Title: 9-AMINOCARBONYLSUBSUTED DERIVATIVES OF GLYCICYCLOINES

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(54) Title: 9-AMINOCARBONYLSUBSUTED DERIVATIVES OF GLYCICYCLOINES

(57) Abstract: This invention provides compounds of Formula (I) having the structure where $R_1$, $R_2$, $R_3$ and A are defined in the specification or a pharmaceutically acceptable salt thereof useful as antibacterial agents. Compounds according to Formula (II): where $Q$, $R_4$, $R_5$, and $R_6$ and A are defined in the specification are useful as chemical intermediates.
9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES

This application claims priority from U.S. Application No. 60/713,122 filed August 31, 2005 the entire disclosure of which is incorporated herein by reference.

FIELD OF THE INVENTION

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

BACKGROUND OF THE INVENTION

Since 1947 a variety of tetracycline antibiotics have been synthesized and 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 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 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, 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,

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 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.


In U.S. Pat. No. 5,021,407 a method of overcoming the resistance of 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 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 glycylcyclines of this application.

SUMMARY OF THE INVENTION

This invention is concerned with 9-aminocarbonylsubstituted derivatives of glycylcyclines 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.

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

\[ \text{(I)} \]

wherein:

\[ \text{A is a moiety or is absent;} \]

\[ R_1 \] is selected from hydrogen, -OH, amino, -NR\text{\textsubscript{7}}R\text{\textsubscript{8}}, 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, heterocycl 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, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl 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, alkyi, 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, heterocycl 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, heterocycl 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, haloalky, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl 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)-, CH$_3$-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;

$R_3$ is the moiety $R_g$.

$R_4$ 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, alkoxy carbonyl, aryl-C(O)-, CH$_3$-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, alkenyl 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, aryl 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, aikyl, 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, aryl, -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;

R\textsubscript{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, aroyloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aroyloxy 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)-, CH\textsubscript{3}-C(O)-NH-, aralkyl, aroyloxy, heterocyclyl and phenyl, and cycloalkyl of 3 to 6 carbon atoms;

R\textsubscript{7} and R\textsubscript{8} are each independently H or alkyl of 1 to 12 carbon atoms or R\textsubscript{7} and R\textsubscript{8} when optionally taken together with the nitrogen atom to which each is attached form a 3 to 8 membered heterocyclyl ring;

R\textsubscript{9} is aralkyl of 7 to 16 carbon atoms optionally substituted or alkyl of 1 to 12 carbon atoms;
R\textsubscript{10} is H or alkyl of 1 to 12 carbon atoms;

or a pharmaceutically acceptable salt thereof.

An embodiment of this invention provides compounds of Formula I wherein R\textsubscript{i} is -NR\textsubscript{7}R\textsubscript{8}, R\textsubscript{7} is hydrogen, R\textsubscript{8} is methyl, ethyl, n-propyl, n-butyl, 1-methylethyl, 1-methylpropyl, 2-methylpropyl or 1,1-dimethylethyl or a pharmaceutically acceptable salt thereof.

Another embodiment of this invention provides compounds of Formula I wherein R\textsubscript{1} is -NR\textsubscript{7}R\textsubscript{8}, R\textsubscript{7} is methyl or ethyl, R\textsubscript{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.

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

or a pharmaceutically acceptable salt thereof.

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

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

![Chemical Structure](image)

or a pharmaceutically acceptable salt thereof.

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

![Chemical Structure](image)

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

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

An additional embodiment of this invention provides compounds of Formula I wherein \( A \) is the moiety,

\[
\text{\[ \text{structure image} \]}
\]

\( R_3 \) is the moiety

\[
\text{\[ \text{structure image} \]}
\]

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

A further embodiment of this invention provides compounds of Formula I wherein \( A \) is the moiety
$R_3$ is the moiety,

$R_4$ is 1,1-dimethylethyl and

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

An additional embodiment of this invention provides compounds of Formula I wherein:

$A$ is a moiety

$R_1$ is $-NR_7R_8$.
$R_2$ is hydrogen;
$R_3$ is the moiety

\[
\begin{align*}
R_4 & \text{ is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, and aryloxy wherein said aryl and aryloxy is optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryloxy and phenyl; }
\end{align*}
\]

$R_5$ 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, alkoxy carbonyl, aryl-C(O)-, CH$_3$C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH$_2$(CO)OCH$_2$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, aryloxy and
phenyl, heteroaryl optionally substituted, aryl of 6, 10 or 14 carbon atoms optionally substituted, cycloalkyl 3 to 6 ring atoms, aryl-\(\text{CH}=\text{CH}-\), cycloalkyl-alkyl; and adamantyl;

\(R_6\) is hydrogen;

\(R_7\) and \(R_8\) are each independently \(\text{H}\) or alkyl of 1 to 12 carbon atoms;

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

\(R_{10}\) is \(\text{H}\);

or a pharmaceutically acceptable salt thereof.

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

\(((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,

\(((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,

\(((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,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,11-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,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,11-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,

(^[^-[(SaR. βaSys.iOaS^g-CaminocarbonylHy-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,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,11-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,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,11-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)-1,11-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,

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,11-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\}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\}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\}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\}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\}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\}amino]carbonyl\}oxy)methyl 4-tert-butylbenzoate,

(\{[(2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl\}amino]carbonyl\}oxy)methyl 1.1'-biphenyl-4-carboxylate,
(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1-tetrahydroxy-10,12-dioxo-5,6a,6a,7,10,10a,12-octahydropyretacren-2-yl)amino)-2-oxoethyl)(propyl)amino)carbonyl)oxy)methyl 1,1'-biphenyl-4-carboxylate,

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

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1-tetrahydroxy-10,12-dioxo-δ,δ,δ,e,β,aJ.10JOa.12-octahydropyretacren-2-yl)amino)-2-oxoethyl)(propyl)amino)carbonyl)oxy)methyl 4-tert-butylbenzoate,

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

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

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

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1-tetrahydroxy-10,12-dioxo-5,6a,6a,7,10,10a,12-octahydropyretacren-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-octahydropyrene-2-yl)amino)-2-oxoethyl)(propyl)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-octahydropyrene-2-yl)amino)-2-oxoethyl)(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-octahydropyrene-2-yl)amino)-2-oxoethyl)(propyl)amino)carbonyl)oxy)methyl adamantane-1-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-octahydropyrene-2-yl)amino)-2-oxoethyl)(propyl)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-octahydropyrene-2-yl)amino)-2-oxoethyl)(propyl)amino)carbonyl)oxy)methyl adamantane-1-carboxylate,
Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

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

ethyl 2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1-tetrahydroxy-10,12-dioxo-δ,5a,6,6aJJO.10a.12-octahydrorotenacen-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-octahydrotetracene-2-yl]amino)-2-oxoethyl(propyl)carbamate.

Additional further embodiments of the invention are the following specifically preferred 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-octahydrotetracene-2-yl]amino)-2-oxoethyl)(butyl)amino[carbonyl]oxy)methyl thiophene-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-octahydrotetracene-2-yl]amino)-2-oxoethyl)(propyl)amino[carbonyl]oxy)methyl thiophene-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-octahydrotetracene-2-yl]amino)-2-oxoethyl)(butyl)amino[carbonyl]oxy)methyl thiophene-3-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-octahydrotetracene-2-yl]amino)-2-oxoethyl)(propyl)amino[carbonyl]oxy)methyl thiophene-3-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-octahydrotetracene-2-yl]amino)-2-oxoethyl)(butyl)amino[carbonyl]oxy)methyl thiophene-3-carboxylate,

Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:
(\{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-2-yl]amino)-2-oxoethyl\})(tert-butyl)amino]carbonyl]oxy)methyl propionate,

(\{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-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,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-2-yl]amino)-2-oxoethyl\})(tert-butyl)amino]carbonyl]oxy)methyl 3,5-dimethylbenzoate,

(\{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-2-yl]amino)-2-oxoethyl\})(tert-butyl)amino]carbonyl]oxy)methyl 4-fluorobenzoate,

(\{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-2-yl]amino)-2-oxoethyl\})(tert-butyl)amino]carbonyl]oxy)methyl 3-methylbutanoate,

(\{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-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,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-2-yl]amino)-2-oxoethyl\})(tert-butyl)amino]carbonyl]oxy)methyl 4-(trifluoromethyl)benzoate,

(\{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,1\}-aminooctahydrotetracen-2-yl]amino)-2-oxoethyl\})(tert-butyl)amino]carbonyl]oxy)methyl cyclopropanecarboxylate,
(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1-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-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,

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,

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1-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,

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1-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-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,

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1-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 2,6-dinitrobenzoate,

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((^aR,aS,aS,aS)-9-laminocarbonyl)-4,7-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,

(((2-([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((^aR,aS,aS,aS)-9-laminocarbonyl)-4,7-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,

(((2-([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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-1,0,1,2-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,

(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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-(acetylaminobenzoate,

(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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

(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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:

\[
\begin{align*}
   & ([\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-1,2\text{-dioxo}-5,5a,6,6a,7,10,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ 4-fluorobenzoate}, \\
   & ([\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-10,12\text{-dioxo}-\delta,\delta a,6,6a,7,10,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ 3,5-dimethylbenzoate}, \\
   & ([\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-0,12\text{-dioxo}-\delta,\delta a,6,6a,7,10,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ pivalate}, \\
   & ([\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-1,0,12\text{-dioxo}-\delta,\delta a,6,6a,7,\delta a,6,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ 3,3-dimethylbutanoate}, \\
   & ([\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-10,12\text{-dioxo}-5,5a,6,6a,7,10,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ 2,2-dimethylbutanoate}, \\
   & ([\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-0,1,2\text{-dioxo}-\delta,\delta a,6,6a,7,10,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ 2-ethylbutanoate}, \\
   & ([\{(\delta aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11\text{-}\text{tetrahydroxy}-1,0,1,2\text{-dioxo}-\delta,\delta a,6,6a,7,10,10a,12\text{-octahydrotetracen-2-yl}\text{amino}\text{carbonyl}\text{oxy}]\text{methyl} \text{ thiophene-2-carboxylate},
\end{align*}
\]
Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

- \(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)carbonyl)oxy)methyl cyclopentylacetate,
- \(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10^-dioxo-5,6,6a,7-\delta,6,\delta aJ.10.10a.12-octahydrotetracen-2-yl)amino)carbonyl)oxy)methyl 4-tert-butylbenzoate.
Further embodiments of the invention are the following specifically preferred compounds of Formula I or pharmaceutically acceptable salts thereof:

(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,7,10,12-octahydrotetracen-2-yl]amino)-2-oxoethyl(propyl)carbamate,

(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,7,10,12-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,7,10,12-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,1 1-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)-1,8,1 1-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl(butyl)carbamate and

[5-(4-methoxyphenyl)-2-oxo-1,3-dioxol-4-yl]methyl 2-[[[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1 1-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 (H):

\[
\begin{align*}
\text{R}_4 & \text{ is selected from hydrogen, alkyl of 1 to 12 carbon atoms, optionally substituted} \\
\text{with 1 to 3 substituents independently selected from the group halogen, amino,} \\
\text{cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl,} \\
\text{hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-} \\
\text{cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, aroylxy and} \\
\text{N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, aroylxy and aryl of N-(alkyl} \\
\text{of 1 to 12 carbon atoms)-aryl may optionally be substituted with 1 to 3 substituents} \\
\text{independently selected from halogen, nitro, cyano, aikenyl, hydroxyl, alkyl, haloalkyl,}
\end{align*}
\]
alkoxy, amino, alkyiamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl 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, alkyiamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl 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, alkyiamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl 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, alkyiamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aryl 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, heterocycl of 3 to 8 ring atoms, aryl of 6, 10 or 14 carbon atoms, arylxy 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, alkyiamino, dialkylamino, carboxyl, alkoxy carbonyl, aryl-C(O)-, CH₃-C(O)-NH-, aralkyl, aryloxy, heterocycl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aryl of 7 to 13 carbon atoms optionally substituted, SR³, heteroaryl optionally substituted and heteroaryl carbonyl optionally substituted;
C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH₃(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;

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, alkoxy carbonyl, aryl-C(O)-, CH₃- C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, and cycloalkyl of 3 to 6 carbon atoms;

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

Q is -OR, Cl, Br or I;

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

\[
\begin{align*}
\text{R}_{12} & \text{ is alkyl of 1 to 6 carbon atoms.}
\end{align*}
\]
The compounds having Formula II are useful as chemical intermediates for making the compounds having formula I and the pharmaceutically acceptable salt thereof where in: A is a moiety

\[
\begin{align*}
R_4 & \quad \quad \quad \quad \\
\text{N} & \quad \quad \quad \quad \quad \\
\text{O} & \quad \quad \quad \quad \quad \\
\end{align*}
\]

and R₃ is the moiety

\[
\begin{align*}
R_5 & \quad \quad \quad \quad \\
\text{O} & \quad \quad \quad \quad \\
R_6 & \quad \quad \quad \quad \\
R_8 & \quad \quad \quad \quad \\
R_{10} & \quad \quad \quad \quad \\
\end{align*}
\]

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 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.

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
and $R_{12}$ is alkyl of 1 to 6 carbon atoms.

Another embodiment of the invention provides compounds of Formula II wherein $R_8$ and $R_{10}$ are H.

