated in the above formula are intended to be included within the scope of the present invention. For instance, compounds of

10 Formula (I) which exist as tautomers are depicted below:



The present invention accordingly provides a pharmaceutical composition

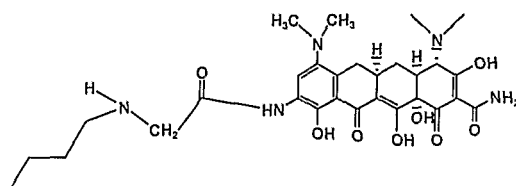
15 which comprises a compound of this invention in combination or association with a pharmaceutically acceptable carrier. In particular, the present invention provides a pharmaceutical composition which comprises an effective amount of a compound of this invention and a pharmaceutically acceptable carrier.

20 Proton sponge is [1,8-bis(dimethylamino)naphthalene, N,N,N',N'-tetramethyl-1,8-naphthalenediamine].

Alkali metal carbonate includes lithium, potassium and sodium carbonate.

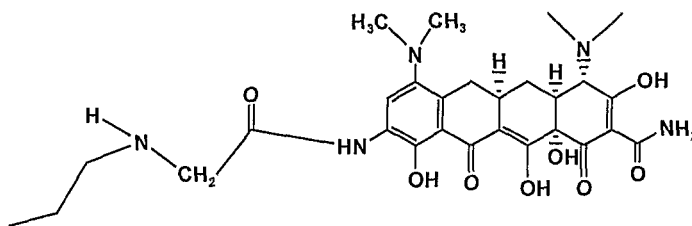
25 DMPU is 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone.

N-butyl-glycylcycline (N-bu-glycyl) is



N-propyl-glycylcycline (N-prop-glycyl) is

5



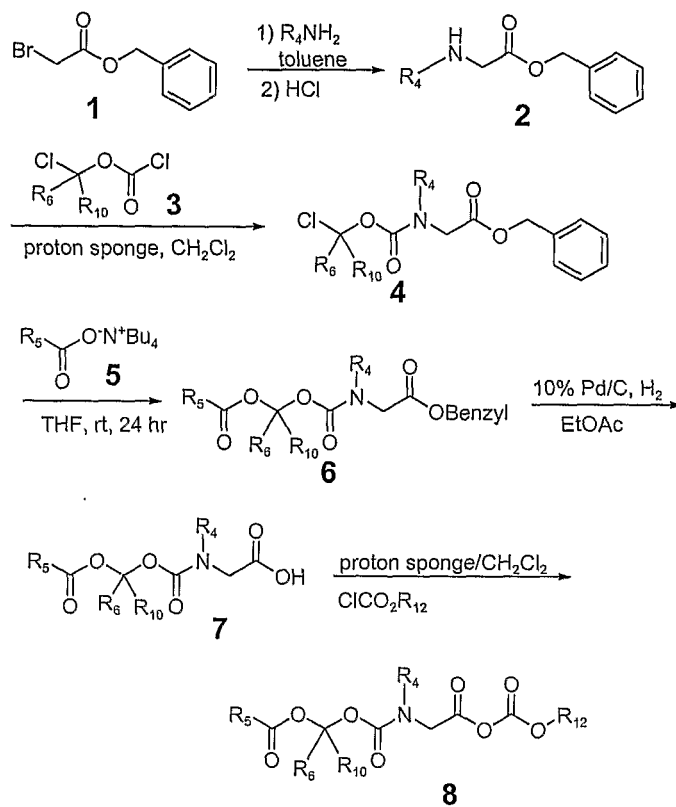
DESCRIPTION OF THE PREFERRED EMBODIMENTS

The compounds of this invention may be prepared according to the following
5 schemes: (1) from commercially available starting materials or: (2) from known starting materials which can be prepared as described in literature procedures or: (3) from new intermediates described in the schemes and experimental procedures.

The synthesis of acyloxy intermediate 8 is shown in Scheme 1. Reaction of amine
10 R_4NH_2 , preferably t-butylamine, with ester 1 provides the substituted amino ester 2. Preparation of the intermediate 4 is accomplished by using Proton Sponge as base to effect the acylation of substituted amino ester 2 with chloromethyl chloroformate 3. Treatment of intermediate 4 with the tetrabutylammonium salt 5 of carboxylic acids gives the benzyl protected acyloxy intermediate 6. The benzyl protecting group is
15 removed by catalytic reduction to give carboxylic acid 7 which is activated to a mixed anhydride with chloroformate $ClCO_2R_{12}$ where R_{12} is alkyl of 1 to 6 carbon atoms, for example iso-butyl chloroformate to give acyloxycarbamate intermediate 8. In an alternate route, silyl esters may optionally be used in place of the benzyl ester of
20 intermediate 4, treating with the appropriate carboxylic acid followed by deblocking the silyl ester with tetrabutylammonium fluoride or magnesium bromide to afford carboxylic acid 7. Optionally, carboxylic acid 7 may be activated through the use of coupling agents not limited to di-t-butyl dicarbonate (Boc_2O); e.g., benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (also known as Bop); benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate (also
25 known as PyBop); O-benzotriazole-N,N',N'-tetramethyl-uronium-hexafluorophosphate (HBTU); Bromotris-pyrrolidino-phosphonium hexafluorophosphate; 2-Chloro-N-methylpyridinium iodide (CMPI); dicyclohexylcarbodiimide (DCC); 1,3-diisopropylcarbodiimide (DIC); 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (EDC); or Carbonyl diimidazole.

30

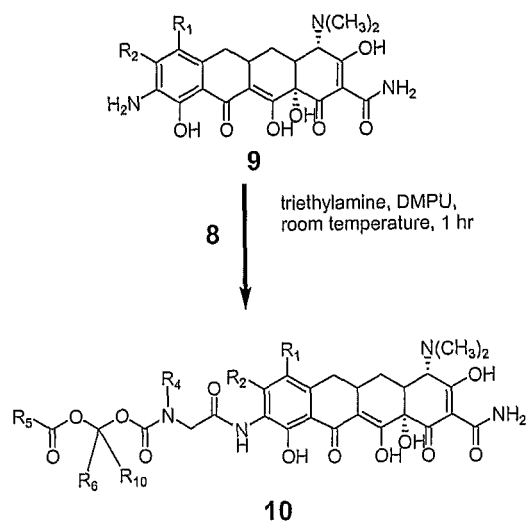
SCHEME 1



5

As shown in Scheme 2, reaction of activated acyloxycarbamate intermediate 8 with 7,8-disubstituted-9-aminotetracycline 9 in the presence of triethylamine and DMPU gives acyloxycarbamate 10.

Scheme 2

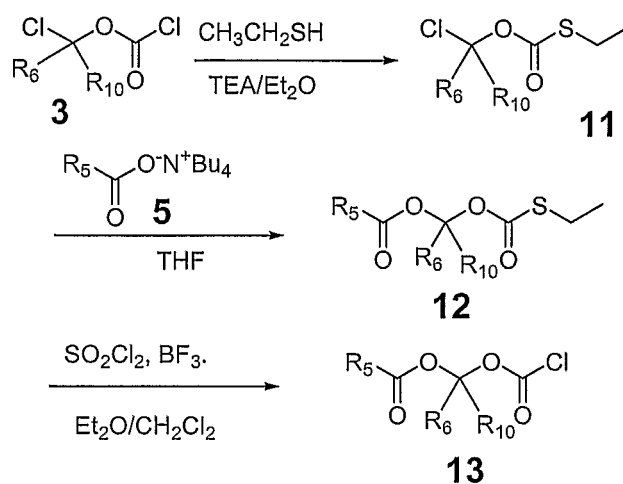


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Additional acyloxy carbamate compounds may be synthesized via routes as shown in Schemes 3 and 4. Treatment of chloromethyl chloroformate 3 with ethanethiol in the presence of triethylamine (TEA) gives carbonothioate 11. Compound 12 is prepared by reacting carbonothioate 11 with carboxylic acid tetrabutylammonium salt 5 in tetrahydrofuran. Chlorination of compound 12 with sulfuryl chloride in the presence of catalytic amount of boron trifluoroetherate affords chloro intermediate 13 (using the methods described in M. Folkmann and F.J. Lund, *Synthesis*, December 1990, 1159-1166).

15

Scheme 3

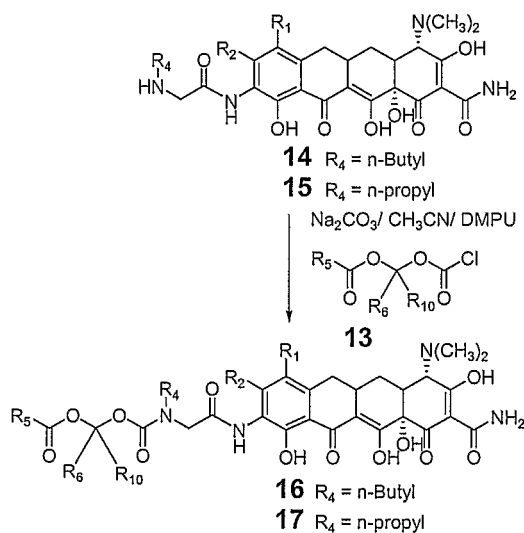


5

As further seen in Scheme 4 acyloxycarbamates 16 and 17 where R_4 is preferably n-butyl or n-propyl are synthesized by treatment of either 14 or 15 where R_4 is preferably n-butyl or n-propyl with the chloro intermediate 13 to give

10 acyloxycarbamates 16 and 17 respectively.

Scheme 4

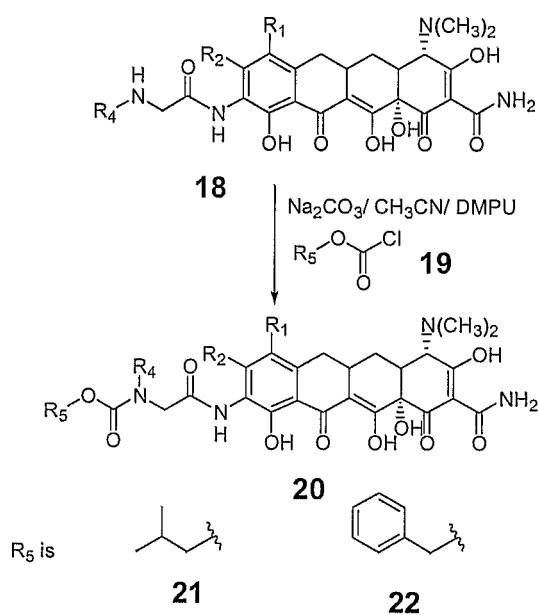


15

As shown in Scheme 5, carbamates of glycylcycline where R_4 is preferably propyl 18 may also be prepared by reaction with chloro intermediate 19 in the presence of an alkali metal carbonate preferably sodium carbonate, and DMPU in acetonitrile to afford preferred compounds (21 and 22).

5

Scheme 5

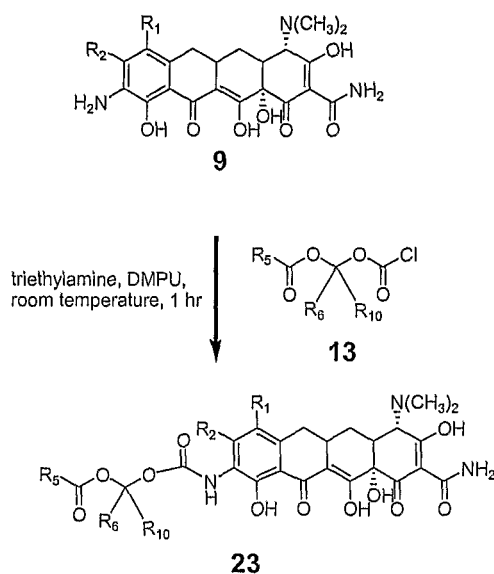


10

R_4 is preferably propyl

15

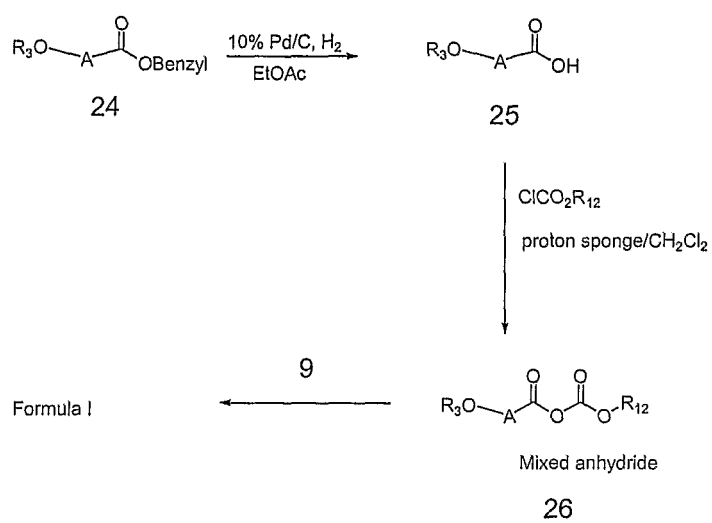
Scheme 6



- 5 As shown in Scheme 6, reaction of chloro intermediate 13 with 7,8-disubstituted-9-aminotetracycline 9 in the presence of triethylamine and DMPU gives carbamate 23.

- As further shown in Scheme 7, compounds of Formula I may generally be prepared
- 10 by removal of the benzyl protecting group from benzyl protected acyloxy intermediate 24 to give carboxylic acid 25 which is activated to a mixed anhydride with a chloroformate $ClCO_2R_{12}$ where R_{12} is alkyl of 1 to 6 carbon atoms, for example isobutyl chloroformate to give acyloxycarbamate intermediate 26. Further reaction of
- 15 7,8-disubstituted-9-aminotetracycline 9 with acyloxycarbamate mixed anhydride intermediate 26 in the presence of triethylamine and DMPU affords compounds of Formula (I).

Scheme 7



Reactions are performed in a solvent appropriate to the reagents and materials employed and suitable for the transformation being effected. It is understood by those skilled in the art of organic synthesis that the various functionalities present on the molecule must be consistent with the chemical transformations proposed. This may necessitate judgement as to the order of synthetic steps, protecting groups, if required, and deprotection conditions. Substituents on the starting materials may be incompatible with some of the reaction conditions. Such restrictions to the substituents which are compatible with the reaction conditions will be apparent to one skilled in the art.

Some of the compounds of the hereinbefore described schemes have center of asymmetry. The compounds may, therefore, exist in at least two and often more stereoisomeric forms. The present invention encompasses all stereoisomers of the compounds whether free from other stereoisomers or admixed with other stereoisomers in any proportion and thus includes, for instance, racemic mixture of enantiomers as well as the diastereomeric mixture of isomers. The absolute configuration of any compound may be determined by conventional X-ray crystallography.

The compounds of the invention may be obtained as metal complexes such as aluminum, calcium, iron, magnesium, manganese and complex salts; inorganic and organic salts and corresponding Mannich base adducts using methods known to those skilled in the art (Richard C. Larock, Comprehensive Organic Transformations, VCH Publishers, 411-415, 1989). Preferably, the compounds of the invention are obtained as inorganic salts such as hydrochloric, hydrobromic, hydroiodic, phosphoric, nitric or sulfate; or organic salts such as acetate, benzoate, citrate, cysteine or other amino acids, fumarate, glycolate, maleate, succinate, tartrate alkylsulfonate or arylsulfonate. In all cases, the salt formation occurs with the C(4)-dimethylamino group. The salts are preferred for oral and parenteral administration.

Standard Pharmacological Test Procedures

Methods for in Vitro Antibacterial evaluation

5

The minimum inhibitory concentration (MIC)

Antimicrobial susceptibility testing. The in vitro activities of the antibiotics are determined by the broth microdilution method as recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (1). Mueller-Hinton II broth (MHBII)(BBL Cockeysville, MD) is the medium employed in the testing procedures. Microtiter plates containing serial dilutions of each antimicrobial agent are inoculated with each organism to yield the appropriate density (10^5 CFU/ml) in a 100 μ l final volume. The plates are incubated for 18 - 22 hours at 35°C in ambient air. The minimal inhibitory concentration for all isolates is defined as the lowest concentration of antimicrobial agent that completely inhibits the growth of the organism as detected by the unaided eye.

1. NCCLS. 2000. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards: M7-A5, vol. 20. National Committee for Clinical Laboratory Standards, Wayne, PA.

25 Standard Pharmacological Test Procedures

Presented in Tables I-XIII are representative compounds of Formula I which were evaluated against a panel of 40 selected gram-positive and gram-negative bacteria strains by pre-incubation in water, mouse serum or human serum. Representative compounds were first incubated in mouse serum for an hour prior to the in vitro testing against a panel of selected gram-positive and gram-negative bacteria strains. All compounds were also pre-incubated in water for an hour prior to testing as

control. Representative compounds of Formula I were incubated in human serum prior to MIC determination. Representative compounds of Formula I which demonstrated in vivo activity were further subjected to various stability tests. A summary of the in vitro testing data of representative examples of Formula I are shown in Table 1. Expanded in vitro data of selected examples (87 and 27) are shown in Table 2 and 5 respectively. MICs of representative examples of Formula I are further shown in Tables 3 and 4. Table 6 presents in vitro and in vivo activity of representative examples of compounds of Formula I against Staph. aureus Smith in mice. Table 7 presents in vivo (oral, iv) and in vitro (MIC) activity of representative examples of compounds of Formula I against E. coli in mice. Table 8 presents in vivo (oral, iv) and in vitro (MIC) activity of representative examples of compounds of Formula I, against Staph aureus Smith in mice. Table 9 presents in vitro (MIC) activity of representative examples of compounds of Formula I against E. Coli in human serum and water and also against Staph in human serum and water. Table 10 presents in vivo single oral dose (SOD) and single intravenous dose (SIV) ED₅₀ data for representative examples of compounds of Formula I against Staph. Smith and E. Coli #311 in mammals.

TABLE I
ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water
	Example 1	Example 1	Example 2	Example 2	Example 3	Example 3	Example 4	Example 4
E. coli GC 2236	1	16	4	32	1	>64	1	64
E. coli GC 2231	1	64	4	64	2	>64	1	64
E. coli GC 2235	0.50	16	2	64	1	>64	1	64
E. coli GC 2232	0.50	16	2	64	2	>64	1	64
E. coli GC 2233	1	16	1	64	1	>64	1	64
E. coli GC 2234	0.50	16	1	64	1	>64	1	64
E. coli GC 2270	0.50	16	1	64	1	>64	1	64
E. coli GC 2271	0.50	16	1	64	1	>64	0.50	64
E. coli GC 2272	1	16	1	64	1	>64	1	64
E. coli GC 4559	1	32	1	64	2	>64	2	>64
E. coli GC 4560	0.50	2	0.25	4	0.50	32	0.25	8
E. coli GC 6465	8	>64	8	64	8	>64	4	>64
E. coli GC 3226	1	32	4	64	2	>64	2	64
E. coli GC 2203	0.50	16	2	64	1	>64	1	64
E. coli GC 1073	1	32	4	64	2	>64	1	>64
Salmonella spp. GC 235	1	64	8	>64	2	>64	2	>64

TABLE I (Cont)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES

OF FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water
Example 1	Example 1	Example 2	Example 2	Example 3	Example 3	Example 4	Example 4	Example 4
Salmonella spp. GC 566	2	64	8	>64	4	>64	4	>64
S. cholerae GC 1355	8	>64	>64	>64	16	>64	8	>64
S. typhimurium GC 2172	4	>64	>64	>64	8	>64	4	>64
P. aeruginosa GC 2214	32	>64	>64	>64	32	>64	32	>64
S. aureus GC 1131	1	4	2	4	2	4	1	4
S. aureus GC 6466	1	1	1	2	1	4	0.50	2
S. aureus GC 6467	4	4	4	8	4	32	2	8
S. aureus GC 1079	2	4	8	8	2	32	1	4
S. aureus GC 4536	2	4	2	4	2	4	1	4
S. aureus GC 2216	1	4	2	4	1	4	0.50	4
S. aureus GC 6335	2	4	8	8	2	8	1	4
S. aureus GC 6469	2	8	2	4	4	32	2	16

TABLE I (Cont)
ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water
	Example 1	Example 1	Example 2	Example 2	Example 3	Example 3	Example 4	Example 4
<i>S. epidermidis</i> GC 4935	2	8	8	8	4	8	2	4
<i>E. faecalis</i> GC 4555	1	4	2	4	1	8	1	8
<i>E. faecalis</i> GC 2265	1	4	4	8	2	32	2	8
<i>E. faecalis</i> GC 2267	2	8	4	4	2	32	1	8
<i>E. faecalis</i> GC 2242	1	4	4	4	2	16	1	4
<i>E. faecium</i> GC 4556	1	4	4	8	2	16	1	4
<i>E. faecium</i> GC 2243	1	2	1	4	1	4	0.50	2
<i>S. pneumoniae</i> * GC 4465	0.50	0.25	0.50	0.25	0.12	0.25	<0.06	0.12
<i>S. pneumoniae</i> + GC 4465	2	2	2	4	1	2	2	4
<i>S. pyogenes</i> GC 4563	0.25	0.50	0.25	0.25	0.12	0.25	0.12	0.25
<i>S. agalactiae</i> GC 4564	0.50	1	2	2	1	2	0.25	0.50
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64

TABLE II

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 5	Water Example 5	Mouse Serum Example 6	Water Example 6	Mouse Serum Example 7	Water Example 7	Mouse Serum Example 8	Water Example 8
<i>E. coli</i> GC 2236	2	16	2	8	0.25	2	1	32
<i>E. coli</i> GC 2231	2	64	2	64	2	16	2	>64
<i>E. coli</i> GC 2235	1	16	1	8	0.50	4	1	16
<i>E. coli</i> GC 2232	2	32	2	32	0.50	4	1	32
<i>E. coli</i> GC 2233	2	32	2	16	0.50	4	1	32
<i>E. coli</i> GC 2234	1	32	1	16	1	4	1	32
<i>E. coli</i> GC 2270	1	16	1	8	0.50	4	1	64
<i>E. coli</i> GC 2271	1	16	1	8	0.50	4	1	32
<i>E. coli</i> GC 2272	1	32	1	16	0.50	4	1	32
<i>E. coli</i> GC 4559	2	32	2	16	1	8	1	64
<i>E. coli</i> GC 4560	0.50	4	0.25	2	0.25	0.50	0.50	4
<i>E. coli</i> GC 6465	8	>64	4	>64	16	>64	8	>64
<i>E. coli</i> GC 3226	2	32	2	16	0.50	8	2	64
<i>E. coli</i> GC 2203	1	32	2	16	0.50	4	1	32
<i>E. coli</i> GC 1073	2	32	2	16	0.50	8	1	32
<i>Salmonella</i> spp. GC 235	2	32	2	16	2	8	4	64
<i>Salmonella</i> spp. GC 566	4	64	4	64	1	16	4	>64

TABLE II (Cont)
ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCILCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water
	Example 5	Example 5	Example 6	Example 6	Example 7	Example 7	Example 8	Example 8	Example 8	Example 8
<i>S. cholerae</i> GC 1355	16	>64	16	>64	16	>64	32	>64		
<i>S. typhimurium</i> GC 2172	8	>64	8	>64	4	>64	8	>64		
<i>P. aeruginosa</i> GC 2214	32	>64	32	>64	16	>64	32	>64		
<i>S. aureus</i> GC 1131	0.50	1	0.50	1	1	1	1	2		
<i>S. aureus</i> GC 6466	0.25	0.50	0.25	1	0.50	0.50	0.50	1		
<i>S. aureus</i> GC 6467	2	4	2	4	4	4	4	8		
<i>S. aureus</i> GC 1079	2	2	2	4	1	4	2	4		
<i>S. aureus</i> GC 4536	1	1	0.50	2	1	1	0.50	2		
<i>S. aureus</i> GC 2216	0.50	2	0.50	2	0.50	0.50	0.50	4		
<i>S. aureus</i> GC 6335	0.50	1	0.50	2	1	1	1	4		
<i>S. aureus</i> GC 6469	2	4	2	4	2	4	2	8		
<i>S. epidermidis</i> GC 4935	1	2	1	4	2	2	2	8		

TABLE II (Cont)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLOLINES OF FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum		Water		Mouse Serum		Water		Mouse Serum		Water		Mouse Serum		Water	
	Example 5	Example 5	Example 5	Example 5	Example 6	Example 6	Example 6	Example 6	Example 7	Example 7	Example 7	Example 7	Example 8	Example 8	Example 8	Example 8
E. faecalis GC 4555	1	4	1	4	1	4	1	4	0.50	1	0.50	1	0.50	8	8	8
E. faecalis GC 2265	2	4	2	4	2	4	2	4	1	2	1	2	2	8	8	8
E. faecalis GC 2267	2	4	1	4	1	4	1	4	1	2	1	2	2	8	8	8
E. faecalis GC 2242	1	2	1	2	1	2	1	2	1	1	1	1	1	4	4	4
E. faecium GC 4556	1	2	1	2	1	2	1	2	0.50	1	0.50	1	1	4	4	4
E. faecium GC 2243	0.50	1	0.50	2	0.50	2	0.50	2	0.25	0.12	0.25	0.12	0.25	2	2	2
S. pneumoniae* GC 4465	<0.06	0.12	0.12	0.25	0.12	0.25	0.12	0.25	0.25	0.12	0.25	0.12	<0.06	0.25	0.25	0.25
S. pneumoniae+ GC 4465	2	4	2	2	2	2	2	2	4	2	4	2	1	4	4	4
S. pyogenes GC 4563	0.12	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.12	0.50	0.50	0.50
S. agalactiae GC 4564	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.25	0.50	0.25	0.50	0.25	0.50	0.50	0.50
c. albicans GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE III

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 9	Water Example 9	Mouse Serum Example 10	Water Example 10	Mouse Serum Example 11	Water Example 11	Mouse Serum Example 12	Water Example 12
<i>E. coli</i> GC 2236	1	8	0.50	8	0.50	8	1	16
<i>E. coli</i> GC 2231	2	64	2	32	2	64	2	64
<i>E. coli</i> GC 2235	0.50	4	0.25	4	0.25	4	1	16
<i>E. coli</i> GC 2232	1	8	0.50	8	1	16	0.50	32
<i>E. coli</i> GC 2233	0.50	4	0.50	8	0.25	8	1	32
<i>E. coli</i> GC 2234	0.50	8	0.50	8	0.50	16	1	16
<i>E. coli</i> GC 2270	0.50	4	0.50	8	0.50	8	0.50	32
<i>E. coli</i> GC 2271	0.50	8	0.25	8	0.25	4	0.50	16
<i>E. coli</i> GC 2272	0.50	8	0.50	8	0.25	4	1	16
<i>E. coli</i> GC 4559	1	8	0.50	16	0.50	32	1	64
<i>E. coli</i> GC 4560	0.25	1	0.12	0.12	0.12	0.12	0.25	1
<i>E. coli</i> GC 6465	4	>64	8	>64	8	>64	8	>64
<i>E. coli</i> GC 3226	2	16	0.50	16	0.50	>64	2	64
<i>E. coli</i> GC 2203	0.50	4	0.50	8	0.25	16	1	32
<i>E. coli</i> GC 1073	1	8	0.50	16	0.50	16	1	64
<i>Salmonella</i> spp. GC 235	1	8	0.50	32	0.50	64	1	64
<i>Salmonella</i> spp. GC 566	2	64	2	>64	2	>64	4	>64
<i>S. cholerae</i> GC 1355	64	>64	16	>64	32	>64	16	>64

TABLE III (Cont)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water
	Example 9	Example 9	Example 10	Example 10	Example 11	Example 11	Example 12	Example 12	Example 12	Example 12
S. typhimurium GC 2172	8	>64	4	>64	4	>64	4	>64	4	>64
P. aeruginosa GC 2214	16	>64	16	>64	16	>64	32	>64	32	>64
S. aureus GC 1131	<0.06	0.25	0.12	0.12	0.25	0.25	1	0.25	1	2
S. aureus GC 6466	0.12	0.12	0.12	0.12	0.25	0.25	0.50	0.25	0.50	1
S. aureus GC 6467	1	2	2	2	4	4	4	4	4	16
S. aureus GC 1079	2	1	0.50	1	2	4	2	4	2	8
S. aureus GC 4536	0.50	0.50	0.25	0.50	0.50	0.50	1	0.50	1	2
S. aureus GC 2216	0.25	0.50	0.25	0.50	0.50	0.50	1	0.50	1	4
S. aureus GC 6335	0.25	0.50	0.25	0.50	1	1	1	1	1	2
S. aureus GC 6469	1	2	1	2	4	4	4	4	4	16
S. epidermidis GC 4935	0.25	1	0.50	1	1	2	4	2	4	8
E. faecalis GC 4555	0.50	2	0.50	1	0.50	1	0.50	1	0.50	4

TABLE III (Cont)

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

	Mouse Example 9	Serum Example 9	Water Example 9	Mouse Example 10	Serum Example 10	Water Example 10	Mouse Example 11	Serum Example 11	Water Example 11	Mouse Example 12	Serum Example 12	Water Example 12
<i>E. faecalis</i> GC 2265	1		2	1	1	1	2	2	4	2	2	8
<i>E. faecalis</i> GC 2267	1		2	1	1	2	2	2	2	2	2	8
<i>E. faecalis</i> GC 2242	0.50		1	0.25	0.25	0.50	0.25	0.25	0.50	2	2	4
<i>E. faecium</i> GC 4556	0.25		0.50	0.25	0.25	0.50	0.25	0.25	0.50	1	1	4
<i>E. faecium</i> GC 2243	0.25		0.50	<0.06	<0.06	0.12	0.12	0.12	0.25	0.50	0.50	4
<i>S. pneumoniae</i> * GC 4465	<0.06		<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	0.12
<i>S. pneumoniae</i> + GC 4465	2		2	1	1	1	2	2	2	4	4	8
<i>S. pyogenes</i> GC 4563	<0.06		<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	<0.06	0.12	0.12	0.25
<i>S. agalactiae</i> GC 4564	0.12		0.25	<0.06	<0.06	0.12	<0.06	<0.06	<0.06	0.25	0.25	0.25
<i>c. albicans</i> GC 3066	>64		>64	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE IV

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCILCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 13	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum Water
		Example 13	Example 14	Example 14	Example 15	Example 15	Example 16
E. coli GC 2236	2	8	>64	>64	>64	64	>64
E. coli GC 2231	2	16	>64	>64	>64	>64	>64
E. coli GC 2235	2	8	32	64	32	16	64
E. coli GC 2232	2	8	>64	>64	>64	>64	>64
E. coli GC 2233	2	8	>64	>64	>64	>64	>64
E. coli GC 2234	1	8	>64	>64	>64	>64	>64
E. coli GC 2270	1	8	>64	>64	64	>64	>64
E. coli GC 2271	2	8	>64	>64	64	>64	>64
E. coli GC 2272	2	8	>64	>64	>64	>64	>64
E. coli GC 4559	4	16	>64	>64	>64	>64	>64
E. coli GC 4560	1	4	4	4	1	2	4
E. coli GC 6465	8	>64	>64	>64	>64	>64	>64
E. coli GC 3226	2	16	>64	>64	>64	64	>64
E. coli GC 2203	2	8	32	64	32	16	64
E. coli GC 1073	2	16	>64	>64	>64	>64	>64
Salmonella spp. GC 235	2	16	>64	>64	>64	>64	>64

TABLE IV (Cont)

	Mouse Serum	Water	Example 13	Mouse Serum	Water	Example 14	Mouse Serum	Water	Example 15	Mouse Serum	Water	Example 16	Water	Example 17
Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13	Example 13
Salmonella spp.														
GC 566	8	64		>64		>64		>64		>64		>64		>64
S. choleraesuis														
GC 1355	16	>64		>64		>64		>64		>64		>64		>64

TABLE IV (Cont)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 13	Water Example 13	Mouse Serum Example 14	Water Example 14	Mouse Serum Example 15	Water Example 15	Mouse Serum Example 16	Water Example 16
<i>S. typhimurium</i> GC 2172	8	64	>64	>64	>64	>64	>64	>64
<i>P. aeruginosa</i> GC 2214	32	>64	>64	>64	>64	>64	>64	>64
<i>S. aureus</i> GC 1131	2	2	1	2	2	4	2	4
<i>S. aureus</i> GC 6466	1	2	2	8	2	4	4	8
<i>S. aureus</i> GC 6467	4	8	2	4	16	16	8	8
<i>S. aureus</i> GC 1079	4	4	1	2	2	4	2	4
<i>S. aureus</i> GC 4536	1	2	2	2	2	4	2	4
<i>S. aureus</i> GC 2216	2	4	2	4	2	4	2	4
<i>S. aureus</i> GC 6335	2	4	1	4	4	4	4	4
<i>S. aureus</i> GC 6469	4	8	2	4	4	8	4	8
<i>S. epidermidis</i> GC 4935	4	8	8	8	16	16	8	8
<i>E. faecalis</i> GC 4555	2	4	2	8	4	8	4	8

TABLE IV (Cont)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum		Water		Mouse Serum		Water		Mouse Serum		Water		Mouse Serum		Water	
	Example 13		Example 13		Example 14		Example 14		Example 15		Example 15		Example 16		Example 16	
E. faecalis GC 2265	4		8		2		8		8		8		4		8	
E. faecalis GC 2267	4		8		2		8		8		8		4		8	
E. faecalis GC 2242	4		8		2		8		8		8		8		8	
E. faecium GC 4556	2		8		4		8		8		8		4		8	
E. faecium GC 2243	2		4		2		4		8		8		4		8	
S. pneumoniae* GC 4465	0.50		0.50		2		4		2		2		4		4	
S. pneumoniae+ GC 4465	8		8		4		4		4		4		8		8	
S. pyogenes GC 4563	0.50		1		2		4		2		2		4		8	
S. agalactiae GC 4564	1		2		16		16		8		8		16		16	
c. albicans GC 3066	>64		>64		>64		>64		>64		>64		>64		>64	

TABLE V

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 21	Water Example 21	Mouse Serum Example 22	Water Example 22	Mouse Serum Example 23	Water Example 23	Mouse Serum Example 24	Water Example 24
<i>E. coli</i> GC 2236	1	>64	2	>64	2	>64	1	>64
<i>E. coli</i> GC 2231	1	>64	2	>64	2	>64	2	>64
<i>E. coli</i> GC 2235	0.50	>64	1	>64	1	>64	0.50	>64
<i>E. coli</i> GC 2232	1	>64	2	>64	1	>64	0.50	>64
<i>E. coli</i> GC 2233	1	>64	2	>64	2	>64	1	>64
<i>E. coli</i> GC 2234	0.50	>64	1	>64	1	>64	0.50	>64
<i>E. coli</i> GC 2270	1	>64	1	>64	1	>64	0.50	>64
<i>E. coli</i> GC 2271	0.50	>64	1	>64	1	>64	0.50	>64
<i>E. coli</i> GC 2272	1	>64	1	>64	1	>64	1	>64
<i>E. coli</i> GC 4559	1	>64	2	>64	2	>64	1	>64
<i>E. coli</i> GC 4560	0.25	>64	0.50	>64	0.50	8	0.25	64
<i>E. coli</i> GC 6465	4	>64	8	>64	4	>64	8	>64
<i>E. coli</i> GC 3226	8	>64	8	>64	8	>64	1	>64
<i>E. coli</i> GC 2203	0.50	>64	1	>64	1	>64	0.50	>64
<i>E. coli</i> GC 1073	1	>64	2	>64	1	>64	1	>64
<i>Salmonella</i> spp. GC 235	2	>64	2	>64	2	>64	1	>64
<i>Salmonella</i> spp. GC 566	4	>64	4	>64	4	>64	2	>64
<i>S. cholerae</i> GC 1355	16	>64	16	>64	16	>64	32	>64

TABLE V (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water	Mouse Serum	Water
Example 21	Example 21	Example 21	Example 22	Example 22	Example 22	Example 23	Example 23	Example 23	Example 24	Example 24
S. typhimurium GC 2172	4	>64	8	>64	>64	4	>64	>64	8	>64
P. aeruginosa GC 2214	>64	>64	>64	>64	>64	>64	>64	>64	16	>64
S. aureus GC 1131	1	64	1	4	2	1	2	2	1	2
S. aureus GC 6466	1	64	0.50	2	0.50	0.25	0.50	0.50	0.25	0.50
S. aureus GC 6467	4	>64	4	>64	>64	4	8	>64	4	>64
S. aureus GC 1079	4	>64	2	32	32	2	4	64	2	64
S. aureus GC 4536	2	32	1	2	2	1	2	4	1	4
S. aureus GC 2216	1	64	1	4	4	1	4	4	0.50	4
S. aureus GC 6335	2	64	2	8	8	2	4	16	2	16
S. aureus GC 6469	4	>64	4	64	64	4	4	>64	4	>64
S. epidermidis GC 4935	2	64	2	16	16	2	4	16	2	16
E. faecalis GC 4555	1	64	2	64	64	1	4	64	1	64
E. faecalis GC 2265	1	64	2	64	64	1	4	32	2	32
E. faecalis GC 2267	2	64	4	64	64	2	8	64	4	64
E. faecalis GC 2242	2	32	2	32	32	2	4	4	2	4
E. faecium GC 4556	2	64	2	64	64	2	4	32	1	32
E. faecium GC 2243	0.50	8	1	8	8	0.50	4	2	0.50	2
S. pneumoniae* GC 4465	0.25	0.50	0.50	1	1	0.12	0.12	<0.06	<0.06	<0.06

