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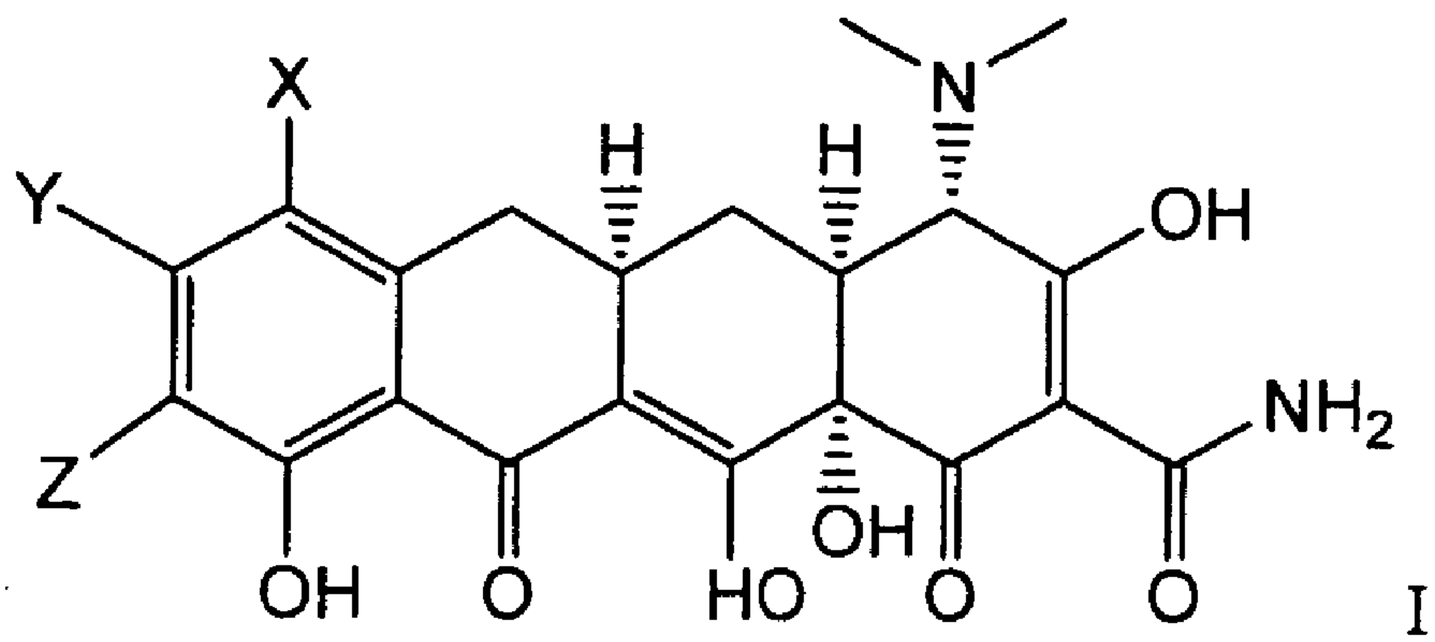
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(54) Titre : COMPOSES DE TETRACYCLINE
(54) Title: TETRACYCLINE COMPOUNDS



I

(57) Abrégé/Abstract:
The present invention is directed to a compound represented by Structural Formula (I): or a pharmaceutically ac-ceptable salt thereof. The variables for Structural Formula I are defined herein. Also described is a pharmaceutical composition comprising the compound of Structural Formula I and its therapeutic use.

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(13) **C**

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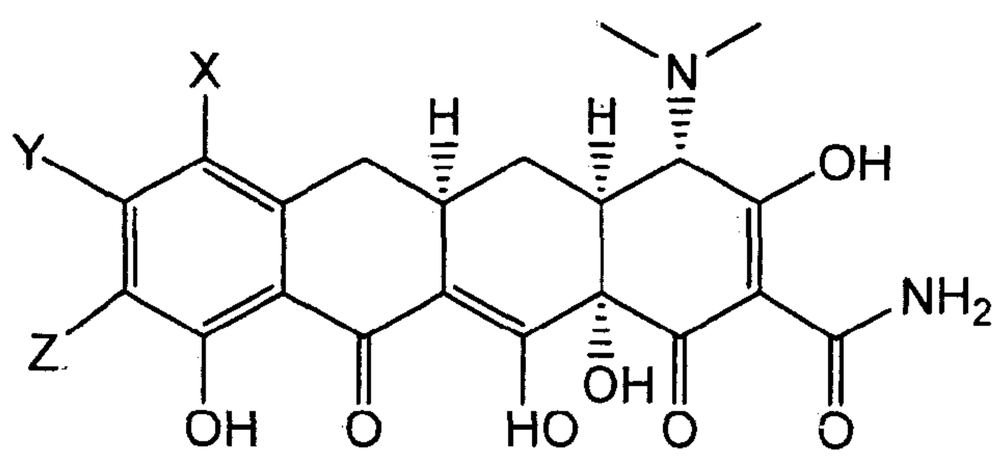
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(54) Title: TETRACYCLINE COMPOUNDS



(I)

(57) Abstract: The present invention is directed to a compound represented by Structural Formula (I): or a pharmaceutically acceptable salt thereof. The variables for Structural Formula I are defined herein. Also described is a pharmaceutical composition comprising the compound of Structural Formula I and its therapeutic use.

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JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __2___

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TETRACYCLINE COMPOUNDS

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No.: 61/215,757, filed on May 8, 2009.

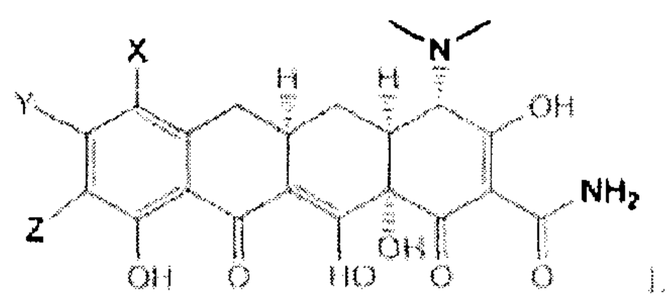
BACKGROUND OF THE INVENTION

The tetracyclines are broad spectrum anti-microbial agents that are widely used in human and veterinary medicine. The total production of tetracyclines by fermentation or semi-synthesis is measured in the thousands of metric tons per year.

The widespread use of tetracyclines for therapeutic purposes has led to the emergence of resistance to these antibiotics, even among highly susceptible bacterial species. Therefore, there is need for new tetracycline analogs with improved antibacterial activities and efficacies against other tetracycline responsive diseases or disorders.

SUMMARY OF THE INVENTION

Compounds of Formula I are new tetracycline analogs with improved antibacterial activities and efficacies against other tetracycline responsive diseases or disorders:



I.

Pharmaceutically acceptable salts of the compound of Formula I are also included.

Values for the variables in Formula I are provided below:

X is selected from hydrogen, bromo, fluoro, chloro, C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -$S(O)_m$-C_1-C_6 alkyl, C_3-C_7 cycloalkyl, -O-C_3-C_7 cycloalkyl, -$S(O)_m$-C_3-C_7 cycloalkyl, -CN, -$N(R^4)(R^5)$, and -NH-C(O)-(C_1-C_6 alkylene)-$N(R^4)(R^5)$, wherein

each alkyl, alkylene or cycloalkyl in the group represented by X is optionally substituted with fluoro;

Y is selected from fluoro, -C_1-C_6 alkyl, and -$[C(R^{1a})(R^{1b})]_m$-$N(R^2)(R^3)$;

Z is selected from hydrogen, fluoro, bromo, -CN, -$[C(R^{1a})(R^{1b})]_n$-$N(R^2)(R^3)$, -$N(R^4)(R^5)$, NO_2, -NH-C(O)-C_1-C_4 alkylene-$N(R^4)(R^5)$, C_1-C_6 alkyl, -NH-C(O)-C_1-C_6 alkyl, -NH-$S(O)_m$-C_1-C_6 alkyl, -NH-$S(O)_m$-C_3-C_{10} carbocyclyl, -NH-$S(O)_m$-(4-13 membered) heterocyclyl;

each R^{1a} and R^{1b} is independently selected from hydrogen, C_1-C_4 alkyl, and C_3-C_{10} carbocyclyl;

R^2 is selected from hydrogen, C_1-C_{12} alkyl, -C_0-C_6 alkylene-C_3-C_{10} carbocyclyl, and -C_0-C_6 alkylene-(4-13 membered) heterocyclyl;

R^3 is selected from hydrogen, C_1-C_8 alkyl, -C_0-C_6 alkylene-C_3-C_{10} carbocyclyl, -C_0-C_6 alkylene-(4-13 membered) heterocyclyl, -C(O)-C_1-C_6 alkyl, -C_0-C_6 alkylene-$C(O)N(R^4)(R^5)$, -C(O)-C_1-C_6 alkylene-$N(R^4)(R^5)$, -C_2-C_6 alkylene-$N(R^4)(R^5)$, -$S(O)_m$-C_1-C_6 alkyl, -$S(O)_m$-C_3-C_{10} carbocyclyl, and -$S(O)_m$-(4-13 membered) heterocyclyl, wherein each alkyl, carbocyclyl, alkylene or heterocyclyl in the group represented by R^2 or R^3 is optionally and independently substituted with one or more substituents independently selected from fluoro, chloro, -OH, -O-C_1-C_4 alkyl, C_1-C_4 alkyl, fluoro-substituted-C_1-C_4 alkyl, -$N(R^4)(R^5)$, C_3-C_{10} carbocyclyl or a (4-13 membered) heterocyclyl; or

R^2 and R^3 taken together with the nitrogen atom to which they are bound form a (4-7 membered) monocyclic heterocylic ring, or a (6-13 membered) bicyclic, spirocyclic or bridged heterocylic ring, wherein the (4-7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring optionally comprises 1 to 4 additional heteroatoms independently selected from N, S and O; and wherein the (4-7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring is optionally substituted with one or more substituents independently selected from C_3-C_{10} carbocyclyl, (4-13 membered) heterocyclyl, fluoro, chloro, -OH, C_1-C_4 fluoroalkyl, C_1-C_4 alkyl, -O-C_3-C_{10} carbocyclyl, -O-(4-13 membered) heterocyclyl, -C_0-C_4 alkyl-O-C_1-C_4 alkyl, -C_0-C_4 alkyl-O-C_1-C_4 fluoroalkyl, =O, -C(O)-C_1-C_4 alkyl, -$C(O)N(R^4)(R^5)$, -$N(R^4)$-C(O)-C_1-C_4 alkyl, and -C_0-C_4 alkylene-$N(R^4)(R^5)$,

and wherein each carbocyclyl or heterocyclyl substituent is optionally substituted with fluoro, chloro, -OH, C_1-C_4 fluoroalkyl, C_1-C_4 alkyl, -O-C_1-C_4 alkyl, -O-C_1-C_4 fluoroalkyl, $-NH_2$, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

each of R^4 and R^5 is independently selected from hydrogen and C_1-C_4 alkyl; or

R^4 and R^5 taken together with the nitrogen atom to which they are bound form a (4-7 membered) heterocylic ring optionally comprising one additional heteroatom selected from N, S and O, wherein the (4-7 membered) heterocylic ring is optionally substituted with fluoro, chloro, -OH, fluoro-substituted C_1-C_4 alkyl, -C_1-C_4 alkyl, or -C_1-C_4 alkylene-O-C_1-C_4 alkyl, and is optionally benzofused;

m is 0, 1 or 2; and

n is 1 or 2,

with the proviso that when Z is -NH-C(O)-C_1-C_4 alkyl-N(R^4)(R^5), X is other than fluoro.

Another embodiment of the present invention is directed to a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound disclosed herein or a pharmaceutically acceptable salt thereof. The pharmaceutical composition is used in therapy, such as treating an infection in a subject.

Another embodiment of the present invention is a method of treating an infection in a subject comprising administering to the subject an effective amount of a compound disclosed herein or a pharmaceutically acceptable salt thereof.

Another embodiment of the present invention is the use of a compound disclosed herein or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for treating an infection in a subject.

Another embodiment of the present invention is the use of a compound disclosed herein or a pharmaceutically acceptable salt thereof for therapy, such as treating an infection in a subject.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1A-1C provide MIC values for the indicated compound.

FIGS. 2A-2K provide compounds in accordance with Structure Formula I.

FIGS. 3A-3EE provide compounds in accordance with Structure Formula I.

FIGS. 4A-4Z provide compounds in accordance with Structure Formula I.

FIGS. 5A-5O provide compounds in accordance with Structure Formula I.

FIGS. 6A- 6FF provide compounds in accordance with Structure Formula I.

FIGS. 7A-7J provide MIC values for compounds of the invention.

FIGS. 8A-8D provide MIC values for compounds of the invention.

FIGS. 9A-9M provide MIC values for compounds of the invention.

FIGS. 10A-10I provide MIC values for compounds of the invention.

FIGS. 11A-11G provide MIC values for compounds of the invention.

The foregoing will be apparent from the following more particular description of example embodiments of the invention, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating embodiments of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a compound represented by Structural Formula I or a pharmaceutically acceptable salt thereof. Values and alternative values for the variables in Structural Formula I are defined as the following:

X is hydrogen, bromo, fluoro, chloro, C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -$S(O)_m$-C_1-C_6 alkyl, C_3-C_7 cycloalkyl, -O-C_3-C_7 cycloalkyl, -$S(O)_m$-C_3-C_7 cycloalkyl, -CN, -$N(R^4)(R^5)$ or -NH-C(O)-(C_1-C_6 alkylene)-$N(R^4)(R^5)$. Each alkyl, alkylene or cycloalkyl in the group represented by X is optionally substituted with fluoro. In another embodiment, X is fluoro, chloro, -CN or -$N(CH_3)_2$. Alternatively, X is fluoro, chloro or -$N(CH_3)_2$. In another alternative, X is fluoro. In yet another alternative, X is chloro. In yet another alternative, X is -$N(CH_3)_2$. In yet another embodiment, X is hydrogen. In still another embodiment when Z is -NH-C(O)-C_1-C_4 alkyl-$N(R^4)(R^5)$, X is other than fluoro.

Y is fluoro, -C_1-C_6 alkyl, or -$[C(R^{1a})(R^{1b})]_m$-$N(R^2)(R^3)$. In another embodiment, Y is fluoro, methyl, -$CH(R^{1a})$-$N(R^2)(R^3)$, -$(CH_2)_2$-$N(R^2)(R^3)$, -NH(pyridyl), -NH(C_1-C_8 alkyl), -NHC(O)-C_1-C_3 alkylene-piperidine, -NHC(O)-C_1-C_3 alkylene-pyrrolidine or -$NHS(O)_2$-phenyl, wherein each piperidine and each pyrrolidine in the group represented by Y is optionally substituted with one

or more -C_1-C_6 alkyl. In another embodiment, Y is fluoro, methyl or -$CH(R^{1a})$-$N(R^2)(R^3)$. Alternatively, Y is -$CH(R^{1a})$-$N(R^2)(R^3)$. In another alternative, Y is fluoro. In yet another alternative, Y is -NHR^3.

Z is hydrogen, fluoro, bromo, -CN, -$[C(R^{1a})(R^{1b})]_n$-$N(R^2)(R^3)$, -$N(R^4)(R^5)$, NO_2, -NH-C(O)-C_1-C_4 alkylene-$N(R^4)(R^5)$, C_1-C_6 alkyl, -NH-C(O)-C_1-C_6 alkyl, -NH-$S(O)_m$-C_1-C_6 alkyl, -NH-$S(O)_m$-C_3-C_{10} carbocyclyl or -NH-$S(O)_m$-(4-13 membered) heterocyclyl. In another embodiment, Z is hydrogen, NH_2 or -CH_2-NH-CH_2-$C(CH_3)_3$. In another embodiment, Z is hydrogen. Alternatively, Z is -$[C(R^{1a})(R^{1b})]_n$-$N(R^2)(R^3)$ or -$N(R^4)(R^5)$.

Each R^{1a} and R^{1b} is independently hydrogen, C_1-C_4 alkyl or C_3-C_{10} carbocyclyl. In another alternative, R^{1a} is hydrogen or methyl.

R^2 is hydrogen, C_1-C_{12} alkyl, -C_0-C_6 alkylene-C_3-C_{10} carbocyclyl, and -C_0-C_6 alkylene-(4-13 membered) heterocyclyl. Each alkyl, carbocyclyl, alkylene or heterocyclyl in the group represented by R^2 is optionally and independently substituted with one or more substituents independently selected from fluoro, chloro, -OH, -O-C_1-C_4 alkyl, C_1-C_4 alkyl, fluoro-substituted-C_1-C_4 alkyl, -$N(R^4)(R^5)$, C_3-C_{10} carbocyclyl and a (4-13 membered) heterocyclyl. In another alternative, R^2 is hydrogen, C_1-C_3 straight chained alkyl, C_1-C_3 straight chained fluoroalkyl, cyclopropyl or -CH_2-cyclopropyl. Alternatively, R^2 is hydrogen, C_1-C_3 straight chained alkyl or -CH_2-cyclopropyl.

R^3 is hydrogen, C_1-C_8 alkyl, -C_0-C_6 alkylene-C_3-C_{10} carbocyclyl, -C_0-C_6 alkylene-(4-13 membered) heterocyclyl, -C(O)-C_1-C_6 alkyl, -C_0-C_6 alkylene-$C(O)N(R^4)(R^5)$, -C(O)-C_1-C_6 alkylene-$N(R^4)(R^5)$, -C_2-C_6 alkylene-$N(R^4)(R^5)$, -$S(O)_m$-C_1-C_6 alkyl, -$S(O)_m$-C_3-C_{10} carbocyclyl or -$S(O)_m$-(4-13 membered) heterocyclyl. When R^2 is hydrogen or C_1-C_2 alkyl, R^3 is additionally benzyl. Each alkyl, carbocyclyl, alkylene or heterocyclyl in the group represented by R^3 is optionally and independently substituted with one or more substituents independently selected from fluoro, chloro, -OH, -O-C_1-C_4 alkyl, C_1-C_4 alkyl, fluoro-substituted-C_1-C_4 alkyl, -$N(R^4)(R^5)$, C_3-C_{10} carbocyclyl and a (4-13 membered) heterocyclyl. In another alternative, R^3 is hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_2-C_6 alkylene-O-C_1-

C_3 alkyl, -C_3-C_{10} cycloalkyl, -C_3-C_{10}cycloalkyl-substituted C_1-C_3 alkyl, cyclopropyl-substituted cyclopropyl, -$(CH_2)_2$-phenyl or -$S(O)_2$-phenyl. Alternatively, R^3 is hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_1-C_6 alkylene-O-C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkyl-substituted C_1-C_3 alkyl, -$(CH_2)_2$-phenyl, and when R^2 is hydrogen or -C_1-C_2 alkyl, R^3 is additionally benzyl. In another embodiment, R^3 is selected from hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_1-C_6 alkylene-O-C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, -$(CH_2)_2$-phenyl and C_3-C_{10} cycloalkyl-substituted C_1-C_3 alkyl, wherein each cycloalkyl in the group represented by R^3 is optionally substituted with-C_1-C_3 alkyl or optionally benzofused.

Alternatively, R^2 and R^3 taken together with the nitrogen atom to which they are bound form a (4-7 membered) monocyclic heterocylic ring, or a (6-13 membered) bicyclic, spirocyclic or bridged heterocylic ring, wherein the (4-7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring optionally comprises 1 to 4 additional heteroatoms independently selected from N, S and O. The (4-7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring is optionally substituted with one or more substituents independently selected from C_3-C_{10} carbocyclyl, (4-13 membered) heterocyclyl, fluoro, chloro, -OH, C_1-C_4 fluoroalkyl, C_1-C_4 alkyl, -O-C_3-C_{10} carbocyclyl, -O-(4-13 membered) heterocyclyl, -C_0-C_4 alkyl-O-C_1-C_4 alkyl, -C_0-C_4 alkyl-O-C_1-C_4 fluoroalkyl, =O, -C(O)-C_1-C_4 alkyl, -C(O)N(R^4)(R^5), -N(R^4)-C(O)-C_1-C_4 alkyl, and -C_0-C_4 alkylene-N(R^4)(R^5), and wherein each carbocyclyl or heterocyclyl substituent is optionally substituted with fluoro, chloro, -OH, C_1-C_4 fluoroalkyl, C_1-C_4 alkyl, -O-C_1-C_4 alkyl, -O-C_1-C_4 fluoroalkyl, -NH_2, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$. In another embodiment, R^2 and R^3 taken together with the nitrogen atom to which they are bound form a ring selected from pyrrolidine, piperidine, piperazine or morpholine, wherein the ring is optionally substituted with one or more substituents independently selected from -OH, -C_1-C_3 alkyl and -C_1-C_3 alkylene-O-C_1-C_3 alkyl, and wherein the ring is optionally benzofused or spirofused to cyclopropyl. Alternatively, R^2 and R^3 taken together with the nitrogen atom to which they are bound form a ring selected from pyrrolidine and piperidine, wherein

the ring is optionally substituted with one or more substituents independently selected from fluoro, C_1-C_3 alkyl and -C_1-C_3 alkylene-O-C_1-C_3 alkyl, and wherein the ring is optionally benzofused or spirofused to cyclopropyl.

Each of R^4 and R^5 is independently hydrogen or C_1-C_4 alkyl.

Alternatively, R^4 and R^5 taken together with the nitrogen atom to which they are bound form a (4-7 membered) heterocylic ring optionally comprising one additional heteroatom selected from N, S and O, wherein the (4-7 membered) heterocylic ring is optionally substituted with fluoro, chloro, -OH, fluoro-substituted C_1-C_4 alkyl, -C_1-C_4 alkyl, or -C_1-C_4 alkylene-O- C_1-C_4 alkyl, and is optionally benzofused.

Each m is independently 0, 1 or 2.

n is 1 or 2.

In a second embodiment, the compound of the present invention is represented by Structural Formula I or a pharmaceutically acceptable salt thereof wherein, Y is fluoro, methyl, -CH(R^{1a})-N(R^2)(R^3), -(CH_2)$_2$-N(R^2)(R^3), -NH(pyridyl), -NH(C_1-C_8 alkyl), -NHC(O)-C_1-C_3 alkylene-piperidine, -NHC(O)-C_1-C_3 alkylene-pyrrolidine or -NHS(O)$_2$-phenyl, and each piperidine and each pyrrrolidine in the group represented by Y is optionally substituted with one or more -C_1-C_6 alkyl; R^{1a} is hydrogen or methyl; R^2 is hydrogen, C_1-C_3 straight chained alkyl, C_1-C_3 straight chained fluoroalkyl, cyclopropyl or -CH_2-cyclopropyl; R^3 is hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_2-C_6 alkylene-O-C_1-C_3 alkyl, -C_3-C_{10} cycloalkyl, -C_3-C_{10}cycloalkyl-substituted C_1-C_3 alkyl, cyclopropyl-substituted cyclopropyl, -(CH_2)$_2$-phenyl or -S(O)$_2$-phenyl, and when R^2 is hydrogen or C_1-C_2 alkyl, R^3 is additionally benzyl; or R^2 and R^3 taken together with the nitrogen atom to which they are bound form a ring selected from pyrrolidine, piperidine, piperazine or morpholine, wherein the ring is optionally substituted with one or more substituents independently selected from -OH, -C_1-C_3 alkyl and -C_1-C_3 alkylene-O-C_1-C_3 alkyl, and wherein the ring is optionally benzofused or spirofused to cyclopropyl; and values and alternative values for the remainder of the variables are as described above.

In a third embodiment, the compound of the present invention is represented by Structural Formula I or a pharmaceutically acceptable salt thereof wherein, Y is

fluoro, methyl or -CH(R^{1a})-N(R^2)(R^3); R^{1a} is hydrogen or methyl; R^2 is hydrogen, C_1-C_3 straight chained alkyl or -CH_2-cyclopropyl; R^3 is hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_1-C_6 alkylene-O-C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkyl-substituted C_1-C_3 alkyl, wherein each cycloalkyl in the group represented by R^3 is optionally substituted with-C_1-C_3 alkyl or optionally benzofused, or -$(CH_2)_2$-phenyl, and when R^2 is hydrogen or -C_1-C_2 alkyl, R^3 is additionally benzyl; or R^2 and R^3 taken together with the nitrogen atom to which they are bound form a ring selected from pyrrolidine and piperidine, wherein the ring is optionally substituted with one or more substituents independently selected from fluoro, -C_1-C_3 alkyl and -C_1-C_3 alkylene-O-C_1-C_3 alkyl, and wherein the ring is optionally benzofused or spirofused to cyclopropyl; and values and alternative values for the remainder of the variables are as described above.

In a fourth embodiment the compound of the present invention is represented by Structural Formula I or a pharmaceutically acceptable salt thereof wherein, X is fluoro, chloro, -CN or -$N(CH_3)_2$; Z is hydrogen, NH_2 or -CH_2-NH-CH_2-$C(CH_3)_3$; and values and alternative values for the remainder of the variables are as described above for Structural Formula I or for the second or third embodiment.

In another embodiment of a compound of Formula I:

X is selected from OCH3, CF3, Cl, F, and N(CH3)2;

Z is hydrogen and when X is F, Z is additionally selected from NH2, NH(C1 C2 alkyl), and N(C1 C2 alkyl)2; and

Y is CH2 NR2R3; wherein

R2 is selected from hydrogen, and C1-C3 alkyl; and

R3 is selected from hydrogen, C1-C8 alkyl, C0-C6 alkylene C3-C10 carbocyclyl, C0-C6 alkylene (4-13 membered) heterocyclyl, and C2 C6 alkylene N(R4)(R5), wherein each carbocyclyl or heterocyclyl in the group represented by R3 is optionally and independently substituted with one or more substituents independently selected from fluoro, OH, O C1 C3 alkyl, C1-C3 alkyl, fluoro-substituted C1-C3 alkyl, N(R4)(R5), C3-C10 carbocyclyl or a (4-13 membered) heterocyclyl; or

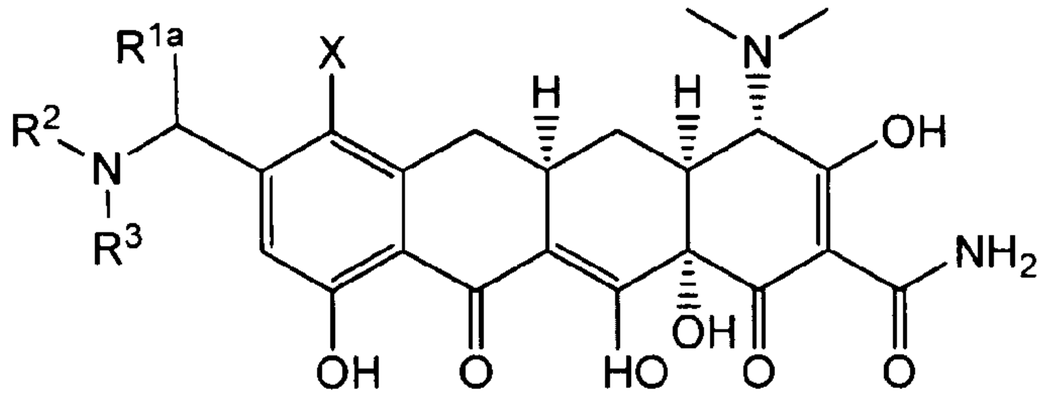
R2 and R3 taken together with the nitrogen atom to which they are bound form a (4 7 membered) saturated monocyclic heterocylic ring, or a (6-13 membered)

saturated bicyclic, spirocyclic or bridged heterocylic ring, wherein the (4 7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring is optionally substituted with one or more substituents independently selected from C3-C10 carbocyclyl, (4-13 membered) heterocyclyl, fluoro, OH, -C1 C3 fluoroalkyl, -C1 C3 alkyl, O C3-C10 carbocyclyl, O (4-13 membered) heterocyclyl, C0 C2 alkylene O C1 C3 alkyl, C0 C2 alkylene O C1 C3 fluoroalkyl, =O, and C0-C4 alkylene N(R4)(R5), and wherein each carbocyclyl or heterocyclyl substituent is optionally substituted with fluoro, OH, C1 C3 fluoroalkyl, C1 C3 alkyl, O C1 C3 alkyl, O C1 C3 fluoroalkyl, NH2, NH(C1 C4 alkyl), or N(C1 C4 alkyl)2; and

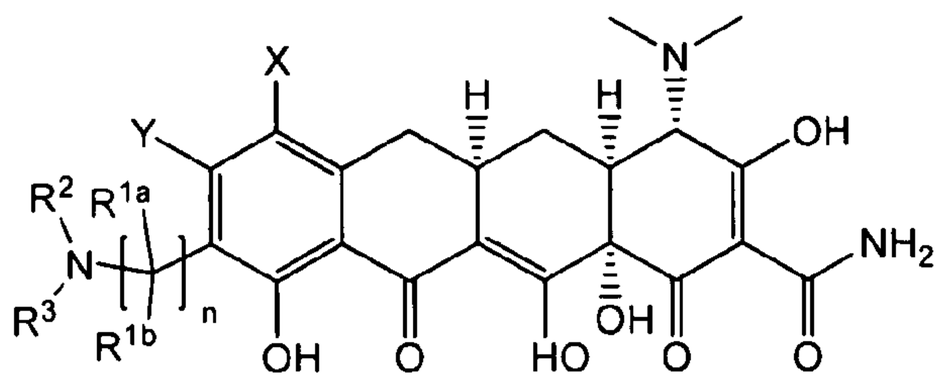
each of R4 and R5 is independently selected from hydrogen and C1 C4 alkyl.

In one specific aspect of this embodiment X is OCH3. In another specific aspect, X is CF3. In still another specific aspect, X is Cl. In another specific aspect, X is F and Z is hydrogen. In another specific aspect, X is F and Z is selected from NH2, NH(C1 C2 alkyl), and N(C1 C2 alkyl)2. In still another specific aspect X is N(CH3)2.

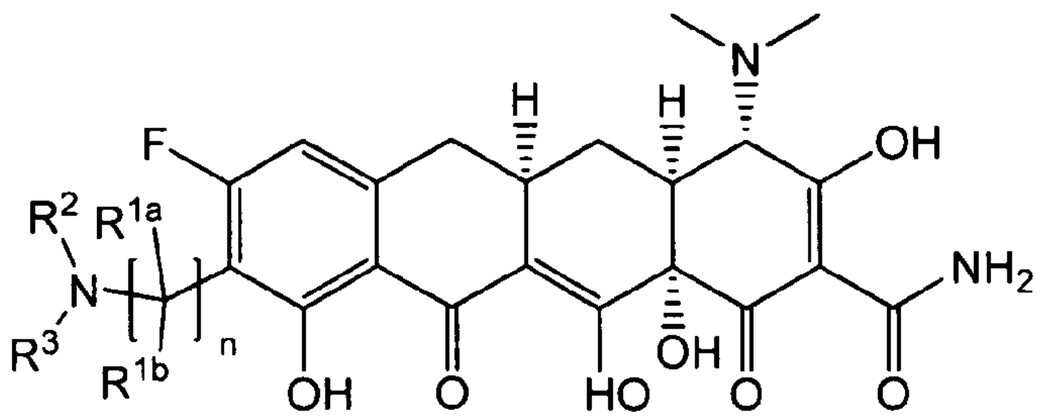
A fifth embodiment is a compound of Structural Formulas II, III, IIIa or IV or a pharmaceutically acceptable salt thereof:



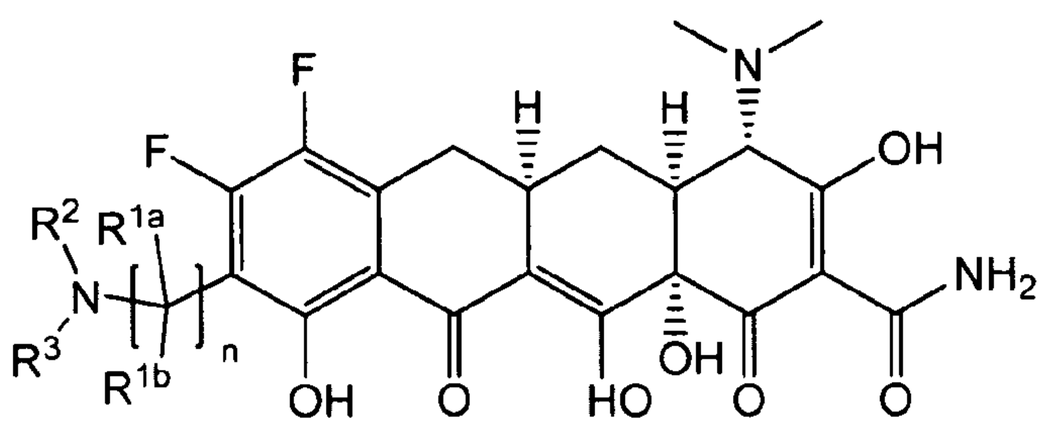
II,



III,



IIIa, or

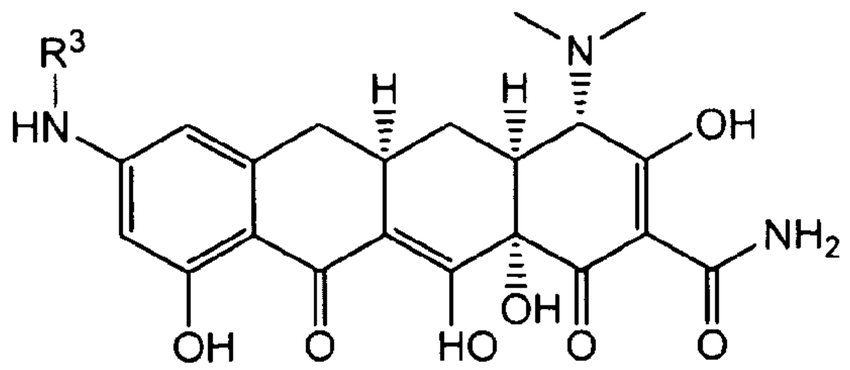


IV.

Values and alternative values for the variables in Structural Formulas II, III, IIIa and IV are as defined for Structural Formula I or in the second or in the third embodiment. Alternatively, values for the variables in Structural Formula II are as defined in the fourth embodiment. In Structural Formula II, X is preferably fluoro, chloro or $-N(CH_3)_2$.

In a sixth embodiment, the compound of the present invention is represented by Structural Formula I or a pharmaceutically acceptable salt thereof wherein, Y is $-NHR^3$; R^3 is pyridyl, C_1-C_8 alkyl, $-C(O)-C_1$-C_3 alkylene-piperidine or $-C(O)-C_1$-C_3 alkylene-pyrrolidine. Each piperidine or pyrrolidine in the group represented by R^3 is optionally substituted with one or more C_1-C_3 alkyl. Values and alternative values for the remainder of the variables are as defined for Structural Formula I above or in the second or in the third embodiment.

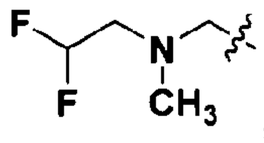
A seventh embodiment is a compound of Structural Formula V or a pharmaceutically acceptable salt thereof:

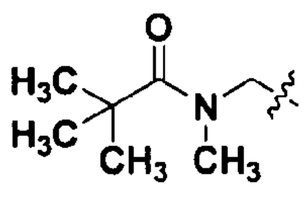


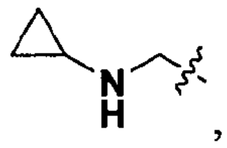
V,

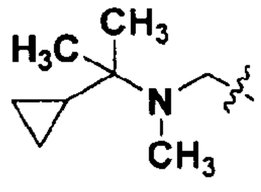
and values and alternative values for the remainder of the variables are as defined in the preceding paragraph.

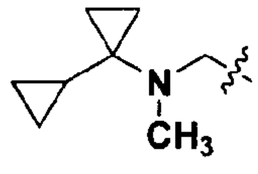
Specific examples of compounds of the invention are represented by Structural Formula II, wherein:

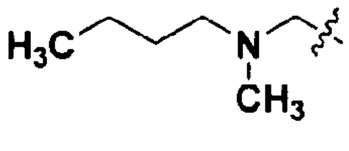
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-54;

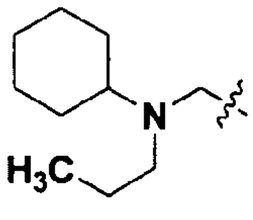
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-9;

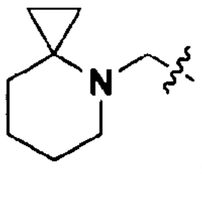
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S4-5-1;

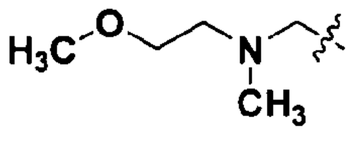
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-29;

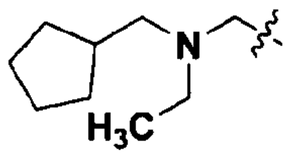
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-60;

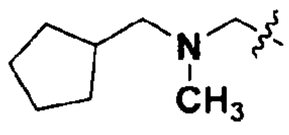
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-42;

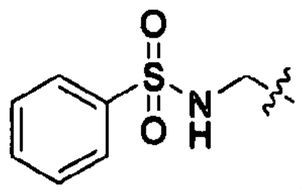
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-67;

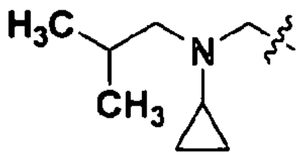
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-11;

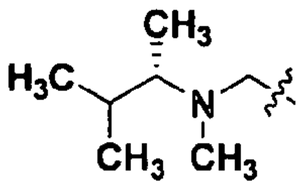
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S4-5-5;

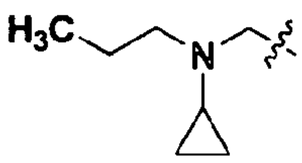
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-62;

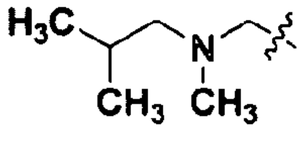
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-46;

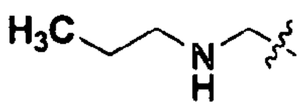
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-6;

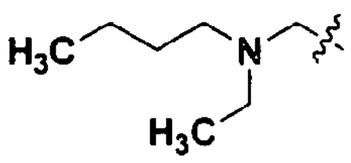
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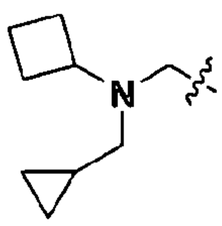
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-59

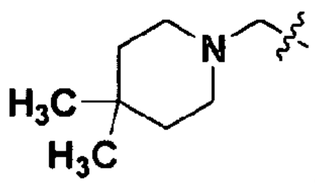
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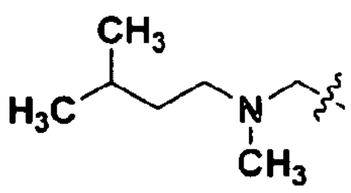
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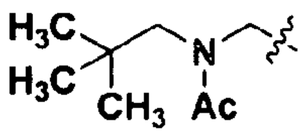
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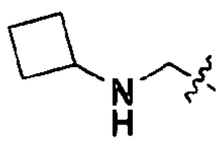
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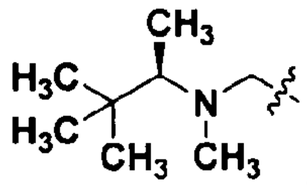
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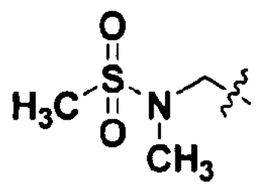
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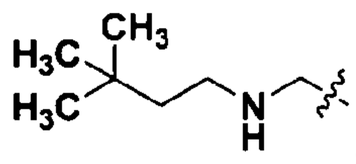
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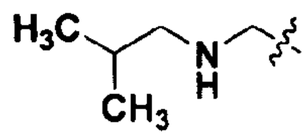
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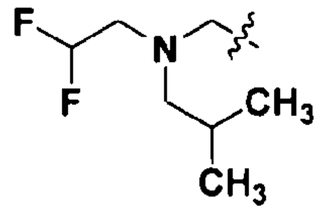
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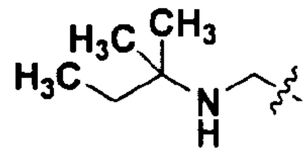
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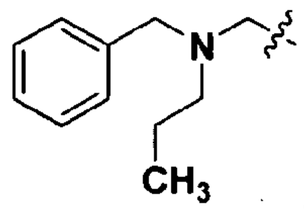
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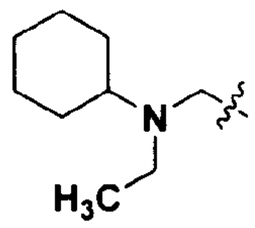
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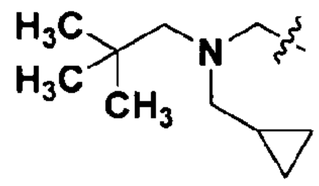
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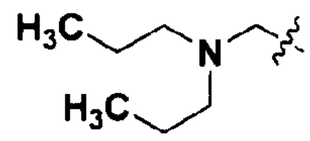
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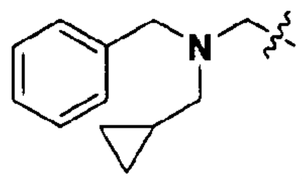
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-5;

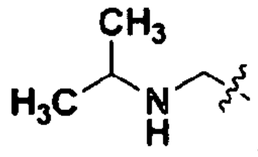
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-47;

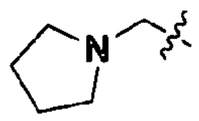
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-66;

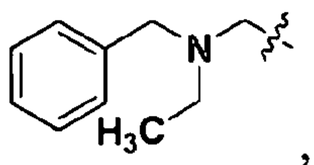
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-35;

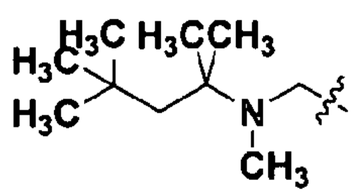
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-2;

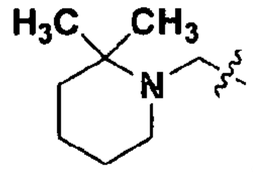
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-48;

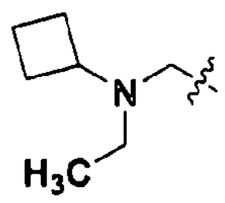
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-2;

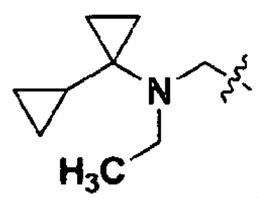
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S3-5-5;

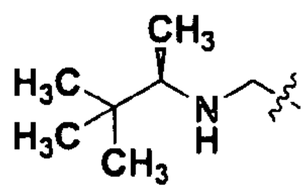
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-49;

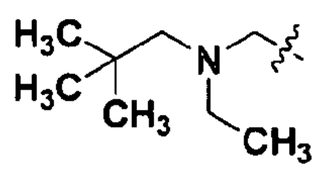
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-30;

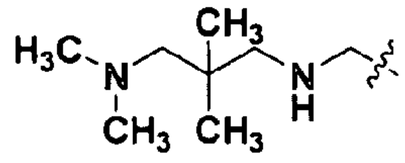
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S6-4-1;

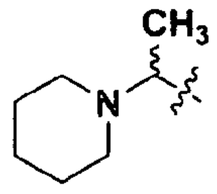
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-52;

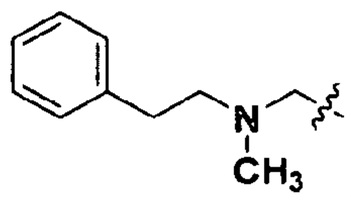
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-61;

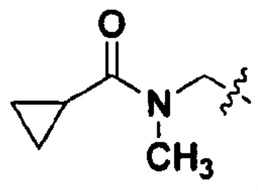
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-6;

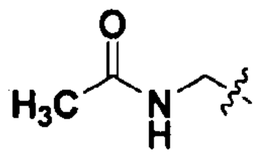
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-43;

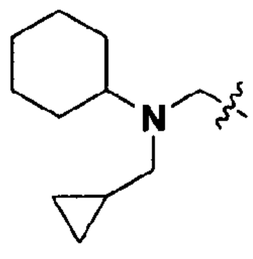
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S3-5-6;

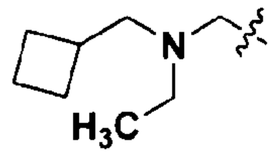
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S5-5-1;

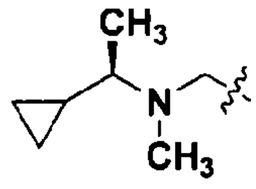
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-43;

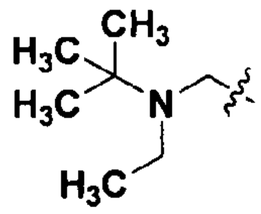
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-8;

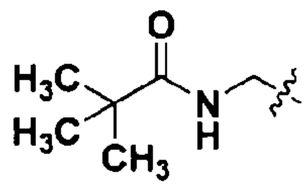
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-1;

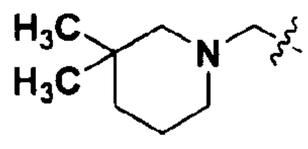
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-68;

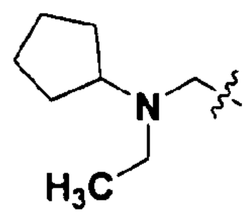
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-69;

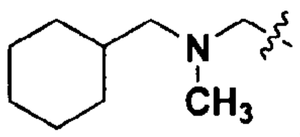
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-8;

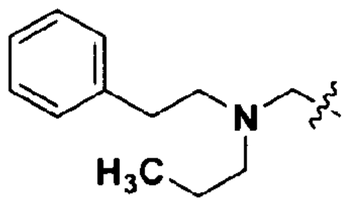
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-31;

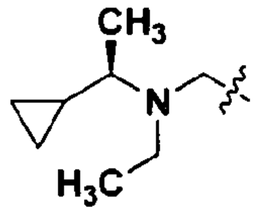
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-2;

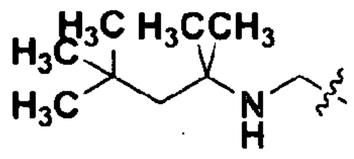
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-16;

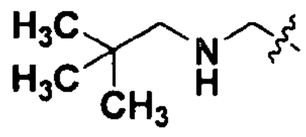
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-32;

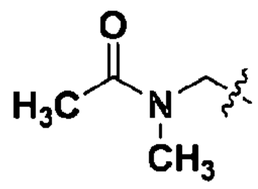
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-47;

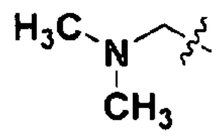
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-57;

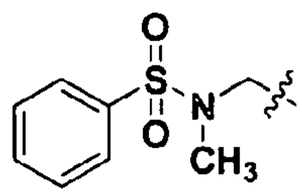
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-9;

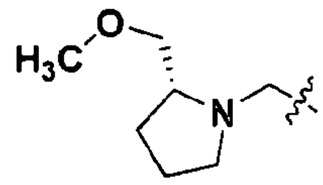
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-7;

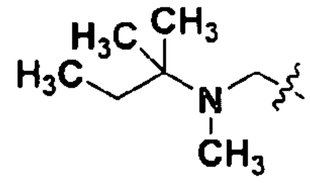
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-1;

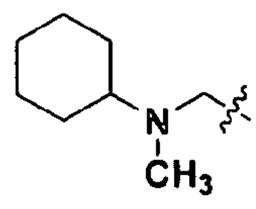
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-7;

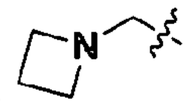
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-13;

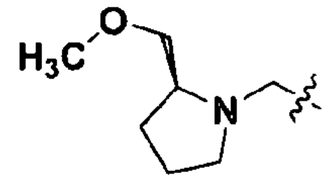
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-12;

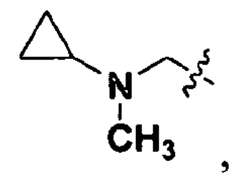
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-45;

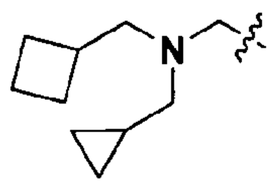
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-28;

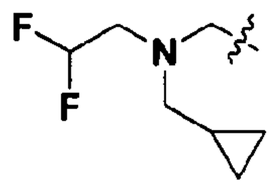
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-65;

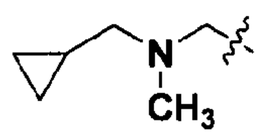
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-54;

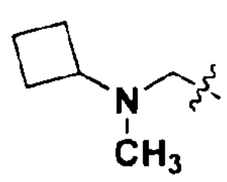
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-3;

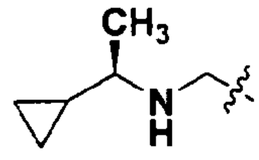
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-26;

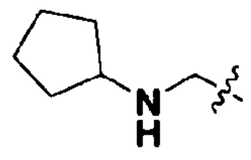
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-71;

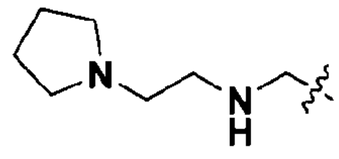
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-55;

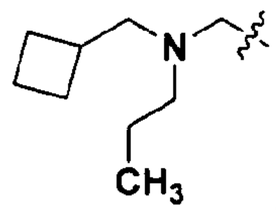
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S4-5-6;

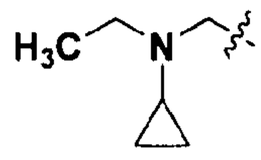
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-51;

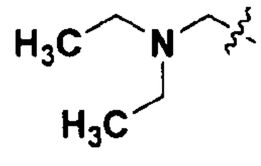
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-17;

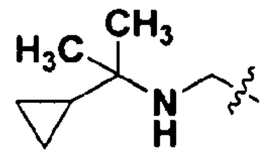
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-4;

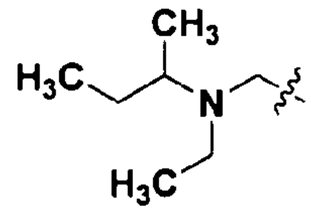
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# 3-5-4;

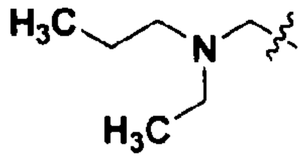
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-70;

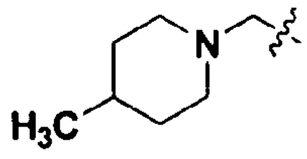
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-45;

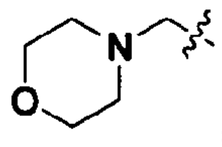
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S4-5-3;

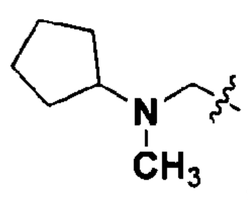
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-6;

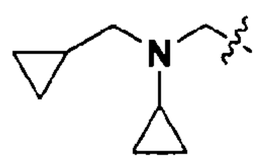
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-63;

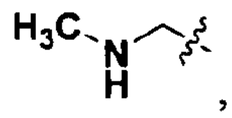
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-40;

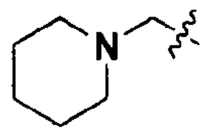
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-19;

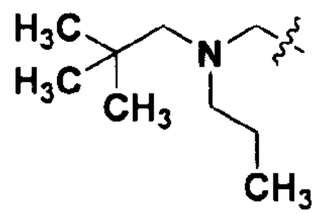
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-9;

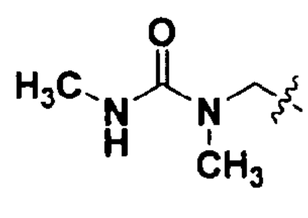
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-27;

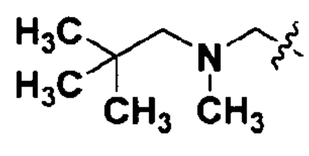
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-14;

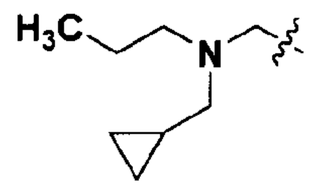
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-17;

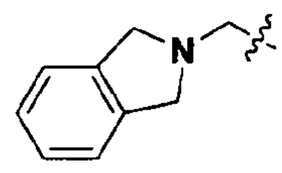
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-8;

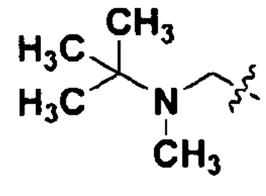
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# 2-4-44;

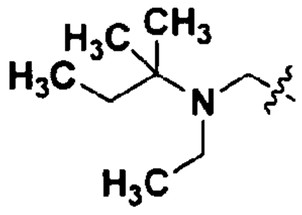
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-10;

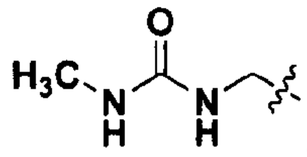
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-21;

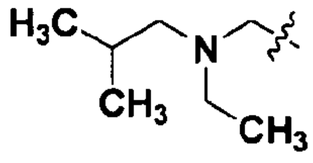
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-38;

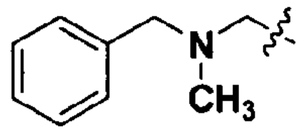
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-39;

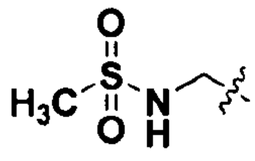
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-25;

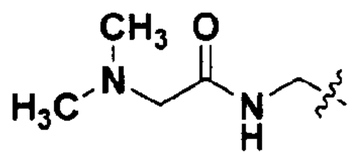
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-33;

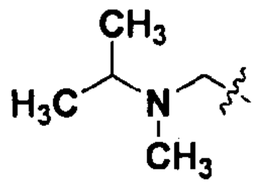
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-3;

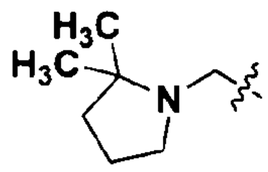
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-50;

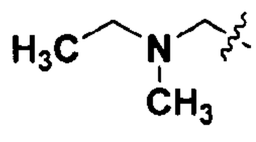
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-46;

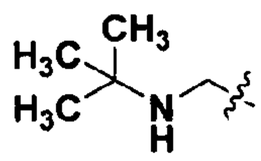
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-5;

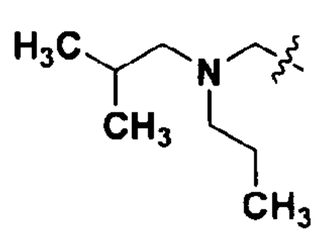
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S7-4-4;

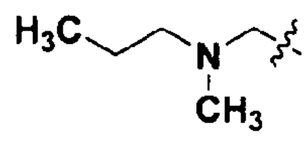
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-24;

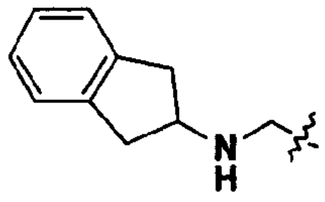
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-12;

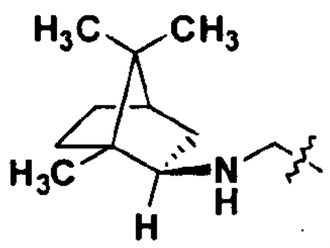
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S4-5-2;

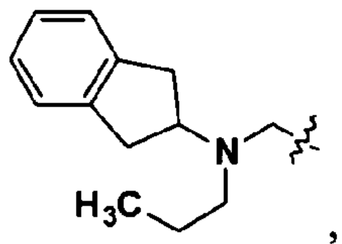
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-3;

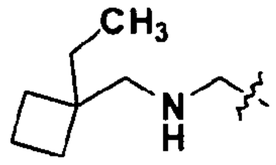
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-49;

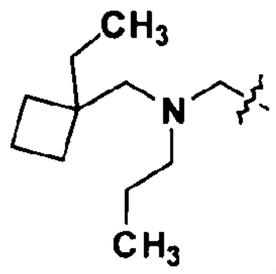
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-41;

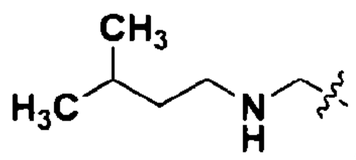
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-90;

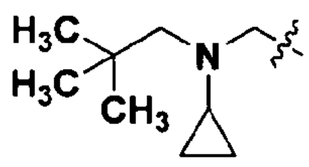
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-114;

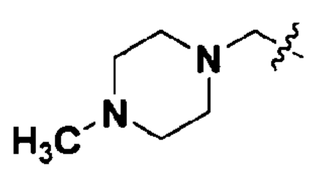
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-88;

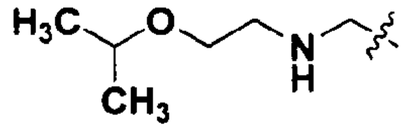
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-91;

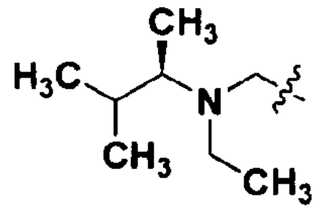
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S1-14-94;

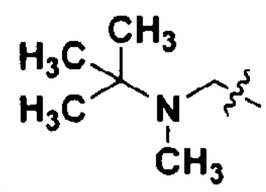
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-15;

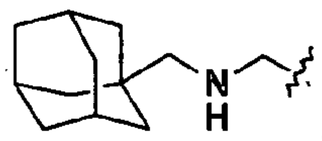
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-48;

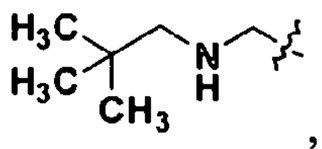
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S4-5-4;

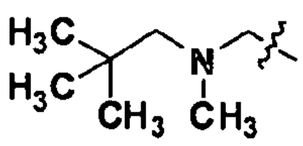
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S3-53;

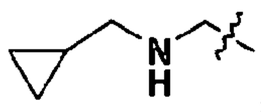
X is fluoro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S2-4-58;

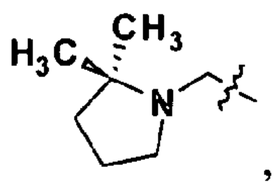
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-11;

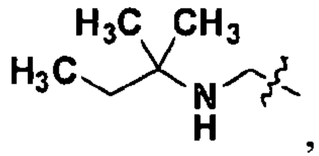
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-9;

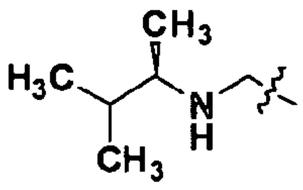
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-5;

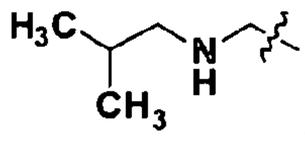
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-11;

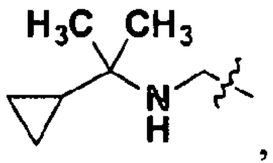
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-6;

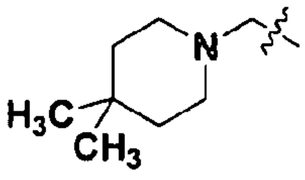
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-4;

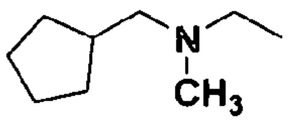
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-2;

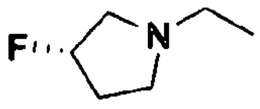
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-8;

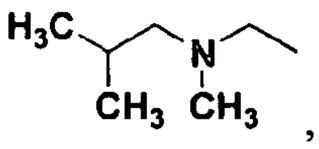
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-1;

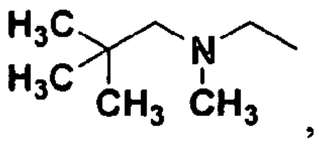
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-3;

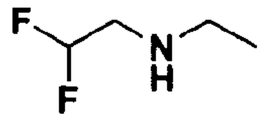
X is chloro and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S15-13-16;

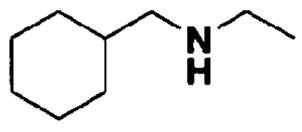
X is $-N(CH_3)_2$ and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S16-10-21;

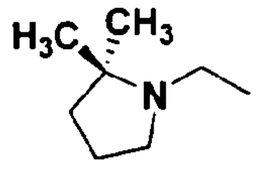
X is $-N(CH_3)_2$ and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S16-10-26;

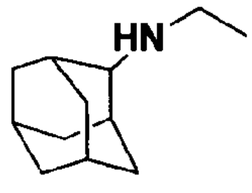
X is $-N(CH_3)_2$ and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S16-10-20;

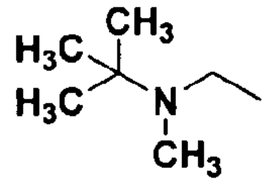
X is $-N(CH_3)_2$ and -CH(R^{1a})-NR^2R^3 is , Cmpd.# S16-10-9;

X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is , Cmpd.# S16-10-13;

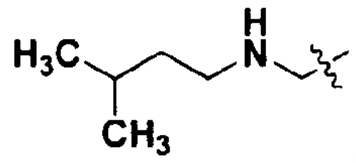
X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is , Cmpd.# S16-10-15;

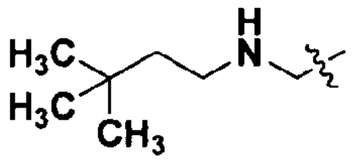
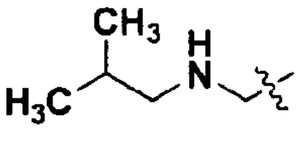
X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is , Cmpd.# S16-10-15;

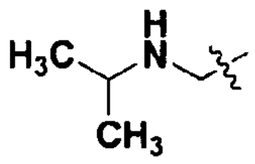
X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is , Cmpd.# S16-10-18; or

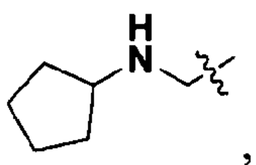
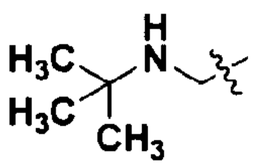
X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is , Cmpd.# S1-14-54.

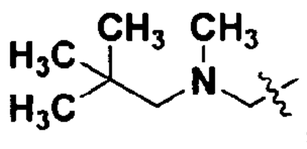
Other specific examples of compounds of the invention are represented by Structural Formulas IIIa, wherein:

$-[C(R^{1a})(R^{1b})]_n-N(R^2)(R^3)$ is , Cmpd.#S20-10-5;

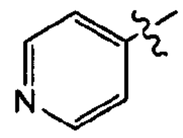
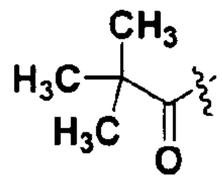
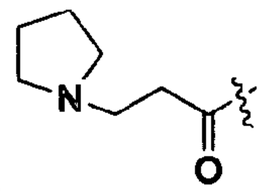
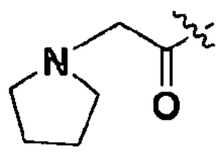
, Cmpd.#S20-10-6; , Cmpd.#S20-10-2;

, Cmpd.# S20-10-7;

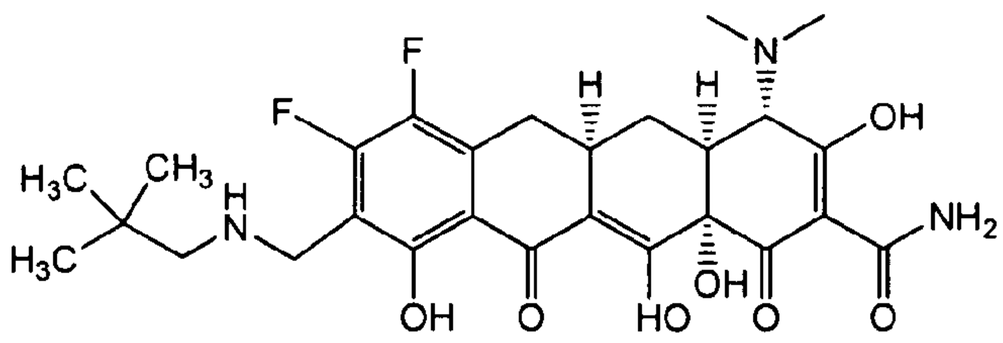
, Cmpd.# S20-10-8; , Cmpd.# S20-10-3; or

, Cmpd.# S20-10-4.

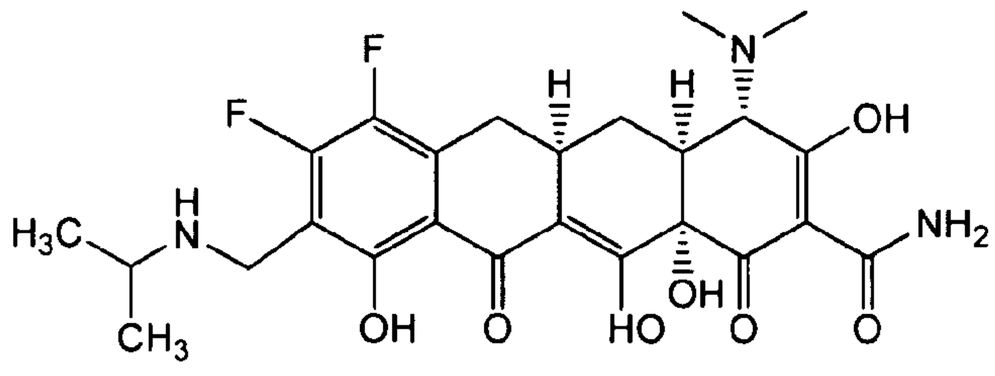
Additional specific examples of compounds of the invention are represented by Structural Formula V, wherein:

R^3 is , Cmpd.# S22-6; , Cmpd.# S21-12-6; , Cmpd.# S21-12-2; or , Cmpd.# S21-12-1.

Additional specific examples of the compounds of the present invention are represented by Structural Formula IVa and IVb, or a pharmaceutically acceptable salt thereof:



IVa and



IVb.

Methods of preparation of the exemplified compounds are provided in Exemplification section.

DEFINITIONS

"Alkyl" means a saturated aliphatic branched or straight-chain monovalent hydrocarbon radical having the specified number of carbon atoms. Thus, "(C_1-C_{12}) alkyl" means a radical having from 1- 12 carbon atoms in a linear or branched arrangement. "(C_1-C_{12})alkyl" includes methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl and dodecyl. Unless otherwise specified, suitable substitutions for a "substituted alkyl" include halogen, -OH, -O-C_1-C_4 alkyl, C_1-C_4 alkyl, fluoro-substituted-C_1-C_4 alkyl, -O-C_1-C_4 fluoroalkyl, -NH_2, -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)$_2$, C_3-C_{10} carbocyclyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl or naphthalenyl), a (4-13 membered)

heterocyclyl (e.g., pyrrolidine, piperidine, piperazine, tetrahydrofuran, tetrahydropyran or morpholine) or -N(R^4)(R^5), wherein R^4 and R^5 are as described above.

As used here, the term "alkylene" refers to a divalent alkyl group that has two points of attachment to the rest of the compound. An alkyl moiety of an alkylene group, alone or as a part of a larger moiety (alkoxy, alkylammonium, and the like) is preferably a straight chained or branched saturated aliphatic group with 1 to about 12 carbon atoms, e.g., methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *tert*-butyl, pentyl, hexyl, heptyl or octyl, or a saturated cycloaliphatic group with 3 to about 12 carbon atoms. Non-limiting examples of alkylene groups include a divalent C1-6 groups such as methylene (-CH_2-), ethylene (-CH_2CH_2-), n-propylene (-$CH_2CH_2CH_2$-), isopropylene (-$CH_2CH(CH_3)$-), and the like. Examples of a divalent C1-6 alkyl group include, for example, a methylene group, an ethylene group, an ethylidene group, an n-propylene group, an isopropylene group, an isobutylene group, an s-butylene group, an n-butylene group, and a t-butylene group.

"Cycloalkyl" means a saturated aliphatic cyclic hydrocarbon radical having the specified number of carbon atoms. (C_3-C_6)cycloalkyl includes cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.The cycloalkyl can be (3-7 membered) monocyclic, (6-13 membered) fused bicyclic, (4-13 membered) bridged bicyclic, (6-13 membered) spiro bicyclic or bridged tricyclic (e.g., adamantyl). Suitable substituents for a "substituted cycloalkyl" include, but are not limited to halogen, -OH, -O-C_1-C_4 alkyl, C_1-C_4 alkyl, fluoro-substituted-C_1-C_4 alkyl, C_3-C_{10} carbocyclyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl or naphthalenyl), a (4-13 membered) heterocyclyl (e.g., pyrrolidine, piperidine, piperazine, tetrahydrofuran, tetrahydropyran or morpholine), or -N(R^4)(R^5), wherein R^4 and R^5 are as described above.

"Heterocycle" means a saturated or partially unsaturated (4-13 membered) heterocyclic ring containing 1, 2, 3 or 4 heteroatoms independently selected from N, O or S, and includes for example heteroaryl. When one heteroatom is S, it can be optionally mono- or di-oxygenated (i.e. -S(O)- or -$S(O)_2$-). The heterocycle can be

(4-7 membered) monocyclic, (6-13 membered) fused bicyclic, (6-13 membered) bridged bicyclic, or (6-13 membered) spiro bicyclic.

Examples of monocyclic heterocycle include, but not limited to, azetidine, pyrrolidine, piperidine, piperazine, hexahydropyrimidine, tetrahydrofuran, tetrahydropyran, morpholine, thiomorpholine, thiomorpholine 1,1-dioxide, tetrahydro-2H-1,2-thiazine, tetrahydro-2H-1,2-thiazine 1,1-dioxide, isothiazolidine, or isothiazolidine 1,1-dioxide.

A fused bicyclic heterocycle has two rings which have two adjacent ring atoms in common. The first ring is a monocyclic heterocycle and the second ring is a cycloalkyl, partially unsaturated carbocycle, phenyl or heteroaryl (e.g., pyrrole, imidazole, pyrazole, oxazole, isoxazole, thiazole, isothiazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-oxadiazole, 1,2,5-thiadiazole, 1,2,5-thiadiazole 1-oxide, 1,2,5-thiadiazole 1,1-dioxide, 1,3,4-thiadiazole, pyridine, pyrazine, pyrimidine, pyridazine, 1,2,4-triazine, 1,3,5-triazine, and tetrazole).

A spiro bicyclic heterocycle has two rings which have only one ring atom in common. The first ring is a monocyclic heterocycle and the second ring is a cycloalkyl, partially unsaturated carbocycle or a monocyclic heterocycle. For example, the second ring is a (C_3-C_6)cycloalkyl. Example of spiro bicyclic heterocycle includes, but not limited to, azaspiro[4.4]nonane, 7-azaspiro[4.4]nonane, azaspiro[4.5]decane, 8-azaspiro[4.5]decane, azaspiro[5.5]undecane, 3-azaspiro[5.5]undecane and 3,9-diazaspiro[5.5]undecane.

A bridged bicyclic heterocycle has two rings which have three or more adjacent ring atoms in common. The first ring is a monocyclic heterocycle and the other ring is a cycloalkyl (such as (C_3-C_6)cycloalkyl), partially unsaturated carbocycle or a monocyclic heterocycle. Examples of bridged bicyclic heterocycles include, but are not limited to, azabicyclo[3.3.1]nonane, 3-azabicyclo[3.3.1]nonane, azabicyclo[3.2.1]octane, 3-azabicyclo[3.2.1]octane, 6-azabicyclo[3.2.1]octane and azabicyclo[2.2.2]octane, 2-azabicyclo[2.2.2]octane.

"Heteroaryl" means a (5-12 membered) monovalent heteroaromatic monocyclic or bicyclic ring radical. A heteroaryl contains 1, 2, 3 or 4 heteroatoms independently selected from N, O, and S. Heteroaryls include, but are not limited to pyrrole, imidazole, pyrazole, oxazole, isoxazole, thiazole, isothiazole, 1,2,3-

triazole, 1,2,4-triazole, 1,3,4-oxadiazole, 1,2,5-thiadiazole, 1,2,5-thiadiazole 1-oxide, 1,2,5-thiadiazole 1,1-dioxide, 1,3,4-thiadiazole, pyridine, pyrazine, pyrimidine, pyridazine, 1,2,4-triazine, 1,3,5-triazine, and tetrazole. Bicyclic heteroaryl rings include, but are not limited to, bicyclo[4.4.0] and bicyclo[4.3.0] fused ring systems such as indolizine, indole, isoindole, indazole, benzimidazole, benzthiazole, purine, quinoline, isoquinoline, cinnoline, phthalazine, quinazoline, quinoxaline, 1,8-naphthyridine, and pteridine.

"Carbocyclyl" and "carbocycle" both mean (3-10 membered) saturated, partially saturated or unsaturated aliphatic cyclic hydrocarbon ring and includes for example aryl. "Carbocyclyl" includes, but are not limited to C_3-C_6 cycloalkyl and aryl. C_3-C_6 cycloalkyl includes, but is not limited to optionally substituted cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

"Aryl" means an aromatic monocyclic or polycyclic (e.g. bicyclic or tricyclic) carbocyclic ring system. Aryl systems include, but not limited to, phenyl, naphthalenyl, fluorenyl, indenyl, azulenyl, and anthracenyl.

"Alkoxy" means an alkyl radical attached through an oxygen linking atom. "(C_1-C_4)-alkoxy" includes methoxy, ethoxy, propoxy, and butoxy.

"Alkylthio" means an alkyl radical attached through a sulfur linking atom. "(C_1-C_4)alkylthio" include methylthio, ethylthio, propylthio and butylthio.

"Alkylsulfinyl" means an alkyl radical attached through a -S(O)- linking group. "(C_1-C_4)alkylsulfinyl" include methylsulfinyl, ethylsulfinyl, propylsulfinyl and butylsulfinyl.

"Alkylsulfonyl" means an alkyl radical attached through a -$S(O)_2$- linking group. "(C_1-C_4)alkylsulfonyl" include methylsulfonyl, ethylsulfonyl, propylsulfonyl and butylsulfonyl.

Haloalkyl and halocycloalkyl include mono, poly, and perhaloalkyl groups where each halogen is independently selected from fluorine, chlorine, and bromine.

"Cycloalkoxy" means a cycloalkyl radical attached through an oxygen linking atom. "(C_3-C_6)cycloalkoxy" includes cyclopropyloxy, cyclobutyloxy, cyclopentyloxy and cyclohexyloxy.

"Aryloxy" means an aryl moiety attached through an oxygen linking atom. Aryloxy includes, but not limited to, phenoxy.

"Arylthio" means an aryl moiety attached through a sulfur linking atom. Arylthio includes, but not limited to, phenylthio.

"Arylsulfinyl" means an aryl moiety attached through a -S(O)- linking group. Arylsulfinyl includes, but not limited to, phenylsulfinyl.

"Arylsulfonyl" means an aryl moiety attached through a $-S(O)_2-$ linking group. Arylsulfonyl includes, but not limited to, phenylsulfonyl.

"Hetero" refers to the replacement of at least one carbon atom member in a ring system with at least one heteroatom selected from N, S, and O. A hetero ring system may have 1, 2, or 3 carbon atom members replaced by a heteroatom.

"Halogen" and "halo" are interchangeably used herein and each refers to fluorine, chlorine, bromine, or iodine.

Another embodiment of the present invention is a pharmaceutical composition comprising one or more pharmaceutically acceptable carrier and/or diluent and a compound disclosed herein or a pharmaceutically acceptable salt thereof.

"Pharmaceutically acceptable carrier" means non-therapeutic components that are of sufficient purity and quality for use in the formulation of a composition of the invention that, when appropriately administered to an animal or human, typically do not produce an adverse reaction, and that are used as a vehicle for a drug substance (i.e. a compound of the present invention).

"Pharmaceutically acceptable diluent" means non-therapeutic components that are of sufficient purity and quality for use in the formulation of a composition of the invention that, when appropriately administered to an animal or human, typically do not produce an adverse reaction, and that are used as a diluting agent for a drug substance (i.e. a compound of the present invention).

Pharmaceutically acceptable salts of the compounds of the present invention are also included. For example, an acid salt of a compound of the present invention containing an amine or other basic group can be obtained by reacting the compound with a suitable organic or inorganic acid, resulting in pharmaceutically acceptable

anionic salt forms. Examples of anionic salts include the acetate, benzenesulfonate, benzoate, bicarbonate, bitartrate, bromide, calcium edetate, camsylate, carbonate, chloride, citrate, dihydrochloride, edetate, edisylate, estolate, esylate, fumarate, glyceptate, gluconate, glutamate, glycollylarsanilate, hexylresorcinate, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isethionate, lactate, lactobionate, malate, maleate, mandelate, mesylate, methylsulfate, mucate, napsylate, nitrate, pamoate, pantothenate, phosphate/diphosphate, polygalacturonate, salicylate, stearate, subacetate, succinate, sulfate, tannate, tartrate, teoclate, tosylate, and triethiodide salts.

Salts of the compounds of the present invention containing a carboxylic acid or other acidic functional group can be prepared by reacting with a suitable base. Such a pharmaceutically acceptable salt may be made with a base which affords a pharmaceutically acceptable cation, which includes alkali metal salts (especially sodium and potassium), alkaline earth metal salts (especially calcium and magnesium), aluminum salts and ammonium salts, as well as salts made from physiologically acceptable organic bases such as trimethylamine, triethylamine, morpholine, pyridine, piperidine, picoline, dicyclohexylamine, N,N'-dibenzylethylenediamine, 2-hydroxyethylamine, bis-(2-hydroxyethyl)amine, tri-(2-hydroxyethyl)amine, procaine, dibenzylpiperidine, dehydroabietylamine, N,N'-bisdehydroabietylamine, glucamine, N-methylglucamine, collidine, quinine, quinoline, and basic amino acids such as lysine and arginine.

The invention also includes various isomers and mixtures thereof. Certain of the compounds of the present invention may exist in various stereoisomeric forms.Stereoisomers are compounds which differ only in their spatial arrangement. Enantiomers are pairs of stereoisomers whose mirror images are not superimposable, most commonly because they contain an asymmetrically substituted carbon atom that acts as a chiral center. "Enantiomer" means one of a pair of molecules that are mirror images of each other and are not superimposable. Diastereomers are stereoisomers that are not related as mirror images, most commonly because they contain two or more asymmetrically substituted carbon atoms. "*R*" and "*S*" represent the configuration of substituents around one or more

chiral carbon atoms. When a chiral center is not defined as R or S, a mixture of both configurations is present.

"Racemate" or "racemic mixture" means a compound of equimolar quantities of two enantiomers, wherein such mixtures exhibit no optical activity; i.e., they do not rotate the plane of polarized light.

The compounds of the invention may be prepared as individual isomers by either isomer-specific synthesis or resolved from an isomeric mixture. Conventional resolution techniques include forming the salt of a free base of each isomer of an isomeric pair using an optically active acid (followed by fractional crystallization and regeneration of the free base), forming the salt of the acid form of each isomer of an isomeric pair using an optically active amine (followed by fractional crystallization and regeneration of the free acid), forming an ester or amide of each of the isomers of an isomeric pair using an optically pure acid, amine or alcohol (followed by chromatographic separation and removal of the chiral auxiliary), or resolving an isomeric mixture of either a starting material or a final product using various well known chromatographic methods.

When the stereochemistry of a disclosed compound is named or depicted by structure, the named or depicted stereoisomer is at least 60%, 70%, 80%, 90%, 99% or 99.9% by weight pure relative to the other stereoisomers. When a single enantiomer is named or depicted by structure, the depicted or named enantiomer is at least 60%, 70%, 80%, 90%, 99% or 99.9% by weight optically pure. Percent optical purity by weight is the ratio of the weight of the enantiomer over the weight of the enantiomer plus the weight of its optical isomer.

The present invention also provides a method of treating a subject with a tetracycline-responsive disease or disorder comprising administering to the subject an effective amount of a compound of the present invention or a pharmaceutically acceptable salt thereof.

"Tetracycline-responsive disease or disorder" refers to a disease or disorder that can be treated, prevented, or otherwise ameliorated by the administration of a tetracycline compound of the present invention. Tetracycline-responsive disease or disorder includes infections, cancer, inflammatory disorders, autoimmune disease, arteriosclerosis, corneal ulceration, emphysema, arthritis, osteoporosis,

osteoarthritis, multiple sclerosis, osteosarcoma, osteomyelitis, bronchiectasis, chronic pulmonary obstructive disease, skin and eye diseases, periodontitis, osteoporosis, rheumatoid arthritis, ulcerative colitis, inflammatory disorders, tumor growth and invasion, metastasis, acute lung injury, stroke, ischemia, diabetes, aortic or vascular aneurysms, skin tissue wounds, dry eye, bone, cartilage degradation, malaria, senescence, diabetes, vascular stroke, neurodegenerative disorders, cardiac disease, juvenile diabetes, acute and chronic bronchitis, sinusitis, and respiratory infections, including the common cold; acute and chronic gastroenteritis and colitis; acute and chronic cystitis and urethritis; acute and chronic dermatitis; acute and chronic conjunctivitis; acute and chronic serositis; uremic pericarditis; acute and chronic cholecystis; cystic fibrosis, acute and chronic vaginitis; acute and chronic uveitis; drug reactions; insect bites; burns and sunburn, bone mass disorder, acute lung injury, chronic lung disorders, ischemia, stroke or ischemic stroke, skin wound, aortic or vascular aneurysm, diabetic retinopathy, hemorrhagic stroke, angiogenesis, and other states for which tetracycline compounds have been found to be active (see, for example, U. S. Patent Nos. 5,789,395; 5,834,450; 6,277,061 and 5,532,227). Compounds of the invention can be used to prevent or control important mammalian and veterinary diseases such as diarrhea, urinary tract infections, infections of skin and skin structure, ear, nose and throat infections, wound infection, mastitis and the like. In addition, methods for treating neoplasms using tetracycline compounds of the invention are also included (van der Bozert et al., Cancer Res., 48: 6686-6690 (1988)).

Infections that can be treated using compounds of the invention (i.e. compound of Structural Formula (I)) or a pharmaceutically acceptable salt thereof include, but are not limited to, skin infections, GI infections, urinary tract infections, genito-urinary infections, respiratory tract infections, sinuses infections, middle ear infections, systemic infections, cholera, influenza, bronchitis, acne, malaria, sexually transmitted disease including syphilis and gonorrhea, Legionnaires' disease, Lyme disease, Rocky Mountain spotted fever, Q fever, typhus, bubonic plague, gas gangrene, hospital acquired infections, leptospirosis, whooping cough, anthrax and infections caused by the agents responsible for lymphogranuloma venereum,

inclusion conjunctivitis, or psittacosis. Infections can be bacterial, fungal, parasitic and viral infections (including those which are resistant to other tetracycline compounds).

In one embodiment, the infection can be caused bacteria. In another embodiment, the infection is caused by a Gram-positive bacteria. In a specific aspect of this embodiment, the infection is caused by a Gram-positive bacteria selected from *S. aureus, S.pneumoniae, P. granulosum* and *P. acnes.*

In another embodiment, the infection is caused by a Gram-negative bacteria. In a specific aspect of this embodiment, the infection is caused by a Gram-negative bacteria selected from *E. coli* or *B. thetaiotaomicron.*

In another embodiment, the infection is caused by an organism selected from the group consisting of *K. pneumoniae, Salmonella, E. hirae, A. baumanii, B. catarrhalis, H. influenzae, P. aeruginosa, E. faecium, E. coli, S. aureus,* and *E. faecalis.* In another embodiment, the infection is caused by an organism selected from the group consisting of rickettsiae, chlamydiae, and *Mycoplasma pneumoniae.* In another embodiment, the infection is caused by an organism resistant to tetracycline. In another embodiment, the infection is caused by an organism resistant to methicillin. In another embodiment, the infection is caused by an organism resistant to vancomycin. In another embodiment the infection is a *Bacillus anthracis* infection. "*Bacillus anthracis* infection" includes any state, diseases, or disorders caused or which result from exposure or alleged exposure to *Bacillus anthracis* or another member of the *Bacillus cereus* group of bacteria.

In a further embodiment, the tetracycline responsive disease or disorder is not a bacterial infection. In another embodiment, the tetracycline compounds of the invention are essentially non-antibacterial. For example, non-antibacterial compounds of the invention may have MIC values greater than about 4 μg/ml (as measured by assays known in the art and/or the assay given in Example 22). Tetracycline responsive disease or disorder also includes diseases or disorders associated with inflammatory process associated states (IPAS). The term "inflammatory process associated state" includes states in which inflammation or inflammatory factors (e.g., matrix metalloproteinases (MMPs), nitric oxide (NO), TNF, interleukins, plasma proteins, cellular defense systems, cytokines, lipid

metabolites, proteases, toxic radicals, adhesion molecules, etc.) are involved or are present in an area in aberrant amounts, e.g., in amounts which may be advantageous to alter, e.g., to benefit the subject. The inflammatory process is the response of living tissue to damage. The cause of inflammation may be due to physical damage, chemical substances, micro-organisms, tissue necrosis, cancer or other agents. Acute inflammation is short-lasting, lasting only a few days. If it is longer lasting however, then it may be referred to as chronic inflammation.

IPASs include inflammatory disorders. Inflammatory disorders are generally characterized by heat, redness, swelling, pain and loss of function. Examples of causes of inflammatory disorders include, but are not limited to, microbial infections (e.g., bacterial and fungal infections), physical agents (e.g., burns, radiation, and trauma), chemical agents (e.g., toxins and caustic substances), tissue necrosis and various types of immunologic reactions.

Examples of inflammatory disorders can be treated using the compounds of the invention (i.e. compound of Structural Formula (I)) or a pharmaceutically acceptable salt thereof include, but are not limited to, osteoarthritis, rheumatoid arthritis, acute and chronic infections (bacterial and fungal, including diphtheria and pertussis); acute and chronic bronchitis, sinusitis, and upper respiratory infections, including the common cold; acute and chronic gastroenteritis and colitis; inflammatory bowel disorder; acute and chronic cystitis and urethritis; vasculitis; sepsis; nephritis; pancreatitis; hepatitis; lupus; inflammatory skin disorders including, for example, eczema, dermatitis, psoriasis, pyoderma gangrenosum, acne rosacea, and acute and chronic dermatitis; acute and chronic conjunctivitis; acute and chronic serositis (pericarditis, peritonitis, synovitis, pleuritis and tendinitis); uremic pericarditis; acute and chronic cholecystis; acute and chronic vaginitis; acute and chronic uveitis; drug reactions; insect bites; burns (thermal, chemical, and electrical); and sunburn.

IPASs also include matrix metalloproteinase associated states (MMPAS). MMPAS include states characterized by aberrant amounts of MMPs or MMP activity. Examples of matrix metalloproteinase associated states ("MMPAS's") can be treated using compounds of the invention or a pharmaceutically acceptable salt thereof,

include, but are not limited to, arteriosclerosis, corneal ulceration, emphysema, osteoarthritis, multiple sclerosis (Liedtke et al., Ann. Neurol. 1998, 44: 35-46; Chandler et al., J. Neuroimmunol. 1997, 72: 155-71), osteosarcoma, osteomyelitis, bronchiectasis, chronic pulmonary obstructive disease, skin and eye diseases, periodontitis, osteoporosis, rheumatoid arthritis, ulcerative colitis, inflammatory disorders, tumor growth and invasion (Stetler-Stevenson et al., Annu. Rev. Cell Biol. 1993, 9: 541 -73; Tryggvason et al., Biochim. Biophys. Acta 1987, 907: 191-217; Li et al., Mol. Carcillog. 1998, 22: 84-89)), metastasis, acute lung injury, stroke, ischemia, diabetes, aortic or vascular aneurysms, skin tissue wounds, dry eye, bone and cartilage degradation (Greenwald et al., Bone 1998,22 : 33-38; Ryan et al., Curr. Op. Rheumatol. 1996, 8: 238- 247). Other MMPAS include those described in U. S. Pat. Nos. 5,459, 135; 5,321,017; 5,308,839; 5,258,371 ; 4,935,412; 4,704,383, 4,666,897, and RE 34,656.

In a further embodiment, the IPAS include disorders described in U.S. Patents Nos. 5,929,055; and 5,532,227.

Tetracycline responsive disease or disorder also includes diseases or disorders associated with NO associated states. The term "NO associated states" includes states which involve or are associated with nitric oxide (NO) or inducible nitric oxide synthase (iNOS). NO associated state includes states which are characterized by aberrant amounts of NO and/or iNOS. Preferably, the NO associated state can be treated by administering tetracycline compounds of the invention. The disorders, diseases and states described in U. S. Patents Nos. 6,231,894; 6,015,804; 5,919,774; and 5,789,395 are also included as NO associated states.

Examples of diseases or disorders associated with NO associated states can be treated using the compounds of the present invention (i.e. compound of Structural Formula (I)) or a pharmaceutically acceptable salt thereof include, but are not limited to, malaria, senescence, diabetes, vascular stroke, neurodegenerative disorders (Alzheimer's disease and Huntington's disease), cardiac disease

(reperfusion-associated injury following infarction), juvenile diabetes, inflammatory disorders, osteoarthritis, rheumatoid arthritis, acute, recurrent and chronic infections (bacterial, viral and fungal); acute and chronic bronchitis, sinusitis, and respiratory infections, including the common cold; acute and chronic gastroenteritis and colitis; acute and chronic cystitis and urethritis; acute and chronic dermatitis; acute and chronic conjunctivitis; acute and chronic serositis (pericarditis, peritonitis, synovitis, pleuritis and tendonitis); uremic pericarditis; acute and chronic cholecystis; cystic fibrosis, acute and chronic vaginitis; acute and chronic uveitis; drug reactions; insect bites; burns (thermal, chemical, and electrical); and sunburn.

In another embodiment, the tetracycline responsive disease or disorder is cancer. Examples of cancers that can be treated using the compounds of the invention (i.e. compound of Structural Formula (I)) or a pharmaceutically acceptable salt thereof include all solid tumors, i.e., carcinomas e.g., adenocarcinomas, and sarcomas. Adenocarcinomas are carcinomas derived from glandular tissue or in which the tumor cells form recognizable glandular structures. Sarcomas broadly include tumors whose cells are embedded in a fibrillar or homogeneous substance like embryonic connective tissue. Examples of carcinomas which may be treated using the methods of the invention include, but are not limited to, carcinomas of the prostate, breast, ovary, testis, lung, colon, and breast. The methods of the invention are not limited to the treatment of these tumor types, but extend to any solid tumor derived from any organ system. Examples of treatable cancers include, but are not limited to, colon cancer, bladder cancer, breast cancer, melanoma, ovarian carcinoma, prostate carcinoma, lung cancer, and a variety of other cancers as well. The methods of the invention also cause the inhibition of cancer growth in adenocarcinomas, such as, for example, those of the prostate, breast, kidney, ovary, testes, and colon. In one embodiment, the cancers treated by methods of the invention include those described in U. S. Patent Nos. 6,100,248; 5,843,925; 5,837,696; or 5,668,122.

Alternatively, the tetracycline compounds may be useful for preventing or reducing the likelihood of cancer recurrence, for example, to treat residual cancer following surgical resection or radiation therapy. The tetracycline compounds useful

according to the invention are especially advantageous as they are substantially nontoxic compared to other cancer treatments.

In a further embodiment, the compounds of the invention are administered in combination with standard cancer therapy, such as, but not limited to, chemotherapy.

Examples of tetracycline responsive states can be treated using the compounds of the invention (i.e. compound of Structural Formula (I)) or a pharmaceutically acceptable salt thereof also include neurological disorders which include both neuropsychiatric and neurodegenerative disorders, but are not limited to, such as Alzheimer's disease, dementias related to Alzheimer's disease (such as Pick's disease), Parkinson's and other Lewy diffuse body diseases, senile dementia, Huntington's disease, Gilles de la Tourette's syndrome, multiple sclerosis, amyotrophic lateral sclerosis (ALS), progressive supranuclear palsy, epilepsy, and Creutzfeldt-Jakob disease; autonomic function disorders such as hypertension and sleep disorders, and neuropsychiatric disorders, such as depression, schizophrenia, schizoaffective disorder, Korsakoff s psychosis, mania, anxiety disorders, or phobic disorders; learning or memory disorders, e. g., amnesia or age-related memory loss, attention deficit disorder, dysthymic disorder, major depressive disorder, mania, obsessive-compulsive disorder, psychoactive substance use disorders, anxiety, phobias, panic disorder, as well as bipolar affective disorder, e. g., severe bipolar affective (mood) disorder (BP-I), bipolar affective neurological disorders, e. g. , migraine and obesity.

Further neurological disorders include, for example, those listed in the American Psychiatric Association's Diagnostic and Statistical manual of Mental Disorders (DSM).

In another embodiment, the tetracycline responsive disease or disorder is diabetes. Diabetes that can be treated using the compounds of the invention or a pharmaceutically acceptable salt thereof include, but are not limited to, juvenile diabetes, diabetes mellitus, diabetes type I, or diabetes type II. In a further embodiment, protein glycosylation is not affected by the administration of the tetracycline compounds of the invention. In another embodiment, the tetracycline

compound of the invention is administered in combination with standard diabetic therapies, such as, but not limited to insulin therapy.

In another embodiment, the tetracycline responsive disease or disorder is a bone mass disorder. Bone mass disorders that can be treated using the compounds of the invention or a pharmaceutically acceptable salt thereof include disorders where a subjects bones are disorders and states where the formation, repair or remodeling of bone is advantageous. For examples bone mass disorders include osteoporosis (e. g. , a decrease in bone strength and density), bone fractures, bone formation associated with surgical procedures (e. g., facial reconstruction), osteogenesis imperfecta (brittle bone disease), hypophosphatasia, Paget's disease, fibrous dysplasia, osteopetrosis, myeloma bone disease, and the depletion of calcium in bone, such as that which is related to primary hyperparathyroidism. Bone mass disorders include all states in which the formation, repair or remodeling of bone is advantageous to the subject as well as all other disorders associated with the bones or skeletal system of a subject which can be treated with the tetracycline compounds of the invention. In a further embodiment, the bone mass disorders include those described in U. S. Patents Nos. 5,459, 135; 5,231,017; 5,998,390; 5,770,588; RE 34,656; 5,308,839; 4,925,833; 3,304,227; and 4,666,897.

In another embodiment, the tetracycline responsive disease or disorder is acute lung injury. Acute lung injuries that can be treated using the compounds of the invention or a pharmaceutically acceptable salt thereof include adult respiratory distress syndrome (ARDS), post-pump syndrome (PPS), and trauma. Trauma includes any injury to living tissue caused by an extrinsic agent or event. Examples of trauma include, but are not limited to, crush injuries, contact with a hard surface, or cutting or other damage to the lungs.

The tetracycline responsive disease or disorder of the invention also includes chronic lung disorders. Examples of chronic lung disorders that can be treated using the compounds of the invention or a pharmaceutically acceptable salt thereof include, but are not limited, to asthma, cystic fibrosis, chronic obstructive pulmonary disease (COPD), and emphysema. In a further embodiment, the acute and/or chronic lung disorders that can be treated using the compounds of the

invention or a pharmaceutically acceptable salt thereof include those described in U. S. Patents No. 5,977,091 ; 6,043,231 ; 5,523,297; and 5,773,430.

In yet another embodiment, the tetracycline responsive disease or disorder is ischemia, stroke, or ischemic stroke.

In a further embodiment, the tetracycline compounds of the invention or a pharmaceutically acceptable salt thereof can be used to treat such disorders as described above and in U. S. Patents No. 6,231,894; 5,773,430; 5,919,775 and 5,789,395.

In another embodiment, the tetracycline responsive disease or disorder is a skin wound. The invention also provides a method for improving the healing response of the epithelialized tissue (e.g., skin, mucosae) to acute traumatic injury (e.g., cut, burn, scrape, etc.). The method includes using a tetracycline compound of the invention or a pharmaceutically acceptable salt thereof to improve the capacity of the epithelialized tissue to heal acute wounds. The method may increase the rate of collagen accumulation of the healing tissue. The method may also decrease the proteolytic activity in the epithelialized tissue by decreasing the collagenolytic and/or gellatinolytic activity of MMPs. In a further embodiment, the tetracycline compound of the invention or a pharmaceutically acceptable salt thereof is administered to the surface of the skin (e. g., topically). In a further embodiment, the tetracycline compound of the invention or a pharmaceutically acceptable salt thereof is used to treat a skin wound, and other such disorders as described in, for example, U. S. Patent Nos. 5,827,840; 4,704,383; 4,935,412; 5,258,371 ; 5,308,839, 5,459, 135; 5,532,227; and 6,015,804.

In yet another embodiment, the tetracycline responsive disease or disorder is an aortic or vascular aneurysm in vascular tissue of a subject (e.g., a subject having or at risk of having an aortic or vascular aneurysm, etc.). The tetracycline compound or a pharmaceutically acceptable salt thereof may be effective to reduce the size of the vascular aneurysm or it may be administered to the subject prior to the onset of the vascular aneurysm such that the aneurysm is prevented. In one embodiment, the vascular tissue is an artery, e.g., the aorta, e.g., the abdominal aorta. In a further

embodiment, the tetracycline compounds of the invention are used to treat disorders described in U. S. Patent Nos. 6,043,225 and 5,834,449.

The compounds of the invention or a pharmaceutically acceptable salt thereof can be used alone or in combination with one or more therapeutic agent in the methods of the invention disclosed herein.

The language "in combination with" another therapeutic agent or treatment includes co-administration of the tetracycline compound and with the other therapeutic agent or treatment as either a single combination dosage form or as multiple, separate dosage forms, administration of the tetracycline compound first, followed by the other therapeutic agent or treatment and administration of the other therapeutic agent or treatment first, followed by the tetracycline compound.

The other therapeutic agent may be any agent that is known in the art to treat, prevent, or reduce the symptoms of a tetracycline-responsive disease or disorder. The choice of additional therapeutic agent(s) is based upon the particular tetracycline-responsive disease or disorder being treated. Such choice is within the knowledge of a treating physician. Furthermore, the other therapeutic agent may be any agent of benefit to the patient when administered in combination with the administration of a tetracycline compound.

As used herein, the term "subject" means a mammal in need of treatment, e.g., companion animals (e.g., dogs, cats, and the like), farm animals (e.g., cows, pigs, horses, sheep, goats and the like) and laboratory animals (e.g., rats, mice, guinea pigs and the like). Typically, the subject is a human in need of the specified treatment.

As used herein, the term "treating" or 'treatment" refers to obtaining desired pharmacological and/or physiological effect. The effect can be prophylactic or therapeutic, which includes achieving, partially or substantially, one or more of the following results: partially or totally reducing the extent of the disease, disorder or syndrome; ameliorating or improving a clinical symptom or indicator associated with the disorder; delaying, inhibiting or decreasing the likelihood of the progression of the disease, disorder or syndrome; or partially or totally delaying, inhibiting or

reducing the likelihood of the onset or development of disease, disorder or syndrome.

"Effective amount" means that amount of active compound agent that elicits the desired biological response in a subject. Such response includes alleviation of the symptoms of the disease or disorder being treated. In one embodiment, the effective amount of a compound of the invention is from about 0.01 mg/kg/day to about 1000 mg/kg/day, from about 0.1 mg/kg/day to about 100 mg/kg/day, or from about 0.5 mg/kg/day to about 50 mg/kg/day.

The invention further includes the process for making the composition comprising mixing one or more of the present compounds and an optional pharmaceutically acceptable carrier; and includes those compositions resulting from such a process, which process includes conventional pharmaceutical techniques.

The compositions of the invention include ocular, oral, nasal, transdermal, topical with or without occlusion, intravenous (both bolus and infusion), and injection (intraperitoneally, subcutaneously, intramuscularly, intratumorally, or parenterally). The composition may be in a dosage unit such as a tablet, pill, capsule, powder, granule, liposome, ion exchange resin, sterile ocular solution, or ocular delivery device (such as a contact lens and the like facilitating immediate release, timed release, or sustained release), parenteral solution or suspension, metered aerosol or liquid spray, drop, ampoule, auto-injector device, or suppository; for administration ocularly, orally, intranasally, sublingually, parenterally, or rectally, or by inhalation or insufflation.

Compositions of the invention suitable for oral administration include solid forms such as pills, tablets, caplets, capsules (each including immediate release, timed release, and sustained release formulations), granules and powders; and, liquid forms such as solutions, syrups, elixirs, emulsions, and suspensions. Forms useful for ocular administration include sterile solutions or ocular delivery devices. Forms useful for parenteral administration include sterile solutions, emulsions, and suspensions.

The compositions of the invention may be administered in a form suitable for once-weekly or once-monthly administration. For example, an insoluble salt of the active compound may be adapted to provide a depot preparation for

intramuscular injection (e.g., a decanoate salt) or to provide a solution for ophthalmic administration.

The dosage form containing the composition of the invention contains an effective amount of the active ingredient necessary to provide a therapeutic effect. The composition may contain from about 5,000 mg to about 0.5 mg (preferably, from about 1,000 mg to about 0.5 mg) of a compound of the invention or salt form thereof and may be constituted into any form suitable for the selected mode of administration. The composition may be administered about 1 to about 5 times per day. Daily administration or post-periodic dosing may be employed.

For oral administration, the composition is preferably in the form of a tablet or capsule containing, e.g., 500 to 0.5 milligrams of the active compound. Dosages will vary depending on factors associated with the particular patient being treated (e.g., age, weight, diet, and time of administration), the severity of the condition being treated, the compound being employed, the mode of administration, and the strength of the preparation.

The oral composition is preferably formulated as a homogeneous composition, wherein the active ingredient is dispersed evenly throughout the mixture, which may be readily subdivided into dosage units containing equal amounts of a compound of the invention. Preferably, the compositions are prepared by mixing a compound of the invention (or pharmaceutically acceptable salt thereof) with one or more optionally present pharmaceutical carriers (such as a starch, sugar, diluent, granulating agent, lubricant, glidant, binding agent, and disintegrating agent), one or more optionally present inert pharmaceutical excipients (such as water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, and syrup), one or more optionally present conventional tableting ingredients (such as corn starch, lactose, sucrose, sorbitol, talc, stearic acid, magnesium stearate, dicalcium phosphate, and any of a variety of gums), and an optional diluent (such as water).

Binder agents include starch, gelatin, natural sugars (e.g., glucose and beta-lactose), corn sweeteners and natural and synthetic gums (e.g., acacia and tragacanth). Disintegrating agents include starch, methyl cellulose, agar, and bentonite.

Tablets and capsules represent an advantageous oral dosage unit form.Tablets may be sugarcoated or filmcoated using standard techniques. Tablets may also be coated or otherwise compounded to provide a prolonged, control-release therapeutic effect. The dosage form may comprise an inner dosage and an outer dosage component, wherein the outer component is in the form of an envelope over the inner component. The two components may further be separated by a layer which resists disintegration in the stomach (such as an enteric layer) and permits the inner component to pass intact into the duodenum or a layer which delays or sustains release. A variety of enteric and non-enteric layer or coating materials (such as polymeric acids, shellacs, acetyl alcohol, and cellulose acetate or combinations thereof) may be used.

Compounds of the invention may also be administered via a slow release composition; wherein the composition includes a compound of the invention and a biodegradable slow release carrier (e.g., a polymeric carrier) or a pharmaceutically acceptable non-biodegradable slow release carrier (e.g., an ion exchange carrier).

Biodegradable and non-biodegradable slow release carriers are well known in the art. Biodegradable carriers are used to form particles or matrices which retain an active agent(s) and which slowly degrade/dissolve in a suitable environment (e.g., aqueous, acidic, basic and the like) to release the agent. Such particles degrade/dissolve in body fluids to release the active compound(s) therein. The particles are preferably nanoparticles (e.g., in the range of about 1 to 500 nm in diameter, preferably about 50-200 nm in diameter, and most preferably about 100 nm in diameter). In a process for preparing a slow release composition, a slow release carrier and a compound of the invention are first dissolved or dispersed in an organic solvent. The resulting mixture is added into an aqueous solution containing an optional surface-active agent(s) to produce an emulsion. The organic solvent is then evaporated from the emulsion to provide a colloidal suspension of particles containing the slow release carrier and the compound of the invention.

The compound disclosed herein may be incorporated for administration orally or by injection in a liquid form such as aqueous solutions, suitably flavored syrups, aqueous or oil suspensions, flavored emulsions with edible oils such as cottonseed oil, sesame oil, coconut oil or peanut oil and the like, or in elixirs or

similar pharmaceutical vehicles. Suitable dispersing or suspending agents for aqueous suspensions, include synthetic and natural gums such as tragacanth, acacia, alginate, dextran, sodium carboxymethylcellulose, methylcellulose, polyvinyl-pyrrolidone, and gelatin. The liquid forms in suitably flavored suspending or dispersing agents may also include synthetic and natural gums. For parenteral administration, sterile suspensions and solutions are desired. Isotonic preparations, which generally contain suitable preservatives, are employed when intravenous administration is desired.

The compounds may be administered parenterally *via* injection. A parenteral formulation may consist of the active ingredient dissolved in or mixed with an appropriate inert liquid carrier. Acceptable liquid carriers usually comprise aqueous solvents and other optional ingredients for aiding solubility or preservation. Such aqueous solvents include sterile water, Ringer's solution, or an isotonic aqueous saline solution. Other optional ingredients include vegetable oils (such as peanut oil, cottonseed oil, and sesame oil), and organic solvents (such as solketal, glycerol, and formyl). A sterile, non-volatile oil may be employed as a solvent or suspending agent. The parenteral formulation is prepared by dissolving or suspending the active ingredient in the liquid carrier whereby the final dosage unit contains from 0.005 to 10% by weight of the active ingredient. Other additives include preservatives, isotonizers, solubilizers, stabilizers, and pain-soothing agents. Injectable suspensions may also be prepared, in which case appropriate liquid carriers, suspending agents and the like may be employed.

Compounds of the invention may be administered intranasally using a suitable intranasal vehicle.

Compounds of the invention may also be administered topically using a suitable topical transdermal vehicle or a transdermal patch.

For ocular administration, the composition is preferably in the form of an ophthalmic composition. The ophthalmic compositions are preferably formulated as eye-drop formulations and filled in appropriate containers to facilitate administration to the eye, for example a dropper fitted with a suitable pipette. Preferably, the compositions are sterile and aqueous based, using purified water. In addition to the

compound of the invention, an ophthalmic composition may contain one or more of: a) a surfactant such as a polyoxyethylene fatty acid ester; b) a thickening agents such as cellulose, cellulose derivatives, carboxyvinyl polymers, polyvinyl polymers, and polyvinylpyrrolidones, typically at a concentration n the range of about 0.05 to about 5.0% (wt/vol); c) (as an alternative to or in addition to storing the composition in a container containing nitrogen and optionally including a free oxygen absorber such as Fe), an anti-oxidant such as butylated hydroxyanisol, ascorbic acid, sodium thiosulfate, or butylated hydroxytoluene at a concentration of about 0.00005 to about 0.1% (wt/vol); d) ethanol at a concentration of about 0.01 to 0.5% (wt/vol); and e) other excipients such as an isotonic agent, buffer, preservative, and/or pH-controlling agent. The pH of the ophthalmic composition is desirably within the range of 4 to 8.

In certain embodiments, the composition of this invention includes one or more additional agents. The other therapeutic agent may be ay agent that is capable of treating, preventing or reducing the symptoms of a tetracycline-responsive disease or disorder. Alternatively, the other therapeutic agent may be any agent of benefit to a patient when administered in combination with the tetracycline compound in this invention.

The following abbreviations are used in the synthesis examples below.

Abbreviations

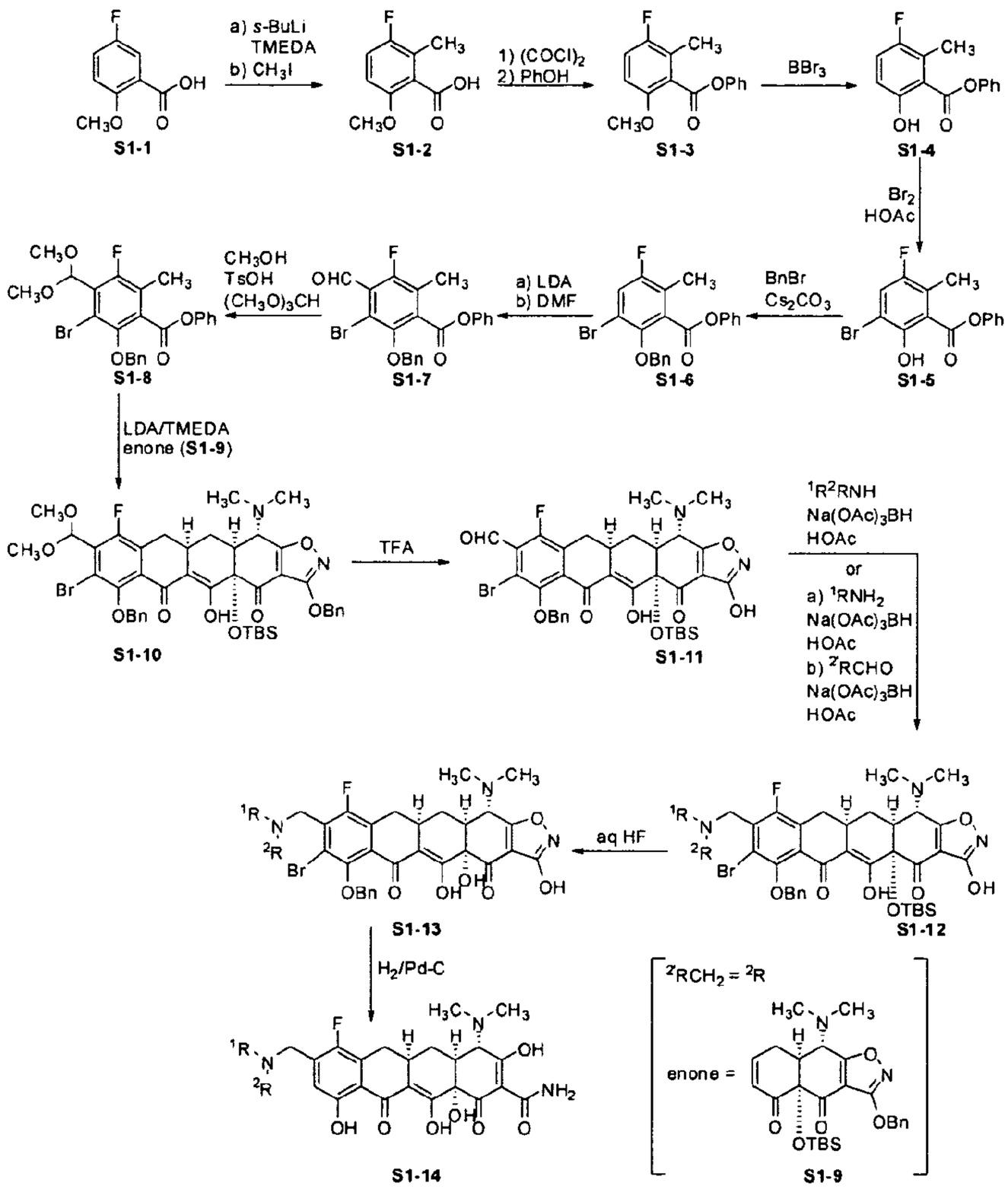
Ac	acetyl
AIBN	2,2'-azobis(2-methylpropionitrile)
aq	aqueous
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bu	butyl
Cbz	benzyloxycarbonyl
Cy	tricyclohexylphosphine
dba	dibenzylideneacetone
DIBAL-H	diisobutylaluminum hydride
DIEA	*N,N*-diisopropylethylamine
DMAP	4-(dimethylamino)pyridine

DME	1,2-dimethoxyethane
DMF	*N,N*-dimethylformamide
DMPU	1,3-dimethyl-3,4-5,6-tetrahydro-2(1*H*)-pyrimidone
DMSO	dimethyl sulfoxide
EDC	*N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide
ESI	electrospray ionization
Et	ethyl
EtOAc	ethyl acetate
HPLC	high performance liquid chromatography
HOBt	1-hydroxybenzotriazole
i	iso
IBX	2-iodoxybenzoic acid
LDA	lithium diisopropylamide
LHMDS	lithium bis(trimethylsilyl)amide
LTMP	lithium 2,2,6,6-tetramethylpiperidide
MeOH	methanol
Ms	methanesulfonyl
MS	mass spectrometry
MTBE	methyl *tert*-butyl ether
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance spectrometry
Ph	phenyl
Pr	propyl
s	secondary
t	tertiary
TMEDA	*N,N,N'N'*-tetramethylethylenediamine
TBS	*tert*-butyldimethylsilyl
TEA	triethylamine
Tf	trifluoromathanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride

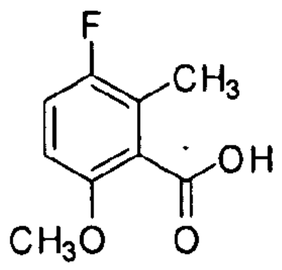
	THF	tetrahydrofuran
	TLC	thin layer chromatography
	Ts	*para*-toluenesulfonyl
	TsOH	*para*-toluenesulfonic acid
5	Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

Example 1. Synthesis of Compounds via Scheme 1.

Scheme 1

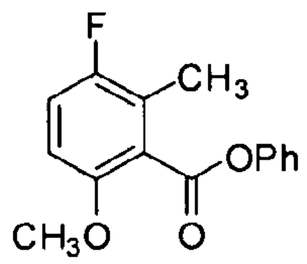


The following compounds were prepared according to Scheme 1.



S1-2

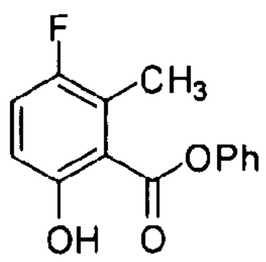
To a THF solution of 5-fluoro-2-methoxybenzoic acid (**S1-1**, 0.50 g, 2.94 mmol, 1.0 equiv, Aldrich 523097) cooled at -78 °C was added a THF solution of *s*-BuLi (4.60 mL, 1.40 M/cyclohexane, 6.44 mmol, 2.2 equiv) and TMEDA (0.97 mL, 6.47 mmol, 2.2 equiv). The reaction was stirred at -78 °C for 2 hrs. Iodomethane (1.10 mL, 17.64 mmol, 6.0 equiv) was added to the reaction mixture dropwise. The reaction was allowed to warm to 25 °C over 1 h and stirred at 25 °C for 1 h. Aqueous NaOH (6 N, 20 mL) was added. The resulting mixture was extracted with *t*-butylmethyl ether (20 mL × 2). The aqueous layer was acidified with hydrochloric acid (6 N) to pH 1 and extracted with EtOAc (20 mL × 4). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give 0.51 g of crude **S1-2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (dd, J = 9.8, 8.5 Hz, 1 H), 6.75 (dd, J = 9.8, 3.7 Hz, 1 H), 3.86 (s, 3 H), 2.34 (d, J = 2.4 Hz, 3 H); MS (ESI) *m/z* 185.12 (M+H).



S1-3

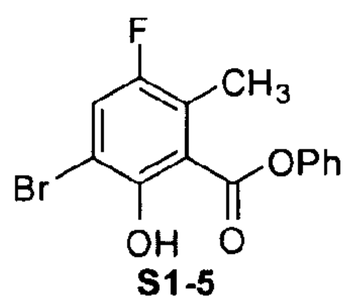
Oxalyl chloride (0.95 mL, 11.10 mmol, 5.5 equiv) was added to a dichloromethane solution (15 mL, anhydrous) of **S1-2** (0.51 g, 2.00 mmol, 1.0 equiv). DMF (0.1 mL) was added to the resulting mixture. The reaction was stirred at 25 °C for 1 h and concentrated. The resulting solid was redissovled in 15 mL of anhydrous dichloromethane. Phenol (0.52 g, 5.50 mmol, 2.8 equiv), DMAP (0.67 g, 5.60 mmol, 2.8 equiv), and triethylamine (1.90 mL, 13.90 mmol, 7.0 equiv) were added to the reaction mixture. The reaction was stirred at 25 °C for 12 hrs and concentrated. EtOAc and H_2O were added to the residue. The organic layer was washed with aqueous NaOH (1 N), H_2O, and brine, dried over sodium sulfate, and concentrated. Flash chromatography on silica gel (40:1 hexanes/EtOAc) yielded

0.40 g of compound **S1-3** (52%, 2 steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.41 (m, 2 H), 7.31-7.24 (m, 3 H), 7.08 (dd, *J* = 9.2, 9.2 Hz, 1 H), 6.77 (dd, *J* = 9.2, 3.7 Hz, 1 H), 3.88 (s, 3 H), 2.36 (d, *J* = 2.3 Hz, 3 H); MS (ESI) *m/z* 261.12 (M+H).



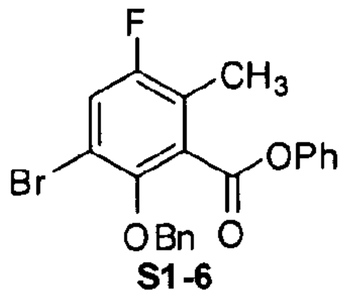
S1-4

BBr_3 (1.85 mL, 1 M/dichloromethane, 1.85 mmol, 1.2 equiv) was added to a dichloromethane solution (8 mL) of **S1-3** (0.40 g, 1.54 mmol, 1.0 equiv) at -78 °C. The reaction was stirred from -78 °C to 25 °C for 1.5 hrs, quenched by saturated aqueous $NaHCO_3$, and concentrated. EtOAc and H_2O were added to the reaction mixture. The aqueous layer was extracted with EtOAc. The combined EtOAc extracts were dried over sodium sulfate and concentrated under reduced pressure to yield 0.36 g of crude **S1-4**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.66 (s, 1 H), 7.50-7.44 (m, 2 H), 7.36-7.31 (m,1 H), 7.26-7.18 (m, 3 H), 6.86 (dd, *J* = 9.3, 4.9 Hz, 1 H), 2.60 (d, *J* = 2.4 Hz, 3 H); MS (ESI) *m/z* 245.11 (M-H).



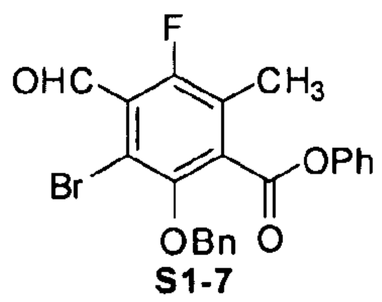
S1-5

Compound **S1-4** (4.92 g, 95% purity, 20.00 mmol, 1.0 equiv) was dissolved in acetic acid (50 mL). Bromine (1.54 mL, 30.00 mmol, 1.5 equiv) was added *via* syringe at rt. After stirring at rt for 2 hrs, LC/MS indicated that the starting material was consumed. The reaction mixture was diluted with EtOAc, washed with water (3 x 100 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give 7.06 g of compound **S1-5** as a light yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.14 (s, 1 H), 7.52 (d, *J* = 9.2 Hz, 1 H), 7.49-7.43 (m, 2 H), 7.36-7.30 (m, 1 H), 7.21-7.16 (m, 2 H), 2.55 (d, *J* = 2.3 Hz, 3 H).



S1-6

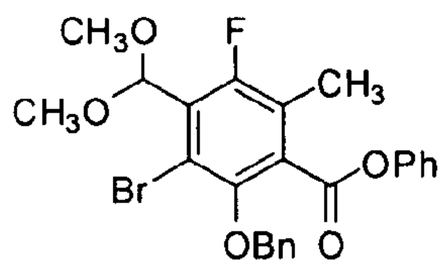
Compound **S1-5** (crude, 1.06 g, 2.97 mmol, 1.0 equiv) was dissolve in acetone (20 mL), added with potassium carbonate (0.82 g, 5.94 mmol, 2.0 equiv), and cooled to 0 °C in an ice-bath. Benzyl bromide (540 µL, 4.45 mmol, 1.5 equiv) was added dropwise. After 2 hrs, LC/MS indicated that 40% of the starting material was consumed. The reaction mixture was heated to 50 °C for another hour and the starting material was completely consumed. The reaction mixture was diluted with EtOAc (100 mL), washed with water and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give 2.2 g of crude **S1-6**, which was purified by column chromatography (Biotage 10 g column, 2 to 5% EtOAc in hexanes gradient), yielding 1.03 g (84%, two steps) of the pure compound **S1-6** as an colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2 H), 7.40-7.33 (m, 6 H), 7.25 (t, J = 7.3 Hz, 1 H), 7.04 (d, J = 8.6 Hz, 2 H), 5.09 (s, 2 H), 2.32 (d, J = 1.8 Hz, 3 H).



S1-7

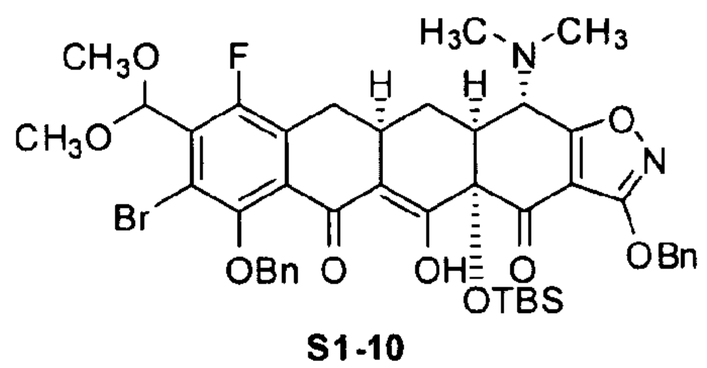
An LDA/THF solution was prepared by adding *n*-BuLi (1.6 M/hexanes, 5.10 mL, 8.16 mmol, 1.5 equiv) to diisopropylamine (1.15 mL, 8.16 mmol, 1.5 equiv) in THF (15 mL) at -78 °C. The reaction mixture was warmed to -20 °C and stirred for 15 min. After the LDA solution was cooled to -78 °C, compound **S1-6** (2.26 g, 5.44 mmol, 1.0 equiv) in THF (5 mL) was added dropwise. An orange-red solution was formed. After 10 min, DMF (1.26 mL, 16.30 mmol, 3.0 equiv) was added dropwise. The reaction solution was allowed to warm to -20 °C in 1 h and quenched by saturated aqueous NH_4Cl. LC/MS indicated that the starting material was consumed. The reaction mixture was diluted with EtOAc (100 mL), washed with water and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. This gave 2.42 g of crude **S1-7**, which was purified by column chromatography

(Biotage 24 g column, 5 to 10% EtOAc in hexanes gradient), yielding 2.23 g (92%) of the pure compound **S1-7** as a light yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1 H), 7.51-7.47 (m, 2 H), 7.40-7.33 (m, 5 H), 7.27 (t, J = 7.3 Hz, 1 H), 7.06-7.02 (m, 2 H), 5.12 (s, 2 H), 2.37 (d, J = 2.3 Hz, 3 H).



S1-8

To a solution of compound **S1-7** (10 g, 22.60 mmol, 1.0 equiv) in MeOH was added trimethylorthoformate (4.8 g, 45.20 mmol, 2.0 equiv) and $TsOH\cdot H_2O$ (0.13 g, 0.68 mmol, 0.03 equiv) at rt. The reaction mixture was heated to reflux overnight and concentrated under reduced pressure. The residue was diluted with H_2O and extracted with EtOAc. The organic layer was dried over sodium sulfate and evaporated to dryness. The crude product was purified by column chromatography on silica gel (petroleum ether:EtOAc from 100:1 to 30:1) to afford compound **S1-8** as a light yellow solid (10g, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.45 (m, 2 H), 7.25-7.35 (m, 5 H), 7.16-7.21 (m, 1 H), 6.98 (d, J = 8.0 Hz, 2 H), 5.71 (s, 1 H), 5.04 (s, 2 H), 3.46 (s, 6 H), 2.29 (d, J = 2.4 Hz, 3 H).

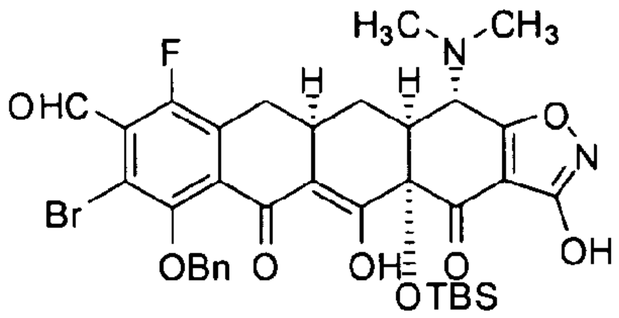


S1-10

Compound **S1-8** (1.37 g, 2.80 mmol, 3.0 equiv) and enone **S1-9** (0.45 g, 0.93 mmol, 1.0 equiv) were dissolved in dry THF (5 mL) under N_2. Freshly prepared LDA/TMEDA/THF (0.71 M/THF, 7.9 mL, 5.60 mmol, 2.0 equiv) was added to the solution at -78 °C. The solution was stirred at -78 °C for about 10 min, and then the temperature was slowly increased from -78 °C to -10 °C over 20 min. The reaction mixture was quenched by saturated aqueous NH_4Cl (50 mL) and extracted with EtOAc (50 ml x 3). The organic phase was dried over sodium sulfate and evaporated under reduced pressure to afford the crude product. The crude product was purified by column chromatography on silica gel (petroleum ether: EtOAc: from 50:1 to

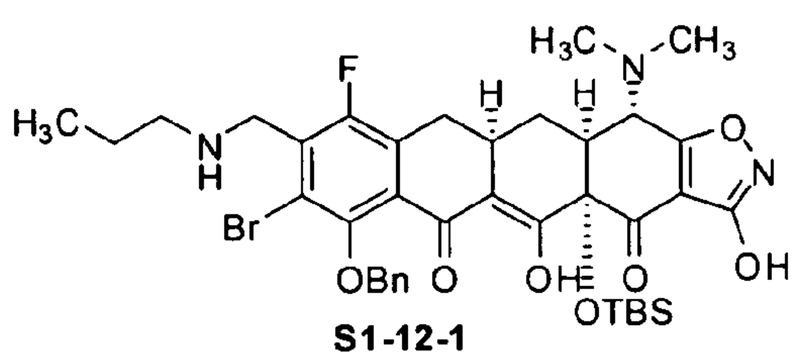
15:1) to give the desired compound **S1-10** (0.60 g, 0.68 mmol, 74%): ^{1}H NMR (400 MHz, CD_3OD) δ 15.97 (s, 1 H), 7.61-7.59 (m, 2 H), 7.55-7.53 (m, 2 H)□7.42-7.40 (m, 6 H), 5.83 (s, 1 H), 5.40 (s, 2 H), 5.02-4.97 (m, 2 H)□3.96 (d, *J* = 10.8 Hz, 1 H), 3.57 (s, 6 H), 3.35-3.26 (m, 1 H), 3.09-2.95 (m, 1 H), 2.67-2.58 (m, 1 H), 2.53 (s, 6 H), 2.50-2.39 (m, 1 H), 2.21-2.10 (m, 1 H), 1.58 (s, 9 H), 0.31 (s, 3 H), 0.16 (s, 3 H); MS (ESI) *m/z* 877.3 (M+H).

Preparation of LDA/TMEDA/THF: To diisopropylamine (1.1 g, 10.90 mmol, 1.0 equiv) and TMEDA (5 mL) in dry THF (5 mL) at -78 °C was added *n*-BuLi (4.8 mL, 2.5 M/hexanes, 12.00 mmol, 1.1 equiv) dropwise under N_2. The solution was stirred at -78 °C for 1 h. The prepared LDA/TMEDA/THF solution was about 0.71 M and was used immediately.



S1-11

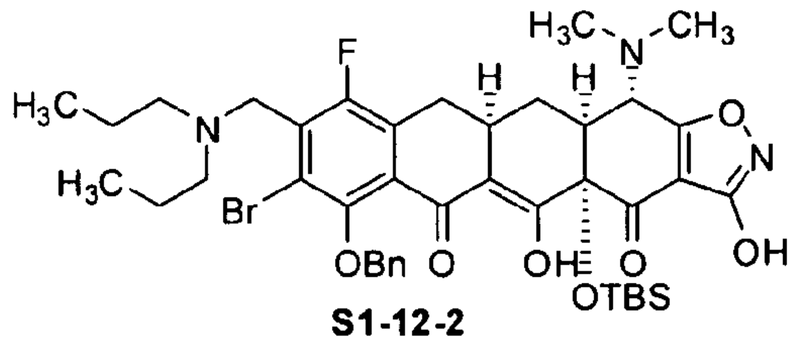
Compound **S1-10** (50 mg, 0.057 mmol, 1.0 equiv) was dissolved in dry dichloromethane (1 mL). TFA (0.5 mL) was added. The solution was stirred at 10 °C for 1 h. LC-MS analysis showed the complete consumption of starting material. The reaction mixture was washed with H_2O (10 mL x 3) and concentrated under reduced pressure to give crude **S1-11**, which was used for the next step without further purification: MS (ESI) *m/z* 741.1 (M+H).



S1-12-1

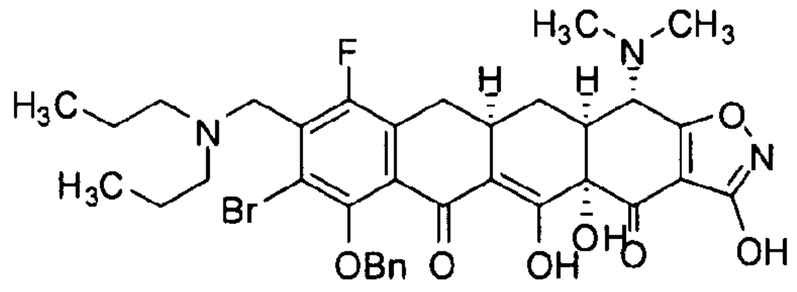
Compound **S1-11** (crude, 0.057 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (2 mL). HOAc (20 μL) and *n*-propylamine (49 mg, 0.34 mmol, 6.0 equiv) were added. The mixture was stirred for 1 h. $Na(OAc)_3BH$ (73 mg, 0.34 mmol, 6.0 equiv) was added and the resulting mixture was stirred for another hour. The mixture was washed with H_2O (10 mL) and concentrated to give crude **S1-12-1**,

which was used for the next step without further purification: MS (ESI) *m/z* 786.2 (M+H).



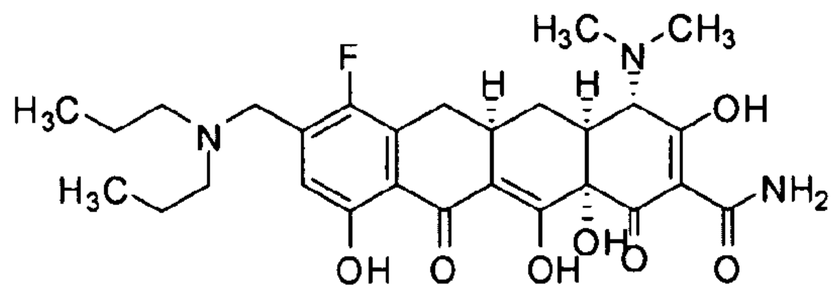
S1-12-2

Compound **S1-12-1** (crude, 0.057 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (2 mL). HOAc (20 μL) and propionaldehyde (49 mg, 0.34 mmol, 6.0 equiv) were added. The mixture was stirred for 1 h. $Na(OAc)_3BH$ (73 mg, 0.34 mmol, 6.0 equiv) was added and the resulting mixture was stirred for another hour. The mixture was washed with H_2O (10 mL) and concentrated to give crude **S1-12-2**, which was used for the next step without further purification: MS (ESI) *m/z* 828.2 (M+H).



S1-13-2

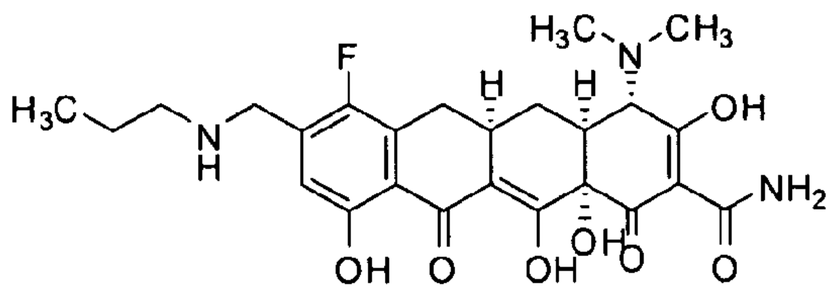
Compound **S1-12-2** (crude, 0.057 mmol, 1.0 equiv) was dissolved in THF (5 mL) in a polypropylene tube at rt. Aqueous HF (2 mL, 48-50%) was added. The reaction mixture was stirred at rt for 1 h. The resulting mixture was carefully poured into an aqueous solution of K_2HPO_4. The pH of the mixture was adjusted to 7-8 by adding more aqueous K_2HPO_4. The mixture was extracted with EtOAc (20 mL), and the EtOAc extract was concentrated to give crude **S1-13-2**, which was used for the next step without further purification: MS (ESI) *m/z* 714.0 (M+H).



S1-14-2

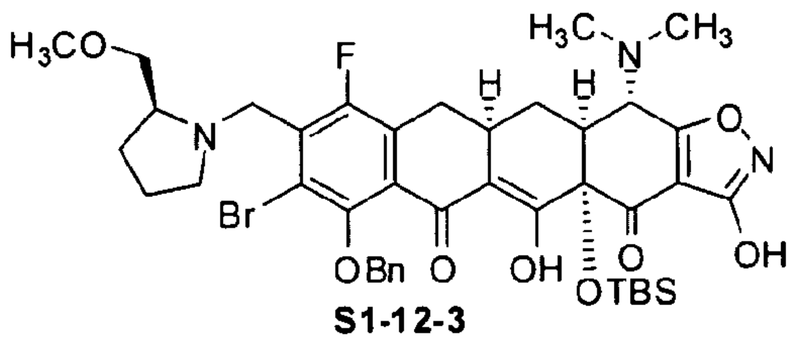
Compound **S1-13-2** (crude, 0.057 mmol, 1.0 equiv) was dissolved in MeOH (5 mL). HCl/MeOH(1 mL, 4 M) and 10% Pd-C (15 mg) was added. The reaction

mixture was purged with hydrogen and stirred under H_2 (balloon) at rt for 1 h. The mixture was filtered and concentrated. The crude compound was purified by preparative HPLC using similar conditions for **S2-4-1** to afford the desired compound **S1-14-2** as a yellow solid (10 mg, 32%, 5 steps): ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 6.0 Hz, 1 H), 4.41 (s, 2 H), 4.10 (s, 1 H), 3.18-2.91 (m, 13 H), 2.37-2.23 (m, 2 H), 1.83-1.73 (m, 4 H), 1.67-1.58 (m, 1 H), 0.96 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 546.2 (M+H).



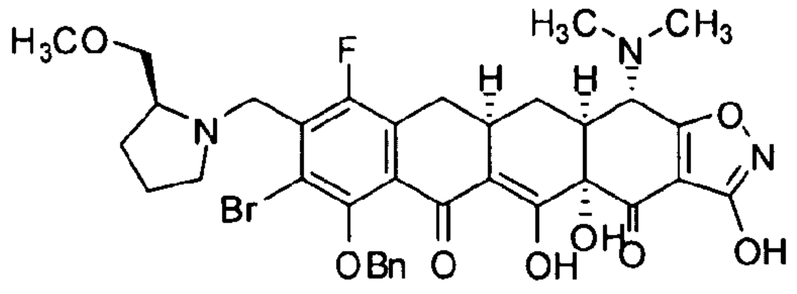
S1-14-1

Similarly, compound **S1-14-1** was prepared driectly from **S1-12-1** *via* HF treatment followed by hydrogenation: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, J = 6.0 Hz, 1 H), 4.27 (s, 2 H), 4.12 (s, 1 H), 3.21 (dd, J = 15.1, 4.6 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.94 (d, J = 6.9 Hz, 2 H), 3.14-2.98 (m, 2 H), 2.21-2.39 (m, 2 H), 1.82-1.71 (m, 2 H), 1.70-1.58 (m, 1 H), 1.02 (t, J = 7.6 Hz, 3 H); MS (ESI) *m/z* 504.44 (M+H).



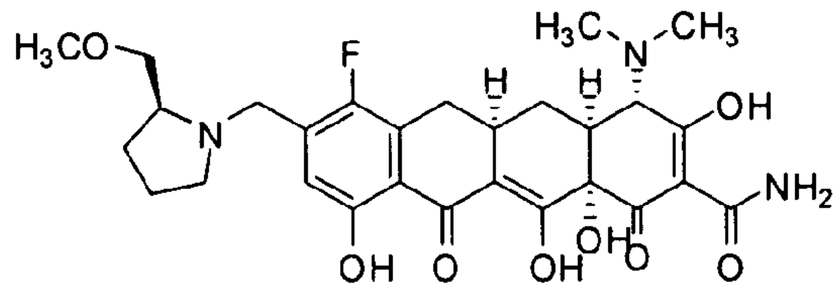
S1-12-3

Compound **S1-11** (crude, 0.057 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (2 mL). HOAc (20 μL) and (*S*)-(+)-2-(methyoxymethyl)pyrrolidine (49 mg, 0.34 mmol, 6.0 equiv) were added. The mixture was stirred at rt for 1 h. $Na(OAc)_3BH$ (73 mg,0.34 mmol, 6.0 equiv) was added and the resulting mixture was stirred for another hour. The mixture was washed with H_2O (10 mL) and concentrated to give crude **S1-12-3**, which was used for the next step without further purification: MS (ESI) *m/z* 842.3 (M+H).



S1-13-3

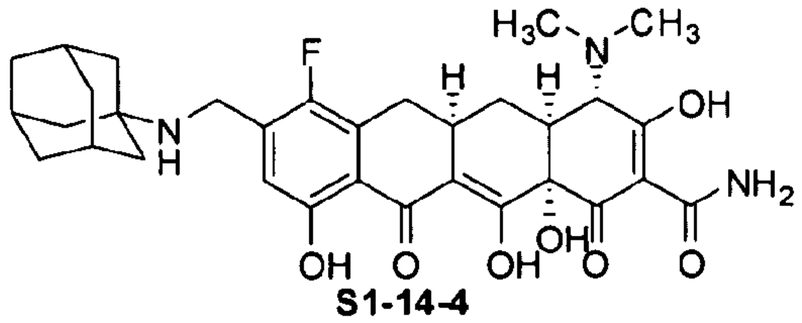
Compound **S1-12-3** (crude, 0.057 mmol, 1.0 equiv) was dissolved in THF (5 mL) in a polypropylene tube at rt. Aqueous HF (2 mL, 48-50%) was added. The reaction mixture was stirred at rt for 1 h. The resulting mixture was poured into an aqueous solution of K_2HPO_4. The pH of the mixture was adjusted to 7-8 with more aqueous K_2HPO_4. The mixture was extracted with EtOAc (20 mL), and the EtOAc extract was concentrated to give crude **S1-13-3**, which was used for the next step without further purification: MS (ESI) *m/z* 728.2 (M+H).



S1-14-3

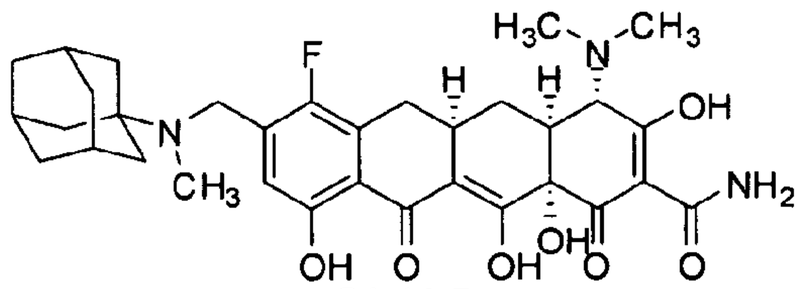
Compound **S1-13-3** (crude, 0.057 mmol, 1.0 equiv) was dissolved in MeOH (5 mL). HCl/MeOH (1 mL, 4 M) and 10% Pd-C (15 mg) was added. The reaction mixture was purged with hydrogen and stirred under H_2 (balloon) at rt for 1 h. The mixture was filtered and concentrated. The crude product was purified by preparative HPLC using similar conditions for **S2-4-1** to afford the desired compound **S1-14-3** as a yellow solid (10 mg, 31%, 4 steps): ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, *J* = 5.6 Hz, 1 H), 4.68 (d, *J* = 13.2 Hz, 1 H), 4.29 (d, *J* = 13.2 Hz, 1 H), 4.10 (s, 1 H), 3.85-3.82 (m, 1 H), 3.71-3.59 (m, 2 H), 3.46-3.41 (m, 1 H), 3.39 (s, 3 H), 3.26-2.93 (m, 10 H), 2.33-2.24 (m, 3 H), 2.22-2.09 (m, 1 H), 1.95-1.81 (m, 2 H), 1.63-1.55 (m, 1 H); MS (ESI) *m/z* 560.1 (M+H).

The following compounds were prepared similarly to **S1-14-1**, **S1-14-2**, or **S1-14-3**.



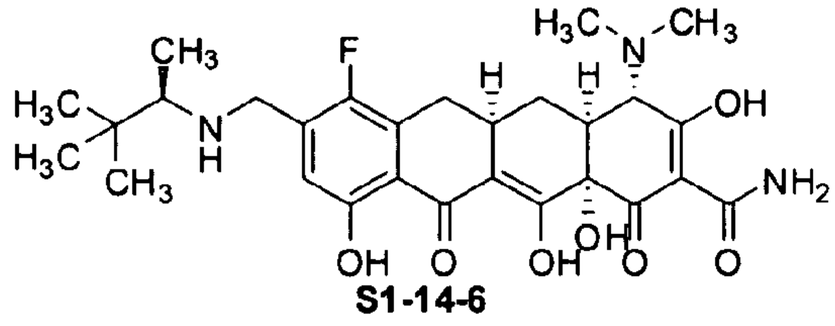
S1-14-4

S1-14-4: ^{1}H NMR (400 MHz, CD_3OD with DCl) δ 7.09 (d, *J* = 5.96 Hz, 1 H), 4.23 (s, 2 H), 4.16 (s, 1 H), 3.26-2.94 (m, 9 H), 2.38-2.20 (m, 5 H), 2.12-2.00 (m, 6 H), 1.84-1.71 (m, 6 H), 1.70-1.56 (m, 1 H); MS (ESI) *m/z* 596.18 (M+H).



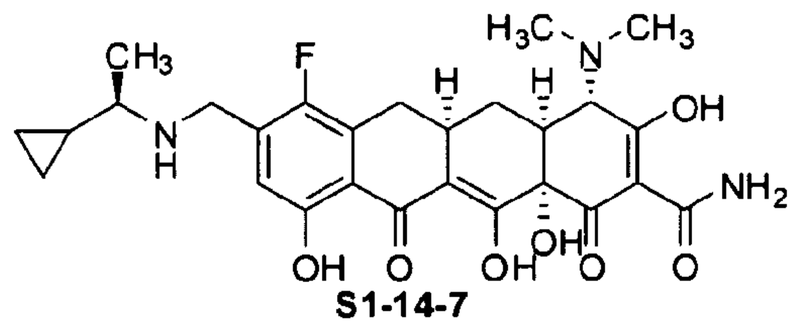
S1-14-5

S1-14-5: ^{1}H NMR (400 MHz, CD_3OD with DCl) δ 7.09 (d, *J* = 5.5 Hz, 1 H), 4.89-4.79 (m, 1 H), 4.17 (s, 1 H), 3.98-3.89 (m, 1 H), 3.26-2.94 (m, 9 H), 2.74 (s, 3 H), 2.38-2.05 (m, 11 H), 1.84-1.71 (m, 6 H), 1.70-1.56 (m, 1 H); MS (ESI) *m/z* 610.19 (M+H).



S1-14-6

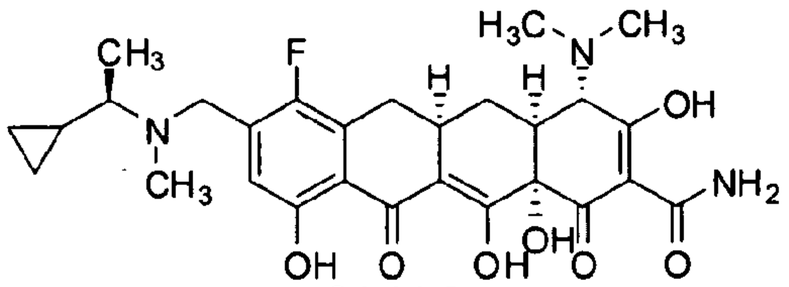
S1-14-6: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.40 (d, *J* = 14.2 Hz, 1 H), 4.34 (d, *J* = 14.2 Hz, 1 H), 4.10 (s, 1 H), 3.21 (dd, *J* = 15.5, 4.6 Hz, 1 H), 3.04 (s, 3 H), 2.95 (s, 3 H), 3.17-2.97 (m, 2 H), 2.34 (t, *J* = 14.7 Hz, 1 H), 2.28-2.20 (m, 1 H), 1.69-1.59 (m, 1 H), 1.34 (d, *J* = 6.9 Hz, 3 H), 1.00 (s, 9 H); MS (ESI) *m/z* 546.30 (M+H).



S1-14-7

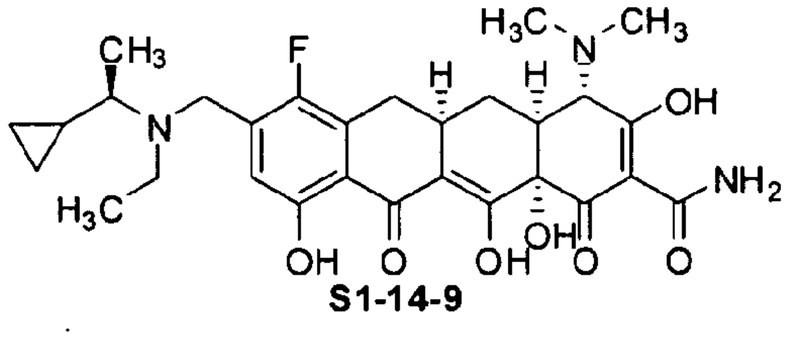
S1-14-7: ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, *J* = 6.0 Hz, 1 H), 4.40 (d, *J* = 14.2 Hz, 1 H), 4.29 (d, *J* = 14.2 Hz, 1 H), 4.10 (s, 1 H), 3.21 (dd, *J* = 15.5, 4.6 Hz,

1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.17-2.97 (m, 2 H), 2.73 (m, 1 H), 2.34 (t, J = 14.7 Hz, 1 H), 2.23 (m, 1 H), 1.69-1.59 (m, 1 H), 1.46 (d, J = 6.9 Hz, 3 H), 1.00 (s, 9 H), 1.07-0.99 (m, 1 H), 0.79-0.72 (m, 2 H), 0.63-0.55 (m, 1 H), 0.41-0.32 (m, 1 H); MS (ESI) *m/z* 530.25 (M+H).



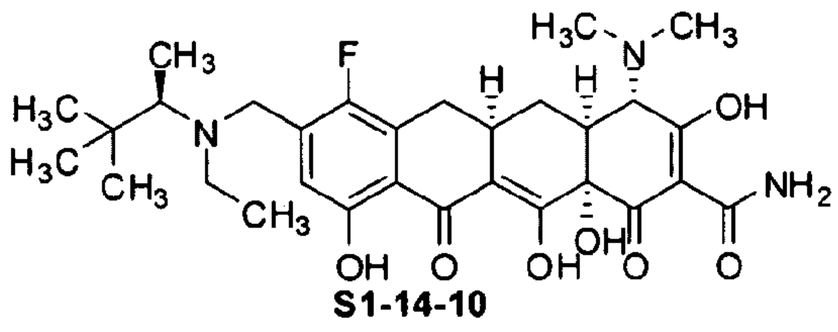
S1-14-8

S1-14-8: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.69 (dd, J = 30.2, 13.3 Hz, 1 H), 4.20 (dd, J = 30.2, 13.3 Hz, 1 H), 4.11 (s, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.26-2.97 (m, 3 H), 2.85 (d, J = 21.1 Hz, 3 H), 2.36 (t, J = 14.6 Hz, 1 H), 2.29-2.21 (m, 1 H), 1.69-1.60 (m, 1 H), 1.52 (t, J = 5.0 Hz, 3 H), 1.30-1.12 (m, 1 H), 0.90-0.74 (m, 2 H), 0.72-0.64 (m, 1 H), 0.59-0.51 (m, 1 H), 0.49-0.37 (m, 1 H); MS (ESI) *m/z* 544.28 (M+H).



S1-14-9

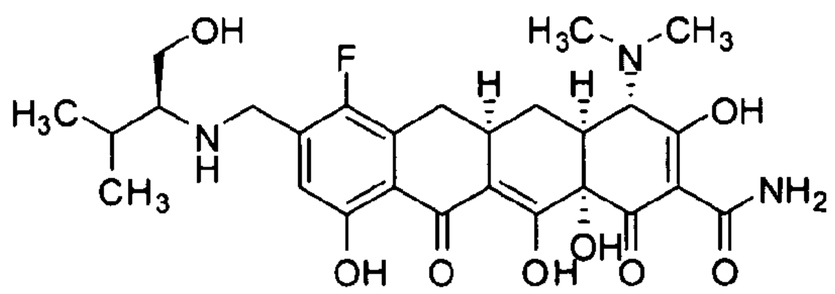
S1-14-9: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 6.0 Hz, 1 H), 4.73 (dd, J = 29.8, 13.3 Hz, 1 H), 4.25 (dd, J = 30.2, 13.3 Hz, 1 H), 4.10 (s, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.50-2.97 (m, 5 H), 2.36 (t, J = 14.6 Hz, 1 H), 2.28-2.20 (m, 1 H), 1.70-1.60 (m, 1 H), 1.48 (dd, J = 18.3, 6.4 Hz, 3 H), 1.29 (dt, J = 30.7, 6.4 Hz, 1 H), 0.90-0.73 (m, 2 H), 0.65-0.49 (m, 2 H), 0.46-0.37 (m, 1 H); MS (ESI) *m/z* 558.29 (M+H).



S1-14-10

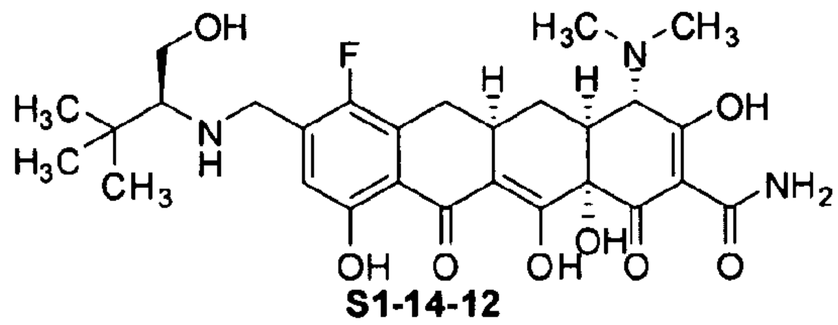
S1-14-10: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 6.0 Hz, 1 H), 4.58 (d, J = 13.2 Hz, 1 H), 4.17 (d, J = 13.2 Hz, 1 H), 4.11 (s, 1 H), 3.63-3.55 (m, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.25-2.97 (m, 5 H), 2.36 (t, J = 14.7 Hz, 1 H), 2.30-2.22 (m, 1

H), 1.71-1.61 (m, 1 H), 1.36 (d, *J* = 6.9 Hz, 3 H), 1.21 (s, 9 H); MS (ESI) *m/z* 574.32 (M+H).



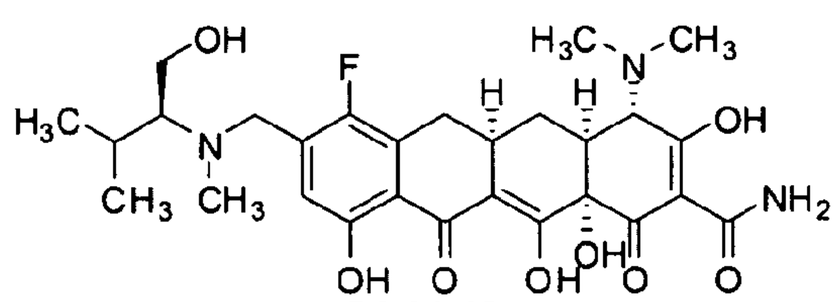
S1-14-11

S1-14-11: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.39 (t, *J* = 13.3 Hz, 2 H), 4.13 (s, 1 H), 3.93 (dd, *J* = 12.3, 2.7 Hz, 1 H), 3.80 (dd, *J* = 12.4, 6.9 Hz, 1 H), 3.06 (s, 3 H), 2.97 (s, 3 H), 3.23-2.97 (m, 4 H), 2.37-2.23 (m, 2 H), 2.22-2.16 (m, 1 H), 2.13 (d, *J* = 1.4 Hz, 1 H), 1.68-1.58 (m, 1 H), 1.06 (dd, *J* = 23.4, 6.4 Hz, 6 H); MS (ESI) *m/z* 548.25 (M+H).



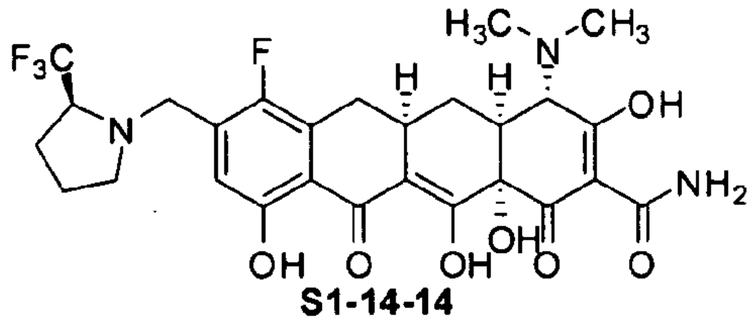
S1-14-12

S1-14-12: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 6.0 Hz, 1 H), 4.48 (m, 2 H), 4.13 (s, 1 H), 3.98 (dd, *J* = 12.4, 2.7 Hz, 1 H), 3.85 (dd, *J* = 11.0, 7.8 Hz, 1 H), 3.06 (s, 3 H), 2.98 (s, 3 H), 3.23-2.97 (m, 4 H), 2.40-2.23 (m, 2 H), 2.10 (d, *J* = 1.4 Hz, 1 H), 1.69-1.59 (m, 1 H), 1.06 (s, 9 H); MS (ESI) *m/z* 562.26 (M+H).



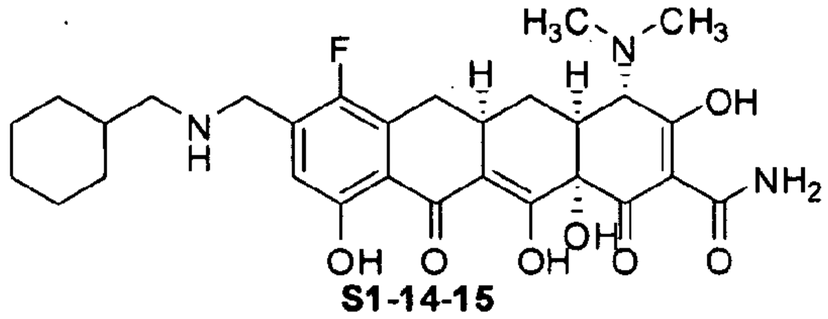
S1-14-13

S1-14-13: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (br, s, 1 H), 4.71 (d, *J* = 13.3 Hz, 1 H), 4.39 (d, *J* = 13.3 Hz, 1 H), 4.13 (s, 1 H), 4.04-3.88 (m, 2 H), 3.80 (dd, *J* = 12.4, 6.9 Hz, 1 H), 3.06 (s, 3 H), 2.97 (s, 3 H), 3.23-2.92 (m, 7 H), 2.47-2.23 (m, 3 H), 1.69-1.59 (m, 1 H), 1.18-1.02 (m, 6 H); MS (ESI) *m/z* 562.27 (M+H).



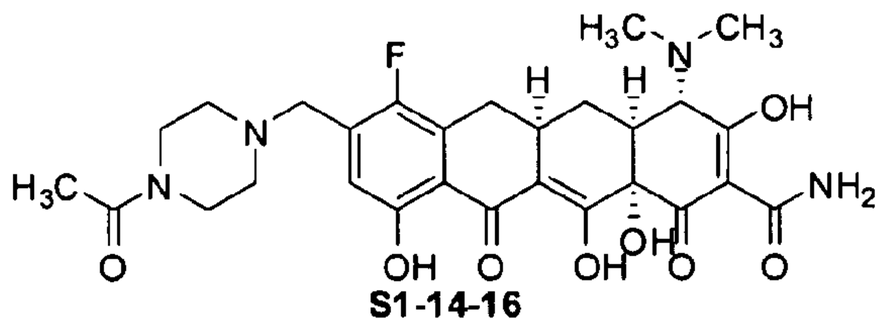
S1-14-14

S1-14-14: ^{1}H NMR (400 MHz, CD_3OD) δ 6.98 (d, J = 5.5 Hz, 1 H), 4.25 (d, J = 14.7 Hz, 1 H), 4.05 (d, J = 14.7 Hz, 1 H), 4.08 (s, 1 H), 3.81-3.73 (m, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.27-2.97 (m, 4 H), 2.76 (m, 1 H), 2.35-2.17 (m, 3 H), 2.09-1.99 (m, 1 H), 1.99-1.87 (m, 2 H), 1.69-1.59 (m, 1 H); MS (ESI) *m/z* 584.26 (M+H).



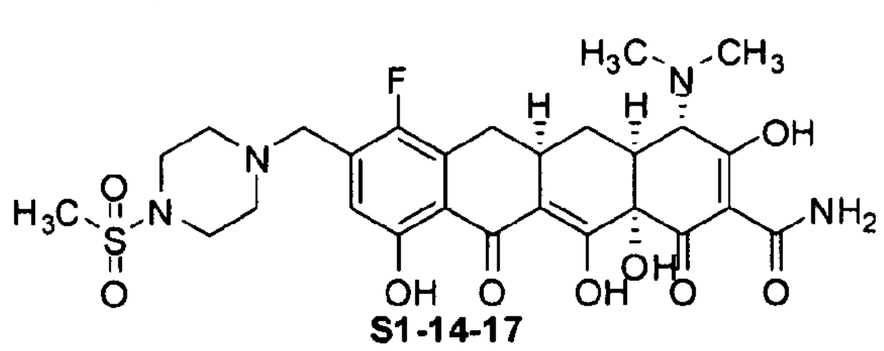
S1-14-15

S1-14-15: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 5.9 Hz, 1 H), 4.27 (s, 2 H), 4.12 (s, 1 H), 3.02 (s, 3 H), 3.27-2.96 (m, 8 H), 2.40-2.24 (m, 2 H), 1.87-1.58 (m, 7 H), 1.40-1.19 (m, 3 H), 1.11-0.98 (m, 2 H); MS (ESI) *m/z* 558.31 (M+H).



S1-14-16

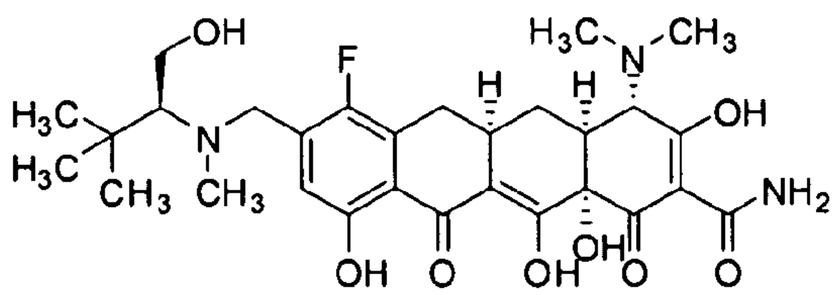
S1-14-16: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.5 Hz, 1 H), 4.45 (s, 2 H), 4.10 (s, 1 H), 3.27-2.98 (m, 7 H), 3.04 (s, 3 H), 2.97 (s, 3 H), 2.37 (t, J = 15.1 Hz, 1 H), 2.27-2.17 (m, 1 H), 2.14 (s, 3 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 573.26 (M+H).