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

$\text{O} \quad \text{O} \quad \text{R}_{12}$

1. $\text{O} \quad \text{O} \quad \text{4-tert-butylbenzoate},$

2. $\text{O} \quad \text{O} \quad \text{2,2-dimethylbutanoate},$

3. $\text{O} \quad \text{O} \quad \text{2-methylpropanoate},$

4. $\text{O} \quad \text{O} \quad \text{cyclopentanecarboxylate},$

5. $\text{O} \quad \text{O} \quad \text{4-methylbenzoate},$

6. $\text{O} \quad \text{O} \quad \text{heptanoate},$

7. $\text{O} \quad \text{O} \quad \text{propionate},$

8. $\text{O} \quad \text{O} \quad \text{cyclohexanecarboxylate},$
(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3,5-dimethylbenzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 4-fluorobenzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3-methylbutanoate,

benzyl N-(tert-butyl)-N-(((cyclopentylacetyl)oxy)methoxy)carbonyl)glycinate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl A-(trifluoromethyl)benzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl cyclopropanecarboxylate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl adamantane-1-carboxylate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl pentanoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl cyclobutanecarboxylate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3-cyclohexylpropanoate,

benzyl N-(tert-butyl)-N-(((4-fluorophenoxy)acetyl)oxy)methoxy)carbonyl)glycinate,

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)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,

15

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl A-methoxybenzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 1H-indole-2-carboxylate,

20

benzyl N-(tert-butyl)-N-(((diphenylacetyl)oxy)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-difluorobenzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 2-fluorobenzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 2-(trifluoromethyl)benzoate,

(((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 4-(1H-pyrrol-1-yl)benzoate,

(((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,

(((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-trimethoxybenzoate,

(((2-(benzyloxy)-2-oxoethyl)(3-tert-butyl)amino)carbonyl)oxy)methyl 3,5-dimethoxybenzoate,

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]carbonyl]oxy)methyl 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


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,

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,
N-(tert-butyl)-N-\{[(cyclohexylcarbonyloxy)methoxy]carbonyl\}glycine,
N-(tert-butyl)-N-\{[(3,5-dimethylbenzoyl)oxy]methoxy\}carbonyl\}glycine,
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,
N-(tert-butyl)-N-\{[(4-(trifluoromethyl)benzoyl)oxy]methoxy\}carbonyl\}glycine,
N-(tert-butyl)-N-\{[(cyclopropylcarbonyloxy)methoxy]carbonyl\}glycine,
N-(tert-butyl)-N-\{[(pentanoyloxy)methoxy]carbonyl\}glycine,
N-(tert-butyl)-N-\{[(4-cyclohexylpropanoyl)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,
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,

N-(tert-butyl)-N-{[[(1-benzofuran-2-ylcarbonyl)oxy]methoxy]carbonyl}glycine,

N-(tert-butyl)-N-{[[(1-methyl-1H-pyrrol-2-yl)carbonyl]oxy]methoxy}carbonyl]glycine,

N-(tert-butyl)-N-{[[(1,1'-biphenyl-4-ylcarbonyl)oxy]methoxy]carbonyl}glycine,

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,

N-(tert-butyl)-N-{[[(1-naphthoyloxy)methoxy]carbonyl}glycine,

N-(tert-butyl)-N-{[[(2-naphthoyloxy)methoxy]carbonyl]glycine,

N-(tert-butyl)-N-{[[(1H-indol-2-ylcarbonyl)oxy]methoxy]carbonyl}glycine,

N-(tert-butyl)-N-{[[(2,6-difluorobenzoyl)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]glycine,
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,
N-[[[3,5-bis(trifluoromethyl)phenyl]acetyl]oxy]methoxy]carbonyl]glycine,
N-(tert-butyl)-N-[[[4-(heptyloxy)benzoyl]oxy]methoxy]carbonyl]glycine,
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-(acetylamino)benzoyl]oxy]methoxy]carbonyl]glycine,
N-[[[9-anthrylcarbonyl]oxy]methoxy]carbonyl]glycine and
N-[[[4-benzoylbenzoyl]oxy]methoxy]carbonyl]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 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 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, alkoxy carbonyl, 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 1,1-dimethylethyl also termed t-butyl. In some 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.

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, wherein said aryl and arylo 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. In some embodiments of the invention alkenyl is a vinyl moiety \( \text{CH}_2=\text{CH}^- \).

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

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)-, CH\(_3\)-C(O)-NH-, aralkyl, aryloxyl, heterocyclic and phenyl. In particular, aryl is phenyl or 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.

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.

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

As used herein the term alkylnyl 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 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.

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, 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.

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, arylO- refers to a arylO- group.

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

The present invention accordingly provides a pharmaceutical composition 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.

Proton sponge is \([1,8\text{-bis(dimethylamino)naphthalene}, \, \text{N,N,N',N'-tetramethyl-1,8-naphthalenediamine}]\).

Alkali metal carbonate includes lithium, potassium and sodium carbonate.

DMPU is 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone.
N-butyl-glycylcycline (N-bu-glycyl) is

\[ \text{Diagram of N-butyl-glycylcycline} \]

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

\[ \text{Diagram of N-propyl-glycylcycline} \]
DESCRIPTION OF THE PREFERRED EMBODIMENTS

The compounds of this invention may be prepared according to the following 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 R₄NH₂, 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 removed by catalytic reduction to give carboxylic acid 7 which is activated to a mixed anhydride with chloroformate ClCO₂Rᵢ₂ where Rᵢ₂ is alkyi of 1 to 6 carbon atoms, for example iso-butyl chloroformate to give acyloxy carbamate intermediate 8. In an alternate route, silyl esters may optionally be used in place of the benzyl ester of 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 (BoC₂O); e.g., benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (also known asBop); benzotriazole-1 -yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate (also known as PyBop); 0-benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluoro-phosphate (HBTU); Bromotris-pyrrolidino-phosphonium hexafluorophosphate; 2-Chloro-N-methylpyridinium iodide (CMPI); dicyclohexylcarbodiimide (DCC); 1,3-diisopropylcarbodiimide (DIG); 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (EDC); or Carbonyl diimidazole.
As shown in Scheme 2, reaction of activated acyloxycarbamate intermediate 8 with Z,S-disubstituted-9-aminotetracycline 9 in the presence of triethylamine and DMPU gives acyloxycarbamate 10.
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 FJ. Lund, Synthesis, December 1990, 1159-1166).
As further seen in Scheme 4 acyloxycarbamates 16 and 17 where R₄ is preferably n-butyl or n-propyl are synthesized by treatment of either 14 or 15 where R₄ is preferably n-butyl or n-propyl with the chloro intermediate 13 to give acyloxycarbamates 16 and 17 respectively.
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).

Scheme 5

$R_5$ is preferably propyl
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 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 $\text{CICO}_2\text{R}_{12}$ where $\text{R}_{12}$ is alkyl of 1 to 6 carbon atoms, for example isobutyl chloroformate to give acyloxy carbamate intermediate 26. Further reaction of 7,8-disubstituted-9-aminotetracycline 9 with acyloxy carbamate mixed anhydride intermediate 26 in the presence of triethylamine and DMPU affords compounds of Formula (I).
Scheme 7

\[ \text{Formula I} \]
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

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 µl 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.


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 also against Staph in human serum and water. Table 10 presents in vivo single oral dose (SOD) and single intravenous dose (SIV) ED$_{50}$ data for representative examples of compounds of Formula I against Staph. Smith and E. Coli #31 1 in mammals.
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<th>1</th>
<th>Mouse Water</th>
<th>16</th>
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### TABLE I (Cont)

**ANTIBACTERIAL ACTIVITY OF -AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCICYCLINES**

**OF FORMULA I**

**MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

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TABLE I (Cont)

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYL-SUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF
FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC (μG/ML)

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# TABLE II

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCyclines OF FORMULA I**

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ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYL SUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I
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**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I**

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### TABLE III (Cont)

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

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

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TABLE IV (Cont)

ANTIBACTERIAL ACTIVITY OF γ-AMINOCARBONYL-SUBSTITUTED DERIVATIVES OF GLYCYLCYC LINES OF FORMULA I
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## TABLE IV (Cont)

ANTIBACTERIAL ACTIVITY OF \(-\)-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

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### TABLE V

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I**

**MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

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

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S. pyogenes GC 4563
S. agalactiae GC 4564
c. albicans GC 3066
### TABLE V

**ANTIBACTERIAL ACTIVITY OF \(-\)**AMINOCARBONYL**SUBSTITUTED DERIVATIVES OF GLYC**ACYCLINES OF FORMULA I**

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TABLE VII (CONT)

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

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<td>S. agaiactiae GC 4564</td>
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### TABLE VIII

**ANTIBACTERIAL ACTIVITY OF \( \text{\textregistered} \)-AMINOCARBONYL SUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I**

**MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

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TABLE VIII (CONT)

ANTIBACTERIAL ACTIVITY OF $\alpha$-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I

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S. pneumoniae+ GC
4465
S. pyogenes GC 4563
S . agalactiae GC 4564
c . albicans GC 3066

E . faecium GC 2243
S. pneumoniae* GC

E. faecium GC 4556

E . faecalis GC 2242

E. faecalis GC 2267

E . faecalis GC 2265

E. faecalis GC 4555

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0.25

0.12

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0.25

1

2
1
1
1
1

Mouse
Water
Serum
Human Serum Water
Mouse Serum
Example 45 Example 45 Example 45
Example 46 Example 46

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0.12

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0.25

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0.50

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Human Serum Water
Example 46
Example 47

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0.25
1
>64

0.50

0.25
2

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4
4
4
4
2

1
1
1
1
1
0.50

Mouse Serum Human Serum
Example 47
Example 47

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


### TABLE IX

**ANTIBACTERIAL ACTIVITY OF α-AVIINOCARBONYL-SUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I**

**MINIMAL INHIBITORY CONCENTRATION MIC (UG/ML)**

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# TABLE X

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYL SUBSTITUTED DERIVATIVES OF GLYCYLCYCLINES OF FORMULA I**

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### TABLE X (CONT)

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

MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)

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### TABLE XI

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

**MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

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TABLE XII

ANTIBACTERIAL ACTIVITY OF $\text{N}$-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I

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### TABLE XII (CONT)

**ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCYLCYCLOINES OF FORMULA I**

**MINIMAL INHIBITORY CONCENTRATION MIC(UG/ML)**

<table>
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<th>Water</th>
<th>Mouse Serum</th>
<th>Human Serum</th>
<th>Water</th>
<th>Mouse Serum</th>
<th>Human Serum</th>
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<td>Example 62</td>
<td>Example 62</td>
<td>Example 63</td>
<td>Example 63</td>
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- **E. faecium GC 4556**
  - Mouse: 2
  - Human: 0.50
  - Example: 1
  - MIC: 0.50
  - Example: 1
  - MIC: 0.50
  - Example: 0.50
  - MIC: 0.25
  - Example: 4

- **E. faecium GC 2243**
  - Mouse: 0.50
  - Human: 0.25
  - Example: 1
  - MIC: 0.50
  - Example: 0.50
  - MIC: 0.50
  - Example: 0.50
  - MIC: 0.25
  - Example: 0.25

- **S. pneumoniae**
  - Mouse: 0.12
  - Human: 0.12
  - Example: 0.25
  - MIC: 0.12
  - Example: 0.12
  - MIC: 0.12
  - Example: 0.12
  - MIC: 0.12

- **S. pneumoniae**
  - Mouse: 0.50
  - Human: 0.50
  - Example: 1
  - MIC: 1
  - Example: 0.50
  - MIC: 0.50
  - Example: 0.50
  - MIC: 0.50

- **S. pyogenes GC 4563**
  - Mouse: 0.50
  - Human: 0.25
  - Example: 0.25
  - MIC: 0.25
  - Example: 0.25
  - MIC: 0.12
  - Example: 0.12
  - MIC: 0.12

- **S. agalactiae GC 4564**
  - Mouse: 0.25
  - Human: 0.25
  - Example: 0.25
  - MIC: 0.25
  - Example: 0.25
  - MIC: 0.12
  - Example: 0.25
  - MIC: 0.25

- **c. albicans GC 3066**
  - Mouse: >64
  - Human: >64
  - Example: >64
  - MIC: >64
  - Example: >64
  - MIC: >64
  - Example: >64
  - MIC: >64

91
|                  | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water | Mouse Serum | Water |
|------------------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|
| **E. coli**      |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |             |       |
| GC 2236         | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     |
| GC 2231         | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     |
| GC 2232         | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     |
| GC 2233         | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     | 2           | 4     |
| GC 2234         | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     |
| GC 2270         | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     | 0.50        | 1     |
| GC 2271         | 0.50        | 0.50  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  |
| GC 2272         | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  | 0.25        | 0.12  |
| GC 4559         | 0.12        | 0.06  | <0.06       | <0.06 | <0.06       | <0.06 | <0.06       | <0.06 | <0.06       | <0.06 | <0.06       | <0.06 | <0.06       | <0.06 | <0.06       | <0.06 | <0.06       | <0.06 |
| GC 4560         | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  |
| GC 4561         | 0.50        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  | 0.25        | 0.25  |
| GC 4562         | 8           | 64    | 4           | 64    | 4           | 64    | 4           | 64    | 4           | 64    | 4           | 64    | 4           | 64    | 4           | 64    |
| GC 4563         | 1           | 8     | 2           | 8     | 2           | 8     | 2           | 8     | 2           | 8     | 2           | 8     | 2           | 8     | 2           | 8     |
| GC 4564         | 1           | 4     | 1           | 4     | 1           | 4     | 1           | 4     | 1           | 4     | 1           | 4     | 1           | 4     | 1           | 4     |
| GC 4565         | 4           | 16    | 4           | 16    | 4           | 16    | 4           | 16    | 4           | 16    | 4           | 16    | 4           | 16    | 4           | 16    |
| GC 4566         | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    |
| GC 1534         | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    | 32          | 32    |

**TABLE XIII**

ANTIBACTERIAL ACTIVITY OF 9-AMINOCARBONYL-SUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I
**TABLE XIII (CONT)**

ANTIBACTERIAL ACTIVITY OF -AMINOCARBONYLSUBSTITUTED DERIVATIVES OF GLYCICYCLINES OF FORMULA I

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TABLE XIII (CONT)

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

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

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\(^a\) 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)

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<sup>a</sup> 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>
<thead>
<tr>
<th>Ex Number</th>
<th>E. coli (Mouse Serum)</th>
<th>E. coli (Water)</th>
<th>Staph (Mouse Serum)</th>
<th>Staph (Water)</th>
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* 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)

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<tr>
<th>Ex Number</th>
<th>E. coli (Mouse Serum)</th>
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* 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.

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<table>
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</tr>
<tr>
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<tr>
<td>E. coli, tet (M₃,S₁,O) Tet (M)</td>
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<td>E. coli (susceptible)</td>
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<td>E. coli (IMP)</td>
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<td>S. aureus, tet (M)</td>
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<td>S. aureus, tet (K), efflux</td>
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<td>S. aureus (susceptible)</td>
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<tr>
<td>Streptococcus spp.</td>
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<td>C. albicans</td>
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* 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.