TABLE V (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum	Water Example 21	Mouse Serum	Water Example 22	Mouse Serum	Water Example 23	Mouse Serum	Water Example 24
	Example 21	21	Example 22	22	Example 23	23	Example 24	24
<i>S. pneumoniae</i> + GC 4465	4	4	4	16	4	8	2	1
<i>S. pyogenes</i> GC 4563	0.25	0.12	0.50	1	0.12	0.25	<0.06	<0.06
<i>S. agalactiae</i> GC 4564	0.50	8	1	8	0.25	0.25	0.50	8
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64

TABLE VI

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCILCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 25	Water Example 25	Mouse Serum Example 26	Water Example 26	Mouse Serum Example 27	Water Example 27	Mouse Serum Example 28	Water Example 28
<i>E. coli</i> GC 2236	2	64	2	>64	0.50	64	0.50	>64
<i>E. coli</i> GC 2231	2	>64	4	>64	1	>64	1	>64
<i>E. coli</i> GC 2235	1	32	1	64	0.50	64	0.50	>64
<i>E. coli</i> GC 2232	1	>64	1	>64	0.50	64	0.50	>64
<i>E. coli</i> GC 2233	2	32	2	>64	0.50	64	0.50	>64
<i>E. coli</i> GC 2234	1	>64	1	>64	0.50	64	0.25	>64
<i>E. coli</i> GC 2270	1	>64	1	>64	0.50	64	0.50	>64
<i>E. coli</i> GC 2271	1	32	1	>64	0.50	64	0.25	>64
<i>E. coli</i> GC 2272	2	64	2	64	0.50	32	0.50	>64
<i>E. coli</i> GC 4559	2	>64	2	>64	0.50	>64	0.50	>64
<i>E. coli</i> GC 4560	0.50	2	0.50	8	0.25	1	0.25	>64
<i>E. coli</i> GC 6465	8	>64	8	>64	4	>64	8	>64
<i>E. coli</i> GC 3226	2	>64	2	>64	0.50	>64	0.50	>64
<i>E. coli</i> GC 2203	1	>64	1	>64	0.50	>64	0.50	>64
<i>E. coli</i> GC 1073	2	>64	2	>64	0.50	>64	0.50	>64
<i>Salmonella</i> spp. GC 235	2	>64	2	>64	1	>64	0.50	>64
<i>Salmonella</i> spp. GC 566	4	>64	4	>64	1	>64	2	>64
<i>S. choleraesuis</i> GC 1355	32	>64	32	>64	16	>64	16	>64

TABLE VI (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCILCYCLINES OF FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Mouse Serum Example 25	Water Example 25	Mouse Serum Example 26	Water Example 26	Mouse Serum Example 27	Water Example 27	Mouse Serum Example 28	Water Example 28
<i>S. typhimurium</i> GC 2172	8	>64	16	>64	4	>64	8	>64
<i>P. aeruginosa</i> GC 2214	32	>64	32	>64	8	>64	16	>64
<i>S. aureus</i> GC 1131	0.50	0.50	0.50	0.50	0.12	0.25	0.50	32
<i>S. aureus</i> GC 6466	0.25	0.25	0.25	0.25	0.12	0.25	0.50	4
<i>S. aureus</i> GC 6467	2	2	1	4	2	2	4	64
<i>S. aureus</i> GC 1079	1	2	1	2	1	2	2	64
<i>S. aureus</i> GC 4536	0.50	0.50	0.25	0.50	0.12	0.12	0.50	32
<i>S. aureus</i> GC 2216	0.50	1	0.50	0.50	0.25	0.25	0.50	32
<i>S. aureus</i> GC 6335	0.50	0.50	0.50	1	0.25	0.50	1	16
<i>S. aureus</i> GC 6469	2	4	1	2	1	2	4	64
<i>S. epidermidis</i> GC 4935	1	2	1	2	0.25	1	1	32
<i>E. faecalis</i> GC 4555	1	2	1	4	0.25	1	0.25	64
<i>E. faecalis</i> GC 2265	2	2	2	8	1	2	2	64
<i>E. faecalis</i> GC 2267	2	4	2	4	1	2	2	64
<i>E. faecalis</i> GC 2242	2	2	2	4	0.50	0.50	0.50	4
<i>E. faecium</i> GC 4556	1	4	1	4	0.50	1	0.50	32
<i>E. faecium</i> GC 2243	0.50	1	1	2	0.12	0.25	0.25	0.25
<i>S. pneumoniae</i> * GC 4465	0.12	0.25	0.25	0.25	<0.06	<0.06	<0.06	<0.06

TABLE VI (CONT)

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

	Mouse Serum Water		Mouse Serum Water		Mouse Serum Water		Mouse Serum Water		Mouse Serum Water	
	Example 25	Example 25	Example 25	Example 26	Example 26	Example 26	Example 27	Example 27	Example 28	Example 28
<i>S. pneumoniae</i> + GC 4465	4	4	4	4	4	4	1	2	2	0.50
<i>S. pyogenes</i> GC 4563	0.12	0.25	0.25	0.25	0.25	0.25	<0.06	<0.06	<0.06	<0.06
<i>S. agalactiae</i> GC 4564	0.50	0.50	0.50	1	2	2	0.12	0.12	0.25	0.50
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE VII

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water	Mouse Serum	Mouse Serum	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum
	Example 42	Example 42	Example 42	Example 42	Example 43	Example 43	Example 44	Example 44	Example 44
E. coli GC 2236	>64	4	>64	>64	>64	0.50	>64	2	>64
E. coli GC 2231	>64	4	>64	>64	>64	0.50	>64	2	>64
E. coli GC 2235	>64	4	>64	>64	>64	0.25	>64	2	>64
E. coli GC 2232	>64	4	>64	>64	>64	0.50	>64	2	>64
E. coli GC 2233	>64	4	>64	>64	>64	0.50	>64	2	>64
E. coli GC 2234	>64	4	>64	>64	>64	0.25	>64	2	>64
E. coli GC 2270	>64	4	>64	>64	>64	0.25	>64	2	>64
E. coli GC 2271	>64	4	>64	>64	>64	0.25	>64	2	>64
E. coli GC 2272	>64	4	>64	>64	>64	0.50	>64	2	>64
E. coli GC 4559	>64	8	>64	>64	>64	0.50	>64	4	>64
E. coli GC 4560	8	2	8	32	<0.06	16	4	2	4
E. coli GC 6465	>64	16	>64	>64	2	>64	>64	8	>64
E. coli GC 3226	>64	16	>64	>64	1	>64	>64	4	>64
E. coli GC 2203	>64	8	>64	>64	0.50	>64	>64	2	>64
E. coli GC 1073	>64	8	>64	>64	0.50	>64	>64	4	>64
Salmonella spp. GC 235	>64	16	>64	>64	0.50	>64	>64	4	>64
Salmonella spp. GC 566	>64	32	>64	>64	2	>64	>64	8	>64

TABLE VII (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCINES OF FORMULA I									
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)									
	Water	Mouse Serum	Mouse Serum	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum
	Example 42	Example 42	Example 42	Example 42	Example 43	Example 43	Example 43	Example 44	Example 44
S. cholerae GC 1355	>64	64	>64	>64	4	>64	>64	16	>64
S. typhimurium GC 2172	>64	64	>64	>64	2	>64	>64	8	>64
P. aeruginosa GC 2214	>64	>64	>64	>64	16	>64	>64	>64	>64
S. aureus GC 1131	4	2	2	64	1	16	4	2	2
S. aureus GC 6466	4	2	4	64	0.50	16	2	2	2
S. aureus GC 6467	8	4	4	>64	0.50	32	4	2	2
S. aureus GC 1079	4	2	4	64	1	32	4	2	2
S. aureus GC 4536	8	2	4	32	1	16	4	2	2
S. aureus GC 2216	4	2	2	64	0.50	32	2	2	2
S. aureus GC 6335	4	2	4	64	1	64	4	2	4
S. aureus GC 6469	4	2	4	>64	1	32	4	2	2

TABLE VII (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I										
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)										
	Water	Mouse Serum	Mouse Serum	Water	Mouse Serum	Mouse Serum	Water	Mouse Serum	Human Serum	Human Serum
	Example 42	Example 42	Example 42	Example 42	Example 43	Example 43	Example 43	Example 43	Example 44	Example 44
	8	4	4	32	2	4	4	4	2	4
<i>S. epidermidis</i> GC 4935	4	2	4	32	0.50	8	4	4	2	4
<i>E. faecalis</i> GC 4555	8	2	4	32	0.50	8	4	4	2	4
<i>E. faecalis</i> GC 2265	4	2	4	32	0.50	4	4	4	2	4
<i>E. faecalis</i> GC 2267	8	4	4	16	0.50	4	4	4	2	4
<i>E. faecalis</i> GC 2242	8	2	4	16	0.50	8	4	4	2	4
<i>E. faecium</i> GC 4556	4	2	4	0.25	0.12	0.25	4	4	2	4
<i>E. faecium</i> GC 2243	4	2	4	0.50	<0.06	1	2	2	1	2
<i>S. pneumoniae</i> * GC 4465	8	4	8	2	2	2	4	4	4	4
<i>S. pneumoniae</i> + GC 4465	4	2	4	<0.06	<0.06	<0.06	2	2	1	4
<i>S. pyogenes</i> GC 4563	8	2	8	2	<0.06	2	4	4	1	4
<i>S. agalactiae</i> GC 4564	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>c. albicans</i> GC 3066										

TABLE VIII

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCINES OF FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum
	Example 45	Example 45	Example 45	Example 46	Example 46	Example 46	Example 47	Example 47	Example 47
E. coli GC 2236	16	1	4	64	0.50	4	>64	1	32
E. coli GC 2231	32	1	4	64	0.50	4	>64	1	32
E. coli GC 2235	16	0.50	4	64	0.50	4	>64	1	16
E. coli GC 2232	16	1	4	64	0.50	4	>64	1	16
E. coli GC 2233	16	1	4	64	0.50	4	>64	0.50	16
E. coli GC 2234	16	0.50	4	64	0.50	4	>64	1	16
E. coli GC 2270	32	0.50	4	>64	0.50	4	>64	0.50	16
E. coli GC 2271	16	0.50	4	64	0.50	4	>64	1	16
E. coli GC 2272	16	1	8	64	1	4	>64	1	16
E. coli GC 4559	64	1	8	>64	1	8	>64	2	64
E. coli GC 4560	2	0.25	0.50	4	0.50	1	16	1	4
E. coli GC 6465	>64	2	16	>64	2	16	>64	2	>64
E. coli GC 3226	64	1	8	>64	1	16	>64	2	32
E. coli GC 2203	32	0.50	4	>64	0.50	8	>64	1	32
E. coli GC 1073	64	1	8	>64	1	8	>64	2	32
Salmonella spp. GC 235	>64	1	8	>64	1	16	>64	2	64
Salmonella spp. GC 566	>64	2	32	>64	2	16	>64	4	>64

TABLE VIII (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum
	Example 45	Example 45	Example 45	Example 46	Example 46	Example 46	Example 47	Example 47	Example 47
<i>S. cholerae</i> GC 1355	>64	4	32	>64	2	32	>64	4	>64
<i>S. typhimurium</i> GC 2172	>64	2	32	>64	2	32	>64	4	>64
<i>P. aeruginosa</i> GC 2214	>64	16	>64	>64	16	>64	>64	32	>64
<i>S. aureus</i> GC 1131	1	0.50	0.50	0.50	0.50	0.50	2	1	2
<i>S. aureus</i> GC 6466	0.50	0.25	0.25	0.25	0.25	0.25	2	1	1
<i>S. aureus</i> GC 6467	2	1	1	1	1	0.50	4	1	2
<i>S. aureus</i> GC 1079	1	0.50	0.12	0.50	0.50	0.50	2	1	2
<i>S. aureus</i> GC 4536	1	0.50	0.50	0.50	0.50	0.50	4	1	1
<i>S. aureus</i> GC 2216	1	1	0.50	1	0.50	0.50	2	1	1
<i>S. aureus</i> GC 6335	2	1	0.50	1	1	0.50	2	1	2
<i>S. aureus</i> GC 6469	1	1	0.50	1	1	0.50	4	1	2
<i>S. epidermidis</i> GC 4935	2	1	1	2	1	1	4	2	4

TABLE VIII (CONT)
ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water Example 45	Mouse Serum Example 45	Human Serum Example 45	Water Example 46	Mouse Serum Example 46	Human Serum Example 46	Water Example 47	Mouse Serum Example 47	Human Serum Example 47
<i>E. faecalis</i> GC 4555	2	1	2	2	0.50	0.50	4	1	4
<i>E. faecalis</i> GC 2265	4	0.50	1	2	0.50	1	4	1	4
<i>E. faecalis</i> GC 2267	2	0.50	1	2	0.50	1	4	1	4
<i>E. faecalis</i> GC 2242	2	1	1	1	0.50	1	4	1	4
<i>E. faecium</i> GC 4556	2	1	1	1	0.50	1	4	1	4
<i>E. faecium</i> GC 2243	2	0.50	1	0.50	0.25	0.25	2	0.50	2
<i>S. pneumoniae</i> * GC 4465	0.50	0.25	0.25	0.12	0.12	0.12	0.50	0.25	0.50
<i>S. pneumoniae</i> + GC 4465	4	2	2	1	1	1	4	2	2
<i>S. pyogenes</i> GC 4563	0.50	0.25	0.25	0.25	0.12	0.25	0.25	0.12	0.25
<i>S. agalactiae</i> GC 4564	0.50	0.25	0.50	0.25	0.25	0.25	1	0.50	1
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE IX

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCLYCINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum
Example 48	Example 48	Example 48	Example 48	Example 49	Example 49	Example 49	Example 50	Example 50	Example 50
E. coli GC 2236	64	0.25	16	16	0.50	4	32	1	8
E. coli GC 2231	64	0.50	16	16	0.50	8	64	1	8
E. coli GC 2235	32	0.25	16	8	0.50	4	32	1	4
E. coli GC 2232	64	0.25	16	16	0.50	4	32	1	8
E. coli GC 2233	64	0.25	16	8	0.25	4	32	1	8
E. coli GC 2234	64	0.50	16	16	0.25	4	64	1	8
E. coli GC 2270	64	0.50	16	16	0.50	4	32	1	8
E. coli GC 2271	32	0.25	8	8	0.25	4	32	1	4
E. coli GC 2272	64	0.25	8	8	0.50	2	32	1	4
E. coli GC 4559	>64	0.25	32	16	0.50	8	64	2	16
E. coli GC 4560	2	0.12	1	1	0.12	0.50	4	0.50	2
E. coli GC 6465	>64	2	>64	>64	2	32	>64	2	16
E. coli GC 3226	>64	0.50	32	16	0.50	8	32	1	8
E. coli GC 2203	64	0.25	16	8	0.25	4	32	1	8
E. coli GC 1073	64	0.50	32	32	0.50	8	32	2	8
Salmonella spp. GC 235	>64	0.50	32	32	1	16	>64	2	32
Salmonella spp. GC 566	>64	2	>64	64	2	32	>64	4	32
S. cholerae GC 1355	>64	4	>64	>64	4	64	>64	4	64

TABLE IX (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water	Mouse Serum		Human Serum	Water		Mouse Serum		Human Serum		Water		Mouse Serum		Human Serum	
		Example 48	Example 48	Example 48	Example 48	Example 48	Example 49	Example 49	Example 49	Example 49	Example 50	Example 50	Example 50	Example 50	Example 50	Example 50
<i>S. typhimurium</i> GC 2172	>64	4	>64	>64	>64	>64	4	32	>64	>64	>64	>64	4	32	>64	>64
<i>P. aeruginosa</i> GC 2214	>64	16	>64	>64	>64	>64	32	>64	>64	>64	>64	>64	32	>64	>64	>64
<i>S. aureus</i> GC 1131	0.25	0.25	0.25	0.25	0.50	0.50	0.50	0.50	0.50	0.50	1	0.25	0.50	0.50	0.50	0.50
<i>S. aureus</i> GC 6466	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.25	0.25	0.25	0.25	0.25	0.25
<i>S. aureus</i> GC 6467	2	1	0.50	0.50	2	2	1	1	1	1	2	0.25	0.25	0.25	0.25	0.25
<i>S. aureus</i> GC 1079	1	0.25	0.25	0.25	0.50	0.50	0.50	0.50	0.50	0.50	2	0.50	0.50	0.50	0.50	0.50
<i>S. aureus</i> GC 4536	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.50	0.50	0.25	0.25	0.25	0.25
<i>S. aureus</i> GC 2216	0.50	0.25	0.25	0.25	0.50	0.50	0.25	0.25	0.25	0.25	2	2	1	0.50	0.50	0.50
<i>S. aureus</i> GC 6335	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1
<i>S. aureus</i> GC 6469	1	0.50	1	1	1	1	1	1	1	1	2	2	1	1	1	1
<i>S. epidermidis</i> GC 4935	1	0.50	0.50	0.50	2	2	1	1	1	1	4	4	2	2	2	2
<i>E. faecalis</i> GC 4555	2	0.12	4	4	4	4	0.25	0.50	0.50	0.50	4	4	1	1	2	2

TABLE IX (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water Example 48	Mouse Serum Example 48	Human Serum Example 48	Water Example 49	Mouse Serum Example 49	Human Serum Example 49	Water Example 50	Mouse Serum Example 50	Human Serum Example 50
<i>E. faecalis</i> GC 2265	2	0.50	1	2	0.50	1	4	1	2
<i>E. faecalis</i> GC 2267	2	0.50	1	4	0.50	1	4	1	2
<i>E. faecalis</i> GC 2242	1	0.50	1	2	0.50	1	2	1	1
<i>E. faecium</i> GC 4556	1	0.50	1	2	0.50	1	2	1	1
<i>E. faecium</i> GC 2243	0.50	0.25	0.25	0.50	0.25	0.25	0.50	0.25	0.25
<i>S. pneumoniae</i> * GC 4465	0.12	0.12	0.12	0.12	0.12	0.12	<0.06	<0.06	<0.06
<i>S. pneumoniae</i> + GC 4465	0.25	0.25	0.25	1	1	1	0.50	0.50	0.50
<i>S. pyogenes</i> GC 4563	0.12	0.12	0.12	0.12	0.12	0.12	0.25	0.12	0.12
<i>S. agalactiae</i> GC 4564	0.12	0.12	0.12	0.25	0.12	0.12	0.25	0.25	0.25
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE X

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCCLINES OF FORMULA I											
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)											
Water Example 51	Mouse Serum Example 51	Human Serum Example 51	Water Example 52	Mouse Serum Example 52	Human Serum Example 52	Water Example 53	Mouse Serum Example 53	Human Serum Example 53			
E. coli GC 2236	>64	2	32	8	1	8	32	1	16		
E. coli GC 2231	>64	2	32	16	1	8	64	1	16		
E. coli GC 2235	>64	1	32	4	0.50	4	32	0.50	8		
E. coli GC 2232	>64	2	32	8	0.50	4	32	0.50	8		
E. coli GC 2233	>64	2	32	8	0.50	8	32	1	16		
E. coli GC 2234	>64	1	32	8	0.50	4	16	0.50	8		
E. coli GC 2270	>64	1	32	4	0.50	4	32	1	8		
E. coli GC 2271	>64	1	32	4	0.50	4	16	0.50	8		
E. coli GC 2272	>64	2	32	4	0.50	4	16	0.25	8		
E. coli GC 4559	>64	2	32	8	1	8	32	1	16		
E. coli GC 4560	32	1	8	2	0.25	2	2	0.50	2		
E. coli GC 6465	>64	4	32	64	2	16	>64	4	32		
E. coli GC 3226	>64	2	64	16	1	16	32	1	16		
E. coli GC 2203	>64	2	32	8	0.50	8	32	1	16		
E. coli GC 1073	>64	2	64	4	1	8	32	1	16		
Salmonella spp. GC 235	>64	2	64	16	1	16	64	2	64		
Salmonella spp. GC 566	>64	4	64	64	2	32	>64	2	32		
S. cholerae GC 1355	>64	8	>64	>64	4	>64	>64	8	64		
S. typhimurium GC 2172	>64	8	64	64	4	64	>64	4	64		

TABLE X (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water Example 51	Mouse Serum Example 51	Human Serum Example 51	Water Example 52	Mouse Serum Example 52	Human Serum Example 52	Water Example 53	Mouse Serum Example 53	Human Serum Example 53
<i>P. aeruginosa</i> GC 2214	>64	64	>64	>64	64	>64	>64	64	>64
<i>S. aureus</i> GC 1131	1	0.50	0.50	2	0.50	1	1	1	1
<i>S. aureus</i> GC 6466	1	0.25	0.25	2	0.50	1	0.50	0.50	0.50
<i>S. aureus</i> GC 6467	2	0.50	1	4	0.50	4	2	1	1
<i>S. aureus</i> GC 1079	2	0.50	1	2	0.50	1	1	0.50	0.50
<i>S. aureus</i> GC 4536	1	0.50	0.50	2	0.50	0.50	1	0.25	0.50
<i>S. aureus</i> GC 2216	1	0.50	0.50	4	0.50	1	1	0.50	0.50
<i>S. aureus</i> GC 6335	1	0.50	0.50	4	1	2	1	0.50	0.50
<i>S. aureus</i> GC 6469	2	1	1	4	0.50	2	2	1	1
<i>S. epidermidis</i> GC 4935	4	2	2	4	1	4	2	1	2
<i>E. faecalis</i> GC 4555	16	1	8	4	0.50	2	2	0.50	2
<i>E. faecalis</i> GC 2265	8	1	4	4	1	4	4	1	0.50
<i>E. faecalis</i> GC 2267	16	2	4	4	0.50	4	4	0.50	2

TABLE X (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I									
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)									
	Water	Mouse Serum	Human Serum	Water Example 51	Mouse Serum Example 51	Human Serum Example 51	Water Example 52	Mouse Serum Example 52	Human Serum Example 52
	Example 51	Example 51	Example 51	Example 51	Example 51	Example 51	Example 52	Example 52	Example 52
	Water	Mouse Serum	Human Serum	Water Example 53	Mouse Serum Example 53	Human Serum Example 53	Water Example 53	Mouse Serum Example 53	Human Serum Example 53
E. faecalis GC 2242	8	2	4	4	0.50	4	4	0.50	2
E. faecium GC 4556	8	2	8	4	0.50	2	2	0.50	2
E. faecium GC 2243	4	1	4	1	0.25	1	0.50	0.25	0.25
S. pneumoniae* GC 4465	1	0.50	2	0.12	<0.06	0.25	0.12	0.12	0.25
S. pneumoniae+ GC 4465	1	1	2	2	1	4	2	2	1
S. pyogenes GC 4563	2	0.50	2	0.25	0.12	0.25	0.25	0.12	0.25
S. agalactiae GC 4564	2	1	4	0.50	0.12	0.50	0.50	<0.06	0.50
c. albicans GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE XI

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLOLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

	Water Example 58	Mouse Serum Example 58	Human Serum Example 58	Water Example 59	Mouse Serum Example 59	Human Serum Example 59	Water Example 60	Mouse Serum Example 60	Human Serum Example 60
<i>E. coli</i> GC 2236	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2231	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2235	>64	>64	>64	>64	>64	>64	>64	64	64
<i>E. coli</i> GC 2232	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2233	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2234	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2270	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2271	>64	>64	>64	>64	>64	>64	>64	64	64
<i>E. coli</i> GC 2272	>64	>64	>64	>64	64	>64	64	32	32
<i>E. coli</i> GC 4559	>64	>64	>64	>64	64	>64	>64	>64	>64
<i>E. coli</i> GC 4560	4	4	4	4	4	4	2	1	1
<i>E. coli</i> GC 6465	>64	>64	>64	>64	32	>64	>64	>64	>64
<i>E. coli</i> GC 3226	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 2203	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>E. coli</i> GC 1073	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>Salmonella</i> spp. GC 235	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>Salmonella</i> spp. GC 566	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>S. cholerae</i> GC 1355	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>S. typhimurium</i> GC 2172	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE XI (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCLYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water Example 58	Mouse Serum Example 58	Human Serum Example 58	Water Example 59	Mouse Serum Example 59	Human Serum Example 59	Water Example 60	Mouse Serum Example 60	Human Serum Example 60
<i>P. aeruginosa</i> GC 2214	>64	>64	>64	>64	>64	>64	>64	>64	>64
<i>S. aureus</i> GC 1131	4	2	4	4	4	4	8	2	2
<i>S. aureus</i> GC 6466	4	2	4	8	4	4	8	4	4
<i>S. aureus</i> GC 6467	4	2	4	4	4	4	8	4	4
<i>S. aureus</i> GC 1079	8	2	4	8	4	2	4	2	2
<i>S. aureus</i> GC 4536	4	2	4	4	4	4	4	2	2
<i>S. aureus</i> GC 2216	4	2	4	4	4	4	4	2	2
<i>S. aureus</i> GC 6335	4	4	4	4	4	4	8	8	8
<i>S. aureus</i> GC 6469	4	2	4	4	4	4	4	2	2
<i>S. epidermidis</i> GC 4935	8	4	4	4	4	4	16	8	8
<i>E. faecalis</i> GC 4555	8	4	4	4	4	4	4	4	2
<i>E. faecalis</i> GC 2265	4	4	4	4	4	4	8	8	4
<i>E. faecalis</i> GC 2267	4	2	4	4	4	4	8	8	4
<i>E. faecalis</i> GC 2242	4	2	4	4	2	4	8	8	4
<i>E. faecium</i> GC 4556	4	2	4	4	4	4	4	4	4
<i>E. faecium</i> GC 2243	4	2	4	4	4	8	4	2	2
<i>S. pneumoniae</i> * GC 4465	2	2	4	4	4	4	2	1	1
<i>S. pneumoniae</i> + GC 4465	8	4	4	8	4	8	4	4	2
<i>S. pyogenes</i> GC 4563	4	4	4	4	4	4	2	1	0.50
<i>S. agalactiae</i> GC 4564	8	8	16	8	8	8	4	4	4
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE XII

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

	Water Example 61	Mouse Serum Example 61	Human Serum Example 61	Water Example 62	Mouse Serum Example 62	Human Serum Example 62	Water Example 63	Mouse Serum Example 63	Human Serum Example 63
<i>E. coli</i> GC 2236	16	0.50	4	4	0.50	8	>64	1	>64
<i>E. coli</i> GC 2231	32	1	8	8	0.50	4	>64	1	>64
<i>E. coli</i> GC 2235	16	0.50	4	4	0.50	2	>64	0.50	>64
<i>E. coli</i> GC 2232	16	0.50	4	8	1	2	>64	1	>64
<i>E. coli</i> GC 2233	16	1	8	8	2	4	>64	1	>64
<i>E. coli</i> GC 2234	16	0.50	8	8	1	2	>64	1	64
<i>E. coli</i> GC 2270	16	0.50	4	8	0.50	2	>64	0.50	64
<i>E. coli</i> GC 2271	16	0.50	4	4	1	2	>64	0.50	>64
<i>E. coli</i> GC 2272	8	0.50	4	8	1	4	>64	1	>64
<i>E. coli</i> GC 4559	64	1	8	16	1	8	>64	2	>64
<i>E. coli</i> GC 4560	1	0.25	1	0.50	0.25	0.50	16	0.50	2
<i>E. coli</i> GC 6465	>64	1	32	>64	2	8	>64	2	>64
<i>E. coli</i> GC 3226	32	0.50	8	8	1	4	>64	1	>64
<i>E. coli</i> GC 2203	32	0.50	8	16	1	4	>64	1	>64
<i>E. coli</i> GC 1073	32	0.50	8	16	0.50	4	>64	2	>64
<i>Salmonella</i> spp. GC 235	>64	1	16	>64	1	8	>64	1	>64
<i>Salmonella</i> spp. GC 566	>64	1	32	>64	1	16	>64	1	>64
<i>S. choleraesuis</i> GC 1355	>64	2	64	>64	2	32	>64	2	>64

TABLE XII (CONT)
ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYL CYCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	Water Example 61	Mouse Serum Example 61	Human Serum Example 61	Water Example 62	Mouse Serum Example 62	Human Serum Example 62	Water Example 63	Mouse Serum Example 63	Human Serum Example 63
<i>S. typhimurium</i> GC 2172	>64	1	64	>64	2	16	>64	2	>64
<i>P. aeruginosa</i> GC 2214	>64	8	>64	>64	16	>64	>64	32	>64
<i>S. aureus</i> GC 1131	0.50	0.50	0.50	0.50	0.50	0.50	4	1	1
<i>S. aureus</i> GC 6466	0.50	0.50	0.50	0.25	0.50	0.50	2	0.50	1
<i>S. aureus</i> GC 6467	1	0.50	0.50	0.50	1	0.50	16	2	4
<i>S. aureus</i> GC 1079	1	0.25	0.50	0.50	1	0.50	8	1	2
<i>S. aureus</i> GC 4536	0.50	0.50	0.50	0.50	0.50	0.50	4	1	1
<i>S. aureus</i> GC 2216	1	0.50	0.50	0.50	0.50	0.50	4	1	1
<i>S. aureus</i> GC 6335	1	0.50	1	0.50	1	0.50	4	1	1
<i>S. aureus</i> GC 6469	2	0.50	0.50	1	1	0.50	16	1	2
<i>S. epidermidis</i> GC 4935	1	0.50	1	0.50	0.50	0.50	4	2	2
<i>E. faecalis</i> GC 4555	2	1	2	1	1	0.50	4	1	2
<i>E. faecalis</i> GC 2265	2	0.50	2	1	0.50	0.50	8	1	2
<i>E. faecalis</i> GC 2267	2	0.50	2	1	0.50	0.50	16	1	2
<i>E. faecalis</i> GC 2242	2	0.50	2	0.50	0.50	0.50	1	1	1

TABLE XII (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I									
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)									
	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum	Water	Mouse Serum	Human Serum
	Example 61	Example 61	Example 61	Example 62	Example 62	Example 62	Example 63	Example 63	Example 63
E. faecium GC 4556	2	0.50	2	1	1	1	0.50	1	4
E. faecium GC 2243	0.50	0.25	1	0.50	0.50	0.50	0.50	0.25	0.25
S. pneumoniae* GC 4465	0.12	0.12	0.25	0.12	0.12	0.12	0.12	0.12	0.12
S. pneumoniae+ GC 4465	0.50	0.50	0.50	0.50	1	0.50	0.50	0.50	0.50
S. pyogenes GC 4563	0.50	0.25	0.25	0.25	0.25	0.12	0.12	0.12	0.12
S. agalactiae GC 4564	0.25	0.25	0.50	0.25	0.25	0.12	0.25	0.25	0.25
c. albicans GC 3066	>64	>64	>64	>64	>64	>64	>64	>64	>64

TABLE XIII

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	MouseSerum Example 108	Water Example 108	MouseSerum Example 109	Water Example 109	MouseSerum Example 109	Water Example 109	MouseSerum Example 110	Water Example 110	
E. coli GC 2236	0.50	2	0.50	1	0.50	2	1	2	2
E. coli GC 2231	2	4	0.50	1	1	2	4	8	8
E. coli GC 2235	0.50	1	0.25	0.50	0.50	1	0.50	1	1
E. coli GC 2232	1	2	0.50	1	0.50	2	1	2	2
E. coli GC 2233	0.50	1	0.25	0.50	1	2	0.50	1	1
E. coli GC 2234	0.50	2	0.12	0.25	0.25	2	1	2	2
E. coli GC 2270	0.50	1	0.25	0.50	0.25	2	1	1	1
E. coli GC 2271	0.50	0.50	0.12	0.25	0.25	1	1	2	2
E. coli GC 2272	0.25	0.50	0.25	0.25	0.50	2	1	1	1
E. coli GC 4559	0.50	1	0.12	0.25	1	2	2	2	2
E. coli GC 4560	0.12	0.25	<0.06	<0.06	0.25	0.25	0.25	0.50	0.50
E. coli GC 6465	8	64	1	4	4	16	64	>64	>64
E. coli GC 3226	0.50	1	0.50	1	1	4	2	4	4
E. coli GC 2203	0.50	1	0.50	1	0.50	2	1	4	4
E. coli GC 1073	0.50	2	0.50	1	1	4	2	8	8
Salmonella spp. GC 235	1	4	1	2	1	4	4	8	8
Salmonella spp. GC 566	1	8	2	4	2	4	16	32	32
S. cholerae GC 1355	32	64	8	32	8	32	>64	>64	>64

TABLE XIII (CONT)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

	MouseSerum Example 108	Water Example 108	MouseSerum Example 109	Water Example 109	MouseSerum Example 109	Water Example 109	MouseSerum Example 110	Water Example 110
<i>S. typhimurium</i> GC 2172	4	32	4	16	4	16	64	>64
<i>P. aeruginosa</i> GC 2214	16	32	16	>64	32	>64	>64	>64
<i>S. aureus</i> GC 1131	0.25	0.50	1	2	1	4	2	4
<i>S. aureus</i> GC 6466	0.50	1	0.50	1	0.50	4	1	2
<i>S. aureus</i> GC 6467	2	8	2	4	2	8	32	>64
<i>S. aureus</i> GC 1079	2	4	2	4	2	8	16	16
<i>S. aureus</i> GC 4536	0.50	1	1	2	1	4	4	4
<i>S. aureus</i> GC 2216	0.50	1	1	2	0.50	8	2	4
<i>S. aureus</i> GC 6335	1	2	2	4	1	4	8	8
<i>S. aureus</i> GC 6469	0.25	1	1	2	2	8	32	32
<i>S. epidermidis</i> GC 4935	1	2	2	4	2	8	4	8
<i>E. faecalis</i> GC 4555	0.50	0.50	0.50	1	0.50	1	1	2
<i>E. faecalis</i> GC 2265	1	2	1	2	1	4	8	4

TABLE XIII (CONT)

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCCLINES OF FORMULA I
MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

	MouseSerum	Water	MouseSeru m	Water	MouseSeru m	Water	MouseSeru m	Water	MouseSeru m	Water
	Example 108	Example 108	Example 109	Example 109	Example 109	Example 109	Example 109	Example 109	Example 110	Example 110
<i>E. faecalis</i> GC 2267	1	2	1	2	1	4	8	4		
<i>E. faecalis</i> GC 2242	0.50	1	1	1	1	2	1	1		
<i>E. faecium</i> GC 4556	0.50	1	1	2	1	2	1	2		
<i>E. faecium</i> GC 2243	0.50	0.50	0.50	0.50	0.50	1	0.50	0.50		
<i>S. pneumoniae</i> * GC 4465	0.12	0.12	<0.06	0.12	<0.06	0.25	0.25	0.12		
<i>S. pneumoniae</i> + GC 4465	1	2	1	1	1	2	4	2		
<i>S. pyogenes</i> GC 4563	0.12	0.12	<0.06	0.12	0.12	0.25	0.12	<0.06		
<i>S. agalactiae</i> GC 4564	0.12	0.12	0.12	0.25	<0.06	0.25	0.25	0.25		
<i>c. albicans</i> GC 3066	>64	>64	>64	>64	>64	>64	>64	>64		

Table 1. In vitro activity (MIC)^a of representative examples of formula I

Ex Number	Minimum inhibitory concentration MIC (μ g/ml)			
	E.coli (Mouse Serum)	E.coli (Water)	Staph (Mouse Serum)	Staph (Water)
1	0.5-1	16-64	1-4	1-8
2	1-4	32-64	1-8	2-8
3	1-2	>64	1-4	4-32
4	0.5-2	64->64	0.5-2	2-16
5	1-2	16-64	0.25-2	0.5-4
6	1-2	8-64	0.5-2	1-4
7	0.25-2	2-16	0.5-4	0.5-4
8	1-2	16->64	0.5-4	1-8
9	0.5-2	4-64	<0.06-2	0.12-2
10	0.25-2	4-32	0.25-2	0.12-2
11	0.25-2	4->64	0.25-4	0.25-4
12	0.5-2	16-64	0.5-4	1-16
13	1-4	8-16	1-4	2-8
14	32->64	64->64	1-8	2-8
15	32->64	32->64	2-16	4-16
16	16->16	64->64	2-8	4-8
17	0.5-2	32-64	1-4	2-32
18	0.5-2	4-8	1-4	1-4
19	0.5-2	32->64	0.5-4	1-8
20	0.5-2	>64	1-4	64->64
21	0.5-8	>64	1-4	32->64
22	1-8	>64	0.5-4	2->64
23	1-8	>64	0.25-4	0.5-8
24	0.5-2	>64	0.25-4	0.5->64
25	1-2	32->64	0.25-2	0.5-4
26	1-4	64->64	0.25-1	0.25-4
27	0.5-1	32->64	0.12-2	0.12-2
28	0.25-1	>64	0.5-4	4-64
29	0.5-1	>64	0.25-2	1-4
30	0.5-1	32->64	0.25-2	1-8
31	0.5-1	16->64	0.25-2	0.5-4
32	0.5-1	1-4	0.25-2	0.5-4
33	0.5-2	32->64	0.12-2	0.12-2

5 ^a Range of MIC (minimum inhibitory concentration) for E. coli and Staph., including MRSA which are selected from those E. coli and Staph., presented in Tables I-XIII.