S1-14-17

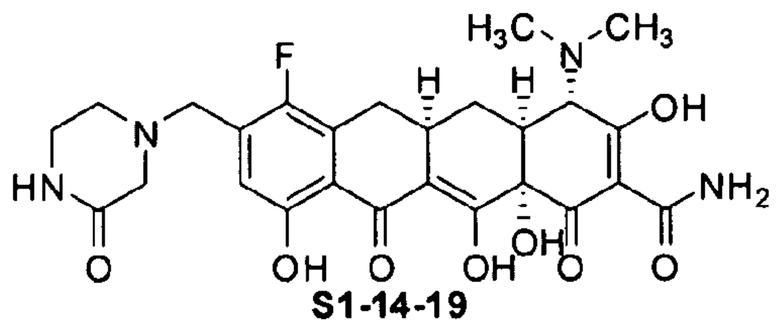
S1-14-17: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, J = 5.5 Hz, 1 H), 4.47 (s, 2 H), 4.09 (s, 1 H), 3.27-2.98 (m, 7 H), 3.04 (s, 3 H), 2.97 (s, 3 H), 2.96 (s, 3 H),

2.36 (t, J = 15.1 Hz, 1 H), 2.26-2.18 (m, 1 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 609.20 (M+H).



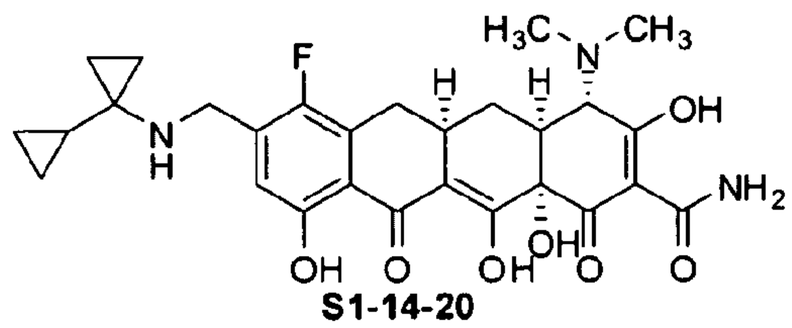
S1-14-18

S1-14-18: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.77 (d, J = 13.3 Hz, 1 H), 4.55 (d, J = 13.3 Hz, 1 H), 4.12-4.06 (m, 3 H), 3.14 (s, 3 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.23-2.97 (m, 4 H), 2.42-3.34 (m, 1 H), 2.23 (m, 1 H), 1.70-1.60 (m, 1 H), 1.02 (s, 9 H); MS (ESI) *m/z* 576.27 (M+H).



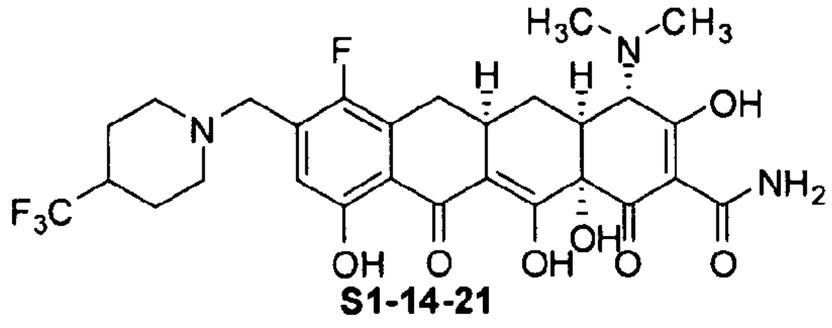
S1-14-19

S1-14-19: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 5.5 Hz, 1 H), 4.53 (s, 2 H), 4.08 (s, 1 H), 3.90 (s, 2 H), 3.67-3.55 (m, 4 H), 3.27-2.98 (m, 3 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.38 (t, J = 15.1 Hz, 1 H), 2.27-2.19 (m, 1 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 545.19 (M+H).



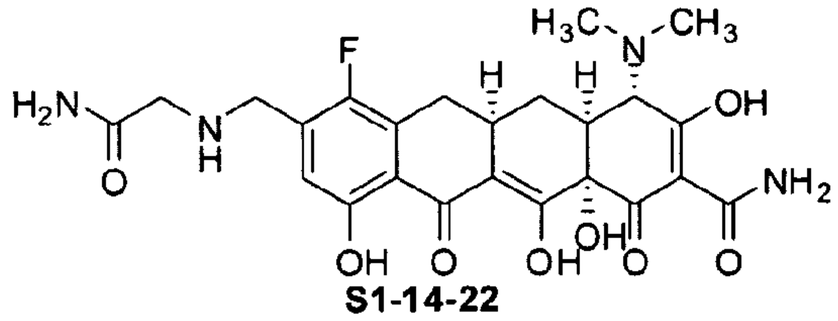
S1-14-20

S1-14-20: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, J = 5.9 Hz, 1 H), 4.51 (d, J = 4.1 Hz, 2 H), 4.07 (s, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.25-2.96 (m, 3 H), 2.35 (t, J = 15.1 Hz, 1 H), 2.26-2.18 (m, 1 H), 1.70-1.60 (m, 1 H), 1.59-1.51 (m, 1 H), 1.02-0.94 (m, 2 H), 0.86-0.78 (m, 2 H), 0.76-0.68 (m, 2 H), 0.43-0.35 (m, 2 H); MS (ESI) *m/z* 542.29 (M+H).



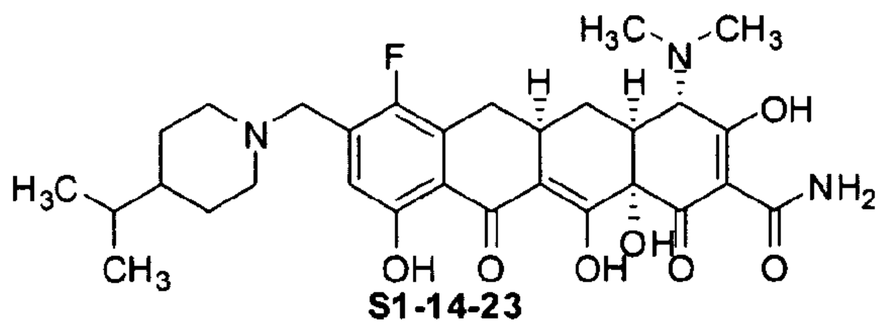
S1-14-21

S1-14-21: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.5 Hz, 1 H), 4.41 (s, 2 H), 4.08 (s, 1 H), 3.72-3.64 (m, 2 H), 3.24-2.98 (m, 5 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.65-2.55 (m, 1 H), 2.37 (t, J = 15.1 Hz, 1 H), 2.24-2.10 (m, 3 H), 1.90-1.77 (m, 2 H), 1.71-1.61 (m, 1 H); MS (ESI) *m/z* 598.30 (M+H).



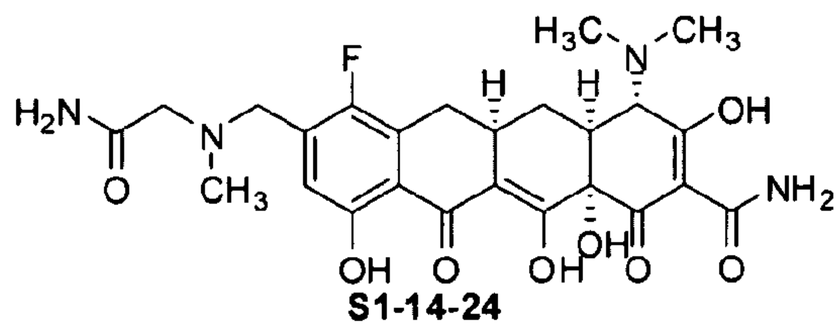
S1-14-22

S1-14-22: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, J = 6.0 Hz, 1 H), 4.32 (s, 2 H), 4.09 (s, 1 H), 3.87 (s, 2 H), 3.24-2.98 (m, 3 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.35 (t, J = 15.1 Hz, 1 H), 1.98, (s, 1.5 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 519.23 (M+H).



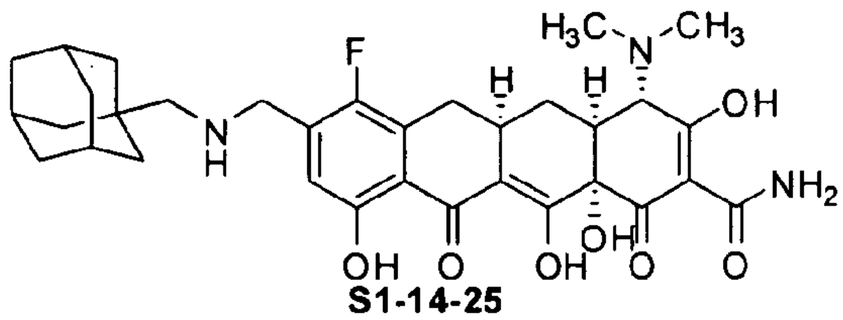
S1-14-23

S1-14-23: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 5.5 Hz, 1 H), 4.34 (s, 2 H), 4.08 (s, 1 H), 3.58-3.50 (m, 2 H), 3.24-2.98 (m, 5 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 2.36 (t, J = 15.1 Hz, 1 H), 2.23 (m, 1 H), 2.02-1.92 (m, 2 H), 1.69-1.59 (m, 1 H), 1.54-1.40 (m, 3 H), 1.40-1.32 (m, 1 H), 0.91 (d, J = 6.4 Hz, 6 H); MS (ESI) *m/z* 572.27 (M+H).



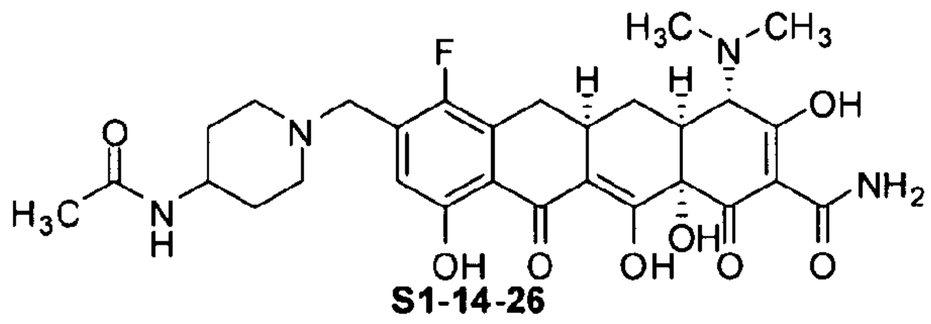
S1-14-24

S1-14-24: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, *J* = 6.0 Hz, 1 H), 4.51-2.43 (m, 2 H), 4.08 (s, 1 H), 4.04 (s, 2 H), 3.24-2.98 (m, 3 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 2.92 (s, 3 H), 2.35 (t, *J* = 15.1 Hz, 1 H), 2.28-2.18 (m, 1 H), 1.69-1.59 (m, 1 H); MS (ESI) *m/z* 533.29 (M+H).



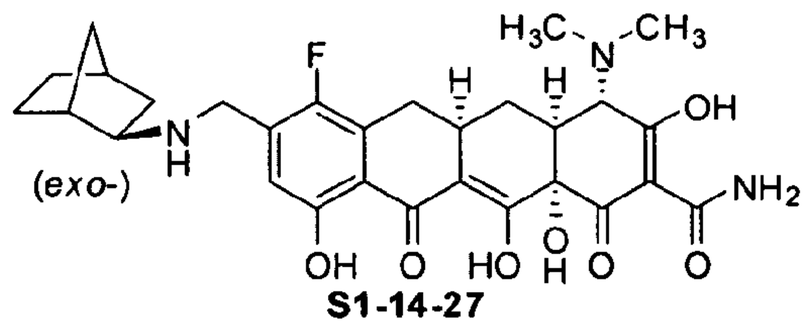
S1-14-25

S1-14-25: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, *J* = 5.5 Hz, 1 H), 4.31 (s, 2 H), 4.10 (s, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.27-2.96 (m, 3 H), 2.77 (s, 2 H), 2.61 (s, 1 H), 2.36 (t, *J* = 15.1 Hz, 1 H), 2.28-2.20 (m, 1 H), 1.84-1.76 (m, 4 H), 1.75-1.66 (m, 5 H), 1.63 (br, s, 5 H), 1.59 (br, s, 2 H); MS (ESI) *m/z* 610.28 (M+H).



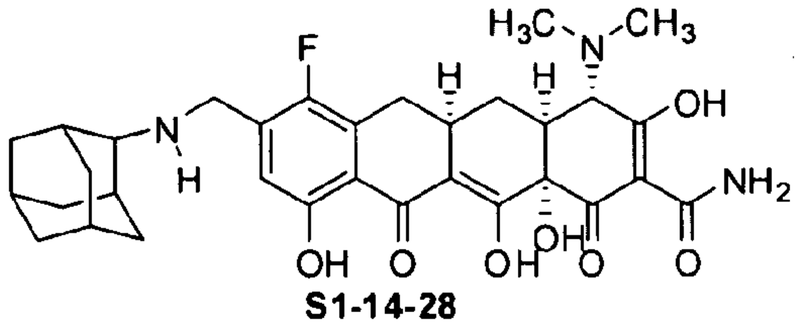
S1-14-26

S1-14-26: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (br, s, 1 H), 4.37 (s, 2 H), 4.07 (s, 1 H), 3.92-2.84 (m, 1 H), 3.61-3.54 (m, 2 H), 3.24-2.98 (m, 5 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 2.36 (t, *J* = 15.1 Hz, 1 H), 2.24-2.10 (m, 2 H), 2.18-1.96 (m, 1 H), 1.91 (s, 3 H), 1.80-1.59 (m, 3 H); MS (ESI) *m/z* 587.24 (M+H).



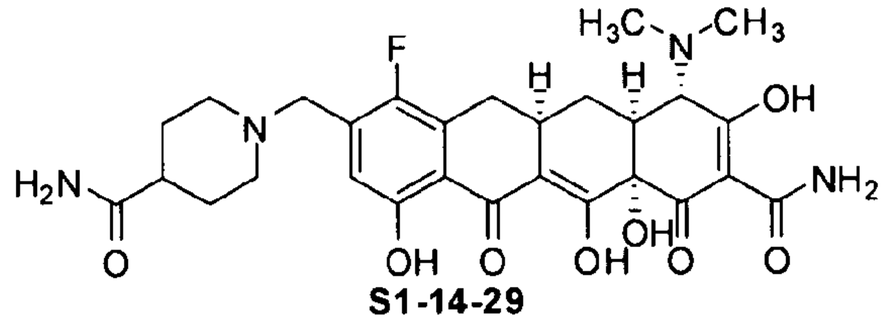
S1-14-27

S1-14-27: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, *J* = 5.5 Hz, 1 H), 4.24 (s, 2 H), 4.09 (s, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.27-2.96 (m, 4 H), 2.57 (d, *J* = 4.2 Hz, 1 H), 2.43 (s, 1 H), 2.34 (t, *J* = 15.1 Hz, 1 H), 2.27-2.19 (m, 1 H), 1.87 (dd, *J* = 13.7, 7.8 Hz, 1 H), 1.73-1.52 (m, 5 H), 1.35 (d, *J* = 11.0 Hz, 1 H), 1.28-1.20 (m, 2 H); MS (ESI) *m/z* 556.30 (M+H).



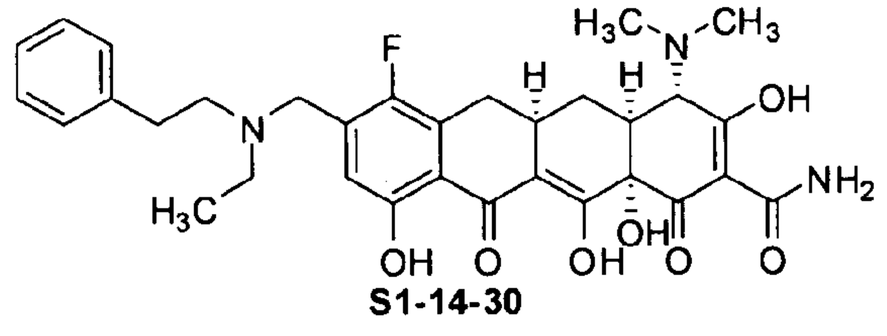
S1-14-28

S1-14-28: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.9 Hz, 1 H), 4.31 (s, 2 H), 4.09 (s, 1 H), 3.47 (s, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.27-2.96 (m, 3 H), 2.57 (d, J = 4.2 Hz, 1 H), 2.43 (s, 1 H), 2.35 (t, J = 15.5 Hz, 1 H), 2.26 (s, 2 H), 2.29-2.20 (m, 1 H), 2.04-1.89 (m, 6 H), 1.87-1.73 (m, 6 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 596.36 (M+H).



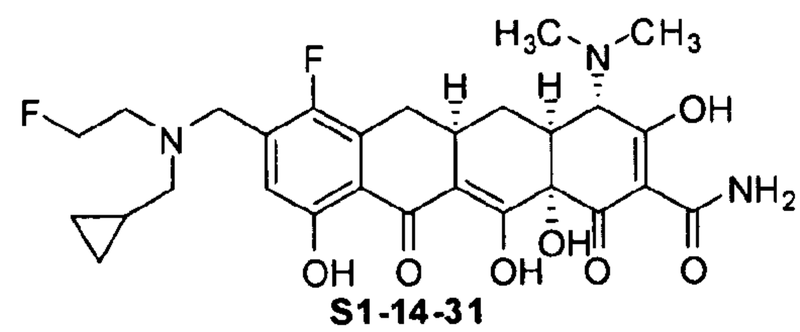
S1-14-29

S1-14-29: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.9 Hz, 1 H), 4.39 (s, 2 H), 4.10 (s, 1 H), 3.65-3.56 (m, 2 H), 3.24-2.98 (m, 5 H), 3.04 (s, 3 H), 2.97 (s, 3 H), 2.60-2.52 (m, 1 H), 2.37 (t, J = 15.1 Hz, 1 H), 2.28-2.20 (m, 1 H), 2.13-2.02 (m, 2 H), 1.97-1.88 (m, 2 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 573.28 (M+H).



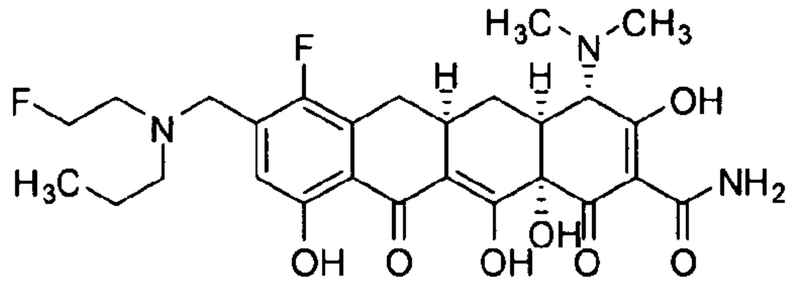
S1-14-30

S1-14-30: ^{1}H NMR (400 MHz, CD_3OD) δ 7.25-7.19 (m, 5 H), 7.02 (d, J = 5.6 Hz,1 H), 4.42 (s, 2 H), 3.98 (s, 1 H), 3.34-3.21 (m, 4 H), 3.15-2.85 (m, 11 H), 2.30-2.18 (m, 2 H), 1.62-1.52 (m, 1 H), 1.33 (t, J = 7.2 Hz,3 H); MS (ESI) *m/z* 594.1 (M+H).



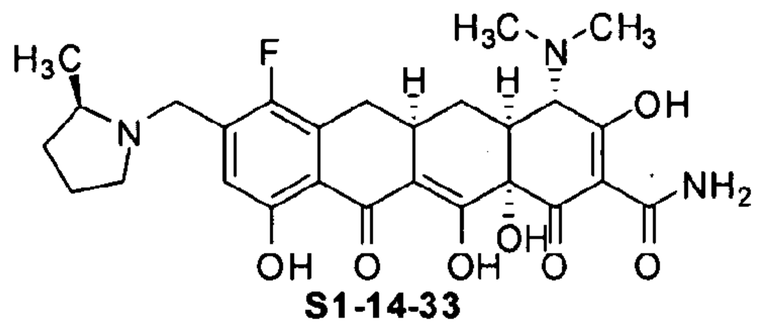
S1-14-31

S1-14-31: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, *J* = 5.6 Hz, 1 H), 4.88 (t, *J* = 4.4 Hz, 1 H), 4.55 (t, *J* = 4.4 Hz, 1 H), 4.01 (s, 1 H), 3.70-3.50 (m, 2 H), 3.17 (d, *J* = 7.2 Hz, 2 H), 3.10-2.87 (m, 11 H), 2.31-2.12 (m, 2 H), 1.57-1.54 (m, 1 H), 1.13-1.08 (m, 1 H), 0.74-0.72 (m, 2 H),0.41-0.37 (m, 2 H); MS (ESI) *m/z* 562.1 (M+H).



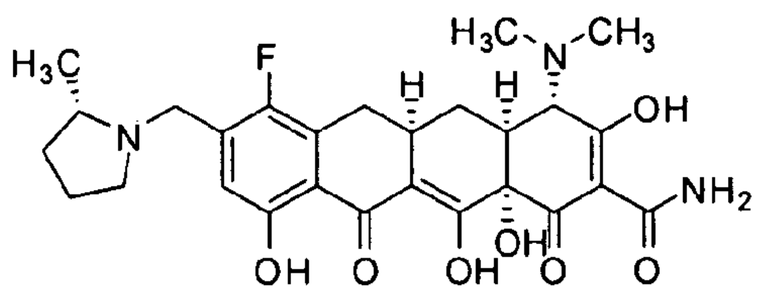
S1-14-32

S1-14-32: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, *J* = 5.6 Hz, 1 H), 4.87 (t, *J* = 4.0 Hz, 1 H), 4.74 (t, *J* = 4.0 Hz 1 H), 4.43 (s, 2 H), 4.02 (s, 1 H), 3.60-3.51 (m, 2 H), 3.20-2.88 (m, 11 H), 2.31-2.15 (m, 2 H),1.78-1.7 (m, 2 H), 1.58-1.55 (m, 1 H), 0.93 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 550.1 (M+H).



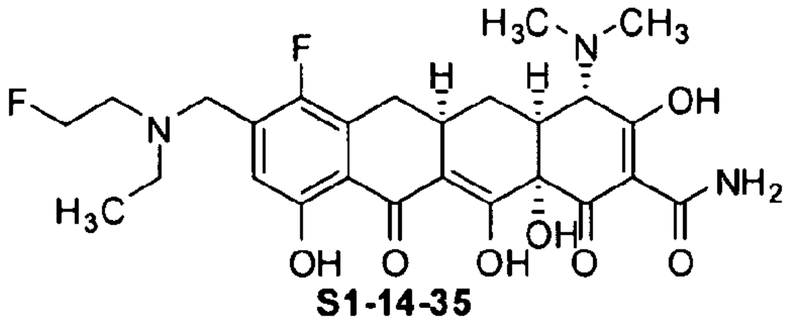
S1-14-33

S1-14-33: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, *J* = 5.6 Hz, 1 H), 4.56 (d, *J* = 13.2 Hz, 1 H), 4.13 (d, *J* = 13.2 Hz,1 H), 4.01 (s, 1 H), 3.56-3.36 (m, 2 H), 3.16-2.86 (m, 10 H), 2.33-2.16 (m, 3 H), 2.07-1.91 (m, 2 H), 1.73-1.67 (m, 1 H), 1.61-1.52 (m, 1 H), 1.42 (d, *J* = 6.4 Hz, 3 H) ; MS (ESI) *m/z* 575.2 (M+H).

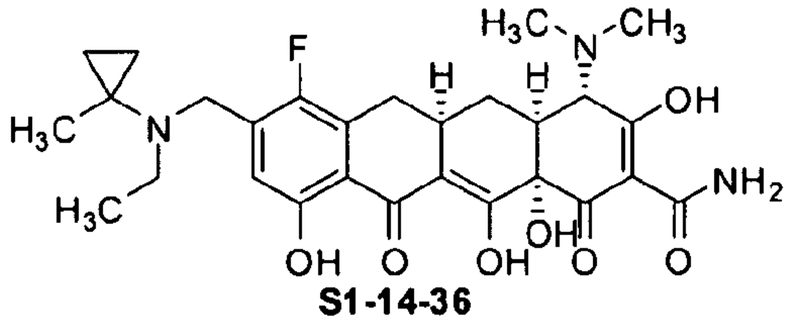


S1-14-34

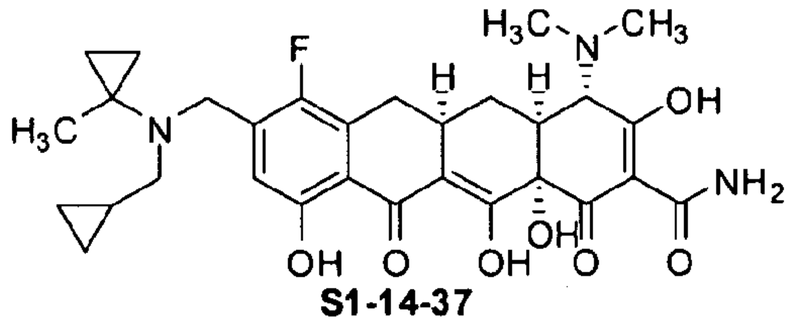
S1-14-34: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, *J* = 5.6 Hz, 1 H), 4.56 (d, *J* = 13.2 Hz, 1 H), 4.13 (d, *J* = 13.2 Hz,1 H), 4.01 (s, 1 H), 3.56-3.36 (m, 2 H), 3.16-2.86 (m, 10 H), 2.33-2.16 (m, 3 H), 2.07-1.91 (m, 2 H), 1.73-1.67 (m, 1 H), 1.61-1.52 (m, 1 H), 1.42 (d, *J* = 6.4 Hz, 3 H) ; MS (ESI) *m/z* 575.2 (M+H).


S1-14-35

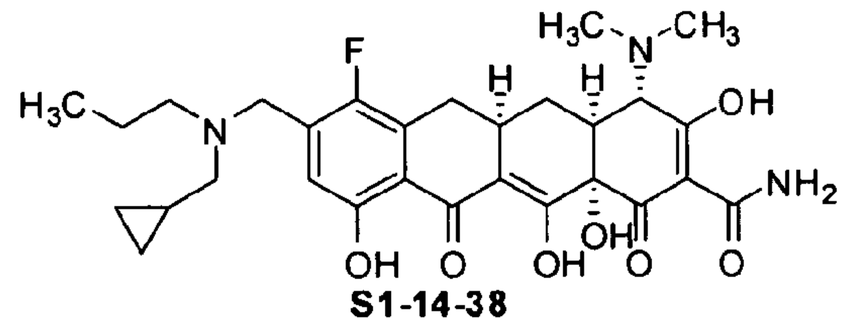
S1-14-35: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.96 (t, J = 6.0 Hz, 1 H), 4.78 (t, J = 6.0 Hz, 1 H), 4.51 (s, 2 H), 4.11 (s, 1 H), 3.72-3.59 (m, 2 H), 3.40 (q, J = 6.8 Hz, 2 H), 3.24-2.97 (m, 9 H), 2.39-2.24 (m, 2 H), 1.69-1.60 (m, 1 H), 1.41 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 536.1 (M+H).


S1-14-36

S1-14-36: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 6.0 Hz, 1 H), 4.62-4.47 (m, 2 H), 4.12 (s, 1 H), 3.50-3.44 (m,2 H), 3.23-2.98 (m, 9 H), 2.38-2.25 (m, 2 H), 1.69-1.66 (m, 1 H), 1.55 (s, 3 H), 1.42-1.39 (t, J = 7.2 Hz,3 H), 1.39-1.35 (m, 3 H), 094-0.86 (m, 3 H); MS (ESI) *m/z* 544.2 (M+H).

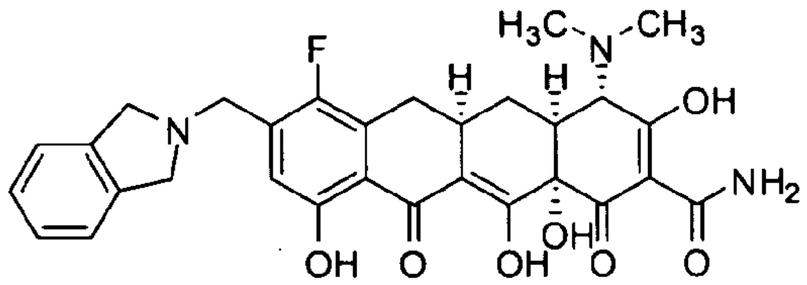

S1-14-37

S1-14-37: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.59 (s, 2 H), 4.10 (s, 1 H), 3.24-2.97 (m, 11 H), 2.40-2.24 (m, 2 H), 1.70-1.59 (m, 1 H), 1.56 (s, 3 H), 1.21-1.15 (m, 1 H), 0.93-0.89 (m, 2 H), 0.79-0.77 (m, 2 H), 0.69-0.66 (m, 1 H), 0.59-0.56 (m, 1 H), 0.47-0.46 (m, 2 H); MS (ESI) *m/z* 570.1 (M+H).


S1-14-38

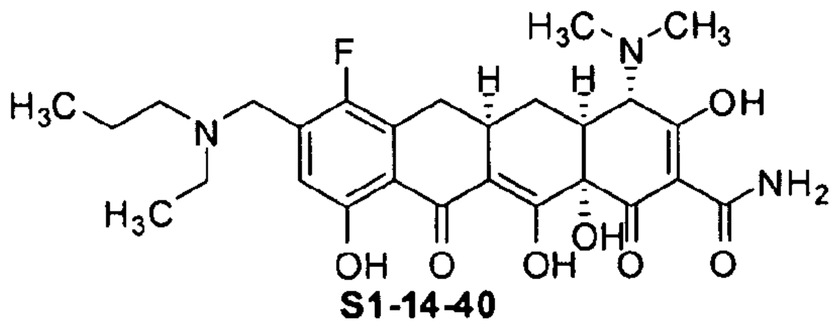
S1-14-38: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.63-4.60 (m, 1 H), 4.50-4.47 (m, 1 H), 4.11 (s, 1 H), 3.13-2.98 (m, 11 H), 2.39-2.24 (m,

2 H), 1.94-1.92 (m, 1 H), 1.75-1.70 (m, 1 H);1.66-1.63 (m, 1 H), 1.58 (s, 3 H), 1.38-1.29 (m, 1 H), 1.02 (t, J = 7.2 Hz, 3 H),0.92-0.87 (m, 3 H); MS (ESI) *m/z* 558.1 (M+H).



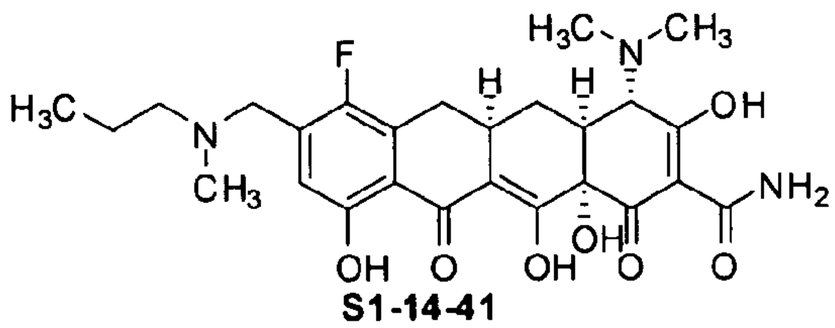
S1-14-39

S1-14-39: ^{1}H NMR (400 MHz, CD_3OD) δ 7.34 (s, 4 H), 7.04 (d, J = 5.2 Hz, 1 H), 4.71-4.63 (m, 4 H), 4.63 (s, 2 H) 3.99 (s, 1 H), 3.17-2.87 (m, 9 H), 2.28-2.15 (m, 2 H) 1.61-1.51 (m, 1 H); MS (ESI) *m/z* 564.2 (M+H).



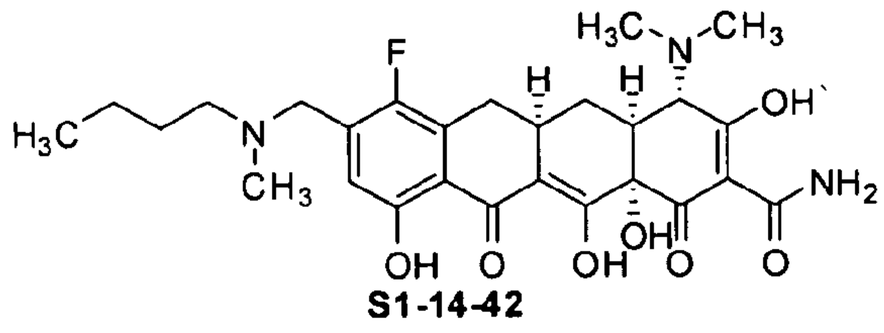
S1-14-40

S1-14-40: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.6 Hz, 1 H), 4.42 (d, J = 4.0 Hz, 2 H), 4.12 (s, 1 H), 3.29-2.90 (m, 13 H), 2.41-2.22 (m, 2 H), 1.90-1.75 (m, 2 H), 1.71-1.60 (M, 1 H); 1.38 (t, J = 7.2 Hz, 3 H), 1.05 (t, J = 7.2 Hz, 3 H), MS (ESI) *m/z* 530.2 (M+H).



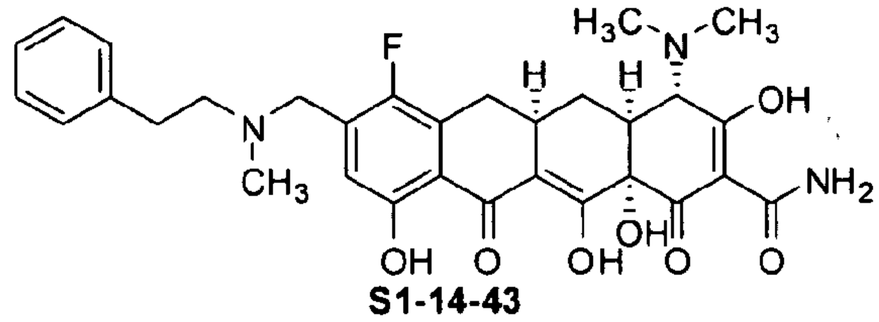
S1-14-41

S1-14-41: ^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (d, J = 5.2 Hz, 1 H), 4.48 (d, J = 13.2 Hz, 1 H), 4.27 (d, J = 13.2 Hz, 1 H), 4.09 (d, J = 4.4 Hz, 1 H), 3.22-2.92 (m, 11 H), 2.84 (s, 3 H), 2.38-2.22 (m, 2 H), 1.87-1.70 (m, 2 H), 1.68-1.62 (m, 1 H), 1.03 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 518.0 (M+H).



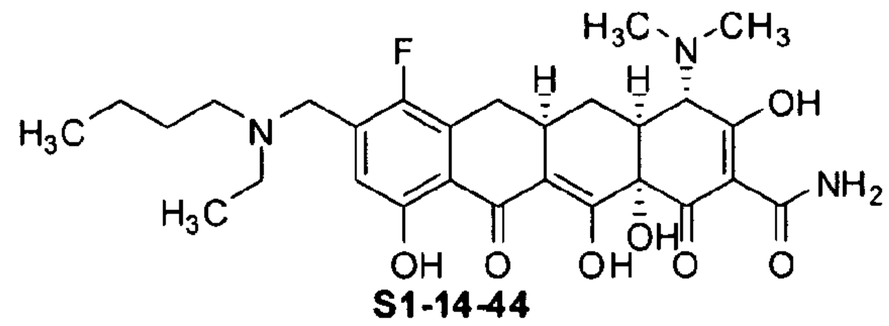
S1-14-42

S1-14-42: ^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (d, J = 5.6 Hz, 1 H), 4.51 (d, J = 13.6 Hz, 1 H), 4.28 (d, J = 13.6 Hz, 1 H), 4.09 (s, 1 H), 3.20-2.95 (m, 11 H), 2.83 (s, 3 H), 2.40-2.13 (m, 2 H), 1.79-1.71 (m, 2 H), 1.69-1.57 (m, 1 H), 1.46-1.35 (m, 2 H), 0.98 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 532.1 (M+H).



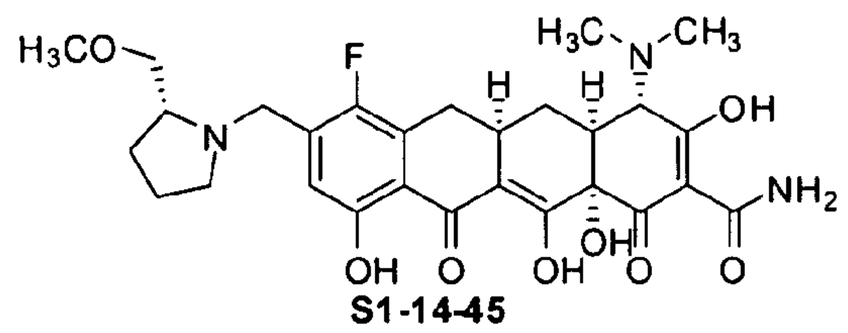
S1-14-43

S1-14-43: ^{1}H NMR (400 MHz, CD_3OD) δ 7.27-7.16 (m, 5 H), 7.01 (d, J = 5.6 Hz, 1 H), 4.52-4.48 (m, 1 H), 4.29-4.25 (m, 1 H), 4.03 (s, 1 H), 3.45-3.25 (m, 2 H), 3.15-2.88 (m, 11 H), 2.84 (s, 3 H), 2.30-2.16 (m, 2 H), 1.60-1.54 (m, 1 H), MS (ESI) *m/z* 580.1 (M+H).



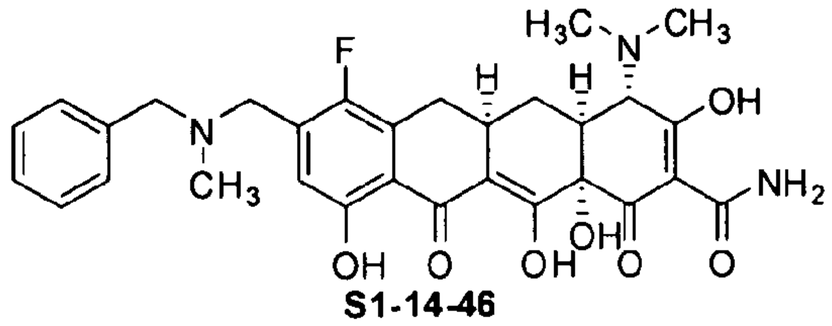
S1-14-44

S1-14-44: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 4.8 Hz, 1 H), 4.40 (s, 2 H), 4.11 (s, 1 H), 3.29-2.95 (m, 13 H), 2.37-2.23 (m, 2 H), 1.79-1.71 (m, 2 H), 1.67-1.58 (m, 1 H), 1.45-1.38 (m, 2 H), 1.37 (t, J = 7.2 Hz, 3 H), 0.95 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 546.2 (M+H).



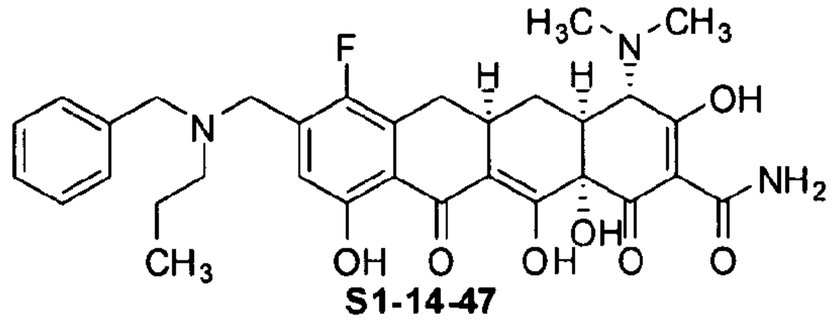
S1-14-45

S1-14-45: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, J = 5.6 Hz, 1 H), 4.70 (d, J = 13.2 Hz, 1 H), 4.29 (d, J = 13.2 Hz, 1 H), 4.09 (s, 1 H), 3.86-3.83 (m, 1 H), 3.73-3.60 (m, 2 H), 3.49-3.41 (m, 1 H), 3.40 (s, 3 H), 3.22-2.95 (m, 10 H), 2.37-2.26 (m, 3 H), 2.22-1.84 (m, 3 H), 1.68-1.57 (m, 1 H), MS (ESI) *m/z* 560.1 (M+H).



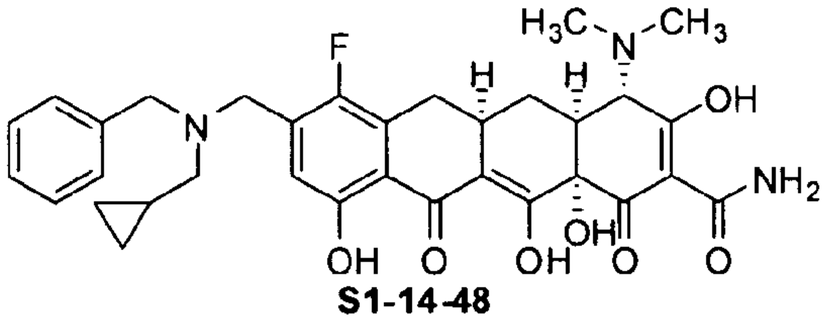
S1-14-46

S1-14-46: ^{1}H NMR (400 MHz, CD_3OD) δ 7.47-7.41 (m, 5 H), 6.95 (d, *J* = 6.0 Hz, 1 H), 4.41-4.36 (m, 2 H), 4.34-4.18 (m, 2 H), 4.02 (s, 1 H), 3.12-2.88 (m, 9 H), 2.72 (s, 3 H), 2.28-2.12 (m, 2 H), 1.60-1.50 (m, 1 H); MS (ESI) *m/z* 565.2 (M+H).



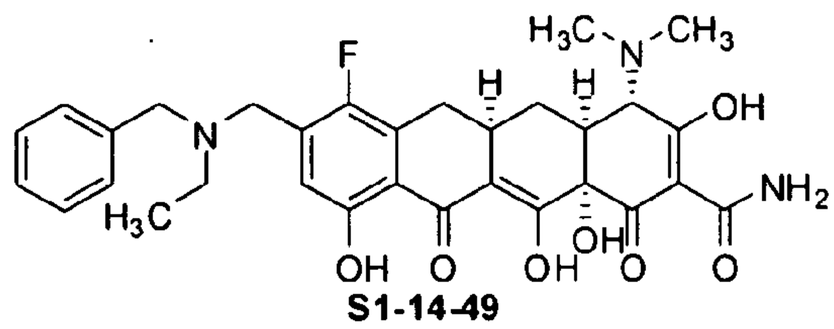
S1-14-47

S1-14-47: ^{1}H NMR (400 MHz, CD_3OD) δ 7.58-7.49 (m, 5 H), 6.99 (d, *J* = 5.6 Hz, 1 H), 4.49-4.42 (m, 4 H), 4.13 (s, 1 H), 3.18-2.97 (m, 11 H), 2.35-2.23 (m, 2 H), 1.91-1.88 (m, 2 H), 1.68-1.47 (m, 1 H), 0.97 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 594.2 (M+H).



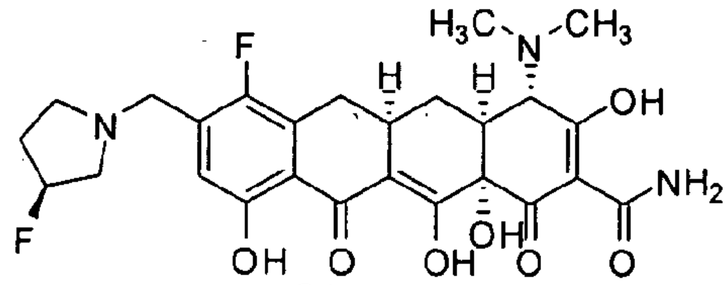
S1-14-48

S1-14-48: ^{1}H NMR (400 MHz, CD_3OD) δ 7.53-7.49 (m, 5 H), 6.96 (d, *J* = 5.2 Hz, 1 H), 4.62-4.35 (m, 4 H), 4.09 (s, 1 H), 3.20-2.96 (m, 11 H), 2.35-2.21 (m, 2 H), 1.67-1.48 (m, 1 H), 1.26-1.13 (m, 1 H), 0.86-0.74 (m, 2 H), 0.44-0.33 (m, 2 H); MS (ESI) *m/z* 606.1 (M+H).



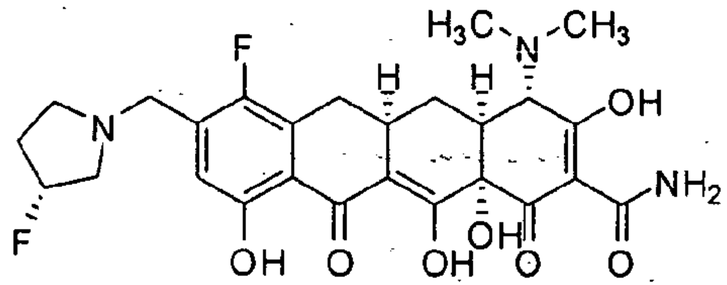
S1-14-49

S1-14-49: ^{1}H NMR (400 MHz, CD_3OD) δ 7.53-7.48 (m, 5 H), 6.96 (d, *J* = 5.6 Hz, 1 H), 4.48-4.34 (m, 4 H), 4.09 (s, 1 H), 3.26-2.87 (m, 11 H), 2.35-2.20 (m, 2 H), 1.62-1.56 (m, 1 H), 1.44 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 580.1 (M+H).



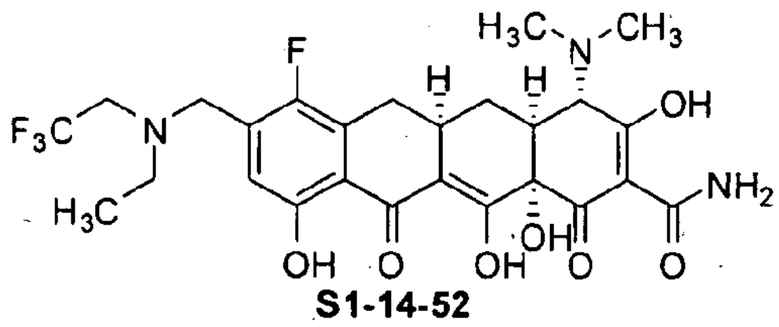
S1-14-50

S1-14-50: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, *J* = 5.6 Hz, 1 H), 5.47 (d, *J* = 52 Hz, 1 H), 4.55 (s, 2 H), 4.12 (s, 1 H), 3.95-3.47 (m, 4 H), 3.24-2.98 (m, 9 H), 2.70-2.62 (m, 1 H), 2.39-2.25 (m, 3 H), 1.69-1.61 (m, 1 H); MS (ESI) *m/z* 534.1 (M+H).



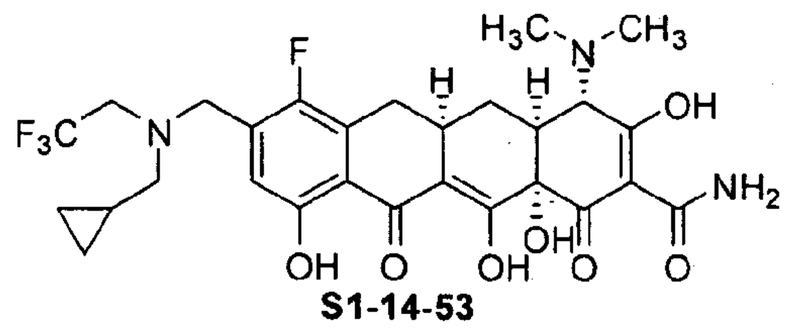
S1-14-51

S1-14-51: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 6 Hz, 1 H), 5.47 (d, *J* = 52.4 Hz, 1 H), 4.54 (s, 2 H), 4.11 (s, 1 H), 3.92-3.39 (m, 4 H), 3.26-2.98 (m, 9 H), 2.70-2.62 (m, 1 H), 2.40-2.23 (m, 3 H), 1.71-1.62 (m, 1 H); MS (ESI) *m/z* 534.1 (M+H).

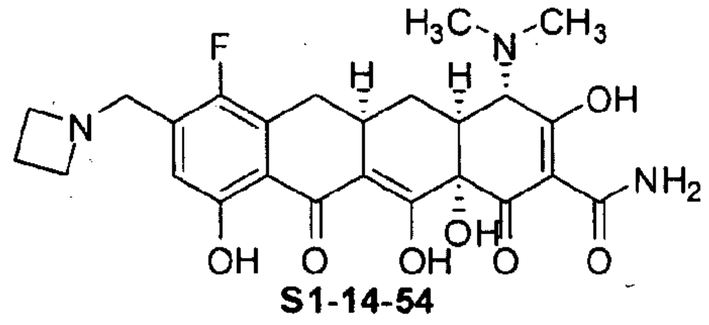


S1-14-52

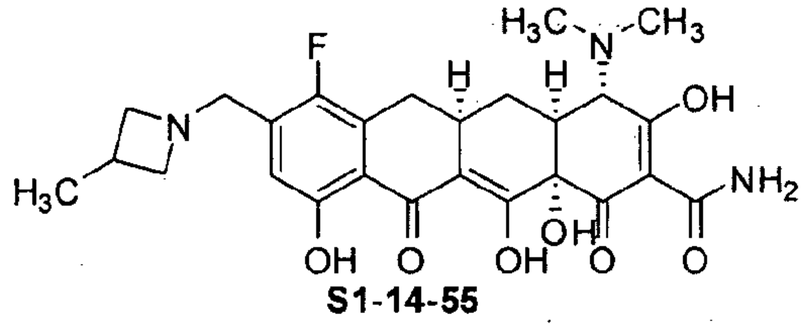
S1-14-52: ^{1}H NMR (400 MHz, CD_3OD) δ 6.98 (d, *J* = 5.6 Hz, 1 H), 4.07 (s, 1 H), 3.93 (s, 2 H), 3.31 (q, *J* = 9.2 Hz, 2 H), 3.19-2.89 (m, 9 H), 2.77 (q, *J* = 7.2 Hz, 2 H), 2.34-2.15 (m, 2 H), 1.68-1.57 (m, 1 H), 1.11 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 572.1 (M+H).


S1-14-53

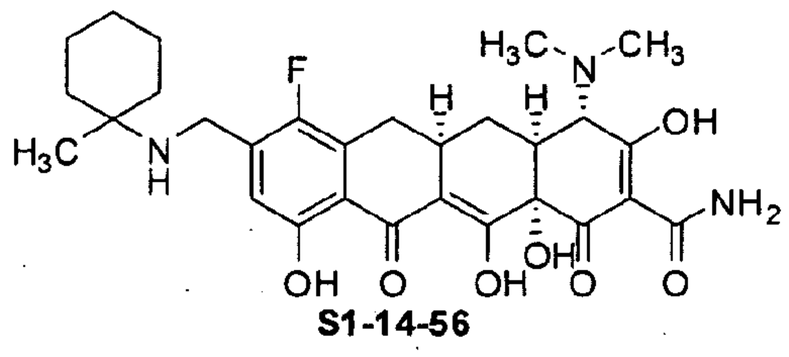
S1-14-53: ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, J = 6.0 Hz, 1 H), 4.20 (s, 2 H), 4.09 (s, 1 H), 3.76-3.65 (m, 2 H), 3.74 (q, J = 7.2 Hz, 2 H), 3.20-2.96 (m, 9 H), 2.81 (d, J = 6.8 Hz, 2 H), 2.34-2.21 (m, 2 H), 1.68-1.56 (m, 1 H), 1.07-0.98 (m, 1 H), 0.65-0.58 (m, 2 H), 0.27-0.23 (m, 2 H); MS (ESI) *m/z* 598.1 (M+H).


S1-14-54

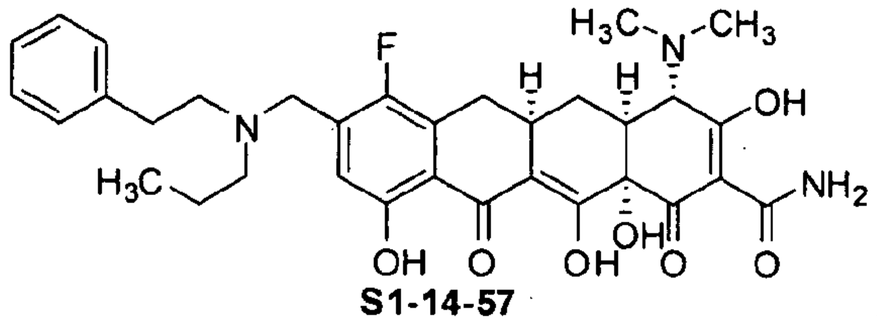
S1-14-54: ^{1}H NMR (400 MHz, CD_3OD) δ 6.97 (d, J = 6.0 Hz, 1 H), 4.45 (s, 2 H), 4.25-4.17 (m, 4 H), 4.09 (s, 1 H), 3.21-2.95 (m, 9 H), 2.61-2.51 (m, 1 H), 2.49-2.38 (s, 1 H), 2.32-2.18 (m, 2 H), 1.65-1.53 (m, 1 H); MS (ESI) *m/z* 502.1 (M+H).


S1-14-55

S1-14-55: ^{1}H NMR (400 MHz, CD_3OD) δ 6.98 (d, J = 6.0 Hz, 1 H), 4.50-4.42 (m□2H), 4.29-4.21 (m, 2 H), 4.09 (s, 1 H), 3.92-3.85 (m□2H), 3.22-2.97 (m, 9 H), 2.28-2.33 (m, 2 H), 1.66 (ddd, J = 11.6, 11.2, 11.6 Hz, 1 H), 1.33 (d, J = 6.8 Hz, 1 H), 1.28 (d, J = 6.8 Hz, 2 H); MS (ESI) *m/z* 516.1 (M+H).

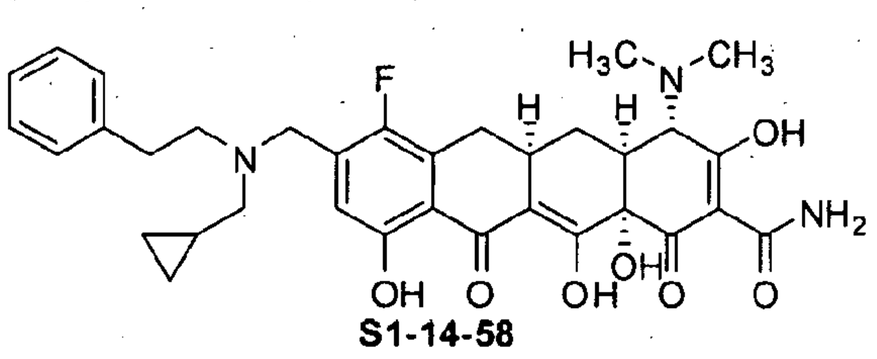

S1-14-56

S1-14-56: ^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (d, J = 5.2 Hz, 1 H), 4.24 (s, 2 H), 4.10 (s, 1 H), 3.24-2.97 (m, 9 H), 2.28-2.23 (m, 2 H), 1.98-1.56 (m, 10 H), 1.55 (s, 3 H); MS (ESI) *m/z* 558.1 (M+H).



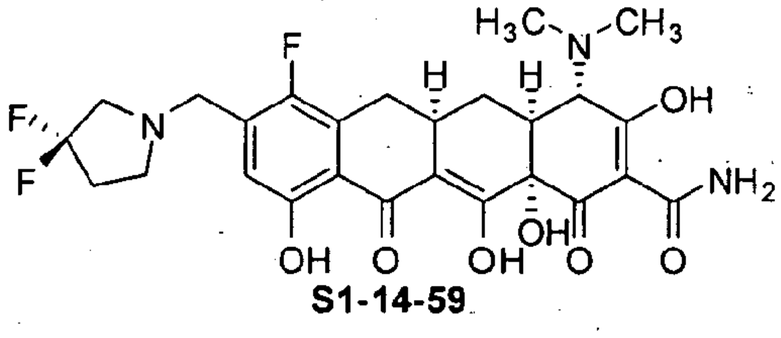
S1-14-57

S1-14-57: ^{1}H NMR (400 MHz, CD_3OD) δ 7.36-7.32 (m, 2 H), 7.29-7.27 (m, 3 H), 7.12 (d, J = 5.6 Hz, 1 H), 4.53 (s, 2 H), 4.11 (s, 1 H), 3.40 (t, 2 H), 3.28-2.94 (m, 13 H), 2.43-2.22 (m, 2 H), 1.92-1.61 (m, 3 H), 1.02 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 607.3 (M+H).



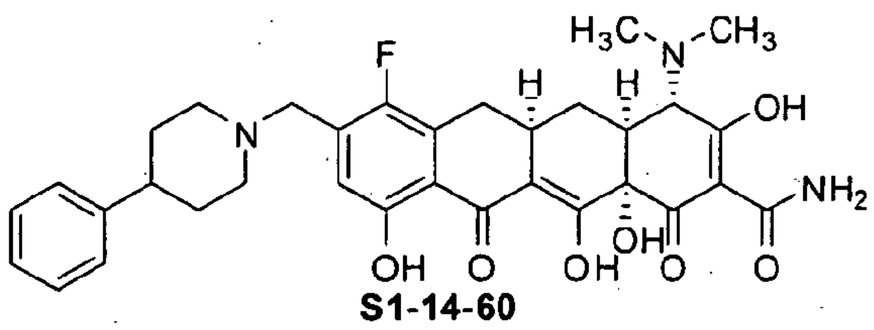
S1-14-58

S1-14-58: ^{1}H NMR (400 MHz, CD_3OD) δ 7.26-7.19 (m, 5 H), 7.05 (d, J = 5.6 Hz, 1 H), 4.61-4.42 (m, 2 H), 4.03 (s, 1 H), 3.47-3.33 (m, 2 H), 3.17 (d, J = 7.2 Hz, 1 H), 3.11-2.88 (m,11 H), 2.32-2.14 (m,2 H), 1.61-1.51 (m, 1 H), 1.21-1.11 (m, 1 H),0.74-0.72 (m, 2 H), 0.41-0.38 (m, 2 H); MS (ESI) *m/z* 620.3 (M+H).



S1-14-59

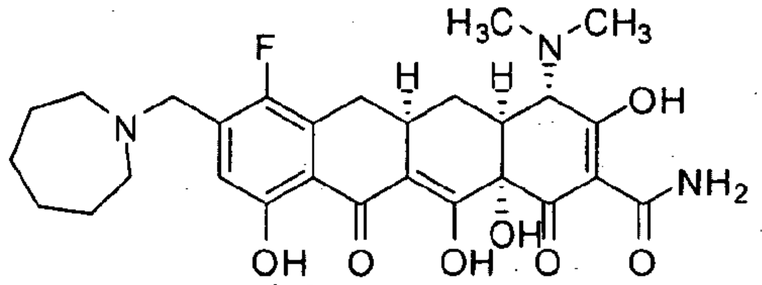
S1-14-59: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, J = 5.6 Hz, 1 H), 4.48 (s, 2 H), 4.01 (s, 1 H), 3.87 (t, J = 11.6 Hz, 2 H), 3.87 (t, J = 7.6 Hz, 2 H), 3.18-2.88 (m, 9 H), 2.18-2.07 (m, 2 H), 2.33-2.11 (m, 2 H), 1.56-1.51 (m, 1 H); MS (ESI) *m/z* 552.2 (M+H).



S1-14-60

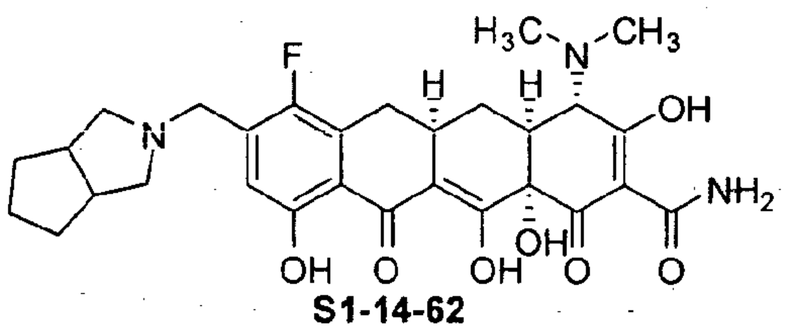
S1-14-60: ^{1}H NMR (400 MHz, CD_3OD) δ 7.24-7.11 (m, 5 H), 7.07 (d, J = 4.8 Hz, 1 H), 4.35 (s, 2 H), 4.04 (s, 1 H), 3.60-3.57 (m, 3 H), 3.16-2.80 (m, 11 H),

2.31-2.17 (m, 2 H), 2.06-1.96 (s, 4 H), 1.63-1.52 (m, 1 H); MS (ESI) *m/z* 606.2 (M+H).



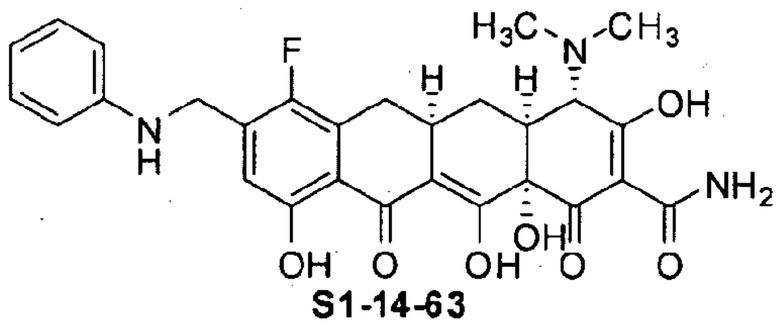
S1-14-61

S1-14-61: ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, *J* = 5.6 Hz, 1 H), 4.35 (s, 2 H), 4.03 (s, 1 H), 3.45-3.40 (m, 2 H), 3.23-2.90 (m, 11 H), 2.32-2.16 (m, 2 H), 2.07-1.81 (m, 4 H), 1.79-1.65 (m, 4 H), 1.63-1.53 (m, 1 H); MS (ESI) *m/z* 544.2 (M+H).



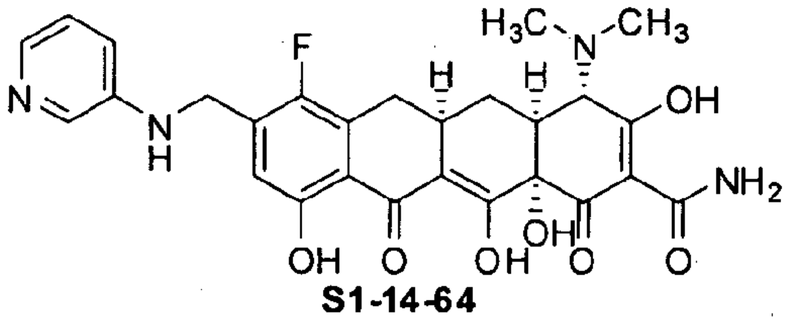
S1-14-62

S1-14-62: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, *J* = 6.0 Hz, 1 H), 4.37 (s, 2 H), 4.03 (s, 1 H), 3.72-3.65 (m, 2 H), 3.19-2.84 (m, 11 H), 2.82-2.65 (m, 2 H), 2.32-2.16 (m, 2 H), 1.70-1.41 (m, 7 H); MS (ESI) *m/z* 556.2 (M+H).



S1-14-63

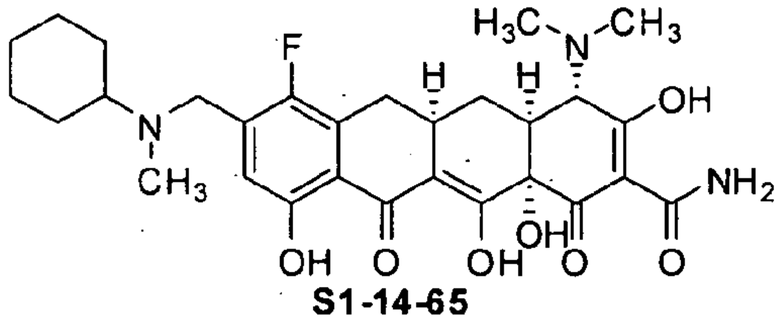
S1-14-63: ^{1}H NMR (400 MHz, CD_3OD) δ 7.59-7.34 (m, 5 H), 6.94 (d, *J* = 5.6 Hz, 1 H), 4.63 (s, 2 H), 4.10 (s, 1 H), 3.19-2.97 (m, 9 H), 2.34-2.23 (m, 2 H), 1.68 (ddd, *J* = 13.2, 13.2, 13.2 Hz, 1 H); MS (ESI) *m/z* 538.2 (M+H).



S1-14-64

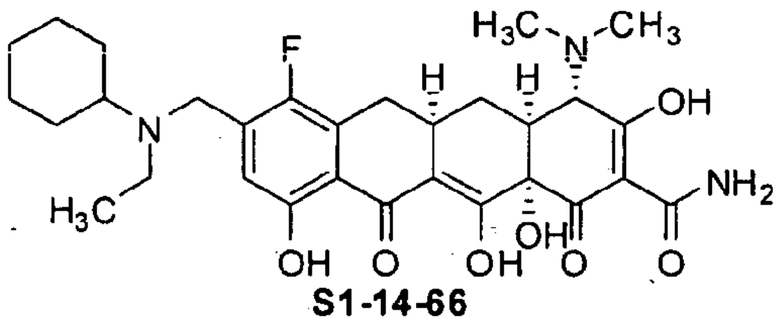
S1-14-64: ^{1}H NMR (400 MHz, CD_3OD) δ 7.97 (s, 1 H), 7.91 (t, *J* = 2.8 Hz, 1 H), 7.66-7.65 (m, 2 H), 6.74 (d, *J* = 5.6 Hz, 1 H), 4.46 (s, 2 H), 4.00 (s, 1 H),3.25-

2.88 (m, 9 H), 2.27-2.12 (m, 2 H), 1.56 (ddd, *J* = 13.6, 13.6, 13.6 Hz, 1 H); MS (ESI) *m/z* 539.2 (M+H).



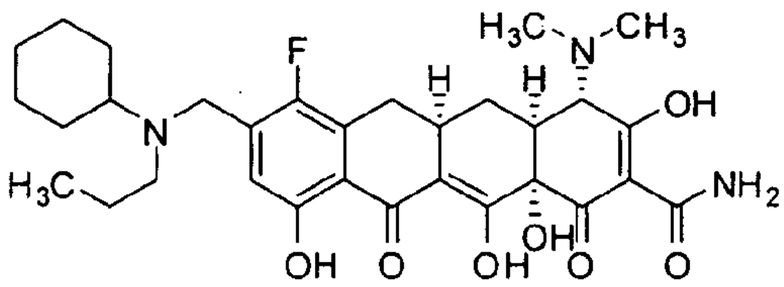
S1-14-65

S1-14-65: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 5.6 Hz, 1 H), 4.62 (d, *J* = 13.2 Hz, 1 H), 4.19 (d, *J* = 13.2 Hz, 1 H), 4.17 (s, 1 H), 3.41-2.35 (m, 1 H),3.25-2.99 (m, 9 H), 2.71 (s, 3 H), 2.41-2.27 (m, 2 H), 2.24-2.17 (m, 2 H); 2.05-1.92 (m, 2 H), 1.78-1.558 (m, 4 H), 1.50-1.37 (M, 2 H), 1.35-1.20 (m, 1 H); MS (ESI) *m/z* 558.2 (M+H).



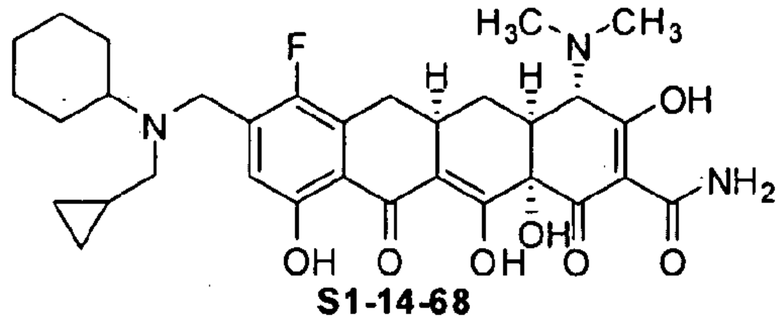
S1-14-66

S1-14-66: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, *J* = 6.0 Hz, 1 H), 4.57 (d, *J* = 13.6 Hz, 1 H), 4.21 (d, *J* = 13.6 Hz, 1 H), 4.10 (s, 1 H), 3.44-3.35 (m, 1 H), 3.30-2.95 (m, 11 H), 2.38-2.20 (m, 2 H), 2.15-2.05 (m, 2 H), 2.00-1.90 (m, 2 H), 1.75-1.55 (m, 4 H), 1.50-1.35 (m, 2 H), 1.35-1.20 (m, 1 H), 1.32 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 572.2 (M+H).



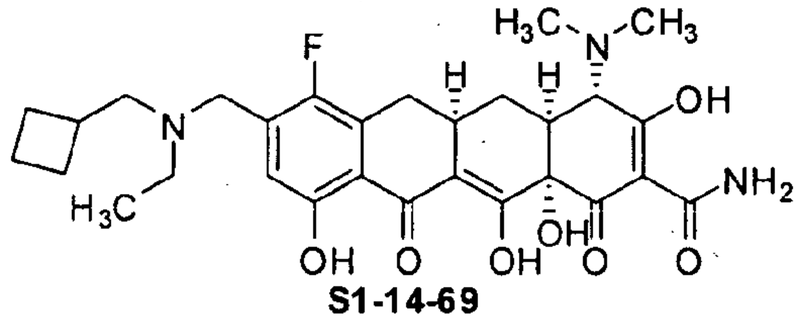
S1-14-67

S1-14-67: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, *J* = 5.6 Hz, 1 H), 4.56 (d, *J* = 13.6 Hz, 1 H), 4.25 (d, *J* = 13.6 Hz, 1 H), 4.11 (s, 1 H), 3.40-3.32 (m, 1 H), 3.25-2.95 (m, 11 H), 2.40-2.21 (m, 2 H), 2.17-2.06 (m, 2 H), 1.99-1.90 (m, 2 H), 1.85-1.56 (m, 6 H), 1.47-1.20 (m, 3 H), 0.96 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 586.2 (M+H).



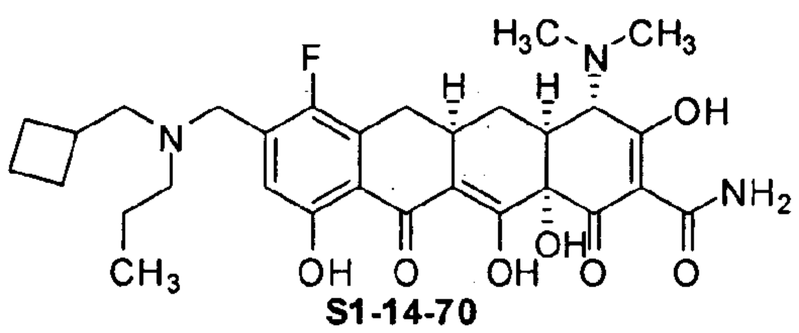
S1-14-68

S1-14-68: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.9 Hz, 1 H), 4.56 (d, J = 12.0 Hz, 1 H), 4.32 (d, J = 12.0 Hz, 1 H), 4.11 (s, 1 H), 3.56-3.48 (m, 1 H), 3.21-2.93 (m, 11 H), 2.39-2.21 (m, 2 H), 2.18-2.04 (m, 2 H), 2.0-1.9 (m, 2 H), 1.81-1.56 (m, 4 H), 1.46-1.20 (m, 3 H), 1.15-1.03 (s, 1 H), 0.78-0.69 (m, 2 H), 0.45-0.35 (m, 2 H); MS (ESI) *m/z* 598.2 (M+H).



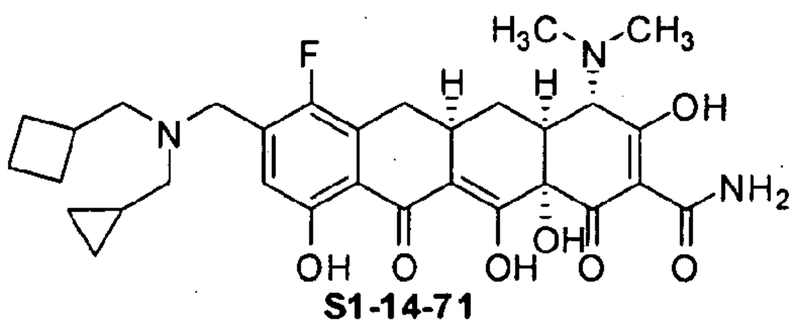
S1-14-69

S1-14-69: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.6 Hz, 1 H), 4.30 (s, 2 H), 4.11 (s, 1 H), 3.28-2.95 (m, 13 H), 2.90-2.79 (m, 1 H), 2.40-2.15 (m, 4 H), 2.07-1.81 (m, 4 H), 1.57-1.29 (m, 1 H), 1.39-1.33 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 557.2 (M+H).



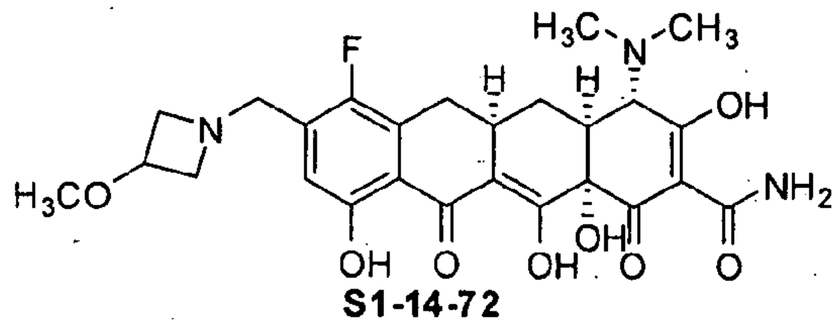
S1-14-70

S1-14-70: ^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (d, J = 5.6 Hz, 1 H), 4.36 (s, 2 H), 4.10 (s, 1 H), 3.28-2.96 (m, 13 H), 2.90-2.80 (m, 1 H), 2.40-2.14 (m, 4 H), 2.06-1.72 (m, 6 H), 1.67-1.55 (m, 1 H), 1.02-0.96 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 572.2 (M+H).



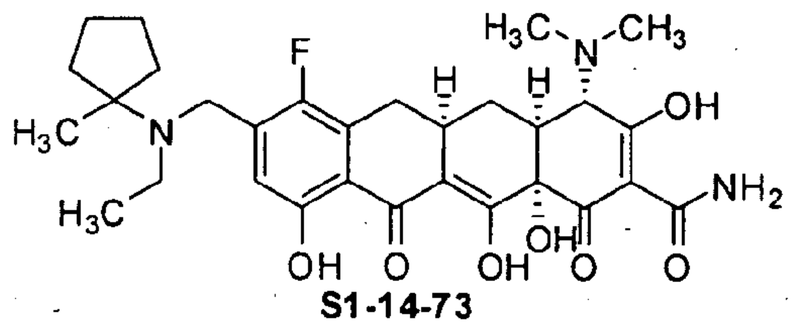
S1-14-71

S1-14-71: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 5.6 Hz, 1 H), 4.55-4.36 (m, 2 H), 4.12 (s, 1 H), 3.43-2.80 (m, 13 H), 2.39-2.12 (m, 4 H), 2.08-1.80 (m, 5 H), 1.70-1.56 (m, 1 H), 1.21-1.12 (m, 1 H), 0.82-0.72 (m, 2 H), 0.49-0.39 (m, 2 H); MS (ESI) *m/z* 584.2 (M+H).



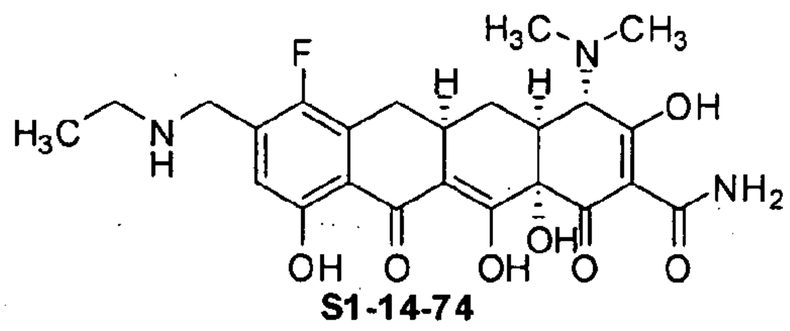
S1-14-72

S1-14-72: ^{1}H NMR (400 MHz, CD_3OD) δ 6.98 (dd, *J* = 2.0, 6.0 Hz, 1 H), 4.55-4.45 (m, 3 H), 4.45-3.38 (m, 2 H), 4.18-4.02 (m, 3 H), 3.33 (s, 3 H), 3.22-2.95 (m, 9 H), 2.37-2.22 (m, 2 H), 1.68-1.58 (m, 1 H); MS (ESI) *m/z* 532.1 (M+H).



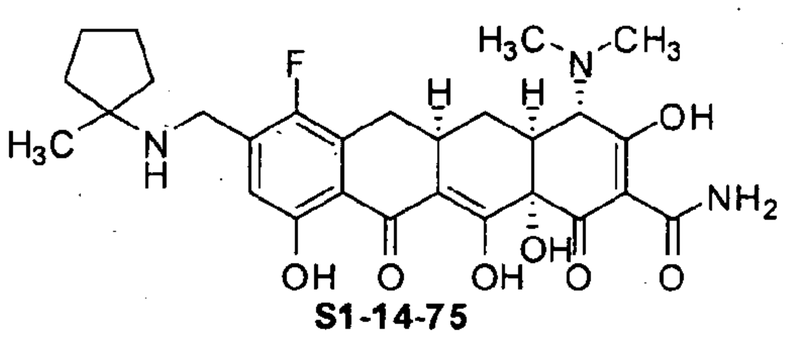
S1-14-73

S1-14-73: ^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (d, *J* = 5.6 Hz, 1 H), 4.60-4.51 (m, 1 H), 4.52-4.45 (m, 1 H), 4.11 (s, 1 H), 3.25-2.92 (m, 11 H), 2.41-2.20 (m, 2 H), 2.08-1.75 (m, 8 H), 1.68-1.59 (m, 1 H), 1.50 (s, 3 H), 1.14 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 572.2 (M+H).



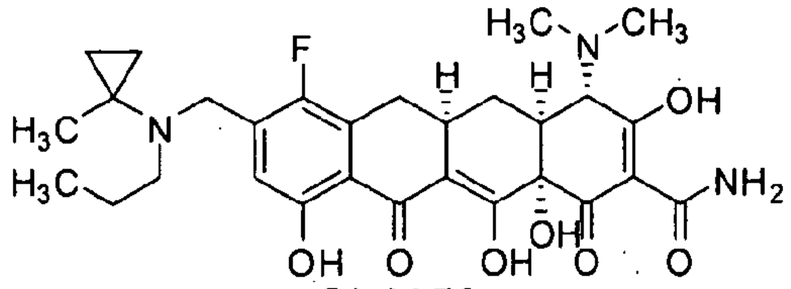
S1-14-74

S1-14-74: ^{1}H NMR (400 MHz, CD_3OD) δ 7.02 (d, *J* = 5.6 Hz, 1 H), 4.25 (s, 2 H), 4.11 (s, 1 H), 3.22-2.98 (m, 11 H), 2.36-2.23 (m, 2 H), 1.68-1.58 (m, 1 H), 1.33 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 490.4 (M+H).



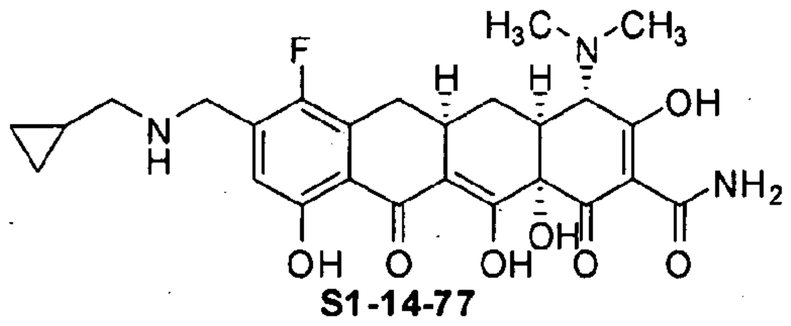
S1-14-75

S1-14-75: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.6 Hz, 1 H), 4.23 (s, 2 H), 4.11 (s, 1 H), 3.25-2.91 (m, 9 H), 2.39-2.20 (m, 2 H), 2.00-1.75 (m, 8 H), 1.68-1.59 (m, 1 H), 1.49 (s, 3 H); MS (ESI) *m/z* 544.3 (M+H).



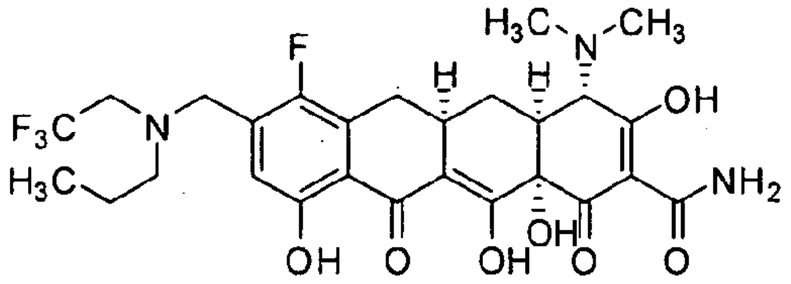
S1-14-76

S1-14-76: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 6.0 Hz, 1 H), 4.64-4.47 (m, 2 H), 4.11 (s, 1 H), 3.25-2.98 (m, 11 H), 2.39-2.24 (m, 2 H), 1.98-1.90 (m, 1 H), 1.80-1.70 (m, 1 H), 1.68-1.60 (m, 1 H), 1.55 (s, 3 H), 1.38-1.29 (m, 1 H), 1.02 (t, J = 7.2 Hz, 3 H), 0.98-0.82 (m, 3 H); MS (ESI) *m/z* 558.1 (M+H).



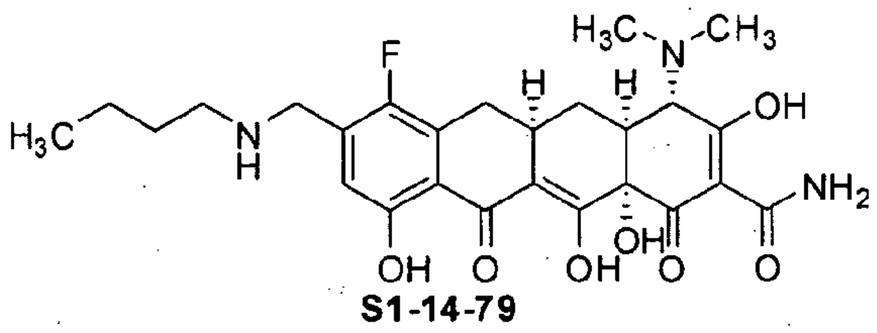
S1-14-77

S1-14-77: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 5.6 Hz, 1 H), 4.30 (s, 2 H), 4.12 (s, 1 H), 3.24-2.98 (m, 11 H), 2.37-2.25 (m, 2 H), 1.69-1.60 (m, 1 H), 1.19-1.14 (m, 1 H), 0.79-0.73 (m, 2 H), 0.48-0.42 (m, 2 H); MS (ESI) *m/z* 516.0 (M+H).



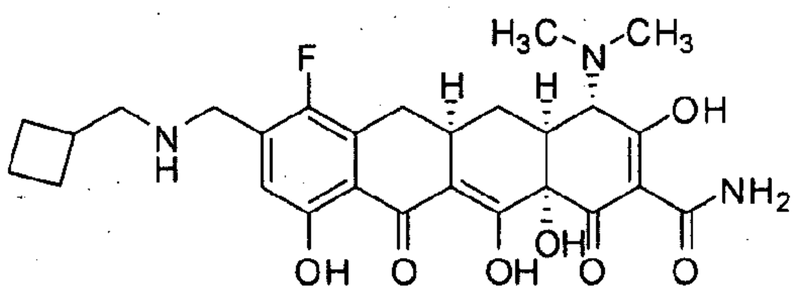
S1-14-78

S1-14-78: ^{1}H NMR (400 MHz, CD_3OD) δ 6.97 (d, J = 5.6 Hz, 1 H), 4.07 (s, 1 H), 3.96 (s, 2 H), 3.38 (t, J = 9.6 Hz, 2 H), 3.20-2.94 (m, 9 H),2.68 (t, J = 7.6 Hz, 2 H), 2.35-2.25 (m, 2 H), 1.58-1.50 (m, 3 H), 0.88 (t, J = 7.2 Hz, 3 H),; MS (ESI) *m/z* 586.1 (M+H).



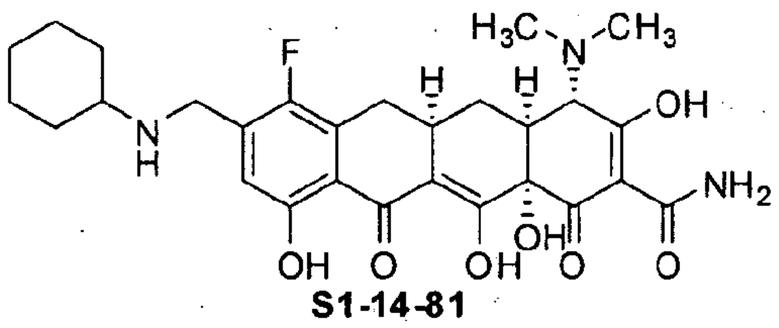
S1-14-79

S1-14-79: ^{1}H NMR (400 MHz, CD_3OD) δ 6.94 (d, J = 6.0 Hz, 1 H), 4.18 (s, 2 H), 4.02 (s, 1 H), 3.15-2.82 (m, 11 H), 2.28-2.15 (m, 2 H), 1.66-1.51 (m, 3 H), 1.40-1.30 (m, 2 H), 0.90 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 518.1 (M+H).



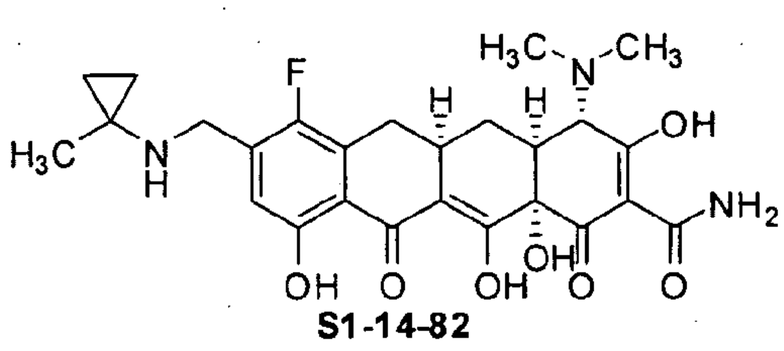
S1-14-80

S1-14-80: ^{1}H NMR (400 MHz, CD_3OD) δ 6.91 (d, J = 5.6 Hz, 1 H), 4.12 (s, 2 H), 4.00 (s, 1 H), 3.10-2.84 (m, 11 H), 2.62-2.54 (m, 1 H), 2.24-2.05 (m, 4 H), 1.89-1.71 (m, 4 H), 1.56-1.47 (m, 1 H); MS (ESI) *m/z* 530.1 (M+H).



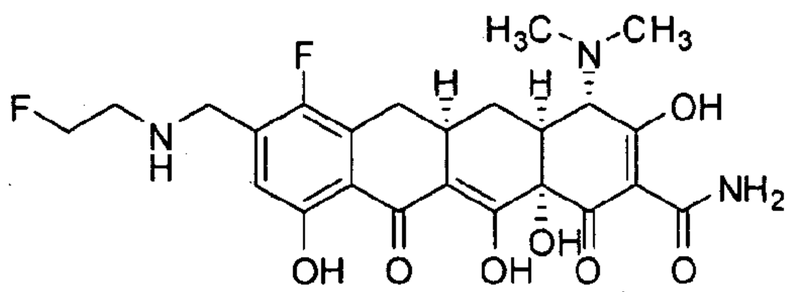
S1-14-81

S1-14-81: ^{1}H NMR (400 MHz, CD_3OD) δ 6.92 (d, J = 5.2 Hz, 1 H), 4.16 (s, 2 H), 4.00 (s, 1 H), 3.10-2.84 (m, 10 H), 2.23-2.06 (m, 4 H), 1.79-1.76 (m, 2 H), 1.61-1.50 (m, 2 H), 1.32-1.10 (m, 5 H); MS (ESI) *m/z* 530.1 (M+H).



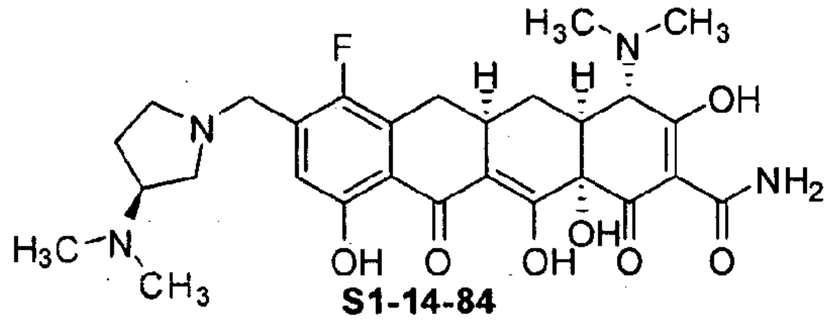
S1-14-82

S1-14-82: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, J = 6.0 Hz, 1 H), 4.36 (s, 2 H), 4.10 (s, 1 H), 3.22-2.95 (m, 9 H), 2.32-2.23 (m, 2 H), 1.67-1.59 (m, 1 H), 1.56 (s, 3 H), 1.12-1.09 (m, 2 H), 0.86-0.83 (m, 2 H); MS (ESI) *m/z* 516.0 (M+H).



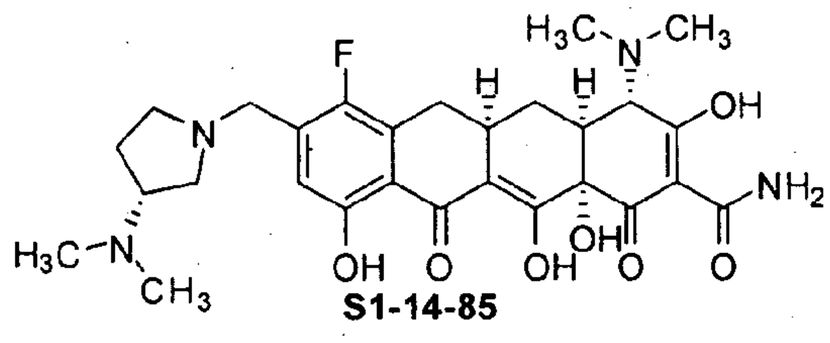
S1-14-83

S1-14-83: ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, J = 5.2 Hz, 1 H), 4.86 (d, J = 4.4 Hz, 1 H), 4.72 (d, J = 4.4 Hz, 1 H), 4.35 (s, 2 H), 4.11 (s, 1 H), 3.52 (d, J = 4.0 Hz, 1 H), 3.45 (d, J = 4.0 Hz, 1 H),3.23-2.95 (m, 9 H), 2.36-2.24 (m, 2 H), 1.68-1.58 (m, 1 H); MS (ESI) *m/z* 508.0 (M+H).



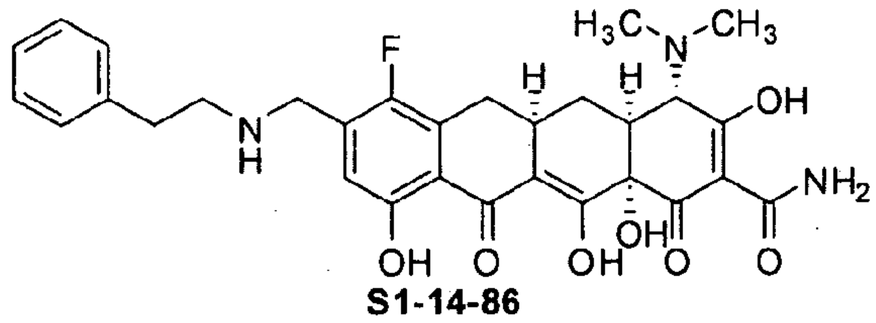
S1-14-84

S1-14-84: ^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (d, J = 5.6 Hz, 1 H), 4.61-4.55 (m, 2 H), 4.30-4.19 (m,1 H), 4.11 (s, 1 H), 4.05-3.50 (m, 4 H), 3.23-2.90 (m, 15 H), 2.70-2.60 (m, 1 H), 2.55-2.45 (m, 1 H), 2.35-2.20 (m, 2 H), 1.68-1.57 (m, 1 H); MS (ESI) *m/z* 559.1 (M+H).



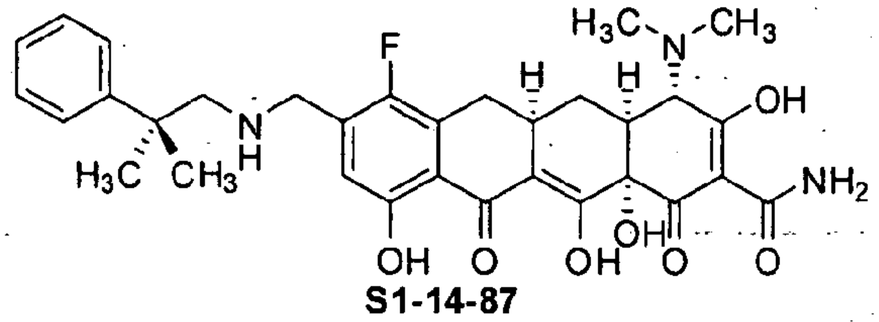
S1-14-85

S1-14-85: ^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (d, J = 6.06 Hz, 1 H), 4.55 (s, 2 H), 4.25-4.18 (m,1 H), 4.09 (s, 1 H), 3.95-3.48 (m, 4 H), 3.23-2.95 (m, 15 H), 2.65-2.58 (m, 1 H), 2.45-2.39 (m, 1 H), 2.38-2.19 (m, 2 H), 1.70-1.58 (m, 1 H); MS (ESI) *m/z* 559.1 (M+H).



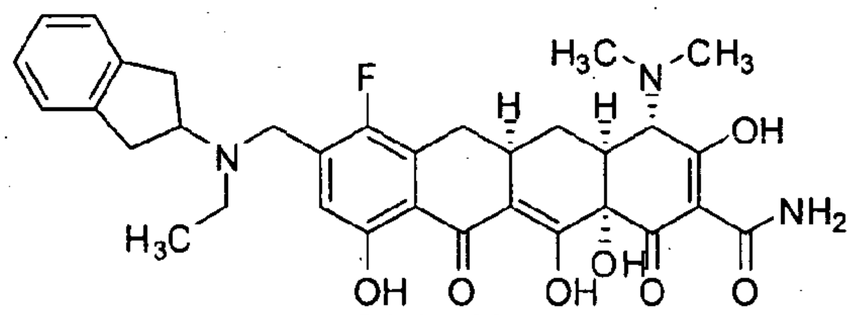
S1-14-86

S1-14-86: ^{1}H NMR (400 MHz, CD_3OD) δ 7.28-7.16 (m, 5 H), 6.93 (d, *J* = 6.0 Hz, 1 H), 4.23 (s, 2 H), 4.00 (s, 1 H), 3.25 (t, *J* = 7.6 Hz, 2 H), 3.21-2.88 (m, 11 H), 2.28-2.14 (m, 2 H), 1.61-1.50 (m, 1 H); MS (ESI) *m/z* 566.1 (M+H).



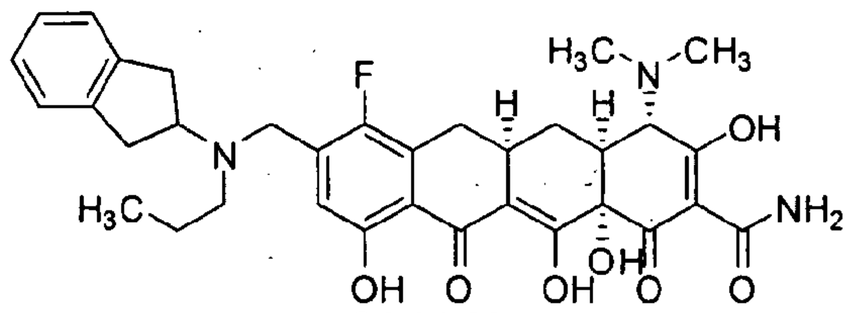
S1-14-87

S1-14-87: ^{1}H NMR (400 MHz, CD_3OD) δ 7.38-7.27 (m, 5 H), 6.90 (d, *J* = 6.0 Hz, 1 H), 4.20 (s, 2 H), 4.10 (s, 1 H), 3.20-2.98 (m, 11 H), 2.29-2.20 (m, 2 H), 1.69-1.60 (m, 1 H), 1.44 (s, 6 H); MS (ESI) *m/z* 594.0 (M+H).



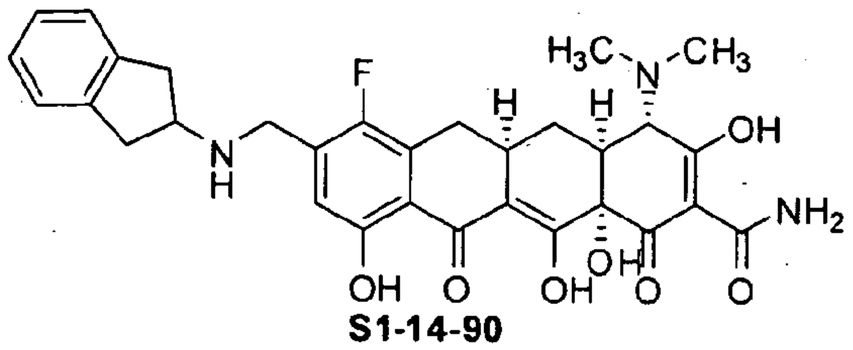
S1-14-88

S1-14-88: ^{1}H NMR (400 MHz, CD_3OD) δ 7.29-7.23 (m, 4 H), 7.11 (d, *J* = 6.0 Hz, 1 H), 4.49-4.43 (m, 3 H), 4.10 (s, 1 H), 3.57-3.48 (m, 4 H), 3.24-2.98 (m, 11 H), 2.40-2.25 (m, 2 H), 1.66-1.58 (m, 1 H), 1.41 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 605.9 (M+H).



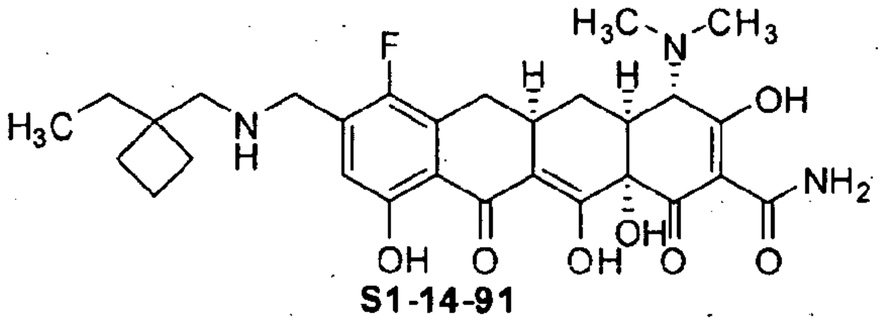
S1-14-89

S1-14-89: ^{1}H NMR (400 MHz, CD_3OD) δ 7.22-7.16 (m, 4 H), 7.05 (d, *J* = 6.0 Hz, 1 H), 4.48-4.41 (m, 3 H), 4.05 (s, 1 H), 3.60-3.46 (m, 4 H), 3.18-2.95 (m, 11 H), 2.35-2.17 (m, 2 H), 1.82-1.68 (m, 2 H), 1.62-1.52 (m, 1 H), 0.90 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 620.3 (M+H).



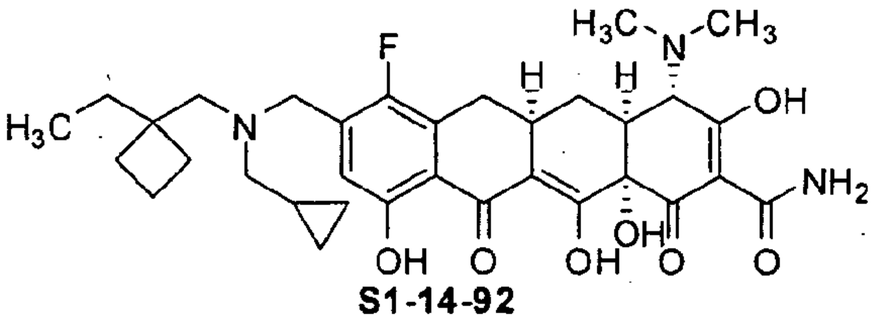
S1-14-90

S1-14-90: ^{1}H NMR (400 MHz, CD_3OD) δ 7.18-7.10 (m, 4 H), 6.95 (d, *J* = 6.0 Hz, 1 H), 4.25 (s, 2 H), 4.11-4.04 (m, 1 H), 4.00 (s, 1 H), 3.40-3.34 (m, 2 H), 3.19-2.85 (m, 11 H), 2.26-2.12 (m, 2 H), 1.57-1.51 (m, 1 H); MS (ESI) *m/z* 578.4 (M+H).



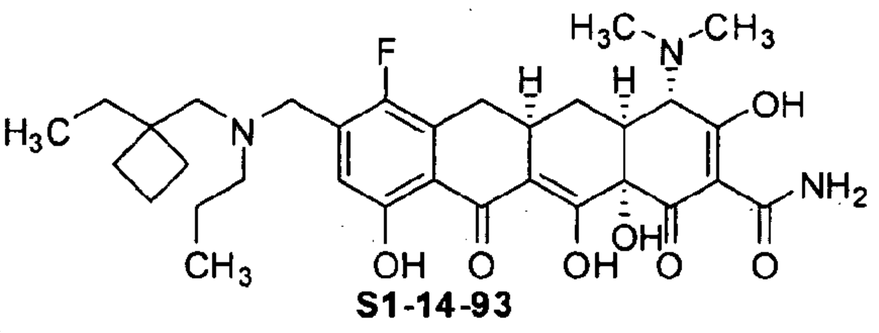
S1-14-91

S1-14-91: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 5.6 Hz, 1 H), 4.34 (s, 2 H), 4.13 (s, 1 H), 3.20-2.89 (m, 11 H), 2.31-2.25 (m, 2 H), 1.90-1.73 (m, 6 H), 1.60-1.48 (m, 3 H), 0.86 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 558.1 (M+H).



S1-14-92

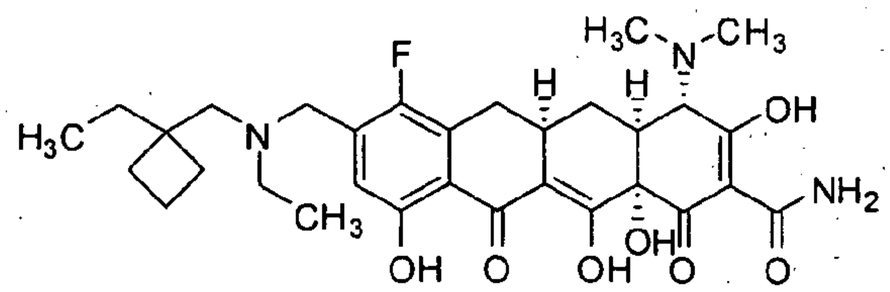
S1-14-92: ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, *J* = 5.6 Hz, 1 H), 4.38 (s, 2 H), 4.03 (s, 1 H), 3.18-2.85 (m, 13 H), 2.30-2.15 (m, 2 H), 1.90-1.75 (m, 6 H), 1.70-1.518 (m, 3 H), 1.20-1.11 (m, 1 H), 0.81 (t, *J* = 7.2 Hz, 3 H), 0.78-0.69 (m, 2 H), 0.45-0.36 (m, 2 H); MS (ESI) *m/z* 612.1 (M+H).



S1-14-93

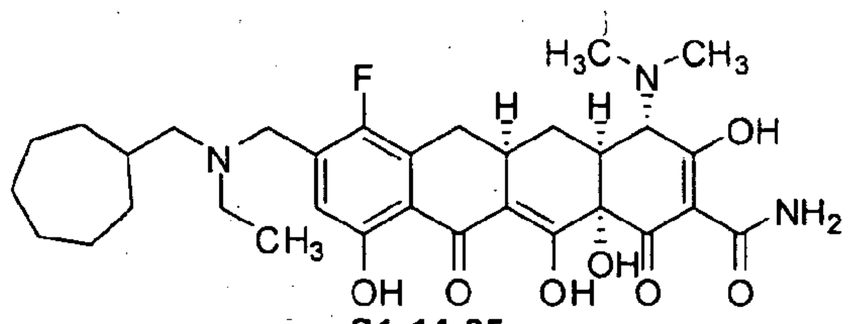
S1-14-93: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 5.6 Hz, 1 H), 4.38-4.34 (m, 2 H), 4.03 (s, 1 H), 3.36-3.29 (m, 1 H), 3.19-2.88 (m, 12 H), 2.36-2.25 (m,

2 H), 2.00-1.81 (m, 8 H), 1.72-1.50 (m, 3 H), 0.91 (t, J = 7.2 Hz, 3 H), 0.82 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 600.2 (M+H).



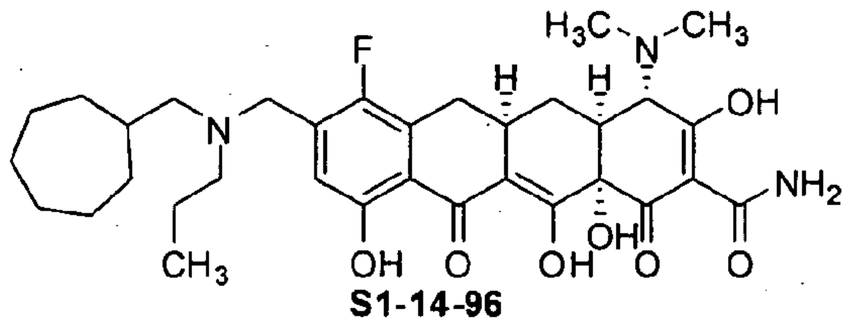
S1-14-94

S1-14-94: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.6 Hz, 1 H), 4.38-4.34 (m, 2 H), 4.11 (s, 1 H), 3.38-3.30 (m, 1 H), 3.25-2.95 (m, 12 H), 2.36-2.25 (m, 2 H), 2.05-1.85 (m, 6 H), 1.78-1.61 (m, 3 H), 1.45 (t, J = 7.2 Hz, 3 H), 0.90 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 586.0 (M+H).



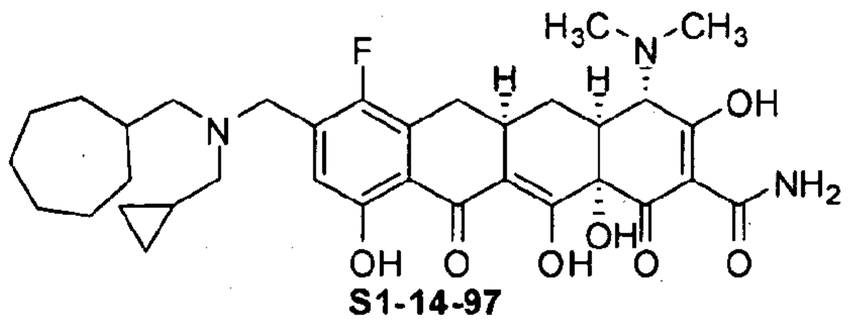
S1-14-95

S1-14-95: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, J = 5.2 Hz, 1 H), 4.40 (d, J = 13.2 Hz, 1 H), 4.28 (d, J = 13.6 Hz, 1 H), 4.04 (s, 1 H), 3.22-2.81 (m, 13 H), 2.31-2.17 (m, 2 H), 2.06-1.93 (m, 2 H), 1.82-1.43 (m, 9 H), 1.31 (t, J = 7.2 Hz, 3 H), 1.25-1.14 (m, 3 H); MS (ESI) *m/z* 600.3 (M+H).



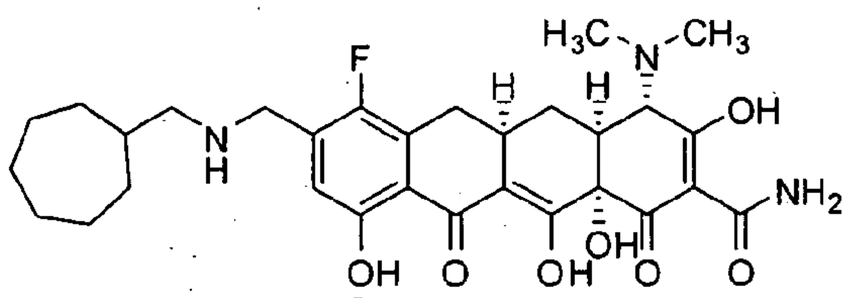
S1-14-96

S1-14-96: ^{1}H NMR (400 MHz, CD_3OD) δ 7.02 (d, J = 6 Hz, 1 H), 4.42-4.29 (m, 2 H), 4.05 (s, 1 H), 3.22-2.81 (m, 13 H), 2.31-2.17 (m, 2 H), 2.06-1.93 (m, 2 H), 1.82-1.43 (m, 11 H), 1.31 (t, J = 7.2 Hz, 3 H), 1.25-1.14 (m, 3 H), MS (ESI) *m/z* 600.3 (M+H).



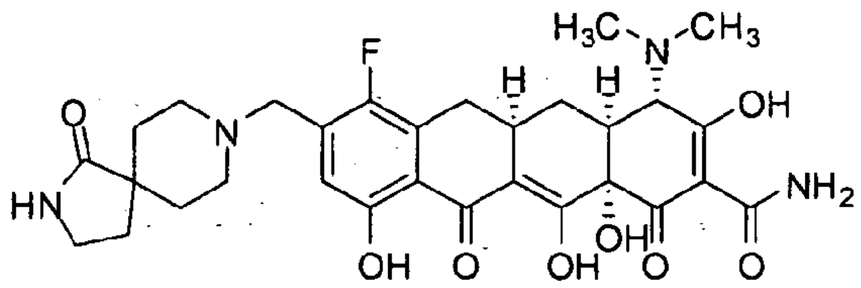
S1-14-97

S1-14-97: ^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (d, J = 5.2 Hz, 1 H), 4.54 (s, 2 H), 4.16 (s, 1 H), 3.23-3.01 (m, 13 H), 2.42-2.29 (m, 2 H), 2.14-2.05 (m, 1 H), 1.92-1.83 (m, 1 H), 1.79-1.45 (m, 9 H), 1.48-1.21 (m, 4 H), 0.86-0.75 (m, 2 H), 0.55-0.47 (m, 2 H); MS (ESI) *m/z* 626.2 (M+H).



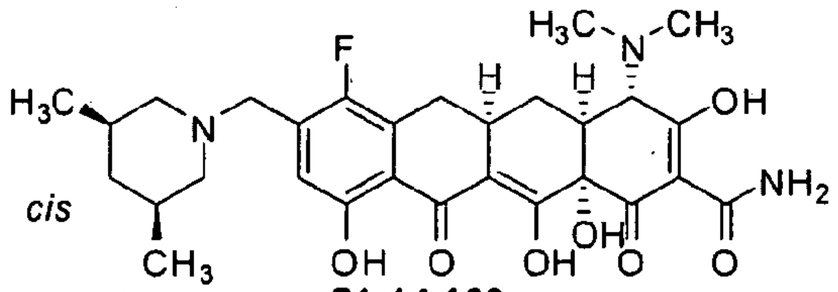
S1-14-98

S1-14-98: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.6 Hz, 1 H), 4.29 (s, 2 H), 4.13 (s, 1 H), 3.21-2.96 (m, 11 H), 2.38-2.25 (m, 2 H), 2.02-1.91 (m, 1 H), 1.85-1.47 (m, 11 H), 1.37-1.26 (m, 2 H); MS (ESI) *m/z* 572.2 (M+H).



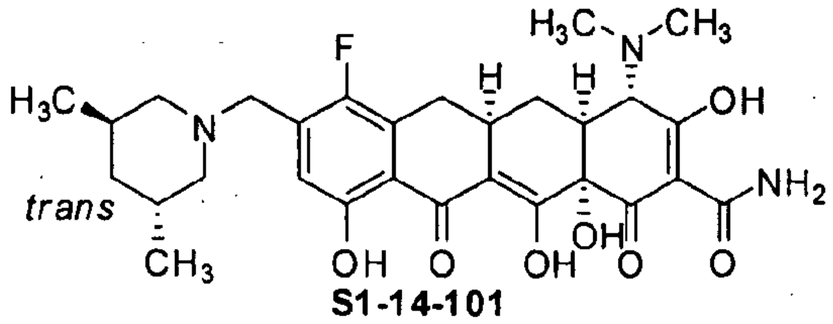
S1-14-99

S1-14-99: ^{1}H NMR (400 MHz, CD_3OD) δ 6.97 (d, J = 5.6 Hz, 1 H), 4.31 (s, 2 H), 4.00 (s, 1 H), 3.57-3.44 (m, 3 H), 3.27-3.22 (m, 2 H), 3.13-2.85 (m, 10 H), 2.28-2.21 (m, 1 H), 2.15-2.08 (m, 2 H), 2.04-1.89 (m, 3 H), 1.85-1.77 (m, 1 H), 1.70-1.66 (m, 1 H), 1.60-1.48 (m, 1 H); MS (ESI) *m/z* 599.2 (M+H).



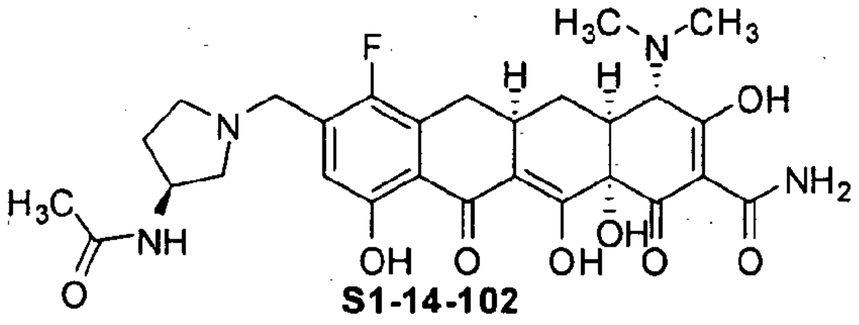
S1-14-100

S1-14-100: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, J = 6.0 Hz, 1 H), 4.29 (s, 2 H), 4.03 (s, 1 H), 3.40-3.29 (m, 1 H), 3.23-2.81 (m, 10 H), 2.63-2.56 (m, 1 H), 2.32-2.07 (m, 4 H), 1.62-1.49 (m, 2 H), 1.35-1.25 (m, 1 H), 1.10 (d, J = 7.6 Hz, 3 H), 0.90 (d, J = 7.6 Hz, 3 H), 0.89-0.78 (m, 1 H); MS (ESI) *m/z* 558.3 (M+H).



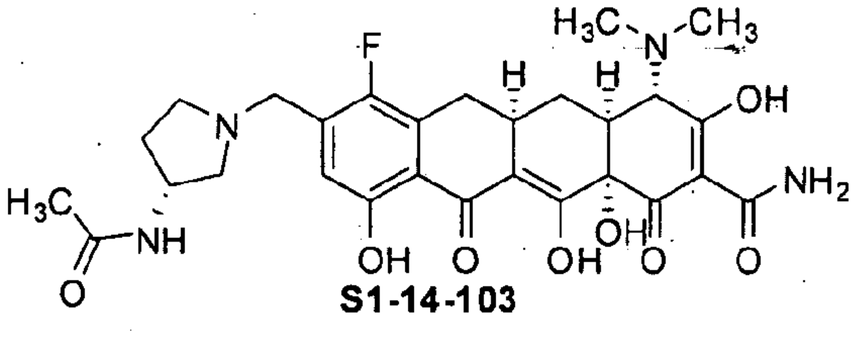
S1-14-101

S1-14-101: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.6 Hz, 1 H), 4.37 (s, 2 H), 4.11 (s, 1 H), 3.43-3.37 (m, 2 H), 3.23-2.97 (m, 9 H), 2.68-2.60 (m, 2 H), 2.42-2.24 (m, 2 H), 1.98-1.81 (m, 3 H), 1.71-1.58 (m, 1 H), 0.99 (d, J = 7.6 Hz, 6 H), 0.95-0.85 (m, 1 H); MS (ESI) *m/z* 558.6 (M+H).



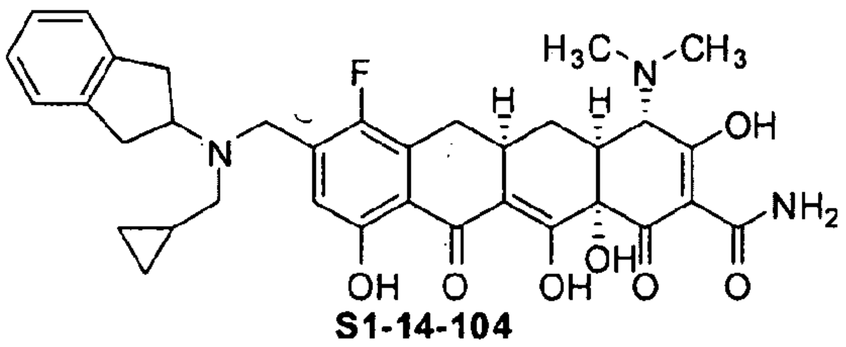
S1-14-102

S1-14-102: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 6.0 Hz, 1 H), 4.53-4.48 (m, 2 H), 4.42-4.38 (m, 1 H), 4.10 (s, 1 H), 3.92-3.62 (m, 2 H), 3.55-3.50 (m, 2 H), 3.25-2.96 (m, 9 H), 2.62-2.51 (m, 1 H), 2.40-2.21 (m, 2 H), 2.19-2.02 (m, 2 H), 1.96 (d, J = 7.2 Hz, 3 H), 1.71-1.60 (m, 1 H); MS (ESI) *m/z* 573.3 (M+H).



S1-14-103

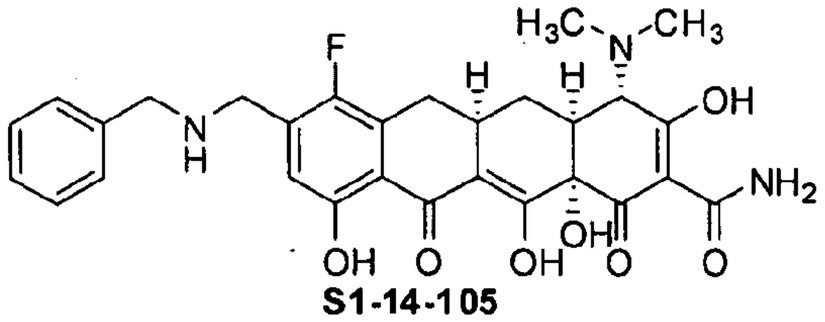
S1-14-103: ^{1}H NMR (400 MHz, CD_3OD) δ 7.12 (d, J = 6.0 Hz, 1 H), 4.57-4.46 (m, 3 H), 4.15 (s, 1 H), 3.90-3.83 (m, 1 H), 3.68-3.51 (m, 3 H), 3.24-2.98 (m, 9 H), 2.62-2.55 (m, 1 H), 2.39-2.25 (m, 2 H), 2.21-2.05 (m, 2 H), 1.98 (d, J = 10 Hz, 3 H), 1.67-1.60 (m, 1 H); MS (ESI) *m/z* 572.9 (M+H).



S1-14-104

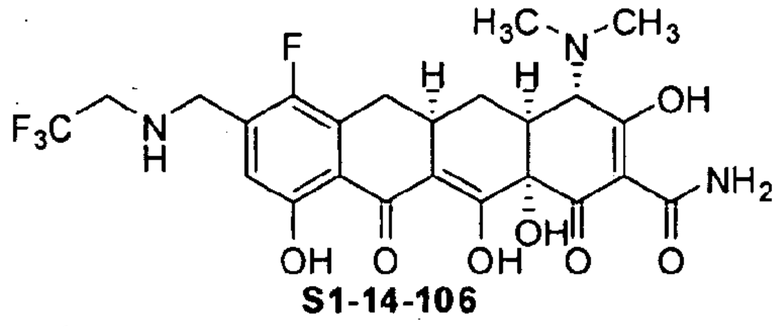
S1-14-104: ^{1}H NMR (400 MHz, CD_3OD) δ 7.22-7.16 (m, 4 H), 7.02 (d, J = 6.0 Hz, 1 H), 4.52-4.38 (m, 3 H), 4.05 (s, 1 H), 3.45-3.32 (m, 4 H), 3.18-2.95 (m, 11

H), 2.32-2.15 (m, 2 H), 1.61-1.52 (m, 1 H), 1.15-1.08 (m, 1 H), 0.73-0.67 (m, 2 H), 0.39-0.33 (m, 2 H); MS (ESI) *m/z* 632.0 (M+H).



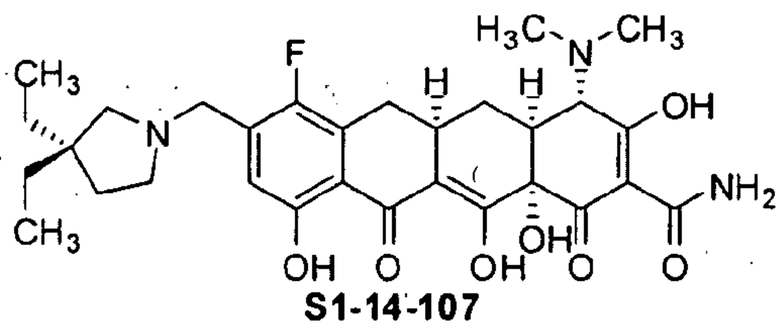
S1-14-105

S1-14-105: ^{1}H NMR (400 MHz, CD_3OD) δ 7.44-7.37 (m, 5 H), 6.93 (d, *J* = 5.6 Hz, 1 H), 4.23 (s, 2 H), 4.21 (s, 2 H), 4.03 (s, 1 H), 3.25-2.88 (m, 9 H), 2.27-2.15 (m, 2 H), 1.59-1.50 (m, 1 H); MS (ESI) *m/z* 552.0 (M+H).



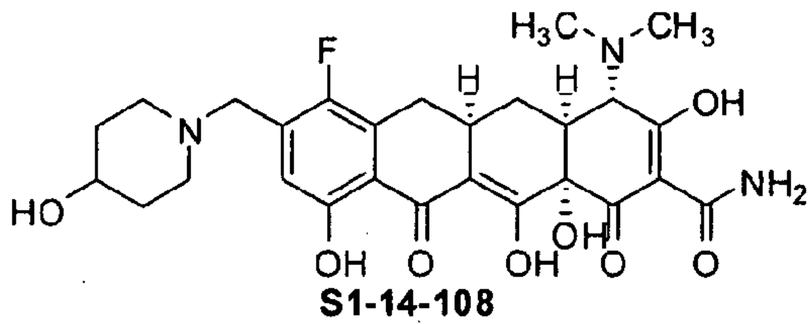
S1-14-106

S1-14-106: ^{1}H NMR (400 MHz, CD_3OD) δ 6.97 (d, *J* = 5.6 Hz, 1 H), 4.34 (s, 2 H), 4.05 (d, *J* = 8.8 Hz, 2 H), 4.02 (s, 1 H), 3.25-2.88 (m, 9 H), 2.30-2.15 (m, 2 H), 1.61-1.51 (m, 1 H); MS (ESI) *m/z* 544.1 (M+H).



S1-14-107

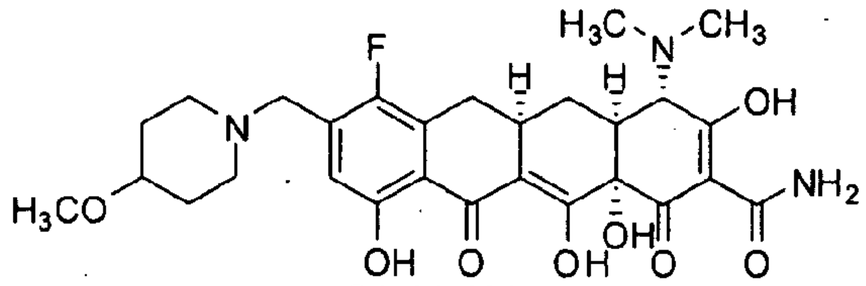
S1-14-107: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, *J* = 5.2 Hz, 1 H), 4.39 (s, 2 H), 4.04 (s, 1 H), 3.58-3.49 (m, 1 H), 3.48-3.44 (m, 1 H), 3.18-2.88 (m, 11 H), 2.32-2.15 (m, 2 H), 1.98-1.88 (m, 1 H), 1.82-1.73 (m, 1 H), 1.62-1.41 (m, 5 H), 0.82 (m, *J* = 7.2 Hz, 3 H), 0.78 (m, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 572.1 (M+H).



S1-14-108

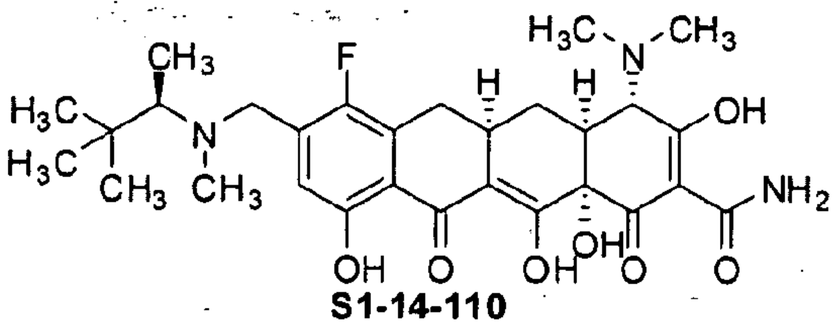
S1-14-108: ^{1}H NMR (400 MHz, CD_3OD) δ 6.99 (t, *J* = 6.0 Hz, 1 H), 4.29-4.28 (m, 2 H), 4.01 (s, 1 H), 4.00-3.98 (m,1 H), 3.33-3.29 (m, 2 H), 3.18-2.95 (m, 11

H), 2.31-2.27 (m, 2 H), 2.17-2.04 (m, 2 H), 1.95-1.84 (m, 2 H), 1.57-1.49 (m, 1 H); MS (ESI) *m/z* 546.9 (M+H).



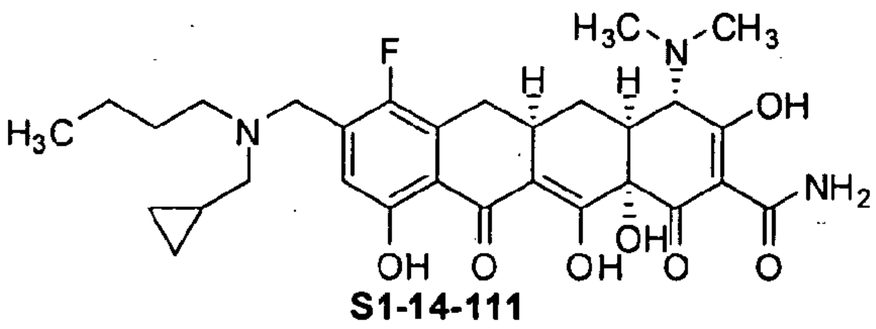
S1-14-109

S1-14-109: ^{1}H NMR (400 MHz, CD_3OD) δ 6.98 (t, *J* = 5.6 Hz, 1 H), 4.30-4.28 (m, 2 H), 4.01 (s, 1 H), 4.00-3.98 (m,1 H), 3.55-3.48 (m, 2 H), 3.39-3.37 (m, 1 H), 3.26 (s, 3 H), 3.18-2.95 (m, 11 H), 2.32-2.16 (m, 3 H), 2.06-2.02 (m, 1 H), 1.85-1.78 (m, 2 H), 1.62-1.50 (m, 1 H); MS (ESI) *m/z* 560.0 (M+H).



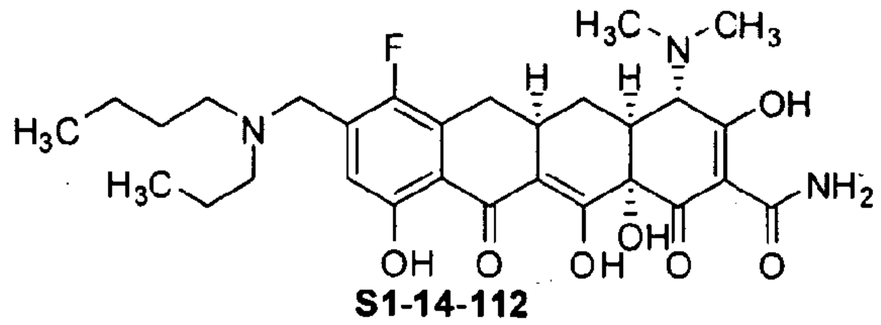
S1-14-110

S1-14-110: ^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (d, *J* = 6.0 Hz, 1 H), 4.55 (d, *J* = 13.2 Hz, 1 H), 4.39 (d, *J* = 13.2 Hz, 1 H), 4.10 (s, 1 H), 3.51-3.43 (m, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.89 (s, 3 H), 3.25-2.97 (m, 3 H), 2.35 (t, *J* = 14.7 Hz, 1 H), 2.29-2.21 (m, 1 H), 1.69-1.59 (m, 1 H), 1.38 (d, *J* = 6.9 Hz, 3 H), 1.00 (s, 9 H); MS (ESI) *m/z* 560.25 (M+H).



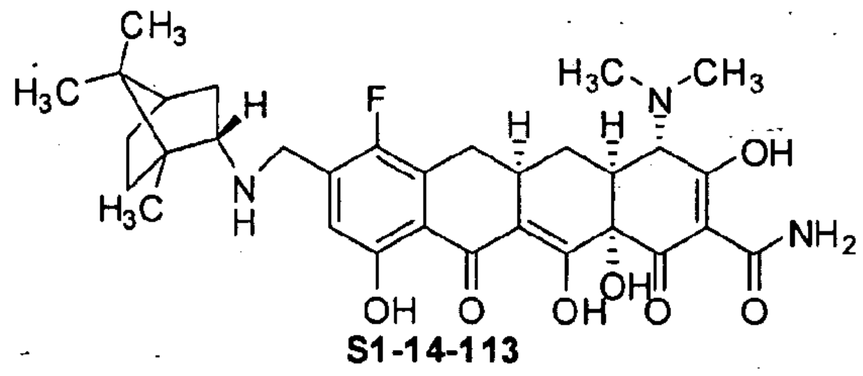
S1-14-111

S1-14-111: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 6.5 Hz, 1 H), 4.55 (d, *J* = 12.2 Hz, 1 H), 4.44 (d, *J* = 12.2 Hz, 1 H), 4.12 (s, 1 H), 2.95-3.05 (m, 13 H), 2.22-2.40 (m, 2 H), 1.59-1.75 (m, 3 H), 1.35-1.45 (m, 2 H), 1.12-1.25 (m, 1 H), 0.95 (t, *J*-7.7 Hz, 3 H), 0.75-0.85 (m, 2 H), 0.40-0.50 (m, 2 H); MS (ESI) *m/z* 572.2 (M+H).



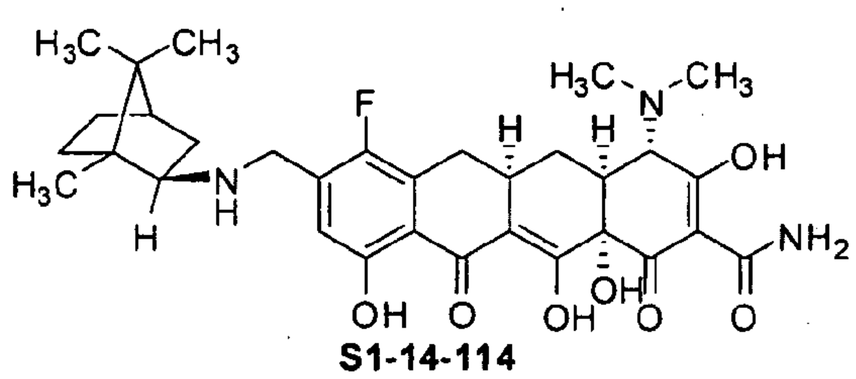
S1-14-112

S1-14-112: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, J = 5.6 Hz, 1 H), 4.35 (s, 2 H), 4.00 (s, 1 H), 2.70-3.20 (m, 12 H), 2.12-2.31 (m, 2 H), 1.50-1.80 (m, 6 H), 1.15-1.40 (m, 2 H), 0.85-0.95 (m, 6 H); MS (ESI) *m/z* 560.1.



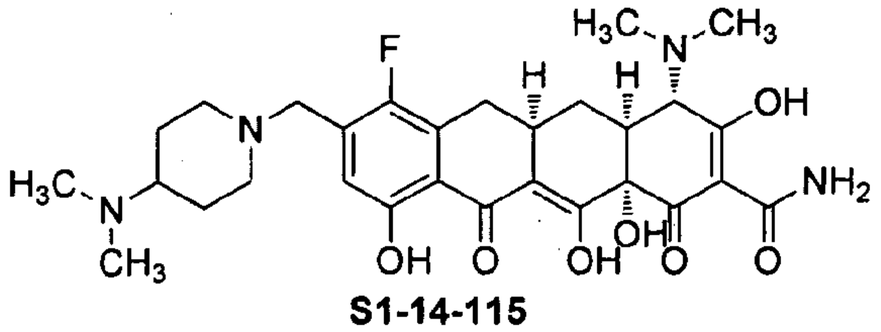
S1-14-113

S1-14-113: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 6.0 Hz, 1 H), 4.30 (s, 2 H), 4.06 (s, 1 H), 3.23-3.16 (m, 1 H), 3.17-2.95 (m, 9 H), 2.39-2.30 (m, 2 H), 2.26-2.19 (m, 1 H), 1.90-1.81 (m, 1 H), 1.78 (t, J = 4.6, 1 H), 1.67-1.54 (m, 4 H), 1.42-1.33 (m, 1 H), 1.21 (dd, J = 13.7, 4.1 Hz, 1 H), 1.01 (s, 3 H), 0.93 (s, 3 H), 0.89 (s, 3 H); MS (ESI) *m/z* 598.33 (M+H).



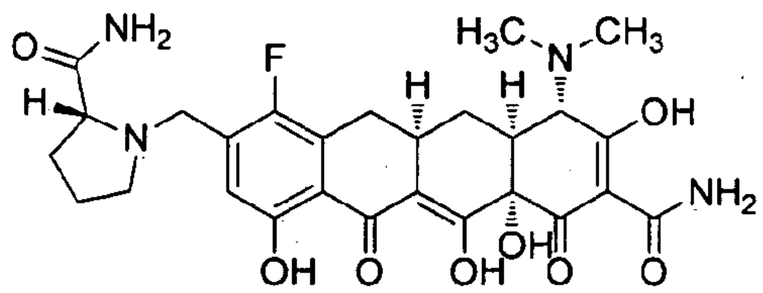
S1-14-114

S1-14-114: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 6.0 Hz, 1 H), 4.37 (d, J = 13.3 Hz, 1 H), 4.20 (d, J = 13.3 Hz, 1 H), 4.09 (s, 1 H), 3.23-3.16 (m, 1 H), 3.17-2.96 (m, 9 H), 2.35 (t, J = 14.7 Hz, 1 H), 2.28-2.21 (m, 1 H), 2.13-2.06 (m, 1 H), 1.92-1.77 (m, 4 H), 1.74-1.60 (m, 2 H), 1.24-1.17 (m, 1 H), 1.08 (s, 3 H), 0.98 (s, 3 H), 0.92 (s, 3 H); MS (ESI) *m/z* 598.28 (M+H).



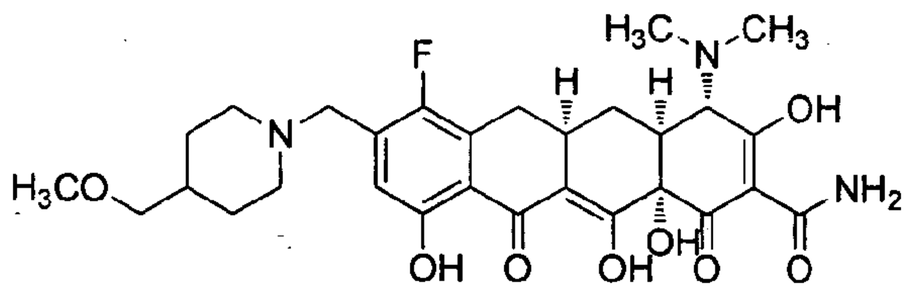
S1-14-115

^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, *J* = 5.2 Hz, 1 H), 4.37 (s, 2 H), 4.07 (s, 1 H)□3.66-3.55 (m, 3 H), 3.19-2.92 (m, 11 H), 2.84 (s, 6 H), 2.40-1.98 (m, 6H), 1.63-1.53 (m, 1H); MS (ESI) *m/z* 573.1 (M+H)



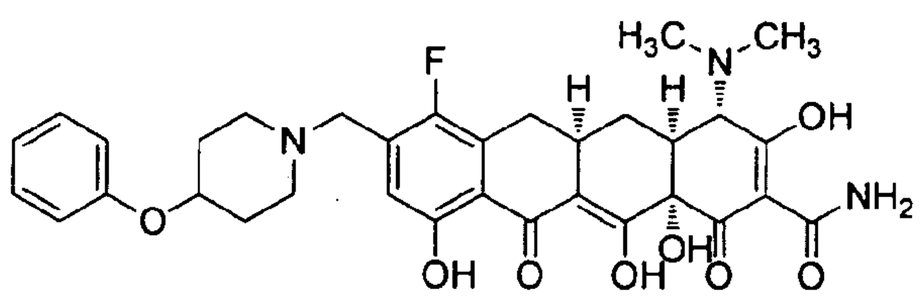
S1-14-116

^{1}H NMR (400 MHz, CD_3OD) δ 6.96 (d, *J* = 5.6 Hz, 1 H), 4.44-4.33 (m, 2 H), 4.19 (t, *J* = 8.4 Hz, 1 H), 4.02 (s, 1 H), 3.59-3.57 (m, 1H), 3.40-3.30 (m, 1 H), 3.14-3.11(m, 2 H), 3.03-2.88 (m, 7 H), 2.56-2.50 (m, 1 H), 2.28-2.20 (m, 1 H), 2.17-2.13 (m, 2 H), 1.97-1.90 (m, 2 H), 1.60-1.51 (m, 1 H); MS (ESI) *m/z* 559.2 (M+H).



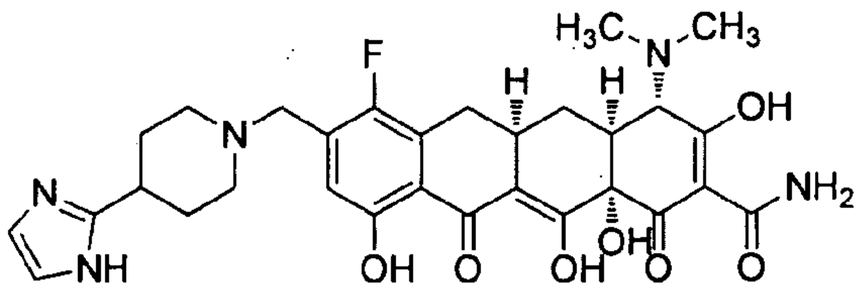
S1-14-117

^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, *J* = 5.2 Hz, 1 H), 4.36 (s, 2 H), 4.13 (s, 1 H), 3.56 (d, *J* =11.6 Hz, 2 H), 3.28 (s, 3 H), 3.26 (d, *J* =5.6 Hz, 2 H), 3.22-2.97 (m, 11 H), 2.35-2.25 (m, 2 H), 1.98-1.90 (m, 3 H), 1.67-1.56 (m, 3 H); MS (ESI) *m/z* 574.2 (M+H).



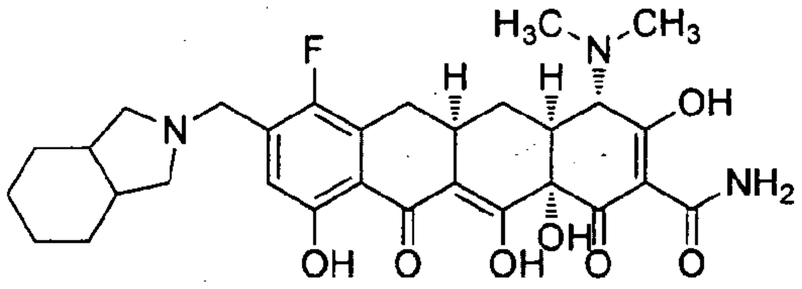
S1-14-118

^{1}H NMR (400 MHz, CD_3OD) δ 7.30-7.23 (m, 2 H), 7.14 (d, *J* = 4.4 Hz, 1 H), 7.01-6.91 (m, 3 H), 4.44 (s, 2 H), 4.11 (s, 1 H), 3.64 (d, *J* = 12 Hz, 1 H), 3.45 (s, 3 H), 3.23-3.18 (m, 1 H), 3.11-2.96 (m, 9 H), 2.36-2.16 (m, 6 H), 1.68-1.61 (m, 1 H); MS (ESI) *m/z* 622.2 (M+H).



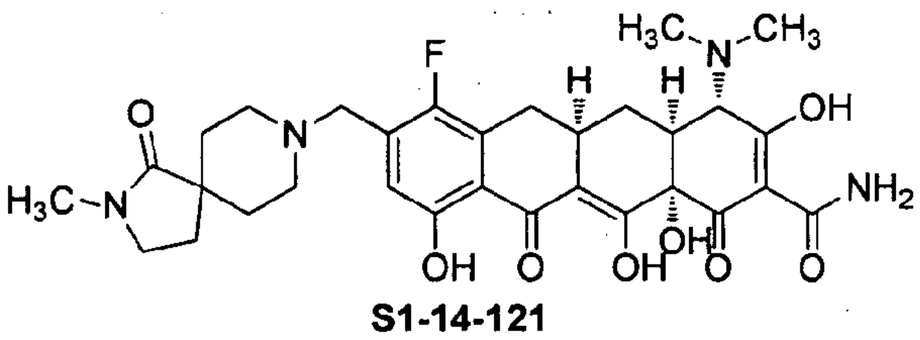
S1-14-119

^{1}H NMR (400 MHz, CD_3OD) δ 7.49 (s, 2 H), 7.19 (d, J = 5.6 Hz, 1 H), 4.46 (s, 2 H), 4.13 (s, 1 H), 3.72 (d, J = 12 Hz, 2 H), 3.53-3.49 (m, 1 H), 3.41-3.35 (m, 2 H), 3.23-2.98 (m, 9 H), 2.39-2.24 (m, 6 H), 1.68-1.58(m, 1 H) ; MS (ESI) *m/z* 596.2 (M+H).



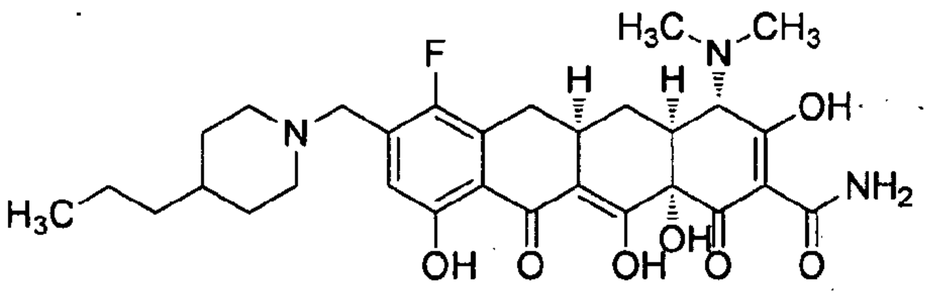
S1-14-120

^{1}H NMR (400 MHz, CD_3OD) δ 7.15-7.11(m, 1 H), 4.49 (d, J = 9.2 Hz, 2 H), 4.11 (s, 1 H), 3.64-3.60 (m, 1 H), 3.49-3.34 (m, 1 H), 3.34-3.33 (m, 1 H), 3.22-2.96 (m, 10 H), 2.60-2.51 (m, 1 H), 2.43-2.20 (m, 3 H), 1.78-1.50 (m, 7 H), 1.42-1.40 (m, 2 H); MS (ESI) *m/z* 570.2 (M+H).



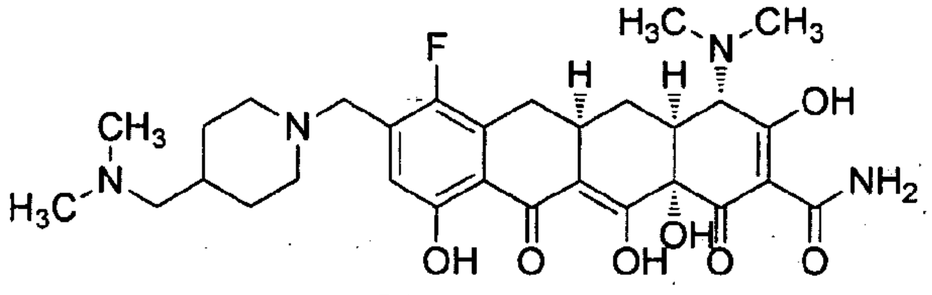
S1-14-121

^{1}H NMR (400 MHz, CD_3OD) δ 7.13-7.12(m, 1 H), 4.48 (s, 2 H), 4.15 (s, 1 H), 3.74-3.56 (m, 2 H), 3.46-3.37 (m, 3 H), 3.28-3.17(m, 2 H), 3.11-2.97 (m, 8 H), 2.82 (d, J =12.8 Hz, 3 H), 2.33-2.26 (m, 2 H), 2.17-1.92 (m, 5 H), 1.75 (d, J =14.4 Hz, 1 H), 1.67-1.68(m, 1 H); MS (ESI) *m/z* 613.3 (M+H).



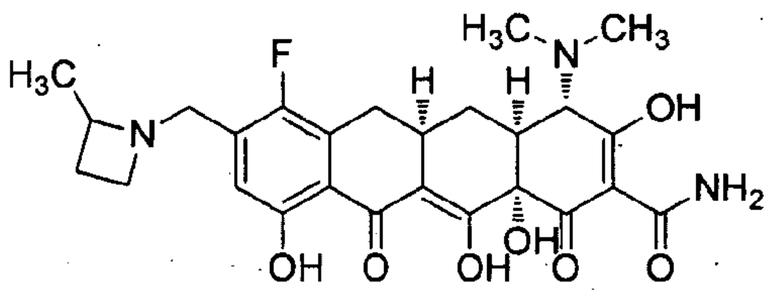
S1-14-122

^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.36 (s, 2 H), 4.15 (s, 1 H), 3.53 (d, *J* = 11.2 Hz, 2 H), 3.25-2.98 (m, 11 H), 2.29 (d, *J* = 13.2 Hz, 2 H), 1.94 (d, *J* = 14 Hz, 2 H), 1.75-1.51 (m, 4 H), 1.37-1.23 (m, 4 H), 091-0.88 (t, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 572.3 (M+H).



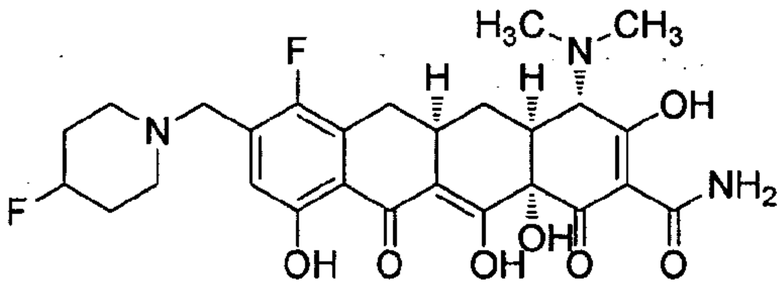
S1-14-123

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (d, *J* = 5.6 Hz, 1 H), 4.42 (s, 2 H), 4.14 (s, 1 H), 3.63 (d, *J* = 11.2 Hz, 2 H), 3.25-3.12 (m, 6 H), 3.07-2.93 (m, 13 H), 2.40-2.30 (m, 3 H), 2.11 (d, *J* = 14 Hz, 2 H), 1.74-1.65 (m, 3 H); MS (ESI) *m/z* 587.3 (M+H).



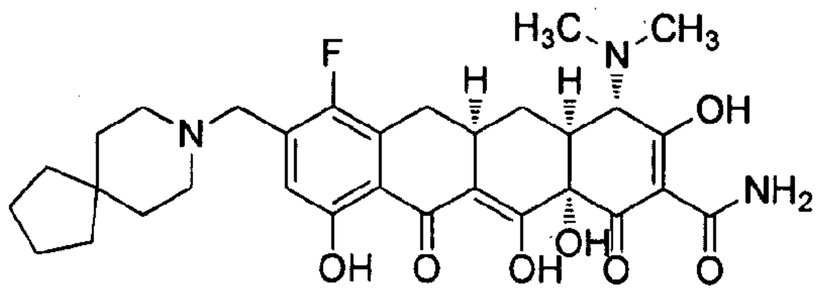
S1-14-124

^{1}H NMR (400 MHz, CD_3OD) δ 6.96 (d, *J* = 4.8 Hz, 1 H), 4.59-4.57 (m, 1 H), 4.41-4.31 (m, 2 H), 4.04-3.93 (m, 3 H), 3.13-2.88 (m, 9 H), 2.50-2.46 (m, 1 H), 2.28-2.16 (m, 3 H), 1.61-1.50(m, 1 H), 1.34 (d, *J* = 4.8 Hz, 3 H); MS (ESI) *m/z* 516.2 (M+H).



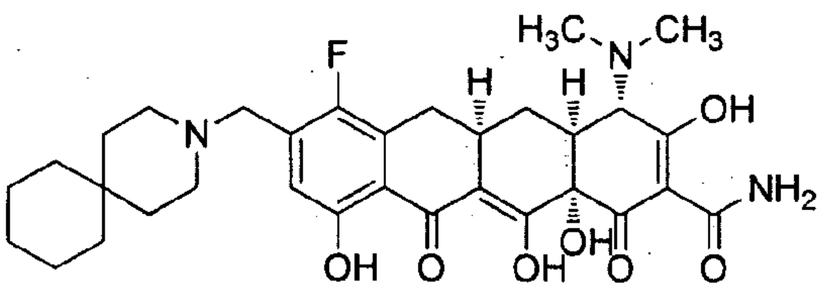
S1-14-125

^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (d, *J* = 5.6 Hz, 1 H), 5.04-5.02 (m, 0.5 H), 4.90-4.88 (m, 0.5 H), 4.41 (s, 2 H), 4.12 (s, 1 H), 3.65-3.33 (m, 4 H), 3.25-2.97 (m, 9 H), 2.37-2.03 (m, 6 H), 1.67-1.58 (m, 1 H); MS (ESI) *m/z* 548.2 (M+H).



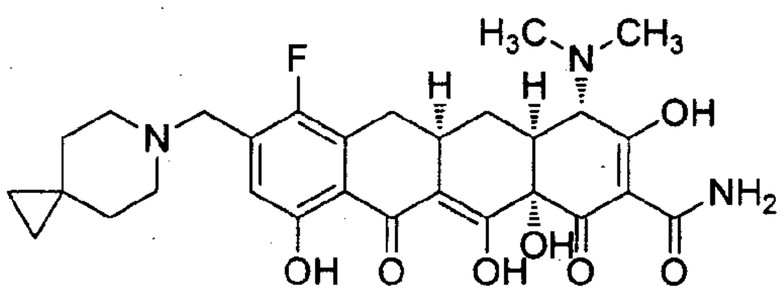
S1-14-126

^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, J = 5.6 Hz, 1 H), 4.38 (s, 2 H), 4.11 (s, 1 H)□3.45-3.42 (m, 2 H), 3.22-2.97 (m, 11 H), 2.36-2.24 (m, 2 H),1.85-1.54 (m, 11 H), 1.50-1.45 (m, 2 H); MS (ESI) *m/z* 584.3 (M+H)



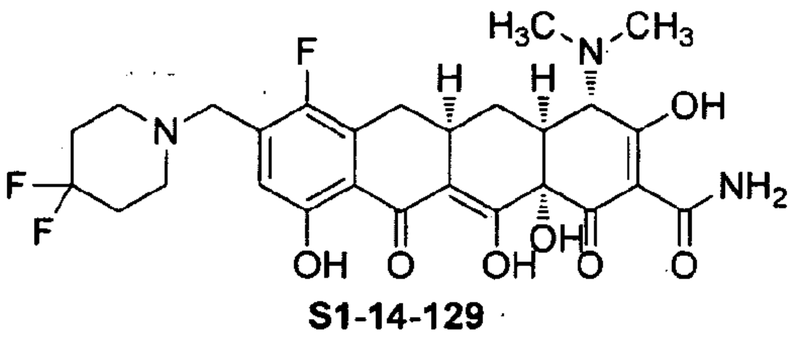
S1-14-127

^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.6 Hz, 1 H), 4.38 (s, 2 H), 4.11 (s, 1 H), 3.40-3.30 (m, 2 H), 3.23-2.97(m, 11 H), 2.36-2.24 (m, 2 H), 1.90-1.87 (m, 2 H), 1.64-1.32 (m, 13 H); MS (ESI) *m/z* 597.9 (M+H).



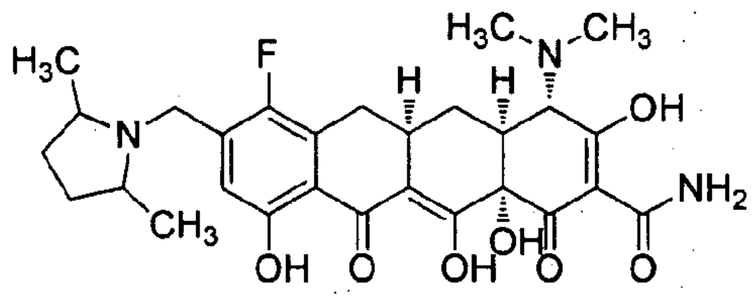
S1-14-128

^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, J = 5.6 Hz, 1 H), 4.41 (s, 2 H), 4.11 (s, 1 H), 3.54-3.51 (m, 2 H), 3.22-2.97 (m, 11 H), 2.37-2.18 (m, 4 H), 1.68-1.62 (m, 1 H), 1.22-1.19 (m, 2 H), 0.53-0.50 (m, 4 H); MS (ESI) *m/z* 556.2 (M+H).



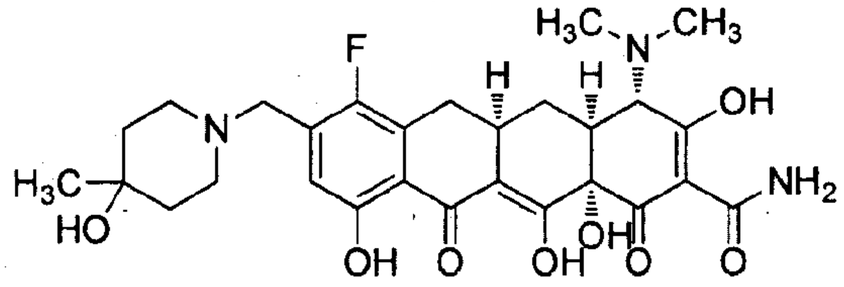
S1-14-129

^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (d, J = 5.6 Hz, 1 H), 4.47 (s, 2 H), 4.11 (s, 1 H), 3.66-3.50 (m, 2 H), 3.46-3.32 (m, 2 H), 3.22-2.97 (m, 9 H), 2.38-2.24 (m, 6 H), 1.68-1.58 (m, 1 H); MS (ESI) *m/z* 566.2 (M+H).



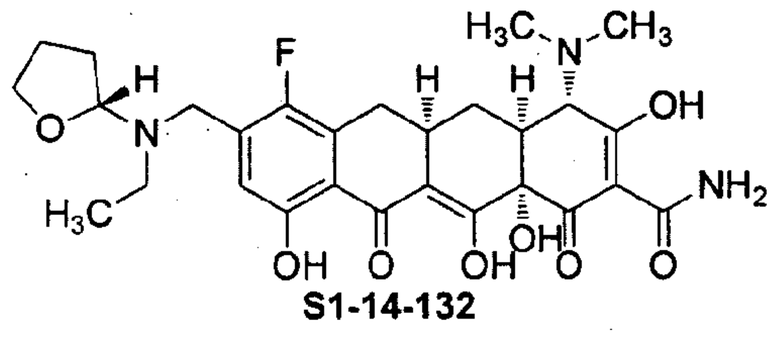
S1-14-130

^{1}H NMR (400 MHz, MeOD) δ 7.11 and 7.10 (each s, total 1 H), 4.50 (s, 2 H), 4.13 (s, 1 H), 3.73-3.64 (m, 2 H), 3.27-2.95 (m, 9 H), 2.40-2.25 (m, 4 H), 1.79-1.75 (m, 2 H), 1.70-1.60 (m, 1 H), 1.42 (d, *J* = 7.2 Hz, 6 H); MS (ESI) *m/z* 544.1 (M+H).



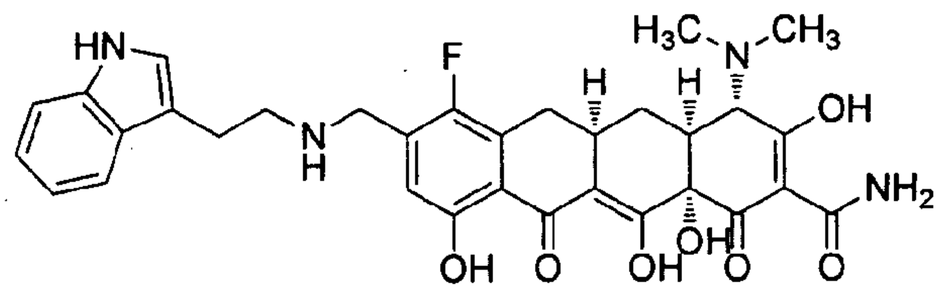
S1-14-131

^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, *J* = 5.6 Hz, 1 H), 4.30 (s, 2 H), 4.05 (s, 1 H), 3.29-3.22 (m, 4 H), 3.13 -2.89 (m, 9 H), 2.27-2.17 (m, 2 H), 1.85-1.80 (m, 2 H), 1.72-1.68 (m, 2 H), 1.60-1.51 (m, 1 H), 1.19 (s, 3 H); MS (ESI) m/z 560.0 (M+H).



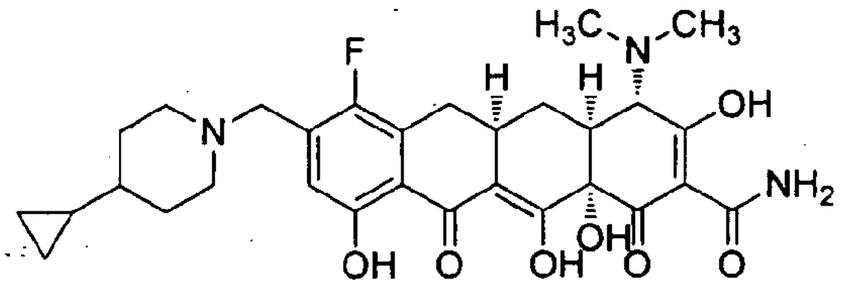
S1-14-132

^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (dd, *J* = 11.0, 5.5 Hz, 1 H), 4.61 (dd, *J* = 26.7, 14.2 Hz, 1 H), 4.47-4.27 (m, 2 H), 4.10 (s, 1 H), 4.00-3.82 (m, 2 H), 3.43-3.30 (m, 2 H), 3.25-2.94 (m, 11 H), 2.42-2.32 (m, 1 H), 2.29-2.11 (m, 2 H), 2.03-1.90 (m, 2 H), 1.71-1.56 (m, 2 H), 1.38 (t, *J* = 7.3 Hz, 3 H); MS (ESI) *m/z* 574.20 (M+H).



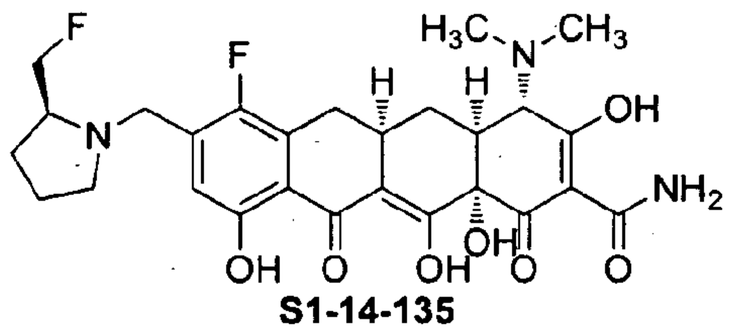
S1-14-133

^{1}H NMR (400 MHz, CD_3OD) δ 7.53 (d, J = 7.6 Hz, 1 H), 7.36 (d, J = 8.0 Hz, 1 H), 7.19 (s, 1 H), 7.11 (t, J = 7.6 Hz, 1 H), 7.04-7.00 (m, 2 H), 4.33-4.26 (m, 2 H), 4.11 (s, 1 H), 3.42-3.37 (m, 2 H), 3.26-2.95 (m, 11 H), 2.33-2.23 (m, 2 H), 1.68-1.59 (m, 1 H);MS (ESI) *m/z* 605.0 (M+H).