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

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<th>E. coli (water)</th>
<th>Staph. (mouse serum)</th>
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<td>64-&gt;64</td>
</tr>
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<td>32-&gt;64</td>
</tr>
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<td>0.5-4</td>
<td>2-&gt;64</td>
</tr>
<tr>
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<td>&gt;64</td>
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<td>0.5-8</td>
</tr>
<tr>
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<td>0.25-4</td>
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<td>8-32</td>
<td>2-4</td>
<td>4-16</td>
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<td>38</td>
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<td>0.5-2</td>
<td>1-8</td>
</tr>
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<td>1-4</td>
<td>16-32</td>
<td>1-4</td>
<td>2-16</td>
</tr>
</tbody>
</table>

*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 4. In vitro activity (MIC)\textsuperscript{a} of representative examples of compounds of Formula I

<table>
<thead>
<tr>
<th>Ex. No.</th>
<th>E. coli (mouse serum)</th>
<th>E. coli (water)</th>
<th>Staph. (mouse serum)</th>
<th>Staph. (water)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>1-2</td>
<td>16-64</td>
<td>0.25-2</td>
<td>0.5-4</td>
</tr>
<tr>
<td>6</td>
<td>1-2</td>
<td>8-64</td>
<td>0.5-2</td>
<td>1-4</td>
</tr>
<tr>
<td>7</td>
<td>0.25-2</td>
<td>2-16</td>
<td>0.5-4</td>
<td>0.5-4</td>
</tr>
<tr>
<td>8</td>
<td>1-2</td>
<td>16-64</td>
<td>0.5-4</td>
<td>1-8</td>
</tr>
<tr>
<td>9</td>
<td>0.5-2</td>
<td>4-64</td>
<td>0.06-1</td>
<td>0.12-2</td>
</tr>
<tr>
<td>10</td>
<td>0.25-2</td>
<td>4-32</td>
<td>0.25-2</td>
<td>0.12-2</td>
</tr>
<tr>
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<td>4-&gt;64</td>
<td>0.25-4</td>
<td>0.25-4</td>
</tr>
<tr>
<td>19</td>
<td>0.5-2</td>
<td>32-&gt;64</td>
<td>0.5-4</td>
<td>1-8</td>
</tr>
<tr>
<td>24</td>
<td>0.5-2</td>
<td>&gt;64</td>
<td>0.25-4</td>
<td>0.5-&gt;64</td>
</tr>
<tr>
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<td>1-2</td>
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<td>0.25-2</td>
<td>0.5-4</td>
</tr>
<tr>
<td>26</td>
<td>1-4</td>
<td>64-&gt;64</td>
<td>0.25-1</td>
<td>0.25-4</td>
</tr>
<tr>
<td>27</td>
<td>0.5-1</td>
<td>32-&gt;64</td>
<td>0.12-2</td>
<td>0.12-2</td>
</tr>
<tr>
<td>28</td>
<td>0.25-1</td>
<td>&gt;64</td>
<td>0.5-4</td>
<td>4-64</td>
</tr>
<tr>
<td>31</td>
<td>0.5-1</td>
<td>16-&gt;64</td>
<td>0.25-2</td>
<td>0.5-4</td>
</tr>
<tr>
<td>33</td>
<td>0.5-2</td>
<td>32-&gt;64</td>
<td>0.12-2</td>
<td>0.12-2</td>
</tr>
<tr>
<td>35</td>
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<td>8-64</td>
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<td>2-4</td>
</tr>
<tr>
<td>40</td>
<td>1-2</td>
<td>16-&gt;64</td>
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<td>0.25-2</td>
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<tr>
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<td>16-64</td>
<td>0.5-4</td>
<td>1-8</td>
</tr>
</tbody>
</table>

\textsuperscript{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 5. *In vitro* activity (MIC) of Example 27

<table>
<thead>
<tr>
<th></th>
<th>water</th>
<th>Mouse serum</th>
<th>Human serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli, tet(A-D), 64-&gt;64</td>
<td>64-64</td>
<td>0.5-1</td>
<td>4-16</td>
</tr>
<tr>
<td>E. coli, tet (M,S,O) Tet (M)</td>
<td>0.5</td>
<td>0.5</td>
<td>4-8</td>
</tr>
<tr>
<td>E. coli (susceptible)</td>
<td>0.5</td>
<td>0.5</td>
<td>16</td>
</tr>
<tr>
<td>E. coli (IMP)</td>
<td>0.25</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>S. aureus, tet (M)</td>
<td>0.12</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td>S. aureus, tet (K), efflux</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>S. aureus (susceptible) a</td>
<td>0.12</td>
<td>0.12</td>
<td>0.5</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>0.12-1</td>
<td>0.12-1</td>
<td>0.5-2</td>
</tr>
<tr>
<td>Streptococcus spp.</td>
<td>0.06-2</td>
<td>&lt;0.06-0.12</td>
<td>0.12-2</td>
</tr>
<tr>
<td>C. albicans</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
</tbody>
</table>

* a Strain used for *in vivo* testing

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.

<table>
<thead>
<tr>
<th>Ex. No.</th>
<th>SOD^b</th>
<th>SIV^c</th>
<th>MIC^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>5.68</td>
<td>1.43</td>
<td>8</td>
</tr>
<tr>
<td>44</td>
<td>4</td>
<td>0.75</td>
<td>4</td>
</tr>
<tr>
<td>45</td>
<td>5.9</td>
<td>0.66</td>
<td>1</td>
</tr>
<tr>
<td>47</td>
<td>14</td>
<td>1.2</td>
<td>4</td>
</tr>
<tr>
<td>48</td>
<td>10.1</td>
<td>1.1</td>
<td>0.25</td>
</tr>
<tr>
<td>49</td>
<td>16</td>
<td>0.92</td>
<td>0.25</td>
</tr>
<tr>
<td>50</td>
<td>16.88</td>
<td>1.65</td>
<td>0.5</td>
</tr>
<tr>
<td>52</td>
<td>10.69</td>
<td>1.29</td>
<td>2</td>
</tr>
<tr>
<td>53</td>
<td>5.08</td>
<td>0.73</td>
<td>1</td>
</tr>
<tr>
<td>54</td>
<td>8.4</td>
<td>0.83</td>
<td>0.5</td>
</tr>
<tr>
<td>87</td>
<td>12.82</td>
<td>0.83</td>
<td>32</td>
</tr>
</tbody>
</table>

^a MIC (minimum inhibitory concentration)

^b SOD (Single oral dose)

^c SIV (Single intravenous dose)

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.

<table>
<thead>
<tr>
<th>Ex. No.</th>
<th>SOD(^b)</th>
<th>SIV(^c)</th>
<th>MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>&gt;64</td>
<td>3.17</td>
<td>&gt;64</td>
</tr>
<tr>
<td>42</td>
<td>30.3</td>
<td>3.1</td>
<td>&gt;64</td>
</tr>
<tr>
<td>44</td>
<td>42.8</td>
<td>2.85</td>
<td>&gt;64</td>
</tr>
<tr>
<td>45</td>
<td>64</td>
<td>1.8</td>
<td>64</td>
</tr>
<tr>
<td>48</td>
<td>29.8</td>
<td>1.7</td>
<td>&gt;64</td>
</tr>
<tr>
<td>49</td>
<td>49</td>
<td>2.2</td>
<td>64</td>
</tr>
<tr>
<td>50</td>
<td>29.8</td>
<td>1.7</td>
<td>&gt;64</td>
</tr>
<tr>
<td>52</td>
<td>43.7</td>
<td>3.78</td>
<td>8</td>
</tr>
<tr>
<td>53</td>
<td>46.88</td>
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<td>54</td>
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<td>&gt;64</td>
</tr>
<tr>
<td>87</td>
<td>60.4</td>
<td>3.6</td>
<td>&gt;64</td>
</tr>
</tbody>
</table>

\(^a\) 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.

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

<table>
<thead>
<tr>
<th>Ex. No.</th>
<th>SOD&lt;sup&gt;b&lt;/sup&gt;</th>
<th>SIV&lt;sup&gt;c&lt;/sup&gt;</th>
<th>MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.7</td>
<td>0.6</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>8.51</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>19</td>
<td>8.05</td>
<td>0.31</td>
<td>1</td>
</tr>
<tr>
<td>26</td>
<td>8.79</td>
<td>0.43</td>
<td>0.5</td>
</tr>
<tr>
<td>27</td>
<td>3.9</td>
<td>0.44</td>
<td>0.12</td>
</tr>
<tr>
<td>28</td>
<td>6.61</td>
<td>0.6</td>
<td>32</td>
</tr>
<tr>
<td>33</td>
<td>4.91</td>
<td>0.48</td>
<td>0.12</td>
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<td>35</td>
<td>3.5</td>
<td>0.43</td>
<td>4</td>
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<td>0.84</td>
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<td>38</td>
<td>5.3</td>
<td>0.6</td>
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<tr>
<td>40</td>
<td>4.65</td>
<td>0.39</td>
<td>0.5</td>
</tr>
</tbody>
</table>

<sup>a</sup> MIC (minimum inhibitory concentration)

<sup>b</sup> SOD (Single oral dose)

<sup>c</sup> SIV (Single intravenous dose)
<table>
<thead>
<tr>
<th>Ex No.</th>
<th>E.coli (Human Serum)</th>
<th>E.coli (Water)</th>
<th>Staph (Human Serum)</th>
<th>Staph (Water)</th>
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<tr>
<td>4</td>
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<td>16-&gt;64</td>
<td>0.12-1</td>
<td>0.25-4</td>
</tr>
<tr>
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<td>0.25-2</td>
<td>0.5-4</td>
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<td>&gt;64</td>
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<td>4-8</td>
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<tr>
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<td>&gt;64</td>
<td>4-64</td>
<td>32-&gt;64</td>
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<td>0.5-2</td>
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<td>&gt;64</td>
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<td>Ex. No.</td>
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<td>ED_{50} (mg/kg) Staph. Smith</td>
<td>PO - RAT 20 mg/kg</td>
</tr>
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<td>--------</td>
<td>-----</td>
<td>-----</td>
<td>----------------------------</td>
<td>------------------</td>
</tr>
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<td>&gt;32</td>
<td>&gt;2</td>
</tr>
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<td>0.59</td>
<td>&gt;32</td>
<td>&gt;2</td>
</tr>
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<td>&gt;2</td>
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<td>&gt;2</td>
</tr>
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<td>&gt;32</td>
<td>&gt;2</td>
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<td>&gt;2</td>
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<td>&gt;2</td>
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<td>0.82</td>
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<td>8.05</td>
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<td>&gt;2</td>
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When the compounds of the invention are employed as antibacteriais, they can be combined with one or more pharmaceutically acceptable carriers, for example, 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 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 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, 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 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 oils such as com, 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.

Reference Compound 1
(Tert-butyl-chloromethoxycarbonyl-amino)-acidic acid benzyl ester.

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 than 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

Reference Compound 2
3,3-Dimethyl-butyric acid (benzyloxy carbonyl methyl tert-butyl carbamoyloxy)-methyl
ester

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

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 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

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<td>9</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl propionate</td>
<td>MS (ESI) m/z 352.17; HRMS: calcd for C18H25NO6 + H+, 352.17546; found (ESI+,[M+H]+), 352.17551;</td>
</tr>
<tr>
<td>10</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl cyclohexanecarboxylate</td>
<td>MS (ESI) m/z 406.26;</td>
</tr>
<tr>
<td>11</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl 3,5-dimethylbenzoate</td>
<td>MS (ESI) m/z 428.25; HRMS: calcd for C18H25NO6 + H+, 352.17546; found (ESI+,[M+H]+), 352.17551;</td>
</tr>
<tr>
<td>12</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl 4-fluorobenzoate</td>
<td>MS (ESI) m/z 418.2; HRMS: calcd for C20H29NO6 + Na+, 402.18871; found (ESI+,[M+Na]+), 402.18882;</td>
</tr>
<tr>
<td>13</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl 3-methylbutanoate</td>
<td>MS (ESI) m/z 380.27; HRMS: calcd for C20H29NO6 + Na+, 402.18871; found (ESI+,[M+Na]+), 402.18882;</td>
</tr>
<tr>
<td>14</td>
<td>benzyl N-({tert-buty}-N-{(cyclopentylacetyl)oxy}[methoxy]carbonyl)glycinate</td>
<td>MS (ESI) m/z 406.2;</td>
</tr>
<tr>
<td>15</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl 4-(trifluoromethyl)benzoate</td>
<td>MS (CI(ISOBUTANE)) m/z 468.13;</td>
</tr>
<tr>
<td>16</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl cyclopropanecarboxylate</td>
<td>MS (ESI) m/z 364.26;</td>
</tr>
<tr>
<td>17</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl adamantane-1-carboxylate</td>
<td>MS (ESI) m/z 458.3;</td>
</tr>
<tr>
<td>18</td>
<td>((([(2-({benzylxy}-2-oxoethyl)({tert-buty}-amino)carbonyl]oxy)methyl pentanoate</td>
<td>MS (ESI) m/z 380.2;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>19</td>
<td>(((2-(benzyloxy)-2-oxoethyl) (tert-buty1)amino)carbonyloxy)methyl cyclobutanecarboxylate</td>
<td>MS (ESI) m/z 378.2; MS (ESI) m/z 400.2;</td>
</tr>
<tr>
<td>20</td>
<td>(((2-(benzyloxy)-2-oxoethyl) (tert-buty1)amino)carbonyloxy)methyl 3-cyclohexylpropanoate</td>
<td>MS (ESI) m/z 434.3; MS (ESI) m/z 451.3; HRMS: calcd for C24H35NO6 + Na+, 456.23566; found (ESI+), [M+NA]1+, 456.23661;</td>
</tr>
<tr>
<td>21</td>
<td>benzyl N-(tert-buty1)-N-(((4-fluorophenoxy)acetyl)oxy)methoxy)carbonyl]glycinate</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>benzyl N-(tert-buty1)-N-(((cyclohexylacetetyl)oxy)methoxy)carbonyl]glycinate</td>
<td>MS (ESI) m/z 420.2; MS (ESI) m/z 442.2;</td>
</tr>
<tr>
<td>23</td>
<td>(((2-(benzyloxy)-2-oxoethyl) (tert-buty1)amino)carbonyloxy)methyl 2,6-dimethylbenzoate</td>
<td>MS (ESI) m/z 428.2;</td>
</tr>
<tr>
<td>24</td>
<td>benzyl N-(tert-buty1)-N-(((phenylacetetyl)oxy)methoxy)carbonyl]glycinate</td>
<td>MS (ESI) m/z 414.2; MS (ESI) m/z 436.2; HRMS: calcd for C23H27NO6 + H+, 414.19112; found (ESI+), [M+H]1+, 414.19143;</td>
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<tr>
<td>25</td>
<td>(((2-(benzyloxy)-2-oxoethyl) (tert-buty1)amino)carbonyloxy)methyl pivalate</td>
<td>MS (ESI) m/z 380.1; MS (ESI) m/z 781.3; HRMS: calcd for C20H29NO6 + H+, 380.20677; found (ESI+), [M+H]1+, 380.20649;</td>
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<td>Ref. Cpd. No.</td>
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<td>Spectra</td>
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<tr>
<td>26</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1-benzofuran-2-carboxylate</td>
<td>MS (ESI) m/z 440; MS (ESI) m/z 901.1; HRMS: calcd for C24H25NO7 + H+, 440.17038; found (ESI+, [M+H]+), 440.17005;</td>
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<td>27</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1-methyl-1H-pyrrole-2-carboxylate</td>
<td>MS (ESI) m/z 403.3; MS (ESI) m/z 827.7;</td>
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<tr>
<td>28</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1,1′-biphenyl-4-carboxylate</td>
<td>MS (ESI) m/z 476.2; HRMS: calcd for C28H29NO6 + Na+, 498.18871; found (ESI+, [M+Na]+), 498.18857;</td>
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<tr>
<td>29</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 4-methoxybenzoate</td>
<td>MS (ESI) m/z 430.3; MS (ESI) m/z 452.3;</td>
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<tr>
<td>30</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1H-indole-2-carboxylate</td>
<td>MS (ESI) m/z 439.1; HRMS: calcd for C24H26N2O6 + Na+, 461.16831; found (ESI+, [M+Na]+), 461.168;</td>
</tr>
<tr>
<td>31</td>
<td>benzyl N-(tert-butyl)-N-(((diphenylacetlyloxy)methoxy)carbonyl)glycinate</td>
<td>MS (ESI) m/z 490.2;</td>
</tr>
<tr>
<td>32</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1-naphthoate</td>
<td>MS (ESI) m/z 450.1;</td>
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<tr>
<td>33</td>
<td>(((2-benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 2-naphthoate</td>
<td>MS (ESI) m/z 450.1;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>34</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1-methyl-1H-indole-3-carboxylate</td>
<td>MS (ESI) m/z 453.3; MS (ESI) m/z 905.6; MS (ESI) m/z 927.5;</td>
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<tr>
<td>35</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl quinoline-2-carboxylate</td>
<td>MS (ESI) m/z 451.2; MS (ESI) m/z 901.4;</td>
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<tr>
<td>36</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl nicotinate</td>
<td>MS (ESI) m/z 401.1;</td>
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<tr>
<td>37</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl isonicotinate</td>
<td>MS (ESI) m/z 401;</td>
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<tr>
<td>38</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 2,6-difluorobenzoate</td>
<td>MS (ESI) m/z 436.2; MS (ESI) m/z 893.4; MS (ESI) m/z 453.2;</td>
</tr>
<tr>
<td>39</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 2-fluorobenzoate</td>
<td>MS (ESI) m/z 418.2; MS (ESI) m/z 857.5; MS (ESI) m/z 440.2;</td>
</tr>
<tr>
<td>40</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 2-(trifluoromethyl)benzoate</td>
<td>MS (ESI) m/z 468.1; MS (ESI) m/z 490.2;</td>
</tr>
<tr>
<td>41</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 4-(1H-pyrrol-1-yl)benzoate</td>
<td>MS (ESI) m/z 465.1; MS (ESI) m/z 482.1;</td>
</tr>
<tr>
<td>42</td>
<td>(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 1,1'-biphenyl-2-carboxylate</td>
<td>MS (ESI) m/z 476.3; MS (ESI) m/z 493.3; MS (ESI) m/z 951.6;</td>
</tr>
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<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>43</td>
<td>(((((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 2,4,6-trimethylbenzoate</td>
<td>MS (ESI) m/z 442.3; MS (ESI) m/z 459.3;</td>
</tr>
<tr>
<td>44</td>
<td>(((((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 4-isopropoxybenzoate</td>
<td>MS (ESI) m/z 458.3;</td>
</tr>
<tr>
<td>45</td>
<td>(((((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3,4,5-trimethoxybenzoate</td>
<td>MS (ESI) m/z 490.3; MS (ESI) m/z 996.5; MS (ESI) m/z 979.5;</td>
</tr>
<tr>
<td>46</td>
<td>(((((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3,5-dimethoxybenzoate</td>
<td>MS (ESI) m/z 460.3; MS (ESI) m/z 936.5; MS (ESI) m/z 913.5;</td>
</tr>
<tr>
<td>47</td>
<td>3-phenyl-acrylic acid (benzyloxy carbonylmethyl-tert-butyl carbamoyloxy)-methyl ester</td>
<td>PE added cpd</td>
</tr>
<tr>
<td>48</td>
<td>(((((2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 3-methyl-1-benzofuran-2-carboxylate</td>
<td>MS (ESI) m/z 454.2; MS (ESI) m/z 907.5; HRMS: calcld for C25H27NO7 + Na+, 476.16797; found (ESI, [M+Na]1+), 476.16858;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>50</td>
<td>(((2-{benzyloxy}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 4-(heptyloxy)benzoate</td>
<td>MS (ESI) m/z 514.3; HRMS: calcld for C29H39NO7 + H+, 514.27993; found (ESI+, [M+H]1+), 514.28023;</td>
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<tr>
<td>51</td>
<td>(((2-{benzyloxy}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 2-(2-phenylethyl)benzoate</td>
<td>MS (ESI) m/z 526.2;</td>
</tr>
<tr>
<td>52</td>
<td>(((2-{benzyloxy}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 4-(dodecyloxy)benzoate</td>
<td>MS (ESI) m/z 584.3; HRMS: calcld for C34H49NO7 + H+, 584.35818; found (ESI+, [M+H]1+), 584.3574;</td>
</tr>
<tr>
<td>53</td>
<td>(((2-{benzyloxy}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 4-(acetylamo)benzoate</td>
<td>MS (ESI) m/z 457.2; MS (ESI) m/z 913.4; HRMS: calcld for C24H28N2O7 + Na+, 479.17887; found (ESI+, [M+NA]1+), 479.17909;</td>
</tr>
<tr>
<td>54</td>
<td>(((2-{benzyloxy}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl anthracene-9-carboxylate</td>
<td>MS (ESI) m/z 500.2; MS (ESI) m/z 999.5;</td>
</tr>
<tr>
<td>55</td>
<td>(((2-{benzyloxy}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 4-benzoylbenzoate</td>
<td>MS (ESI) m/z 504.2;</td>
</tr>
</tbody>
</table>
Reference Compound 56