Table 1 (Cont)

Ex Number	Minimum inhibitory concentration MIC ^a (μg/ml)			
	E.coli (Mouse Serum)	E.coli (Water)	Staph (Mouse Serum)	Staph (Water)
34	0.5-1	4-16	0.25-4	0.25-4
35	4-8	8-64	2-4	2-4
36	2-8	8-32	2-4	4-16
37	2-4	4-32	1-4	2-4
38	0.5-4	64->64	0.5-2	1-8
39	1-4	16-32	1-4	2-16
40	1-2	16->64	0.25-2	0.25-2
41	0.5-4	16-64	0.5-4	1-8
42	4-16	>64	2-4	4-8
43	0.25-2	>64	0.5-2	32->64
44	2-8	>64	2	2-4
45	0.5-2	16->64	0.25-1	0.5-2
46	0.5-2	64->64	0.25-1	0.25-2
47	0.5-2	>64	1-2	2-4
48	0.25-2	32->64	0.12-2	0.12-2
49	0.25-2	8->64	0.12-1	0.12-2
50	1-2	32-64	0.25-2	0.25-4
51	1-2	>64	0.25-2	1-4
52	0.5-1	4-16	0.5-1	2-4
53	0.25-1	16-64	0.25-1	0.5-2
54	0.5-1	>64	0.5-2	1-4
55	0.5-8	64->64	1-2	2-8
56	0.25-2	8->64	0.25-1	1-4
57	0.5-4	>64	0.5-2	4-16
58	>64	>64	2-4	4-8
59	32->64	>64	4	4-8
60	32->64	64->64	2-8	4-16
61	0.5-1	8->64	0.25-0.5	0.5-2
62	0.5-2	4->64	0.5-1	0.25-1
63	0.5-2	>64	0.5-2	2-16
64	<0.12	<0.12 - 1	<0.12 - 0.25	<0.12 - 0.5
	<0.12 -			
65	0.5	16	<0.12 - 0.5	<0.12 - 1
66	>128	>128	1-16	2-16
	<0.12 -			
67	0.25	8-32	<0.12 - 0.25	<0.12 - 1
68	<0.12 - 1	2-8	<0.12 - 0.25	<0.12 - 1

^a Range of MIC (minimum inhibitory concentration) for E. coli and Staph., including MRSA which are selected from those E. coli and Staph., presented in Tables I-XIII.

Table 1 (Cont)

Ex Number	Minimum inhibitory concentration MIC ^a (μ g/ml)			
	E.coli (Mouse Serum)	E.coli (Water)	Staph (Mouse Serum)	Staph (Water)
	<0.12 -			
69	0.5	8-64	<0.12 - 0.25	<0.12 - 1
70	4-8	>64	1-4	2-4
71	0.12-0.25	>64	0.5-1	32-64
72	0.5-1	>64	0.5-1	4-8
73	0.5-1	>64	1-4	4-8
74	0.25-1	>64	0.5-4	64->64
75	16->64	>64	8-16	16-32
76	16->64	>64	8-16	8-32
77	8->64	>64	2-4	4-32
78	16-64	>64	8	8-32
79	16->64	>64	4	4-8
80	16->64	64->64	4-8	4-16
81	0.5-1	8-16	0.5-2	4-8
82	64->64	>64	4-16	4-8
83	64->64	>64	8-32	2-16
84	2-4	>64	0.5-2	0.5-4
85	1-2	>64	1-2	4-16
86	8-16	>64	2-8	8
87	64->64	>64	32-64	>64
88	0.5-2	8-16	1-4	4-16
89	0.25-1	4-8	0.5-1	1-4
90	2-4	>64	0.25-2	1-16
91	0.5-2	>64	0.12-0.25	0.25-2
92	4-8	>64	4	8-32
93	1-4	64->64	1-2	32-64
94	32-64	>64	16-32	>64
95	>64	>64	16->64	>64
96	0.25-1	64->64	0.25-1	4-16
97	4-8	>64	1-4	4-8
98	1-4	>64	0.5-2	2-4
99	1-2	>64	0.5-2	2-4
100	2	64->64	0.5-1	2-4
101	1	16-32	0.5-2	4-16
102	0.5-1	>64	0.5-1	64->64
103	8-16	>64	8-16	64->64
104	8-16	>64	16-64	64->64
105	2	>64	1-2	16->64

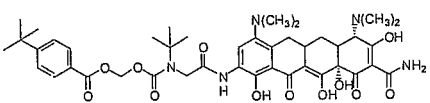
^a Range of MIC (minimum inhibitory concentration) for E. coli and Staph., including MRSA which are selected from those E. coli and Staph., presented in Tables I-XIII.

Table 1 (Cont)

Ex Number	Minimum inhibitory concentration MIC ^a (μ g/ml)			
	E.coli (Mouse Serum)	E.coli (Water)	Staph (Mouse Serum)	Staph (Water)
106	>64	>64	>64	>64
107	>64	0.5-1	2-8	0.5-1
108	0.5-2	0.5-4	0.25-2	1-8
109	0.25-1	1-4	0.5-2	4-8
110	0.5-4	1-8	1-32	2->64
111	0.25-1	1-4	0.5-8	1-16
112	1-4	2-8	2-8	4-16
113	1-4	2-16	4-16	4-32

^a Range of MIC (minimum inhibitory concentration) for E. coli and Staph., including MRSA which are selected from those E. coli and Staph., presented in Tables I-XIII.

5 Table 2. In vitro activity (MIC) of Example 87.

Example 87			
			
	water	Mouse serum	Human serum
E. coli, tet(A-D), efflux	>64	0.25-0.5	>64
E. coli, tet (M,S,O) Tet (M)	>64	0.25-0.5	>64
E. coli (susceptible)	>64	0.5	>64
E. coli (IMP)	32	<0.06	16
S. aureus, tet (M)	64	0.5	16
S. aureus, tet (K), efflux	64	1	32
S. aureus (susceptible) ^a	32	1	16
Enterococcus spp.	0.25-32	0.12-0.5	0.25-8
Streptococcus spp.	0.5-2	<0.06	1-2
C. albicans	>64	>64	>64

^a Strain used for the in vivo testing

Representative examples of compounds of Formula I were further evaluated for oral efficacy, stability in physiological pH in mouse serum and human plasma.

5

Table 3. In vitro activity (MIC)^a of representative examples of compounds of Formula I

Minimum inhibitory concentration (MIC), $\mu\text{g/mL}$				
Ex. No.	E. coli (mouse serum)	E. coli (water)	Staph. (mouse serum)	Staph. (water)
1	0.5-1	16-64	1-4	1-8
2	1-4	32-64	1-8	2-8
3	1-2	>64	1-4	4-32
4	0.5-2	64->64	0.5-2	2-16
12	0.5-2	16-64	0.5-4	1-16
13	1-4	8-16	1-4	2-8
17	0.5-2	32-64	1-4	2-32
18	0.5-2	4-8	1-4	1-4
20	0.5-2	>64	1-4	64->64
21	0.5-8	>64	1-4	32->64
22	1-8	>64	0.5-4	2->64
23	1-8	>64	0.25-4	0.5-8
29	0.5-1	>64	0.25-2	1-4
30	0.5-1	32->64	0.25-2	1-8
34	0.5-1	4-16	0.25-4	0.25-4
36	2-8	8-32	2-4	4-16
38	0.5-4	64->64	0.5-2	1-8
39	1-4	16-32	1-4	2-16

^a Range of MIC (minimum inhibitory concentration) for E. coli and Staph., including MRSA which are selected from those E. coli and Staph., presented in Tables I-XIII.

15

Table 4. In vitro activity (MIC)^a of representative examples of compounds of Formula

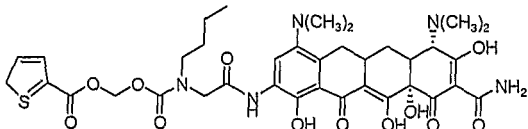
5 I

Ex. No.	Minimum inhibitory concentration (MIC), μ g/mL			
	E. coli (mouse serum)	E. coli (water)	Staph. (mouse serum)	Staph. (water)
5	1-2	16-64	0.25-2	0.5-4
6	1-2	8-64	0.5-2	1-4
7	0.25-2	2-16	0.5-4	0.5-4
8	1-2	16->64	0.5-4	1-8
9	0.5-2	4-64	0.06-1	0.12-2
10	0.25-2	4-32	0.25-2	0.12-2
11	0.25-2	4->64	0.25-4	0.25-4
19	0.5-2	32->64	0.5-4	1-8
24	0.5-2	>64	0.25-4	0.5->64
25	1-2	32->64	0.25-2	0.5-4
26	1-4	64->64	0.25-1	0.25-4
27	0.5-1	32->64	0.12-2	0.12-2
28	0.25-1	>64	0.5-4	4-64
31	0.5-1	16->64	0.25-2	0.5-4
33	0.5-2	32->64	0.12-2	0.12-2
35	4-8	8-64	2-4	2-4
40	1-2	16->64	0.25-2	0.25-2
41	0.5-4	16-64	0.5-4	1-8

^a Range of MIC (minimum inhibitory concentration) for E. coli and Staph. including MRSA which are selected from those E. coli and Staph., presented in Tables I-XIII.

10

Table 5. In vitro activity (MIC) of Example 27

Example 27			
			
	water	Mouse serum	Human serum
E. coli, tet(A-D), efflux	64->64	0.5-1	4-16
E. coli, tet (M,S,O) Tet (M)	0.5	0.5	4-8
E. coli (susceptible)	0.5	0.5	16
E. coli (IMP)	0.25	0.25	0.5
S. aureus, tet (M)	0.12	0.12	0.25
S. aureus, tet (K), efflux	1	1	1
S. aureus (susceptible) ^a	0.12	0.12	0.5
Enterococcus spp.	0.12-1	0.12-1	0.5-2
Streptococcus spp.	<0.06- 0.12	<0.06-0.12	0.12-2
C. albicans	>64	>64	>64

^a Strain used for in vivo testing

- 5 Representative examples of compounds of Formula I were tested for the oral efficacy using *S. aureus* Smith in mice. The summary of in vivo and in vitro activities of selected compounds are listed in Table 6.

Table 6. In vitro and in vivo activity of representative examples of compounds of Formula I against Staph. aureus Smith in mice.

Ex. No.	ED ₅₀ mg/kg (Staph aureus Smith)		μg/mL (Staph aureus Smith)
	SOD ^b	SIV ^c	MIC ^a
42	5.68	1.43	8
44	4	0.75	4
45	5.9	0.66	1
47	14	1.2	4
48	10.1	1.1	0.25
49	16	0.92	0.25
50	16.88	1.65	0.5
52	10.69	1.29	2
53	5.08	0.73	1
54	8.4	0.83	0.5
87	12.82	0.83	32

5 ^a MIC (minimum inhibitory concentration)

^b SOD (Single oral dose)

^c SIV (Single intravenous dose)

10 Representative examples of compounds of Formula I were tested in vivo against gram-negative bacteria (*E. coli*) in mice. Results of the tests (MIC, oral and IV) are list in Table 7.

Table 7. In vivo (oral, iv) and in vitro (MIC)^a activity of representative examples of compounds of Formula I against *E. coli* in mice .

Ex. No.	ED ₅₀ mg/kg (<i>E. coli</i>)		μg/mL (<i>E. coli</i>)
	SOD ^b	SIV ^c	MIC
5	>64	3.17	>64
42	30.3	3.1	>64
44	42.8	2.85	>64
45	64	1.8	64
48	29.8	1.7	>64
49	49	2.2	64
50	29.8	1.7	>64
52	43.7	3.78	8
53	46.88	2.25	32
54	29.2	2.16	>64
87	60.4	3.6	>64

5 ^a MIC (minimum inhibitory concentration)

^b SOD (Single oral dose)

^c SIV (Single intravenous dose)

Test results of in vivo activity are shown in Table 8 for representative examples of compounds of Formula I .

- 5 Table 8. In vivo (oral, iv) and in vitro (MIC)^a activity of representative examples of compounds of Formula I, against Staph aureus Smith in mice .

Ex. No.	ED ₅₀ mg/kg (Staph aureus Smith)		μg/mL (Staph aureus Smith)
	SOD ^b	SIV ^c	MIC
1	4.7	0.6	4
5	8.51	0.5	1
19	8.05	0.31	1
26	8.79	0.43	0.5
27	3.9	0.44	0.12
28	6.61	0.6	32
33	4.91	0.48	0.12
35	3.5	0.43	4
36	5.15	0.84	8
38	5.3	0.6	2
40	4.65	0.39	0.5

^a MIC (minimum inhibitory concentration)

^b SOD (Single oral dose)

10 ^c SIV (Single intravenous dose)

Table 9

Ex No.	Minimum inhibitory concentration (MIC), $\mu\text{g/mL}$			
	E.coli (Human Serum)	E.coli (Water)	Staph (Human Serum)	Staph (Water)
4	8-32	32->64	0.5-4	2-8
19	8-32	16->64	0.12-1	0.25-4
27	4-16	64->64	0.25-2	0.5-4
42	>64	>64	2-4	4-8
43	>64	>64	4-64	32->64
44	>64	>64	2-4	2-4
45	4-16	16->64	0.12-1	0.5-2
46	4-16	64->64	0.25-1	0.25-2
47	16->64	>64	1-4	2-4
48	8->64	32->64	0.12-2	0.12-2
49	4-32	8->64	0.12-1	0.12-2
50	4-16	32-64	0.25-2	0.25-4
51	32-64	>64	0.25-2	1-4
52	4-16	4-16	0.5-4	2-4
53	8-16	16-64	0.5-2	0.5-2
54	16-32	>64	0.5-2	1-4
55	32->64	64->64	1-4	2-8
56	4-32	8->64	0.25-2	1-4
57	>64	>64	1-8	4-16
58	>64	>64	4	4-8
59	>64	>64	2-4	4-8
60	32->64	64->64	2-8	4-16
61	4-32	8->64	0.5-1	0.5-2
62	2-8	4->64	0.5	0.25-1
63	64->64	>64	1-4	2-16
102	64->64		>64	
105	64->64		8->64	

Table 10

Ex. No.	ED ₅₀ (mg/kg) Staph Smith		ED ₅₀ mg/kg E. coli #311		IV - RAT 2 mg/kg			PO - RAT 20 mg/kg		
	SOD	SIV	SOD	SIV	Cmax	AUC	T _{1/2}	Cmax	AUC	%BA
1										
2	13.27	0.71								
3	16.05	0.59								
4	11.6	0.39	>32	>2						
5	8.51	0.5								
6	20.05	0.87								
7	16.1	0.52								
8	16.63	0.48								
9	11.27	0.32								
10	13.62	0.36								
11	30.27	0.59								
12	15.02	1								
13	10.98	0.82								
14	>32	>2								
16	>32	>2								
17	59.9	1.07								
18	29.02	0.6								
19	8.05	0.31	>32	>2						
20	19.4	0.6								
21	>32	0.77								
22	18.77	0.43								

Table 10 (cont)

Ex. No.	ED ₅₀ (mg/kg) Staph Smith		ED ₅₀ mg/kg E. coli #311		IV - RAT 2 mg/kg		PO - RAT 20 mg/kg		%BA	
	SOD	SIV	SOD	SIV	Cmax	AUC	T1/2	Cmax		AUC
23	19.01	0.47								
24	27	0.59								
25	15.71	0.56								
26	8.79	0.43								
27	3.9	0.44	>32	>2						
28	6.61	0.6	>32	>2						
29	13.67	0.43								
30	15.1	0.41								
31	11.11	0.31								
32	7.7	0.56								
33	4.91	0.45								
34	12.86	0.71								
35	3.5	0.43								
36	5.15	0.84								
37	4.1	0.55								
38	5.3	0.6								
39	13.3	0.6								
40	4.65	0.39								
41	11.3	0.83								
42	5.68	1.43	30.3	3.1	4.1	1.6	5.1	0.22	0.64	8.1
43	12.82	0.83	60.4	3.6	6.5	2.4	3.5	0.05	0.27	2.3
44	4	0.75	42.8	2.85						
45	5.9	0.66	64	1.8						

Table 10 (cont)

Ex. No.	ED ₅₀ (mg/kg) Staph Smith		ED ₅₀ mg/kg E. coli #311		IV - RAT 2 mg/kg		PO - RAT 20 mg/kg			
	SOD	SIV	SOD	SIV	Cmax	AUC	T1/2	Cmax	AUC	%BA
46	8.4	0.83	29.2	2.16						
47	14	1.2	>64	3.17						
48	10.1	1.1	29.8	1.7						
49	16.6	0.92	49	2.2						

Table 10 (cont)

Ex. No.	ED ₅₀ (mg/kg) Staph Smith		ED ₅₀ mg/kg E. coli #311		IV - RAT 2 mg/kg			PO - RAT 20 mg/kg		
	SOD	SIV	SOD	SIV	Cmax	AUC	T1/2	Cmax	AUC	%BA
50	16.88	1.65	>64	2.59						
52	10.69	1.29	43.7	3.78						
53	5.08	0.73	46.88	2.25						
54	>16	1.17	>32	3.72						
55	>16	1.81	32	4.69						
56	>16	0.79								
57	6.36	1.17								
58			>32	>8						
59			>32	>8						
60			>32	>8						
61			>32	2-4						
62			>32	4-8						
63			>32	4-8						
71	>32	1	>32	>4						
74	>32	1.08	>32	>4						
81	16-32	>4								
82	21.97	0.52								
90	16-32	0.5-1								
91	11.73	1.21								
93	>32	0.5-1								
96	16-32	1-2	>32	2-4						
102	19.81	1.59	>32	2-4						

Table 10 (cont)

Ex No	ED ₅₀ (mg/kg) Staph Smith		ED ₅₀ mg/kg E. coli #311		SIV		IV - RAT 2 mg/kg		T _{1/2}		PO - RAT 20 mg/kg		%BA
	SOD	SIV	SOD	SIV	Cmax	AUC	Cmax	AUC	Cmax	AUC	Cmax	AUC	
108	>32	>2											
109	19.94	0.76											
110	31.94	0.6											
112	6.12	0.48											
113	7.01	0.4											

Table 10 (cont)

Table 10 (cont.)																
Ex No	IV - DOG				Oral - DOG				IV - MONKEY				Oral - MONKEY			
	2 mg/kg				10 mg/kg				2 mg/kg				10 mg/kg			
	Cmax	AUC	T1/2	Cmax	AUC	%BA	Cmax	AUC	T1/2	Cmax	AUC	T1/2	Cmax	AUC	%BA	
1	10.8	8.3	14.9	0.11	0.67	1.6%	9.1	3.3	17.6	no levels detected						
27	1.9	9.8	10.7	0.018	0.22	0.5%	20	9.3	7.3	0.04	0.21	0.5%				
28	0.55	6	7.8	0.09	0.74	2.5%	0.77	3.6	13.2	0.05	0.23	1.3%				

When the compounds of the invention are employed as antibacterials, they can be combined with one or more pharmaceutically acceptable carriers, for example,
5 solvents, diluents and the like, and may be administered orally in such forms as tablets, capsules, dispersible powders, granules, or suspensions containing, for example, from about 0.05 to 5% of suspending agent, syrups containing, for example, from about 10 to 50% of sugar, and elixirs containing, for example, from about 20 to 50% ethanol, and the like, or parenterally in the form of sterile injectable
10 solutions or suspensions containing from about 0.05 to 5% suspending agent in an isotonic medium. Such pharmaceutical preparations may contain, for example, from about 25 to about 90% of the active ingredient in combination with the carrier, more usually between about 5% and 60% by weight.

An effective amount of compound from 2.0 mg/kg of body weight to 100.0 mg/kg of
15 body weight may be administered one to five times per day via any typical route of administration including but not limited to oral, parenteral (including subcutaneous, intravenous, intramuscular, intrasternal injection or infusion techniques), topical or rectal, in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles. It will be understood,
20 however, that the specific dose level and frequency of dosage for any particular patient may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular
25 condition, and the host undergoing therapy.

These active compounds may be administered orally as well as by intravenous, intramuscular, or subcutaneous routes. Solid carriers include starch, lactose, dicalcium phosphate, microcrystalline cellulose, sucrose and kaolin, while liquid
carriers include sterile water, polyethylene glycols, non-ionic surfactants and edible
30 oils such as corn, peanut and sesame oils, as are appropriate to the nature of the active ingredient and the particular form of administration desired. Adjuvants customarily employed in the preparation of pharmaceutical compositions may be

advantageously included, such as flavoring agents, coloring agents, preserving agents, and antioxidants, for example, vitamin E, ascorbic acid, BHT and BHA.

The preferred pharmaceutical compositions from the standpoint of ease of preparation and administration are solid compositions, particularly tablets and hard-filled or liquid-filled capsules. Oral administration of the compounds is preferred.

These active compounds may also be administered parenterally or intraperitoneally.

Solutions or suspensions of these active compounds as a free base or pharmacologically acceptable salt can be prepared in water suitably mixed with a

surfactant such as hydroxy-propylcellulose. Dispersions can also be prepared in

glycerol, liquid, polyethylene glycols and mixtures thereof in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

The pharmaceutical forms suitable for injectable use include sterile aqueous

solutions or dispersions and sterile powders for the extemporaneous preparation of

sterile injectable solutions or dispersions. In all cases, the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the

conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacterial and fungi. The carrier can

be a solvent or dispersion medium containing, for example, water, ethanol, polyol

(e.g., glycerol, propylene glycol and liquid polyethylene glycol), suitable mixtures thereof, and vegetable oil.

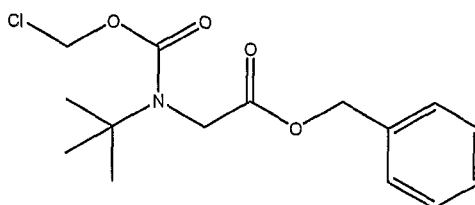
The present invention further provides a method of treating bacterial infections in warm-blooded animals including man, which comprises providing to the afflicted warm-blooded animals an antibacterially effective amount of a compound or a pharmaceutical composition of a compound of the invention.

The invention will be more fully described in conjunction with the following specific examples which are not to be construed as limiting the scope of the invention.

5

Reference Compound 1

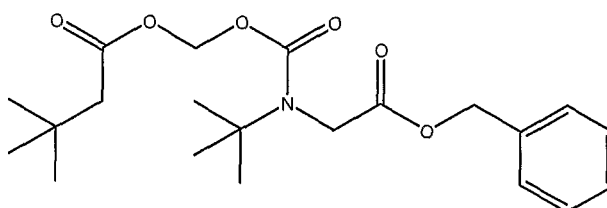
(Tert-butyl-chloromethoxycarbonyl-amino)-acetic acid benzyl ester.



- 10 To a solution of tert-butylamino-acetic acid benzyl ester in dichloromethane is added two equivalents of [1,8-bis(dimethylamino)naphthalene, N,N,N',N'-tetramethyl-1,8-naphthalenediamine]. The reaction mixture is then cooled in an ice bath and one equivalent of chloromethyl chloroformate is added. The reaction is then warm to room temperature and continue to stir for 24 hr. It is then washed with water and then
- 15 brine.

Reference Compound 2

- 20 3,3-Dimethyl-butyrac acid (benzyloxycarbonylmethyl-tert-butyl-carbamoyloxy)-methyl ester



- 25 Tert-butylacetic acid and 1.0 M tetrabutylammonium hydroxide in methanol is stirred for an hour, methanol is removed and THF is added. To this solution is then added benzyl N-(tert-butyl)-N-[(chloromethoxy)carbonyl]glycinate and stirred at room temperature for 24 hr. Solvent is removed and residue is diluted with ether, then

washed with water, then brine. It is dried over magnesium sulfate, filtered and solvent removed. MS (ESI) m/z 394.25

5

Reference Compounds 3-55 (Table A)

Substantially following the method described in detail hereinabove in Reference Compound 2 using (tert-butyl-chloromethoxycarbonyl-amino)-acidic acid benzyl ester
 10 from Reference Compound 1 and the appropriate carboxylic acid, the reference compounds 3-55 of this invention listed below in Table A are prepared.

Table A

15

Ref. Cpd. No.	Name	Spectra
3	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate	MS (ESI) m/z 456.23
4	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate	MS m/z 01-400386LMS;
5	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-methylpropanoate	MS (ESI) m/z 366.24; HRMS: calcd for C ₁₉ H ₂₇ NO ₆ + Na ⁺ , 388.17306; found (ESI ⁺ , [M+NA] ¹⁺), 388.17295;
6	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclopentanecarboxylate	MS (ESI) m/z 392.23;
7	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate	MS (ESI) m/z 414.24; MS (ESI) m/z 436.23; HRMS: calcd for C ₂₃ H ₂₇ NO ₆ + Na ⁺ , 436.17306; found (ESI ⁺ , [M+NA] ¹⁺), 436.17291;

Ref. Cpd. No.	Name	Spectra
8	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl heptanoate	MS (ESI) m/z 408.24;
9	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl propionate	MS (ESI) m/z 352.17; HRMS: calcd for C ₁₈ H ₂₅ NO ₆ + H ⁺ , 352.17546; found (ESI ⁺ , [M+H] ⁺), 352.17551;
10	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate	MS (ESI) m/z 406.26;
11	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate MS (ESI) m/z 428.25; MS (ESI) m/z 87.54;	MS (ESI) m/z 428.25; MS (ESI) m/z 87.54;
12	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate	MS (ESI) m/z 418.2; MS (ESI) m/z 440.2;
13	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-methylbutanoate	MS (ESI) m/z 380.27; HRMS: calcd for C ₂₀ H ₂₉ NO ₆ + Na ⁺ , 402.18871; found (ESI ⁺ , [M+NA] ¹⁺), 402.18882;
14	benzyl N-(tert-butyl)-N-({[(cyclopentylacetyl)oxy]methoxy}carbonyl)glycinate	MS (ESI) m/z 406.2;
15	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(trifluoromethyl)benzoate	MS (CI(ISOBUTANE)) m/z 468.13;
16	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclopropanecarboxylate	MS (ESI) m/z 364.26;
17	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate	MS (ESI) m/z 458.3;
18	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl pentanoate	MS (ESI) m/z 380.2;

Ref. Cpd. No.	Name	Spectra
19	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclobutanecarboxylate	MS (ESI) m/z 378.2; MS (ESI) m/z 400.2;
20	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-cyclohexylpropanoate	MS (ESI) m/z 434.3; MS (ESI) m/z 451.3; HRMS: calcd for C ₂₄ H ₃₅ NO ₆ + Na ⁺ , 456.23566; found (ESI ⁺ , [M+NA] ¹⁺), 456.23661;
21	benzyl N-(tert-butyl)-N-([[(4-fluorophenoxy)acetyl]oxy]methoxy)carbonyl]glycinate	
22	benzyl N-(tert-butyl)-N-([[(cyclohexylacetyl)oxy]methoxy]carbonyl)glycinate	MS (ESI) m/z 420.2; MS (ESI) m/z 442.2;
23	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,6-dimethylbenzoate	MS (ESI) m/z 428.2;
24	benzyl N-(tert-butyl)-N-([[(phenylacetyl)oxy]methoxy]carbonyl)glycinate	MS (ESI) m/z 414.2; MS (ESI) m/z 436.2; HRMS: calcd for C ₂₃ H ₂₇ NO ₆ + H ⁺ , 414.19112; found (ESI ⁺ , [M+H] ¹⁺), 414.19143;
25	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl pivalate	MS (ESI) m/z 380.1; MS (ESI) m/z 781.3; HRMS: calcd for C ₂₀ H ₂₉ NO ₆ + H ⁺ , 380.20677; found (ESI ⁺ , [M+H] ¹⁺), 380.20649;

Ref. Cpd. No.	Name	Spectra
26	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-benzofuran-2-carboxylate	MS (ESI) m/z 440; MS (ESI) m/z 901.1; HRMS: calcd for C ₂₄ H ₂₅ NO ₇ + H ⁺ , 440.17038; found (ESI ⁺ , [M+H] ¹⁺), 440.17005;
27	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-pyrrole-2-carboxylate	MS (ESI) m/z 403.3; MS (ESI) m/z 827.7;
28	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate	MS (ESI) m/z 476.2; HRMS: calcd for C ₂₈ H ₂₉ NO ₆ + Na ⁺ , 498.18871; found (ESI ⁺ , [M+NA] ¹⁺), 498.18857;
29	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate	MS (ESI) m/z 430.3; MS (ESI) m/z 452.3;
30	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1H-indole-2-carboxylate	MS (ESI) m/z 439.1; HRMS: calcd for C ₂₄ H ₂₆ N ₂ O ₆ + Na ⁺ , 461.16831; found (ESI ⁺ , [M+NA] ¹⁺), 461.168;
31	benzyl N-(tert-butyl)-N-({[(diphenylacetyl)oxy]methoxy}carbonyl)glycinate	MS (ESI) m/z 490.2;
32	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-naphthoate	MS (ESI) m/z 450.1;
33	({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-naphthoate	MS (ESI) m/z 450.1;

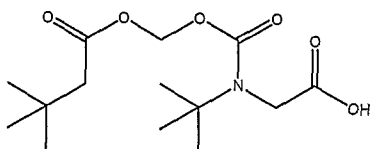
Ref. Cpd. No.	Name	Spectra
34	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-indole-3-carboxylate	MS (ESI) m/z 453.3; MS (ESI) m/z 905.6; MS (ESI) m/z 927.5;
35	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl quinoline-2-carboxylate	MS (ESI) m/z 451.2; MS (ESI) m/z 901.4;
36	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl nicotinate	MS (ESI) m/z 401.1;
37	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl isonicotinate	MS (ESI) m/z 401;
38	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,6-difluorobenzoate	MS (ESI) m/z 436.2; MS (ESI) m/z 893.4; MS (ESI) m/z 453.2;
39	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-fluorobenzoate	MS (ESI) m/z 418.2; MS (ESI) m/z 857.5; MS (ESI) m/z 440.2;
40	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-(trifluoromethyl)benzoate	MS (ESI) m/z 468.1; MS (ESI) m/z 490.2;
41	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(1H-pyrrol-1-yl)benzoate	MS (ESI) m/z 465.1; MS (ESI) m/z 482.1;
42	({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-2-carboxylate	MS (ESI) m/z 476.3; MS (ESI) m/z 493.3; MS (ESI) m/z 951.6;

Ref. Cpd. No.	Name	Spectra
43	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,4,6-trimethylbenzoate	MS (ESI) m/z 442.3; MS (ESI) m/z 459.3;
44	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-isopropoxybenzoate	MS (ESI) m/z 458.3;
45	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,4,5-trimethoxybenzoate	MS (ESI) m/z 490.3; MS (ESI) m/z 996.5; MS (ESI) m/z 979.5;
46	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-dimethoxybenzoate	MS (ESI) m/z 460.3; MS (ESI) m/z 936.5; MS (ESI) m/z 919.5;
47	3-phenyl-acrylic acid (benzyloxycarbonylmethyl-tert-butyl-carbamoyloxy)-methyl ester	PE added cpd
48	({[[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-methyl-1-benzofuran-2-carboxylate	MS (ESI) m/z 454.2; MS (ESI) m/z 907.5; HRMS: calcd for C ₂₅ H ₂₇ NO ₇ + Na ⁺ , 476.16797; found (ESI, [M+NA] ¹⁺), 476.16858;

Ref. Cpd. No.	Name	Spectra
49	benzyl N-({[3,5-bis(trifluoromethyl)phenyl]acetyl}oxy)methoxy]carbonyl)-N-(tert-butyl)glycinate	MS m/z 01-305267LMS; HRMS: calcd for C ₂₅ H ₂₅ F ₆ NO ₆ + Na ⁺ , 572.14783; found (ESI ⁺ , [M+NA] ¹⁺), 572.14702;
50	([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(heptyloxy)benzoate	MS (ESI) m/z 514.3; HRMS: calcd for C ₂₉ H ₃₉ NO ₇ + H ⁺ , 514.27993; found (ESI ⁺ , [M+H] ¹⁺), 514.28023;
51	([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-(2-phenylethyl)benzoate	MS (ESI) m/z 526.2;
52	([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(dodecyloxy)benzoate	MS (ESI) m/z 584.3; HRMS: calcd for C ₃₄ H ₄₉ NO ₇ + H ⁺ , 584.35818; found (ESI ⁺ , [M+H] ¹⁺), 584.3574;
53	([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(acetylamino)benzoate	MS (ESI) m/z 457.2; MS (ESI) m/z 913.4; HRMS: calcd for C ₂₄ H ₂₈ N ₂ O ₇ + Na ⁺ , 479.17887; found (ESI ⁺ , [M+NA] ¹⁺), 479.17909;
54	([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl anthracene-9-carboxylate	MS (ESI) m/z 500.2; MS (ESI) m/z 999.5;
55	([2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-benzoylbenzoate	MS (ESI) m/z 504.2;

Reference Compound 56

3,3-Dimethyl-butyrlic (tert-butyl-carboxymethyl-carbamoyloxy)-methyl ester.



5

The product from Reference Compound 2, 10% palladium on carbon in ethyl acetate is hydrogenated in a Parr shaker at ca. 40 psi for about an hour. The catalyst is
10 filtered and solvent removed to give the corresponding carboxylic acid product of the example MS(ESI) m/z 394.25.

15

Reference Examples 57-108 (Table B)

Substantially following the method described in detail hereinabove in Reference Compound 56 the reference compounds 57-108 of this invention listed below in Table B are prepared using the appropriate benzyl esters of Reference Compounds
20 3-55.