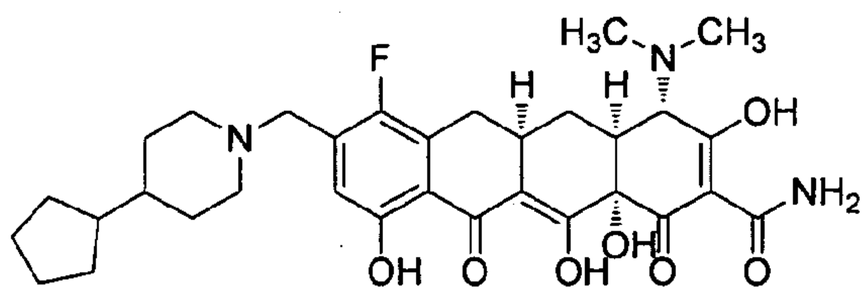
S1-14-134

^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, J = 5.6 Hz, 1 H), 4.24 (s, 2 H), 4.02 (s, 1 H), 3.45-3.42 (m, 2 H), 3.11-2.87 (m, 11 H), 2.26-2.15 (m, 3 H), 1.93-1.89 (m, 2 H), 1.60-1.48 (m, 3 H), 0.80-0.69 (m, 1 H), 0.50-0.40 (m, 1 H), 0.35-0.33 (m, 2 H), 0.07-0.02 (m, 2 H); MS (ESI) *m/z* 570.0 (M+H).



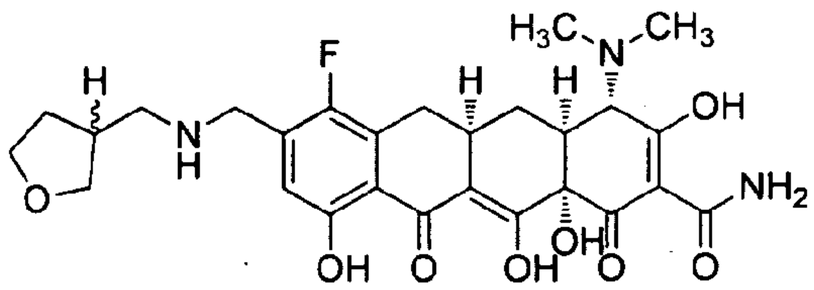
S1-14-135

^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, J = 5.6 Hz, 1 H), 4.41 (s, 2 H), 4.09 (s, 1 H), 3.79 -3.66 (m, 1 H), 3.61-3.52 (m, 1 H), 3.46-3.37 (m, 2 H), 3.26-2.93 (m, 10 H), 2.43-2.33 (m, 1 H), 2.27-2.20 (m, 1 H), 2.18-2.05 (m, 2 H), 1.95-1.72 (m, 2 H), 1.72 -1.60 (m, 1 H); MS (ESI) *m/z* 548.14 (M+H).



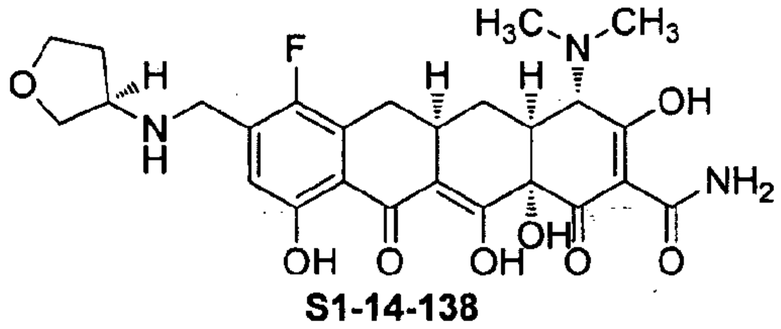
S1-14-136

^{1}H NMR (400 MHz, CD_3OD) δ 6.98 (d, J = 5.6 Hz, 1 H), 4.26 (s, 2 H), 4.00 (s, 1 H), 3.47-3.44 (m, 2 H), 3.15-2.89 (m, 11 H), 2.32-2.25 (m, 1 H), 2.17-2.14 (m, 1 H), 1.95-1.92 (m, 3 H), 1.76-1.66 (m, 2 H), 1.64-1.02 (m, 10 H); MS (ESI) *m/z* 598.1 (M+H).



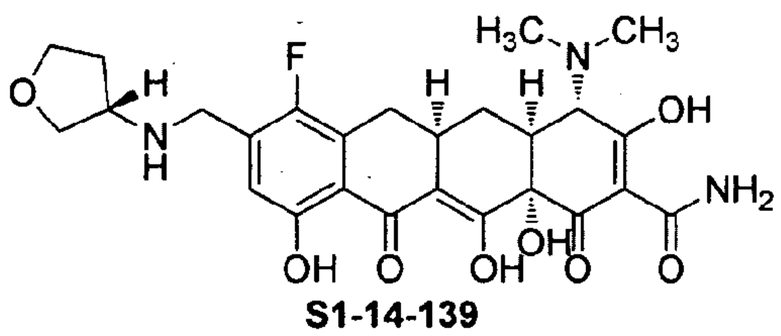
S1-14-137

^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (d, J = 5.9 Hz, 1 H), 4.31 (s, 2 H), 4.09 (s, 1 H), 3.95-3.85 (m, 2 H), 3.75 (t, J = 7.3 Hz, 1 H), 3.54 (dd, J = 8.7, 5.5 Hz, 1 H), 3.20-2.90 (m, 11 H), 2.70-2.59 (m, 1 H), 2.40- 2.30 (m, 1 H), 2.28-2.13 (m, 2 H), 1.75-1.59 (m, 2 H); MS (ESI) *m/z* 546.16 (M+H).



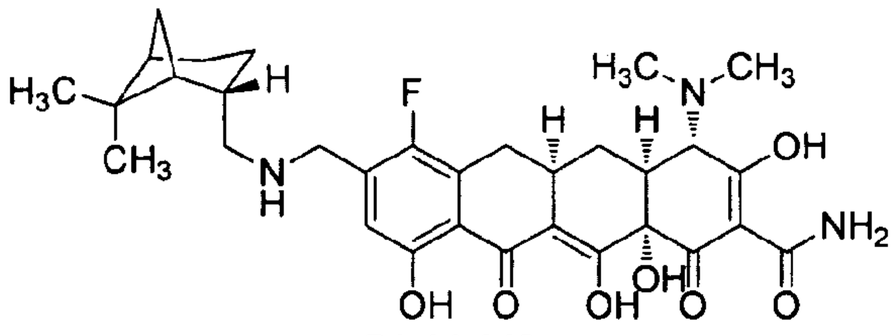
S1-14-138

^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, J = 5.9 Hz, 1 H), 4.30 (s, 2 H), 4.18-3.94 (m, 4 H), 3.90-3.80 (m, 1 H), 3.80-3.65 (m, 1 H), 3.24-2.85 (m, 9 H), 2.50-2.20 (m, 3 H), 2.18-2.00 (m, 1 H), 1.70-1.57 (m, 1 H); MS (ESI) *m/z* 532.11 (M+H).



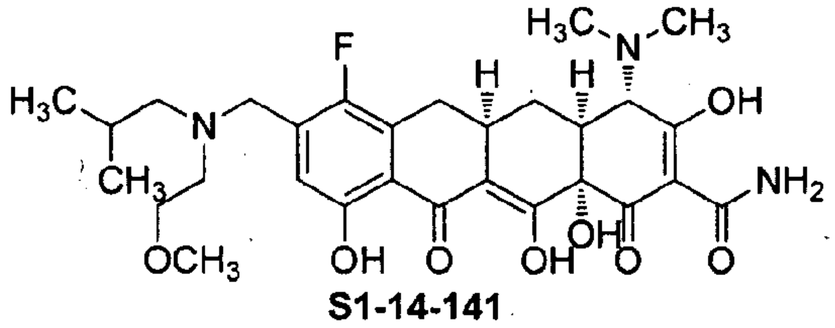
S1-14-139

^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, J = 5.9 Hz, 1 H), 4.31 (d, J = 5.0 Hz, 2 H), 4.23-4.15 (m, 1 H), 4.08 (s, 1 H), 3.95-3.88 (m, 1 H), 3.85-3.78 (m, 1 H), 3.25-3.16 (m, 1 H), 3.15-2.93 (m, 9 H), 2.39-2.29 (m, 1 H), 2.27-2.19 (m, 1 H), 2.17-2.07 (m, 1 H), 2.00-1.91 (m, 2 H), 1.70-1.56 (m, 2 H); MS (ESI) *m/z* 546.13 (M+H).



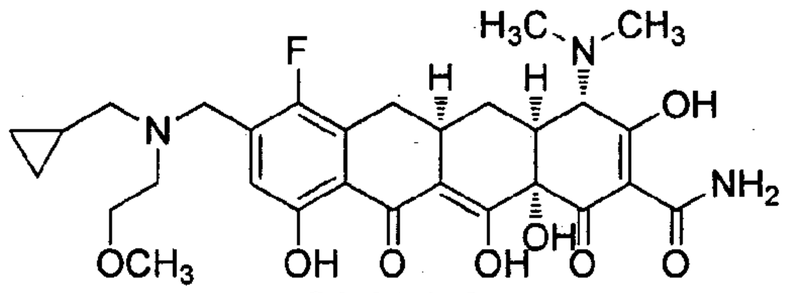
S1-14-140

^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (d, J = 5.5 Hz, 1 H), 4.28 (s, 2 H), 4.10 (s, 1 H), 3.24 -2.83 (m, 11 H), 2.54-2.40 (m, 3 H), 2.39-2.30 (m, 1 H), 2.28-2.21 (m, 1 H), 2.11-1.90 (m, 5 H), 1.70-1.50 (m, 2 H), 1.23 (s, 3 H), 1.01 (s, 3 H); MS (ESI) *m/z* 598.19 (M+H).



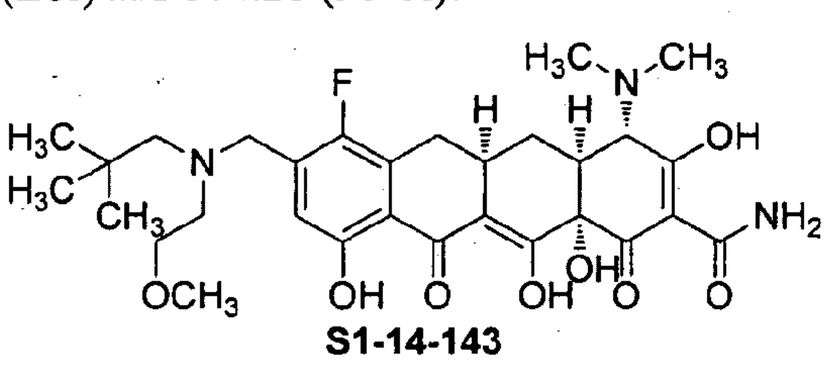
S1-14-141

^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.51 (d, J = 1.7 Hz, 2 H), 4.09 (s, 1 H), 3.78 (t, J = 4.8 Hz, 2 H), 3.46-3.40 (m, 5 H), 3.24 -2.94 (m, 11 H), 2.37 (t, J = 14.7 Hz, 1 H), 2.28-2.17 (m, 2 H), 1.72-1.60 (m, 1 H), 1.09-1.01 (m, 6 H); MS (ESI) *m/z* 576.24 (M+H).



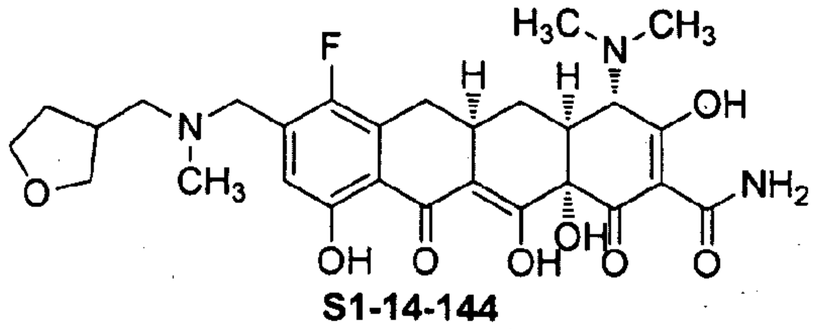
S1-14-142

^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 5.9 Hz, 1 H), 4.55 (d, J = 3.7 Hz, 2 H), 4.07 (s, 1 H), 3.77 (t, J = 4.8 Hz, 2 H), 3.66-3.54 (m, 1 H), 3.41 (s, 3 H), 3.48-3.37 (m, 1 H), 3.25 -2.90 (m, 11 H), 2.43-2.33 (m, 1 H), 2.28-2.20 (m, 1 H), 1.71-1.60 (m, 1 H), 1.25-1.15 (m, 1 H), 1.85-1.75 (m, 2 H), 0.50-0.42 (m, 2 H); MS (ESI) *m/z* 574.21 (M+H).



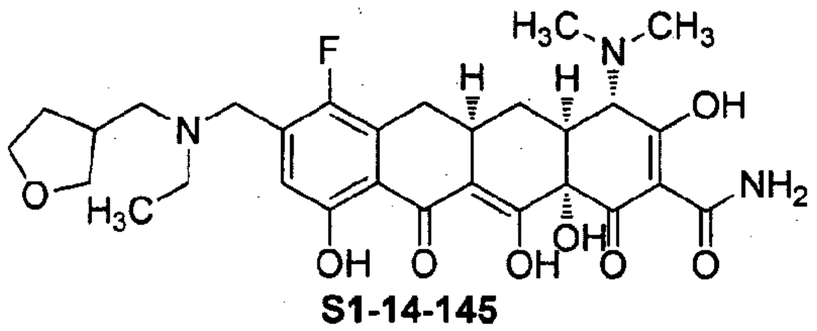
S1-14-143

^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (d, J = 6.0 Hz, 1 H), 4.56 (br, 2 H), 4.09 (s, 1 H), 3.80 (br, 2 H), 3.55-3.46 (m, 2 H), 3.42 (s, 3 H), 3.44-3.39 (m, 1 H), 3.22-2.92 (m, 10 H), 2.42-2.33 (m, 1 H), 2.27-2.20 (m, 1 H), 1.72-1.60 (m, 1 H), 1.09 (s, 9 H); MS (ESI) *m/z* 590.21 (M+H).



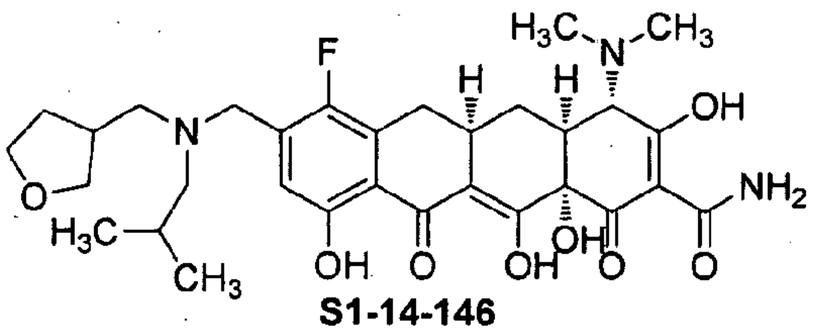
S1-14-144

^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.9 Hz, 1 H), 4.64-4.52 (m, 1 H), 4.38-4.22 (m, 1 H), 4.10 (s, 1 H), 3.98-3.82 (m, 2 H), 3.76 (t, J = 7.3 Hz, 1 H), 3.55-3.45 (m, 1 H), 3.27-2.88 (m, 14 H), 2.85-2.73 (m, 1 H), 2.42- 2.32 (m, 1 H), 2.28-2.19 (m, 2 H), 1.77-1.59 (m, 2 H); MS (ESI) *m/z* 560.21 (M+H).



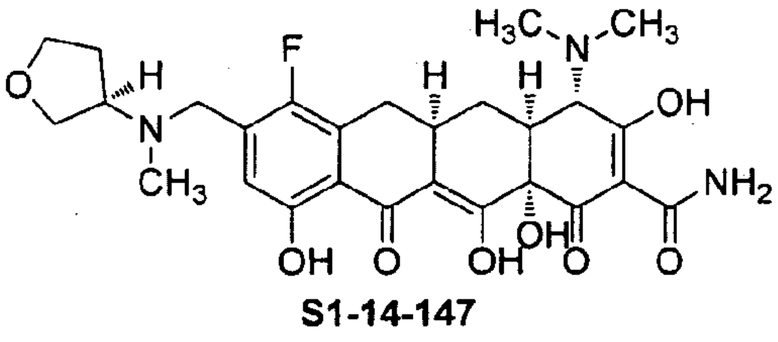
S1-14-145

^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.9 Hz, 1 H), 4.55-4.39 (m, 2 H), 4.08 (s, 1 H), 3.98-3.82 (m, 2 H), 3.75 (t, J = 7.3 Hz, 1 H), 3.53-3.40 (m, 1 H), 3.36-2.92 (m, 13 H), 2.80-2.71 (m, 1 H), 2.43- 2.33 (m, 1 H), 2.28-2.18 (m, 2 H), 1.73-1.59 (m, 2 H), 1.40 (t, J = 7.3 Hz, 3 H); MS (ESI) *m/z* 574.28 (M+H).



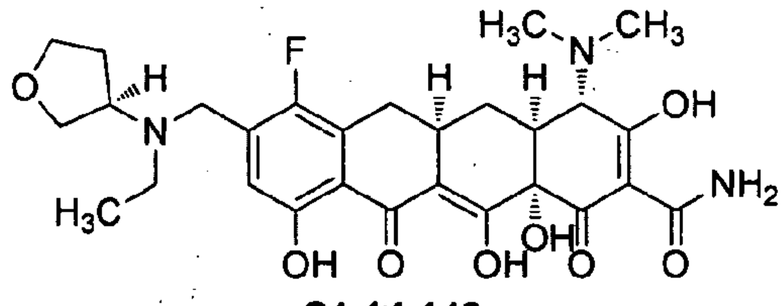
S1-14-146

^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.9 Hz, 1 H), 4.60-4.40 (m, 2 H), 4.09 (s, 1 H), 4.02-3.94 (m, 1 H), 3.92-3.84 (m, 1 H), 3.83-3.73 (m, 1 H), 3.52-3.43 (m, 1 H), 3.36-2.92 (m, 13 H), 2.83-2.71 (m, 1 H), 2.43- 2.34 (m, 1 H), 2.33 - 2.18 (m, 3 H), 1.75-1.60 (m, 2 H), 1.06 (dd, J = 13.7, 6.9 Hz, 6 H); MS (ESI) *m/z* 602.30 (M+H).



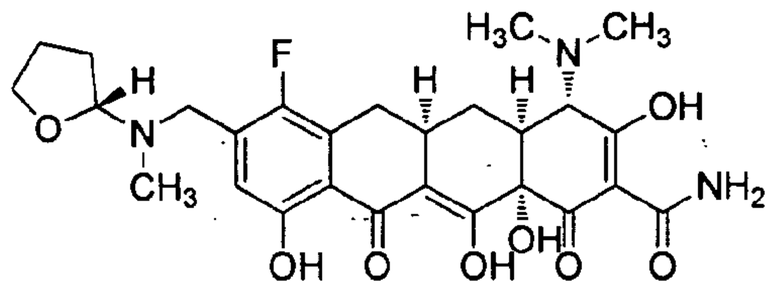
S1-14-147

^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, *J* = 6.0 Hz, 1 H), 4.60-4.42 (m, 1 H), 4.36-4.22 (m, 2 H), 4.22-4.09 (m, 2 H), 4.10 (s, 1 H), 3.84 (dd, *J* = 11.4, 6.0 Hz, 1 H), 3.78-3.67 (m, 1 H), 3.24-3.17 (m, 1 H), 3.17-2.92 (m, 8 H), 2.83 (s, 3 H), 2.54-2.20 (m, 4 H), 1.70-1.59 (m, 1 H); MS (ESI) *m/z* 546.14 (M+H).



S1-14-148

^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.48 (d, *J* = 13.7 Hz, 1 H), 4.43-4.11 (m, 4 H), 4.09 (s, 1 H), 3.90-3.78 (m, 1 H), 3.76-3.64 (m, 1 H), 3.40-3.27 (m, 2 H), 3.24-3.18 (m, 1 H), 3.17-2.92 (m, 8 H), 2.50-2.20 (m, 4 H), 1.71-1.59 (m, 1 H), 1.45-1.32 (m, 3 H); MS (ESI) *m/z* 560.19 (M+H).

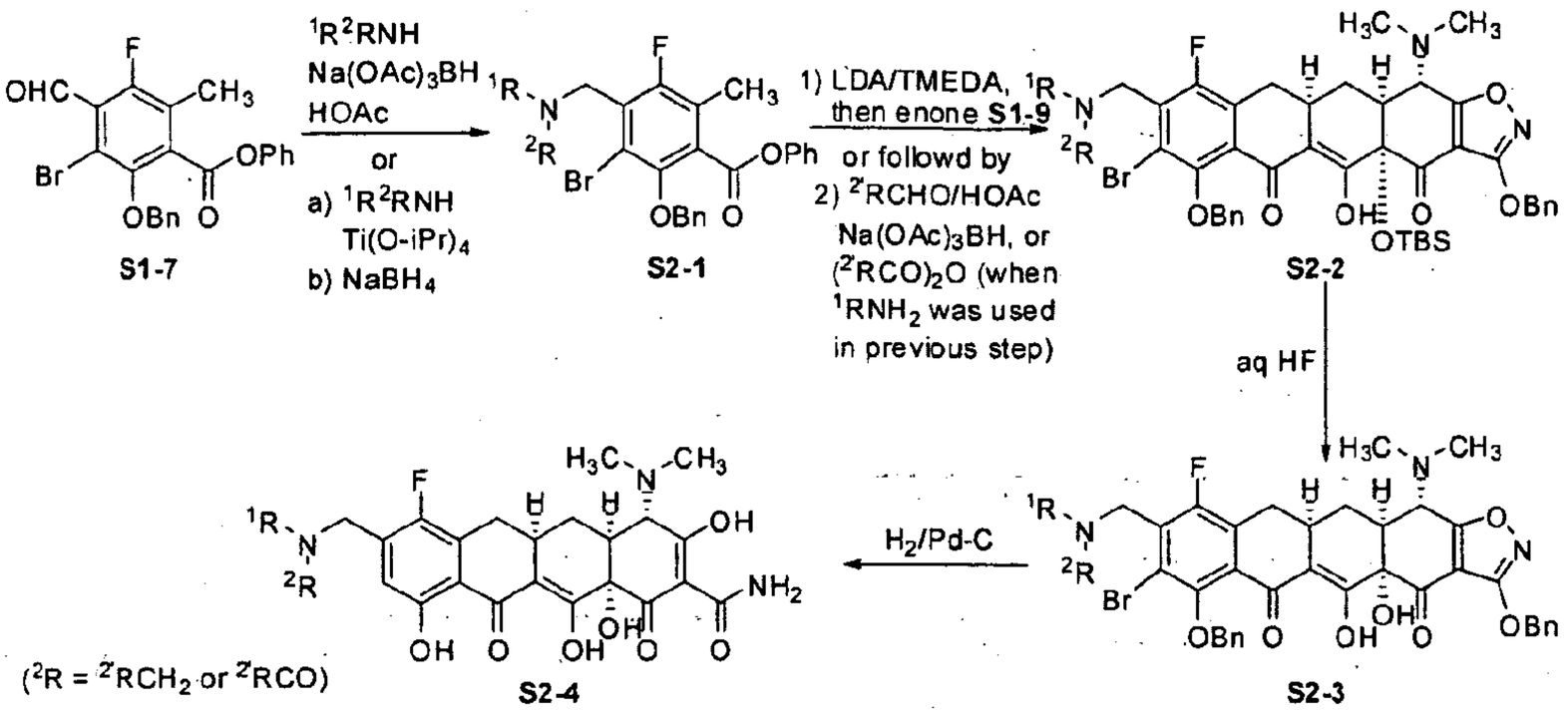


S1-14-149

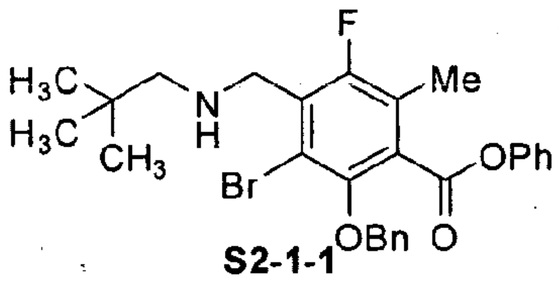
^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (dd, *J* = 11.9, 5.9 Hz, 1 H), 4.63 (t, *J* = 11.7 Hz, 1 H), 4.44-4.25 (m, 2 H), 4.09 (s, 1 H), 4.00-3.82 (m, 2 H), 3.47-3.39 (m, 1 H), 3.25-2.87 (m, 11 H), 2.42-2.31 (m, 1 H), 2.27-2.10 (m, 2 H), 2.02-1.90 (m, 2 H), 1.71-1.56 (m, 2 H); MS (ESI) *m/z* 560.18 (M+H).

Example 2. Synthesis of Compounds via Scheme 2.

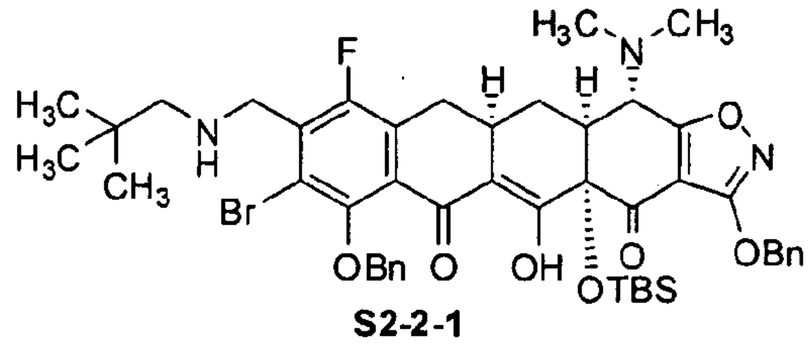
Scheme 2



The following compounds were prepared according to Scheme 2.

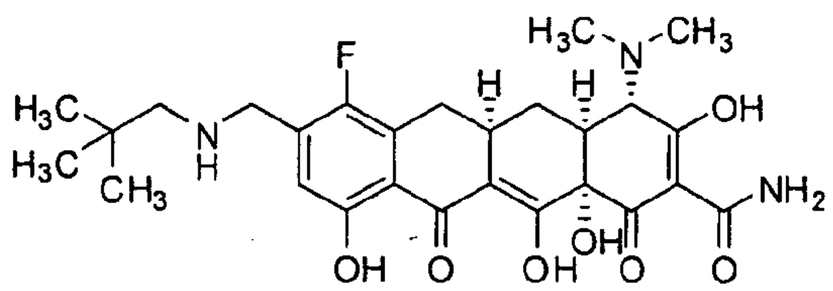


Compound **S1-7** (0.25 g, 0.56 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (4 mL). Neopentylamine (98 mg, 0.11 mmol, 2.0 equiv) was added *via* a syringe, followed by the addition of acetic acid (64 µL, 0.11 mmol) under a nitrogen atmosphere. After stirring at rt for 1 h, sodium triacetoxyborohydride (0.36 g, 1.68 mmol, 3.0 equiv) was added to the reaction mixture. LC/MS indicated that the starting material was consumed after overnight. The reaction mixture was diluted with dichloromethane, washed with saturated aqueous $NaHCO_3$ (3 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (Biotage 10 g column, 10% to 20% EtOAc in hexanes gradient), yielding pure compound **S2-1-1** as a colorless oil (0.25 g, 86%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.47 (m, 2 H), 7.40-7.33 (m, 6 H), 7.25 (t, J = 6.9 Hz, 1 H), 7.04 (d, J = 8.2 Hz, 2 H), 5.10 (s, 2 H), 4.04 (d, J = 2.3 Hz, 2 H), 2.35 (d, J = 1.8 Hz, 3 H), 2.30 (s, 2 H), 0.89 (s, 9 H).



S2-2-1

LDA/THF was prepared by adding *n*-BuLi (0.29 mL, 1.6 M/hexanes, 0.46 mmol, 3.0 equiv) to diisopropylamine (65 µL, 0.46 mmol, 3.0 equiv) in 3 mL dry THF under a nitrogen atmosphere in a flame dried schenck flask at -78 °C. The resulting solution was warmed to -20 °C and stirred for another 15 min. After the LDA solution was cooled down to -78 °C, TMEDA (69 µL, 0.46 mmol, 3.0 equiv) was added slowly *via* a syringe. Compound **S2-1-1** (0.10 g, 0.20 mmol, 1.3 equiv) was dissolved in 1 mL dry THF and added into the LDA solution slowly *via* a syringe. A dark-red color appeared as soon as addition started. After stirring for 10 min, enone **S1-9** (74 mg, 0.15 mmol, 1.0 equiv) in 1 mL dry THF was added slowly a *via* syringe. After 10 min, LC/MS indicated that the enone was consumed and the product present. The reaction mixture was allowed to slowly warm to -20 °C in 1 h. A phosphate buffer solution (pH 7, 10 mL) was added, followed by the addition of 20 mL saturated aqueous ammonium chloride. The resulting mixture was extracted with dichloromethane (3 x 15 mL). The combined extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting orange-red oil was purified by column chromatography (Biotage 10 g column, 10% to 30% EtOAc in hexanes gradient) to yield the desired compound **S2-2-1** (90 mg, 65%).

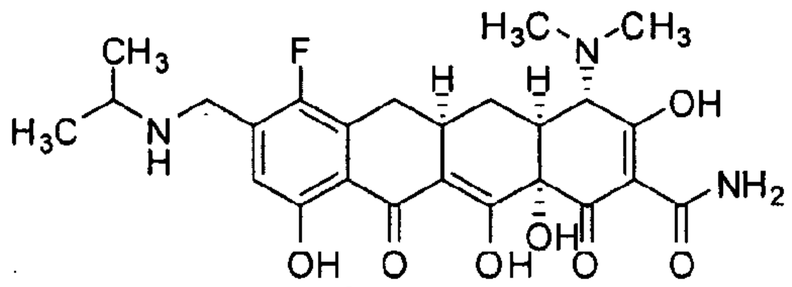


S2-4-1

Aqueous HF (0.3 mL, 48-50%) was added to a CH_3CN solution (1.0 mL) of 7 (20 mg) in a plastic vial at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The resulting mixture was poured into an aqueous solution (10 mL) of K_2HPO_4 (2 g). The solution was extracted with EtOAc (3 x 15 mL). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give the crude intermediate.

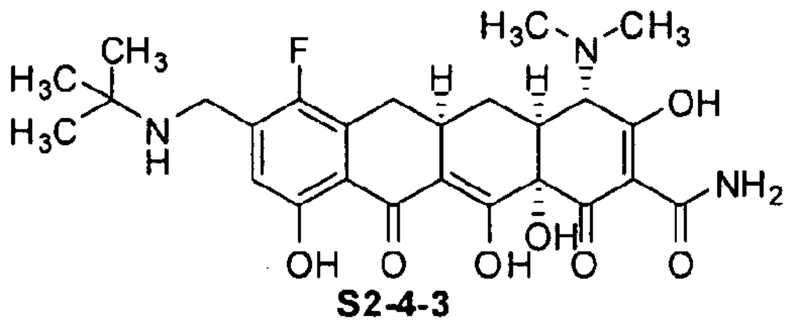
10% Pd-C (5 mg) was added to a MeOH solution (2 mL) of the above crude intermediate. HCl/MeOH (0.5 mL, 0.5 N) was also added. The reaction mixture was stirred under H_2 (balloon) at 25 °C for 2 hrs and filtered through a pad of Celite. The filtrate was concentrated to give the crude product. The crude product was purified by HPLC on a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, sample in 2.0 mL (0.05 N HCl), gradient elution with 0→70% B over 15 min, mass-directed fraction collection] to yield the desired product **S2-4-1** as a yellow solid (8 mg, 66%, 2 steps): ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.42 (s, 2 H), 4.14 (s, 1 H), 3.21 (dd, J = 15.5, 4.6 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.92 (s, 2 H), 3.17 -2.97 (m, 2 H), 2.39-2.22 (m, 2 H), 1.70-1.58 (m, 1 H), 1.06 (s, 9 H); MS (ESI) *m/z* 532.49 (M+H).

The following compounds were prepared according to the methods for **S2-4-1**, substituting the appropriate amine for isobutylamine.



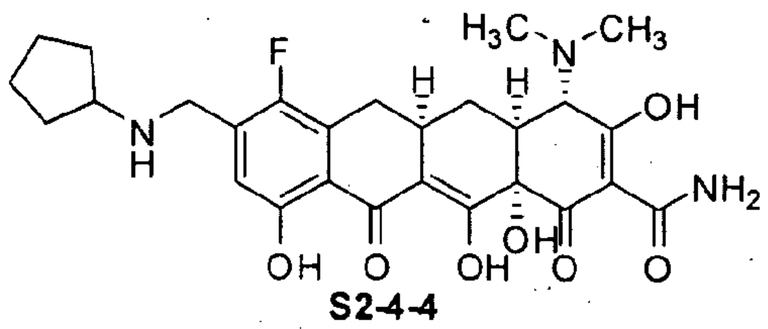
S2-4-2

S2-4-2: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.08 (d, J = 5.96 Hz, 1 H), 4.27 (s, 2 H), 4.16 (s, 1 H), 3.51 (hept, J = 6.9 Hz, 1 H), 3.28-2.94 (m, 9 H), 2.38-2.26 (m, 2 H), 1.60 (dd, J = 13.3, 11.0 Hz, 1 H), 1.41 (d, J = 6.9 Hz, 6 H); MS (ESI) *m/z* 504.28 (M+H).



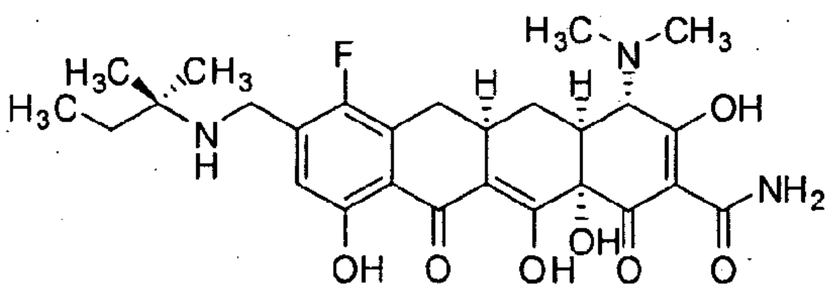
S2-4-3

S2-4-3: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.09 (d, J = 5.92 Hz, 1 H), 4.22 (s, 2 H), 4.16 (s, 1 H), 3.28-2.94 (m, 9 H), 2.38-2.26 (m, 2 H), 1.60 (dd, J = 14.0, 11.0 Hz, 1 H), 1.47 (s, 9 H); MS (ESI) *m/z* 518.28 (M+H).



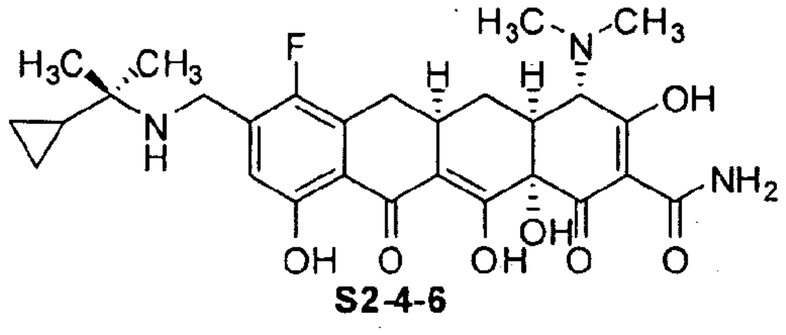
S2-4-4

S2-4-4: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.07 (d, J = 5.96 Hz, 1 H), 4.26 (s, 2 H), 4.16 (s, 1 H), 3.66 (quint, J = 6.9 Hz, 1 H), 3.34-2.94 (m, 11 H), 2.36-2.24 (m, 2 H), 2.23-2.12 (m, 2 H), 1.90-1.54 (m, 5 H); MS (ESI) *m/z* 530.23 (M+H).



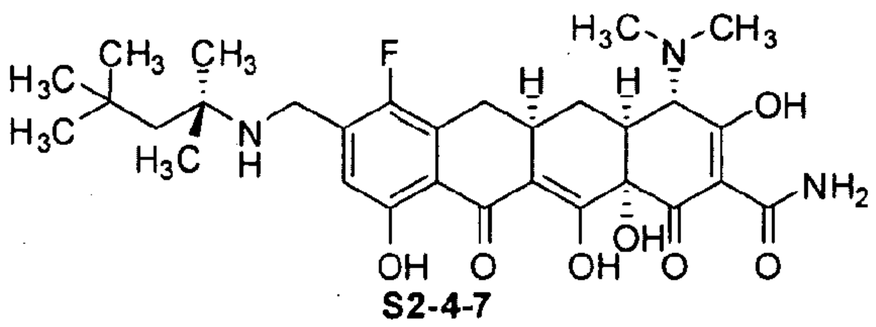
S2-4-5

S2-4-5: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.08 (d, J = 5.96 Hz, 1 H), 4.21 (s, 2 H), 4.15 (s, 1 H), 3.26-2.96 (m, 9 H), 2.36-2.24 (m, 2 H), 1.82 (q, J = 7.32 Hz, 2 H), 1.69-1.55 (m, 1 H), 1.42 (s, 6 H), 1.02 (d, J = 7.32 Hz, 3 H); MS (ESI) *m/z* 532.24 (M+H).



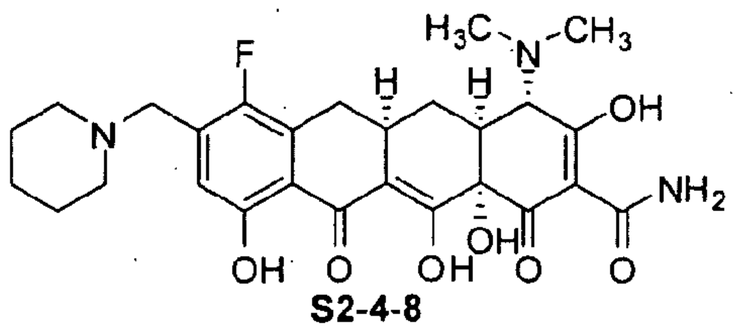
S2-4-6

S2-4-6: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.11 (d, J = 5.96 Hz, 1 H), 4.33 (s, 2 H), 4.16 (s, 1 H), 3.26-2.94 (m, 9 H), 2.36-2.25 (m, 2 H), 1.69-1.55 (m, 1 H), 1.33 (s, 6 H), 1.29-1.20 (m, 1 H), 0.72-0.64 (m, 2 H), 0.63-0.56 (m, 2 H); MS (ESI) *m/z* 544.24 (M+H).



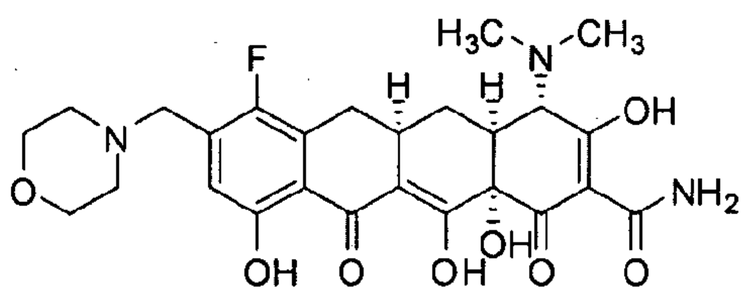
S2-4-7

S2-4-7: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.11 (d, J = 5.48 Hz, 1 H), 4.24 (s, 2 H), 4.18 (s, 1 H), 3.28-2.96 (m, 9 H), 2.37-2.26 (m, 2 H), 1.84 (s, 2 H), 1.69-1.54 (m, 7 H), 1.10 (s, 9 H); MS (ESI) *m/z* 574.28 (M+H).



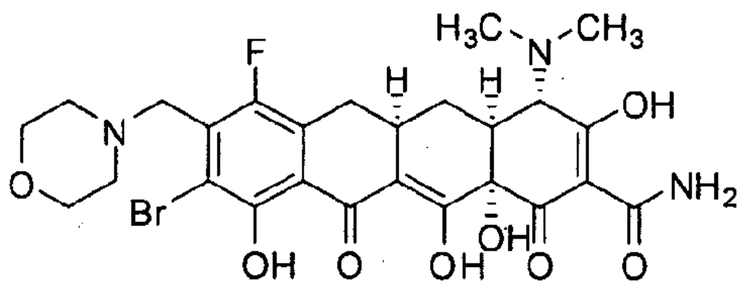
S2-4-8

S2-4-8: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.15 (d, J = 5.96 Hz, 1 H), 4.37 (s, 2 H), 4.17 (s, 1 H), 3.56-3.48 (m, 2 H), 3.40-2.94 (m, 11 H), 2.38-2.26 (m, 2 H), 1.99-1.78 (m, 5 H), 1.70-1.48 (m, 2 H); MS (ESI) *m/z* 530.29 (M+H).



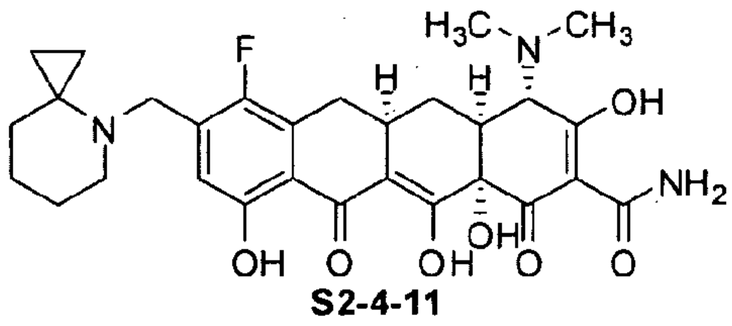
S2-4-9

S2-4-9: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.17 (d, J = 5.96 Hz, 1 H), 4.45 (s, 2 H), 4.16 (s, 1 H), 4.08-3.98 (m, 2 H), 3.92-3.80 (m, 2 H), 3.52-3.42 (m, 2 H), 3.38-2.94 (m, 11 H), 2.38-2.25 (m, 2 H), 1.70-1.55 (m, 1 H); MS (ESI) *m/z* 532.27 (M+H).



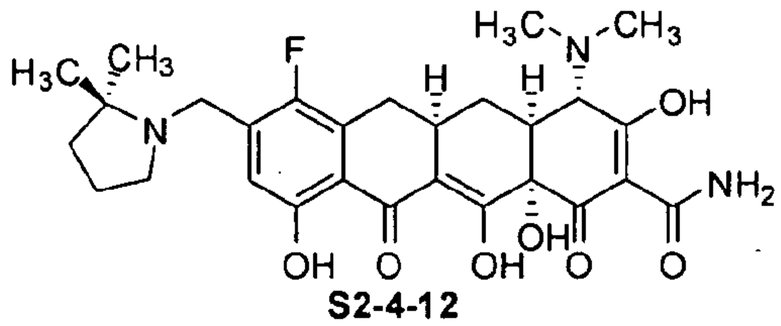
S2-4-10

S2-4-10: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 4.69 (s, 2 H), 4.17 (s, 1 H), 4.10-3.98 (m, 2 H), 3.95-3.84 (m, 2 H), 3.34-2.94 (m, 13 H), 2.38-2.25 (m, 2 H), 1.71-1.57 (m, 1 H); MS (ESI) *m/z* 610.2, 612.19 (M+H).

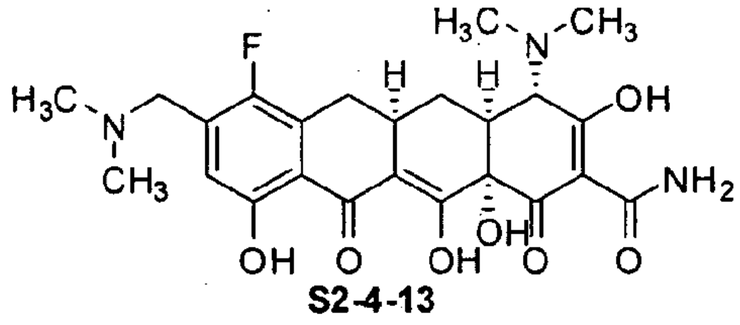


S2-4-11

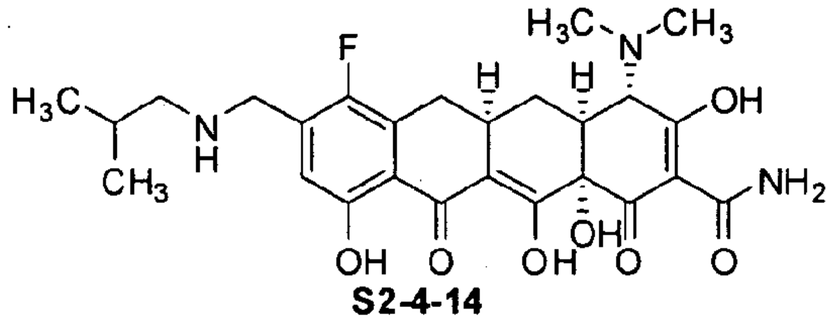
S2-4-11: ^{1}H NMR (400 MHz, CD3OD/DCl) δ 7.15 (br s, 1 H), 4.76-4.58 (m, 2 H), 4.17 (s, 1 H), 3.40-2.92 (m, 11 H), 2.60-2.48 (m, 1 H), 2.38-2.15 (m, 3 H), 1.99-1.82 (m, 2 H), 1.82-1.55 (m, 2 H), 1.45-1.36 (m, 1 H), 1.22-1.14 (m, 1 H), 1.10-0.99 (m, 1 H), 0.99-0.80 (m, 2 H); MS (ESI) *m/z* 556.20 (M+H).


S2-4-12

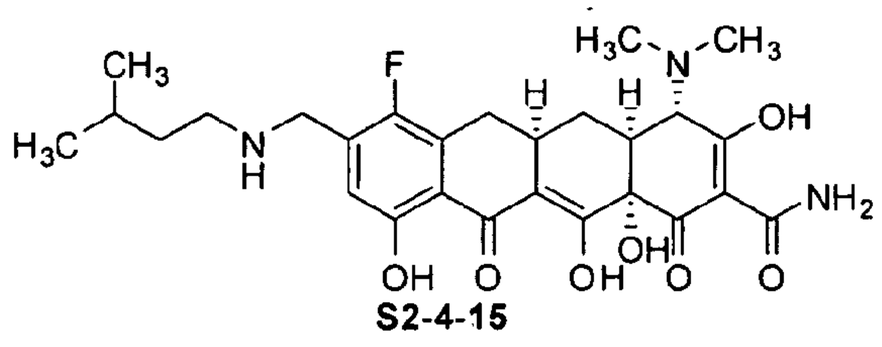
S2-4-12: ^{1}H NMR (400 MHz, CD3OD/DCl) δ 7.12 (d, *J* = 5.96 Hz, 1 H), 4.56 (d, *J* = 3.2 Hz, 1 H), 4.17 (s, 1 H), 4.10 (d, *J* = 3.2 Hz, 1 H), 3.54-3.45 (m, 2 H), 3.26-2.96 (m, 9 H), 2.39-2.26 (m, 2 H), 2.23-1.95 (m, 4 H), 1.70-1.56 (m, 4 H), 1.44 (s, 3 H); MS (ESI) *m/z* 544.22 (M+H).


S2-4-13

S2-4-13: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.42 (s, 2 H), 4.14 (s, 1 H), 3.06 (s, 3 H), 2.98 (s, 3 H), 2.92 (s, 6 H), 3.24-2.97 (m, 3 H), 2.37-2.25 (m, 2 H), 1.70-1:57 (m, 1 H); MS (ESI) *m/z* 490.43 (M+H).

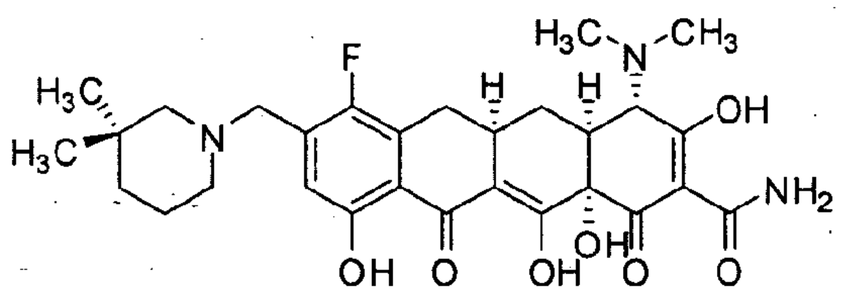

S2-4-14

S2-4-14: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.28 (s, 2 H), 4.14 (s, 1 H), 3.21 (dd, *J* = 15.5, 4.6 Hz, 1 H), 3.06 (s, 3 H), 2.97 (s, 3 H), 2.94 (d, *J* = 6.9 Hz, 2 H), 3.17-2.97 (m, 2 H), 2.35-2.25 (m, 2 H), 2.12-2.02 (m, 1 H), 1.70-1.58 (m, 1 H), 1.04 (d, *J* = 6.9 Hz, 6 H); MS (ESI) *m/z* 518.47 (M+H).


S2-4-15

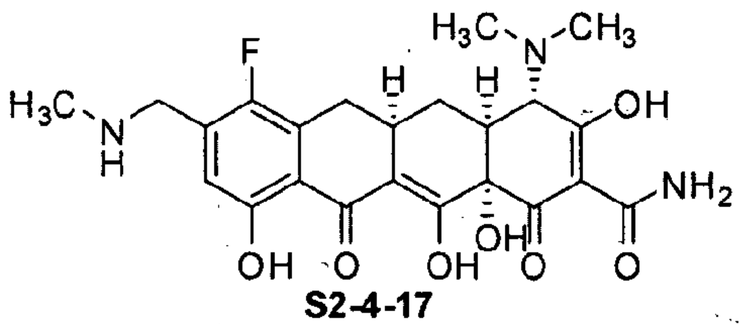
S2-4-15: ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (d, *J* = 6.0 Hz, 1 H), 4.28 (s, 2 H), 4.12 (s, 1 H), 3.21 (dd, *J* = 15.1, 4.6 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.94

(d, J = 6.9 Hz, 2 H), 3.16-2.98 (m, 4 H), 2.38-2.22 (m, 2 H), 1.72-1.58 (m, 4 H), 0.97 (d, J = 6.4 Hz, 6 H); MS (ESI) *m/z* 532.50 (M+H).



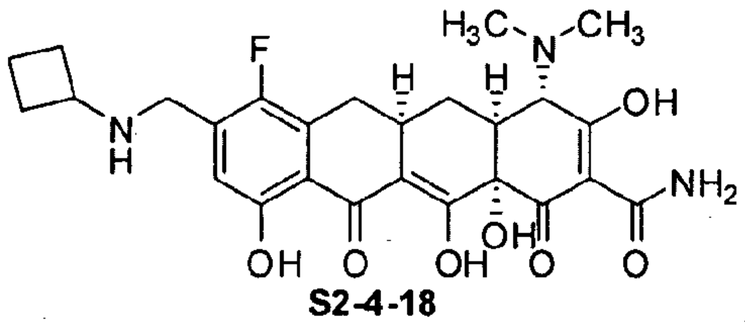
S2-4-16

S2-4-16: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.5 Hz, 1 H), 4.37 (s, 2 H), 4.10 (s, 1 H), 3.50 (m, 1 H), 3.27-2.93 (m, 5 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.85 (m, 1 H), 2.36 (t, J = 15.1 Hz, 1 H), 2.29-2.21 (m, 1 H), 1.99-1.81 (m, 2 H), 1.72-1.53 (m, 2 H), 1.49-1.38 (m, 1 H), 1.12 (s, 3 H), 1.02 (s, 3 H); MS (ESI) *m/z* 558.49 (M+H).



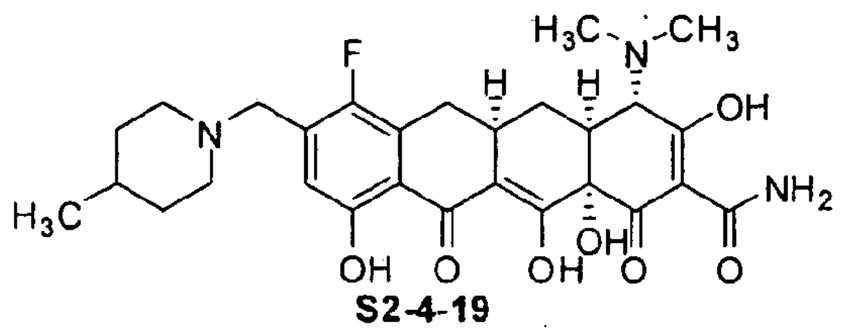
S2-4-17

S2-4-17: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (d, J = 6.0 Hz, 1 H), 4.17 (s, 2 H), 4.10 (s, 1 H), 3.21 (dd, J = 15.1, 4.6 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.84 (s, 3 H), 3.14-2.98 (m, 2 H), 2.21-2.39 (m, 2 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 476.31 (M+H).

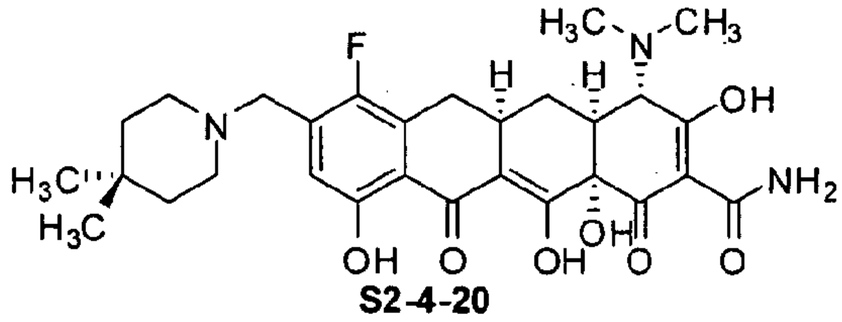


S2-4-18

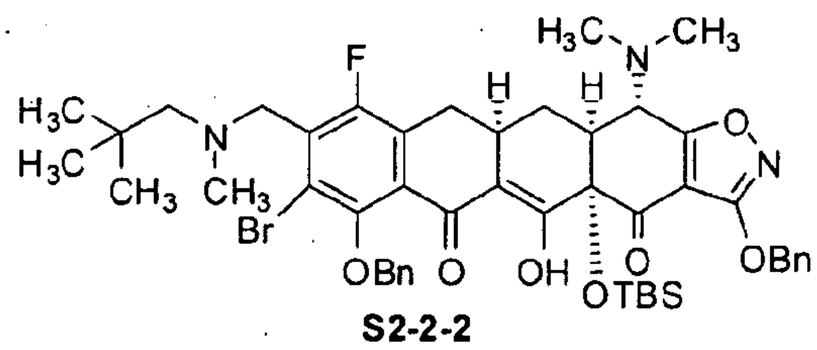
S2-4-18: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (d, J = 6.0 Hz, 1 H), 4.14 (s, 2 H), 4.10 (s, 1 H), 3.84 (m, 1 H), 3.21 (dd, J = 15.5, 4.6 Hz, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.14-2.97 (m, 2 H), 2.36 (t, J = 14.7 Hz, 1 H), 2.40-2.30 (m, 3 H), 2.28-2.17 (m, 3 H), 1.93 (m, 2 H), 1.68-1.58 (m, 1 H); MS (ESI) *m/z* 516.34 (M+H).


S2-4-19

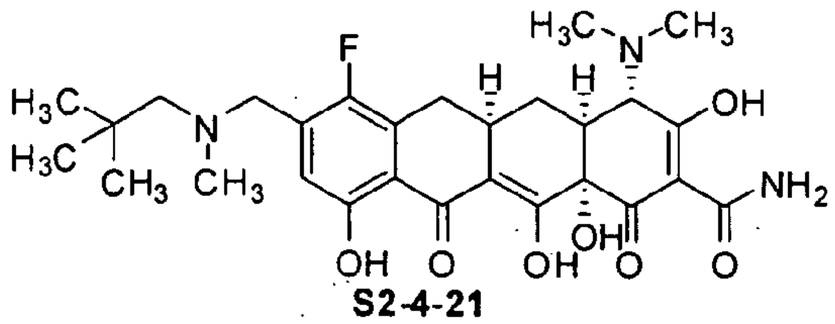
S2-4-19: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.5 Hz, 1 H), 4.35 (s, 2 H), 4.12 (s, 1 H), 3.51 (m, 2 H), 3.24-2.98 (m, 5 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.34 (t, J = 15.1 Hz, 1 H), 2.29-2.21 (m, 1 H), 1.96-1.85 (m, 2 H), 1.79-1.56 (m, 2 H), 1.54-1.40 (m, 2 H),0.99 (d, J = 6.4 Hz, 3 H); MS (ESI) *m/z* 544.25 (M+H).


S2-4-20

S2-4-20: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.5 Hz, 1 H), 4.39 (s, 2 H), 4.09 (s, 1 H), 3.38 (m, 2 H), 3.24-2.98 (m, 5 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.35 (t, J = 15.1 Hz, 1 H), 2.27-2.19 (m, 1 H), 1.77-1.58 (m, 5 H), 1.09 (s, 3 H), 1.03 (s, 3 H); MS (ESI) *m/z* 558.29 (M+H).


S2-2-2

Compound **S2-2-1** (30 mg, 0.033 mmol) was dissolved in 1,2-dichloroethane (2 mL). Formaldehyde solution (12 μL, 0.16 mmol, 5.0 equiv) and acetic acid (9 μL, 0.17 mmol) were added *via* a syringe under a nitrogen atmosphere. After stirring at rt for 1 h, sodium triacetoxyborohydride (21 mg, 0.16 mmol) was added to the reaction mixture. LC/MS indicated that the starting material was consumed after 2 hrs. The reaction mixture was diluted with dichloromethane, washed with $NaHCO_3$ (saturated aqueous solution, 3 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure, yielding 26 mg of crude compound **S2-2-2**, which was used without further purification.

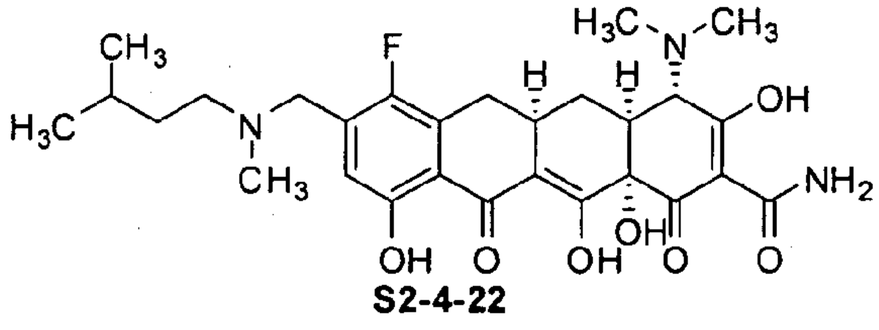


S2-4-21

Aqueous HF (0.3 mL, 48-50%) solution was added to a CH_3CN solution (1.0 mL) of **S2-2-2** (crude, 26 mg) in a plastic vial at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The resulting mixture was poured into an aqueous solution (10 mL) of K_2HPO_4 (2 g). The solution was extracted with EtOAc (3 x 15 mL). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give the crude intermediate.

Pd-C (5 mg, 10wt%) was added to MeOH solution (2 mL) of the crude intermediate. HCl in MeOH (0.5 N, 0.5 mL) was added. The reaction was stirred under H_2 (balloon) at 25 °C for 2 hrs and filtered through a pad of Celite. The filtrate was concentrated, and the crude product was purified by HPLC on a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, sample in 2.0 mL (0.05 N HCl), gradient elution with 0→70% B over 15 min, mass-directed fraction collection]. Fractions containing the desired product were collected and freeze-dried, yielding product **S2-4-21** as a yellow solid 19 mg (> 95% for 3 steps): ^{1}H NMR (400 MHz, CD_3OD) δ 7.12 (d, J = 5.8 Hz, 1 H), 4.58 (d, J = 13.3 Hz, 1 H), 4.36 (d, J = 13.3 Hz, 1 H), 4.11 (s, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.95 (s, 5 H), 3.26-3.01 (m, 3 H), 2.37 (t, J = 14.6 Hz, 1 H), 2.29-2.22 (m, 1 H), 1.71-1.61 (m, 1 H), 1.08 (s, 9 H); MS (ESI) *m/z* 546.37 (M+H).

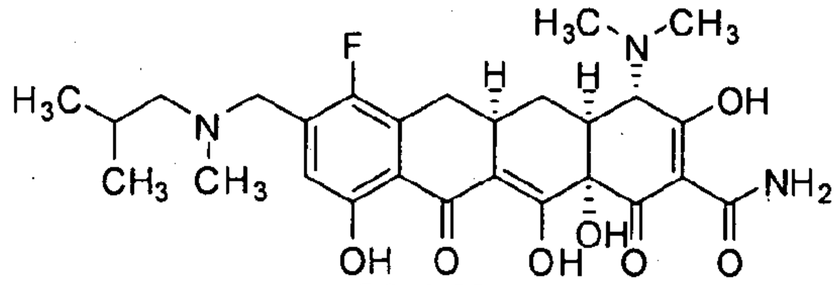
The following compounds were prepared according to the methods for **S2-4-21** above, using either formaldehyde or substituting the appropriate aldehyde for formaldehyde.



S2-4-22

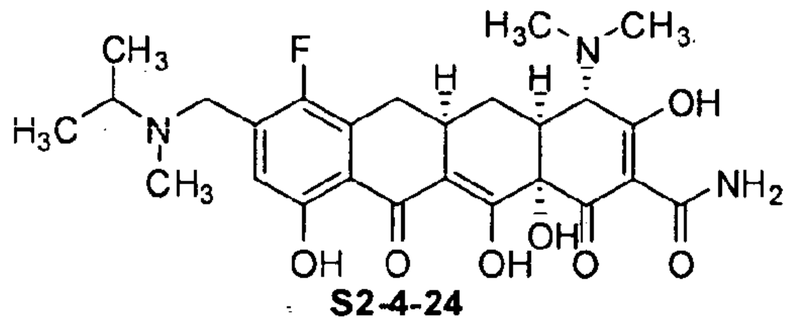
S2-4-22: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.13 (d, J = 5.48 Hz, 1 H), 4.60-4.48 (m, 1 H), 4.36-4.26 (m, 1 H), 4.17 (s, 1 H), 3.40-2.94 (m, 11 H), 2.85 (s, 3

H), 2.38-2.26 (m, 2 H), 1.78-1.56 (m, 4 H), 1.00-0.92 (m, 6 H); MS (ESI) *m/z* 546.30 (M+H).



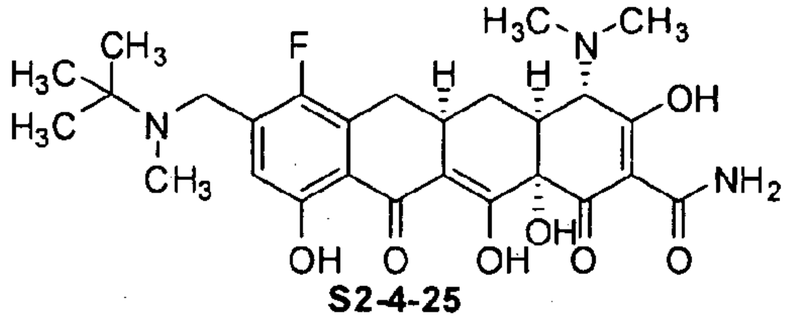
S2-4-23

S2-4-23: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.11 (d, J = 5.96 Hz, 1 H), 4.63-4.52 (m, 1 H), 4.33-4.24 (m, 1 H), 4.16 (s, 1 H), 3.26-2.94 (m, 11 H), 2.87 (s, 3 H), 2.38-2.26 (m, 3 H), 1.70-1.56 (m, 1 H), 1.10-1.02 (m, 6 H); MS (ESI) *m/z* 532.31 (M+H).



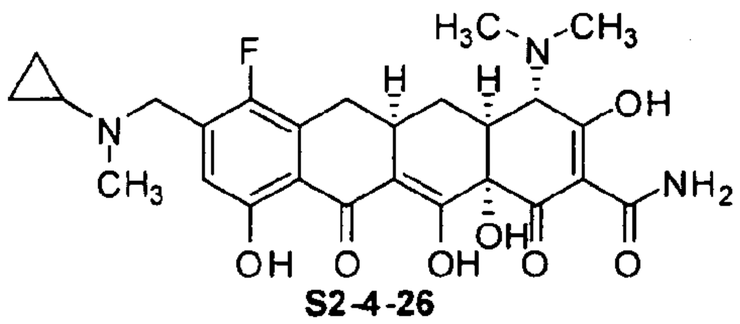
S2-4-24

S2-4-24: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.13 (d, J = 5.92 Hz, 1 H), 4.60-4.50 (m, 1 H), 4.24-4.14 (m, 2 H), 3.76-3.66 (m, 1 H), 3.26-2.94 (m, 9 H), 2.79 (s, 3 H), 2.40-2.26 (m, 2 H), 1.70-1.58 (m, 1 H), 1.50-1.40 (m, 6 H); MS (ESI) *m/z* 518.31 (M+H).



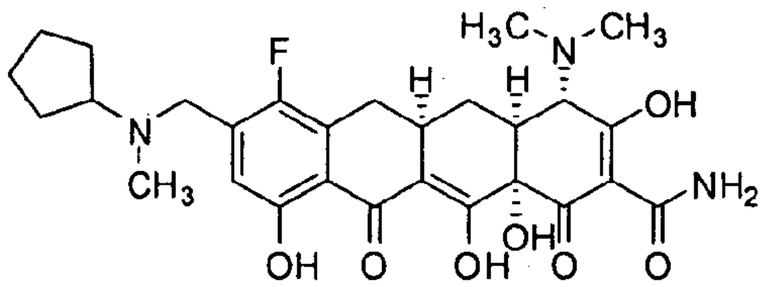
S2-4-25

S2-4-25: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.10 (d, J = 4.1 Hz, 1 H), 4.80-4.72 (m, 1 H), 4.15 (s, 1 H), 4.04-3.96 (m, 1 H), 3.26-2.94 (m, 9 H), 2.78-2.74 (m, 3 H), 2.39-2.25 (m, 2 H), 1.72-1.53 (m, 10 H); MS (ESI) *m/z* 532.30 (M+H).



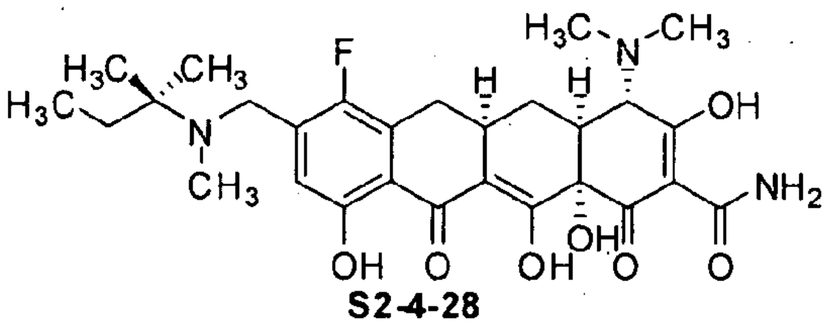
S2-4-26

S2-4-26: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.13 (d, J = 5.5 Hz, 1 H), 4.64-4.46 (m, 2 H), 4.17 (s, 1 H), 3.26-2.94 (m, 12 H), 2.39-2.25 (m, 2 H), 1.70-1.56 (m, 1 H), 1.14-1.04 (m, 1 H), 0.98-0.85 (m, 4 H); MS (ESI) *m/z* 516.22 (M+H).



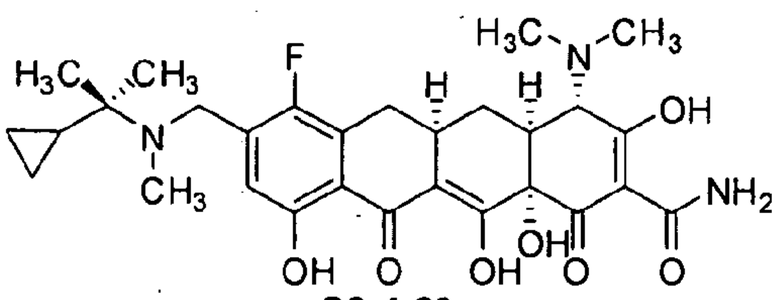
S2-4-27

S2-4-27: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.12 (d, J = 5.5 Hz, 1 H), 4.62-4.53 (m, 1 H), 4.28-4.20 (m, 1 H), 4.17 (s, 1 H), 3.84-3.74 (m, 1 H), 3.26-2.94 (m, 9 H), 2.79 (s, 3 H), 2.39-2.25 (m, 3 H), 2.23-2.13 (m, 1 H), 1.97-1.81 (m, 4 H), 1.80-1.55 (m, 3 H); MS (ESI) *m/z* 544.27 (M+H).



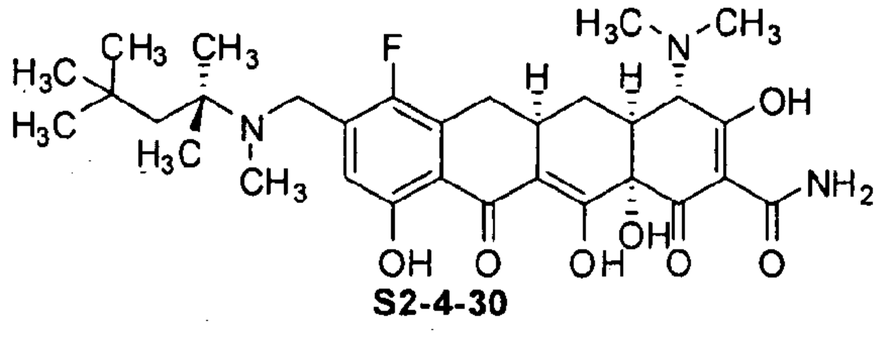
S2-4-28

S2-4-28: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.10 (d, J = 5.96 Hz, 1 H), 4.80-4.71 (m, 1 H), 4.18 (s, 1 H), 4.06-3.98 (m, 1 H), 3.26-2.95 (m, 9 H), 2.76 (s, 3 H), 2.37-2.25 (m, 2 H), 2.01-1.89 (m, 2 H), 1.69-1.54 (m, 1 H), 1.51 (s, 3 H), 1.48 (s, 3 H), 1.07 (t, J = 6.4 Hz, 3 H); MS (ESI) *m/z* 546.27 (M+H).

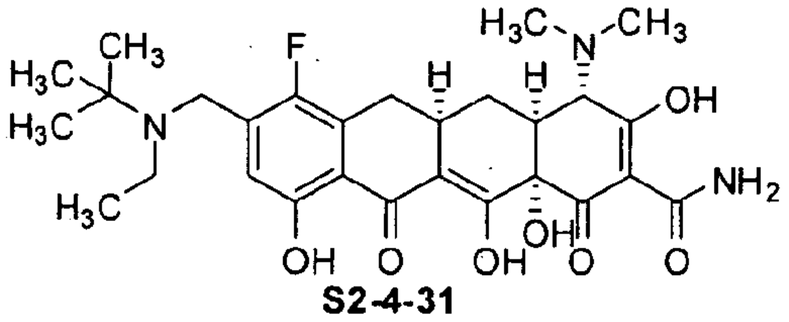


S2-4-29

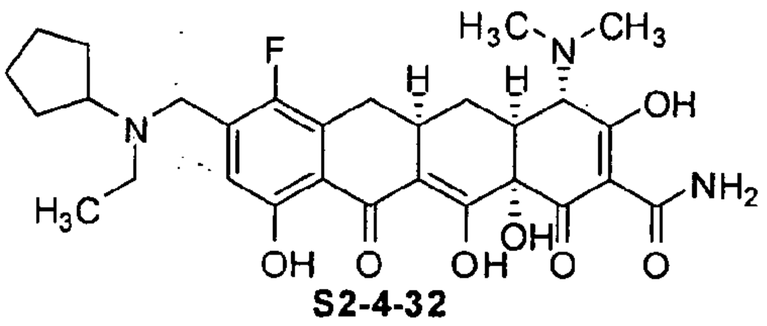
S2-4-29: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.11 (d, J = 5.0 Hz, 1 H), 4.96-4.88 (m, 1 H), 4.16 (s, 1 H), 4.10-4.01 (m, 1 H), 3.26-2.95 (m, 9 H), 2.82 (s, 3 H), 2.39-2.25 (m, 2 H), 1.70-1.58 (m, 1 H), 1.50-1.28 (m, 7 H), 0.82-0.59 (m, 4 H); MS (ESI) *m/z* 558.28 (M+H).


S2-4-30

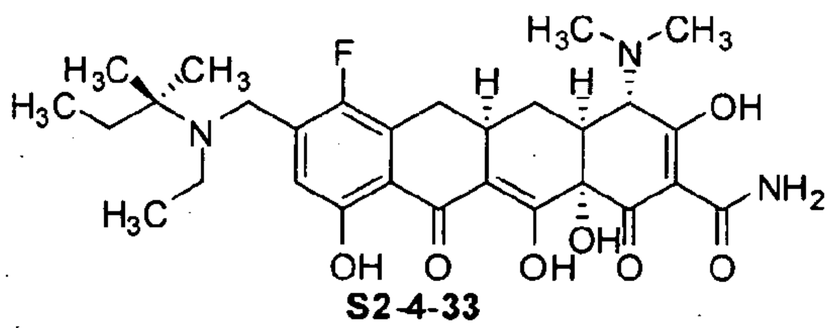
S2-4-30: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.10 (d, J = 5.5 Hz, 1 H), 4.82-4.74 (m, 1 H), 4.17 (s, 1 H), 4.05-3.97 (m, 1 H), 3.28-2.95 (m, 9 H), 2.76 (s, 3 H), 2.38-2.26 (m, 2 H), 2.01-1.80 (m, 2 H), 1.76-1.56 (m, 7 H), 1.12 (s, 9 H); MS (ESI) *m/z* 588.29 (M+H).


S2-4-31

S2-4-31: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.21 (d, J = 5.0 Hz, 1 H), 4.70-4.61 (m, 1 H), 4.32-4.26 (m, 1 H), 4.19 (s, 1 H), 3.56-3.45 (m, 1 H), 3.34-2.95 (m, 10 H), 2.40-2.26 (m, 2 H), 1.72-1.55 (m, 10 H), 1.19 (t, J = 7.3 Hz, 3 H); MS (ESI) *m/z* 546.26 (M+H).

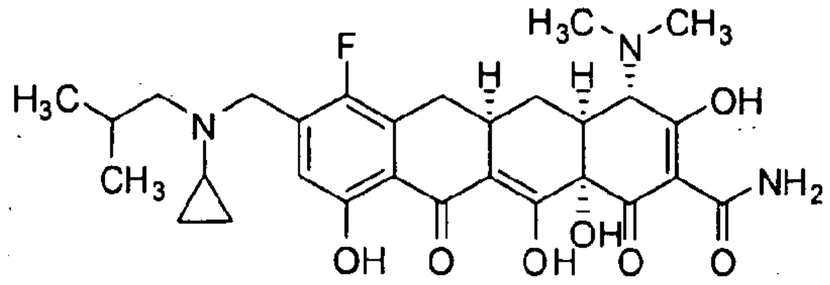

S2-4-32

S2-4-32: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.12 (d, J = 4.1 Hz, 1 H), 4.51-4.34 (m, 2 H), 4.16 (s, 1 H), 3.92-3.82 (m, 1 H), 3.34-2.94 (m, 11 H), 2.40-2.08 (m, 4 H), 1.98-1.79 (m, 4 H), 1.78-1.55 (m, 3 H), 1.36 (t, J = 7.4 Hz, 3 H); MS (ESI) *m/z* 558.29 (M+H).


S2-4-33

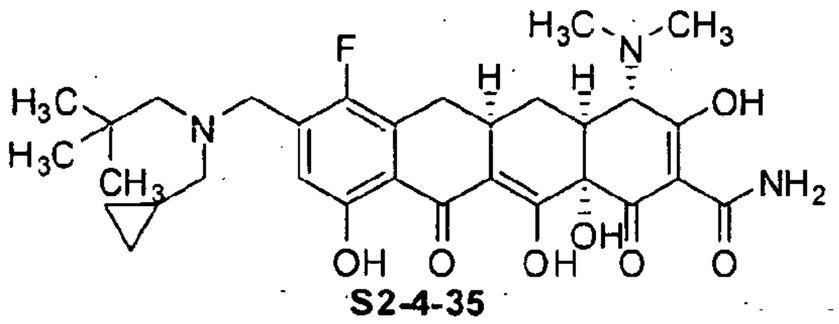
S2-4-33: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.19 (d, J = 5.5 Hz, 1 H), 4.72-4.63 (m, 1 H), 4.34-4.24 (m, 1 H), 4.17 (s, 1 H), 3.59-3.50 (m, 1 H), 3.26-2.96

(m, 10 H), 2.40-2.26 (m, 2 H), 2.04-1.93 (m, 2 H), 1.70-1.50 (m, 7 H), 1.18 (t, J = 7.3 Hz, 3 H), 1.06 (t, J = 7.6 Hz, 3 H); MS (ESI) *m/z* 560.35 (M+H).



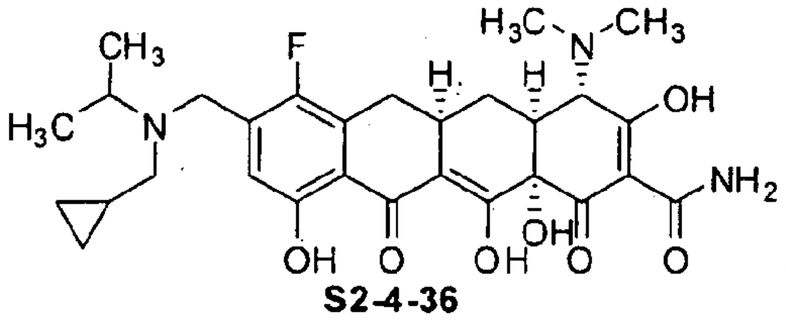
S2-4-34

S2-4-34: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.15 (d, J = 5.5 Hz, 1 H), 4.64-4.44 (m, 2 H), 4.16 (s, 1 H), 3.26-2.94 (m, 11 H), 2.93-2.82 (m, 1 H), 2.41-2.25 (m, 3 H), 1.70-1.56 (m, 1 H), 1.20-1.05 (m, 7 H), 1.05-0.84 (m, 3 H); MS (ESI) *m/z* 558.27 (M+H).



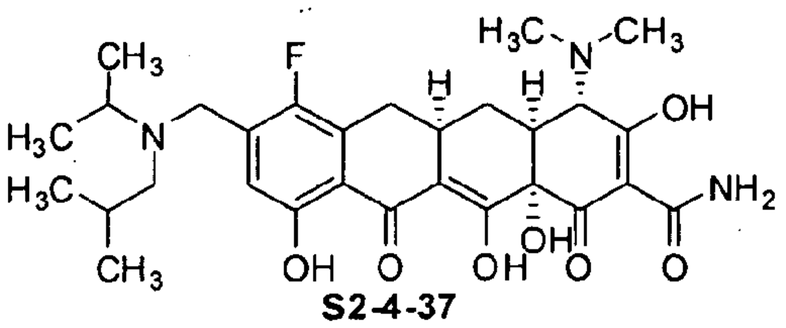
S2-4-35

S2-4-35: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.20 (d, J = 3.2 Hz, 1 H), 4.60-4.49 (m, 2 H), 4.16 (s, 1 H), 3.45-3.36 (m, 1 H), 3.34-2.94 (m, 12 H), 2.40-2.26 (m, 2 H), 1.70-1.56 (m, 1 H), 1.36-1.26 (m, 1 H), 1.07 (s, 9 H), 0.86-0.74 (m, 2 H), 0.57-0.49 (m, 2 H); MS (ESI) *m/z* 586.33 (M+H).



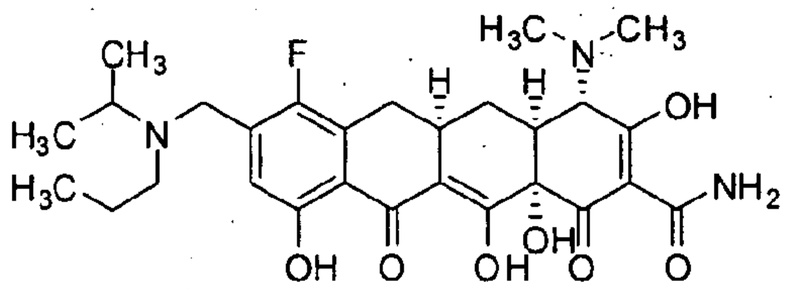
S2-4-36

S2-4-36: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.13 (d, J = 5.5 Hz, 1 H), 4.54-4.33 (m, 2 H), 4.16 (s, 1 H), 3.98-3.86 (m, 1 H), 3.26-2.94 (m, 11 H), 2.40-2.24 (m, 2 H), 1.70-1.56 (m, 1 H), 1.52-1.35 (m, 6 H), 1.20-1.08 (m, 1 H), 0.80-0.70 (m, 2 H), 0.50-0.40 (m, 2 H); MS (ESI) *m/z* 558.21 (M+H).



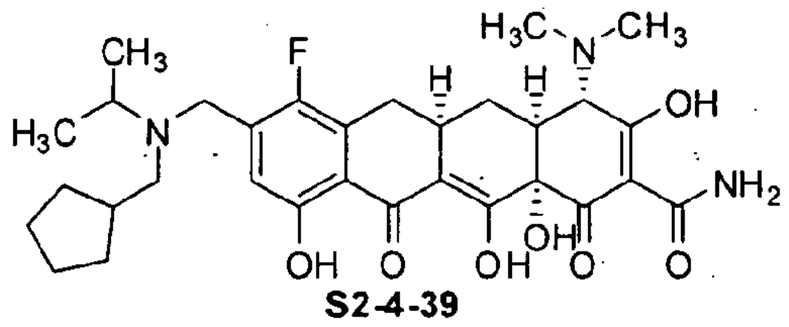
S2-4-37

S2-4-37: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.18 (d, J = 5.96 Hz, 1 H), 4.52-4.35 (m, 2 H), 4.17 (s, 1 H), 3.82-3.70 (m, 1 H), 3.26-2.94 (m, 11 H), 2.41-2.28 (m, 2 H), 2.04-1.93 (m, 1 H), 1.71-1.58 (m, 1 H), 1.52-1.38 (m, 6 H), 1.08-1.02 (d, J = 6.9 Hz, 3 H), 1.00-0.94 (d, J = 6.4 Hz, 3 H); MS (ESI) *m/z* 560.20 (M+H).



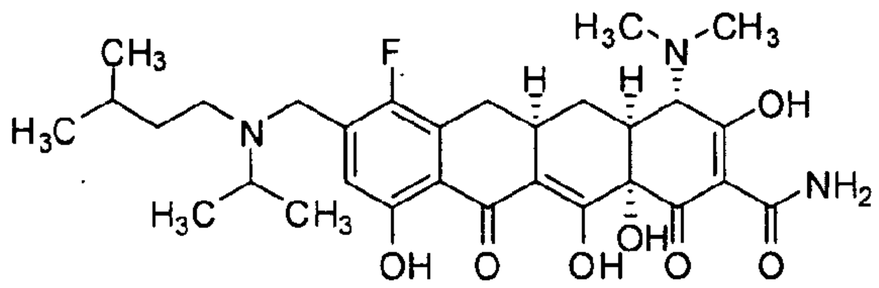
S2-4-38

S2-4-38: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.11 (d, J = 5.5 Hz, 1 H), 4.54-4.44 (m, 1 H), 4.28-4.22 (m, 1 H), 4.15 (s, 1 H), 3.80-3.72 (m, 1 H), 3.36-2.94 (m, 11 H), 2.40-2.26 (m, 2 H), 1.88-1.54 (m, 3 H), 1.50-1.38 (m, 6 H), 1.03-0.94 (m, 3 H); MS (ESI) *m/z* 546.20 (M+H).



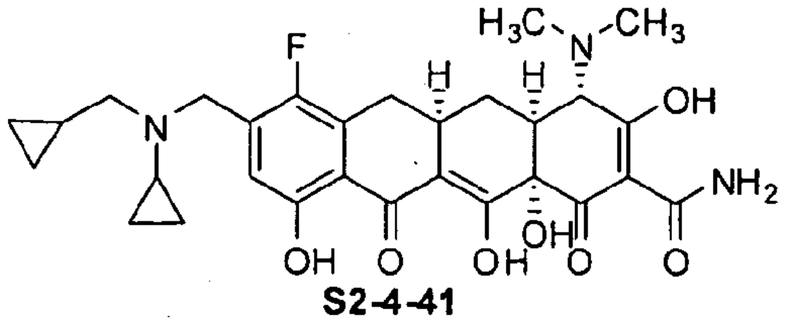
S2-4-39

S2-4-39: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.17 (d, J = 5.5 Hz, 1 H), 4.52-4.33 (m, 2 H), 4.17 (s, 1 H), 3.84-3.72 (m, 1 H), 3.36-2.94 (m, 11 H), 2.40-2.16 (m, 3 H), 1.99-1.83 (m, 2 H), 1.75-1.53 (m, 5 H), 1.52-1.42 (m, 6 H), 1.34-1.15 (m, 2 H); MS (ESI) *m/z* 586.26 (M+H).



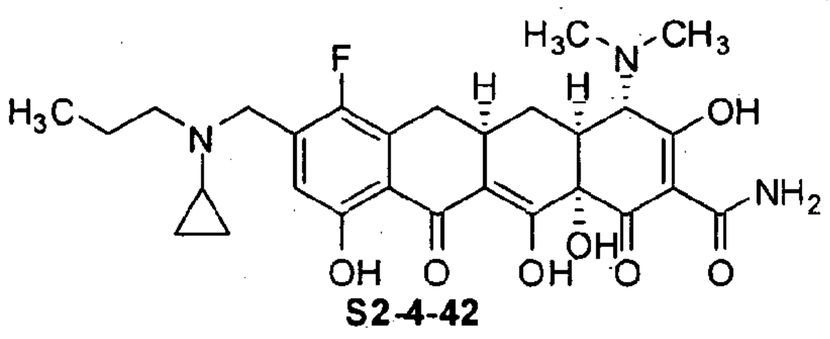
S2-4-40

S2-4-40: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.14 (d, J = 5.5 Hz, 1 H), 4.56-4.47 (m, 1 H), 4.33-4.24 (m, 1 H), 4.17 (s, 1 H), 3.84-3.72 (m, 1 H), 3.36-2.94 (m, 11 H), 2.40-2.25 (m, 2 H), 1.75-1.54 (m, 4 H), 1.52-1.40 (m, 6 H), 1.02-0.88 (m, 6 H); MS (ESI) *m/z* 574.26 (M+H).



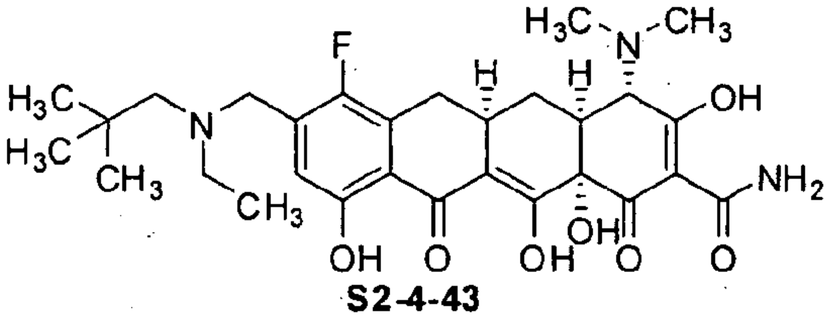
S2-4-41

S2-4-41: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.9 Hz, 1 H), 4.64 (br, s, 1 H), 4.57 (br, s, 1 H), 4.10 (s, 1 H), 3.21 (dd, J = 15.1, 4.6 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.15-2.89 (m, 5 H), 2.36 (m, 1 H), 2.29-2.21 (m, 1 H), 1.70-1.60 (m, 1 H), 1.33-1.23 (m, 1 H), 1.10-0.85 (m, 3 H), 0.85-0.79 (m, 2 H), 0.78-0.67 (m, 1 H), 0.53-0.47 (m, 2 H); MS (ESI) *m/z* 556.33 (M+H).



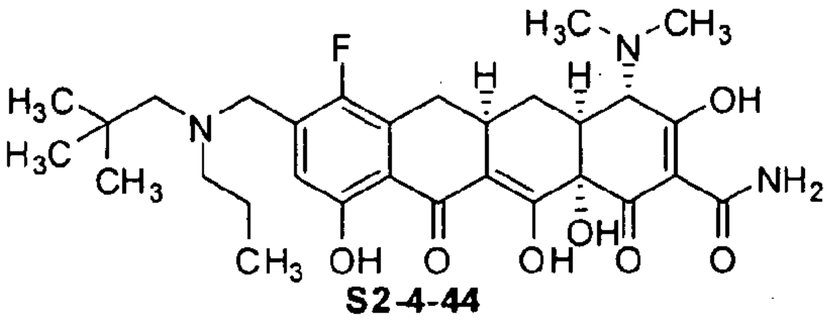
S2-4-42

S2-4-42: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, J = 5.5 Hz, 1 H), 4.54 (d, J = 6.4 Hz, 2 H), 4.12 (s, 1 H), 3.21 (dd, J = 15.1, 4.6 Hz, 1 H), 3.17-2.95 (m, 4 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.92-2.87 (m, 1 H), 2.36 (t, J = 13.8 Hz, 1 H), 2.29-2.21 (m, 1 H), 1.9-1.84 (m, 2 H), 1.70-1.60 (m, 1 H), 1.03 (t, J = 7.3 Hz, 3 H), 1.10-0.85 (m, 3 H), 0.82-0.68 (m, 1 H); MS (ESI) *m/z* 544.33 (M+H).



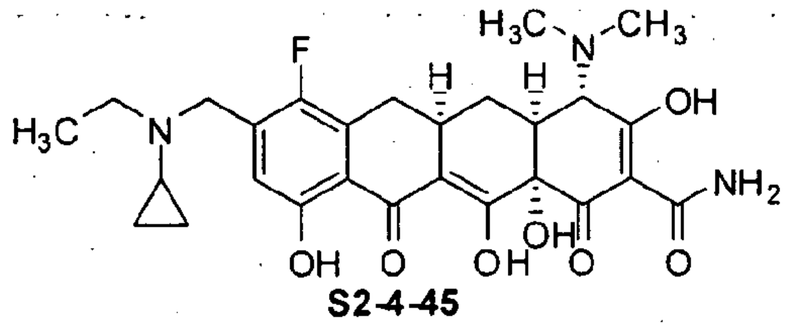
S2-4-43

S2-4-43: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 5.5 Hz, 1 H), 4.51 (d, J = 13.3 Hz, 1 H), 4.39 (d, J = 13.3 Hz, 1 H), 4.07 (s, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.25-2.96 (m, 7 H), 2.42-2.33 (m, 1 H), 2.26-2.18 (m, 1 H), 1.70-1.60 (m, 1 H), 1.43 (t, J = 7.3 Hz, 3 H), 1.06 (s, 9 H); MS (ESI) *m/z* 560.50 (M+H).



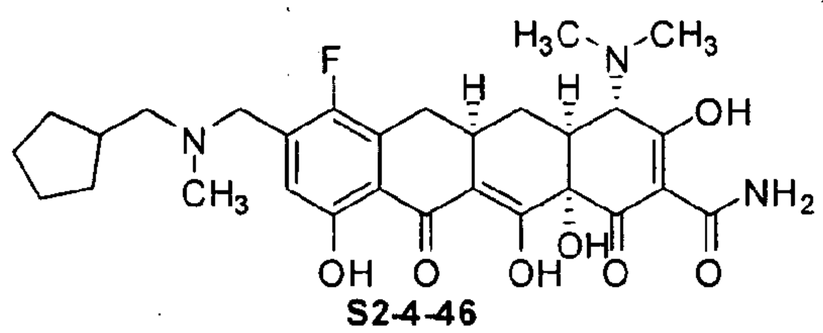
S2-4-44

S2-4-44: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 5.5 Hz, 1 H), 4.52 (d, J = 13.3 Hz, 1 H), 4.41 (d, J = 13.3 Hz, 1 H), 4.07 (s, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 3.25-2.96 (m, 7 H), 2.43-2.33 (m, 1 H), 2.27-2.19 (m, 1 H), 1.98-1.88 (m, 1 H), 1.86-1.74 (m, 1 H), 1.71-1.61 (m, 1 H), 1.08 (s, 9 H), 1.01 (t, J = 6.9 Hz, 3 H); MS (ESI) *m/z* 574.52 (M+H).



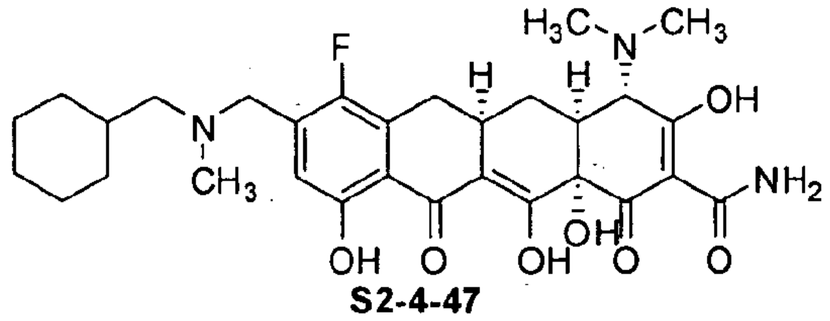
S2-4-45

S2-4-45: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 5.5 Hz, 1 H), 4.53 (d, J = 6.8 Hz, 2 H), 4.10 (s, 1 H), 3.41 (q, J = 7.3 Hz, 2 H), 3.21 (dd, J = 15.1, 4.6 Hz, 1 H), 3.17-2.95 (m, 2 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.93-2.85 (m, 1 H), 2.36 (t, J = 13.8 Hz, 1 H), 2.29-2.20 (m, 1 H), 1.69-1.59 (m, 1 H), 1.46 (t, J = 7.3 Hz, 3 H), 1.10-0.84 (m, 3 H), 0.79-0.69 (m, 1 H); MS (ESI) *m/z* 530.38 (M+H).



S2-4-46

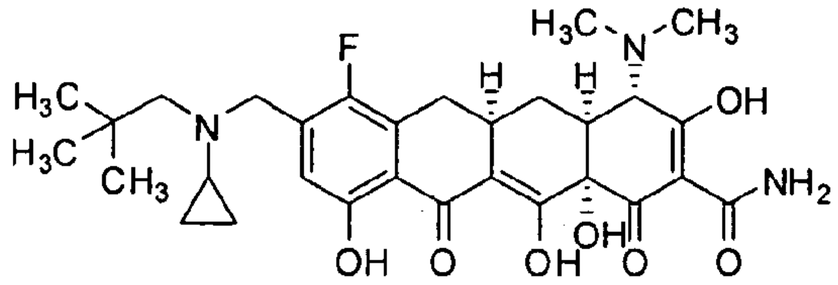
S2-4-46: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.9 Hz, 1 H), 4.58 (d, J = 13.3 Hz, 1 H), 4.26 (d, J = 13.3 Hz, 1 H), 4.10 (s, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.87 (s, 5 H), 3.27-2.96 (m, 3 H), 2.43-2.32 (m, 2 H), 2.28-2.20 (m, 1 H), 2.03-1.91 (m, 2 H), 1.78-1.60 (m, 5 H), 1.36-1.20 (m, 2 H); MS (ESI) *m/z* 558.40 (M+H).



S2-4-47

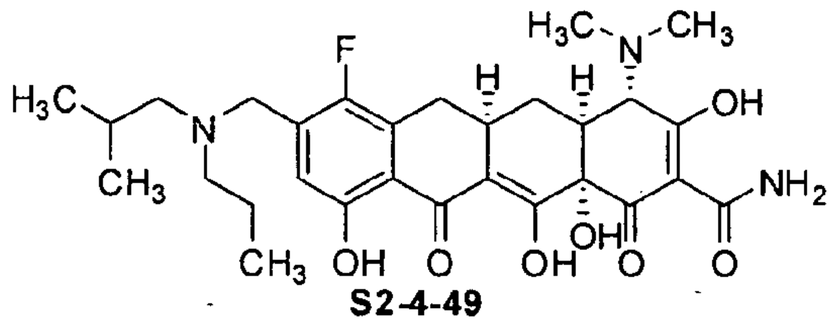
S-2-4-47: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 5.9 Hz, 1 H), 4.56 (d, J = 13.3 Hz, 1 H), 4.23 (d, J = 13.3 Hz, 1 H), 4.09 (s, 1 H), 3.04 (s, 3 H), 2.97 (s, 3 H), 2.86 (s, 5 H), 3.27-2.96 (m, 3 H), 2.37 (t, J = 13.8 Hz, 1 H), 2.28-2.20 (m, 1 H),

1.96-1.59 (m, 7 H), 1.44-1.30 (m, 2 H), 1.29-1.19 (m, 1 H), 1.13-0.95 (m, 2 H); MS (ESI) *m/z* 572.41 (M+H).



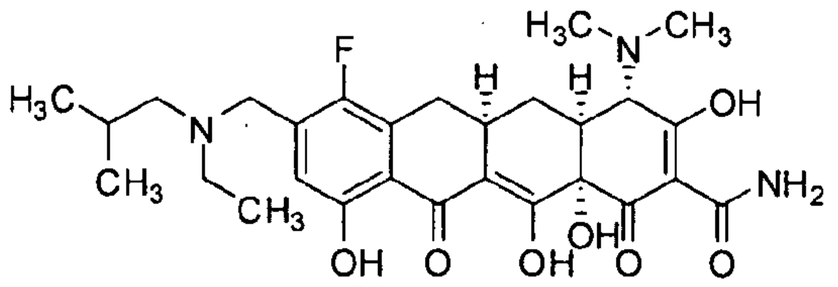
S2-4-48

S2-4-48: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, *J* = 5.5 Hz, 1 H), 4.52 (d, *J* = 13.3 Hz, 1 H), 4.41 (d, *J* = 13.3 Hz, 1 H), 4.07 (s, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 3.25-2.96 (m, 6 H), 2.43-2.33 (m, 1 H), 2.27-2.19 (m, 1 H), 1.66 (m, 1 H), 1.08 (s, 9 H), 1.10-0.85 (m, 3 H), 0.81-0.71 (m, 1 H); MS (ESI) *m/z* 572.43 (M+H).



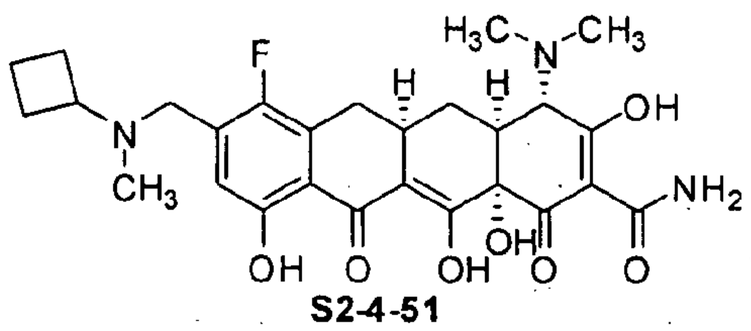
S2-4-49

S2-4-49: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.50 (d, *J* = 13.7 Hz, 1 H), 4.37 (d, *J* = 13.7 Hz, 1 H), 4.28 (s, 2 H), 4.10 (s, 1 H), 3.21 (dd, *J* = 15.5, 4.6 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.17-2.98 (m, 6 H), 2.37 (t, *J* = 14.7 Hz, 1 H), 2.29-2.12 (m, 2 H), 1.93-1.73 (m, 2 H), 1.71-1.61 (m, 1 H), 1.09-0.98 (m, 9 H); MS (ESI) *m/z* 560.35 (M+H).



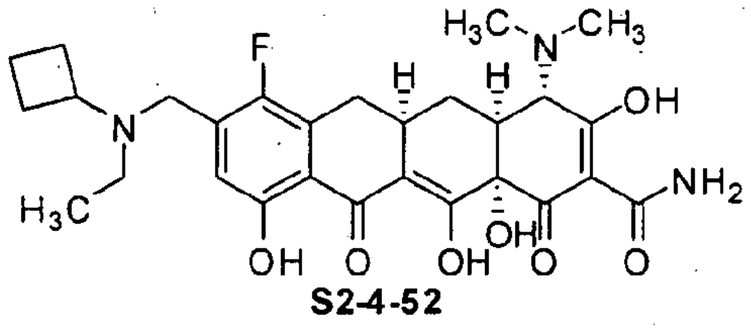
S2-4-50

S-2-4-50: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, *J* = 6.0 Hz, 1 H), 4.50 (d, *J* = 13.5 Hz, 1 H), 4.34 (d, *J* = 13.5 Hz, 1 H), 4.28 (s, 2 H), 4.10 (s, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.27-2.97 (m, 7 H), 2.36 (t, *J* = 14.7 Hz, 1 H), 2.28-2.12 (m, 2 H), 1.70-1.60 (m, 1 H), 1.39 (t, *J* = 6.9 Hz, 3 H), 1.05 (dd, *J* = 15.1, 6.4 Hz, 6 H); MS (ESI) *m/z* 546.39 (M+H).



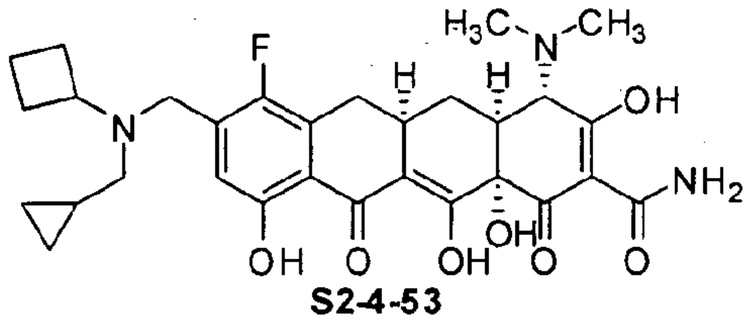
S2-4-51

S2-4-51: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 6.0 Hz, 1 H), 4.41 (d, J = 12.4 Hz, 1 H), 4.14 (d, J = 12.4 Hz, 1 H), 4.12 (s, 1 H), 3.88 (m, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.25-2.97 (m, 3 H), 2.70 (s, 3 H), 2.43-2.22 (m, 6 H), 1.96-1.77 (m, 2 H), 1.69-1.59 (m, 1 H); MS (ESI) *m/z* 530.34 (M+H).



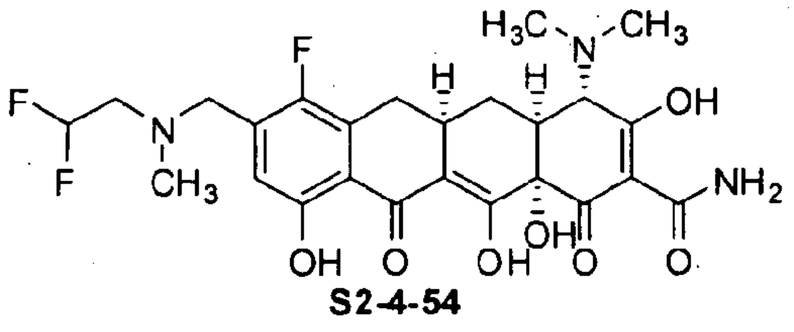
S2-4-52

S2-4-52: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 6.0 Hz, 1 H), 4.31 (br, s, 2 H), 4.14 (s, 1 H), 4.00-3.92 (m, 1 H), 3.06 (s, 3 H), 2.97 (s, 3 H), 3.26-2.97 (m, 5 H), 2.42-2.22 (m, 6 H), 1.92-1.77 (m, 2 H), 1.69-1.59 (m, 1 H), 1.35 (t, J = 6.8 Hz, 3 H); MS (ESI) *m/z* 544.35 (M+H).



S2-4-53

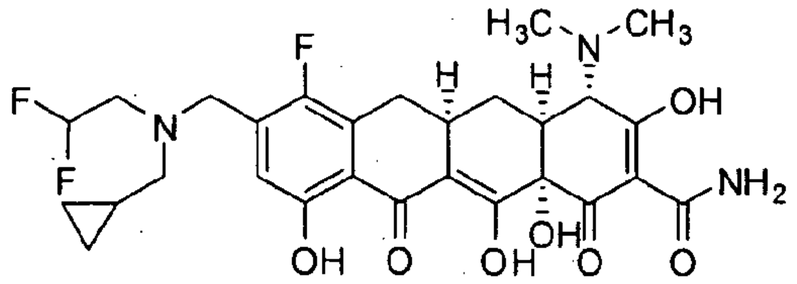
S2-4-53: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, J = 6.0 Hz, 1 H), 4.48 (m, 1 H), 4.37 (m, 1 H), 4.13 (s, 1 H), 4.04 (m, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.25-2.95 (m, 5 H), 2.45-2.13 (m, 6 H), 1.89-1.74 (m, 2 H), 1.69-1.59 (m, 1 H), 1.19-1.11 (m, 1 H), 0.81-0.72 (m, 2 H), 0.46-0.36 (m, 2 H); MS (ESI) *m/z* 570.39 (M+H).



S2-4-54

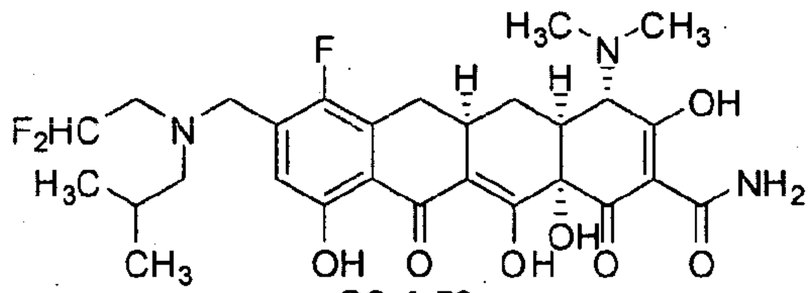
S2-4-54: ^{1}H NMR (400 MHz, CD_3OD) δ 7.09 (d, J = 5.0 Hz, 1 H), 6.48 (t, J = 53.6 Hz, 1 H), 4.55 (s, 2 H), 4.11 (s, 1 H), 3.83 (t, J = 14.2 Hz, 2 H), 3.05 (s, 3 H),

3.01 (s, 3 H), 2.97 (s, 3 H), 3.25-2.98 (m, 5 H), 2.37 (t, J = 14.7 Hz, 1 H), 2.29-2.21 (m, 1 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 540.31 (M+H).



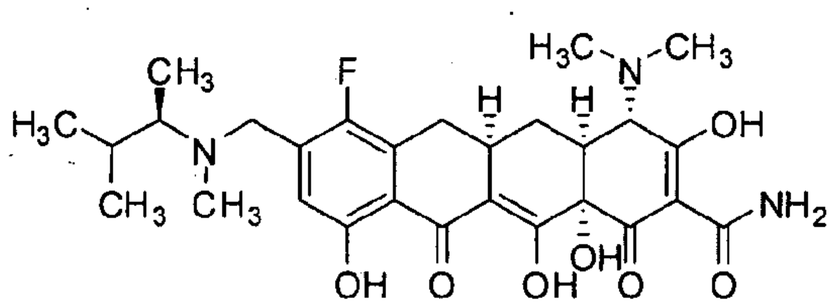
S2-4-55

S2-4-55: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (br, s, 1 H), 6.51 (t, J = 53.6 Hz, 1 H), 4.64 (s, 2 H), 4.12 (s, 1 H), 3.87 (t, J = 14.2 Hz, 2 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.25-2.98 (m, 7 H), 2.44-2.22 (m, 2 H), 1.70-1.61 (m, 1 H), 1.27-1.19 (m, 1 H), 0.88-0.80 (m, 2 H), 0.55-0.45 (m, 2 H); MS (ESI) *m/z* 580.34 (M+H).



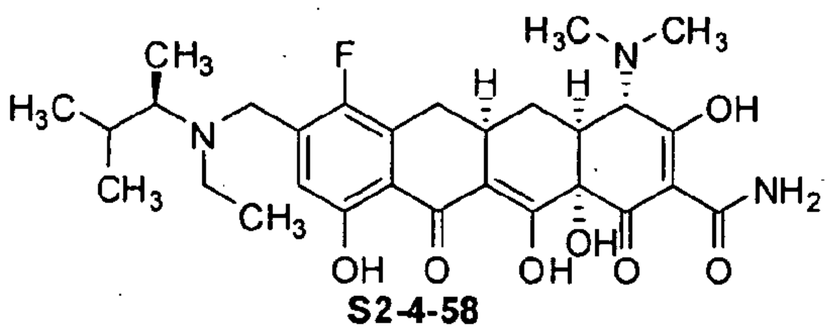
S2-4-56

S2-4-56: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 5.0 Hz, 1 H), 6.38 (t, J = 53.6 Hz, 1 H), 4.40 (br, s, 2 H), 4.09 (s, 1 H), 3.56 (m, 2 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 3.22-2.98 (m, 5 H), 2.35 (t, J = 14.2 Hz, 1 H), 2.28-2.08 (m, 2 H), 1.69-1.59 (m, 1 H), 1.02 (d, J = 6.9 Hz, 6 H); MS (ESI) *m/z* 582.34 (M+H).



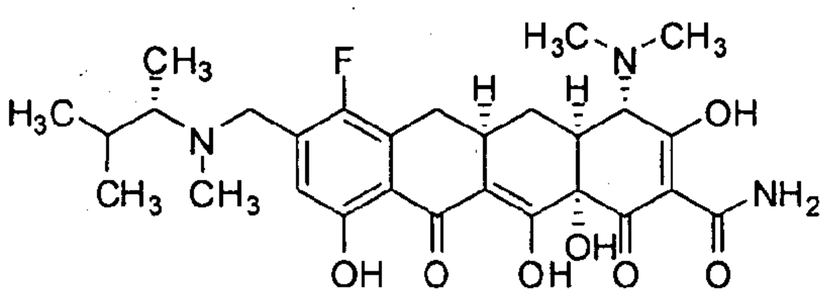
S2-4-57

S2-4-57: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (t, J = 6.0 Hz, 1 H), 4.61 (dd, J = 18.3, 13.7 Hz, 1 H), 4.18 (dd, J = 78.3, 13.7 Hz, 1 H), 4.10 (s, 1 H), 3.87 (t, J = 14.2 Hz, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.84 (s, 3 H), 3.25-2.98 (m, 3 H), 2.42-2.20 (m, 3 H), 1.70-1.60 (m, 1 H), 1.41 (dd, J = 30.2, 6.9 Hz, 3 H), 1.13 (dd, J = 30.2, 6.9 Hz, 3 H), 1.04 (dd, J = 15.6, 6.9 Hz, 3 H); MS (ESI) *m/z* 546.30 (M+H).



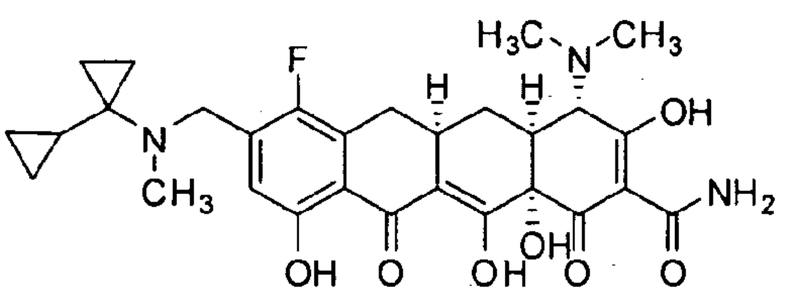
S2-4-58

S2-4-58: ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (m, 1 H), 4.08 (s, 1 H), 4.61 (dd, *J* = 18.3, 13.7 Hz, 1 H), 4.18 (dd, *J* = 78.3, 13.7 Hz, 1 H), 3.47 (m, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 3.41-2.97 (m, 5 H), 2.42-2.20 (m, 3 H), 1.70-1.60 (m, 1 H), 1.37 (dd, *J* = 30.2, 6.9 Hz, 3 H), 1.29 (t, *J* = 6.9 Hz, 3 H), 1.13 (dd, *J* = 30.2, 6.9 Hz, 3 H), 1.03 (dd, *J* = 15.6, 6.9 Hz, 3 H); MS (ESI) *m/z* 560.33 (M+H).



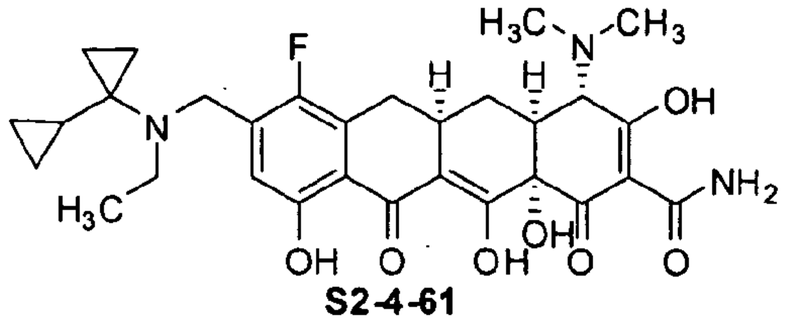
S2-4-59

S2-4-59: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (t, *J* = 6.0 Hz, 1 H), 4.61 (dd, *J* = 18.3, 13.7 Hz, 1 H), 4.18 (dd, *J* = 78.3, 13.7 Hz, 1 H), 4.10 (s, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.27-2.98 (m, 4 H), 2.83 (s, 3 H), 2.42-2.20 (m, 3 H), 1.70-1.60 (m, 1 H), 1.41 (dd, *J* = 30.2, 6.9 Hz, 3 H), 1.13 (dd, *J* = 30.2, 6.9 Hz, 3 H), 1.04 (dd, *J* = 15.6, 6.9 Hz, 3 H); MS (ESI) *m/z* 546.32 (M+H).



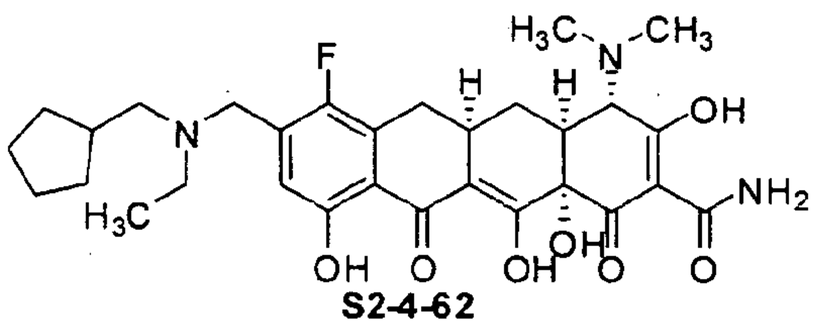
S2-4-60

S2-4-60: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 5.9 Hz, 1 H), 4.75 (d, *J* = 13.3 Hz, 1 H), 4.60 (d, *J* = 13.3, 1 H), 4.10 (s, 1 H), 3.04 (s, 3 H), 3.02 (s, 3 H), 2.96 (s, 3 H), 3.25-2.96 (m, 3 H), 2.41-2-20 (m, 2 H), 1.70-1.59 (m, 2 H), 1.19-1.01 (m, 2 H), 0.96-0.88 (m, 1 H), 0.86-0.70 (m, 3 H), 0.43-0.31 (m, 2 H); MS (ESI) *m/z* 556.31 (M+H).



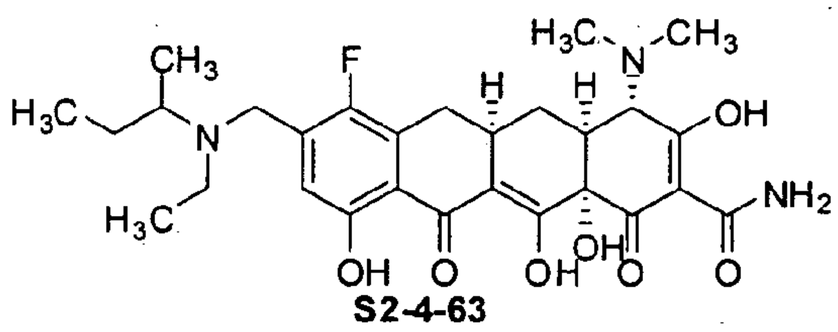
S2-4-61

S2-4-61: ^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (d, *J* = 5.9 Hz, 1 H), 4.75 (d, *J* = 13.3 Hz, 1 H), 4.60 (d, *J* = 13.3, 1 H), 4.10 (s, 1 H), 3.05 (s, 3 H), 2.96 (s, 3 H), 3.25-2.96 (m, 5 H), 2.41-2-20 (m, 2 H), 1.70-1.59 (m, 2 H), 1.35 (t, *J* = 6.8 Hz, 3 H), 1.19-1.01 (m, 2 H), 0.96-0.88 (m, 1 H), 0.86-0.70 (m, 3 H), 0.43-0.31 (m, 2 H); MS (ESI) *m/z* 570.32 (M+H).



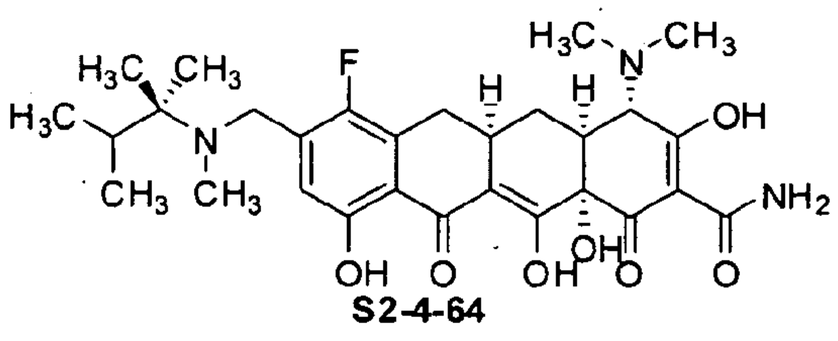
S2-4-62

S2-4-62: ^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (d, *J* = 6.0 Hz, 1 H), 4.51-4.33 (m, 2 H), 4.17 (s, 1 H), 3.27-3.19 (m, 1 H), 3.08 (s, 3 H), 2.99 (s, 3 H), 3.17-2.97 (m, 4 H), 2.38-2.27 (m, 2 H), 2.27-2.18 (m, 1 H), 1.99-1.83 (m, 2 H), 1.74-1.55 (m, 5 H), 1.43 (t, *J* = 7.3 Hz, 3 H), 1.32-1.14 (m, 2 H); MS (ESI) *m/z* 572.39 (M+H).



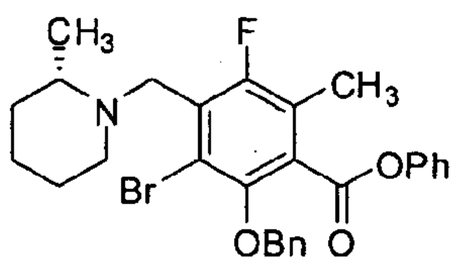
S2-4-63

S2-4-63: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11-7.07 (m, 1 H), 4.61 (dd, *J* = 18.3, 13.7 Hz, 1 H), 4.29, 4.09 (ABq, *J* = 13.7 Hz, 1 H), 4.11 (s, 1 H), 3.51-3.43 (m, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 3.41-2.97 (m, 5 H), 2.34 (t, *J* = 6.9 Hz, 1 H), 2.27-2.20 (m, 1 H), 2.06-1.95 (m, 1 H), 1.74-1.59 (m, 2 H), 1.44 (d, *J* = 6.1 Hz, 3 H), 1.29 (t, *J* = 6.9 Hz, 3 H), 1.08 (t, *J* = 7.6 Hz, 3 H); MS (ESI) *m/z* 546.38 (M+H).



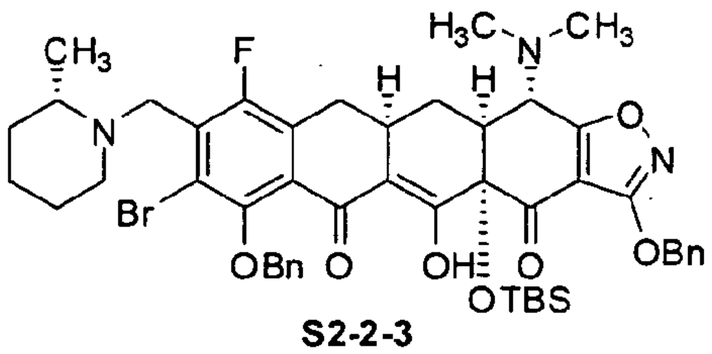
S2-4-64

S2-4-64: ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (d, *J* = 6.0 Hz, 1 H), 4.80-4.71 (m, 1 H), 4.18 (s, 1 H), 4.06-3.98 (m, 1 H), 3.26-2.95 (m, 9 H), 2.76 (s, 3 H), 2.42-2.30 (m, 2 H), 2.01-1.89 (m, 1 H), 1.69-1.54 (m, 1 H), 1.51 (s, 3 H), 1.48 (s, 3 H), 1.02 (d, *J* = 6.4 Hz, 6 H); MS (ESI) *m/z* 560.23 (M+H).



S2-1-3

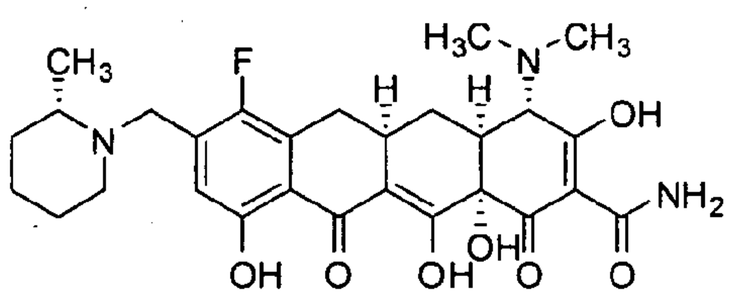
Compound **S1-7** (89 mg, 0.20 mmol, 1.0 equiv) and (*S*)-2-methylpiperidine (60 μL, 0.50 mmol, 2.5 equiv) were dissolved in 1,2-dichloroethane (2 mL). Titanium(IV) isopropoxide (0.18 mL, 0.60 mmol, 3.0 equiv) was added at rt. After stirring at rt overnight, LC/MS indicated that most of the starting material was consumed and the intermediate formed. MeOH (1 mL) and sodium borohydride (40 mg, 1.1 mmol, 5.5 equiv, added in 4 equal portions) were added until the intermediate was completely converted to the product. The reaction mixture was diluted with dichloromethane, washed with saturated aqueous sodium bicarbonate, water (2 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (Biotage 10 g column, 10% to 50% EtOAc in hexanes gradient), yielding 86 mg (82%) of the desired compound **S2-1-3** as a colorless oil.



S2-2-3

LDA was prepared by adding *n*-BuLi (0.24 mL, 1.6 M/hexanes, 0.38 mmol, 3.0 equiv) to diisopropylamine (53 μL, 0.38 mmol, 3.0 equiv) in 2 mL dry THF under a nitrogen atmosphere in a flame dried schenck flask cooled at -78 °C. The resulting solution was warmed to -20 °C and stirred for 15 min. After the LDA solution was cooled down to -78 °C, TMEDA (57 μL, 0.38 mmol, 3.0 equiv) was added slowly *via* a syringe, followed by the dropwise addition of compound **S2-1-3**

(86 mg, 0.16 mmol, 1.3 equiv) in 1 mL dry THF (a dark-red color appeared as soon as addition started). After stirring for 10 min, enone **S1-9** (54 mg, 0.13 mmol, 1.0 equiv) in 1 mL dry THF was added slowly *via* a syringe. After 10 min, LC/MS indicated that the enone was consumed and the product present. The reaction mixture was allowed to slowly warm to -30 °C in 1 h, added with a phosphate buffer (pH 7, 10 mL) and saturated aqueous ammonium chloride (20 mL), and extracted with dichloromethane (3 x 15 mL). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting orange-red oil was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; injection volume: 4.0 mL (CH_3CN); gradient: 20→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product were collected and concentrated at rt to remove most of the acetonitrile. The resulting mostly aqueous solution was extracted with EtOAc. The EtOAc extract was dried (sodium sulfate) and concentrated to give 26 mg (23%) of the desired compound **S2-2-3**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.00 (br, s, 1 H), 7.58-7.54 (m, 2 H), 7.51-7.47 (m, 2 H), 7.40-7.31 (m, 6 H), 5.35 (s, 2 H), 4.98 (q, J = 11.0 Hz, 2 H), 4.13-4.07 (m, 1 H), 3.93 (d, J = 11.0 Hz, 1 H), 3.42 (d, J = 12.2 Hz, 1 H), 3.24 (dd, J = 15.9, 4.9 Hz, 1 H), 3.03-2.93 (m, 1 H), 2.69-2.62 (m, 1 H), 2.58-2.51 (m, 1 H), 2.48 (s, 6 H), 2.50-2.40 (m, 3 H), 2.19-2.10 (m, 2 H), 1.66-1.58 (m, 2 H), 1.48-1.26 (m, 4 H), 1.22 (d, J = 6.1 Hz, 3 H), 0.81 (s, 9 H), 0.26 (s, 3 H), 0.12 (s, 3 H).

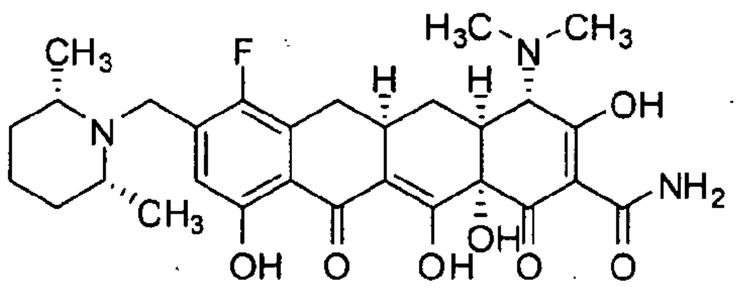


S2-4-65

Aqueous HF (0.3 mL, 48-50%) was added to a CH_3CN solution (1.0 mL) of **S2-2-3** (26 mg) in a plastic vial at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The resulting mixture was poured into an aqueous solution (10 mL) of K_2HPO_4 (2 g). The solution was extracted with EtOAc (3 x 15 mL). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give the crude intermediate (18 mg).

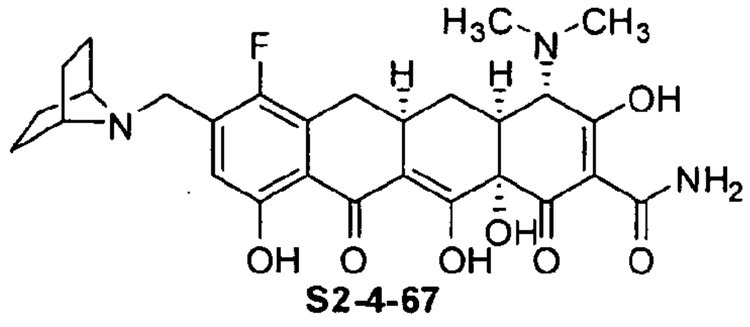
Pd-C (10 mg, 10wt%) was added to a MeOH solution (2 mL) of the above crude intermediate. HCl/MeOH (0.5 mL, 0.5 N) was also added. The reaction was stirred under H_2 (balloon) at 25 °C for 2 hrs and filtered through a pad of Celite. The filtrate was concentrated, and the crude product was purified by HPLC on a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, sample in 2.0 mL (0.05 N HCl), gradient elution with 0→70% B over 15 min, mass-directed fraction collection] to yield the desired product **S2-4-65** as a yellow solid (9 mg, 59%, two steps): ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (d, J = 6.0 Hz, 1 H), 4.76 (d, J = 13.7 Hz, 1 H), 4.15 (d, J = 13.7 Hz, 1 H), 4.10 (s, 1 H), 3.40-3.32 (m, 2 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.27-2.96 (m, 4 H), 2.42-2.32 (m, 1 H), 2.27-2.21 (m, 1 H), 1.92-1.80 (m, 2 H), 1.73-1.58 (m, 3 H), 1.56 (d, J = 6.4 Hz, 3 H); MS (ESI) *m/z* 544.26 (M+H).

The following compounds were prepared according to the methods of **S2-4-65**, substituting the appropriate amine for 2-methylpiperidine.



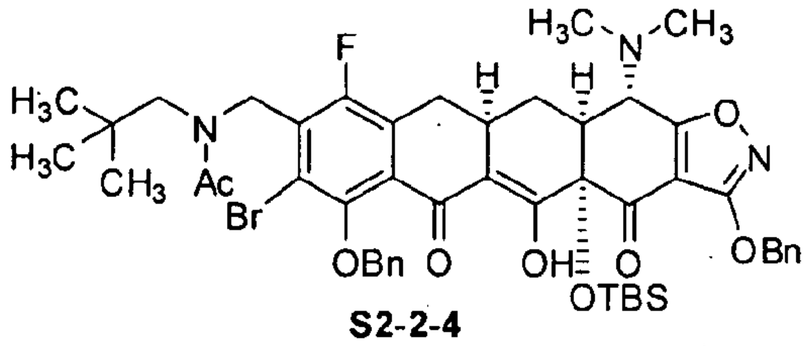
S2-4-66

S2-4-66: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (dd, J = 8.2, 6.0 Hz, 1 H), 4.40 (s, 2 H), 4.09 (s, 1 H), 3.68-3.57 (m, 2 H), 3.24-2.98 (m, 3 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.40-2.32 (m, 1 H), 2.29-2.21 (m, 1 H), 2.05-1.58 (m, 7 H), 1.54 (d, J = 6.0 Hz, 3 H), 1.35 (d, J = 6.0 Hz, 3 H); MS (ESI) *m/z* 558.31 (M+H).



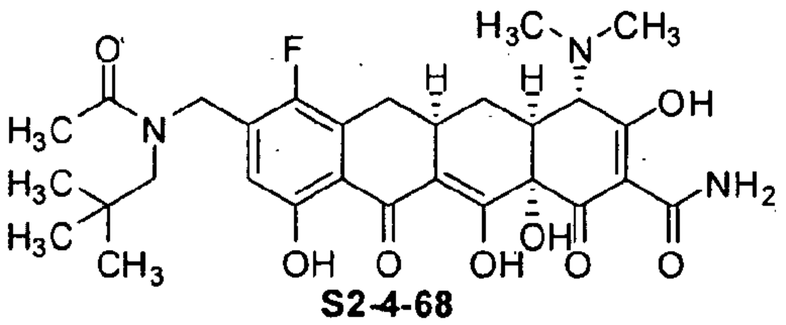
S2-4-67

S2-4-67: ^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (d, J = 6.0 Hz, 1 H), 4.33 (s, 2 H), 4.15 (br, s, 2 H), 4.09 (s, 1 H), 3.04 (s, 3 H), 2.97 (s, 3 H), 3.23-2.96 (m, 3 H), 2.38-2.29 (m, 3 H), 2.27-2.20 (m, 1 H), 2.08-2.01 (m, 2 H), 1.86-1.80 (m, 2 H), 1.71-1.61 (m, 1 H); MS (ESI) *m/z* 542.26 (M+H).



S2-2-4

Acetic anhydride (3.6 µL, 0.038 mmol, 2.0 equiv) was added to a solution of **S2-2-1** (17 mg, 0.019 mmol, 1.0 equiv) in dichloromethane (1 mL). After 2 hrs, the reaction mixture was concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 µm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 90→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 5.0-6.0 min, were collected and concentrated under reduced pressure to give 12 mg (66%) of the desired compound **S2-2-4**: ^1H NMR (400 MHz, $CDCl_3$) δ 16.02-15.88 (m, 1 H), 7.58-7.44 (m, 4 H), 7.40-7.28 (m, 6 H), 5.36 (s, 2 H), 5.03-4.70 (m, 4 H), 3.94 (br s, 1 H), 3.30-3.14 (m, 3 H), 3.04-2.93 (m, 1 H), 2.64-2.32 (m, 9 H), 2.16-2.06 (m, 4 H), 1.04-0.94 (m, 9 H), 0.81 (s, 9 H), 0.24 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 944.61, 946.61 (M+H).

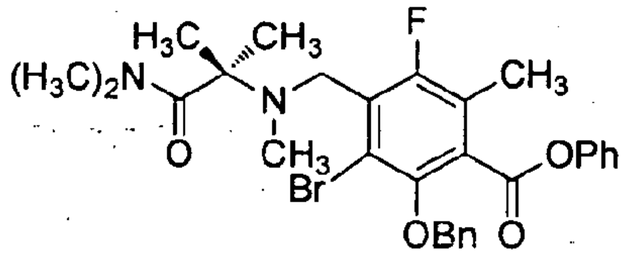


S2-4-68

A solution of compound **S2-2-4** (12 mg, 0.013 mmol) in 1,4-dioxane (0.80 mL) was treated with HF (0.40 mL, 48-50% aqueous solution) at rt. After stirring overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL). This mixture was extracted with EtOAc (3 times), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield the crude intermediate.

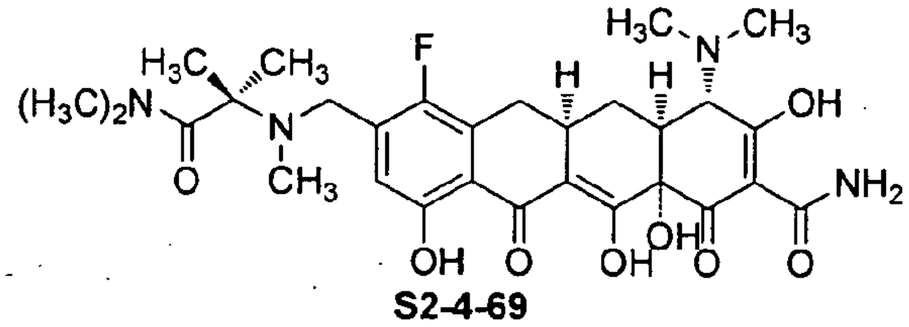
The above crude intermediate was dissolved in MeOH (1 mL)/1,4-dioxane (1 mL). HCl/MeOH (0.5 mL, 0.5 N) and 10% Pd-C (Degussa, 2 mg) were added, and an atmosphere of hydrogen was introduced. After 2 hrs, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude product

was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 9.8-11.4 min, were collected and freeze-dried to yield the desired compound **S2-4-68** (5 mg, 69%): ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.14 (d, J = 5.5 Hz, 1 H), 4.40 (s, 2 H), 4.15 (s, 1 H), 3.82-3.56 (m, 5 H), 3.26-2.94 (m, 9 H), 2.36-2.24 (m, 2 H), 2.24-1.98 (br m, 9 H), 1.70-1.55 (m, 1 H); MS (ESI) *m/z* 574.33 (M+H).



S2-1-2

Compound **S2-1-2** was prepared from **S1-7** using similar procedures to that of **S15-15-2**. A colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 2.3, 7.8 Hz, 2 H), 7.33-7.38 (m, 5 H), 7.25 (t, J = 7.8 Hz , 1 H), 7.05 (d, J = 7.8 Hz, 2 H), 5.10 (s, 2 H), 3.81 (s, 2 H), 3.43 (s, 3 H), 2.93 (s, 3 H), 2.34 (s, 3 H), 2.07 (s, 3 H), 1.45 (s, 6 H); MS (ESI) *m/z* 571.2 (M+H), calcd for $C_{29}H_{32}BrFN_2O_4$ 571.15.



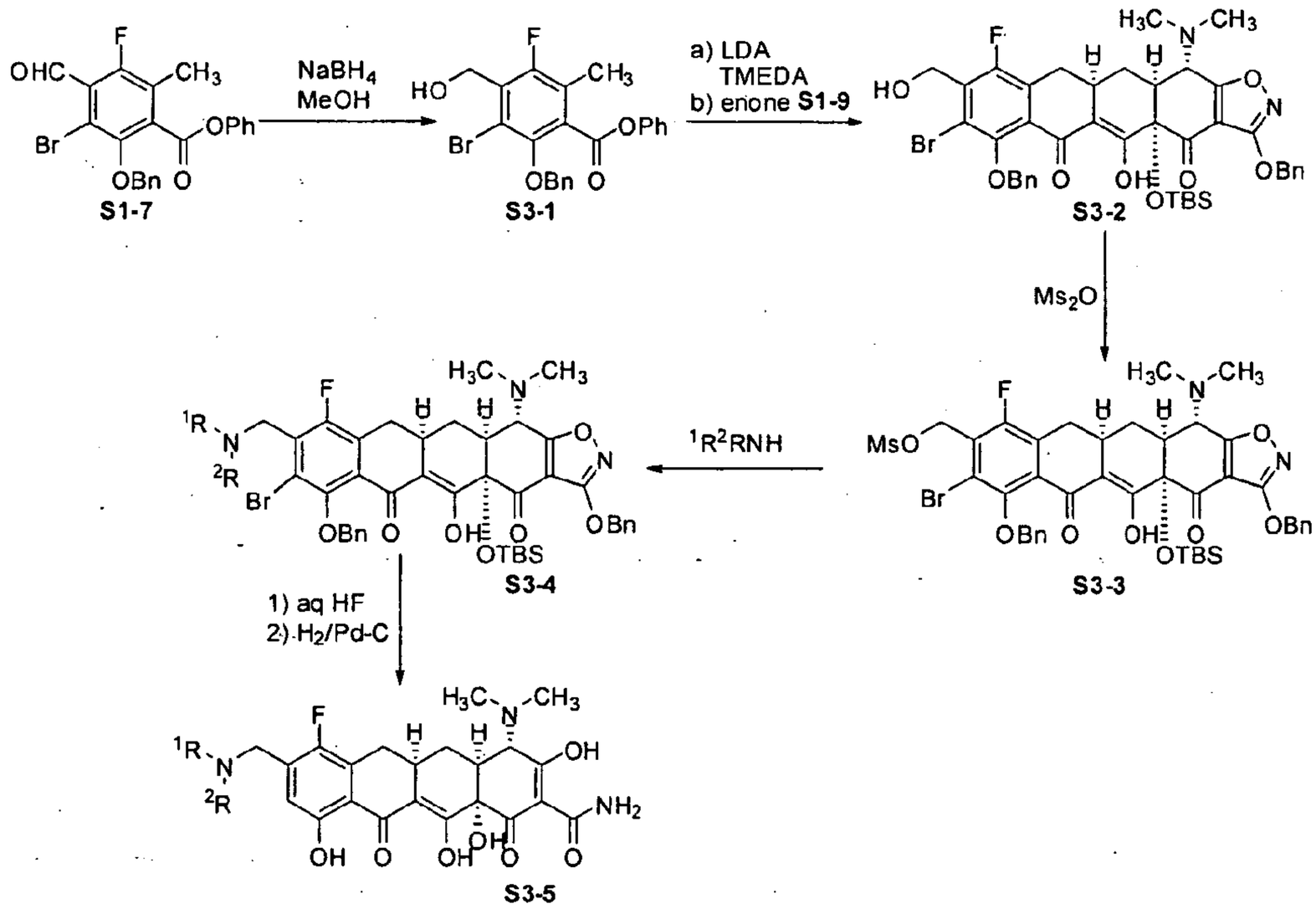
S2-4-69

Compound **S2-4-69** was prepared from **S2-1-2** using similar procedures to that of **S2-4-1**. The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 10→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 10.20-10.80 min, were collected and freeze-dried to give the desired product **S2-4-69** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ

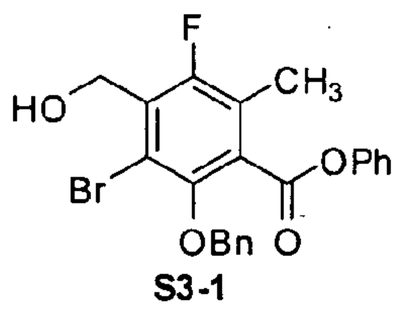
7.39 (d, J = 5.8 Hz, 1 H), 4.23 (d, J = 12.4 Hz, 1 H), 4.15 (d, J = 12.4 Hz, 1 H), 4.10 (s, 1 H), 2.97-3.16 (m, 15 H), 2.71 (s, 3 H), 2.35 (dd, J = 15.1 Hz, 1 H), 2.23-2.26 (m, 1 H), 1.86 (s, 3H), 1.66 (s, 3 H), 1.60-1.70 (m, 1 H); MS (ESI) *m/z* 589.5 (M+H), calcd for $C_{29}H_{38}FN_4O_8$ 589.26.

Example 3. Synthesis of Compounds via Scheme 3.

Scheme 3

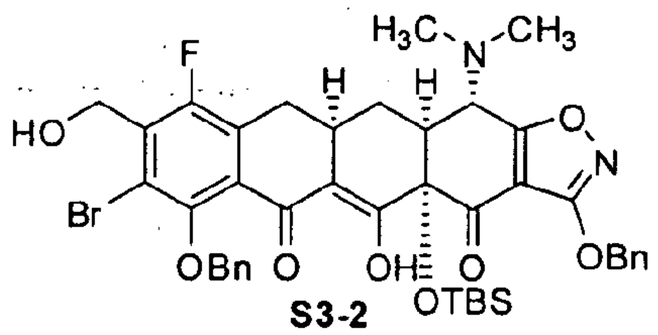


The following compounds were prepared according to Scheme 3.



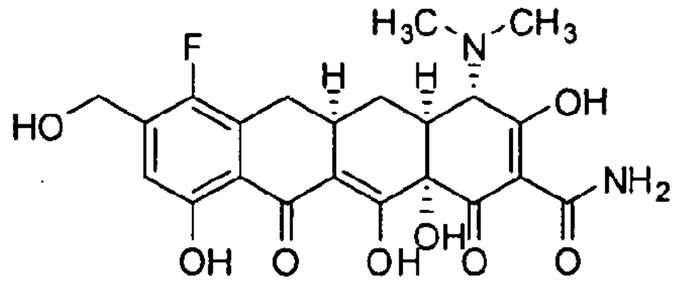
Compound **S1-7** (0.42 g, 0.94 mmol, 1.0 equiv) was dissolved in MeOH (5 mL). Sodium borohydride (76 mg, 2.00 mmol, 2.1 equiv) was added in several portions. During the addition, gas evolution was observed. After stirring at rt for 30 min, LC/MS indicated that the starting material was consumed. The reaction mixture was diluted with EtOAc, washed with water (2 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude

material was purified by column chromatography (Biotage 10 g column, 5% to 20% EtOAc in hexanes gradient), yielding 0.37 g (88%) of the desired compound **S3-1** as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1 H), 7.49 (dd, J = 7.8, 2.3 Hz, 2 H), 7.40-7.33 (m, 5 H), 7.25 (t, J = 7.8 Hz, 1 H), 7.07-7.02 (m, 2 H), 5.10 (s, 2 H), 4.91 (dd, J = 6.9, 2.3 Hz, 2 H), 2.35 (d, J = 2.3 Hz, 3 H).



S3-2

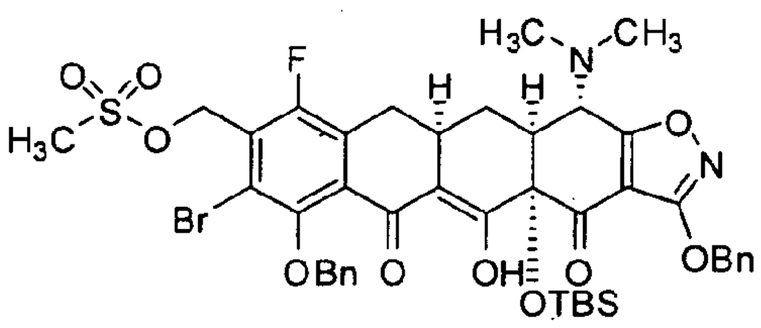
LDA was freshly prepared by adding *n*-BuLi (1.6 M/hexanes, 1.59 mmol, 3.0 equiv) to diisopropylamine (0.22 mL, 1.59 mmol, 3.0 equiv) in 10 mL dry THF under a nitrogen atmosphere in a flame dried schenck flask at -78 °C. The pale solution was warmed to -20 °C and stirred for 15 min. After the LDA solution was cooled down to -78 °C with a dry ice/acetone bath, TMEDA (0.24 mL, 1.59 mmol, 3.0 equiv) was added slowly *via* a syringe. Compound **S3-1** (0.28 g, 0.64 mmol, 1.2 equiv) in 2 mL dry THF was added to slowly *via* a syringe. A dark-red color appeared as soon as the addition started. After stirring at -78 °C for 10 min, enone **S1-9** (0.26 g, 0.53 mmol, 1.0 equiv) 2 mL dry THF was added slowly *via* a syringe. After 10 min, LC/MS indicated that the enone was consumed and the product present. The reaction mixture was allowed to slowly warm to -20 °C in 1 h. Phosphate buffer (pH 7, 10 mL) was added, followed by the addition of 20 mL saturated aqueous ammonium chloride. The resulting mixture was extract with dichloromethane (3 x 15 mL). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting orange-red oil was purified by column chromatography (Biotage 24 g column, 10% to 30% EtOAc in hexanes gradient) yielding 0.22 g of compound **S3-2** (50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.1 (br, s, 1 H), 7.58-7.54 (m, 2 H), 7.51-7.47 (m, 2 H), 7.41-7.32 (m, 6 H), 5.36 (s, 2 H), 4.95 (dd, J = 26.6, 9.6 Hz, 2 H), 4.89 (d, J = 7.8 Hz, 2 H), 3.92 (d, J = 10.6 Hz, 1 H), 3.25 (dd, J = 15.6, 4.1Hz, 1 H), 3.04-2.94 (m, 1 H), 2.59-2.53 (m, 1 H), 2.49 (s, 6 H), 2.40 (t, J = 15.6 Hz, 1 H), 2.20-2.10 (m, 2 H), 0.81 (s, 9 H), 0.26 (s, 3 H), 0.12 (s, 3 H).



S3-5-1

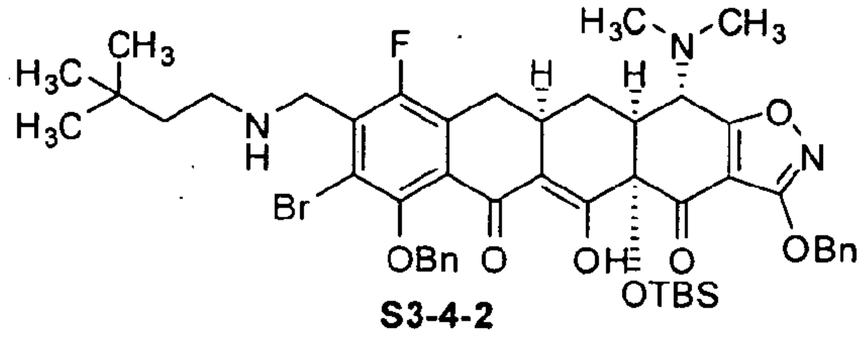
Aqueous HF (0.3 mL, 48-50%) solution was added to a CH_3CN solution (1.0 mL) of **S3-2** (5 mg, 0.06 mmol) in a plastic vial at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The reaction mixture was poured into an aqueous solution (10 mL) of K_2HPO_4 (2 g). The solution was extracted with EtOAc (3 x 15 mL). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give the crude intermediate.

Pd-C (5 mg, 10wt%) was added to a MeOH solution (2 mL) of the crude intermediate. HCl in MeOH (0.5 mL, 0.5 N) was added and the reaction was stirred under H_2 (balloon) at 25 °C for 2 hrs. The catalyst was filtered off with a pad of Celite. The filtrate was concentrated to afford the crude product, which was purified by HPLC on a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, sample in 2.0 mL (0.05 N HCl), gradient elution with 0→70% B over 15 min, mass-directed fraction collection], yielding 2 mg of the desired product **S3-5-1** as a yellow solid (54%, two steps): ^{1}H NMR (400 MHz, CD_3OD) δ 6.94 (d, J = 6.0 Hz, 1 H), 4.33 (s, 2 H), 4.12 (s, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 3.18-2.95 (m, 3 H), 2.27 (t, J = 16.4 Hz, 1 H), 2.24-2.17 (m, 1 H), 1.67-1.57 (m, 1 H); MS (ESI) *m/z* 463.37 (M+H).



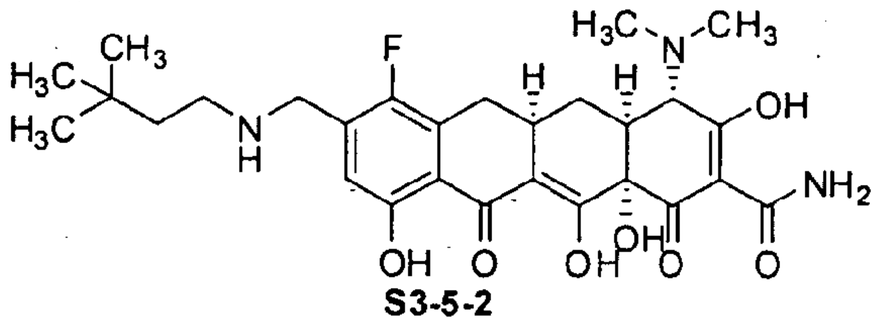
S3-3

Methanesulfonic anhydride (99 mg, 0.57 mmol, 3.0 equiv) was added to a solution of **S3-2** (0.16 g, 0.19 mmol, 1.0 equiv) in THF (4 mL). After 1 h, triethylamine (0.079 mL, 0.57 mmol, 3.0 equiv) was added. After 1 h, additional methanesulfonic anhydride (0.16 g, 0.95 mmol, 5.0 equiv) was added. After 1 h, the reaction mixture was used without concentration in subsequent reactions: MS (ESI) *m/z* 911.45, 913.44 (M+H).



S3-4-2

3,3-Dimethylbutylamine (0.063 mL, 0.47 mmol, 10 equiv) was added to a solution of **S3-3** in THF (1 mL, 0.047 mmol, 1.0 equiv). After 1 h, additional 3,3-dimethylbutylamine (0.13 mL, 0.95 mmol, 20 equiv) was added. After 30 minutes, the reaction mixture was concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 20→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.2-9.0 min, were collected and freeze-dried to yield 10 mg (22%) of compound **S3-4-2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.10-15.79 (br s, 1 H), 7.60-7.45 (m, 4 H), 7.43-7.28 (m, 6 H), 5.35 (s, 2 H), 5.04-4.84 (m, 2 H), 3.90 (d, *J* = 11.0 Hz, 1 H), 3.32-3.19 (m, 1 H), 3.06-2.93 (m, 1 H), 2.86-2.76 (m, 1 H), 2.60-2.34 (m, 10 H), 2.18-2.10 (m, 1 H), 1.70-1.58 (m, 4 H), 0.99-0.76 (m, 18 H), 0.26 (s, 3 H), 0.11 (s, 3 H); MS (ESI) *m/z* 916.54, 918.49 (M+H).



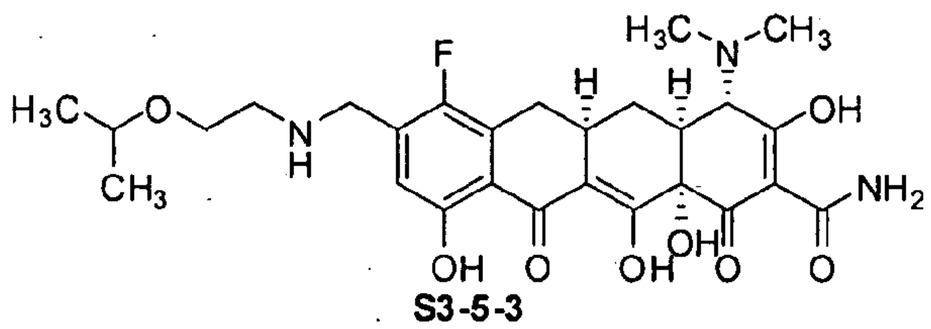
S3-5-2

A solution of compound **S3-4-2** (10 mg, 0.011 mmol) in 1,4-dioxane (0.80 mL) was treated with HF (0.40 mL, 48-50% aqueous solution). After stirring overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL). This mixture was extracted with EtOAc (3 times). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield the crude intermediate.

The above crude intermediate was dissolved in MeOH (1 mL), 1,4-dioxane (1 mL), and 0.5 N HCl/MeOH (0.4 mL). 10% Pd-C (Degussa, 2 mg) was added, and

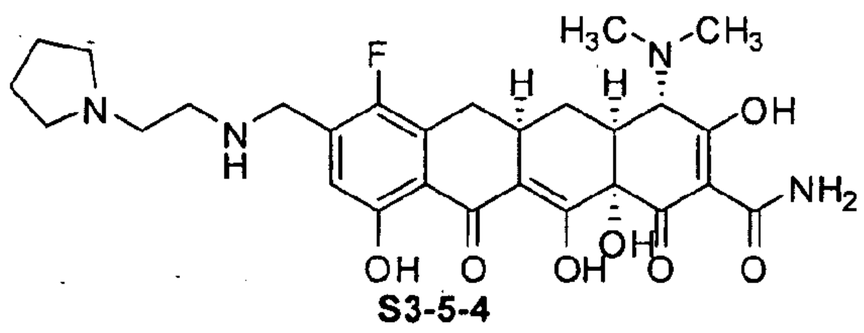
an atmosphere of hydrogen was introduced. After 2 hrs, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.2-9.6 min, were collected and freeze-dried to yield 5 mg (69%) of compound **S3-5-2**: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.08 (d, J = 5.48 Hz, 1 H), 4.29 (s, 2 H), 4.16 (s, 1 H), 3.34-2.96 (m, 11 H), 2.36-2.25 (m, 2 H), 1.71-1.58 (m, 3 H), 0.97 (s, 9 H); MS (ESI) *m/z* 546.32 (M+H).

The following compounds were prepared according to the methods of **S3-5-2**, substituting the appropriate amine for 3,3-dimethylbutylamine:



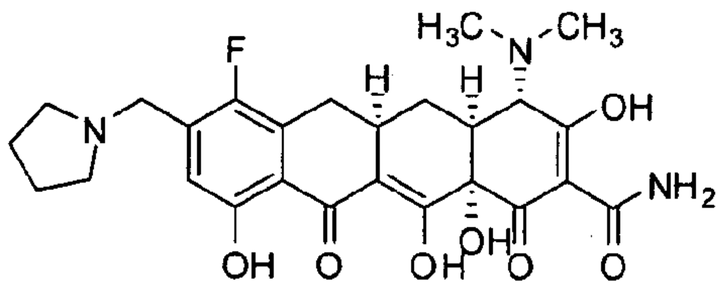
S3-5-3

S3-5-3: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.07 (d, J = 5.96 Hz, 1 H), 4.32 (s, 2 H), 4.17 (s, 1 H), 3.80-3.65 (m, 3 H), 3.36-2.96 (m, 11 H), 2.38-2.25 (m, 2 H), 1.62 (dd, J = 14.0, 11.4 Hz, 1 H), 1.18 (d, J = 6.4 Hz, 6 H); MS (ESI) *m/z* 548.30 (M+H).



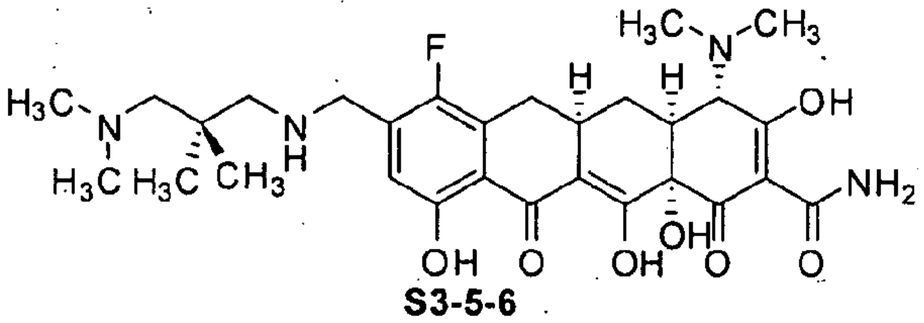
S3-5-4

S3-5-4: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 6.55 (d, J = 5.60 Hz, 0.45 H), 6.45 (d, J = 5.52 Hz, 0.55 H), 4.78 (s, 1.1 H), 4.67 (s, 0.9 H), 4.15 (s, 1 H), 3.40-2.96 (m, 16 H), 2.32-2.20 (m, 4 H), 2.10 (s, 2 H), 1.62 (m, 1 H), 1.02 (s, 4 H); MS (ESI) *m/z* 559.33 (M+H).



S3-5-5

S3-5-5: ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (d, J = 6.0 Hz, 1 H), 4.46 (s, 2 H), 4.09 (s, 1 H), 3.04 (s, 3 H), 2.97 (s, 3 H), 3.27-2.97 (m, 3 H), 2.37 (m, 1 H), 2.28-2.14 (m, 3 H), 2.08-2.00 (m, 2 H), 1.72-1.62 (m, 1 H); MS (ESI) *m/z* 516.40 (M+H).

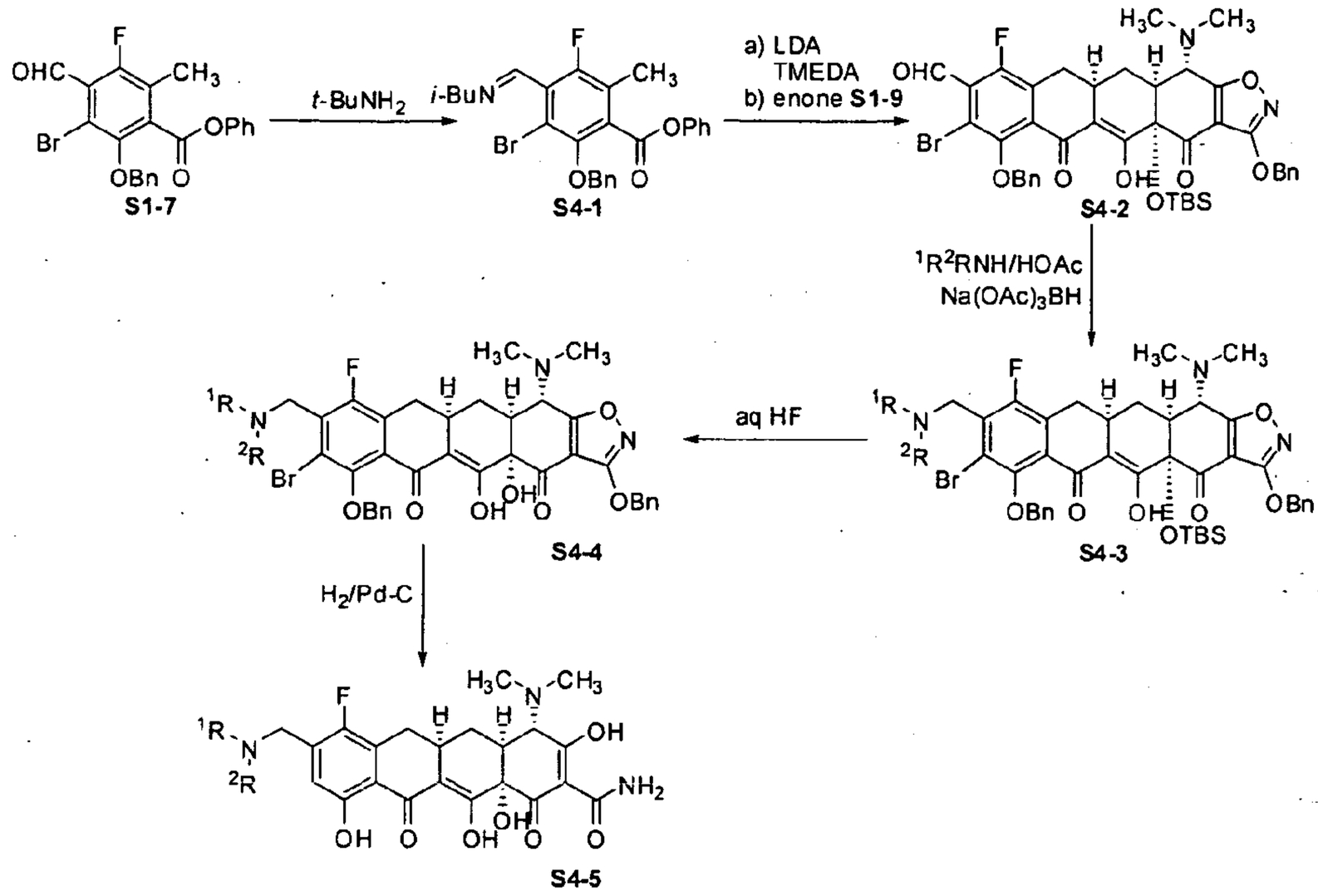


S3-5-6

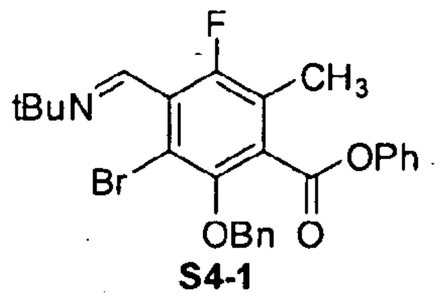
S3-5-6: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.22 (d, J = 5.96 Hz, 1 H), 4.39 (s, 2 H), 4.17 (s, 1 H), 3.40 (s, 2 H), 3.26-2.90 (m, 17 H), 2.40-2.25 (m, 2 H), 1.70-1.57 (m, 1 H), 1.32 (s, 6 H); MS (ESI) *m/z* 575.37 (M+H).