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

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 filtered and solvent removed to give the corresponding carboxylic acid product of the example MS(ESI) m/z 394.25.

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 3-55.
<table>
<thead>
<tr>
<th>Ref. Cpd. No.</th>
<th>Name</th>
<th>Spectra</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>N-(tert-butyl)-N-(((4-tert-butylbenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 366.18</td>
</tr>
<tr>
<td>58</td>
<td>N-(tert-butyl)-N-(((isobutyroxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 274.05; MS (ESI) m/z 549.13; HRMS: calcd for C12H21NO6 + H+, 276.14416; found (ESI+), [M+H]1+, 276.14314;</td>
</tr>
<tr>
<td>59</td>
<td>N-(tert-butyl)-N-(((cyclopentylcarbonyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 300.04; MS (ESI) m/z 601.1; HRMS: calcd for 2 C14H23NO6 - H+, 601.29780; found (ESI-), [2M-H]1-, 601.29741;</td>
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<tr>
<td>60</td>
<td>N-(tert-butyl)-N-(((4-methylbenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 324.19; HRMS: calcd for C16H21NO6 + Na+, 346.12611; found (ESI+), [M+Na]1+, 346.12625;</td>
</tr>
<tr>
<td>61</td>
<td>N-(tert-butyl)-N-(((heptanoyloxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 316.25; MS (ESI) m/z 633.54;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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</tr>
<tr>
<td>62</td>
<td>N-(tert-butyl)-N-(((propionyloxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 260.05; MS (ESI) m/z 521.13; HRMS: calcd for C11H19NO6 + Na+, 284.11046; found (ESI, [M+Na]+), 284.11017;</td>
</tr>
<tr>
<td>63</td>
<td>N-(tert-butyl)-N-(((cyclohexylcarbonyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 314.06; MS (ESI) m/z 629.14; HRMS: calcd for 2 C15H25NO6 - H+, 629.32910; found (ESI-, [2M-H]1-), 629.32842;</td>
</tr>
<tr>
<td>64</td>
<td>N-(tert-butyl)-N-(((3,5-dimethylbenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 338.16;</td>
</tr>
<tr>
<td>65</td>
<td>N-(tert-butyl)-N-(((4-fluorobenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 326; MS (ESI) m/z 653; HRMS: calcd for C15H18FNO6 + Na+, 350.10103; found (ESI+, [M+Na]+), 350.10131;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>66</td>
<td>N-((tert-butyl)-N-(((3-methylbutanoyl)oxy)methoxy)carbonyl)glycine</td>
<td>HRMS: calcld for C13H23NO6 + Na+, 312.14176; found (ESI+, [M+Na]+), 312.14197;</td>
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<tr>
<td>67</td>
<td>N-((tert-butyl)-N-(((cyclopentylacetyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 314; HRMS: calcld for C15H25NO6 + H+, 316.17546; found (ESI+, [M+H]+), 316.17503;</td>
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<tr>
<td>68</td>
<td>N-((tert-butyl)-N-(((4-(trifluoromethyl)benzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 376; HRMS: calcld for C12H19NO6 + Na+, 296.11046; found (ESI+, [M+Na]+), 296.11061;</td>
</tr>
<tr>
<td>69</td>
<td>N-((tert-butyl)-N-(((cyclopropylcarbonyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 368.21; MS (ESI) m/z 757.37;</td>
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<tr>
<td>70</td>
<td>N-(((1-adamantylcarbonyl)oxy)methoxy)carbonyl)-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 368.21; MS (ESI) m/z 757.37;</td>
</tr>
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<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>71</td>
<td>N-(tert-butyl)-N-[[pentanoyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 288; MS (ESI) m/z 577.1; HRMS: calcd for C13H23NO6 + H+, 290.15982; found (ESI+, [M+H]+), 290.15951;</td>
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<td>72</td>
<td>N-(tert-butyl)-N-[[cyclobutylcarbonyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 288.1; MS (ESI) m/z 310.1; HRMS: calcd for C13H21NO6 + H+, 288.14416; found (ESI+, [M+H]+), 288.14435;</td>
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<td>73</td>
<td>N-(tert-butyl)-N-[[3-cyclohexylpropanoyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 344.2; MS (ESI) m/z 709.4; HRMS: calcd for C17H29NO6 + Na+, 366.18871; found (ESI+, [M+Na]+), 366.18863;</td>
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<tr>
<td>74</td>
<td>N-(tert-butyl)-N-[[4-fluorophenoxy]acetyl][oxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 356.1;</td>
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<tr>
<td>75</td>
<td>N-(tert-butyl)-N-[[cyclohexylacetoyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 328; MS (ESI) m/z 657.1;</td>
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<td>Ref. Cpd. No.</td>
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<td>Spectra</td>
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<tr>
<td>76</td>
<td>N-(tert-buty1)-N-(((2,6-dimethylbenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 338.2;</td>
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<tr>
<td>77</td>
<td>N-(tert-buty1)-N-(((phenylacetyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 322.1; HRMS: calcd for C16H21NO6 + H+, 324.14416; found (ESI+, [M+H]1+), 324.14351;</td>
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<tr>
<td>78</td>
<td>N-(tert-buty1)-N-(((2,2-dimethylpropanoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 288.1; HRMS: calcd for C13H23NO6 + H+, 290.15982; found (ESI+, [M+H]1+), 290.15965;</td>
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<td>79</td>
<td>N-(((1-benzofuran-2-ylcarbonyl)oxy)methoxy)carbonyl)-N-(tert-buty1)glycine</td>
<td>MS (ESI) m/z 350; HRMS: calcd for C17H19NO7 + H+, 350.12343; found (ESI+, [M+H]1+), 350.12327;</td>
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<td>80</td>
<td>N-(tert-buty1)-N-(((1-methyl-1H-pyrrol-2-yl)carbonyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 313; MS (ESI) m/z 647.1;</td>
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<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
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<tr>
<td>81</td>
<td>N-((((1,1'-biphenyl-4-ylcarbonyl)oxy)methoxy)carbonyl)-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 386.2; HRMS: calcld for C21H23NO6 + Na+ 408.14176; found (ESI+,[M+NA]1+), 408.14195;</td>
</tr>
<tr>
<td>82</td>
<td>N-(tert-butyl)-N-((((4-methoxybenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 338.1; MS (ESI) m/z 677.3; HRMS: calcld for C16H21NO7 + Na+, 362.12102; found (ESI+, [M+NA]1+), 362.12095;</td>
</tr>
<tr>
<td>83</td>
<td>N-(tert-butyl)-N-((((1H-indol-2-ylcarbonyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 349.2; HRMS: calcld for C17H20N2O6 + Na+, 371.12136; found (ESI+, [M+NA]1+), 371.12148;</td>
</tr>
<tr>
<td>84</td>
<td>N-(tert-butyl)-N-((((diphenylacetoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 298.2;</td>
</tr>
<tr>
<td>85</td>
<td>N-(tert-butyl)-N-((((1-naphthoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 358.2; MS (ESI) m/z 717.4; MS (ESI) m/z 1076.6;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>86</td>
<td>N-(tert-butyl)-N-[[2-naphthoyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 360.1; MS (ESI) m/z 472.1;</td>
</tr>
<tr>
<td>87</td>
<td>N-(tert-butyl)-N-[[[1-methyl-1H-indol-3-yl]carbonyl]oxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 361.2; MS (ESI) m/z 1085.7; MS (ESI) m/z 723.5; HRMS: calcd for C18H22N2O6 + H+, 363.15506; found (ESI+), [M+H]1+, 363.15556;</td>
</tr>
<tr>
<td>88</td>
<td>N-(tert-butyl)-N-[[[quinolin-2-yl]carbonyl]oxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 359.2; MS (ESI) m/z 1079.7; MS (ESI) m/z 719.4;</td>
</tr>
<tr>
<td>89</td>
<td>N-(tert-butyl)-N-[[[pyridin-3-yl]carbonyl]oxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 309.2; MS (ESI) m/z 929.5; MS (ESI) m/z 619.3;</td>
</tr>
<tr>
<td>90</td>
<td>N-(tert-butyl)-N-[[isonicotinoyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 311.1; MS (ESI) m/z 333.1;</td>
</tr>
<tr>
<td>91</td>
<td>N-(tert-butyl)-N-[[[2,6-difluorobenzoyl]oxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 390.2; MS (ESI) m/z 689.3;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>92</td>
<td>N-(tert-butyl)-N-((((2-fluorobenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 326.2; MS (ESI) m/z 980.6; MS (ESI) m/z 653.3;</td>
</tr>
<tr>
<td>93</td>
<td>N-(tert-butyl)-N-((((2-(trifluoromethyl)benzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 422.1; MS (ESI) m/z 753;</td>
</tr>
<tr>
<td>94</td>
<td>N-(tert-butyl)-N-(((4-pyrrolidin-1-ylbenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 379.2;</td>
</tr>
<tr>
<td>95</td>
<td>N-(((1,1'-biphenyl)-2-ycarbonyl)oxy)methoxy)carbonyl)-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 384.3; MS (ESI) m/z 1154.7; MS (ESI) m/z 769.5;</td>
</tr>
<tr>
<td>96</td>
<td>N-(tert-butyl)-N-((((mesitylcarbonyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 701.5; MS (ESI) m/z 386.2; MS (ESI) m/z 1052.8;</td>
</tr>
<tr>
<td>97</td>
<td>N-(tert-butyl)-N-((((4-isopropoxybenzoyl)oxy)methoxy)carbonyl)glycine</td>
<td>MS (ESI) m/z 733.3; MS (ESI) m/z 1100.3; MS (ESI) m/z 412.2; HRMS: calcd for C18H25NO7 + H+, 368.17038; found (ESI+), [M+H]+, 368.17069;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>98</td>
<td>N-(tert-butyl)-N-[[3,4,5-trimethoxybenzoyl]oxy]methoxy]carbonylglycine</td>
<td>MS (ESI) m/z 398; MS (ESI) m/z 797.2; MS (ESI) m/z 1195.9; HRMS: calcd for C18H25NO9 + H+, 400.16021; found (ESI+, [M+H]+1+), 400.1610</td>
</tr>
<tr>
<td>99</td>
<td>N-(tert-butyl)-N-[[3,5-dimethoxybenzoyl]oxy]methoxy]carbonylglycine</td>
<td>MS (ESI) m/z 368.1; MS (ESI) m/z 737.1; MS (ESI) m/z 414; HRMS: calcd for C17H23NO8 + H+, 370.14965; found (ESI+, [M+H]+1+), 370.15016;</td>
</tr>
<tr>
<td>100</td>
<td>N-(tert-butyl)-N-[[2E]-3-phenylprop-2-enoyl]oxy]methoxy]carbonylglycine</td>
<td>MS (ESI) m/z 334.2; MS (ESI) m/z 669.4; MS (ESI) m/z 1004.6; HRMS: calcd for C17H21NO6 + Na+, 358.12611; found (ESI+, [M+Na]+1+), 358.12763;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>101</td>
<td>N-(tert-butyl)-N-[(3-methyl-1-benzofuran-2-yl)carbonyloxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 725.4; MS (ESI) m/z 1088.6; MS (ESI) m/z 398.2; HRMS: calcd for C18H21NO7 + H+, 364.13908; found (ESI, [M+H]+), 364.13956;</td>
</tr>
<tr>
<td>102</td>
<td>N-[(3,5-bis(trifluoromethyl)phenyl]acetyl]oxy)methoxy]carbonyl]-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 458.1; MS (ESI) m/z 917.1; HRMS: calcd for C18H19F6NO6 + H+, 460.11893; found (ESI+, [M+H]+), 460.11854;</td>
</tr>
<tr>
<td>103</td>
<td>N-(tert-butyl)-N-[(4-(heptyloxy)benzoyl]oxy)methoxy]carbonyl]glycine</td>
<td>MS (ESI) m/z 422.2; MS (ESI) m/z 468.3; MS (ESI) m/z 845.3; HRMS: calcd for C22H33NO7 + H+, 424.23298; found (ESI+, [M+H]+), 424.23295;</td>
</tr>
<tr>
<td>Ref. Cpd. No.</td>
<td>Name</td>
<td>Spectra</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>105</td>
<td>N-(tert-butyl)-N-[[[4-(dodecyloxy)benzoyl]oxy]methoxy]carbonyl]glycine</td>
<td>MS (ESI+) m/z 494.31095; MS (ESI+) m/z 494.31123; HRMS: calcd for C27H43NO7 + H+, 494.31123; found (ESI+), [M+H]+, 494.31095;</td>
</tr>
<tr>
<td>106</td>
<td>N-[[[4-(acetylamino)benzoyl]oxy]methoxy]carbonyl]-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 367.1; MS (ESI) m/z 733.1;</td>
</tr>
<tr>
<td>107</td>
<td>N-[[[9-anthrylcarbonyl]oxy]methoxy]carbonyl]-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 408.3; MS (ESI) m/z 1226.7; MS (ESI) m/z 817.5;</td>
</tr>
<tr>
<td>108</td>
<td>N-[[[4-benzoylbenzoyl]oxy]methoxy]carbonyl]-N-(tert-butyl)glycine</td>
<td>MS (ESI) m/z 414.2;</td>
</tr>
</tbody>
</table>
Reference Compound 109
3,3-Dimethyl-butyric acid [tert-butyl-(2-isobutoxycarbonyloxy-2-oxo-ethyl)-carbamoyloxy)-methyl ester.