25

Table B

Ref. Cpd. No.	Name	Spectra
57	N-(tert-butyl)-N-({[(4-tert-butylbenzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 366.18
58	N-(tert-butyl)-N-({[(isobutyryloxy)methoxy]carbonyl}glycine	MS (ESI) m/z 274.05; MS (ESI) m/z 549.13; HRMS: calcd for C ₁₂ H ₂₁ NO ₆ + H ⁺ , 276.14416; found (ESI ⁺ , [M+H] ¹⁺), 276.14314;
59	N-(tert-butyl)-N-({[(cyclopentylcarbonyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 300.04; MS (ESI) m/z 601.1; HRMS: calcd for 2 C ₁₄ H ₂₃ NO ₆ - H ⁺ , 601.29780; found (ESI ⁻ , [2M-H] ¹⁻), 601.29741;
60	N-(tert-butyl)-N-({[(4-methylbenzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 324.19; HRMS: calcd for C ₁₆ H ₂₁ NO ₆ + Na ⁺ , 346.12611; found (ESI ⁺ , [M+NA] ¹⁺), 346.12625;
61	N-(tert-butyl)-N-({[(heptanoyloxy)methoxy]carbonyl}glycine	MS (ESI) m/z 316.25; MS (ESI) m/z 633.54;

Ref. Cpd. No.	Name	Spectra
62	N-(tert-butyl)-N-[(propionyloxy)methoxy]carbonyl)glycine	MS (ESI) m/z 260.05; MS (ESI) m/z 521.13; HRMS: calcd for C ₁₁ H ₁₉ NO ₆ + Na ⁺ , 284.11046; found (ESI, [M+NA] ⁺), 284.11017;
63	N-(tert-butyl)-N-([(cyclohexylcarbonyl)oxy]methoxy)carbonyl)glycine	MS (ESI) m/z 314.06; MS (ESI) m/z 629.14; HRMS: calcd for 2 C ₁₅ H ₂₅ NO ₆ - H ⁺ , 629.32910; found (ESI-, [2M-H] ¹⁻), 629.32842;
64	N-(tert-butyl)-N-([(3,5-dimethylbenzoyl)oxy]methoxy)carbonyl)glycine	MS (ESI) m/z 338.16;
65	N-(tert-butyl)-N-([(4-fluorobenzoyl)oxy]methoxy)carbonyl)glycine	MS (ESI) m/z 326; MS (ESI) m/z 653; HRMS: calcd for C ₁₅ H ₁₈ FNO ₆ + Na ⁺ , 350.10103; found (ESI ⁺ , [M+NA] ¹⁺), 350.10131;

Ref. Cpd. No.	Name	Spectra
66	N-(tert-butyl)-N-({[(3-methylbutanoyl)oxy]methoxy}carbonyl)glycine	HRMS: calcd for C ₁₃ H ₂₃ NO ₆ + Na ⁺ , 312.14176; found (ESI ⁺ , [M+NA] ¹⁺), 312.14197;
67	N-(tert-butyl)-N-({[(cyclopentylacetyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 314; MS (ESI) m/z 629.1; HRMS: calcd for C ₁₅ H ₂₅ NO ₆ + H ⁺ , 316.17546; found (ESI ⁺ , [M+H] ¹⁺), 316.17503;
68	N-(tert-butyl)-N-({[(4-(trifluoromethyl)benzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 376; MS (ESI) m/z 752.9;
69	N-(tert-butyl)-N-({[(cyclopropylcarbonyl)oxy]methoxy}carbonyl)glycine	HRMS: calcd for C ₁₂ H ₁₉ NO ₆ + Na ⁺ , 296.11046; found (ESI ⁺ , [M+NA] ¹⁺), 296.11061;
70	N-({[(1-adamantylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine	MS (ESI) m/z 368.21; MS (ESI) m/z 757.37;

Ref. Cpd. No.	Name	Spectra
71	N-(tert-butyl)-N-[(pentanoyloxy)methoxy]carbonyl]glycine	MS (ESI) m/z 288; MS (ESI) m/z 577.1; HRMS: calcd for C ₁₃ H ₂₃ NO ₆ + H ⁺ , 290.15982; found (ESI ⁺ , [M+H] ¹⁺), 290.15951;
72	N-(tert-butyl)-N-([(cyclobutylcarbonyl)oxy]methoxy)carbonyl]glycine	MS (ESI) m/z 288.1; MS (ESI) m/z 310.1; HRMS: calcd for C ₁₃ H ₂₁ NO ₆ + H ⁺ , 288.14416; found (ESI ⁺ , [M+H] ¹⁺), 288.14435;
73	N-(tert-butyl)-N-([(3-cyclohexylpropanoyl)oxy]methoxy)carbonyl]glycine	MS (ESI) m/z 344.2; MS (ESI) m/z 709.4; HRMS: calcd for C ₁₇ H ₂₉ NO ₆ + Na ⁺ , 366.18871; found (ESI ⁺ , [M+NA] ¹⁺), 366.18863;
74	N-(tert-butyl)-N-([(4-fluorophenoxy)acetyl]oxy]methoxy)carbonyl]glycine	MS (ESI) m/z 356.1;
75	N-(tert-butyl)-N-([(cyclohexylacetyl)oxy]methoxy)carbonyl]glycine	MS (ESI) m/z 328; MS (ESI) m/z 657.1;

Ref. Cpd. No.	Name	Spectra
76	N-(tert-butyl)-N-({[(2,6-dimethylbenzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 338.2;
77	N-(tert-butyl)-N-({[(phenylacetyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 322.1; MS (ESI) m/z 645.2; HRMS: calcd for C ₁₆ H ₂₁ NO ₆ + H ⁺ , 324.14416; found (ESI ⁺ , [M+H] ¹⁺), 324.14351;
78	N-(tert-butyl)-N-({[(2,2-dimethylpropanoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 288.1; MS (ESI) m/z 577.1; HRMS: calcd for C ₁₃ H ₂₃ NO ₆ + H ⁺ , 290.15982; found (ESI ⁺ , [M+H] ¹⁺), 290.15965;
79	N-({[(1-benzofuran-2-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine	MS (ESI) m/z 350; MS (ESI) m/z 721; HRMS: calcd for C ₁₇ H ₁₉ NO ₇ + H ⁺ , 350.12343; found (ESI ⁺ , [M+H] ¹⁺), 350.12327;
80	N-(tert-butyl)-N-([{[(1-methyl-1H-pyrrol-2-yl)carbonyl]oxy}methoxy}carbonyl)glycine	MS (ESI) m/z 313; MS (ESI) m/z 647.1;

Ref. Cpd. No.	Name	Spectra
81	N-({[(1,1'-biphenyl-4-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine	MS (ESI) m/z 386.2; HRMS: calcd for C ₂₁ H ₂₃ NO ₆ + Na ⁺ , 408.14176; found (ESI ⁺ , [M+NA] ¹⁺), 408.14195;
82	N-(tert-butyl)-N-({[(4-methoxybenzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 338.1; MS (ESI) m/z 677.3; HRMS: calcd for C ₁₆ H ₂₁ NO ₇ + Na ⁺ , 362.12102; found (ESI ⁺ , [M+NA] ¹⁺), 362.12095;
83	N-(tert-butyl)-N-({[(1H-indol-2-ylcarbonyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 349.2; HRMS: calcd for C ₁₇ H ₂₀ N ₂ O ₆ + Na ⁺ , 371.12136; found (ESI ⁺ , [M+NA] ¹⁺), 371.12148;
84	N-(tert-butyl)-N-({[(diphenylacetyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 298.2;
85	N-(tert-butyl)-N-({[(1-naphthoyloxy)methoxy]carbonyl}glycine	MS (ESI) m/z 358.2; MS (ESI) m/z 717.4; MS (ESI) m/z 1076.6;

Ref. Cpd. No.	Name	Spectra
86	N-(tert-butyl)-N-[[2-naphthoyloxy)methoxy]carbonyl]glycine	MS (ESI) m/z 360.1; MS (ESI) m/z 472.1;
87	N-(tert-butyl)-N-[[[(1-methyl-1H-indol-3-yl)carbonyl]oxy]methoxy]carbonyl]glycine	MS (ESI) m/z 361.2; MS (ESI) m/z 1085.7; MS (ESI) m/z 723.5; HRMS: calcd for C ₁₈ H ₂₂ N ₂ O ₆ + H ⁺ , 363.15506; found (ESI ⁺ , [M+H] ⁺), 363.15556;
88	N-(tert-butyl)-N-([quinolin-2-ylcarbonyl]oxy)methoxy]carbonyl]glycine	MS (ESI) m/z 359.2; MS (ESI) m/z 1079.7; MS (ESI) m/z 719.4;
89	N-(tert-butyl)-N-([pyridin-3-ylcarbonyl]oxy)methoxy]carbonyl]glycine	MS (ESI) m/z 309.2; MS (ESI) m/z 929.5; MS (ESI) m/z 619.3;
90	N-(tert-butyl)-N-[[[isonicotinoyloxy)methoxy]carbonyl]glycine	MS (ESI) m/z 311.1; MS (ESI) m/z 333.1;
91	N-(tert-butyl)-N-([2,6-difluorobenzoyl]oxy)methoxy]carbonyl]glycine	MS (ESI) m/z 390.2; MS (ESI) m/z 689.3;

Ref. Cpd. No.	Name	Spectra
92	N-(tert-butyl)-N-({[2-fluorobenzoyl]oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 326.2; MS (ESI) m/z 980.6; MS (ESI) m/z 653.3;
93	N-(tert-butyl)-N-({[2-(trifluoromethyl)benzoyl]oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 422.1; MS (ESI) m/z 753;
94	N-(tert-butyl)-N-({[4-pyrrolidin-1-ylbenzoyl]oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 379.2;
95	N-({[1,1'-biphenyl-2-ylcarbonyl]oxy]methoxy}carbonyl)-N-(tert-butyl)glycine	MS (ESI) m/z 384.3; MS (ESI) m/z 1154.7; MS (ESI) m/z 769.5;
96	N-(tert-butyl)-N-({[mesitylcarbonyl]oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 701.5; MS (ESI) m/z 386.2; MS (ESI) m/z 1052.8;
97	N-(tert-butyl)-N-({[4-isopropoxybenzoyl]oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 733.3; MS (ESI) m/z 1100.3; MS (ESI) m/z 412.2; HRMS: calcd for C ₁₈ H ₂₅ NO ₇ + H ⁺ , 368.17038; found (ESI ⁺ , [M+H] ¹⁺), 368.17069;

Ref. Cpd. No.	Name	Spectra
98	N-(tert-butyl)-N-({[(3,4,5-trimethoxybenzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 398; MS (ESI) m/z 797.2; MS (ESI) m/z 1195.9; HRMS: calcd for C ₁₈ H ₂₅ NO ₉ + H ⁺ , 400.16021; found (ESI ⁺ , [M+H] ¹⁺), 400.1610
99	N-(tert-butyl)-N-({[(3,5-dimethoxybenzoyl)oxy]methoxy}carbonyl)glycine	MS (ESI) m/z 368.1; MS (ESI) m/z 737.1; MS (ESI) m/z 414; HRMS: calcd for C ₁₇ H ₂₃ NO ₈ + H ⁺ , 370.14965; found (ESI ⁺ , [M+H] ¹⁺), 370.15016;
100	N-(tert-butyl)-N-([{[(2E)-3-phenylprop-2-enoyl]oxy}methoxy]carbonyl)glycine	MS (ESI) m/z 334.2; MS (ESI) m/z 669.4; MS (ESI) m/z 1004.6; HRMS: calcd for C ₁₇ H ₂₁ NO ₆ + Na ⁺ , 358.12611; found (ESI ⁺ , [M+NA] ¹⁺), 358.12763;

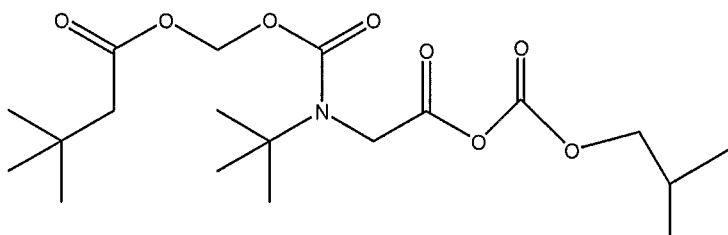
Ref. Cpd. No.	Name	Spectra
101	N-(tert-butyl)-N-[[[[(3-methyl-1-benzofuran-2-yl)carbonyl]oxy}methoxy]carbonyl]glycine	MS (ESI) m/z 725.4; MS (ESI) m/z 1088.6; MS (ESI) m/z 398.2; HRMS: calcd for C ₁₈ H ₂₁ NO ₇ + H ⁺ , 364.13908; found (ESI, [M+H] ¹⁺), 364.13956;
102	N-[[[3,5-bis(trifluoromethyl)phenyl]acetyl]oxy}methoxy]carbonyl]-N-(tert-butyl)glycine	MS (ESI) m/z 458.1; MS (ESI) m/z 917.1; HRMS: calcd for C ₁₈ H ₁₉ F ₆ NO ₆ + H ⁺ , 460.11893; found (ESI ⁺ , [M+H] ¹⁺), 460.11854;
103	N-(tert-butyl)-N-[[[4-(heptyloxy)benzoyl]oxy}methoxy]carbonyl]glycine	MS (ESI) m/z 422.2; MS (ESI) m/z 468.3; MS (ESI) m/z 845.3; HRMS: calcd for C ₂₂ H ₃₃ NO ₇ + H ⁺ , 424.23298; found (ESI ⁺ , [M+H] ¹⁺), 424.23295;

Ref. Cpd. No.	Name	Spectra
104	N-(tert-butyl)-N-([2-(2-phenylethyl)benzoyl]oxy)methoxy)carbonyl]glycine	MS (ESI+) m/z 414.19088; MS (ESI+) m/z 414.19112; HRMS: calcd for C ₂₃ H ₂₇ NO ₆ + H ⁺ , 414.19112; found (ESI+, [M+H] ⁺), 414.19088;
105	N-(tert-butyl)-N-([4-(dodecyloxy)benzoyl]oxy)methoxy)carbonyl]glycine	MS (ESI+) m/z 494.31095; MS (ESI+) m/z 494.31123; HRMS: calcd for C ₂₇ H ₄₃ NO ₇ + H ⁺ , 494.31123; found (ESI+, [M+H] ⁺), 494.31095;
106	N-([4-(acetylamino)benzoyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine	MS (ESI) m/z 367.1; MS (ESI) m/z 733.1;
107	N-([9-anthrylcarbonyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine	MS (ESI) m/z 408.3; MS (ESI) m/z 1226.7; MS (ESI) m/z 817.5;
108	N-([4-benzoylbenzoyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine	MS (ESI) m/z 414.2;

Reference Compound 109

3,3-Dimethyl-butylric acid [tert-butyl-(2-isobutoxycarbonyloxy-2-oxo-ethyl)-
carbamoxyloxy]-methyl ester.

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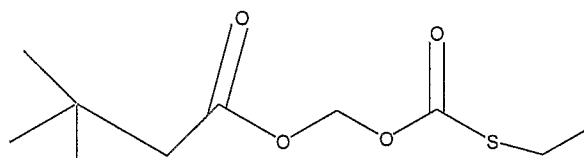


To a solution of Reference Compound 56 in dichloromethane at room temperature is added 1.2 equivalent of [1,8-bis(dimethylamino)naphthalene, N,N,N',N'-tetramethyl-
10 1,8-naphthalenediamine] and 0.95 equivalent of iso-butylchloroformate. The reaction is stirred for 24 hour, diluted with dichloromethane, washed with dilute HCl, brine, then water. It is dried with sodium sulfate. Solvent removed and the product is used in the next step without further purification.

15

Reference Compound 110

3,3-Dimethylbutyric acid ethylsulfanylcabonyloxymethyl ester

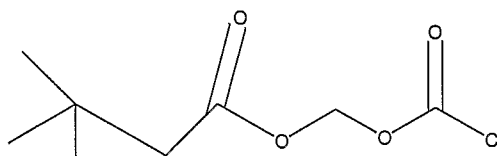


20 To a solution of t-butylacetic acid (0.025 mol, 3 g) in methanol is added tetrabutylammonium hydroxide (1M/methanol, 25 ml). The mixture is stirred for 1 h and the solvent removed to a residue. The residue is dissolved in 150 ml of methylene chloride and 150 ml of water and a solution of O-chloromethyl S-ethyl carbonothioate (0.025 mol, 3.85 f) in 50 ml of methylene chloride added. The mixture
25 is stirred at room temperature for 24 h. The methylene chloride layer is separated, washed with water, brine and dried over sodium sulfate. The solvent is removed under vacuo and the residue stirred in 300 ml of ether for 24 h. The resulting white

solid is filtered, the solid discarded and the solvent removed from the filtrate to give 6 g of a crude oil.

Reference Compound 111

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To a stirred solution of 3,3-dimethylbutyric acid ethylsulfanylcabonyloxymethyl ester (Reference Compound 110) (0.025 ml, 6 g) in methylene chloride at -20°C (dry ice/carbon tetrachloride) is added sulfonyl chloride (0.025 mol, 3.5 g). After 10 min, 0.1 ml of boron trifluoride etherate is added. The mixture is stirred at 0°C for 1 h, at room temperature for 30 min. The volatiles are removed by distillation to yield 4.9 g of the desired acid chloride.

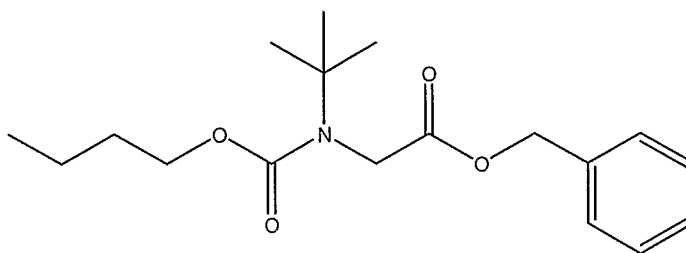
15

Following the procedure of Reference Compound 111 the corresponding acid chloride used in Examples 112 to 120 was prepared.

Reference Compound 112

20

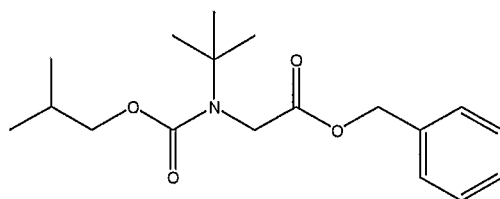
benzyl N-(butoxycarbonyl)-N-(tert-butyl)glycinate



Reference Compound 113

benzyl N-(tert-butyl)-N-(isobutoxycarbonyl)glycinate

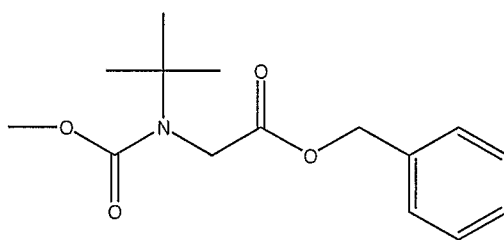
5



Reference Compound 114

benzyl N-(tert-butyl)-N-(methoxycarbonyl)glycinate

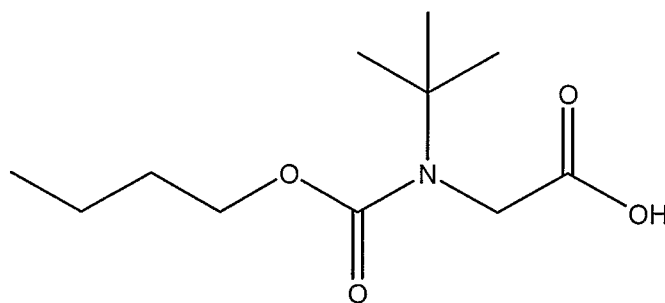
10



15

Reference Compound 115

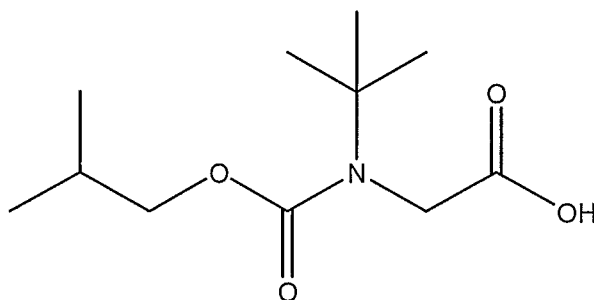
N-(butoxycarbonyl)-N-(tert-butyl)glycine



20

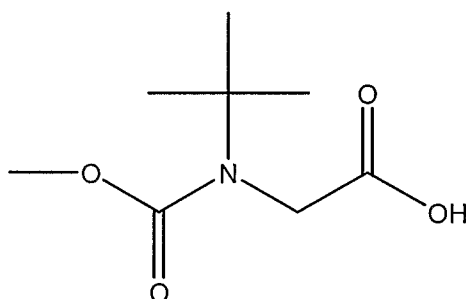
Reference Compound 116
N-(tert-butyl)-N-(isobutoxycarbonyl)glycine

5



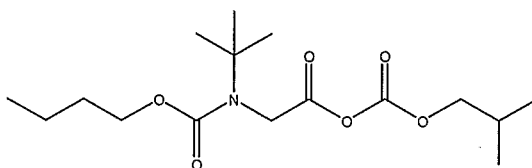
10

Reference Compound 117
N-(tert-butyl)-N-(methoxycarbonyl)glycine



15

Reference Compound 118
isobutoxycarbonyl N-(butoxycarbonyl)-N-(tert-butyl)glycinate

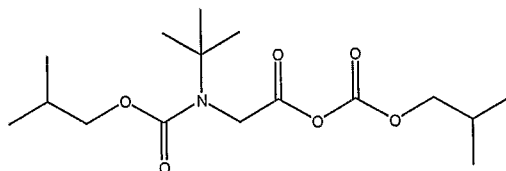


20

Reference Compound 119

isobutoxycarbonyl N-(tert-butyl)-N-(isobutoxycarbonyl)glycinate

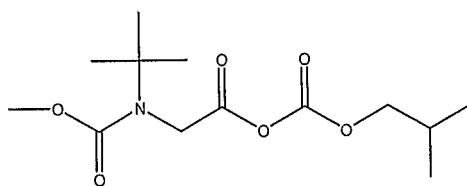
5



Reference compound 120

isobutoxycarbonyl N-(tert-butyl)-N-(methoxycarbonyl)glycinate

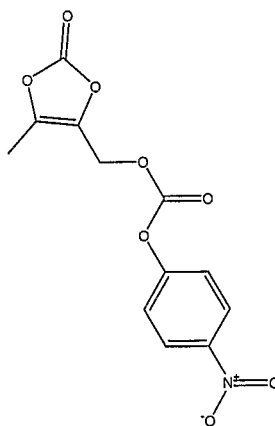
10



15

Reference Compound 121

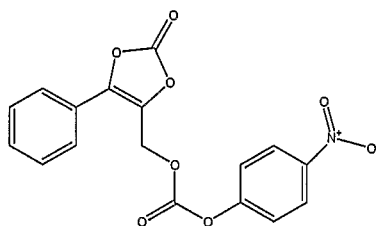
(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-nitrophenyl carbonate



The product of the Reference Example was prepared using the conditions described by R. Sakamoto et al, Chem. Pharm. Bull. 32(6), 2241-2248(1984).

Reference Compound 122

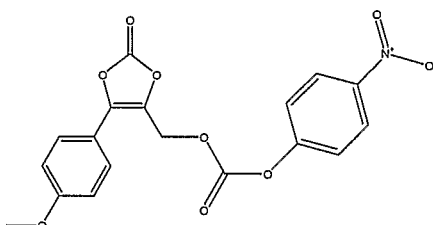
5 4-nitrophenyl (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl carbonate



10 The product of the Reference Example was prepared using the conditions described by R. Sakamoto et al, Chem. Pharm. Bull. 32(6), 2241-2248(1984).

Reference Compound 123

15 [5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 4-nitrophenyl carbonate

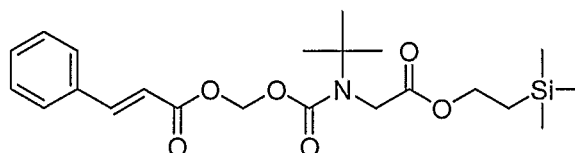


20 The product of the Reference Example was prepared using the conditions described by R. Sakamoto et al, Chem. Pharm. Bull. 32(6), 2241-2248(1984).

25

Reference Compound 124

4-tert-butyl-10,10-dimethyl-3,6-dioxo-2,7-dioxa-4-aza-10-silaundec-1-yl (2E)-3-phenylacrylate



5

Trans-cinnamic acid (23.1 mmol) and 1.0 M tetrabutylammonium hydroxide (22.2 mmol) in methanol are stirred for one hour, and the methanol is removed. THF is added. To this solution is added 2-(trimethylsilyl)ethyl 2-(tert-butyl((chloromethoxy)carbonyl)amino)-acetate (18.5 mmol) and the mixture is stirred at room temperature for 24 hr. The solvent is removed and the residue is diluted with ether. The resulting solution is washed with water and brine. The organic layer is dried over magnesium sulfate, filtered and concentrated under reduced pressure to yield 5.01 g (61%) MS (ESI) m/z 436.3.

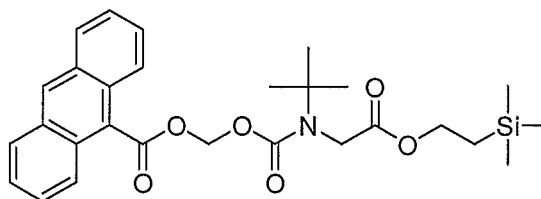
10

Using substantially the same procedure as described above for Reference Compound 124 the following reference compounds were prepared from the appropriate carboxylic acids:

15

Reference Compound 125

4-tert-butyl-10,10-dimethyl-3,6-dioxo-2,7-dioxa-4-aza-10-silaundec-1-yl anthracene-9-carboxylate



MS (ESI) m/z 510.3

25

Reference Compound 126

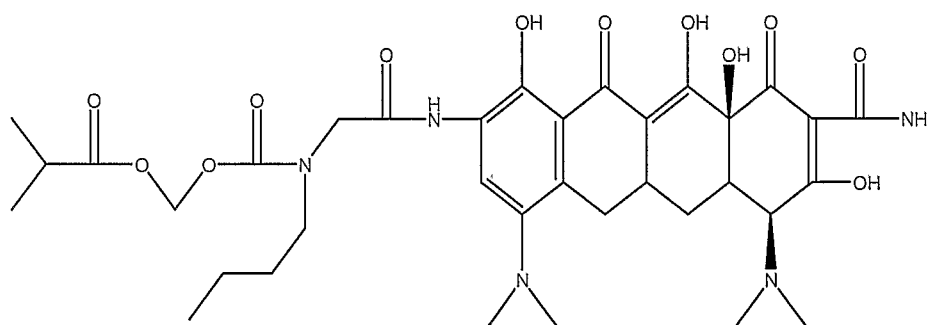
4-tert-butyl-10,10-dimethyl-3,6-dioxo-2,7-dioxa-4-aza-10-silaundecyl 4-benzoylbenzoate

5

MS (ESI) m/z 536.2

Example 1

10 {[(2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 2-methylpropanoate



15

To a solution of n-Butylglycylcycline in acetonitrile/DMPA (1:5), sodium carbonate is added. The reaction mixture is stirred for 5 min and propanoic acid, 2-methyl-[(chlorocarbonyl)oxy]methyl ester prepared according to the methods described in M. Folkmann and F.J. Lund, *Synthesis*, December 1990, 1159-1166, is added. Stirring is continued for about 30 to 45 minute (or monitored by MS (ES)). Upon completion of the reaction, 0.5 mL of methanol is added and the mixture poured slowly into a mixture of isopropanol and ether. 1.0M HCl in ether is added and the solid is filtered. The solid is dissolved in water and is extracted with methylene chloride to give the product of the Example. MS (ESI) m/z 730.28 (M+H);

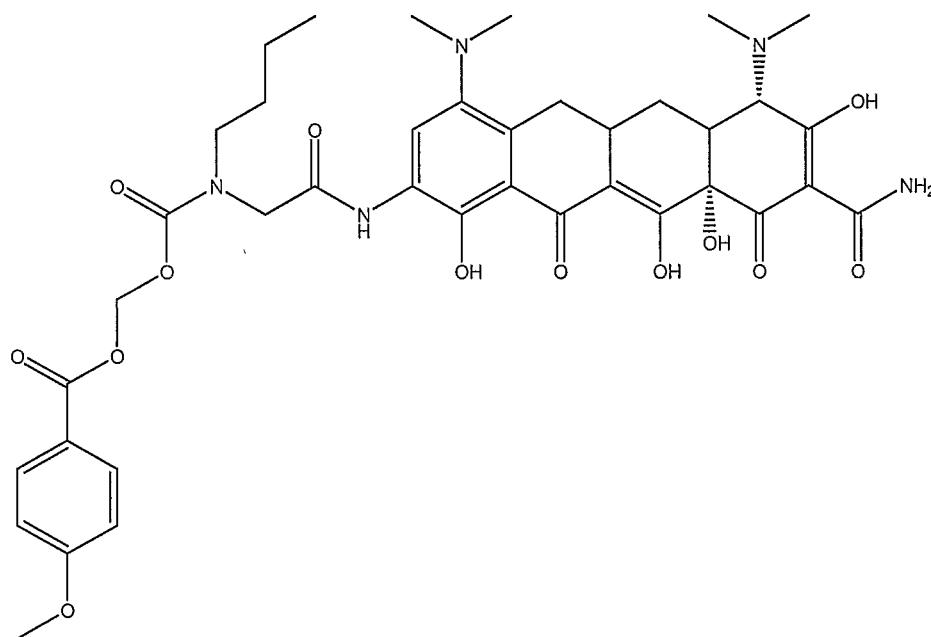
25

Following the procedure of Example 1, and the corresponding acid chloride prepared by methods described in M. Folkmann and F.J. Lund, Synthesis, December 1990, 1159-1166 and N-butylglycylcycline or N-propylglycylcycline the following Examples 2-41 are prepared.

5

Example 2

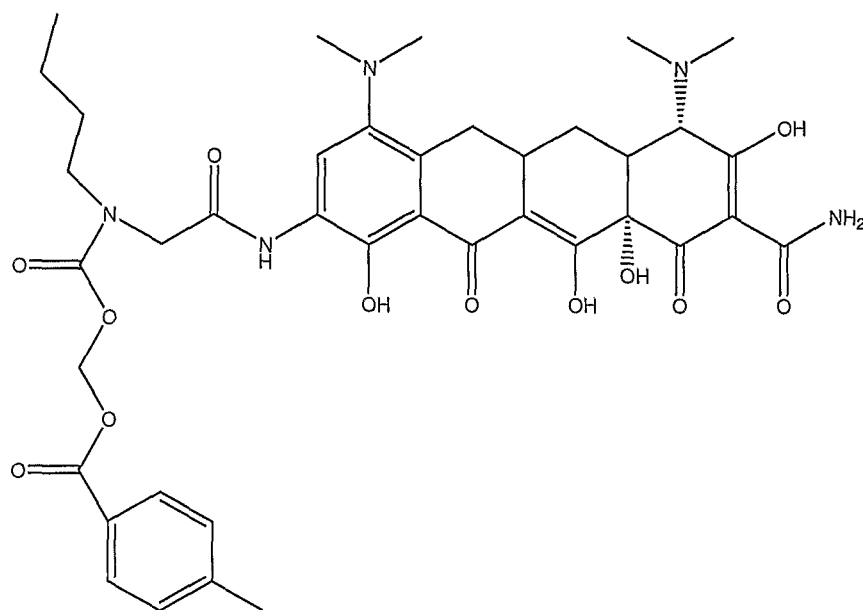
10 {[(2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate



15 The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy)methyl 4-methoxybenzoate and N-butylglycylcycline to give the product of the Example.

Example 3

5 {{{[2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate



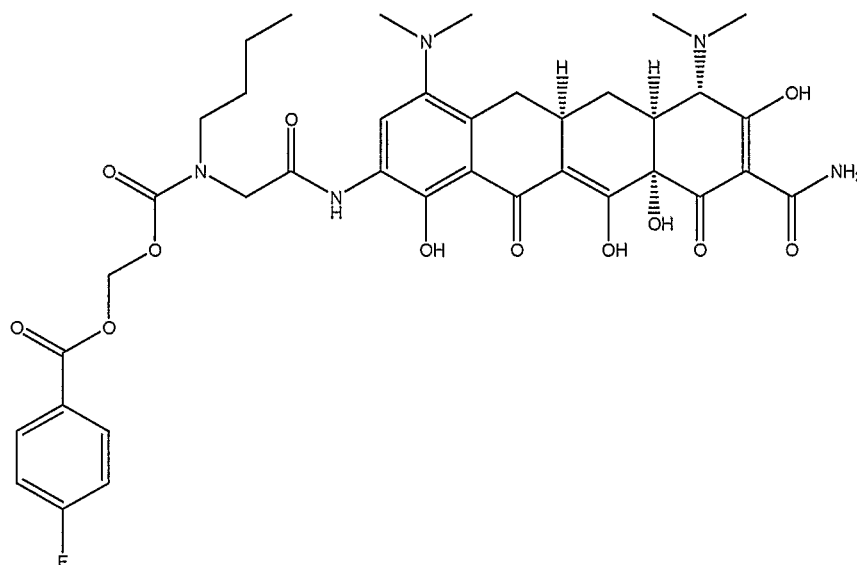
10

The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 4-methylbenzoate and N-butylglycylcyclocline to give the product of the Example.

15 MS (ESI) m/z 778.3 ((M+H)⁺);

Example 4

5 ({[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate



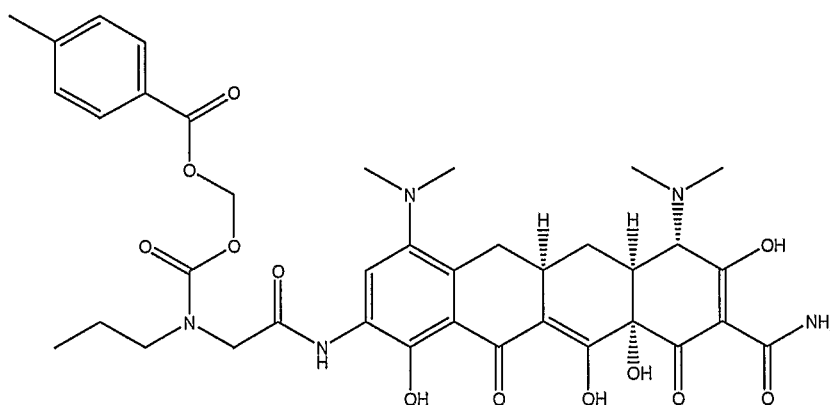
10 The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy)methyl 4-fluorobenzoate and N-butylglycylcycline to give the product of the Example.

MS (ESI) m/z 782.3 ($(M+H)^+$);

15

Example 5

20 ({[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 4-methylbenzoate



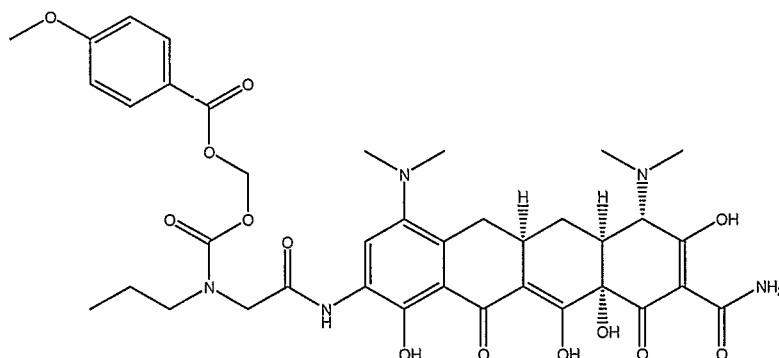
The title compound is prepared by the procedure of Example 1, using

- 5 [(chlorocarbonyl)oxy]methyl 4-methylbenzoate and N-propylglycylcycline to give the product of the Example.

MS (ESI) m/z 764.3 ((M+H)+);

Example 6

- 10 ([[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl)oxy]methyl 4-methoxybenzoate



15

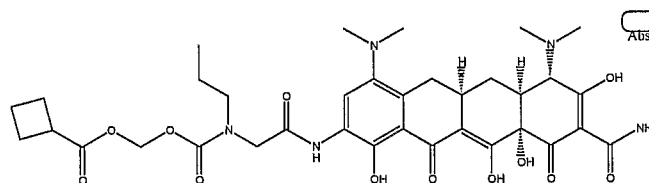
The title compound is prepared by the procedure of Example 1, using

[(chlorocarbonyl)oxy]methyl 4-methoxybenzoate and N-propylglycylcycline to give the product of the Example.

- 20 MS (ESI) m/z 780.3 ((M+H)+);

Example 7

5 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl cyclobutanecarboxylate



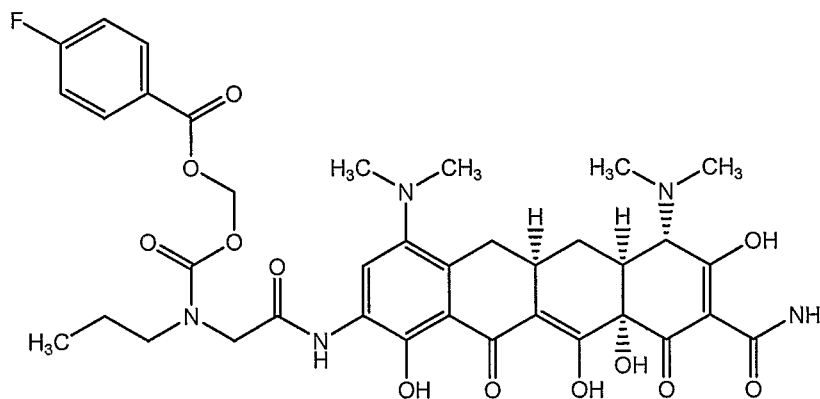
10

The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl cyclobutanecarboxylate and N-propylglycylcycline to give the product of the Example.

15 MS (ESI) m/z 728.3 ((M+H)⁺);

Example 8

20 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate



The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 4-fluorobenzoate and N-propylglycylcycline to give the product of the Example.

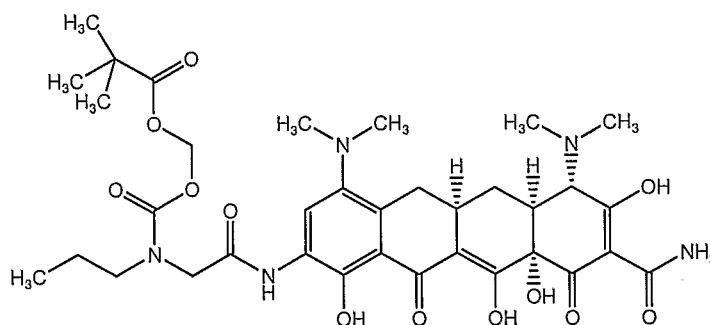
5

MS (ESI) m/z 768.3 ((M+H)⁺);

Example 9

10

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl pivalate



15

The title compound is prepared by the procedure of Example 1, using Propanoic acid, 2,2-dimethyl-, [(chlorocarbonyl)oxy]methyl ester and N-propylglycylcycline to give the product of the Example.

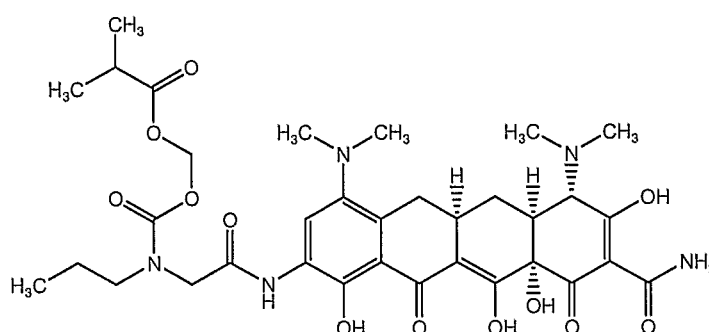
20

MS (ESI) m/z 730.3 ((M+H)⁺);

25

Example 10

- 5 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 2-methylpropanoate



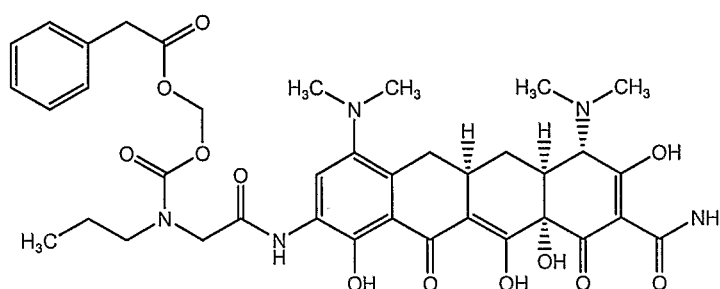
10

The title compound is prepared by the procedure of Example 1, using propanoic acid, 2-methyl-,[(chlorocarbonyl)oxy]methyl ester and N-propylglycylcycline to give the product of the Example.