Example 4. Synthesis of Compounds via Scheme 4.

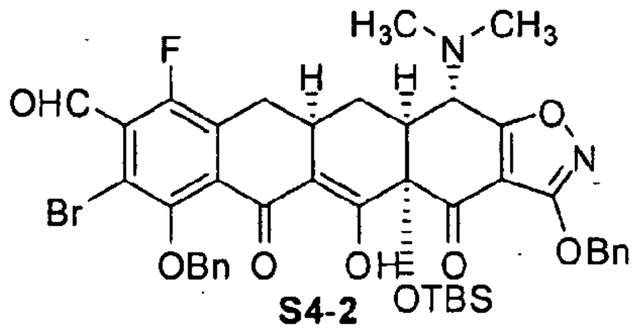
Scheme 4



The following compounds were prepared according to Scheme 4.

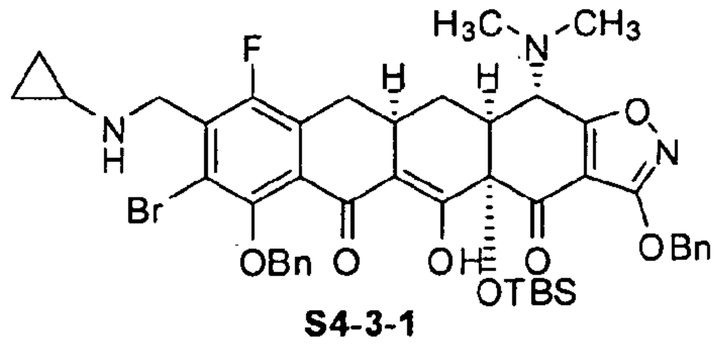


Compound **S1-7** (0.50 g, 1.14 mmol, 1.0 equiv) and *t*-butylamine (0.60 mL, 5.68 mmol, 5.0 equiv) were stirred at rt in toluene (5 mL) overnight. The reaction mixture was concentrated under reduced pressure. ^{1}H NMR indicated a 4:1 mixture of **S4-1**:**S1-7**. The material was redissolved in toluene (5 mL). *t*-Butylamine (0.60 mL, 5.68 mmol, 5.0 equiv) and 4Å molecular sieves (0.50 g) were added. After stirring at rt overnight, the reaction mixture was filtered through Celite and concentrated to give crude **S4-1** (with ~10% **S1-7**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1 H), 7.38 (d, J = 6.0 Hz, 2 H), 7.45-7.32 (m, 5 H), 7.31-7.14 (m, 3 H), 5.11 (s, 2 H), 2.35 (s, 3 H), 1.38 (s, 9 H).



S4-2

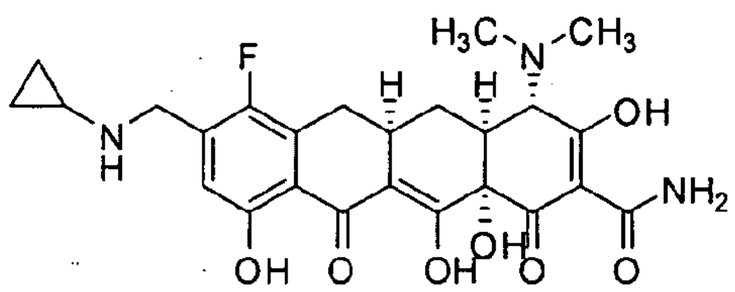
A solution of **S4-1** (0.56 g, 1.13 mmol, 1.2 equiv) in THF (5 mL) was added to a solution of LHMDS (1.4 mL, 1.0 M/THF, 1.40 mmol, 1.5 equiv) and TMEDA (1.02 mL, 6.78 mmol, 6.0 equiv) in THF (10 mL) at -78 °C. No color change was observed. Additional LDA (1.22 mL, 1.2 M/THF, 1.47 mmol, 1.3 equiv) was added dropwise, immediately producing a red colored solution. The reaction was stirred at -78 °C for 5 min. A solution of enone **S1--9** (0.45 g, 0.94 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to the reaction mixture. The reaction was stirred from -78 °C to -20 °C for 1 h, quenched by saturated aqueous NH_4Cl, and extracted with EtOAc. The combined EtOAc extracts were dried (sodium sulfate) and concentrated to yield the crude product, which was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 µm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 90→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 5.8-7.4 min, were collected and concentrated under reduced pressure to give 0.23 g (29%) of pure **S4-2** (The imine hydrolyzed to the aldehyde on concentration): ^1H NMR (400 MHz, $CDCl_3$) δ 15.79 (s, 1 H), 10.33 (s, 1 H), 7.60-7.45 (m, 4 H), 7.45-7.30 (m, 6 H), 5.28 (s, 2 H), 4.98 (q, J = 9.2 Hz, 2 H), 3.89 (d, J = 10.4 Hz, 1 H), 3.30-3.22 (m, 1 H), 3.08-2.95 (m, 1 H), 2.62-2.57 (m, 1 H), 2.52-2.32 (m, 8 H), 2.20-2.12 (m, 1 H), 0.81 (s, 9 H), 0.26 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 831.56, 833.55 (M+H).



S4-3-1

Cyclopropylamine (0.030 mL, 0.42 mmol, 7.0 equiv) was added to a solution of **S4-2** (50 mg, 0.060 mmol, 1.0 equiv) and acetic acid (0.024 mL, 0.42 mmol, 7.0 equiv) in dichloromethane (1 mL). After 30 min., sodium triacetoxyborohydride (64

mg, 0.30 mmol, 5.0 equiv) was added. After an additional 3 hrs, the mixture was quenched by $NaHCO_3$ (saturated, aqueous solution) and pH 7 phosphate buffer. The mixture was extracted with dichloromethane, and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 20→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.6-10.4 min, were collected and freeze-dried to yield 8 mg of compound **S4-3-1** (16%, ~90% pure by ^1H NMR): ^1H NMR (400 MHz, $CDCl_3$) δ 16.00-15.79 (br s, 1 H), 7.60-7.45 (m, 4 H), 7.43-7.26 (m, 6 H), 4.97 (q, J = 9.4 Hz, 2 H), 4.37 (br s, 2 H), 3.90 (d, J = 10.4 Hz, 1 H), 3.30-3.22 (m, 1 H), 3.08-2.95 (m, 1 H), 2.62-2.27 (m, 12 H), 2.18-2.10 (m, 1 H), 0.88-0.74 (m, 11 H), 0.70-0.62 (m, 2 H), 0.26 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 872.43, 874.41 (M+H).



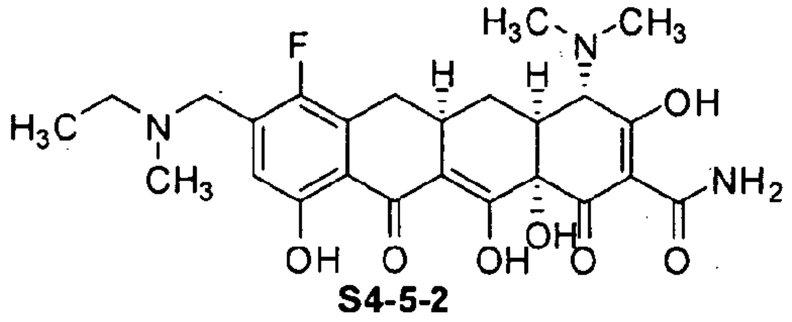
S4-5-1

A solution of compound **S4-3-1** (8 mg, 0.0094 mmol) in 1,4-dioxane (1 mL) was treated with HF (0.40 mL, 48-50% aqueous solution). After stirring at rt overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL). This mixture was extracted with EtOAc (3 times), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield the crude product.

The above crude product was dissolved in MeOH (1 mL), 1,4-dioxane (1 mL), and 0.5 N HCl/MeOH (0.5 mL). 10% Pd-C (Degussa, 2 mg) was added, and an atmosphere of hydrogen was introduced. After 2 hrs, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10

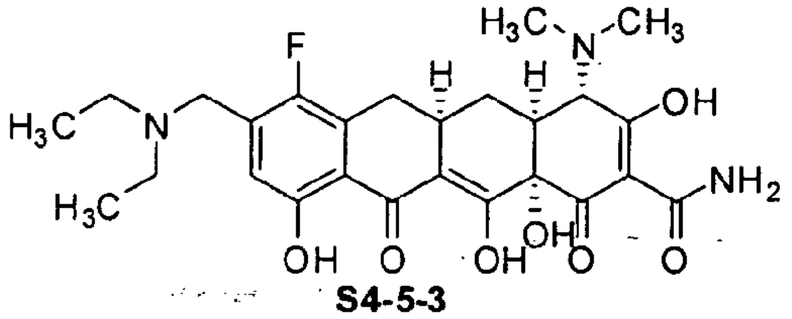
min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.8-7.6 min, were collected and freeze-dried to yield 3 mg (56%) of compound **S4-5-1**: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.08 (d, J = 5.96 Hz, 1 H), 4.38 (s, 2 H), 4.18 (s, 1 H), 3.34-2.96 (m, 9 H), 2.86-2.79 (m, 1 H), 2.36-2.25 (m, 2 H), 1.62 (dd, J = 14.0, 11.0 Hz, 1 H), 1.02-0.86 (m, 4 H); MS (ESI) *m/z* 502.22 (M+H).

The following compounds were prepared according to the methods of **S4-5-1**, substituting the appropriate amines for cyclopropylamine.



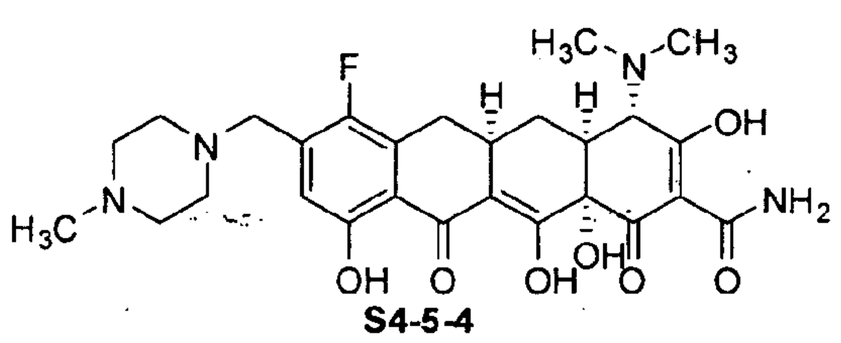
S4-5-2

S4-5-2: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.11 (d, J = 5.48 Hz, 1 H), 4.51 (dd, J = 13.3, 6.4 Hz, 1 H), 4.31 (dd, J = 13.3, 6.4 Hz, 1 H), 4.16 (s, 1 H), 3.42-3.10 (m, 4 H), 3.10-2.97 (m, 7 H), 2.85 (s, 3 H), 2.39-2.25 (m, 2 H), 1.62 (dd, J = 14.0, 11.0 Hz, 1 H), 1.41 (t, J = 7.3 Hz, 3 H); MS (ESI) *m/z* 504.22 (M+H).



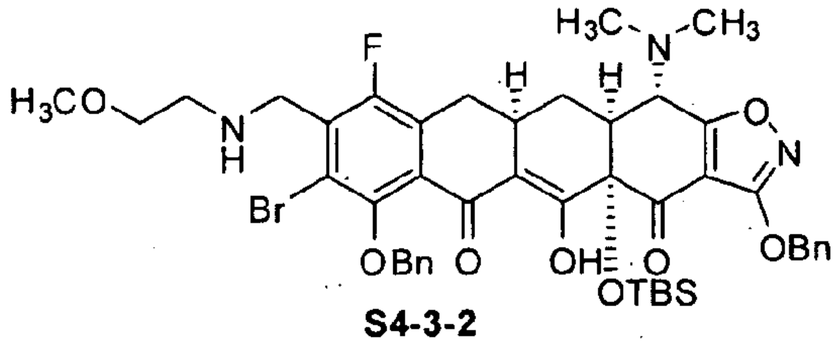
S4-5-3

S4-5-3: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.10 (d, J = 5.96 Hz, 1 H), 4.23 (s, 2 H), 4.17 (s, 1 H), 3.35-2.96 (m, 13 H), 2.40-2.25 (m, 2 H), 1.63 (dd, J = 14.0, 11.0 Hz, 1 H), 1.39 (t, J = 7.1 Hz, 6 H); MS (ESI) *m/z* 518.24 (M+H).



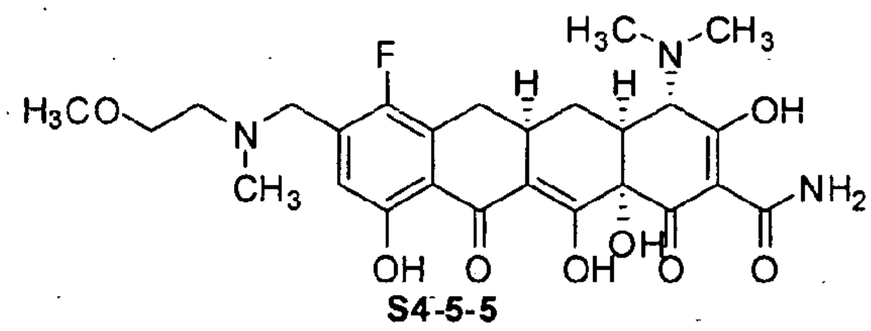
S4-5-4

S4-5-4: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.22 (d, J = 5.48 Hz, 1 H), 4.60 (s, 2 H), 4.16 (s, 1 H), 3.98-3.60 (br m, 8 H), 3.24-2.94 (m, 12 H), 2.40-2.24 (m, 2 H), 1.64 (dd, J = 14.0, 11.0 Hz, 1 H); MS (ESI) *m/z* 545.26 (M+H).



S4-3-2

Prepared according to the method of compound **S4-3-1** above, substituting 2-methoxyethylamine for cyclopropylamine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.00-15.79 (br s, 1 H), 7.58-7.45 (m, 4 H), 7.42-7.30 (m, 6 H), 5.36 (s, 2 H), 5.02-4.88 (m, 2 H), 4.35-4.20 (m, 2 H), 3.95-3.88 (m, 1 H), 3.75-58 (m, 2 H), 3.35 (s, 3 H), 3.30-3.19 (m, 1 H), 3.08-2.95 (br m, 3 H), 2.62-2.36 (m, 9 H), 2.18-2.10 (m, 1 H), 0.81 (s, 9 H), 0.26 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 890.55, 892.53 (M+H).



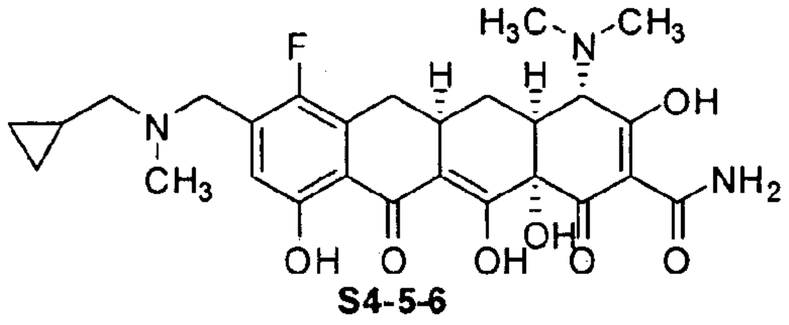
S4-5-5

Formaldehyde (37% aqueous solution, 0.0092 mL, 0.12 mmol, 5.0 equiv) was added to a solution of compound **S4-3-2** (22 mg, 0.025 mmol) in dichloromethane (1 mL) and HOAc (0.0071 mL, 0.12 mmol, 5.0 equiv). After 30 minutes, $Na(OAc)_3BH$ (16 mg, 0.074 mmol, 3.0 equiv) was added. After 2 hrs, the mixture was quenched by $NaHCO_3$ (saturated, aqueous solution) and pH 7 phosphate buffer. This mixture was extracted with dichloromethane, and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure.

The above crude intermediate was dissolved in 1,4-dioxane (0.80 mL) and treated with HF (0.40 mL, 48-50% aqueous solution) at rt. After stirring overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL) and extracted with EtOAc (3 times). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure.

The above crude intermediate was dissolved in MeOH (1 mL), 1,4-dioxane (1 mL), and 0.5 N HCl/MeOH (0.5 mL). 10% Pd-C (Degussa, 2 mg) was added, and an atmosphere of hydrogen was introduced. After 2 hrs, the reaction mixture was filtered through Celite and concentrated under reduced pressure to afford the crude

product, which was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.5-7.6 min, were collected and freeze-dried to yield 11 mg of compound **S4-5-5** (75%, 3 steps): ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.10 (d, J = 5.52 Hz, 1 H), 4.59 (dd, J = 13.3, 7.8 Hz, 1 H), 4.34 (dd, J = 13.3, 7.8 Hz, 1 H), 4.17 (s, 1 H), 3.84-3.72 (m, 2 H), 3.54-3.35 (m, 5 H), 3.34-2.96 (m, 9 H), 2.91 (s, 3 H), 2.38-2.25 (m, 2 H), 1.70-1.55 (m, 1 H); MS (ESI) *m/z* 534.25 (M+H).

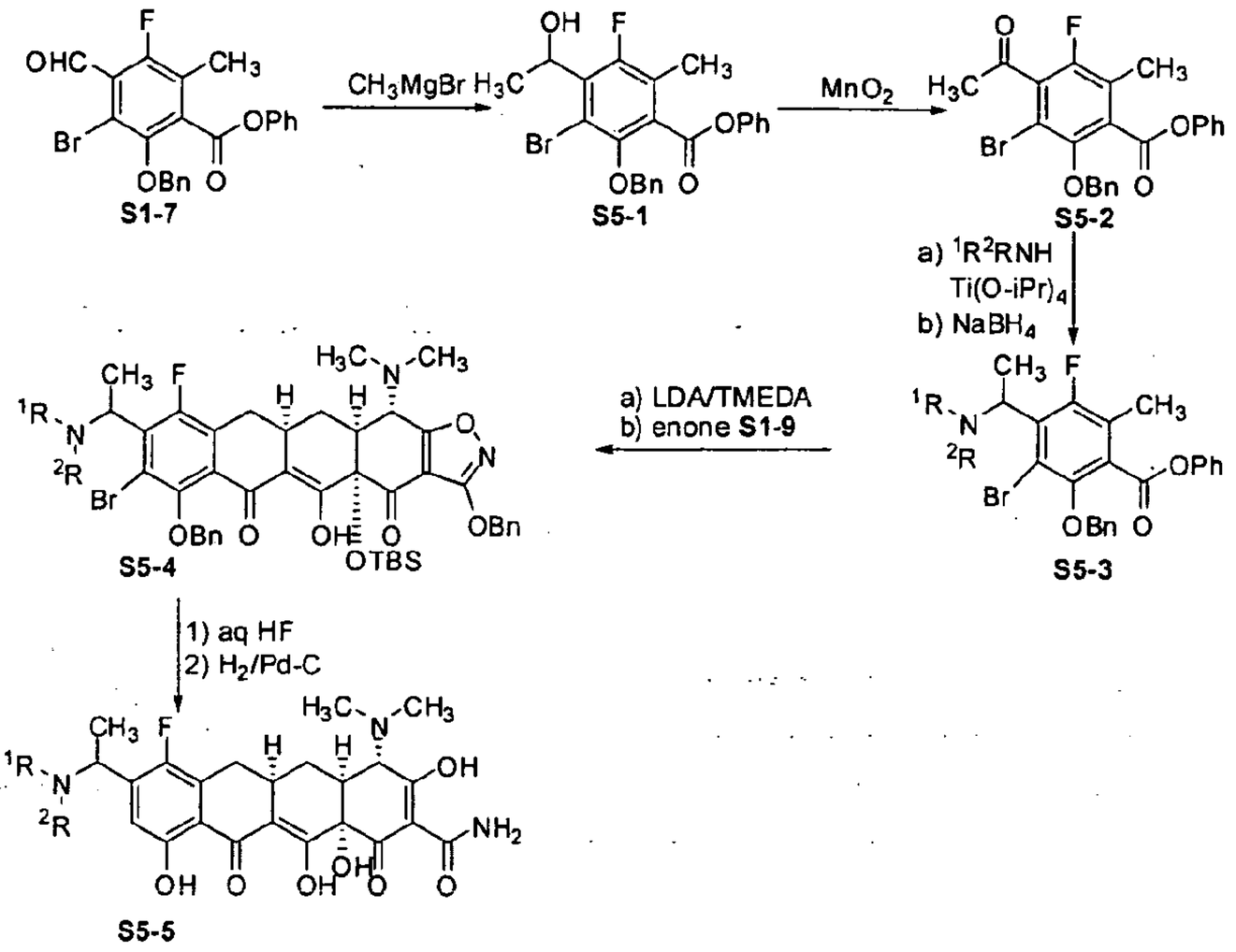


S4-5-6

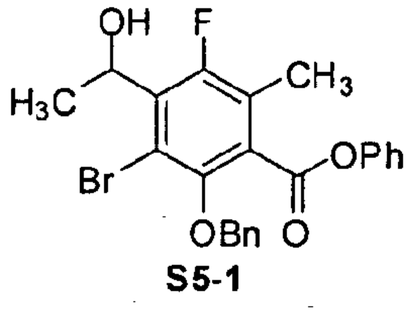
Prepared according to the methods of **S4-5-5**, substituting cyclopropanemethylamine for 2-methoxyethylamine: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.12 (d, J = 5.52 Hz, 1 H), 4.62 (dd, J = 13.3, 7.8 Hz, 1 H), 4.32 (dd, J = 13.3, 7.8 Hz, 1 H), 4.16 (s, 1 H), 3.35-2.96 (m, 11 H), 2.90 (s, 3 H), 2.40-2.26 (m, 2 H), 1.63 (dd, J = 14.0, 11.4 Hz, 1 H), 1.30-1.17 (m, 1 H), 0.86-0.74 (m, 2 H), 0.56-0.43 (m, 2 H); MS (ESI) *m/z* 530.25 (M+H).

Example 5. Synthesis of Compounds via Scheme 5.

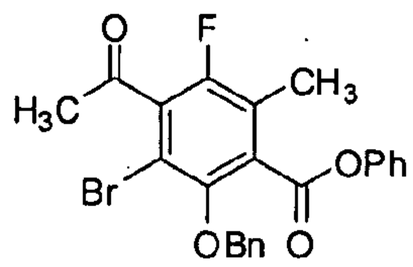
Scheme 5



The following compounds were prepared according to Scheme 5.

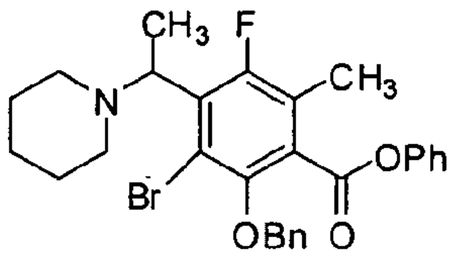


Methylmagnesium bromide (0.51 mL, 3.0 M/Et_2O, 1.53 mmol, 1.0 equiv) was added to a solution of compound **S1-7** (0.67 g, 1.52 mmol, 1.0 equiv) in THF (8 mL) at -78 °C. After 30 minutes, the reaction mixture was quenched by NH_4Cl (saturated, aqueous solution) and extracted with EtOAc. The extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The material was purified by column chromatography on silica (Biotage 10 g prepacked column, 0% to 25% EtOAc in hexanes gradient), yielding 0.50 g (72%) of compound **S5-1**: R_f 0.35 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 2 H), 7.40-7.32 (m, 5 H), 7.28-7.20 (m, 1 H), 7.08-7.00 (m, 2 H), 5.41 (q, *J* = 6.9 Hz, 1 H), 5.09 (s, 2 H), 2.34 (s, 1 H), 1.63 (d, *J* = 6.9 Hz, 3 H); MS (ESI) *m/z* 481.14, 483.1 (M+Na).



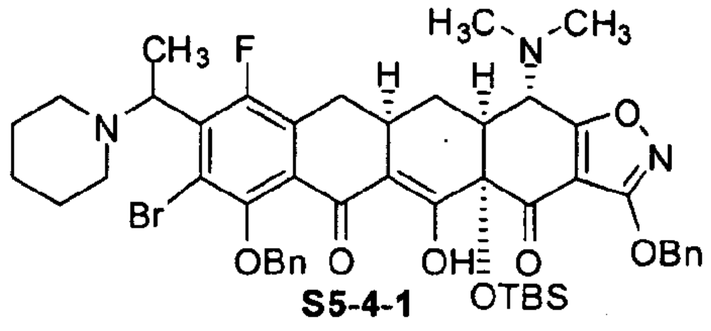
S5-2

Manganese dioxide (activated, 0.20 g, 2.07 mmol, 5.0 equiv) was added to a solution of compound **S5-1** (0.19 g, 0.41 mmol, 1.0 equiv) in dichloromethane (5 mL). After stirring overnight, the reaction was ~30% complete. Additional manganese dioxide (activated, 0.20 g, 2.07 mmol, 5.0 equiv) was added. After stirring overnight, the reaction mixture was diluted with EtOAc (20 mL) and filtered through Celite. The filtrate was concentrated under reduced pressure, yielding 0.16 g (83%) of compound **S5-2**: R_f 0.24 (10% EtOAc/hexanes); MS (ESI) *m/z* 479.10, 481.10 (M+Na).



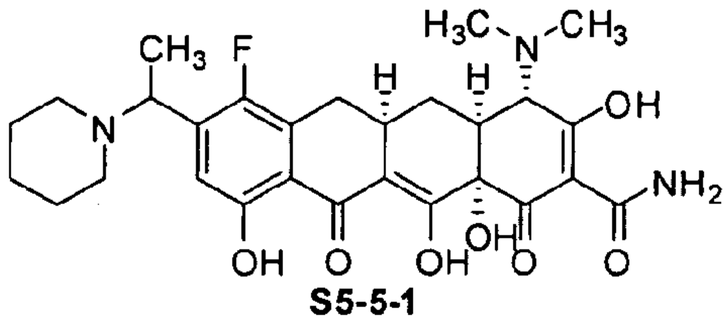
S5-3-1

Compound **S5-2** (55 mg, 0.12 mmol, 1.0 equiv), piperidine (0.059 mL, 0.60 mmol, 5.0 equiv), and titanium(IV) isopropoxide (0.18 mL, 0.60 mmol, 5.0 equiv) were stirred in dichloromethane (0.20 mL) overnight. Additional piperidine (0.20 mL, 2.00 mmol, 1.7 equiv) and titanium(IV) isopropoxide (0.20 mL, 0.67 mmol, 5.6 equiv) were added, and the reaction mixture was heated to 50 °C overnight. The reaction mixture was diluted with MeOH (2 mL) and $NaBH_4$ (15 mg, 0.40 mmol, 3.3 equiv) was added. Additional $NaBH_4$ (10 mg portions, 0.26 mmol, 2.2 equiv) was added every 30 minutes for 4 hrs, resulting in ~75% conversion. More MeOH (10 mL) and $NaBH_4$ (0.10 g, 2.64 mmol, 22 equiv) were added. After bubbling ceased, the reaction mixture was concentrated under reduced pressure. The resulting solids were dissolved in EtOAc, washed with $NaHCO_3$ (saturated, aqueous solution, 3 times) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure, yielding 55 mg (87% crude) of compound **S5-3-1**. The material was concentrated from toluene (2 times) and used without further purification: R_f 0.35 (30% EtOAc/hexanes; MS (ESI) *m/z* 526.18, 528.17 (M+H).



S5-4-1

n-Butyllithium (0.074 mL, 2.5 M/hexanes, 0.18 mmol, 2.25 equiv) was added to diisopropylamine (0.026 mL, 0.18 mmol, 2.25 equiv) in THF (2 mL) at -40 °C. The reaction mixture was cooled to -78 °C, and TMEDA (0.072 mL, 0.48 mmol, 6.0 equiv) was added. A solution of compound **S5-3-1** (55 mg, 0.10 mmol, 1.25 equiv) in THF (1 mL) was added dropwise. The reaction was stirred at -78 °C for 5 min. A solution of enone **S1-9** (39 mg, 0.080 mmol, 1.0 equiv) in THF (0.5 mL) was added dropwise to the reaction mixture. Additional LDA (20.050 mL, 2.0 M/heptane/THF/ethylbenzene, 0.10 mmol, 1.25 equiv) was added. The reaction was stirred from -78 °C to -20 °C for 45 minutes, quenched by saturated aqueous NH_4Cl, and extracted with EtOAc (2 times). The combined EtOAc extracts were dried (sodium sulfate) and concentrated to yield the crude product, which was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 20→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 7.2-8.6 min, were collected and freeze-dried to give 26 mg of compound **S5-4-1** (36%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.0-15.9 (m, 1 H), 7.58-7.45 (m, 4 H), 7.40-7.28 (m, 6 H), 5.35 (s, 2 H), 5.03-4.89 (m, 2 H), 4.52-4.34 (br s, 1 H), 3.92 (d, J = 10.4 Hz, 1 H), 3.29-3.19 (m, 1 H), 3.06-2.93 (m, 1 H), 2.78-2.58 (m, 1 H), 2.58-2.34 (m, 11 H), 2.22-1.76 (br m, 2 H), 1.72-1.36 (br m, 9 H), 0.88-0.76 (m, 9 H), 0.26 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 914.30, 916.32 (M+H).



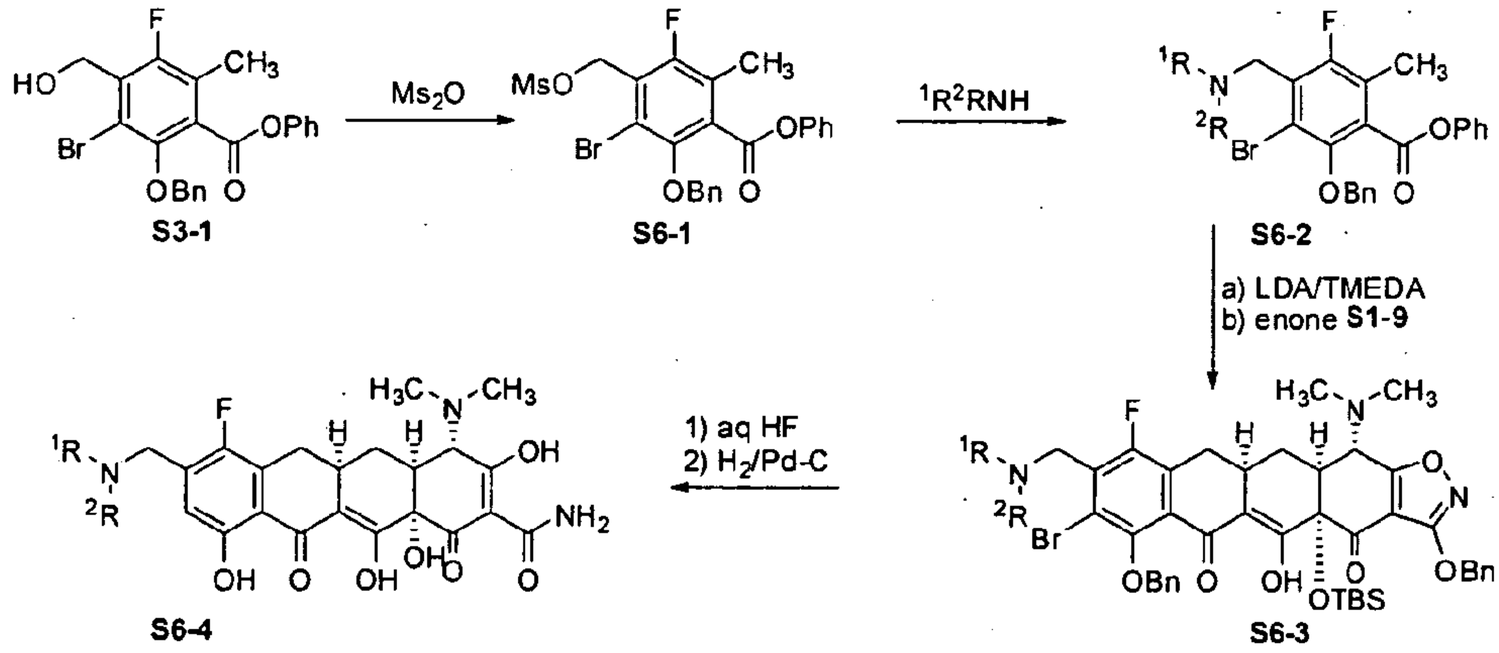
S5-5-1

A solution of compound **S5-4-1** (26 mg, 0.028 mmol) in 1,4-dioxane (1 mL) was treated with HF (0.40 mL, 48-50% aqueous solution). After stirring overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL). This mixture was extracted with EtOAc (3 times). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure.

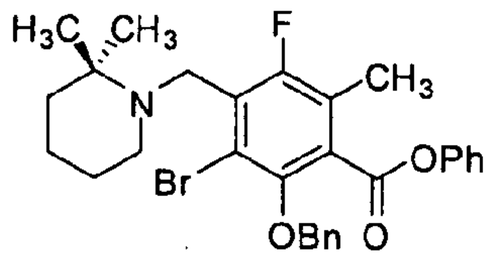
The above material was dissolved in MeOH (2 mL), 1,4-dioxane (2 mL), and 0.5 N HCl/MeOH (0.5 mL). 10% Pd-C (Degussa, 5 mg) was added, and an atmosphere of hydrogen was introduced. After 2 hrs, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.8-8.2 min, were collected and freeze-dried to yield 12 mg (68%) of compound **S5-5-1**: ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 7.17 (d, J = 5.0 Hz, 1 H), 4.80-4.68 (m, 1 H), 4.15 (s, 1 H), 3.80-3.72 (m, 1 H), 3.42-3.30 (m, 1 H), 3.26-2.78 (m, 11 H), 2.40-2.25 (m, 2 H), 2.05-1.71 (m, 8 H), 1.70-1.40 (m, 2 H); MS (ESI) *m/z* 544.15 (M+H).

Example 6. Synthesis of Compounds via Scheme 6.

Scheme 6



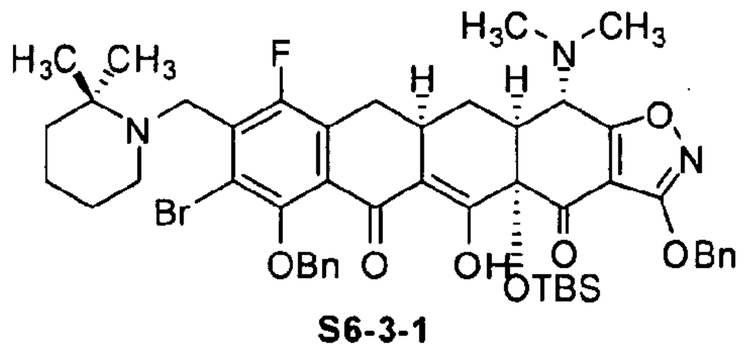
The following compounds were prepared according to Scheme 6.



S6-2-1

Compound **S3-1** (0.36 g, 0.81 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (15 mL) with triethylamine (0.57 mL, 4.07 mmol, 5.0 equiv). Methanesulfonic anhydride (0.71 g, 4.07 mmol, 5.0 equiv) was added in one portion at 0 °C. During the addition, color change was observed. After stirring at rt for one hour, LC/MS indicated that the starting material was consumed. The reaction mixture was diluted with dichloromethane, quenched by pH 7 phosphate buffer, washed with water (2 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude intermediate was used without further purification.

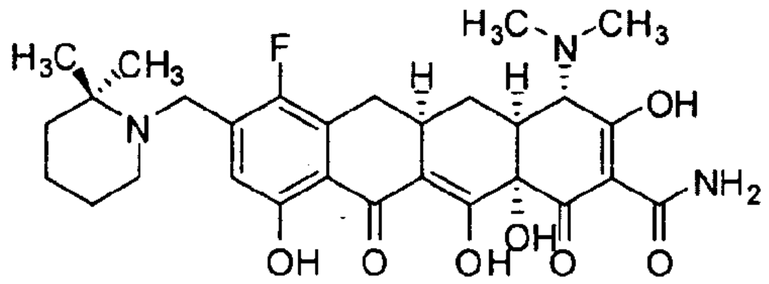
The above crude intermediate (0.16 g, 0.30 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (2 mL) with diisopropylethylamine (0.13 mL, 0.72 mmol, 2.4 equiv). 2,2-Dimethyl piperidine hydrochloric salt (54 mg, 0.36 mmol, 1.2 equiv) was first neutralized with sodium hydroxide solution and then was added to reaction mixture in one portion at rt. After stirring at 60 °C for four days, LC/MS indicated that most of the starting material was consumed. The reaction mixture was diluted with dichloromethane, washed with water (2 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford the desired product **S6-2-1**, which was used without further purification.



S6-3-1

A solution of LDA was prepared by adding *n*-BuLi (0.31 mL, 1.6 M/hexanes, 0.50 mmol, 2.5 equiv) to diisopropylamine (71 µL, 0.50 mmol, 2.5 equiv) in 2 mL dry THF under a nitrogen atmosphere in a flame dried schenck flask at -78 °C. The pale solution was warmed to -20 °C, stirred for 15 min, and cooled down to -78 °C. TMEDA (75 µL, 0.50 mmol, 2.5 equiv) was added slowly *via* a

syringe, followed by the dropwise addition of compound **S6-2-1** (crude, 0.30 mmol, 1.5 equiv)/THF (1 mL). A dark-red color appeared as soon as addition started. After stirring for 10 min, enone **S1-9** (96 mg, 0.20 mmol, 1.0 equiv) in 1 mL dry THF was added slowly *via* a syringe. After 10 min, LC/MS indicated that the enone was consumed and the product present. The reaction mixture was allowed to slowly warm to -20 °C in 1 h. Phosphate buffer (pH 7, 10 mL) and saturated aqueous ammonium chloride (20 mL) were added. The resulting mixture was extracted with dichloromethane (3 x 15 mL), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield crude **S6-3-1** as a red-orange oil (97 mg).



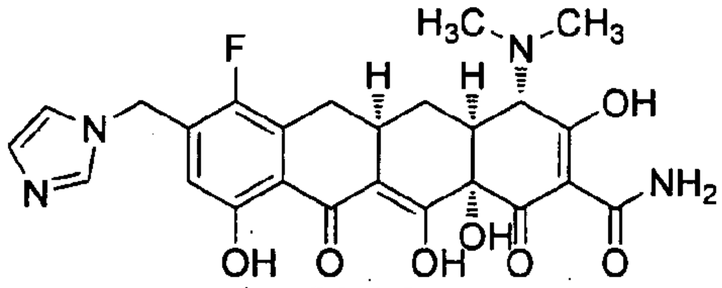
S6-4-1

Aqueous HF (0.3 mL, 48-50%) was added to a CH_3CN solution (1.0 mL) of **S6-3-1** (97 mg) in a plastic vial at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The reaction mixture was poured into an aqueous solution (10 mL) of K_2HPO_4 (2 g). The solution was extracted with EtOAc (3 x 15 mL). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give the crude intermediate (18 mg).

Pd-C (5 mg, 10wt%) was added to a MeOH solution (2 mL) of the above crude intermediate. HCl in MeOH (0.5 N, 0.5 mL) was added. The reaction was stirred under H_2 (balloon) at 25 °C for 2 hrs and filtered through a pad of Celite. The filtrate was concentrated, and the crude product was purified by HPLC on a Polymerx 10 μ RP-γ100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, sample in 2.0 mL (0.05 N HCl), gradient elution with 0→70% B over 15 min, mass-directed fraction collection]. Fractions containing the desired product were collected and freeze-dried, yielding 9 mg of the desired product **S6-4-1** as a yellow solid (5%, five steps): ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (d, J = 5.5 Hz, 1 H), 4.75 (dd, J = 13.7, 7.3 Hz, 1 H), 4.08 (s, 1 H), 3.92 (dd, J = 13.7, 7.3 Hz, 1 H), 3.32 (m, 2 H), 3.24-2.98 (m, 3 H), 3.03 (s, 3 H), 2.96 (s, 3 H),

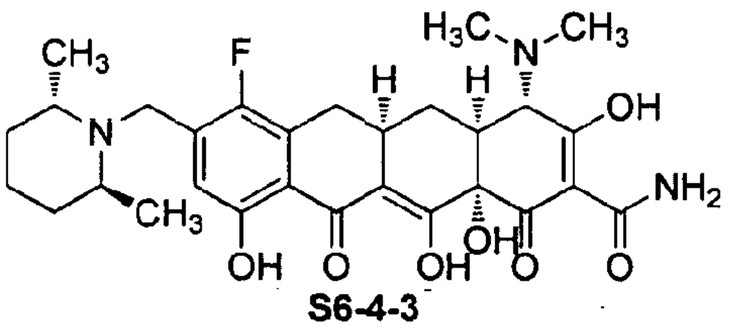
2.37 (t, J = 15.1 Hz, 1 H), 2.27-2.20 (m, 1 H), 1.91-1.82 (m, 2 H), 1.80-1.63 (m, 5 H), 1.63 (s, 3 H), 1.50 (s, 3 H); MS (ESI) *m/z* 558.30 (M+H).

The following compounds were prepared similarly to **S6-4-1.**



S6-4-2

^{1}H NMR (400 MHz, CD_3OD) δ 9.11 (s, 1 H), 7.68 (m, 1 H), 7.62 (m, 1 H), 6.86 (d, J = 5.9 Hz, 1 H), 5.54 (s, 2 H), 4.07 (s, 1 H), 3.22-2.93 (m, 9 H), 2.37 -2.27 (m, 1 H), 2.24-2.17 (m, 1 H), 1.70 -1.57 (m, 1 H); MS (ESI) *m/z* 513.17 (M+H).

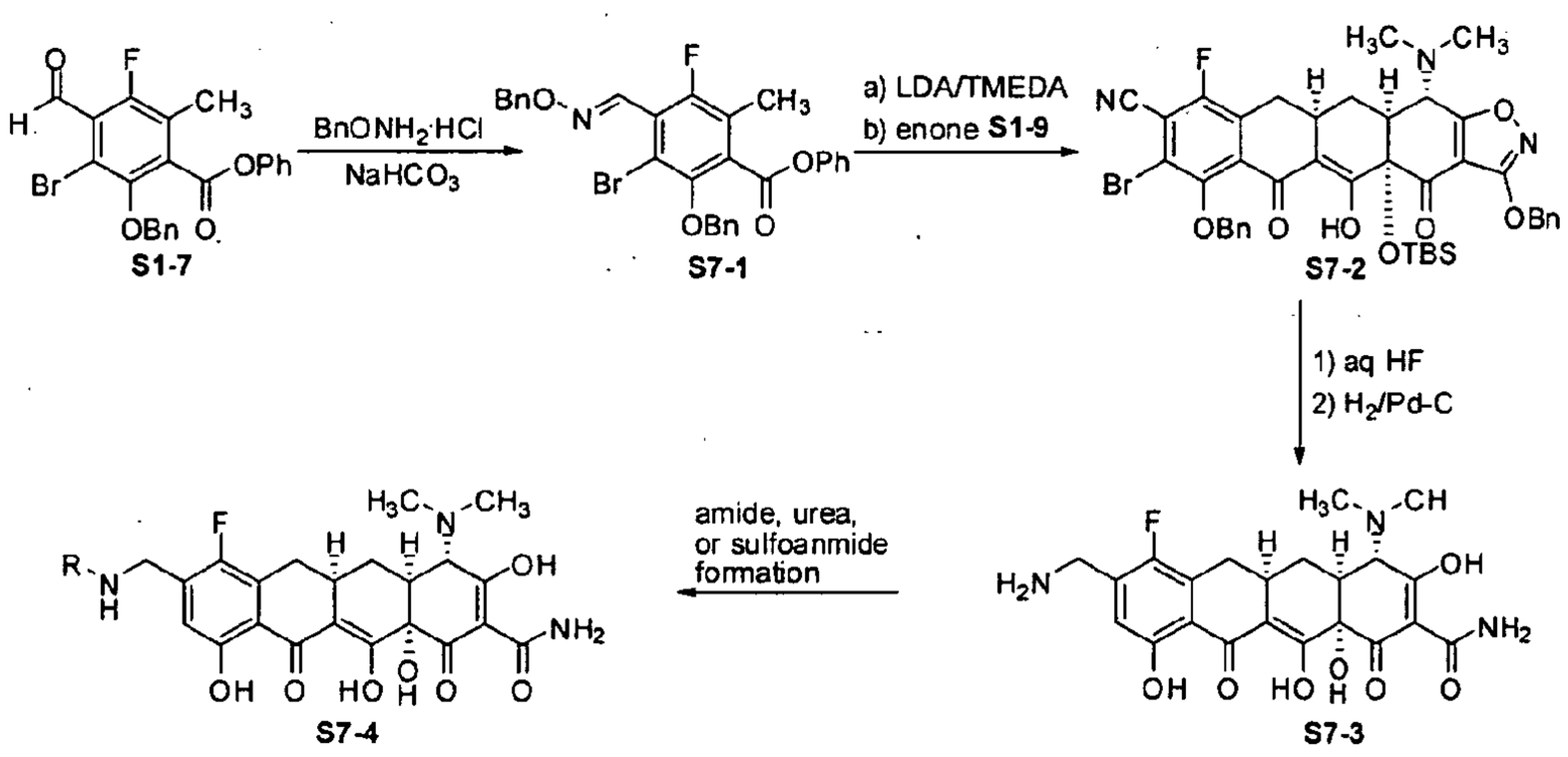


S6-4-3

^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (dd, J = 8.2, 6.0 Hz, 1 H), 4.39 (s, 2 H), 4.10 (s, 1 H), 3.65-3.54 (m, 2 H), 3.24-92 (m, 9 H), 2.43-2.32 (m, 1 H), 2.28-2.17 (m, 1 H), 2.07-1.58 (m, 7 H), 1.51 (d, J = 6.0 Hz, 3 H), 1.39 (d, J = 6.0 Hz, 3 H); MS (ESI) *m/z* 558.61 (M+H).

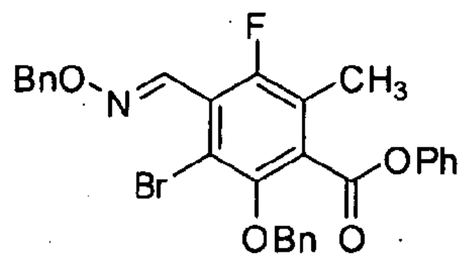
Example 7. Synthesis of Compounds via Scheme 7.

Scheme 7



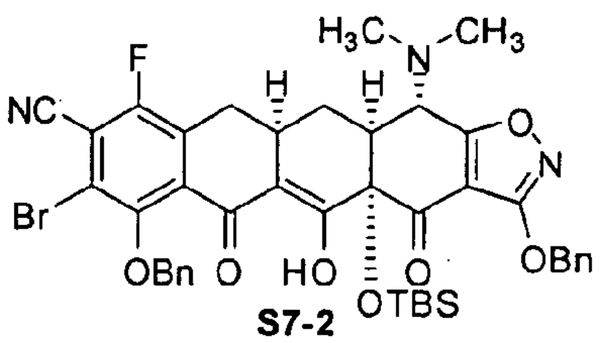
S1-7 **S7-1** **S7-2** **S7-3** **S7-4**

The following compounds were prepared according to Scheme 7.



S7-1

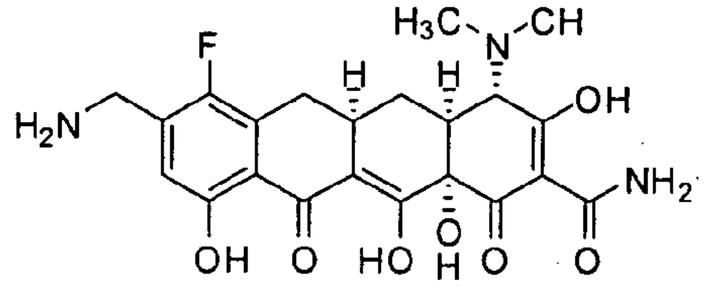
To a solution of sodium bicarbonate (0.21 g, 2.48 mmol, 1.1 equiv) in water (10 mL) was added *O*-benzylhydroxylamine hydrochloride (0.40 g, 2.48 mmol, 1.1 equiv). The solution was heated until all solid dissolved. Compound **S1-7** (1.00 g, 2.26 mmol, 1.0 equiv) in EtOH (6 mL) and 1,4-dioxane (6 mL) were added. The solution was heated until all solid dissolved, and then stirred at rt for 2 hrs. The mixture was diluted with EtOAc (100 mL), washed with brine (20 mL x 3), dried (sodium sulfate), and concentrated. The residue was purified by flash chromatography on silica gel, eluting with hexanes/EtOAc (30:1 to 5:1) to afford 1.10 g (89%) of compound **S7-1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1 H), 7.48-7.24 (comp, 13 H), 7.03-6.96 (comp, 2 H), 5.22 (s, 2 H), 5.03 (s, 2 H), 2.30 (d, J = 2.4 Hz, 3 H); MS (ESI) *m/z* 548.16 (M+H).



S7-2

To a solution of LDA (0.38 mL, 1.0 M/THF, 0.38 mmol, 2.9 equiv) in THF (1 mL) was added TMEDA (57 µL, 0.38 mmol, 2.9 equiv) at -78 °C. After stirring for 5 min, a solution of compound **S7-1** (89 mg, 0.16 mmol, 1.2 equiv) in THF (0.3 mL) was added dropwise to the LDA solution. After complete addition, the reaction mixture was stirred at -78 °C for 10 min. A solution of enone **S1-9** (60 mg, 0.13 mmol, 1.0 equiv) in THF (0.3 mL) was added dropwise. The mixture was slowly warmed to -20 °C over 30 min. The mixture was quenched by phosphate buffer (pH 8, 1.5 mL) and saturated ammonium chloride solution (0.5 mL). The aqueous layer was extracted with EtOAc (3 mL x 4). All organic layers were combined, dried (sodium sulfate), and concentrated. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18

OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; injection volume: 2.0 mL (CH_3CN); gradient: 80→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.1-8.3 min, were collected and freeze-dried to give 33 mg of **S7-2** (32%): ^1H NMR (400 MHz, $CDCl_3$) δ 15.71 (s, 1 H), 7.55-7.24 (comp, 10 H), 5.35 (s, 2 H), 4.99 (d, J = 9.8 Hz, 1 H), 4.95 (d, J = 9.8 Hz, 1 H), 3.87 (d, J = 10.4 Hz, 1 H), 3.24 (dd, J = 16.5, 4.6 Hz, 1 H), 3.07-2.97 (m, 1 H), 2.49 (s, 6 H), 2.64-2.33 (comp, 3 H), 2.20-2.12 (m, 1 H), 0.80 (s, 9 H), 0.26 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 828.16 (M+H).

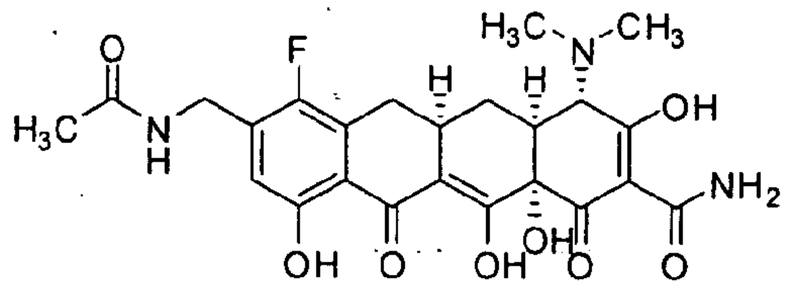


S7-3

To a solution of **S7-2** (33 mg, 0.040 mmol) in acetonitrile (1 mL) was added HF (0.3 mL, 48-50% solution in water). The mixture was stirred at 0 °C for 63 hrs and rt for 3 hrs. The mixture was quenched by potassium phosphate dibasic solution (prepared from 8 g K_2HPO_4 and 8 mL water). The aqueous layer was extracted with EtOAc (8 mL x 5). All organic layers were combined, dried (sodium sulfate) and concentrated to afford the crude intermediate.

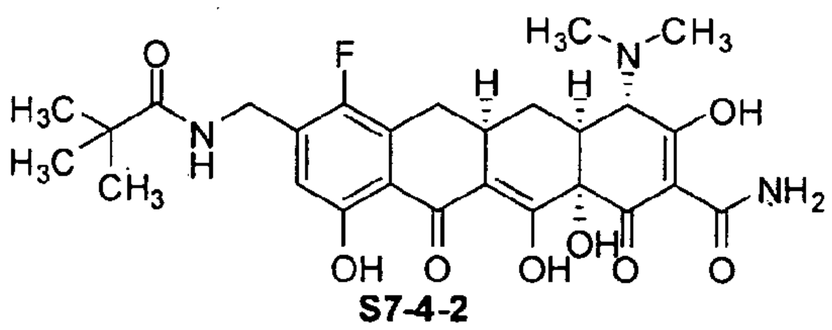
To the above crude intermediate in MeOH/dioxane solution (1:1, 1.4 mL) was added Pd-C (15 mg, 10wt%) and HCl/MeOH (0.5 N, 0.25 mL). The reaction was bubbled with H_2 (balloon) at 25 °C for 90 min. The mixture was filtered through a small Celite plug and flashed with MeOH. The filtrate was concentrated to yield the crude product, which was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-1 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 4.5 mL (0.05 N HCl/water); gradient: 0→50% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.9-8.1 min, were collected and freeze-dried to yield 10 mg of primary **S7-3** (55% for 2 steps): ^1H NMR (400 MHz, CD_3OD) δ 6.95 (d, J = 6.1 Hz, 1 H), 4.18 (s, 2 H), 4.09 (s, 1 H), 3.04 (s, 3 H), 2.96

(s, 3 H), 3.22-2.90 (comp, 3 H), 2.39-2.28 (m, 1 H), 2.28-2.18 (m, 1 H), 1.70-1.57 (m, 1 H); MS (ESI) *m/z* 462.12 (M+H).



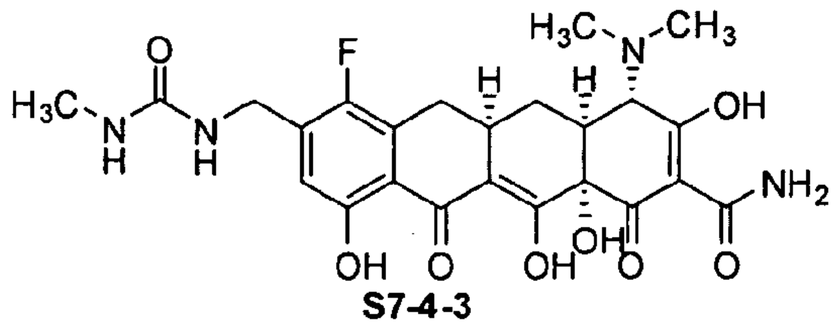
S7-4-1

To a solution of compound **S7-3** (10 mg, 0.020 mmol, 1.0 equiv) and Ac_2O (diluted 20 times in dichloromethane, 45 μL, 0.020 mmol, 1.0 equiv) in DMF (1.5 mL) was added Et_3N (15 μL, 0.11 mmol, 5.5 equiv) at 0 °C. The mixture was stirred for 30 min and then submitted to preparative reverse phase HPLC purification on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 3.0 mL (0.05 N HCl/water); gradient: 0→70% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 9.4-10.6 min, were collected and freeze-dried to yield 4 mg of **S7-4-1** (40%): ^{1}H NMR (400 MHz, CD_3OD) δ 6.73 (d, J = 5.5 Hz, 1 H), 4.38 (d, J = 1.8 Hz, 2 H), 4.07 (s, 1 H), 3.15 (dd, J = 15.3, 4.3 Hz, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.10-2.92 (comp, 2 H), 2.32-2.23 (m, 1 H), 2.22-2.15 (m, 1 H), 2.01 (s, 3 H), 1.68-1.56 (m, 1 H); MS (ESI) *m/z* 504.10 (M+H).



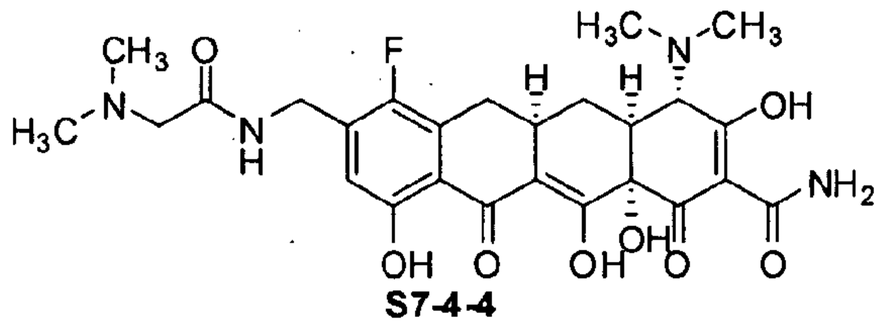
S7-4-2

S7-4-2 was prepared according to the procedure for the preparation of **S7-4-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 6.65 (d, J = 6.1 Hz, 1 H), 4.41 (d, J = 16.5 Hz, 1 H), 4.35 (d, J = 16.5 Hz, 1 H), 4.06 (s, 1 H), 3.15 (dd, J = 15.3, 4.6 Hz, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.10-2.91 (comp, 2 H), 2.33-2.22 (m, 1 H), 2.22-2.14 (m, 1 H), 1.68-1.56 (m, 1 H), 1.22 (s, 9 H); MS (ESI) *m/z* 546.27 (M+H).



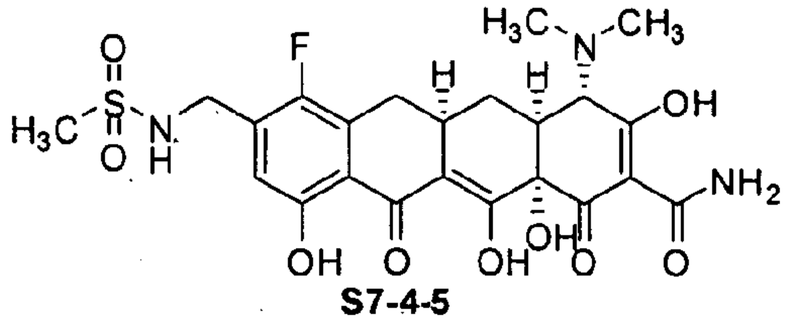
S7-4-3

To a solution of compound **S7-3** (11 mg, 0.020 mmol, 1.0 equiv) and methyl isocyanate (1.4 mg, 0.020 mmol, 1.0 equiv) in DMF (1.5 mL) was added Et_3N (18 μL, 0.13 mmol, 6.5 equiv) at 0 °C. The mixture was stirred for 10 min and then submitted to preparative reverse phase HPLC purification on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 3.3 mL (0.05 N HCl/water); gradient: 0→70% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 9.3-10.6 min, were collected and freeze-dried to yield 4 mg of **S7-4-3** (31%): ^{1}H NMR (400 MHz, CD_3OD) δ 6.74 (d, J = 6.1 Hz, 1 H), 4.37 (d, J = 17.3 Hz, 1 H), 4.32 (d, J = 17.3 Hz, 1 H), 4.06 (s, 1 H), 3.15 (dd, J = 15.9, 4.6 Hz, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.10-2.92 (comp, 2 H), 2.72 (s, 3 H), 2.32-2.22 (m, 1 H), 2.22-2.15 (m, 1 H), 1.67-1.56 (m, 1 H); MS (ESI) *m/z* 519.08 (M+H).



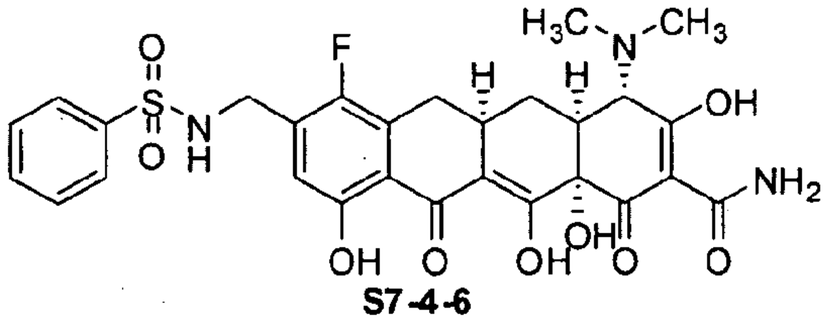
S7-4-4

S7-4-4 was prepared from **S7-3** according to the procedure for the preparation of **S7-4-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 6.79 (d, J = 6.1 Hz, 1 H), 4.49 (d, J = 5.5 Hz, 2 H), 4.07 (s, 1 H), 4.03 (s, 2 H), 3.15 (dd, J = 15.2, 4.3 Hz, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 2.94 (s, 6 H), 3.10-2.92 (comp, 2 H), 2.33-2.23 (m, 1 H), 2.22-2.17 (m, 1 H), 1.68-1.56 (m, 1 H); MS (ESI) *m/z* 547.11 (M+H).



S7-4-5

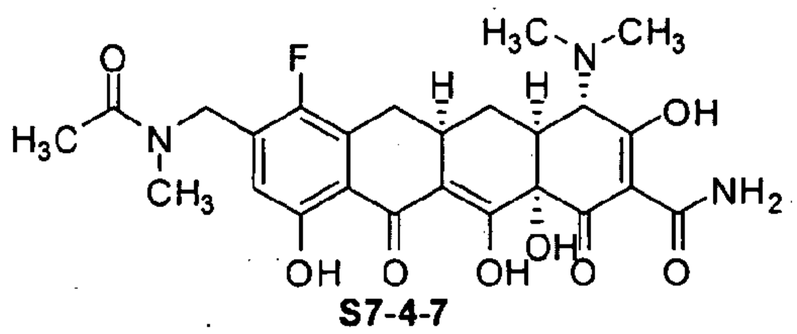
To a solution of compound **S7-3** (11 mg, 0.020 mmol, 1.0 equiv) and methanesulfonic anhydride (5 mg, 0.030 mmol, 1.5 equiv) in DMF (1.5 mL) was added Et_3N (18 μL, 0.13 mmol, 6.5 equiv) at 0 °C. The mixture was stirred for 50 min and then submitted to preparative reverse phase HPLC purification on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 3 mL (0.05 N HCl/water); gradient: 0→70% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 10.3-11.6 min, were collected and freeze-dried to yield 3 mg of **S7-4-5** (22%): ^{1}H NMR (400 MHz, CD_3OD) δ 6.93 (d, J = 6.1 Hz, 1 H), 4.29 (s, 2 H), 4.06 (s, 1 H), 3.16 (dd, J = 15.9, 4.6 Hz, 1 H), 3.03 (s, 3 H), 2.94 (s, 3 H), 2.93 (s, 3 H), 3.10-2.92 (comp, 2 H), 2.34-2.23 (m, 1 H), 2.23-2.16 (m, 1 H), 1.68-1.57 (m, 1 H); MS (ESI) *m/z* 540.04 (M+H).



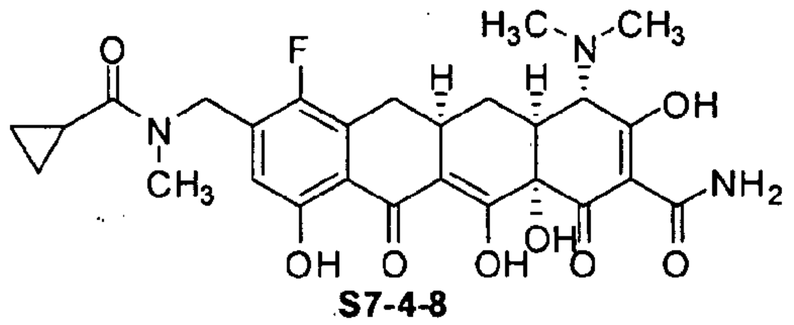
S7-4-6

S7-4-6 was prepared according to the procedure for the preparation of **S7-4-5**: ^{1}H NMR (400 MHz, CD_3OD) δ 7.79 (d, J = 7.4 Hz, 2 H), 7.59-7.48 (comp, 3 H), 6.76 (d, J = 6.1 Hz, 1 H), 4.12 (s, 2 H), 4.06 (s, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.15-2.91 (comp, 3 H), 2.24-2.13 (comp, 2 H), 1.67-1.54 (m, 1 H); MS (ESI) *m/z* 602.22 (M+H).

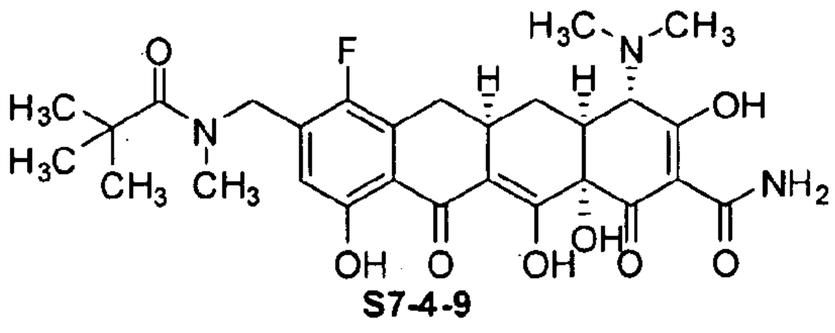
The following compounds were prepared from **S2-4-17** using similar amide, urea, or sulfonamide formation conditions.


S7-4-7

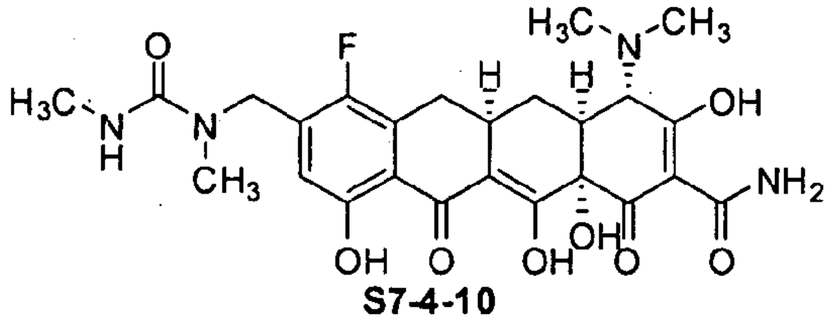
To a solution of **S2-4-17** (8 mg, 0.020 mmol, 1.0 equiv) and Ac_2O (diluted 20 times in dichloromethane, 38 μL, 0.020 mmol, 1.0 equiv) in DMF/acetonitrile (1:1, 2 mL) was added Et_3N (9 μL, 0.070 mmol, 3.5 equiv) at rt. The mixture was stirred for 30 min and then submitted to preparative reverse phase HPLC purification on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 1.5 mL (0.05 N HCl/water); gradient: 0→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.1-9.0 min, were collected and freeze-dried to yield 5 mg of **S7-4-7** (52%): ^1H NMR (400 MHz, CD_3OD) δ 6.62 (d, J = 6.1 Hz, 1 H), 4.67-4.60 (m, 2 H), 4.07 (s, 1 H), 3.09 (s, 3 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.21-2.90 (comp, 3 H), 2.36-2.12 (comp, 5 H), 1.68-1.58 (m, 1 H); MS (ESI) *m/z* 518.12 (M+H).


S7-4-8

S7-4-8: ^1H NMR (400 MHz, CD_3OD) δ 6.64-6.56 (m, 1 H), 4.63 (br s, 2 H), 4.07 (s, 1 H), 3.25 (s, 3 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.21-2.92 (comp, 3 H), 2.35-2.16 (comp, 2 H), 2.07-1.99 (m, 1 H), 1.70-1.57 (m, 1 H), 0.94-0.76 (comp, 4 H); MS (ESI) *m/z* 544.25 (M+H).

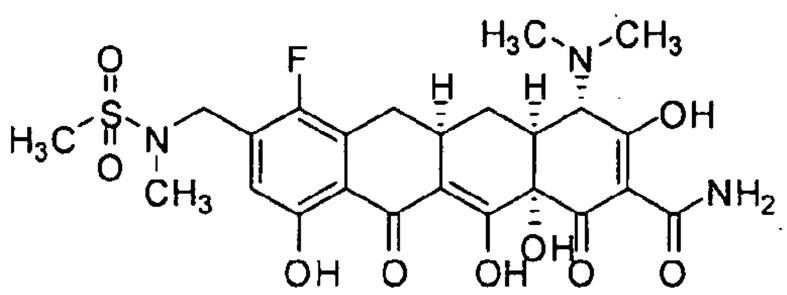

S7-4-9

S7-4-9: ^{1}H NMR (400 MHz, CD_3OD) δ 6.53 (d, J = 6.1 Hz, 1 H), 4.63 (d, J = 4.3 Hz, 2 H), 4.06 (s, 1 H), 3.17 (s, 3 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.20-2.92 (comp, 3 H), 2.37-2.16 (comp, 2 H), 1.68-1.58 (m, 1 H), 1.32 (s, 9 H); MS (ESI) *m/z* 560.30 (M+H).



S7-4-10

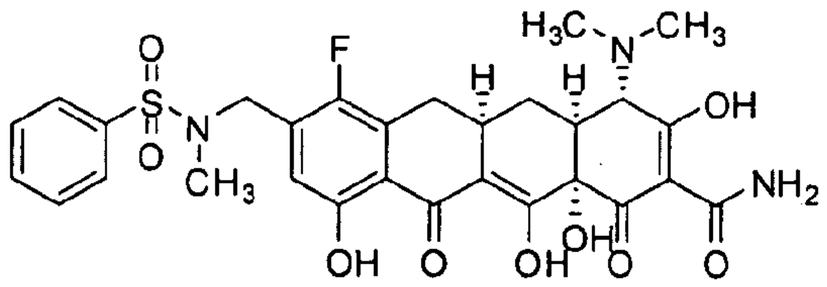
To a solution of **S2-4-17** (15 mg, 0.030 mmol, 1.0 equiv) and methyl isocyanate (2 mg, 0.030 mmol, 1.0 equiv) in DMF (1.5 mL) was added Et_3N (22 μL, 0.16 mmol, 5.3 equiv) at 0 °C. The mixture was stirred for 30 min and then submitted to preparative reverse phase HPLC purification on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 2.6 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.4-10.2 min, were collected and freeze-dried to yield 14 mg of **S7-4-10** (83%): ^{1}H NMR (400 MHz, CD_3OD) δ 6.59 (d, J = 6.1 Hz, 1 H), 4.55 (s, 2 H), 4.07 (s, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 2.91 (s, 3 H), 3.19-2.89 (comp, 3 H), 2.75 (s, 3 H), 2.32-2.16 (comp, 2 H), 1.68-1.57 (m, 1 H); MS (ESI) *m/z* 533.11 (M+H).



S7-4-11

To a solution of **S2-4-17** (15 mg, 0.030 mmol, 1.0 equiv) and methanesulfonic anhydride (6 mg, 0.030 mmol, 1.0 equiv) in DMF (1.5 mL) was added Et_3N (22 μL, 0.16 mmol, 5.3 equiv) at 0 °C. The mixture was stirred at 0 °C for 30 min and rt for 20 min. The mixture was submitted to preparative reverse phase HPLC purification on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min;

Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 3 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 9.8-11.6 min, were collected and freeze-dried to yield 7 mg of **S7-4-11** (38%): ^{1}H NMR (400 MHz, CD_3OD) δ 6.90 (d, J = 5.5 Hz, 1 H), 4.38 (s, 2 H), 4.07 (s, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 2.94 (s, 3 H), 3.19-2.93 (comp, 3 H), 2.83 (s, 3 H), 2.34-2.16 (comp, 2 H), 1.69-1.58 (m, 1 H); MS (ESI) *m/z* 554.06 (M+H).

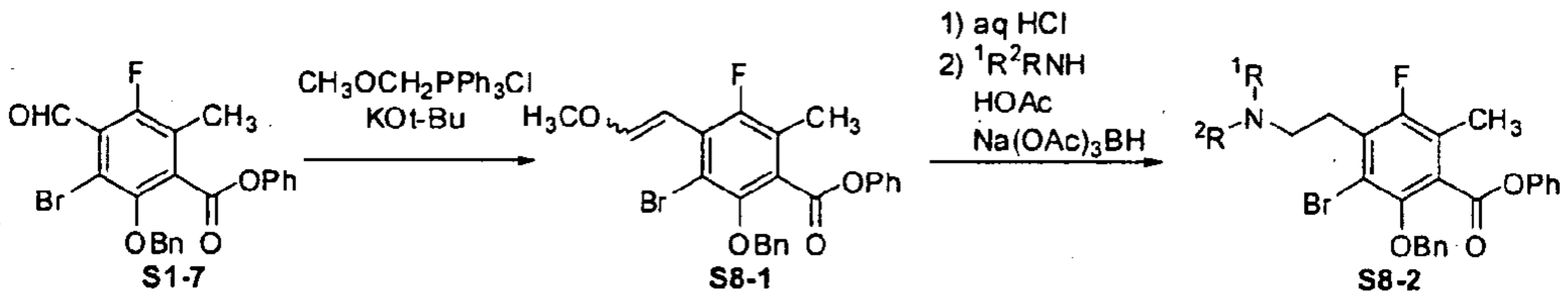


S7-4-12

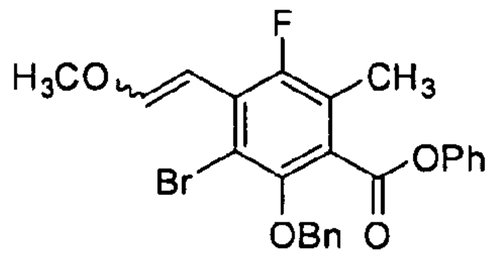
S7-4-12 was prepared according to the procedure for the preparation of **S7-4-11**: ^{1}H NMR (400 MHz, CD_3OD) δ 7.85 (dd, J = 7.4, 1.8 Hz, 2 H), 7.72-7.60 (comp, 3 H), 6.87 (d, J = 6.1 Hz, 1 H), 4.25 (d, J = 1.8 Hz, 2 H), 4.06 (s, 1 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 3.15-2.92 (comp, 3 H), 2.71 (s, 3 H), 2.32-2.16 (comp, 2 H), 1.68-1.57 (m, 1 H); MS (ESI) *m/z* 616.20 (M+H).

Example 8. Synthesis of Compounds via Scheme 8.

Scheme 8

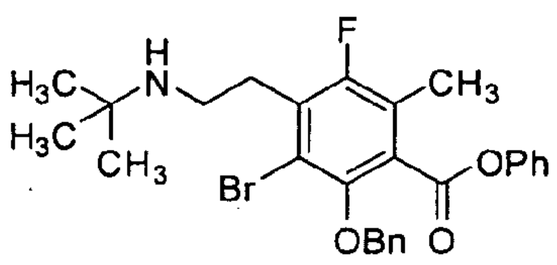


The following compounds were prepared according to Scheme 8.



S8-1

(Methoxymethyl)triphenylphosphonium chloride (0.46 g, 1.35 mmol, 2.0 equiv) was added to a suspension of potassium *t*-butoxide (0.15 g, 1.35 mmol, 2.0 equiv) in THF (3 mL), resulting in a red colored mixture. After 15 minutes, a solution of compound **S1-7** (0.30 g, 0.68 mmol, 1.0 equiv) in THF (2 mL) was added, resulting in a yellowish orange mixture. After 1 h, the reaction mixture was quenched by water (15 mL) and extracted with EtOAc (2 x 20 mL). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The material was purified by column chromatography on silica (Biotage 10 g prepacked column, 0% to 6% EtOAc in hexanes gradient). The two regioisomeric compounds mostly co-eluted and were combined, yielding 0.23 g (73%) of compound **S8-1** (^{1}H NMR indicated a 2:1 mixture of cis and trans isomers): R_f 0.40, 0.34 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 2 H), 7.40-7.32 (m, 5.66 H), 7.28-7.20 (m, 1 H), 7.04 (d, J = 8.2 Hz, 2 H), 6.31 (d, J = 6.8 Hz, 0.34 H), 5.93 (d, J = 12.8 Hz, 0.66 H), 5.22 (d, J = 6.8 Hz, 0.34 H), 5.08 (s, 2 H), 3.77 (s, 2 H), 3.73 (s, 1 H), 2.36-2.31 (m, 3 H); MS (ESI) *m/z* 493.26, 495.26 (M+Na).

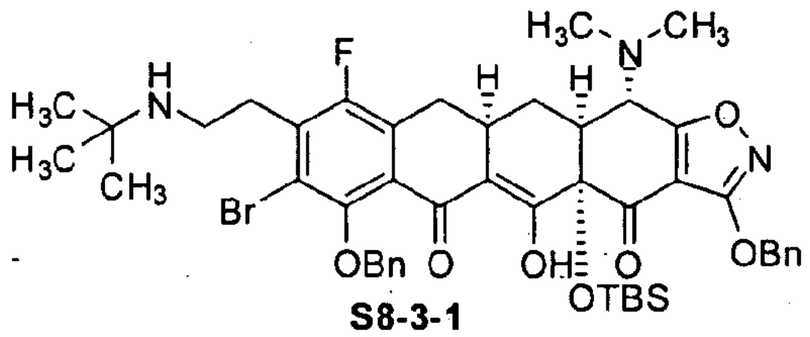


S8-2-1

A solution of **S8-1** (0.35 g, 0.74 mmol) in 6 N HCl in water (2 mL) and THF (6 mL) was heated to 70 °C. After 4 hrs, the reaction mixture was cooled to room temperature and diluted with EtOAc (25 mL). The layers were separated, and the EtOAc layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure, yielding 0.32 g (95%) of crude aldehyde intermediate: MS (ESI) *m/z* 479.19, 481.15 (M+Na).

The aldehyde intermediate (0.10 g, 0.13 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (2 mL) and HOAc (0.054 mL, 0.94 mmol, 7.2 equiv) and *t*-

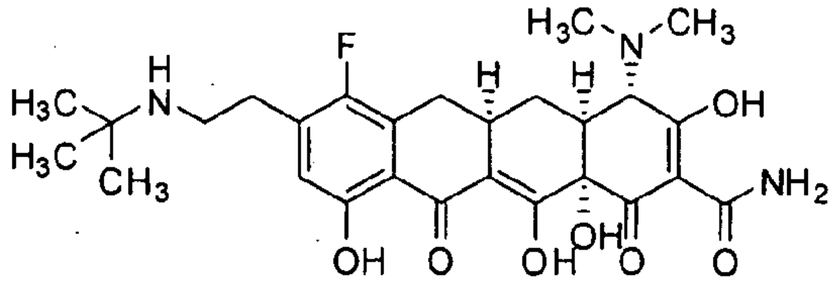
butylamine (0.099 mL, 0.94 mmol, 7.2 equiv) were added. After 15 minutes, $Na(OAc)_3BH$ (0.14 g, 0.67 mmol, 5.2 equiv) was added. After stirring overnight, the reaction mixture was quenched by $NaHCO_3$ (saturated, aqueous solution), diluted with dichloromethane (20 mL), washed with $NaHCO_3$ (saturated, aqueous solution, 10 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The material was purified by column chromatography on silica (Biotage 5 g prepacked column, 0% to 60% EtOAc in hexanes gradient), yielding 20 mg (28%) of compound **S8-2-1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 2 H), 7.40-7.32 (m, 5 H), 7.28-7.20 (m, 1 H), 7.04 (d, J = 8.2 Hz, 2 H), 5.10 (s, 2 H), 3.25-2.98 (m, 2 H), 2.90-2.70 (m, 2 H), 2.35 (s, 3 H), 1.17 (br s, 9 H); MS (ESI) *m/z* 514.31, 516.3 (M+H).



S8-3-1

A solution of **S8-2-1** (20 mg, 0.038 mmol, 1.2 equiv) in THF (1 mL) was added to a solution of LDA (1.2 M/THF/heptane/ethylbenzene, 0.058 mL, 0.070 mmol, 2.2 equiv) and TMEDA (0.028 mL, 0.19 mmol, 6.0 equiv) in THF (2 mL) at -78 °C, giving a red colored solution. The reaction was stirred at -78 °C for 5 min. A solution of enone **S1-9** (15 mg, 0.032 mmol, 1.0 equiv) in THF (0.5 mL) was added dropwise to the reaction mixture. The reaction was stirred from -78 °C to -20 °C for 1 h, quenched by saturated aqueous NH_4Cl, and extracted with EtOAc (2 times). The combined EtOAc extracts were dried (sodium sulfate) and concentrated to yield the crude product. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 20→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 7.0-8.0 min, were collected and freeze-dried to give 18 mg of pure compound **S8-3-1** (62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.45 (m, 4 H), 7.40-7.28 (m, 6 H), 5.35 (s, 2 H), 5.00-4.87 (m, 2 H), 3.91 (d, J = 10.4 Hz, 1 H), 3.54-3.15 (m, 3 H), 3.02-2.88 (m, 3

H), 2.58-2.32 (m, 9 H), 2.17-2.08 (m, 1 H), 1.48-1.20 (br s, 9 H), 0.80 (s, 9 H), 0.26 (s, 3 H), 0.11 (s, 3 H); MS (ESI) *m/z* 902.48, 904.45 (M+H).



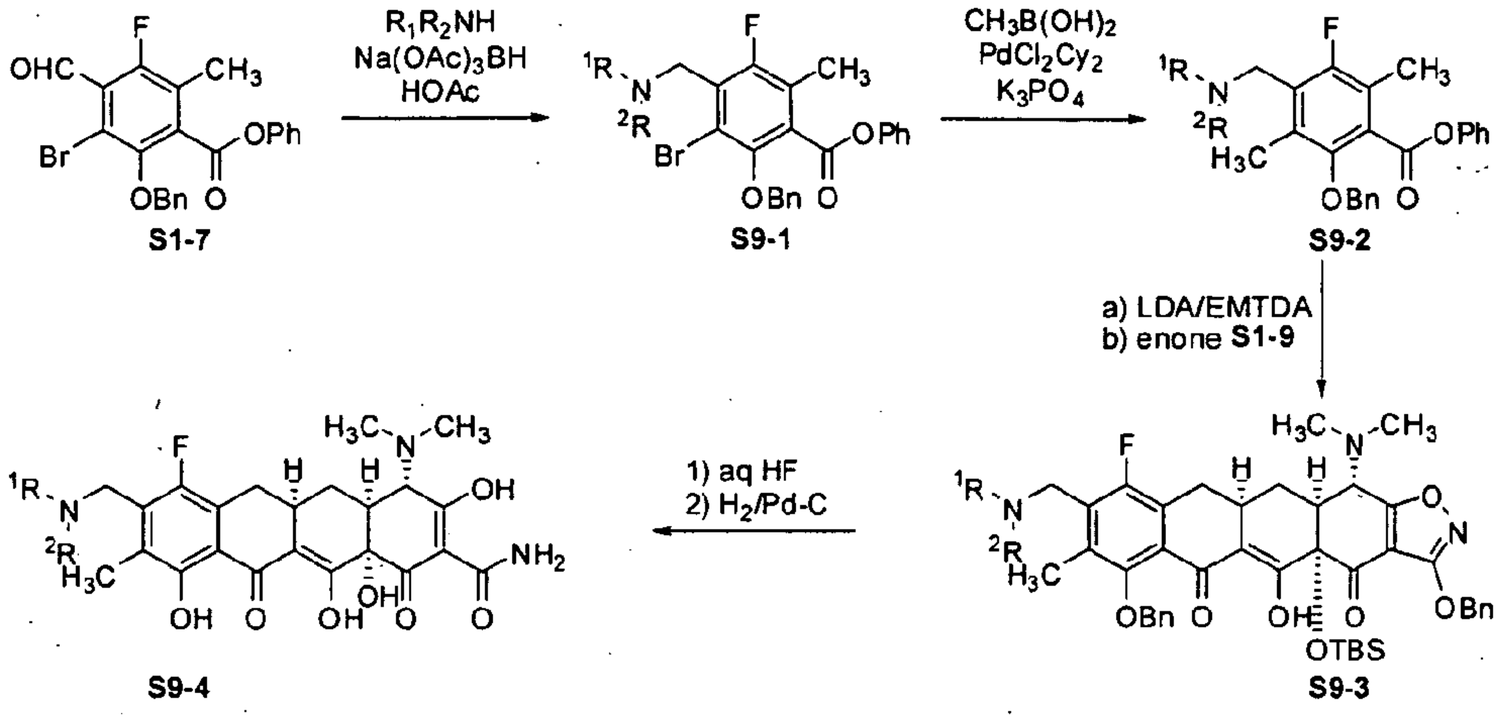
S8-4-1

A solution of compound **S8-3-1** (18 mg, 0.020 mmol) in 1,4-dioxane (0.80 mL) was treated with HF (0.40 mL, 48-50% aqueous solution). After stirring overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL). This mixture was extracted with EtOAc (3 times), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure.

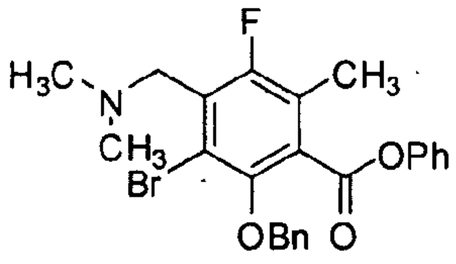
The above material was dissolved in MeOH (1 mL), 1,4-dioxane (1 mL), and 0.5 N HCl/MeOH (0.4 mL). 10% Pd-C (Degussa, 2 mg) was added, and an atmosphere of hydrogen was introduced. After 2 hrs, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 7.0-8.4 min, were collected and freeze-dried to yield 8 mg of compound **S8-4-1** (64%): ^{1}H NMR (400 MHz, CD_3OD/DCl) δ 6.86 (d, J = 5.5 Hz, 1 H), 4.14 (s, 1 H), 3.34-2.94 (m, 13 H), 2.33-2.21 (m, 2 H), 1.70-1.55 (m, 1 H), 1.49 (s, 9 H); MS (ESI) *m/z* 532.31 (M+H).

Example 9. Synthesis of Compounds via Scheme 9.

Scheme 9

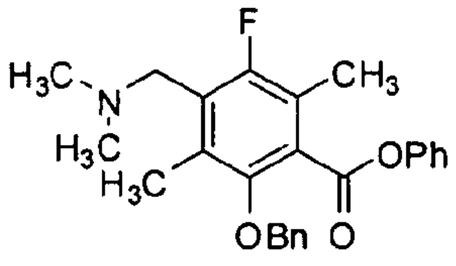


The following compounds were prepared according to Scheme 9.



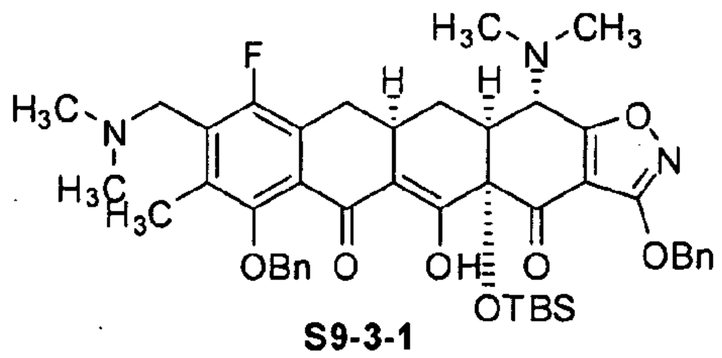
S9-1-1

Compound **S1-7** (0.25 g, 0.56 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (4 mL). Dimethylamine (0.56 mL, 2.0 M/THF, 1.12 mmol, 2.0 equiv) and acetic acid (64 μL, 1.12 mmol, 2.0 equiv) were added under a nitrogen atmosphere. After stirring at rt for 1 h, sodium triacetoxyborohydride (0.36 g, 1.68 mmol, 3.0 equiv) was added to reaction mixture. After overnight, LC/MS indicated that the starting material was consumed. The reaction mixture was diluted with dichloromethane, washed with $NaHCO_3$ (saturated aqueous solution, 3 x 10 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Biotage 10 g column, 10% to 30% EtOAc in hexanes gradient), yielding 0.21 g (78%) of the pure compound **S9-1-1** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.47 (m, 2 H), 7.40-7.33 (m, 5 H), 7.26 (t, J = 7.8 Hz, 1 H), 7.07-7.03 (m, 2 H), 5.11 (s, 2 H), 3.66 (d, J = 2.3 Hz, 2 H), 2.37 (d, J = 2.3 Hz, 3 H), 2.35 (s, 6 H).



S9-2-1

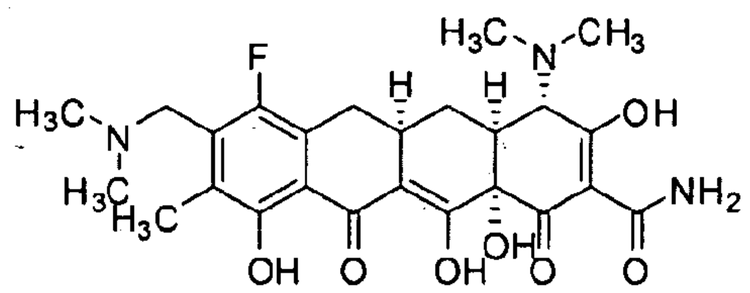
Compound **S9-1-1** (0.10 g, 0.21 mmol), methylboronic acid (38 mg, 0.64 mmol), dichlorobis(tricyclohexylphosphine)palladium(II) (4 mg, 0.011 mmol) and K_3PO_4 (0.14 g, 0.64 mmol) were heated to 80 °C in toluene (2 mL) and water (5 drops). After 5 hrs, additional K_3PO_4 (0.14 g, 0.64 mmol) and methylboronic acid (38 mg, 0.64 mmol) were added. The reaction mixture was heated to 100 °C. After one hour, the reaction mixture was cooled to rt and let stand for 3 days. Additional dichlorobis-(tricyclohexylphosphine)palladium(II) (5 mg, 0.015 mmol) and methylboronic acid (38 mg, 0.64 mmol) were added, followed by enough K_3PO_4 to give a saturated aqueous layer. This was heated to 110 °C. After 2 hrs, the reaction was complete. Upon cooling to rt, the reaction mixture was diluted with EtOAc, washed with water (2 times) and brine (1 time), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The material was purified by column chromatography on silica (Biotage 5 g prepacked column, 0% to 6% MeOH in dichloromethane gradient), yielding 81 mg (93%) of compound **S9-2-1**. The compound was ~80-90% pure and contaminated with phosphine ligand: R_f 0.49 (10% MeOH/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.30 (m, 7 H), 7.30-7.20 (m, 1 H), 7.12-7.04 (m, 2 H), 4.96 (s, 2 H), 2.80-2.20 (m, 9 H), 1.56 (s, 3 H); MS (ESI) *m/z* 408.34 (M+H).



S9-3-1

n-Butyllithium (2.5 M/hexanes, 0.14 mL, 0.35 mmol, 2.3 equiv) was added to a -40 °C solution of diisopropylamine (0.050 mL, 0.35 mmol, 2.3 equiv) in THF (5 mL). The reaction mixture was cooled to -78 °C, and TMEDA (0.14 mL, 0.92 mmol, 6.1 equiv) was added. A solution of **S9-2-1** (81 mg, 0.20 mmol, 1.3 equiv) in THF (2 mL) was added dropwise. A solution of enone **S1-9** (74 mg, 0.15 mmol, 1.0 equiv) in THF (1 mL) was added dropwise to the reaction mixture. The reaction was stirred from -78 °C to -20 °C for 1 h, quenched by saturated aqueous NH_4Cl, and extracted with EtOAc (2 times). The combined EtOAc extracts were dried (sodium sulfate) and concentrated to yield the crude product. The crude

product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; gradient: 50→100% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 2.5-3.6 min, were collected and freeze-dried to give 34 mg of compound **S9-3-1** (28%, contaminated with the phosphine ligand): MS (ESI) *m/z* 796.53 (M+H).



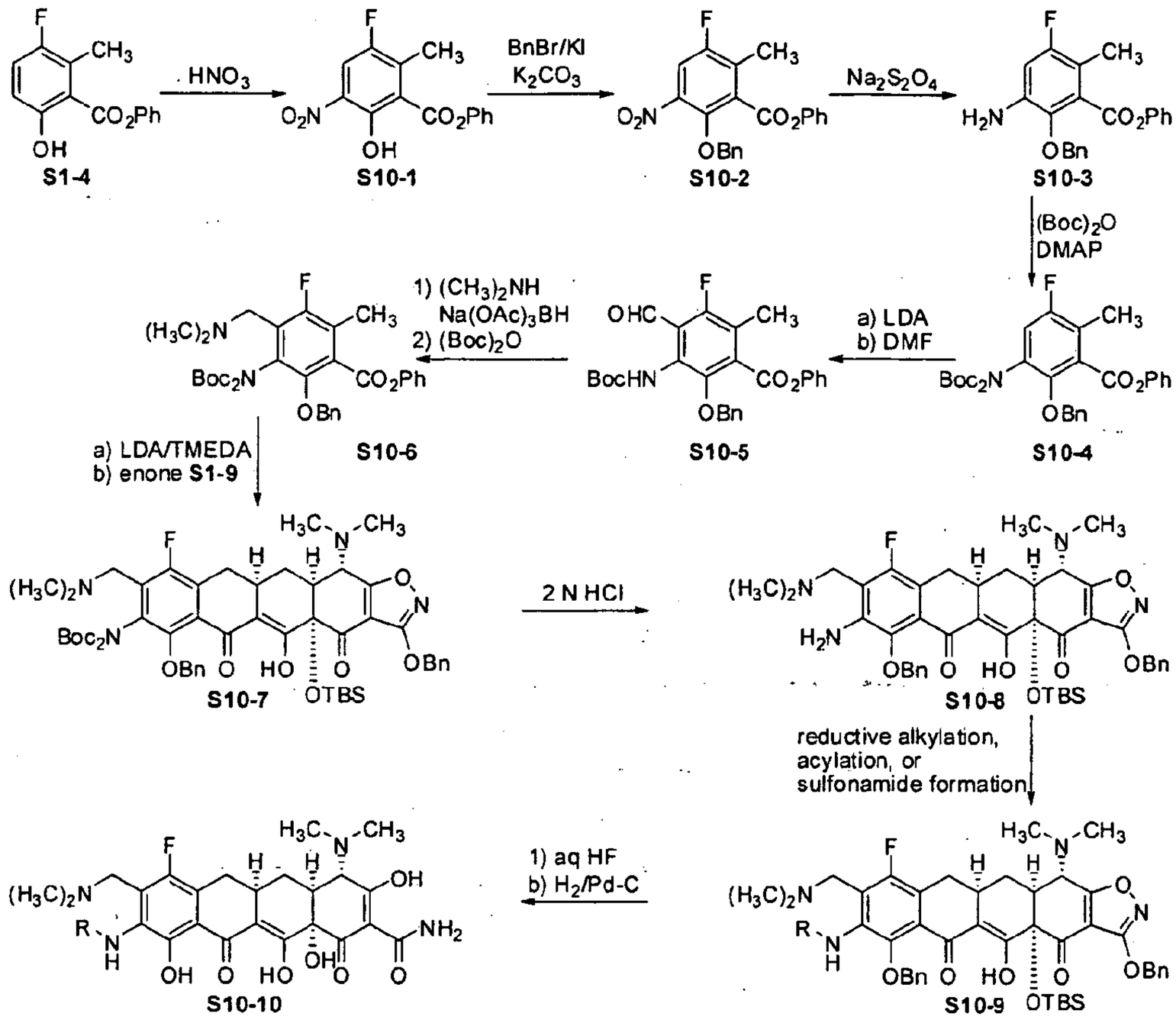
S9-4-1

A solution of compound **S9-3-1** (34 mg, 0.043 mmol) in 1,4-dioxane (0.9 mL) was treated with HF (0.40 mL, 48-50% aqueous solution). After stirring overnight, the mixture was poured into a solution of K_2HPO_4 (4.8 g) in water (20 mL). This mixture was extracted with EtOAc (3 times), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure.

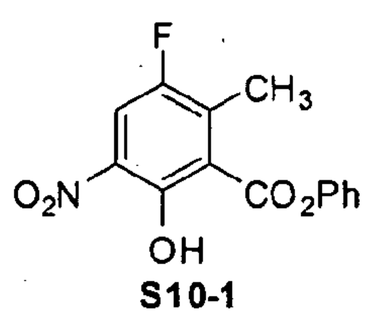
The above crude material was dissolved in MeOH (2 mL), 1,4-dioxane (2 mL), and 0.5 N HCl/MeOH (0.5 mL). 10% Pd-C (Degussa, 10 mg) was added, and an atmosphere of hydrogen was introduced. Upon completion, the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, gradient elution with 0→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.6-7.6 min, were collected and freeze-dried to yield 10 mg of compound **S9-4-1** (41%): ^1H NMR (400 MHz, CD_3OD/DCl) δ 4.52 (s, 2 H), 4.15 (s, 1 H), 3.24-2.92 (m, 15 H), 2.36 (s, 3 H), 2.34-2.24 (m, 2 H), 1.70-1.56 (m, 1 H); MS (ESI) *m/z* 504 (M+H).

Example 10. Synthesis of Compounds via Scheme 10.

Scheme 10



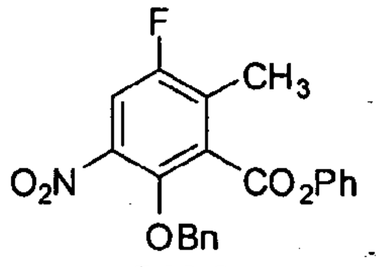
The following compounds were prepared according to Scheme 10.



S10-1

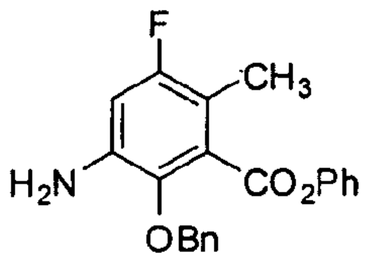
To a 250 mL round bottom flask was added compound **S1-4** (14.47g, 56.30 mmol, 1.0 equiv, crude), tetrabutylammonium bromide (0.90 g, 2.80 mmol, 0.05 equiv), 1,2-dichloroethane (60 mL), and water (60 mL). The clear bi-layer was cooled in a 20 °C water bath. Nitric acid (7.2 mL, 70 wt%, 112.60 mmol, 2.0 equiv) was added. After the addition, the reaction temperature slowly rose to 26 °C. The reaction was stirred at room temperature overnight (19 hrs). TLC (heptane/EtOAc = 9.5/0.5) showed the reaction was complete. The organic layer was separated, washed with water (60mL x 2) and brine, and dried over anhydrous sodium sulfate. The solvent was removed to give compound **S10-1** as a brown oil, which solidified on

standing (17.71 g, quantitative). The crude product was used directly for the next step.



S10-2

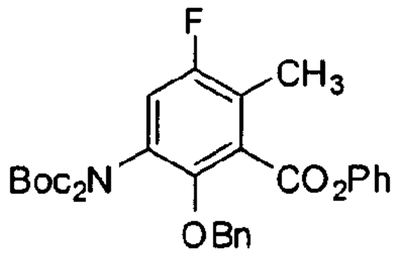
To a 250 mL round bottom flask was added compound **S10-1** (17.7 g, 56.30 mmol 1.0 equiv), acetone (177 mL), anhydrous potassium carbonate (15.6 g, 113.00 mmol, 2.0 equiv), and potassium iodide (0.47 g, 2.80 mmol, 0.05 equiv). To the stirred suspension at room temperature was added benzyl bromide (7.03 mL, 59.10 mmol, 1.05 equiv). The suspension was then heated to 56 °C for 4 hrs. TLC (heptane/EtOAc = 9/1) showed the reaction was complete. The solid was removed by filtration and washed with acetone (30 mL). The filtrated was concentrated to give a paste. The paste was partitioned between methyl t-butyl ether (MTBE, 120 mL) and water (80 mL). The organic layer was washed with water (80 mL) and brine, dried over anhydrous sodium sulfate, and concentrated to give compound **S10-2** as a brown oil (21.09 g, 98%). The crude product was used directly for the next step.



S10-3

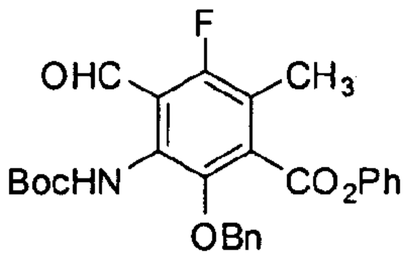
To a 1 L round bottom flask was added compound **S10-2** (21.08 g, 55.40 mmol, 1.0 equiv) and THF (230 mL). The solution was cooled in a cold water bath to 10 °C. To another 500 mL round bottom flask containing water (230 mL), sodium hydrosulfite ($Na_2S_2O_4$, 56.7 g, 276.80 mmol, 5.0 equiv) was added slowly with stirring. The aqueous solution of sodium hydrosulfite was added to the THF solution of compound **S10-2**. The temperature quickly rose from 10 °C to 20.4 °C after the addition. The yellow suspension was stirred while the cold water bath slowly warmed up to room temperature overnight to give an orange cloudy solution. The reaction temperature during this period was between 15 °C to 19 °C. TLC (heptane/EtOAc = 9/1) showed the reaction was complete. The orange cloudy

solution was diluted with EtOAc (460 mL). The organic layer was washed with water (150 mL x 2) and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to give the crude product as a brown oil. The crude product was purified by flash silica gel column eluted with heptane/EtOAc 9/1 to yield the desired product **S10-3** (15.83 g, 80%, 3 steps).



S10-4

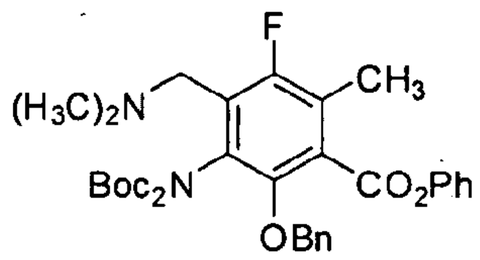
Di-*t*-butyl dicarbonate (10.56 g, 48.40 mmol, 2.5 equiv) and DMAP (0.12 g, 0.97 mmol, 0.05 equiv) were added to the solution of **S10-3** (6.80 g, 19.40 mmol, 1.0 equiv) in anhydrous DMF (39 mL). The resulting mixture was stirred at rt for 20 hrs and diluted with EtOAc. The solution was washed with H_2O (three times) and brine, dried over sodium sulfate, filtered and concentrated. Further purification of the residue by flash chromatography (silica gel, 95:5 hexanes/EtOAc) yielded compound **S10-4** as a white solid (8.70 g, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 18H), 2.36 (d, J = 1.8 Hz, 3 H), 4.92 (s, 2 H), 6.96-7.02 (m, 3 H), 7.22-7.38 (m, 8 H); MS (ESI) *m/z* 574.3 (M+Na), calcd for $C_{31}H_{34}FNO_3Na$ 574.2.



S10-5

To compound **S10-4** (4.80 g, 8.70 mmol, 1.0 equiv) in anhydrous THF (50 mL) at -78 °C was added LDA (7.25 mL, 1.8 M/heptane/ethylbenzene/THF, 13.05 mmol, 1.5 equiv) dropwise over a period of 2 min. The resulting deep red-brown solution was stirred at -78 °C for 30 min. Anhydrous DMF (1.35 mL, 17.44 mmol, 2.0 equiv) was added. The resulting light brown solution was stirred at -78 °C for 30 min. The reaction was quenched at -78 °C with HOAc (0.90 mL), warmed up to rt, diluted with EtOAc (200 mL), washed with water (500 mL x 1), saturated aqueous sodium bicarbonate (100 mL x 1), and brine (100 mL x 1). The EtOAc solution was dried over sodium sulfate and concentrated under reduced pressure. Flash column

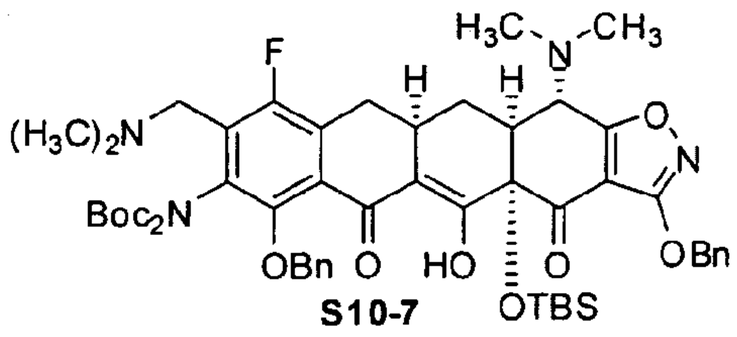
chromatography on silica gel with 0%-15% EtOAc/hexanes yielded the desired product **S10-5** as an orange solid (2.55 g, 61%): R_f 0.50 (20% EtOAc/hexanes): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1 H), 7.39 (br s, 1 H), 7.30-7.42 (m, 7 H), 7.23-7.30 (m, 1 H), 7.07 (d, J = 7.3 Hz, 2 H), 4.96 (s, 2 H), 2.36 (d, J = 2.4 Hz, 3 H), 1.44 (s, 9 H); MS (ESI) *m/z* 480.1 (M+H), calcd for $C_{27}H_{26}FNO_6$ 479.2.



S10-6

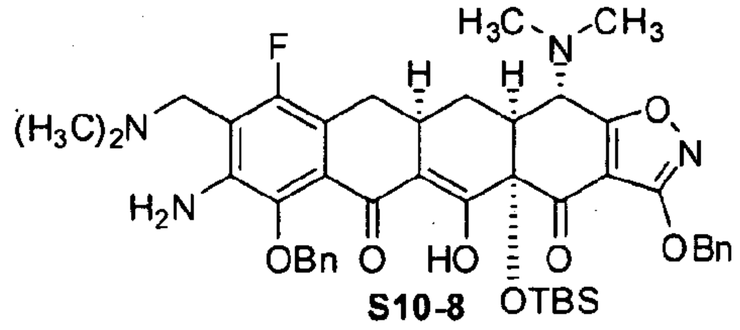
To a solution of **S10-5** (0.40 g, 0.83 mmol, 1.0 equiv) in 1,2-dichloroethane (8.4 mL) was added dimethylamine (33% in EtOH, 0.57 mL, 4.18 mmol, 5.0 equiv) and acetic acid (0.14 mL, 2.50 mmol, 3.0 equiv). The mixture was stirred at rt for 2 hrs. $Na(OAc)_3BH$ (0.53 g, 2.50 mmol, 3.0 equiv) was added, and the reaction was stirred for 15 hrs. The mixture was diluted with EtOAc (15 mL). The organic layer was washed two times with potassium phosphate dibasic solution (prepared from 2 g K_2HPO_4 and 5 mL water), dried (sodium sulfate) and concentrated.

To the above residue in DMF (8 mL) was added Boc_2O (0.24 g, 1.08 mmol, 1.3 equiv), DMAP (10 mg, 0.080 mmol, 0.1 equiv) and Et_3N (0.58 mL, 4.20 mmol, 5.1 equiv). The reaction was stirred at rt for 2 hrs. Sodium hydride (60% dispersion in mineral oil, 0.18 g, 4.40 mmol, 5.3 equiv) was added, and the mixture was stirred for 2 hrs. The mixture was quenched by brine (2 mL) and diluted with EtOAc (100 mL). The organic layer was washed with brine (30 mL x 5), dried (sodium sulfate) and concentrated. The residue was purified by flash chromatography on silica gel, eluting with hexanes/EtOAc (5:1) to afford 0.52 g of compound **60** (quant. yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.18 (comp, 8 H), 7.02-6.96 (comp, 2 H), 4.96 (s, 2 H), 3.37 (s, 2 H), 2.37 (d, J = 2.4 Hz, 3 H), 2.22 (s, 6 H), 1.36 (s, 18 H); MS (ESI) *m/z* 609.33 (M+H).



S10-7

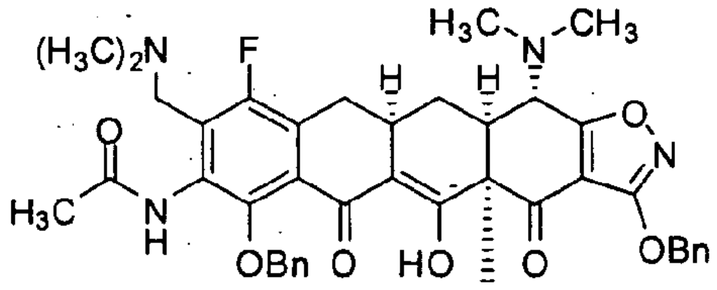
To a solution of *i*-Pr_2NH (0.27 mL, 1.93 mmol, 3.0 equiv) in THF (7 mL) was added a solution of *n*-BuLi (0.89 mL, 2.17 M/hexanes, 1.93 mmol, 3.0 equiv) dropwise at -78 °C. The reaction was allowed to warm to 0 °C, stirred at 0 °C for 25 min, and then cooled to -78 °C. TMEDA (0.29 mL, 1.93 mmol, 3.0 equiv) was added, and the mixture was stirred at -78 °C for 5 min. A solution of compound **S10-6** (0.51 g, 0.83 mmol, 1.3 equiv) in THF (0.5 mL) was added dropwise to the LDA solution over 5 min. Once addition was complete, the reaction mixture was stirred at -78 °C for 30 min. A solution of enone **S1-9** (0.31 g, 0.64 mmol, 1.0 equiv) in THF (0.5 mL) was added dropwise over 2 min. The mixture was slowly warmed to -20 °C over 40 min and quenched by phosphate buffer (pH 7, 10 mL). The aqueous layer was extracted with EtOAc (20 mL x 3). All organic layers were combined, dried (sodium sulfate), and concentrated. The residue was purified by flash chromatography on silica gel, eluting with hexanes/EtOAc (20:1 to 3:1) to afford 0.56 g of compound **S10-7** (87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.96 (s, 1 H), 7.50-7.24 (comp, 10 H), 5.35 (s, 2 H), 4.93 (d, J = 9.8 Hz, 1 H), 4.83 (d, J = 9.8 Hz, 1 H), 3.94 (d, J = 12.2 Hz, 1 H), 3.35 (s, 2 H), 3.31-3.23 (m, 1 H), 3.05-2.94 (m, 1 H), 2.49 (s, 6 H), 2.59-2.36 (comp, 3 H), 2.21 (s, 6 H), 2.20-2.10 (m, 1 H), 1.37 (s, 9 H), 1.32 (s, 9 H), 0.81 (s, 9 H), 0.27 (s, 3 H), 0.12 (s, 3 H); MS (ESI) *m/z* 997.42 (M+H).



S10-8

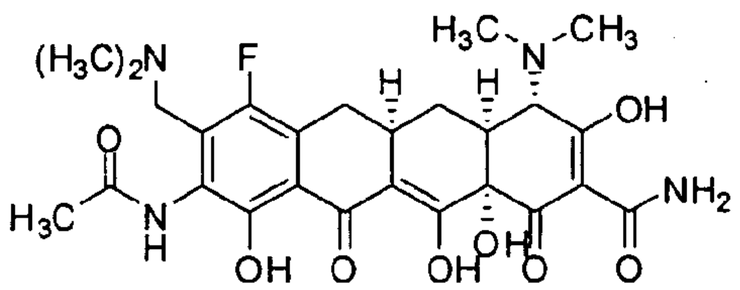
To a solution of compound **S10-7** in 1,4-dioxane (4 mL) was added HCl in 1,4-dioxane (4 N, 4 mL). The mixture was stirred for 3 hrs and then concentrated under reduced pressure. Potassium phosphate dibasic solution (prepared from 2 g K_2HPO_4 and 5 mL water) was added. The mixture was extracted with EtOAc (10 mL x 3). All organic layers were combined, dried (sodium sulfate) and concentrated to afford 0.45 g (quant. yield) of compound **S10-8**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.15 (s, 1 H), 7.57-7.24 (comp, 10 H), 5.35 (s, 2 H), 4.90 (d, J = 11.9 Hz, 1 H), 4.82 (d, J = 11.9 Hz, 1 H), 3.97 (d, J = 10.4 Hz, 1 H), 3.50 (s, 2 H), 3.17-3.09 (m, 1

H), 3.03-2.93 (m, 1 H), 2.48 (s, 6 H), 2.18 (s, 6 H), 2.57-2.08 (comp, 4 H), 0.82 (s, 9 H), 0.27 (s, 3 H), 0.13 (s, 3 H); MS (ESI) *m/z* 797.36 (M+H).



S10-9-1

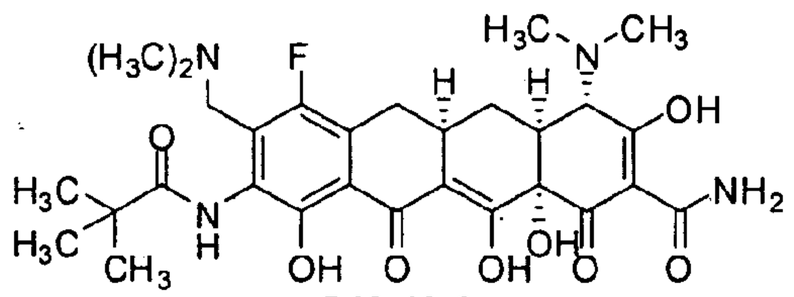
To a solution of compound **S10-8** (14 mg, 0.020 mmol, 1.0 equiv) and Et_3N (37 μL, 0.26 mmol, 13 equiv) in dichloromethane (2 mL) was added a solution of AcCl (2.2 μL, 0.030 mmol, 1.5 equiv) in dichloromethane (0.4 mL). The reaction was stirred at rt for 1 h, quenched by MeOH (0.3 mL), and then concentrated under reduced pressure. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; injection volume: 2.0 mL (CH_3CN); gradient: 30→70% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.2-7.0 min, were collected and freeze-dried to give 14 mg of **S10-9-1** (96%): ^1H NMR (400 MHz, $CDCl_3$) δ 15.98 (s, 1 H), 7.54-7.24 (comp, 10 H), 5.35 (s, 2 H), 4.96-4.83 (m, 2 H), 3.94 (d, J = 9.8 Hz, 1 H), 3.47 (s, 2 H), 3.26-3.18 (m, 1 H), 3.05-2.95 (m, 1 H), 2.49 (s, 6 H), 2.23 (s, 6 H), 2.60-2.10 (comp, 4 H), 2.00 (s, 3 H), 0.82 (s, 9 H), 0.27 (s, 3 H), 0.13 (s, 3 H); MS (ESI) *m/z* 839.34 (M+H).



S10-10-1

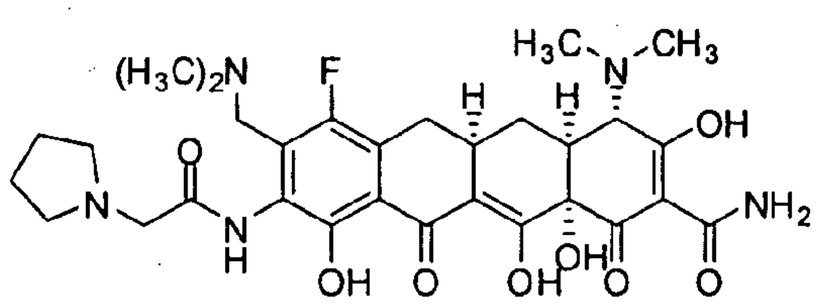
To a solution of **S10-9-1** (14 mg, 0.020 mmol) in 1,4-dioxane (3 mL) was added a solution of HF (0.3 mL of 48-50% solution in water). The mixture was stirred for 4 hrs and then quenched by potassium phosphate dibasic solution (prepared from 2 g K_2HPO_4 and 5 mL water). The mixture was extracted with EtOAc (5 mL x 3). All organic layers were combined, dried (sodium sulfate) and concentrated.

To the above residue in MeOH/dioxane solution (1:1, 4 mL) was added Pd-C (10 mg, 10wt%) and HCl in MeOH (0.5 N, 0.3 mL). The reaction was bubbled with H_2 (balloon) at 25 °C for 30 min. The mixture was filtered through a small Celite plug. The filtrate was concentrated to yield the crude product. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-1 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 2.1 mL (0.05 N HCl/water); gradient: 0→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 5.1-5.3 min, were collected and freeze-dried to yield 1 mg of **S10-10-1** (11% for 2 steps): ^{1}H NMR (400 MHz, CD_3OD) δ 4.36 (s, 2 H), 4.10 (s, 1 H), 3.05 (s, 3 H), 2.96 (s, 3 H), 2.94 (s, 6 H), 3.22-2.88 (comp, 3 H), 2.45-2.34 (m, 1 H), 2.28 (s, 3 H), 2.28-2.21 (m, 1 H), 1.73-1.61 (m, 1 H); MS (ESI) *m/z* 547.22 (M+H).



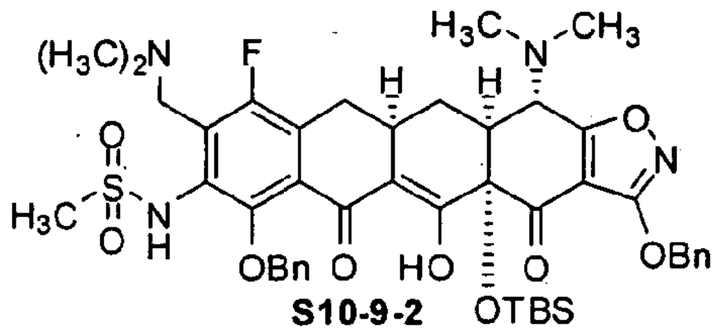
S10-10-2

S10-10-2 was prepared according to the procedure for the preparation of **S10-10-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 4.30 (s, 2 H), 4.09 (s, 1 H), 3.05 (s, 3 H), 2.96 (s, 3 H), 2.94 (s, 6 H), 3.22-2.90 (comp, 3 H), 2.46-2.36 (m, 1 H), 2.29-2.20 (comp, 1 H), 1.74-1.62 (m, 1 H), 1.39 (s, 9 H); MS (ESI) *m/z* 589.18 (M+H).



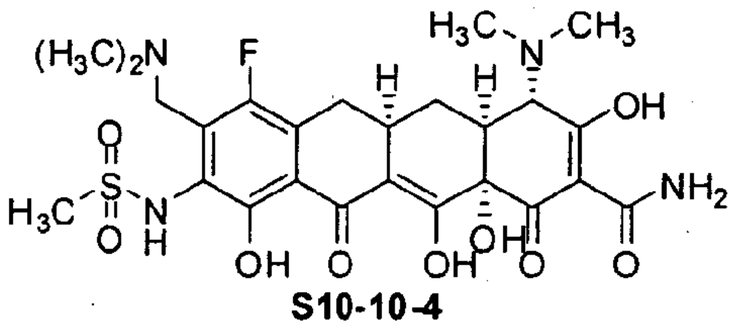
S10-10-3

S10-10-3 was prepared according to the procedure for the preparation of **S10-10-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 4.49 (s, 2 H), 4.47 (s, 2 H), 4.11 (s, 1 H), 3.86-3.76 (m, 2 H), 3.38-3.32 (m, 2 H), 3.04 (s, 3 H), 2.99 (s, 3 H), 2.96 (s, 6 H), 3.24-2.90 (comp, 3 H), 2.45-2.36 (m, 1 H), 2.30-2.00 (comp, 5 H), 1.72-1.60 (m, 1 H); MS (ESI) *m/z* 616.25 (M+H).



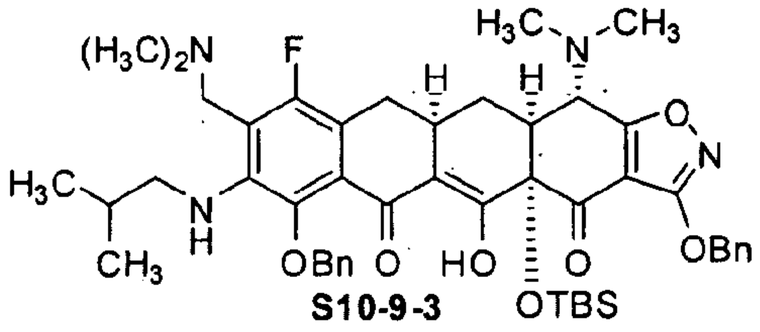
S10-9-2

To a solution of compound **S10-8** (59 mg, 0.070 mmol, 1.0 equiv) and Et_3N (0.15 mL, 1.11 mmol, 16 equiv) in dichloromethane (2 mL) was added methanesulfonic anhydride (28 mg, 0.30 mmol, 4.3 equiv). The reaction was stirred at rt for 1 h. The mixture was purified by flash chromatography on silica gel, eluting with hexanes/EtOAc (20:1 to 2:1) to afford 10 mg of compound **S10-9-2** (15%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.01 (s, 1 H), 7.54-7.24 (comp, 10 H), 5.35 (s, 2 H), 4.96 (s, 2 H), 3.93 (d, *J* = 10.4 Hz, 1 H), 3.68 (d, *J* = 13.7 Hz, 1 H), 3.62 (d, *J* = 13.7 Hz, 1 H), 3.24-3.17 (m, 1 H), 3.00 (s, 3 H), 3.06-2.98 (m, 1 H), 2.48 (s, 6 H), 2.27 (s, 6 H), 2.59-2.11 (comp, 4 H), 0.83 (s, 9 H), 0.27 (s, 3 H), 0.14 (s, 3 H); MS (ESI) *m/z* 875.38 (M+H).



S10-10-4

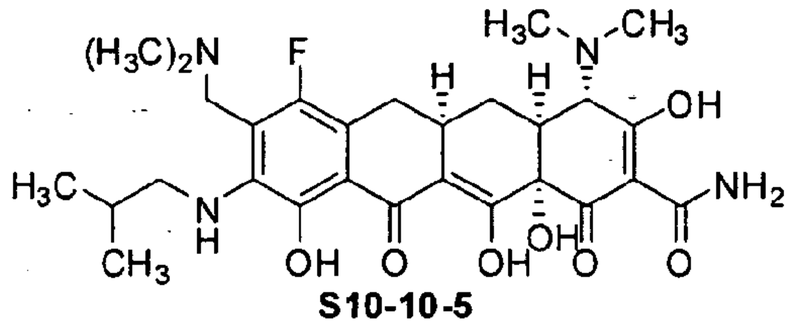
S10-10-4 was prepared from **S10-9-2** according to the procedure for the preparation of **S10-10-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 4.67 (d, *J* = 13.4 Hz, 1 H), 4.63 (d, *J* = 13.4 Hz, 1 H), 4.10 (s, 1 H), 3.11 (s, 3 H), 3.04 (s, 3 H), 2.99 (s, 3 H), 2.96 (s, 6 H), 3.24-2.90 (comp, 3 H), 2.46-2.35 (m, 1 H), 2.29-2.22 (comp, 1 H), 1.72-1.61 (m, 1 H); MS (ESI) *m/z* 583.10 (M+H).



S10-9-3

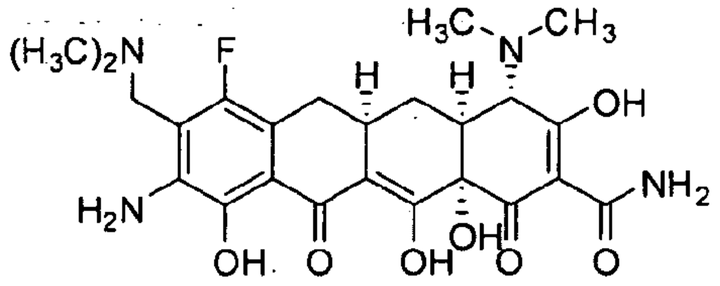
To a solution of compound **S10-8** (27 mg, 0.030 mmol, 1.0 equiv) and acetic acid (6 μL, 0.10 mmol, 3.3 equiv) in 1,2-dichloroethane (1 mL) was added isobutyraldehyde (16 μL, 0.17 mmol, 5.6 equiv). The mixture was stirred at rt for 2

hrs. $Na(OAc)_3BH$ (22 mg, 0.10 mmol, 3.3 equiv) was added, and the reaction was stirred for 3 hrs. Another portion of $Na(OAc)_3BH$ (22 mg, 0.10 mmol, 3.3 equiv) was added, and the reaction was stirred for another 3 hrs. The mixture was diluted with EtOAc (10 mL). The organic layer was washed four times with potassium phosphate dibasic solution (prepared from 0.5 g K_2HPO_4 and 1 mL water), dried (sodium sulfate) and concentrated. The residue was purified by flash chromatography on silica gel, eluting with hexanes/EtOAc (20:1 to 10:1) to afford 23 mg of compound **S10-9-3** (80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.27 (s, 1 H), 7.55-7.24 (comp, 10 H), 5.83-5.56 (br, 1 H), 5.35 (s, 2 H), 4.89 (d, J = 10.4 Hz, 1 H), 4.81 (d, J = 10.4 Hz, 1 H), 3.97 (d, J = 10.4 Hz, 1 H), 3.48 (s, 2 H), 3.22-3.07 (comp, 3 H), 2.97-2.87 (m, 1 H), 2.48 (s, 6 H), 2.55-2.30 (comp, 3 H), 2.23 (s, 6 H), 2.14-2.06 (m, 1 H), 1.78-1.66 (m, 1 H), 0.89 (d, J = 1.8 Hz, 3 H), 0.87 (d, J = 1.8 Hz, 3 H), 0.82 (s, 9 H), 0.26 (s, 3 H), 0.13 (s, 3 H); MS (ESI) *m/z* 853.39 (M+H).



S10-10-5

S10-10-5 was prepared from **S10-9-3** according to the procedure for the preparation of **S10-10-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 4.51 (s, 2 H), 4.08 (s, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 2.90 (s, 6 H), 3.21-2.82 (comp, 5 H), 2.36-2.25 (m, 1 H), 2.25-2.17 (m, 1 H), 1.93-1.81 (m, 1 H), 1.69-1.58 (m, 1 H), 1.04 (d, J = 2.4 Hz, 3 H), 1.02 (d, J = 2.4 Hz, 3 H); MS (ESI) *m/z* 561.18 (M+H).

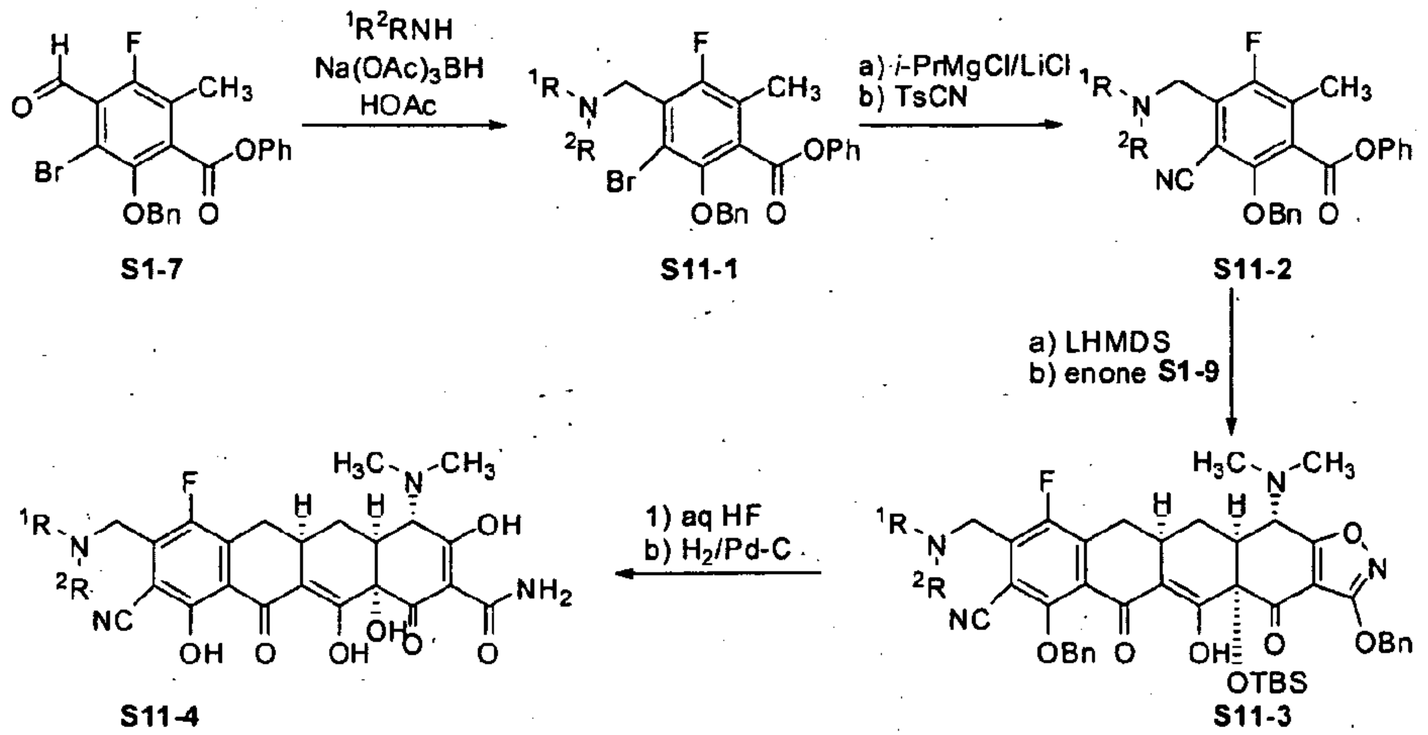


S10-10-6

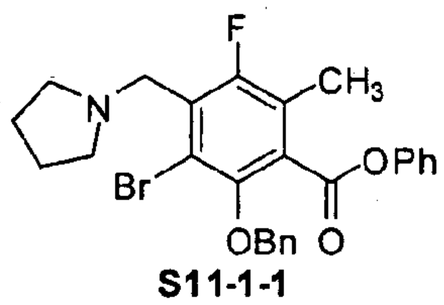
S10-10-6 was prepared from **S10-8** *via* HF treatment followed by hydrogenation according to the procedure for the preparation of **S10-10-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 4.42 (s, 2 H), 4.08 (s, 1 H), 3.14 (dd, J = 21.4, 4.9 Hz, 1 H), 3.03 (s, 3 H), 2.96 (s, 3 H), 2.92 (s, 6 H), 3.09-2.88 (comp, 2 H), 2.26-2.17 (comp, 2 H), 1.66-1.54 (m, 1 H); MS (ESI) *m/z* 505.12 (M+H).

Example 11. Synthesis of Compounds via Scheme 11.

Scheme 11

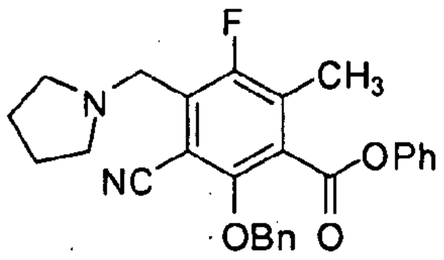


The following compounds were prepared according to Scheme 11.



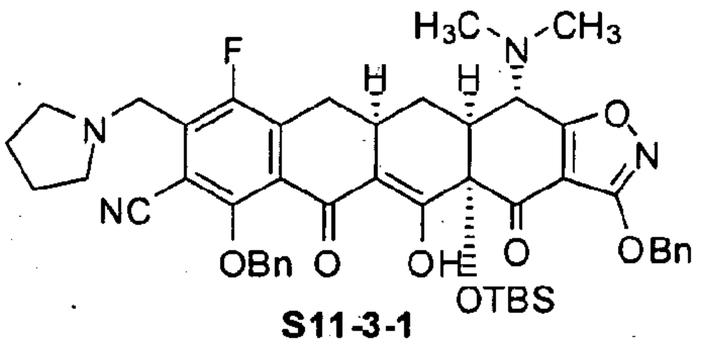
S11-1-1

Compound **S1-7** (0.44 g, 1.00 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (5 mL) and pyrrolidine (0.25 mL, 3.00 mmol, 3.0 equiv) was added *via* a syringe followed by acetic acid (0.17 mL, 3.00 mmol, 3.0 equiv) under a nitrogen atmosphere. After stirring at rt for 1 h, sodium triacetoxyborohydride (0.32 g, 1.50 mmol, 1.5 equiv) was added to reaction mixture. The reaction was stirred at rt overnight. Another 1.0 equiv of reagents were added. LC/MS indicated that the starting material was consumed after stirring for another 2 hrs. The reaction mixture was diluted with dichloromethane, washed with $NaHCO_3$ (saturated aqueous solution, 3 x 20 mL) and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give crude compound **S11-1-1** (0.53 g), which was used without further purification: ^1H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1 H), 7.53-7.49 (m, 2 H), 7.40-7.33 (m, 5 H), 7.26 (t, J = 7.8 Hz, 1 H), 7.09-7.05 (m, 2 H), 5.13 (s, 2 H), 3.94 (d, J = 2.7 Hz, 2 H), 2.66 (br, s, 2 H), 2.35 (d, J = 2.3 Hz, 3 H), 1.82-1.76 (m, 2 H).



S11-2-1

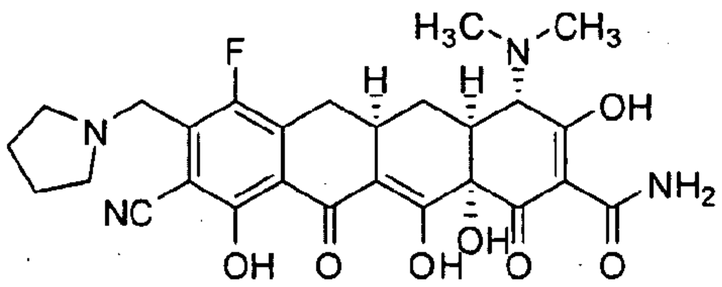
Isopropylmagnesium chloride/lithium chloride (0.30 mL, 1.2 M/THF, 0.36 mmol, 1.8 equiv) was added to compound **S11-1-1** (0.10 g, 0.20 mmol, 1.0 equiv) in THF (2 mL) under a nitrogen atmosphere at -78 °C. The resulting solution was warmed up to rt and stirred for another 45 min. After the solution was cooled down to -78 °C, TsN_3 (91 mg, 0.50 mmol, 2.5 equiv) in THF (1 mL) was added slowly *via* a syringe. The reaction was warmed to -40 °C and stirred for another 45 min. LC/MS indicated that the starting materials was consumed and the product present. The reaction mixture was allowed to slowly warm to -20 °C. Saturated aqueous sodium bicarbonate (10 mL) was added. The resulting mixture was extracted with dichloromethane (3 x 15 mL), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield crude **S11-2-1** (0.15 g) as a pale yellow oil.



S11-3-1

Compound **S11-2-1** (crude, 0.15 g, 0.20 mmol, 1.5 equiv) and enone **S1-9** (64 mg, 0.13 mmol, 1.0 equiv) were dissolved in 2 mL dry THF under a nitrogen atmosphere in a flame dried schenck flask at -78 °C. LHMDS (0.40 mL, 1.0 M/THF, 0.40 mmol, 3.1 equiv) was added slowly *via* a syringe. A red-orange color appeared. The reaction was warmed to -30 °C and stirred for another 15 min. Phosphate buffer (pH 7, 10 mL) was added, followed by the addition of 20 mL saturated aqueous ammonium chloride. The resulting mixture was extracted with dichloromethane (3 x 15 mL), and the combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The red-orange oil was purified by preparative reverse phase HPLC purification on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent

A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; injection volume: 4.0 mL (CH_3CN); gradient: 0→50% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product were collected and concentrated at rt to remove most of the acetonitrile. The resulting mostly aqueous solution was extracted with EtOAc. The EtOAc extract was dried (sodium sulfate) and concentrated to give 20 mg of compound **S11-3-1** (12% for 3 steps).



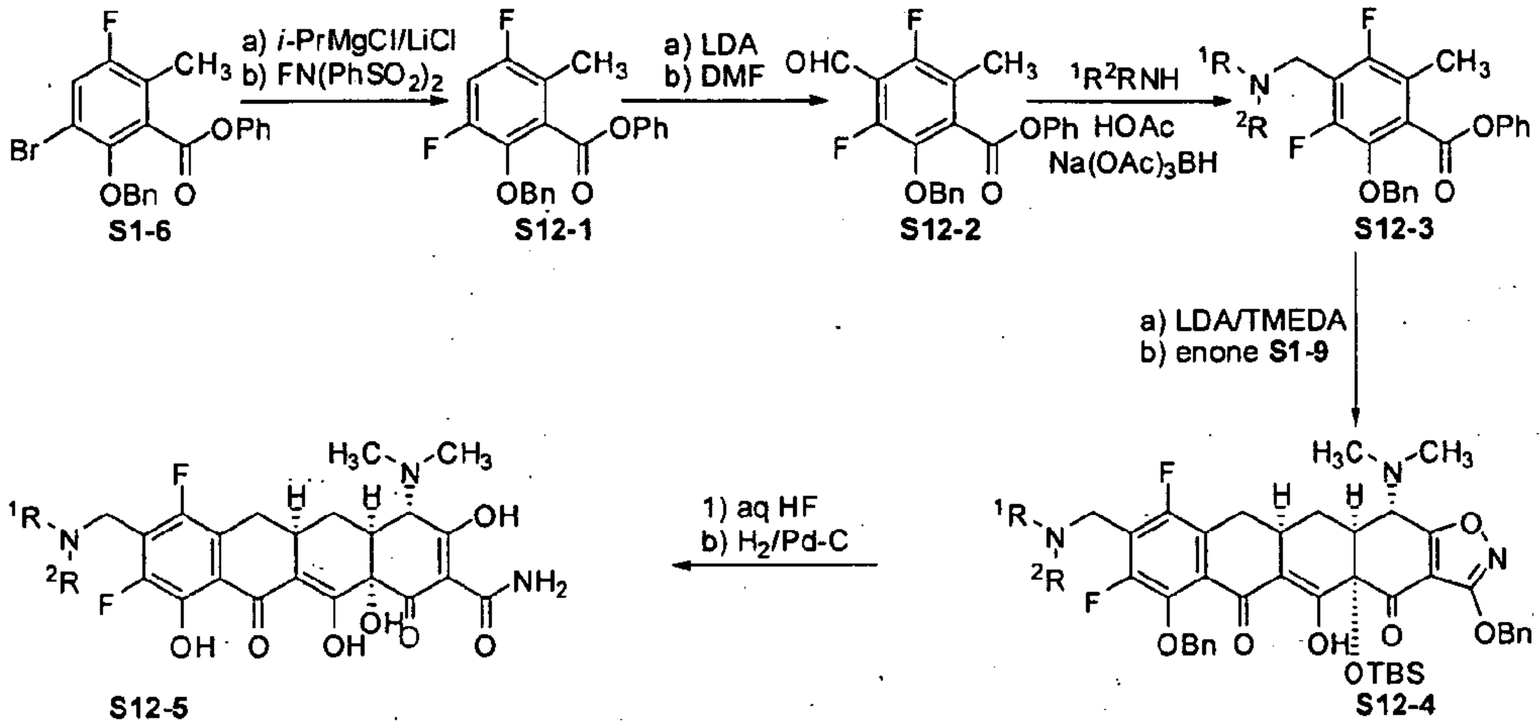
S11-4-1

Aqueous HF (0.3 mL, 48-50%) was added to a CH_3CN solution (1.0 mL) of **S11-3-1** (20 mg) in a plastic vial at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The reaction solution was poured into an aqueous solution (10 mL) of K_2HPO_4 (2 g). The mixture was extracted with EtOAc (3 x 15 mL). The combined EtOAc extracts were dried over sodium sulfate and concentrated to give the crude intermediate (18 mg).

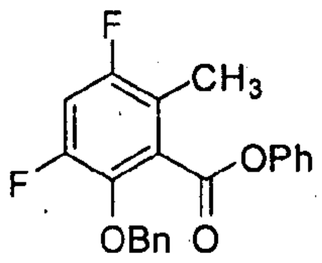
Pd-C (5 mg, 10wt%) was added to a MeOH solution (2 mL) of the above crude intermediate. HCl in MeOH (0.5 N, 0.5 mL) was added. The reaction was stirred under H_2 (balloon) at 25 °C for 45 min and filtered through a pad of Celite. The filtrate was concentrated to afford the crude product, which was purified by reverse phase HPLC on a Polymerx 10 μ RP-γ100 R column [30 × 21.20 mm, 10 micron, solvent A: 0.05 N HCl, solvent B: CH_3CN, sample in 2.0 mL (0.05 N HCl), gradient elution with 0→70% B over 15 min, mass-directed fraction collection]. Fractions containing the desired product were collected and freeze-dried, yielding 8 mg of the desired product **S11-4-1** as a yellow solid (65% for two steps): ^1H NMR (400 MHz, CD_3OD) δ 4:64 (s, 2 H), 4.12 (s, 1 H), 3.68 (m, 2 H), 3.32 (m, 2 H), 3.05 (s, 3 H), 2.96 (s, 3 H), 3.27-2.97 (m, 3 H), 2.45 (m, 1 H), 2.30-2.13 (m, 3 H), 2.13-2.00 (m, 2 H), 1.69-1.59 (m, 1 H); MS (ESI) *m/z* 541.27 (M+H).

Example 12. Synthesis of Compounds via Scheme 12.

Scheme 12

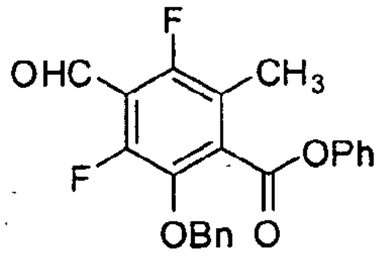


The following compounds were prepared according to Scheme 12.



S12-1

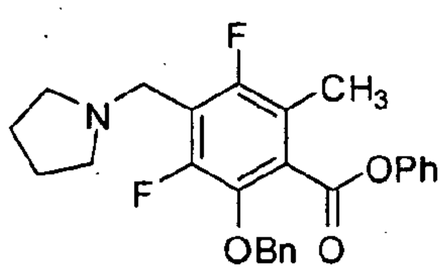
iPrMgCl•LiCl (4.00 mL, 1.2 M/THF, 4.80 mmol, 2.0 equiv) was added to a THF solution (12 mL) of **S1-6** (1.00 g, 2.40 mmol,) at 0 °C. The reaction was stirred at 0 °C for 30 min. $(PhSO_2)_2NF$ (1.50 g, 4.80 mmol, 2.0 equiv) was added to the reaction mixture. The reaction was stirred at 0 °C for 30 min and allowed to warm to 25 °C over 1 h, quenched by saturated aqueous NH_4Cl, and extracted with EtOAc. The EtOAc extract was dried (sodium sulfate) and concentrated to give the crude product. Flash chromatography on silica gel (30:1 hexanes/EtOAc) yielded 0.50 g of compound **S12-1** (59%).



S12-2

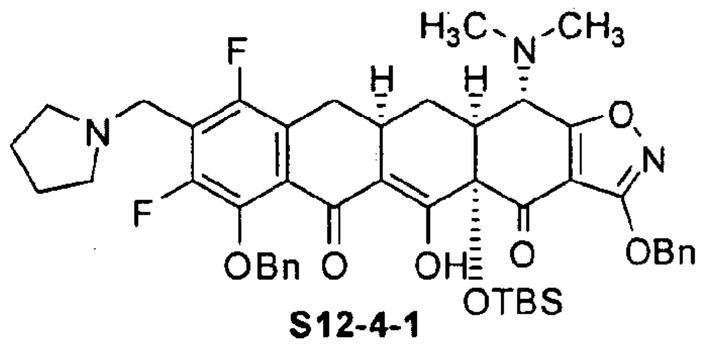
n-BuLi (6.50 mL, 1.6 M/hexanes, 10.40 mmol, 1.5 equiv) was added to a THF solution (15 mL) of diisopropylamine (1.50 mL, 10.40 mmol, 1.5 equiv) at 0 °C. The reaction was stirred at 0 °C for 30 min and cooled to -78 °C. To the mixture was added a THF solution (15 mL) of **S12-1** (2.29 g, 6.47 mmol, 1.0 equiv). The reaction was stirred at -78 °C for 20 min and DMF (1.50 mL, 19.40 mmol,

3.0 equiv) was added. The reaction was allowed to warm to 25 °C over 1 h and quenched by saturated aqueous NH_4Cl. The resulting mixture was extracted with EtOAc. The EtOAc extract was dried over sodium sulfate and concentrated. Flash chromatography on silica gel (10:1 hexanes/EtOAc) yielded 1.70 g of compound **S12-2** (69%).



S12-3-1

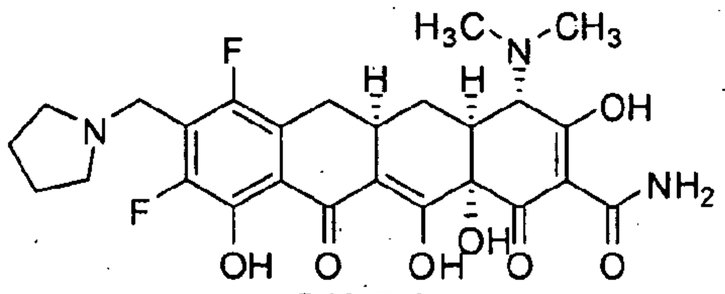
Pyrrolidine (65 µL, 0.79 mmol, 5.0 equiv), $Na(OAc)_3BH$ (68 mg, 0.32 mmol, 2.0 equiv), and HOAc (47 µL) were added to a dichloromethane solution (3 mL) of **S12-2** (60 mg, 0.16 mmol, 1.0 equiv). The reaction was stirred at 25 °C for 1 h and quenched by H_2O. The resulting mixture was extracted with dichloromethane. The dichloromethane extract was dried (sodium sulfate) and concentrated to give crude **S12-3-1**.



S12-4-1

A THF solution (1 mL) of crude **S12-3-1** (0.14 mmol, 1.7 equiv) was added to a THF solution (1 mL) of LDA (0.17 mL, 1.8 M/THF/heptane/ethylbenzene, 0.31 mmol, 3.7 equiv) and TMEDA (84 µL, 0.56 mmol, 6.7 equiv). The reaction was stirred at -78 °C for 10 min. A THF solution (1 mL) of enone **S1-9** (40 mg, 0.084 mmol, 1.0 equiv) was added to the reaction at -78 °C. The reaction was stirred at -78 °C for 30 min and allowed to warm to 25 °C over 1 h, quenched by saturated aqueous NH_4Cl, and extracted with EtOAc. The EtOAc extract was dried (sodium sulfate) and concentrated. The crude product was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 µm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; injection volume: 4.0 mL (CH_3CN); gradient: 50→100% B over 15 min; mass-directed fraction collection].

Fractions containing the desired product were collected and concentrated at 25 °C to remove most of the acetonitrile. The resulting aqueous solution was extracted with EtOAc, and the EtOAc extract was dried (sodium sulfate) and concentrated to give 16 mg of **S12-4-1** (23%).

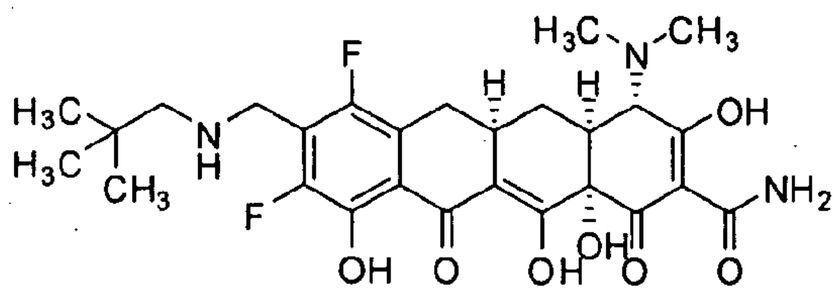


S12-5-1

Aqueous HF (0.5 mL, 48-50%) was added to a CH_3CN solution (2 mL) of **S12-4-1** (16 mg, 0.019 mmol) in a polypropylene tube at 25 °C. The reaction was stirred at 25 °C for 18 hrs. The resulting mixture was poured into an aqueous solution of K_2HPO_4 (4 g, dissolved in 30 mL water). The mixture was extracted with EtOAc, and the EtOAc extract was dried (sodium sulfate) and concentrated to yield the crude intermediate.

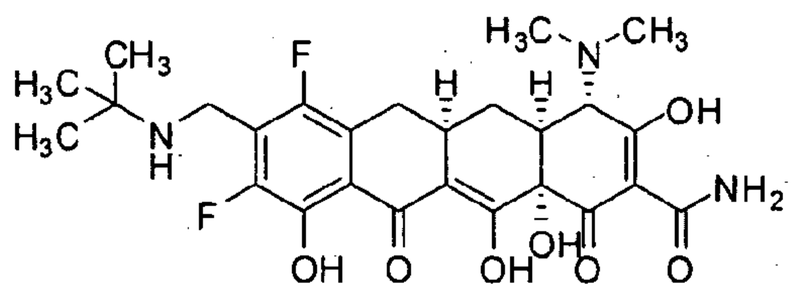
Pd-C (8 mg, 10wt%) was added to a HCl/MeOH solution (0.5N, 2 mL) of the above crude product. The reaction was purged with hydrogen and stirred under H_2 (balloon) at 25 °C for 4 hrs. The reaction mixture was filtered through a small Celite plug. The filtrate was concentrated to yield the crude product, which was purified by preparative reverse phase HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 0→70% B over 7 min, 70→100% over 3 min, and 100% over 5 min; mass-directed fraction collection]. Fractions containing the desired product were collected and freeze-dried to yield 2 mg of compound **S12-5-1**: ^{1}H NMR (400 MHz, CD_3OD) δ 4.58 (s, 2 H), 4.10 (s, 1 H), 3.71-3.67 (m, 2 H), 3.30-2.92 (m, 5 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 2.41-2.32 (m, 1 H), 2.29-2.15 (m, 3 H), 2.10-1.98 (m, 2 H), 1.72-1.60 (m, 1 H); MS (ESI) *m/z* 534.23 (M+H).

The following compounds were prepared similarly to **S12-5-1**.



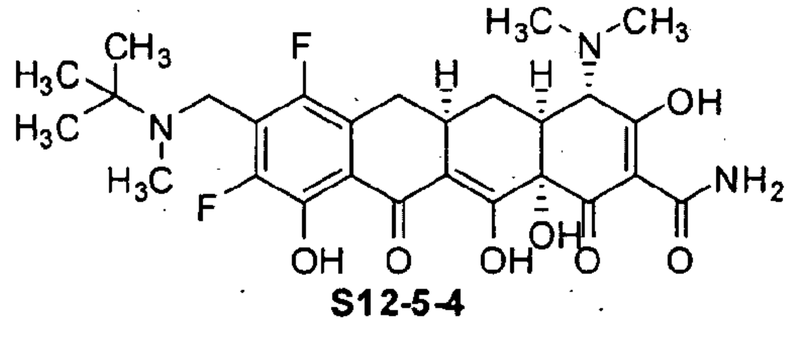
S12-5-2

S12-5-2: ^{1}H NMR (400 MHz, CD_3OD) δ 4.43 (s, 2 H), 4.08 (s, 1 H), 3.29-2.92 (m, 3 H), 3.04 (s, 3 H), 3.00 (s, 2 H), 2.96 (s, 3 H), 2.39-2.28 (m, 1 H), 2.26-2.19 (m, 1 H), 1.70-1.59 (m, 1 H), 1.06 (s, 9 H); MS (ESI) *m/z* 550.16 (M+H).



S12-5-3

S12-5-3: ^{1}H NMR (400 MHz, CD_3OD) δ 4.32 (s, 2 H), 4.10 (s, 1 H), 3.24-2.93 (m, 3 H), 3.04 (s, 3 H), 2.95 (s, 3 H), 2.39-2.20 (m, 2 H), 1.70-1.58 (m, 1 H), 1.48 (s, 9 H); MS (ESI) *m/z* 536.24 (M+H).

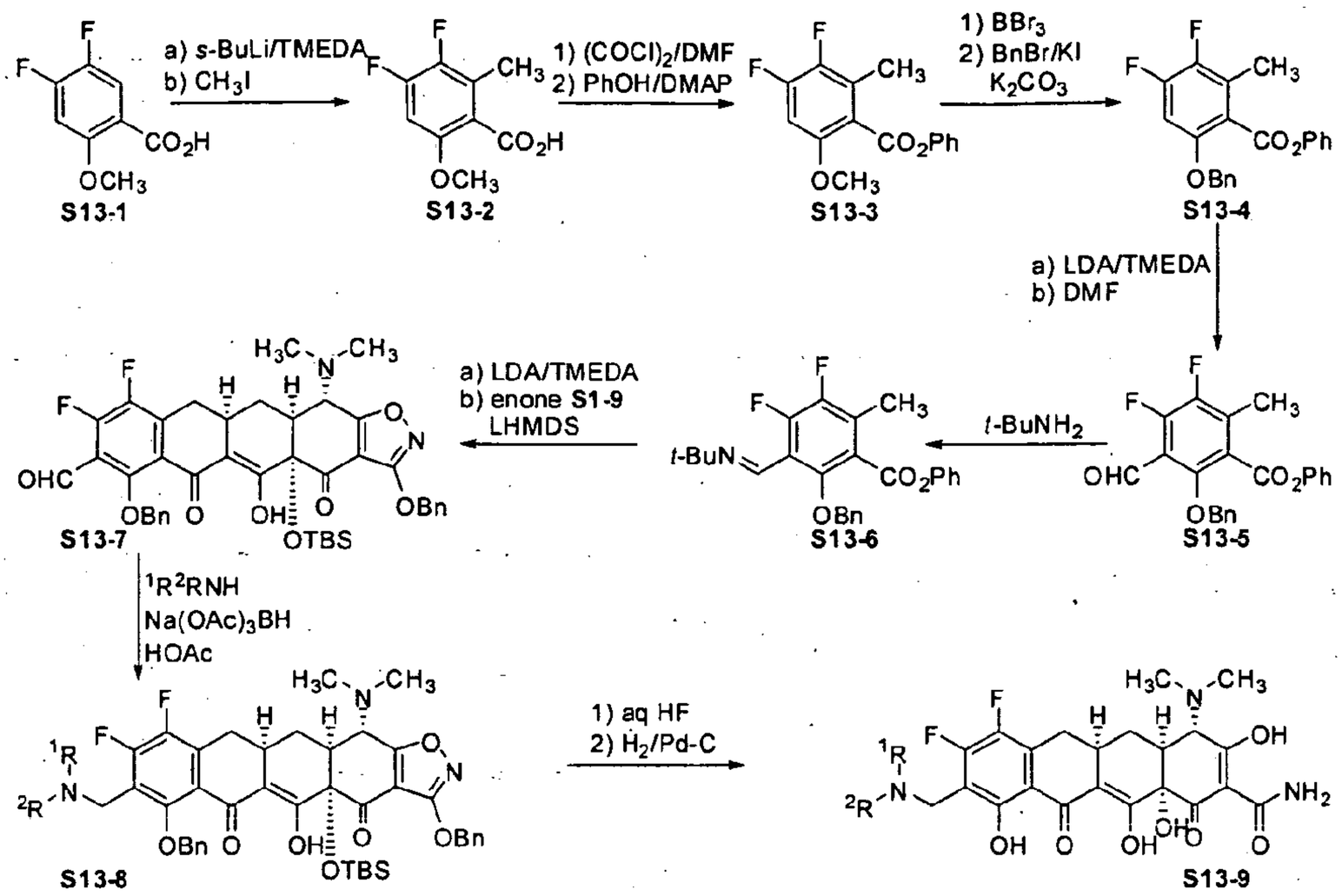


S12-5-4

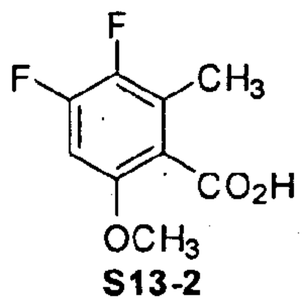
S12-5-4: ^{1}H NMR (400 MHz, CD_3OD) δ 4.19 (s, 2 H), 4.11 (s, 1 H), 3.25-2.95 (m, 3 H), 3.06 (s, 3 H), 2.96 (s, 3 H), 2.80 (s, 3 H), 2.42-2.21 (m, 2 H), 1.71-1.58 (m, 1 H), 1.58 (s, 9 H); MS (ESI) *m/z* 550.26 (M+H).

Example 13. Synthesis of Compounds via Scheme 13.

Scheme 13



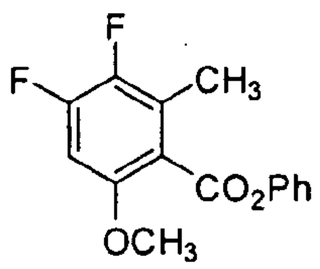
The following compounds were prepared according to Scheme 13



S13-2

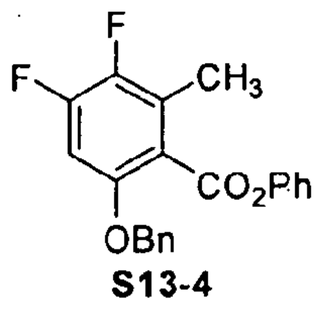
A solution of benzoic acid **S13-1** (5.00 g, 26.60 mmol, 1.0 equiv) in THF (40 mL) was added dropwise to a solution of *s*-BuLi (41.76 mL, 1.4 M/cyclohexane, 58.50 mmol, 2.2 equiv) and TMEDA (8.77 mL, 58.50 mmol, 2.2 equiv) in THF (40 mL) at -78 °C *via* a cannula over 30 min. The resulting red-orange thick reaction mixture was stirred at -78 °C for 2 hrs, slowly changing to a yellow brownish suspension. Iodomethane (8.30 mL, 133.00 mmol, 5.0 equiv) was added at -78 °C slowly. The resulting yellow suspension was then stirred at rt for 30 min. Water (50 mL) was added, and the resulting mixture was concentrated to remove most of the THF. Aqueous NaOH (40 mL, 6 N) was added, and the resulting mixture was extracted with methyl *t*-butyl ether (2 x 60 mL). The combined organic phases were extracted with aqueous NaOH (40 mL, 3 N). The combined aqueous layers were acidified with 6 N HCl (~ 65 mL) to pH 1, and extracted with EtOAc (120 mL, then

80 mL). The combined EtOAc extracts were dried over magnesium sulfate, filtered and concentrated to afford crude **S13-2** as an orange solid (**S13-2**:regio*n*-isomer:**S13-1** = ~1.2:0.8:1 by ^{1}H NMR).



S13-3

The above crude product was dissolved in dry dichloromethane (100 mL). Oxalyl chloride (2.78 mL, 31.89 mmol, 1.2 equiv) was added, followed by a few drops of DMF. The reaction mixture was stirred at rt for 1h, concentrated and further dried under high vacuum. The residue was re-dissolved in dry dichloromethane (100 mL). Phenol (2.75 g, 29.26 mmol, 1.1 equiv), triethylamine (7.40 mL, 53.20 mmol, 2.0 equiv), and DMAP (0.10 g, 0.82 mmol, 0.03 equiv) were added. The reaction mixture was stirred at rt for 1h. The solvent was evaporated and the residue was dissolved in EtOAc (200 mL). The organic layer was washed with 1 N HCl (60 mL), 1 N NaOH (70 mL), water (50 mL) and brine (60 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography (1-4% EtOAc/hexanes) to afford the desired product **S13-3** as a white solid (1.39 g, 19% over two steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.43 (m, 2 H), 7.31-7.29 (m, 1 H), 7.26-7.24 (m, 2 H), 6.67 (dd, *J* = 6.0, 11.4 Hz, 1 H), 3.84 (s, 3 H), 2.41 (s, 3 H); MS (ESI) *m/z* 277.22 (M-H).