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-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.

Reference Compound 110
3,3-Dimethylbutyric acid ethylsulfanylcarbonyloxymethyl ester

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 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

To a stirred solution of 3,3-dimethylbutyric acid ethylsulfanylcarbonyloxyethyl ester (Reference Compound 110) (0.025 ml, 6 g) in methylene chloride at -20°C (dry ice/carbon tetrachloride) is added sulfuryl 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.

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

Reference Compound 112

benzyl N-(butoxycarbonyl)-N-(tert-butyl)glycinate
Reference Compound 113
benzyl N-(tert-butyl)-N-(isobutoxycarbonyl)glycinate

Reference Compound 114
benzyl N-(tert-butyl)-N-(methoxycarbonyl)glycinate

Reference Compound 115
N-(butoxycarbonyl)-N-(tert-butyl)glycine
Reference Compound 116
N-(tert-butyl)-N-(isobutoxycarbonyl)glycine

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

Reference Compound 118
isobutoxycarbonyl N-(butoxycarbonyl)-N-(tert-butyl)glycinate
Reference Compound 119
iso-butoxycarbonyl N-(tert-butyl)-N-(iso-butoxycarbonyl)glycinate

Reference compound 120
iso-butoxycarbonyl N-(tert-butyl)-N-(methoxycarbonyl)glycinate

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

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

Reference Compound 123

[5-(4-methoxyphenyl)-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 124

4-tert-butyl-1,0,1,0-dimethyl-3,6-dioxo-2,7-dioxa-4-aza-1,0-silaundec-1-yl (2E)-3-phenylacrylate

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.

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

Reference Compound 125

4-tert-butyl-1,0,1,0-dimethyl-3,6-dioxo-2,7-dioxa-4-aza-1,0-silaundec-1-yl anthracene-9-carboxylate

MS (ESI) m/z 510.3
Reference Compound 126
4-tert-butyl-1,0,10-dimethyl-3,6-dioxo-2,7-dioxa-4-aza-10-silaundecyl 4-benzoylbenzoate

MS (ESI) m/z 536.2

Example 1

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

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);
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.

**Example 2**

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

![Chemical Structure](image)

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

\[
\text{Example 3} \\
(\text{[(2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1,10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydr}
\text{tetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl 4-methylbenzoate
\]

\[
\begin{align*}
\text{N} & \text{N} \\
\text{O} & \text{O} \\
\text{N} & \text{N} \\
\text{O} & \text{O} \\
\end{align*}
\]

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

\[
\text{MS (ESI) m/z 778.3 ((M+H)+);}
\]
Example 4

\[
\{(2-((((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2-0110X0-5,53,6,63,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl}oxy)methyl\] 4-fluorobenzoate

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

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

Example 5

\[
\{(2-((((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino]carbonyl}oxy)methyl\] 4-methylbenzoate

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

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.

MS (ESI) m/z 780.3 ((M+H)+);
Example 7

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

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

MS (ESI) m/z 728.3 ((M+H)+);

Example 8

\[((2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1-
tetrahydroxy-1,2-dioxo-5,6,6a,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.

\[ \text{MS (ESI) m/z 768.3 ((M+H)^+)}; \]

Example 9

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

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.

\[ \text{MS (ESI) m/z 730.3 ((M+H)^+)}; \]
Example 10

\[
\text{MS (ESI) m/z 716.3 ((M+H)+);} 
\]

Example 11

\[
\text{MS (ESI) m/z 716.3 ((M+H)+);} 
\]
The title compound is prepared by the procedure of Example 1, using benzeneacetic acid, [(chlorocarbonyl)oxy]methyl ester and N-propylglyclyclycline to give the product of the Example.

\[ \text{MS (ESI) } m/z \ 764.3 \ (\text{(M+H)}^+) \]

Example 12

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

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

\[ \text{MS (ESI) } m/z \ 778.3 \ (\text{(M+H)}^+) \]
Example 13

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

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

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

Example 14

benzyl 2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-
tetrahydroxy-1,2-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 benzyl chloroformate and N-propylglycylcycline in the presence of sodium carbonate and DMPU in acetonitrile to give the product of the Example.

MS (ESI) m/z 706.3 ((M+H)+);
HRMS: calcd for $C_{36}H_{43}N_5O_{10} \cdot HCl$, 741.2777; found (ESI), 706.31 133;

Example 15

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

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

isobutyl 2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2-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.

MS (ESI) m/z 672.3 ((M+H)+);
MS (ESI) m/z 336.9 ((M+2H)2+);
HRMS: calcd for $C_{33}H_{45}N_5O_{10}$ *HCl, 707.2933; found (ESI+), 672.32618

Example 17

$\text{[2-}{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl}$(butyl)amino]carbonyloxy)methyl heptanoate
The title compound is prepared by the procedure of Example 1, using heptanoic acid, [(chlorocarbonyl)oxy]methyl ester and N-butylglycylcycline to give the product of the Example.

MS (ESI+) m/z 772.2 (M+H);
HRMS: calcd for C_{36}H_{53}N_{5}O_{12} · 2.00 HCl, 843.3224; found (ESI+), 772.37696;

Example 18

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

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

MS (ESI) m/z 742.3 ((M+H)+);
HRMS: calcd for C_{36}H_{47}N_{5}O_{12} · 2.00 HCl, 813.2755; found (ESI+), 742.32898;
Example 19

\[ \text{\{^-\[(\text{SaR.eaS.ZS.10aSJ- 9-Caminocarbonyl)}-4,7\text{-bis(dimethylamino)}J-i \ ,\delta.iOa.H-tetrahydroxy-1 0,1 2-0110X0-5,53,6,63,7, 10, 10a, 12\text{-octahydrotetracen-2-yl][amino)}-2-oxoethyl\text{(propyl)amino[carbonyl]oxy)}methyl \text{ heptanoate} \]

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.

MS (ESI) m/z 758.4 ((M+H)+);
HRMS: calcd for C_{37}H_{51}N_{5}O_{12} · HCl, 793.3301; found (ESI+), 758.36175;

Example 20

\[ \text{\{[2-\[(5aR,6aS,7S, 10aS)-9-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1 \ ,8, 10a, 11\text{-tetrahydroxy-1 0,1 2-dioxo-5,5a,6,6a,7, 10, 10a, 12\text{-octahydrotetracen-2-yl][amino)}-2-oxoethyl\text{(butyl)amino[carbonyl]oxy)}methyl \text{ 4-tert-butylbenzoate} \]

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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.

MS (ESI+) m/z 820.2 (M+H);
HRMS: calcd for C_{42}H_{53}N_{5}O_{12} · HCl, 855.3458; found (ESI+), 820.37684;
MS (ESI) m/z 840.3 ((M+H)+);

HRMS: calcd for C_{44}H_{49}N_{5}O_{12}·HCl, 875.3145; found (ESI+), 840.34378;

Example 22

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

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.

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

HRMS: calcd for C_{40}H_{49}N_{5}O_{12}·2.00 HCl, 863.2911; found (ESI+), 792.34378;

Example 23

\[
\text{[(2-}[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,6,8,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl](butyl)amino]carbonyl]oxy)methyl thiophene-2-carboxylate
\]
The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl thiophene-2-carboxylate and N-butylglycylcycline to give the product of the Example.

MS (ESI) m/z 770.1 ([M+H]+);
HRMS: calcd for C_{36}H_{43}N_{12}O_{12}S·HCl, 805.2396; found (ESI+), 770.27084;

Example 24

\(((2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-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.

MS (ES!) m/z 826.4 ((M+H)+);
MS (ESI) m/z 414 ((M+2H)2+);
HRMS: calcd for C_{43}H_{47}N_{5}O_{12}·HCl, 861.2988; found (ESI+), 826.32782;

Example 25

\(((2-\{\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10,12-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

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.
MS (ESI) m/z 756.3 ((M+H)+);
MS (ESI) m/z 378.9 ((M+2H)2+);
HRMS: calcd for C_{35}H_{44}N_{5}O_{12}S·HCl, 791.2239; found (ESI+), 756.2532;

Example 26

\{[\{(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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

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.

MS (ESI) m/z 778.3 ((M+H)+);
HRMS: calcd for C_{39}H_{47}N_{5}O_{12}·HCl, 813.2988; found (ESI+), 778.32984;

Example 27

\{\{(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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
The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxyjmethyl thiophene-3-carboxylate and N-propylglycylcycline to give the product of the Example.

MS (ESI) m/z 756.3 ([(M+H)+]);
HRMS: calcd for C₃₅H₄₁N₅O₁₂·HCl, 791.2239; found (ESI+), 756.2547;

Example 28

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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
The title compound is prepared by the procedure of Example 1, using [(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+);
HRMS: calcd for C₄₁H₅₅N₅O₁₂ · HCl, 841.3301; found (ESI+), 806.36024;
Example 29

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

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.

MS (ESI) m/z 770.3 ((M+H)+);
HRMS: calcd for C_{36}H_{43}N_{5}O_{12}S·HCl, 805.2396; found (ESI+), 770.27028;

Example 30

\[ \left( \left( \left( 5aR,eaS,10aS^\wedge \right) -9\text{-Caminocarbonyl}\right) -4,7\text{-bis(dimethylamino)}-1,8,10a,11\text{-tetrahydroxy}-10,12\text{-dioxo}-5,6a,6a,7,10,10a,12\text{-octahydotetracen-2-yl}\right) \text{amino}\right) \text{-2-oxoethyl}\right) \text{-(butyl)amino} \text{carbonyl} \text{oxy} \text{methyl 2-furoate} \]
The title compound is prepared by the procedure of Example 1, using [(chlorocarbonyl)oxy]methyl 2-furoate and N-butylglyclyclycline to give the product of the Example.

MS (ESI) m/z 752.2 ((M-H)-);
HRMS: calcd for C_{36}H_{43}N_{5}O_{13}·HCl, 789.2624; found (ESI+), 754.29242;

Example 31

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,12-tetrahydroxy-10,12-dioxo-5,6a,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);

Example 32

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

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.
MS (ESI) m/z 716.14 (M+H);
HRMS: calcd for C_{34}H_{45}N_{5}O_{12}, 715.3065; found (ESI+), 716.31469;

Example 33

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

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

MS (ESI) m/z 756.08 (M+H);
HRMS: calcd for C_{37}H_{49}N_{5}O_{12}, 755.3378; found (ESI+), 756.34507;

Example 34

\[ [(2-[(7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(butyl)amino]carbonyl]oxy)methyl cyclohexanecarboxylate \]
The title compound is prepared by the procedure of Example 1, using 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: calcld for C_{38}H_{55}N_{5}O_{12}· HCl, 805.3301; found (ESI+), 770.36093;

Example 35

\[ \{(\text{^-}[\text{5aR.eaS.10aSJ-9}^{\text{'}}\text{aminocarbonylH.Z-bis(dimethylaminoJ-i.}  \delta\text{iOa.i i -}\text{tetrahydroxy-1,12-dioxo-5,6,6a,7, 10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(propyl)amino[carbonyl]oxy)methyl 3,3-dimethylbutanoate} \]

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 the product of the Example.
MS m/z 00-30476 1LMS;
HRMS: calcd for C_{36}H_{49}N_{5}O_{12} · HCl, 779.3145; found (ESI+), 744.34539;

Example 36

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

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.

MS m/z 00-304762LMS;
HRMS: calcd for C_{37}H_{51}N_{5}O_{12} · HCl, 793.3301; found (ESI+), 758.36071;

Example 37

\[
((2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,1-
tetrahydroxy-1,2-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl\}[amino]-2-
oxoethyl)(propyl)amino)carbonyl]oxy)methyl 2,2-dimethylbutanoate
\]
The title compound is prepared by the procedure of Example 1, using
[(chlorocarbonyl)oxy]methyl 2,2-dimethylbutanoate and N-propylglycylcycline to give the product of the Example.