- 15 MS (ESI) m/z 716.3 ((M+H)+);

Example 11

- 20 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl phenylacetate



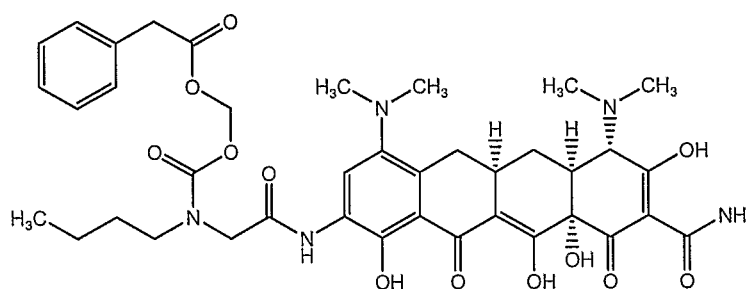
The title compound is prepared by the procedure of Example 1, using benzeneacetic acid, [(chlorocarbonyl)oxy]methyl ester and N-propylglycylcycline to give the product of the Example.

5

MS (ESI) m/z 764.3 ((M+H)+

Example 12

10 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl]oxy)methyl phenylacetate



15

The title compound is prepared by the procedure of Example 1, using benzeneacetic acid, [(chlorocarbonyl)oxy]methyl ester and N-butylglycylcycline to give the product of the Example.

20

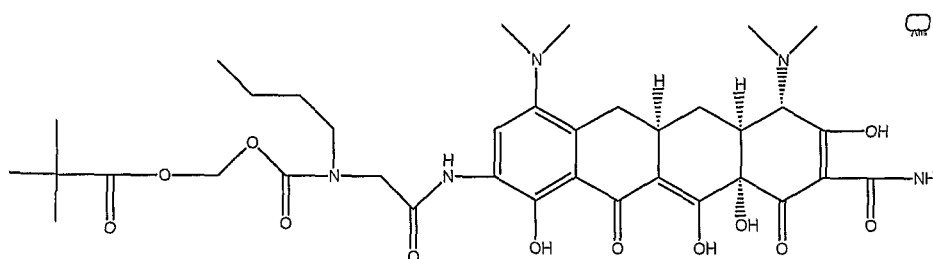
MS (ESI) m/z 778.3 ((M+H)+);

Example 13

5

{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl pivalate

10



The title compound is prepared by the procedure of Example 1, using propanoic acid, 2,2-dimethyl-, [(chlorocarbonyl)oxy]methyl ester and N-butylglycylcyclyne to give the product of the Example.

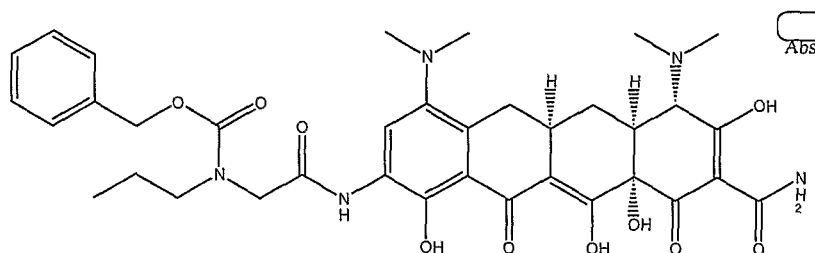
15

MS (ESI) m/z 744.3 ((M+H)+);

Example 14

20 benzyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate

25



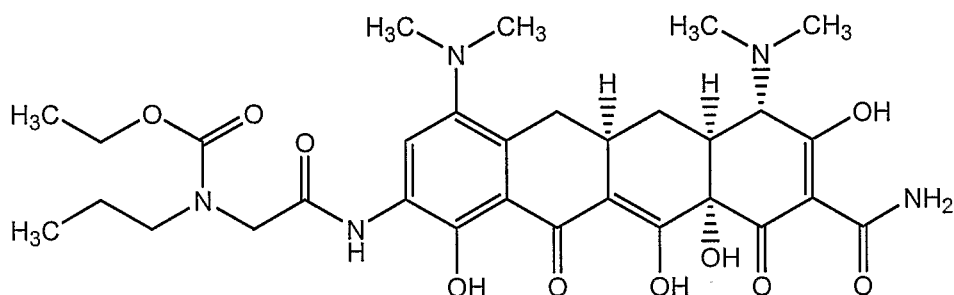
The title compound is prepared by the procedure of Example 1, using benzyl chloroformate and N-propylglycylcycline in the presence of sodium carbonate and DMPU in acetonitrile to give the product of the Example.

- 5 MS (ESI) m/z 706.3 ((M+H)⁺);
 HRMS: calcd for $C_{36}H_{43}N_5O_{10} \cdot HCl$, 741.2777; found (ESI), 706.31133;

Example 15

10

ethyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate



15

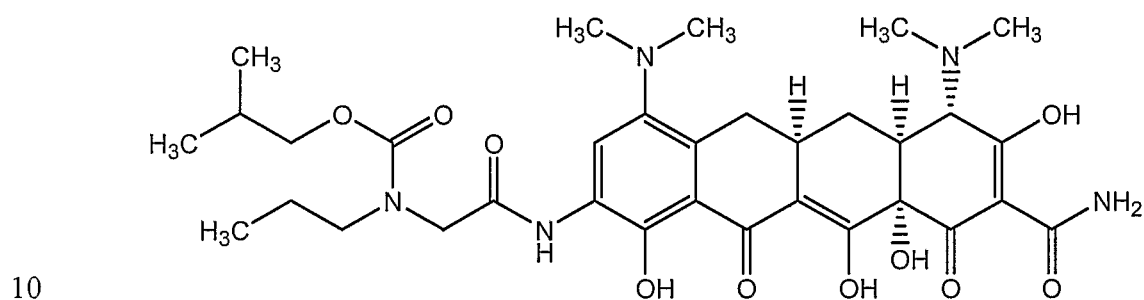
The title compound is prepared by the procedure of Example 1, using ethyl chloroformate and N-propylglycylcycline in the presence of sodium carbonate and DMPU in acetonitrile to give the product of the Example.

20

MS (ESI) m/z 644.3 ((M+H)⁺);
 HRMS: calcd for $C_{31}H_{41}N_5O_{10} \cdot HCl$, 679.2620; found (ESI⁺), 644.29398;

Example 16

- 5 isobutyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate



The title compound is prepared by the procedure of Example 1, using isobutyl chloroformate and N-propylglycylcycline in the presence of sodium carbonate and DMPU in acetonitrile to give the product of the Example.

15

MS (ESI) m/z 672.3 ((M+H)+);

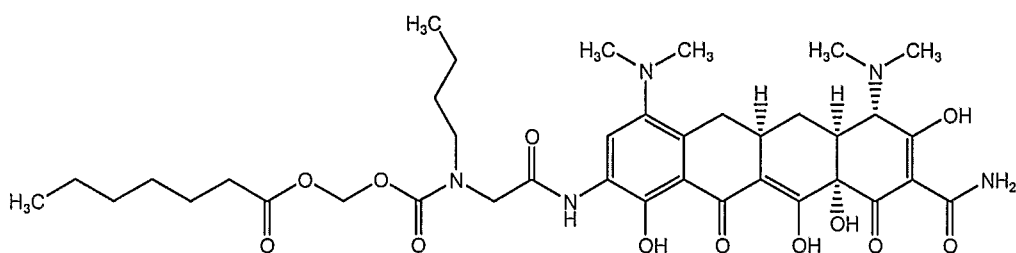
MS (ESI) m/z 336.9 ((M+2H)2+);

HRMS: calcd for $C_{33}H_{45}N_5O_{10} \cdot HCl$, 707.2933; found (ESI+), 672.32618

20

Example 17

- ({[(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl heptanoate
- 25



The title compound is prepared by the procedure of Example 1, using heptanoic acid, [(chlorocarbonyl)oxy]methyl ester and N-butylglycylcyclohexene to give the product of the Example.

MS (ESI+) m/z 772.2 (M+H);

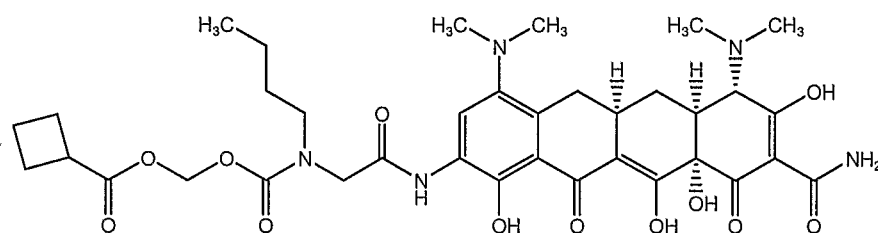
HRMS: calcd for C₃₈H₅₃N₅O₁₂ · 2.00 HCl, 843.3224; found (ESI+), 772.37696;

10

Example 18

(([(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl]oxy)methyl cyclobutanecarboxylate

15



The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl cyclobutanecarboxylate and N-butylglycylcyclohexene to give the product of the Example.

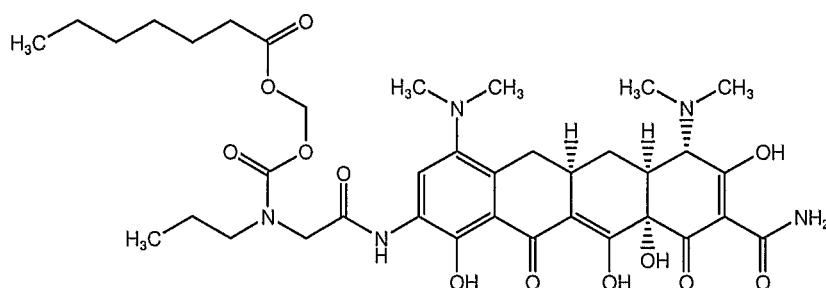
MS (ESI) m/z 742.3 ((M+H)+);

HRMS: calcd for C₃₆H₄₇N₅O₁₂ · 2.00 HCl, 813.2755; found (ESI+), 742.32898;

25

Example 19

- 5 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl heptanoate



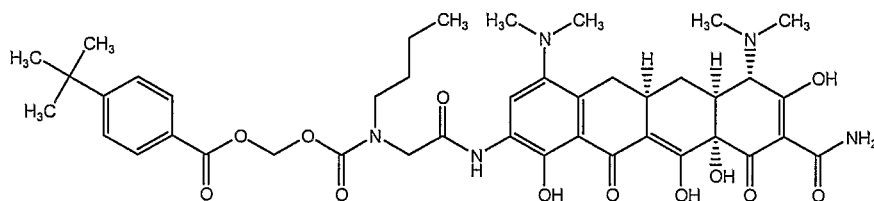
10

The title compound is prepared by the procedure of Example 1, using Heptanoic acid, [(chlorocarbonyl)oxy]methyl ester and N-propylglycylcycline to give the product of the Example.

- 15 MS (ESI) m/z 758.4 ((M+H)⁺);
 HRMS: calcd for $C_{37}H_{51}N_5O_{12} \cdot HCl$, 793.3301; found (ESI⁺), 758.36175;

Example 20

- 20 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate



25

The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 4-tert-butylbenzoate and N-butylglycylcycline to give the product of the Example.

5

MS (ESI+) m/z 820.2 (M+H);

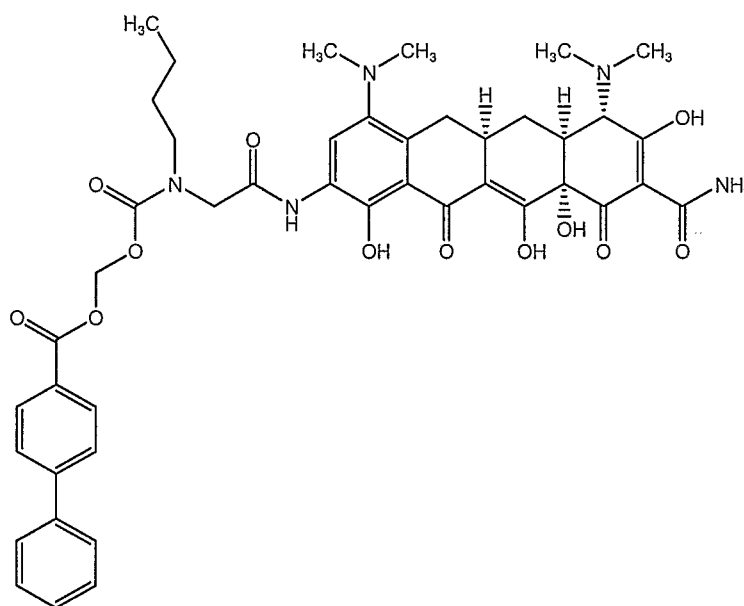
HRMS: calcd for $C_{42}H_{53}N_5O_{12} \cdot HCl$, 855.3458; found (ESI+), 820.37684;

10

Example 21

((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(butyl)amino]carbonyloxy)methyl 1,1'-biphenyl-4-carboxylate

15



The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl biphenyl-4-carboxylate and N-butylglycylcycline to give the product of the Example.

20

MS (ESI) m/z 840.3 ((M+H)+);

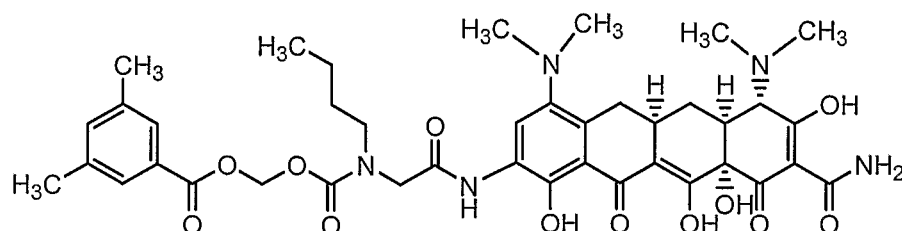
HRMS: calcd for $C_{44}H_{49}N_5O_{12} \cdot HCl$, 875.3145; found (ESI+), 840.34337;

5

Example 22

((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(butyl)amino]carbonyloxy)methyl 3,5-dimethylbenzoate

10



The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 3,5-dimethylbenzoate and N-butylglycylcycline to give the product of the Example.

15

MS (ESI) m/z 792.3 ((M+H)+);

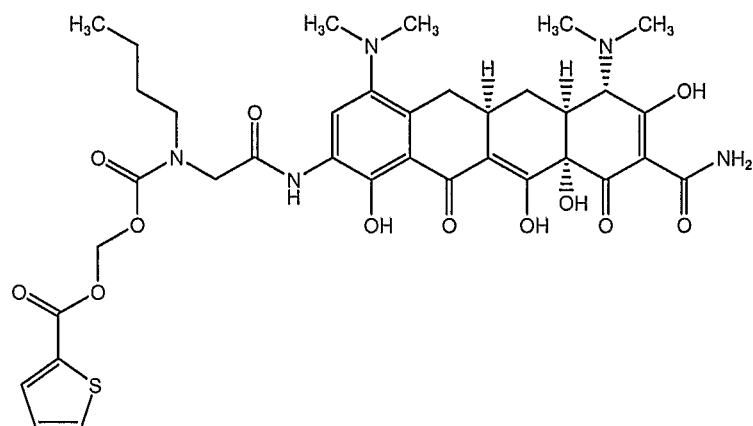
HRMS: calcd for $C_{40}H_{49}N_5O_{12} \cdot 2.00 HCl$, 863.2911; found (ESI+), 792.34378;

20

Example 23

((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(butyl)amino]carbonyloxy)methyl thiophene-2-carboxylate

25



The title compound is prepared by the procedure of Example 1, using
 [(chlorocarbonyl)oxy]methyl thiophene-2-carboxylate and N-butylglycylcycline to give
 5 the product of the Example.

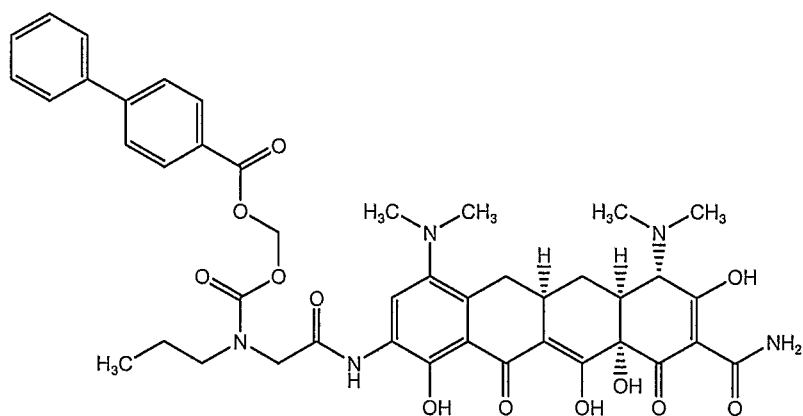
MS (ESI) m/z 770.1 ((M+H)+);

HRMS: calcd for $C_{36}H_{43}N_5O_{12}S \cdot HCl$, 805.2396; found (ESI+), 770.27084;

10

Example 24

15 {[(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate



The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl biphenyl-4-carboxylate and N-propylglycylcycline to give the product of the Example.

5

MS (ESI) m/z 826.4 ((M+H)+);

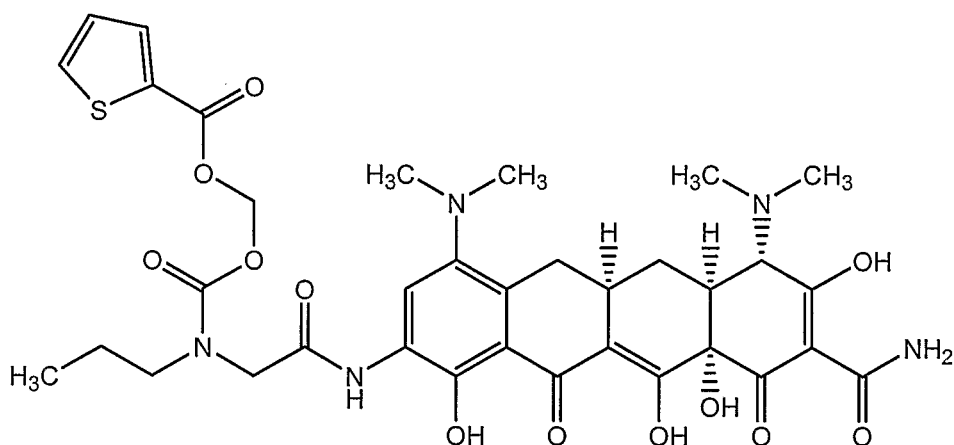
MS (ESI) m/z 414 ((M+2H)²⁺);

HRMS: calcd for C₄₃H₄₇N₅O₁₂ · HCl, 861.2988; found (ESI+), 826.32782;

10

Example 25

15 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl thiophene-2-carboxylate



20

The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl thiophene-2-carboxylate and N-propylglycylcycline to give the product of the Example.

25

MS (ESI) m/z 756.3 ((M+H)+);

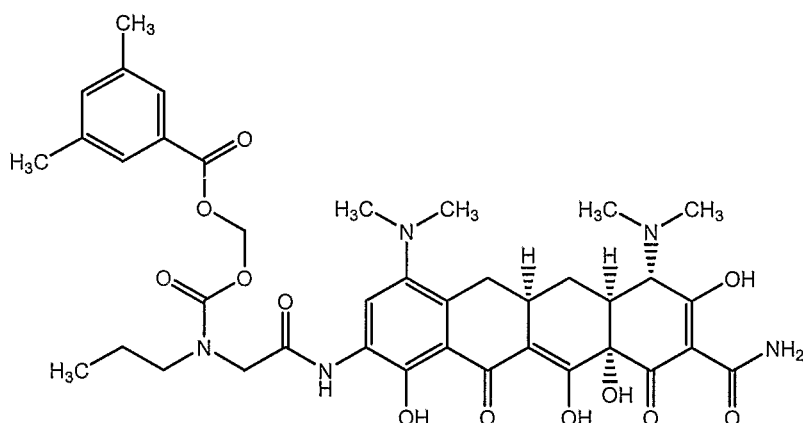
MS (ESI) m/z 378.9 ((M+2H)2+);

HRMS: calcd for $C_{35}H_{41}N_5O_{12}S \cdot HCl$, 791.2239; found (ESI+), 756.2532;

5

Example 26

10 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate



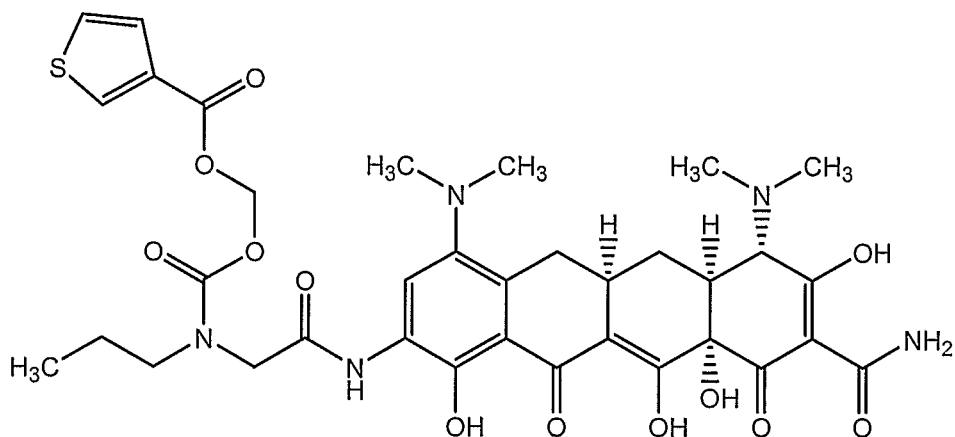
15 The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy)methyl 3,5-dimethylbenzoate and N-propylglycylcycline to give the product of the Example.

20 MS (ESI) m/z 778.3 ((M+H)+);

HRMS: calcd for $C_{39}H_{47}N_5O_{12} \cdot HCl$, 813.2988; found (ESI+), 778.32984;

Example 27

25 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl thiophene-3-carboxylate



5

10 The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl thiophene-3-carboxylate and N-propylglycylcycline to give the product of the Example.

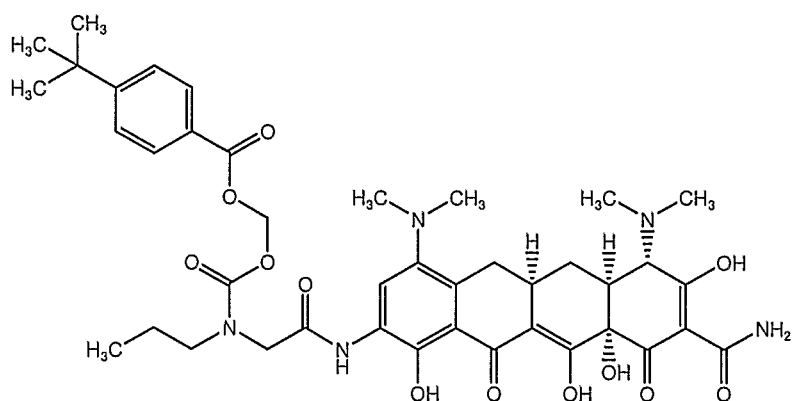
15 MS (ESI) m/z 756.3 ((M+H)⁺);
HRMS: calcd for $C_{35}H_{41}N_5O_{12}S \cdot HCl$, 791.2239; found (ESI⁺), 756.2547;

Example 28

20

(([(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl]oxy)methyl 4-tert-butylbenzoate

25



The title compound is prepared by the procedure of Example 1, using

- 5 [(chlorocarbonyl)oxy]methyl 4-tert-butylbenzoate and N-propylglycylcycline to give the product of the Example.

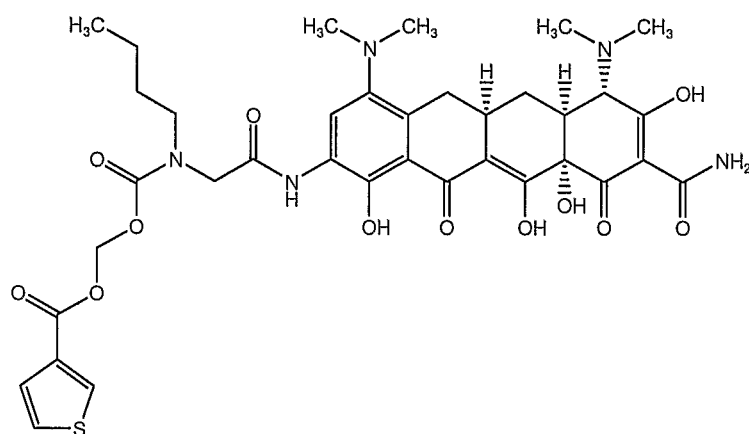
MS (ESI) m/z 806.4 ((M+H)+);

MS (ESI) m/z 403.9 ((M+2H)²⁺);

- 10 HRMS: calcd for C₄₁H₅₁N₅O₁₂ · HCl, 841.3301; found (ESI+), 806.36024;

Example 29

5 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl thiophene-3-carboxylate



10

The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl thiophene-3-carboxylate and N-butylglycylcycline to give the product of the Example.

15

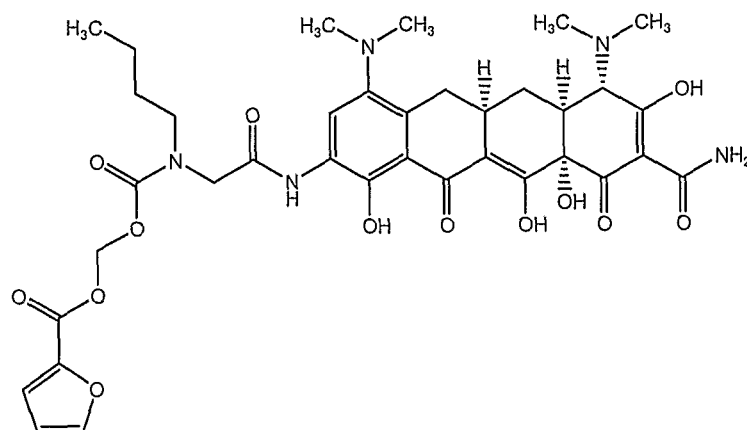
MS (ESI) m/z 770.3 ((M+H)⁺);

HRMS: calcd for $C_{36}H_{43}N_5O_{12}S \cdot HCl$, 805.2396; found (ESI⁺), 770.27028;

20

Example 30

25 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 2-furoate



5

The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 2-furoate and N-butylglycylcycline to give the product of the Example.

10

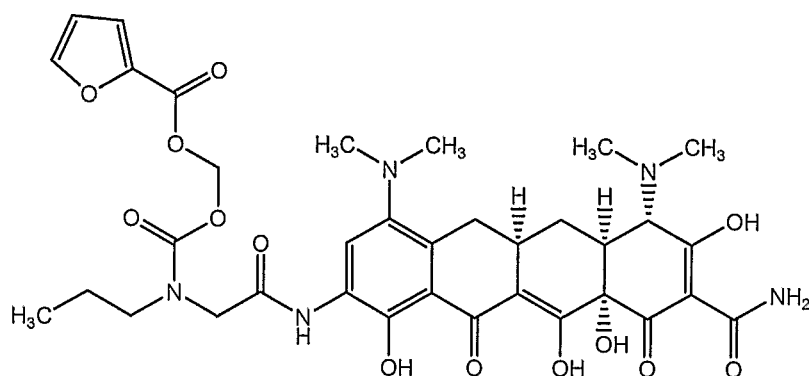
MS (ESI) m/z 752.2 ((M-H)-);

HRMS: calcd for $C_{36}H_{43}N_5O_{13} \cdot HCl$, 789.2624; found (ESI+), 754.29242;

Example 31

15

{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 2-furoate



The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 2-furoate and N-propylglycylcycline to give the product of the Example.

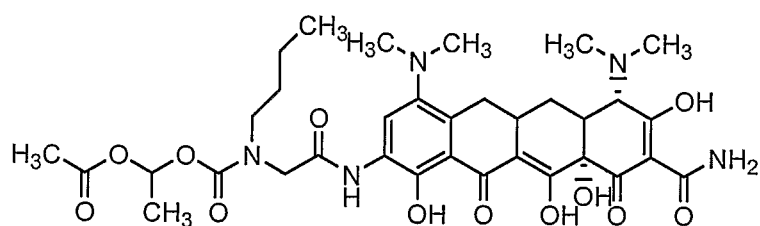
MS (ESI) m/z 740.19 (M+H);

10

Example 32

1-({[(2-{{(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(butyl)amino]carbonyl}oxy)ethyl acetate

15



The title compound is prepared by the procedure of Example 1, using 1-[(chlorocarbonyl)oxy]ethyl acetate and N-butylglycylcycline to give the product of the Example.

20

MS (ESI) m/z 716.14 (M+H);

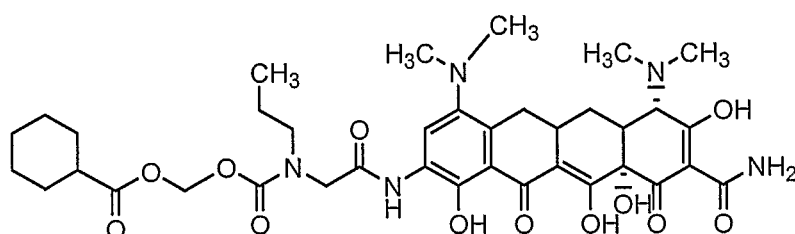
HRMS: calcd for C₃₄H₄₅N₅O₁₂, 715.3065; found (ESI+), 716.31469;

Example 33

5

((2-(((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate

10



The title compound is prepared by the procedure of Example 1, using cyclohexanecarboxylic acid, [(chlorocarbonyl)oxy]methyl ester and N-propylglycylcycline to give the product of the Example.

15

MS (ESI) m/z 756.08 (M+H);

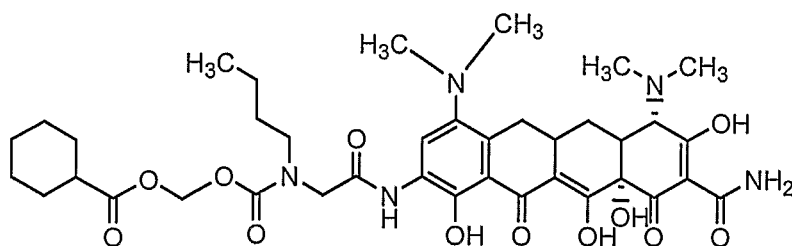
HRMS: calcd for C₃₇H₄₉N₅O₁₂, 755.3378; found (ESI+), 756.34507;

20

Example 34

((2-(((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate

25



The title compound is prepared by the procedure of Example 1, using
 5 cyclohexanecarboxylic acid, [(chlorocarbonyl)oxy]methyl ester and N-
 butylglycylcycline to give the product of the Example.

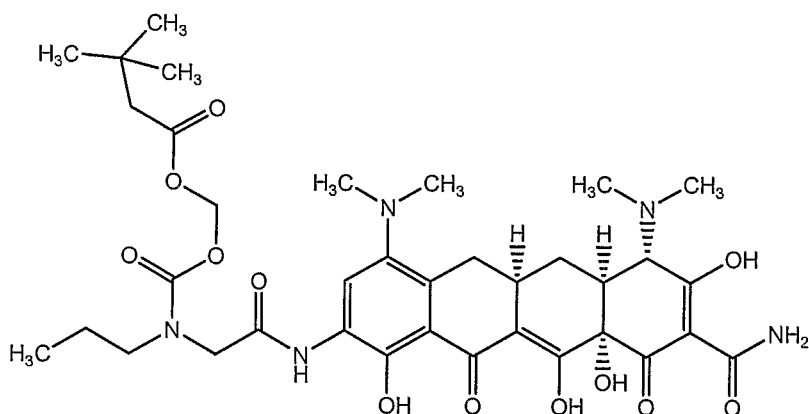
MS (ESI) m/z 70.64 (M+H);

HRMS: calcd for $C_{38}H_{51}N_5O_{12} \cdot HCl$, 805.3301; found (ESI+), 770.36093;

10

Example 35

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-
 tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-
 15 oxoethyl](propyl)amino]carbonyl]oxy)methyl 3,3-dimethylbutanoate



The title compound is prepared by the procedure of Example 1, using butanoic acid,
 3,3-dimethyl-, [(chlorocarbonyl)oxy]methyl ester and N-propylglycylcycline to give
 20 the product of the Example.

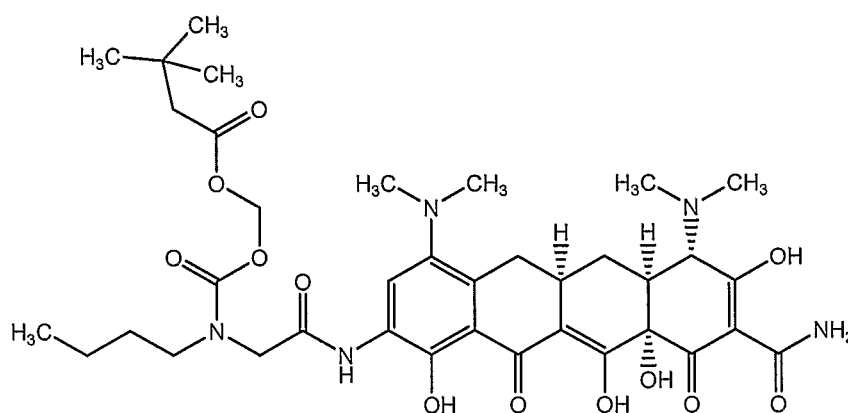
MS m/z 00-304761LMS;

HRMS: calcd for $C_{36}H_{49}N_5O_{12} \cdot HCl$, 779.3145; found (ESI+), 744.34539;

Example 36

5

{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate



10

The title compound is prepared by the procedure of Example 1, using Butanoic acid, 3,3-dimethyl-, [(chlorocarbonyl)oxy]methyl ester and N-butylglycylcycline to give the product of the Example.

15

MS m/z 00-304762LMS;

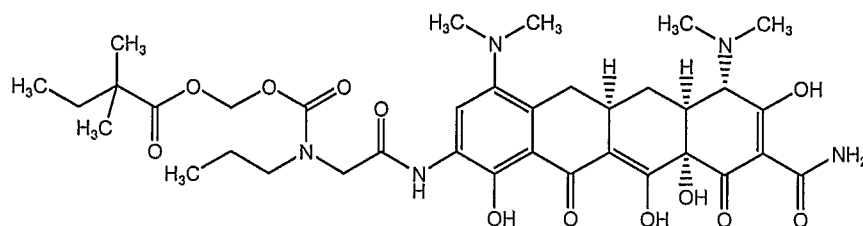
HRMS: calcd for $C_{37}H_{51}N_5O_{12} \cdot HCl$, 793.3301; found (ESI+), 758.36071;

Example 37

20

{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate

25



The title compound is prepared by the procedure of Example 1, using
 [(chlorocarbonyl)oxy]methyl 2,2-dimethylbutanoate and N-propylglycylcycline to give
 5 the product of the Example.

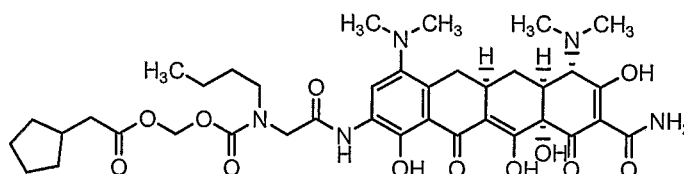
MS m/z 00-304763LMS;

HRMS: calcd for $C_{36}H_{49}N_5O_{12} \cdot HCl$, 779.3145; found (ESI+), 744.3452;

10 Example 38

([[[(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl]oxy)methyl cyclopentylacetate

15



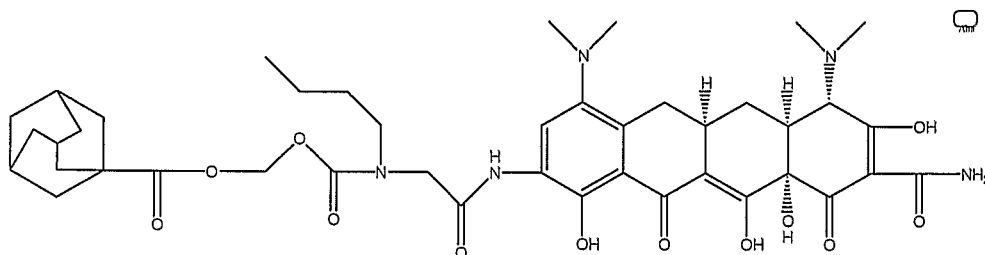
20 The title compound is prepared by the procedure of Example 1, using
 [(chlorocarbonyl)oxy]methyl cyclopentylacetate and N-butylglycylcycline to give the
 product of the Example.

25 MS (ESI) m/z 770.7 (M+H);

HRMS: calcd for $C_{38}H_{51}N_5O_{12} \cdot HCl$, 805.3301; found (ESI+), 770.36062;

Example 39

5 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate



10 The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl adamantane-1-carboxylate and N-butylglycylcycline to give the product of the Example.