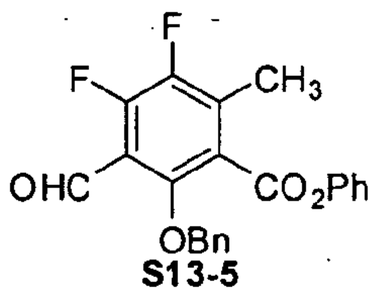


S13-4

A solution of BBr_3 in dichloromethane (6.00 mL, 1.0 M, 6.00 mmol, 1.2 equiv) was added slowly to compound **S13-3** (1.39 g, 5.00 mmol, 1.0 equiv) in dichloromethane (25 mL) at -78 °C. The resulting orange solution was allowed to warm to 0 °C in 30 min and kept at that temperature for 10 min [monitored by LC-MS or TLC (product is slightly more polar)]. Saturated aqueous $NaHCO_3$ was added. The mixture was stirred at rt for 5 min and dichloromethane was evaporated. The residue was extracted with EtOAc (60 mL, then 20 mL). The organic extracts

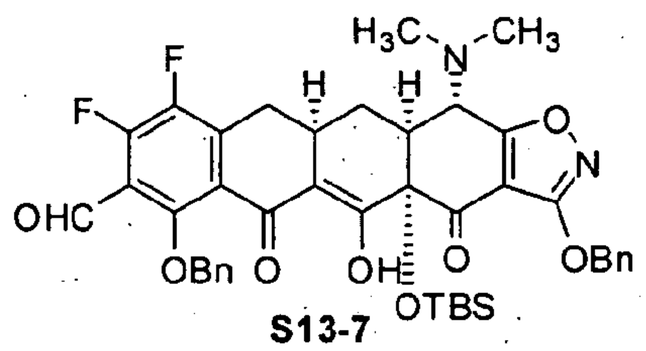
were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated to give the crude intermediate (1.27 g) as a waxy solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.07 (s, 1 H), 7.47-7.44 (m, 2 H), 7.34-7.30 (m, 1 H), 7.19-7.17 (m, 2 H), 6.69 (dd, J = 6.7, 11.0 Hz, 1 H), 2.63 (d, J = 3.0 Hz, 3 H); MS (ESI) *m/z* 263.20 (M-H).

Benzylbromide (0.24 mL, 2.04 mmol, 1.2 equiv), K_2CO_3 powder (0.47 g, 3.41 mmol, 2.0 equiv) and KI (14 mg, 0.085 mmol, 0.05 equiv) were added to the above crude intermediate (0.45 g, 1.70 mmol, 1.0 equiv) in acetone (3.4 mL). The mixture was heated at reflux for 4.5 hrs, cooled to rt, and diluted with EtOAc (50 mL) and water (30 mL). The organic phase was separated, washed with brine, dried over magnesium sulfate, and concentrated. The residue was purified by flash column chromatography (1-4% EtOAc/hexanes) to afford the desired product **S13-4** as a crystalline white solid (0.50 g, 79% over 2 steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.31 (m, 7 H), 7.28-7.24 (m, 1 H), 7.10-7.08 (m, 2 H), 6.71 (dd, J = 6.1, 11.6 Hz, 1 H), 5.10 (s, 2 H), 2.41 (d, J = 1.8 Hz, 3 H); MS (ESI) *m/z* 353.21 (M-H).



S13-5

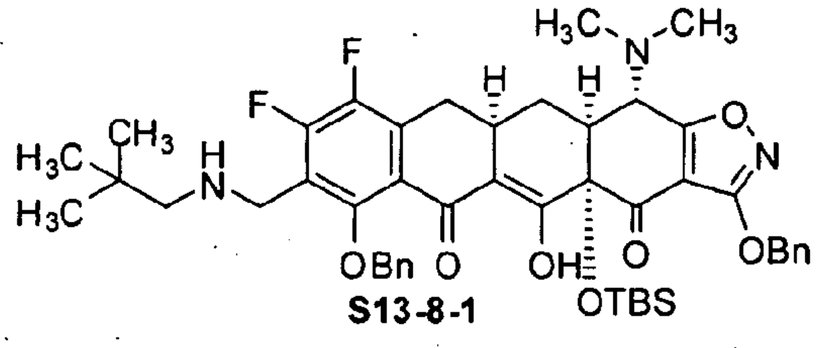
A solution of compound **S13-4** (0.38 g, 1.08 mmol, 1.0 equiv) in THF (4 mL) was added *via* a cannula dropwise to a solution of LDA (1.01 mL, 1.62 mmol, 1.5 equiv) and TMEDA (0.24 mL, 1.62 mmol, 1.5 equiv) in THF (6 mL) at -78 °C. The resulting red orange solution was stirred at -78 °C for 5 min. DMF (0.17 mL, 2.16 mmol, 2.0 equiv) was added. The reaction was stirred at -78 °C for 1 h. Saturated aqueous NH_4Cl (30 mL) was added dropwise to the reaction mixture at -78 °C. The resulting mixture was then warmed up to rt and extracted with EtOAc (60 mL, then 20 mL). The combined EtOAc extracts were dried (sodium sulfate), filtered and concentrated. The residue was purified by flash column chromatography (1-20% EtOAc/hexanes) to afford the desired product **S13-5** as a colorless oil (0.26 g, 62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.35 (m, 7 H), 7.29-7.25 (m, 1 H), 7.06-7.04 (m, 2 H), 5.10 (s, 2 H), 2.48 (d, J = 2.4 Hz, 3 H); MS (ESI) *m/z* 381.24 (M-H).



S13-7

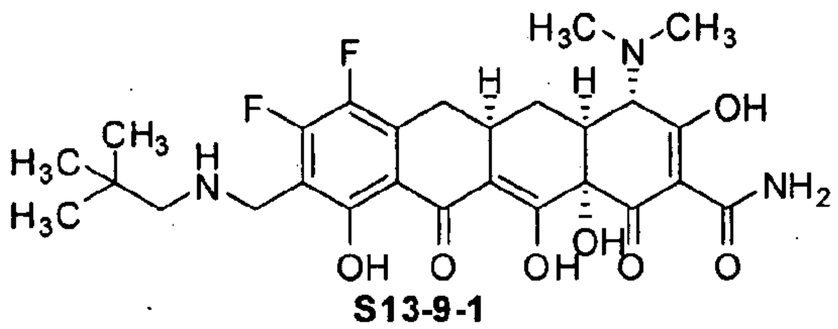
t-$BuNH_2$ (96 μL, 0.91 mmol, 5.0 equiv) was added to a mixture of aldehyde **S13-5** (69 mg, 0.18 mmol, 1.0 equiv) and sodium sulfate in toluene (1 mL). The resulting light greenish reaction mixture was stirred at rt overnight. The solids were filtered off. The filtrate was concentrated under reduced pressure to afford the crude imine, which was used directly in the next step.

A solution of the above imine (0.18 mmol, 1.0 equiv) in THF (1.5 mL) was added *via* a cannula dropwise to a solution of LDA (0.16 mL, 0.26 mmol, 1.4 equiv) and TMEDA (38 μL, 0.26 mmol, 1.4 equiv) in THF (4 mL) at -78 °C. The resulting red-purple reaction mixture was then stirred at -78 °C for 5 min. A solution of enone **S1-9** (70 mg, 0.15 mmol, 0.8 equiv) in THF (1.5 mL) was added *via* a cannula. The resulting dark purple solution was stirred at -78 °C for 8 min, and LHMDS solution (0.18 mL, 1.0 M/THF, 0.18 mmol, 1.0 equiv) was added. The reaction mixture was warmed to -10 °C over 1 h 25 min, quenched by saturated aqueous NH4Cl (20 mL), and extracted with EtOAc (50 mL, then 20 mL). The combined EtOAc extracts were dried (sodium sulfate), filtered and concentrated. The residue was purified by a preparative reverse phase HPLC on a Waters Autopurification system using a Sunfire Prep C18 OBD column [5 μm, 19 × 50 mm; flow rate, 20 mL/min; Solvent A: H_2O with 0.1% HCO_2H; Solvent B: CH_3CN with 0.1% HCO_2H; injection volume: 4.0 mL (CH_3CN); gradient: 80→100% B in A over 10 min; mass-directed fraction collection]. Fractions containing the desired product were collected and concentrated at rt to yield the desired product **S13-7** (23 mg, 20%): ^1H NMR (400 MHz, $CDCl_3$) δ 15.85 (br s, 1 H), 10.10 (s, 1 H), 7.70-7.68 (m, 1 H), 7.52-7.49 (m, 3 H), 7.40-7.31 (m, 6 H), 5.36 (s, 2 H), 5.06, 4.98 (ABq, J = 10.4 Hz, 2 H), 3.91 (d, J = 11.0 Hz, 1 H), 3.34 (dd, J = 4.3, 15.9 Hz, 1 H), 3.07-3.00 (m, 1 H), 2.61-2.58 (m, 1 H), 2.54-2.34 (m, 2 H), 2.50 (s, 6 H), 2.20-2.16 (m, 1 H), 0.82 (s, 9 H), 0.28 (s, 3 H), 0.14 (s, 3 H); MS (ESI) *m/z* 771.53 (M+H).



S13-8-1

Neopentylamine (17 μL, 0.15 mmol, 5.0 equiv), acetic acid (8 μL, 0.15 mmol, 5.0 equiv) and sodium triacetoxyborohydride (12 mg, 0.058 mmol, 2.0 equiv) were added sequentially to a solution of aldehyde **S13-7** (23 mg, 0.029 mmol, 1.0 equiv) in 1,2-dichloroethane (1 mL) at 23 °C. After stirring for 1 h, the reaction mixture was quenched by the addition of saturated aqueous sodium bicarbonate and pH 7 phosphate buffer (1:1, 15 mL) and extracted with dichloromethane (50 mL). The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated to afford crude **S13-8-1**, which was used directly in the next step.

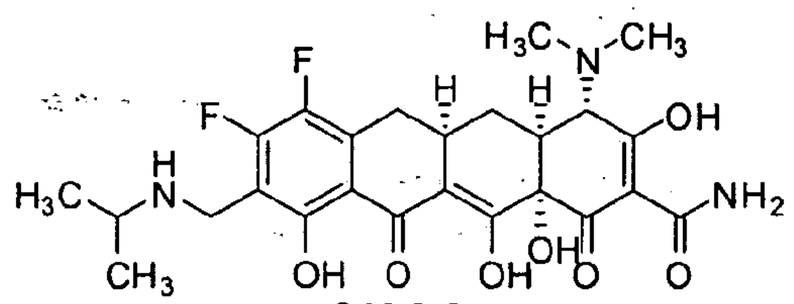


S13-9-1

Aqueous HF (48-50%, 0.3 mL) was added to a solution of compound **S13-8-1** in acetonitrile (0.7 mL) in a polypropylene reaction vessel at 23 °C. The reaction was stirred vigorously at 23 °C overnight and poured into aqueous K_2HPO_4 (3.6 g dissolved in 20 mL water). The mixture was extracted with EtOAc (2 x 25 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was used directly in the next step without further purification.

Pd-C (10wt%, 7 mg) was added into a solution of the above crude product in a mixture of HCl/MeOH (0.5 N, 0.12 mL, 2.0 equiv) and MeOH (2 mL) at 23 °C. The reaction vessel was sealed and purged with hydrogen by briefly evacuating the flask followed by flushing with hydrogen gas (1 atm). The reaction was stirred at 23 °C for 30 min. The reaction mixture was then filtered through a small Celite pad. The filtrate was concentrated. The residue was purified by a preparative reverse phase HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-1 100A column [10 μm, 150 × 21.20 mm; flow rate, 20 mL/min; Solvent A:

0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 3.0 mL (0.05 N HCl/water); gradient: 5→40% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 12.6-13.1 min, were collected and freeze-dried to yield compound **S13-9-1** (4 mg, 23% for 3 steps): ^{1}H NMR (400 MHz, CD_3OD) δ 4.38 (s, 2 H), 4.10 (s, 1 H), 3.11-2.96 (m, 11 H), 2.39 (t, J = 15.1 Hz, 1 H), 2.26-2.23 (m, 1 H), 1.70-1.60 (m, 1 H), 1.07 (s, 9 H); MS (ESI) *m/z* 550.40 (M+H).

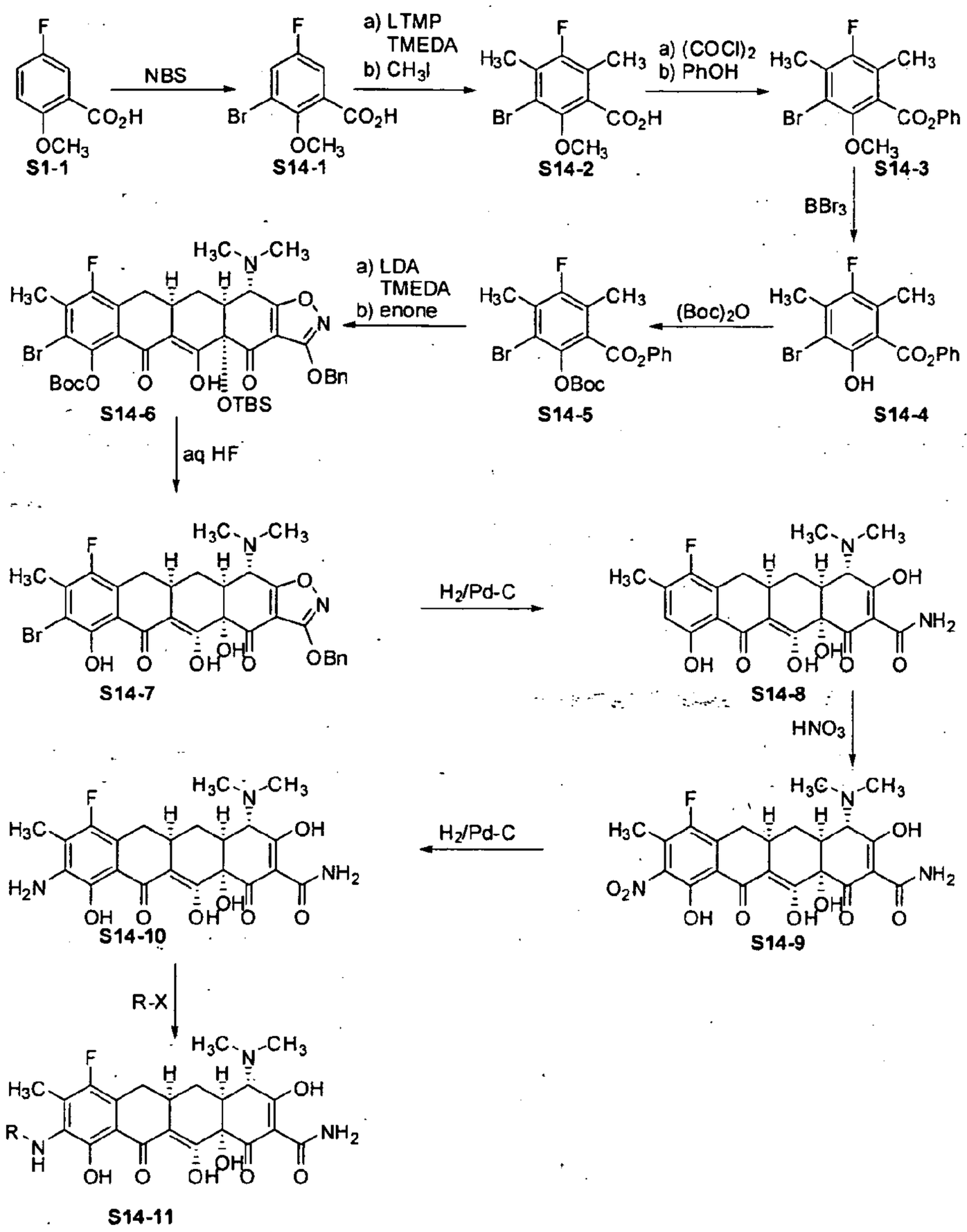


S13-9-2

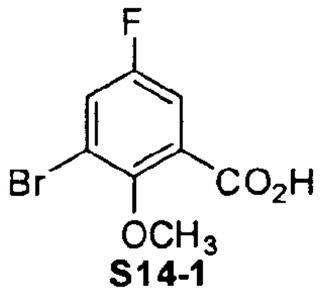
S13-9-2 was prepared similarly: ^{1}H NMR (400 MHz, CD_3OD) δ 4.31 (s, 2 H), 4.11 (s, 1 H), 3.57-2.50 (hept, J = 6.4 Hz, 1 H), 3.04-2.96 (m, 9 H), 2.39 (t, J = 15.1Hz, 1 H), 2.27-2.24 (m, 1 H), 1.70-1.60 (m, 1 H), 1.43 (t, J = 6.4 Hz, 6 H); MS (ESI) *m/z* 522.41 (M+H).

Example 14. Synthesis of Compounds via Scheme 14.

Scheme 14

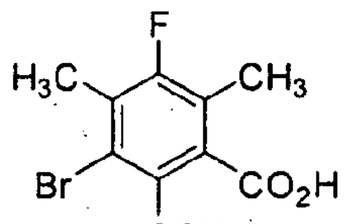


The following compounds were prepared according to Scheme 14.



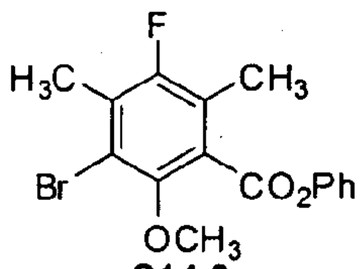
To compound **S1-1** (5.00 g, 29.38 mmol, 1.0 equiv) in sulfuric acid (10 mL) and trifluoroacetic acid (20 mL) at rt was added NBS (5.75 g, 32.30 mmol, 1.1 equiv). The pale solution was stirred at rt for 3 hrs. The resulting pale suspension was carefully poured onto 500 g crushed ice. The mixture was extracted with EtOAc

(200 mL x 1, 100 mL x 3). The EtOAc extracts were combined, dried over sodium sulfate, and concentrated under reduced pressure. The light yellow residue was suspended in minimum dichloromethane. The solid was collected, washed with cold dichloromethane (5 mL x 3), and dried under vacuum overnight to yield the desired product **S14-1** as a white crystalline solid (5.49 g, 75%): R_f 0.55 (0.5% HOAc/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74-7.77 (m, 1 H), 7.24-7.55 (m, 1 H), 4.01 (s, 3 H); MS (ESI) *m/z* 247.1 (M-H), calcd for $C_8H_6BrFO_3$ 248.0.



S14-2

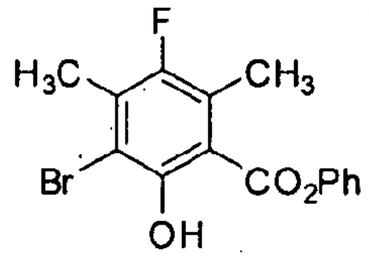
To compound **S14-1** (0.25 g, 1.00 mmol, 1.0 equiv) in anhydrous THF (5 mL) at -78 °C was added TMEDA (0.75 mL, 5.00 mmol, 5.0 equiv) and LTMP (4.00 mmol, freshly prepared, in 4 mL THF) dropwise. The cloudy deep red solution was stirred at -78 °C for 30 min. Iodomethane (0.31 mL, 5.00 mmol, 5.0 equiv) was added dropwise at -78 °C. The resulting pale suspension was allowed to warm to rt and was stirred overnight. Aqueous HCl (1 N) was added to the reaction until pH 1-2. The mixture was extracted with EtOAc (100 mL x 1, 20 mL x 3). The EtOAc extracts were combined, dried over sodium sulfate, and concentrated under reduced pressure to afford crude **S14-2** as an orange solid (0.30 g).



S14-3

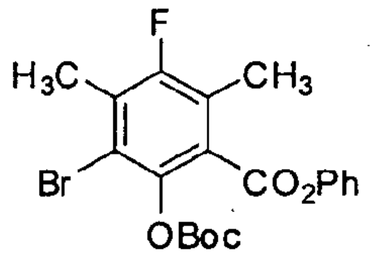
The compound **S14-2** was dissolved in dry dichloromethane (10 mL). Anhydrous DMF (2 drops) and oxalyl chloride (0.43 mL, 5.00 mmol, 5.0 equiv) were added dropwise at rt. The yellow solution was stirred at rt for 30 min and concentrated under reduced pressure. The residue was redissolved in dry dichloromethane (10 mL). Phenol (0.14 g, 1.50 mmol, 1.5 equiv), DIEA (0.70 mL, 4.00 mmol, 4.0 equiv), and DMAP (12 mg, 0.10 mmol, 0.1 equiv) were added. The reaction was stirred at rt overnight, diluted with saturated aqueous sodium bicarbonate (50 mL), and extracted with dichloromethane (50 mL x 3). The

dichloromethane extracts were combined, dried over sodium sulfate, and concentrated under reduced pressure. Flash column chromatography on silica gel using 0% to 5% EtOAc/hexanes yielded the desired product **S14-3** as a pale oil (0.13 g, 37%, 2 steps): R_f 0.70 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.50 (m, 2 H), 7.16-7.23 (m, 3 H), 3.94 (s, 3 H), 2.38 (s, 3 H), 2.32 (s, 3 H); MS (ESI) *m/z* 351.1 (M-H), calcd for $C_{16}H_{14}BrFO_3$ 352.0.



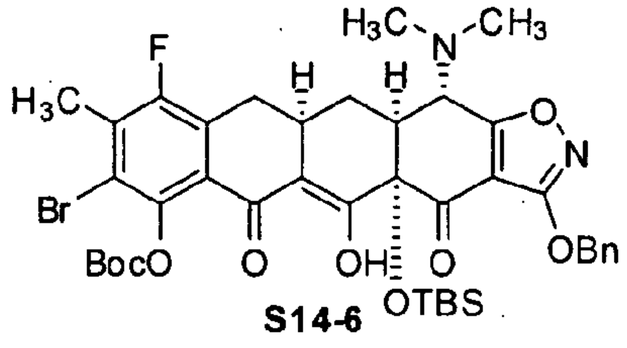
S14-4

Compound **S14-3** (0.13 g, 0.37 mmol, 1.0 equiv) was dissolved in anhydrous dichloromethane (4 mL) and the solution was cooled to -78 °C. BBr_3 (0.93 mL, 1.0 M/dichloromethane, 0.93 mmol, 2.5 equiv) was added dropwise. The orange-brown solution was warmed to -10 °C with stirring over a period of 2 hrs. The reaction was quenched by saturated aqueous sodium bicarbonate (20 mL) and extracted with EtOAc (20 mL x 3). The extracts were combined, dried over sodium sulfate, and concentrated under reduced pressure to yield crude **S14-4** as a pale solid (0.13 g).



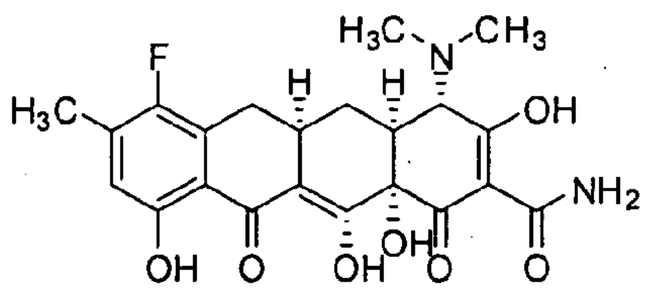
S14-5

Phenol **S14-4** was dissolved in dichloromethane. Di-*t*-butyl dicarbonate (0.12 g, 0.56 mmol, 1.5 equiv), DIEA (0.13 mL, 0.74 mmol, 2.0 equiv), and DMAP (5 mg, 0.040 mmol, 0.1 equiv) were added. The reaction was stirred at rt overnight and concentrated under reduced pressure. Flash column chromatography on silica gel using 0% to 2% EtOAc/hexanes yielded the desired compound **S14-5** as a white solid (0.14 g, 88%, 2 steps): R_f 0.25 (3% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 77.40-7.49 (m, 2 H), 7.18-7.32 (m, 3 H), 2.42 (d, J = 3.0 Hz, 3 H), 2.38 (d, J = 2.5 Hz, 3 H), 1.45 (s, 9 H); MS (ESI) *m/z* 437.1 (M-H), calcd for $C_{20}H_{20}BrFO_3$ 438.0.



S14-6

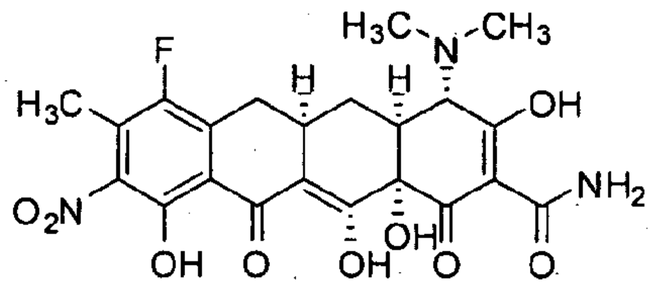
To diisopropylamine (0.090 mL, 0.64 mmol, 5.0 equiv) in anhydrous THF at -78 °C was added *n*-BuLi (0.40 mL, 1.6 M/hexanes, 0.64 mmol, 5.0 equiv). The colorless solution was stirred at 0 °C for 10 min and cooled to -78 °C. TMEDA (0.29 mL, 1.92 mmol, 15 equiv) was added, followed by the dropwise addition of compound **S14-5** (0.14 g, 0.32 mmol, 2.5 equiv, in 3 mL THF) over a period of 5 min. The deep red solution was stirred at -78 °C for 15 min. Enone **S1-9** (62 mg, 0.13 mmol, 1.0 equiv, in 3 mL THF) was added. The reaction was warmed from -78 °C to -10 °C with stirring over a period of 30 min, quenched by HOAc (0.12 mL) and saturated aqueous ammonium chloride (50 mL), and extracted with EtOAc (100 mL x 1, 50 mL x 2). The EtOAc extracts were combined, dried over sodium sulfate, and concentrated under reduced pressure. Reverse phase HPLC purification yielded the desired product **S14-6** as a light-yellow solid (36 mg, 34%): R_f 0.45 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.69 (br s, 1 H), 7.45-7.50 (m, 2 H), 7.30-7.40 (m, 3 H), 5.34 (s, 2 H), 3.97 (br s, 1 H), 3.20-3.30 (br m, 1 H), 2.98-3.07 (br m, 1 H), 2.1-2.7 (m, 11 H), 1.5-1.6 (m, 11 H), 0.80 (s, 9 H), 0.23 (s, 3 H), 0.11 (s, 3 H); MS (ESI) *m/z* 827.3 (M+H), calcd for $C_{40}H_{48}BrFN_3O_9Si$ 826.2.



S14-8

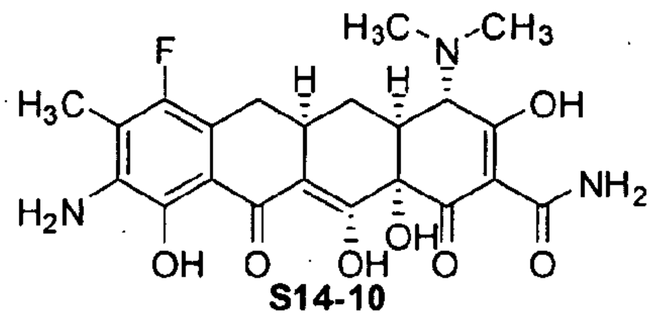
Compound **S14-6** (36 mg, 0.044 mmol) was dissolved in acetonitrile (1.5 mL). Aqueous HF (0.75 mL, 48-50%) was added. The yellow solution was stirred at rt overnight, diluted with aqueous K_2HPO_4 (3.2 g in 16 mL water), and extracted with dichloromethane (20 mL x 3). The dichloromethane extracts were combined, dried over sodium sulfate, and concentrated under reduced pressure to yield crude **S14-7** as a bright-yellow solid (31 mg): MS (ESI) *m/z* 613.2 (M+H), calcd for $C_{29}H_{26}BrFN_2O_7$ 612.1.

The above crude product **S14-7** was dissolved in MeOH (4 mL) and dioxane (2 mL). 10% Pd-C (19 mg, 0.0090 mmol, 0.2 equiv) was added. The mixture was purged with hydrogen and stirred under 1 atm hydrogen atmosphere at rt for 1 h. The catalyst was filtered off with a small Celite pad and washed with MeOH (5 mL x 3). The yellow filtrate was concentrated under reduced pressure to yield crude **S14-8** as a yellow solid (27 mg). 10% of the crude product was purified with reverse phase HPLC using similar conditions for **S2-4-1** to yield compound **S14-8** as a yellow solid (2 mg, 71%, 2 steps, HCl salt): ^{1}H NMR (400 MHz, CD_3OD) δ 6.69 (d, J = 6.1 Hz, 1 H), 4.06 (s, 1 H), 2.80-3.50 (m, 3 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 2.10-2.40 (m, 2 H), 2.27 (s, 3 H), 1.56-1.68 (m, 1 H); MS (ESI) *m/z* 447.1 (M+H), calcd for $C_{22}H_{23}FN_2O_7$ 446.2.



S14-9

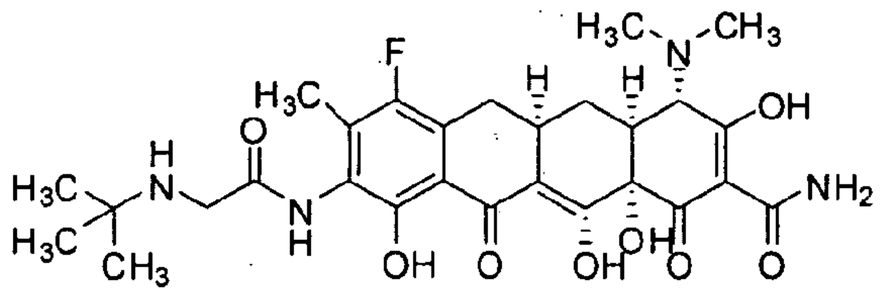
Compound **S14-8** (90% of crude from above, 0.40 mmol) was dissolved in cold sulfuric acid (2 mL, 0 °C). Nitric acid (0.12 mL, 0.5 M in sulfuric acid, 0.060 mmol, 1.5 equiv) was added. The deep brown solution was stirred at 0 °C for 1 h. The resulting deep red solution was added dropwise into ether (100 mL) with stirring. The yellow solid was collected onto a small Celite pad, washed with ether (5 mL x 4, discarded), and eluted with MeOH (5 mL x 3). The yellow MeOH solution was collected and concentrated under reduced pressure to yield the desired compound **S14-9** as a yellow solid (27 mg): MS (ESI) *m/z* 492.3 (M+H), calcd for $C_{22}H_{22}FN_3O_9$ 491.1.



S14-10

Compound **S14-9** (25 mg, 0.036 mmol) was dissolved in MeOH (4 mL). 10% Pd-C (15 mg, 0.0070 mmol, 0.2 equiv) was added. The mixture was purged with hydrogen and stirred at rt under 1 atm hydrogen atmosphere for 4 hrs. The

catalyst was filtered off with a small Celite pad and washed with MeOH (5 mL x 3). The yellow filtrate was concentrated under reduced pressure. HPLC purification using similar conditions for **S2-4-1** yielded the desired product **S14-10** as a deep red solid (6 mg, 31%, 3 steps, bis-HCl salt): ^{1}H NMR (400 MHz, CD_3OD) δ 4.09 (s, 1 H), 2.80-3.50 (m, 3 H), 3.03 (s, 3 H), 2.95 (s, 3 H), 2.30-2.40 (m, 1 H), 2.34 (s, 3 H), 2.19-2.27 (m, 1 H), 1.60-1.62 (m, 1 H); MS (ESI) *m/z* 462.1 (M+H), calcd $C_{22}H_{24}FN_3O_7$ 461.2.

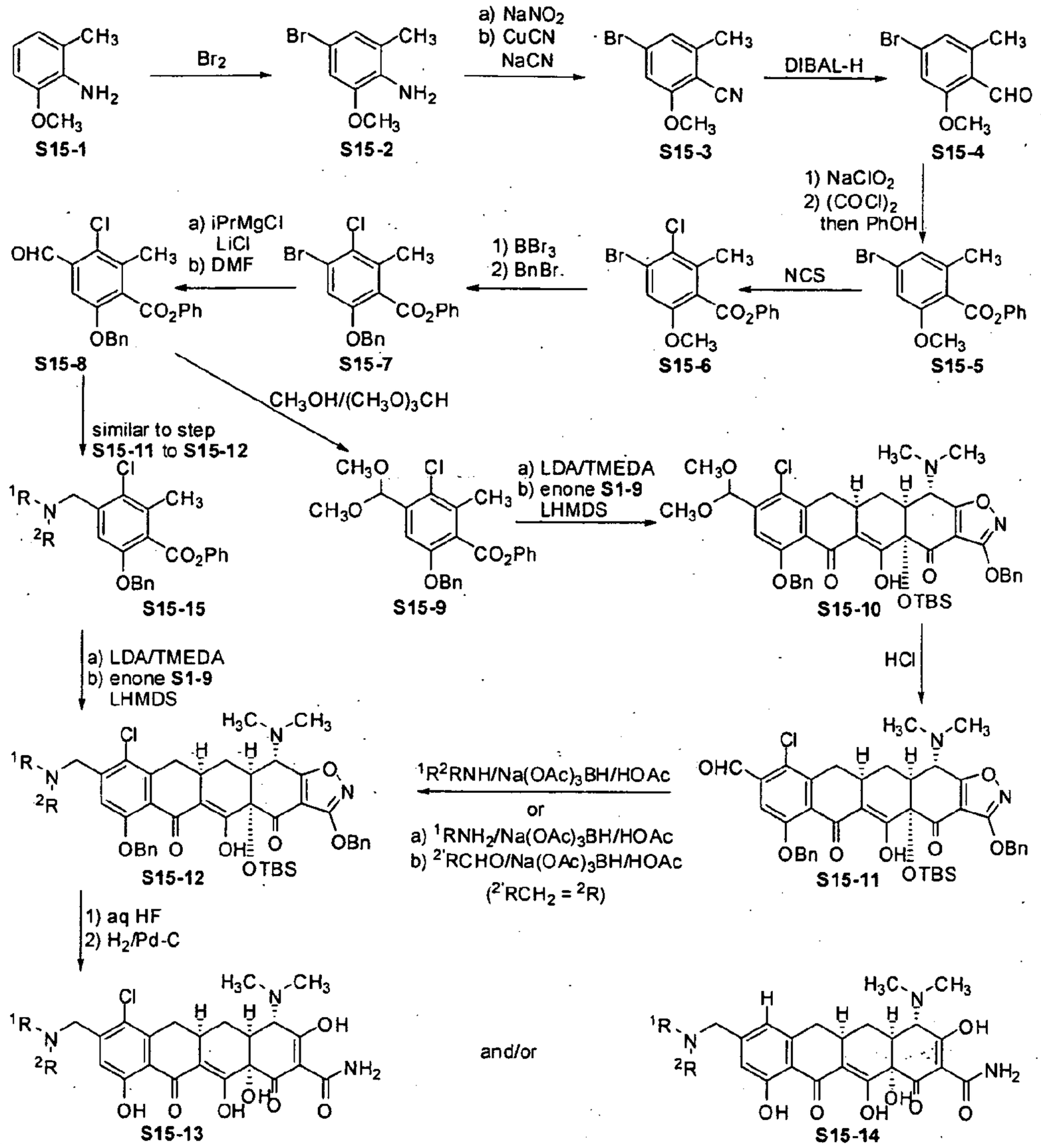


S14-11-1

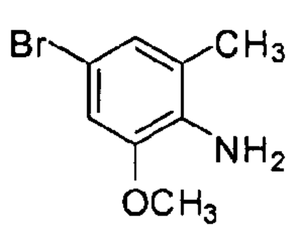
Compound **S14-10** (4 mg, 0.0075 mmol, 1.0 equiv) was dissolved in acetonitrile/DMPU (0.1 mL, 1:1 v/v). *t*-Butylaminoacetyl chloride (2 mg, HCl salt, 0.011 mmol, 1.5 equiv, prepared by treating *t*-butylaminoacetic acid with excess thionyl chloride followed by concentration under reduced pressure) was added. The deep red solution was stirred at rt for 3 hrs and quenched by aqueous HCl (2 mL, 0.1 N). HPLC purification using similar conditions for **S2-4-1** yielded the desired product **S14-11** as a yellow solid (2 mg, 41%, bis-HCl salt): ^{1}H NMR (400 MHz, CD_3OD) δ 4.08 (br s, 3 H), 2.78-3.50 (m 3 H), 3.04 (s, 3 H), 2.95 (s, 3 H), 2.18-2.37 (m, 2 H), 2.21 (s, 3 H), 1.60-1.62 (m, 1 H), 1.42 (s, 9 H); MS (ESI) *m/z* 575.4 (M+H), calcd for $C_{28}H_{35}FN_4O_8$ 574.2.

Example 15. Synthesis of Compounds via Scheme 15.

Scheme 15



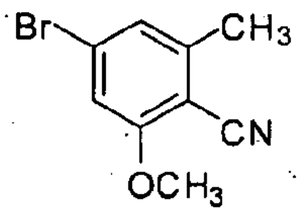
The following compounds were prepared according to Scheme 15.



S15-2

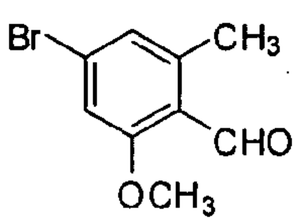
To an ice-cooled solution of 2-methoxy-6-methylaniline (**S15-1**, 25.12 g, 183.10 mmol, 1 equiv) in MeOH (79 mL) and HOAc (25 mL) was added a solution of bromine (9.41 mL, 183.10 mmol) in HOAc (79 mL) dropwise *via* an addition funnel. The reaction mixture was allowed to warm to rt and stirred for 2 hrs after

complete addition. EtOAc (150 mL) was added, and the solid was collected by filtration and washed with more EtOAc, yielding 37.20 g of compound **S15-2** as an off-white solid (HBr salt).



S15-3

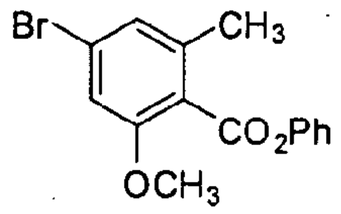
4-Bromo-2-methoxy-6-methylaniline (**S15-2**, HBr salt, 20.00 g, 92.70 mmol, 1.0 equiv) was suspended in concentrated HCl (22 mL) and crushed ice (76 g) cooled in an ice-bath. A solution of $NaNO_2$ (6.52 g, 94.60 mmol, 1.02 equiv) in H_2O (22 mL) was added dropwise. The resulting mixture was stirred at 0 °C for 30 min and neutralized with aqueous Na_2CO_3. A suspension of CuCN (10.4 g, 115.90 mmol, 1.25 equiv) in H_2O (44 mL) was mixed with a solution of NaCN (14.4 g, 294.80 mmol, 3.18 equiv) in 22 mL of H_2O, and cooled in an ice-bath. The initial diazonium salt mixture was then added to the CuCN and NaCN mixture with vigorous stirring while maintaining the temperature at 0 °C (toluene (180 mL) was also added in portions during the addition). The reaction mixture was stirred at 0 °C for 1 h, rt for 2 hrs, and 50 °C for another 1 h. After cooling to rt, the layers were separated. The aqueous layer was extracted with toluene. The combined organic layers were washed with brine, dried over magnesium sulfate, and concentrated. The residue was passed through a silica gel plug, washed with toluene, and concentrated to yield 14.50 g of compound **S15-3** as a light yellow solid.



S15-4

To a solution of **S15-3** (11.34 g, 50.20 mmol, 1.0 equiv) in THF (100 mL) was added 1.5 M DIBAL-H in toluene (40.10 mL, 60.20 mmol, 1.2 equiv) slowly at -78 °C. The reaction was allowed to warm to rt gradually and stirred overnight. After re-cooled to 0 °C, the reaction was carefully quenched by 1 N HCl. The resulting mixture was stirred at rt for 1 h and extracted three times with EtOAc. The combined EtOAc layers were washed with H_2O, saturated aqueous $NaHCO_3$ and

brine, dried over magnesium sulfate, and concentrated to provide compound **S15-4** as a yellow solid, which was used directly in the next step.

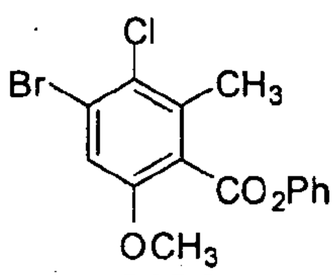


S15-5

To a suspension of **S15-4** (50.20 mmol, 1.0 equiv) in *t*-BuOH (200 mL) was added a solution of $NaClO_2$ (11.34 g, 100.30 mmol, 2.0 equiv) and NaH_2PO_4 (34.6 g, 250.80 mmol, 5.0 equiv) in H_2O (100 mL) *via* an addition funnel. After complete addition, 2-methyl-2-butene (42.40 mL, 0.40 mol, 8 equiv)) was added. The resulting homogenous solution was stirred at rt for 30 min, and volatiles were removed. The residue was suspended in 150 mL of H_2O. The solution was acidified to pH ~ 1 with 1 N HCl and extracted three times with *t*-butyl methyl ether. The combined organic solution was extracted three times with 1 N NaOH. The combined aqueous solution was acidified with 6 N HCl, and extracted three times with EtOAc. The combined EtOAc extracts were washed with brine, dried over magnesium sulfate, and concentrated to provide 8.64 g of the benzoic acid intermediate (**15-4-a**) as an off-white solid, which was used directly in the next step.

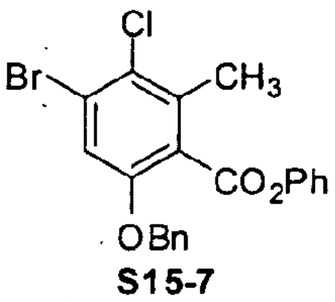
To a solution of the above benzoic acid (8.64 g, 35.20 mmol, 1.0 equiv) in dichloromethane (70 mL) was added oxalyl chloride (3.76 mL, 42.30 mmol, 1.2 equiv), followed by a couple of drops of DMF (caution: gas evolution). The mixture was stirred at rt for 30 min and the volatiles were evaporated under reduce pressure. The residue was further dried under high vacuum to afford the crude benzoyl chloride. The crude benzoyl chloride was re-dissolved in dichloromethane (70 mL). Triethylamine (12.3 mL, 88.10 mmol, 2.5 equiv), phenol (3.98 g, 42.30 mmol, 1.2 equiv) and DMAP (0.43 g, 3.52 mmol, 0.1 equiv) were added. The mixture was stirred at rt for 1 h. The solvent was evaporated. The residue was suspended in EtOAc, and the precipitate was filtered off. The organic solution was then washed with 1 N HCl (three times), H_2O, saturated aqueous $NaHCO_3$, and brine, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography gave compound **S15-5** (10.05 g, 89%) as an off-white solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.45 (m, 2 H), 7.22-7.27 (m, 3 H), 7.04 (d, J = 0.9

Hz, 1 H), 6.97 (d, J = 0.9 Hz, 1 H), 3.87 (s, 3 H), 2.42 (s, 3 H),; MS (ESI) *m/z* 319.0 (M-H), calcd for $C_{15}H_{12}BrO_3$ 319.0.



S15-6

To a solution of compound **S15-5** (2.52 g, 7.87 mmol, 1.0 equiv) in acetonitrile (16 mL) was added NCS (1.10 g, 8.27 mmol, 1.05 equiv) in one portion. The resulting mixture was heated in a 60 °C oil bath for 45 hrs. The solvent was evaporated. The residue was redissolved in Et_2O (400 mL), washed with 1 N NaOH, H_2O and brine, dried over sodium sulfate, and concentrated to provide 2.76 g of compound **S15-6** as a white solid. This material was used directly in the next step without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, J = 7.8, 7.8 Hz, 2 H), 7.22-7.28 (m, 3 H), 7.13 (s, 1 H), 3.87 (s, 3 H), 2.51 (s, 3 H); MS (ESI) *m/z* 353.0 (M-H), calcd for $C_{15}H_{11}BrClO_3$ 352.97.

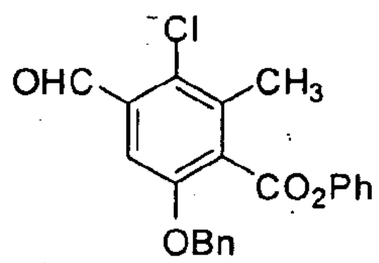


S15-7

Compound **S15-6** (2.76 g, 7.76 mmol, 1.0 equiv) was dissolved in anhydrous dichloromethane (78 mL) and cooled to -78 °C. A solution of boron tribromide (1.0 M in dichloromethane, 7.76 mL, 7.76 mmol, 1.0 equiv) was added dropwise at -78 °C. The resulting yellow solution was stirred at -78 °C for 15 min, and at 0 °C for 30 min. Saturated aqueous $NaHCO_3$ was added. The mixture was stirred at rt for 10 min., and extracted with EtOAc three times. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated to provide 2.69 g of the phenol intermediate as an off-white solid. This material was used directly in the next step without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 7.8, 7.8 Hz, 2 H), 7.32 (dd, J = 7.8, 7.8 Hz, 1 H), 7.27 (s, 1 H), 7.19 (d, J = 7.8 Hz, 2 H), 2.83 (s, 3 H); MS (ESI) *m/z* 339.0 (M-H), calcd for $C_{14}H_9BrClO_3$ 338.95.

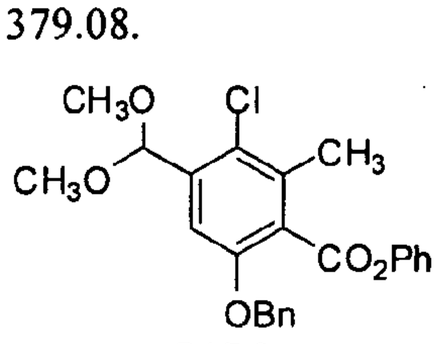
The above phenol (2.65 g, 7.76 mmol, 1.0 equiv) was dissolved in acetone (40 mL), and added with K_2CO_3 (2.14 g, 15.5 mmol, 2.0 equiv) and benzylbromide

(0.97 mL, 8.15 mmol, 1.05 equiv) at rt. After stirring overnight at rt, the solution was filtered through a bed of Celite. The solid cake was further washed with three portions of EtOAc. The combined organic solution was concentrated. The residue was purified by flash chromatography to yield 2.97 g (89%) of compound **S15-7** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.43 (m, 7 H), 7.19-7.26 (m, 2 H), 7.05 (d, J = 7.8 Hz, 2 H), 5.11 (s, 2 H), 2.51 (s, 3 H); MS (ESI) *m/z* 429.0 (M-H), calcd for $C_{21}H_{15}BrClO_3$ 429.00.



S15-8

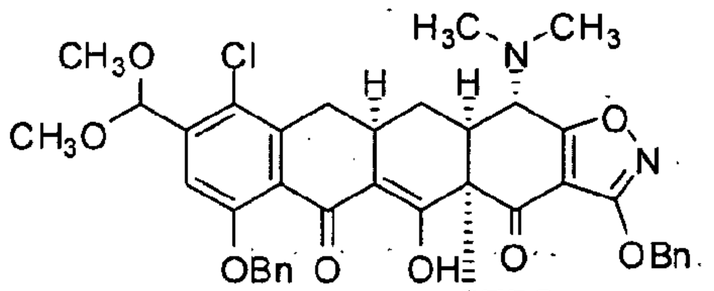
To a solution of compound **S15-7** (1.98 g, 4.59 mmol, 1.0 equiv) in anhydrous THF (23 mL) was added *i*-PrMgCl·LiCl (7.65 mL, 1.2 M/THF, 9.18 mmol, 2.0 equiv) dropwise at -78 °C under a N_2 atmosphere. After 10 min, the temperature was raised to 0 °C and the reaction was stirred for 1 h at 0 °C. DMF (1.80 mL, 22.90 mmol, 5.0 equiv) was then added. The reaction was warmed to rt, stirred for 30 min at rt, and quenched by saturated aqueous NH_4Cl. The layers were separated and the aqueous layer was further extracted twice with EtOAc. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated. Purification of the residue by flash chromatography gave compound **S15-8** (1.45 g, 83%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (s, 1 H), 7.33-7.44 (m, 8 H), 7.25-7.27 (m, 1 H), 7.05 (d, J = 7.8 Hz, 2 H), 5.19 (s, 2 H), 2.51 (s, 3 H); MS (ESI) *m/z* 379.1 (M-H), calcd for $C_{22}H_{16}ClO_4$ 379.08.



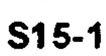
S15-9

To a solution of aldehyde **S15-8** (1.66 g, 4.37 mmol, 1.0 equiv) in MeOH (22 mL) was added trimethylorthoformate (2.40 mL, 21.90 mmol, 5.0 equiv) and TsOH (83 mg, 0.44 mmol, 0.1 equiv). The reaction was heated to 65 °C for 4 hrs. The solvent was evaporated. The residue was redissolved in EtOAc (200 mL), washed

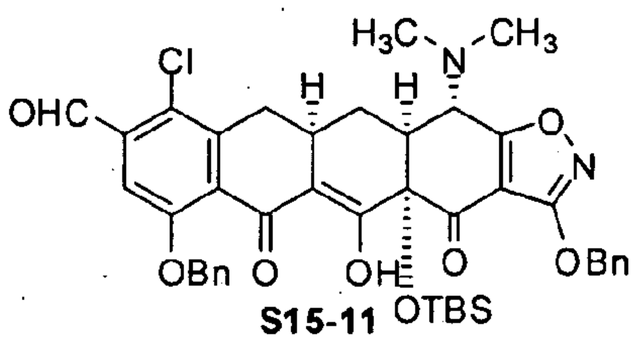
with saturated aqueous $NaHCO_3$ and brine, dried over sodium sulfate, and concentrated. Purification of the residue by flash chromatography gave compound **S15-9** (1.75 g, 94%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 2 H), 7.34-7.37 (m, 5 H), 7.20-7.25 (m, 2 H), 7.07 (d, J = 7.8 Hz, 2 H), 5.62 (s, 1 H), 5.19 (s, 2 H), 3.36 (s, 6 H), 2.48 (s, 3 H); MS (ESI) *m/z* 425.10 (M-H), calcd for $C_{24}H_{22}ClO_5$ 425.12.



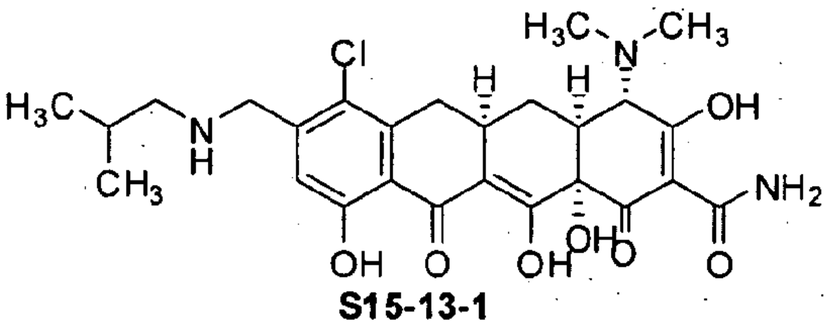
S15-10



A solution of *n*-BuLi in hexanes (2.37 mL, 2.2 M, 5.23 mmol, 1.2 equiv) was added dropwise to a solution of *i*-Pr_2NH (0.77 mL, 5.45 mmol, 1.25 equiv) in THF (27 mL) at -78 °C under a N_2 atmosphere. The resulting solution was stirred at -78 °C for 20 min and 0 °C for 5 min, and then re-cooled to -78 °C. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA, 0.85 mL, 5.67 mmol, 1.30 equiv) was added, followed by the dropwise addition of **S15-9** (2.05 g, 4.80 mmol, 1.1 equiv) in THF (30 mL) *via* a cannula. After complete addition, the resulting dark-red mixture was stirred for another hour at -78 °C and then cooled to -100 °C. A solution of enone **S1-9** (2.10 g, 4.36 mmol, 1.0 equiv) in THF (30 mL) was added dropwise *via* a cannula. The resulting red mixture was slowly warmed to -78 °C. LHMDS (4.36 mL, 1.0 M/THF, 4.36 mmol, 1.0 equiv) was then added and the reaction was slowly warmed to -5 °C. Saturated aqueous NH_4Cl was added. The resulting mixture was extracted three times with EtOAc. The combined EtOAc extracts were washed with brine, dried (sodium sulfate), and concentrated. Purification of the residue by flash chromatography gave compound **S15-10** (3.20 g, 90%) as a light yellow foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.16 (s, 3 H), 7.22-7.52 (m, 11 H), 5.55 (s, 1 H), 5.38 (s, 2 H), 5.29 (d, J = 11.4 Hz, 1 H), 5.24 (d, J = 11.4 Hz, 1 H), 3.97 (d, J = 10.4 Hz, 1 H), 3.46 (dd, J = 4.9, 15.9 Hz, 1 H), 3.38 (s, 3 H), 3.29 (s, 3 H), 2.96-3.04 (m, 1 H), 2.45-2.58 (m, 9 H), 2.15 (d, J = 14.6 Hz, 1 H), 0.84 (s, 9 H), 0.28 (s, 3 H); MS (ESI) *m/z* 815.30 (M+H), calcd for $C_{44}H_{52}ClN_2O_9Si$ 815.31.


S15-11

To a solution of compound **S15-10** (1.48 g, 1.82 mmol, 1.0 equiv) in THF (15 mL) was added 3 N HCl (3 mL) at 0 °C. The resulting mixture was stirred at rt for 4 hrs, diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, dried over sodium sulfate, and concentrated. Purification of the residue by flash chromatography gave aldehyde **S15-11** (1.05 g, 75%) as a light yellow foam: ^1H NMR (400 MHz, $CDCl_3$) δ 15.8 (s, 1 H), 10.5 (s, 1 H), 7.28-7.50 (m, 11 H), 5.36 (s, 2 H), 5.28 (d, J = 11.4 Hz, 1 H), 5.23 (d, J = 11.4 Hz, 1 H), 3.94 (d, J = 10.4 Hz, 1 H), 3.48 (dd, J = 4.9, 15.9 Hz, 1 H), 2.96-3.06 (m, 1 H), 2.44-2.60 (m, 9 H), 2.16 (d, J = 14.6 Hz, 1 H), 0.82 (s, 9 H), 0.26 (s, 3 H), 0.14 (s, 3 H); MS (ESI) *m/z* 769.30 (M+H), calcd for $C_{42}H_{46}ClN_2O_8Si$ 769.26.


S15-13-1

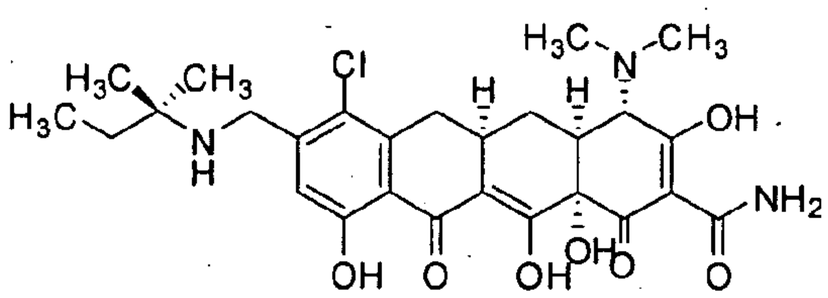
Compound **S15-11** (30 mg, 0.039 mmol, 1.0 equiv) was dissolved in 1,2-dichloroethane (1.0 mL). Isobutylamine (14 µL, 0.12 mmol, 3.0 equiv) and acetic acid (7 µL, 0.12 mmol, 3.0 equiv) were added. After stirring at rt for 1 h, sodium triacetoxyborohydride (17 mg, 0.078 mmol, 2.0 equiv) was added. Stirring was continued overnight. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted three times with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated to give the crude intermediate, which was used directly in the next step without further purification.

In a plastic vial, the above amine intermediate was dissolved in CH_3CN (1 mL). Aqueous HF (48-50%, 0.25 mL) was added. After stirring at rt for 16 hrs, the reaction mixture was poured into aqueous solution (12.5 mL) of K_2HPO_4 (1.75 g)

and extracted three times with dichloromethane. The combined organic phases were washed with brine, dried, and concentrated to yield the crude intermediate.

The above crude intermediate was dissolved in EtOAc (2.0 mL). Pd-C (10wt%, 8 mg, 30% w/w) was added. The reaction flask was briefly evacuated and re-filled with hydrogen. The reaction mixture was stirred at rt and monitored by LC-MS. After the reaction was complete, MeOH (5 mL) and 0.5 N HCl/MeOH (0.5 mL) were added. The mixture was stirred for 30 min, and filtered through a small pad of Celite. The filtrate was concentrated to give the crude product, which was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 7.85-8.95 min, were collected and freeze-dried to give the desired product **S15-13-1** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 7.16 (s, 1 H), 4.38 (s, 2 H), 4.12 (s, 1 H), 3.40 (dd, J = 4.6, 16.0 Hz, 1 H), 2.96-3.11 (m, 10 H), 2.41 (dd, J = 14.0, 14.0 Hz, 1 H), 2.24-2.28 (m, 1 H), 2.08-2.13 (m, 1 H), 1.60-1.70 (m, 1 H), 1.06 (d, J = 6.4 Hz, 6 H); MS (ESI) *m/z* 534.2 (M+H), calcd for $C_{26}H_{33}ClN_3O_7$ 534.19.

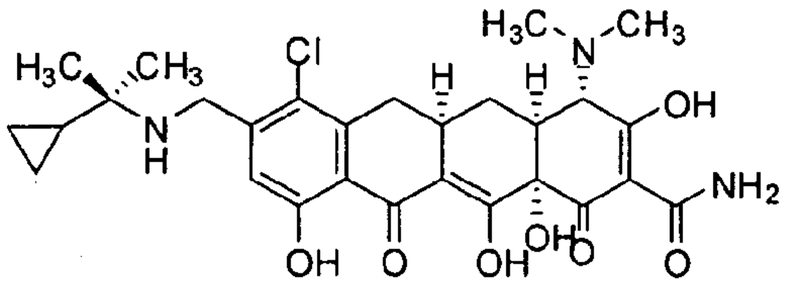
The following compounds were prepared similarly to **S15-13-1**.



S15-13-2

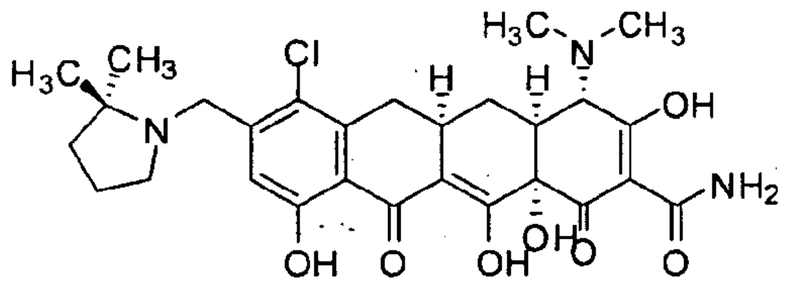
The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.00-9.50 min, were collected and freeze-dried to give the desired product **S15-13-2** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.33 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, J = 4.6, 16.0 Hz, 1 H), 2.96-3.10 (m, 8 H), 2.40 (dd, J = 15.0, 15.0 Hz, 1 H), 2.25-2.28 (m, 1 H), 1.84 (q, J = 7.3 Hz, 2 H), 1.60-1.70 (m, 1 H),

1.44 (s, 6 H), 1.04 (t, J = 7.3 Hz, 3 H); MS (ESI) *m/z* 548.3 (M+H), calcd for $C_{27}H_{35}ClN_3O_7$ 548.21.



S15-13-3

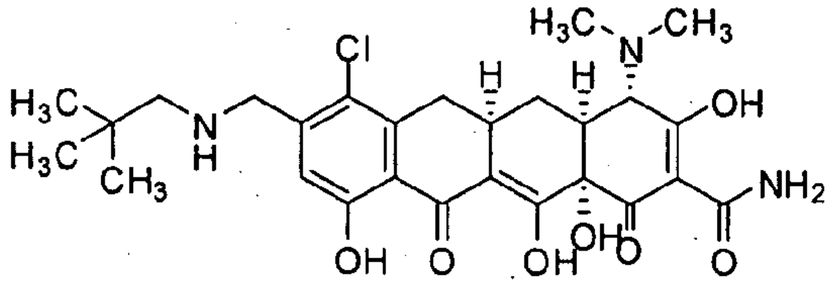
The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 8.35-9.80 min, were collected and freeze-dried to give the desired product **S15-13-3** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.44 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, J = 4.6, 16.0 Hz, 1 H), 2.96-3.10 (m, 8 H), 2.41 (dd, J = 15.0, 15.0 Hz, 1 H), 2.23-2.28 (m, 1 H), 1.60-1.70 (m, 1 H), 1.34 (s, 6 H), 1.21-1.26 (m, 1 H), 0.69-0.72 (m, 2 H), 0.60-0.63 (m, 2 H); MS (ESI) *m/z* 560.3 (M+H), calcd for $C_{28}H_{35}ClN_3O_7$ 560.21.



S15-13-4

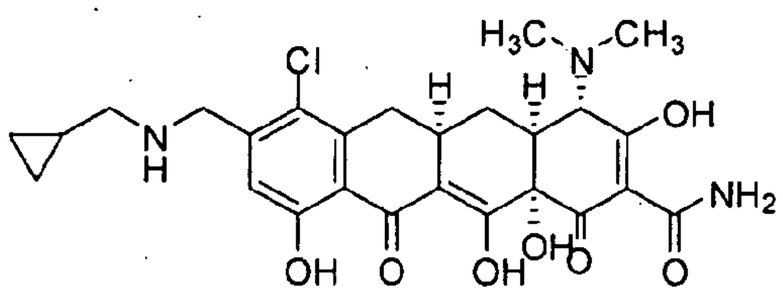
The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 7.15-8.50 min, were collected and freeze-dried to give the desired product **S15-13-4** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.72 (t, J = 13.2 Hz, 1 H), 4.10-4.15 (m, 2 H), 3.38-3.55 (m, 2 H), 2.95-3.10 (m, 8 H), 2.41 (dd, J = 15.0, 15.0 Hz, 1 H), 1.96-2.28 (m, 5 H), 1.96-2.28 (m, 5 H), 1.66 (s, 3 H), 1.63-

1.66 (m, 1 H), 1.45 (s, 3 H); MS (ESI) *m/z* 560.3 (M+H), calcd for $C_{28}H_{35}ClN_3O_7$ 560.21.



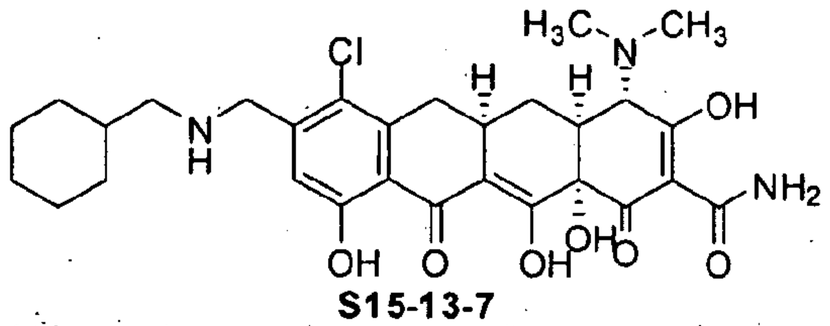
S15-13-5

The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 7.65-8.50 min, were collected and freeze-dried to give the desired product **S15-13-5** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.24 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, *J* = 4.6, 16.0 Hz, 1 H), 2.94-3.14 (m, 10 H), 2.41 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.24-2.30 (m, 1 H), 1.60-1.70 (m, 1 H), 1.08 (s, 9 H); MS (ESI) *m/z* 548.3 (M+H), calcd for $C_{27}H_{35}ClN_3O_7$ 548.21.



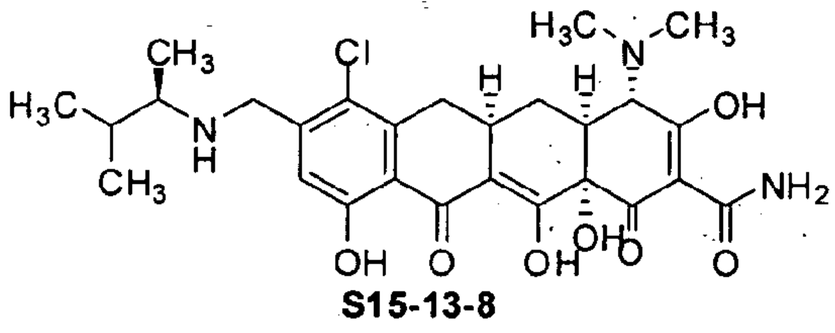
S15-13-6

The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 13.80-14.90 min, were collected and freeze-dried to give the desired product **S15-13-6** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (s, 1 H), 4.40 (s, 2 H), 4.13 (s, 1 H), 3.40 (dd, *J* = 4.6, 16.0 Hz, 1 H), 2.94-3.14 (m, 10 H), 2.40 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.25-2.28 (m, 1 H), 1.60-1.70 (m, 1 H), 1.16-1.21 (m, 1 H), 0.72-0.77 (m, 2 H), 0.43-0.47 (m, 2 H); MS (ESI) *m/z* 532.2 (M+H), calcd for $C_{26}H_{31}ClN_3O_7$ 532.18.



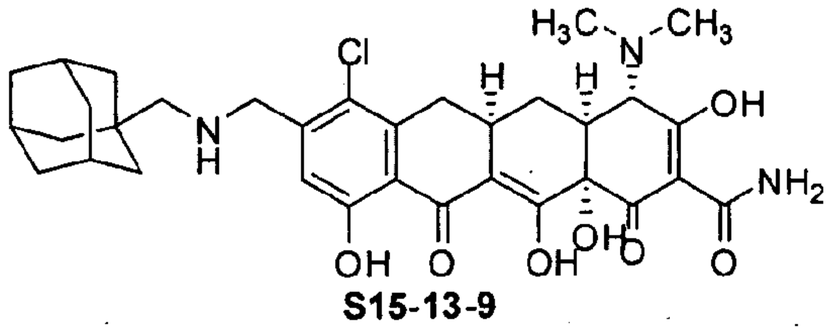
S15-13-7

The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 15.55-16.00 min, were collected and freeze-dried to give the desired product **S15-13-7** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (s, 1 H), 4.37 (s, 2 H), 4.12 (s, 1 H), 3.40 (dd, *J* = 4.6, 16.0 Hz, 1 H), 2.94-3.14 (m, 10 H), 2.40 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.24-2.28 (m, 1 H), 1.60-1.88 (m, 7 H), 1.21-1.35 (m, 3 H), 1.01-1.09 (m, 2 H); MS (ESI) *m/z* 574.3 (M+H), calcd for $C_{29}H_{37}ClN_3O_7$ 574.22.



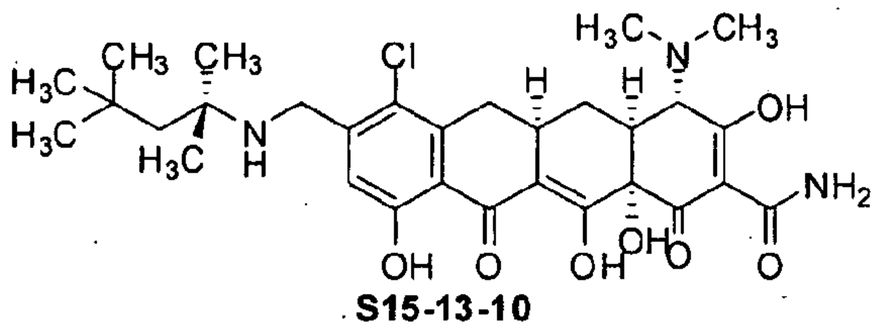
S15-13-8

The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 13.85-14.90 min, were collected and freeze-dried to give the desired product **S15-13-8** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.18 (s, 1 H), 4.40 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, *J* = 4.6, 16.0 Hz, 1 H), 3.32-3.36 (m, 1 H), 2.94-3.11 (m, 8 H), 2.40 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.20-2.28 (m, 2 H), 1.60-1.70 (m, 1 H), 1.34 (d, *J* = 6.8 Hz, 3 H), 1.06 (d, *J* = 6.8 Hz, 3 H), 1.01 (d, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 548.2 (M+H), calcd for $C_{27}H_{35}ClN_3O_7$ 548.21.



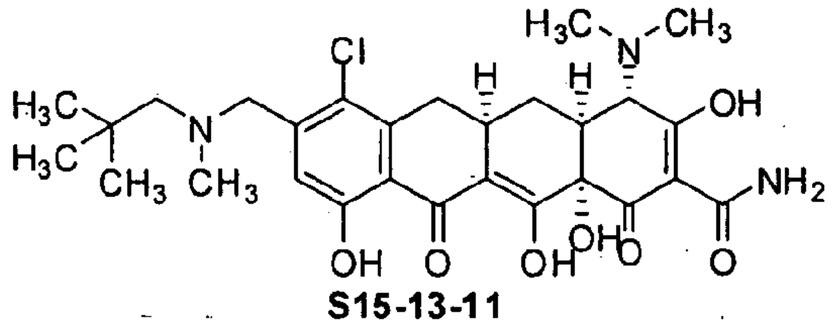
S15-13-9

The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 9.60-10.85 min, were collected and freeze-dried to give the desired product **S15-13-9** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.41 (s, 2 H), 4.15 (s, 1 H), 3.40 (dd, *J* = 4.6, 16.0 Hz, 1 H), 2.83-3.15 (m, 10 H), 2.39 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.26-2.32 (m, 1 H), 2.03 (br. s, 3 H), 1.59-1.81 (m, 13 H); MS (ESI) *m/z* 626.3 (M+H), calcd for $C_{33}H_{41}ClN_3O_7$ 626.26.



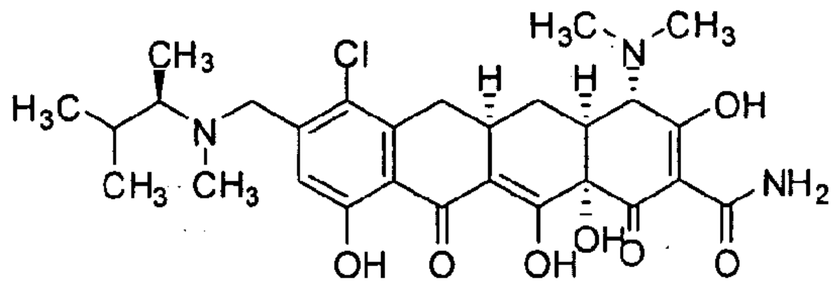
S15-13-10

The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 10→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 15.15-16.45 min, were collected and freeze-dried to give the desired product **S15-13-10** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.34 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, *J* = 4.6, 16.0 Hz, 1 H), 2.94-3.15 (m, 8 H), 2.40 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.24-2.28 (m, 1 H), 1.83 (s, 2 H), 1.60-1.70 (m, 1 H), 1.58 (s, 6 H), 1.11 (s, 9 H); MS (ESI) *m/z* 590.3 (M+H), calcd for $C_{30}H_{41}ClN_3O_7$ 590.26.



S15-13-11

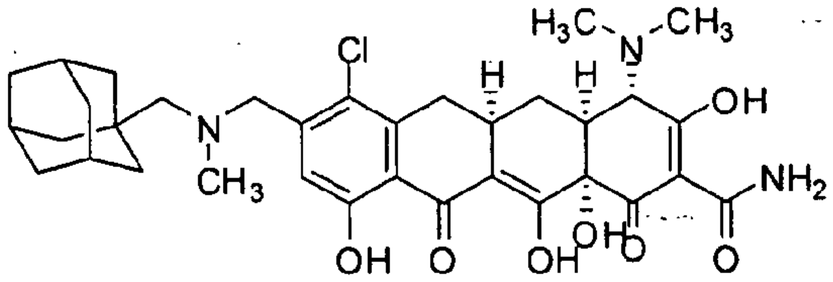
To a solution of compound **S15-13-5** (12 mg, 0.022 mmol, 1.0 equiv) in DMF (0.5 mL) was added sequentially triethylamine (6 μL, 0.045 mmol, 2.0 equiv), HCHO (37wt% in H_2O, 5 μL, 0.067 mmol, 3.0 equiv) and $InCl_3$ (0.5 mg, 0.0022 mmol, 0.1 equiv) at rt. After stirring for 5 min, $Na(OAc)_3BH$ (10 mg, 0.045 mmol, 2.0 equiv) was added. Stirring was continued for another hour. HCl/MeOH (0.20 mL, 0.5 N) was added. The resulting mixture was added dropwise to vigorously stirring diethyl ether (100 mL). The precipitate was collected onto a small Celite pad and washed three times with more diethyl ether. The Celite pad was then eluted several times with MeOH. The MeOH solution was collected and concentrated to provide the crude product, which was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 13.90-15.40 min, were collected and freeze-dried to give the desired product **S15-13-11** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.28 (s, 1 H), 4.71-4.78 (m, 1 H), 4.43-4.48 (m, 1 H), 4.13 (s, 1 H), 3.41 (dd, J = 4.6, 16.0 Hz, 1 H), 2.94-3.15 (m, 13 H), 2.44 (dd, J = 15.0, 15.0 Hz, 1 H), 2.24-2.28 (m, 1 H), 1.60-1.70 (m, 1 H), 1.09 (s, 9 H); MS (ESI) *m/z* 562.2 (M+H), calcd for $C_{28}H_{37}ClN_3O_7$ 562.22.



S15-13-12

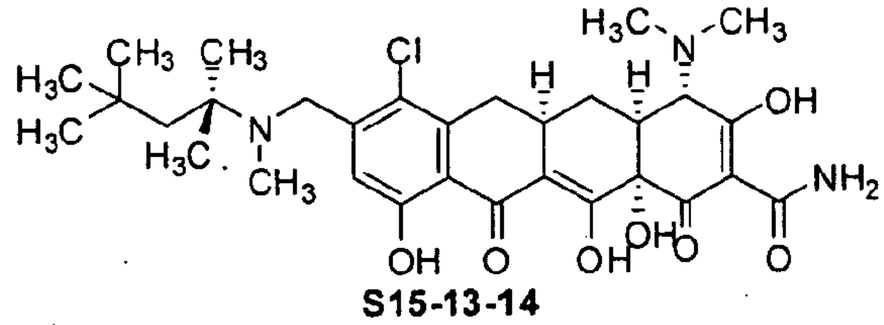
Compound **S15-13-12** was prepared similarly from **S15-13-8**. The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow

rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 0→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 14.15-15.25 min, were collected and freeze-dried to give the desired product **S15-13-12** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.26-4.76 (m, 2 H), 4.12 (s, 1 H), 3.34-3.44 (m, 2 H), 2.82-3.11 (m, 11 H), 2.18-2.47 (m, 3 H), 1.60-1.70 (m, 1 H), 1.39-1.46 (m, 3 H), 1.03-1.08 (m, 6 H); MS (ESI) *m/z* 562.2 (M+H), calcd for $C_{28}H_{37}ClN_3O_7$ 562.22.



S15-13-13

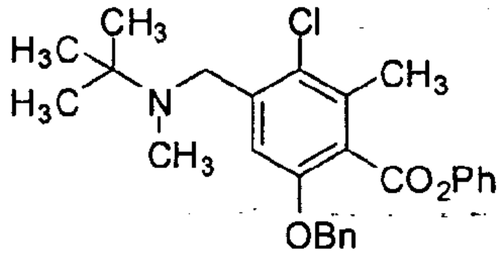
Compound **S15-13-13** was prepared similarly from **S15-13-9**. The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 17.00-18.85 min, were collected and freeze-dried to give the desired product **S15-13-13** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.68-4.74 (m, 1 H), 4.43-4.47 (m, 1 H), 4.12 (s, 1 H), 3.42 (dd, *J* = 4.6, 16.0 Hz, 1 H), 2.94-3.12 (m, 13 H), 2.45 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.24-2.29 (m, 1 H), 2.02 (br. s, 3 H), 1.57-1.81 (m, 13 H); MS (ESI) *m/z* 640.2 (M+H), calcd for $C_{34}H_{43}ClN_3O_7$ 640.27.



S15-13-14

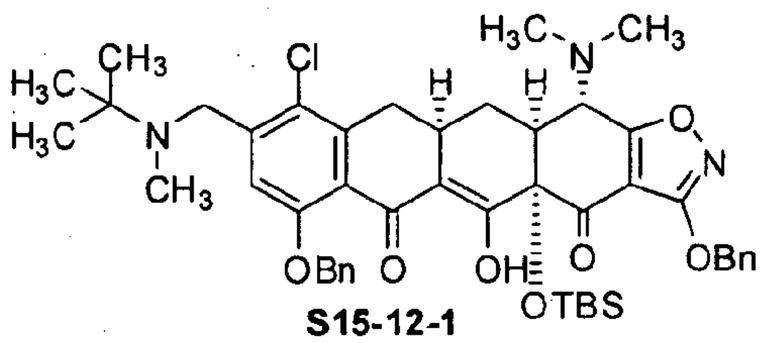
Compound **S15-13-14** was prepared similarly from **S15-13-10**. The crude product was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection

volume: 4.0 mL (0.05 N HCl/water); gradient: 10→100% B over 20 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 16.35-17.65 min, were collected and freeze-dried to give the desired product **S15-13-14** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.12-4.18 (m, 1 H), 4.11 (s, 1 H), 3.40-3.50 (m, 2 H), 2.94-3.15 (m, 8 H), 2.75 (s, 3 H), 2.39-2.48 (m, 1 H), 2.24-2.28 (m, 1 H), 1.83-2.00 (m, 2 H), 1.73 (s, 3 H), 1.60-1.70 (m, 1 H), 1.63 (s, 3 H), 1.14 (s, 9 H); MS (ESI) *m/z* 604.3 (M+H), calcd for $C_{31}H_{43}ClN_3O_7$ 604.27.



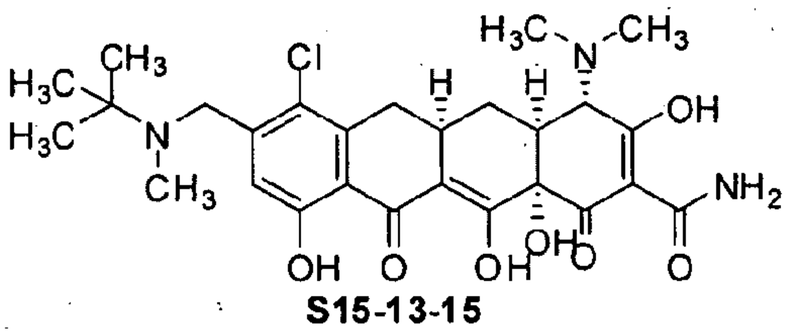
S15-15-1

To a solution of compound **S15-8** (0.39 g, 1.02 mmol, 1.0 equiv) in 1,2-dichloroethane (10 mL) was added *t*-butylamine (0.13 mL, 1.22 mmol, 1.2 equiv) and acetic acid (0.18 mL, 3.05 mmol, 3.0 equiv). After stirring at rt for 2.5 hrs, sodium triacetoxyborohydride (0.43 g, 2.03 mmol, 2.0 equiv) was added. Stirring was continued overnight. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted three times with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated to give the crude intermediate as an off-white oil. The crude intermediate was redissolved in 1,2-dichloroethane (10 mL). Formaldehyde (37wt% in H_2O, 0.76 mL, 10.20 mmol, 10 equiv) and acetic acid (0.18 mL, 3.05 mmol, 3.0 equiv) were added After stirring at rt for 1 h, sodium triacetoxyborohydride (0.43 g, 2.03 mmol, 2.0 equiv) was added. Stirring was continued for another hour. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted three times with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated. Purification of the residue by flash chromatography gave compound **S15-15-1** (0.35 g) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 2 H), 7.20-7.40 (m, 7 H), 7.12 (d, J = 7.8 Hz, 2 H), 5.18 (s, 2 H), 3.59 (s, 2 H), 2.44 (s, 3 H), 2.09 (s, 3 H), 1.10 (s, 9 H); MS (ESI) *m/z* 452.3 (M+H), calcd for $C_{27}H_{31}ClNO_3$ 452.19.



S15-12-1

Compound **S15-12-1** was prepared by the procedure of **S15-10** employing compound **S15-15-1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.0 (s, 1 H), 7.22-7.52 (m, 11 H), 5.36 (s, 2 H), 5.27 (s, 2 H), 3.97 (d, *J* = 10.4 Hz, 1 H), 3.55 (s, 2 H), 3.42 (dd, *J* = 4.9, 15.9 Hz, 1 H), 2.93-3.04 (m, 1 H), 2.43-2.53 (m, 9 H), 2.13 (d, *J* = 14.6 Hz, 1 H), 2.01 (s, 3 H), 1.07 (s, 9 H), 0.84 (s, 9 H), 0.28 (s, 3 H), 0.13 (s, 3 H); MS (ESI) *m/z* 840.4 (M+H), calcd for $C_{47}H_{59}ClN_3O_7Si$ 840.37.

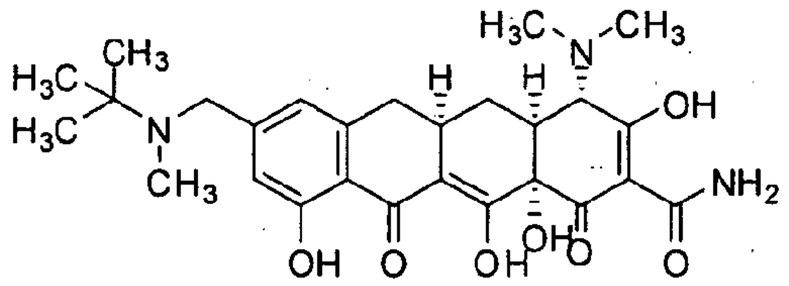


S15-13-15

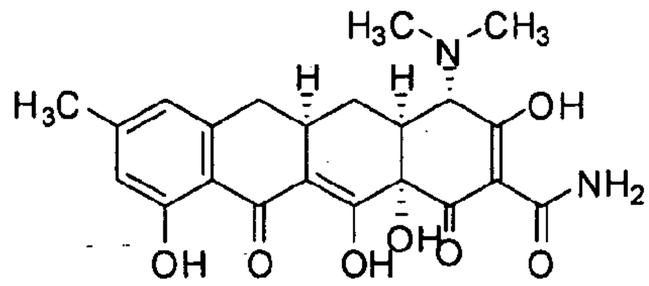
In a plastic vial, compound **S15-12-1** (85 mg, 0.10 mmol) was dissolved in CH_3CN (2 mL). Aqueous HF (48-50%, 0.5 mL) was added. After stirring at rt for 7 hrs, the reaction mixture was poured into an aqueous solution (25 mL) of K_2HPO_4 (3.5 g). The resulting mixture was extracted three times with dichloromethane. The combined organic phases were washed with brine, dried, and concentrated under reduced pressure to yield the crude desilylated product.

The above crude intermediate was dissolved in EtOAc (6 mL). Pd-C (10wt%, 22 mg) was added. The reaction flask was briefly evacuated and re-filled with hydrogen. The reaction mixture was stirred at rt and monitored by LC-MS. After the reaction was complete, MeOH (5 mL) and 0.5 N HCl/MeOH (0.5 mL) were added. The mixture was stirred for 30 min and filtered through a small pad of Celite. The filtrate was concentrated to give the crude product, which was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: MeOH; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 20→100% B over 10 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.30-8.85 min, were collected and freeze-

dried to give the desired product **S15-13-15** as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.80-4.87 (m, 1 H), 4.12-4.20 (m, 1 H), 4.12 (s, 1 H), 3.38-3.40 (m, 1 H), 2.96-3.11 (m, 8 H), 2.75 (s, 3 H), 2.38-2.40 (m, 1 H), 2.24-2.28 (m, 1 H), 1.60-1.70 (m, 1 H), 1.57 (s, 9 H); MS (ESI) *m/z* 548.2 (M+H), calcd for $C_{27}H_{35}ClN_3O_7$ 548.21.



S15-14-1



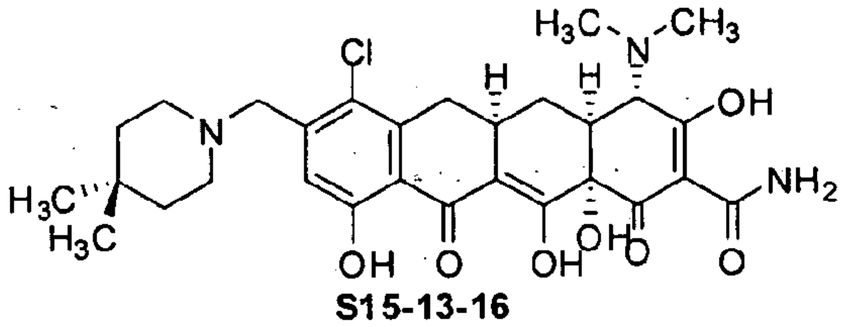
S15-14-2

Alternatively, the crude desilylated product of **S15-12-1** (13 mg) was dissolved in 0.5 N HCl/MeOH (0.07 mL). The volatiles were evaporated. The residue was redissolved in MeOH (2 mL) and added with Pd-C (10wt%, 7 mg). The reaction flask was briefly evacuated and re-filled with hydrogen. The reaction mixture was stirred at rt and monitored by LC-MS. After all the reaction was complete, the reaction mixture was filtered through a small pad of Celite. The filtrate was concentrated to yield the crude product, which was purified by HPLC on a Waters Autopurification system using a Phenomenex Polymerx 10 μ RP-γ 100 R column [30 × 21.20 mm, 10 micron; flow rate, 20 mL/min; Solvent A: 0.05 N HCl/water; Solvent B: CH_3CN; injection volume: 4.0 mL (0.05 N HCl/water); gradient: 10→50% B over 15 min; mass-directed fraction collection]. Fractions containing the desired product, eluting at 6.08-8.75 min, were collected and freeze-dried to give the following two products.

S15-14-1, a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (s, 1 H), 6.93 (s, 1 H), 4.65 (d, J = 12.8 Hz, 1 H), 4.08 (s, 1 H), 3.90 (d, J = 12.8 Hz, 1 H), 2.96-3.11 (m, 9 H), 2.70 (s, 3 H), 2.58-2.68 (m, 1 H), 2.19-2.22 (m, 1 H), 1.60-1.70 (m, 1 H), 1.53 (s, 9 H); MS (ESI) *m/z* 514.3 (M+H), calcd for $C_{27}H_{36}N_3O_7$ 514.25.

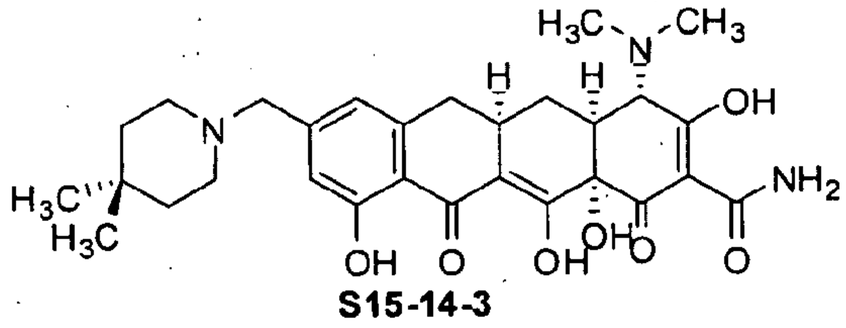
S15-14-2, a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 6.62 (s, 1 H), 6.59 (s, 1 H), 4.06 (s, 1 H), 2.77-3.11 (m, 9 H), 2.51 (dd, J = 14.2, 14.2 Hz, 1 H), 2.30 (s, 3 H), 2.14-2.17 (m, 1 H), 1.52-1.62 (m, 1 H); MS (ESI) *m/z* 429.3 (M+H), calcd for $C_{22}H_{25}N_2O_7$ 429.16.

The following compounds were prepared using similar procedures to that of **S15-13-1**, **S15-13-11**, **S15-13-15** or **S15-14-1**.



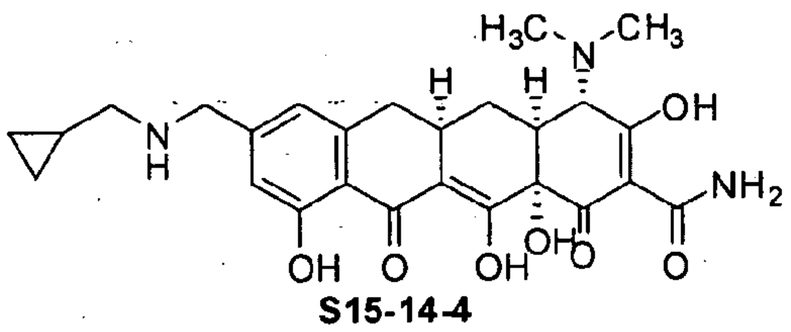
S15-13-16

S15-13-16, a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.53 (s, 2 H), 4.13 (s, 1 H), 3.30-3.45 (m, 5 H), 2.96-3.15 (m, 8 H), 2.40 (dd, *J* = 15.9, 15.9 Hz, 1 H), 2.25-2.29 (m, 1 H), 1.61-1.79 (m, 5 H), 1.09 (s, 3 H), 1.03 (s, 3 H); MS (ESI) *m/z* 574.3 (M+H), calcd for $C_{29}H_{37}ClN_3O_7$ 574.22.



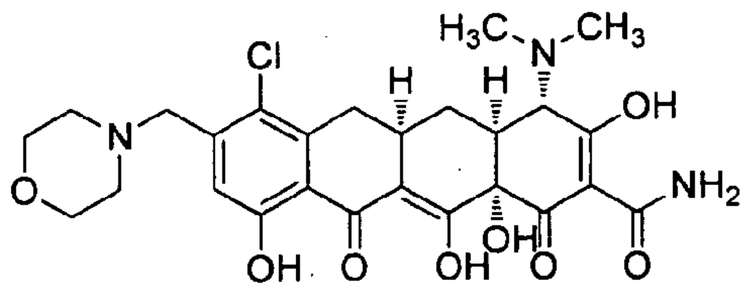
S15-14-3

S15-14-3, a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 7.00 (s, 1 H), 6.95 (s, 1 H), 4.28 (s, 2 H), 4.09 (s, 1 H), 2.96-3.15 (m, 13 H), 2.61 (dd, *J* = 15.9, 15.9 Hz, 1 H), 2.18-2.22 (m, 1 H), 1.59-1.75 (m, 5 H), 1.09 (s, 3 H), 1.04 (s, 3 H); MS (ESI) *m/z* 540.3 (M+H), calcd for $C_{29}H_{38}N_3O_7$ 540.26.



S15-14-4

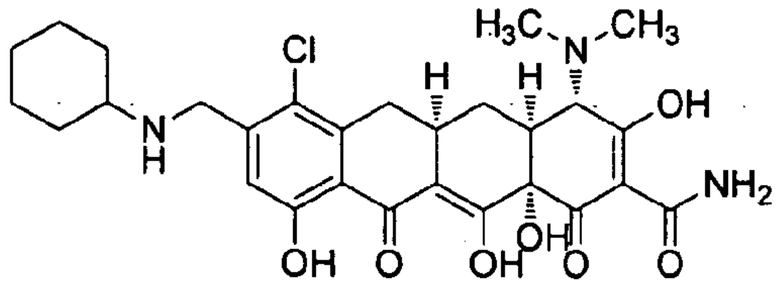
S15-14-4, a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) δ 6.97 (s, 1 H), 6.90 (s, 1 H), 4.18 (s, 2 H), 4.09 (s, 1 H), 2.94-3.14 (m, 11 H), 2.60 (dd, *J* = 15.0, 15.0 Hz, 1 H), 2.19-2.22 (m, 1 H), 1.59-1.65 (m, 1 H), 1.10-1.15 (m, 1 H), 0.71-0.74 (m, 2 H), 0.40-0.43 (m, 2 H); MS (ESI) *m/z* 497.2 (M+H), calcd for $C_{26}H_{32}N_3O_7$ 497.22.



S15-13-17

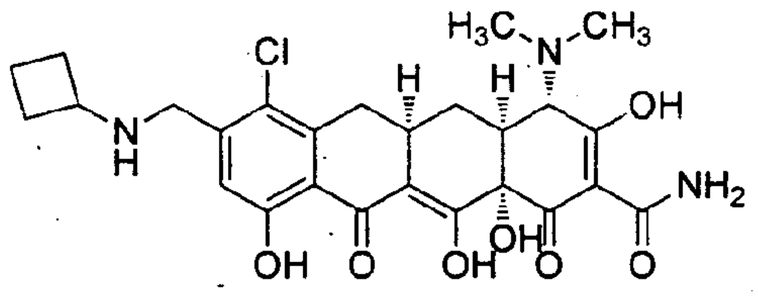
^{1}H NMR (400 MHz, CD_3OD) δ 7.31 (s, 1 H), 4.56 (dd, *J* = 19.2 Hz, 13.6 Hz, 2 H), 4.15 (s, 1 H), 4.08-3.98 (m, 2 H), 3.90-3.79 (m, 2 H), 3.53-3.33 (m, 5 H), 3.20-

2.90 (m, 8 H), 2.45-2.36 (m, 1 H), 2.32-2.25 (m, 1 H), 1.71-160 (m, 1 H); MS (ESI) *m/z* 548.1 (M+H).



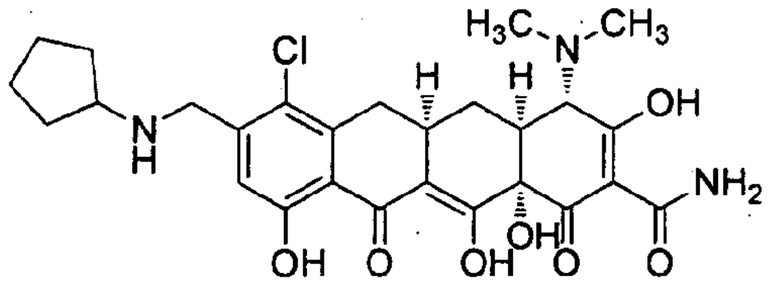
S15-13-18

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.40 (s, 2 H), 4.14 (s, 1 H), 3.50-3.36 (m, 1 H), 3.32-3.21 (m, 1 H), 3.18-2.90 (m, 8 H), 2.48-2.36 (m, 1 H), 2.31-2.20 (m, 3 H), 1.98-1.88 (m, 2 H), 1.80-1.60 (m, 2 H), 1.50-1.35 (m, 4 H), 1.34-1.20 (m, 1 H); MS (ESI) *m/z* 560.1 (M+H).



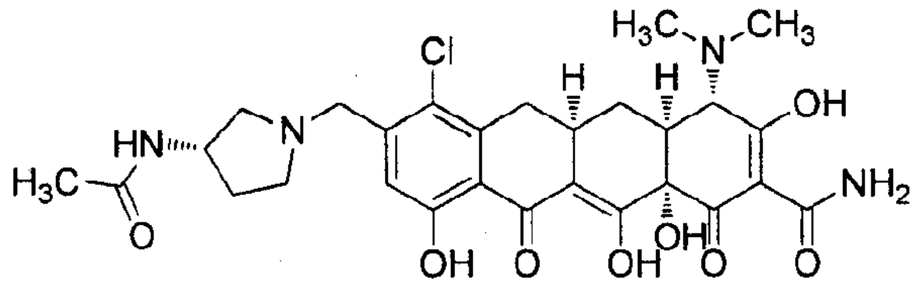
S15-13-19

^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.26 (s, 2 H), 4.13 (s, 1 H), 3.95-3.86 (m, 1 H), 3.45-3.37 (m, 1 H), 3.18-2.95 (m, 8 H), 2.45-2.33 (m, 3 H), 2.32-2.20 (m, 3 H), 2.02-1.90 (m, 2 H), 1.72-1.60 (m, 1 H); MS (ESI) *m/z* 532.1 (M+H).



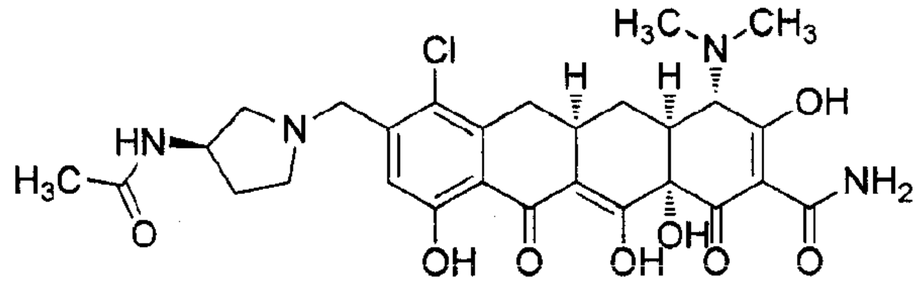
S15-13-20

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.38 (s, 2 H), 4.13 (s, 1 H), 3.79-3.65 (m, 1 H), 3.45-3.38 (m, 1 H), 3.17-2.95 (m, 8 H), 2.48-2.38 (m, 1 H), 2.30-2.15 (m, 3 H), 1.91-1.78 (m, 2 H), 1.80-1.67 (m, 5 H); MS (ESI) *m/z* 546.1 (M+H).



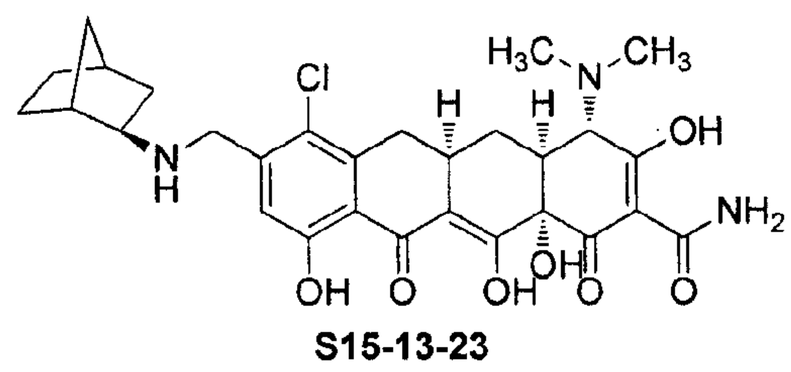
S15-13-21

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.72-4.56 (m, 2 H), 4.50-4.32 (m, 1 H), 4.14 (s, 1 H), 3.97-3.78 (m, 1 H), 3.75-3.50 (m, 2 H), 3.46-3.38 (m, 1 H), 3.20-2.90 (m, 9 H), 2.70-2.52 (m, 1 H), 2.50-2.38 (m, 1 H), 2.32-2.24 (m, 1 H), 2.20-2.05 (m, 1 H), 1.97 (s, 3 H), 1.73-1.61 (m, 1 H); MS (ESI) *m/z* 589.0 (M+H).



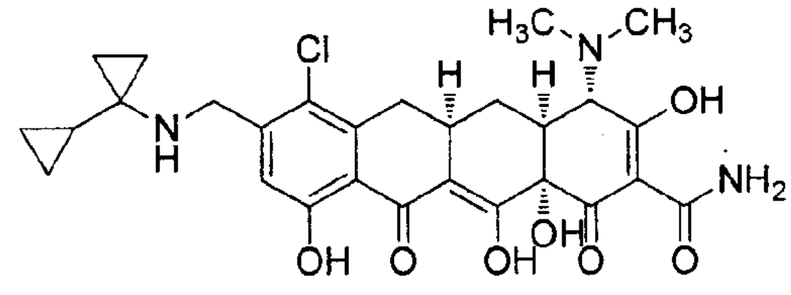
S15-13-22

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.72-4.56 (m, 2 H), 4.48-4.33 (m, 1 H), 4.14 (s, 1 H), 3.98-3.79 (m, 1 H), 3.75-3.50 (m, 2 H), 3.45-3.38 (m, 1 H), 3.18-2.90 (m, 9 H), 2.70-2.51 (m, 1 H), 2.50-2.38 (m, 1 H), 2.32-2.24 (m, 1 H), 2.20-2.05 (m, 1 H), 1.97 (s, 3 H), 1.73-1.61 (m, 1 H); MS (ESI) *m/z* 589.0 (M+H).



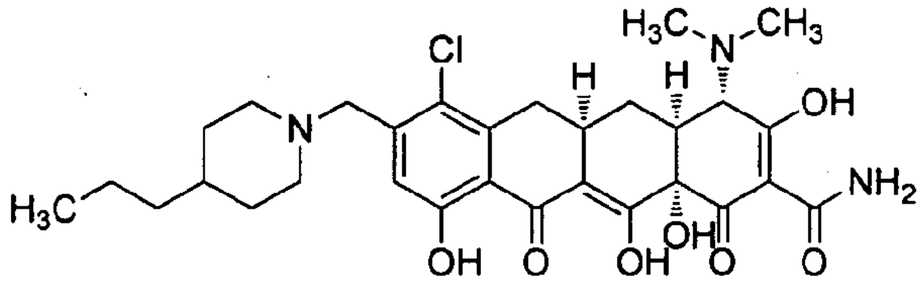
S15-13-23

^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.42-4.32 (m, 2 H), 4.16 (s, 1 H), 3.71-3.60 (m, 1 H), 3.46-3.41 (m, 1 H), 3.20-2.95 (m, 8 H), 2.71 (br s, 1 H), 2.46-2.25 (m, 4 H), 2.20-2.18 (m, 1 H), 1.75-1.52 (m, 4 H), 1.60-1.50 (m, 2 H), 1.50-1.41 (m, 1 H), 1.24-1.16 (m, 1 H); MS (ESI) *m/z* 572.2 (M+H).



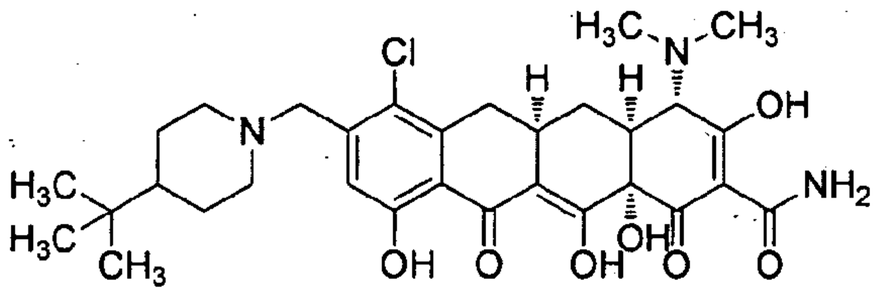
S15-13-24

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.64 (s, 2 H), 4.14 (s, 1 H), 3.48-3.39 (m, 1 H), 3.10-2.95 (m, 8 H), 2.48-2.38 (m, 1 H), 2.32-2.25 (m, 1 H), 1.68-1.59 (m, 1 H), 1.50-1.39 (m, 1 H), 1.05-0.97 (m, 2 H), 0.88-0.82 (m, 2 H), 0.78-0.73 (m, 2 H), 0.45-0.38 (m, 2 H); MS (ESI) *m/z* 558.1 (M+H).



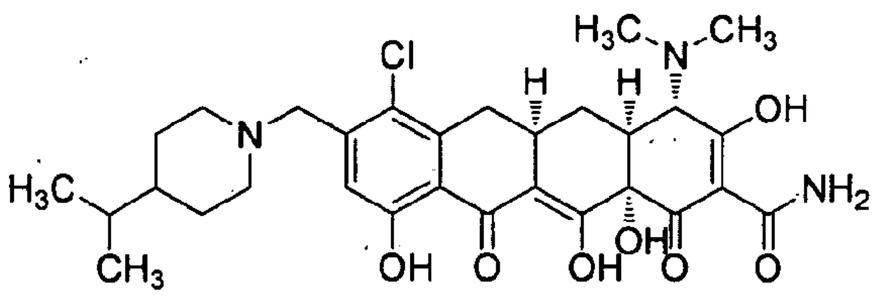
S15-13-25

^{1}H NMR (400 MHz, CD_3OD) δ 7.27 (s, 1 H), 4.51 (s, 2 H), 4.15 (s, 1 H), 3.62-3.53 (m, 2 H), 3.47-3.38 (m, 1 H), 3.24-2.90 (m, 10 H), 2.49-2.37 (m, 1 H), 2.32-2.25 (m, 1 H), 2.02-1.93 (m, 2 H), 1.70-1.58 (m, 2 H), 1.57-1.24 (m, 6 H), 1.00-0.89 (m, 3 H); MS (ESI) *m/z* 588.2 (M+H).



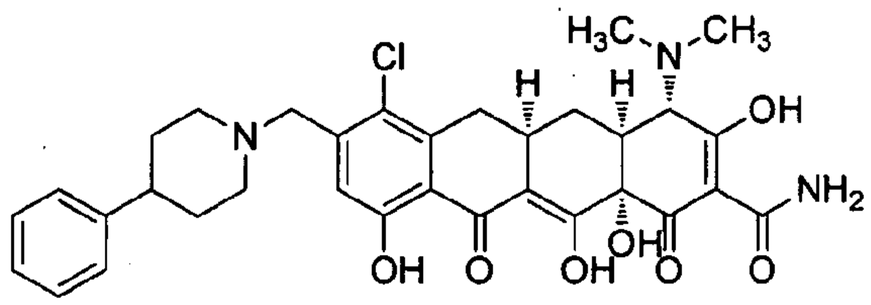
S15-13-26

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.49 (s, 2 H), 4.13 (s, 1 H), 3.65-3.58 (m, 2 H), 3.49-3.38 (m, 1 H), 3.20-2.95 (m, 10 H), 2.49-2.38 (m, 1 H), 2.31-2.24 (m, 1 H), 2.02-1.93 (m, 2 H), 1.71-1.55 (m, 3 H), 1.48-1.38 (m, 1 H), 0.91 (s, 9 H); MS (ESI) *m/z* 602.2 (M+H).



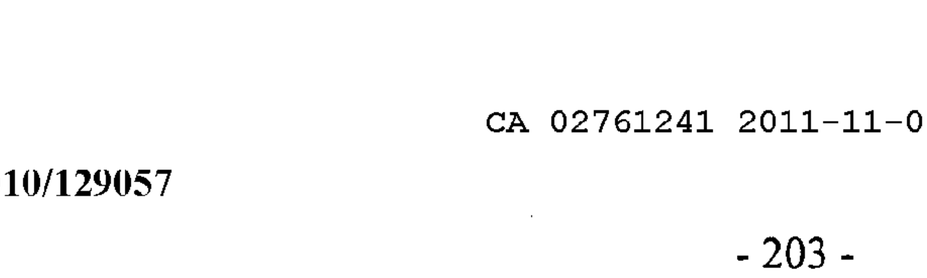
S15-13-27

^{1}H NMR (400 MHz, CD_3OD) δ 7.27 (s, 1 H), 4.51 (s, 2 H), 4.15 (s, 1 H), 3.65-3.56 (m, 2 H), 3.48-3.38 (m, 1 H), 3.23-2.95 (m, 10 H), 2.48-3.38 (m, 1 H), 2.32-2.26 (m, 1 H), 2.02-1.93 (m, 2 H), 1.72-1.38 (m, 5 H), 0.95 (d, J = 6.4 Hz, 6 H); MS (ESI) *m/z* 588.3 (M+H).



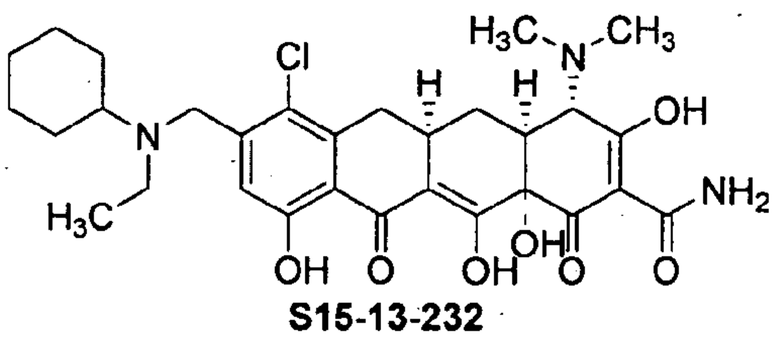
S15-13-28

^{1}H NMR (400 MHz, CD_3OD) δ 7.47-7.20 (m, 6 H), 4.58 (s, 2 H), 4.14 (s, 1 H), 3.75-3.65 (m, 1 H), 3.57-3.35 (m, 2 H), 3.20-2.85 (m, 9 H), 2.61-2.40 (m, 2 H), 2.31-2.19 (m, 1 H), 2.18-2.00 (m, 4 H), 1.73-1.60 (m, 1 H); MS (ESI) *m/z* 622.0 (M+H).



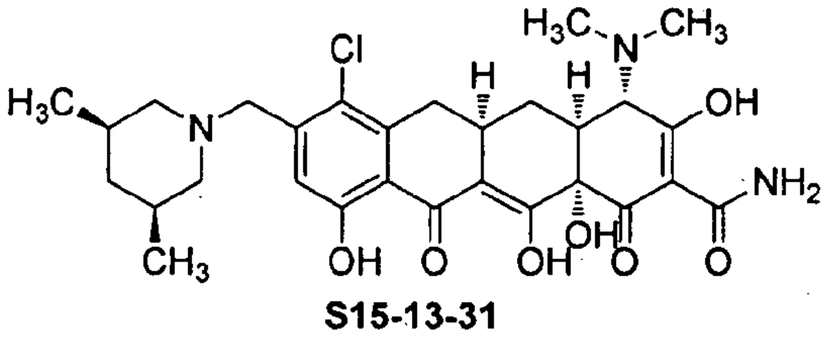
S15-13-29

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.51 (s, 2 H), 4.14 (s, 1 H), 3.64-3.57 (m, 2 H), 3.46-3.37 (m, 1 H), 3.32 (s, 3 H), 3.30-2.25 (m, 2 H), 3.25-2.95 (m, 10 H), 2.48-2.38 (m, 1 H), 2.31-2.24 (m, 1 H), 2.02-1.98 (m, 3 H), 1.71-1.52 (m, 3 H); MS (ESI) *m/z* 590.0 (M+H).



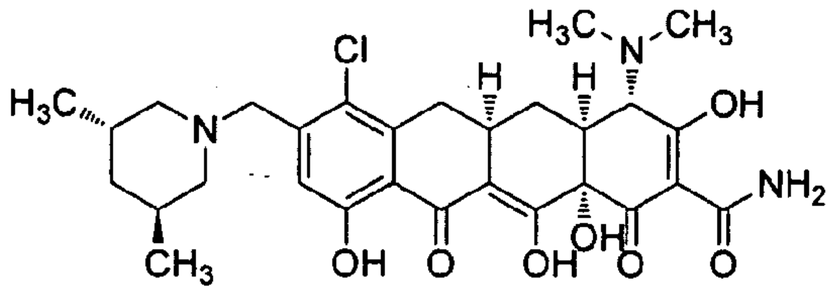
S15-13-232

MS (ESI) *m/z* 588.1.4 (M+H), calcd for $C_{30}H_{39}ClN_3O_9$ 588.24.



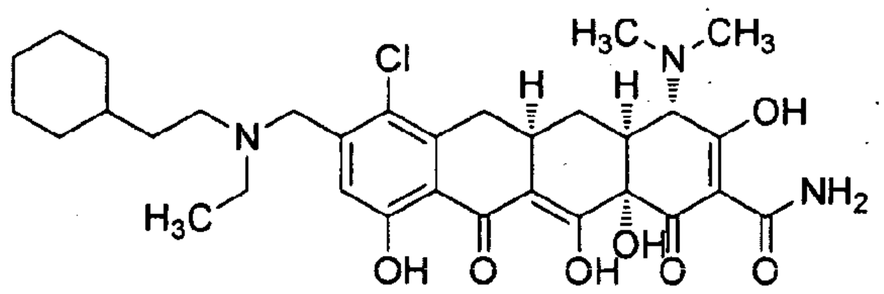
S15-13-31

^{1}H NMR (400 MHz, CD_3OD) δ 7.30 (s, 1 H), 4.53 (dd, *J* = 18.4 Hz, 13.6 Hz, 2 H), 4.15 (s, 1 H), 3.48-3.38 (m, 3 H), 3.20-2.95 (m, 8 H), 2.80-2.70 (m, 2 H), 2.48-2.38 (m, 1 H), 2.34-2.26 (m, 1 H), 2.10-1.95 (m, 2 H), 1.91-1.82 (m, 1 H), 1.72-1.61 (m, 1 H), 1.00 (d, *J* = 6.4 Hz, 6 H); MS (ESI) *m/z* 574.5 (M+H).



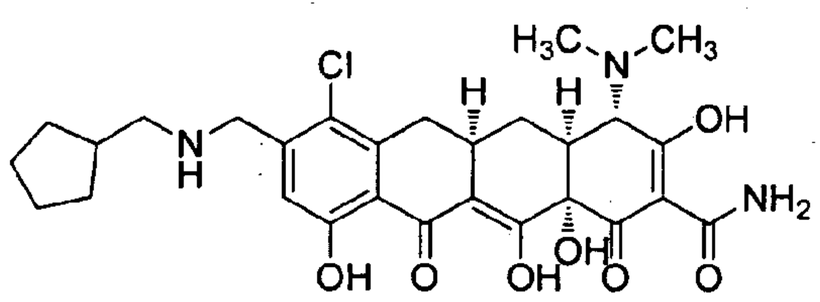
S15-13-32

^{1}H NMR (400 MHz, CD_3OD) δ 7.32 (s, 1 H), 4.60-4.32 (m, 2 H), 4.15 (s, 1 H), 3.50-3.38 (m, 2 H), 3.20-2.94 (m, 9 H), 2.83-2.70 (m, 1 H), 2.48-2.38 (m, 1 H), 2.35-2.10 (m, 3 H), 2.08-1.95 (m, 1 H), 1.72-1.53 (m, 2 H), 1.50-1.40 (m, 1 H), 1.19 (d, J = 6.8 Hz, 3 H), 0.99 (d, J = 6.8 Hz, 3 H); MS (ESI) *m/z* 574.3 (M+H).



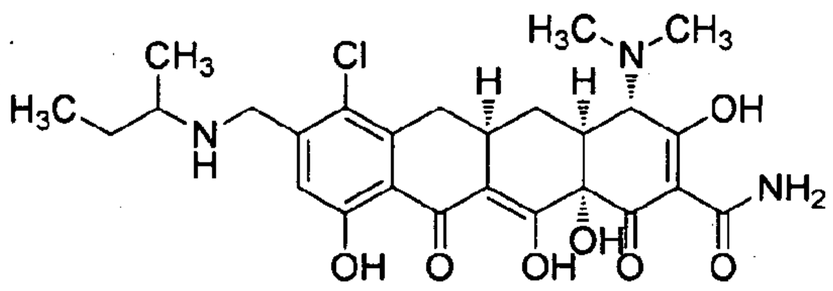
S15-13-33

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.56-4.48 (m, 2 H), 4.13 (s, 1 H), 2.43-3.39 (m, 1 H), 3.20-2.95 (m, 12 H), 2.45-2.38 (m, 1 H), 2.29-2.26 (m, 1 H), 1.80-1.59 (m, 8 H), 1.42-1.12 (m, 7 H), 1.08-0.93 (m, 2 H); MS (ESI) *m/z* 616.1 (M+H).



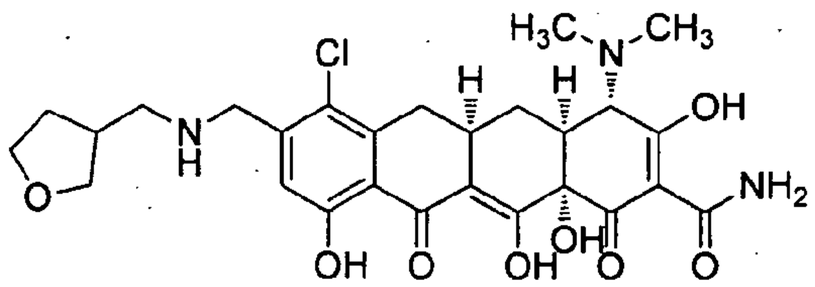
S15-13-34

^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (s, 1 H), 4.30 (s, 2 H), 4.02 (s, 1 H), 3.35-3.28 (m, 1 H), 3.08-2.85 (m, 10 H), 2.38-2.28 (m, 1 H), 2.21-2.10 (m, 2 H), 1.90-1.78 (m, 2 H), 1.68-1.49 (m, 5 H), 1.28-1.12 (m, 2 H); MS (ESI) *m/z* 560.3 (M+H).



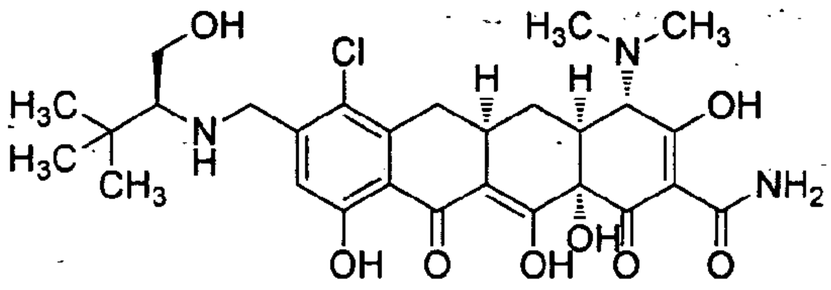
S15-13-35

^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.38 (s, 2 H), 4.13 (s, 1 H), 3.44-3.30 (m, 2 H), 3.18-2.88 (m, 8 H), 2.45-2.35 (m, 1 H), 2.31-2.24 (m, 1 H), 2.03-1.90 (m, 1 H), 1.70-1.58 (m, 2 H), 1.43 (d, *J* = 7.0 Hz, 3 H), 1.05 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 534.0 (M+H).



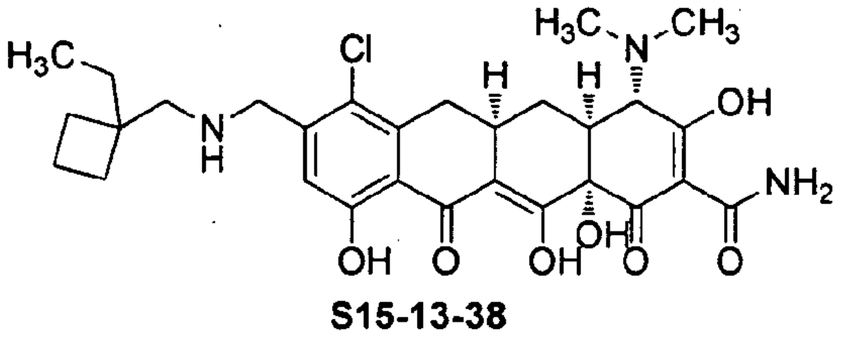
S15-13-36

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.40 (s, 2 H), 4.11 (s, 1 H), 3.92-3.86 (m, 2 H), 3.80-3.70 (m, 1 H), 3.57-3.54 (m, 1 H), 3.42-3.34 (m, 1 H), 3.22-3.19 (m, 1 H), 3.15-2.85 (m, 8 H), 2.72-2.60 (m, 1 H), 2.43-2.35 (m, 1 H), 2.28-2.13 (m, 2 H), 1.76-1.58 (m, 2 H); MS (ESI) *m/z* 562.1 (M+H).



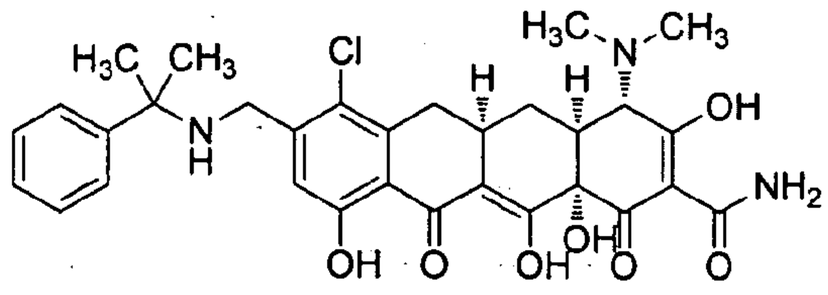
S15-13-37

^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.57 (s, 2 H), 4.10 (s, 1 H), 3.97 (dd, *J* = 12.0 Hz and 8.0 Hz, 1 H), 3.86 (dd, *J* = 12.0 Hz and 7.6 Hz, 1 H), 3.41 (dd, *J* = 16.4 Hz and 4.8 Hz, 1 H), 3.13-2.94 (m, 9 H), 2.44-2.37 (m, 1 H), 2.28-2.20 (m, 1 H), 1.69-1.59 (m, 1 H), 1.08 (s, 9 H); MS (ESI) *m/z* 578.1 (M+H).



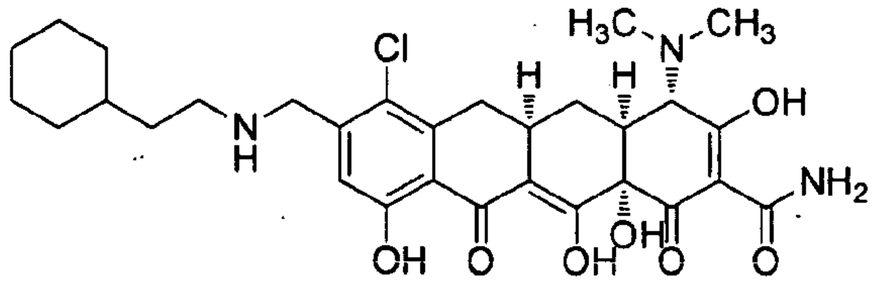
S15-13-38

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.44 (s, 2 H), 4.14 (s, 1 H), 3.42 (dd, *J* = 12.0 Hz and 4.8 Hz, 1 H), 3.22-2.87 (m, 10 H), 2.48-2.38 (m, 1 H), 2.31-2.25 (m, 1 H), 2.00-1.80 (m, 6 H), 1.70-1.58 (m, 3 H), 0.89 (t, *J* = 7.6 Hz, 3 H); MS (ESI) *m/z* 574.2 (M+H).



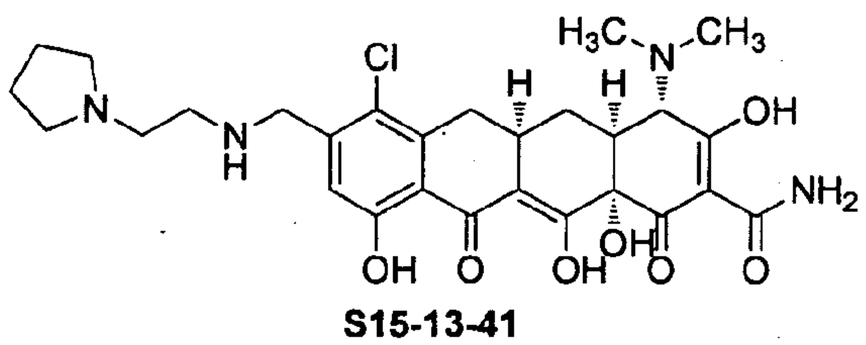
S15-13-39

^{1}H NMR (400 MHz, CD_3OD) δ 7.75-7.65 (m, 2 H), 7.60-7.48 (m, 3 H), 6.97 (s, 1 H), 4.12 (s, 1 H), 4.00 (s, 2 H), 3.37-3.32 (m, 1 H), 3.10-2.95 (m, 8 H), 2.41-2.32 (m, 1 H), 2.30-2.20 (m, 1 H), 1.89 (s, 6 H), 1.70-1.59 (m, 1 H); MS (ESI) *m/z* 596.3 (M+H).



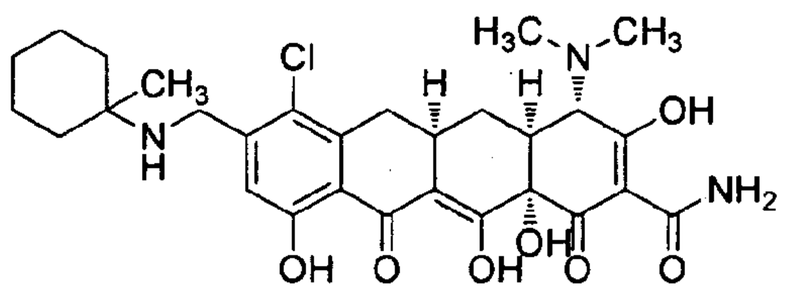
S15-13-40

^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (s, 1 H), 4.38 (s, 2 H), 4.14 (s, 1 H), 3.42 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.23-2.96 (m, 10 H), 2.47-2.38 (m, 1 H), 2.32-2.25 (m, 1 H), 1.81-1.60 (m, 8 H), 1.45-1.17 (m, 4 H), 1.08-0.96 (m, 2 H); MS (ESI) *m/z* 588.2 (M+H).



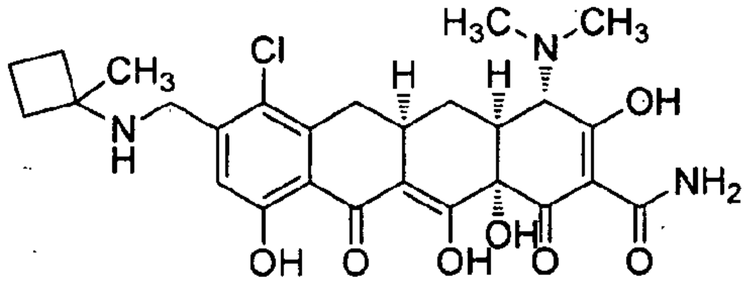
S15-13-41

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.50 (s, 2 H), 4.14 (s, 1 H), 3.90-3.65 (m, 6 H), 3.43 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.20-2.90 (m, 10 H), 2.46-2.35 (m, 1 H), 2.31-2.22 (m, 1 H), 2.20-2.00 (m, 4 H), 1.71-1.60 (m, 1 H); MS (ESI) *m/z* 575.3 (M+H).



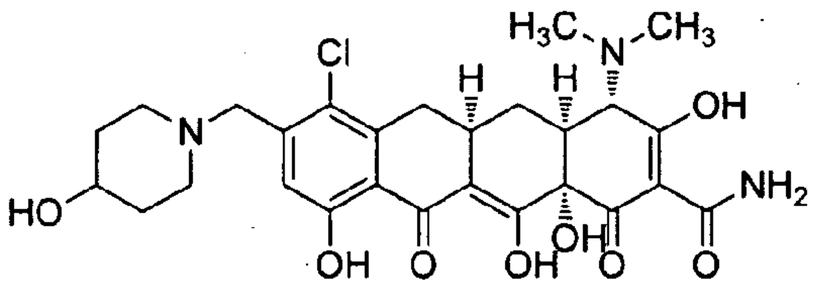
S15-13-42

^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.35 (s, 2 H), 4.11 (s, 1 H), 3.41 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.15-2.95 (m, 8 H), 2.46-2.38 (m, 1 H), 2.28-2.22 (m, 1 H), 2.00-1.93 (m, 2 H), 1.83-1.62 (m, 6 H), 1.61-1.49 (m, 6 H); MS (ESI) *m/z* 574.0 (M+H).



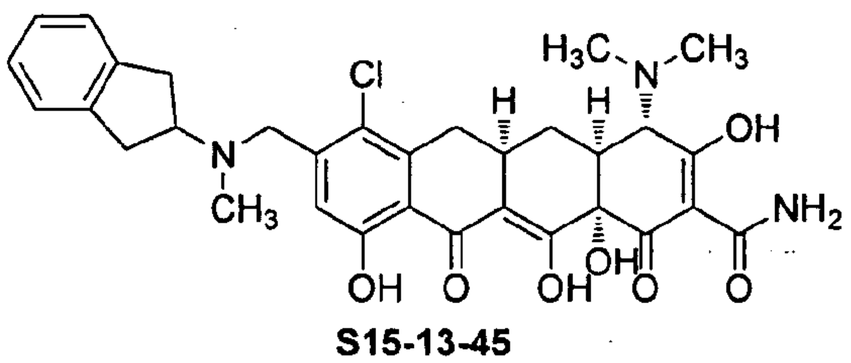
S15-13-43

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.22 (s, 2 H), 4.14 (s, 1 H), 3.41 (dd, *J* = 16.4 Hz and 4.4 Hz, 1 H), 3.18-2.32 (m, 8 H), 2.55-2.35 (m, 3 H), 2.31-2.22 (m, 1 H), 2.18-2.08 (m, 2 H), 2.05-1.93 (m, 2 H), 1.66 (s, 3 H); MS (ESI) *m/z* 546.0 (M+H).



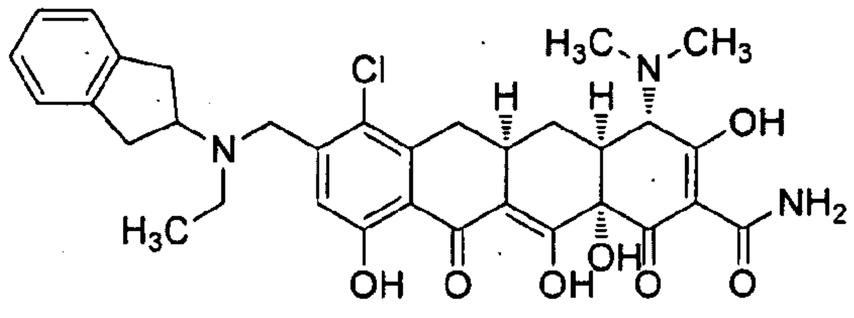
S15-13-44

^{1}H NMR (400 MHz, CD_3OD) δ 7.27 (s, 1 H), 4.55-4.47 (m, 2 H), 4.13 (s, 1 H), 3.86 (m, 1 H), 3.61-3.52 (m, 1 H), 3.50-3.35 (m, 3 H), 3.30-2.94 (m, 9 H), 2.45-2.35 (m, 1 H), 2.31-2.22 (m, 1 H), 2.18-1.98 (m, 2 H), 1.95-1.87 (m, 1 H), 1.85-1.70 (m, 1 H), 1.70-1.56 (m, 1 H); MS (ESI) *m/z* 562.1 (M+H).



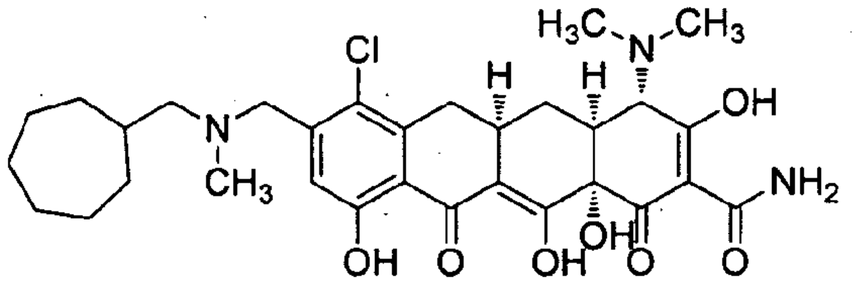
S15-13-45

^{1}H NMR (400 MHz, CD_3OD) δ 7.32-7.23 (m, 5 H), 2.48-2.38 (m, 2 H), 4.13 (s, 1 H), 3.65-3.38 (m, 6 H), 3.20-2.95 (m, 8 H), 2.84 (s, 3 H), 2.50-2.38 (m, 1 H), 2.32-2.25 (m, 1 H), 1.72-1.60 (m, 1 H); MS (ESI) *m/z* 608.0 (M+H).



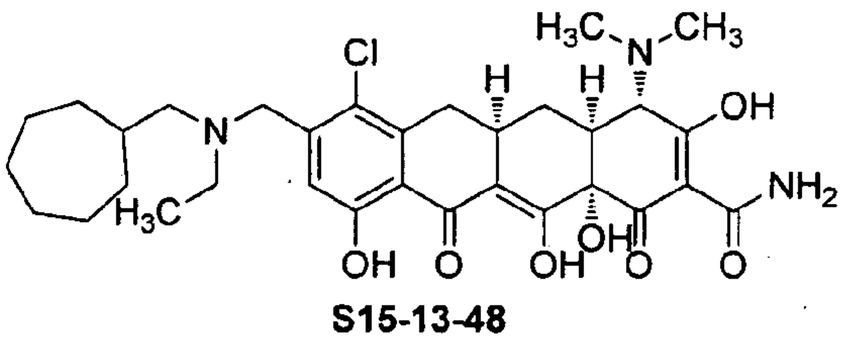
S15-13-46

^{1}H NMR (400 MHz, CD_3OD) δ 7.20-7.35 (m, 5 H), 4.65-4.40 (m, 3 H), 4.14 (s, 1 H), 3.60-3.38 (m, 6 H), 3.20-2.95 (m, 9 H), 2.50-2.39 (m, 1 H), 2.33-2.26 (m, 1 H), 1.73-1.61 (m, 1 H), 1.43 (t, *J* = 7.6 Hz, 3 H); MS (ESI) *m/z* 622.1 (M+H).



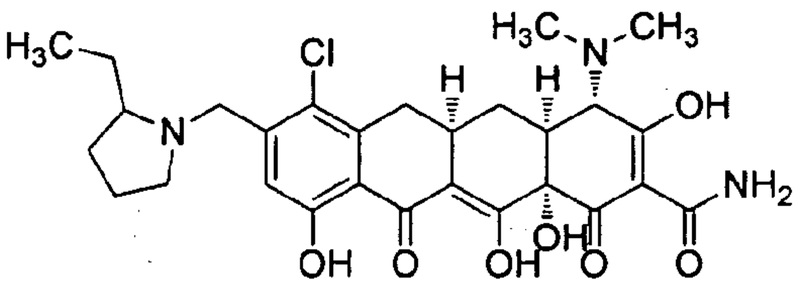
S15-13-47

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.74 (t, *J* = 13.6 Hz, 1 H), 4.32 (t, *J* = 11.6 Hz, 1 H), 4.16 (s, 1 H), 3.43 (dd, *J* = 16.0 Hz and 3.6 Hz, 1 H), 3.26-2.85 (m, 13 H), 2.47-2.40 (m, 1 H), 2.32-2.90 (m, 1 H), 2.20-2.08 (m, 1 H), 1.95-1.50 (m, 11 H), 1.40-1.25 (m, 2 H); MS (ESI) *m/z* 602.0 (M+H).



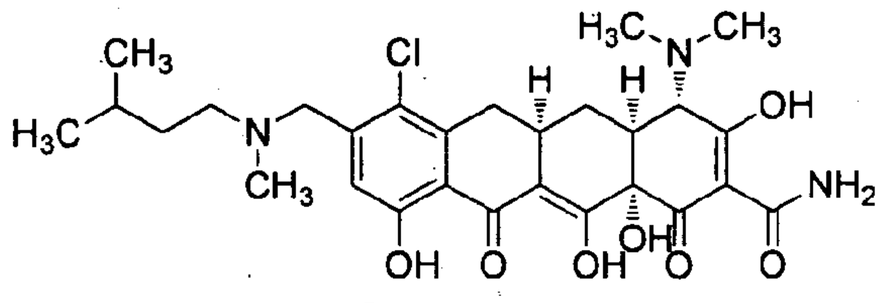
S15-13-48

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.64 (t, *J* = 13.6 Hz, 1 H), 4.49 (t, *J* = 11.6 Hz, 1 H), 4.15 (s, 1 H), 3.44 (dd, *J* = 16.0 Hz and 3.6 Hz, 1 H), 3.22-2.98 (m, 12 H), 2.50-2.40 (m, 1 H), 2.34-2.26 (m, 1 H), 2.10-2.00 (m, 1 H), 1.91-1.80 (m, 1 H), 1.80-1.50 (m, 9 H), 1.44 (t, *J* = 7.6 Hz, 3 H), 1.40-1.23 (m, 3 H); MS (ESI) *m/z* 616.1 (M+H).



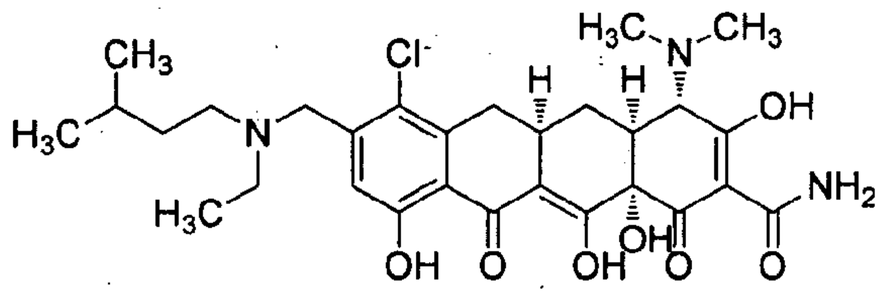
S15-13-49

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.79 (d, *J* = 13.6 Hz, 1 H), 4.35 (d, *J* = 13.2 Hz, 1 H), 4.13 (s, 1 H), 3.60-3.37 (m, 4 H), 3.16-2.94 (m, 8 H), 2.48-2.34 (m, 2 H), 2.30-2.22 (m, 1 H), 2.20-2.08 (m, 2 H), 2.08-1.98 (m,1 H), 1.85-1.71 (m, 1 H), 1.70-1.57 (m, 2 H), 1.06 (t, *J* = 7.6 Hz, 3 H); MS (ESI) *m/z* 560.4 (M+H).



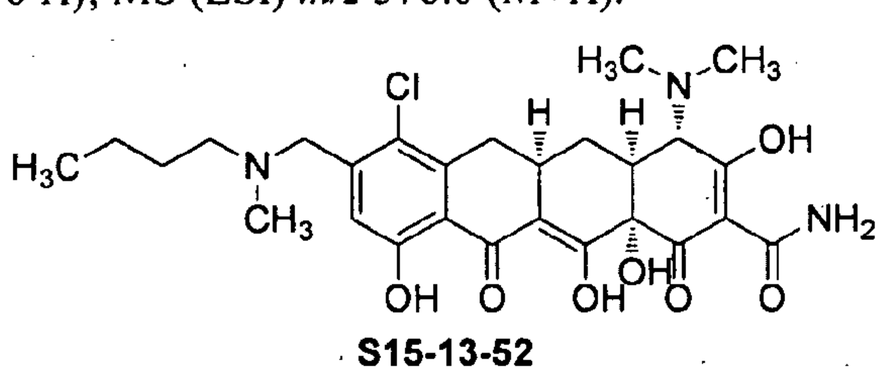
S15-13-50

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.68 (t, *J* = 13.6 Hz, 1 H), 4.39 (t, *J* = 14.0 Hz, 1 H), 4.15 (s, 1 H), 3.43-3.36 (m, 1 H), 3.18-2.72 (m, 13 H), 2.46-2.38 (m, 1 H), 2.30-2.25 (m, 1 H), 1.80-1.60 (m, 4 H), 0.99 (d, *J* = 7.6 Hz, 6 H); MS (ESI) *m/z* 562.1 (M+H).



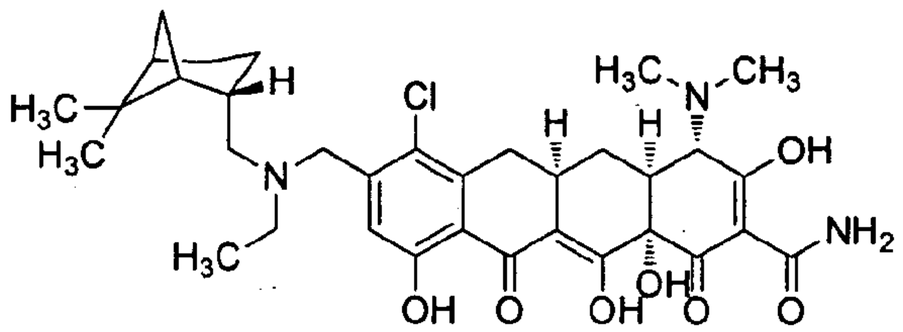
S15-13-51

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.54 (s, 2 H), 4.23 (s, 1 H), 3.42 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.26-2.97 (m, 12 H), 2.48-2.38 (m, 1 H), 2.30-2.23 (m, 1 H), 1.75-1.60 (m, 4 H), 1.40 (t, *J* = 7.6 Hz, 3 H), 0.96 (t, *J* = 7.2 Hz, 6 H); MS (ESI) *m/z* 576.0 (M+H).



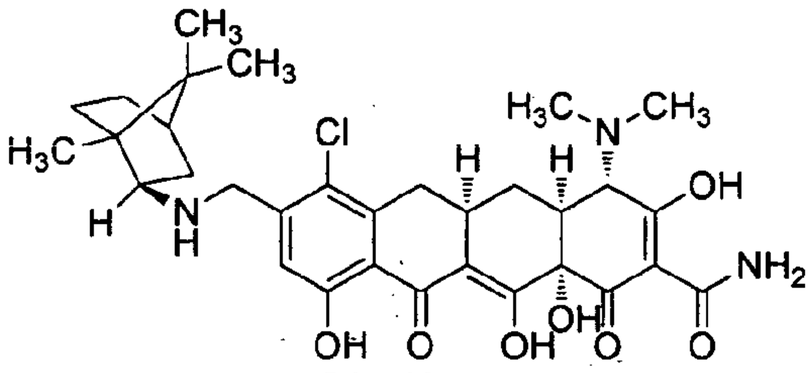
S15-13-52

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.68 (t, *J* = 13.6 Hz, 1 H), 4.39 (t, *J* = 14.0 Hz, 1 H), 4.13 (s, 1 H), 3.40 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.19-2.83 (m, 13 H), 2.49-2.39 (m, 1 H), 2.31-2.25 (m, 1 H), 1.88-1.78 (m, 2 H), 1.71-1.60 (m, 1 H), 1.50-1.39 (m, 2 H), 1.01 (t, *J* = 7.6 Hz, 3 H); MS (ESI) *m/z* 548.0 (M+H).



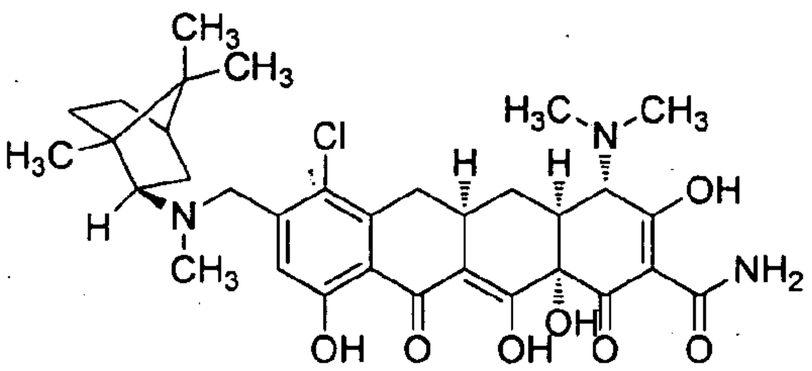
S15-13-53

^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.46 (s, 2 H), 4.06 (s, 1 H), 3.38-3.28 (m, 1 H), 3.20-2.88 (m, 12 H), 2.60-2.28 (m, 3 H), 2.25-2.17 (m, 1 H), 2.11-2.00 (m, 1 H), 1.98-1.90 (m, 1 H), 1.90-1.78 (m, 3 H), 1.64-1.50 (m, 1 H), 1.40-1.28 (m, 2 H), 1.28-1.12 (m, 3 H), 1.03-0.93 (m, 3 H), 0.71 (s, 3 H); MS (ESI) *m/z* 642.2 (M+H).



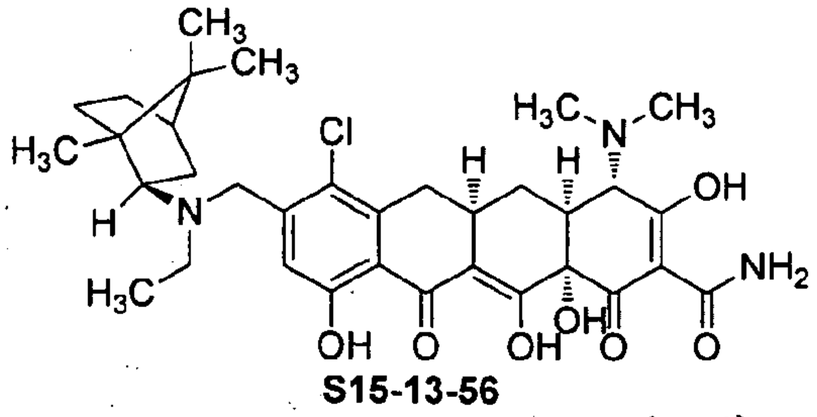
S15-13-54

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.48 (d, *J* = 13.6 Hz, 1 H), 4.29 (d, *J* = 13.6 Hz, 1 H), 4.15 (s, 1 H), 3.42 (dd, *J* = 16.4 Hz and 4.4 Hz, 1 H), 3.18-2.87 (m, 9 H), 2.47-2.35 (m, 1 H), 2.32-2.16 (m, 2 H), 1.99-1.60 (m, 5 H), 1.32-1.20 (m, 2 H), 1.13 (s, 3 H), 1.02 (s, 3 H), 0.94 (s, 3 H); MS (ESI) *m/z* 614.0 (M+H).



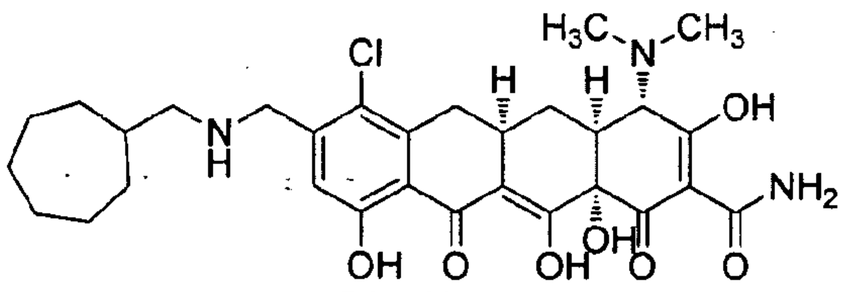
S15-13-55

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.14 (s, 1 H), 3.62-3.50 (m, 1 H), 3.48-3.38 (m, 1 H), 3.20-2.78 (m, 12 H), 2.60-2.49 (m, 1 H), 2.48-2.35 (m, 1 H), 2.32-2.18 (m, 2 H), 2.10-2.02 (m, 1 H), 1.98-1.80 (m, 3 H), 1.80-1.59 (m, 2 H), 1.28 (s, 3 H), 1.05 (s, 3 H), 0.95 (s, 3 H); MS (ESI) *m/z* 628.0 (M+H).



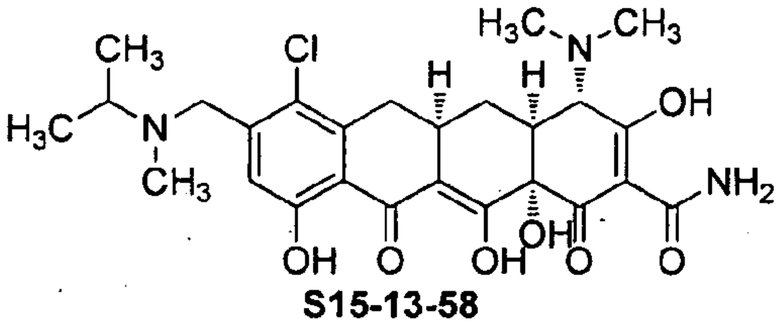
S15-13-56

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.55 (d, *J* = 13.6 Hz, 1 H), 4.29 (d, *J* = 13.6 Hz, 1 H), 4.14 (s, 1 H), 3.71-3.52 (m, 2 H), 3.50-3.38 (m, 2 H), 3.25-2.94 (m, 9 H), 2.58-2.37 (m, 2 H), 2.38-2.24 (m, 2 H), 2.09-1.82 (m, 4 H), 1.80-1.62 (m, 2 H), 1.42 (s, 3 H), 1.28 (s, 3 H), 1.07 (s, 3 H), 0.96 (t, *J* = 8.0 Hz, 3 H); MS (ESI) *m/z* 642.0 (M+H).



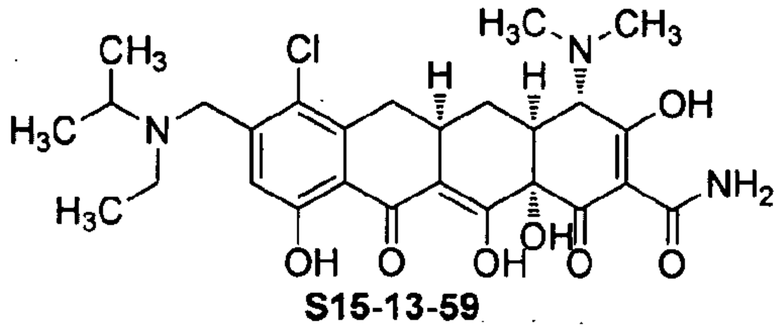
S15-13-57

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.38 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.15-2.97 (m, 10 H), 2.44-2.37 (m, 1 H), 2.30-2.22 (m, 1 H), 2.04-1.92 (m, 1 H), 1.88-1.78 (m, 2 H), 1.78-1.48 (m, 9 H), 1.39-1.27 (m, 2 H); MS (ESI) *m/z* 588.1 (M+H).



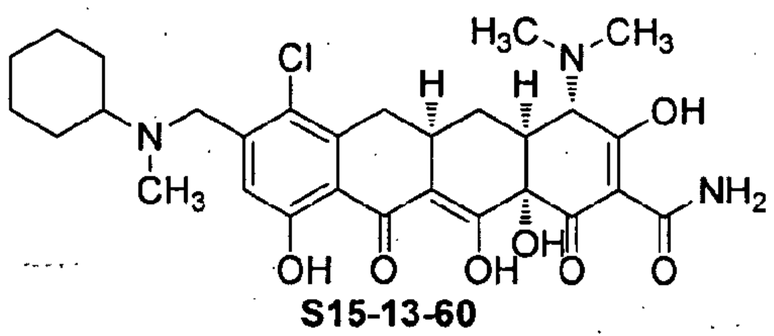
S15-13-58

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.68 (t, *J* = 13.2 Hz, 1 H), 4.29 (t, *J* = 13.2 Hz, 1 H), 4.16 (s, 1 H), 3.80 (m, 1 H), 3.44 (m, 1 H), 3.20-2.90 (m, 8 H), 2.81 (s, 3 H), 2.50-2.38 (m, 1 H), 2.34-2.26 (m, 1 H), 1.73-1.60 (m, 1 H), 1.52 (d, *J* = 5.6 Hz, 3 H), 1.47 (d, *J* = 6.4 Hz, 1 H); MS (ESI) *m/z* 534.0 (M+H).



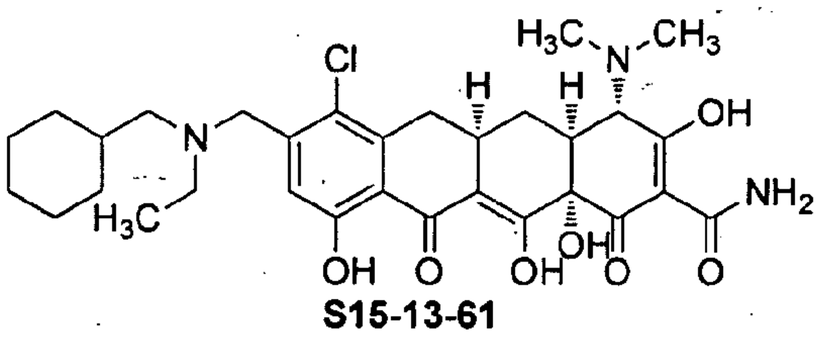
S15-13-59

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.65 (t, *J* = 13.2 Hz, 1 H), 4.39 (t, *J* = 13.2 Hz, 1 H), 4.16 (s, 1 H), 3.91-3.82 (m, 1 H), 3.45 (m, 1 H), 3.28-2.90 (m, 10 H), 2.51-2.40 (m, 1 H), 2.34-2.26 (m, 1 H), 1.75-1.62 (m, 1 H), 1.61 (d, *J* = 7.6 Hz, 3 H), 1.45 (d, *J* = 6.8 Hz, 3 H), 1.37 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 547.9 (M+H).



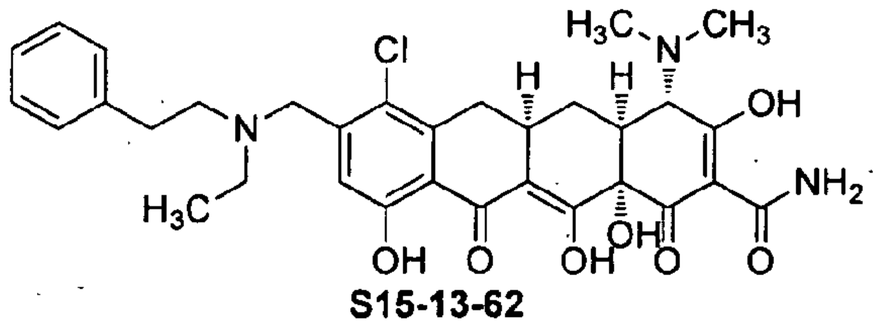
S15-13-60

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.74 (t, *J* = 13.6 Hz, 1 H), 4.29 (t, *J* = 13.2 Hz, 1 H), 4.16 (s, 1 H), 3.50-3.39 (m, 2 H), 3.20-2.97 (m, 8 H), 2.82 (s, 3 H), 2.49-2.38 (m, 1 H), 2.34-2.26 (m, 1 H), 2.20 (m, 2 H), 2.00 (m, 2 H), 1.80-1.55 (m, 4 H), 1.52-1.38 (m, 2 H), 1.35-1.25 (m, 1 H); MS (ESI) *m/z* 574.0 (M+H).



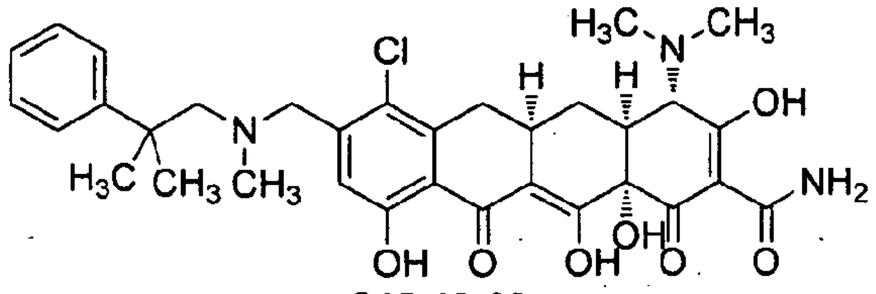
S15-13-61

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.64 (t, *J* = 13.2 Hz, 1 H), 4.51 (t, *J* = 13.2 Hz, 1 H), 4.16 (s, 1 H), 3.45 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.22-2.90 (m, 12 H), 2.51-2.42 (m, 1 H), 2.35-2.26 (m, 1 H), 1.96-1.64 (m, 7 H), 1.43 (t, *J* = 7.2 Hz, 3 H), 1.40-1.20 (m, 3 H), 1.15-0.95 (m, 2 H); MS (ESI) *m/z* 601.9 (M+H).



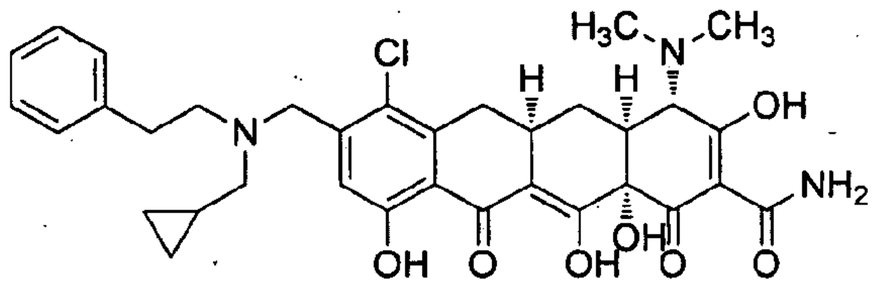
S15-13-62

^{1}H NMR (400 MHz, CD_3OD) δ 7.40-7.26 (m, 6 H), 4.72-4.58 (m, 2 H), 4.16 (s, 1 H), 3.52-2.39 (m, 5 H), 3.21-2.88 (m, 10 H), 2.50-2.39 (m, 1 H), 2.35-2.26 (m, 1 H), 1.74-1.62 (m, 1 H), 1.46 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 610.1 (M+H).



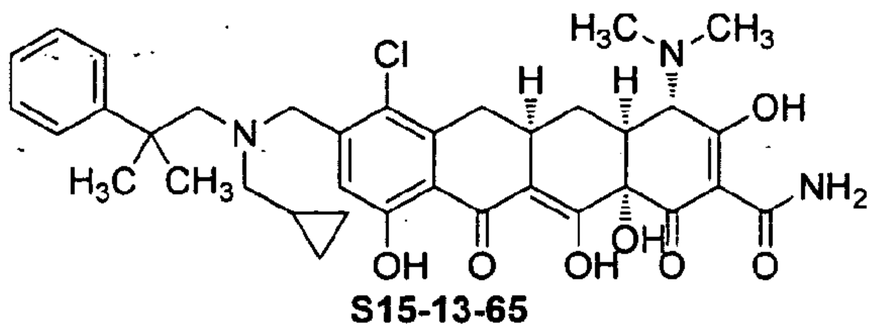
S15-13-63

^{1}H NMR (400 MHz, CD_3OD) δ 7.51 (d, *J* = 7.8 Hz, 2 H), 7.41 (t, *J* = 7.8 Hz, 2 H), 7.30 (br s, 1 H), 7.05 (s, 1 H), 4.41 (t, *J* = 12.4 Hz, 1 H), 4.23 (t, *J* = 12.4 Hz, 1 H), 3.75 (dd, *J* = 31.2 Hz and 13.6 Hz, 2 H), 3.40-3.30 (m, 1 H), 3.20-2.88 (m, 8 H), 2.75 (s, 3 H), 2.45-2.36 (m, 1 H), 2.32-2.25 (m, 1 H), 1.72-1.60 (m, 1 H), 1.58 (s, 3 H), 1.49 (s, 3 H); MS (ESI) *m/z* 624.1 (M+H).



S15-13-64

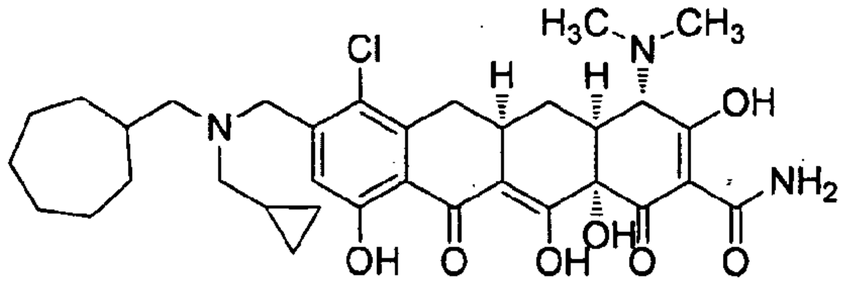
^{1}H NMR (400 MHz, CD_3OD) δ 7.38 (m, 2 H), 7.31-7.28 (m, 4 H), 4.81 (t, *J* = 14.0 Hz, 1 H), 4.68 (t, *J* = 14.0 Hz, 1 H), 4.16 (s, 1 H), 3.60-3.49 (m, 2 H), 3.43 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.36-3.30 (m, 2 H), 3.26-2.97 (m, 10 H), 2.49-2.39 (m, 1 H), 2.34-2.26 (m, 1 H), 1.73-1.62 (m, 1 H), 1.33-1.24 (m, 1 H), 0.87-0.83 (m, 2 H), 0.54-0.51 (m, 2 H); MS (ESI) *m/z* 636.0 (M+H).



S15-13-65

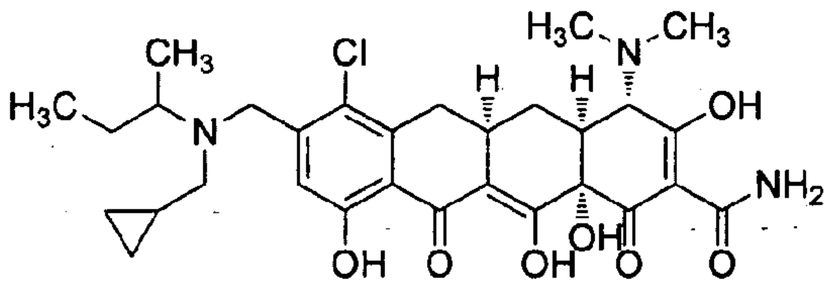
^{1}H NMR (400 MHz, CD_3OD) δ 7.48-7.42 (m, 2 H), 7.42-7.33 (m, 2 H), 7.33-7.25 (m, 1 H), 7.12-7.08 (m, 1 H), 4.57-4.49 (m, 1 H), 4.44-4.34 (m, 1 H), 4.16 (s, 1 H), 3.91-3.82 (m, 1 H), 3.66-3.58 (m, 1 H), 3.36-3.28 (m, 1 H), 3.24-2.97 (m, 10 H), 2.46-2.32 (m, 1 H), 2.32-2.25 (m, 1 H), 1.73-1.60 (m, 1 H), 1.55 (s, 3 H),

1.44 and 1.42 (each s, total 3 H), 1.30-1.18 (m, 1 H), 0.83-0.73 (m, 2 H), 0.40-0.31 (m, 2 H); MS (ESI) *m/z* 664.1 (M+H).