MS m/z 00-304763LMS;
HRMS: calcd for C_{36}H_{49}N_{5}O_{12}·HCl, 779.3145; found (ESI+), 744.3452;

Example 38

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

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.

MS (ESI) m/z 770.7 (M+H);
HRMS: calcd for C_{38}H_{51}N_{5}O_{12}·HCl, 805.3301; found (ESI+), 770.36062;
Example 39

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,10,10a,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(butyl)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-butylglycylcycline to give the product of the Example.

MS (ESI) m/z 822.9 (M+H);
HRMS: calcd for C_{42}H_{55}N_{5}O_{12}·HCl, 857.3614; found (ESI+), 822.39184;

Example 40

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,10,10a,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(propyl)amino)carbonyl)oxy)methyl cyclopentylacetate

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

Example 41

MS (ESI) m/z 754.2 [(M-H)-];
HRMS: calcd for C_{37}H_{49}N_{5}O_{12} · HCl, 791.3145; found (ESI+), 756.34433;

Example 42

MS (ESI) m/z 808.8 (M+H);
HRMS: calcd for C_{41}H_{53}N_{5}O_{12} · HCl, 843.3458; found (ESI+), 808.37604;
To a solution of 9-amino-minocycline monosulfate (0.0055 mol, 3.135g, 1 equivalent) 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-butyric 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 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_{5}O_{12} · HCl, 793.3301; found (ESI+), 758.36201;

Example 43

Prepared according to Scheme II
\[(\{[(2-\{[(5aR,6aS, 7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl\{tert-butyl\}amino\}carbonyl)oxy\}methyl 4-tert-butylbenzoate\]
Reference Compound 57 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminomino-cycline using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 820.37 (M+H);
HRMS: calcd for $C_{42}H_{53}N_{12}O_{12}\cdot HCl$, 855.3458; found (ESI+), 820.3754;
Example 45

Prepared according to Scheme 2

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

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.

MS (ESI) m/z 730.38 (M+H);
HRMS: calcd for C_{35}H_{47}N_{5}O_{12} \cdot HCl, 765.2988; found (ESI+), 730.33002;

Example 46

\[
\{(\{(2-\{(5aR,6aS,7S,10aS)-\text{amine} \text{carbonyl})-4,7\text{-bis(dimethylamino)}-1,8,10a,11\text{-}
\text{tetrahydroxy-10,12-dioxo-5,6a,6a,7,10,10a,12-octahydrotetracen-2-yl}\text{amine} \text{-2-oxoethyl})(\text{tert-butyl})\text{amine}\}\text{carbonyl} \text{oxy})methyl \text{ cyclopentanecarboxylate}
\]
Reference Compound 59 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12}·HCl, 791.3145; found (ESI+), 378.67644;

Example 47

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

Reference Compound 60 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.
MS (ESI) m/z 778.34 (M+H);
HRMS: calcd for C_{39}H_{47}N_{5}O_{12}, 777.3221; found (ESI+), 778.33065;

Example 48

Prepared according to Scheme II

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

Reference Compound 61 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 772.45 (M+H);
HRMS: calcd for C_{38}H_{53}N_{5}O_{12}·HCl, 807.3458; found (ESI+), 772.37695;

Example 49

Prepared according to Scheme II

\[
\text{[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1\}C^\Delta\text{-dioxo}-5,5a,\text{e.e.aJ.10.IOa.12-octahydrotetracen-2-yl\}amino)-2-oxoethyl})(tert-butyl)amino\}carbonyl\}oxy)methyl propionate}
\]
Reference Compound 62 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 716.3 (M+H);
HRMS: calcd for C_{34}H_{46}N_{12}O_{12}·HCl, 751.2832; found (ESI+), 716.31461;

Example 50

\(((2-[[5\text{aR,6aS,7S,10aS}]-9-(\text{aminocarbonyl})-4,7-\text{bis(dimethylamino)}]-1,8,10a,11-\text{tetrahydroxy}-1,0,1,2-\text{dioxo}-5,5a,6,6a,7,10,10a,12-\text{octahydropyrene}-2-y][\text{amino}]-2-\text{oxoethyl})(\text{tert-butyl} \text{amino}][\text{carbonyl}][\text{oxy}]\text{methyl cyclohexane carboxylate}

Reference Compound 63 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 770.36 (M+H);
HRMS: calcd for C_{38}H_{51}N_{5}O_{12} \cdot \text{HCl}, 805.3301; found (ESI-), 768.34546;

Example 51

Prepared according to Scheme 2

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

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

MS (ESI) m/z 792.32 (M+H);
HRMS: calcd for C_{40}H_{49}N_{5}O_{12} \cdot \text{HCl}, 827.3145; found (ESI+), 792.34613;

Example 52

\[
\text{([(2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10a,12-octahydrotetracen-2-yl]amino\}-2-oxoethyl)(tert-butyl)aminojcarbonyl}oxy)methyl \quad 4\text{-fluorobenzoate}
\]
Reference Compound 65 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

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

HRMS: calcd for C_{38}H_{44}F_{12}N_{5}O_{12}·HCl, 817.2737; found (ESI+), 782.30406

Example 53

Prepared according to Scheme 2

(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1C^-dioxo-5,5a,6,6aJ,10.10a.12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 3-methylbutanoate

Reference Compound 66 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.
MS (ESI) m/z 744.37 (M+H);
HRMS: calcd for C_{56}H_{49}N_{5}O_{12} HCl, 779.3145; found (ESI+), 744.34481;

Example 54

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

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

MS (ESI) m/z 770.4 (M+H);
HRMS: calcd for C_{38}H_{51}N_{5}O_{12} HCl, 805.3301; found (ESI+), 770.35888;

Example 55

Prepared according to Scheme 2

\([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2-dioxo-5,6a,7,10,10a,12-octahydrotetracen-2-ylationo]-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl \) 4-(trifluoromethyl)benzoate
Reference Compound 68 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{3}N_{5}O_{12}·HCl, 867.2705; found (ESI+), 832.30055;

Example 56

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

methyl cyclopropanecarboxylate

Reference Compound 69 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12}·HCl, 763.2832; found (ESI+), 728.31289;
Example 57

Prepared according to Scheme 2

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

Reference Compound 70 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12} HCl, 857.3614; found (ESI+), 822.39237

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\text{[amino]-2-oxoethyl(tert-butyl)carbamate} \]
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.

MS (ESI) m/z 686.4 (M+H);
HRMS: calcd for C_{34}H_{47}N_{5}O_{10}·HCl, 721.3090; found (ESI+), 686.34079;

Example 59

isobutyl 2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino\}-2-oxoethyl(tert-butyl)carbamate

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 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_{5}O_{10}·HCl, 721.3090; found (ESI-), 684.32433;

Example 60

methyl 2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino\}-2-oxoethyl(tert-butyl)carbamate
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.

MS (ESI) m/z 644.3 (M+H);
MS (ESI) m/z 322.6 (M+2H);
HRMS: calcd for C\textsubscript{31}H\textsubscript{41}N\textsubscript{5}O\textsubscript{10} - HCl, 679.2620; found (ESI-), 642.27736;

Example 61

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

Reference Compound 71 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12} • HCl, 779.3145; found (ESI+), 744.34613;

Example 62

Prepared according to Scheme II

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

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

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

Example 63

\(((\{(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,10\text{-}
tetrahydroxy-1,2-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl\}amino)-2-
oxoethyl\} tert-butyl)amino\}carbonyl\}oxy)methyl \ 3\text{-}cyclohexylpropanoate
Reference Compound 73 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

Example 64

\[
\begin{align*}
\text{MS (ESI) m/z 796.4 (M-H);} \\
\text{Example 64}
\end{align*}
\]

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

Example 65

\[
\begin{align*}
\text{MS (ESI) m/z 812.4 (M+H);} \\
\text{MS (ESI) m/z 406.7 (M+2H);} \\
\text{HRMS: calcd for } C_{39}H_{40}FN_5O_{13} \cdot HCl, 847.2843; \text{ found (ESI+), 812.31518;} \\
\end{align*}
\]
Reference Compound 75 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{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-1,2-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-aminominocycline 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_{5}O_{12} \cdot HCl, 827.3145; found (ESI+), 792.34423;
Example 67

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

Reference Compound 77 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12} HCl, 813.2988; found (ESI+), 778.3299;

Example 68

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

Reference Compound 78 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12} · HCl, 779.3145; found (ESI+), 744.34434;

Example 69

Prepared according to Scheme II

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

Reference Compound 79 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 804.4 (M+H);
MS (ESI) m/z 402.7 (M+2H);
HRMS: calcd for C_{40}H_{45}N_{5}O_{13} · HCl, 839.2781; found (ESI+), 804.30779;

Example 70

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

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Reference Compound 80 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{6}O_{12}, 766.3174; found (ESI+), 767.32406;

Example 71

\[((2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2-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

Reference Compound 81 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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);
HRMS: calcd for C_{44}H_{49}N_{5}O_{12}·HCl, 875.3145; found (ESI+), 840.34496;
Example 72

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

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

MS (ESI) m/z 792.3 (M-H);
HRMS: calcd for C_{39}H_{47}N_{5}O_{13} * HCl, 829.2937; found (ESI+), 794.3251 1;

Example 73

Prepared according to Scheme II

\[
\text{[(2-[((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl}oxy)methyl 1H-indole-2-carboxylate
\]
Reference Compound 83 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{6}O_{12} \cdot HCl, 838.2941; found (ESI+), 803.3275;

Example 74

10 \{(2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2-0110X0-5,53,6,63,7,10,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy\}methyl diphenylacetate

Reference Compound 84 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{6}O_{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,6,6aJJO.10a.12-octahydrotetracen-2-yl]amino)carbonyl]oxy]\}methyl thiophene-2-carboxylate
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);

HRMS: calcd for C_{30}H_{32}N_{4}O_{n}S·HCl, 692.1555; found (ESI+), 657.18613;

Example 76

Prepared according to scheme 6

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

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.
MS (ESI) m/z 667.2 (M-H);
HRMS: calcd for C_{32}H_{33}FN_{4}O_{11} \cdot HCl, 704.1897; found (ESI+), 669.22024;

Example 77

Prepared according to scheme 6

\[(((\text{5aR,6aS,7S,10aS})-9-\text{(aminocarbonyl)}-4,7-\text{bis(dimethylamino)}-1,8,10a,11-\text{tetrahydroxy}-1,2-\text{O10X0-5,58,6,63,7,10,10a,12-octahydrotetracen-2-yI][amino]carbonyl)oxy]methyl \text{3,5-dimethylbenzoate}}

The title compound is prepared by the procedure of Example 42, using

\[(((\text{chlorocarbonyl)oxy]methyl \text{3,5-dimethylbenzoate}} \text{in place of the Reference Compound 109 to give the product of the example.}}

MS (ESI) m/z 679.2 (M+H);
HRMS: calcd for C_{34}H_{38}N_{4}O_{11} \cdot HCl, 714.2304; found (ESI+), 679.26076;

Example 78

Prepared according to scheme 6

\[(((\text{5aR,6aS,7S,10aS})-9-\text{(aminocarbonyl)}-4,7-\text{bis(dimethylamino)}-1,8,10a,11-\text{tetrahydroxy}-10,12-\text{dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yI][amino]carbonyl)oxy]methyl \text{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_{4}O_{11}\cdot HCl, 666.2304; found (ESI+), 631.26094;

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,δa,δ,δa,7,1i Q1 Qa.12-octa-hydrotetracen-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_{4}O_{11}\cdot HCl, 680.2460; found (ESI+), 645.27632;
Example 80

Prepared according to scheme 6

\[ \{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2^\text{O}X0-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)carbonyl)oxy]methyl \ 2,2-dimethylbutanoate \]

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

MS (ESI) m/z 645.2 (M+H);
HRMS: calcd for C_{31}H_{40}N_{4}O_{n} \cdot \text{HCl}, 680.2460; found (ESI+), 645.27637;

Example 81

\[ \{[(2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,2^\text{O}X0-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy]methyl \ 1\text{-naphthoate} \]
Reference Compound 85 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 812.5 (M-H);
HRMS: calcd for $C_{42}H_{47}N_5O_{12}\cdot HC\text{l}$, 849.2988; found (ESI+), 814.33029;

**Example 82**

$$\begin{align*}
\{[(2-\{(5aR,6aS,7S, 10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1 \ 8, 10a, 11-
tetrahydroxy-1 0,12-dioxo-5,5a,6,6a,7, 10,10a, 12-octahydrotetracen-2-yl[amino]-2-
oxoethyl)\{tert-butyl)amino\}carbonyl\}oxy)methyl 2-naphthoate
\end{align*}$$

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

MS (ESI) m/z 812.5 (M-H);
HRMS: calcd for $C_{42}H_{47}N_5O_{12}\cdot HC\text{l}$, 849.2988; found (ESI+), 814.33004;

**Example 83**

$$\begin{align*}
\{[(2-\{(5aR,6aS,7S, 10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1 \ 8, 10a, 11-
tetrahydroxy-1 0,12-dioxo-5,5a,6,6a,7, 10,10a, 12-octahydrotetracen-2-yl[amino]-2-
oxoethyl)\{tert-butyl)amino\}carbonyl\}oxy)methyl 1-methyl-1 H-indole-3-carboxylate
\end{align*}$$
Reference Compound 87 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{46}N_{6}O_{12} \cdot HCl, 852.3097; found (ESI-), 815.32484;

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-oxyoethyl)(tert-butyl)amino\}carbonyl)oxy)methyl quinoline-2-carboxylate

Reference Compound 88 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{6}O_{12} \cdot HCl, 850.2941; found (ESI+), 815.32509;
Example 85
Prepared according to scheme 6

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

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

\[
\begin{align*}
\text{MS (ESI) m/z 643.4 (M-H);} \\
\text{MS (ESI) m/z 1287.7 (2M-H);} \\
\text{HRMS: calcd for C}_{31}\text{H}_{40}\text{N}_{4}\text{O}_{11} \cdot \text{HCl}, 680.2460; found (ESI+), 645.27618;}
\end{align*}
\]
Example 86
Prepared according to scheme 6

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

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

MS (ESI) m/z 655.3 (M-H);
MS (ESI) m/z 131.17 (2M-H);
HRMS: calcd for C\text{32}H\text{40}N\text{4}O\text{11} \cdot \text{HCl}, 692.2460; found (ESI+), 657.27572;

Example 87
Prepared according to scheme 6

\[
\text{[([(5aR,6aS,7S,10aS)-9(a minocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,12-octahydrotetracen-2-yl]amino}carbonyl)oxy)methyl 4-tert-butylbenzoate}
\]
The title compound is prepared by the procedure of Example 42, using 
[(chlorocarbonyl)oxy]methyl 4-tert-butylbenzoate in place of the Reference 
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_{4}O_{n}HCl, 742.2617; found (ESI+), 707.29336;