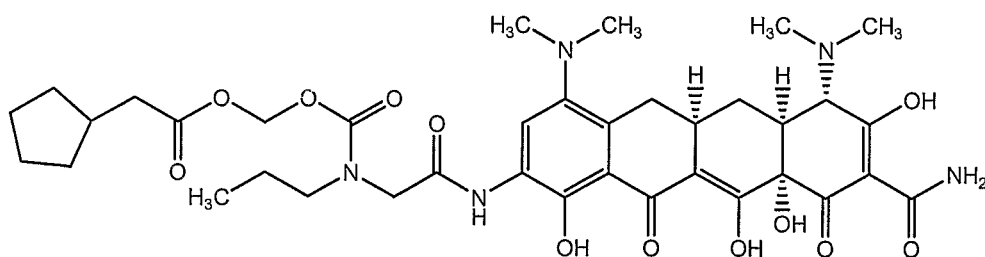
MS (ESI) m/z 822.9 (M+H);

HRMS: calcd for $C_{42}H_{55}N_5O_{12} \cdot HCl$, 857.3614; found (ESI+), 822.39184;

15

Example 40

20 {{{2-[[{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl cyclopentylacetate



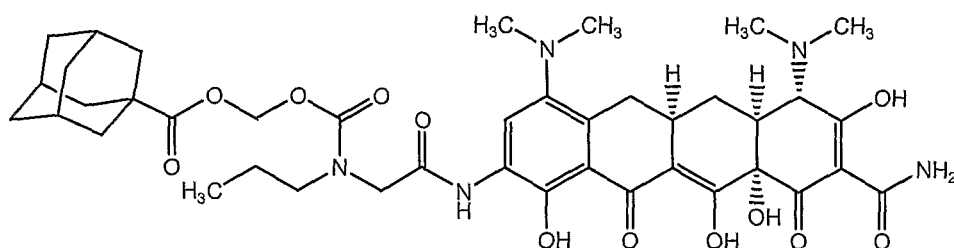
The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl cyclopentylacetate and N-propylglycylcyclohexylamine to give the product of the Example.

5 MS (ESI) m/z 754.2 ((M-H)-);

HRMS: calcd for $C_{37}H_{49}N_5O_{12} \cdot HCl$, 791.3145; found (ESI+), 756.34433;

Example 41

10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl)oxy)methyl adamantane-1-carboxylate



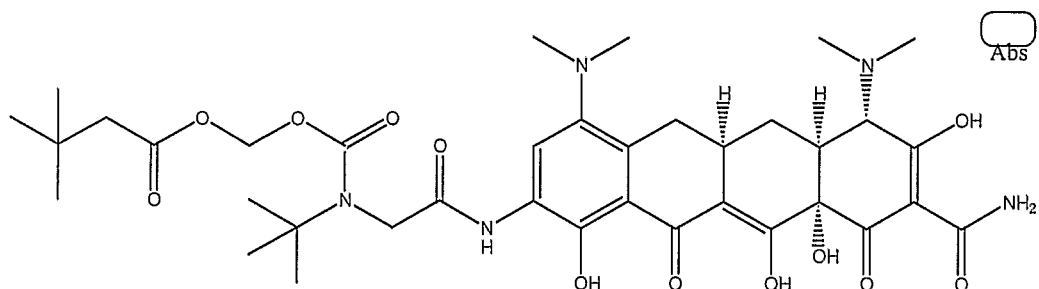
The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl adamantane-1-carboxylate and N-propylglycylcyclohexylamine to give the product of the Example.

MS (ESI) m/z 808.8 (M+H);

HRMS: calcd for $C_{41}H_{53}N_5O_{12} \cdot HCl$, 843.3458; found (ESI+), 808.37604;

Example 42

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 3,3-dimethylbutanoate



5

To a solution of 9-amino-minocycline monosulfate (0.0055 mol, 3.135g, 1 equivalent)
 10 in a mixture of 12 ml of acetonitrile and 50 ml of DMPU is added 1.66 g (3
 equivalents) of triethylamine and Reference Compound 109 (0.012 mole, 4.88g),
 3,3-Dimethyl-butyrlic acid [tert-butyl-(2-isobutoxycarbonyloxy-2-oxo-ethyl)-
 carbamoyloxy]-methyl ester. The reaction is stirred at room temperature for 2 hour, 1
 mL methanol is added, stirred for 5 min. and the mixture is poured onto a mixture of
 15 500 ml of ether and 100 ml of isopropanol. Solid is collected and purified by
 extraction to give 1.5 g of the product of the Example.

MS (ESI) m/z 758.55 (M+H);

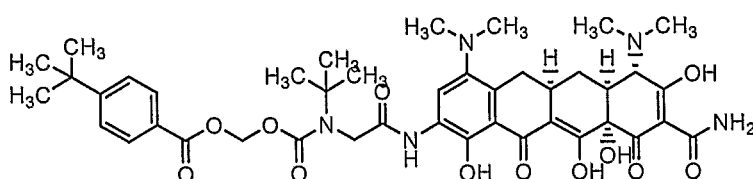
HRMS: calcd for $C_{37}H_{51}N_5O_{12} \cdot HCl$, 793.3301; found (ESI+), 758.36201;

20

Example 43

Prepared according to Scheme II

25 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-
 tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-
 oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 4-tert-butylbenzoate



Reference Compound 57 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline
 5 using the conditions of Example 42 to give the product of the Example.

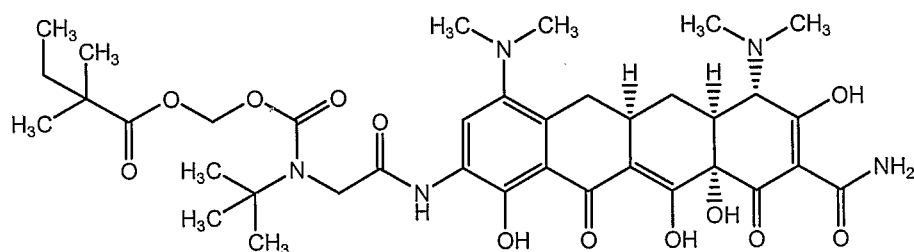
MS (ESI) m/z 820.37 (M+H);

HRMS: calcd for $C_{42}H_{53}N_5O_{12} \cdot HCl$, 855.3458; found (ESI+), 820.37574;

10 Example 44

{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino)-2-oxoethyl)(tert-butyl)amino}carbonyl}oxy)methyl 2,2-dimethylbutanoate

15



The title compound is prepared by reacting the product of the reaction of N-(tert-butyl)-N-{{(2,2-dimethylbutanoyl)oxy}methoxy}carbonyl}glycine using the conditions
 20 of Reference Compound 109 with 9-aminocycline using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 758.63 (M+H);

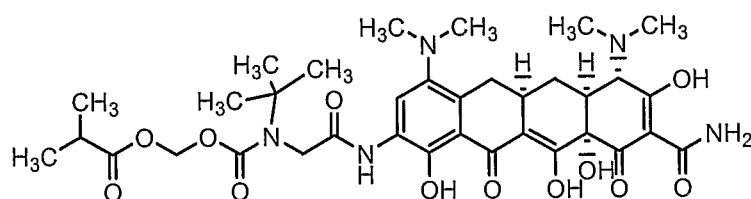
25 HRMS: calcd for $C_{37}H_{51}N_5O_{12} \cdot HCl$, 793.3301; found (ESI+), 758.36119;

Example 45

Prepared according to Scheme 2

- 5 ([[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 2-methylpropanoate

10



Reference Compound 58 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

15

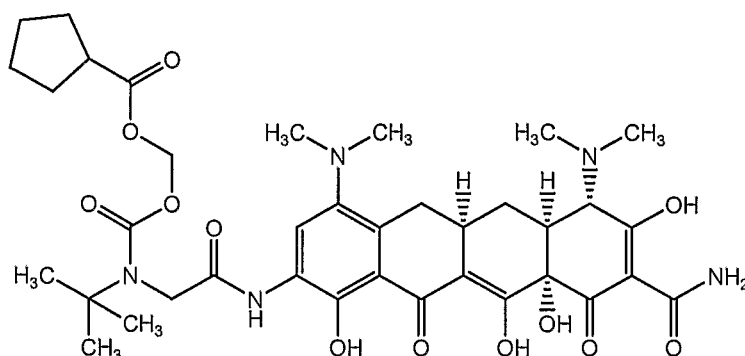
MS (ESI) m/z 730.38 (M+H);HRMS: calcd for $C_{35}H_{47}N_5O_{12} \cdot HCl$, 765.2988; found (ESI+), 730.33002;

20

Example 46

25

([[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclopentanecarboxylate



Reference Compound 59 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocyclohexylamine using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 754.09 ((M-H)⁻);

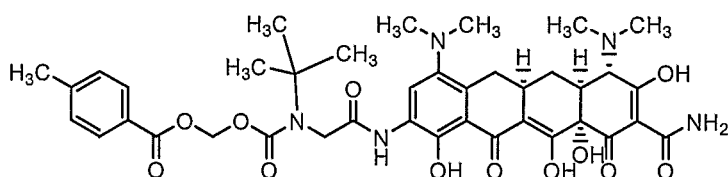
HRMS: calcd for $C_{37}H_{49}N_5O_{12} \cdot HCl$, 791.3145; found (ESI⁺), 378.67644;

10

Example 47

((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino]carbonyloxy)methyl 4-methylbenzoate

15



Reference Compound 60 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocyclohexylamine using the conditions of Example 42 to give the product of the Example.

20

MS (ESI) m/z 778.34 (M+H);

HRMS: calcd for $C_{39}H_{47}N_5O_{12}$, 777.3221; found (ESI+), 778.33065;

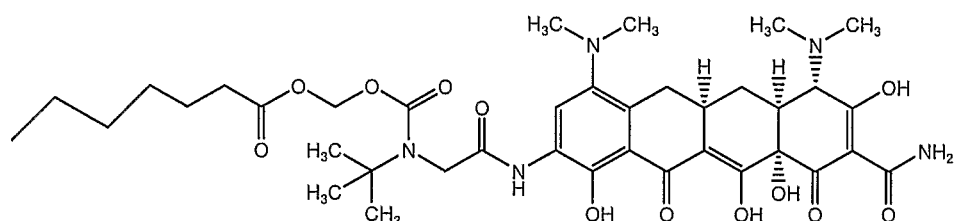
Example 48

5

Prepared according to Scheme II

({[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl heptanoate

10



Reference Compound 61 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

15

MS (ESI) m/z 772.45 (M+H);

HRMS: calcd for $C_{38}H_{53}N_5O_{12} \cdot HCl$, 807.3458; found (ESI+), 772.37695;

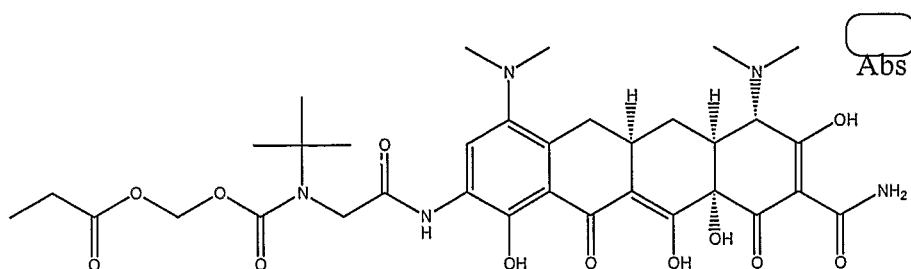
20

Example 49

Prepared according to Scheme II

({[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl propionate

25



Reference Compound 62 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline
 5 using the conditions of Example 42 to give the product of the Example.

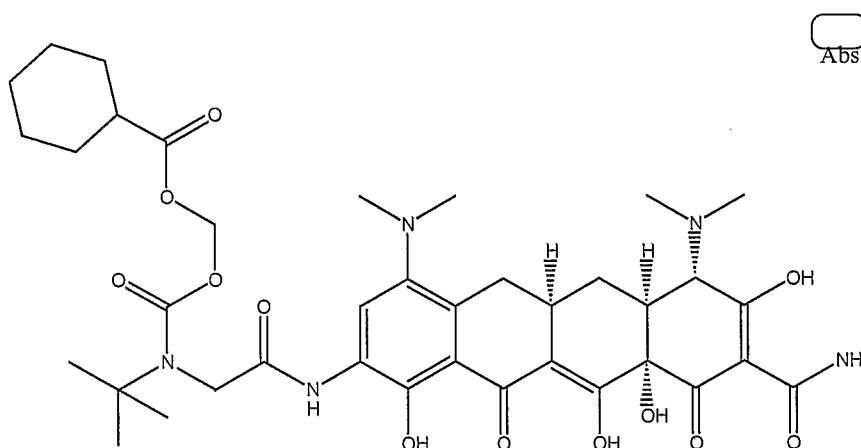
MS (ESI) m/z 716.3 (M+H);

HRMS: calcd for $C_{34}H_{45}N_5O_{12} \cdot HCl$, 751.2832; found (ESI+), 716.31461;

10

Example 50

{{[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyloxy)methyl cyclohexanecarboxylate
 15



Reference Compound 63 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline
 20 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 770.36 (M+H);

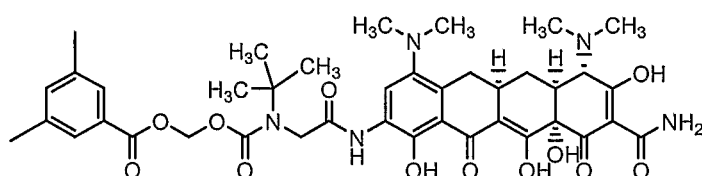
HRMS: calcd for $C_{38}H_{51}N_5O_{12} \cdot HCl$, 805.3301; found (ESI-), 768.34546;

5

Example 51

Prepared according to Scheme 2

10 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate



15

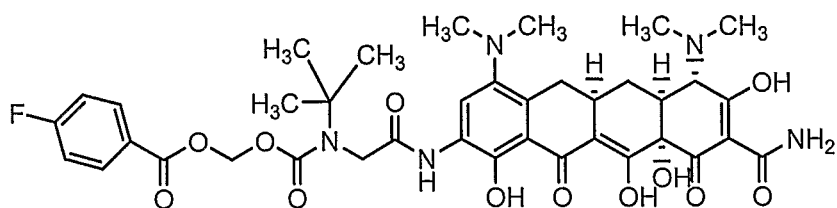
Reference Compound 64 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline using the conditions of Example 42 to give the product of the Example.

20 MS (ESI) m/z 792.32 (M+H);

HRMS: calcd for $C_{40}H_{49}N_5O_{12} \cdot HCl$, 827.3145; found (ESI+), 792.34613;

Example 52

25 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate



- 5 Reference Compound 65 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline using the conditions of Example 42 to give the product of the Example.

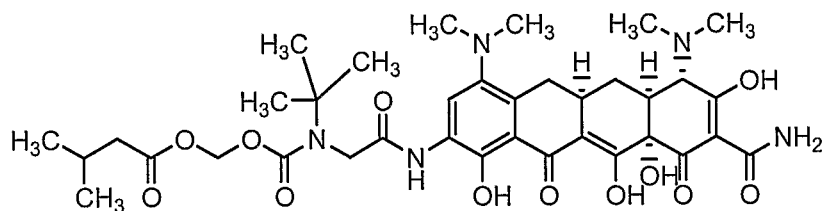
MS (ESI) m/z 782.3 (M+H);

- 10 HRMS: calcd for $C_{38}H_{44}FN_5O_{12} \cdot HCl$, 817.2737; found (ESI+), 782.30406

Example 53

Prepared according to Scheme 2

- 15 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3-methylbutanoate



20

- Reference Compound 66 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline using the conditions of Example 42 to give the product of the Example.
- 25

MS (ESI) m/z 744.37 (M+H);

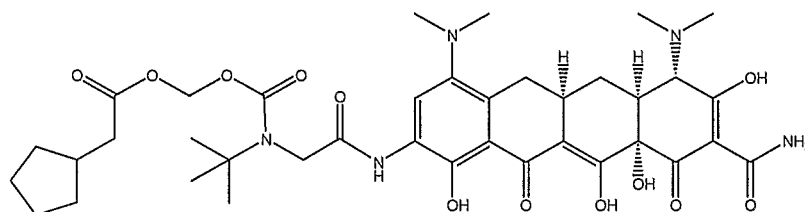
HRMS: calcd for $C_{36}H_{49}N_5O_{12} \cdot HCl$, 779.3145; found (ESI+), 744.34481;

Example 54

5

{{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclopentylacetate

10



Reference Compound 67 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

15

MS (ESI) m/z 770.4 (M+H);

HRMS: calcd for $C_{38}H_{51}N_5O_{12} \cdot HCl$, 805.3301; found (ESI+), 770.35888;

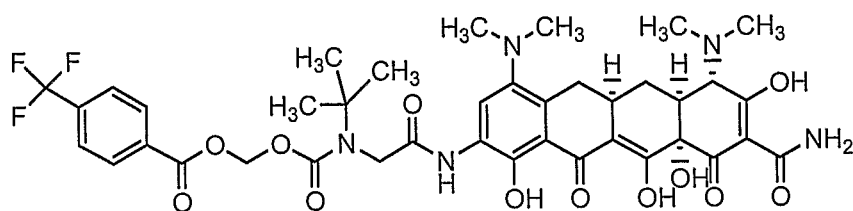
20

Example 55

Prepared according to Scheme 2

{{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(trifluoromethyl)benzoate

25



Reference Compound 68 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycinolide
 5 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 832.2 (M+H);

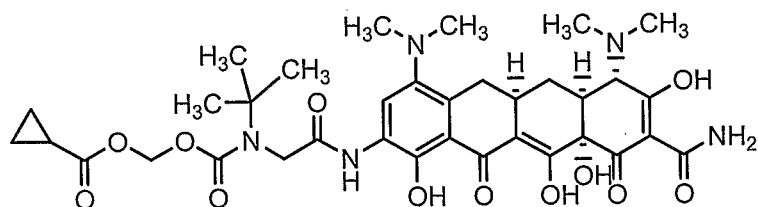
MS (ESI) m/z 416.6 (M+2H);

HRMS: calcd for $C_{39}H_{44}F_3N_5O_{12} \cdot HCl$, 867.2705; found (ESI+), 832.30055;

10

Example 56

{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl cyclopropanecarboxylate
 15



Reference Compound 69 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycinolide
 20 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 728.34 (M+H);

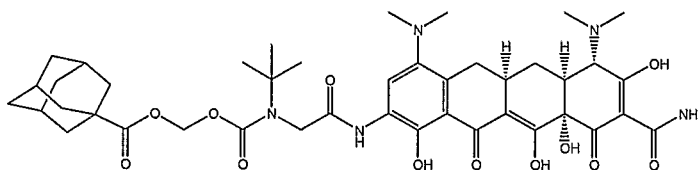
HRMS: calcd for $C_{35}H_{45}N_5O_{12} \cdot HCl$, 763.2832; found (ESI+), 728.31289;

25

Example 57

Prepared according to Scheme 2

- 5 ([[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl adamantane-1-carboxylate



10

- Reference Compound 70 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline
15 using the conditions of Example 42 to give the product of the Example.

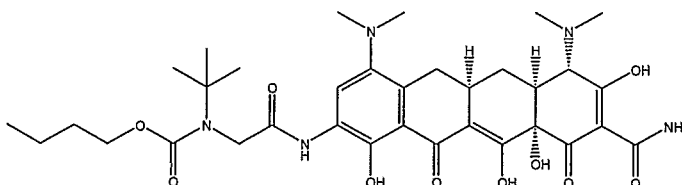
MS (ESI) m/z 822.5 (M+H);HRMS: calcd for $C_{42}H_{55}N_5O_{12} \cdot HCl$, 857.3614; found (ESI+), 822.39237

20

Example 58

butyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](tert-butyl)carbamate

25



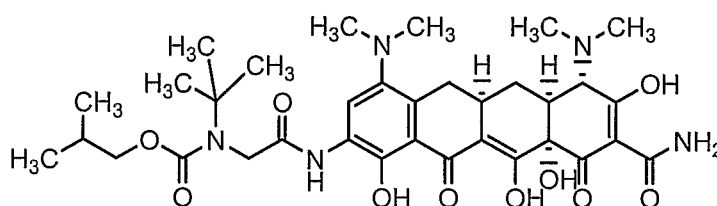
The title compound is prepared by the procedure of Example 42, using 1 equivalent of 9-amino-minocycline and 2 equivalents of isobutoxycarbonyl N-(butoxycarbonyl)-N-(tert-butyl)glycinate Reference Example 118 to give the product of the example.

5 MS (ESI) m/z 686.4 (M+H);

HRMS: calcd for $C_{34}H_{47}N_5O_{10} \cdot HCl$, 721.3090; found (ESI+), 686.34079;

Example 59

10 isobutyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(tert-butyl)carbamate



15

The title compound is prepared by the procedure of Example 42, using 1 equivalent of 9-amino-minocycline and 2 equivalents of isobutoxycarbonyl N-(tert-butyl)-N-(isobutoxycarbonyl)glycinate, Reference Example 119 to give the product of the
20 example.

MS (ESI) m/z 686.3 (M+H);

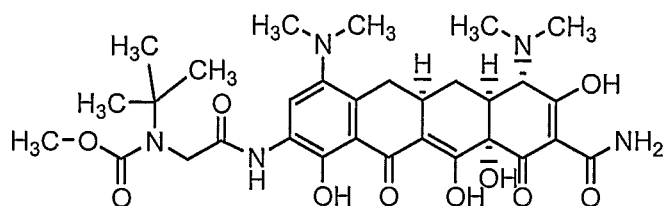
MS (ESI) m/z 1371.7 (2M+H);

HRMS: calcd for $C_{34}H_{47}N_5O_{10} \cdot HCl$, 721.3090; found (ESI-), 684.32433;

25

Example 60

30 methyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(tert-butyl)carbamate



5 The title compound is prepared by the procedure of Example 42, using 1 equivalent of 9-amino-minocycline and 2 equivalents of isobutoxycarbonyl N-(tert-butyl)-N-(methoxycarbonyl)glycinate Reference Example 120 to give the product of the example.

10 MS (ESI) m/z 644.3 (M+H);

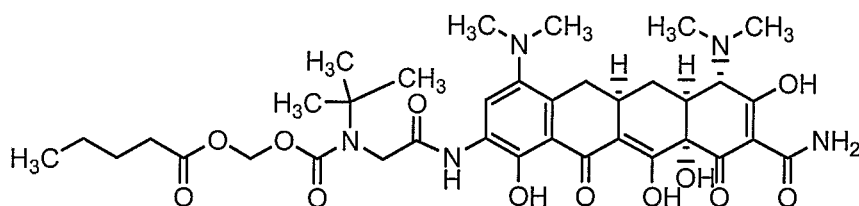
MS (ESI) m/z 322.6 (M+2H);

HRMS: calcd for $C_{31}H_{41}N_5O_{10} \cdot HCl$, 679.2620; found (ESI-), 642.27736;

Example 61

15

(([(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl pentanoate



20

Reference Compound 71 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline
25 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 742 (M-H);

HRMS: calcd for $C_{36}H_{49}N_5O_{12} \cdot HCl$, 779.3145; found (ESI+), 744.34613;

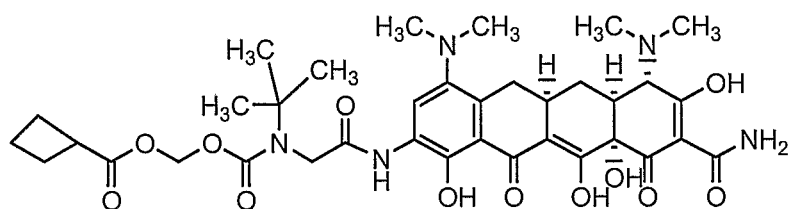
Example 62

5

Prepared according to Scheme II

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclobutanecarboxylate

10



Reference Compound 72 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

15

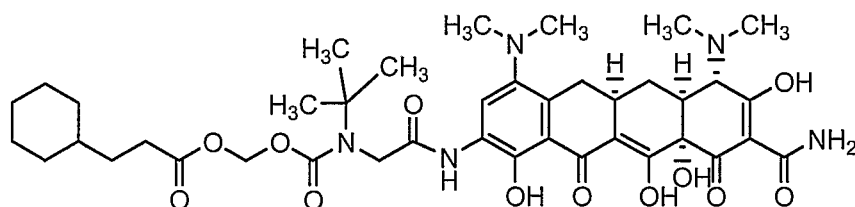
MS (ESI) m/z 742.4 (M+H);

Example 63

20

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3-cyclohexylpropanoate

25



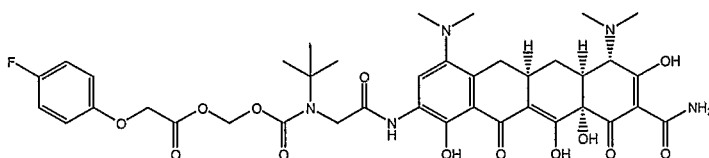
Reference Compound 73 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

5

MS (ESI) m/z 796.4 (M-H);

Example 64

10 {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl (4-fluorophenoxy)acetate



15

Reference Compound 74 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

20 MS (ESI) m/z 812.4 (M+H);

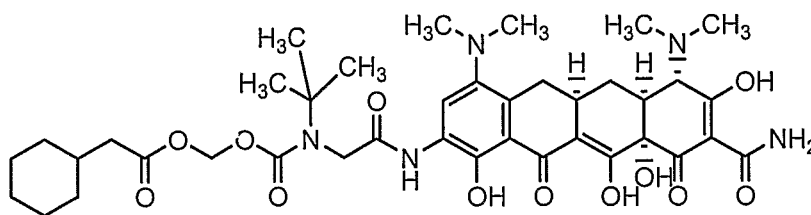
MS (ESI) m/z 406.7 (M+2H);

HRMS: calcd for $C_{39}H_{46}FN_5O_{13} \cdot HCl$, 847.2843; found (ESI+), 812.31518;

Example 65

25

{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclohexylacetate



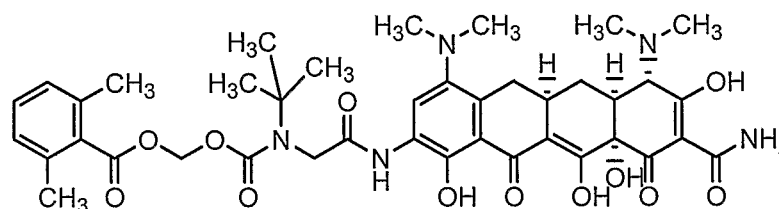
Reference Compound 75 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline
5 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 782.2 (M-H);

HRMS: calcd for $C_{39}H_{53}N_5O_{12} \cdot HCl$, 819.3458; found (ESI+), 784.37621;

Example 66

{{[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2,6-dimethylbenzoate



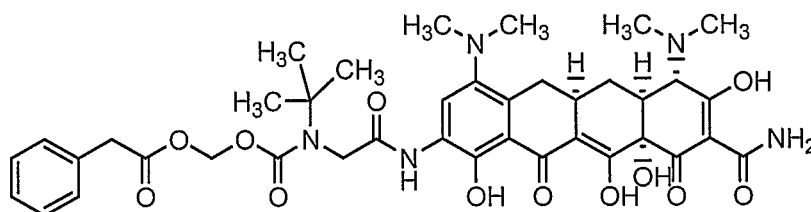
Reference Compound 76 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline
20 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 790.4 (M-H);

HRMS: calcd for $C_{40}H_{49}N_5O_{12} \cdot HCl$, 827.3145; found (ESI+), 792.34423;

Example 67

5 {[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl phenylacetate



Reference Compound 77 is reacted under the conditions of Reference Compound
10 109 and the product of said reaction is further contacted with 9-aminocycline
using the conditions of Example 42 to give the product of the Example.

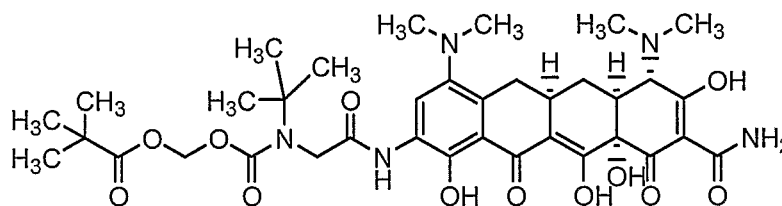
MS (ESI) m/z 778.3 (M+H);

HRMS: calcd for $C_{39}H_{47}N_5O_{12} \cdot HCl$, 813.2988; found (ESI+), 778.3299;

15

Example 68

20 {[(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl pivalate



Reference Compound 78 is reacted under the conditions of Reference Compound
25 109 and the product of said reaction is further contacted with 9-aminocycline
using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 744.5 (M+H);

HRMS: calcd for $C_{36}H_{49}N_5O_{12} \cdot HCl$, 779.3145; found (ESI+), 744.34434;

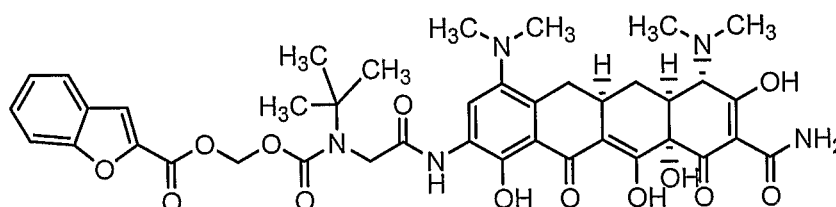
Example 69

5

Prepared according to Scheme II

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 1-benzofuran-2-carboxylate

10



Reference Compound 79 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

15

MS (ESI) m/z 804.4 (M+H);

MS (ESI) m/z 402.7 (M+2H);

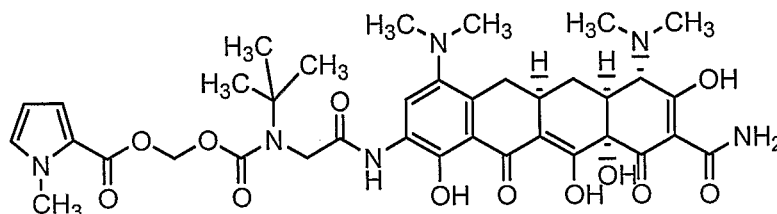
HRMS: calcd for $C_{40}H_{45}N_5O_{13} \cdot HCl$, 839.2781; found (ESI+), 804.30779;

20

Example 70

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 1-benzofuran-2-carboxylate

25



Reference Compound 80 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline
 5 using the conditions of Example 42 to give the product of the Example.

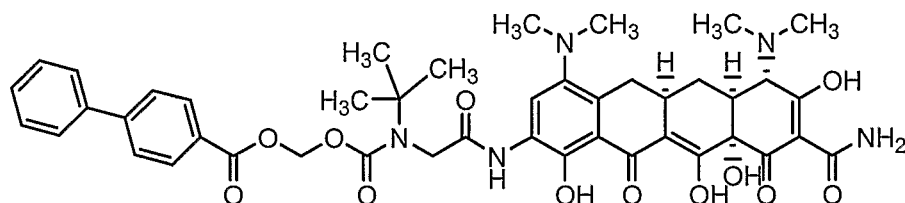
MS (ESI) m/z 767.4 (M+H);

HRMS: calcd for $C_{37}H_{46}N_6O_{12}$, 766.3174; found (ESI+), 767.32406;

10 Example 71

{{[(2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate

15



Reference Compound 81 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline
 20 using the conditions of Example 42 to give the product of the Example.

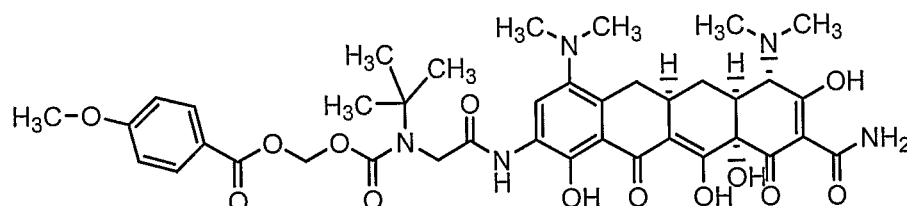
MS (ESI) m/z 838.2 (M-H);

MS (ESI) m/z 113 (TFA-H);

25 HRMS: calcd for $C_{44}H_{49}N_5O_{12} \cdot HCl$, 875.3145; found (ESI+), 840.34496;

Example 72

- 5 {{{2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate



- 10 Reference Compound 82 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminotetracycline using the conditions of Example 42 to give the product of the Example.

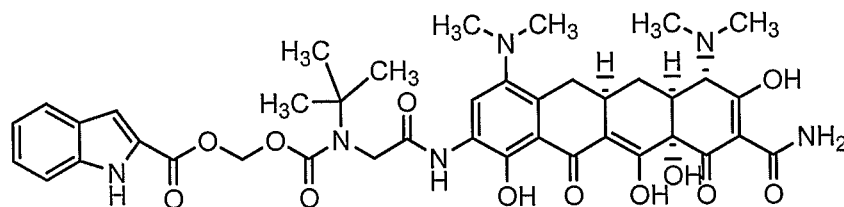
MS (ESI) m/z 792.3 (M-H);

- 15 HRMS: calcd for $C_{39}H_{47}N_5O_{13} \cdot HCl$, 829.2937; found (ESI+), 794.32511;

Example 73

Prepared according to Scheme II

- 20 {{{2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl}amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1H-indole-2-carboxylate



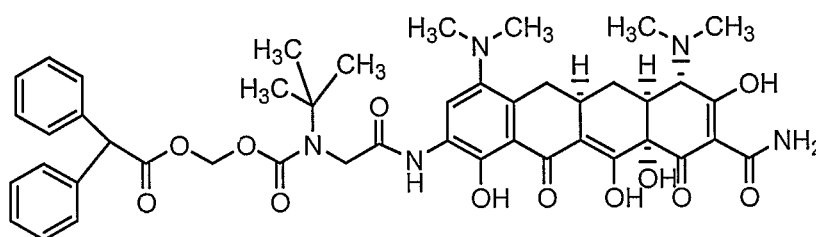
25

Reference Compound 83 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

- 5 MS (ESI) m/z 803.4 (M+H);
 HRMS: calcd for $C_{40}H_{46}N_6O_{12} \cdot HCl$, 838.2941; found (ESI+), 803.32375;

Example 74

- 10 $\{[(2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino\}-2-oxoethyl)(tert-butyl)amino]carbonyl\}oxy\}$ methyl diphenylacetate

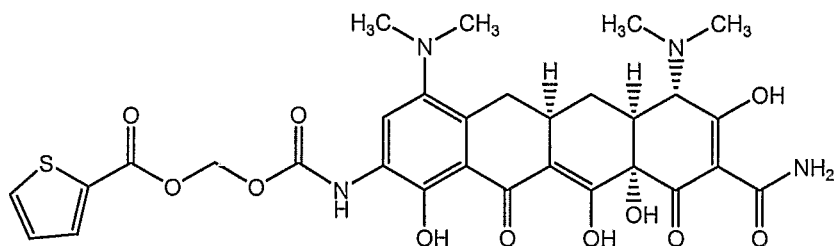


- 15 Reference Compound 84 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

- 20 MS (ESI) m/z 852.4 (M-H);
 HRMS: calcd for $C_{45}H_{51}N_5O_{12} \cdot HCl$, 889.3301; found (ESI-), 852.3463;

Example 75

- 25 Prepared according to scheme 6
 $\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino\}carbonyl\}oxy\}$ methyl thiophene-2-carboxylate



- 5 The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl thiophene-2-carboxylate in place of the Reference Compound 109 to give the product of the example.

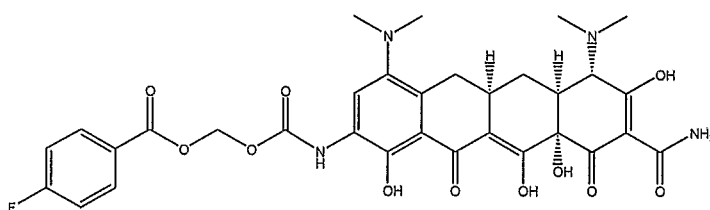
MS (ESI) m/z 655.2 (M-H);

- 10 HRMS: calcd for $C_{30}H_{32}N_4O_{11}S \cdot HCl$, 692.1555; found (ESI+), 657.18613;

Example 76

Prepared according to scheme 6

- 15 [({[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 4-fluorobenzoate



20

The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl 4-fluorobenzoate in place of the Reference Compound 109 to give the product of the example.

25

MS (ESI) m/z 667.2 (M-H);

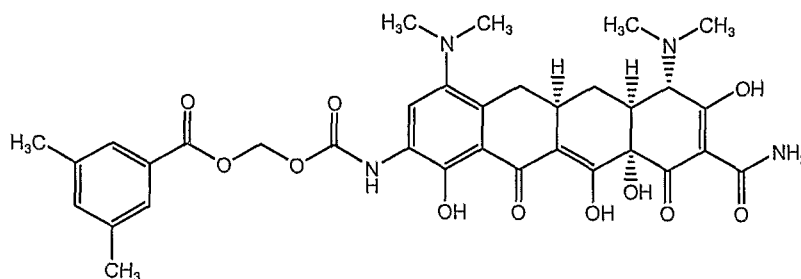
HRMS: calcd for $C_{32}H_{33}FN_4O_{11} \cdot HCl$, 704.1897; found (ESI+), 669.22024;

5

Example 77

Prepared according to scheme 6

10 [({[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 3,5-dimethylbenzoate



15 The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl 3,5-dimethylbenzoate in place of the Reference Compound 109 to give the product of the example.