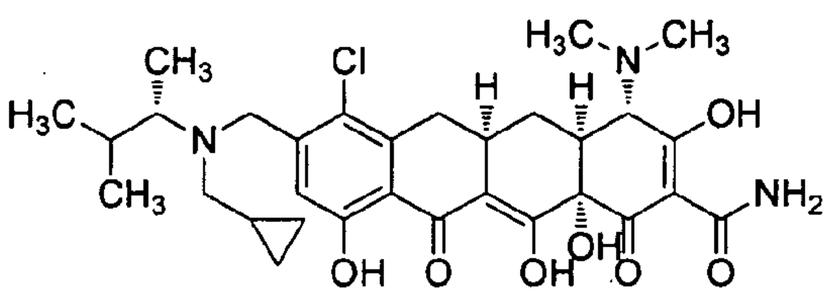
S15-13-66

^{1}H NMR (400 MHz, CD_3OD) δ 7.30 (s, 1 H), 4.74-4.62 (m, 2 H), 4.16 (s, 1 H), 3.45 (dd, *J* = 12.4 Hz and 4.4 Hz, 1 H), 3.39-3.31 (m, 1 H), 3.28-3.22 (m, 2 H), 3.20-2.98 (m, 9 H), 2.53-2.43 (m, 1 H), 2.35-2.26 (m, 1 H), 2.12-2.02 (m, 1 H), 1.92-1.82 (m, 1 H), 1.80-1.45 (m, 10 H), 1.40-1.18 (m, 3 H), 0.90-0.82 (m, 2 H), 0.55-0.48 (m, 2 H); MS (ESI) *m/z* 642.0 (M+H).



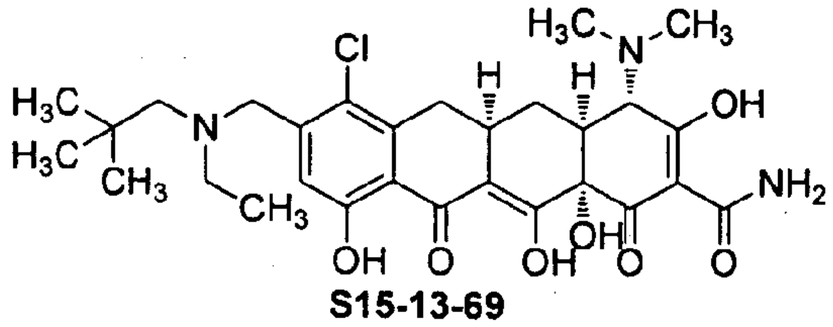
S15-13-67

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 and 7.24 (each s, total 1 H), 4.68-4.59 (m, 1 H), 4.58-4.46 (m, 1 H), 4.15 (s, 1 H), 3.75-3.63 (m, 1 H), 3.48-3.37 (m, 1 H), 3.25-2.98 (m, 11 H), 2.50-2.40 (m, 1 H), 2.33-2.26 (m, 1 H), 2.12-1.92 (m, 1 H), 1.85-1.60 (m, 2 H), 1.54 and 1.44 (each d, *J* = 6.8 Hz, total 3 H), 1.18-1.02 (m, 4 H), 0.82-0.73 (m, 2 H), 0.50-0.38 (m, 2 H); MS (ESI) *m/z* 588.1 (M+H).



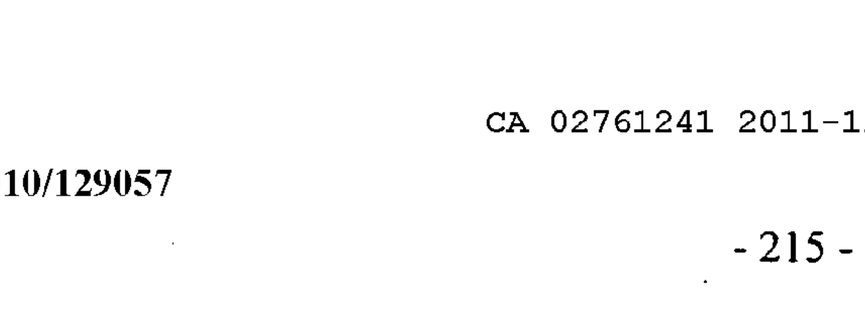
S15-13-68

^{1}H NMR (400 MHz, CD_3OD) δ 7.31 and 7.24 (each s, total 1 H), 4.75-4.64 (m, 1 H), 4.39-4.30 (m, 1 H), 4.16 (s, 1 H), 3.85-3.76 (m, 1 H), 3.48-3.39 (m, 1 H), 3.26-2.98 (m, 10 H), 2.50-2.12 (m, 3 H), 1.73-1.62 (m, 1 H), 1.44 (d, *J* = 6.4 Hz, 3 H), 1.30-1.00 (m, 7 H), 0.88-0.68 (m, 2 H), 0.60-0.38 (m, 2 H); MS (ESI) *m/z* 602.1 (M+H).



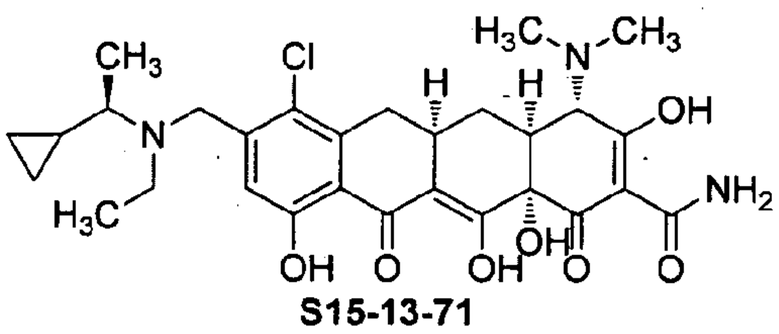
S15-13-69

^{1}H NMR (400 MHz, CD_3OD) δ 7.30 (s, 1 H), 4.70-4.50 (m, 2 H), 4.14 (s, 1 H), 3.48-3.35 (m, 3 H), 3.18-2.86 (m, 10 H), 2.48-2.37 (m, 1 H), 2.31-2.22 (m, 1 H), 1.71-1.58 (m, 1)□1.47 (t, *J* = 6.4 Hz, 3 H), 1.06 (s, 9 H); MS (ESI) *m/z* 576.1 (M+H).



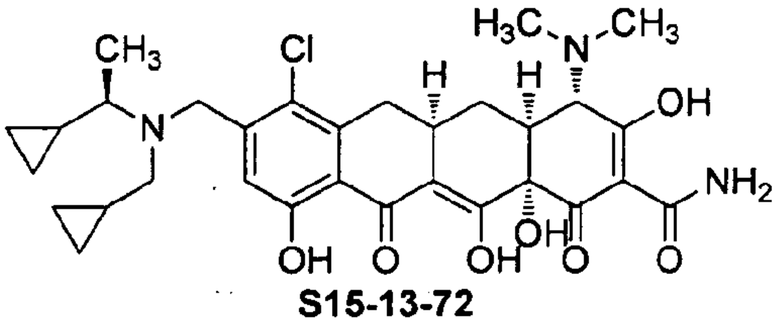
S15-13-70

^{1}H NMR (400 MHz, CD_3OD) δ 7.34 (s, 1 H), 4.77-4.66 (m, 2 H), 4.14 (s, 1 H), 3.49-3.38 (m, 2 H), 3.32-3.18 (m, 1 H), 3.18-2.94 (m, 10 H), 2.50-2.37 (m, 1 H), 2.30-2.22 (m, 1 H), 1.71-1.60 (m, 1 H), 1.38-1.28 (m, 1 H), 1.03 (s, 9 H), 0.90-0.74 (m, 2 H), 0.55-0.44 (m, 2 H); MS (ESI) *m/z* 602.1 (M+H).



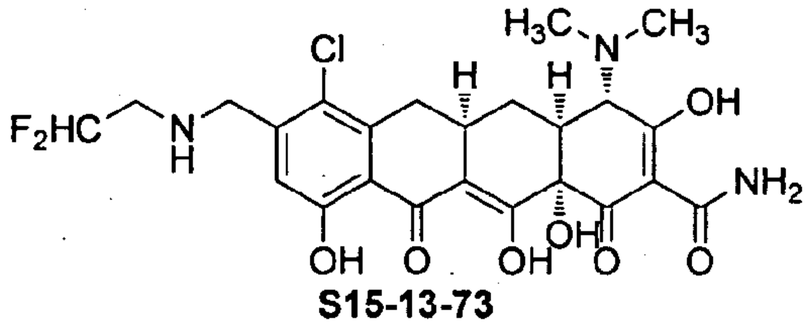
S15-13-71

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.50 and 4.38 (each d, *J* = 13.6 Hz, total 1 H), 4.16 (s, 1 H), 3.52-3.35 (m, 4 H), 3.20-2.98 (m, 9 H), 2.50-2.40 (m, 1 H), 2.34-2.26 (m, 1 H), 1.75-1.62 (m, 1 H), 1.58 and 1.53 (each d, *J* = 6.4 Hz, total 3 H), 1.38 and 1.29 (each t, *J* = 7.2 Hz, total 3 H), 0.96-0.78 (m, 2 H), 0.72-0.40 (m, 2); MS (ESI) *m/z* 574.1 (M+H).



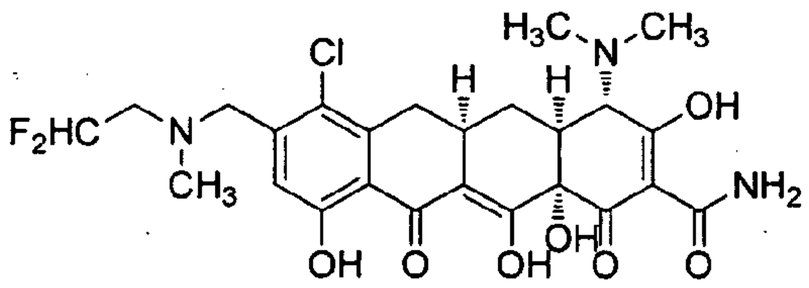
S15-13-72

^{1}H NMR (400 MHz, CD_3OD) δ 7.28 and 7.25 (each s, total 1 H), 4.76-4.72 (m, 1 H), 4.47-4.40 (m, 1 H), 4.14 (s, 1 H), 3.57-3.35 (m, 3 H), 3.20-2.98 (m, 10 H), 2.50-2.40 (m, 1 H), 2.33-2.26 (m, 1 H), 1.74-1.62 (m, 1 H), 1.51 (t, J = 7.2 Hz, 3 H), 1.45-1.22 (m, 1 H), 1.22-1.16 and 1.05-0.95 (each m, total 1 H), 0.90-0.60 (m, 5 H), 0.60-0.34 (m, 3 H); MS (ESI) *m/z* 600.1 (M+H).



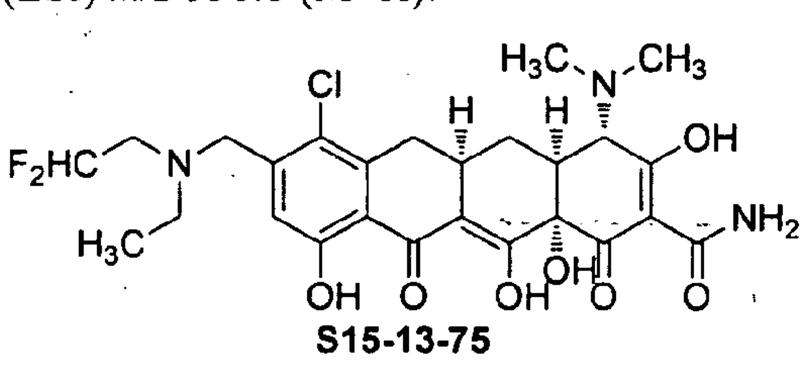
S15-13-73

^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (s, 1 H), 6.36 (tt, J = 53.6 Hz and 3.2 Hz, 1 H), 4.50 (s, 2 H), 4.12 (s, 1 H), 3.71 (dt, J = 15.2 Hz and 3.2 Hz, 2 H), 3.41 (dd, J = 16.0 Hz and 4.8 Hz, 1 H), 3.15-2.95 (m, 8 H), 2.46-2.38 (m, 1 H), 2.30-2.22 (m, 1 H), 1.72-1.61 (m, 1 H); MS (ESI) *m/z* 542.0 (M+H).



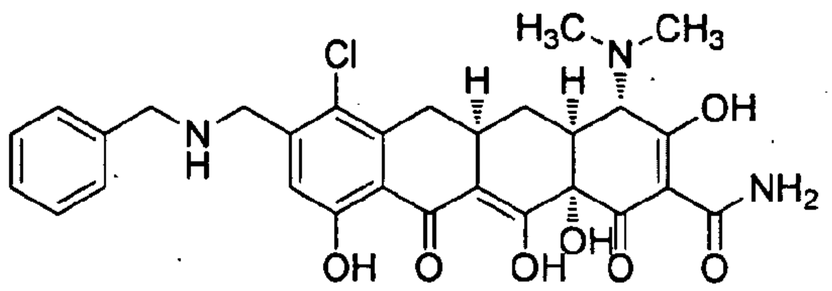
S15-13-74

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 6.50 (tt, J = 53.6 Hz and 3.2 Hz, 1 H), 4.65 (s, 2 H), 4.12 (s, 1 H), 3.90-3.80 (m, 2 H), 3.44-3.38 (m, 1 H), 3.16-2.95 (m, 11 H), 2.47-2.40 (m, 1 H), 2.30-2.23 (m, 1 H), 1.71-1.61 (m, 1 H); MS (ESI) *m/z* 556.0 (M+H).



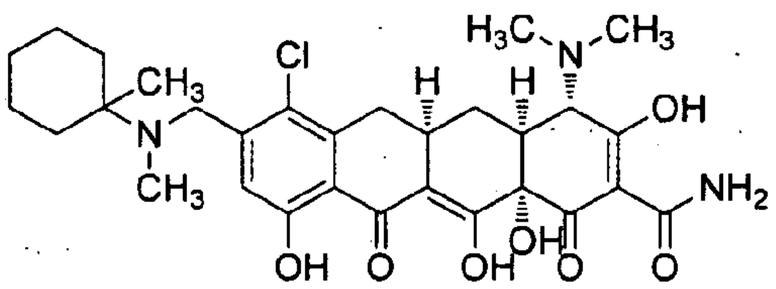
S15-13-75

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 6.51 (br t, J = 55.2 Hz, 1 H), 4.68 (dd, J = 16.8 Hz and 14.8 Hz, 2 H), 4.13 (s, 1 H), 3.86-3.76 (m, 2 H), 3.48-3.39 (m, 3 H), 3.18-2.95 (m, 8 H), 2.47-2.39 (m, 1 H), 2.30-2.24 (m, 1 H), 1.71-1.60 (m, 1 H), 1.44 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 570.0 (M+H).



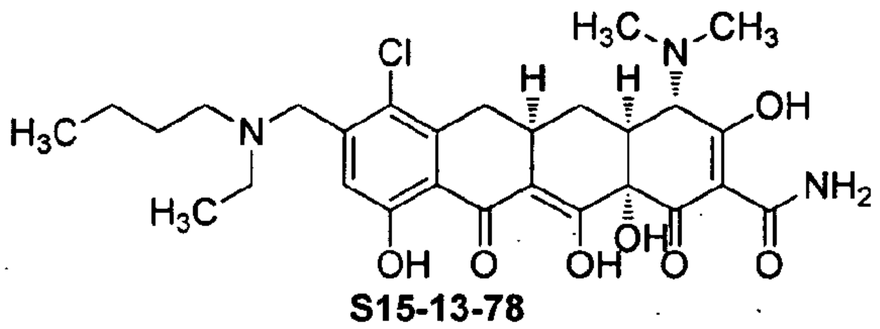
S15-13-76

^{1}H NMR (400 MHz, CD_3OD) δ 7.56-7.48 (m, 5 H), 7.10 (s, 1 H), 4.37 (br s, 4 H), 4.12 (s, 1 H), 3.38 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.14-2.95 (m, 8 H), 2.43-2.35 (m, 1 H), 2.27-2.22 (m, 1 H), 1.70-1.69 (m, 1 H); MS (ESI) *m/z* 568.3 (M+H).



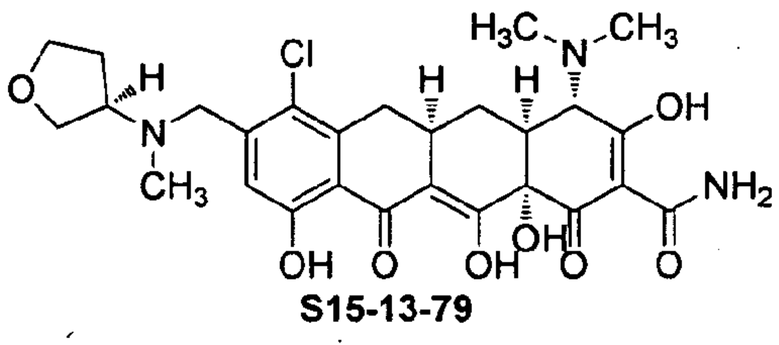
S15-13-77

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.89-4.83 (m, 1 H), 4.17-4.10 (m, 2 H), 3.47-3.37 (m, 1 H), 3.18-2.95 (m, 8 H), 2.76-2.72 (m, 3 H), 2.48-2.22 (m, 3 H), 2.04-1.95 (m, 1 H), 1.91-1.70 (m, 5 H), 1,70-1.50 (m, 6 H), 1.33-1.20 (m, 1 H); MS (ESI) *m/z* 588.4 (M+H).



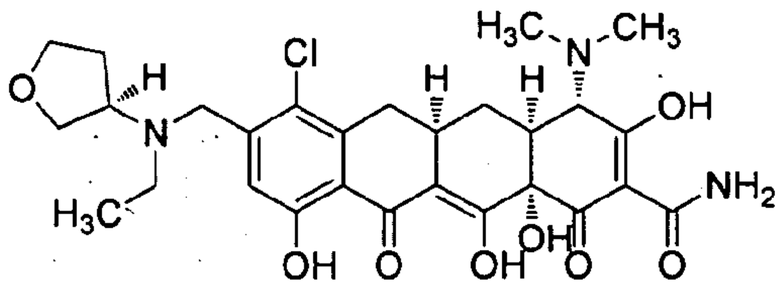
S15-13-78

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.58-4.48 (m, 2 H), 4.13 (s, 1 H), 3.42 (dd, *J* = 16.0 Hz and 4.0 Hz, 1 H), 3.23-2.95 (m, 12 H), 2.46-2.39 (m, 1 H), 2.30-2.27 (m, 1 H), 1.88-1.78 (m, 2 H), 1.70-1.60 (m, 1 H), 1.47-1.36 (m, 5 H), 0.98 (t, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 562.1 (M+H).



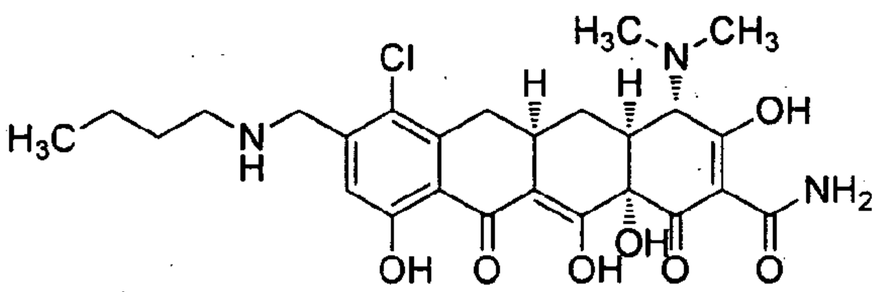
S15-13-79

^{1}H NMR (400 MHz, CD_3OD) δ 7.27 (s, 1 H), 4.44-4.15 (m, 5 H), 3.90-3.76 (m, 2 H), 3.16-2.88 (m, 10 H), 3.00 (s, 3 H), 2.51-2.28 (m, 4 H), 1.75-1.65 (m, 1 H); MS (ESI) *m/z* 562.3 (M+H).



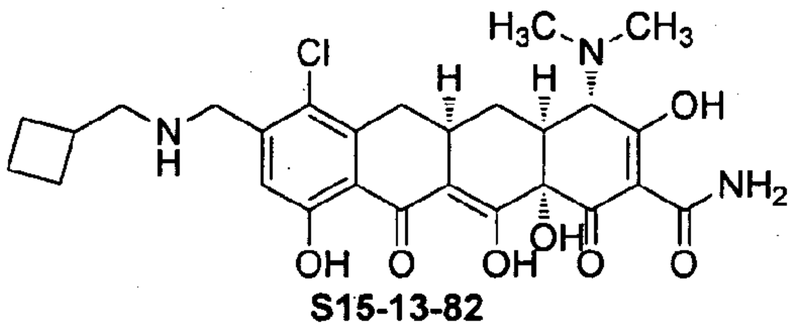
S15-13-80

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.65-4.15 (m, 7 H), 3.86 (s, 1 H), 3.78-3.71 (m, 1 H), 3.16-3.00 (m, 10 H), 2.52-2.28 (m, 4 H), 1.75-1.65 (m, 1 H), 1.44 (s, 3 H); MS (ESI) *m/z* 576.3 (M+H).



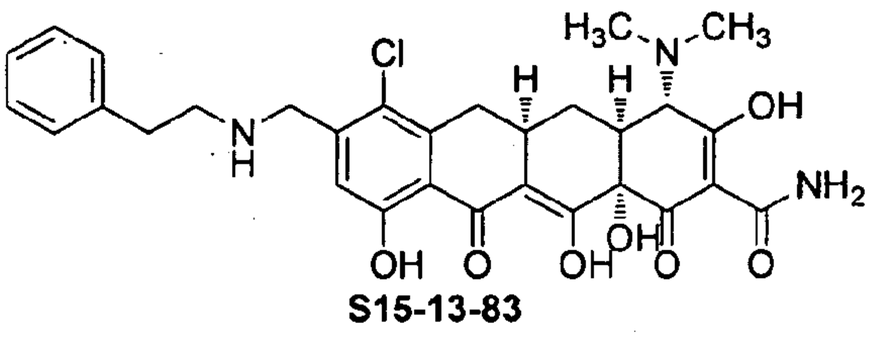
S15-13-81

^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (s, 1 H), 4.37 (s, 2 H), 4.13 (s, 1 H), 3.40 (dd, *J* = 16.0 Hz and 4.0 Hz, 1 H), 3.17-2.97 (m, 10 H), 2.45-2.35 (m, 1 H), 2.30-2.23 (m, 1 H), 1.77-1.64 (m, 3 H), 1.48-1.43 (m, 2 H), 1.00 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 534.0 (M+H).



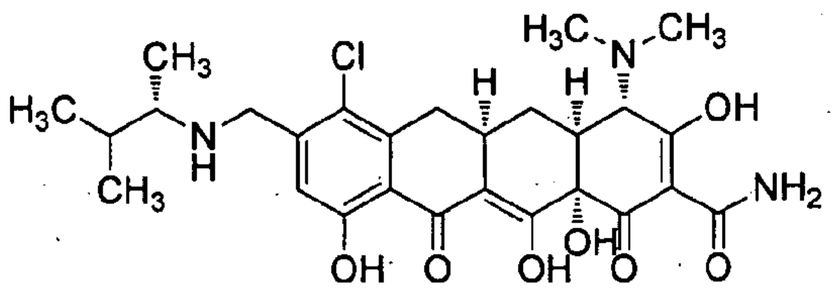
S15-13-82

^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.34 (s, 2 H), 4.13 (s, 1 H), 3.40 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.19-2.97 (m, 10 H), 2.46-2.36 (m,1 H), 2.28-2.18 (m, 3 H), 2.05-1.94 (m, 1 H), 1.92-1.86 (m, 4 H), 1.74-1.59 (m,1 H); MS (ESI) *m/z* 546.0 (M+H).



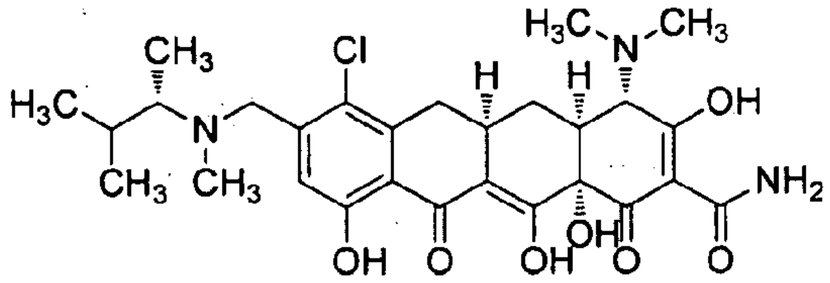
S15-13-83

^{1}H NMR (400 MHz, CD_3OD) δ 7.32-7.15 (m, 5 H), 7.07 (s, 1 H), 4.35 (s, 2 H), 4.04 (s, 1 H), 3.35-3.25 (m, 3 H), 3.08-2.88 (m, 10 H), 2.40-2.30 (m, 1 H), 2.24-2.14 (m, 1 H), 1.65-1.54 (m, 1 H); MS (ESI) *m/z* 582.0 (M+H).



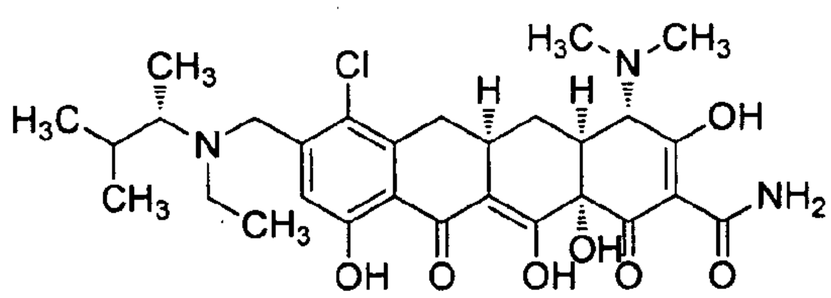
S15-13-84

^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.42 (s, 2 H), 4.14 (s, 1 H), 3.47-3.40 (m, 1 H), 3.18-2.97 (m, 9 H), 2.49-2.39 (m, 1 H), 2.32-2.20 (m, 2 H), 1.74-1.63 (m, 1 H), 1.37 (d, *J* = 6.8 Hz, 3 H), 1.09 (d, *J* = 6.8 Hz, 3 H), 1.04 (d, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 547.9 (M+H).



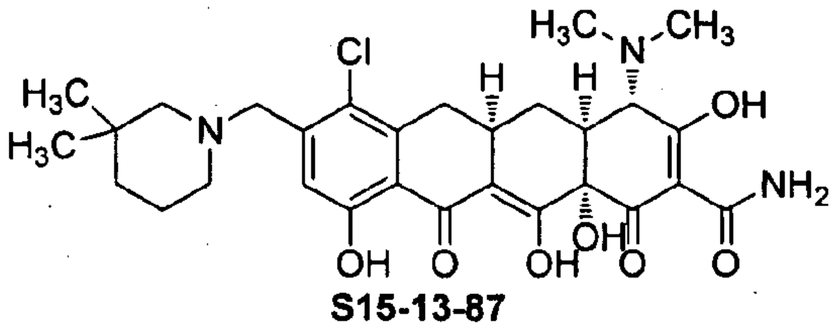
S15-13-85

^{1}H NMR (400 MHz, CD_3OD) δ 7.27 and 7.24 (each s, total 1 H), 4.76-4.70 (m, 1 H), 4.46-4.41 and 4.27-4.15 (each m, total 1 H), 4.15 (s, 1 H), 3.47-3.33 (m, 2 H), 3.20-2.97 (m, 8 H), 2.85 (s, 3 H), 2.49-2.41 (m, 1 H), 2.38-2.26 (m, 1 H), 2.25-2.12 (m, 1 H), 1.72-1.63 (m, 1 H), 1.47 and 1.42 (each d, *J* = 6.8 Hz, total 3 H), 1.20 and 1.06 (each d, *J* = 6.4 Hz, total 3 H), 1.13-1.09 (m, 3 H); MS (ESI) *m/z* 562.1 (M+H).



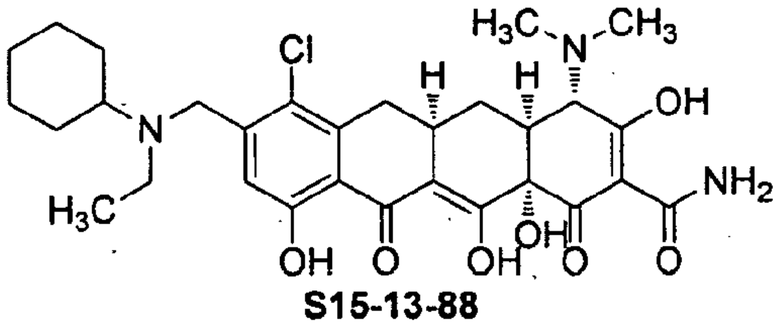
S15-13-86

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 and 7.23 (each s, total 1 H), 4.72-4.67 (m, 1 H), 4.55 and 4.31 (each d, J = 14.0 Hz, total 1 H), 4.15 (s, 1 H), 3.46-3.30 (m, 3 H), 3.20-2.97 (m, 9 H), 2.48-2.40 (m, 1 H), 2.38-2.26 (m, 2 H), 1.72-1.62 (m, 1 H), 1.44-1.31 (m, 6 H), 1.19-1.13 (m, 3 H), 1.09-1.05 (m, 3 H); MS (ESI) *m/z* 576.2 (M+H).



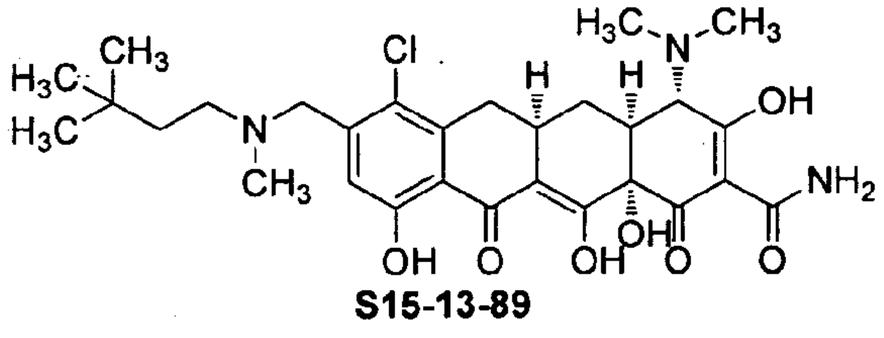
S15-13-87

^{1}H NMR (400 MHz, CD_3OD) δ 7.29 (s, 1 H), 4.60-4.42 (m, 2 H), 4.13 (s, 1 H), 3.60-3.51 (m, 1 H), 3.46-3.38 (m, 1 H), 3.25-2.86 (m, 11 H), 2.48-2.38 (m, 1 H), 2.32-2.24 (m, 1 H), 2.06-1.94 (m, 1 H), 1.90-1.80 (m, 1 H), 1.70-1.53 (m, 2 H), 1.53-1.43 (m, 1 H), 1.13 (s, 3 H), 1.03 (s, 3 H); MS (ESI) *m/z* 574.0 (M+H).



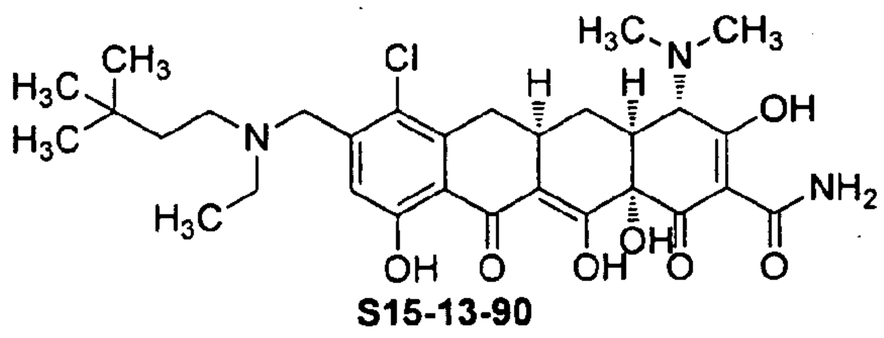
S15-13-88

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.69 (t, *J* = 13.2 Hz, 1 H), 4.35 (t, *J* = 13.2 Hz, 1 H), 4.13 (s, 1 H), 3.47-3.36 (m, 2 H), 3.20-2.95 (m, 10 H), 2.46-2.39 (m, 1 H), 2.29-2.26 (m, 1 H), 2.20-2.10 (m, 2 H), 2.01-1.92 (m, 2 H), 1.82-1.58 (m, 4 H), 1.50-1.37 (m, 2 H), 1.34 (t, *J* = 7.2 Hz, 3 H), 1.34-1.25 (m, 1 H); MS (ESI) *m/z* 588.2 (M+H).



S15-13-89

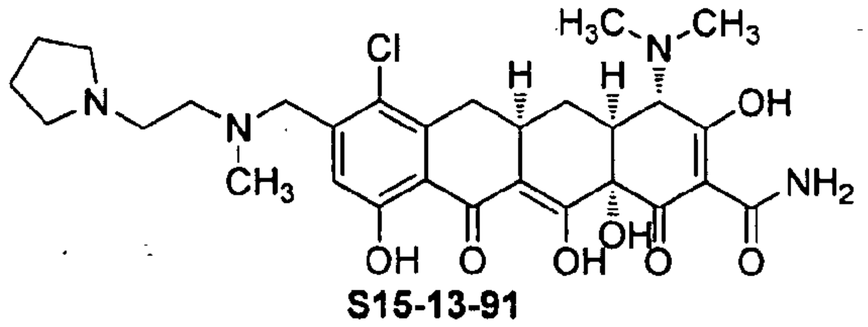
^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.70 (t, *J* = 13.2 Hz, 1 H), 4.39 (t, *J* = 13.2 Hz, 1 H), 4.15 (s, 1 H), 3.47-3.30 (m, 2 H), 3.20-2.95 (m, 9 H), 2.88 (s, 3 H), 2.48-2.40 (m, 1 H), 2.31-2.26 (m, 1 H), 1.77 (t, *J* = 8.4 Hz, 2 H), 1.73-1.61 (m, 1 H), 1.01 (s, 9 H); MS (ESI) *m/z* 576.3 (M+H).



S15-13-90

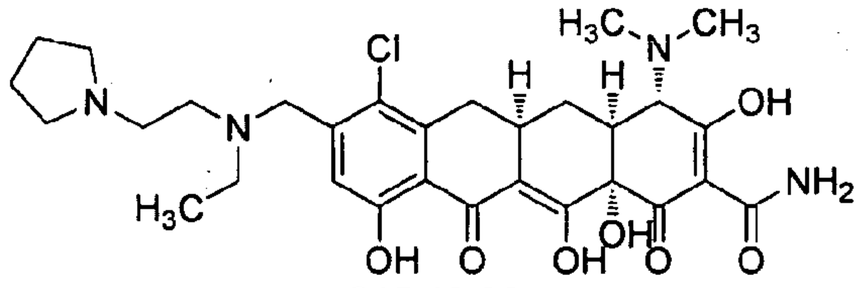
^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.60-4.55 (m, 2 H), 4.14 (s, 1

H), 3.47-3.42 (m, 1 H), 3.20-2.96 (m, 12 H), 2.52-2.43 (m, 1 H), 2.33-2.26 (m, 1 H), 1.77-1.65 (m, 3 H), 1.42 (t, J = 6.8 Hz, 3 H), 1.00 (s, 9 H); MS (ESI) *m/z* 590.3 (M+H).



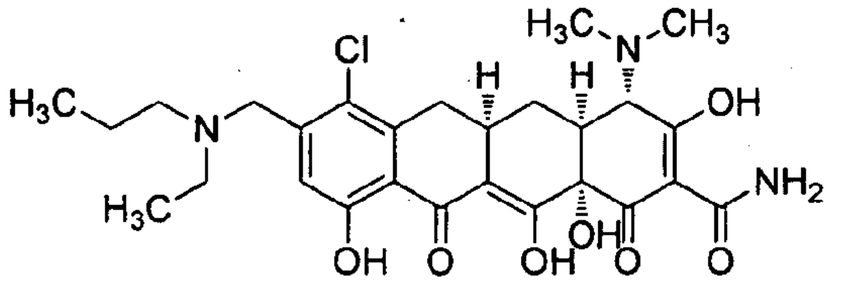
S15-13-91

^{1}H NMR (400 MHz, CD_3OD) δ 7.33 (s, 1 H), 4.60-4.50 (m, 2 H), 4.11 (s, 1 H), 3.80-3.64 (m, 4 H), 3.45-3.36 (m, 1 H), 3.15-2.88 (m, 9 H), 2.65 (s, 6 H), 2.48-2.38 (m, 1 H), 2.28-2.21 (m, 1 H), 2.12 (br s, 4 H), 1.71-1.60 (m, 1 H); MS (ESI) *m/z* 589.2 (M+H).



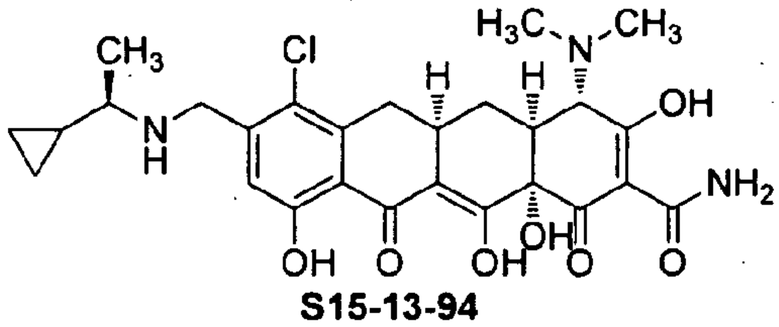
S15-13-92

^{1}H NMR (400 MHz, CD_3OD) δ 7.36 (s, 1 H), 4.60-4.52 (m, 1 H), 4.14 (s, 1 H), 3.82-3.60 (m, 4 H), 3.46-3.38 (m, 1 H), 3.20-2.96 (m, 9 H), 2.68 (s, 6 H), 2.52-2.40 (m, 1 H), 2.30-2.24 (m, 1 H), 2.20-2.09 (m, 4 H), 1.48-1.40 (m, 3 H); MS (ESI) *m/z* 603.4 (M+H).



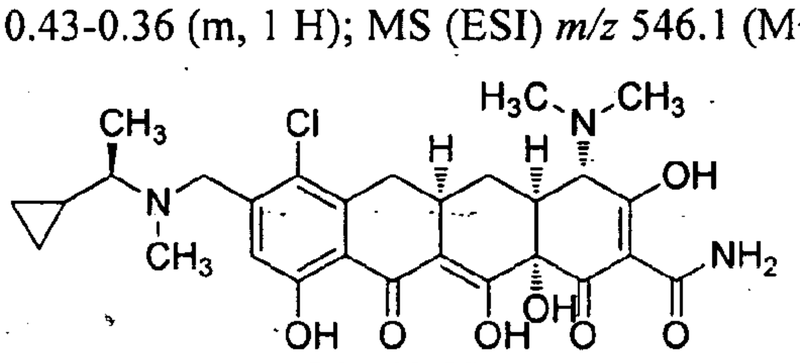
S15-13-93

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.58-4.48 (m, 2 H), 4.13 (s, 1 H), 3.42 (dd, J = 16.4 Hz and 4.4 Hz, 2 H), 3.20-2.96 (m, 11 H), 2.48-2.38 (m, 1 H), 2.31-2.23 (m, 1 H), 1.90-1.77 (m, 2 H), 1.72-1.60 (m, 1 H), 1.39 (t, J = 7.2 Hz, 3 H), 1.02(t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 548.3 (M+H).



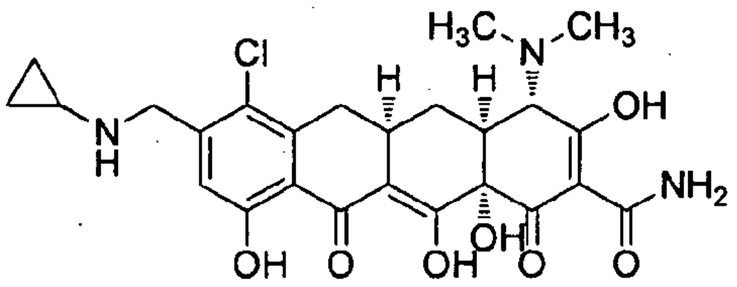
S15-13-94

^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.58-4.50 (m, 1 H), 4.43-4.36 (m, 1 H), 4.13 (s, 1 H), 3.42 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.20-2.93 (m, 9 H), 2.85-2.77 (m, 1 H), 2.46-2.36 (m, 1 H), 2.30-2.26 (m, 1 H), 1.70-1.60 (m, 1 H), 1.50 (d, *J* = 6.8 Hz, 3 H), 1.13-1.04 (m, 1 H), 0.88-0.70 (m, 2 H), 0.68-0.59 (m, 1 H), 0.43-0.36 (m, 1 H); MS (ESI) *m/z* 546.1 (M+H).



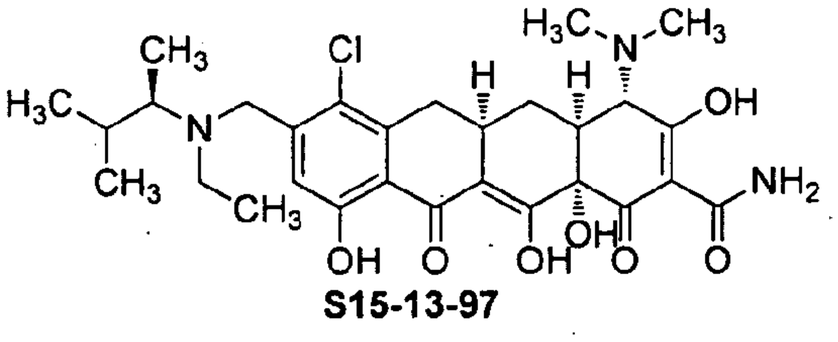
S15-13-95

^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.36-4.24 (m, 2 H), 4.10 (s, 1 H), 3.42-3.35 (m, 1 H), 3.12-2.77 (m, 12 H), 2.47-2.38 (m, 1 H), 2.27-2.23 (m, 1 H), 1.69-1.59 (m, 1 H), 1.57-1.49 (br s, 3 H), 1.33-1.25 and 1.20-1.10 (each m, total 1 H), 0.88-0.73 (m, 2 H), 0.72-0.66 and 0.60-0.52 (each m, total 1 H), 0.48-0.35 (m, 1 H); MS (ESI) *m/z* 560.4 (M+H).



S15-13-96

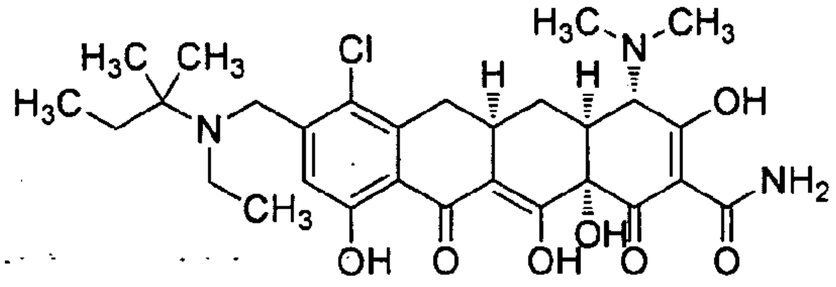
^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.49 (s, 2 H), 4.13 (s, 1 H), 3.41 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.16-2.84 (m, 9 H), 2.44-2.37 (m, 1 H), 2.28-2.25 (m, 1 H), 1.70-1.60 (m, 1 H), 0.97-0.93 (m, 4 H); MS (ESI) *m/z* 518.2 (M+H).



S15-13-97

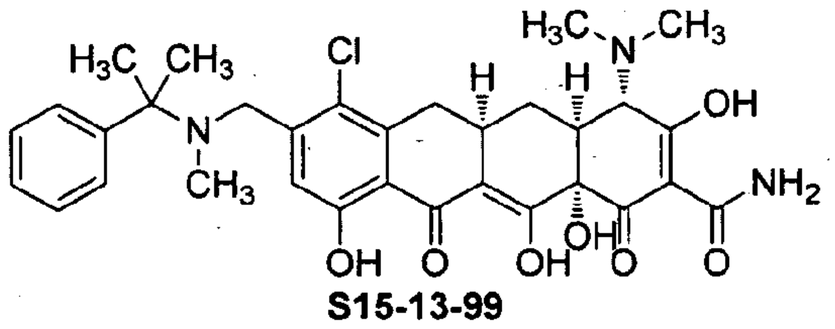
^{1}H NMR (400 MHz, CD_3OD) δ 7.17 and 7.24 (each s, total 1 H), 4.74, 4,67,

4,53 and 4.35 (each d, J = 13.6 Hz, total 2 H), 4.15 (s, 1 H), 3.49-3.36 (m, 3 H), 3.20-2.90 (m, 9 H), 2.50-2.40 (m, 1 H), 2.40-2.28 (m, 2 H), 1.73-1.64 (m, 1 H), 1.47-1.30 (m, 6 H), 1.20-1.12 (m, 3 H), 1.10-1.05 (m, 3 H); MS (ESI) *m/z* 576.2 (M+H).



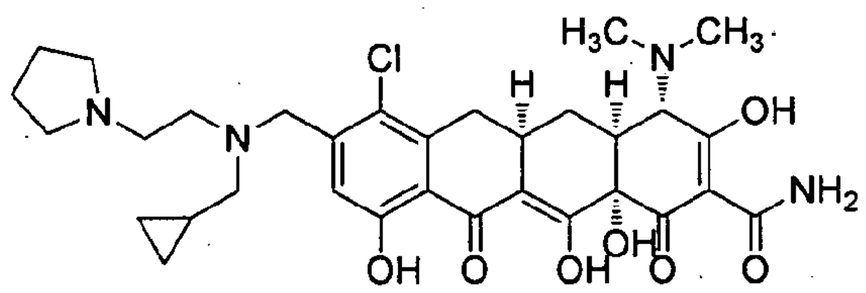
S15-13-98

^{1}H NMR (400 MHz, CD_3OD) δ 7.28 (s, 1 H), 4.77-4.70 (m, 1 H), 4.51-4.44 (m, 1 H), 4.12 (s, 1 H), 3.54-3.38 (m, 2 H), 3.18-2.85 (m, 9 H), 2.48-2.38 (m, 1 H), 2.27-2.24 (m, 1 H), 2.02-1.90 (m, 2 H), 1.70-1.60 (m, 1 H), 1.54 (s, 3 H), 1.53 (s, 3 H), 1.13-1.05 (m, 6 H); MS (ESI) *m/z* 576.2 (M+H).



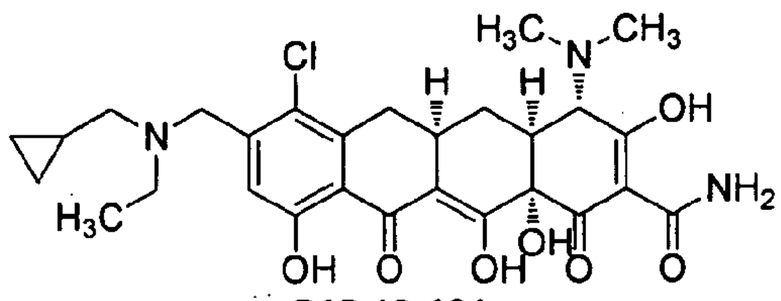
S15-13-99

^{1}H NMR (400 MHz, CD_3OD) δ 7.80-7.76 (m, 2 H), 7.58-7.48 (m, 3 H), 6.97-6.96 (m, 1 H), 4.41-4.35 (m, 1 H), 4.09-4.03 (m, 2 H), 3.15-2.90 (m, 9 H), 2.90-2.80 (m, 3 H), 2.36-2.28 (m, 1 H), 2.25-2.18 (m, 1 H), 1.98 (s, 3 H), 1.95 (s, 3 H), 1.65-1.55 (m, 1 H); MS (ESI) *m/z* 610.1 (M+H).



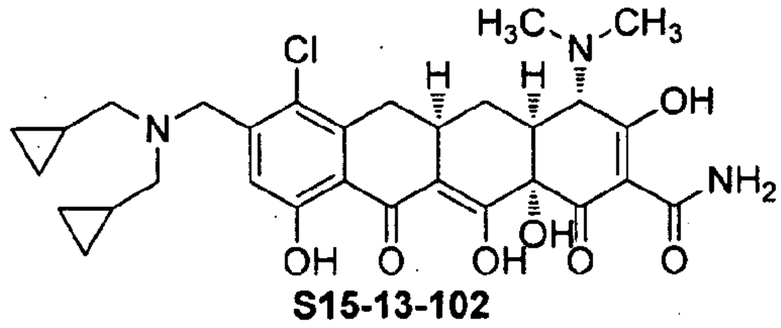
S15-13-100

^{1}H NMR (400 MHz, CD_3OD) δ 7.41 (s, 1 H), 4.85-4.58 (m, 2 H), 4.13 (s, 1 H), 3.87-3.60 (m, 7 H), 3.42 (dd, J = 16.0 Hz and 4.0 Hz, 1 H), 3.20-3.10 (m, 3 H), 3.09-2.95 (m, 8 H), 2.47-2.39 (m, 1 H), 2.28-2.24 (m, 1 H), 2.20-2.00 (m, 4 H), 1.71-1.60 (m, 1 H), 1.35-1.23 (m, 1 H), 0.87-0.80 (m, 2 H), 0.57-0.49 (m, 2 H); MS (ESI) *m/z* 629.2 (M+H).



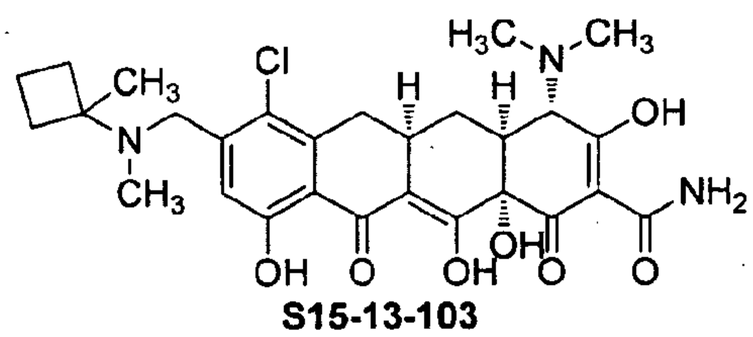
S15-13-101

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.73-4.64 (m, 1 H), 4.57-4.48 (m, 1 H), 4.12 (s, 1 H), 3.44-3.34 (m, 2 H), 3.25-2.95 (m, 11 H), 2.50-2.38 (m, 1 H), 2.30-2.21 (m, 1 H), 1.71-1.60 (m, 1 H), 1.42-1.36 (m, 3 H), 1.25-1.15 (m, 1 H), 0.84-0.77 (m, 2 H), 0.50-0.42 (m, 2 H); MS (ESI) *m/z* 560.3 (M+H).



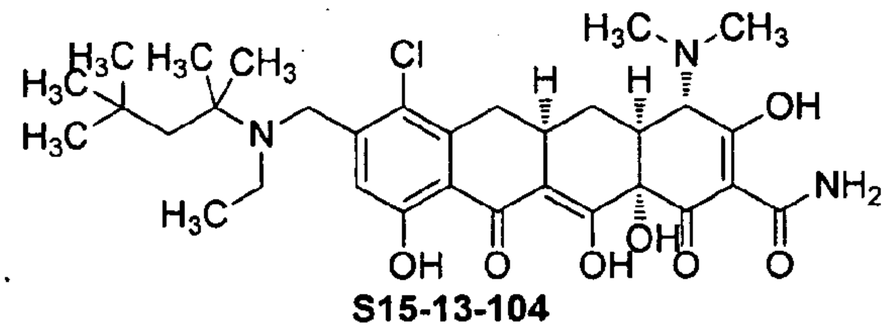
S15-13-102

^{1}H NMR (400 MHz, CD_3OD) δ 7.29 and 7.22 (each s, total 1 H), 4.73-4.68 (m, 2 H), 4.11 (s, 1 H), 3.45-3.35 (m, 1 H), 3.20-2.90 (m, 12 H), 2.49-2.40 (m, 1 H), 2.30-2.21 (m, 1 H), 1.71-1.60 (m, 1 H), 0.82-0.77 (m, 4 H), 0.50-0.39 (m, 4 H); MS (ESI) *m/z* 586.1 (M+H).



S15-13-103

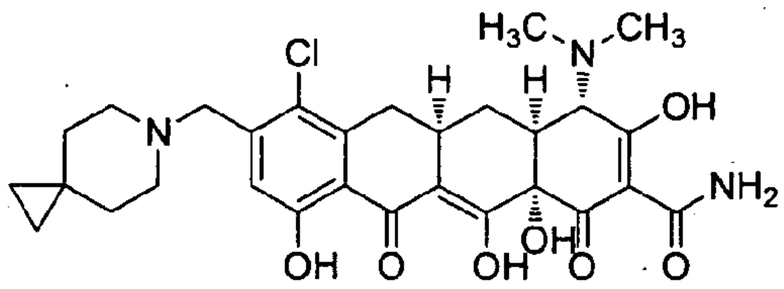
^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.51-4.44 (m, 1 H), 4.20-4.13 (m, 2 H), 3.46-3.39 (m, 1 H), 3.18-2.95 (m, 8 H), 2.71-2.58 (m, 4 H), 2.58-2.37 (m, 2 H), 2.30-2.22 (m, 2 H), 2.10-2.02 (m, 1 H), 2.00-1.87 (m, 2 H), 1.70-1.59 (m, 4 H); MS (ESI) *m/z* 560.1 (M+H).



S15-13-104

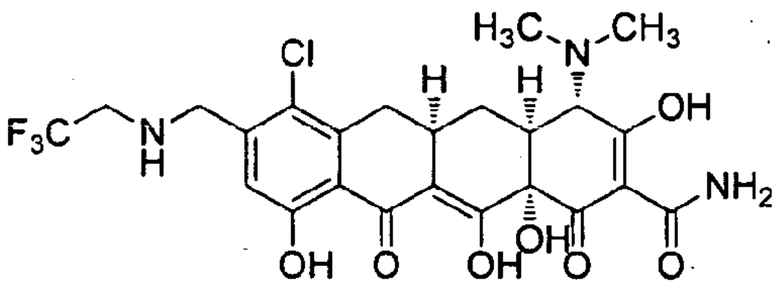
^{1}H NMR (400 MHz, CD_3OD) δ 7.32 (s, 1 H), 4.78-4.71 (m, 1 H), 4.51-4.44 (m, 1 H), 4.14 (s, 1 H), 3.62-3.50 (m, 1 H), 3.48-3.37 (m, 1 H), 3.30-2.95 (m, 9 H),

2.49-2.36 (m, 1 H), 2.30-2.26 (m, 1 H), 1.99-1.90 (m, 2 H), 1.77-1.58 (m, 7 H), 1.17-1.07 (m, 12 H); MS (ESI) *m/z* 618.1 (M+H).



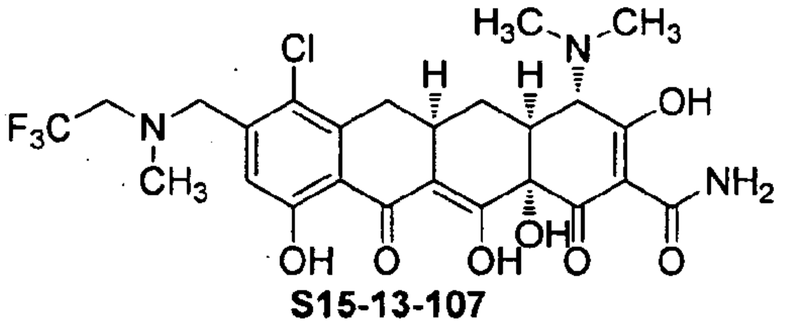
S15-13-105

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.54-4.47 (m, 2 H), 4.08 (s, 1 H), 3.55-3.47 (m, 2 H), 3.37 (dd, *J* = 16.4 Hz and 4.8 Hz, 1 H), 3.11-2.89 (m, 10 H), 2.41-2.34 (m, 1 H), 2.20-2.13 (m, 3 H), 1.65-1.54 (m, 1 H), 1.20-1.16 (m, 2 H), 0.50-0.41 (m, 4 H); MS (ESI) *m/z* 572.2 (M+H).



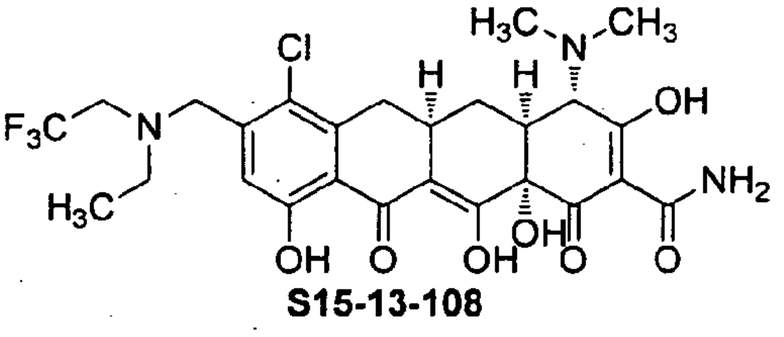
S15-13-106

^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (s, 1 H), 4.46 (s, 2 H), 4.15-4.07 (m, 2 H), 3.35 (dd, *J* = 16.4 Hz and 4.8 Hz, 1 H), 3.10-2.89 (m, 9 H), 2.40-2.32 (m, 1 H), 2.27-2.17 (m, 1 H), 1.65-1.55 (m, 1 H); MS (ESI) *m/z* 560.1 (M+H).



S15-13-107

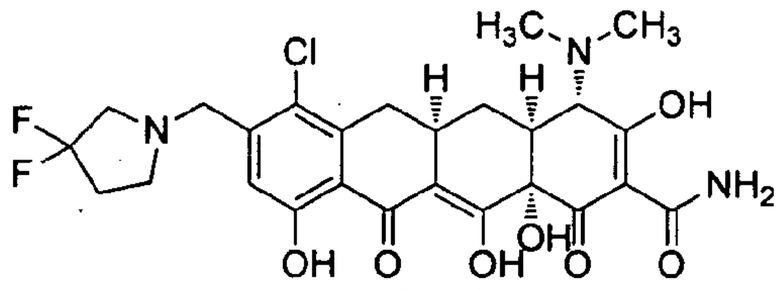
^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.10 (s, 3 H), 3.62-3.55 (m, 2 H), 3.40 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.10-2.95 (m, 8 H), 2.62 (s, 3 H), 2.41-2.32 (m, 1 H), 2.27-2.20 (m, 1 H), 1.69-1.59 (m, 1 H); MS (ESI) *m/z* 574.0 (M+H).



S15-13-108

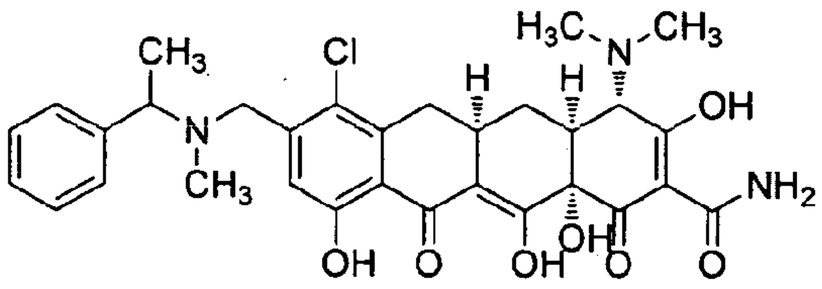
^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (s, 1 H), 4.09 (s, 2 H), 4.05 (s, 1 H), 3.58-3.50 (m, 2 H), 3.33 (dd, *J* = 16.4 Hz and 4.8 Hz, 1 H), 3.05-2.85 (m, 10 H),

2.33-2.25 (m, 1 H), 2.20-2.14 (m, 1 H), 1.63-1.53 (m, 1 H), 1.13 (t, J = 6.8 Hz, 3 H); MS (ESI) *m/z* 588.1 (M+H).



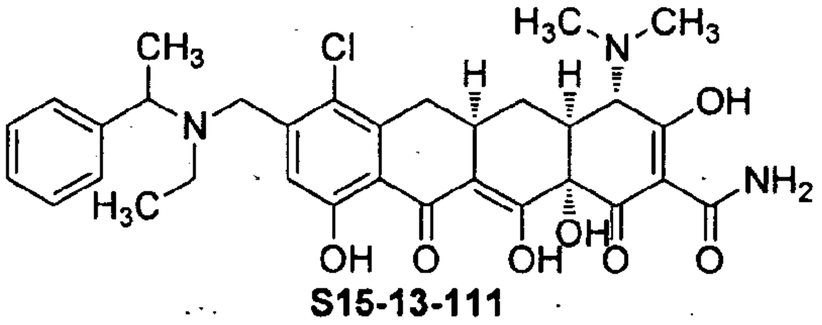
S15-13-109

^{1}H NMR (400 MHz, CD_3OD) δ 7.27 (s, 1 H), 4.78-4.69 (m, 2 H), 4.15 (s, 1 H), 4.07-4.01 (m, 2 H), 3.85-3.81 (m, 2 H), 3.41 (dd, J = 16.0 Hz and 4.4 Hz, 1 H), 3.17-2.95 (m, 8 H), 2.76-2.66 (m, 2 H), 2.43-2.36 (m, 1 H), 2.31-2.27 (m, 1 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 568.0 (M+H).



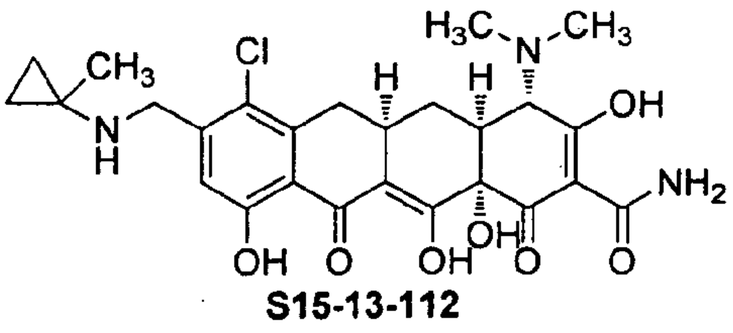
S15-13-110

^{1}H NMR (400 MHz, CD_3OD) δ 7.61-7.51 (m, 5 H), 7.15 and 7.07 (each s, total 1 H), 4.71-4.58 (m, 1 H), 4.18-4.00 (m, 2 H), 3.12-2.70 (m, 13 H), 2.40-2.18 (m, 2 H), 1.86 (br s, 3 H), 1.66-1.52 (m, 1 H); MS (ESI) *m/z* 596.1 (M+H).



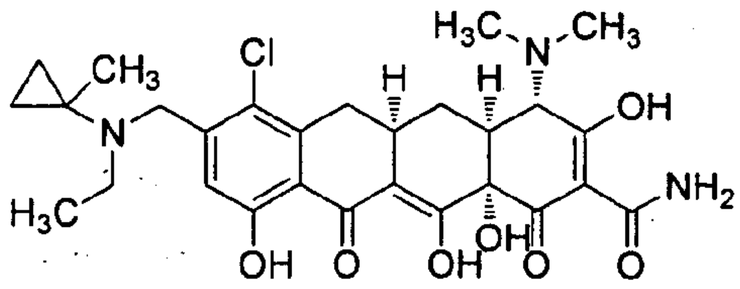
S15-13-111

^{1}H NMR (400 MHz, CD_3OD) δ 7.61-7.50 (m, 5 H), 7.03, 6.99 and 6.97 (each s, total 1 H), 5.02-4.96 (m, 1 H), 4.78-4.70 (m, 1 H), 4.45-4.35 (m, 1 H), 4.34-4.20 (m, 1 H), 4.10 (s, 1 H), 3.49-3.38 (m, 1 H), 3.20-2.91 (m, 8 H), 2.37-2.30 (m, 1 H), 2.23-2.20 (m, 1 H), 1.81 (d, J = 6.0 Hz, 3 H), 1.65-1.52 (m, 1 H), 1.48-1.35 (m, 3 H); MS (ESI) *m/z* 610.2 (M+H).



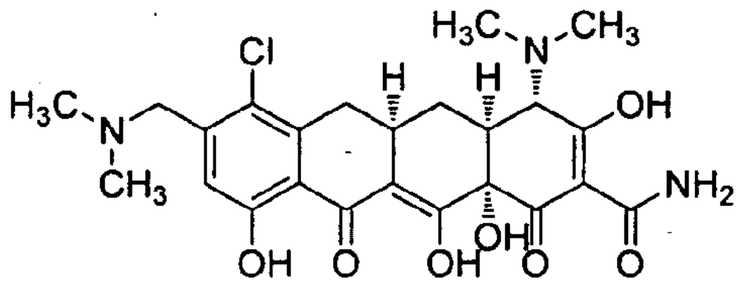
S15-13-112

^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (s, 1 H), 4.45 (s, 2 H), 4.09 (s, 1 H), 3.42-3.35 (m, 1 H), 3.12-2.93 (m, 8 H), 2.43-2.36 (m, 1 H), 2.25-2.22 (m, 1 H), 1.68-1.55 (m, 4 H), 1.15-1.12 (m, 2 H), 0.90-0.87 (m, 2 H); MS (ESI) *m/z* 532.1 (M+H).



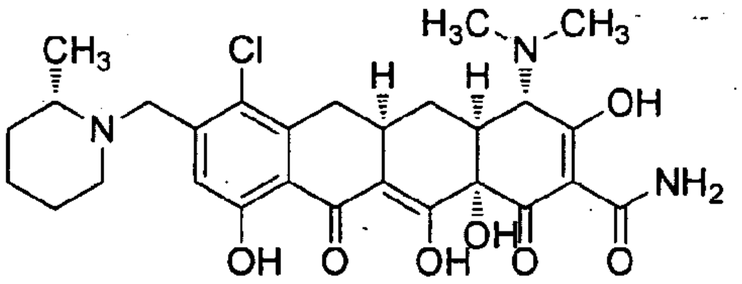
S15-13-113

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.73-4.64 (m, 2 H), 4.12 (s, 1 H), 3.54-3.38 (m, 2 H), 3.18-2.85 (m, 9 H), 2.49-2.38 (m, 1 H), 2.28-2.24 (m, 1 H), 1.70-1.57 (m, 4 H), 1.39 (t, *J* = 7.2 Hz, 3 H), 1.05-0.89 (m, 4 H); MS (ESI) *m/z* 560.1 (M+H).



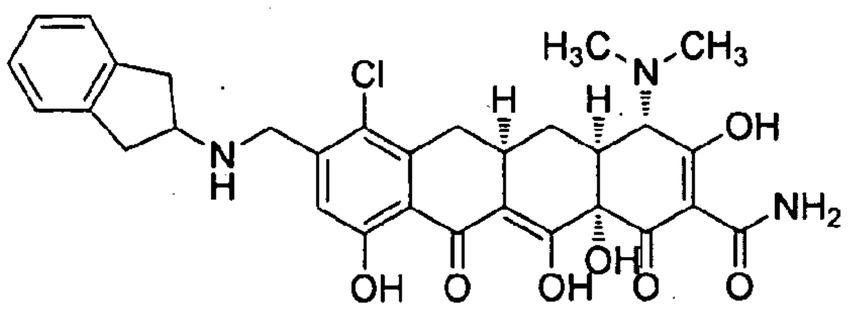
S15-13-114

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.54-4.47 (m, 2 H), 4.12 (s, 1 H), 3.39 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.15-2.85 (m, 14 H), 2.44-2.37 (m, 1 H), 2.28-2.22 (m, 1 H), 1.70-1.59 (m, 1 H); MS (ESI) *m/z* 506.1 (M+H).



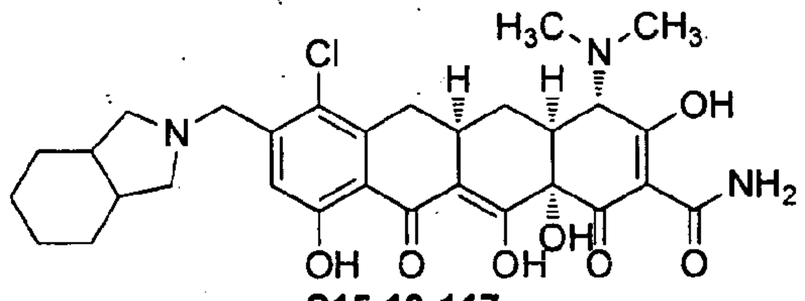
S15-13-115

^{1}H NMR (400 MHz, CD_3OD) δ 7.25-7.20 (m, 1 H), 4.55-4.40 (m, 1 H), 4.29-4.25 (m, 1 H), 4.13 (s, 1 H), 3.50-3.42 (m, 2 H), 3.20-2.88 (m, 10 H), 2.48-2.40 (m, 1 H), 2.30-2.24 (m, 1 H), 2.10-2.00 (m, 1 H), 1.91-1.62 (m, 6 H), 1.59 and 1.52 (each d, J = 6.4 Hz, total 3 H); MS (ESI) *m/z* 560.1 (M+H).



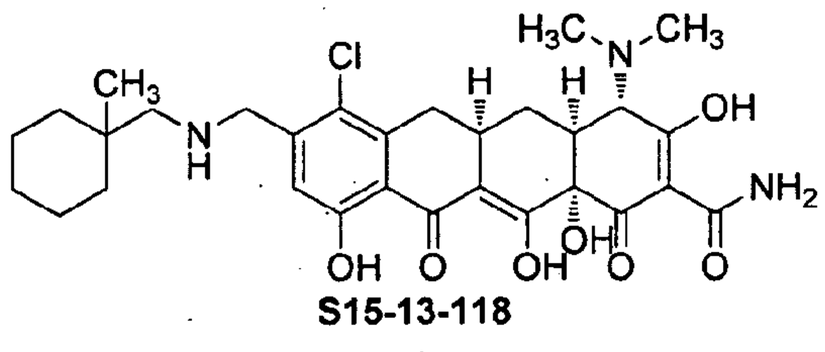
S15-13-116

^{1}H NMR (400 MHz, CD_3OD) δ 7.31-7.18 (m, 5 H), 4.45 (s, 2 H), 4.26 (m,1 H), 4.12 (s, 1 H), 3.50 (dd , *J* = 16.4 Hz and 7.6 Hz, 2 H), 3.23 (dd, *J* = 16.8Hz and 6.4 Hz, 2 H), 3.05-2.97 (m, 9 H), 2.45-2.25 (m, 2 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 594.2 (M+H).



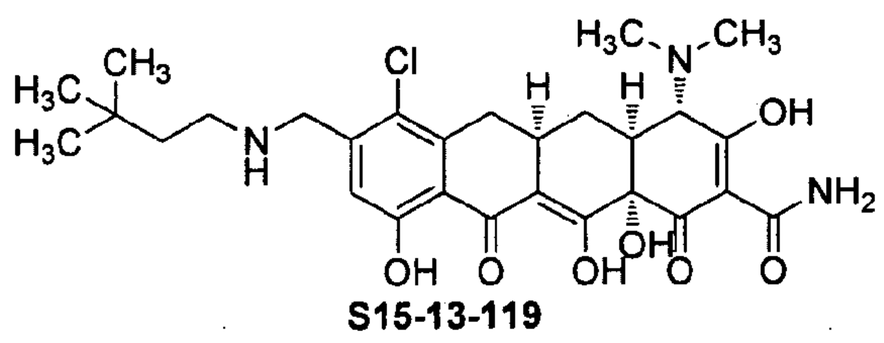
S15-13-117

^{1}H NMR (400 MHz, CD_3OD) δ 7.28 (s, 1 H), 4.63 (d, *J* = 11.2 Hz, 2 H), 4.13 (s, 1 H), 3.68-3.64 (m, 1 H), 3.52-3.51 (m,1 H), 3.43-3.42 (m, 2 H), 3.12-2.89 (m , 9 H), 2.59 (s, 1 H), 2.43-2.-2.37 (m, 2 H), 2.28-2.26 (m.1 H)1.76-1.43 (m, 9 H); MS (ESI) *m/z* 586.2 (M+H).



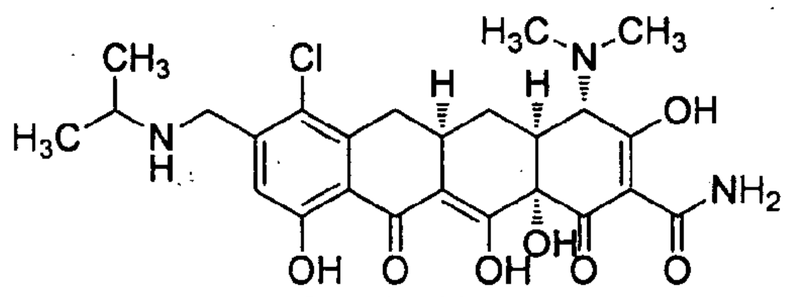
S15-13-118

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.43 (s, 2 H), 4.14 (s, 1 H), 3.11-2.97 (m , 11 H), 2.44-2.41 (m, 1 H), 2.29-2.26 (m, 1 H), 1.70-1.64 (m, 1 H), 1.51-1.41 (m, 10 H), 1.08 (s, 3 H); MS (ESI) *m/z* 558.3 (M+H).



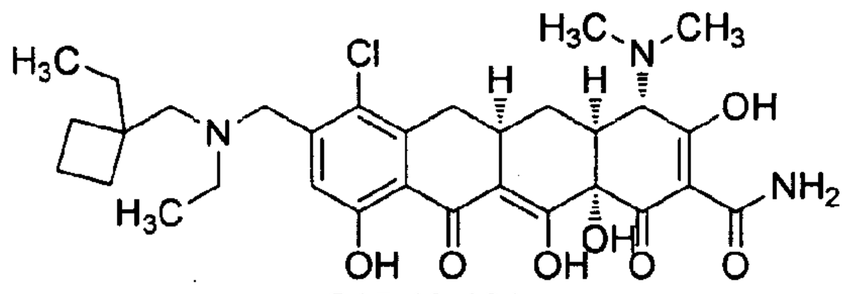
S15-13-119

^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (s, 1 H), 4.39 (s, 2 H), 4.12 (s, 1 H), 3.21-2.97 (m, 11 H), 2.45-2.41 (m, 1 H), 2.28-2.25 (m, 1 H), 1.69-1.66 (m, 3 H), 0.99 (s, 9 H); MS (ESI) *m/z* 562.3 (M+H).



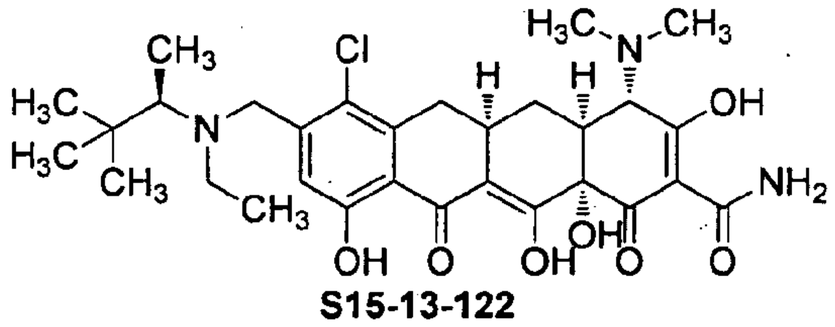
S15-13-120

^{1}H NMR (400 MHz, CD_3OD) δ 7.14 (s, 1 H), 4.36 (s, 2 H), 4.11 (s, 1 H), 3.54-3.51 (m, 1 H) 3.12-2.97 (m, 9 H), 2.45-2.38 (m, 1 H), 2.28-2.25 (m, 1 H), 1.67-1.64 (m, 1 H), 1.43 (d, *J* = 6.4 Hz, 6 H); MS (ESI) *m/z* 519.9 (M+H).



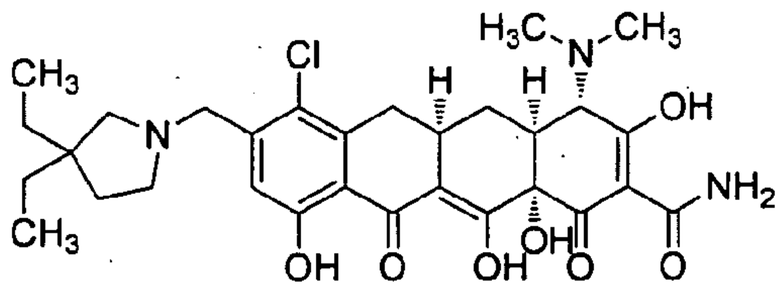
S15-13-121

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.57-4.47 (m, 2 H), 4.14 (s, 1 H), 3.43-3.39 (m, 2 H), 3.21-2.95 (m, 11 H), 2.46-2.38 (m, 1 H), 2.29-2.26 (m, 1 H), 2.05-1.85 (m, 6 H), 1.82-1.72 (m, 2 H), 1.70-1.60 (m, 1 H), 1.46 (t, *J* = 7.2 Hz, 3 H), 0.87 (t, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 602.1 (M+H).



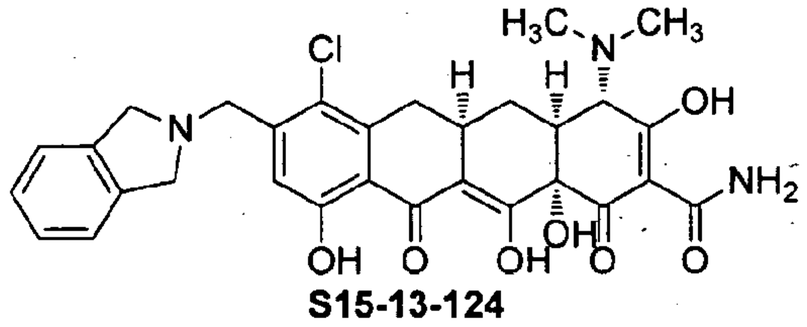
S15-13-122

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 and 7.12 (each s, total 1 H), 4.75-4.70, 4.54-4.44 and 4.34-4.27 (each m, total 2 H), 4.03 (s, 1 H), 3.55-3.46 (m, 1 H), 3.40-3.26 (m, 1 H), 3.18-2.85 (m, 10 H), 2.40-2.30 (m, 1 H), 2.20-2.14 (m, 1 H), 1.61-1.52 (m, 1 H), 1.49 and 1.25 (each t, *J* = 6.8 Hz, total 3 H), 1.40 and 1.35 (each d, *J* = 7.2 Hz, total 3 H), 1.16 (s, 3 H), 0.99 (s, 3 H), 0.85 (s, 3 H); MS (ESI) *m/z* 590.4 (M+H).



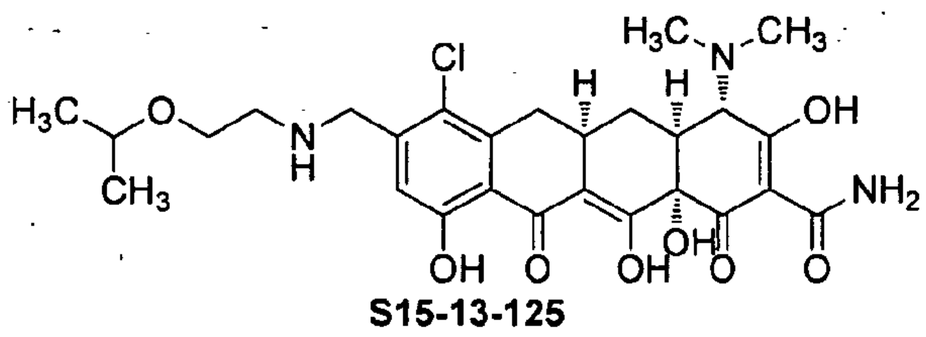
S15-13-123

^{1}H NMR (400 MHz, CD_3OD) δ 7.15 (s, 1 H), 4.52 (br s, 2 H), 4.03 (s, 1 H), 3.55 (s, 1 H), 3.35-3.30 (m, 3 H), 3.03-2.88 (m, 9 H), 2.38-2.30 (m, 1 H), 2.19-2.15 (m, 1 H),1.93-1.77 (m, 2 H)□1.54-1.47 (m, 5 H), 0.83-0.79 (m, 6 H); MS (ESI) *m/z* 588.0 (M+H).



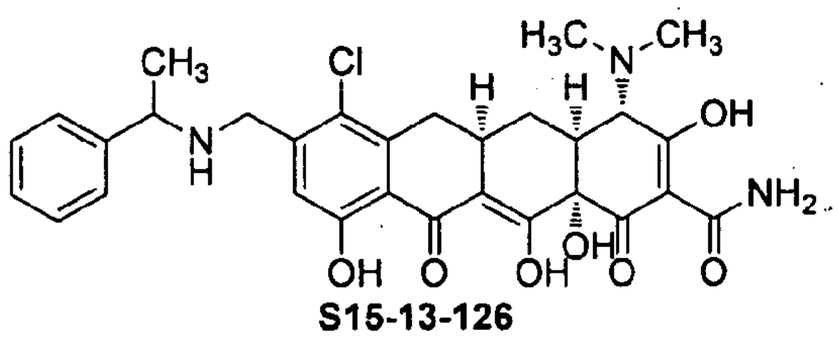
S15-13-124

^{1}H NMR (400 MHz, CD_3OD) δ 7.32 (s, 4 H), 7.12 (s, 1 H), 4.74-4.72 (m, 6 H), 4.03 (s, 1 H), 3.39-3.31 (m, 1 H), 3.05-2.90 (m, 8 H), 2.19-2.16 (m, 1 H), 1.61-1.53 (m, 1 H); MS (ESI) *m/z* 580.0 (M+H).



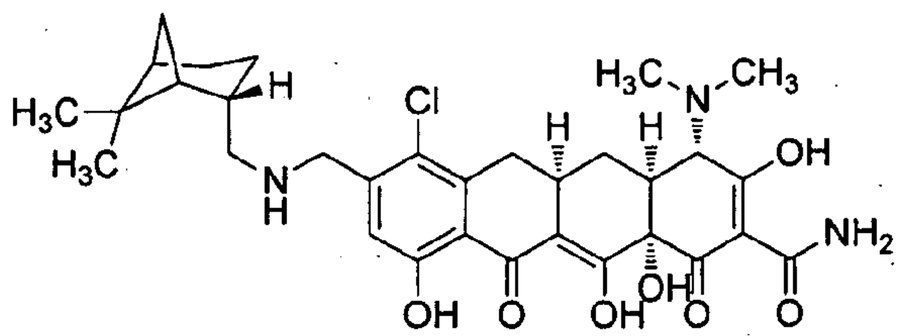
S15-13-125

^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (s, 1 H), 4.35 (s, 2 H), 4.04 (s, 1 H), 3.69-3.61 (m, 3 H), 3.36-3.24 (m, 3 H), 3.03-2.81 (m, 8 H), 2.38-2.30 (m, 1 H), 2.17-2.16 (m, 1 H), 1.63-1.53 (m, 1 H), 1.14-1.12 (m, 6 H); MS (ESI) *m/z* 564.1 (M+H).



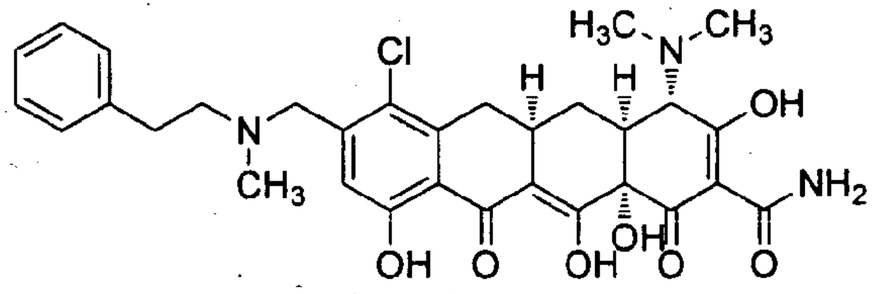
S15-13-126

^{1}H NMR (400 MHz, CD_3OD) δ 7.46-7.42 (m, 5 H), 6.97 (s, 1 H), 4.49-4.47 (m, 1 H), 4.16-3.97 (m, 2 H), 2.99-2.88 (m, 10 H), 2.32-2.25 (m, 2 H), 1.95-1.94 (m, 1 H), 1.69-1.67 (m, 3 H), 1.57-1.52 (m, 1 H); MS (ESI) *m/z* 582.4(M+H).



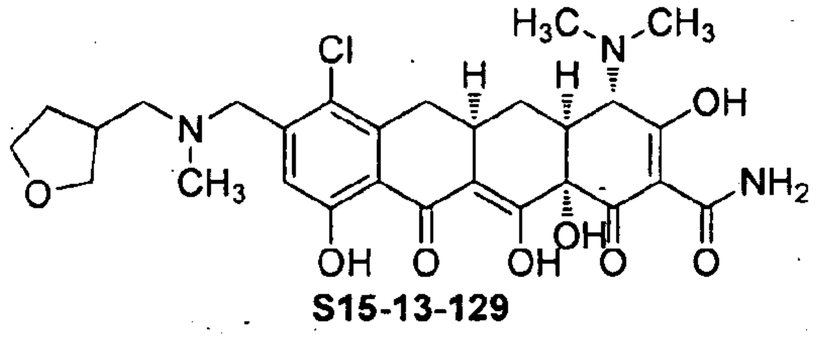
S15-13-127

^{1}H NMR (400 MHz, CD_3OD) δ 7.08 (s, 1 H), 4.31 (s, 2 H), 4.05 (s, 1 H), 3.36-3.31 (m, 2 H), 3.12-2.91 (m, 9 H), 2.47-2.36 (m, 3 H), 2.33-2.29 (m, 1 H), 2.08-1.86 (m, 5 H), 1.60-1.53 (m, 2 H), 1.25-1.14 (s, 3 H), 1.05-0.91 (s, 3 H) ; MS (ESI) *m/z* 614.1 (M+H).



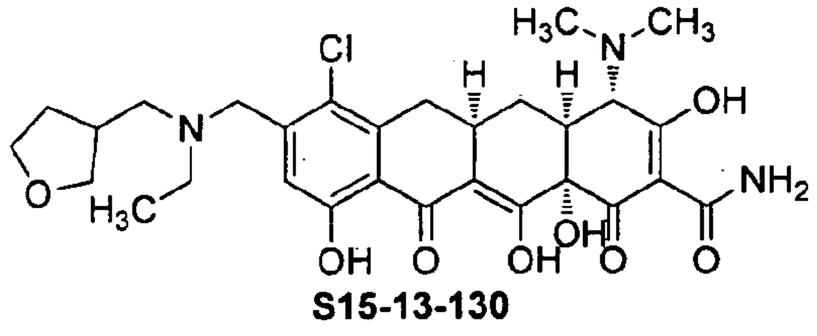
S15-13-128

^{1}H NMR (400 MHz, CD_3OD) δ 7.27-7.16 (m, 6 H), 4.70-4.63 (m, 1 H), 4.41-4.34 (m, 1 H), 4.06 (s, 1 H), 3.48-3.41 (m, 2 H), 3.33-3.29 (m, 1 H), 3.12-2.80 (m, 13 H), 2.35-2.28 (m, 1 H), 2.20-2.17 (m, 1 H), 1.61-1.51 (m, 1 H); MS (ESI) *m/z* 596.0 (M+H).



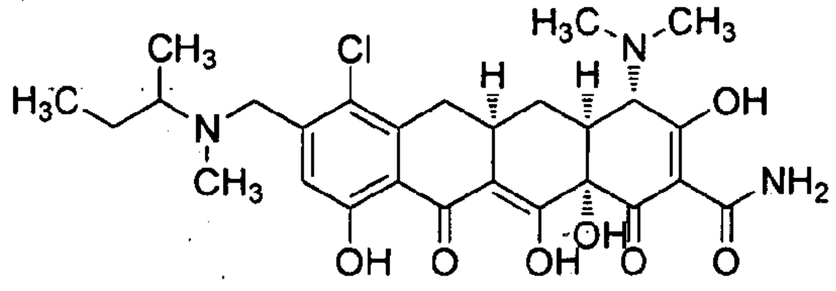
S15-13-129

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.74 (m, 1 H), 4.42 (m, 1 H), 4.15 (s, 1 H), 3.97-3.89 (m, 2 H), 3.80-3.77 (m, 1 H), 3.53 (m, 1 H), 3.39 (s, 3 H), 3.13-2.88 (m, 12 H), 2.46-2.38 (m, 1 H), 2.29-2.26 (m, 2 H), 1.71-1.64 (m, 2 H); MS (ESI) *m/z* 576.1 (M+H).



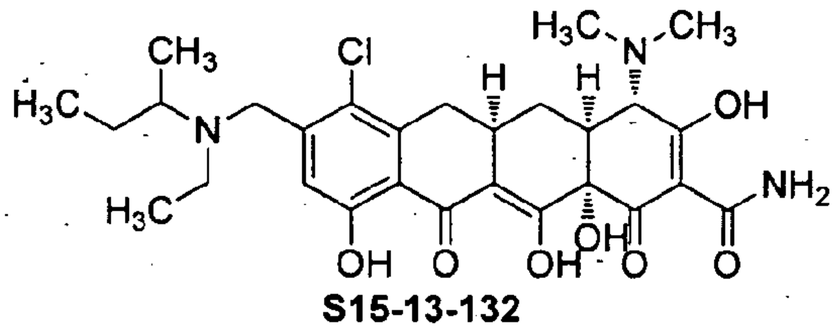
S15-13-130

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.64 -4.53 (m, 2 H), 4.13 (s, 1 H), 3.96-3.87 (m, 2 H), 3.77-3.75 (m, 1 H), 3.52-3.34 (m, 5 H), 3.22-2.79 (m, 10 H), 2.48-2.40 (m, 1 H), 2.28-2.26 (m, 2 H), 1.71-1.65 (m, 2 H), 1.44-1.41 (m, 3 H); MS (ESI) m/z 590.1 (M+H).



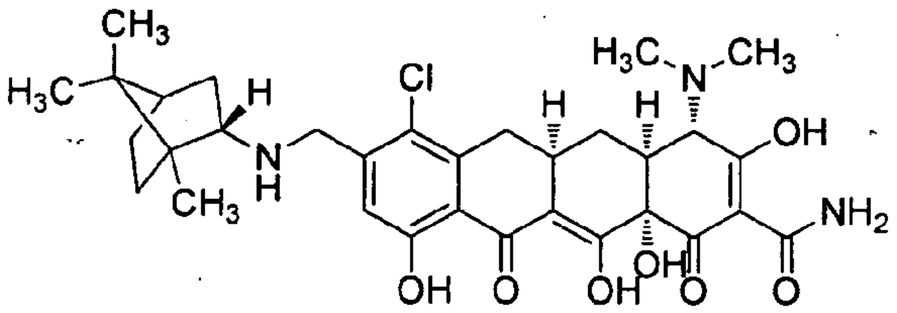
S15-13-131

^{1}H NMR (400 MHz, CD_3OD) δ 7.15 and 7.14 (each s, total 1 H), 4.59-4.54 (m, 1 H), 4.24-4.15 (m, 1 H), 4.05 (s, 1 H), 3.39-3.30 (m, 2 H), 3.03-2.88 (m, 8 H), 2.70 (s, 3 H), 2.37-2.29 (m, 1 H), 2.20-2.17 (m, 1 H), 1.95-1.88 (m, 1 H), 1.70-1.52 (m, 2 H), 1.40-1.34 (m, 3 H), .01-0.95 (m, 3 H); MS (ESI) *m/z* 548.0 (M+H).



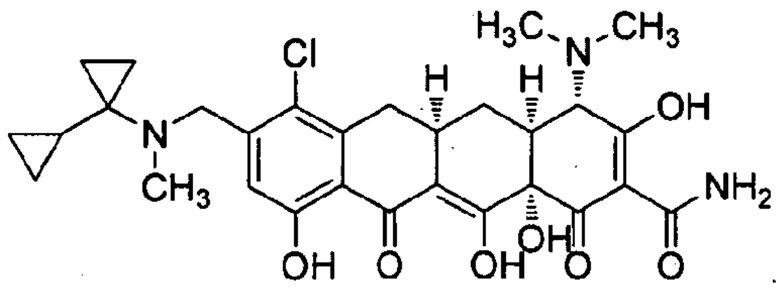
S15-13-132

^{1}H NMR (400 MHz, CD_3OD) δ 7.12 and 7.10 (each s, total 1 H), 4.53 (m, 1 H), 4.28-4.26 (m, 1 H), 4.03 (s, 1 H), 3.41-3.35 (m, 3 H), 3.03-2.87 (m, 9 H), 2.39-2.31 (m, 1 H), 2.18-2.15(m, 1 H), 1.91(m, 1 H),1.71-1.52 (m, 2 H), 1.43-1.23 (m, 6 H); 0.99-0.95 (m, 3 H); MS (ESI) *m/z* 562.1 (M+H)□



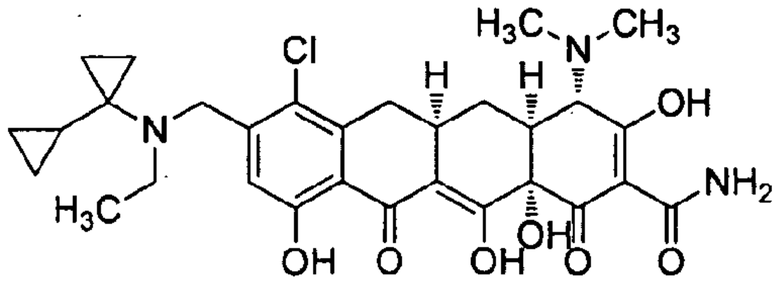
S15-13-133

^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.33 (s, 2 H), 4.04 (s, 1 H), 3.40-3.30 (m, 2 H), 3.12-2.88 (m, 9 H), 2.32-2.18 (m, 2 H), 1.77-1.71 (m, 2 H), 1.53-1.50 (m, 2 H), 1.33-1.20 (m, 3 H), 0.95 (s, 3 H), 0.84 (d, *J* = 9.6 Hz, 6 H); MS (ESI) *m/z* 614.4 (M+H)□



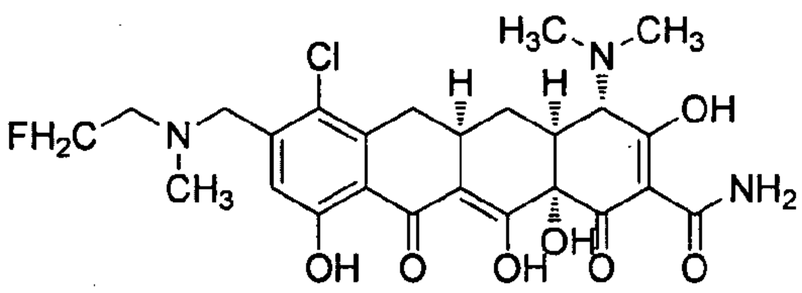
S15-13-134

^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.80-4.61 (m, 2 H), 4.04 (s, 1 H), 3.37-3.27 (m, 1 H), 3.09-2.85 (m, 11 H), 2.38-2.27 (m, 1 H), 2.22-2.15 (m, 1 H), 1.66-1.50 (m, 2 H), 1.22-1.04 (m, 4 H), 0.92-0.81 (m, 1 H), 0.78-0.65 (m, 3 H); MS (ESI) *m/z* 572.2 (M+H).



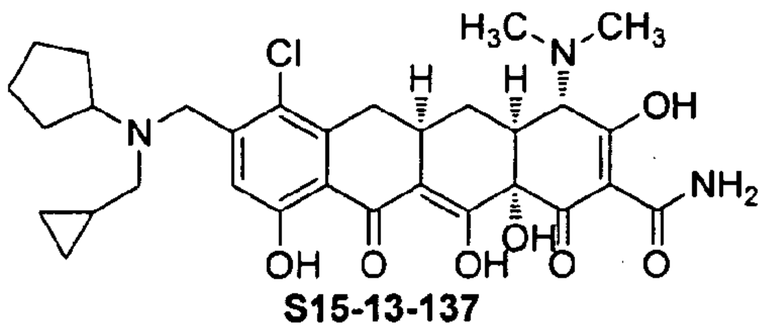
S15-13-135

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.80-4.62 (m, 2 H), 4.05 (s, 1 H), 3.73-3.60 (m, 1 H), 3.42-3.28 (m, 2 H), 3.10-2.85 (m, 8 H), 2.40-2.27 (m, 1 H), 2.22-2.15 (m, 1 H), 1.62-1.50 (m, 2 H), 1.35-1.15 (m, 4 H), 0.97-0.78 (m, 2 H), 0.78-0.60 (m, 3 H), 0.35-0.27 (m, 2 H); MS (ESI) *m/z* 586.2 (M+H).



S15-13-136

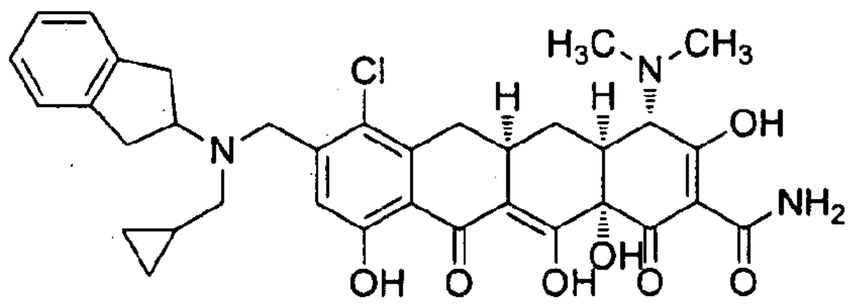
^{1}H NMR (400 MHz, CD_3OD) δ 7.17 (s, 1 H), 4.93 (br s, 2 H), 4.74-4.39 (m, 2 H), 3.65 (br d, J = 27.2 Hz, 2 H), 3.36 (dd, J = 16.4 Hz and 4.4 Hz, 1 H), 3.10-2.89 (m, 11 H), 2.43-2.35 (m, 1 H), 2.25-2.17 (m, 1 H), 1.66-1.55 (m, 1 H); MS (ESI) *m/z* 537.9 (M+H).



S15-13-137

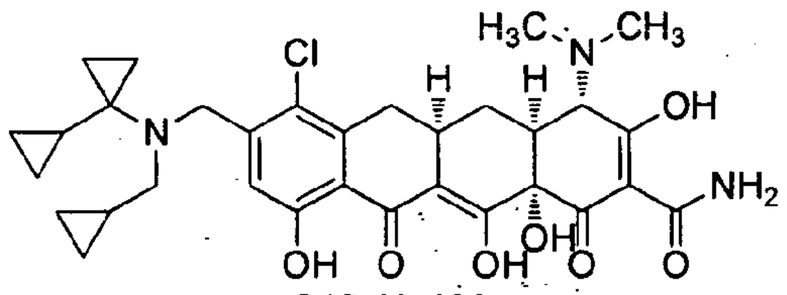
^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.74-4.68 (m, 1 H), 4.59-4.54 (m, 1 H), 4.13 (s, 1 H), 4.08-4.04 (m, 1 H), 3.42 (dd, J = 16.4 Hz and 4.4 Hz, 1 H),

3.18-2.94 (m, 10 H), 2.47-2.40 (m, 1 H), 2.31-2.08 (m, 3 H), 2.05-1.92 (m, 1 H), 1.90-1.79 (m, 3 H), 1.78-1.60 (m, 3 H), 1.20-1.09 (m, 1 H), 0.82-0.70 (m, 2 H), 0.45-0.36 (m, 2 H); MS (ESI) *m/z* 600.0 (M+H).



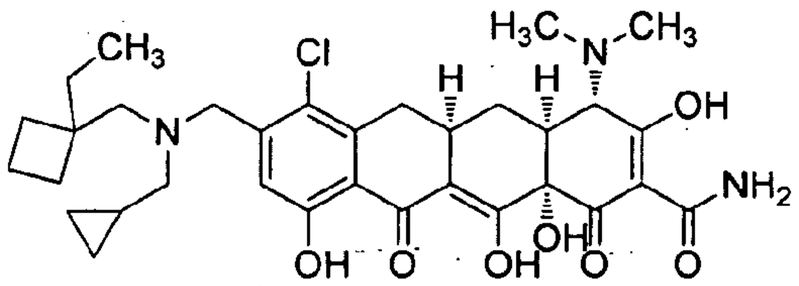
S15-13-138

^{1}H NMR (400 MHz, CD_3OD) δ 7.31-7.18 (m, 5 H), 4.70-4.48 (m, 3 H), 4.12 (s, 1 H), 3.55-3.35 (m, 5 H), 3.18-2.93 (m, 10 H), 2.45-2.37 (m, 1 H), 2.30-2.20 (m, 1 H), 1.70-1.58 (m, 1 H), 1.23-1.10 (m, 1 H), 0.82-0.70 (m, 2 H), 0.43-0.36 (m, 2 H); MS (ESI) *m/z* 648.1 (M+H).



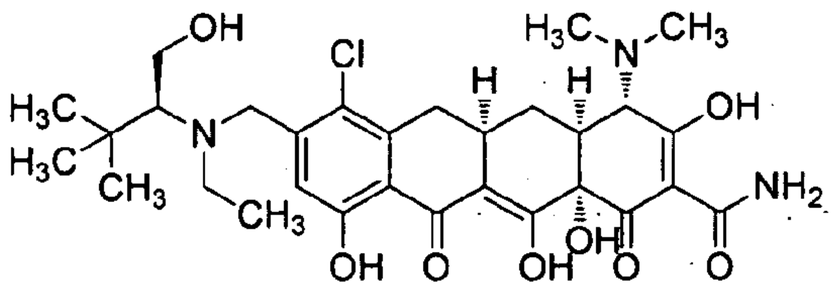
S15-13-139

^{1}H NMR (400 MHz, CD_3OD) δ 7.29 and 7.26 (each s, total 1 H), 4.85-4.73 (m, 1 H), 4.14 (s, 1 H), 3.80-3.73 (m, 1 H), 3.62-3.52 (m, 1 H), 3.48-3.38 (m, 1 H), 3.25-2.86 (m, 9 H), 2.50-2.36 (m, 1 H), 2.30-2.22 (m, 1 H), 1.78-1.60 (m, 2 H), 1.55-1.36 (m, 1 H), 1.27-1.13 (m, 1 H), 1.05-0.68 (m, 8 H), 0.52-0.28 (m, 4 H); MS (ESI) *m/z* 612.1 (M+H).



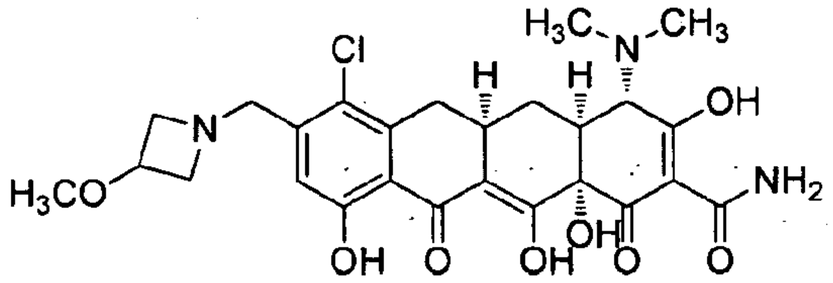
S15-13-140

^{1}H NMR (400 MHz, CD_3OD) δ 7.30 (s, 1 H), 4.70-4.57 (m, 2 H), 4.13 (s, 1 H), 3.58-3.55 (m, 1 H), 3.44-3.39 (m, 1 H), 3.26-2.95 (m, 11 H), 2.48-2.37 (m, 1 H), 2.31-2.24 (m, 1 H), 2.15-1.72 (m, 7 H), 1.71-1.59 (m, 1 H), 1.35-1.24 (m, 3 H), 0.90-0.79 (m, 4 H), 0.55-0.44 (m, 2 H); MS (ESI) *m/z* 627.9 (M+H).



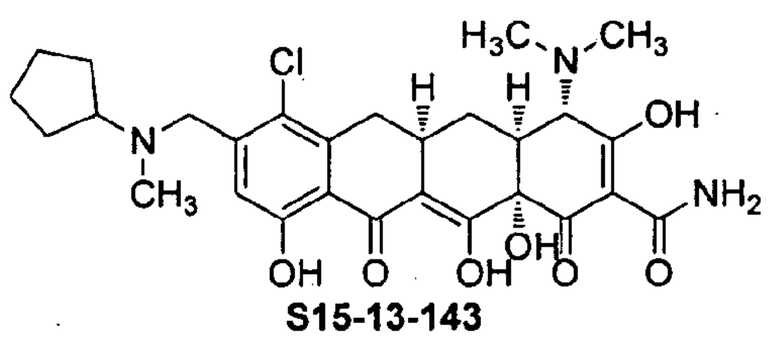
S15-13-141

^{1}H NMR (400 MHz, CD_3OD) δ 7.29 and 7.24 (each s, total 1 H), 4.20-4.08 (m, 3 H), 3.93-3.57 (m, 3 H), 3.48-3.38 (m, 2 H), 3.21-2.89 (m, 9 H), 2.50-2.40 (m, 1 H), 2.32-2.26 (m, 1 H), 1.75-1.60 (m, 1 H), 1.68-1.58 and 1.44-1.36 (each m, total 3 H), 1.31 and 1.01 (each s, total 9 H); MS (ESI) *m/z* 606.1 (M+H).



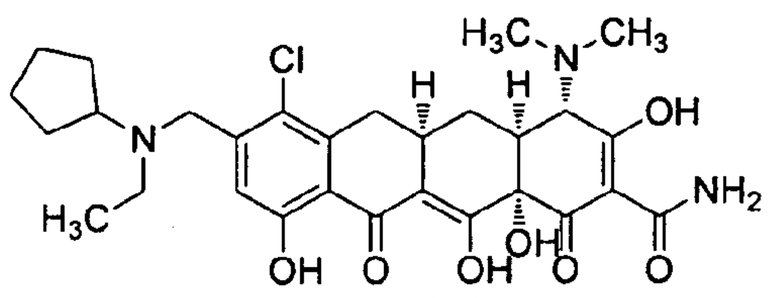
S15-13-142

^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (s, 1 H), 4.64 (s, 2 H), 4.57-4.09 (m, 6 H), 3.39 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.35 (s, 3 H), 3.15-2:95 (m, 8 H), 2.47-2.37 (m, 1 H), 2.28-2.22 (m, 1 H), 1.70-1.57 (m, 1 H); MS (ESI) *m/z* 548.4 (M+H).



S15-13-143

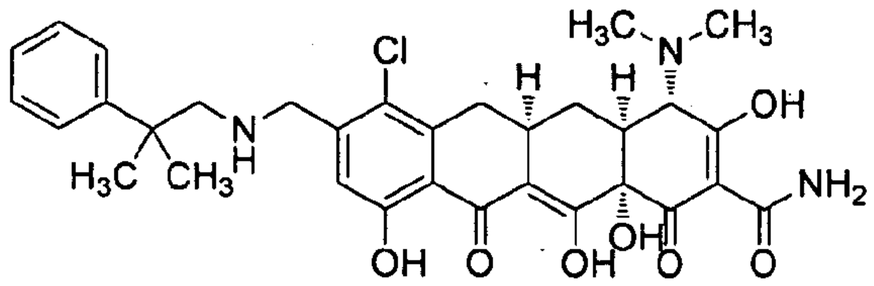
^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.72 (t, *J* = 12.8 Hz, 1 H), 4.33 (t, *J* = 12.4 Hz, 1 H), 4.13 (s, 1 H), 3.88-3.79 (m, 1 H), 3.45-3.37 (m, 1 H), 3.18-2.73 (m, 11 H), 2.48-2.36 (m, 1 H), 2.36-2.14 (m, 3 H), 1.98-1.82 (m, 4 H), 1.78-1.60 (m, 3 H); MS (ESI) *m/z* 560.0 (M+H).



S15-13-144

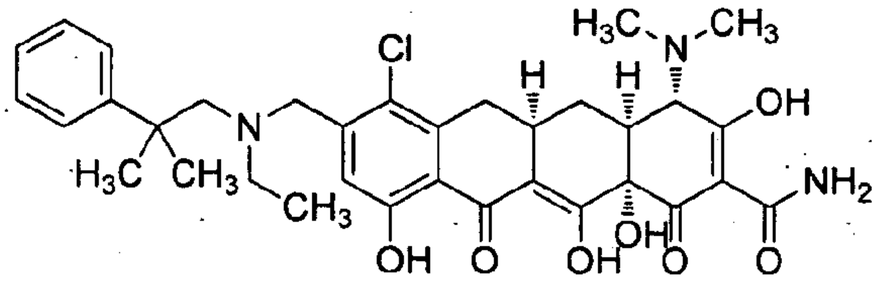
^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.62-4.46 (m, 2 H), 4.23 (s, 1 H), 4.42-4.35 (m, 1 H), 3.43-3.37 (m, 1 H), 3.25-2.95 (m, 10 H), 2.45-2.37 (m, 1 H), 2.31-2.14 (m, 3 H), 2.00-1.80 (m, 4 H), 1.79-1.60 (m, 3 H), 1.36 (t, *J* = 6.8 Hz, 3 H);

MS (ESI) *m/z* 574.1 (M+H).



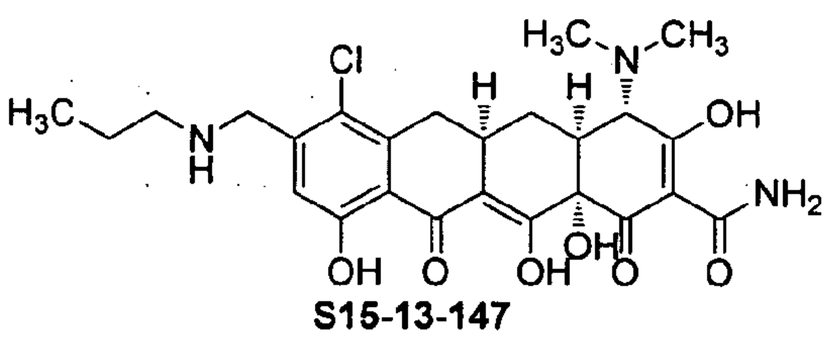
S15-13-145

^{1}H NMR (400 MHz, CD_3OD) δ 7.43-7.28 (m, 5 H), 7.00 (s, 1 H), 7.28 (s, 2 H), 7.11 (s, 1 H), 3.41 (s, 2 H), 3.15-2.95 (m, 9 H), 2.41-2.33 (m, 1 H), 2.26-2.23 (m, 1 H), 1.60-1.59 (m, 1 H), 1.46 (s, 6 H); MS (ESI) *m/z* 610.0 (M+H).



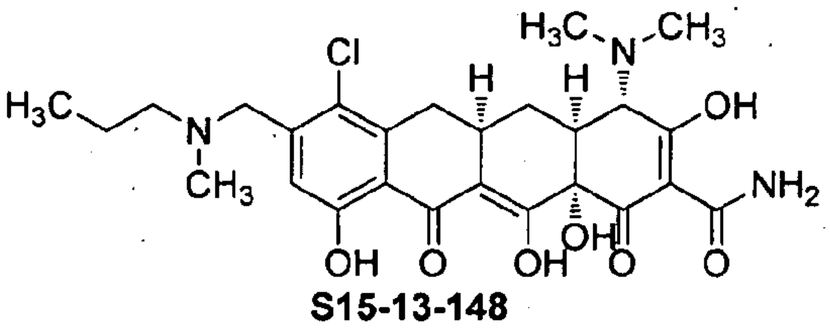
S15-13-146

^{1}H NMR (400 MHz, CD_3OD) δ 7.55-7.27 (m, 5 H), 6.96 and 6.94 (each s, total 1 H), 4.30-4.18 (m, 2 H), 4.12 (s, 1 H), 3.75-3.69 (m, 1 H), 3.63-3.56 (m, 1 H), 3.34 (s, 2 H), 3.24-2.86 (m, 9 H), 2.42-2.30 (m, 1 H), 2.27-2.23 (m, 1 H), 1.69-1.59 (m, 1 H), 1.54 (s, 3 H), 1.45 (s, 3 H), 1.38-1.32 (m, 3 H); MS (ESI) *m/z* 638.1 (M+H).



S15-13-147

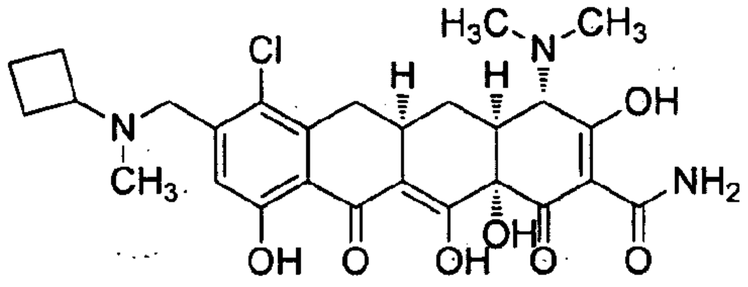
^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.37 (s, 2 H), 4.11 (s, 1 H), 3.41 (dd, *J* = 16.4 Hz and 4.4 Hz, 1 H), 3.15-2.95 (m, 10 H), 2.45-2.37 (m, 1 H), 2.29-2.24 (m, 1 H), 1.84-1.74 (m, 2 H), 1.70-1.60 (m, 1 H), 1.05 (t, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 519.9 (M+H).



S15-13-148

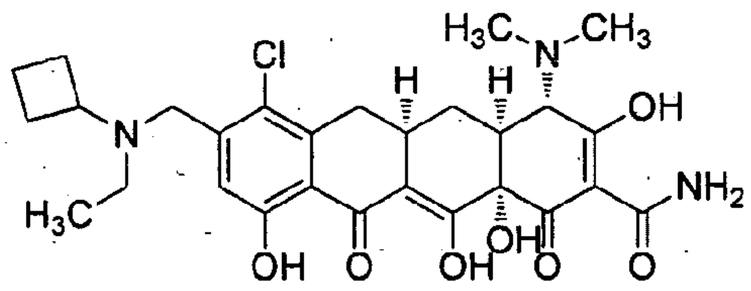
^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.66 (t, *J* = 13.6 Hz, 1 H), 4.38

(t, J = 12.8 Hz, 1 H), 4.13 (s, 1 H), 3.41 (dd, J = 16.0 Hz and 4.0 Hz, 1 H), 3.30-2.95 (m, 10 H), 2.86 (s, 3 H), 2.45-2.38 (m, 1 H), 2.30-2.24 (m, 1 H), 1.91-1.80 (m, 2 H), 1.70-1.60 (m, 1 H), 1.03 (t, J = 7.2 Hz, 3 H); MS (ESI) *m/z* 534.0 (M+H).



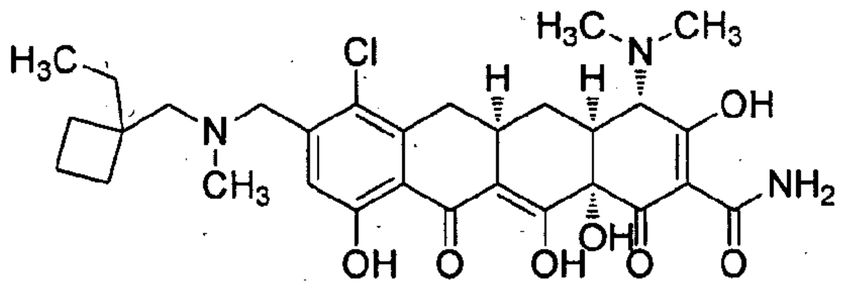
S15-13-149

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.55 (t, J = 14.4 Hz, 1 H), 4.38 (t, J = 14.4 Hz, 1 H), 4.14 (s, 1 H), 3.99-3.93 (m, 1 H), 3.43-3.38 (m, 1 H), 3.17-2.87 (m, 8 H), 2.74 (s, 3 H), 2.46-2.23 (m, 6 H), 1.93-1.75 (m, 2 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 546.0 (M+H).



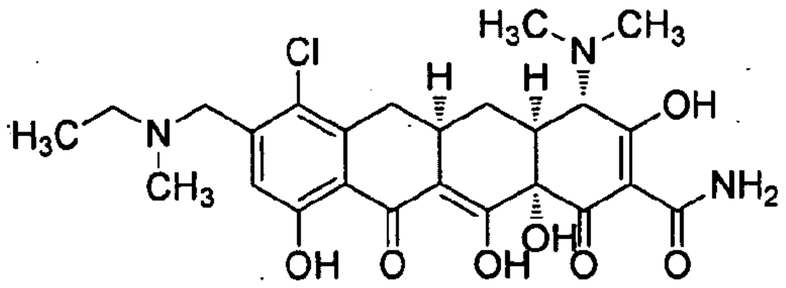
S15-13-150

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.49-4.37 (m, 2 H), 4.13 (s, 1 H), 4.08-3.98 (m, 1 H), 3.41 (dd, J = 16.0 Hz and 4.0 Hz, 1 H), 3.25-2.95 (m, 10 H), 2.47-2.12 (m, 6 H), 1.90-1.75 (m, 2 H), 1.70-1.60 (m, 1 H), 1.38 (t, J = 6.8 Hz, 3 H); MS (ESI) *m/z* 560.0 (M+H).



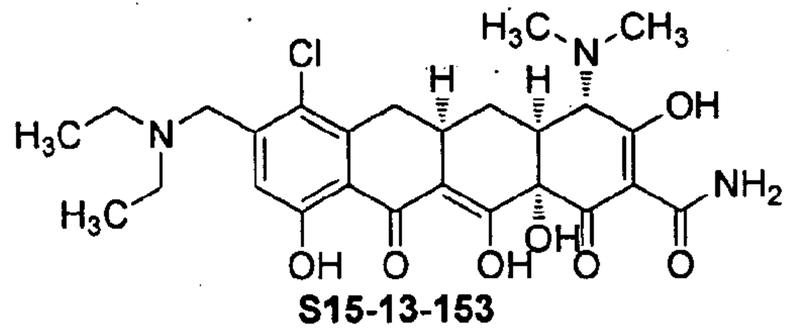
S15-13-151

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.68-4.61 (M, 1 H), 4.44-4.39 (m, 1 H), 4.14 (s, 1 H), 3.44-3.35 (m, 2 H), 3.18-2.88 (m, 11 H), 2.46-2.39 (m, 1 H), 2.30-2.26 (m, 1 H), 2.15-1.60 (m, 8 H), 0.89 (t, J = 6.8 Hz, 3 H); MS (ESI) *m/z* 588.1 (M+H).



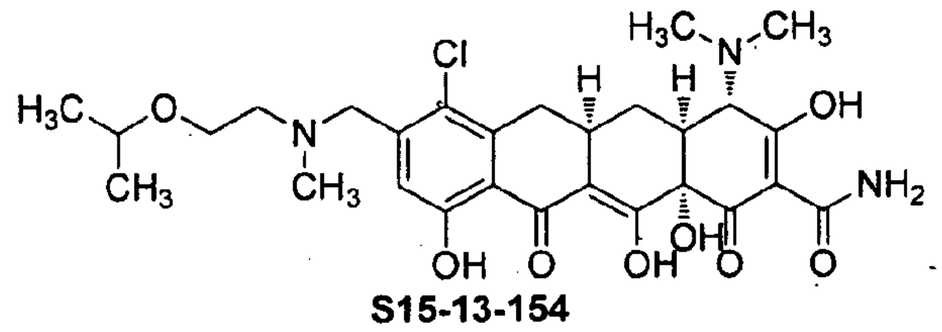
S15-13-152

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.64 (t, *J* = 13.6 Hz, 1 H), 4.38 (t, *J* = 12.8 Hz, 1 H), 4.14 (s, 1 H), 3.45-3.36 (m, 2 H), 3.18-2.95 (m, 9 H), 2.86 (s, 3 H), 2.46-2.38 (m, 1 H), 2.29-2.26 (m, 1 H), 1.70-1.60 (m, 1 H), 1.45 (t, *J* = 6.8 Hz, 3 H); MS (ESI) *m/z* 520.0 (M+H).



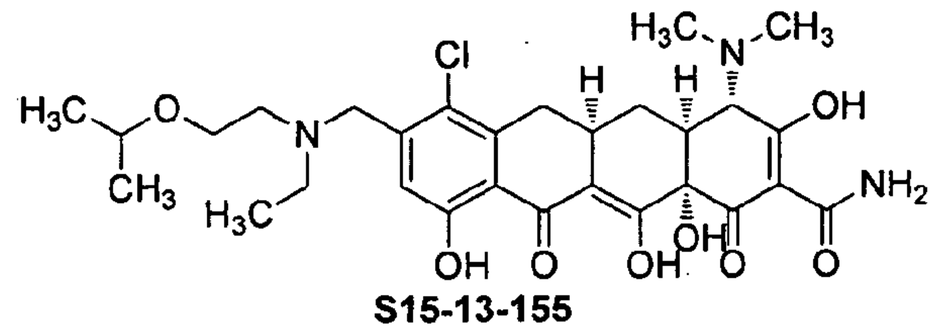
S15-13-153

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.55-4.48 (m, 2 H), 4.13 (s, 1 H), 3.44-3.39 (m, 1 H), 3.18-2.86 (m, 12 H), 2.46-2.39 (m, 1 H), 2.28-2.25 (m, 1 H), 1.70-1.60 (m, 1 H), 1.44-1.37 (m, 6 H); MS (ESI) *m/z* 534.0 (M+H).



S15-13-154

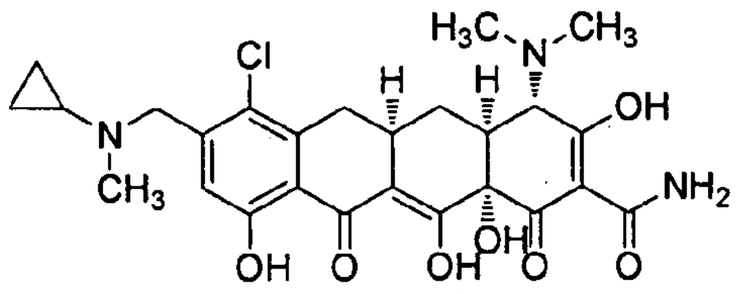
^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.81-4.74 (m, 1 H), 4.44-4.39 (m, 1 H), 4.13 (s, 1 H), 3.84 (br s, 2 H), 3.76-3.68 (m, 1 H), 3.49 (br s, 2 H), 3.41 (dd, *J* = 16.4 Hz and 4.4 Hz, 1 H), 3.18-2.85 (m, 11 H), 2.46-2.39 (m, 1 H), 2.29-2.26 (m, 1 H), 1.70-1.60 (m, 1 H), 1.22-1.18 (m, 6 H); MS (ESI) *m/z* 578.0 (M+H).



S15-13-155

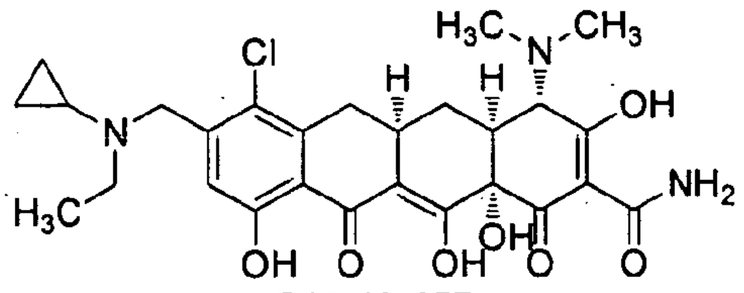
^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.72-4.66 (m, 1 H), 4.57-4.52 (m, 1 H), 4.11 (s, 1 H), 3.83-3.81 (m, 2 H), 3.72-3.66 (m, 1 H), 3.53-3.47 (m, 1 H), 3.45-3.34 (m, 4 H), 3.17-2.95 (m, 9 H), 2.47-2.39 (m, 1 H), 2.28-2.24 (m, 1 H),

1.70-1.60 (m, 1 H), 1.50 (t, J = 6.8 Hz, 3 H), 1.21-1.13 (m, 6); MS (ESI) *m/z* 592.0 (M+H).



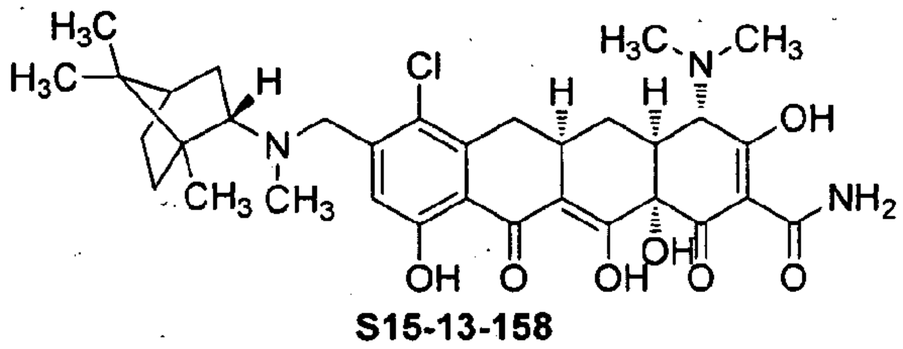
S15-13-156

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.80-4.70 (m, 2 H), 4.13 (s, 1 H), 3.41 (dd, J = 16.0 Hz and 4.4 Hz, 1 H), 3.18-2.96 (m, 12 H), 2.46-2.39 (m, 1 H), 2.29-2.25 (m, 1 H), 1.70-1.60 (m, 1 H), 1.10-0.82 (m, 4 H); MS (ESI) *m/z* 532.0 (M+H).



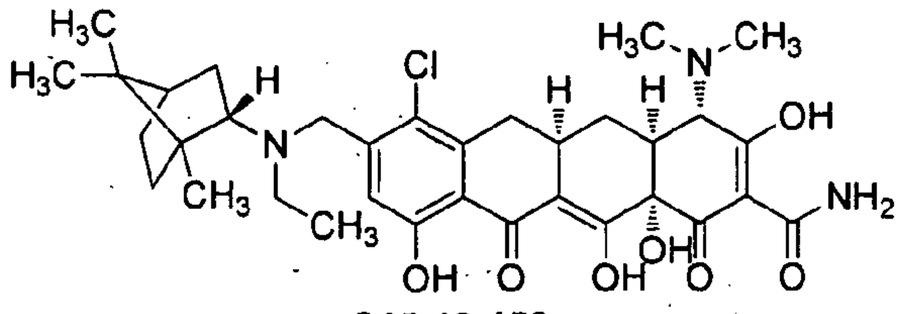
S15-13-157

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.76-4.60 (m, 2 H), 4.13 (s, 1 H), 3.49-3.39 (m, 3 H), 3.18-2.95 (m, 9 H), 2.47-2.39 (m, 1 H), 2.28-2.25 (m, 1 H), 1.70-1.61 (m, 1 H), 1.49 (t, J = 7.6 Hz, 3 H), 1.10-0.80 (m, 3 H), 0.75-0.60 (m, 1 H); MS (ESI) *m/z* 546.0 (M+H).



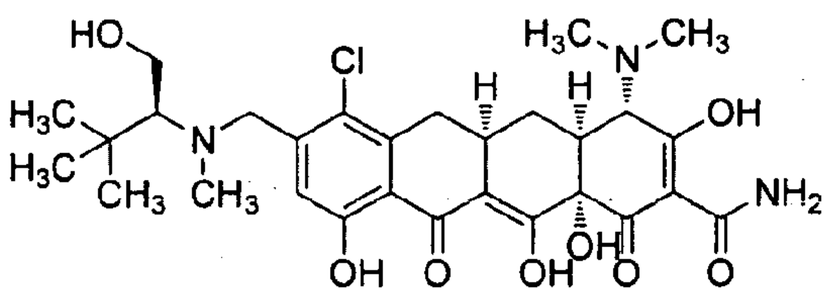
S15-13-158

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.82-4.76 (m, 1 H), 4.33-4.27 (m, 1 H), 4.13 (s, 1 H), 3.75-3.65 (m, 1 H), 3.47-3.39 (m, 1 H), 3.18-2.75 (m, 11 H), 2.51-2.39 (m, 1 H), 2.29-2.25 (m, 1 H), 2.20-1.76 (m, 4 H), 1.70-1.40 (m, 4 H), 1.30 (s, 3 H), 0.99-0.96 (m, 6 H); MS (ESI) *m/z* 628.1 (M+H).



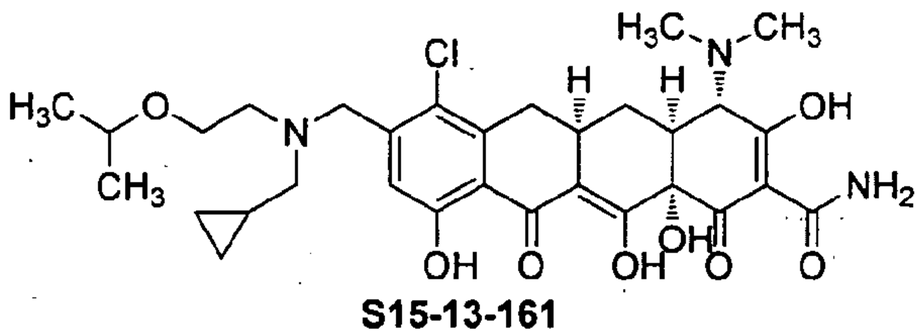
S15-13-159

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 and 7.24 (each s, total 1 H), 4.82-4.73 (m, 1 H), 4.53-4.44 (m, 1 H), 4.13 (s, 1 H), 3.88-3.71 (m, 1 H), 3.48-3.32 (m, 3 H), 3.18-2.95 (m, 8 H), 2.54-2.36 (m, 2 H), 2.29-2.25 (m, 1 H), 1.98-1.85 (m, 2 H), 1.84-1.75 (m, 1 H), 1.70-1.60 (m, 1 H), 1.59-1.40 (m, 3 H), 1.38-1.27 (m, 6 H), 1.00-0.93 (m, 6 H); MS (ESI) *m/z* 642.1 (M+H).



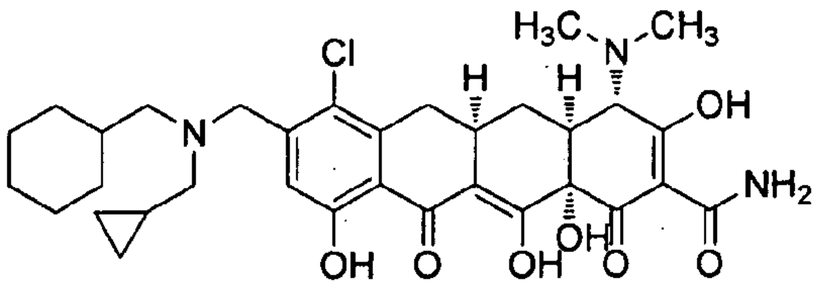
S15-13-160

^{1}H NMR (400 MHz, CD_3OD) δ 7.29 (s, 1 H), 4.97-4.94 (m, 1 H), 4.68-4.65 (m, 1 H), 4.17-4.06 (m, 3 H), 3.45-3.40 (m, 2 H), 3.18-2.95 (m, 11 H), 2.45-2.38 (m, 1 H), 2.30-2.26 (m, 1 H), 1.70-1.61 (m, 1 H), 1.05 (s, 9 H); MS (ESI) *m/z* 592.1 (M+H).



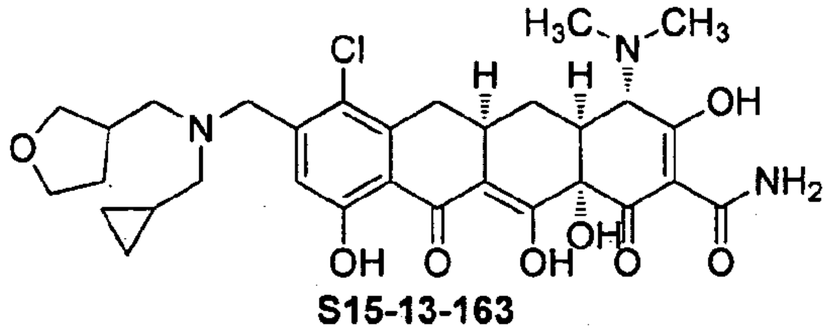
S15-13-161

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.75-4.67 (m, 2 H), 4.12 (s, 1 H), 3.88-3.76 (m, 2 H), 3.75-3.56 (m, 2 H), 3.55-3.37 (m, 2 H), 3.28-2.95 (m, 10 H), 2.46-2.39 (m, 1 H), 2.29-2.25 (m, 1 H), 1.71-1.61 (m, 1 H), 1.30-1.10 (m, 7 H), 0.85-0.74 (m, 2 H), 0.51-0.42 (m, 2 H); MS (ESI) *m/z* 618.1 (M+H).



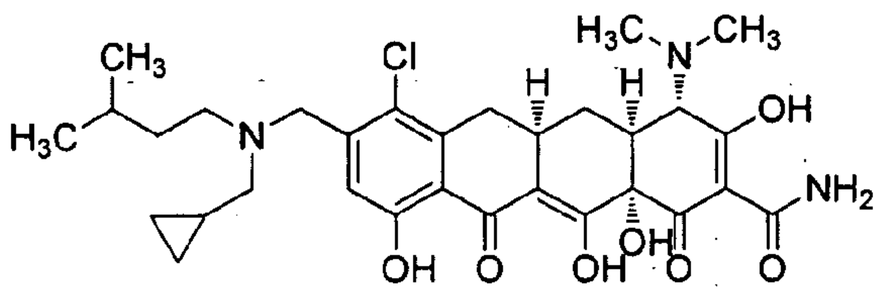
S15-13-162

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.70-4.59 (m, 2 H), 4.12 (s, 1 H), 3.42 (dd, *J* = 16.4 Hz and 4.4 Hz, 1 H), 3.25-2.95 (m, 12 H), 2.47-2.40 (m, 1 H), 2.29-2.25 (m, 1 H), 1.92-1.60 (m, 7 H), 1.40-1.12 (m, 4 H), 1.10-0.90 (m, 2 H), 0.89-0.78 (m, 2 H), 0.52-0.45 (m, 2 H); MS (ESI) *m/z* 628.1 (M+H).



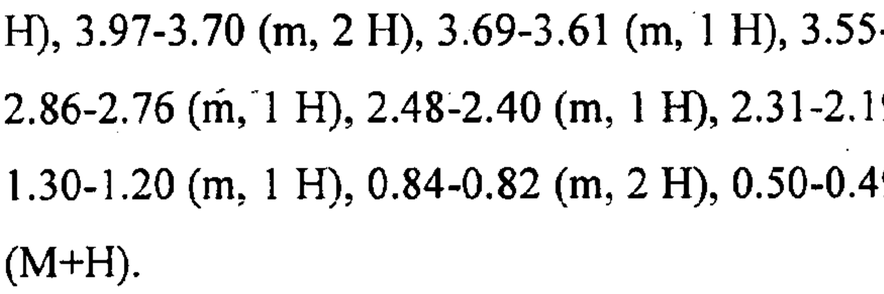
S15-13-163

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (s, 1 H), 4.75-4.60 (m, 2 H), 4.13 (s, 1 H), 3.97-3.70 (m, 2 H), 3.69-3.61 (m, 1 H), 3.55-3.38 (m, 3 H), 3.28-2.95 (m, 11 H), 2.86-2.76 (m, 1 H), 2.48-2.40 (m, 1 H), 2.31-2.19 (m, 2 H), 1.76-1.57 (m, 2 H), 1.30-1.20 (m, 1 H), 0.84-0.82 (m, 2 H), 0.50-0.49 (m, 2 H); MS (ESI) *m/z* 616.1 (M+H).



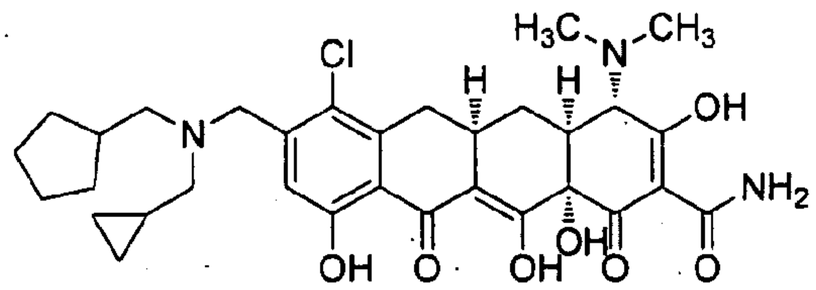
S15-13-164

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.72-4.66 (m, 1 H), 4.58-4.55 (m, 1 H), 4.13 (s, 1 H), 3.42 (dd, J = 16.0 Hz and 4.4 Hz, 1 H), 3.28-2.95 (m, 12 H), 2.48-2.40 (m, 1 H), 2.30-2.25 (m, 1 H), 1.78-1.60 (m, 4 H), 1.25-1.16 (m, 1 H), 0.98-0.95 (m, 6 H), 0.83-0.79 (m, 2 H), 0.48-0.46 (m, 2 H); MS (ESI) *m/z* 602.1 (M+H).



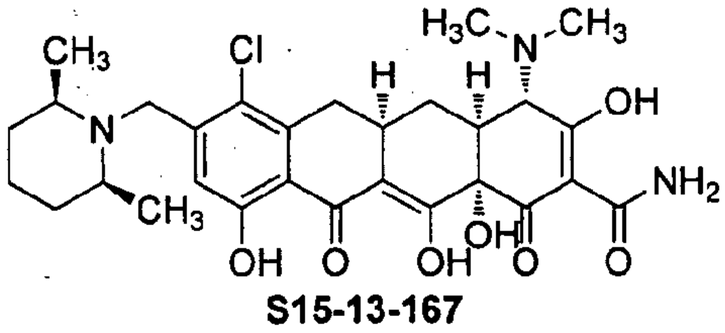
S15-13-165

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1 H), 4.75-4.66 (m, 1 H), 4.60-4.52 (m, 1 H), 4.12 (s, 1 H), 3.47-3.38 (m, 1 H), 3.25-2.95 (m, 12 H), 2.48-2.40 (m, 1 H), 2.30-2.25 (m, 1 H), 1.78-1.61 (m, 3 H), 1.25-1.16 (m, 1 H), 0.94 (s, 9 H), 0.83-0.80 (m, 2 H), 0.49-0.47 (m, 2 H); MS (ESI) *m/z* 616.0 (M+H).



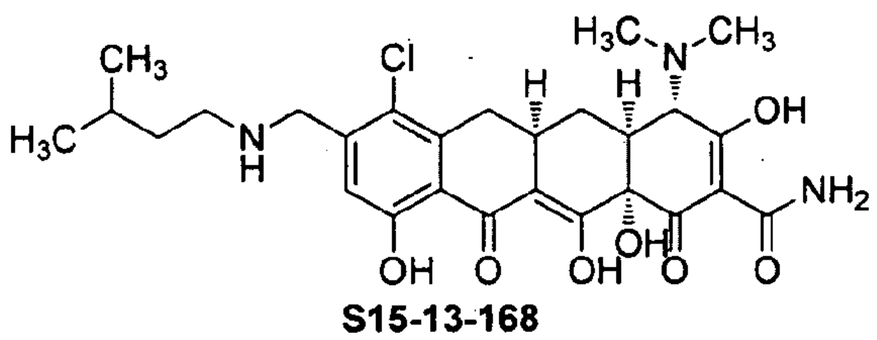
S15-13-166

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.74-4.61 (m, 2 H), 4.13 (s, 1 H), 3.44-3.40 (m, 2 H), 3.28-2.95 (m, 11 H), 2.47-2.35 (m, 2 H), 2.29-2.26 (m, 1 H), 2.00-1.90 (m, 1 H), 1.75-1.59 (m, 5 H), 1.38-1.16 (m, 3 H), 0.85-0.78 (m, 2 H), 0.51-0.46 (m, 2 H); MS (ESI) *m/z* 614.1 (M+H).



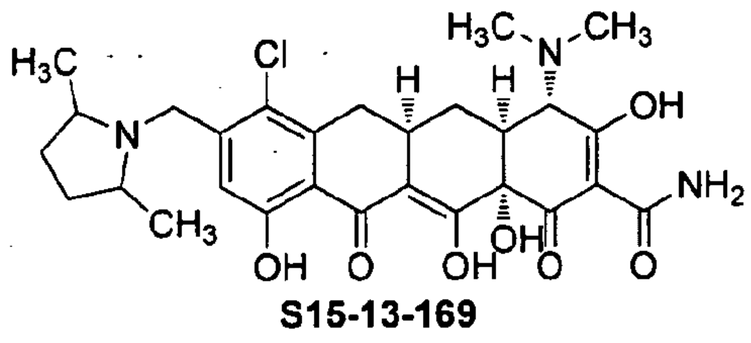
S15-13-167

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.73 (br s, 1 H), 4.48 (dd, *J* = 27.6 Hz and 16.0 Hz, 2 H), 4.10 (br s, 1 H), 3.69-3.46 (m, 2 H), 3.40-3.29 (m, 1 H), 3.10-2.88 (m, 7 H), 2.38-2.20 (m, 2 H), 1.98-1.72 (m, 5 H), 1.71-1.50 (m, 2 H), 1.40-1.18 (m, 6 H); MS (ESI) *m/z* 574.1 (M+H).



S15-13-168

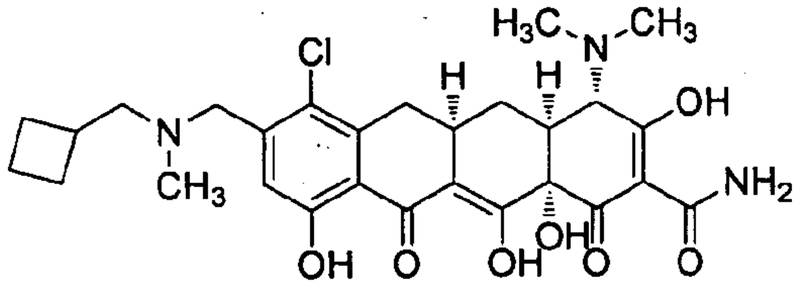
^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (s, 1 H), 4.38 (s, 2 H), 4.11 (s, 1 H), 3.41 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.22-2.87 (m, 10 H), 2.45-2.37 (m, 1 H), 2.28-2.25 (m, 1 H), 1.73-1.64 (m, 4 H), 1.01-0.97 (m, 6 H); MS (ESI) *m/z* 548.0 (M+H).



S15-13-169

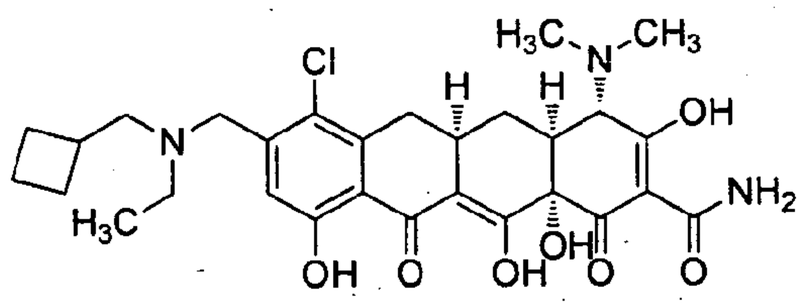
^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.62 (dd, *J* = 18.4 Hz and 13.6

Hz, 2 H), 4.11 (s, 1 H), 3.86-3.81 (m, 2 H), 3.42 (dd, *J* = 16.0 Hz and 4.8 Hz, 1 H), 3.18-2.95 (m, 8 H), 2.49-2.41 (m, 1 H), 2.37-2.24 (m, 3 H), 1.83-1.76 (m, 2 H), 1.72-1.62 (m, 1 H), 1.37-1.33 (m, 6 H); MS (ESI) *m/z* 560.0 (M+H).



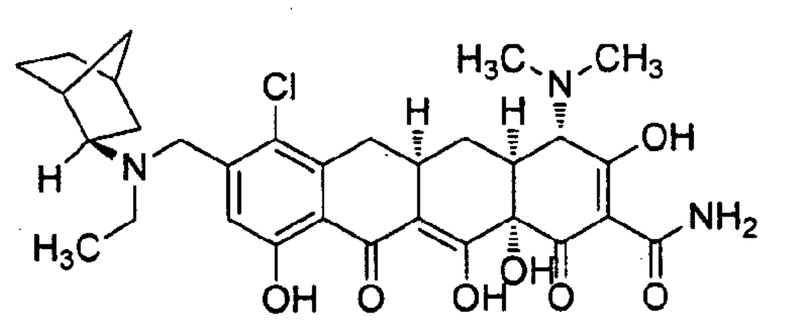
S15-13-170

^{1}H NMR (400 MHz, CD3OD) δ 7.20 (s, 1 H), 4.61 (t, *J* = 12.8 Hz, 1 H), 4.33 (t, *J* = 12.8 Hz, 1 H), 4.13 (s, 1 H), 3.41 (dd, *J* = 16.4 Hz and 4.4 Hz, 1 H), 3.36-3.30 (m, 1 H), 3.18-2.80 (m, 12 H), 2.46-2.38 (m, 1 H), 2.29-1.18 (m, 3 H), 2.10-2.00 (m, 1), 2.00-1.85 (m, 4 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 560.2 (M+H).



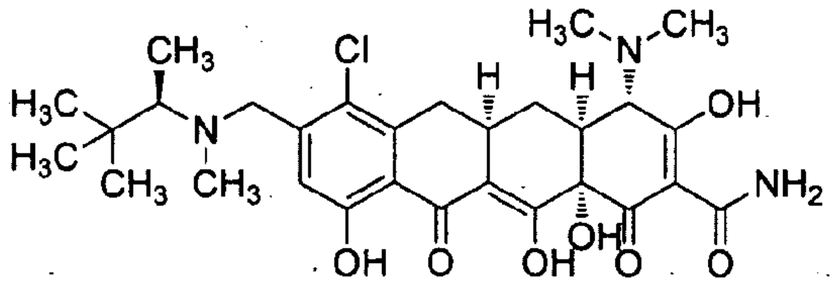
S15-13-171

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.52-4.42 (m, 2 H), 4.12 (s, 1 H), 3.45-3.38 (m, 1 H), 3.28-2.80 (m, 12 H), 2.49-2.40 (m, 1 H), 2.30-2.13 (m, 3 H), 2.08-1.97 (m, 1 H), 1.96-1.80 (m, 4 H), 1.70-1.60 (m, 1 H), 1.38 (t, *J* = 7.2 Hz, 3 H); MS (ESI) *m/z* 574.2 (M+H).



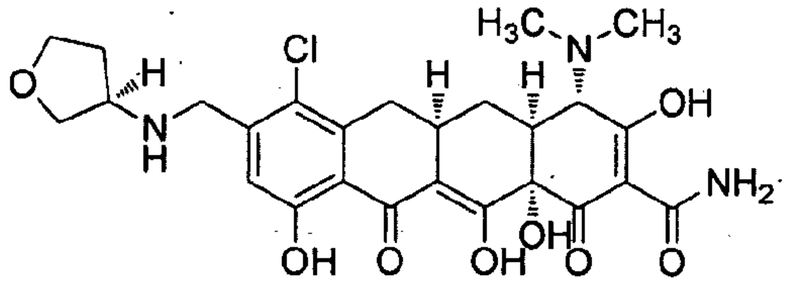
S15-13-172

^{1}H NMR (400 MHz, CD_3OD) δ 7.23 and 7.20 (each s, total 1 H), 4.68-4.42 (m, 2 H), 4.13 (s, 1 H), 3.85-3.75 (m, 1 H), 3.47-3.38 (m, 1 H), 3.18-2.85 (m, 10 H), 2.46-2.01 (m, 3 H), 1.73-1.49 (m, 10 H); MS (ESI) *m/z* 600.1 (M+H).



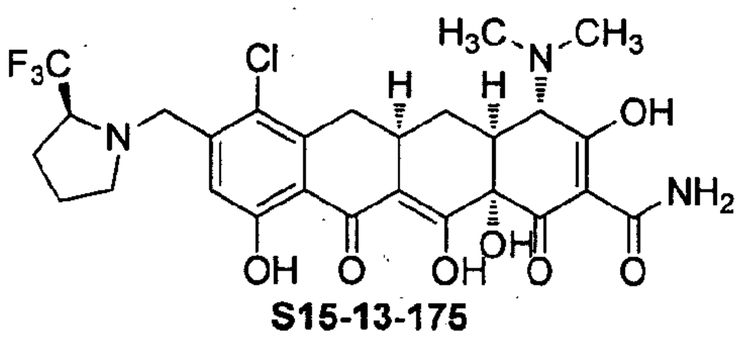
S15-13-173

^{1}H NMR (400 MHz, CD_3OD) δ 7.25 (s, 1 H), 4.70 (d, *J* = 13.2 Hz, 1 H), 4.42 (d, *J* = 13.2 Hz, 1 H), 4.06 (s, 1 H), 3.40 (dd, *J* = 16.4 Hz and 4.8 Hz, 1 H), 3.12-2.80 (m, 12 H), 2.44-2.36 (m, 1 H), 2.23-2.20 (m, 1 H), 1.67-1.57 (m, 1 H), 0.97 (s, 9 H); MS (ESI) *m/z* 576.0 (M+H).



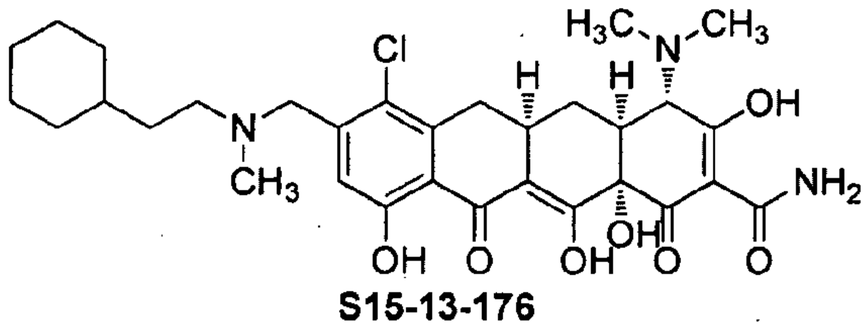
S15-13-174

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.40 (s, 2 H), 4.12-4.05 (m, 4 H), 3.90-3.84 (m, 1 H), 3.78-3.71 (m, 1 H), 3.44-3.37 (m, 1 H), 3.15-2.95 (m, 8 H), 2.50-2.40 (m, 2 H), 2.28-2.23 (m, 1 H), 2.20-2.09 (m, 1 H), 1.71-1.60 (m, 1 H); MS (ESI) *m/z* 548.1 (M+H).



S15-13-175

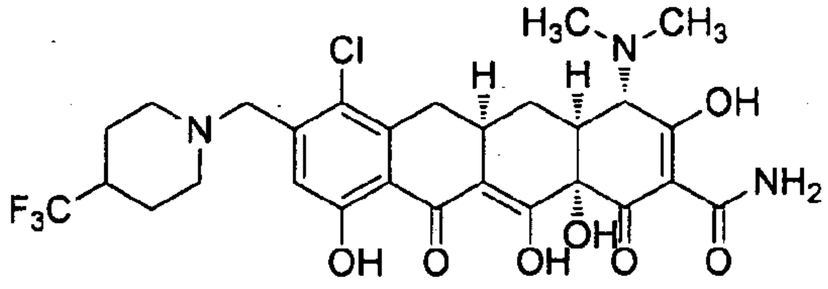
^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.32 (t, *J* = 15.6 Hz, 1 H), 4.17 (t, *J* = 15.6 Hz, 1 H), 4.11 (s, 1 H), 3.90-3.80 (m, 1 H), 3.40 (dd, *J* = 16.0 Hz and 4.4 Hz, 1 H), 3.29-3.20 (m, 1 H), 3.10-2.95 (m, 8 H), 2.83-2.74 (m, 1 H), 2.41-2.20 (m, 3 H), 2.12-1.90 (m, 3 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 599.9 (M+H).



S15-13-176

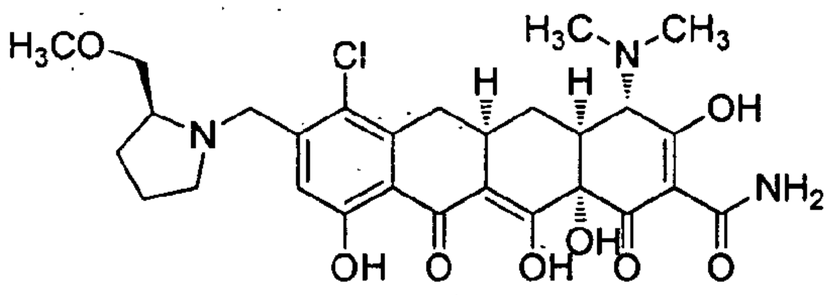
^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.66 (t, *J* = 12.8 Hz, 1 H), 4.37

(t, J = 12.8 Hz, 1 H), 4.13 (s, 1 H), 3.43-3.39 (m, 1 H), 3.20-2.95 (m, 9 H), 2.86 (s, 3 H), 2.46-2.39 (m, 1 H), 2.28-2.25 (m, 1 H), 1.80-1.60 (m, 8 H), 1.44-1.12 (m, 4 H), 1.08-0.96 (m, 2 H); MS (ESI) *m/z* 602.1 (M+H).



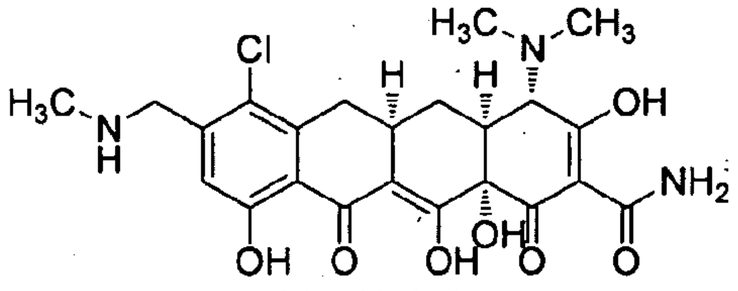
S15-13-177

^{1}H NMR (400 MHz, CD3OD) δ 7.26 (s, 1 H), 4.53 (s, 2 H), 4.11 (s, 1 H), 3.71-3.62 (m, 2 H), 3.40 (dd, J = 16.4 Hz and 4.8 Hz, 1 H), 3.16-2.95 (m, 10 H), 2.70-2.60 (m, 1 H), 2.45-2.38 (m, 1 H), 2.27-2.23 (m, 1 H), 2.17-2.14 (m, 2 H), 1.96-1.83 (m, 2 H), 1.70-1.59 (m, 1 H); MS (ESI) *m/z* 614.1 (M+H).



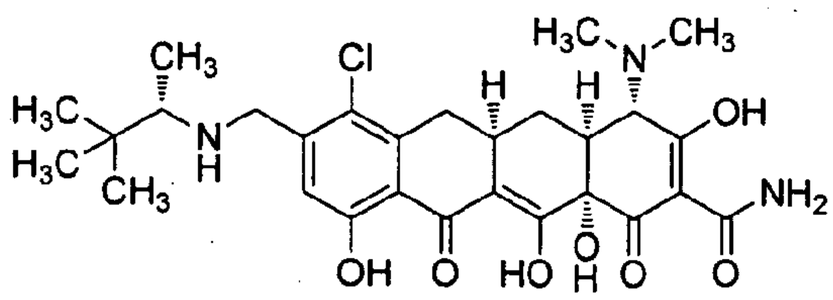
S15-13-178

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.82-4.77 (m, 1 H), 4.39-4.36 (m, 1 H), 4.10 (s, 1 H), 3.92-3.85 (m, 1 H), 3.76-3.72 (m, 1 H), 3.68-3.60 (m, 1 H), 3.51-3.32 (m, 5 H), 3.17-2.95 (m, 9 H), 2.45-2.37 (m, 1), 2.24-2.31 (m, 2 H), 2.20-2.10 (m, 1 H), 2.05-1.87 (m, 2 H), 1.70-1.59 (m, 1 H); MS (ESI) *m/z* 576.1 (M+H).



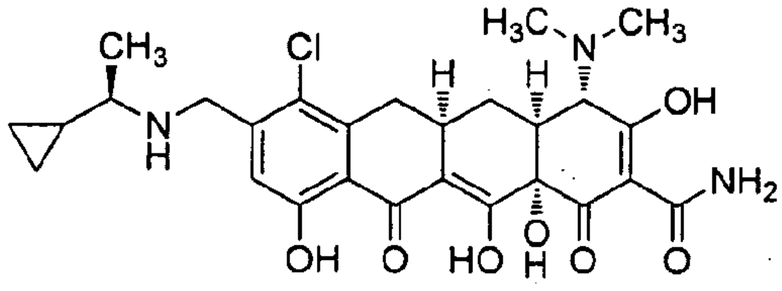
S15-13-179

^{1}H NMR (400 MHz, CD_3OD) δ 7.10 (s, 1 H), 4.36 (s, 2 H), 4.11 (s, 1 H), 3.40 (dd, J = 16.0 Hz and 4.4 Hz, 1 H), 3.16-2.95 (m, 8 H), 2.81 (s, 3 H), 2.45-2.37 (m, 1 H), 2.27-2.24 (m, 1 H), 1.70-1.60 (m, 1 H); MS (ESI) *m/z* 492.1 (M+H).



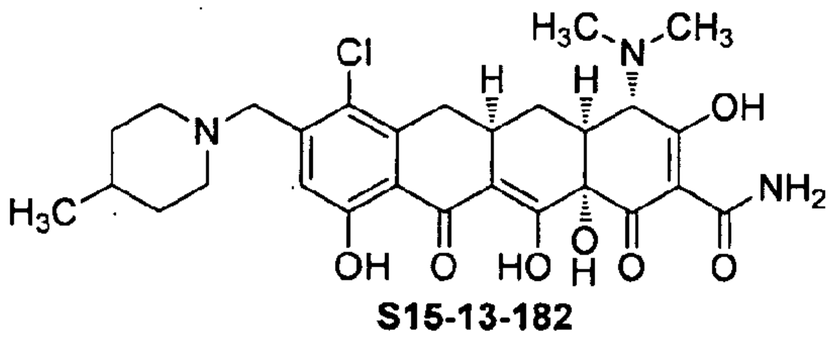
S15-13-180

^{1}H NMR (400 MHz, CD_3OD) δ 7.21 (s, 1 H), 4.50 (d, *J* = 13.7 Hz, 1 H), 4.43 (d, *J* = 13.7 Hz, 1 H), 4.12 (s, 1 H), 3.48-3.38 (m, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.16-2.94 (comp, 3 H), 2.49-2.39 (m, 1 H), 2.30-2.23 (m, 1 H), 1.72-1.61 (m, 1 H), 1.40 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 9 H); MS (ESI) *m/z* 562.22 (M+H).



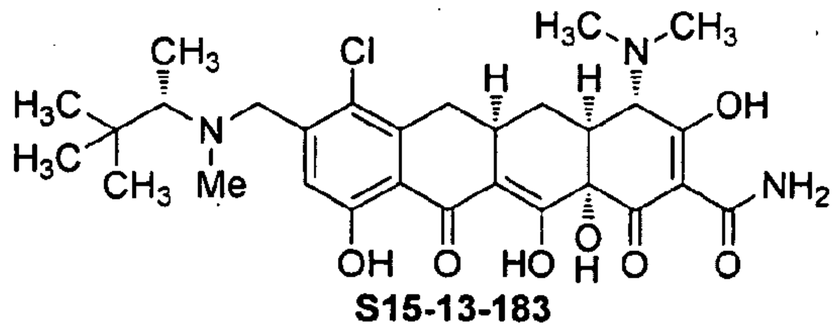
S15-13-181

^{1}H NMR (400 MHz, CD_3OD) δ 7.16 (s, 1 H), 4.52 (d, *J* = 13.4 Hz, 1 H), 4.39 (d, *J* = 13.4 Hz, 1 H), 4.11 (s, 1 H), 3.49-3.36 (m, 1 H), 3.05 (s, 3 H), 2.96 (s, 3 H), 3.14-2.94 (comp, 3 H), 2.48-2.38 (m, 1 H), 2.29-2.22 (m, 1 H), 1.73-1.62 (m, 1 H), 1.50 (d, *J* = 6.7 Hz, 3 H), 1.12-1.03 (m, 1 H), 0.87-0.73 (m, 2 H), 0.67-0.59 (m, 1 H), 0.44-0.36 (m, 1 H); MS (ESI) *m/z* 546.16 (M+H).