Example 88

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

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

MS (ESI) m/z 763.5 (M-H); 
HRMS: calcd for C_{37}H_{44}N_{8}O_{12}HCl, 800.2784; found (ESI+), 765.30896;
Example 89

$$\text{[((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1}$$,

$$10a,11-
$$

tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10a,12-octahydropentacen-2-yl]amino)-2-
$$

$$\text{o xoethyl)(tert-butyl)amino]carbonyl]oxy)methyl isonicotinate}$$

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

HRMS: calcd for $\text{C}_{37}\text{H}_{44}\text{N}_{6}\text{O}_{12}\cdot\text{HCl}$, 800.2784; found (ESI+), 765.3117;

Example 90

$$\text{[((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1}$$,

$$8,10a,11-
$$

tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropentacen-2-yl]amino)-2-
$$

$$\text{o xoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 2,6-difluorobenzoate}$$

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

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

HRMS: calcd for $\text{C}_{38}\text{H}_{43}\text{F}_{2}\text{N}_{5}\text{O}_{12}\cdot\text{HCl}$, 835.2643; found (ESI+), 800.29464;
Example 91

\[
\left[\left(\left(5aR,6aS,7S,10aS\right)-9\text{-amino}-4,7\text{-bis}(\text{dimethylamino})-1,8,10a,11\text{-tetrahydroxy-10J2-dioxo-5,5a6a6a7a7a10a10J2-octahydrotetracen-2-yl}\text{amino}\right)\text{-2-oxoethyl}\right)\text{(tert-butyl)amino} \right)\text{carbonyl} \right)\text{oxy} \text{methyl} \ 2\text{-fluorobenzoate}
\]

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

MS (ESI) m/z 780 (M-H);

HRMS: calcd for C_{38}H_{44}FN_{5}O_{12}\cdot\text{HCl}, 817.2737; found (ESI+), 782.30558;

Example 92

\[
\left[\left(\left(5aR,6aS,7S,10aS\right)-9\text{-amino}-4,7\text{-bis}(\text{dimethylamino})-1,8,10a,11\text{-tetrahydroxy-10,12-dioxo-5a,6a,6a,7,10,10a,12-octahydrotetracen-2-yl}\text{amino}\right)\text{-2-oxoethyl}\right)\text{(tert-butyl)amino} \right)\text{carbonyl} \right)\text{oxy} \text{methyl} \ 2\text{-}(\text{trifluoromethyl})\text{benzoate}
\]
Reference Compound 93 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

HRMS: calcd for C_{39}H_{44}F_{3}N_{5}O_{12}: HCl, 867.2705; found (ESI+), 832.30026;

Example 93

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]

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

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

HRMS: calcd for C_{42}H_{52}N_{6}O_{12}: HCl, 868.3410; found (ESI-), 831.3565;

Example 94

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]

\[ \text{HRMS: calcd for } C_{42}H_{52}N_{6}O_{12}: \text{HCl, 868.3410; found (ESI-), 831.3565;} \]
Reference Compound 95 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

$\text{M}\text{S (ESI)} \text{ m/z } 838.4 \text{ (M-H)}$;
$\text{HRMS: calcd for } C_{44}H_{49}N_5O_{12} \cdot \text{HCl}, 875.3145; \text{ found (ESI+), 840.3455}$;

Example 95

\[
\left\{\left[(2-\{[5aR,6aS,7S,10aS\}-9-(\text{aminocarbonyl})-4,7\text{-bis(dimethylamino)}-1,8,10\text{-octahydrotetracen-2-yl}\text{amino}]\text{oxy})\text{methyl } 2,4,6\text{-trimethylbenzoate}
\right] \right\}
\]

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

$\text{MS (ESI) m/z } 804.5 \text{ (M-H)}$;
$\text{HRMS: calcd for } C_{41}H_{51}N_5O_{12} \cdot \text{HCl}, 841.3301; \text{ found (ESI+), 806.3610}$;
Example 96

\[
[[2-[[5aR,6aS,7S,10aS]-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1-0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl\] 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-aminomycycline 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_{5}O_{13} \cdot HCl, 857.3250; found (ESI-), 820.341 17;

Example 97

\[
[[2-[[5aR,6aS,7S,10aS]-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1-0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino]-2-oxoethyl](tert-butyl)amino]carbonyl]oxy)methyl\] 3,4,5-trimethoxybenzoate

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

\[
\text{Example 98}
\]

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

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

\[
\text{Example 99}
\]

\[
[(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydotetracen-2-yl\}[amino]-2-oxoethyl)(tert-butyl)amino\}carbonyl\}oxy)methyl (2E)-3-phenylprop-2-enoate
\]
Reference Compound 100 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{12} HCl, 825.2988; found (ESI+), 790.33068;

Example 100

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

Reference Compound 101 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{13} HCl, 853.2937; found (ESI+), 818.3234;
Example 101

\[
(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,δ,δ,9aJ.10.10a.12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl [3,5-bis(trifluoromethyl)phenyl]acetate
\]

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);

HRMS: calcd for C_{41}H_{45}F_{6}N_{5}O_{12} \cdot HCl, 949.2736; found (ESI+), 914.30367;

Example 102

\[
(((2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,δ,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyl)oxy)methyl 4-(heptyloxy)benzoate
\]
Reference Compound 103 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

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;

Example 103

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

Reference Compound 104 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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;
Example 104

\[ \text{Reference Compound 105 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominoctylamine using the conditions of Example 42 to give the product of the Example.} \]

\[ \text{MS (ESI) m/z 946.7 (M-H);} \]
\[ \text{HRMS: calcd for } C_{50}H_{69}N_{5}O_{13} \cdot HCl, 983.4659; \text{ found (ESI-), 946.48106;} \]

Example 105

\[ \text{Example 105} \]

\[ \text{Example 104} \]
Reference Compound 106 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline using the conditions of Example 42 to give the product of the Example.

MS (ESI) m/z 819.1 (M-H);
HRMS: calcd for C_{40}H_{48}N_{6}O_{13} · HCl, 856.3046; found (ESI-), 819.32051;

Example 106

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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

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

MS (ESI) m/z 864.3 (M+H);
HRMS: calcd for C_{46}H_{49}N_{5}O_{12} · HCl, 899.3145; found (ESI-), 862.32855;

Example 107

(([(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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
Reference Compound 108 is reacted under the conditions of Reference Compound 109 and the product of said reaction is further contacted with 9-aminominocycline 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_{5}O_{13} ⋅ 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-1,2-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-glycylcylcine (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) ethereal 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);

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

Example 109

(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

The title compound is prepared by the procedure of Example 108, using N-butyi-glycylcycline (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)+);

Example 110

(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-propylglycylcycline (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.

MS (ESI) m/z 790.3 ((M+H)+);
HRMS: calcd for C_{39}H_{43}N_{5}O_{13}, 789.2857; found (ESI+), 790.29243;

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-octahydropyrene-2-yl]amino)-2-oxoethyl(propyl)carbamate

The title compound is prepared by the procedure of Example 108, using N-propylglycylcycline (N-prop-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.

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

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-octahydrortetracen-2-yl]amino)-2-oxoethyl(butyl)carbamate

The title compound is prepared by the procedure of Example 108, using N-butyl-glycylcycline (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.

MS (ESI) m/z 804.12 (M+H);
MS (ESI) m/z 402.58 (M+2H);
HRMS: calcd for C_{40}H_{45}N_{5}O_{13}, 803.3014; found (ESI+), 804.30946;
Example 113

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

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.
WHAT IS CLAIMED IS:

1. A compound represented by Formula (I);

   \[ \text{(I)} \]

   wherein:

   \( A \) is a moiety or is absent;

   \( R_1 \) is selected from hydrogen, -OH, amino, \(-\text{NR}_7\text{R}_8\), 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, alkoxy carbonyl, 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, alkoxy carbonyl,
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;

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, alkoxy carbonyl, 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, 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;

R₃ is the moiety R₉.
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, arloxy and N-(alkyl of 1 to 12 carbon atoms)-aryl, wherein said aryl, arloxy 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, arloxy, 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, arloxy, 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)-, CH₃-C(O)-NH-, aralkyl, arloxy, 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)-, CH$_3$-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, SR$_3$, heteroaryl optionally substituted and heteroaryl carbonyl optionally substituted;

R$_5$ 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)-, CH$_3$-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH$_2$(CO)OCH$_2$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, 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$_2$, cycloalkyl-alkyl; and adamantly;

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 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;

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;

R₈ is aralkyl of 7 to 16 carbon atoms optionally substituted or alkyl of 1 to 12 carbon atoms;
R₁₀ is H or alkyl of 1 to 12 carbon atoms;
or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1, wherein R₁ is -NR₇R₈, R₇ is hydrogen, R₈ is methyl, ethyl, n-propyl, n-butyl, 1-methylpropyl, 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 is methyl, ethyl, n-propyl, 1-methylpropyl, 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 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.

6. A compound according to any one of claims 1 to 5, wherein A is a moiety
7. A compound according to any one of claims 1 to 5, wherein A is absent or a pharmaceutically acceptable salt thereof.

8. A compound according to any one of claims 1 to 7, wherein $R_3$ is a moiety or a pharmaceutically acceptable salt thereof.

9. A compound according to any one of claims 1 to 7, wherein $R_3$ is a moiety or a pharmaceutically acceptable salt thereof.

10. A compound according to any one of claims 1 to 7, wherein $R_3$ is a moiety or a pharmaceutically acceptable salt thereof.
and $R_6$ and $R_{10}$ are H or a pharmaceutically acceptable salt thereof.

11. A compound according to any one of claims 1 to 7, wherein $R_3$ is a moiety

and $R_5$ and $R_{10}$ are H or a pharmaceutically acceptable salt thereof.

12. A compound according to any one of claims 1 to 7, wherein $R_3$ is $R_G$ or a pharmaceutically acceptable salt thereof.

13. A compound according to claim 1, wherein $A$ is the moiety, $R_3$ is the moiety

$R_3$ is the moiety
14. A compound according to claim 1, wherein A is the moiety

\[ R_3 \]

and

\[ R_5 \]

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

15. A compound according to claim 1, wherein

\[ R_4 \]

is 1,1-dimethylethyl and

\[ R_5 \]

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

\[
\begin{align*}
R_4 & \quad \text{is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to 12 carbon atoms, N-alkyl of 1 to 12 carbon atoms, N-cycloalkyl of 3 to 6 carbon atoms, heterocyclyl of 3 to 8 ring atoms, aryl, and aryloxy wherein said aryl and aryloxy is optionally substituted with 1 to 3 substituents independently selected from halogen, nitro, cyano, alkenyl, hydroxyl, alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, carboxyl, alkoxy carbonyl, aryloxy and phenyl;} \\
R_5 & \quad \text{is selected from alkyl of 1 to 12 carbon atoms optionally substituted with 1 to 3 substituents independently selected from the group halogen, amino, cyano, cycloalkyl of 3 to 6 carbon atoms, alkyl of 1 to 12 carbon atoms, phenyl, hydroxyl, alkoxy of 1 to}
\end{align*}
\]
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, alkoxy carbonyl, aryl-C(O)-, CH$_2$-C(O)-NH-, aralkyl, aryloxy, heterocyclyl and phenyl, aralkyl of 7 to 16 carbon atoms optionally substituted, aroyl, -CH$_2$(CO)OCH$_2$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, 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;

R$_6$ is hydrogen;

R$_7$ and R$_8$ are each independently H or alkyl of 1 to 12 carbon atoms;

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 a pharmaceutically acceptable salt thereof.

16. A compound according to claim 1, selected from the group or pharmaceutically acceptable salts thereof:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(2-[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

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

15 [[[2-[[53R,6aS,7S,10aS]-9-(aminocarbonyl)-4,7-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-[[53R,6aS,7S, lOaSJ-9-Caminocarbonyl]-4,7-bis(dimethylamino)\(^{\oplus}\), 8,103,1 1-tetrahydroxy-10,12-dioxo-5,5a,6,63,7,10,10a,12-octahydrotetr3cen-2-yl]amino]-2-oxoethyl]propyl]amino]carbonyl]oxy)methyl 4-tert-butylbenzoate,

25 1- [[[2-[[7S, 10aS^-g-Caminocarbonyl]-4,7-bis(dimethylamino)\(^{-}\), \(^{3}\), 8,10a,11-tetrahydroxy-1 0,1 2-dioxo-5,5a,6,63,7,1 0,103,1 2-oct3hydrotrtr3cen-2-yl]amino]-2-oxoethyl]butyl]3mino[c3rbonyl]oxy]ethy] scetste,

30 [[[2-[[7S,1 03S]-9-(aminocarbonyl)-4,7-bis(dimethyl3mino)-1,8,10a,11-tetrahydroxy-10,1 2-dioxo-5,5a,6,6a,7,1 0,10a,12-oct3hydrotrtr3cen-2-yl]amino]-2-oxoethyl]propyl]amino]c3rbonyl]oxy)methyl cyclohexnscecsrbxosylste,
(\{(2-\{(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropyren-2-yl\}[amino]-2-oxoethyl)(propyl)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-octahydropyren-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-octahydropyren-2-yl\}[amino]-2-oxoethyl)(propyl)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-octahydropyren-2-yl\}[amino]-2-oxoethyl)(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-octahydropyren-2-yl\}[amino]-2-oxoethyl)(propyl)amino][carbonyl]oxy)methyl adamantane-1-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-octahydropyren-2-yl\}[amino]-2-oxoethyl)(propyl)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-octahydropyren-2-yl\}[amino]-2-oxoethyl)(propyl)amino][carbonyl]oxy)methyl adamantane-1-carboxylate,
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


18. 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)(butyl)amino)carbonyl)oxy)methyl thiophene-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)(propyl)amino)carbonyl)oxy)methyl thiophene-2-carboxylate,

(((^^[SaR.eaSJS.10aS^ 9-Caminocarbonyl/Hy-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,

(((2-([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

(((2-([(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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
or pharmaceutically acceptable salts thereof.