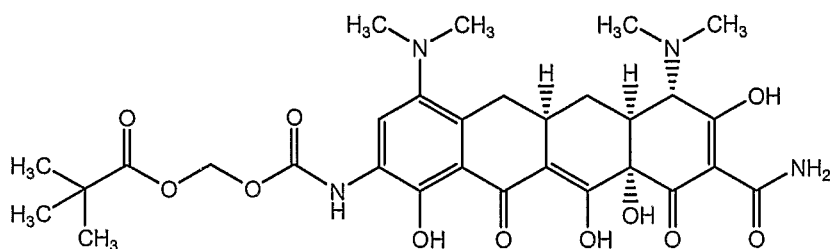
MS (ESI) m/z 679.2 (M+H);

20 HRMS: calcd for $C_{34}H_{38}N_4O_{11} \cdot HCl$, 714.2304; found (ESI+), 679.26076;

Example 78

Prepared according to scheme 6

25 [({[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl pivalate



The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl pivalate in place of the Reference Compound 109 to give the product of the example.

MS (ESI) m/z 631.2 (M+H);

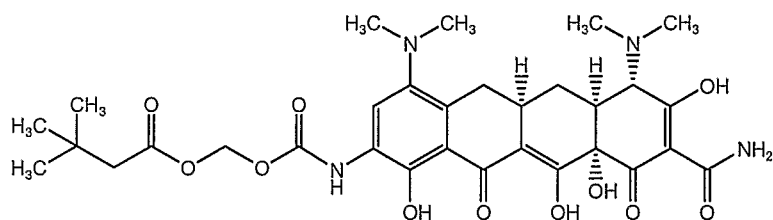
HRMS: calcd for $C_{30}H_{38}N_4O_{11} \cdot HCl$, 666.2304; found (ESI+), 631.26094;

10

Example 79

Prepared according to scheme 6

[[{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 3,3-dimethylbutanoate



The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl 3,3-dimethylbutanoate in place of the Reference Compound 109 to give the product of the example.

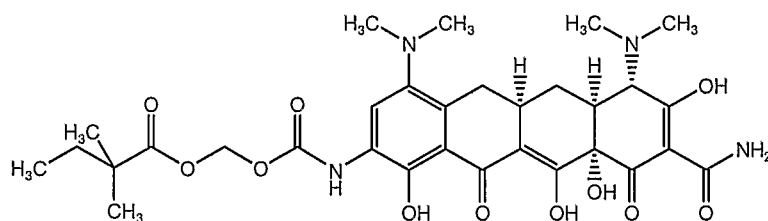
MS (ESI) m/z 643.3 (M-H);

HRMS: calcd for $C_{31}H_{40}N_4O_{11} \cdot HCl$, 680.2460; found (ESI+), 645.27632;

Example 80

Prepared according to scheme 6

- 5 [(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 2,2-dimethylbutanoate



10

The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl 2,2-dimethylbutanoate in place of the Reference Compound 109 to give the product of the example.

15

MS (ESI) m/z 645.2 (M+H);

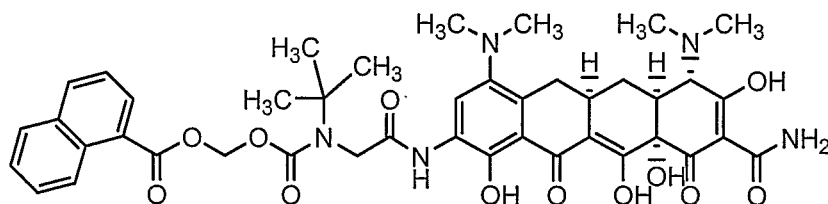
HRMS: calcd for $C_{31}H_{40}N_4O_{11} \cdot HCl$, 680.2460; found (ESI+), 645.27637;

20

Example 81

((2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy]methyl 1-naphthoate

25



Reference Compound 85 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

5

MS (ESI) m/z 812.5 (M-H);

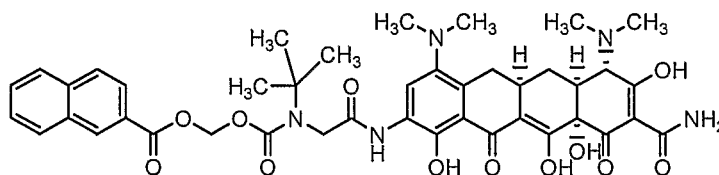
HRMS: calcd for $C_{42}H_{47}N_5O_{12} \cdot HCl$, 849.2988; found (ESI+), 814.33029;

Example 82

10

{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2-naphthoate

15



Reference Compound 86 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

20

MS (ESI) m/z 812.5 (M-H);

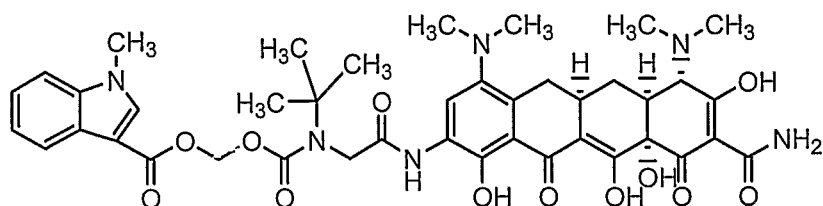
HRMS: calcd for $C_{42}H_{47}N_5O_{12} \cdot HCl$, 849.2988; found (ESI+), 814.33004;

25

Example 83

{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-indole-3-carboxylate

30



Reference Compound 87 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline
 5 using the conditions of Example 42 to give the product of the Example.

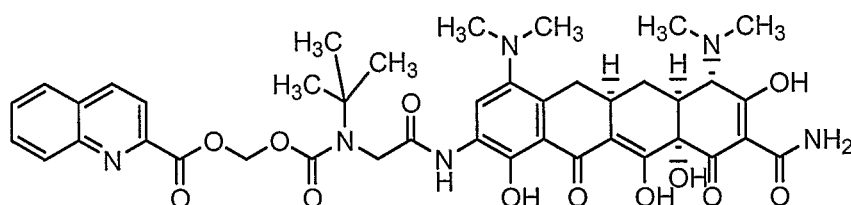
MS (ESI) m/z 815.5 (M-H);

HRMS: calcd for $C_{41}H_{48}N_6O_{12} \cdot HCl$, 852.3097; found (ESI-), 815.32484;

10 Example 84

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl quinoline-2-carboxylate

15



Reference Compound 88 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline
 20 using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 813.5 (M-H);

HRMS: calcd for $C_{41}H_{46}N_6O_{12} \cdot HCl$, 850.2941; found (ESI+), 815.32509;

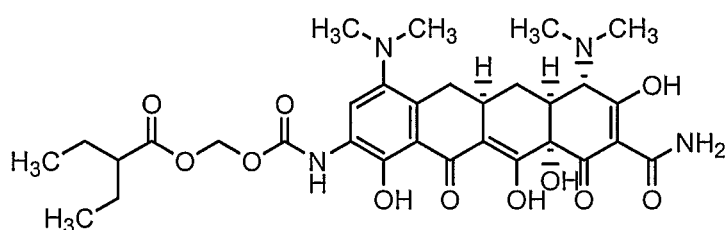
25

Example 85

Prepared according to scheme 6

- 5 [([[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 2-ethylbutanoate

10



15

The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl 2-ethylbutanoate in place of the Reference Compound 109 to give the product of the example.

20

MS (ESI) m/z 643.4 (M-H);

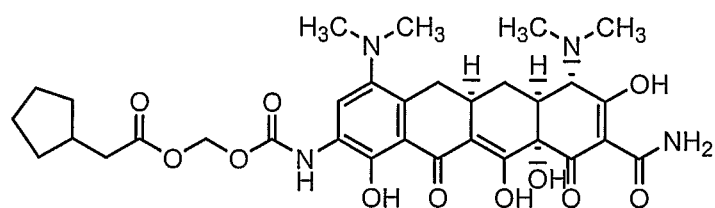
MS (ESI) m/z 1287.7 (2M-H);

HRMS: calcd for $C_{31}H_{40}N_4O_{11} \cdot HCl$, 680.2460; found (ESI+), 645.27618;

Example 86

Prepared according to scheme 6

- 5 [[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl cyclopentylacetate



10

The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl cyclopentylacetate in place of the Reference Compound 109 to give the product of the example.

15

MS (ESI) m/z 655.3 (M-H);

MS (ESI) m/z 1311.7 (2M-H);

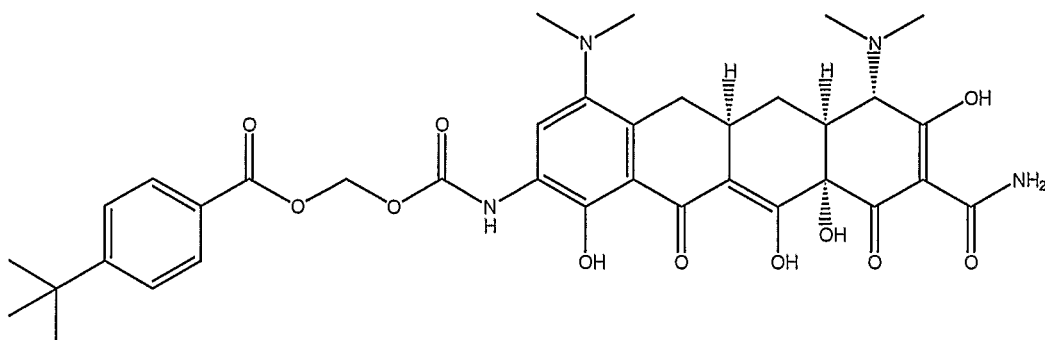
HRMS: calcd for C₃₂H₄₀N₄O₁₁ · HCl, 692.2460; found (ESI+), 657.27572;

20

Example 87

Prepared according to scheme 6

- 25 [[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy]methyl 4-tert-butylbenzoate



The title compound is prepared by the procedure of Example 42, using [(chlorocarbonyl)oxy]methyl 4-tert-butylbenzoate in place of the Reference

5 Compound 109 to give the product of the example.

MS (ESI) m/z 705.1 (M-H);

MS (ESI) m/z 1410.9 (2M-H);

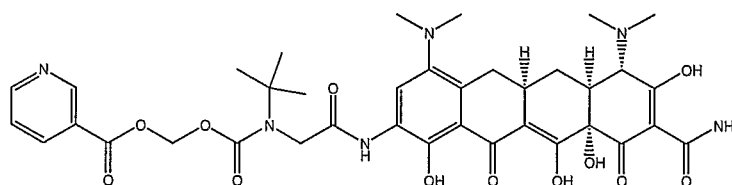
HRMS: calcd for $C_{36}H_{42}N_4O_{11} \cdot HCl$, 742.2617; found (ESI+), 707.29336;

10

Example 88

({[(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl nicotinate

15



Reference Compound 89 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-amininocycline using the conditions of Example 42 to give the product of the Example.

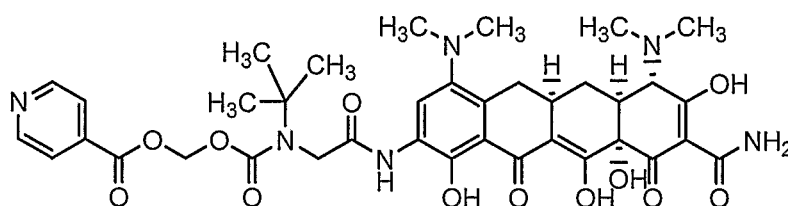
20

MS (ESI) m/z 763.5 (M-H);

HRMS: calcd for $C_{37}H_{44}N_6O_{12} \cdot HCl$, 800.2784; found (ESI+), 765.30896;

Example 89

5 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl isonicotinate



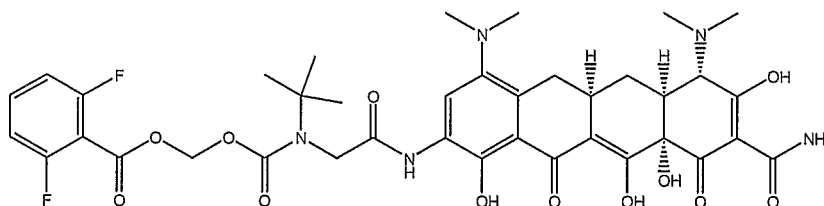
10 Reference Compound 90 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

HRMS: calcd for $C_{37}H_{44}N_6O_{12} \cdot HCl$, 800.2784; found (ESI+), 765.3117;

15

Example 90

20 {{{(2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2,6-difluorobenzoate



Reference Compound 91 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

25

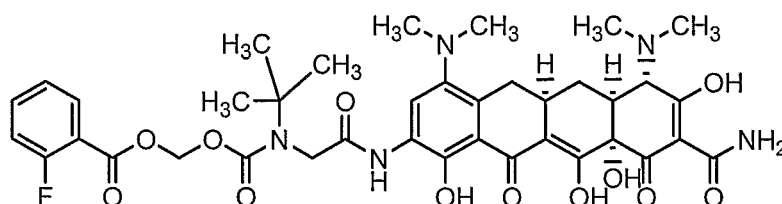
MS (ESI) m/z 798.2 (M-H);

HRMS: calcd for $C_{38}H_{43}F_2N_5O_{12} \cdot HCl$, 835.2643; found (ESI+), 800.29464;

Example 91

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(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 2-fluorobenzoate



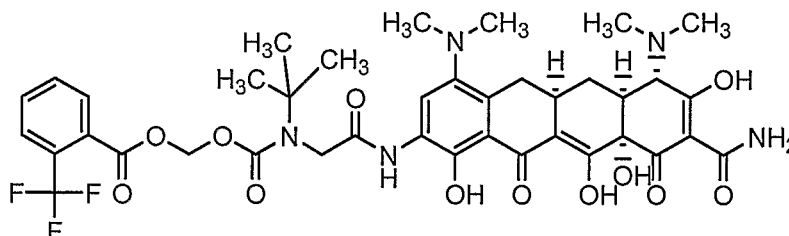
Reference Compound 92 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-amininocycline using the conditions of Example 42 to give the product of the Example.

15 MS (ESI) m/z 780 (M-H);
 HRMS: calcd for $C_{38}H_{44}FN_5O_{12} \cdot HCl$, 817.2737; found (ESI+), 782.30558;

Example 92

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 25

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 2-(trifluoromethyl)benzoate



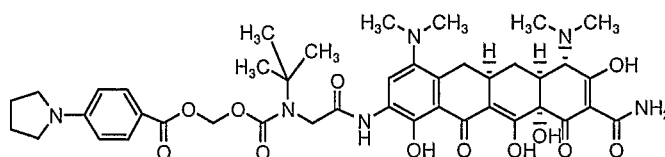
Reference Compound 93 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

- 5 HRMS: calcd for $C_{39}H_{44}F_3N_5O_{12} \cdot HCl$, 867.2705; found (ESI+), 832.30026;

Example 93

- 10 $\{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyloxy\}$ methyl 4-pyrrolidin-1-ylbenzoate

15



Reference Compound 94 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

20

MS (ESI) m/z 833.4 ($M+H$);

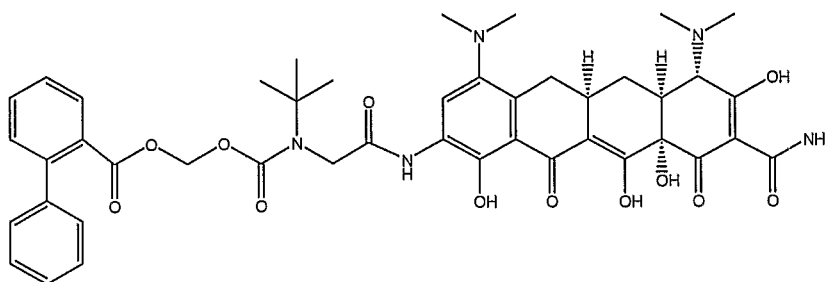
HRMS: calcd for $C_{42}H_{52}N_6O_{12} \cdot HCl$, 868.3410; found (ESI-), 831.3565;

Example 94

25

$\{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyloxy\}$ methyl 1,1'-biphenyl-2-carboxylate

30



Reference Compound 95 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycin
 5 using the conditions of Example 42 to give the product of the Example.

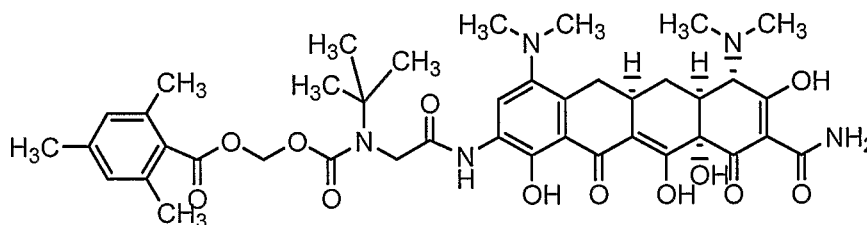
MS (ESI) m/z 838.4 (M-H);

HRMS: calcd for $C_{44}H_{49}N_5O_{12} \cdot HCl$, 875.3145; found (ESI+), 840.34553;

10

Example 95

{{[2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2,4,6-trimethylbenzoate



15

Reference Compound 96 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycin
 20 using the conditions of Example 42 to give the product of the Example.

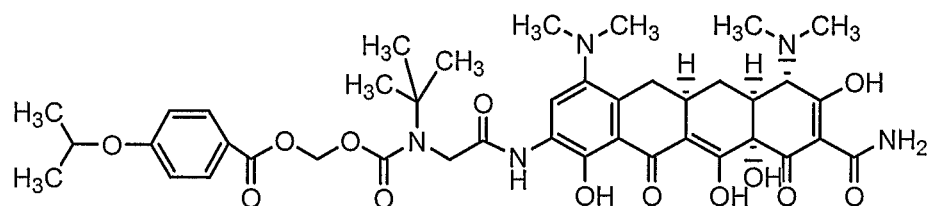
MS (ESI) m/z 804.5 (M-H);

HRMS: calcd for $C_{41}H_{51}N_5O_{12} \cdot HCl$, 841.3301; found (ESI+), 806.36101;

Example 96

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(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 4-isopropoxybenzoate



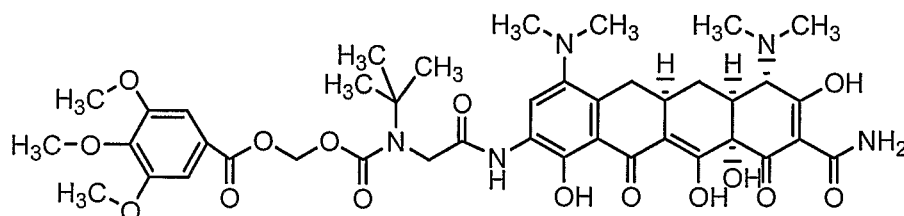
Reference Compound 97 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-amininocycline using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 820.2 (M-H);

HRMS: calcd for $C_{41}H_{51}N_5O_{13} \cdot HCl$, 857.3250; found (ESI-), 820.34117;

Example 97

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 3,4,5-trimethoxybenzoate

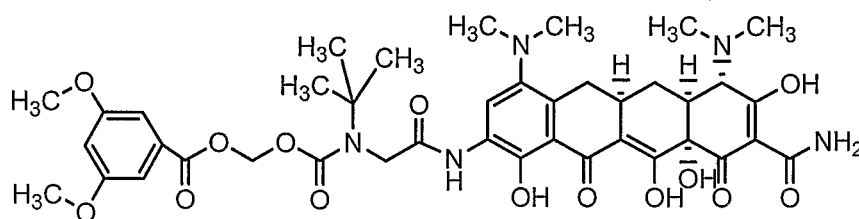


Reference Compound 98 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline using the conditions of Example 42 to give the product of the Example.

- 5 MS (ESI) m/z 852.2 (M-H);
 HRMS: calcd for $C_{41}H_{51}N_5O_{15} \cdot HCl$, 889.3148; found (ESI+), 854.34728;

Example 98

- 10 $\{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl\}oxy\}methyl\ 3,5-dimethoxybenzoate$

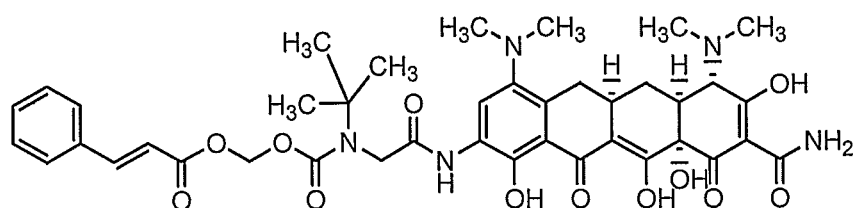


- 15 Reference Compound 99 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminocycline using the conditions of Example 42 to give the product of the Example.

- 20 MS (ESI) m/z 822.1 (M-H);
 HRMS: calcd for $C_{40}H_{49}N_5O_{14}$, 824.3349; found (ESI+), 824.3351;

Example 99

- 25 $\{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl\}oxy\}methyl\ (2E)-3-phenylprop-2-enoate$



Reference Compound 100 is reacted under the conditions of Reference Compound
 5 109 and the product of said reaction is further contacted with 9-aminomycin
 using the conditions of Example 42 to give the product of the Example.

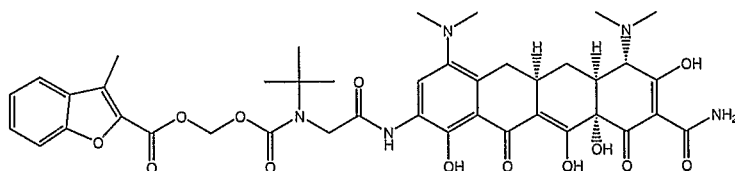
MS (ESI) m/z 788.3 (M-H);

HRMS: calcd for $C_{40}H_{47}N_5O_{12} \cdot HCl$, 825.2988; found (ESI+), 790.33068;

10

Example 100

{{[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-
 tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-
 15 oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-methyl-1-benzofuran-2-carboxylate



Reference Compound 101 is reacted under the conditions of Reference Compound
 20 109 and the product of said reaction is further contacted with 9-aminomycin
 using the conditions of Example 42 to give the product of the Example.

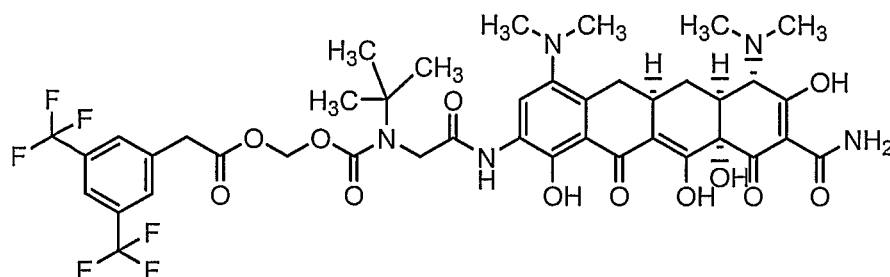
MS (ESI) m/z 816.5 (M-H);

HRMS: calcd for $C_{41}H_{47}N_5O_{13} \cdot HCl$, 853.2937; found (ESI+), 818.3234;

25

Example 101

- 5 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl [3,5-bis(trifluoromethyl)phenyl]acetate



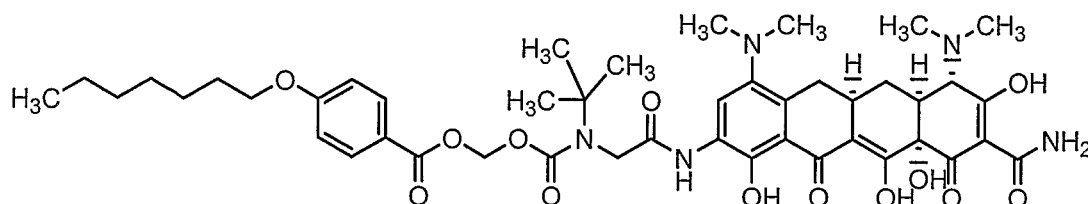
- 10 Reference Compound 102 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycinocycline using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 912 (M-H);

- 15 HRMS: calcd for $C_{41}H_{45}F_6N_5O_{12} \cdot HCl$, 949.2736; found (ESI+), 914.30367;

Example 102

- 20 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 4-(heptyloxy)benzoate



25

Reference Compound 103 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycinocycline using the conditions of Example 42 to give the product of the Example.

5

MS (ESI) m/z 876.1 (M-H);

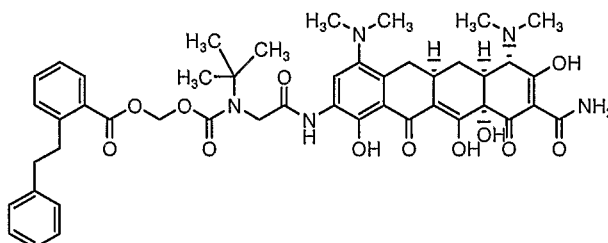
HRMS: calcd for $C_{45}H_{59}N_5O_{13} \cdot HCl$, 913.3876; found (ESI+), 878.41791;

10

Example 103

({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-(2-phenylethyl)benzoate

15



Reference Compound 104 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycinocycline using the conditions of Example 42 to give the product of the Example.

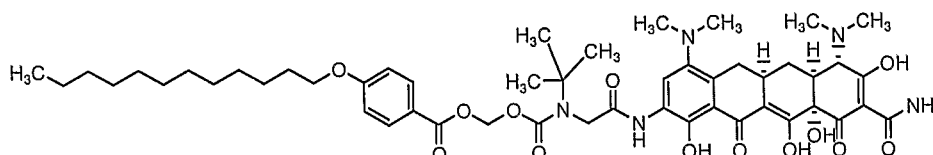
MS (ESI) m/z 866.5 (M-H);

HRMS: calcd for $C_{46}H_{53}N_5O_{12} \cdot HCl$, 903.3458; found (ESI), 868.37357;

25

Example 104

5 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 4-(dodecyloxy)benzoate



10

Reference Compound 105 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycin using the conditions of Example 42 to give the product of the Example.

15

MS (ESI) m/z 946.7 (M-H);

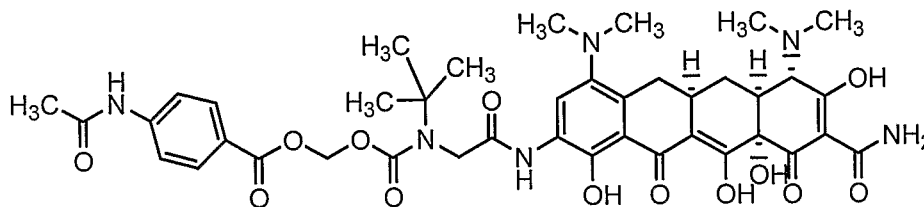
HRMS: calcd for $C_{50}H_{69}N_5O_{13} \cdot HCl$, 983.4659; found (ESI-), 946.48106;

20

Example 105

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 4-(acetamino)benzoate

25



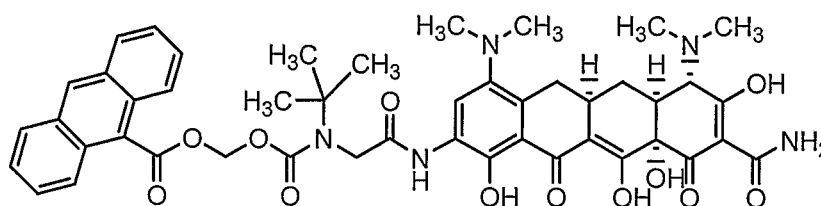
Reference Compound 106 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

5 MS (ESI) m/z 819.1 (M-H);

HRMS: calcd for $C_{40}H_{48}N_6O_{13} \cdot HCl$, 856.3046; found (ESI-), 819.32051;

Example 106

10 CCOC(=O)c1ccc2c(c1)c(c3ccccc32)C(=O)OCCOC(=O)N(C(C)C)CC(=O)Nc4c(O)c(N(C)C)c5c(c4)C(=O)C6C(=O)C(O)C(O)C(=O)C6C(=O)C(O)C(=O)N
 tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl anthracene-9-carboxylate



15

Reference Compound 107 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomincycline using the conditions of Example 42 to give the product of the Example.

20

MS (ESI) m/z 864.3 (M+H);

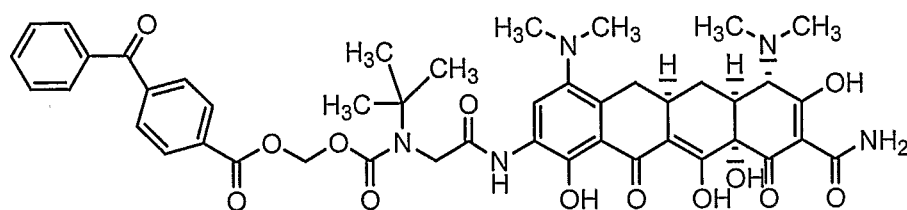
HRMS: calcd for $C_{46}H_{49}N_5O_{12} \cdot HCl$, 899.3145; found (ESI-), 862.32855;

25

Example 107

CCOC(=O)c1ccc2c(c1)c(c3ccccc32)C(=O)OCCOC(=O)N(C(C)C)CC(=O)Nc4c(O)c(N(C)C)c5c(c4)C(=O)C6C(=O)C(O)C(O)C(=O)C6C(=O)C(O)C(=O)N
 tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 4-benzoylbenzoate

30



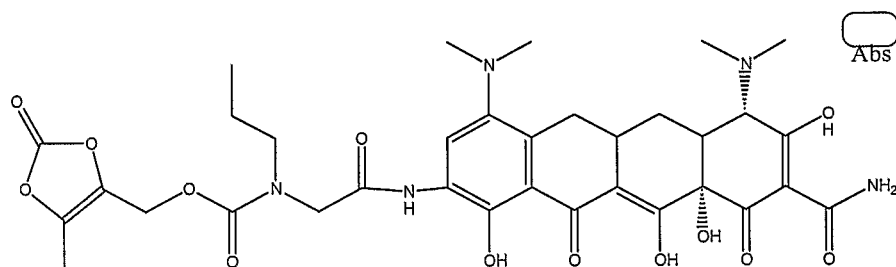
Reference Compound 108 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomycinol using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 866.3 (M-H);

HRMS: calcd for $C_{45}H_{49}N_5O_{13} \cdot HCl$, 903.3094; found (ESI-), 866.32405;

Example 108

(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-[[[(7S,10aR)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate



To a solution of 107 mg (0.166 mmol) of N-propyl-glycylcyclycline (N-prop-glycyl) in DMPU (2 ml) is added 5 equivalents of sodium carbonate (95 mg, 0.9 mmol) followed by 2 equivalents of (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-nitrophenyl carbonate (95 mg, 0.33 mmol) Reference Compound 121 and stirring for 2 hr at room temperature. The reaction mixture is filtered through diatomaceous earth and the filtrate added to a mixture of (1:4)(20 ml) ether:isopropyl alcohol and HCl (1M in ether) is added and the formed solid filtered, redissolved in water, the pH adjusted to

about 2 and extracted with methylene chloride to give 15 mg of the product of the Example.

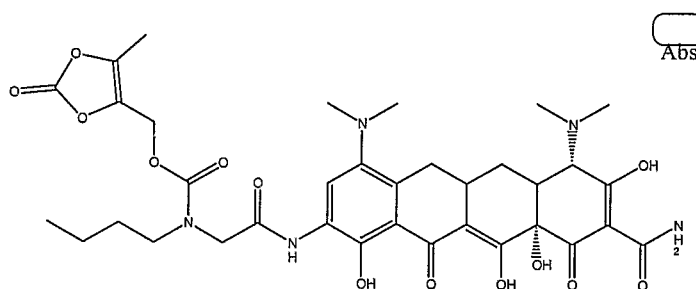
MS (ESI) m/z 728.5 (M+H);

MS (ESI) m/z 364.8 (M+2H);

5 HRMS: calcd for $C_{34}H_{41}N_5O_{13}$, 727.2701; found (ESI+), 728.27606;

Example 109

10 (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate



15

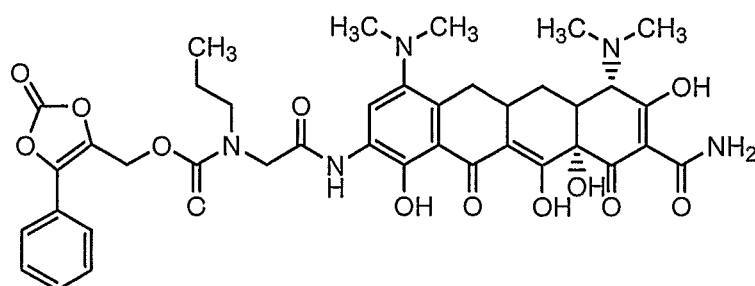
The title compound is prepared by the procedure of Example 108, using N-butylglycylcycline (N-bu-glycyl) and (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-nitrophenyl carbonate Reference Compound 121 to give the product of the Example.

MS (ESI) m/z 742.3 ((M+H)+);

20

Example 110

25 (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl 2-[(7R,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate



The title compound is prepared by the procedure of Example 108, using N-propylglycylcyclohexylamine (N-prop-glycyl) and 4-nitrophenyl (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl carbonate Reference Compound 122 to give the product of the Example.

5

MS (ESI) m/z 790.3 ((M+H)+);

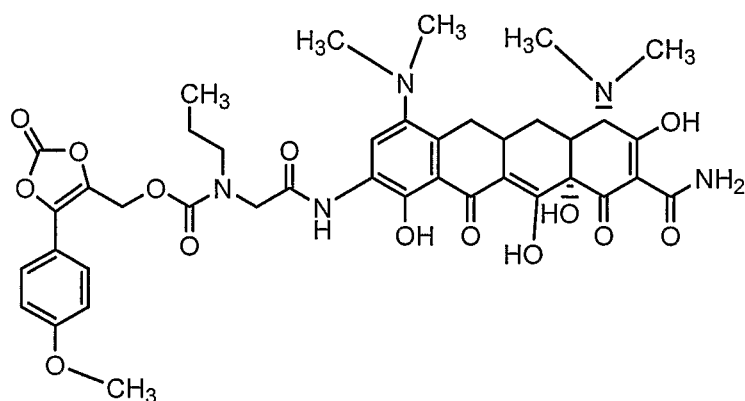
HRMS: calcd for $C_{39}H_{43}N_5O_{13}$, 789.2857; found (ESI+), 790.29243;

10

Example 111

[5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate

15



The title compound is prepared by the procedure of Example 108, using N-propylglycylcyclohexylamine (N-prop-glycyl) and [5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl

20

4-nitrophenyl carbonate Reference Compound 123 to give the product of the Example.

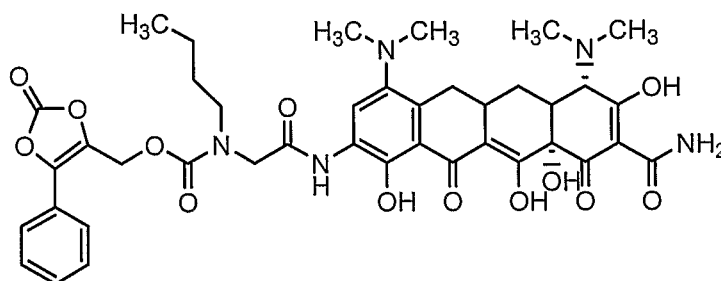
MS (ESI) m/z 820.3 ((M+H)+);

5

Example 112

(2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl 2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate

10



The title compound is prepared by the procedure of Example 108, using N-butylglycylcyclyne (N-bu-glycyl) and 4-nitrophenyl (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl carbonate Reference Compound 122 to give the product of the Example.

15

MS (ESI) m/z 804.12 (M+H);

MS (ESI) m/z 402.58 (M+2H);

20 HRMS: calcd for $C_{40}H_{45}N_5O_{13}$, 803.3014; found (ESI+), 804.30946;

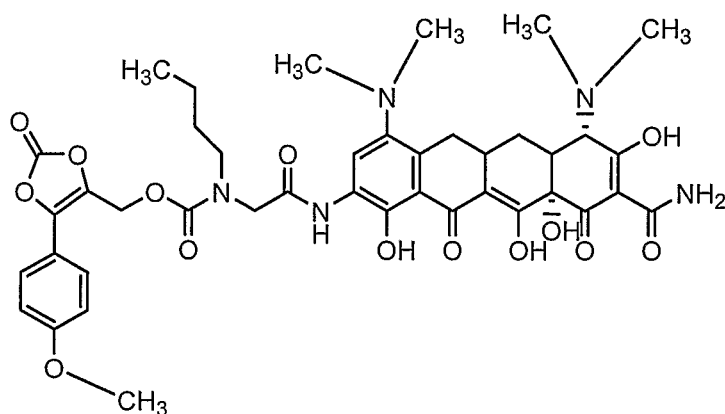
25

Example 113

5

[5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate

10



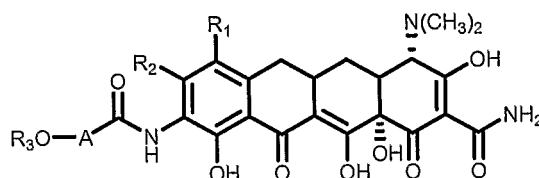
The title compound is prepared by the procedure of Example 108, using N-butyl-glycylcycline (N-bu-glycyl) and [5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 4-nitrophenyl carbonate Reference Compound 123 to give the product of the Example.