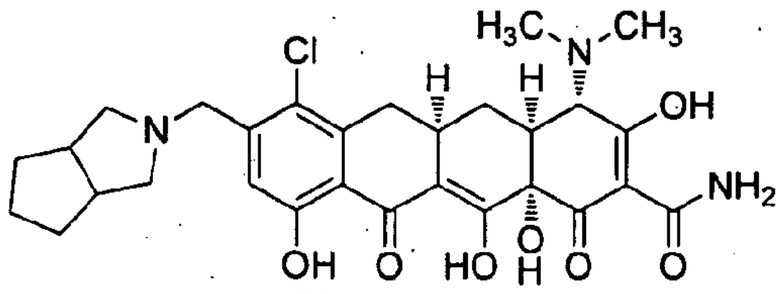
S15-13-182

^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (s, 1 H), 4.49 (s, 2 H), 4.11 (s, 1 H), 3.60-3.37 (comp, 4 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.23-2.94 (comp, 3 H), 2.48-2.39 (m, 1 H), 2.28-2.21 (m, 1 H), 1.97-1.88 (m, 2 H), 1.80-1.61 (m, 2 H), 1.53-1.38 (m, 2 H), 1.01 (d, *J* = 6.1 Hz, 3 H); MS (ESI) *m/z* 560.19 (M+H).



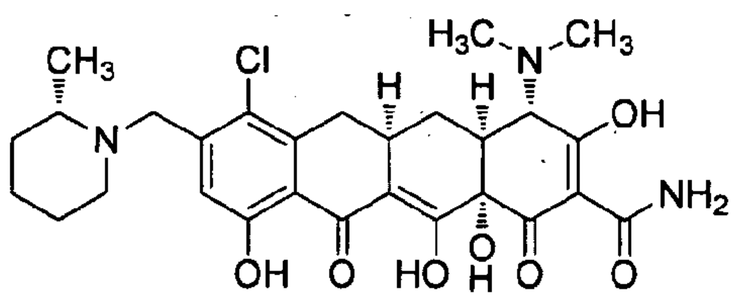
S15-13-183

^{1}H NMR (400 MHz, CD_3OD) δ 7.31 (s, 1 H), 4.71 (d, *J* = 13.4 Hz, 1 H), 4.47 (d, *J* = 13.4 Hz, 1 H), 4.11 (s, 1 H), 3.48-3.38 (m, 1 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 2.90 (s, 3 H), 3.16-2.86 (comp, 3 H), 2.50-2.40 (m, 1 H), 2.29-2.22 (m, 1 H), 1.72-1.60 (m, 1 H), 1.43 (d, *J* = 6.7 Hz, 3 H), 1.02 (s, 9 H); MS (ESI) *m/z* 576.20 (M+H).



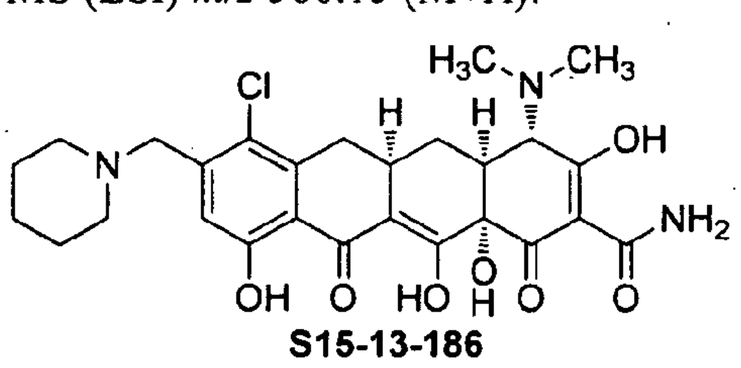
S15-13-184

^{1}H NMR (400 MHz, CD_3OD) δ 7.19 (s, 1 H), 4.57 (s, 2 H), 4.11 (s, 1 H), 3.85-3.76 (m, 2 H), 3.57-3.38 (m, 1 H), 3.05 (s, 3 H), 2.97 (s, 3 H), 3.15-2.81 (comp, 4 H), 2.49-2.39 (m, 1 H), 2.29-2.21 (m, 1 H), 1.95-1.47 (comp, 9 H); MS (ESI) *m/z* 572.14(M+H).



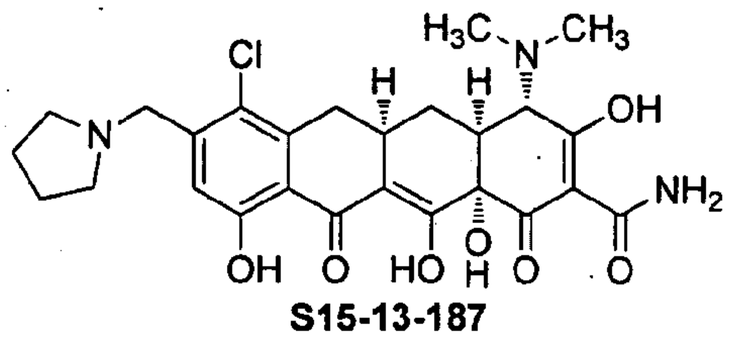
S15-13-185

^{1}H NMR (400 MHz, CD_3OD) δ 7.21-7.18 (m, 1 H), 4.54-4.24 (m, 2 H), 4.10 (s, 1 H), 3.49-3.35 (comp, 3 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.14-2.93 (comp, 3 H), 2.49-2.38 (m, 1 H), 2.28-2.21 (m, 1 H), 2.07-2.00 (m, 1 H), 1.91-1.49 (comp, 9 H); MS (ESI) *m/z* 560.15 (M+H).



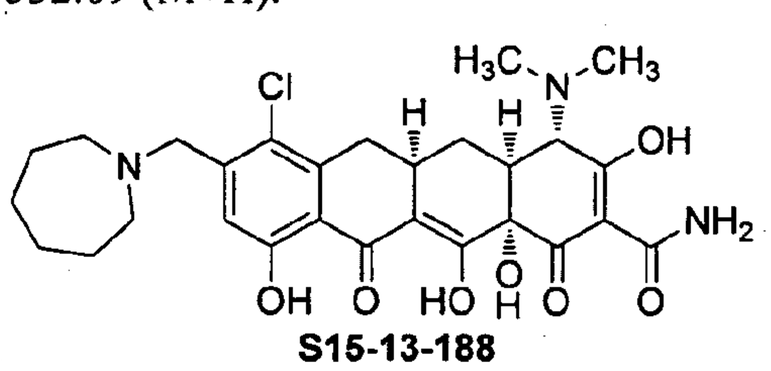
S15-13-186

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.50 (d, *J* = 13.7 Hz, 1 H), 4.46 (d, *J* = 13.7 Hz, 1 H), 4.12 (s, 1 H), 3.57-3.36 (comp, 3 H), 3.05 (s, 3 H), 2.96 (s, 3 H), 3.20-2.94 (comp, 4 H), 2.47-2.37 (m, 1 H), 2.30-2.21 (m, 1 H), 1.99-1.47 (comp, 7 H); MS (ESI) *m/z* 546.10 (M+H).



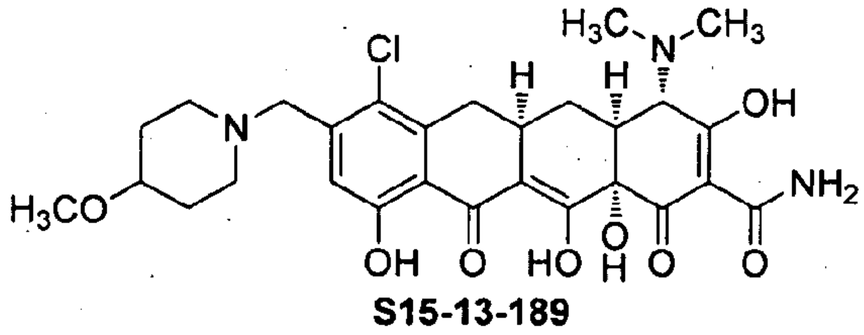
S15-13-187

^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (s, 1 H), 4.58 (s, 2 H), 4.11 (s, 1 H), 3.69-3.56 (m, 2 H), 3.48-3.36 (m, 2 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.16-2.93 (comp, 3 H), 2.46-2.37 (m, 1 H), 2.29-1.98 (comp, 5 H), 1.71-1.59 (m, 1 H); MS (ESI) *m/z* 532.09 (M+H).



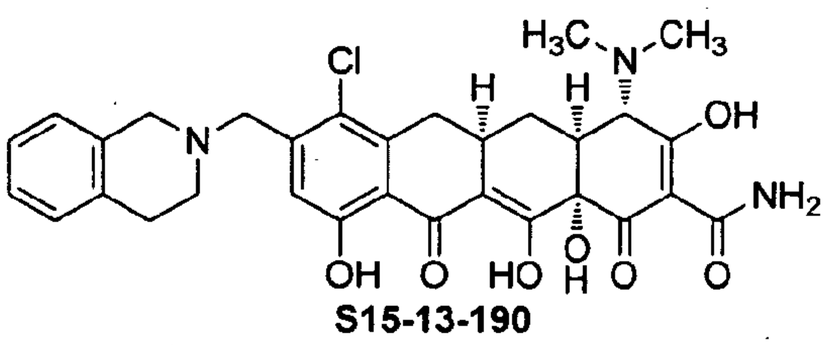
S15-13-188

^{1}H NMR (400 MHz, CD_3OD) δ 7.24 (s, 1 H), 4.53 (s, 2 H), 4.11 (s, 1 H), 3.54-3.33 (comp, 5 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.14-2.93 (comp, 2 H), 2.47-2.38 (m, 1 H), 2.28-2.21 (m, 1 H), 2.06-1.60 (comp, 9 H); MS (ESI) *m/z* 560.15 (M+H).



S15-13-189

^{1}H NMR (400 MHz, CD_3OD) δ 7.25-7.23 (m, 1 H), 4.53-4.47 (m, 2 H), 4.12 (s, 1 H), 3.63-3.34 (comp, 8 H), 3.04 (s, 3 H), 2.96 (s, 3 H), 3.14-2.94 (comp, 3 H), 2.47-2.37 (m, 1 H), 2.31-1.60 (comp, 6 H); MS (ESI) *m/z* 576.15 (M+H).



S15-13-190

^{1}H NMR (400 MHz, CD_3OD) δ 7.34-7.24 (comp, 4 H), 7.21-7.17 (m, 1 H), 4.69 (s, 2 H), 4.54 (s, 2 H), 4.11 (s, 1 H), 3.90-3.53 (m, 2 H), 3.47-3.39 (m, 2 H),

DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME __1___ DE __2___

NOTE: Pour les tomes additionels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

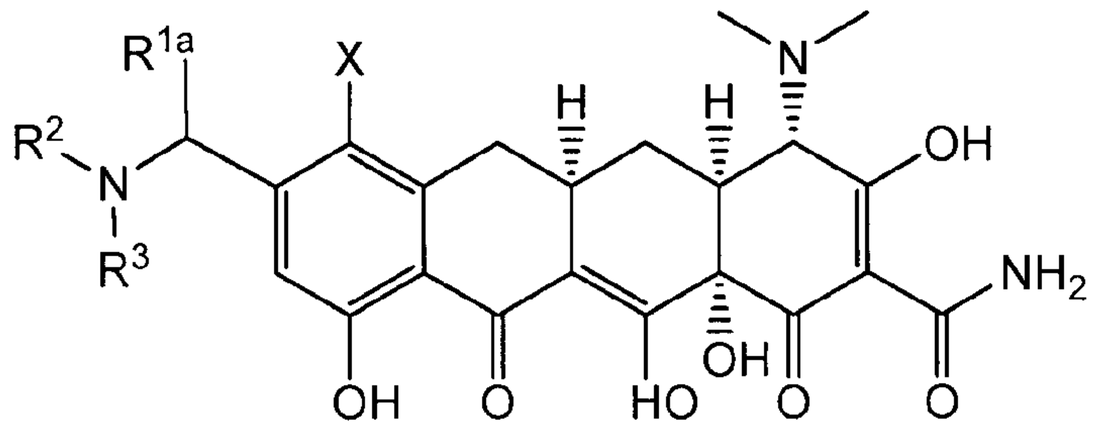
THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __2___

NOTE: For additional volumes please contact the Canadian Patent Office.

CLAIMS:

1. A compound of Formula II:



(II);

or a pharmaceutically acceptable salt thereof, wherein:

X is selected from hydrogen, bromo, fluoro, chloro, C_1-C_6 alkyl, -O-C_1-C_6 alkyl, -S(O)$_m$-C_1-C_6 alkyl, C_3-C_7 cycloalkyl, -O-C_3-C_7 cycloalkyl, -S(O)$_m$-C_3-C_7 cycloalkyl, -CN, -N(R^4)(R^5), and -NH-C(O)-(C_1-C_6 alkylene)-N(R^4)(R^5), wherein each alkyl, alkylene or cycloalkyl in the group represented by X is optionally substituted with fluoro;

R^{1a} is selected from hydrogen, C_1-C_4 alkyl, and C_3-C_{10} carbocyclyl;

R^2 is selected from hydrogen, C_1-C_{12} alkyl, -C_0-C_6 alkylene-C_3-C_{10} carbocyclyl, and -C_0-C_6 alkylene-(4-13 membered) heterocyclyl;

R^3 is selected from hydrogen, C_1-C_8 alkyl, -C_0-C_6 alkylene-C_3-C_{10} carbocyclyl, -C_0-C_6 alkylene-(4-13 membered) heterocyclyl, -C(O)-C_1-C_6 alkyl, -C_0-C_6 alkylene-C(O)N(R^4)(R^5), -C(O)-C_1-C_6 alkylene-N(R^4)(R^5), -C_2-C_6 alkylene-N(R^4)(R^5), -S(O)$_m$-C_1-C_6 alkyl, -S(O)$_m$-C_3-C_{10} carbocyclyl, and -S(O)$_m$-(4-13 membered) heterocyclyl, wherein each alkyl, carbocyclyl, alkylene or heterocyclyl in the group represented by R^2 or R^3 is optionally and independently substituted with one or more substituents independently selected from fluoro, chloro, -OH, -O-C_1-C_4 alkyl, C_1-C_4 alkyl, fluoro-substituted-C_1-C_4 alkyl, -N(R^4)(R^5), C_3-C_{10} carbocyclyl or a (4-13 membered) heterocyclyl; or

R^2 and R^3 taken together with the nitrogen atom to which they are bound form a (4-7 membered) monocyclic heterocylic ring, or a (6-13 membered) bicyclic, spirocyclic or bridged heterocylic ring, wherein the (4-7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring optionally comprises 1 to 4 additional heteroatoms independently selected from N, S and O; and wherein the (4-7 membered) monocyclic heterocylic ring, or the (6-13 membered) bicyclic, spirocyclic or bridged heterocyclic ring is optionally substituted with one or more substituents independently selected from C_3-C_{10} carbocyclyl, (4-13 membered) heterocyclyl, fluoro, chloro, -OH, -C_1-C_4 fluoroalkyl, -C_1-C_4 alkyl, -O-C_3-C_{10} carbocyclyl, -O-(4-13 membered) heterocyclyl, -C_0-C_4 alkylene-O-C_1-C_4 alkyl, -C_0-C_4 alkylene-O-C_1-C_4 fluoroalkyl, =O, -C(O)-C_1-C_4 alkyl, -C(O)N(R^4)(R^5), -N(R^4)-C(O)-C_1-C_4 alkyl, and -C_0-C_4 alkylene-N(R^4)(R^5), and wherein each carbocyclyl or heterocyclyl substituent is optionally substituted with fluoro, chloro, -OH, C_1-C_4 fluoroalkyl, C_1-C_4 alkyl, -O-C_1-C_4 alkyl, -O-C_1-C_4 fluoroalkyl, -NH_2, -NH(C_1-C_4 alkyl), or -N(C_1-C_4 alkyl)$_2$;

each of R^4 and R^5 is independently selected from hydrogen and C_1-C_4 alkyl; or

R^4 and R^5 taken together with the nitrogen atom to which they are bound form a (4-7 membered) heterocylic ring optionally comprising one additional heteroatom selected from N, S and O, wherein the (4-7 membered) heterocylic ring is optionally substituted with fluoro, chloro, -OH, fluoro-substituted C_1-C_4 alkyl, -C_1-C_4 alkyl, or -C_1-C_4 alkylene-O-C_1-C_4 alkyl, and is optionally fused to phenyl; and

each m is independently 0, 1 or 2.

2. The compound of claim 1, wherein:

R^{1a} is selected from hydrogen and methyl;

R^2 is selected from hydrogen, C_1-C_3 straight chained alkyl, C_1-C_3 straight chained fluoroalkyl, cyclopropyl, and -CH_2-cyclopropyl;

R^3 is selected from hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_2-C_6 alkylene-O-C_1-

C_3 alkyl, -C_3-C_{10} cycloalkyl, -C_3-C_{10} cycloalkyl-substituted C_1-C_3 alkyl, cyclopropyl-substituted cyclopropyl, -$(CH_2)_2$-phenyl, and -$S(O)_2$-phenyl, when R^2 is hydrogen or C_1-C_2 alkyl, R^3 is additionally selected from benzyl; or

R^2 and R^3 taken together with the nitrogen atom to which they are bound form a ring selected from pyrrolidine, piperidine, piperazine or morpholine, wherein the ring is optionally substituted with one or more substituents independently selected from -OH, -C_1-C_3 alkyl and -C_1-C_3 alkylene-O-C_1-C_3 alkyl, and wherein the ring is optionally fused to phenyl or spirofused to cyclopropyl.

3. The compound of claim 1, wherein:

R^{1a} is selected from hydrogen and methyl;

R^2 is selected from hydrogen, C_1-C_3 straight chained alkyl and -CH_2-cyclopropyl;

R^3 is selected from hydrogen, C_1-C_8 alkyl, -CH_2-CHF_2, -C_1-C_6 alkylene-O-C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, -$(CH_2)_2$-phenyl and C_3-C_{10} cycloalkyl-substituted C_1-C_3 alkyl, wherein each cycloalkyl in the group represented by R^3 is optionally substituted with-C_1-C_3 alkyl or optionally benzofused and when R^2 is hydrogen or -C_1-C_2 alkyl, R^3 is additionally selected from benzyl; or

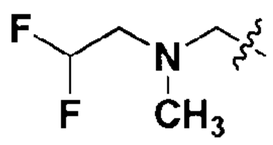
R^2 and R^3 taken together with the nitrogen atom to which they are bound form a ring selected from pyrrolidine and piperidine, wherein the ring is optionally substituted with one or more substituents independently selected from fluoro -C_1-C_3 alkyl and -C_1-C_3 alkylene-O-C_1-C_3 alkyl, and wherein the ring is optionally fused to phenyl or spirofused to cyclopropyl.

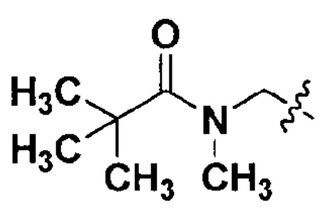
4. The compound of any one of Claims 1 to 3, wherein:

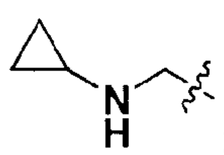
X is selected from fluoro, chloro, -CN, and -$N(CH_3)_2$.

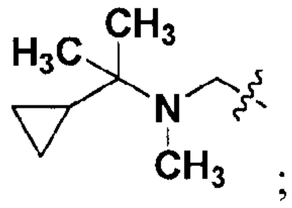
5. The compound of any one of Claims 1 to 4, wherein X is fluoro, chloro, or -$N(CH_3)_2$.

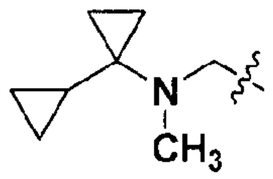
6. The compound of claim 5, wherein:

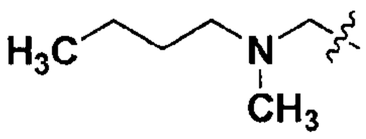
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

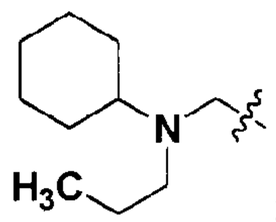
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

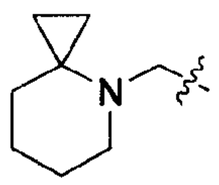
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

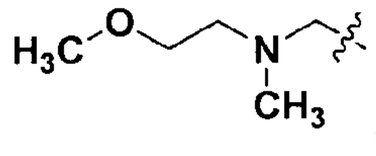
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

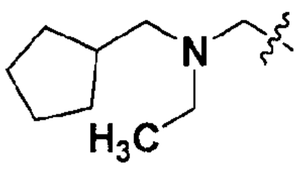
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

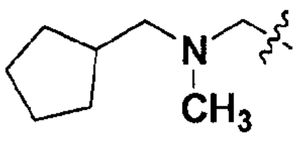
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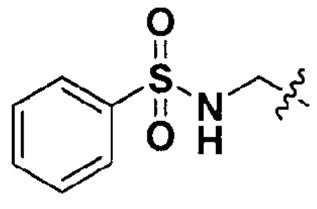
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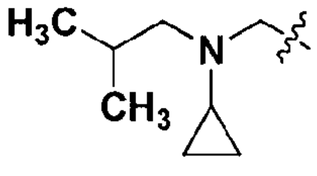
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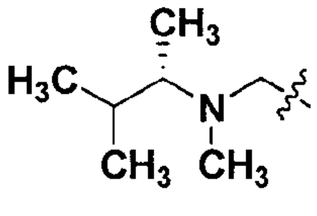
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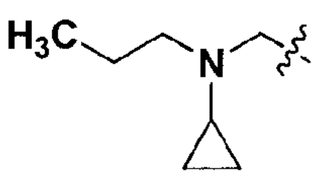
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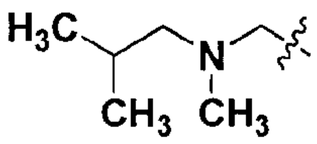
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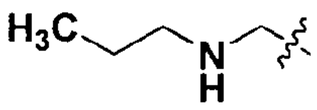
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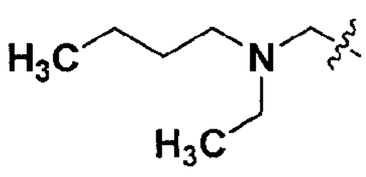
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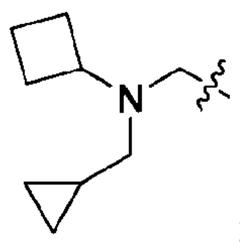
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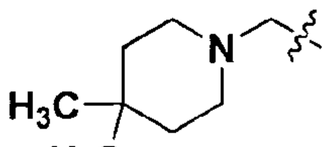
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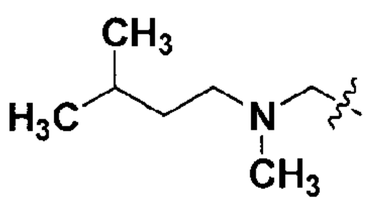
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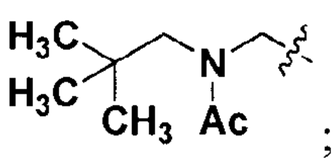
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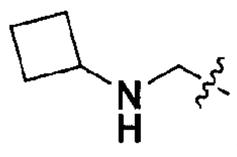
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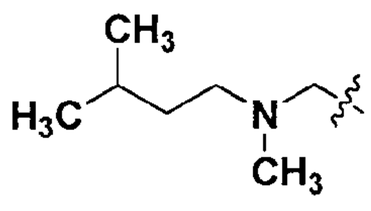
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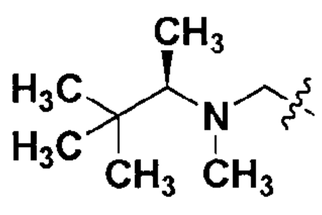
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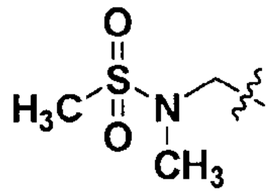
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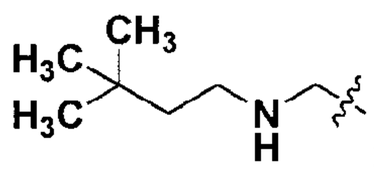
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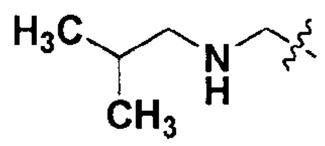
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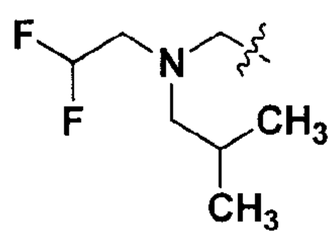
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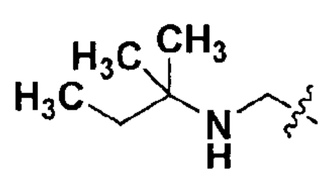
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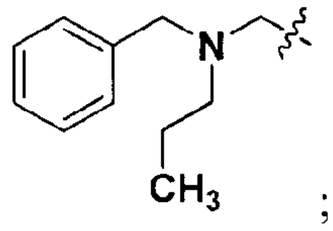
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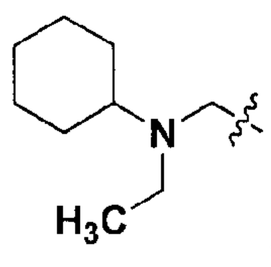
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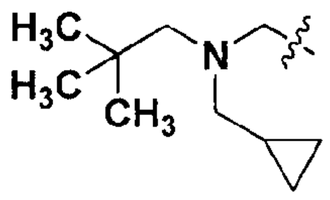
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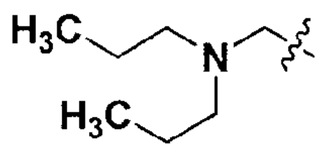
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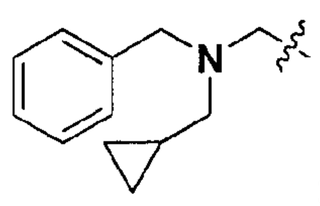
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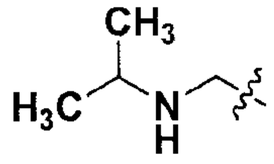
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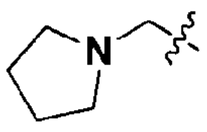
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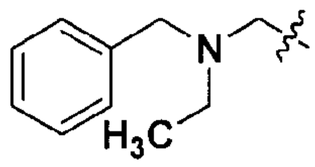
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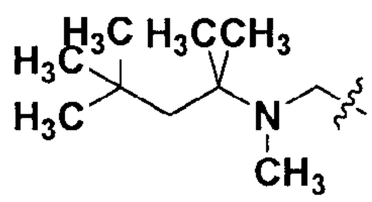
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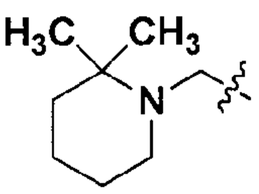
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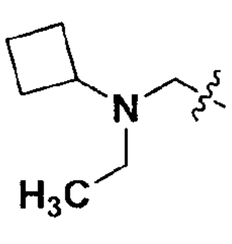
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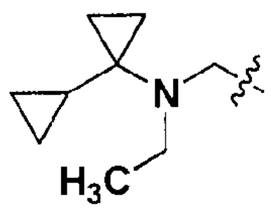
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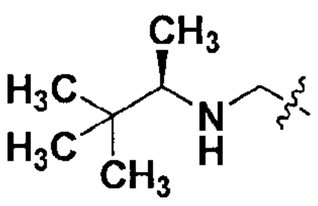
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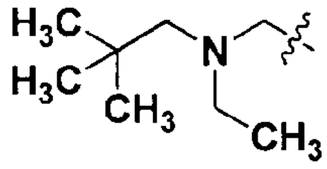
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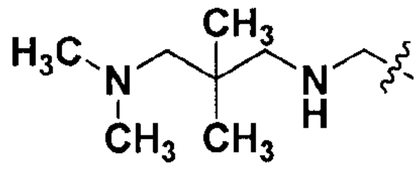
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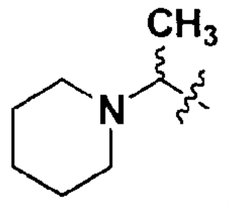
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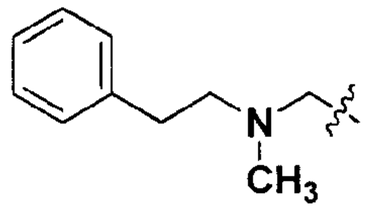
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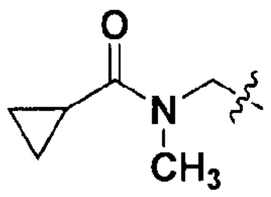
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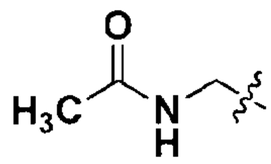
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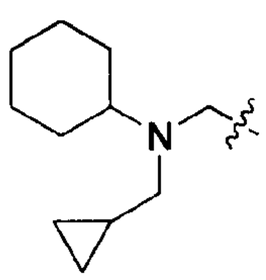
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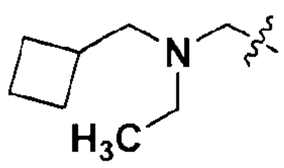
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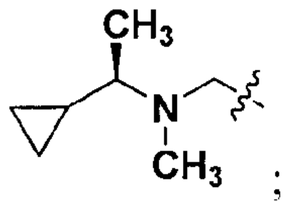
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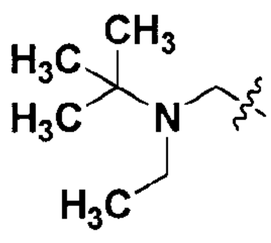
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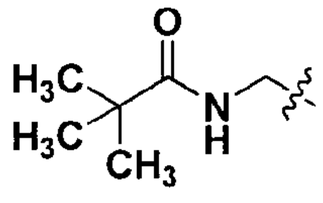
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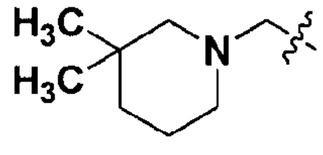
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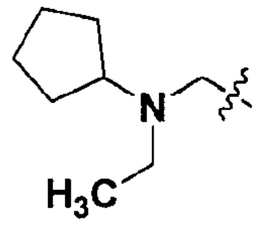
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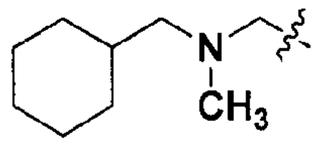
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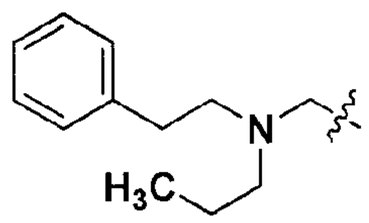
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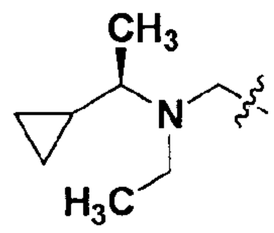
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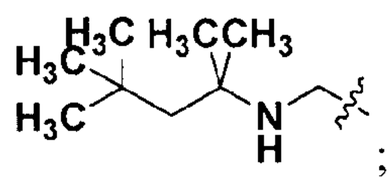
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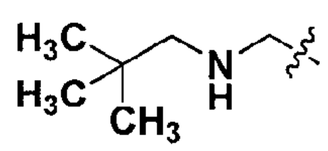
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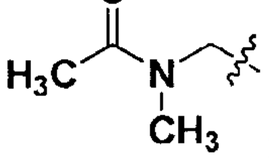
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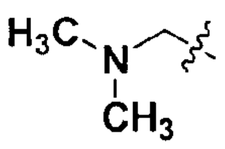
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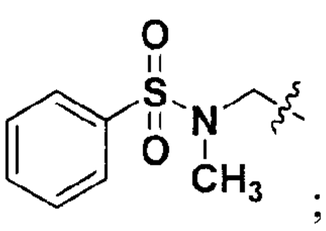
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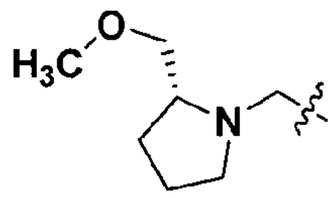
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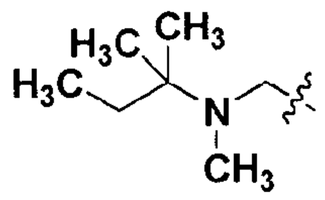
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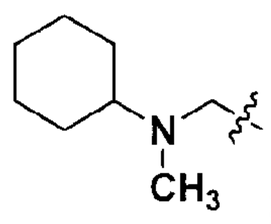
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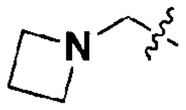
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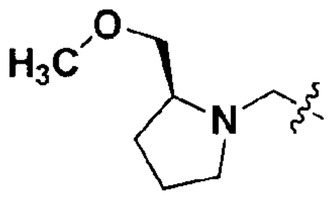
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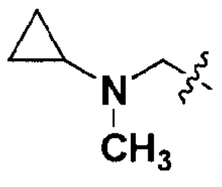
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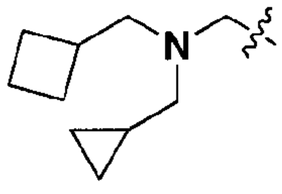
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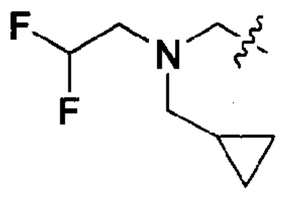
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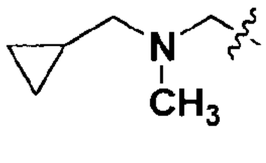
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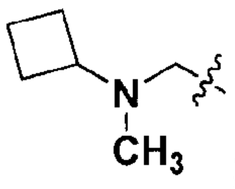
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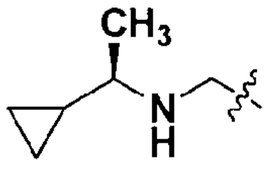
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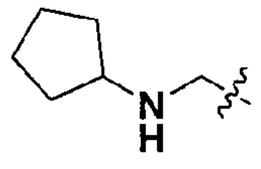
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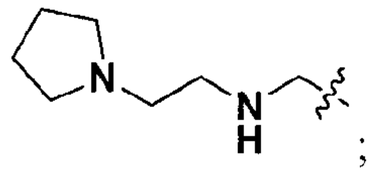
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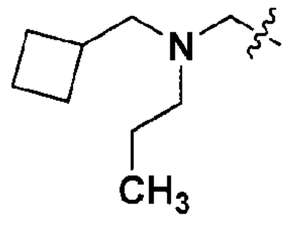
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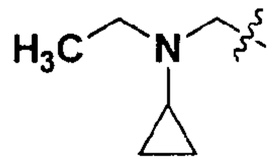
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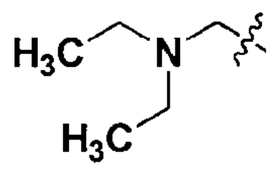
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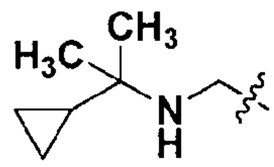
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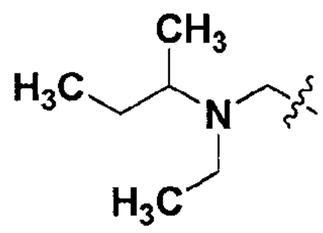
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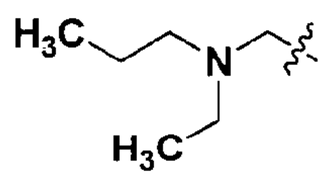
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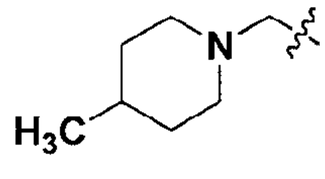
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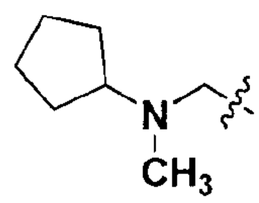
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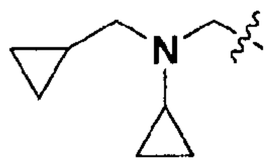
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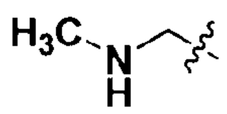
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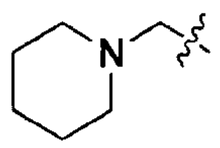
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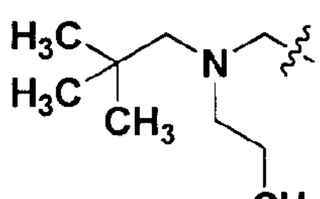
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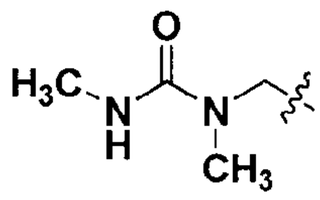
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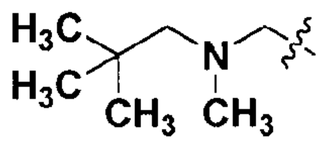
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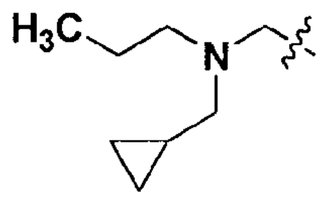
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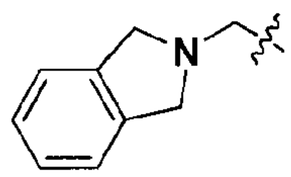
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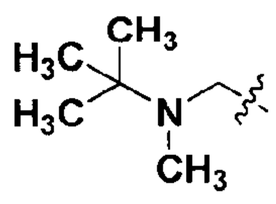
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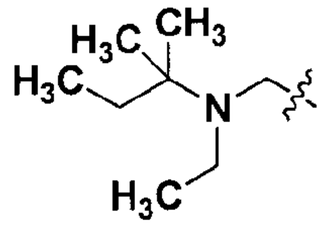
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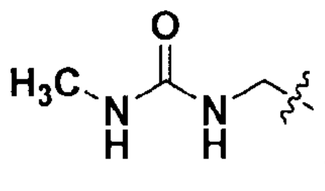
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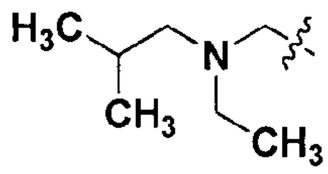
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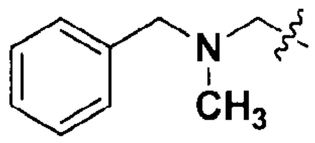
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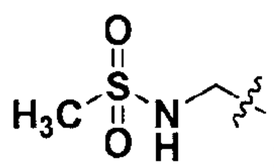
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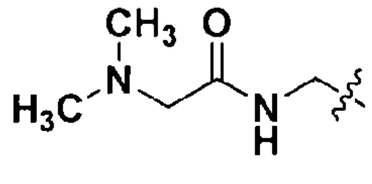
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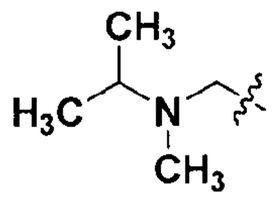
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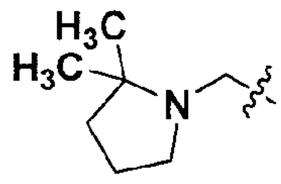
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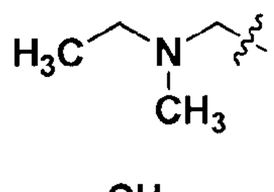
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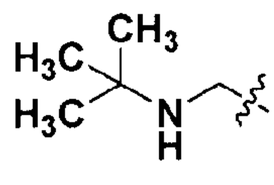
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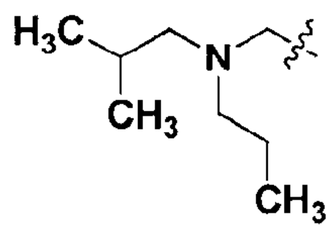
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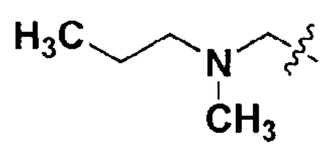
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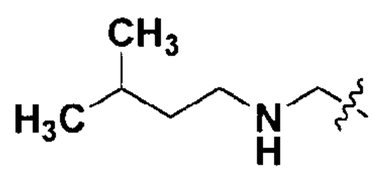
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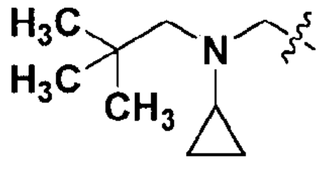
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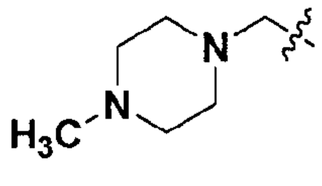
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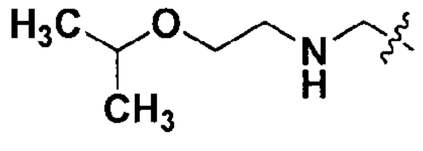
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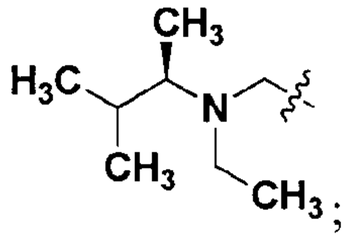
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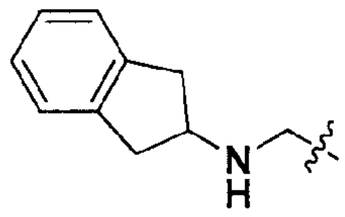
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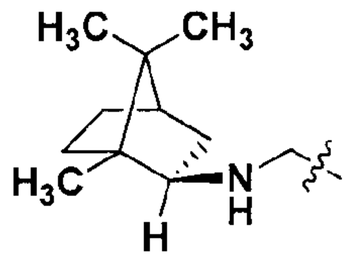
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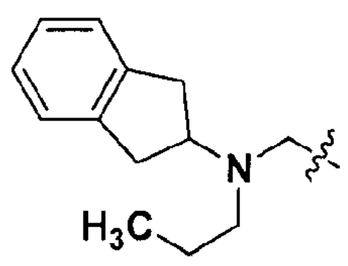
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

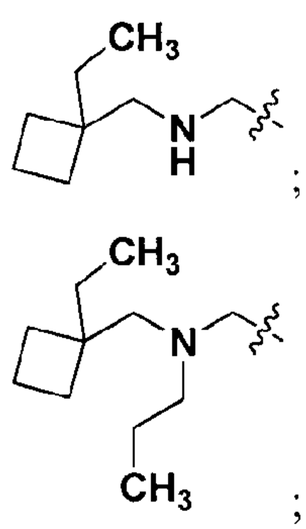
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

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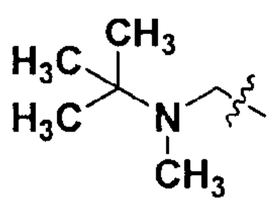
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

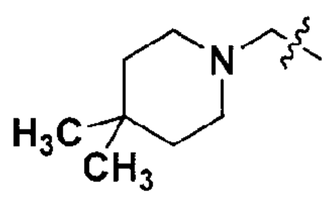
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

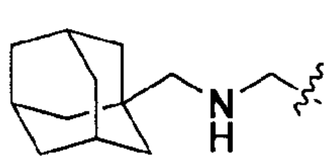
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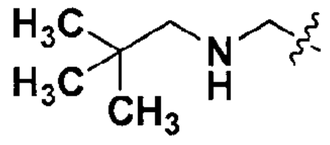
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

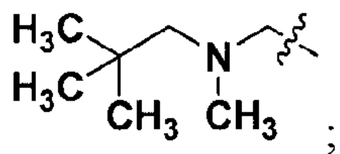
X is fluoro and -CH(R^{1a})-NR^2R^3 is ;

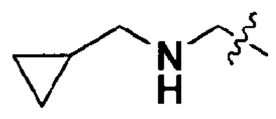
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

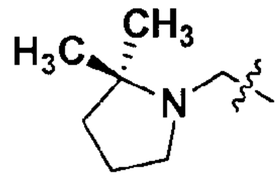
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

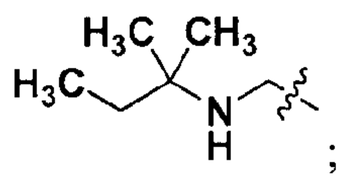
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

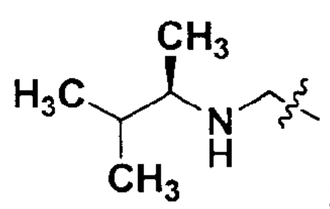
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

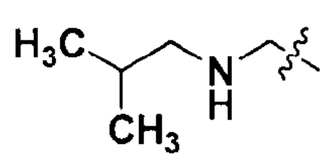
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

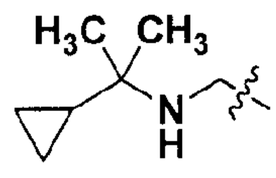
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

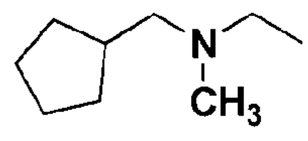
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

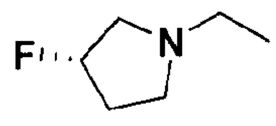
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

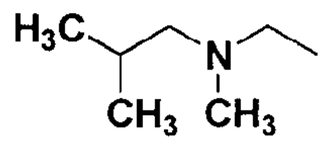
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

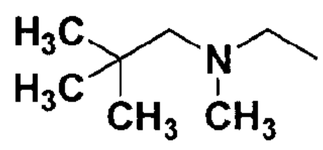
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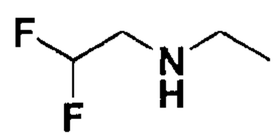
X is chloro and -CH(R^{1a})-NR^2R^3 is ;

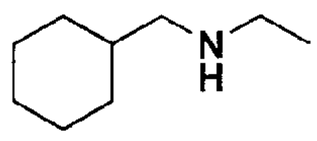
X is $-N(CH_3)_2$ and -CH(R^{1a})-NR^2R^3 is ;

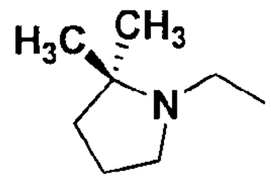
X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is ;

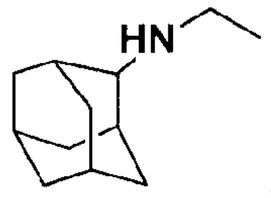
X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is ;

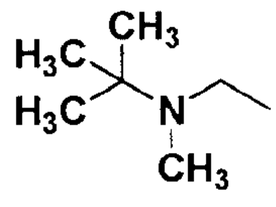
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X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is ; or

X is $-N(CH_3)_2$ and $-CH(R^{1a})-NR^2R^3$ is .

7. The compound of any one of Claims 1-6, for treating an infection in a subject.

8. The compound according to Claim 7, wherein the infection is caused by a Gram-positive organism, or a Gram-negative organism.

9. The compound according to Claim 7, wherein the infection is caused by an organism selected from the group consisting of rickettsiae, chlamydiae, and *Mycoplasma pneumoniae*.

10. The compound according to Claim 7, wherein the infection is caused by an organism resistant to tetracycline.

11. The compound according to Claim 7, wherein the infection is caused by an organism resistant to methicillin.

12. The compound according to Claim 7, wherein the infection is caused by an organism resistant to vancomycin.

13. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and the compound of any one of Claims 1-6.

14. The composition of Claim 13, for treating an infection in a subject.

15. The composition according to Claim 14, wherein the infection is caused by a Gram-positive organism, or a Gram-negative organism.

16. The composition according to Claim 14, wherein the infection is caused by an organism selected from the group consisting of rickettsiae, chlamydiae, and *Mycoplasma pneumoniae*.

17. The composition according to Claim 14, wherein the infection is caused by an organism resistant to tetracycline.

18. The composition according to Claim 14, wherein the infection is caused by an organism resistant to methicillin.

19. The composition according to Claim 14, wherein the infection is caused by an organism resistant to vancomycin.

20. Use of the compound of any one of Claims 1 to 6, or the composition of Claim 13, in the manufacture of a medicament for treating an infection in a subject.

21. The use according to Claim 20, wherein the infection is caused by a Gram-positive organism, or a Gram-negative organism.

22. The use according to Claim 20, wherein the infection is caused by an organism selected from the group consisting of rickettsiae, chlamydiae, and *Mycoplasma pneumoniae.*

23. The use according to Claim 20, wherein the infection is caused by an organism resistant to tetracycline.

24. The use according to Claim 20, wherein the infection is caused by an organism resistant to methicillin.

25. The use according to Claim 20, wherein the infection is caused by an organism resistant to vancomycin.

MIC90 values (µg/ml)

Cmpd. No.	Lot	S. aureus MRSA	S. sapro-phyticus	E. faecalis	Efaecium	S. pneumoniae	E. coli ESBL+	Ecloacae	K. pneumoniae ESBL+	P. mirabilis	A. baumannii	P. aeruginosa
		n=32 isolates	n=15 isolates	n=25 isolates	n=15 isolates	n=19 isolates	n=14 isolates	n=14 isolates	n=16 isolates	n=14 isolates	n=24 isolates	n=35 isolates
S16-10-161	A		(0.5)	(16)	(16)		(1)	(4)	(1)	(16)		(>32)
S24-9-21	A	(2)	(0.5)	(4)	(4)		(0.5)	(2)	(2)	(8)	(2)	
S24-9-23	A	(4)	(0.25)	(8)	(8)		(1)	(2)	(1)	(4)	(1)	
S24-9-25	A	(4)		(4)			(0.25)	(2)	(2)	(32)	(2)	
S15-13-4	A	(4)		(4)			(1)		(2)	(>32)	(2)	
S24-9-17	A	(4)		(8)			(0.5)	(2)	(2)	(16)	(2)	
S3-5-5	A	(8)		(16)			(1)	(2)	(2)	(2)	(2)	
S15-13-194	A			(4)			(0.5)		(1)	(16)	(1)	

FIG. 1A

MIC90 values (µg/ml)

Cmpd. No.	Lot	S. aureus MRSA	S. saprophyticus	E. faecalis	Efaecium	S. pneumoniae	E. coli ESBL+	Ecloacae	K. pneumoniae ESBL+	P. mirabilis	A. baumannii	P. aeruginosa
S25-11-1	A			(8)			(0.5)		(1)	(8)		
S15-13-15	A	(4)		(4)			(1)		(1)	(16)		
S15-13-187	A						(1)	(1)	(1)	(4)		
S25-11-45	A						(0.5)	(2)	(1)	(16)		
S15-13-188	A,B						(0.5)		(2)	(16)		
S15-13-222	A						(0.25)		(0.5)	(4)		
S2-4-19	A						(1)		(2)	(16)		
S2-4-12	A						(1)	(2)	(1)	(>32)		
S15-13-200	A						(1)	(2)	(1)	(32)		

FIG. 1B

Cmpd. No.	Lot	S. aureus MRSA	S. saprophyticus	E. faecalis	Efaecium	S. pneumoniae	E. coli ESBL+	Ecloacae	K. pneumoniae ESBL+	P. mirabilis	A. baumannii	P. aeruginosa
MIC90 values (µg/ml)												
S15-13-223	A	(0.25)	(0.25)	(0.13)	(0.063)	(≤0.016)	(0.5)		(2)	(32)	(4)	(32)
Tigecycline		(2)	(1)	(16)	(0.5)	(0.031)	(16)	(16)	(16)	(>64)	(8)	(32)
PTK 0796		(8)	(0.5)	(16)	(16)	(8)	(>32)			(>64)	(>64)	
Doxycycline		(>32)	(1)	(>32)	(>32)	(>32)	(>32)	(>32)	(>64)	(64)	(>64)	(>32)
Tetracycline		(4)	(4)	(32)	(32)	(1)						(32)
Linezolid		(>32)	(0.5)		(>32)	(1)	(32)	(32)	(64)	(32)	(32)	
Levofloxacin		(8)				(8)	(32)			(64)		
Minocycline												

FIG. 1C

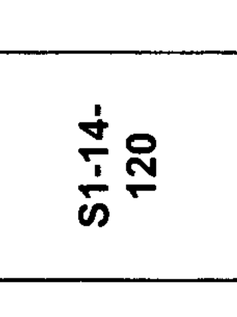
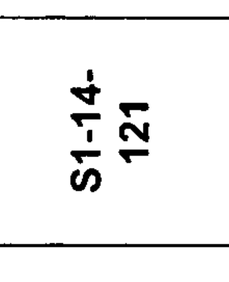
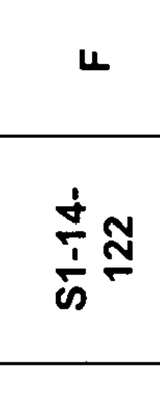
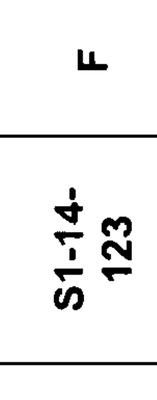
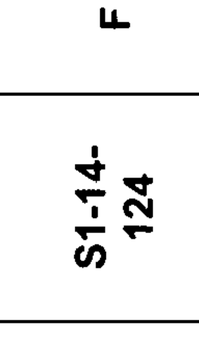
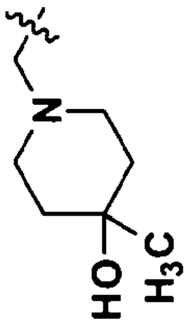
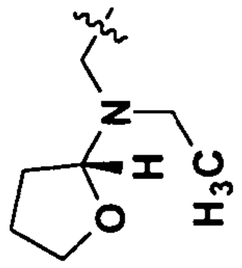
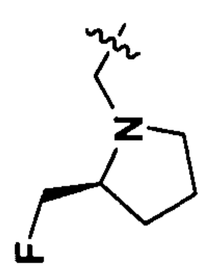
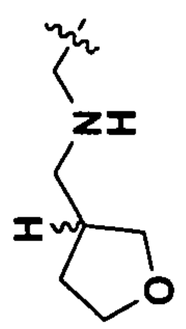
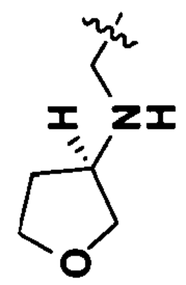
Cmpd	X	Y	Z
S1-14-120	F		H
S1-14-121	F		H
S1-14-122	F		H
S1-14-123	F		H
S1-14-124	F		H
S1-14-115	F		H
S1-14-116	F		H
S1-14-117	F		H
S1-14-118	F		H
S1-14-119	F		H

FIG. 2A

Cmpd	X	Y	Z
S1-14-131	F		H
S1-14-132	F		H
S1-14-135	F		H
S1-14-137	F		H
S114-138	F		H

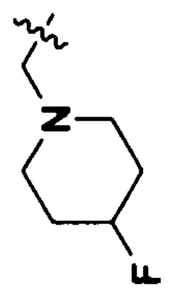
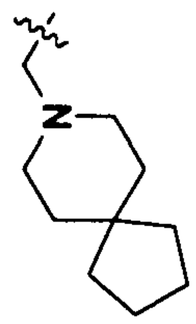
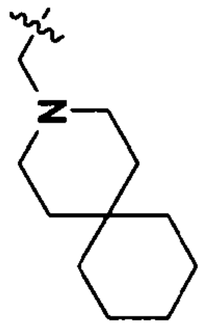
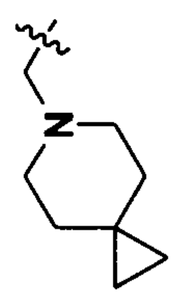
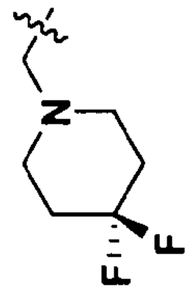
Cmpd	X	Y	Z
S1-14-125	F		H
S1-14-126	F		H
S1-14-127	F		H
S1-14-128	F		H
S1-14-129	F		H

FIG. 2B

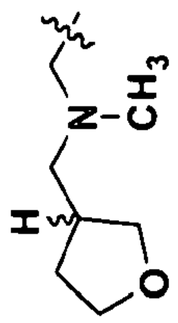
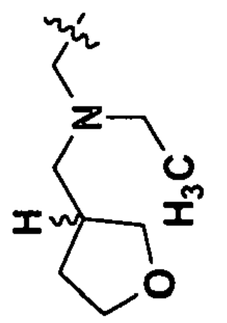
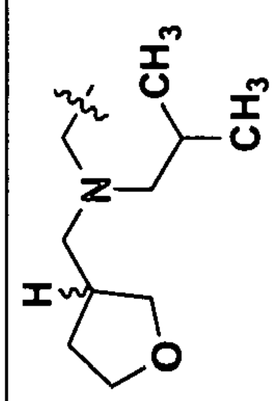
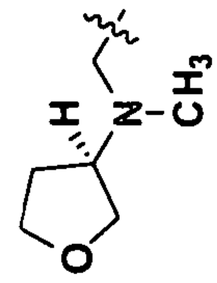
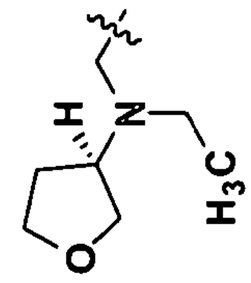
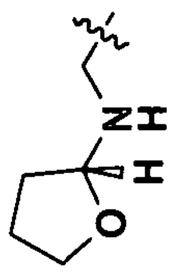
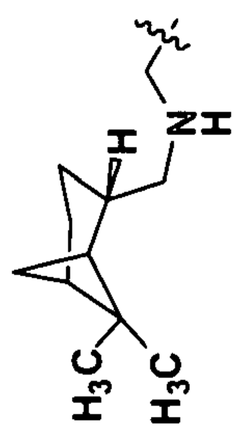
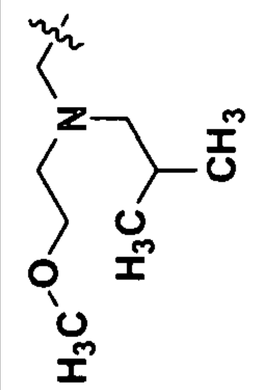
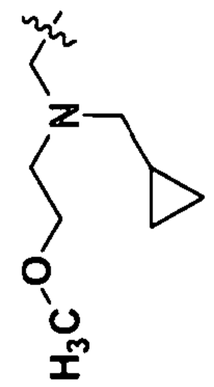
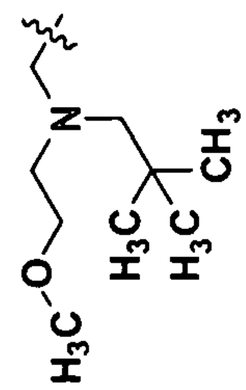
Cmpd	X	Y	Z
S1-14-144	F		H
S1-14-145	F		H
S1-14-146	F		H
S1-14-147	F		H
S1-14-148	F		H
S114-139	F		H
S1-14-140	F		H
S1-14-141	F		H
S1-14-142	F		H
S1-14-143	F		H

FIG. 2C

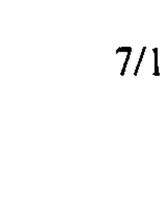
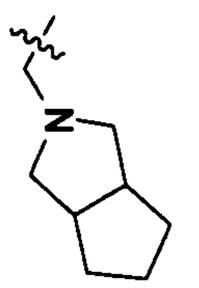
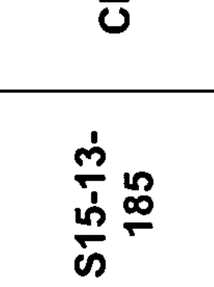
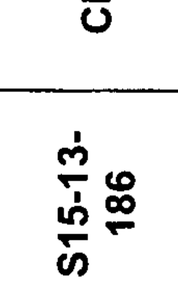
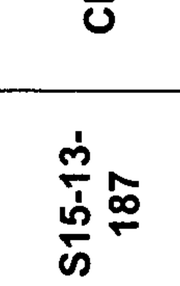
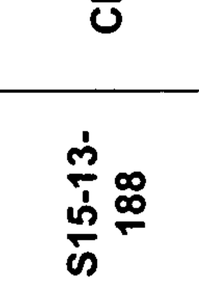
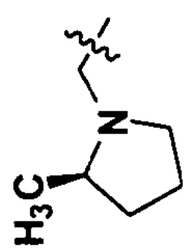
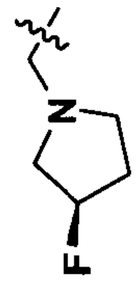
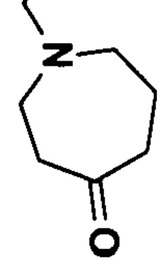
Cmpd	X	Y	Z
S15-13-184	Cl		H
S15-13-185	Cl		H
S15-13-186	Cl		H
S15-13-187	Cl		H
S15-13-188	Cl		H
S1-14-149	F		H
S15-13-180	Cl		H
S15-13-181	Cl		H
S15-13-182	Cl		H
S15-13-183	Cl		H

FIG. 2D

Cmpd	X	Y	Z
S15-13-194	Cl		H
S15-13-195	Cl		H
S15-13-196	Cl		H
S15-13-197	Cl		H
S15-13-198	Cl		H

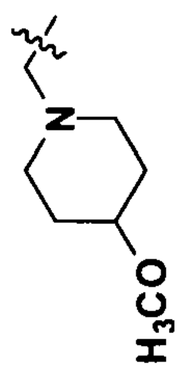
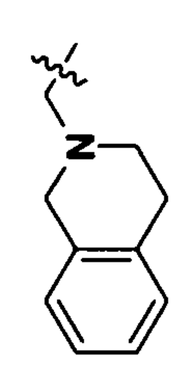
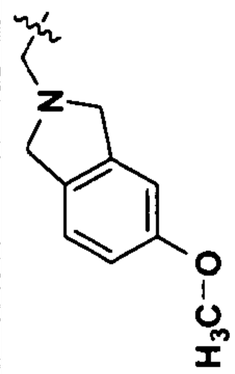
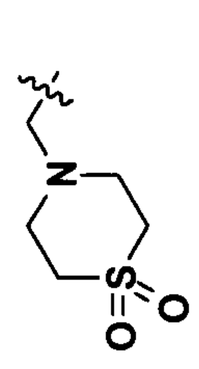
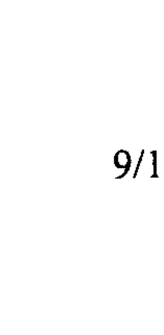
Cmpd	X	Y	Z
S15-13-189	Cl		H
S15-13-190	Cl		H
S15-13-191	Cl		H
S15-13-192	Cl		H
S15-13-193	Cl		H

FIG. 2E

Cmpd	X	Y	Z
S15-13-206	Cl		H
S15-13-207	Cl		H
S15-13-208	Cl		H
S15-13-209	Cl		H
S15-13-210	Cl		H

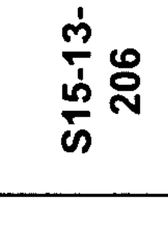
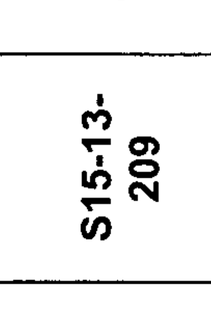
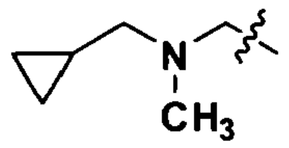
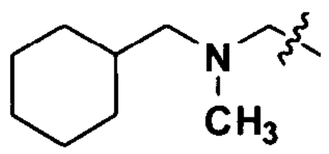
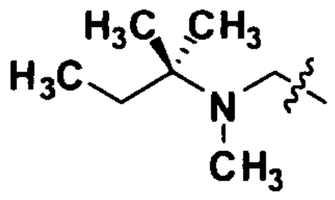
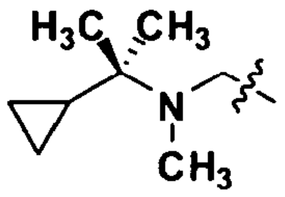
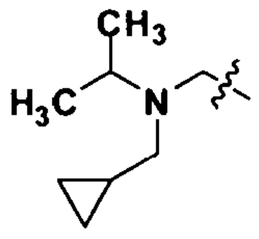
Cmpd	X	Y	Z
S15-13-199	Cl		H
S15-13-200	Cl		H
S15-13-201	Cl		H
S15-13-204	Cl		H
S15-13-205	Cl		H

FIG. 2F

Cmpd	X	Y	Z
S15-13-211	Cl		H
S15-13-212	Cl		H
S15-13-213	Cl		H
S15-13-214	Cl		H
S15-13-215	Cl		H

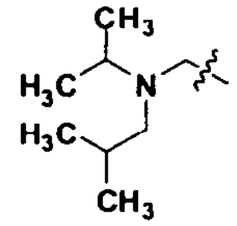
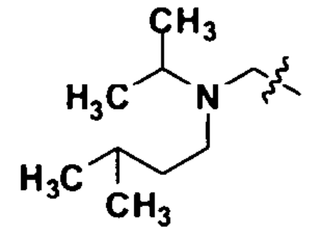
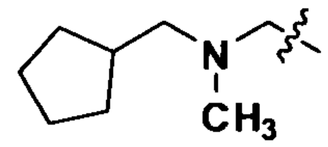
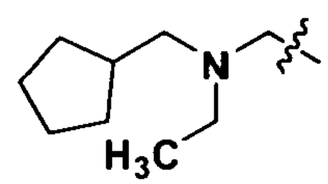
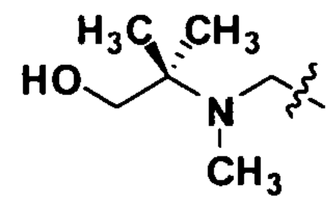
Cmpd	X	Y	Z
S15-13-216	Cl		H
S15-13-217	Cl		H
S15-13-218	Cl		H
S15-13-219	Cl		H
S15-13-220	Cl		H

FIG. 2G

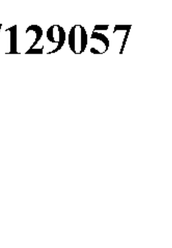
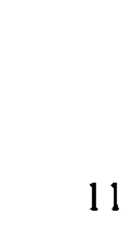
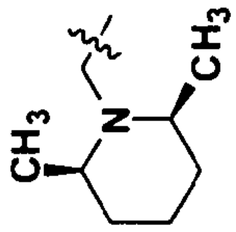
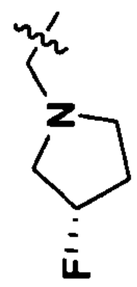
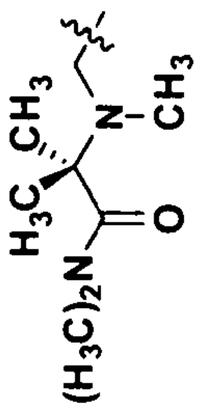
Cmpd	X	Y	Z
S24-9-1	OCH_3		H
S24-9-10	OCH_3		H
S24-9-11	OCH_3		H
S24-9-12	OCH_3		H
S24-9-13	OCH_3		H

FIG. 2H

Cmpd	X	Y	Z
S15-13-221	Cl		H
S15-13-222	Cl		H
S15-13-226	Cl		H
S15-13-227	Cl		H
S15-14-8	H		H

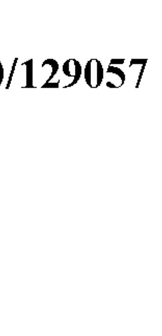
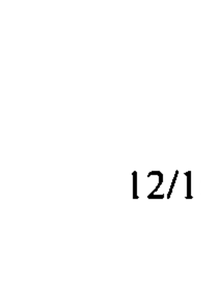
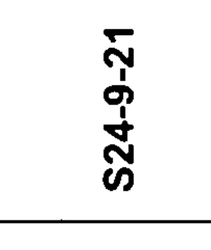
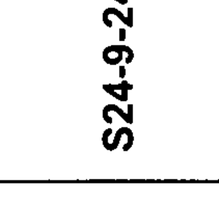
Cmpd	X	Y	Z
S24-9-19	OCH_3		H
S24-9-20	OCH_3		H
S24-9-21	OCH_3		H
S24-9-24	OCH_3		H
S24-9-3	OCH_3		H
S24-9-14	OCH_3		H
S24-9-15	OCH_3		H
S24-9-16	OCH_3		H
S24-9-17	OCH_3		H
S24-9-18	OCH_3		H

FIG. 2I

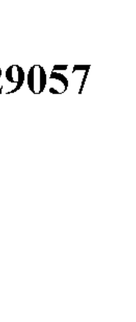
Cmpd	X	Y	Z
S24-9-9	OCH_3		H
S25-11-208	CF_3		H
S27-9-1	F		H
S27-9-2	F		H
S27-9-4	F		H

FIG. 2J

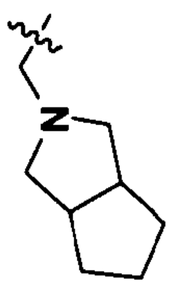
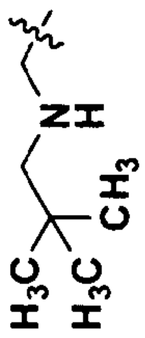
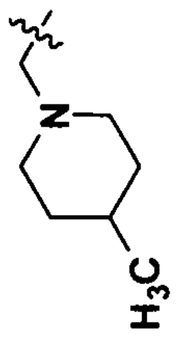
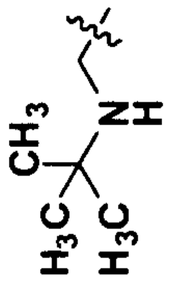
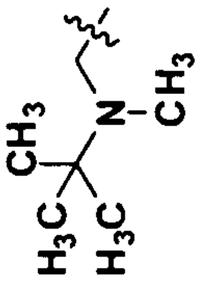
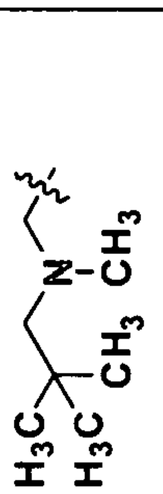
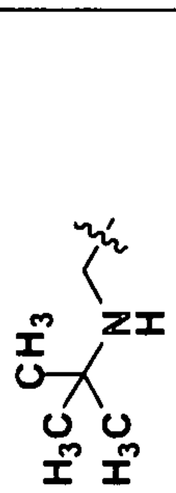
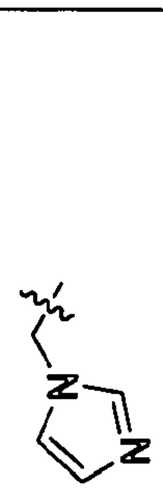
Cmpd	X	Y	Z
S24-9-4	OCH_3		H
S24-9-5	OCH_3		H
S24-9-6	OCH_3		H
S24-9-7	OCH_3		H
S24-9-8	OCH_3		H

FIG. 2K

Cmpd	X	Y	Z
S33-8-1	H		F
S33-8-2	H		F
S33-8-3	H		F
S6-4-2	F		H

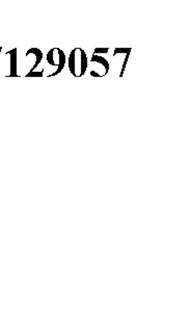
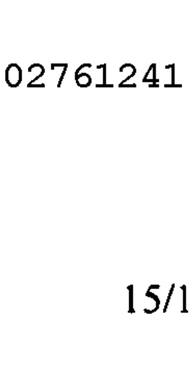
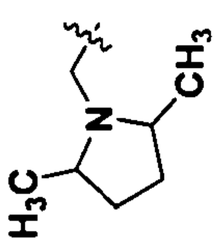
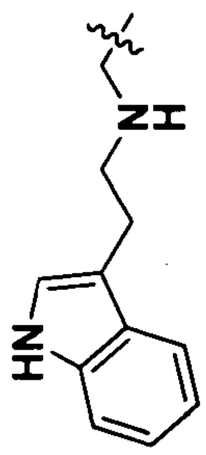
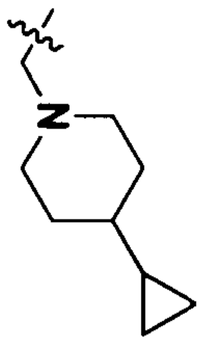
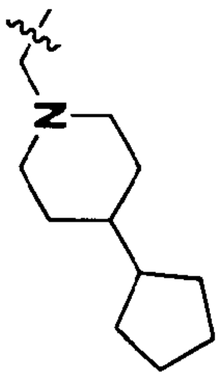
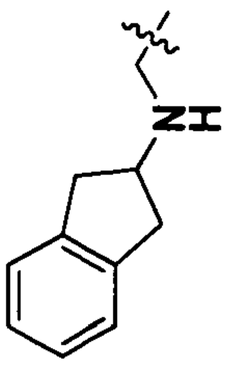
Compound	X	Y	Z
S15-13-117	Cl		H
S15-13-118	Cl		H
S15-13-119	Cl		H
S15-13-120	Cl		H
S15-13-123	Cl		H

FIG. 3A

Compound	X	Y	Z
S1-14-130	F		H
S1-14-133	F		H
S1-14-134	F		H
S1-14-136	F		H
S15-13-116	Cl		H

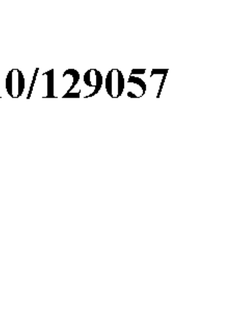
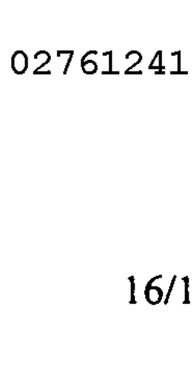
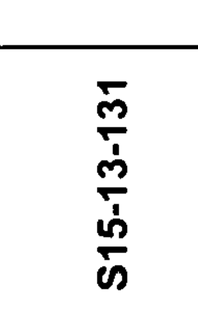
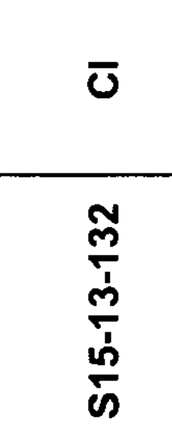
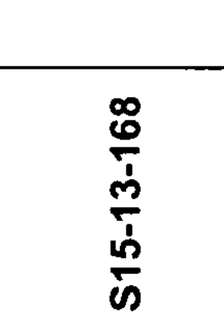
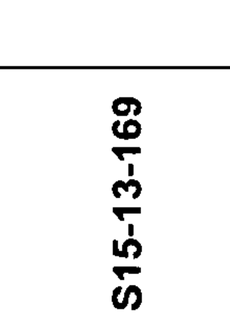
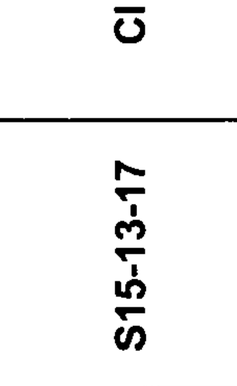
Compound	X	Y	Z
S15-13-131	Cl		H
S15-13-132	Cl		H
S15-13-168	Cl		H
S15-13-169	Cl		H
S15-13-17	Cl		H
S15-13-124	Cl		H
S15-13-125	Cl		H
S15-13-126	Cl		H
S15-13-127	Cl		H
S15-13-128	Cl		H

FIG. 3B

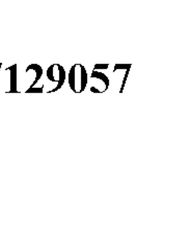
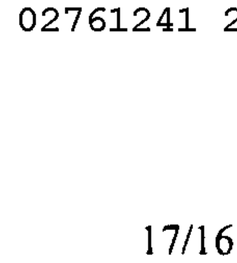
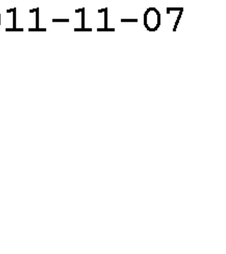
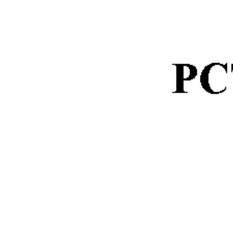
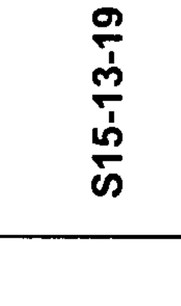
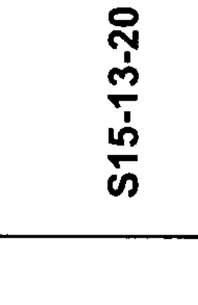
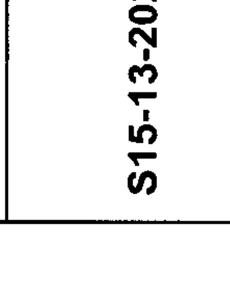
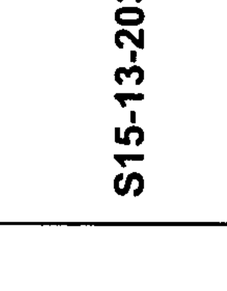
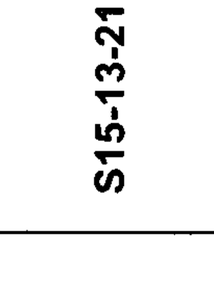
Compound	X	Y	Z
S15-13-19	Cl		H
S15-13-20	Cl		H
S15-13-202	Cl		H
S15-13-203	Cl		H
S15-13-21	Cl		H
S15-13-174	Cl		H
S15-13-175	Cl		H
S15-13-177	Cl		H
S15-13-178	Cl		H
S15-13-18	Cl		H

FIG. 3C

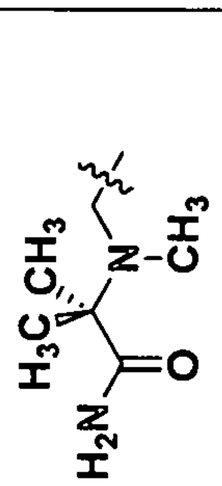
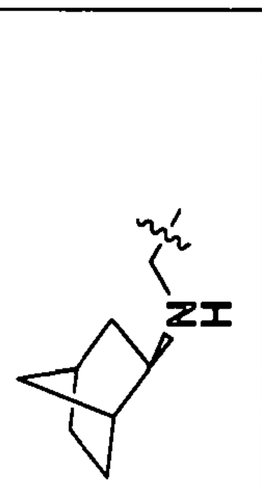
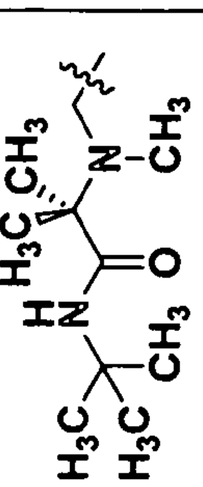
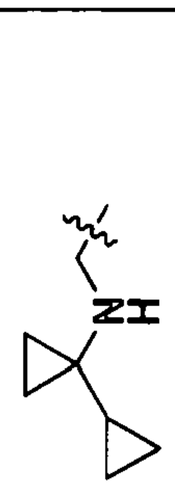
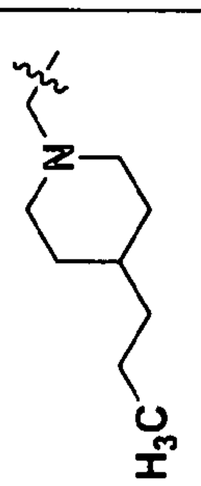
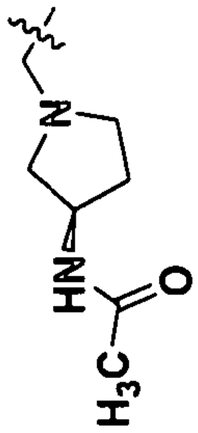
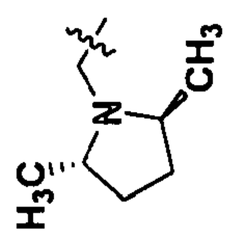
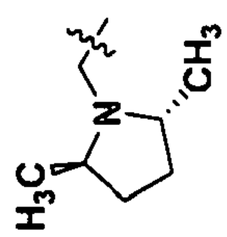
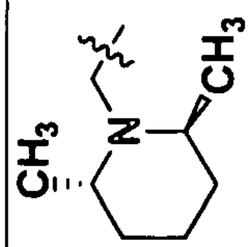
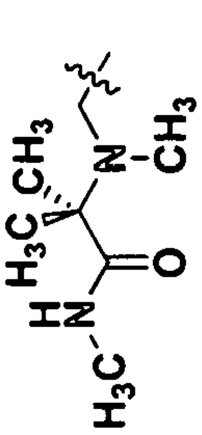
Compound	X	Y	Z
S15-13-229	Cl		H
S15-13-23	Cl		H
S15-13-230	Cl		H
S15-13-24	Cl		H
S15-13-25	Cl		H
S15-13-22	Cl		H
S15-13-223	Cl		H
S15-13-224	Cl		H
S15-13-225	Cl		H
S15-13-228	Cl		H

FIG. 3D

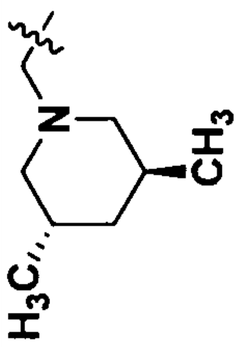
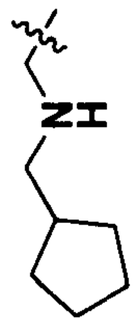
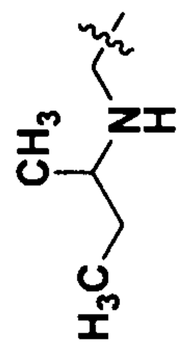
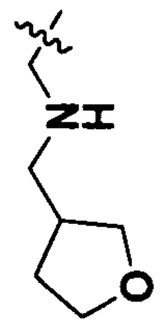
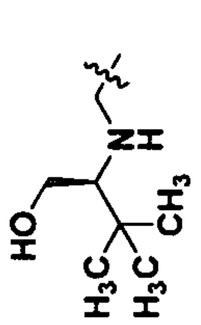
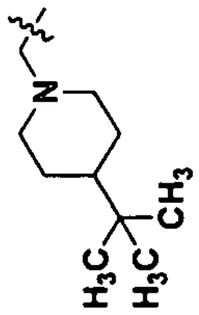
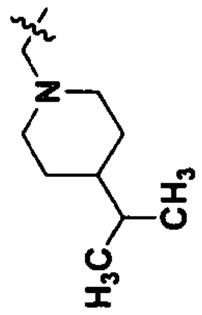
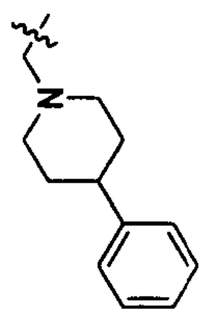
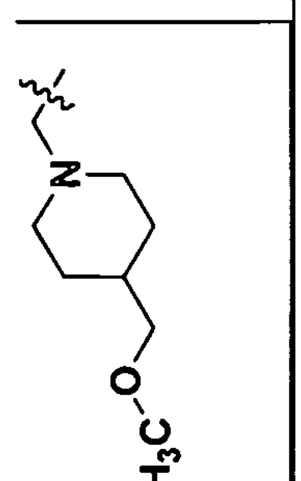
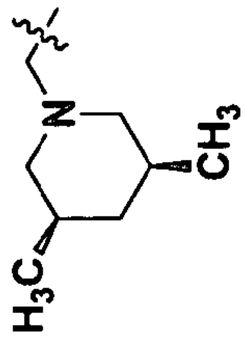
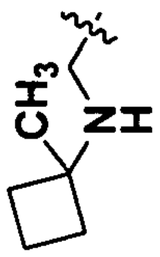
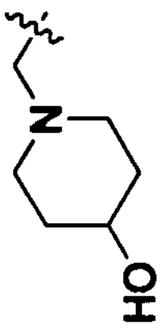
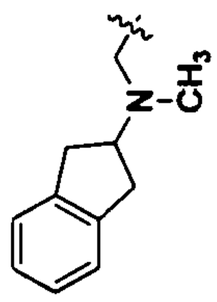
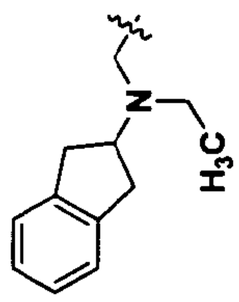
Compound	X	Y	Z
S15-13-32	Cl		H
S15-13-34	Cl		H
S15-13-35	Cl		H
S15-13-36	Cl		H
S15-13-37	Cl		H

FIG. 3E

Compound	X	Y	Z
S15-13-26	Cl		H
S15-13-27	Cl		H
S15-13-28	Cl		H
S15-13-29	Cl		H
S15-13-31	Cl		H

Compound	X	Y	Z
S15-13-43	Cl		H
S15-13-44	Cl		H
S15-13-45	Cl		H
S15-13-46	Cl		H
S15-13-47	Cl		H

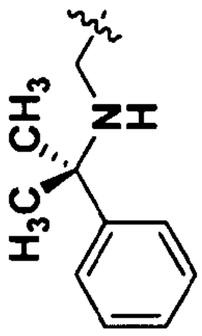
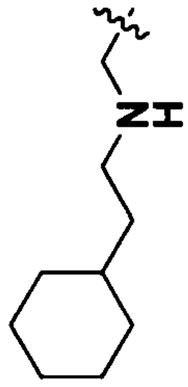
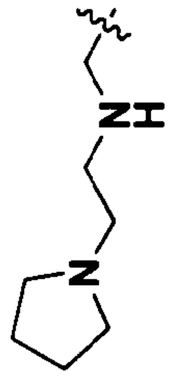
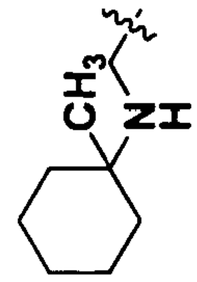
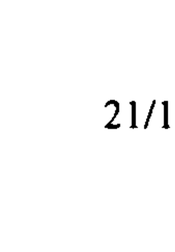
Compound	X	Y	Z
S15-13-38	Cl		H
S15-13-39	Cl		H
S15-13-40	Cl		H
S15-13-41	Cl		H
S15-13-42	Cl		H

FIG. 3F

Compound	X	Y	Z
S15-13-87	Cl		H
S15-14-6	H		H
S16-10-101	$N(CH_3)_2$		H
S16-10-102	$N(CH_3)_2$		H
S16-10-106	$N(CH_3)_2$		H

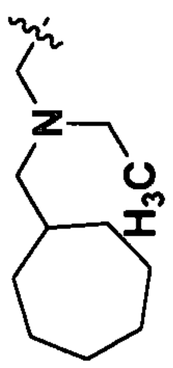
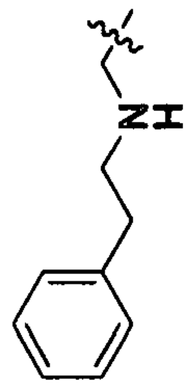
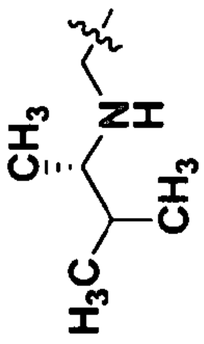
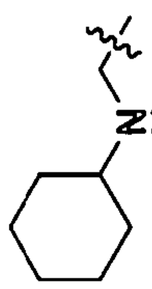
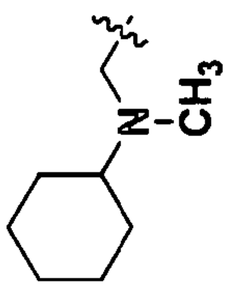
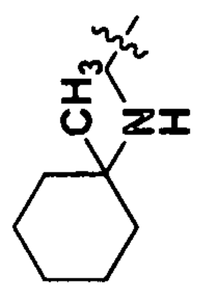
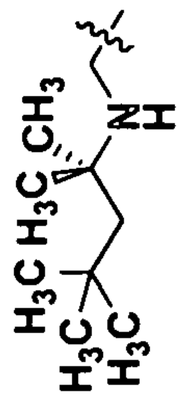
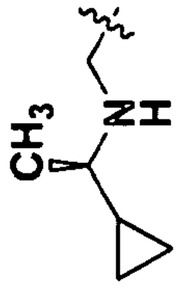
Compound	X	Y	Z
S15-13-48	Cl		H
S15-13-81	Cl		H
S15-13-82	Cl		H
S15-13-83	Cl		H
S15-13-84	Cl		H

FIG. 3G

Compound	X	Y	Z
S16-10-120	$N(CH_3)_2$		H
S16-10-121	$N(CH_3)_2$		H
S16-10-123	$N(CH_3)_2$		H
S16-10-126	$N(CH_3)_2$		H
S16-10-129	$N(CH_3)_2$		H

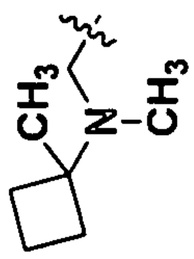
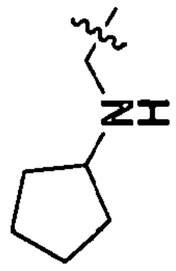
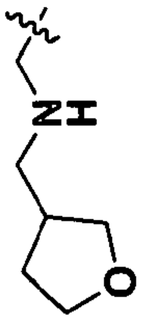
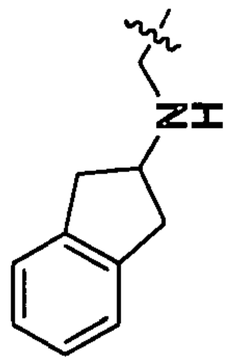
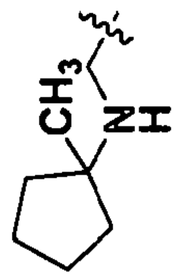
Compound	X	Y	Z
S16-10-107	$N(CH_3)_2$		H
S16-10-110	$N(CH_3)_2$		H
S16-10-116	$N(CH_3)_2$		H
S16-10-117	$N(CH_3)_2$		H
S16-10-119	$N(CH_3)_2$		H

FIG. 3H

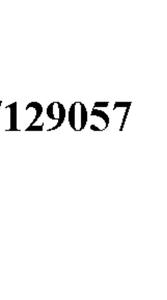
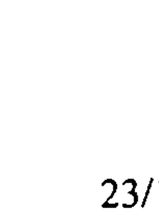
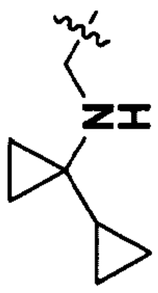
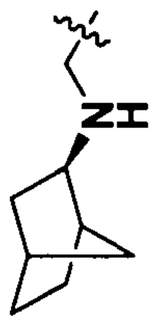
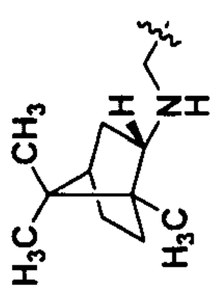
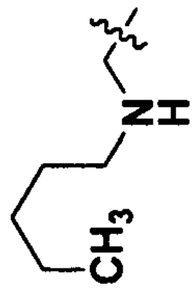
Compound	X	Y	Z
S16-10-143	$N(CH_3)_2$		H
S16-10-144	$N(CH_3)_2$		H
S16-10-145	$N(CH_3)_2$		H
S16-10-146	$N(CH_3)_2$		H
S16-10-147	$N(CH_3)_2$		H

FIG. 31

Compound	X	Y	Z
S16-10-132	$N(CH_3)_2$		H
S16-10-135	$N(CH_3)_2$		H
S16-10-136	$N(CH_3)_2$		H
S16-10-138	$N(CH_3)_2$		H
S16-10-139	$N(CH_3)_2$		H

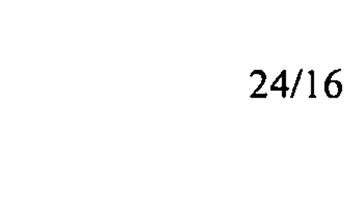
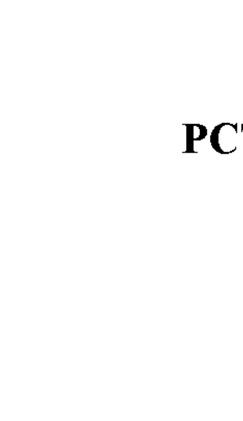
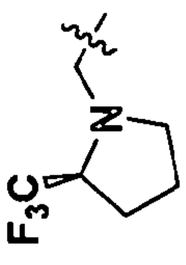
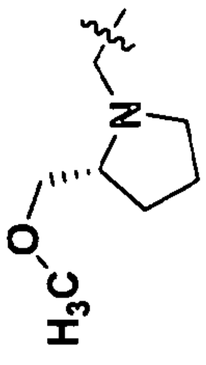
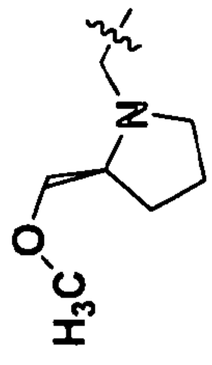
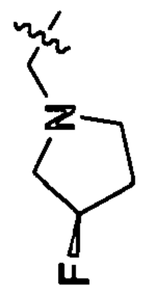
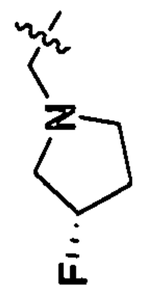
Compound	X	Y	Z
S16-10-153	$N(CH_3)_2$		H
S16-10-154	$N(CH_3)_2$		H
S16-10-155	$N(CH_3)_2$		H
S16-10-156	$N(CH_3)_2$		H
S16-10-157	$N(CH_3)_2$		H

FIG. 3J

Compound	X	Y	Z
S16-10-148	$N(CH_3)_2$		H
S16-10-149	$N(CH_3)_2$		H
S16-10-150	$N(CH_3)_2$		H
S16-10-151	$N(CH_3)_2$		H
S16-10-152	$N(CH_3)_2$		H

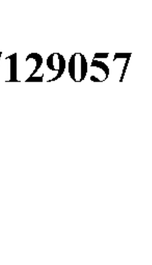
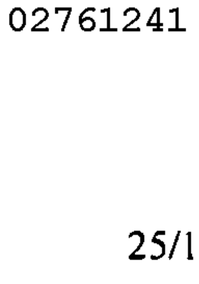
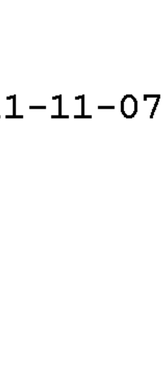
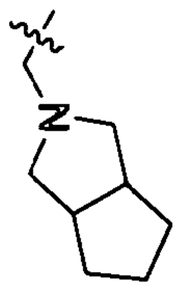
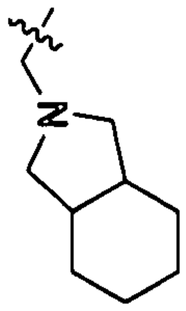
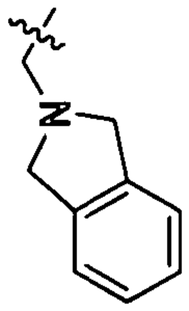
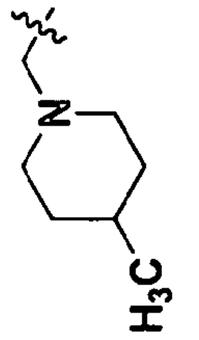
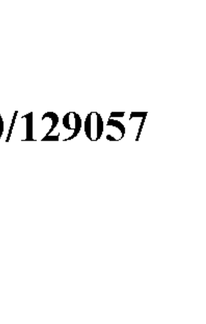
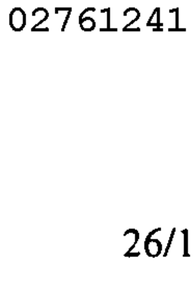
Compound	X	Y	Z
S16-10-163	$N(CH_3)_2$		H
S16-10-164	$N(CH_3)_2$		H
S16-10-165	$N(CH_3)_2$		H
S16-10-166	$N(CH_3)_2$		H
S16-10-167	$N(CH_3)_2$		H
S16-10-158	$N(CH_3)_2$		H
S16-10-159	$N(CH_3)_2$		H
S16-10-160	$N(CH_3)_2$		H
S16-10-161	$N(CH_3)_2$		H
S16-10-162	$N(CH_3)_2$		H

FIG. 3K

Compound	X	Y	Z
S16-10-173	$N(CH_3)_2$		H
S16-10-174	$N(CH_3)_2$		H
S16-10-175	$N(CH_3)_2$		H
S16-10-176	$N(CH_3)_2$		H
S16-10-177	$N(CH_3)_2$		H

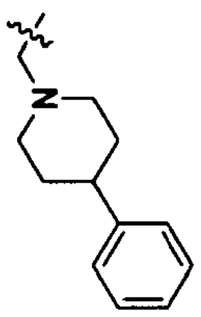
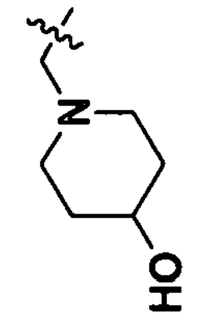
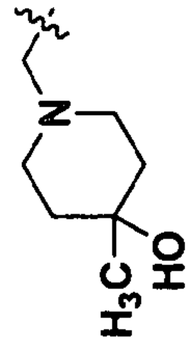
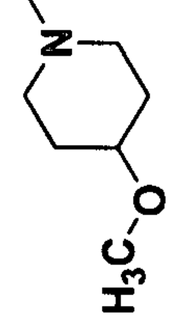
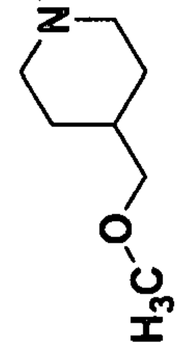
Compound	X	Y	Z
S16-10-168	$N(CH_3)_2$		H
S16-10-169	$N(CH_3)_2$		H
S16-10-170	$N(CH_3)_2$		H
S16-10-171	$N(CH_3)_2$		H
S16-10-172	$N(CH_3)_2$		H

FIG. 3L

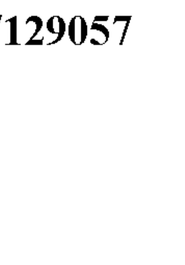
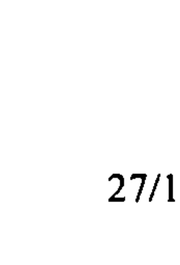
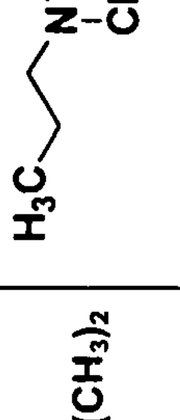
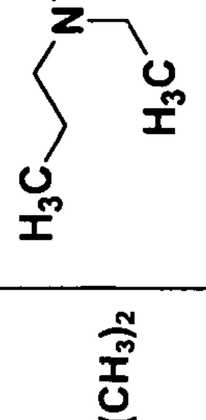
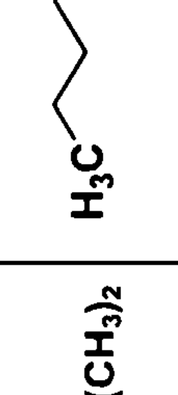
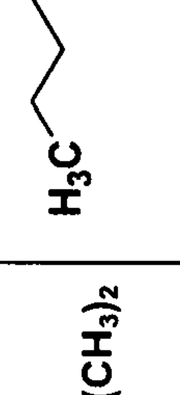
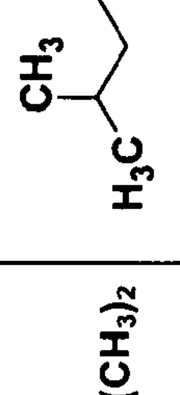
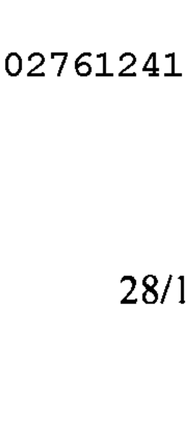
Compound	X	Y	Z
S16-10-37	$N(CH_3)_2$		H
S16-10-38	$N(CH_3)_2$		H
S16-10-39	$N(CH_3)_2$		H
S16-10-40	$N(CH_3)_2$		H
S16-10-42	$N(CH_3)_2$		H
S16-10-178	$N(CH_3)_2$		H
S16-10-179	$N(CH_3)_2$		H
S16-10-28	$N(CH_3)_2$		H
S16-10-33	$N(CH_3)_2$		H
S16-10-36	$N(CH_3)_2$		H

FIG. 3M

Compound	X	Y	Z
S16-10-52	$N(CH_3)_2$		H
S16-10-53	$N(CH_3)_2$		H
S16-10-54	$N(CH_3)_2$		H
S16-10-55	$N(CH_3)_2$		H
S16-10-61	$N(CH_3)_2$		H

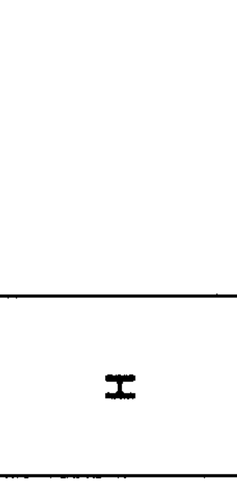
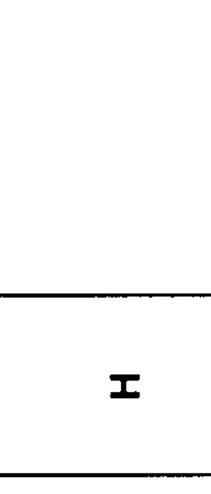
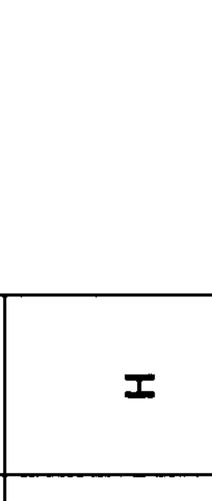
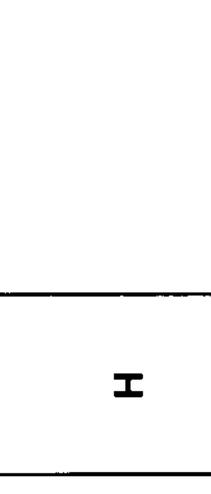
Compound	X	Y	Z
S16-10-43	$N(CH_3)_2$		H
S16-10-45	$N(CH_3)_2$		H
S16-10-46	$N(CH_3)_2$		H
S16-10-48	$N(CH_3)_2$		H
S16-10-49	$N(CH_3)_2$		H

FIG. 3N

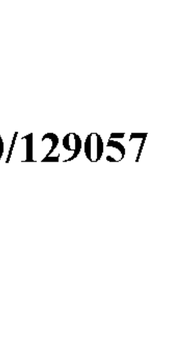
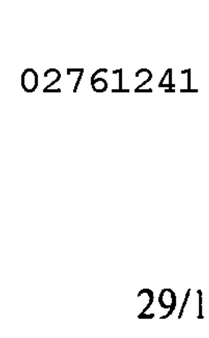
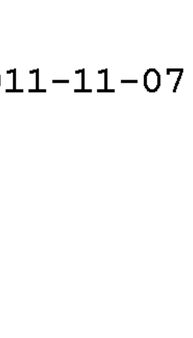
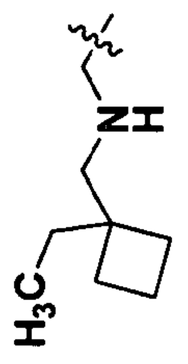
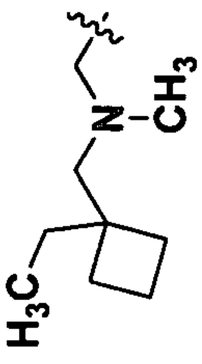
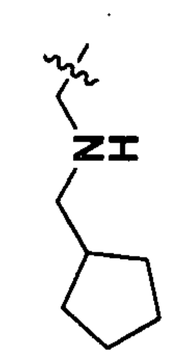
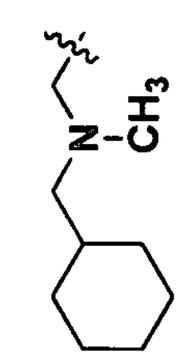
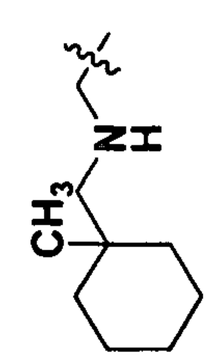
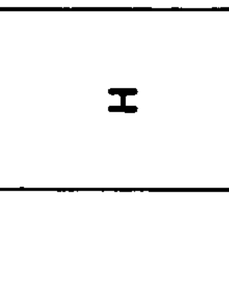
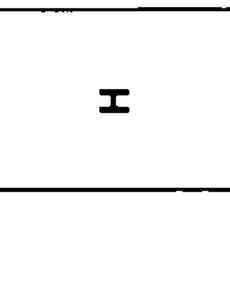
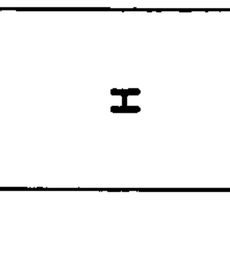
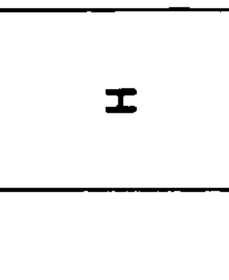
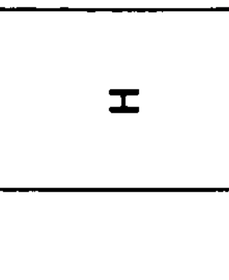
Compound	X	Y	Z
S16-10-72	$N(CH_3)_2$		H
S16-10-73	$N(CH_3)_2$		H
S16-10-74	$N(CH_3)_2$		H
S16-10-75	$N(CH_3)_2$		H
S16-10-79	$N(CH_3)_2$		H

FIG. 30

Compound	X	Y	Z
S16-10-64	$N(CH_3)_2$		H
S16-10-65	$N(CH_3)_2$		H
S16-10-67	$N(CH_3)_2$		H
S16-10-69	$N(CH_3)_2$		H
S16-10-71	$N(CH_3)_2$		H

Compound	X	Y	Z
S16-10-92	$N(CH_3)_2$		H
S16-10-95	OCH_3		H
S2-4-69	F		H
S24-9-125	OCH_3		H
S24-9-126	OCH_3		H

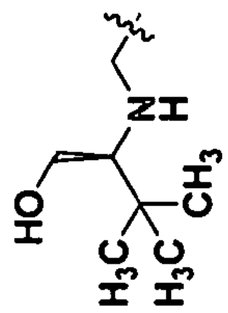
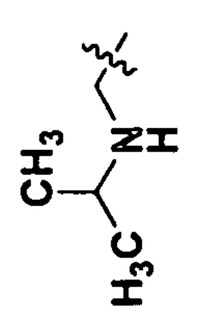
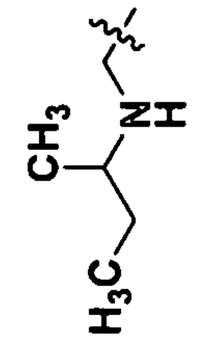
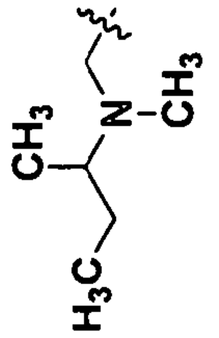
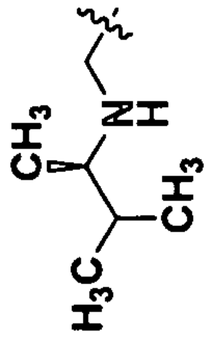
Compound	X	Y	Z
S16-10-83	$N(CH_3)_2$		H
S16-10-86	$N(CH_3)_2$		H
S16-10-88	$N(CH_3)_2$		H
S16-10-89	$N(CH_3)_2$		H
S16-10-91	$N(CH_3)_2$		H

FIG. 3P

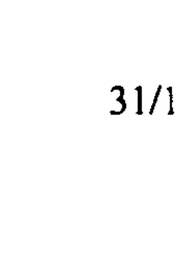
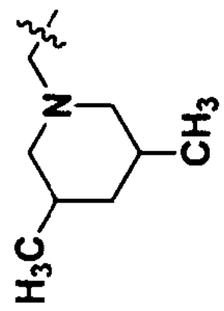
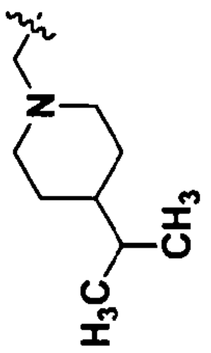
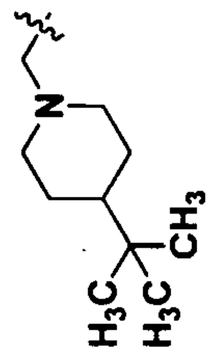
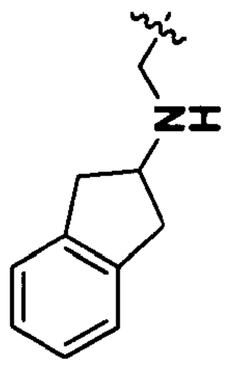
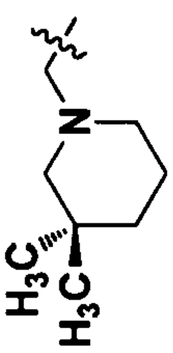
Compound	X	Y	Z
S24-9-132	OCH_3		H
S24-9-180	OCH_3		H
S24-9-2	OCH_3		H
S24-9-22	OCH_3		H
S24-9-23	OCH_3		H

FIG. 3Q

Compound	X	Y	Z
S24-9-127	OCH_3		H
S24-9-128	OCH_3		H
S24-9-129	OCH_3		H
S24-9-130	OCH_3		H
S24-9-131	OCH_3		H

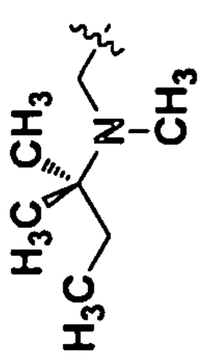
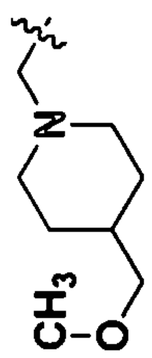
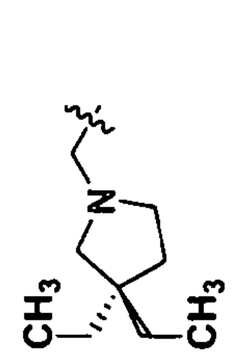
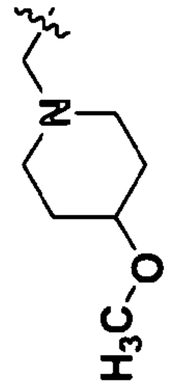
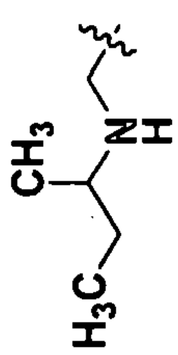
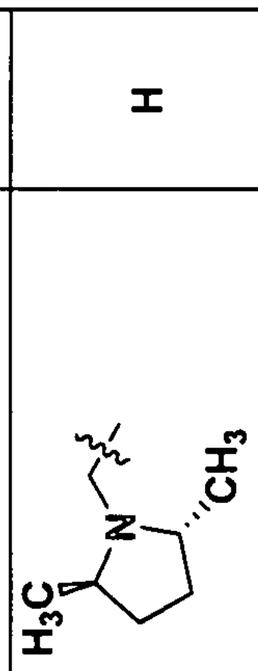
Compound	X	Y	Z
S24-9-31	OCH_3		H
S24-9-32	OCH_3		H
S24-9-80	OCH_3		H
S24-9-81	OCH_3		H
S24-9-82	OCH_3		H
S24-9-25	OCH_3		H
S24-9-26	OCH_3		H
S24-9-27	OCH_3		H
S24-9-28	OCH_3		H
S24-9-30	OCH_3		H

FIG. 3R

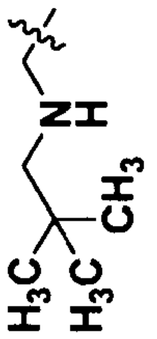
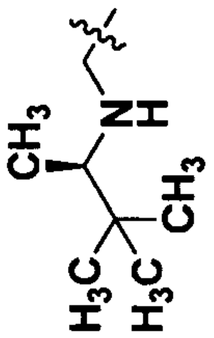
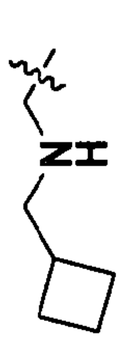
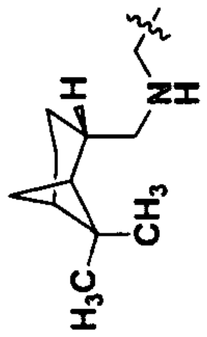
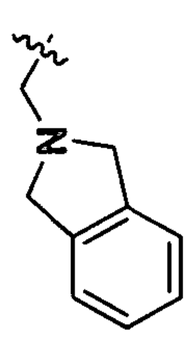
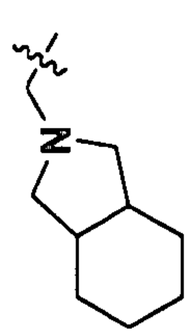
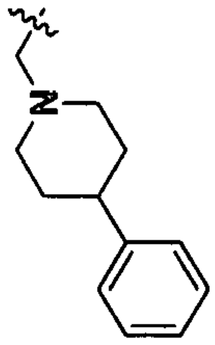
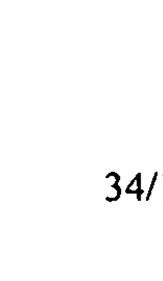
Compound	X	Y	Z
S25-11-10	CF_3		H
S25-11-11	CF_3		H
S25-11-12	CF_3		H
S25-11-13	CF_3		H
S25-11-14	CF_3		H

FIG. 3S

Compound	X	Y	Z
S24-9-83	OCH_3		H
S24-9-84	OCH_3		H
S24-9-92	OCH_3		H
S24-9-93	CF_3		H
S25-11-1	CF_3		H

Compound	X	Y	Z
S25-11-168	CF_3		H
S25-11-169	CF_3		H
S25-11-17	CF_3		H
S25-11-170	CF_3		H
S25-11-171	CF_3		H

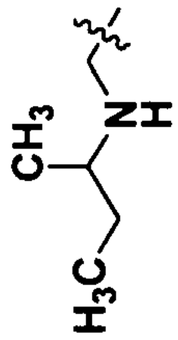
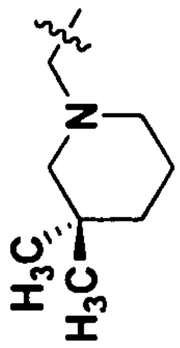
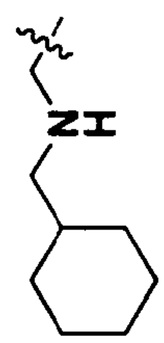
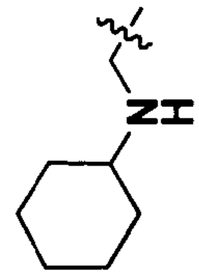
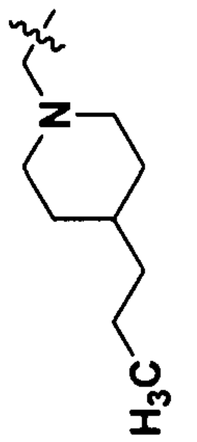
Compound	X	Y	Z
S25-11-15	CF_3		H
S25-11-16	CF_3		H
S25-11-164	CF_3		H
S25-11-165	CF_3		H
S25-11-166	CF_3		H

FIG. 3T

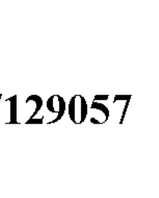
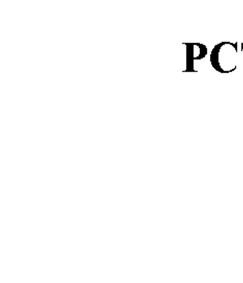
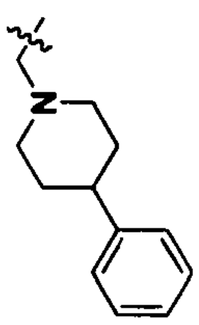
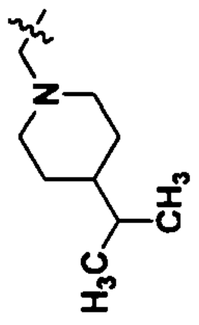
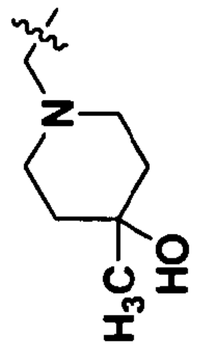
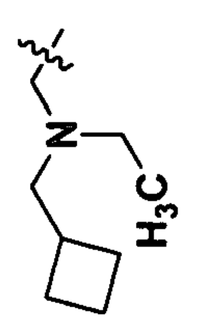
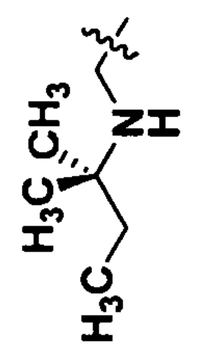
Compound	X	Y	Z
S25-11-177	CF_3		H
S25-11-178	CF_3		H
S25-11-179	CF_3		H
S25-11-18	CF_3		H
S25-11-180	CF_3		H

FIG. 3U

Compound	X	Y	Z
S25-11-172	CF_3		H
S25-11-173	CF_3		H
S25-11-174	CF_3		H
S25-11-175	CF_3		H
S25-11-176	CF_3		H

Compound	X	Y	Z
S25-11-186	CF_3		H
S25-11-187	CF_3		H
S25-11-188	CF_3		H
S25-11-189	CF_3		H
S25-11-19	CF_3		H

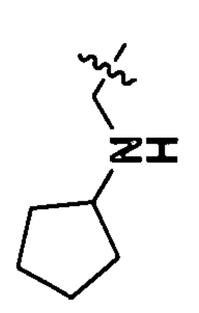
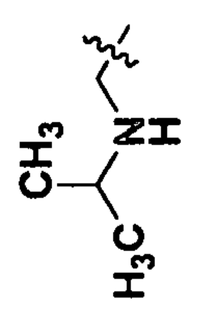
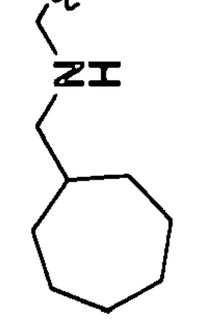
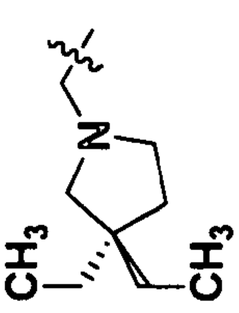
Compound	X	Y	Z
S25-11-181	CF_3		H
S25-11-182	CF_3		H
S25-11-183	CF_3		H
S25-11-184	CF_3		H
S25-11-185	CF_3		H

FIG. 3V

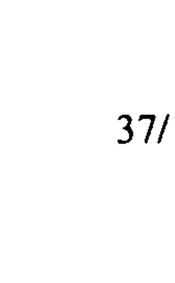
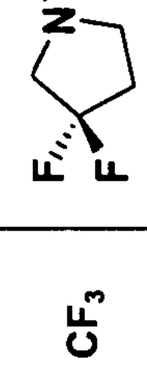
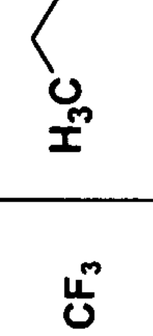
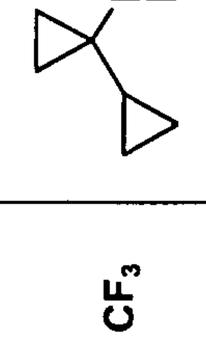
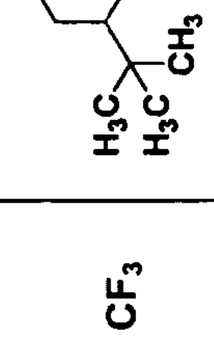
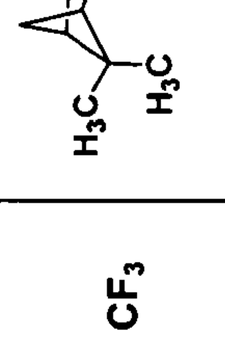
Compound	X	Y	Z
S25-11-199	CF_3		H
S25-11-2	CF_3		H
S25-11-20	CF_3		H
S25-11-200	CF_3		H
S25-11-206	CF_3		H
S25-11-194	CF_3		H
S25-11-195	CF_3		H
S25-11-196	CF_3		H
S25-11-197	CF_3		H
S25-11-198	CF_3		H

FIG. 3W

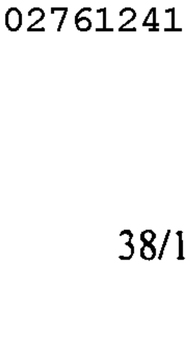
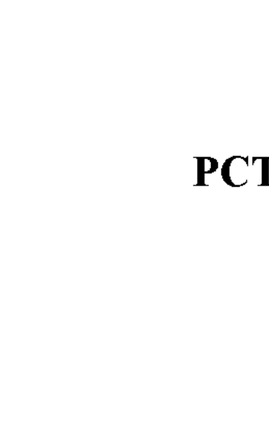
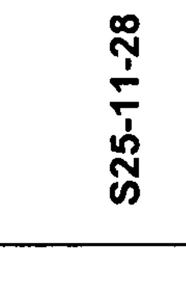
Compound	X	Y	Z
S25-11-24	CF_3		H
S25-11-25	CF_3		H
S25-11-26	CF_3		H
S25-11-27	CF_3		H
S25-11-28	CF_3		H
S25-11-207	CF_3		H
S25-11-208	CF_3		H
S25-11-21	CF_3		H
S25-11-22	CF_3		H
S25-11-23	CF_3		H

FIG. 3X

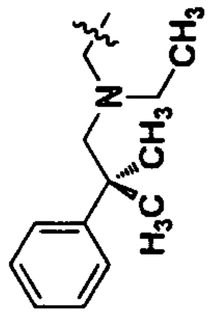
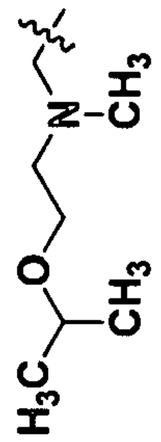
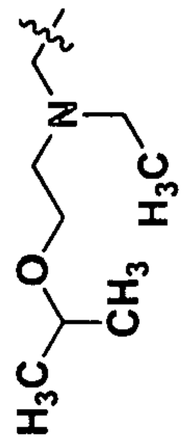
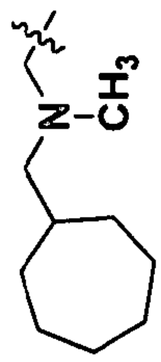
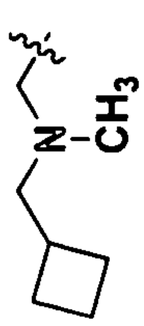
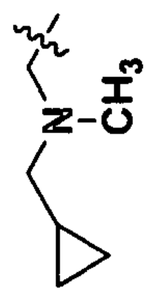
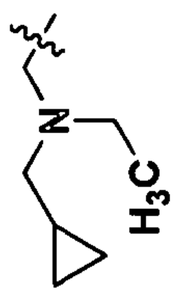
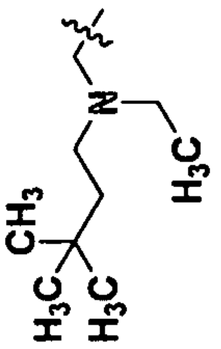
Compound	X	Y	Z
S25-11-33	CF_3		H
S25-11-34	CF_3		H
S25-11-35	CF_3		H
S25-11-36	CF_3		H
S25-11-37	CF_3		H
S25-11-29	CF_3		H
S25-11-3	CF_3		H
S25-11-30	CF_3		H
S25-11-31	CF_3		H
S25-11-32	CF_3		H

FIG. 3Y

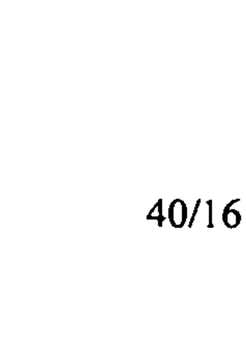
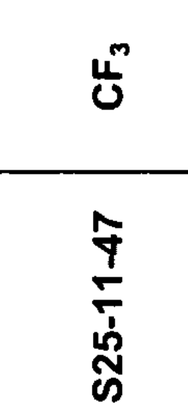
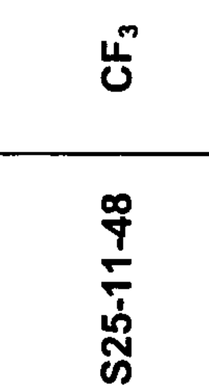
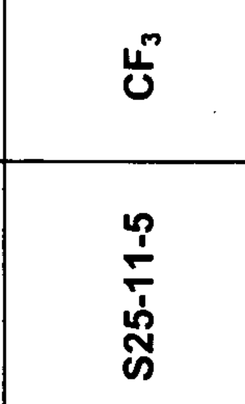
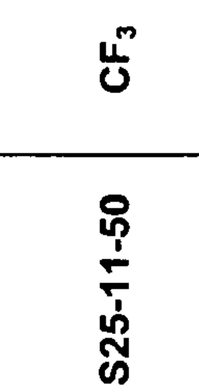
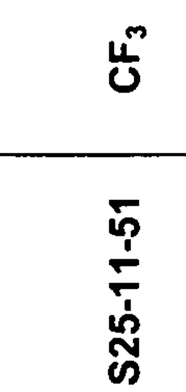
Compound	X	Y	Z
S25-11-47	CF_3		H
S25-11-48	CF_3		H
S25-11-5	CF_3		H
S25-11-50	CF_3		H
S25-11-51	CF_3		H
S25-11-4	CF_3		H
S25-11-43	CF_3		H
S25-11-44	CF_3		H
S25-11-45	CF_3		H
S25-11-46	CF_3		H

FIG. 3Z

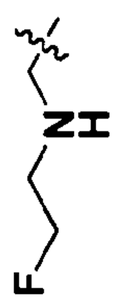
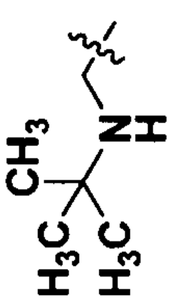
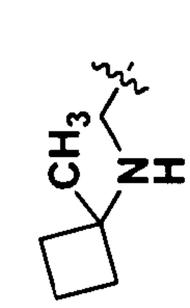
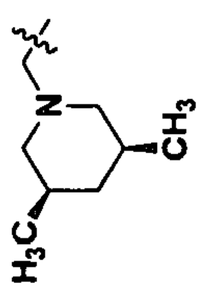
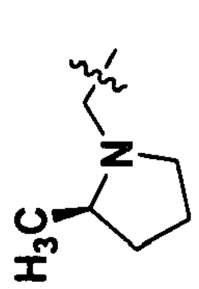
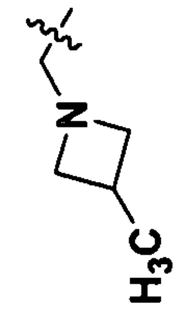
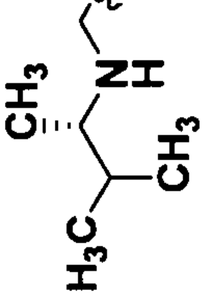
Compound	X	Y	Z
S25-11-57	CF_3		H
S25-11-58	CF_3		H
S25-11-59	CF_3		H
S25-11-6	CF_3		H
S25-11-60	CF_3		H

FIG. 3AA

Compound	X	Y	Z
S25-11-52	CF_3		H
S25-11-53	CF_3		H
S25-11-54	CF_3		H
S25-11-55	CF_3		H
S25-11-56	CF_3		H

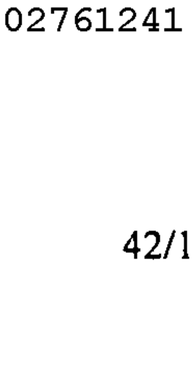
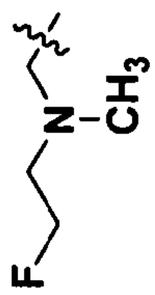
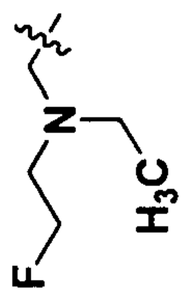
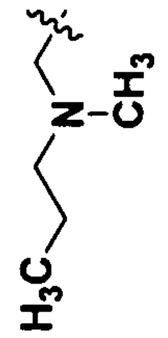
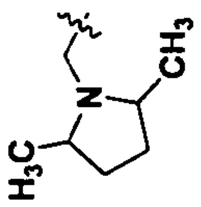
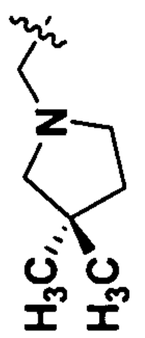
Compound	X	Y	Z
S25-11-66	CF_3		H
S25-11-67	CF_3		H
S25-11-68	CF_3		H
S25-11-69	CF_3		H
S25-11-7	CF_3		H

FIG. 3BB

Compound	X	Y	Z
S25-11-61	CF_3		H
S25-11-62	CF_3		H
S25-11-63	CF_3		H
S25-11-64	CF_3		H
S25-11-65	CF_3		H

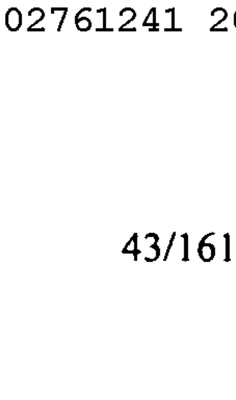
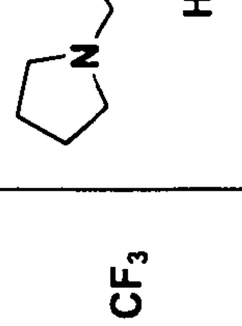
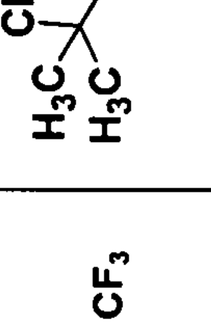
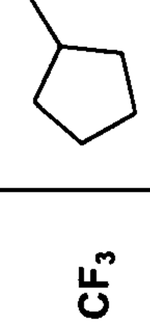
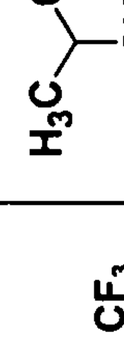
Compound	X	Y	Z
S25-11-75	CF_3		H
S25-11-76	CF_3		H
S25-11-77	CF_3		H
S25-11-78	CF_3		H
S25-11-8	CF_3		H
S25-11-70	CF_3		H
S25-11-71	CF_3		H
S25-11-72	CF_3		H
S25-11-73	CF_3		H
S25-11-74	CF_3		H

FIG. 3CC

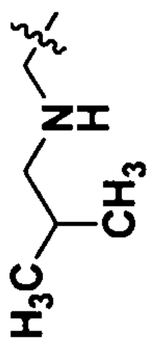
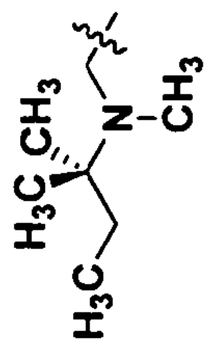
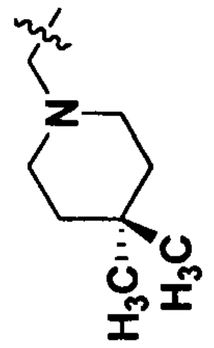
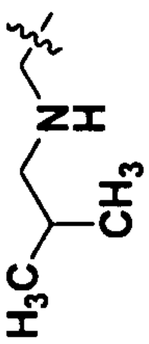
Compound	X	Y	Z
S29-2-1	F		NH_2
S29-2-2	F		NH_2
S29-2-3	Cl		NH_2
S29-2-4	F		$NHCH_3$
S30-4-1	F		$NHCH_3$

FIG. 3DD

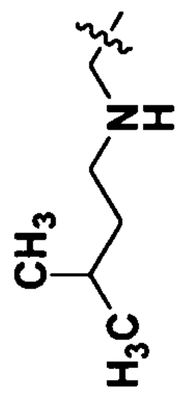
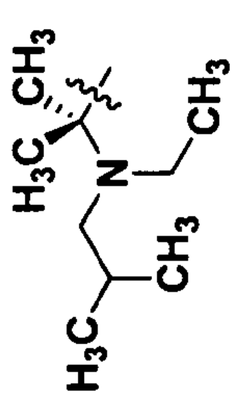
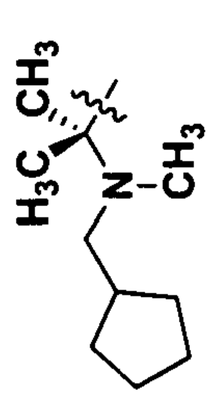
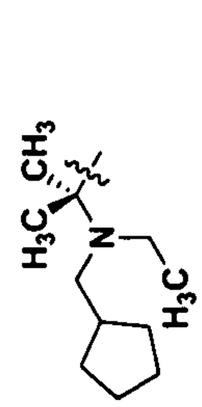
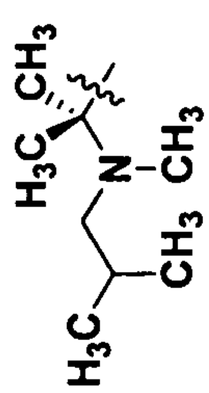
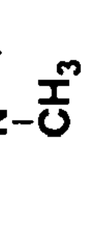
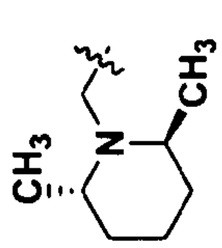
Compound	X	Y	Z
S25-11-9	F		H
S27-9-3	F		H
S27-9-5	F		H
S27-9-6	Cl		H
S27-9-7	F		NH_2

FIG. 3E

Compound	X	Y	Z
S30-4-2	F		H
S6-4-3	Cl		H

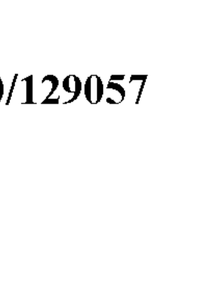
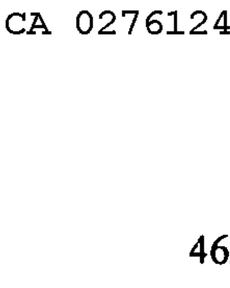
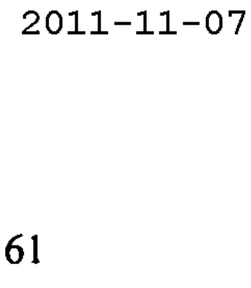
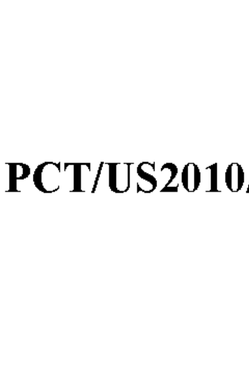
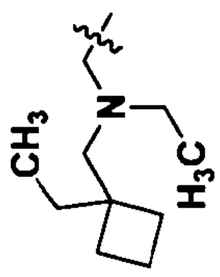
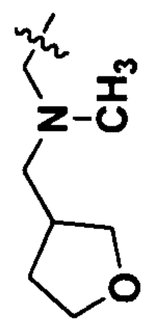
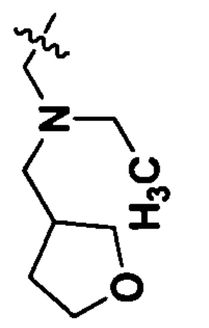
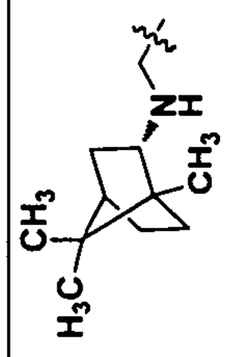
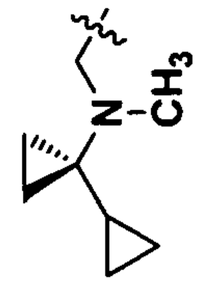
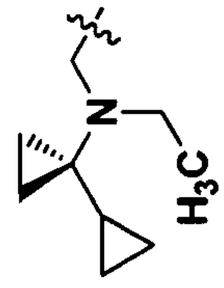
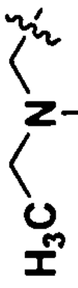
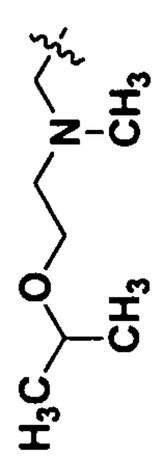
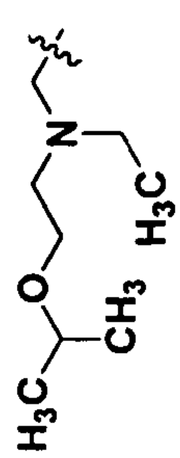
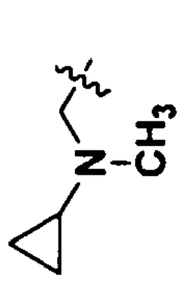
Cmpd	X	Y	Z
S15-13-136	Cl		H
S15-13-142	Cl		H
S15-13-143	Cl		H
S15-13-144	Cl		H
S15-13-145	Cl		H
S15-13-146	Cl		H

FIG. 4A

Cmpd	X	Y	Z
S15-13-121	Cl		H
S15-13-129	Cl		H
S15-13-130	Cl		H
S15-13-133	Cl		H
S15-13-134	Cl		H
S15-13-135	Cl		H

Cmpd	X	Y	Z
S15-13-152	Cl		H
S15-13-153	Cl		H
S15-13-154	Cl		H
S15-13-155	Cl		H
S15-13-156	Cl		H

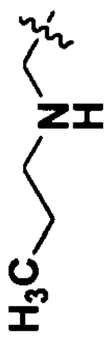
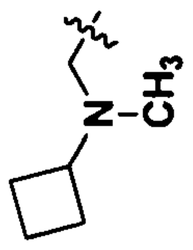
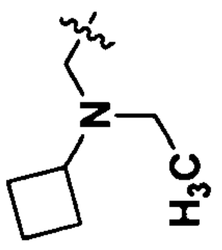
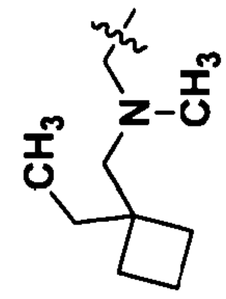
Cmpd	X	Y	Z
S15-13-147	Cl		H
S15-13-148	Cl		H
S15-13-149	Cl		H
S15-13-150	Cl		H
S15-13-151	Cl		H

FIG. 4B

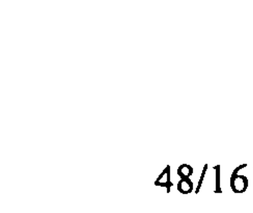
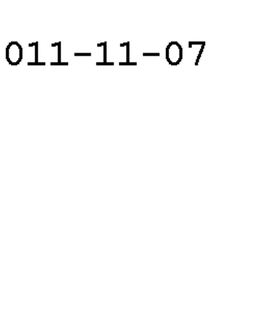
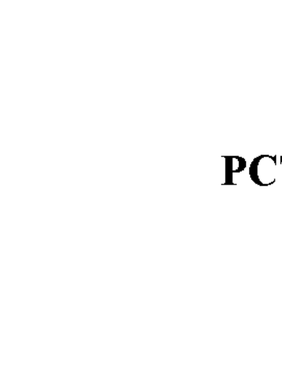
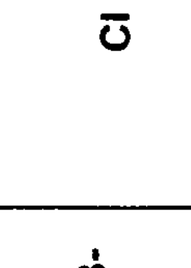
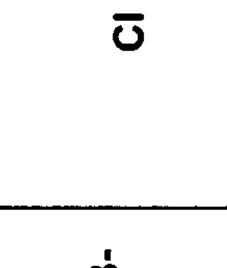
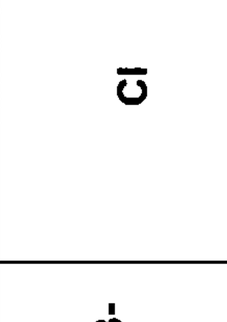
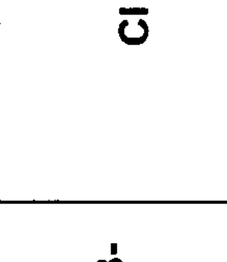
Cmpd	X	Y	Z
S15-13-170	Cl		H
S15-13-171	Cl		H
S15-13-172	Cl		H
S15-13-173	Cl		H
S15-13-176	Cl		H
S15-13-157	Cl		H
S15-13-158	Cl		H
S15-13-159	Cl		H
S15-13-160	Cl		H
S15-13-167	Cl		H

FIG. 4C

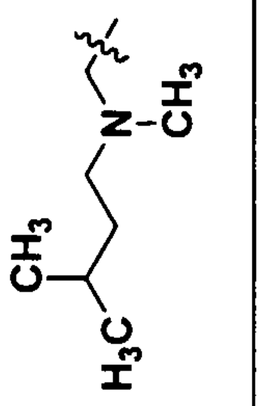
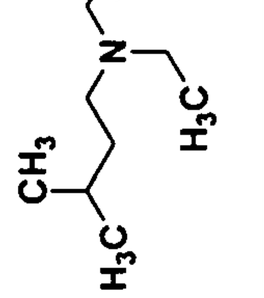
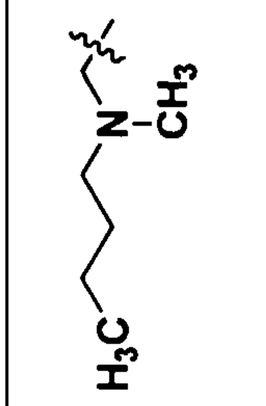
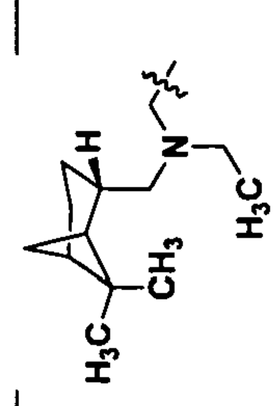
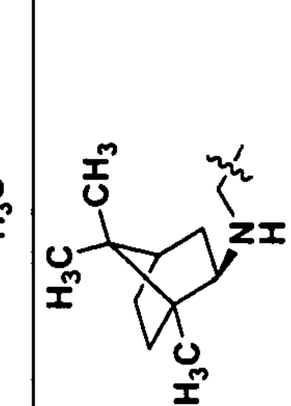
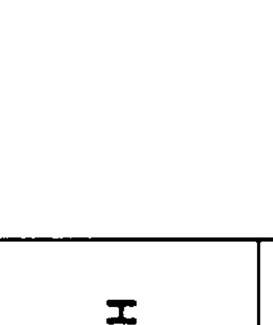
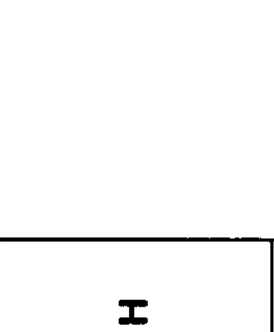
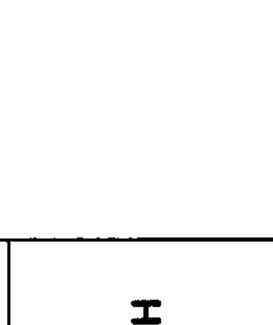
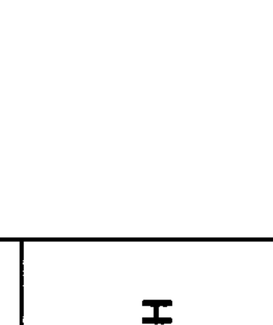
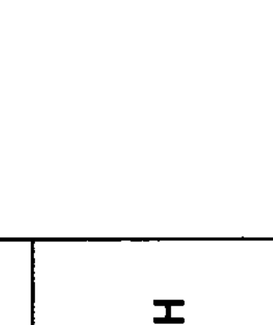
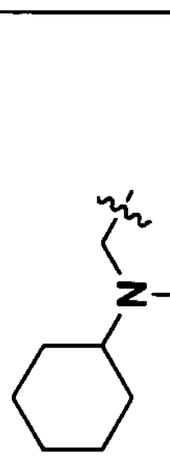
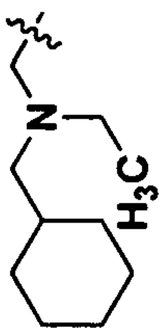
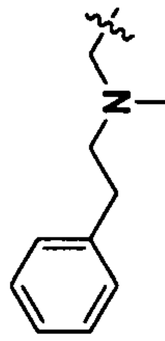
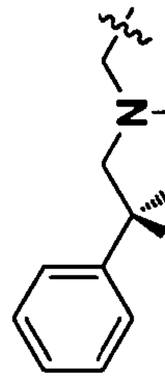
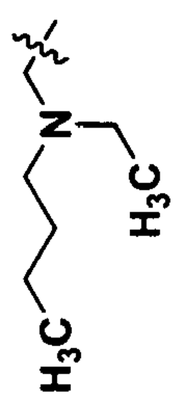
Cmpd	X	Y	Z
S15-13-50	Cl		H
S15-13-51	Cl		H
S15-13-52	Cl		H
S15-13-53	Cl		H
S15-13-54	Cl		H

FIG. 4D

Cmpd	X	Y	Z
S15-13-179	Cl		H
S15-13-227	OCH_3		H
S15-13-30	Cl		H
S15-13-33	Cl		H
S15-13-49	Cl		H

Cmpd	X	Y	Z
S15-13-60	Cl		H
S15-13-61	Cl		H
S15-13-62	Cl		H
S15-13-63	Cl		H
S15-13-78	Cl		H

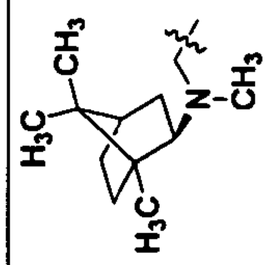
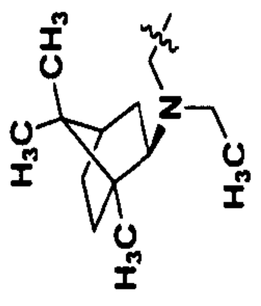
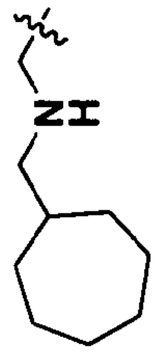
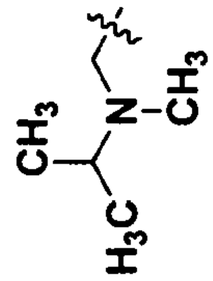
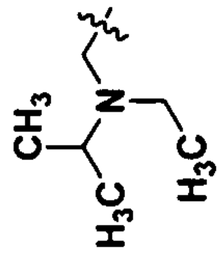
Cmpd	X	Y	Z
S15-13-55	Cl		H
S15-13-56	Cl		H
S15-13-57	Cl		H
S15-13-58	Cl		H
S15-13-59	Cl		H

FIG. 4E

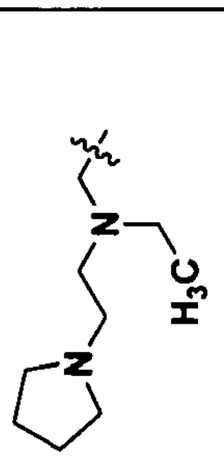
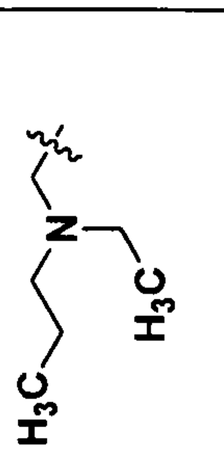
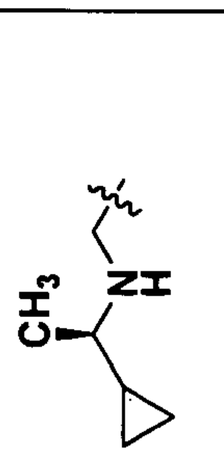
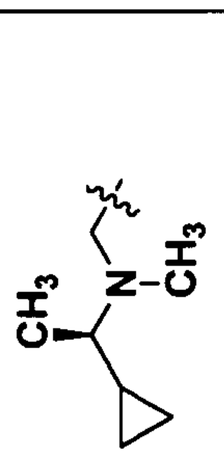
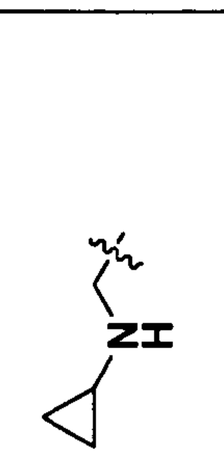
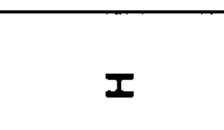
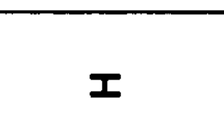
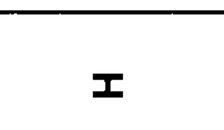
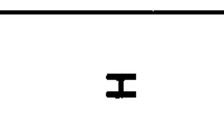
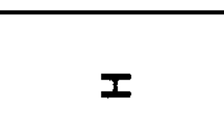
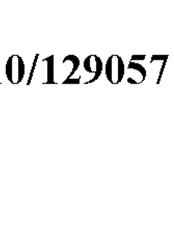
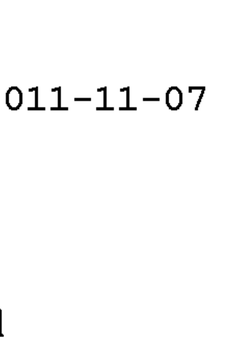
Cmpd	X	Y	Z
S15-13-92	Cl		H
S15-13-93	Cl		H
S15-13-94	Cl		H
S15-13-95	Cl		H
S15-13-96	Cl		H
S15-13-85	Cl		H
S15-13-86	Cl		H
S15-13-89	Cl		H
S15-13-90	Cl		H
S15-13-91	Cl		H

FIG. 4F

Cmpd	X	Y	Z
S16-10-131	$N(CH_3)_2$		H
S16-10-137	$N(CH_3)_2$		H
S16-10-31	$N(CH_3)_2$		H
S16-10-44	$N(CH_3)_2$		H
S16-10-47	$N(CH_3)_2$		H

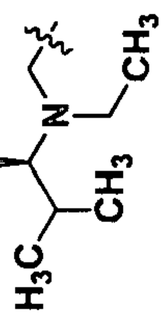
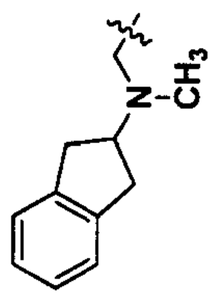
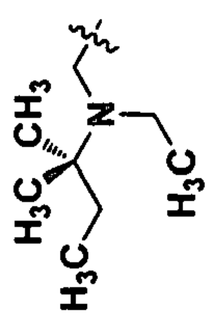
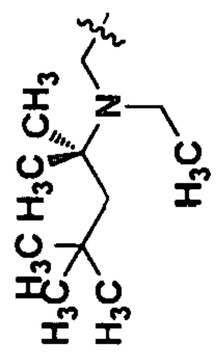
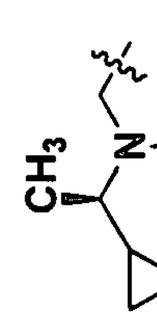
Cmpd	X	Y	Z
S15-13-97	Cl		H
S16-10-118	$N(CH_3)_2$		H
S16-10-125	$N(CH_3)_2$		H
S16-10-128	$N(CH_3)_2$		H
S16-10-130	$N(CH_3)_2$		H

FIG. 4G

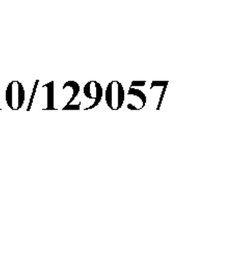
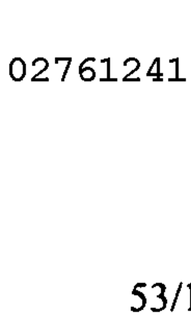
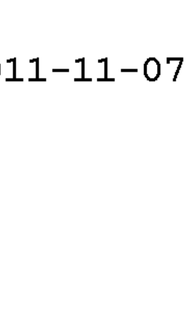
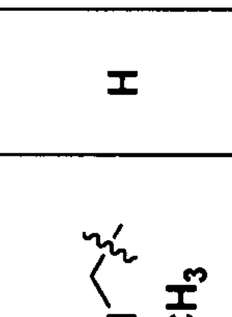
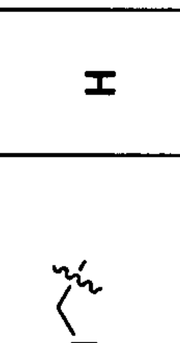
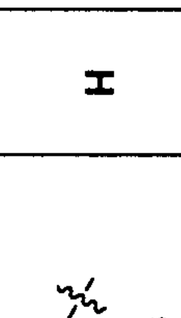
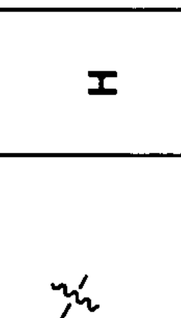
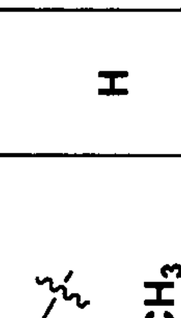
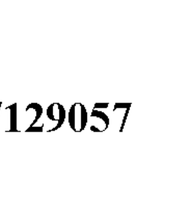
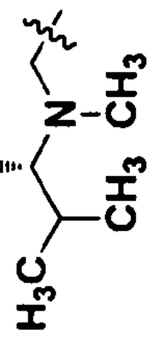
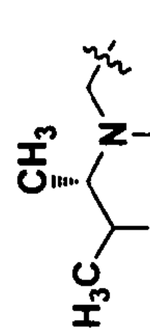
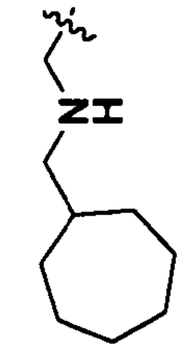
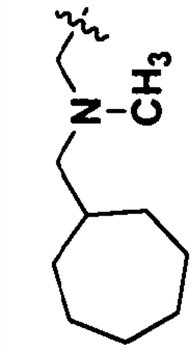
Cmpd	X	Y	Z
S16-10-66	$N(CH_3)_2$		H
S16-10-68	$N(CH_3)_2$		H
S16-10-76	$N(CH_3)_2$		H
S16-10-77	$N(CH_3)_2$		H
S16-10-80	$N(CH_3)_2$		H

FIG. 4H

Cmpd	X	Y	Z
S16-10-50	$N(CH_3)_2$		H
S16-10-51	$N(CH_3)_2$		H
S16-10-56	$N(CH_3)_2$		H
S16-10-57	$N(CH_3)_2$		H
S16-10-58	$N(CH_3)_2$		H

Cmpd	X	Y	Z
S16-10-93	$N(CH_3)_2$		H
S16-10-96	$N(CH_3)_2$		H
S16-10-97	$N(CH_3)_2$		H
S24-9-100	OCH_3		H
S24-9-101	OCH_3		H

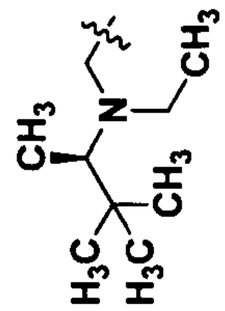
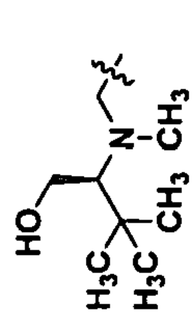
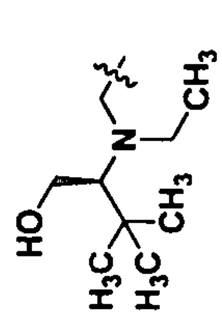
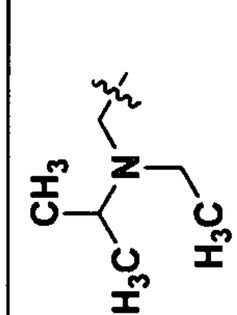
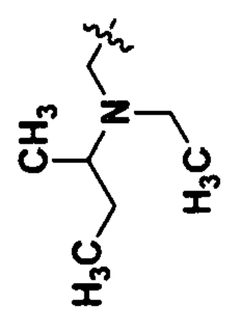
Cmpd	X	Y	Z
S16-10-81	$N(CH_3)_2$		H
S16-10-84	$N(CH_3)_2$		H
S16-10-85	$N(CH_3)_2$		H
S16-10-87	$N(CH_3)_2$		H
S16-10-90	$N(CH_3)_2$		H

FIG. 4I

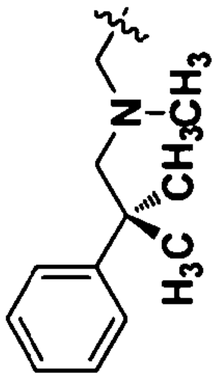
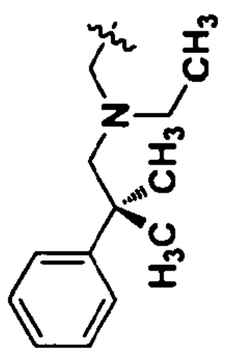
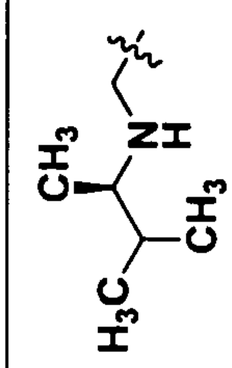
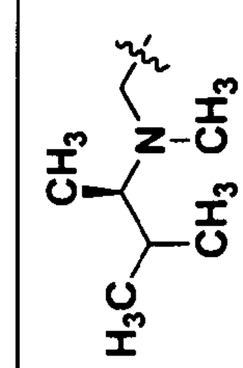
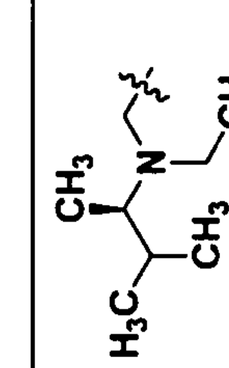
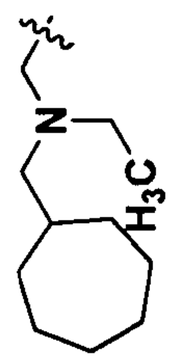
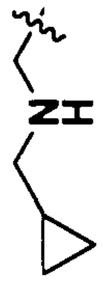
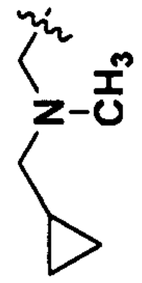
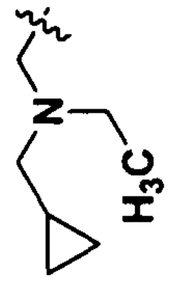
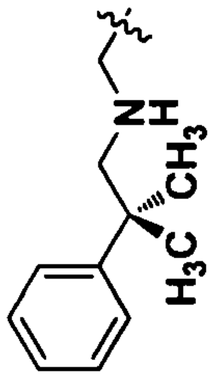
Cmpd	X	Y	Z
S24-9-107	OCH_3		H
S24-9-108	OCH_3		H
S24-9-109	OCH_3		H
S24-9-110	OCH_3		H
S24-9-111	OCH_3		H
S24-9-102	OCH_3		H
S24-9-103	OCH_3		H
S24-9-104	OCH_3		H
S24-9-105	OCH_3		H
S24-9-106	OCH_3		H