19. A compound according to claim 1 selected from the group

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl 2-furoate,}
\]

\[
\text{is pharmaceutically acceptable salts thereof.}
\]

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl propionate,}
\]

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl cyclohexanecarboxylate,}
\]

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl 3,5-dimethylbenzoate,}
\]

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl 4-fluorobenzoate,}
\]

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl 3-methylbutanoate,}
\]

\[
\text{(((2-}^{[(5aR,6aS,7S,10aS)}-9\text{-(aminocarbonyl)}-4,7\text{-bis(dimethylamino)}-1,8,10a,12\text{-octahydrotetracen-2-ylamino)}-2\text{-oxoethyl})(propylamino)carbonyl)oxy)methyl cyclopentylacetate,}
\]
(((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,H-tetrahydroxy-0,12-dioxo-5,5a,6,6a,7,10,10a-octahydro-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl 4-(trifluoromethyl)benzoate,

(((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-0,12-dioxo-5,5a,6,6a,7,10,10a-octahydro-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl cyclopropanecarboxylate,

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-octahydro-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-0,12-dioxo-5,5a,6,6a,7,10,10a-octahydro-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-0,12-dioxo-5,5a,6,6a,7,10,10a-octahydro-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-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-octahydro-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl pentanoate,

(((δ-R eaSJS,10aS)-9*(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-0,12-dioxo-5,5a,6,6a,7,10,10a-octahydro-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl)amino)-2-oxoethyl)(tert-butyl)amino)carbonyloxy)methyl cyclobutanecarboxylate,
(((2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(climethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 3-cyclohexylpropanoate,

(((2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-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-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl cyclohexylacetate,

(((2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl 2,6-dimethylbenzoate,

(((2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrotetracen-2-yl]amino}-2-oxoethyl)(tert-butyl)amino)carbonyl]oxy)methyl phenylacetate,

(((2-{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-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 2-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 2,6-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,

((2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

((2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

((2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

((2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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,

((2-{{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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-\text{-}tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydotetracen-2-yl]amino)-2-oxoethyl)[(tert-butyl]amino]carbonyl]oxy)methyl\} 3,5-dimethoxybenzoate,

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

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

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

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

(\{(2-(((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1-\text{-}tetrahydroxy-10,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydotetracen-2-yl]amino)-2-oxoethyl)[(tert-butyl]amino]carbonyl]oxy)methyl\} 4-(acetylamino)benzoate,
((C(2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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

(((2-((5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-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)c?i"bonyl)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,

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 2,2-dimethylbutanoate,
[\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,Z,10,10a,12-octahydropyrene-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-1,0,12-dioxo-5,5a,6,6a,Z,10,10a,12-octahydropyrene-2-yl]amino}carbonyl]oxy]methyl cyclopentylacetate, and

10

[\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,Z-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropyrene-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-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropyrene-2-yl]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-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropyrene-2-yl]amino}carbonyl]oxy]methyl nicotinate,

25

(\{[(2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropyrene-2-yl]amino}carbonyl]oxy]methyl isonicotinate,

30

(\{[(2-\{[(5aR,6aS,7S,10aS)-9-(aminocarbonyl)-4,7-bis(dimethylamino)-1,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydropyrene-2-yl]amino}carbonyl]oxy]methyl 4-pyrrolidin-1-ylbenzoate,

(δR.eaS.TS.10aSJ-9-aminocarbonylH.y-bis(dimethylamino) )i. β.iOa.H- tetrahydroxy-1,0,1-dioxo-5,5a,6,6a,7,10,10a,12-octahydrötetracen-2-yl]amino)-2-oxoethyl] (tert-butyl)amino]carbonyl]oxy)methyl 1-methyl-1 H-indole-3-carboxylate,

(δR.eaS.TS.10aSJ-9-aaminocarbonylH.y-bis(dimethylamino) )i. β.iOa.H- tetrahydroxy-1,0,1-dioxo-5,5a,6,6a,7,10,10a,12-octahydrötetracen-2-yl]amino)-2-oxoethyl] (tert-butyl)amino]carbonyl]oxy)methyl quinoline-2-carboxylate,

(δR.eaS.TS.10aSJ-9-aaminocarbonylH.y-bis(dimethylamino) )i. β.iOa.H- tetrahydroxy-1,0,1-dioxo-5,5a,6,6a,7,10,10a,12-octahydrötetracen-2-yl]amino)-2-oxoethyl] (tert-butyl)amino]carbonyl]oxy)methyl 1-benzofuran-2-carboxylate, and

or pharmaceutically acceptable salts thereof.

22. A compound according to claim 1 selected from the group

(δ-methyl-2-oxo-1 ,3-dioxol-4-y]methyl 2-[(7S,10aR)-9-(aminocarbonyl)]-4,7-bis(dimethylamino)-1 ,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrötetracen-2-yl]amino)-2-oxoethyl(propyl) carbamate,

(5-methyl-2-oxo-1 ,3-dioxol-4-y]methyl 2-[(7S,10aR)-9-(aminocarbonyl)]-4,7-bis(dimethylamino)-1 ,8,10a,11-tetrahydroxy-1,0,12-dioxo-5,5a,6,6a,7,10,10a,12-octahydrötetracen-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]-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,

(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

[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

or pharmaceutically acceptable salts thereof.

23. A pharmaceutical composition comprising a compound according to anyone of 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, 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.

26. A compound according to Formula (II):
wherein $R_4$, $R_5$, $R_6$, and $R_{10}$ are as defined in claim 1, and

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

$R_{11}$ is H, benzyl optionally substituted with nitro or a moiety of the formula

and $R_{12}$ is alkyl of 1 to 6 carbon atoms.

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, $R_5$ 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.

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
31. A compound according to anyone of claims 26 to 30 wherein \( R_6 \) and \( R_{12} \) are H.

32. A compound according to claim 26 selected from the group:

- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl 4-tert-butylbenzoate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl 2,2-dimethylbutanoate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl 2-methylpropanoate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl cyclopentanecarboxylate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl 4-methylbenzoate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl heptanoate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl propionate,
- \( \{[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino\}carbonyl \)oxy)methyl cyclohexanecarboxylate,
([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 3,5-dimethylbenzoate,

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

([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 3-methylbutanoate,

benzyl N-(tert-butyl)-N-([(cyclopentylacetyl)oxy]methoxy)carbonyl)glycinate,

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

([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl cyclopropanecarboxylate,

([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl adamantane-1-carboxylate,

([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl pentanoate,

([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl cyclobutanecarboxylate,

([(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl)oxy)methyl 3-cyclohexyipropanoate,

benzyl N-(tert-butyl)-N-([(4-fluorophenoxy)acetyl]oxy)methoxy)carbonyl)glycinate,

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,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) pivalate,

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

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 1-methyl-1\(\text{H-}

pyrrole-2-carboxylate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 1,1-T-biphenyl-4-carboxylate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 4-methoxybenzoate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 1H-indole-2-carboxylate,

benzyl N-(tert-butyl)-N-[[(diphenylacetyl)oxy]methoxy]carbonyl]glycinate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 1-naphthoate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 2-naphthoate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) 1-methyl-1\(\text{H-}

indole-3-carboxylate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) quinoline-2-carboxylate,

\(\text{N-(tert-butyl)-N-留[(2-(benzyloxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy}methyl\) nicotinate,
({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino|carbonyl|oxy}methyl isonicotinate,  
({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino|carbonyl|oxy}methyl 2,6-difuorobenzoate,  
({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino|carbonyl|oxy}methyl 2-fluorobenzoate,  
({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino|carbonyl|oxy}methyl 2-(trifluoromethyl)benzoate,  
({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino|carbonyl|oxy}methyl 4-(1 H-pyrrol-1-y1)benzoate,  
({[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,  
({[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-trimethoxybenzoate,  
({[2-(benzyloxy)-2-oxoethyl](tert-butyl)amino|carbonyl|oxy}methyl 3,5-dimethoxybenzoate,  
3-phenyl-acrylic acid (benzyloxy|carbonylmethyl-tert-butyl-carbamoyloxy)-methyl ester,
(1-(tert-butoxy)-2-oxoethyl)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, 

(1-(tert-butoxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 4-(heptyloxy)benzoate, 

10 (1-(tert-butoxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 2-(2-phenylethyl)benzoate, 

(1-(tert-butoxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 4-(dodecyloxy)benzoate, 

15 (1-(tert-butoxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl 4-(acetylamino)benzoate, 

(1-(tert-butoxy)-2-oxoethyl)(tert-butyl)amino]carbonyl]oxy)methyl anthracene-9-carboxylate and 


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, 

30 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-\{([cyclopentylacetoyl]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)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-\{([cyclohexylacetoyl]oxy)methoxy)carbonyl\}glycine,
30  N-(tert-butyl)-N-\{([2,6-dimethylbenzoyl]oxy)methoxy)carbonyl\}glycine,
N-(tert-butyl)-N-\{([phenylacetoyl]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,
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,
N-([(4-methoxybenzoyl)oxy]methoxy)carbonyl)glycine,
N-([(1H-indol-2-ylcarbonyl)oxy]methoxy)carbonyl)glycine,
N-([(diphenylacetyl)oxy]methoxy)carbonyl)glycine,
N-([(1-naphthoyloxy)methoxy]carbonyl)glycine,
N-([(2-naphthoyloxy)methoxy]carbonyl)glycine,
N-([(1-methyl-1H-indol-3-yl)carbonyl]oxy)methoxy)carbonyl]glycine,
N-([(quinolin-2-ylcarbonyl)oxy]methoxy)carbonyl)glycine,
N-([(pyridin-3-ylcarbonyl)oxy]methoxy)carbonyl)glycine,
N-([(isonicotinoyloxy)methoxy]carbonyl)glycine,
N-([(2,6-difluorobenzoyl)oxy]methoxy)carbonyl)glycine,
N-([(2-fluorobenzoyl)oxy]methoxy)carbonyl)glycine,
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,
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,
N-(tert-butyl)-N-([(3,5-dimethoxybenzoyl)oxy]methoxy)carbonyl)glycine,
N-(tert-butyl)-N-([(2E)-3-phenylprop-2-enoyl]oxy)methoxy)carbonyl)glycine,
N-(tert-butyl)-N-([[(3,5-bis(trifluoromethyl)phenyl)acetyl]oxy)methoxy)carbonyl]glycine,
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N-(tert-butyl)-N-([(4-(heptyloxy)benzoyl]oxy)methoxy)carbonyl]glycine,
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-(acetylamino)benzoyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine,
N-([(9-anthrylcarbonyl]oxy)methoxy)carbonyl]-N-(tert-butyl)glycine and
N-((4-benzoylbenzoyl)oxy)methoxy)carbonyl]glycine.

34. A compound according to claim 26 which is
3,3-Dimethyl-butyric acid [tert-butyl-(2-isobutoxycarbonyloxy-2-oxo-ethyl)-carbamoyloxy)-methyl ester.

35. A method for the preparation of compounds represented by Formula (I):

\[
\begin{align*}
\text{R}_3\text{O} - \text{A} - \text{CO} & \text{ represents} \\
\text{R}_5\text{O} - \text{O} - \text{N} & \text{ where } \text{R}_4, \text{R}_5, \text{R}_6, \text{ and } \text{R}_{10} \text{ are as defined in claim 1} \\
\text{R}_4\text{O} - \text{O} - \text{N} & \text{ with a } \delta - \text{disubstituted-9-aminotetracycline of the formula} \\
\end{align*}
\]

or a pharmaceutically acceptable salt thereof comprising the step of:

a. reacting an activated acyloxy carbamate intermediate of the formula

\[
\begin{align*}
\text{R}_5\text{O} - \text{O} - \text{N} & \text{ where } \text{R}_4, \text{R}_5, \text{R}_6, \text{ and } \text{R}_{10} \text{ are as defined in claim 1 and } \text{R}_{12} \text{ is as defined in claim 26} \\
\end{align*}
\]
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, converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.

36. A method for the preparation of compounds represented by Formula (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:

reacting an amine of the formula
wherein $R_1$, $R_2$, $R_4$, $Rs$, $Re$, and $R_{10}$ are as defined in claim 1 with a chloro intermediate of the formula

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

or a pharmaceutically acceptable salt thereof and, if desired, converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.

37. A method for the preparation of compounds represented by Formula (I):
wherein:

\( R_3O - A - CO- \) represents

![Chemical Structure](image)

and \( R_1, R_2, R_4, R_5, Re, \) 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

![Chemical Structure](image)

wherein \( R_i, R_2, \) and \( R_4 \) are as defined in claim 1 with a chloro intermediate of the formula

\[ R_5O - Cl \]

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

![Chemical Structure](image)

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

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{O}
\end{array}
\]

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

\[
\begin{array}{c}
\text{R} \\
\text{R} \\
\text{R}
\end{array}
\]

with a chloro intermediate of the formula

\[
\begin{array}{c}
\text{R} \\
\text{R} \\
\text{Cl}
\end{array}
\]

where \( R_1, R_2, R_5, R_6, \) and \( R_{10} \) are as defined in claim 1

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.

39. A method for the preparation of a compound represented by Formula (I);

wherein:
A, R₁, R₂, and R₃ are as defined in claim 1
or a pharmaceutically acceptable salt thereof comprising:
reacting a carboxylic acid of the formula

where A, and R₃ are as defined above
with a chloroformate CICO₂Rᵢ₂ where Rᵢ₂ 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
and reacting said mixed anhydride with a $\delta$-disubstituted-9-aminotetracycline of the formula

\[
\begin{align*}
\text{Mixed anhydride} \\
R_3O & \overset{\text{A}}{\underset{\text{O}}{\text{O}}} R_12
\end{align*}
\]

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(1 H)-pyrimidinone to afford a compound of Formula (I)

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

or a pharmaceutically acceptable salt thereof and, if desired, converting the compound of Formula (I) into a pharmaceutically acceptable salt thereof.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. C07C237/26 C07C271/22 C07D209/42 C07D213/80 C07D215/48
C07D333/38 A61K31/165...

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

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)
C07C C07D A61K

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

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

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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<tr>
<td>X</td>
<td>WO 01/74761 A (TUFTS COLLEGE [US]) 11 October 2001 (2001-10-11) claims 1,55,83,86</td>
<td>1-5,7, 12, 16-25,39</td>
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<td>WO 02/072031 A2 (PARATEK PHARMACEUTICALS INC [US]) 19 September 2002 (2002-09-19) claims 1,43,72</td>
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</table>

Further documents are listed in the continuation of Box C

See patent family annex

* Special categories of cited documents
  A document defining the general state of the art which is not considered to be of particular relevance
  *E* earlier document but published on or after the international filing date
  *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  *O* document referring to an oral disclosure, use, exhibition or other means
  *P* document published prior to the international filing date but later than the priority date claimed

**Date of the actual completion of the international search**
1 February 2007

**Date of mailing of the international search report**
13/02/2007

**Name and mailing address of the ISA/ European Patent Office, P B 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx 31 651 [ipo nl, Fax (+31-70) 340-3016**

Authorized officer
VOYIAZOGLOU, D
### DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<td>US 5 639 742 A (LEE VING JICK [US] ET AL) 17 June 1997 (1997-06-17)</td>
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Form PCT/ISA/210 (continuation of second sheet) (April 2005)
**INTERNATIONAL SEARCH REPORT**

**Box II** Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. **Claims Nos.:**
   because they relate to subject matter not required to be searched by this Authority, namely:
   
   Although claim 24 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. **Claims Nos.:**
   because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. **Claims Nos.:**
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box III** Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. **As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.**

2. **As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.**

3. **As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:**

4. **No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:**

**Remark on Protest**

- The additional search fees were accompanied by the applicant’s protest.
- No protest accompanied the payment of additional search fees.
<table>
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