20

WHAT IS CLAIMED IS:

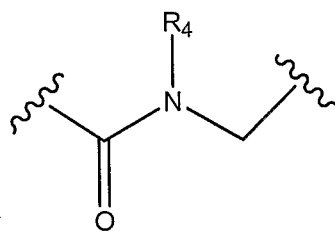
1. A compound represented by Formula (I);

5



(I)

10 wherein:



A is a moiety

or is absent;

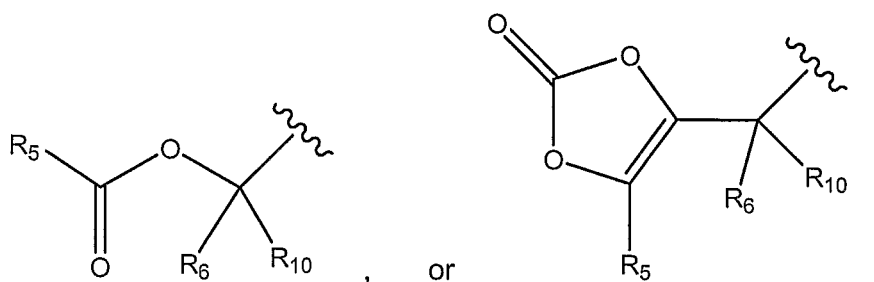
R_1 is selected from hydrogen, $-OH$, amino, $-NR_7R_8$, halogen,
 15 alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents
 independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6
 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12
 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms,
 heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-
 20 aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may
 optionally be substituted with 1 to 3 substituents independently selected from
 halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino,
 dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, $CH_3-C(O)-NH-$, aralkyl, aryloxy,
 heterocyclyl and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted with 1
 25 to 3 substituents independently selected from the group phenyl, heteroaryl, halogen,

amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl and aryl of

N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aryloxy, heterocyclyl and phenyl, and alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, alkyl, hydroxyl, and alkoxy;

10 R₂ is selected from hydrogen, halogen, alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and
15 N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, alkenyl of 2 to 12 carbon atoms
20 optionally substituted with 1 to 3 substituents independently selected from the group phenyl, heteroaryl, halogen, amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl,
25 alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, alkyl, hydroxyl, and alkoxy;

30 R₃ is the moiety R₉,



- 5 R_4 is selected from hydrogen, alkyl of 1 to 12 carbon atoms, optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, $\text{CH}_3\text{-C(O)-NH-}$, aralkyl, aryloxy, heterocyclyl and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group phenyl, heteroaryl, halogen, amino, cyano, alkyl, hydroxyl, alkoxy, aryl, alkynyl and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, $\text{CH}_3\text{-C(O)-NH-}$, aralkyl, aryloxy, heterocyclyl and phenyl, alkynyl of 2 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, alkyl, hydroxyl, and alkoxy, aryl of 6, 10 or 14 carbon atoms said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, $\text{CH}_3\text{-C(O)-NH-}$, aralkyl, aryloxy, heterocyclyl and phenyl, N-(alkyl of 1 to 12 carbon atoms)-aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl,

alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl of 7 to 13 carbon atoms optionally substituted, SR³, heteroaryl optionally substituted and heteroarylcarbonyl optionally substituted;

R₅ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl of 6, 10 or 14 carbon atoms, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl, may be optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH₂(CO)OCH₂aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryloxy and phenyl, alkenyl of 2 to 12 carbon atoms optionally substituted, heteroaryl optionally substituted, aryl of 6, 10 or 14 carbon atoms optionally substituted, alkynyl of 2 to 12 carbon atoms optionally substituted, cycloalkyl 3 to 6 ring atoms, aryl-CH=CH-, cycloalkyl-alkyl; and adamantly;

R₆ is selected from hydrogen, alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aryloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl,

alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and cycloalkyl of 3 to 6 carbon atoms;

- 5 R₇ and R₈ are each independently H or alkyl of 1 to 12 carbon atoms or R₇ and R₈ when optionally taken together with the nitrogen atom to which each is attached form a 3 to 8 membered heterocyclyl ring;

R₉ is aralkyl of 7 to 16 carbon atoms optionally substituted or alkyl of 1 to 12 carbon
10 atoms;

R₁₀ is H or alkyl of 1 to 12 carbon atoms;

or a pharmaceutically acceptable salt thereof.

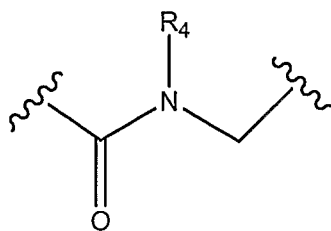
- 15 2. A compound according to claim 1, wherein R₁ is -NR₇R₈, R₇ is hydrogen, R₈ is methyl, ethyl, n-propyl, n-butyl, 1-methylethyl, 1-methylpropyl, 2-methylpropyl or 1,1-dimethylethyl or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1, wherein R₁ is -NR₇R₈, R₇ is methyl or ethyl, R₈
20 is methyl, ethyl, n-propyl, 1-methylethyl, n-propyl, 1-methylpropyl, or 2-methylpropyl or a pharmaceutically acceptable salt thereof.

4. A compound according to claim 1, wherein R₁ is -NR₇R₈, R₇ and R₈ are taken
together with the nitrogen atom to which each is attached form a 3 to 8 membered
25 heterocyclyl ring or a pharmaceutically acceptable salt thereof.

5. A compound according to any one of claims 1 to 5, wherein R₂ is H or a pharmaceutically acceptable salt thereof.

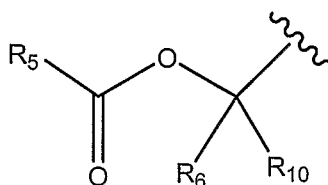
- 30 6. A compound according to any one of claims 1 to 5, wherein A is a moiety



or a pharmaceutically acceptable salt thereof.

7. A compound according to any one of claims 1 to 5, wherein A is absent or a
5 pharmaceutically acceptable salt thereof.

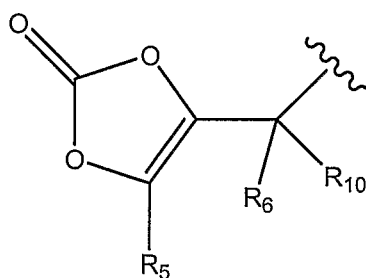
8. A compound according to any one of claims 1 to 7, wherein R_3 is a moiety



10

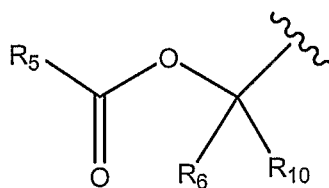
or a pharmaceutically acceptable salt thereof.

9. A compound according to any one of claims 1 to 7, wherein R_3 is a moiety
15



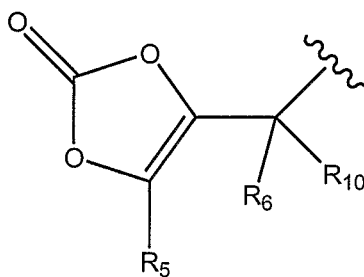
or a pharmaceutically acceptable salt thereof.

20 10. A compound according to any one of claims 1 to 7, wherein R_3 is a moiety



and R_6 and R_{10} are H or a pharmaceutically acceptable salt thereof.

- 5 11. A compound according to any one of claims 1 to 7, wherein R_3 is a moiety

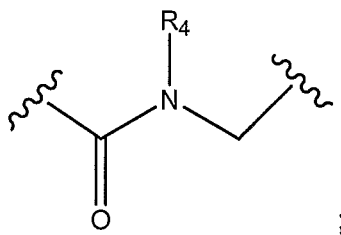


and R_6 and R_{10} are H or a pharmaceutically acceptable salt thereof.

10

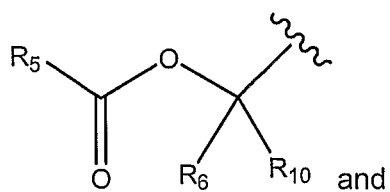
12. A compound according to any one of claims 1 to 7, wherein R_3 is R_9 or a pharmaceutically acceptable salt thereof.

- 15 13. A compound according to claim 1, wherein A is the moiety,



20

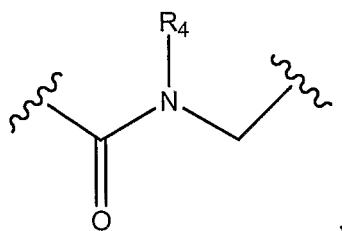
R_3 is the moiety



R_5 is aryl of 6 carbon atoms or a pharmaceutically acceptable salt thereof.

5

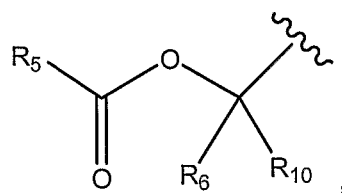
14. A compound according to claim 1, wherein A is the moiety



10

R_3 is the moiety ,

15



R_4 is 1,1-dimethylethyl and

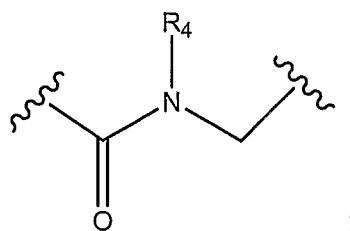
20

R_5 is aryl of 6 carbon atoms or a pharmaceutically acceptable salt thereof.

15. A compound according to claim 1, wherein

A is a moiety

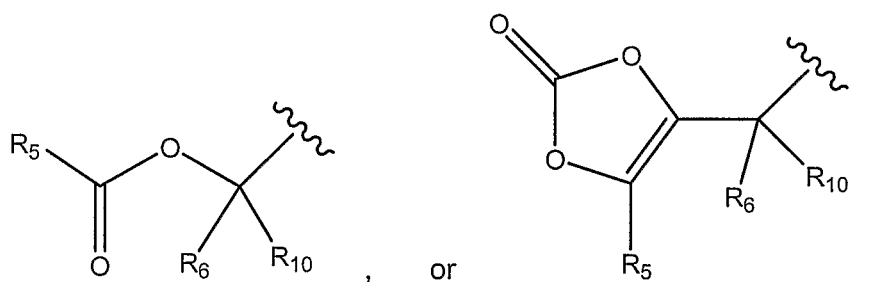
5



R₁ is -NR₇R₈;

R₂ is hydrogen;

10 R₃ is the moiety



15 R₄ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, and aryloxy wherein said aryl and aryloxy is optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, 20 alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryloxy and phenyl;

R₅ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl 25 of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to

12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl of 6, 10 or 14 carbon atoms, and aryloxy wherein said aryl, aryloxy and aryl of N-(alkyl of 1 to 12 carbon atoms)-aryl, may be optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH₂(CO)OCH₂aryl, said aryl optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, aryloxy and phenyl, heteroaryl optionally substituted, aryl of 6, 10 or 14 carbon atoms optionally substituted, cycloalkyl 3 to 6 ring atoms, aryl-CH=CH-, cycloalkyl-alkyl; and adamantyl;

15 R₆ is hydrogen;

R₇ and R₈ are each independently H or alkyl of 1 to 12 carbon atoms;

20 R₉ is aralkyl of 7 to 16 carbon atoms optionally substituted or alkyl of 1 to 12 carbon atoms;

R₁₀ is H;

or a pharmaceutically acceptable salt thereof.

25

16. A compound according to claim 1, selected from the group or pharmaceutically acceptable salts thereof

30 {[(2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyloxy)methyl 2-methylpropanoate,

- (([(2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate,
- 5 (([(2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate,
- 10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate,
- 15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 4-methylbenzoate,
- 20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate,
- 25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate,
- 30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl pivalate,

- ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 2-methylpropanoate,
- 5 ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl phenylacetate,
- 10 ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl phenylacetate,
- 15 ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl pivalate,
- 20 ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl heptanoate,
- 25 ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl cyclobutanecarboxylate,
- 30 ({[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl heptanoate,
- {[(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate,

- (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,
- 5 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate,
- 10 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,
- 15 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate,
- 20 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate,
- 1-(2-(((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)ethyl acetate,
- 25 (((2-(((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate,
- 30 (((2-(((7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate,

- (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate,
- 5 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate,
- 10 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate,
- 15 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl cyclopentylacetate,
- 20 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate,
- 25 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl adamantane-1-carboxylate,
- 30 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3,3-dimethylbutanoate,

- {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-tert-butylbenzoate,
- 5 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2,2-dimethylbutanoate,
- 10 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2-methylpropanoate,
- 15 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl cyclopentanecarboxylate,
- 20 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate,
- 25 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl heptanoate, and
- 30 17. A compound according to claim 1 selected from the group
- benzyl 2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate,

ethyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate, and

5

isobutyl 2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(propyl)carbamate,
or pharmaceutically acceptable salts thereof.

10

18. A compound according to claim 1 selected from the group

15 {{{[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl thiophene-2-carboxylate,

20

{{[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl thiophene-2-carboxylate,

25

{{[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl thiophene-3-carboxylate,

30

{{[2-[[[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 2-furoate, and

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](propyl)amino]carbonyl}oxy)methyl 2-furoate,

5 or pharmaceutically acceptable salts thereof.

19. A compound according to claim 1 selected from the group

10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl propionate,

15 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclohexanecarboxylate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-dimethylbenzoate,

20 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-fluorobenzoate,

25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-methylbutanoate,

30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl cyclopentylacetate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-(trifluoromethyl)benzoate,

5 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl cyclopropanecarboxylate,

10 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl adamantane-1-carboxylate,

butyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(tert-butyl)carbamate,

isobutyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(tert-butyl)carbamate,

20 methyl 2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(tert-butyl)carbamate,

25 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl pentanoate,

30 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl cyclobutanecarboxylate,

- {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3-cyclohexylpropanoate,
- 5 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl (4-fluorophenoxy)acetate,
- 10 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl cyclohexylacetate,
- 15 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 2,6-dimethylbenzoate,
- 20 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl phenylacetate,
- 25 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,
- 30 {{{(2-{{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-naphthoate,

- (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 2-naphthoate,
- 5 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 2,6-difluorobenzoate,
- 10 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 2-fluorobenzoate,
- 15 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 2-(trifluoromethyl)benzoate,
- 20 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 1,1'-biphenyl-2-carboxylate,
- 25 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 2,4,6-trimethylbenzoate,
- 30 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 4-isopropoxybenzoate,
- 30 (((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 3,4,5-trimethoxybenzoate,

- ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-dimethoxybenzoate,
- 5 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl (2E)-3-phenylprop-2-enoate,
- 10 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl [3,5-bis(trifluoromethyl)phenyl]acetate,
- 15 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(heptyloxy)benzoate,
- 20 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-(2-phenylethyl)benzoate,
- 25 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(dodecyloxy)benzoate,
- 30 ([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl anthracene-9-carboxylate,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl 4-benzoylbenzoate, and

- 5 (([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](tert-butyl)amino]carbonyl)oxy)methyl diphenylacetate.

20. A compound according to claim 1 selected from the group

10

[([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl 4-fluorobenzoate,

- 15 [([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl 3,5-dimethylbenzoate,

- 20 [([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl pivalate,

- 25 [([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl 3,3-dimethylbutanoate,

- [([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl 2,2-dimethylbutanoate,

30

[([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl 2-ethylbutanoate,

- [({(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy)methyl thiophene-2-carboxylate,
 5 [({(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy)methyl cyclopentylacetate, and
- 10 [({(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}carbonyl)oxy)methyl 4-tert-butylbenzoate
 or pharmaceutically acceptable salts thereof.
- 15 21. A compound according to claim 1 selected from the group
 ({(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino}carbonyl)oxy)methyl 1H-indole-2-carboxylate,
- 20 ({(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino}carbonyl)oxy)methyl nicotinate,
- 25 ({(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino}carbonyl)oxy)methyl isonicotinate,
- 30 ({(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino}carbonyl)oxy)methyl 4-pyrrolidin-1-ylbenzoate,

{{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 3-methyl-1-benzofuran-2-carboxylate,

5 {{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-indole-3-carboxylate,

10 {{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl quinoline-2-carboxylate,

15 {{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1-benzofuran-2-carboxylate, and

20 {{(2-{{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl-1-methyl-1H-pyrrole-2- carboxylate
or pharmaceutically acceptable salts thereof.

22. A compound according to claim 1 selected from the group

25 (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-{{(7S,10aR)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate,

30 (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-{{(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate,

(2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl 2-[(7R,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate,

- 5 [5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(propyl)carbamate,

- (2-oxo-5-phenyl-1,3-dioxol-4-yl)methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate and
- 10

- [5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl(butyl)carbamate
- 15

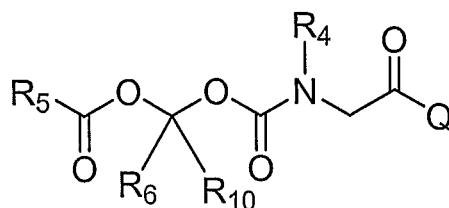
or pharmaceutically acceptable salts thereof.

23. A pharmaceutical composition comprising a compound according to anyone of
20 claims 1 to 22, in association with a pharmaceutically acceptable carrier.

24. A method for the prevention, treatment or control of bacterial infections in warm-blooded animals which comprises providing to said warm-blooded animals an antibacterially effective amount of a compound according to anyone of claims 1 to 22,
25 or a pharmaceutically acceptable salt thereof.

25. Use of a compound according to any one of claims 1 to 22 for the preparation of a medicament for the treatment of bacterial infections.
- 30

26. A compound according to Formula (II):



II

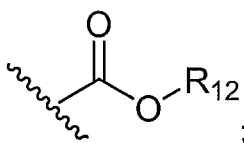
wherein R_4 , R_5 , R_6 , and R_{10} are as defined in claim 1, and

5

Q is $-OR_{11}$, Cl, Br, or I;

R_{11} is H, benzyl optionally substituted with nitro or a moiety of the formula

10



and R_{12} is alkyl of 1 to 6 carbon atoms.

15

27. A compound according to claim 26 wherein R_4 is t-butyl, R_5 is alkyl of 1 to 6 carbon atoms, and R_{11} is benzyl optionally substituted with nitro.

28. A compound according to claim 26 wherein R_4 is alkyl of 1 to 6 carbon atoms,

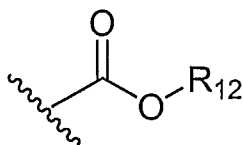
20

R_5 is phenyl optionally substituted and R_{11} is benzyl optionally substituted with nitro.

29. A compound according to claim 26 wherein R_5 is alkyl of 1 to 6 carbon atoms, R_4 is t-butyl and R_{11} is H.

25

30. A compound according to claim 26 wherein R_5 is alkyl of 1 to 6 carbon atoms, R_4 is t-butyl, Q is



and R₁₂ is alkyl of 1 to 6 carbon atoms.

5

31. A compound according to anyone of claims 26 to 30 wherein R₆ and R₁₀ are H.

32. A compound according to claim 26 selected from the group

10

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 4-tert-butylbenzoate,

15

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 2,2-dimethylbutanoate,

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 2-methylpropanoate,

20

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclopentanecarboxylate,

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 4-methylbenzoate,

25

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl heptanoate,

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl propionate,

30

([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclohexanecarboxylate,

- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3,5-dimethylbenzoate,
- 5 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 4-fluorobenzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3-methylbutanoate,
- 10 benzyl N-(tert-butyl)-N-([[(cyclopentylacetyl)oxy]methoxy]carbonyl)glycinate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 4-(trifluoromethyl)benzoate,
- 15 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclopropanecarboxylate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl adamantane-1-carboxylate,
- 20 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl pentanoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl cyclobutanecarboxylate,
- 25 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 3-cyclohexylpropanoate,
- benzyl N-(tert-butyl)-N-([[(4-fluorophenoxy)acetyl]oxy]methoxy]carbonyl)glycinate,
- 30 benzyl N-(tert-butyl)-N-([[(cyclohexylacetyl)oxy]methoxy]carbonyl)glycinate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl 2,6-dimethylbenzoate,

- benzyl N-(tert-butyl)-N-({[(phenylacetyl)oxy]methoxy}carbonyl)glycinate,
- ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl pivalate,
- 5 ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-benzofuran-2-carboxylate,
- ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-pyrrole-2-carboxylate,
- 10 ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-4-carboxylate,
- ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-methoxybenzoate,
- 15 ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1H-indole-2-carboxylate,
- 20 benzyl N-(tert-butyl)-N-({[(diphenylacetyl)oxy]methoxy}carbonyl)glycinate,
- ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-naphthoate,
- 25 ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-naphthoate,
- ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1-methyl-1H-indole-3-carboxylate,
- 30 ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl quinoline-2-carboxylate,
- ({{[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl nicotinate,

- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl isonicotinate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,6-
5 difluorobenzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-fluorobenzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-
10 (trifluoromethyl)benzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(1H-pyrrol-1-
yl)benzoate,
- 15 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 1,1'-biphenyl-2-
carboxylate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2,4,6-
trimethylbenzoate,
20 ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-
isopropoxybenzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,4,5-
25 trimethoxybenzoate,
- ([[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3,5-
dimethoxybenzoate,
- 30 3-phenyl-acrylic acid (benzyloxycarbonylmethyl-tert-butyl-carbamoyloxy)-methyl
ester,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 3-methyl-1-benzofuran-2-carboxylate,

benzyl N-{{[[3,5-bis(trifluoromethyl)phenyl]acetyl}oxy]methoxy]carbonyl}-N-(tert-butyl)glycinate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(heptyloxy)benzoate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 2-(2-phenylethyl)benzoate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(dodecyloxy)benzoate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-(acetylamino)benzoate,

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl anthracene-9-carboxylate and

({[[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino]carbonyl}oxy)methyl 4-benzoylbenzoate.

33. A compound according to claim 26 selected from the group:

N-(tert-butyl)-N-({[(4-tert-butylbenzoyl)oxy]methoxy}carbonyl)glycine,

N-(tert-butyl)-N-{{[(isobutyryloxy)methoxy]carbonyl}glycine,

N-(tert-butyl)-N-{{[(cyclopentylcarbonyl)oxy]methoxy}carbonyl}glycine,

N-(tert-butyl)-N-({[(4-methylbenzoyl)oxy]methoxy}carbonyl)glycine,

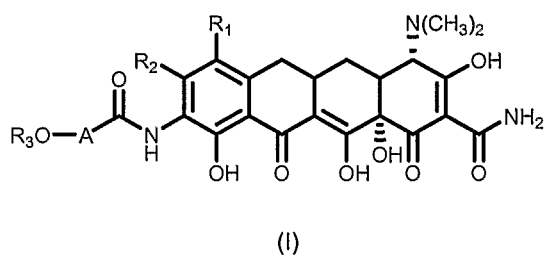
- N-(tert-butyl)-N-([(heptanoyloxy)methoxy]carbonyl)glycine,
- N-(tert-butyl)-N-([(propionyloxy)methoxy]carbonyl)glycine,
- 5 N-(tert-butyl)-N-([(cyclohexylcarbonyl)oxy]methoxy)carbonyl)glycine,
- N-(tert-butyl)-N-([(3,5-dimethylbenzoyl)oxy]methoxy)carbonyl)glycine,
- 10 N-(tert-butyl)-N-([(4-fluorobenzoyl)oxy]methoxy)carbonyl)glycine,
- N-(tert-butyl)-N-([(3-methylbutanoyl)oxy]methoxy)carbonyl)glycine,
- N-(tert-butyl)-N-([(cyclopentylacetyl)oxy]methoxy)carbonyl)glycine,
- 15 N-(tert-butyl)-N-([(4-(trifluoromethyl)benzoyl)oxy]methoxy)carbonyl)glycine,
- N-(tert-butyl)-N-([(cyclopropylcarbonyl)oxy]methoxy)carbonyl)glycine,
- 20 N-([(1-adamantylcarbonyl)oxy]methoxy)carbonyl)-N-(tert-butyl)glycine,
- N-(tert-butyl)-N-([(pentanoyloxy)methoxy]carbonyl)glycine,
- N-(tert-butyl)-N-([(cyclobutylcarbonyl)oxy]methoxy)carbonyl)glycine,
- 25 N-(tert-butyl)-N-([(3-cyclohexylpropanoyl)oxy]methoxy)carbonyl)glycine,
- N-(tert-butyl)-N-([(cyclohexylacetyl)oxy]methoxy)carbonyl)glycine,
- 30 N-(tert-butyl)-N-([(2,6-dimethylbenzoyl)oxy]methoxy)carbonyl)glycine,
- N-(tert-butyl)-N-([(phenylacetyl)oxy]methoxy)carbonyl)glycine,

- N-(tert-butyl)-N-({[(2,2-dimethylpropanoyl)oxy]methoxy}carbonyl)glycine,
- N-({[(1-benzofuran-2-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
- 5 N-(tert-butyl)-N-([{[(1-methyl-1H-pyrrol-2-yl)carbonyl]oxy}methoxy)carbonyl]glycine,
- N-({[(1,1'-biphenyl-4-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
- 10 N-(tert-butyl)-N-({[(4-methoxybenzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(1H-indol-2-ylcarbonyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(diphenylacetyl)oxy]methoxy}carbonyl)glycine,
- 15 N-(tert-butyl)-N-({[(1-naphthoyloxy)methoxy]carbonyl)glycine,
- N-(tert-butyl)-N-({[(2-naphthoyloxy)methoxy]carbonyl)glycine,
- 20 N-(tert-butyl)-N-([{[(1-methyl-1H-indol-3-yl)carbonyl]oxy}methoxy)carbonyl]glycine,
- N-(tert-butyl)-N-({[(quinolin-2-ylcarbonyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-({[(pyridin-3-ylcarbonyl)oxy]methoxy}carbonyl)glycine,
- 25 N-(tert-butyl)-N-({[(isonicotinoyloxy)methoxy]carbonyl)glycine,
- N-(tert-butyl)-N-({[(2,6-difluorobenzoyl)oxy]methoxy}carbonyl)glycine,
- 30 N-(tert-butyl)-N-({[(2-fluorobenzoyl)oxy]methoxy}carbonyl)glycine,
- N-(tert-butyl)-N-([{[(2-(trifluoromethyl)benzoyl]oxy}methoxy)carbonyl]glycine,

- N-(tert-butyl)-N-({[(4-pyrrolidin-1-ylbenzoyl)oxy]methoxy}carbonyl)glycine,
N-({[(1,1'-biphenyl-2-ylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
5 N-(tert-butyl)-N-({[(mesitylcarbonyl)oxy]methoxy}carbonyl)glycine,
N-(tert-butyl)-N-({[(4-isopropoxybenzoyl)oxy]methoxy}carbonyl)glycine,
N-(tert-butyl)-N-({[(3,4,5-trimethoxybenzoyl)oxy]methoxy}carbonyl)glycine,
10 N-(tert-butyl)-N-({[(3,5-dimethoxybenzoyl)oxy]methoxy}carbonyl)glycine,
N-(tert-butyl)-N-({[(2E)-3-phenylprop-2-enoyl]oxy}methoxy}carbonyl)glycine,
15 N-(tert-butyl)-N-({[(3-methyl-1-benzofuran-2-yl)carbonyl]oxy}methoxy}carbonyl)glycine,
N-({[(3,5-bis(trifluoromethyl)phenyl]acetyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine,
20 N-(tert-butyl)-N-({[(4-(heptyloxy)benzoyl]oxy}methoxy}carbonyl)glycine,
N-(tert-butyl)-N-({[(2-(2-phenylethyl)benzoyl]oxy}methoxy}carbonyl)glycine,
25 N-(tert-butyl)-N-({[(4-(dodecyloxy)benzoyl]oxy}methoxy}carbonyl)glycine,
N-({[(4-(acetylamino)benzoyl]oxy}methoxy}carbonyl)-N-(tert-butyl)glycine,
N-({[(9-anthrylcarbonyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine and
30 N-({[(4-benzoylbenzoyl)oxy]methoxy}carbonyl)-N-(tert-butyl)glycine.
34. A compound according to claim 26 which is

3,3-Dimethyl-butyrlic acid [tert-butyl-(2-isobutoxycarbonyloxy-2-oxo-ethyl)-
carbamoyloxy)-methyl ester.

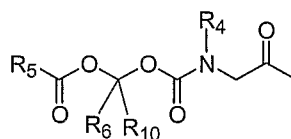
- 5 35. A method for the preparation of compounds represented by Formula (I);



10

wherein:

R₃O - A - CO- represents

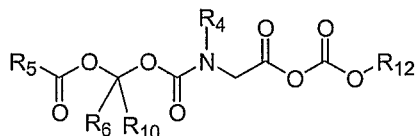


and R₁, R₂, R₄, R₅, R₆, and R₁₀ are as defined in claim 1

15

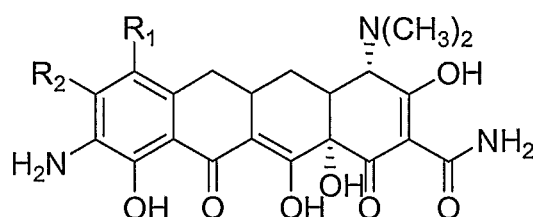
or a pharmaceutically acceptable salt thereof comprising the step of:

- a. reacting an activated acyloxycarbamate intermediate of the formula



20

where R₄, R₅, R₆, and R₁₀ are as defined in claim 1 and R₁₂ is as defined in claim 26
with a 7,8-disubstituted-9-aminotetracycline of the formula



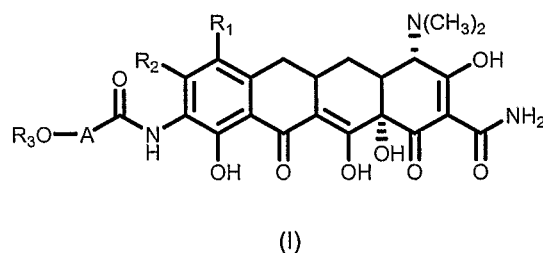
where R_1 , and R_2 are as defined in claim 1

in the presence of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone and triethylamine to afford a compound of Formula (I) and, if desired,

- 5 b. converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.

36. A method for the preparation of compounds represented by Formula (I);

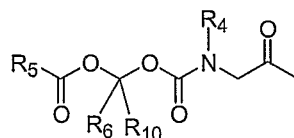
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15

wherein:

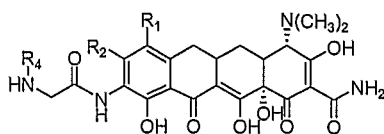
$R_3O - A - CO-$ represents



and R_1 , R_2 , R_4 , R_5 , R_6 , and R_{10} are as defined in claim 1 or a pharmaceutically acceptable salt thereof comprising:

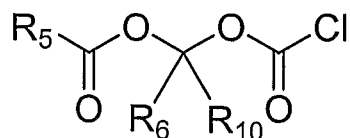
20

reacting an amine of the formula



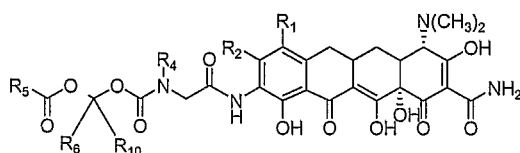
wherein R_1 , R_2 , R_4 , R_5 , R_6 , and R_{10} are as defined in claim 1 with a chloro intermediate of the formula

5



in the presence of an alkali metal carbonate, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone and acetonitrile to afford a compound of the formula

10

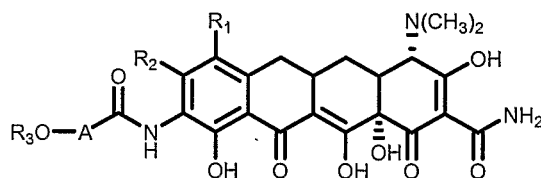


or a pharmaceutically acceptable salt thereof and, if desired, converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.

15

37. A method for the preparation of compounds represented by Formula (I);

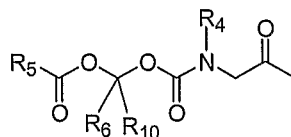
20



(I)

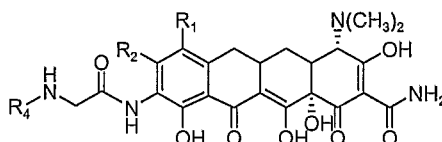
wherein:

$R_3O - A - CO-$ represents

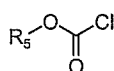


and R_1 , R_2 , R_4 , R_5 , R_6 , and R_{10} are as defined in claim 1 or a pharmaceutically acceptable salt thereof comprising the step of:

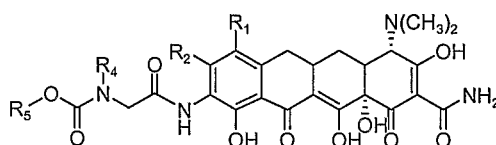
reacting a compound of the formula



wherein R_1 , R_2 , and R_4 are as defined in claim 1 with a chloro intermediate of the formula

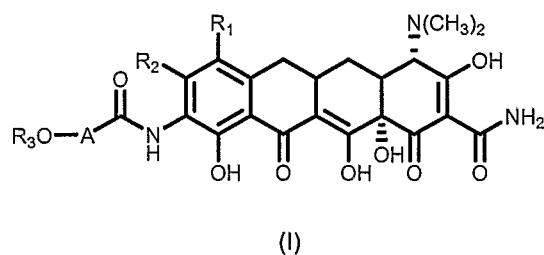


wherein R_5 is as defined in claim 1 in the presence of an alkali metal carbonate, and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone in acetonitrile to give a compound of Formula I



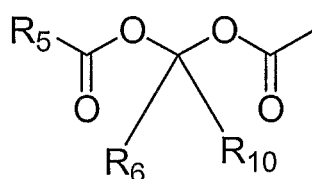
and, if desired, converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.

38. A method for the preparation of a compound represented by Formula (I);



wherein:

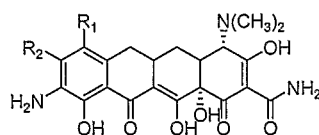
- 5 $R_3O - A - CO-$ represents



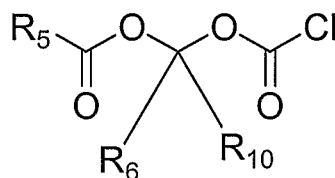
and R_1 , R_2 , R_5 , R_6 , and R_{10} are as defined in claim 1

or a pharmaceutically acceptable salt thereof comprising the step of:

- 10 reacting a 7,8-disubstituted-9-aminotetracycline of the formula

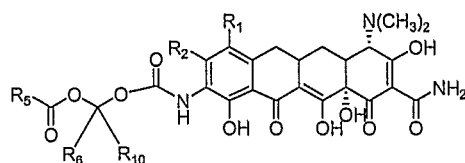


- 15 with a chloro intermediate of the formula



where R_1 , R_2 , R_5 , R_6 , and R_{10} are as defined in claim 1

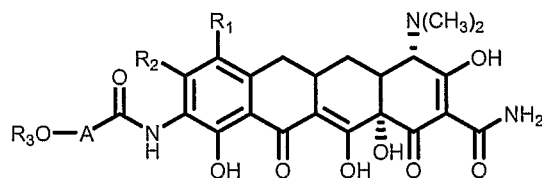
- 20 in the presence of triethylamine and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone to afford a compound of the formula



or a pharmaceutically acceptable salt thereof and, if desired, converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.

5

39. A method for the preparation of a compound represented by Formula (I);



(I)

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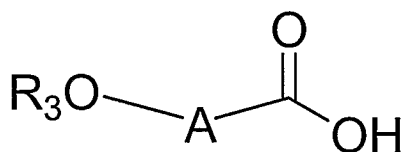
wherein:

A, R₁, R₂, and R₃ are as defined in claim 1

or a pharmaceutically acceptable salt thereof comprising :

15

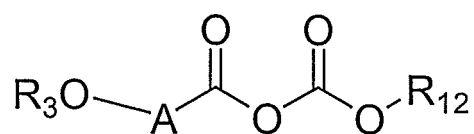
reacting a carboxylic acid of the formula



where A, and R₃ are as defined above

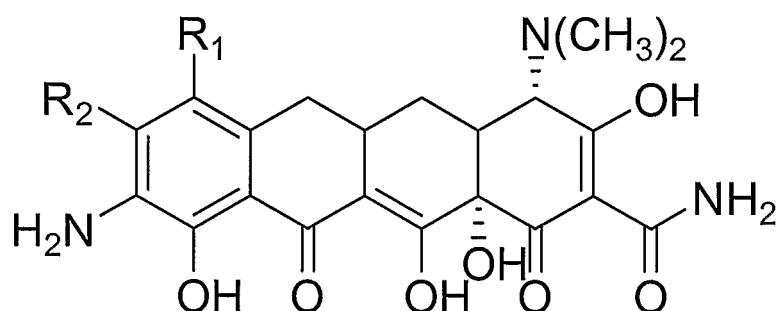
20

with a chloroformate ClCO₂R₁₂ where R₁₂ is alkyl of 1 to 6 carbon atoms in the presence of 1,8-bis(dimethylamino)naphthalene in methylene chloride to give a mixed anhydride of the formula

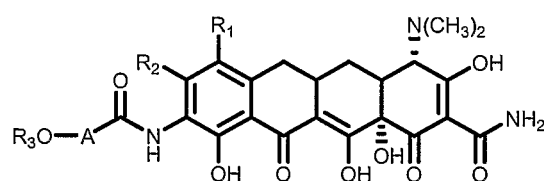


Mixed anhydride

and reacting said mixed anhydride with a 7,8-disubstituted-9-aminotetracycline of the
5 formula



where R_1 , and R_2 are as defined above
in the presence of triethylamine and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-
10 pyrimidinone to afford a compound of Formula (I)



(I)

or a pharmaceutically acceptable salt thereof and, if desired, converting the
15 compound of Formula (I) into a pharmaceutically acceptable salt thereof.