FIG. 4J

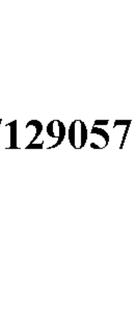
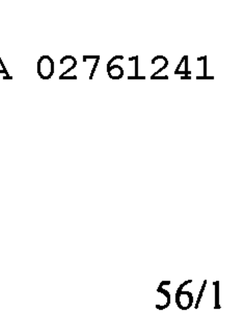
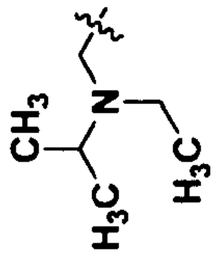
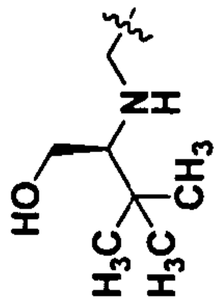
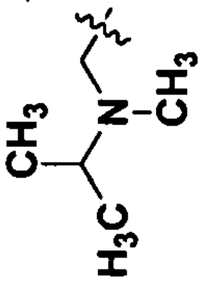
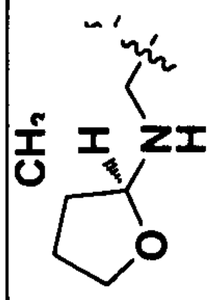
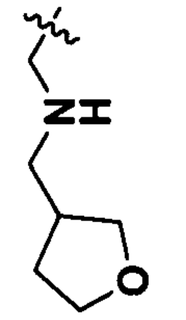
Cmpd	X	Y	Z
S24-9-120	OCH_3		H
S24-9-121	OCH_3		H
S24-9-133	OCH_3		H
S24-9-134	OCH_3		H
S24-9-136	OCH_3		H
S24-9-112	OCH_3		H
S24-9-113	OCH_3		H
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S24-9-116	OCH_3		H
S24-9-119	OCH_3		H

FIG. 4K

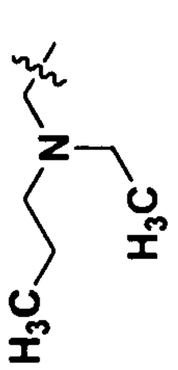
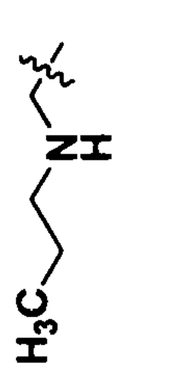
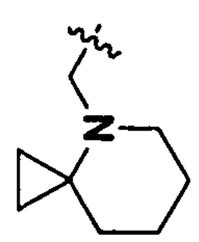
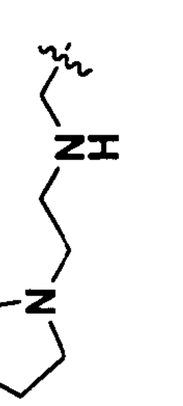
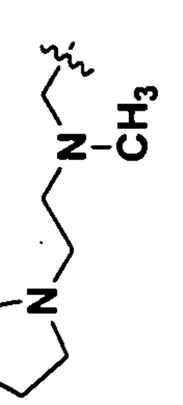
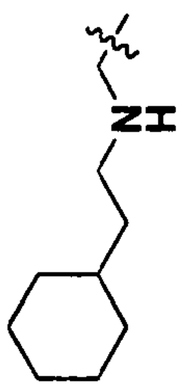
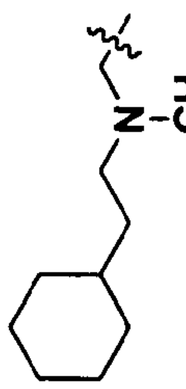
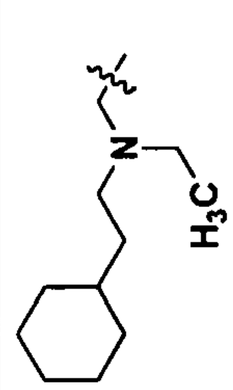
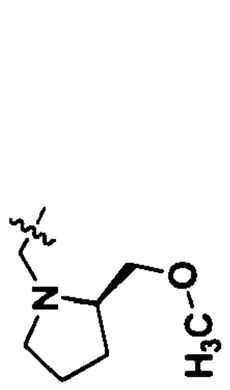
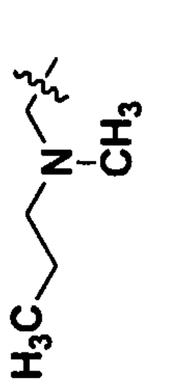
Cmpd	X	Y	Z
S24-9-142	OCH_3		H
S24-9-143	OCH_3		H
S24-9-144	OCH_3		H
S24-9-145	OCH_3		H
S24-9-146	OCH_3		H

FIG. 4L

Cmpd	X	Y	Z
S24-9-137	OCH_3		H
S24-9-138	OCH_3		H
S24-9-139	OCH_3		H
S24-9-140	OCH_3		H
S24-9-141	OCH_3		H

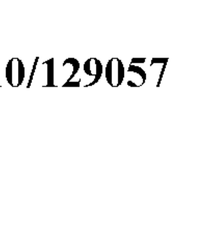
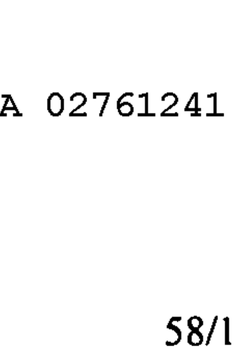
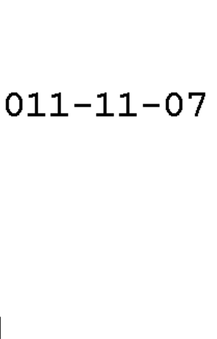
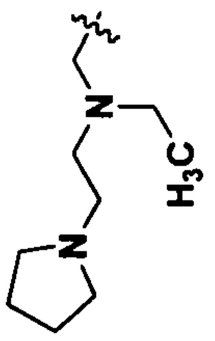
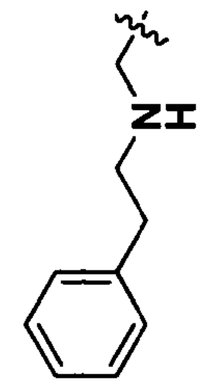
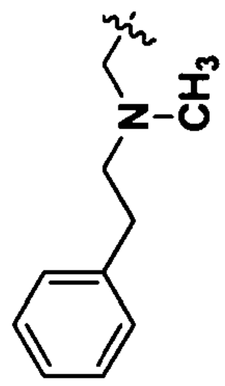
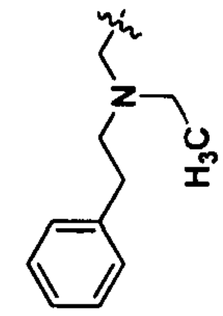
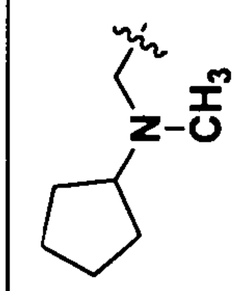
Cmpd	X	Y	Z
S24-9-152	OCH_3		H
S24-9-153	OCH_3		H
S24-9-154	OCH_3		H
S24-9-155	OCH_3		H
S24-9-156	OCH_3		H
S24-9-147	OCH_3		H
S24-9-148	OCH_3		H
S24-9-149	OCH_3		H
S24-9-150	OCH_3		H
S24-9-151	OCH_3		H

FIG. 4M

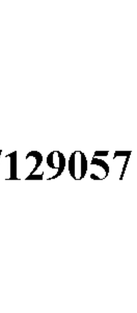
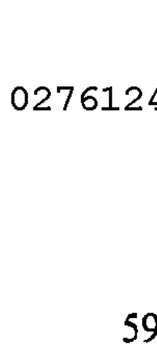
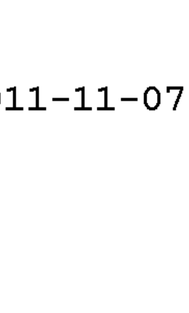
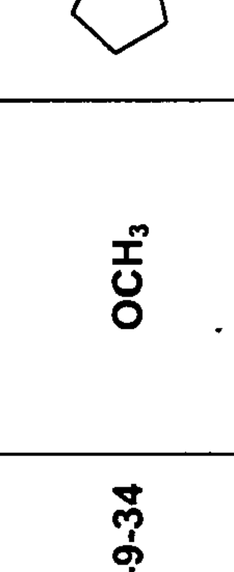
Cmpd	X	Y	Z
S24-9-34	OCH_3		H
S24-9-35	OCH_3		H
S24-9-36	OCH_3		H
S24-9-37	OCH_3		H
S24-9-38	OCH_3		H
S24-9-157	OCH_3		H
S24-9-158	OCH_3		H
S24-9-159	OCH_3		H
S24-9-29	OCH_3		H
S24-9-33	OCH_3		H

FIG. 4N

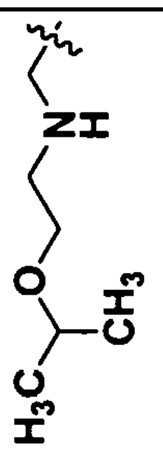
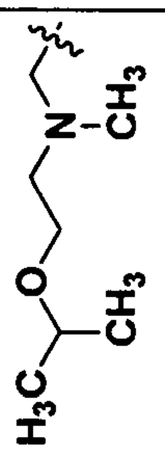
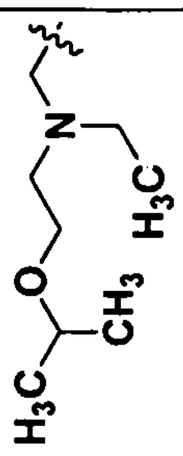
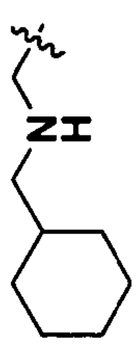
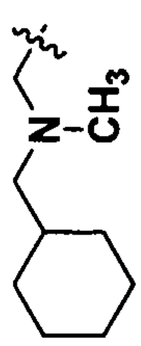
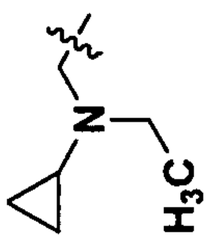
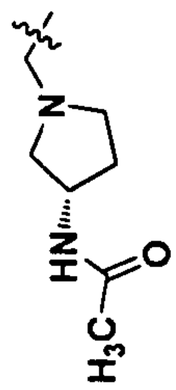
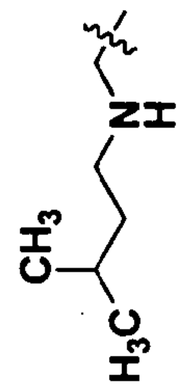
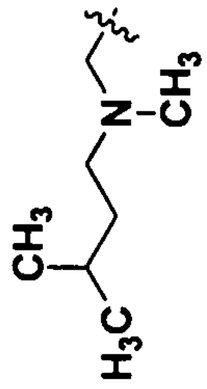
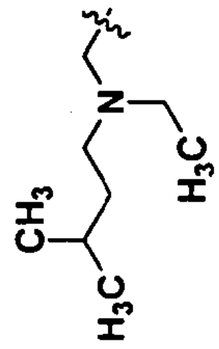
Cmpd	X	Y	Z
S24-9-44	OCH_3		H
S24-9-45	OCH_3		H
S24-9-46	OCH_3		H
S24-9-47	OCH_3		H
S24-9-48	OCH_3		H

FIG. 40

Cmpd	X	Y	Z
S24-9-39	OCH_3		H
S24-9-40	OCH_3		H
S24-9-41	OCH_3		H
S24-9-42	OCH_3		H
S24-9-43	OCH_3		H

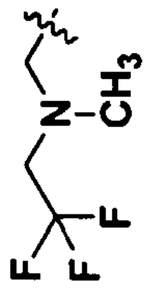
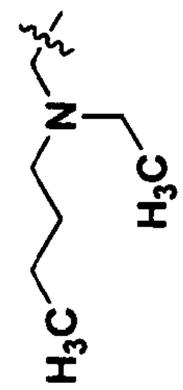
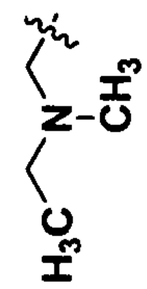
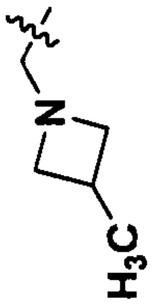
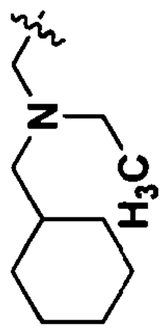
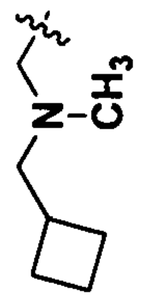
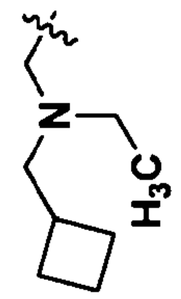
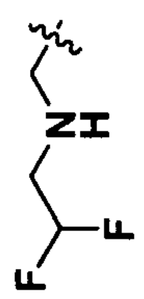
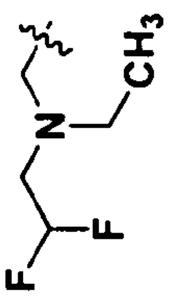
Cmpd	X	Y	Z
S24-9-54	OCH_3		H
S24-9-55	OCH_3		H
S24-9-57	OCH_3		H
S24-9-66	OCH_3		H
S24-9-85	OCH_3		H

FIG. 4P

Cmpd	X	Y	Z
S24-9-49	OCH_3		H
S24-9-50	OCH_3		H
S24-9-51	OCH_3		H
S24-9-52	OCH_3		H
S24-9-53	OCH_3		H

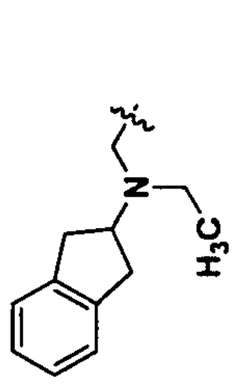
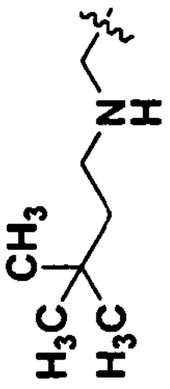
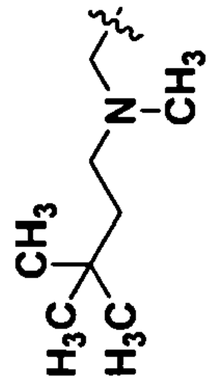
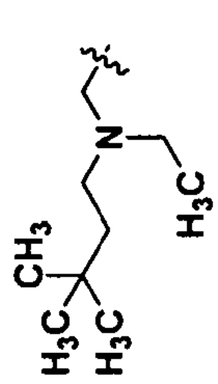
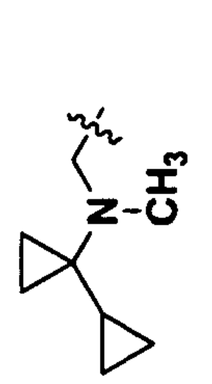
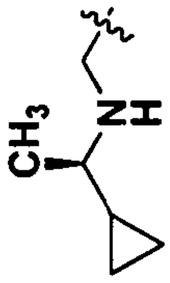
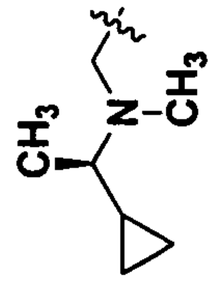
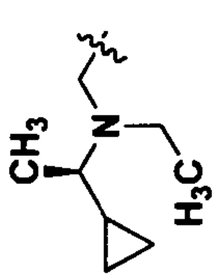
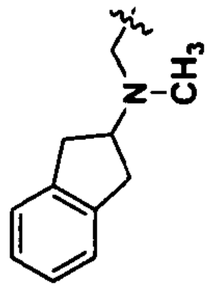
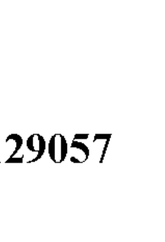
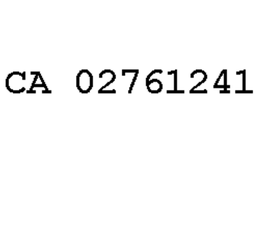
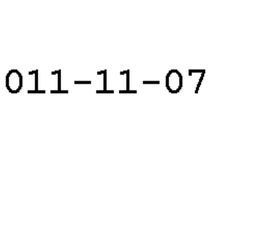
Cmpd	X	Y	Z
S24-9-91	OCH_3		H
S24-9-97	OCH_3		H
S24-9-98	OCH_3		H
S24-9-99	OCH_3		H
S25-11-100	CF_3		H

FIG. 4Q

Cmpd	X	Y	Z
S24-9-86	OCH_3		H
S24-9-87	OCH_3		H
S24-9-88	OCH_3		H
S24-9-89	OCH_3		H
S24-9-90	OCH_3		H

Cmpd	X	Y	Z
S25-11-106	CF_3		H
S25-11-106	CF_3		H
S25-11-107	CF_3		H
S25-11-108	CF_3		H
S25-11-109	CF_3		H

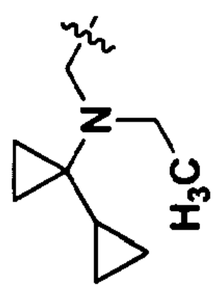
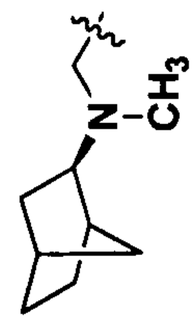
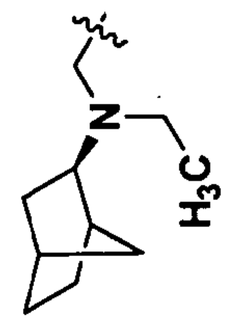
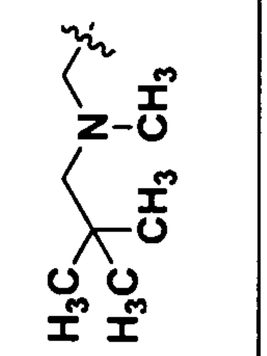
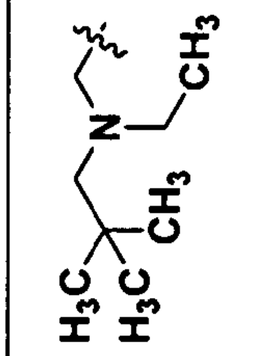
Cmpd	X	Y	Z
S25-11-101	CF_3		H
S25-11-102	CF_3		H
S25-11-103	CF_3		H
S25-11-104	CF_3		H
S25-11-105	CF_3		H

FIG. 4R

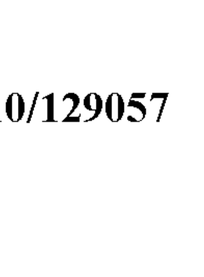
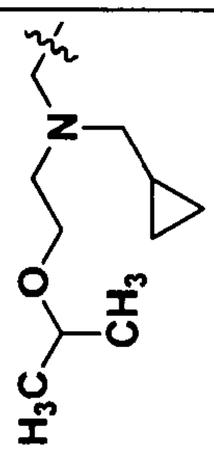
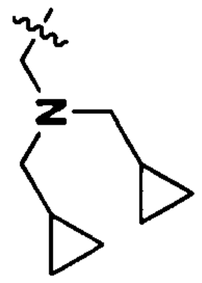
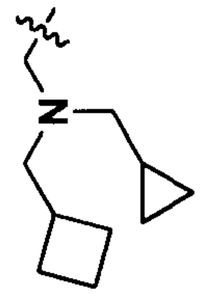
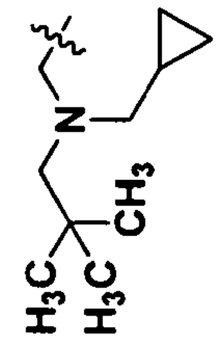
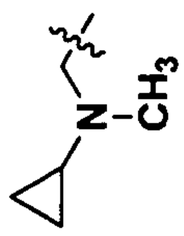
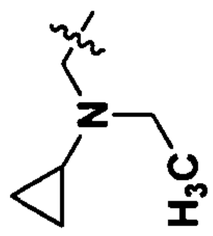
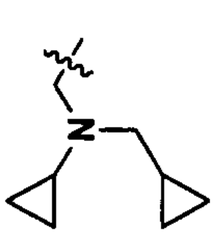
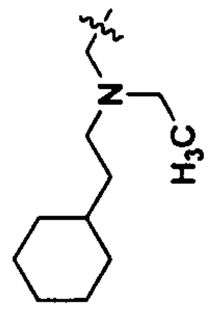
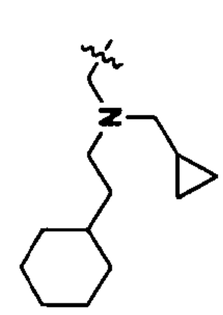
Cmpd	X	Y	Z
S25-11-115	CF_3		H
S25-11-116	CF_3		H
S25-11-117	CF_3		H
S25-11-118	CF_3		H
S25-11-119	CF_3		H
S25-11-110	CF_3		H
S25-11-111	CF_3		H
S25-11-112	CF_3		H
S25-11-113	CF_3		H
S25-11-114	CF_3		H

FIG. 4S

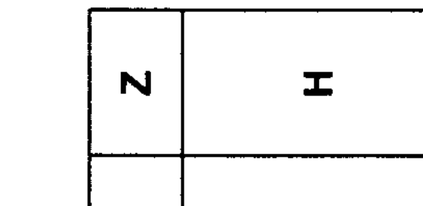
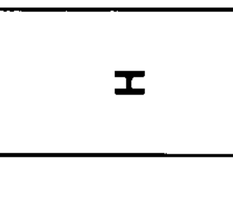
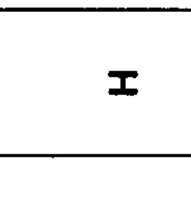
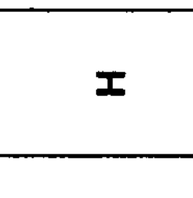
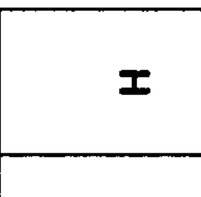
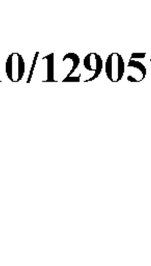
Cmpd	X	Y	Z
S25-11-120	CF_3		H
S25-11-121	CF_3		H
S25-11-122	CF_3		H
S25-11-123	CF_3		H
S25-11-124	CF_3		H
S25-11-125	CF_3		H
S25-11-126	CF_3		H
S25-11-127	CF_3		H
S25-11-128	CF_3		H
S25-11-129	CF_3		H

FIG. 4T

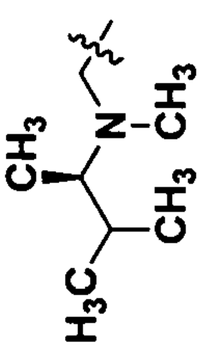
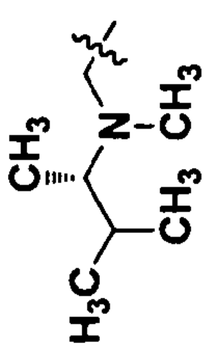
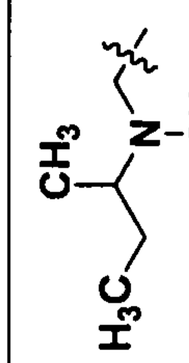
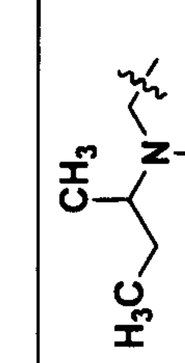
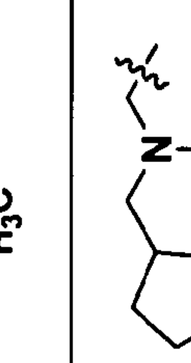
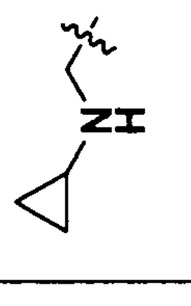
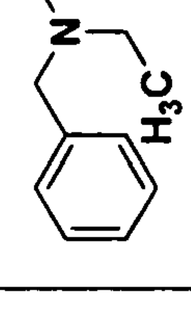
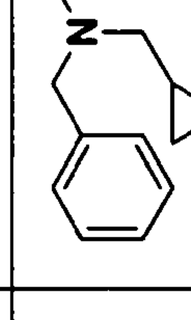
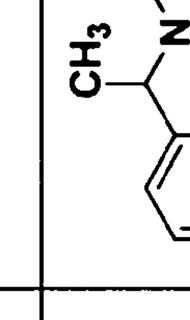
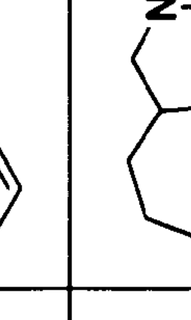
Cmpd	X	Y	Z
S25-11-39	CF_3		H
S25-11-40	CF_3		H
S25-11-41	CF_3		H
S25-11-42	CF_3		H
S25-11-79	CF_3		H

FIG. 4U

Cmpd	X	Y	Z
S25-11-130	CF_3		H
S25-11-131	CF_3		H
S25-11-132	CF_3		H
S25-11-133	CF_3		H
S25-11-38	CF_3		H

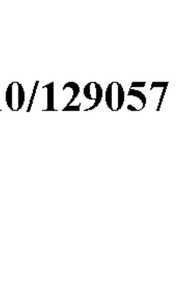
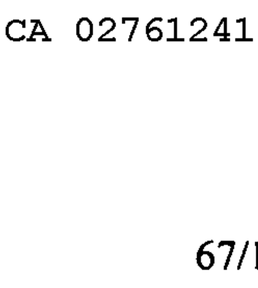
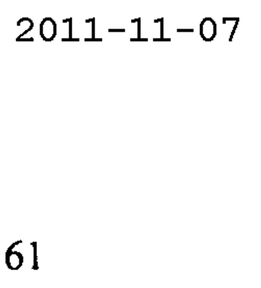
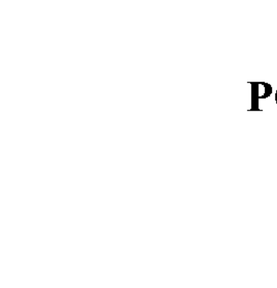
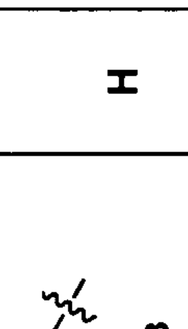
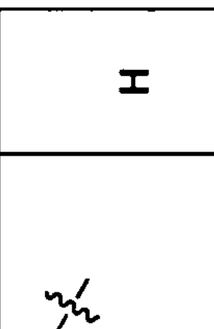
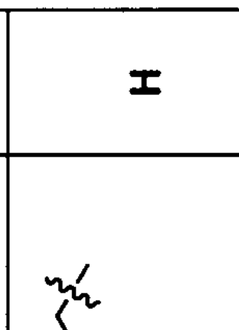
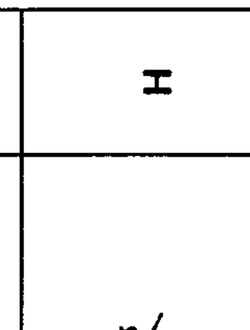
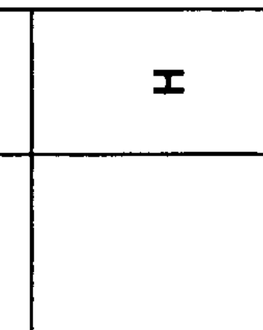
Cmpd	X	Y	Z
S25-11-85	CF_3		H
S25-11-86	CF_3		H
S25-11-87	CF_3		H
S25-11-88	CF_3		H
S25-11-89	CF_3		H
S25-11-80	CF_3		H
S25-11-81	CF_3		H
S25-11-82	CF_3		H
S25-11-83	CF_3		H
S25-11-84	CF_3		H

FIG. 4V

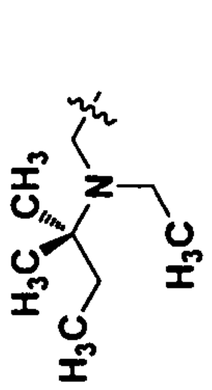
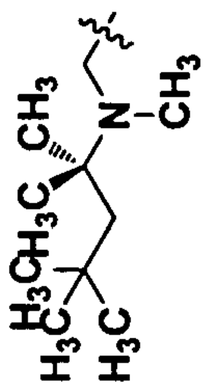
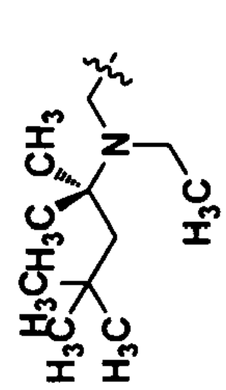
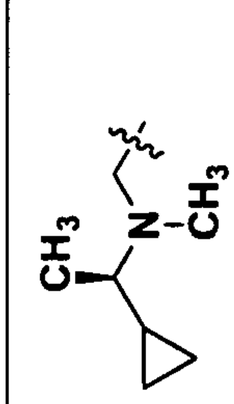
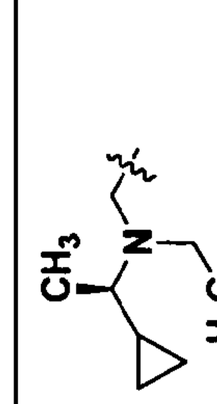
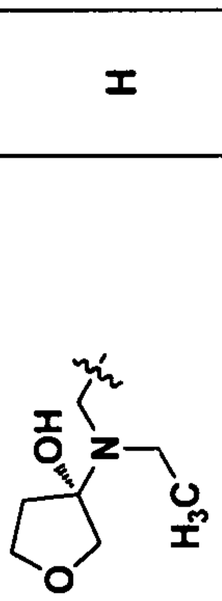
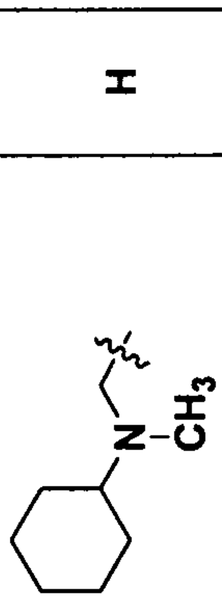
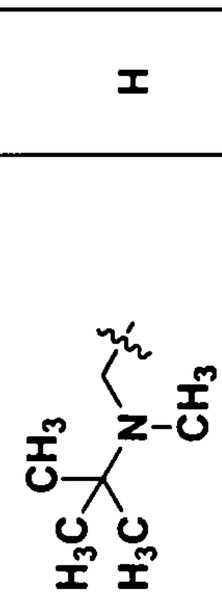
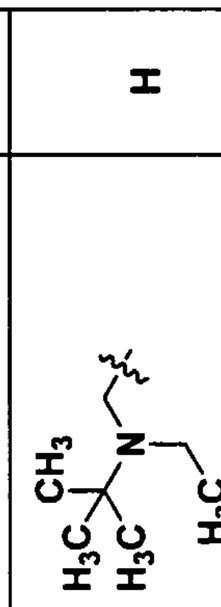
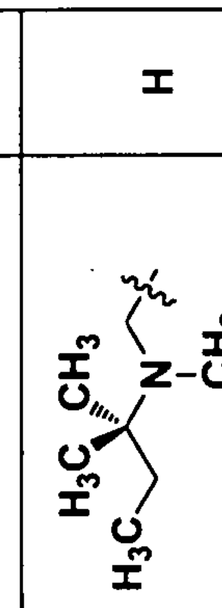
Cmpd	X	Y	Z
S25-11-95	CF_3		H
S25-11-96	CF_3		H
S25-11-97	CF_3		H
S25-11-98	CF_3		H
S25-11-99	CF_3		H
S25-11-90	CF_3		H
S25-11-91	CF_3		H
S25-11-92	CF_3		H
S25-11-93	CF_3		H
S25-11-94	CF_3		H

FIG. 4W

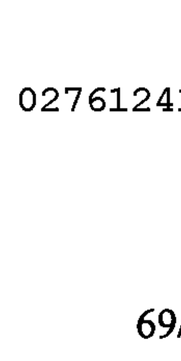
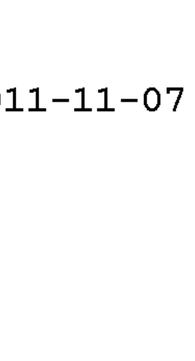
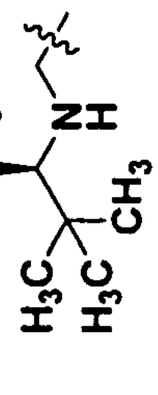
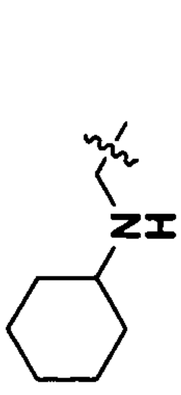
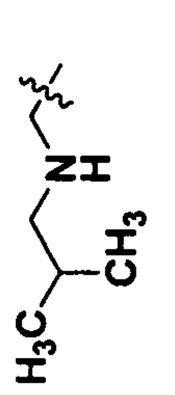
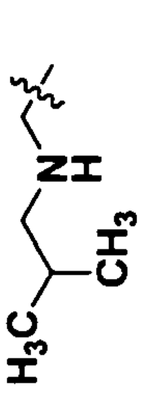
Cmpd	X	Y	Z
S32-6-1-3	$N(CH_2CH_3)_2$		H
S32-6-1-3	$N(CH_2CH_3)_2$		H
S32-6-1-4	$N(CH_2CH_3)_2$		H
S32-6-1-4	$N(CH_2CH_3)_2$		H
S32-6-1-5	$N(CH_2CH_3)_2$		H
S31-7-1			H
S32-6-1-1	$N(CH_2CH_3)_2$		H
S32-6-1-1	$N(CH_2CH_3)_2$		H
S32-6-1-2	$N(CH_2CH_3)_2$		H
S32-6-1-2	$N(CH_2CH_3)_2$		H

FIG. 4X

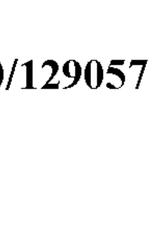
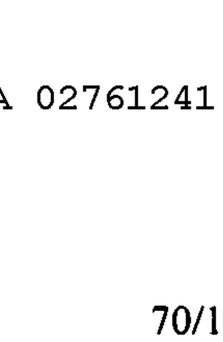
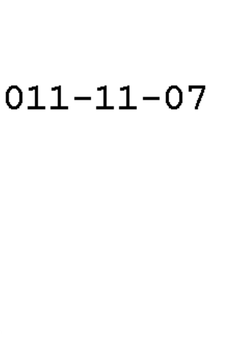
Cmpd	X	Y	Z
S32-6-2-1	$N(CH_3)CH(CH_3)_2$		H
S32-6-2-1	$N(CH_3)CH(CH_3)_2$		H
S32-6-2-2	$N(CH_3)CH(CH_3)_2$		H
S32-6-2-2	$N(CH_3)CH(CH_3)_2$		H
S32-6-2-3	$N(CH_3)CH(CH_3)_2$		H

FIG. 4Y

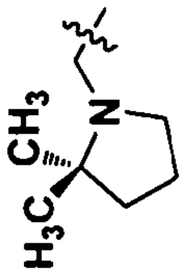
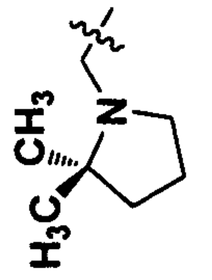
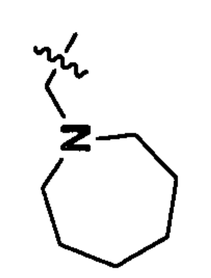
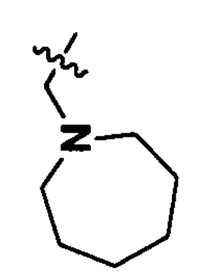
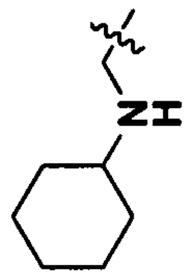
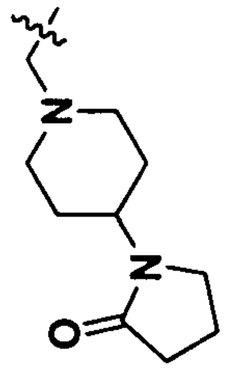
Cmpd	X	Y	Z
S32-6-1-5	$N(CH_2CH_3)_2$		H
S32-6-1-6	$N(CH_2CH_3)_2$		H
S32-6-1-6	$N(CH_2CH_3)_2$		H
S32-6-1-7	$N(CH_2CH_3)_2$		H
S32-6-1-7	$N(CH_2CH_3)_2$		H

FIG. 42

Cmpd	X	Y	Z
S32-6-2-3	$N(CH_3)CH(CH_3)_2$		H
200	OCH_3		H

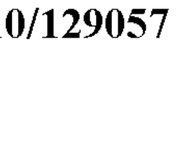
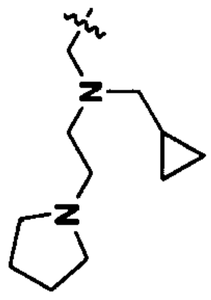
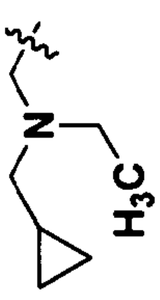
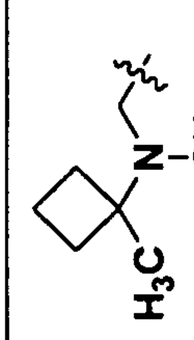
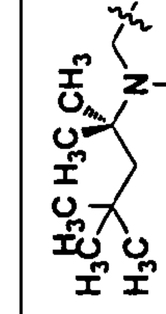
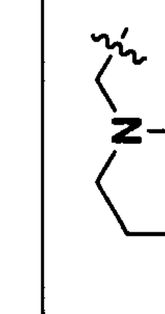
Cmpd #	X	Y	Z
S15-13-106	Cl		H
S15-13-107	Cl		H
S15-13-108	Cl		H
S15-13-109	Cl		H
S15-13-110	Cl		H
S15-13-111	Cl		H
S15-13-100	Cl		H
S15-13-101	Cl		H
S15-13-102	Cl		H
S15-13-103	Cl		H
S15-13-104	Cl		H
S15-13-105	Cl		H

FIG. 5A

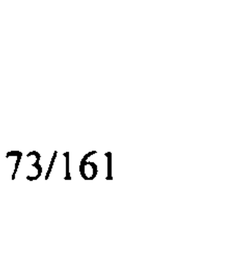
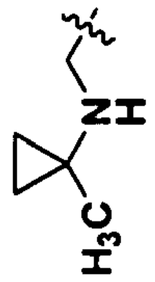
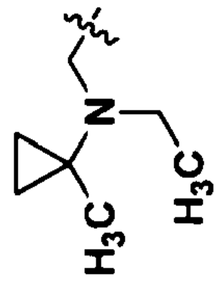
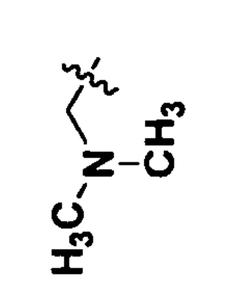
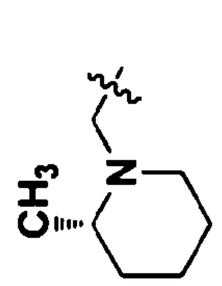
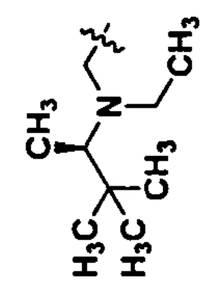
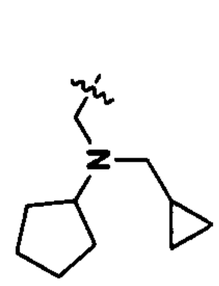
Cmpd #	X	Y	Z
S15-13-138	Cl		H
S15-13-139	Cl		H
S15-13-140	Cl		H
S15-13-141	Cl		H
S15-13-161	Cl		H
S15-13-162	Cl		H

FIG. 5B

Cmpd #	X	Y	Z
S15-13-112	Cl		H
S15-13-113	Cl		H
S15-13-114	Cl		H
S15-13-115	Cl		H
S15-13-122	Cl		H
S15-13-137	Cl		H

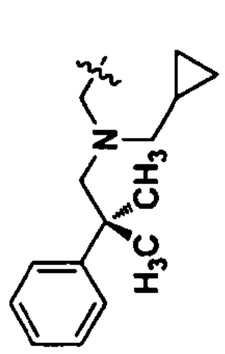
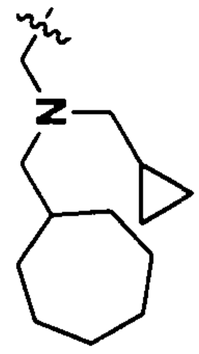
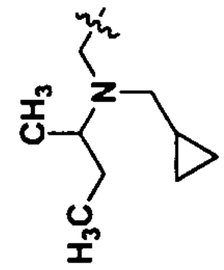
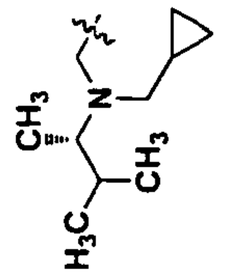
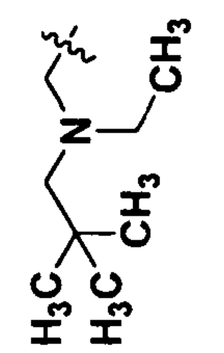
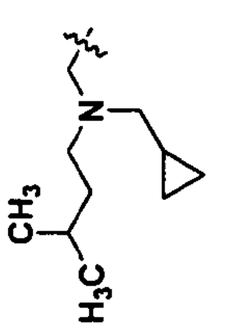
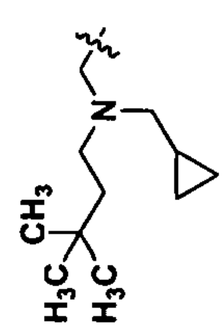
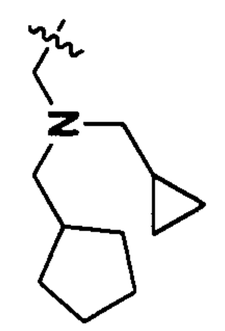
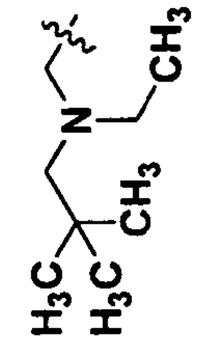
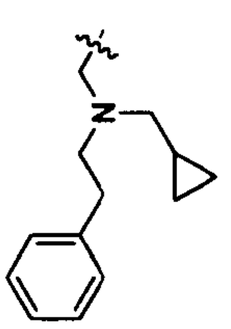
Cmpd #	X	Y	Z
S15-13-65	Cl		H
S15-13-66	Cl		H
S15-13-67	Cl		H
S15-13-68	Cl		H
S15-13-69	Cl		H
S15-13-70	Cl		H

FIG. 5C

Cmpd #	X	Y	Z
S15-13-163	Cl		H
S15-13-164	Cl		H
S15-13-165	Cl		H
S15-13-166	Cl		H
S15-13-227	OCH_3		H
S15-13-64	Cl		H

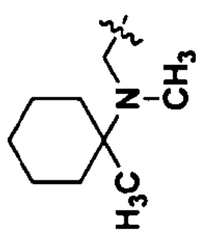
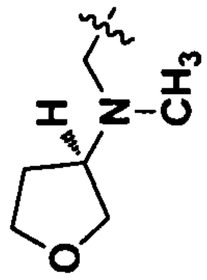
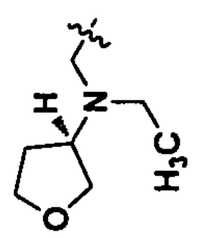
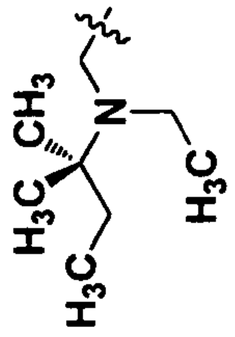
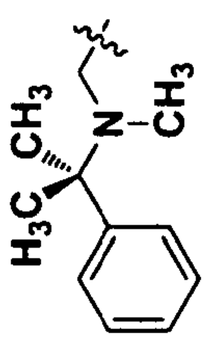
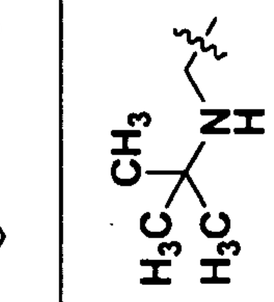
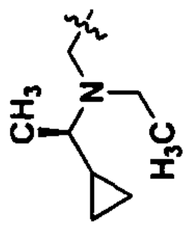
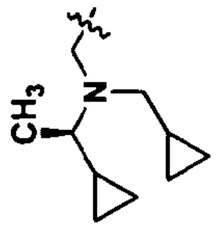
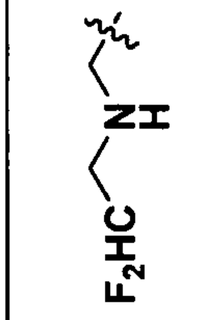
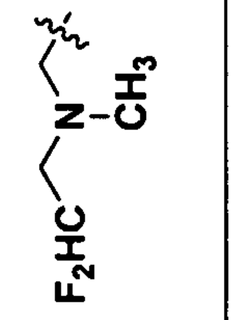
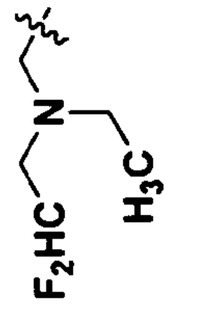
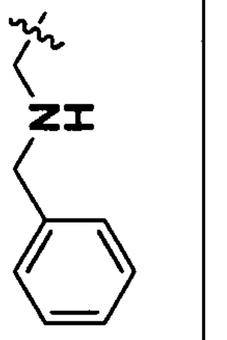
Cmpd #	X	Y	Z
S15-13-77	Cl		H
S15-13-79	Cl		H
S15-13-80	Cl		H
S15-13-98	Cl		H
S15-13-99	Cl		H
S15-14-5	H		H

FIG. 5D

Cmpd #	X	Y	Z
S15-13-71	Cl		H
S15-13-72	Cl		H
S15-13-73	Cl		H
S15-13-74	Cl		H
S15-13-75	Cl		H
S15-13-76	Cl		H

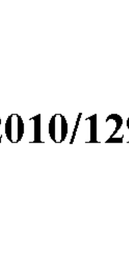
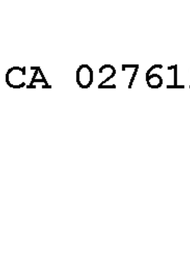
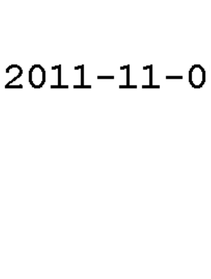
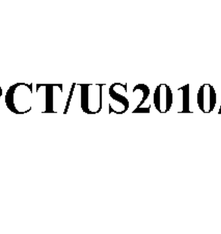
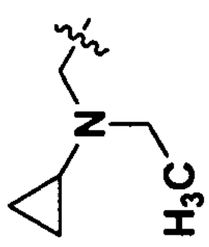
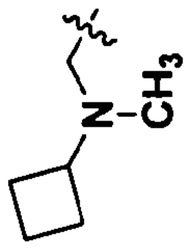
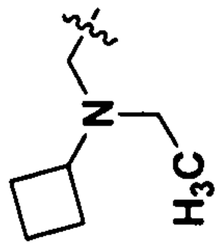
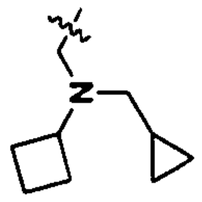
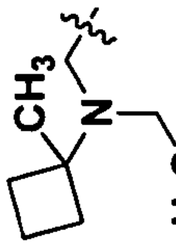
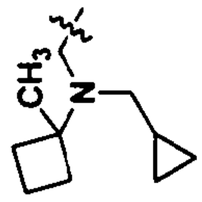
Cmpd #	X	Y	Z
S16-10-111	$N(CH_3)_2$		H
S16-10-112	$N(CH_3)_2$		H
S16-10-113	$N(CH_3)_2$		H
S16-10-114	$N(CH_3)_2$		H
S16-10-115	$N(CH_3)_2$		H
S16-10-122	$N(CH_3)_2$		H

FIG. 5E

Cmpd #	X	Y	Z
S16-10-100	$N(CH_3)_2$		H
S16-10-103	$N(CH_3)_2$		H
S16-10-104	$N(CH_3)_2$		H
S16-10-105	$N(CH_3)_2$		H
S16-10-108	$N(CH_3)_2$		H
S16-10-109	$N(CH_3)_2$		H

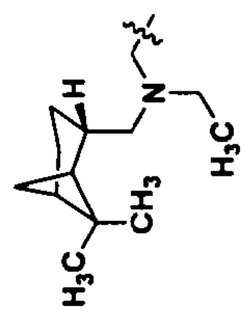
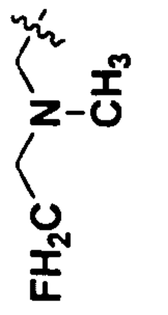
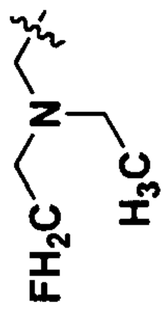
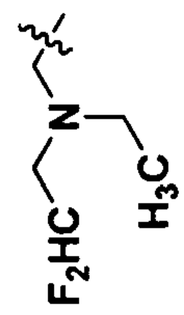
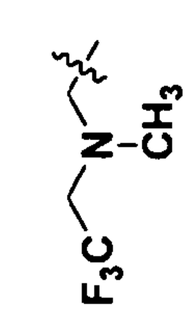
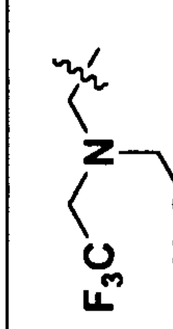
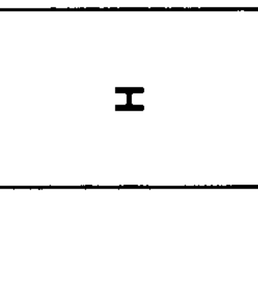
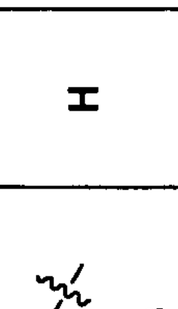
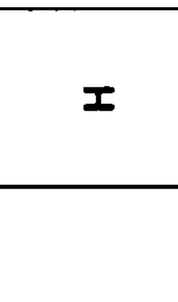
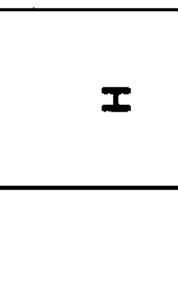
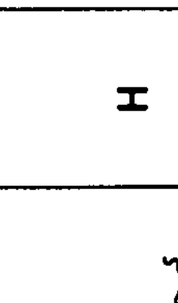
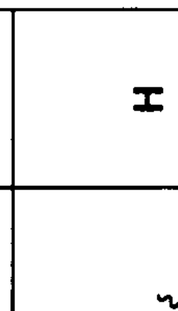
Cmpd #	X	Y	Z
S16-10-142	$N(CH_3)_2$		H
S16-10-29	$N(CH_3)_2$		H
S16-10-30	$N(CH_3)_2$		H
S16-10-32	$N(CH_3)_2$		H
S16-10-34	$N(CH_3)_2$		H
S16-10-35	$N(CH_3)_2$		H

FIG. 5F

Cmpd #	X	Y	Z
S16-10-124	$N(CH_3)_2$		H
S16-10-127	$N(CH_3)_2$		H
S16-10-133	$N(CH_3)_2$		H
S16-10-134	$N(CH_3)_2$		H
S16-10-140	$N(CH_3)_2$		H
S16-10-141	$N(CH_3)_2$		H

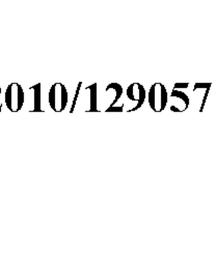
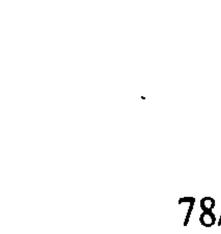
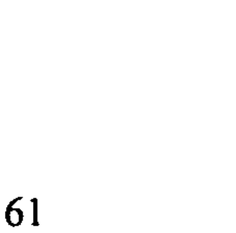
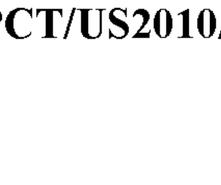
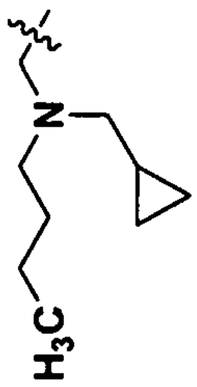
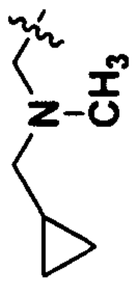
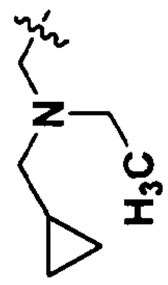
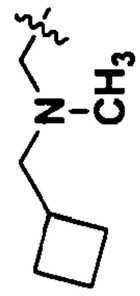
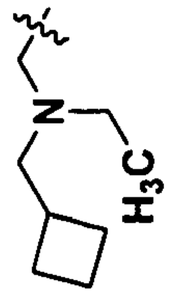
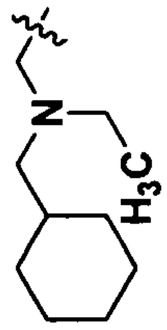
Cmpd #	X	Y	Z
S16-10-78	$N(CH_3)_2$		H
S16-10-82	$N(CH_3)_2$		H
S16-10-94	$N(CH_3)_2$		H
S16-10-98	$N(CH_3)_2$		H
S16-10-99	$N(CH_3)_2$		H
S24-9-117	OCH_3		H

FIG. 5G

Cmpd #	X	Y	Z
S16-10-41	$N(CH_3)_2$		H
S16-10-59	$N(CH_3)_2$		H
S16-10-60	$N(CH_3)_2$		H
S16-10-62	$N(CH_3)_2$		H
S16-10-63	$N(CH_3)_2$		H
S16-10-70	$N(CH_3)_2$		H

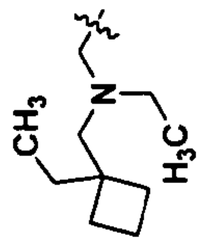
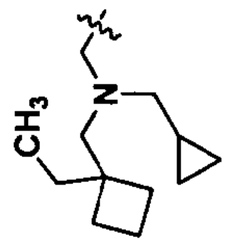
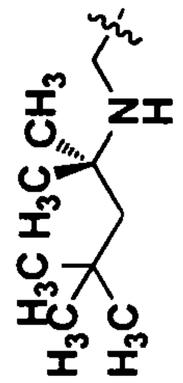
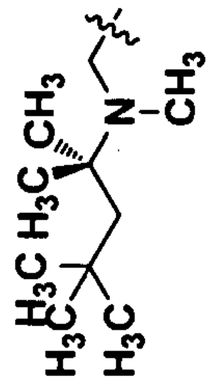
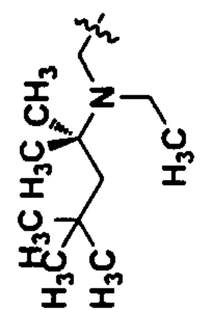
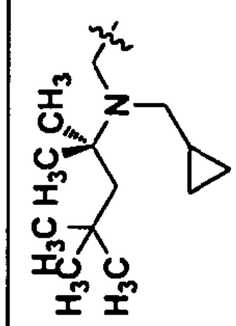
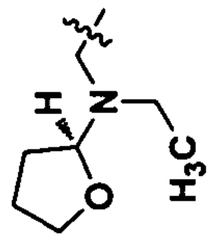
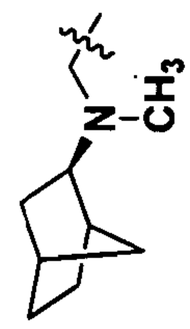
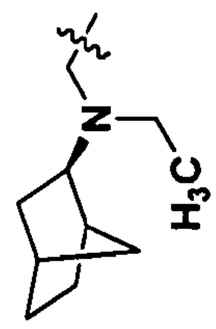
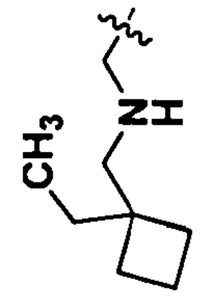
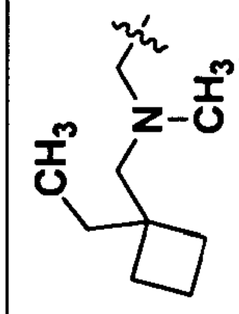
Cmpd #	X	Y	Z
S24-9-162	OCH_3		H
S24-9-163	OCH_3		H
S24-9-164	OCH_3		H
S24-9-165	OCH_3		H
S24-9-166	OCH_3		H
S24-9-167	OCH_3		H

FIG. 5H

Cmpd #	X	Y	Z
S24-9-118	OCH_3		H
S24-9-122	OCH_3		H
S24-9-123	OCH_3		H
S24-9-124	OCH_3		H
S24-9-160	OCH_3		H
S24-9-161	OCH_3		H

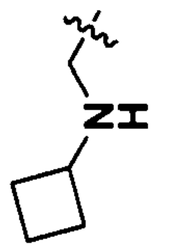
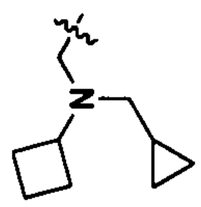
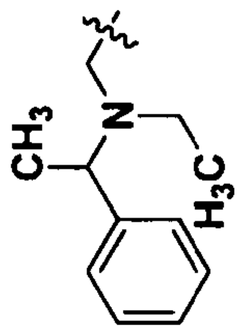
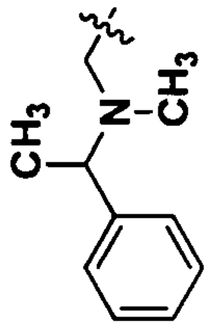
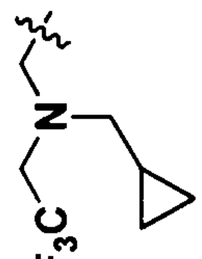
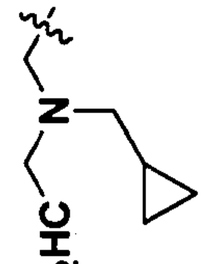
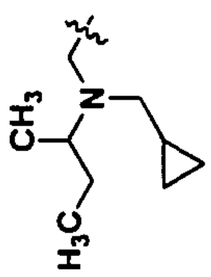
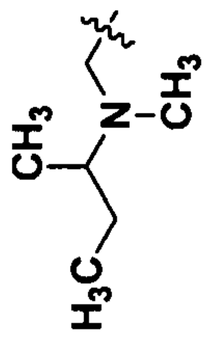
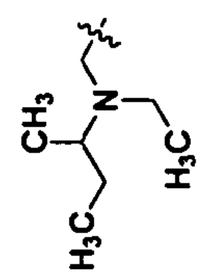
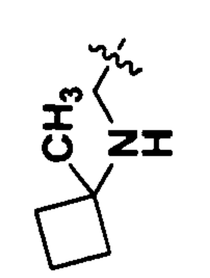
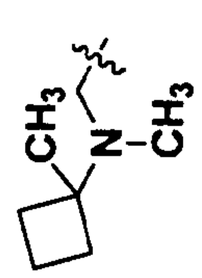
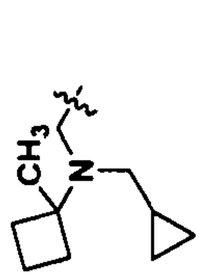
Cmpd #	X	Y	Z
S24-9-174	OCH_3		H
S24-9-175	OCH_3		H
S24-9-179	OCH_3		H
S24-9-182	OCH_3		H
S24-9-56	OCH_3		H
S24-9-58	OCH_3		H
S24-9-168	OCH_3		H
S24-9-169	OCH_3		H
S24-9-170	OCH_3		H
S24-9-171	OCH_3		H
S24-9-172	OCH_3		H
S24-9-173	OCH_3		H

FIG. 51

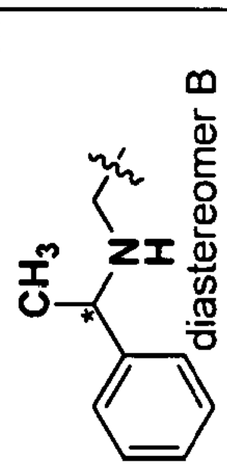
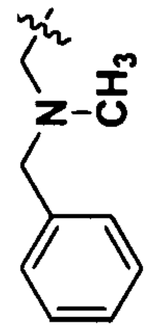
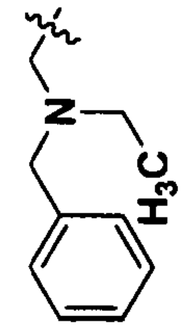
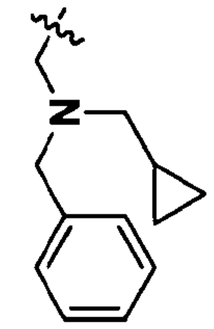
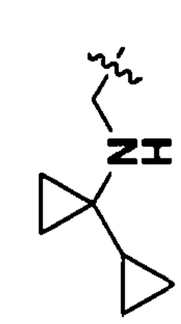
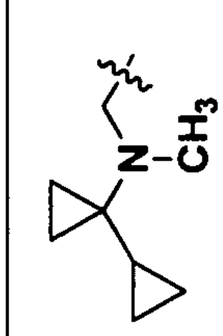
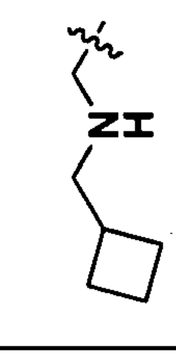
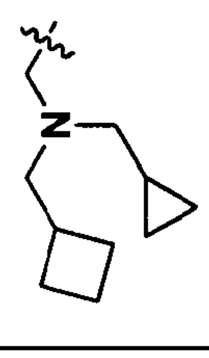
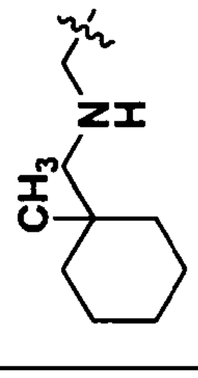
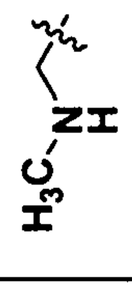
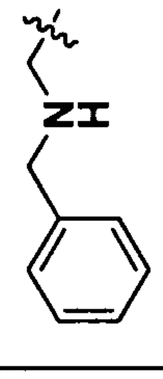
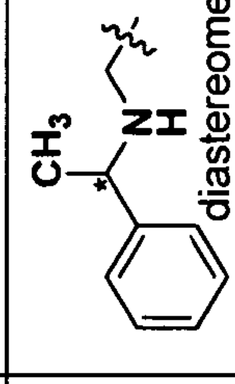
Cmpd #	X	Y	Z
S24-9-65	OCH_3	 diastereomer B	H
S24-9-67	OCH_3		H
S24-9-68	OCH_3		H
S24-9-69	OCH_3		H
S24-9-70	OCH_3		H
S24-9-71	OCH_3		H

FIG. 5J

Cmpd #	X	Y	Z
S24-9-59	OCH_3		H
S24-9-60	OCH_3		H
S24-9-61	OCH_3		H
S24-9-62	OCH_3		H
S24-9-63	OCH_3		H
S24-9-64	OCH_3	 diastereomer A	H

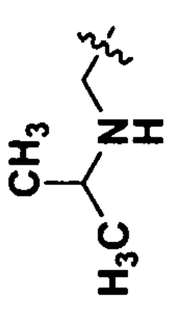
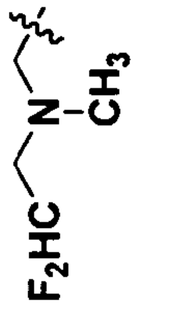
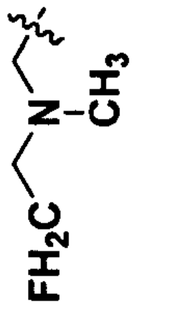
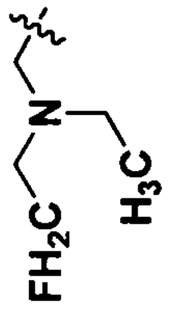
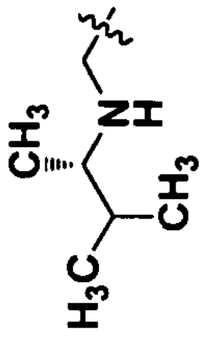
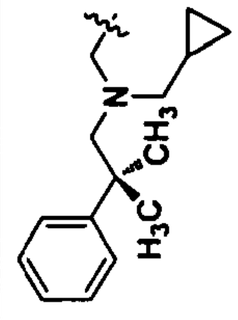
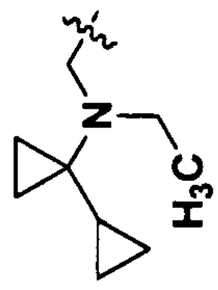
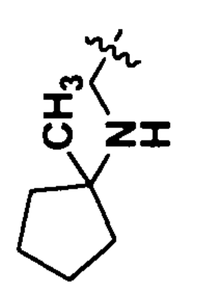
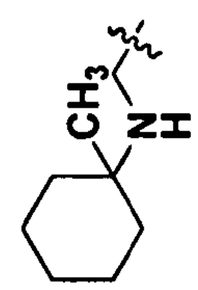
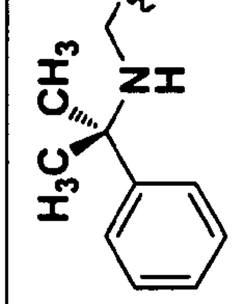
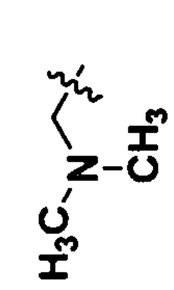
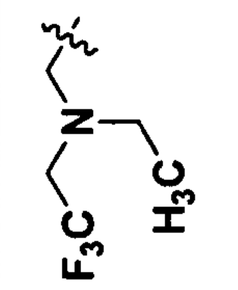
Cmpd #	X	Y	Z
S24-9-78	OCH_3		H
S24-9-79	OCH_3		H
S24-9-94	OCH_3		H
S24-9-95	OCH_3		H
S24-9-96	OCH_3		H
S25-11-134	CF_3		H
S24-9-72	OCH_3		H
S24-9-73	OCH_3		H
S24-9-74	OCH_3		H
S24-9-75	OCH_3		H
S24-9-76	OCH_3		H
S24-9-77	OCH_3		H

FIG. 5K

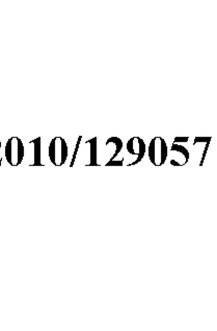
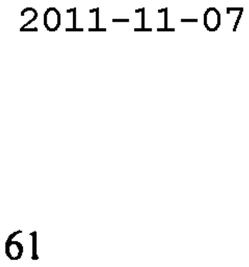
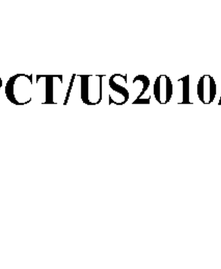
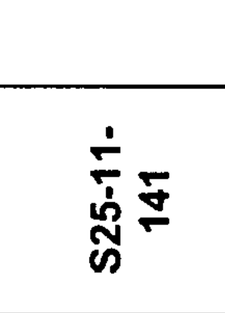
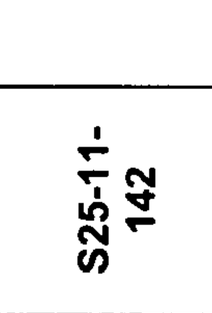
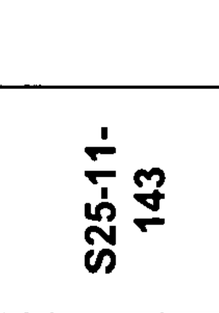
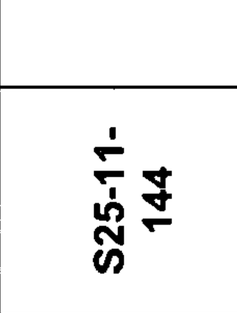
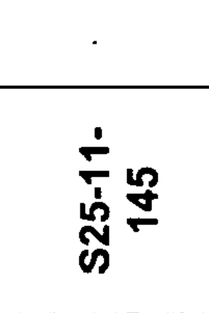
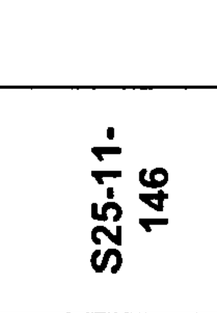
Cmpd #	X	Y	Z
S25-11-141	CF_3		H
S25-11-142	CF_3		H
S25-11-143	CF_3		H
S25-11-144	CF_3		H
S25-11-145	CF_3		H
S25-11-146	CF_3		H

FIG. 5L

Cmpd #	X	Y	Z
S25-11-135	CF_3		H
S25-11-136	CF_3		H
S25-11-137	CF_3		H
S25-11-138	CF_3		H
S25-11-139	CF_3		H
S25-11-140	CF_3		H

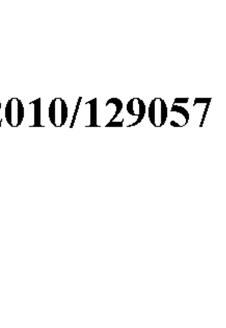
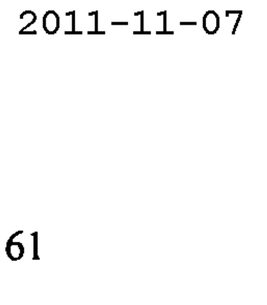
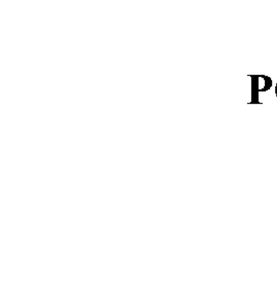
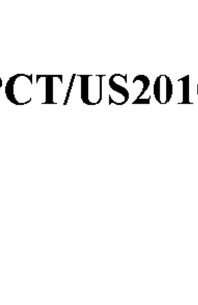
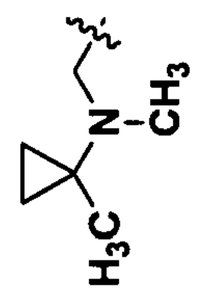
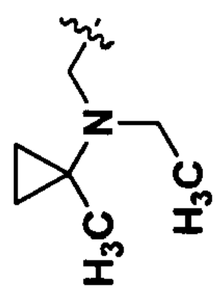
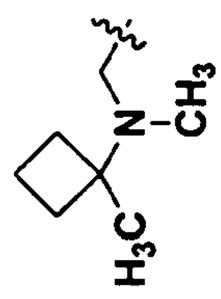
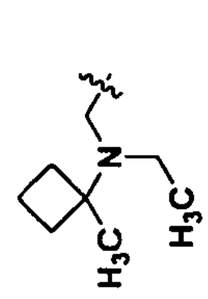
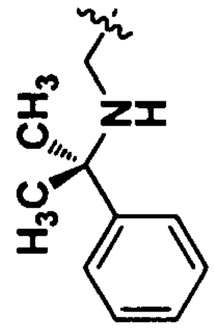
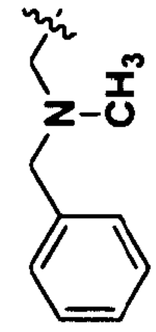
Cmpd #	X	Y	Z
S25-11-153	CF_3		H
S25-11-154	CF_3		H
S25-11-155	CF_3		H
S25-11-156	CF_3	 diastereomer A	H
S25-11-157	CF_3	 diastereomer B	H
S25-11-158	CF_3		H

FIG. 5M

Cmpd #	X	Y	Z
S25-11-147	CF_3		H
S25-11-148	CF_3		H
S25-11-149	CF_3		H
S25-11-150	CF_3		H
S25-11-151	CF_3		H
S25-11-152	CF_3		H

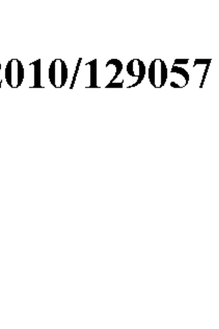
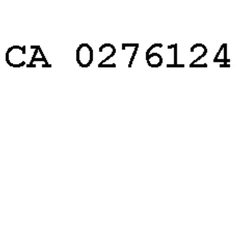
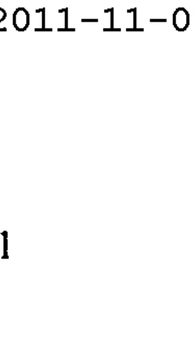
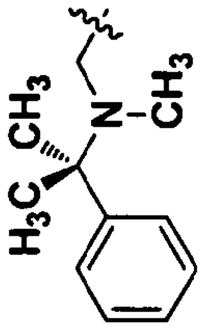
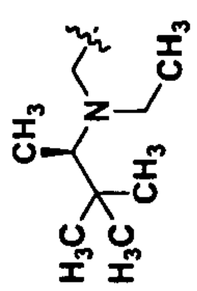
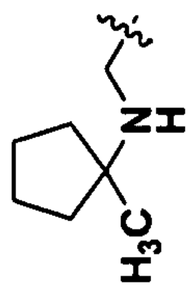
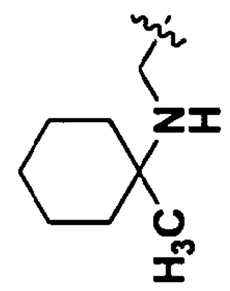
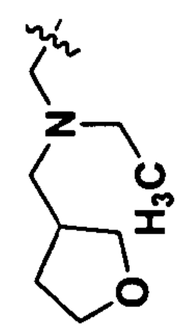
Cmpd #	X	Y	Z
S25-11-190	CF_3		H
S25-11-191	CF_3		H
S25-11-192	CF_3		H
S25-11-193	CF_3		H
S25-11-201	CF_3		H
S25-11-202	CF_3		H

FIG. 5N

Cmpd #	X	Y	Z
S25-11-159	CF_3		H
S25-11-160	CF_3		H
S25-11-161	CF_3		H
S25-11-162	CF_3		H
S25-11-163	CF_3		H
S25-11-167	CF_3		H

Cmpd #	X	Y	Z
S26-7-3	$OCH(CH_3)_2$		H
S26-7-4	$OCH(CH_3)_2$		H

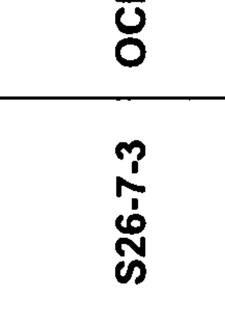
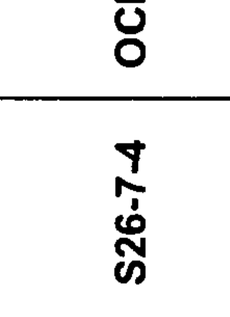
Cmpd #	X	Y	Z
S25-11-203	CF_3		H
S25-11-204	CF_3		H
S25-11-205	CF_3		H
S25-11-209	CF_3		H
S26-7-1	$OCH(CH_3)_2$		H
S26-7-2	$OCH(CH_3)_2$		H

FIG. 50

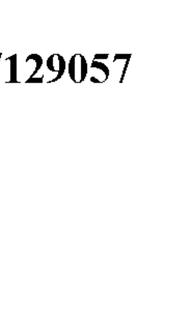
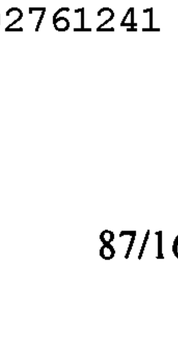
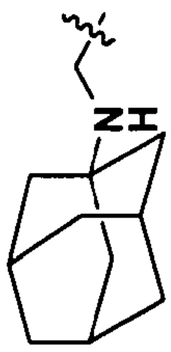
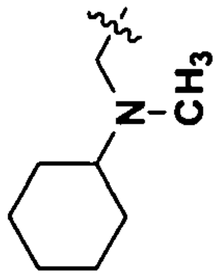
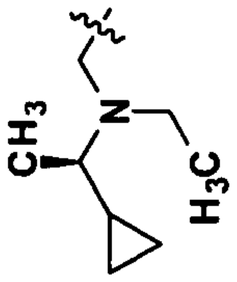
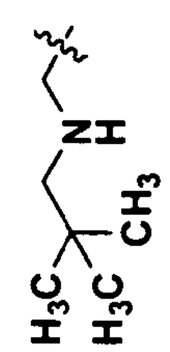
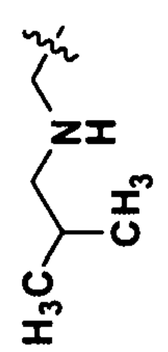
Cmpd	X	Y	Z
S2-4-19	F		H
S2-4-22	F		H
S2-4-23	F		H
S2-4-27	F		H
S2-4-28	F		H

FIG. 6A

Cmpd	X	Y	Z
S1-14-4	F		H
S1-14-65	F		H
S1-14-9	F		H
S2-4-1	F		H
S2-4-14	F		H

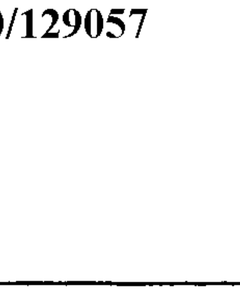
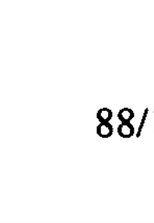
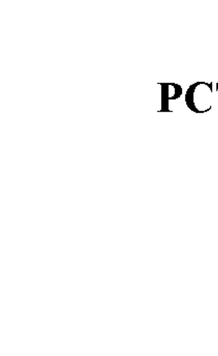
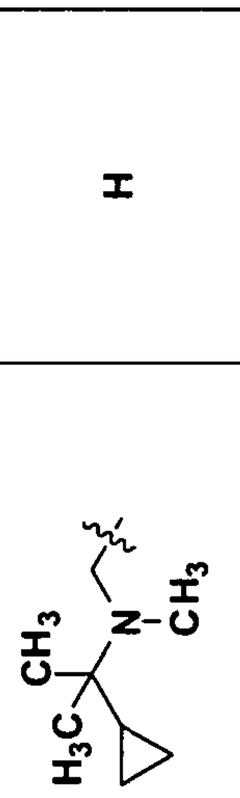
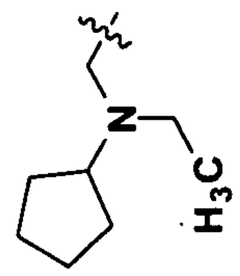
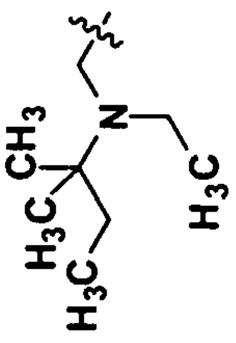
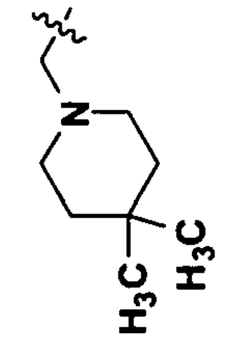
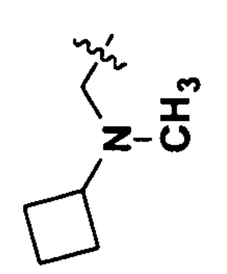
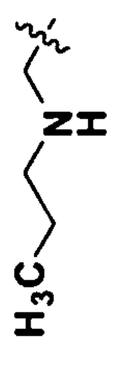
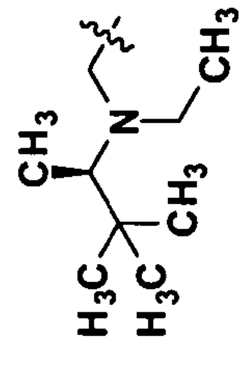
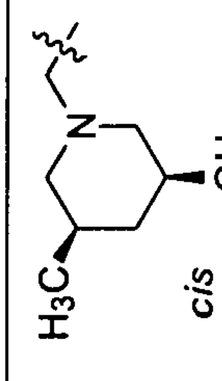
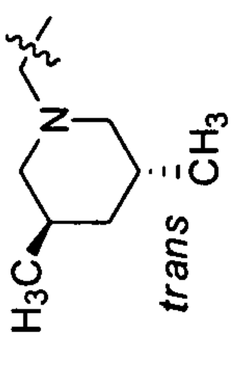
Cmpd	X	Y	Z
S2-4-52	F		H
S2-4-7	F		H
S2-4-8	F		H
S-15-13-1	Cl		H
S15-13-15	Cl		H

FIG. 6B

Cmpd	X	Y	Z
S2-4-29	F		H
S2-4-32	F		H
S2-4-33	F		H
S2-4-50	F		H
S2-4-51	F		H

Cmpd	X	Y	Z
S19-7-2	$N(CH_3)_2$	F	H
S1-14-1	F		H
S1-14-10	F		H
S1-14-100	F	 *cis*	H
S1-14-101	F	 *trans*	H

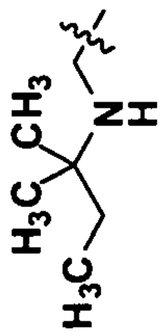
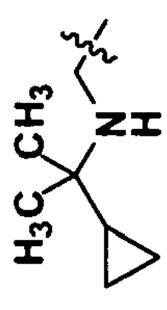
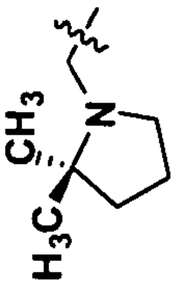
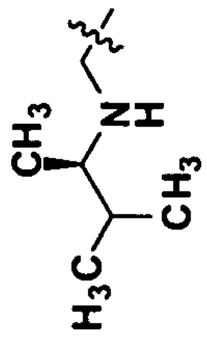
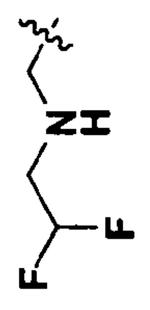
Cmpd	X	Y	Z
S15-13-2	Cl		H
S15-13-3	Cl		H
S15-13-4	Cl		H
S15-13-8	Cl		H
S16-10-13	$N(CH_3)_2$		H

FIG. 6C

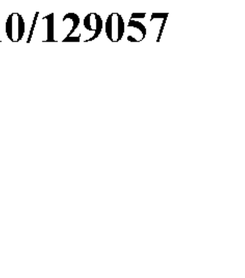
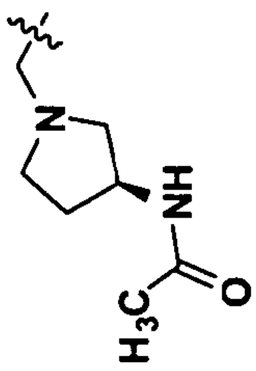
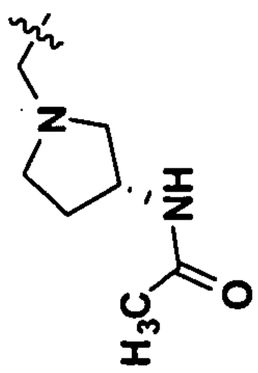
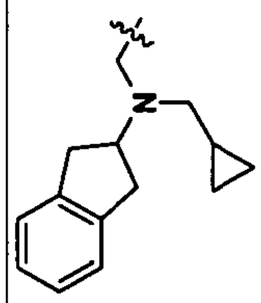
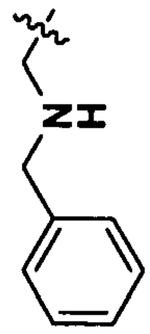
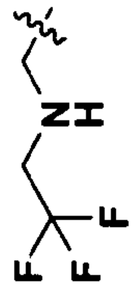
Cmpd	X	Y	Z
S1-14-107	F		H
S1-14-108	F		H
S1-14-109	F		H
S1-14-11	F		H
S1-14-110	F		H
S1-14-102	F		H
S1-14-103	F		H
S1-14-104	F		H
S1-14-105	F		H
S1-14-106	F		H

FIG. 6D

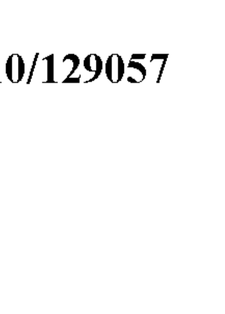
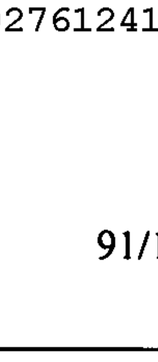
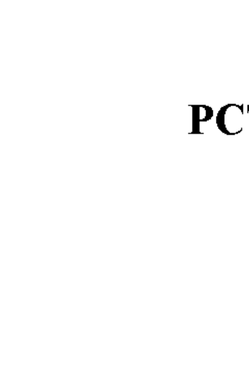
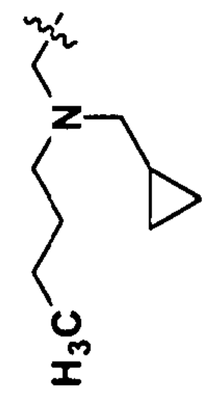
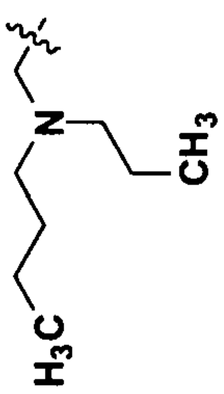
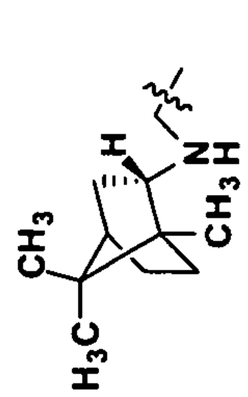
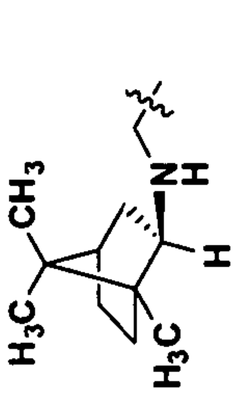
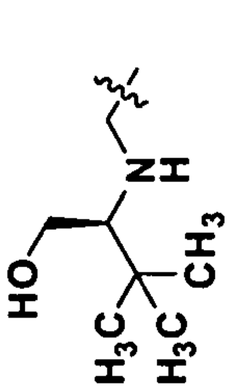
Cmpd	X	Y	Z
S1-14-13	F		H
S1-14-14	F		H
S1-14-15	F		H
S1-14-16	F		H
S1-14-17	F		H

FIG. 6E

Cmpd	X	Y	Z
S1-14-111	F		H
S1-14-112	F		H
S1-14-113	F		H
S1-14-114	F		H
S1-14-12	F		H

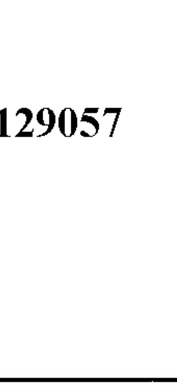
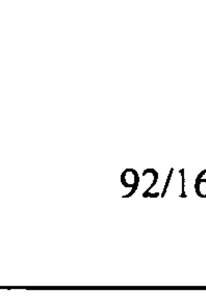
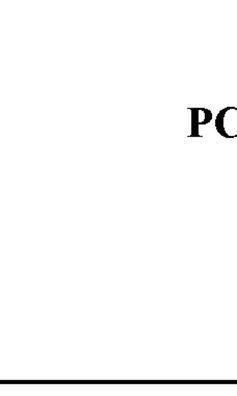
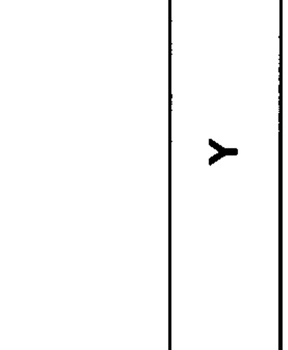
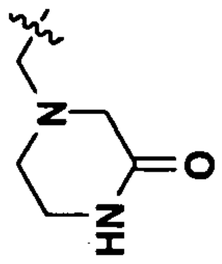
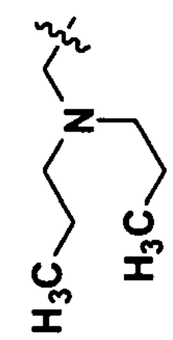
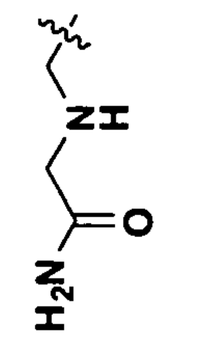
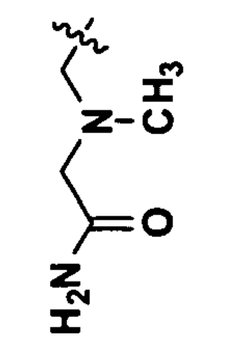
Cmpd	X	Y	Z
S1-14-25	F		H
S1-14-26	F		H
S1-14-27	F		H
S1-14-28	F		H
S1-14-29	F		H
S1-14-18	F		H
S1-14-19	F		H
S1-14-2	F		H
S1-14-22	F		H
S1-14-24	F		H

FIG. 6F

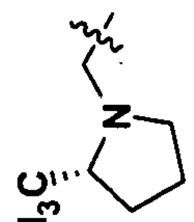
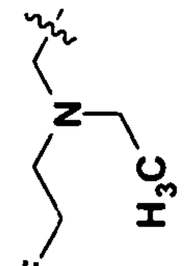
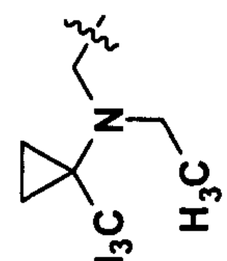
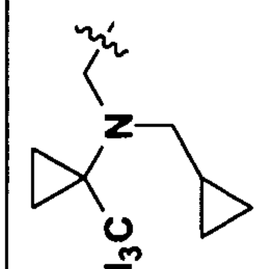
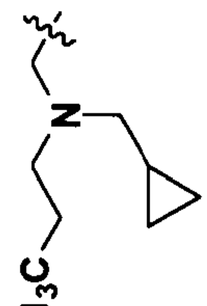
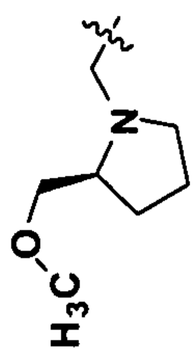
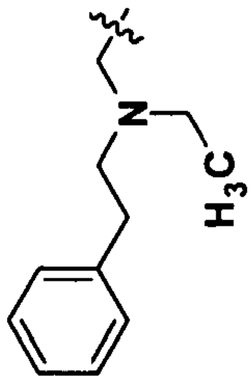
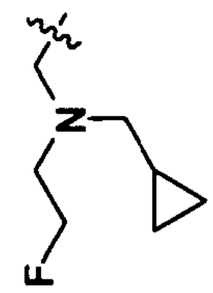
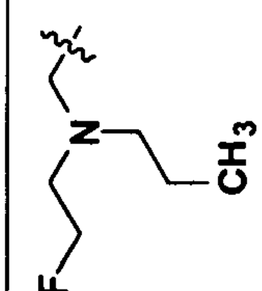
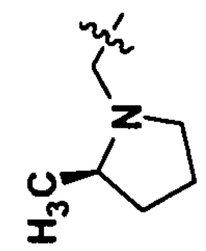
Cmpd	X	Y	Z
S1-14-34	F		H
S1-14-35	F		H
S1-14-36	F		H
S1-14-37	F		H
S1-14-38	F		H

FIG. 6G

Cmpd	X	Y	Z
S1-14-3	F		H
S1-14-30	F		H
S1-14-31	F		H
S1-14-32	F		H
S1-14-33	F		H

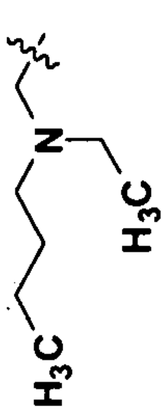
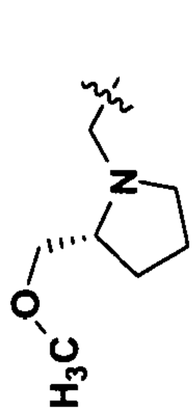
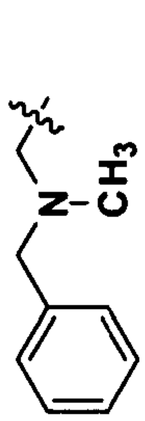
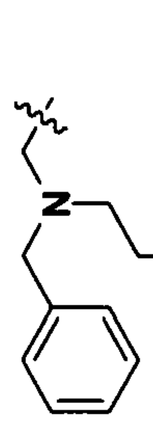
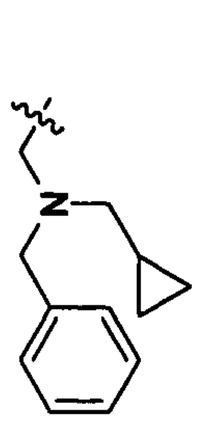
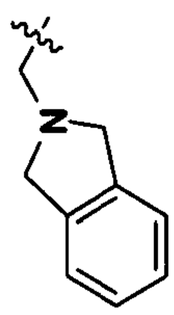
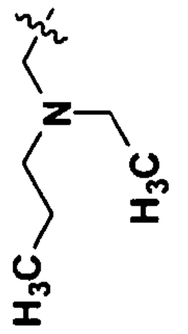
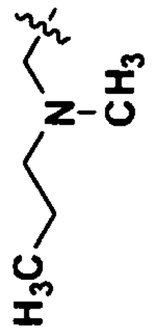
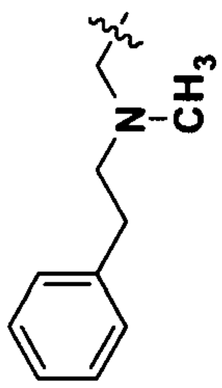
Cmpd	X	Y	Z
S1-14-44	F		H
S1-14-45	F		H
S1-14-46	F		H
S1-14-47	F		H
S1-14-48	F		H

FIG. 6H

Cmpd	X	Y	Z
S1-14-39	F		H
S1-14-40	F		H
S1-14-41	F		H
S1-14-42	F		H
S1-14-43	F		H

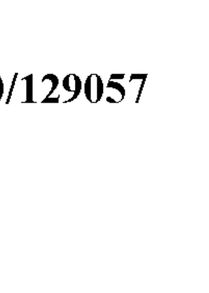
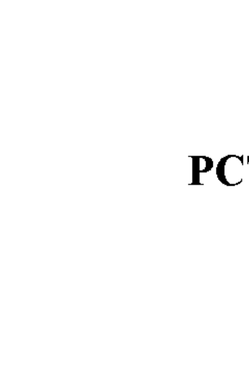
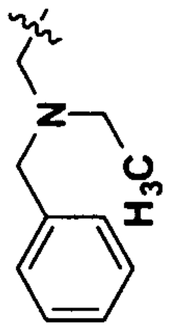
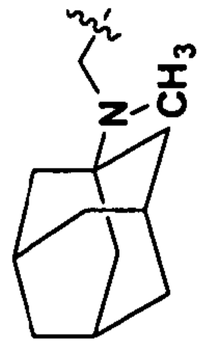
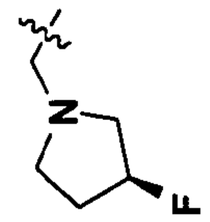
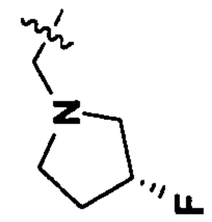
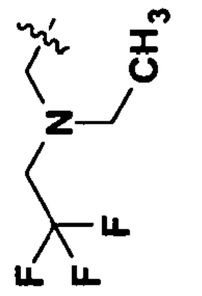
Cmpd	X	Y	Z
S1-14-53	F		H
S1-14-54	F		H
S1-14-55	F		H
S1-14-56	F		H
S1-14-57	F		H

FIG. 19

Cmpd	X	Y	Z
S1-14-49	F		H
S1-14-5	F		H
S1-14-50	F		H
S1-14-51	F		H
S1-14-52	F		H

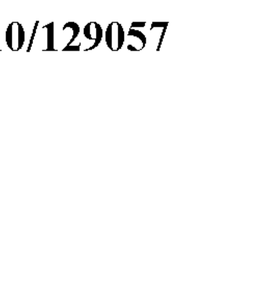
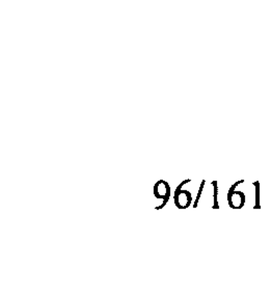
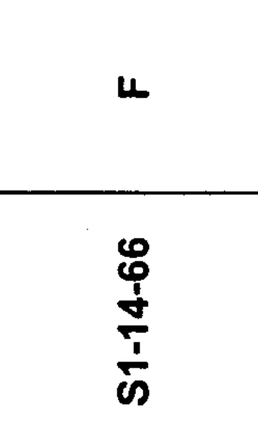
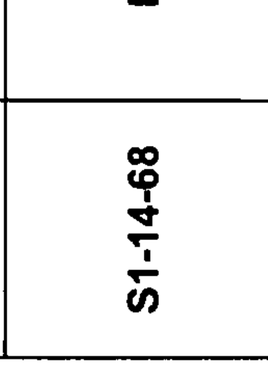
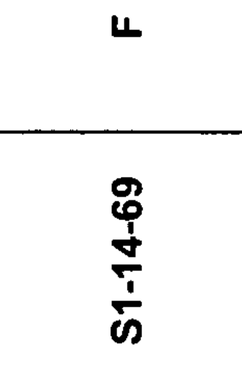
Cmpd	X	Y	Z
S1-14-66	F		H
S1-14-67	F		H
S1-14-68	F		H
S1-14-69	F		H
S1-14-7	F		H
S1-14-58	F		H
S1-14-59	F		H
S1-14-6	F		H
S1-14-60	F		H
S1-14-61	F		H

FIG. 6J

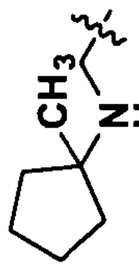
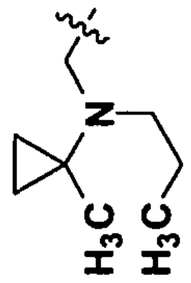
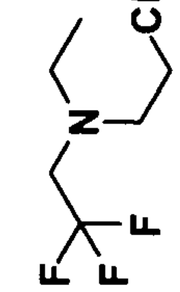
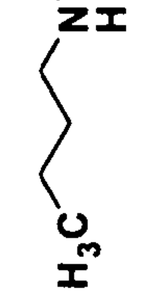
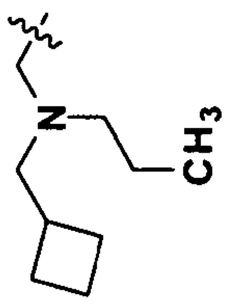
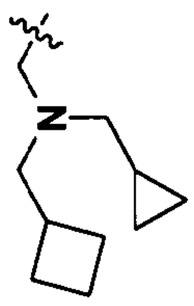
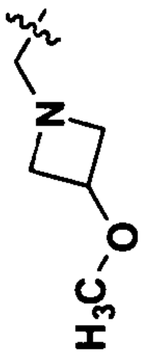
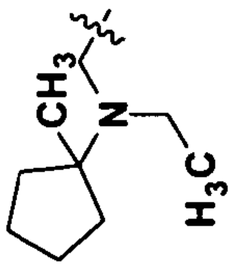
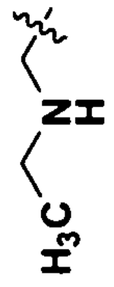
Cmpd	X	Y	Z
S1-14-75	F		H
S1-14-76	F		H
S1-14-77	F		H
S1-14-78	F		H
S1-14-79	F		H

FIG. 6K

Cmpd	X	Y	Z
S1-14-70	F		H
S1-14-71	F		H
S1-14-72	F		H
S1-14-73	F		H
S1-14-74	F		H

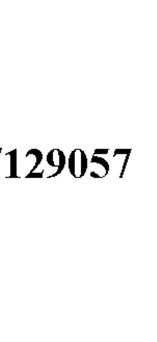
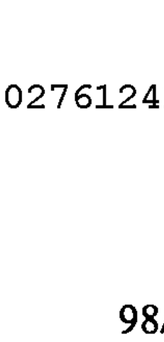
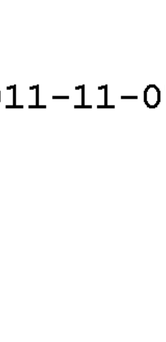
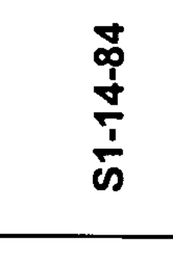
Cmpd	X	Y	Z
S1-14-84	F		H
S1-14-85	F		H
S1-14-86	F		H
S1-14-87	F		H
S1-14-88	F		H
S1-14-8	F		H
S1-14-80	F		H
S1-14-81	F		H
S1-14-82	F		H
S1-14-83	F		H

FIG. 6L

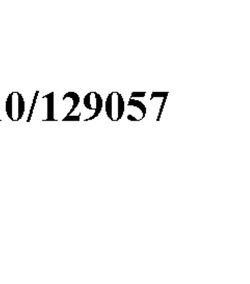
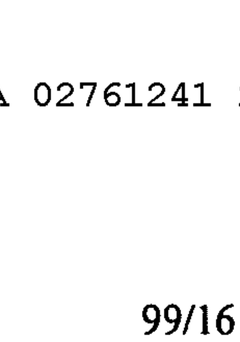
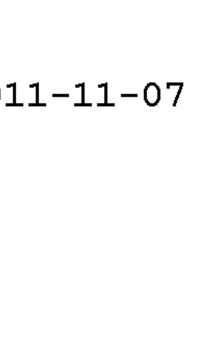
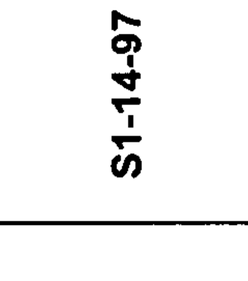
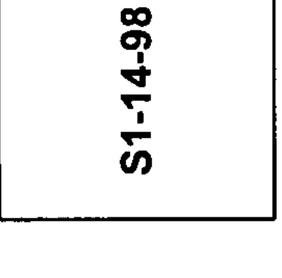
Cmpd	X	Y	Z
S1-14-94	F		H
S1-14-95	F		H
S1-14-96	F		H
S1-14-97	F		H
S1-14-98	F		H
S1-14-89	F		H
S1-14-90	F		H
S1-14-91	F		H
S1-14-92	F		H
S1-14-93	F		H

FIG. 6M

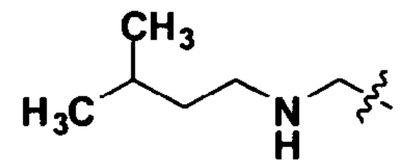
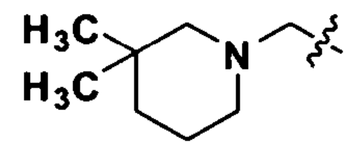
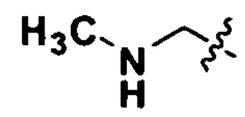
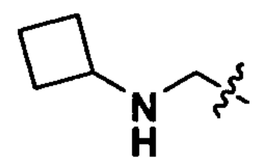
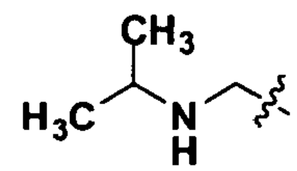
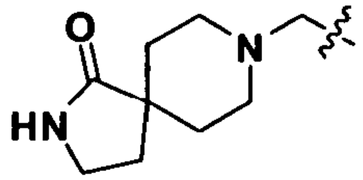
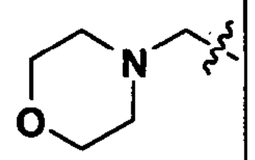
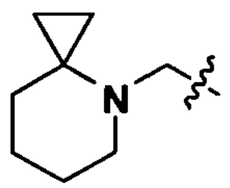
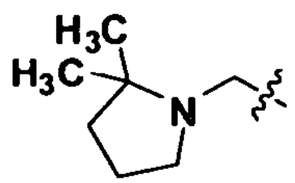
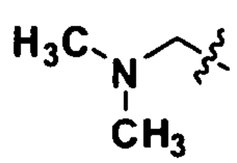
Cmpd	X	Y	Z
S2-4-15	F		H
S2-4-16	F		H
S2-4-17	F		H
S2-4-18	F		H
S2-4-2	F		H
S1-14-99	F		H
S2-4-10	F		Br
S2-4-11	F		H
S2-4-12	F		H
S2-4-13	F		H

FIG. 6N

SUBSTITUTE SHEET (RULE 26)

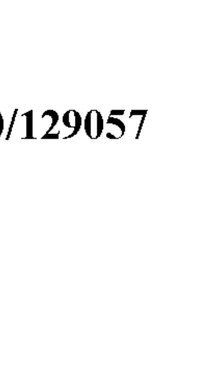
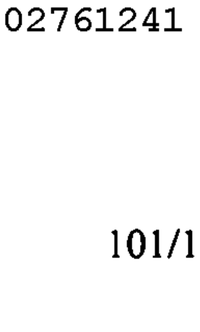
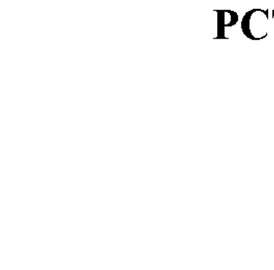
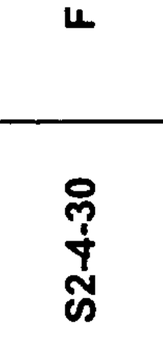
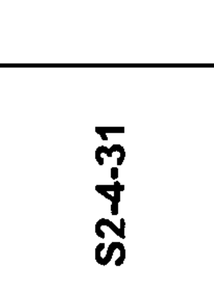
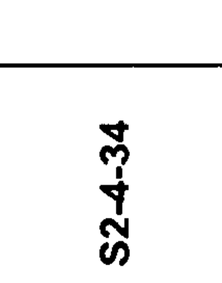
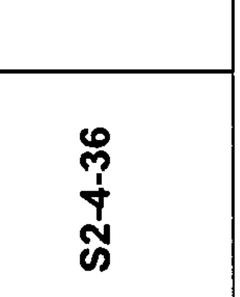
Cmpd	X	Y	Z
S2-4-30	F		H
S2-4-31	F		H
S2-4-34	F		H
S2-4-35	F		H
S2-4-36	F		H
S2-4-21	F		H
S2-4-24	F		H
S2-4-25	F		H
S2-4-26	F		H
S2-4-3	F		H

FIG. 60

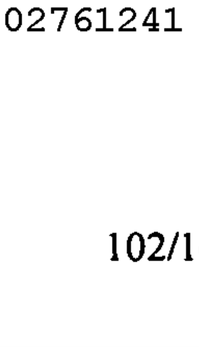
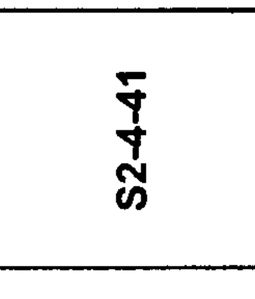
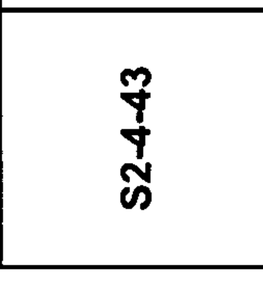
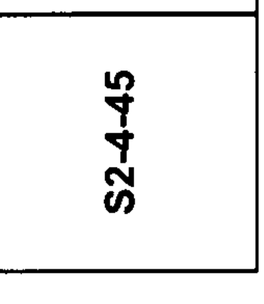
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S2-4-42	F		H
S2-4-43	F		H
S2-4-44	F		H
S2-4-45	F		H
S2-4-37	F		H
S2-4-38	F		H
S2-4-39	F		H
S2-4-4	F		H
S2-4-40	F		H

FIG. 6P

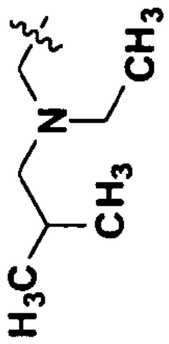
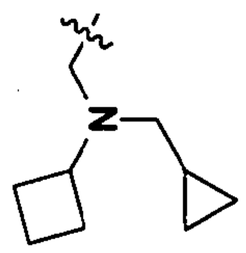
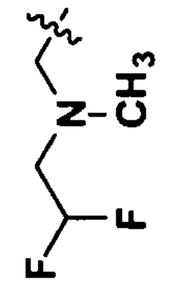
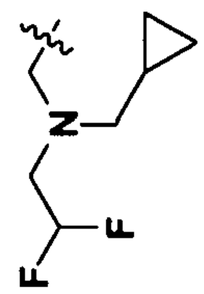
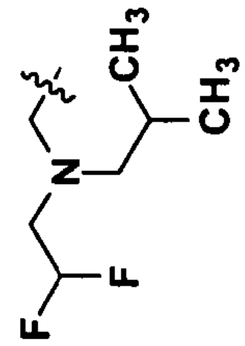
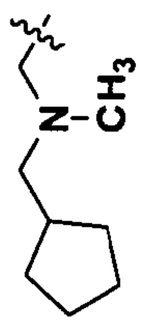
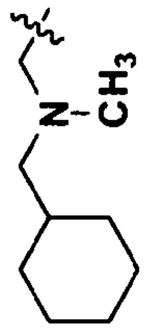
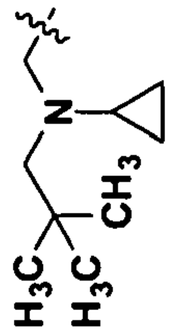
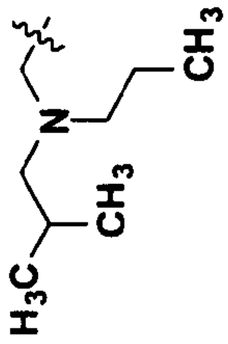
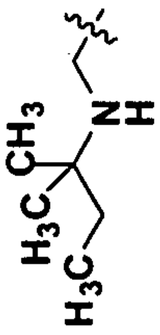
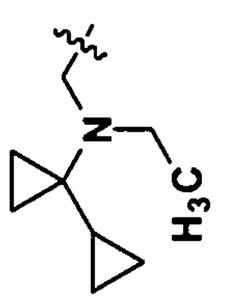
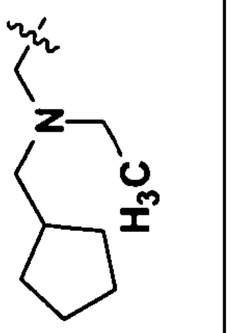
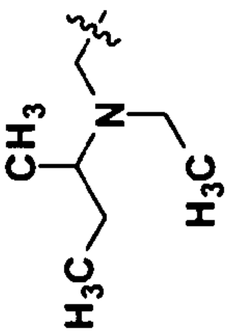
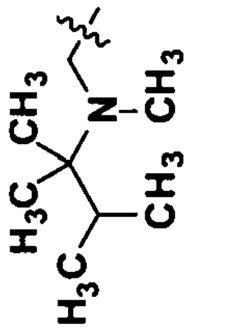
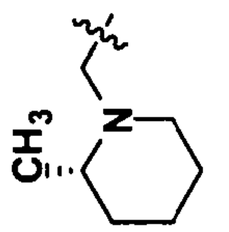
Cmpd	X	Y	Z
S2-4-50	F		H
S2-4-53	F		H
S2-4-54	F		H
S2-4-55	F		H
S2-4-56	F		H
S2-4-46	F		H
S2-4-47	F		H
S2-4-48	F		H
S2-4-49	F		H
S2-4-5	F		H

FIG. 6Q

Cmpd	X	Y	Z
S2-4-61	F		H
S2-4-62	F		H
S2-4-63	F		H
S2-4-64	F		H
S2-4-65	F		H

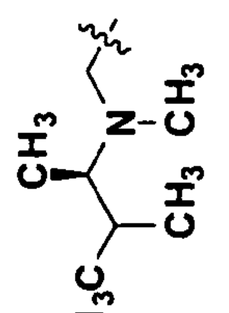
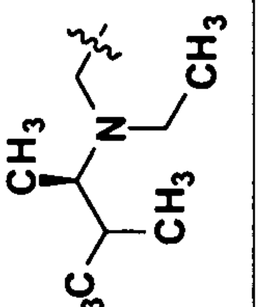
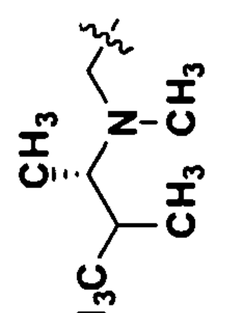
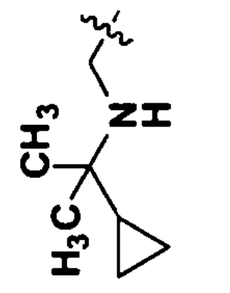
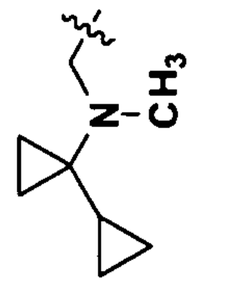
Cmpd	X	Y	Z
S2-4-57	F		H
S2-4-58	F		H
S2-4-59	F		H
S2-4-6	F		H
S2-4-60	F		H

FIG. 6R

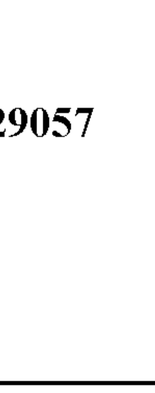
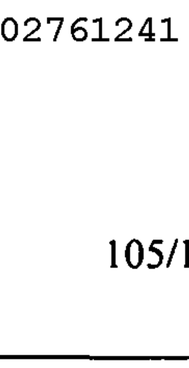
Cmpd	X	Y	Z
S3-5-2	F		H
S3-53	F		H
S3-5-4	F		H
S3-5-5	F		H
S3-5-6	F		H
S2-4-66	F		H
S2-4-67	F		H
S2-4-68	F		H
S2-4-9	F		H
S3-5-1	F	CH2OH	H

FIG. 6S

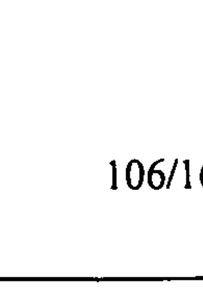
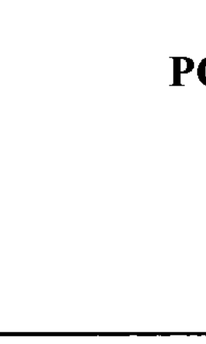
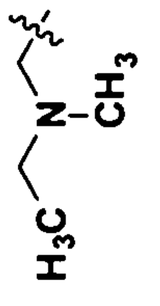
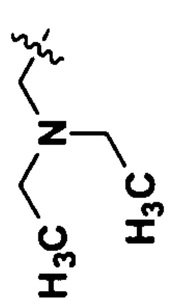
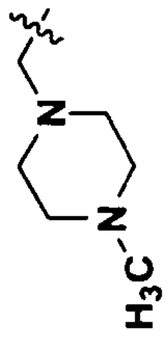
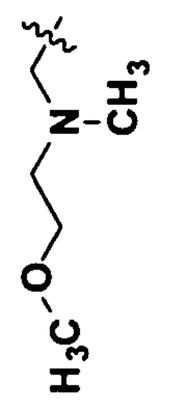
Cmpd	X	Y	Z
S4-5-6	F		H
S5-5-1	F		H
S6-4-1	F		H
S7-4-1	F		H
S7-4-10	F		H

FIG. 6T

Cmpd	X	Y	Z
S4-5-1	F		H
S4-5-2	F		H
S4-5-3	F		H
S4-5-4	F		H
S4-5-5	F		H

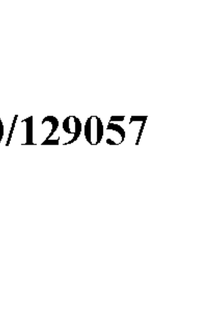
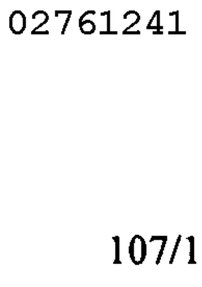
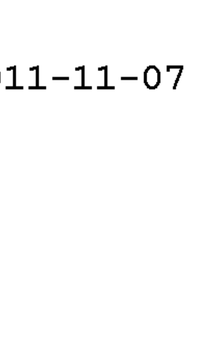
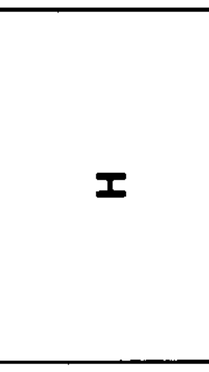
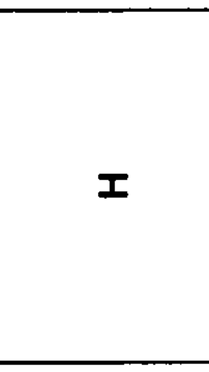
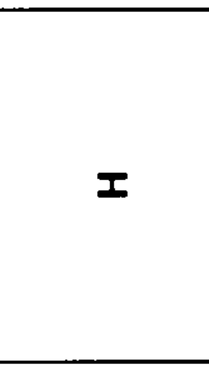
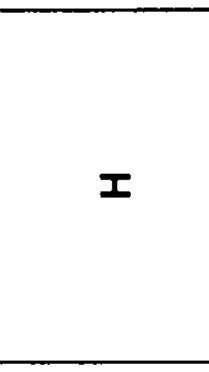
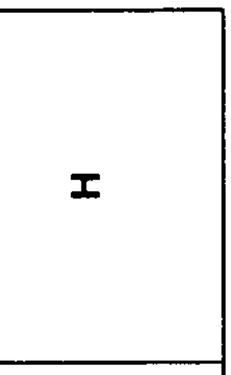
Cmpd	X	Y	Z
S7-4-6	F		H
S7-4-7	F		H
S7-4-8	F		H
S7-4-9	F		H
S8-4-1	F		H

FIG. 6U

Cmpd	X	Y	Z
S7-4-11	F		H
S7-4-12	F		H
S7-4-2	F		H
S7-4-4	F		H
S7-4-5	F		H

Cmpd	X	Y	Z
S12-5-3	F		F
S12-5-4	F		F
S14-10	F	CH3	NH_2
S14-8	F	CH3	H
S14-9	F	CH3	NO_2

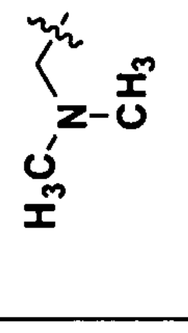
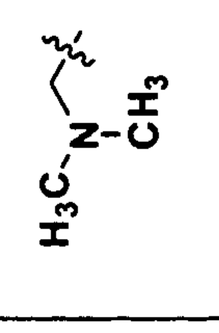
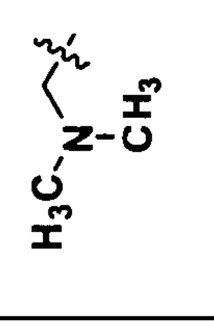
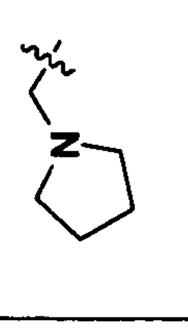
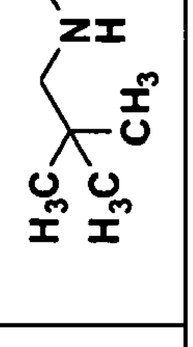
Cmpd	X	Y	Z
S9-4-1	F		CH_3
S10-10-5	F		$NHCH_2C(CH_3)_2$
S10-10-6	F		NH_2
S12-5-1	F		F
S12-5-2	F		F

FIG. 6V

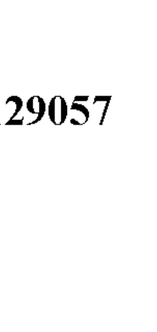
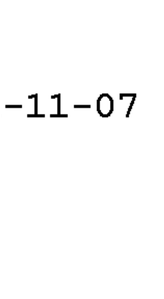
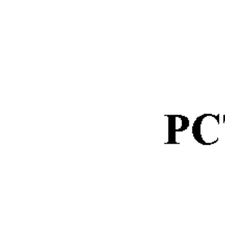
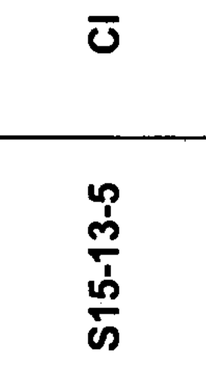
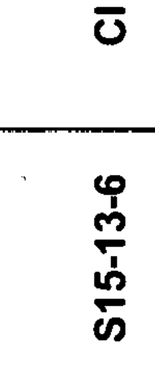
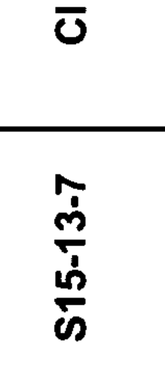
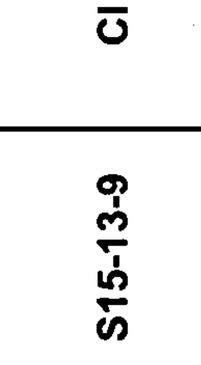
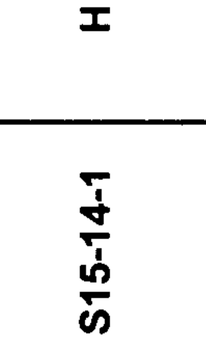
Cmpd	X	Y	Z
S15-13-5	Cl		H
S15-13-6	Cl		H
S15-13-7	Cl		H
S15-13-9	Cl		H
S15-14-1	H		H
S15-13-10	Cl		H
S15-13-11	Cl		H
S15-13-13	Cl		H
S15-13-14	Cl		H
S15-13-16	Cl		H

FIG. 6W

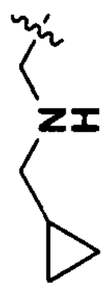
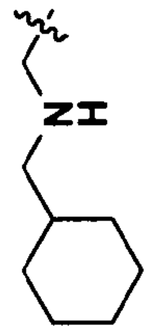
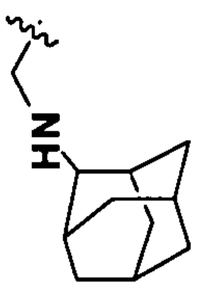
Cmpd	X	Y	Z
S16-10-14	$N(CH_3)_2$		H
S16-10-15	$N(CH_3)_2$		H
S16-10-16	$N(CH_3)_2$		H
S16-10-17	$N(CH_3)_2$		H
S16-10-18	$N(CH_3)_2$		H

FIG. 6X

Cmpd	X	Y	Z
S15-14-2	H	H_3C	H
S15-14-3	H		H
S15-14-4	H		H
S16-10-10	$N(CH_3)_2$		H
S16-10-12	$N(CH_3)_2$		H

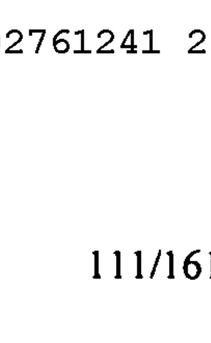
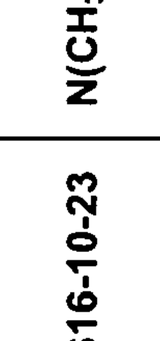
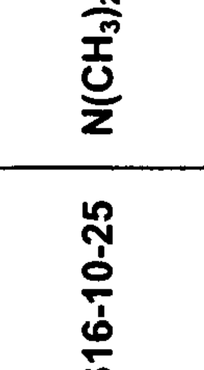
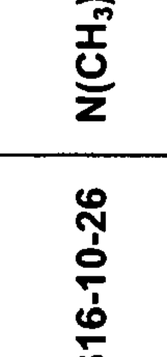
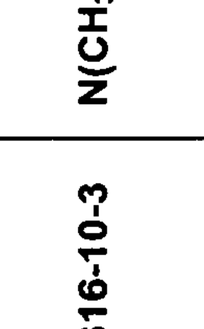
Cmpd	X	Y	Z
S16-10-23	$N(CH_3)_2$		H
S16-10-24	$N(CH_3)_2$		H
S16-10-25	$N(CH_3)_2$		H
S16-10-26	$N(CH_3)_2$		H
S16-10-3	$N(CH_3)_2$		H
S16-10-19	$N(CH_3)_2$		H
S16-10-2	$N(CH_3)_2$		H
S16-10-20	$N(CH_3)_2$		H
S16-10-21	$N(CH_3)_2$		H
S16-10-22	$N(CH_3)_2$		H

FIG. 6Y

Cmpd	X	Y	Z
S17-9-2	CN		H
S19-3	H	F	H
S19-4	NH_2	F	H
S19-5	H	F	NH_2
S21-11	H	N(CH3)2	H

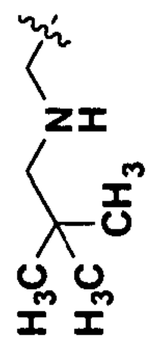
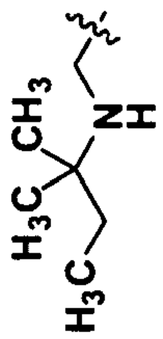
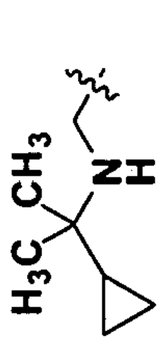
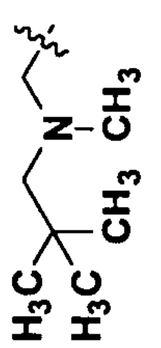
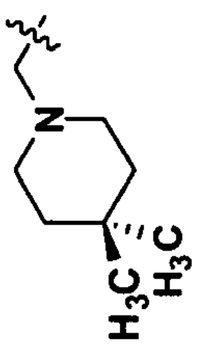
Cmpd	X	Y	Z
S16-10-5	$N(CH_3)_2$		H
S16-10-6	$N(CH_3)_2$		H
S16-10-7	$N(CH_3)_2$		H
S16-10-9	$N(CH_3)_2$		H
S17-9-1	CN		H

FIG. 6Z

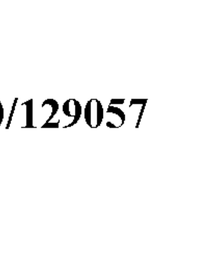
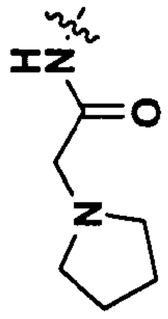
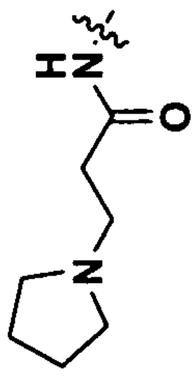
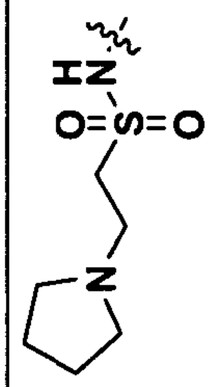
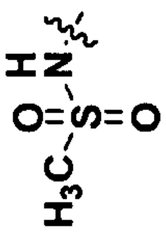
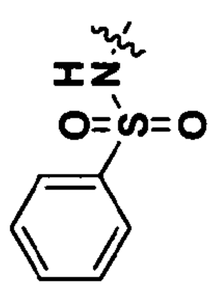
Cmpd	X	Y	Z
S21-12-6	H		H
S22-6	H		H
S22-8-1	H		H
S23-5-1	F		H
S7-4-3	F		H

FIG. 6AA

Cmpd	X	Y	Z
S21-12-1	H		H
S21-12-2	H		H
S21-12-3	H		H
S21-12-4	H		H
S21-12-5	H		H

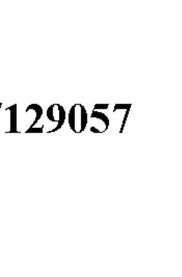
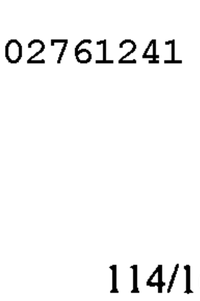
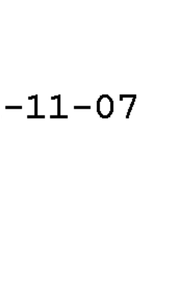
Cmpd	X	Y	Z
S1-14-62	F		H
S1-14-63	F		H
S1-14-64	F		H
S16-10-1	$N(CH_3)_2$		H
S16-10-11	$N(CH_3)_2$		H

FIG. 6BB

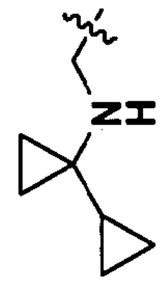
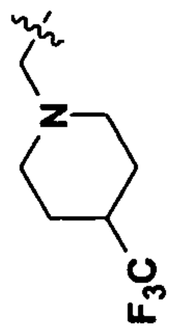
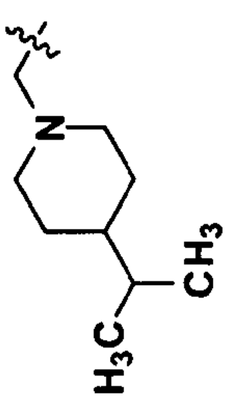
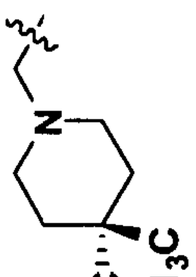
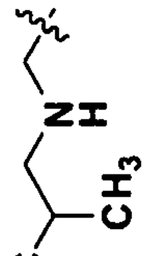
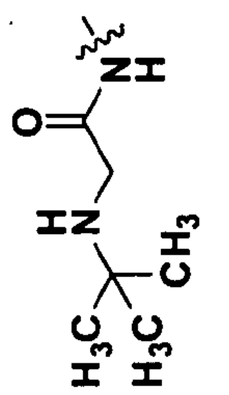
Cmpd	X	Y	Z
S11-4-1	F		CN
S21-10	H	NH2	H
S1-14-20	F		H
S1-14-21	F		H
S1-14-23	F		H

FIG. 6CC

Cmpd	X	Y	Z
S16-10-27	$N(CH_3)_2$		H
S16-10-4	$N(CH_3)_2$		H

Cmpd	X	Y	Z
S19-7-1		F	H

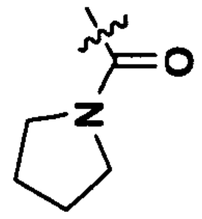
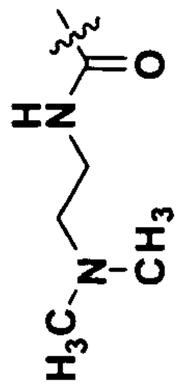
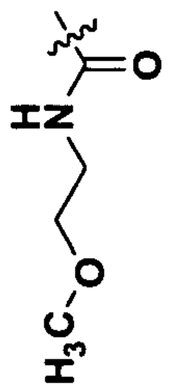
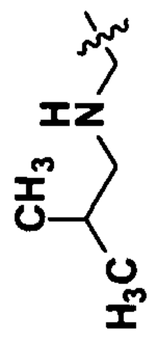
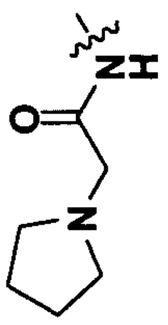
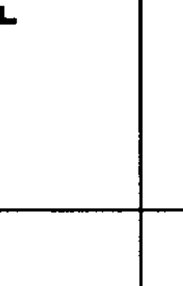
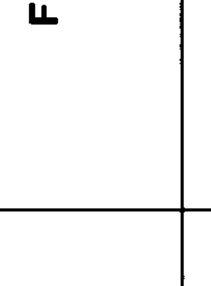
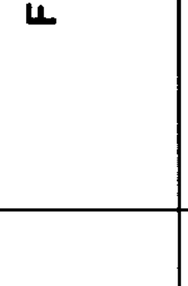
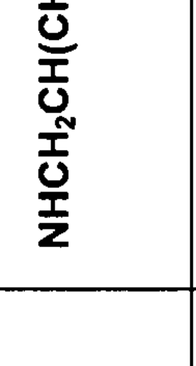
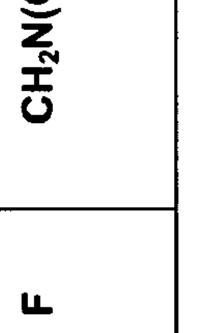
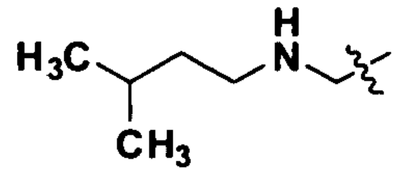
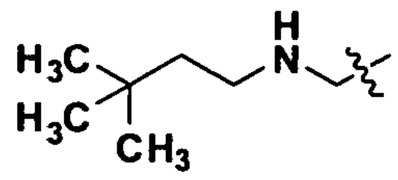
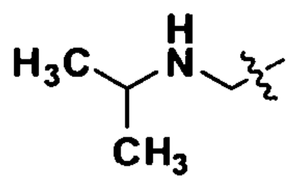
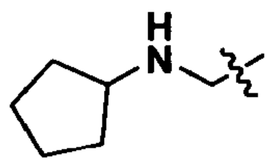
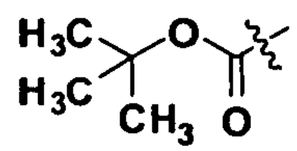
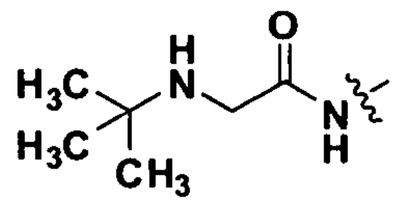
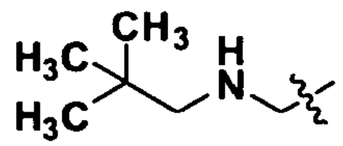
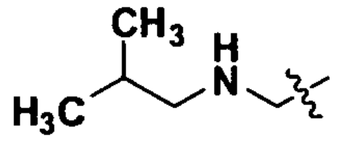
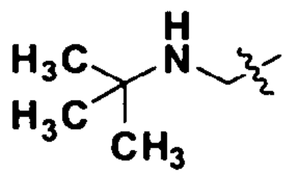
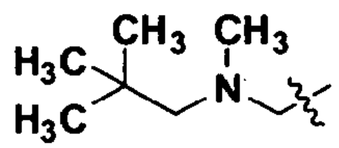
Cmpd	X	Y	Z
S18-9-2	H	F	
S18-9-3	H	F	
S18-9-4	H	F	
S20-10-9	H	$NHCH_2CH(CH_3)_2$	
S10-10-3	F	$CH_2N(CH_3)_2$	
S10-10-1	F	$CH_2N(CH_3)_2$	
S10-10-2	F	$CH_2N(CH_3)_2$	
S10-10-4	F	$CH_2N(CH_3)_2$	
S14-11	F	CH_3	
S18-9-1	H	F	

FIG. 6DD

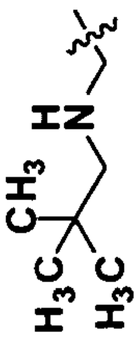
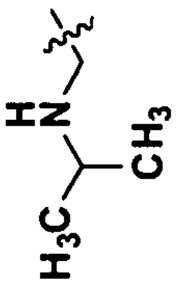
Cmpd	X	Y	Z
S20-10-5	H	F	
S20-10-6	H	F	
S20-10-7	H	F	
S20-10-8	H	F	
S18-7-1	H	F	

Cmpd	X	Y	Z
S19-6-1	H	F	
S19-8-1	H	F	
S20-10-2	H	F	
S20-10-3	H	F	
S20-10-4	H	F	

SUBSTITUTE SHEET (RULE 26)

FIG. 6EE

FIG. 6FF

Cmpd	X	Y	Z
S13-9-1	F	F	
S13-9-2	F	F	

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S1-14-1	B	B	C	B	B	B	A	B	B	B	C	A	A	B	B
S1-14-10	B	B	A	B	B	B	C	C	B	C	C	B	C	B	C
S1-14-100	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-101	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-102	C	C	C	B	C	C	B	C	B	C	C	B	C	C	C
S1-14-103	C	C	C	B	C	C	B	B	B	C	C	B	C	C	C
S1-14-104	C	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-105	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S1-14-106	B	B	B	B	B	B	A	B	B	B	B	B	C	C	C
S1-14-107	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-108	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S1-14-109	C	B	C	B	B	C	B	B	B	B	B	B	B	B	B
S1-14-11	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S1-14-110	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-111	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-112	C	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-113	B	B	B	B	B	B	B	B	B	B	B	B	C	B	B
S1-14-114	A	B	A	B	B	B	C	C	B	C	C	B	C	B	C
S1-14-12	B	B	C	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-13	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-14	B	B	A	B	B	B	C	B	C	C	C	B	C	C	C
S1-14-15	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S1-14-16	B	B	C	B	C	C	B	B	B	C	C	B	C	C	C
S1-14-17	C	B	C	B	B	C	B	B	B	C	C	B	C	C	C
S1-14-18	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-19	C	C	C	B	C	C	B	C	C	C	C	B	C	C	C
S1-14-2	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-20	B	B	B	NT	B	B	A	B	B	B	A	B	B	B	B
S1-14-21	B	B	B	NT	B	B	B	B	B	B	B	B	B	B	B
S1-14-22	C	C	C	B	C	C	C	C	B	C	C	B	C	C	C
S1-14-23	B	B	B	NT	B	B	B	B	B	B	B	B	B	B	B

FIG. 7A

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP153 tetA	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S1-14-24	C	B	C	B	C	C	B	C	C	C	C	C	B	C	C	C
S1-14-25	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-26	C	B	C	B	B	C	B	B	B	B	B	C	B	B	B	B
S1-14-27	B	B	B	B	B	B	A	B	B	B	B	A	B	B	B	A
S1-14-28	B	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-29	C	C	C	B	C	C	B	C	B	B	C	C	B	C	C	C
S1-14-3	B	B	C	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-30	B	B	B	B	B	B	B	B	B	B	B	B	B	C	B	B
S1-14-31	B	B	B	B	B	B	B	B	B	B	B	B	B	C	B	B
S1-14-32	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-33	B	B	C	B	B	B	A	B	B	B	B	A	B	A	B	B
S1-14-34	B	B	C	B	B	B	A	B	B	B	B	A	B	A	B	B
S1-14-35	B	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-36	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-37	B	B	A	B	B	B	C	B	B	B	C	C	B	C	B	B
S1-14-38	C	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-39	B	B	B	B	B	B	C	B	B	B	B	B	B	B	B	B
S1-14-4	B	B	B	A	B	B	A	B	B	B	B	A	B	B	B	B
S1-14-40	B	B	C	B	B	B	A	B	B	B	B	A	B	B	B	B
S1-14-41	B	B	C	B	B	B	A	B	B	B	B	A	B	B	B	B
S1-14-42	B	B	C	B	B	B	A	B	B	B	B	A	B	B	B	B
S1-14-43	B	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-44	B	B	B	B	B	B	A	B	B	B	B	A	B	B	B	B
S1-14-45	B	B	C	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-46	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-47	B	B	A	B	B	B	C	B	C	C	C	B	B	C	C	C
S1-14-48	B	B	B	B	B	B	C	B	C	C	C	C	B	C	C	C
S1-14-49	B	B	B	B	B	B	C	B	C	B	B	C	B	C	B	B
S1-14-5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-50	B	B	B	B	B	B	A	B	B	B	B	A	B	B	B	B
S1-14-51	B	B	B	B	B	B	A	B	B	B	B	A	B	B	B	B

FIG. 7B

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S1-14-52	C	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-53	C	C	B	B	B	B	C	B	C	C	C	B	C	C	C
S1-14-54	B	B	C	B	B	C	B	B	B	B	C	A	B	B	B
S1-14-55	B	B	C	B	B	B	A	B	B	B	B	B	A	B	B
S1-14-56	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S1-14-57	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-58	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-59	B	B	B	B	B	B	B	B	C	B	C	B	C	C	C
S1-14-6	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-60	B	B	B	B	B	B	B	B	B	B	B	B	C	B	B
S1-14-61	B	B	B	B	B	B	A	B	B	B	A	B	A	A	A
S1-14-62	B	B	B	NT	B	B	A	B	B	B	A	B	B	B	A
S1-14-63	B	B	A	NT	B	B	C	B	C	C	C	B	C	C	C
S1-14-64	C	B	B	NT	C	B	B	B	B	C	C	B	C	B	C
S1-14-65	B	B	B	A	B	B	A	B	B	B	A	B	B	B	B
S1-14-66	C	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-67	B	B	B	B	B	B	B	B	B	B	C	B	C	B	B
S1-14-68	B	B	B	B	B	B	B	B	B	B	C	B	C	B	B
S1-14-69	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-7	B	B	B	B	B	B	A	B	B	B	B	B	A	B	B
S1-14-70	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-71	B	B	B	B	B	B	C	B	B	B	C	B	C	B	B
S1-14-72	B	B	C	B	B	B	A	B	B	B	B	B	B	B	B
S1-14-73	B	B	A	B	B	B	A	B	B	B	A	B	B	B	B
S1-14-74	B	B	C	B	B	C	B	B	B	B	C	A	A	B	B
S1-14-75	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-76	B	B	A	B	B	B	C	B	B	B	C	B	C	B	C
S1-14-77	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S1-14-78	B	B	B	B	B	B	C	C	C	C	C	B	C	C	NT
S1-14-79	B	B	C	B	B	B	A	B	B	B	B	B	A	B	B
S1-14-8	B	B	C	B	B	B	A	B	B	B	A	B	B	B	B

FIG. 7C

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S1-14-80	B	B	C	B	B	B	A	B	B	B	A	B	A	B	B
S1-14-81	B	B	B	B	B	B	A	B	B	B	A	B	A	B	B
S1-14-82	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-83	B	B	C	B	B	C	B	B	B	B	B	B	B	B	B
S1-14-84	C	B	C	B	B	C	C	B	B	B	C	B	B	B	B
S1-14-85	C	C	C	B	C	C	B	B	B	B	C	B	B	B	B
S1-14-86	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-87	B	B	B	B	B	B	B	B	B	B	B	B	C	B	B
S1-14-88	B	B	B	B	B	B	C	C	B	C	C	B	C	C	C
S1-14-89	B	B	A	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-9	A	B	B	A	B	B	A	B	B	B	A	B	B	B	A
S1-14-90	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-91	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-92	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-93	B	B	A	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-94	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-95	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-96	C	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-97	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S1-14-98	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S1-14-99	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S2-4-1	B	B	B	A	B	B	A	B	B	B	A	B	B	B	A
S2-4-10	C	C	B	B	B	B	C	B	C	C	C	B	C	C	C
S2-4-11	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-12	A	B	B	B	B	B	A	B	B	A	A	B	B	B	A
S2-4-13	B	B	C	B	B	B	B	B	B	B	B	A	A	B	B
S2-4-14	B	B	C	A	B	B	A	B	B	B	A	B	A	B	B
S2-4-15	B	B	C	B	B	B	A	B	B	B	A	B	B	B	B
S2-4-16	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-17	C	B	C	B	B	C	B	B	B	C	C	B	B	B	B
S2-4-18	B	B	C	B	B	B	B	B	B	B	B	A	A	B	B

FIG. 7D

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S2-4-19	B	A	B	A	B	B	B	B	B	B	A	B	B	B	A
S2-4-2	B	B	C	B	B	C	B	B	B	B	C	A	B	B	B
S2-4-21	B	A	A	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-22	A	A	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-23	A	A	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-24	B	B	C	B	B	B	B	B	B	B	A	B	A	B	A
S2-4-25	B	B	B	B	B	B	A	B	B	A	A	B	A	B	A
S2-4-26	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-27	A	A	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-28	B	A	B	A	B	B	B	B	B	A	A	B	B	B	A
S2-4-29	A	A	B	A	B	B	A	B	B	B	A	B	B	B	A
S2-4-3	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S2-4-30	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S2-4-31	B	B	B	B	B	B	B	B	B	B	A	B	B	B	A
S2-4-32	B	B	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-33	B	A	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-34	B	B	B	B	B	B	C	C	B	C	C	B	C	B	C
S2-4-35	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S2-4-36	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S2-4-37	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S2-4-38	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S2-4-39	B	B	B	B	B	B	C	B	B	B	C	B	C	B	B
S2-4-4	B	B	B	B	B	B	B	B	B	B	B	B	A	B	B
S2-4-40	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S2-4-41	B	B	B	B	B	B	C	B	B	B	B	B	B	B	B
S2-4-42	B	B	B	B	B	B	C	B	B	B	B	B	B	B	B
S2-4-43	B	B	B	B	B	B	C	B	B	B	C	B	C	B	B
S2-4-44	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S2-4-45	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-46	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S2-4-47	B	B	B	B	B	B	C	B	B	B	B	B	B	B	B

FIG. 7E

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S2-4-48	C	B	B	B	B	B	C	C	B	B	C	B	C	C	C
S2-4-49	B	B	B	B	B	B	C	B	B	B	C	B	C	B	B
S2-4-5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S2-4-50	A	A	B	A	B	B	B	B	A	B	A	B	B	B	A
S2-4-50	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-51	B	A	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-52	B	B	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-53	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-54	B	B	B	B	B	B	B	B	B	B	C	B	C	C	C
S2-4-55	B	B	A	B	B	B	C	B	C	C	C	B	C	C	C
S2-4-56	B	B	B	B	B	B	C	C	C	C	C	B	C	C	C
S2-4-57	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-58	B	B	B	B	B	B	C	B	B	B	B	B	C	B	B
S2-4-59	C	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S2-4-6	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S2-4-60	B	B	A	B	B	B	C	B	B	B	B	B	B	B	B
S2-4-61	B	B	A	B	B	B	C	B	B	B	B	B	C	B	B
S2-4-62	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S2-4-63	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S2-4-64	C	C	B	B	B	B	C	B	B	B	C	B	C	B	B
S2-4-65	B	B	B	B	B	B	A	B	B	B	A	B	A	A	A
S2-4-66	B	A	B	B	B	B	A	B	B	B	A	B	B	B	A
S2-4-67	B	B	B	B	B	B	B	B	B	B	C	B	B	B	A
S2-4-68	C	B	B	B	B	B	B	B	C	C	C	B	C	C	C
S2-4-7	B	B	B	A	B	B	B	B	B	B	A	B	B	B	B
S2-4-8	B	B	B	A	B	B	B	B	B	B	A	B	A	A	A
S2-4-9	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S3-5-1	B	B	B	B	B	B	B	B	B	C	B	B	B	B	C
S3-5-2	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S3-53	B	B	C	B	B	C	A	B	B	B	B	B	B	B	B
S3-5-4	C	C	C	B	C	C	B	C	B	C	C	B	B	B	C

FIG. 7F

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S3-5-5	B	B	C	B	B	B	A	B	B	B	B	A	A	B	B
S3-5-6	C	C	C	B	C	C	C	C	B	B	C	B	B	C	B
S4-5-1	B	B	B	B	B	B	A	B	B	B	A	B	A	B	B
S4-5-2	B	B	C	B	B	B	B	B	B	B	B	A	A	B	B
S4-5-3	B	B	C	B	B	B	B	B	B	B	B	B	B	B	B
S4-5-4	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S4-5-5	B	B	C	B	B	C	B	B	B	B	B	B	B	B	B
S4-5-6	B	B	C	B	B	B	A	B	B	B	A	B	A	B	B
S5-5-1	B	B	B	B	B	B	B	B	B	B	A	B	B	B	A
S6-4-1	A	B	B	B	B	B	A	B	B	A	A	B	B	B	A
S7-4-1	B	B	C	B	C	C	B	C	B	C	C	B	C	C	C
S7-4-10	C	B	C	B	C	C	B	C	C	C	C	B	C	C	C
S7-4-11	B	B	C	B	C	C	B	B	B	C	C	B	C	C	C
S7-4-12	B	B	B	B	B	B	B	B	C	C	C	B	C	C	C
S7-4-2	C	B	B	B	C	C	B	B	C	C	C	B	C	C	C
S7-4-3	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C
S7-4-4	C	C	C	B	C	C	B	C	B	B	C	B	B	C	C
S7-4-5	B	B	C	B	C	C	B	C	B	C	C	B	C	C	C
S7-4-6	C	B	B	B	C	C	B	B	B	C	C	B	C	C	C
S7-4-7	B	B	C	B	C	C	B	C	B	C	C	B	C	C	C
S7-4-8	C	B	B	B	B	B	B	B	C	C	C	B	C	C	C
S7-4-9	C	B	B	B	B	B	C	B	C	C	C	B	C	C	C
S8-4-1	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S9-4-1	C	C	C	B	B	B	C	B	B	B	C	B	B	B	C
S10-10-1	C	C	C	NT	C	C	C	C	C	C	C	B	C	C	C
S10-10-2	C	C	C	NT	C	C	C	C	C	C	C	B	C	C	C
S10-10-3	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C
S10-10-4	C	C	C	NT	C	C	C	C	C	C	C	B	C	C	C
S10-10-5	C	C	C	B	B	B	C	B	B	B	C	B	C	C	B
S10-10-6	B	B	B	B	B	B	A	B	B	B	B	A	B	B	A
S11-4-1	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C

FIG. 7G

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S12-5-1	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S12-5-2	C	C	B	B	B	B	C	B	B	B	C	B	C	B	B
S12-5-3	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S12-5-4	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S13-9-1	B	B	B	B	B	A	B	B	B	B	C	B	B	B	B
S13-9-2	C	B	B	B	B	B	B	B	B	C	C	B	B	B	B
S14-10	A	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S14-11	C	C	C	C	B	B	C	B	B	B	C	B	C	C	B
S14-8	B	B	B	B	B	B	C	B	B	B	C	B	C	C	B
S14-9	C	C	B	B	B	B	C	C	C	B	C	B	C	C	B
S-15-13-1	B	B	B	A	B	B	A	B	B	B	A	B	B	B	B
S15-13-10	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S15-13-11	B	B	A	B	B	B	C	B	B	B	A	B	B	B	B
S15-13-13	C	C	B	B	B	B	C	B	C	C	C	B	C	C	B
S15-13-14	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S15-13-15	A	A	B	A	B	B	A	B	A	A	A	B	A	A	B
S15-13-16	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S15-13-2	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S15-13-3	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S15-13-4	B	A	B	A	B	B	A	B	B	A	A	B	B	A	B
S15-13-5	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S15-13-6	B	B	C	B	B	B	B	B	B	B	B	B	A	B	B
S15-13-7	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S15-13-8	B	B	B	A	B	B	A	B	A	B	A	B	A	A	B
S15-13-9	A	B	A	B	B	A	C	C	B	B	C	B	C	B	C
S15-14-1	C	B	C	B	B	C	B	B	B	B	B	B	B	B	B
S15-14-2	B	B	B	B	B	B	B	B	B	B	C	B	C	C	B
S15-14-3	C	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S15-14-4	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-1	C	C	C	NT	C	C	B	C	C	C	C	B	C	C	B
S16-10-10	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B

FIG. 7H

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S16-10-11	B	B	B	NT	B	B	B	B	B	A	B	B	B	B	A
S16-10-12	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-13	A	B	C	A	B	B	A	B	B	B	A	B	B	B	B
S16-10-14	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-15	B	B	B	B	B	B	A	B	B	B	B	B	B	B	B
S16-10-16	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S16-10-17	B	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S16-10-18	A	B	B	B	B	B	A	B	B	B	B	B	B	B	B
S16-10-19	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-2	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-20	B	B	C	B	B	C	A	B	B	B	A	B	B	B	B
S16-10-21	B	B	C	B	B	C	A	B	B	B	B	B	B	B	B
S16-10-22	B	B	C	B	B	C	B	B	B	B	C	B	B	B	A
S16-10-23	B	B	C	B	B	C	B	B	B	B	B	B	B	B	A
S16-10-24	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-25	B	B	B	B	B	B	C	B	B	B	C	B	C	B	B
S16-10-26	B	B	C	B	B	C	A	B	B	B	A	B	B	B	B
S16-10-27	B	B	B	NT	B	B	C	B	B	B	B	B	B	B	B
S16-10-3	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S16-10-4	C	C	C	NT	C	C	B	C	C	C	C	C	C	C	C
S16-10-5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S16-10-6	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S16-10-7	B	B	C	B	B	B	B	B	B	B	C	B	B	B	B
S16-10-9	A	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S17-9-1	C	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S17-9-2	B	B	C	B	B	B	A	B	B	B	B	B	B	B	B
S18-7-1	C	C	B	B	B	B	C	B	C	C	C	B	C	C	C
S18-9-1	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C
S18-9-2	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C
S18-9-3	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C
S18-9-4	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C

FIG. 7I

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S19-3	A	B	B	B	B	B	B	B	B	B	A	B	B	B	B
S19-4	B	B	B	B	B	B	B	B	B	C	B	B	B	B	C
S19-5	A	B	B	B	B	B	B	B	B	B	A	B	B	B	C
S19-6-1	C	C	C	B	B	B	C	B	B	C	C	B	B	B	C
S19-7-1	C	C	C	B	B	C	C	B	B	C	C	B	C	C	C
S19-7-2	A	A	B	A	B	B	B	B	B	B	A	B	B	B	B
S19-8-1	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S20-10-2	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S20-10-3	C	C	B	B	B	B	C	B	B	B	C	B	B	B	B
S20-10-4	C	C	B	B	B	B	C	B	B	B	C	B	C	B	B
S20-10-5	C	C	B	B	B	B	B	B	B	B	C	B	B	B	B
S20-10-6	C	C	B	B	B	B	B	B	B	B	C	B	B	B	B
S20-10-7	C	C	B	B	B	B	C	B	B	B	C	B	B	B	B
S20-10-8	C	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S20-10-9	C	C	B	C	B	B	C	B	C	C	C	B	C	C	C
S21-10	C	C	C	C	C	C	C	C	B	C	C	B	C	C	C
S21-11	C	C	B	B	B	B	C	C	C	C	C	B	C	C	C
S21-12-1	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S21-12-2	C	C	C	B	B	C	C	B	B	B	C	B	B	C	B
S21-12-3	C	C	C	B	C	C	C	C	C	C	C	B	C	C	C
S21-12-4	C	B	C	B	C	C	C	C	C	C	C	B	C	C	C
S21-12-5	C	B	B	B	B	B	C	B	C	C	C	B	C	C	C
S21-12-6	B	B	B	B	B	B	B	B	C	B	C	B	C	C	C
S22-6	B	B	C	B	C	C	B	B	B	C	C	B	B	B	C
S22-8-1	C	C	C	B	C	C	C	C	C	C	C	B	C	C	C
S23-5-1	C	B	B	B	B	B	C	C	C	C	C	B	C	C	C
Minocycline	0.0625	0.0625	8	0.0312	1	16	0.0156	2	0.5	8	0.0625	16	2	1	8
Sancycline	0.5	1		4	8	8	0.25	8	8	32	0.25	33	8	8	32
Tigecycline	0.0625	0.0625	0.125	0.0625	0.0312	0.0625	0.0156	0.0156	0.0312	0.5	0.25	8	0.25	0.125	1

FIG. 7J

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	KP153 tetA	KP109 13883	EC108 13047	EC107 25922	EC155 tetA	AB110 19606	PA111 27853
S15-13-181	B	A	C	A	B	B	A	B	B	A	A	B	B	A	B
S15-13-182	B	A	B	A	B	B	A	B	A	A	B	B	A	A	C
S15-13-183	A	B	A	B	B	B	C	C	C	C	C	B	C	C	C
S15-13-184	B	B	B	A	B	B	A	B	A	B	B	B	A	A	C
S15-13-185	B	B	B	A	B	B	A	B	B	B	B	B	B	A	B
S15-13-186	A	B	B	A	B	B	A	B	A	A	A	A	B	A	A
S15-13-187	A	C	C	A	B	B	A	A	B	A	A	B	B	A	A
S15-13-188	A	B	B	A	B	B	A	B	B	A	A	B	A	A	B
S15-13-189	A	B	B	A	B	B	A	B	B	A	A	B	A	A	B
S15-13-190	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C
S15-13-191	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C
S15-13-192	C	B	C	B	C	B	A	B	B	B	B	B	B	C	C
S15-13-193	B	B	B	B	B	B	B	B	B	B	B	B	B	A	B
S15-13-194	A	B	B	A	B	B	A	B	B	B	B	B	B	A	B
S15-13-195	B	B	C	A	B	B	A	B	B	B	B	B	B	A	B
S15-13-196	B	B	C	A	B	B	A	B	B	B	B	B	C	A	B
S15-13-197	B	B	B	B	B	B	A	B	B	B	B	B	B	A	B
S15-13-198	C	B	C	B	B	B	B	B	B	B	B	B	B	A	B
S15-13-199	A	B	A	B	B	A	C	C	C	C	C	B	B	A	B
S15-13-200	B	B	C	B	B	C	A	B	B	B	B	B	B	A	B
S15-13-201	B	B	A	B	B	B	C	C	C	C	C	B	C	C	C
S15-13-204	B	B	B	A	B	B	A	B	B	B	B	B	B	A	B
S15-13-205	B	B	B	B	B	B	B	C	B	B	B	B	C	B	C
S15-13-206	B	B	A	B	B	B	C	B	B	B	B	B	B	C	B
S15-13-207	B	B	A	B	B	B	C	B	B	B	B	B	B	C	B
S15-13-208	B	B	A	B	B	B	C	B	B	B	B	B	B	C	B
S15-13-209	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S15-13-210	B	B	B	B	B	B	B	B	B	B	B	B	B	A	B
S15-13-211	A	B	C	A	B	B	A	B	B	B	B	B	B	A	B
S15-13-212	B	B	B	B	B	B	C	C	B	B	B	B	B	C	C
S15-13-213	A	B	B	A	B	B	A	B	B	B	B	B	B	C	B
S15-13-214	B	B	B	A	B	B	A	B	B	B	B	B	B	A	C
S15-13-215	B	B	B	B	B	B	B	B	B	B	B	B	B	A	C

FIG. 8A

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP153 tetA	KP109 13883
S15-13-216	C	B	A	B	B	B	C	C	C	C	C	C	C	C	C
S15-13-217	B	B	B	B	B	B	C	B	B	B	C	C	C	C	C
S15-13-218	B	B	B	B	B	B	C	B	B	B	A	C	B	B	B
S15-13-219	B	B	B	B	B	C	C	B	B	B	C	C	C	C	B
S15-13-220	B	A	C	A	B	C	A	B	B	A	C	B	A	B	A
S15-13-221	B	B	B	B	B	B	B	B	B	B	A	C	B	B	B
S15-13-222	B	A	C	A	B	B	A	B	A	A	C	B	A	B	A
S15-13-226	B	B	B	A	B	B	A	B	B	B	A	B	B	A	B
S15-13-227	B	B	B	B	B	B	B	B	C	C	C	C	C	B	B
S15-14-8	C	B	C	B	NT	C	NT	B	B	C	NT	NT	NT	NT	NT
S24-9-1	B	B	C	B	B	C	A	B	B	B	B	B	A	B	B
S24-9-10	B	B	B	B	B	B	A	B	B	A	B	B	A	B	B
S24-9-11	B	B	C	B	B	C	B	B	B	B	C	A	B	B	B
S24-9-12	B	B	B	B	B	B	A	B	B	B	C	B	B	B	B
S24-9-13	B	B	C	B	B	B	B	B	B	B	C	B	B	B	B
S24-9-14	B	B	C	B	B	C	B	B	B	B	C	A	B	B	B
S24-9-15	A	B	C	A	B	C	A	B	B	B	A	B	B	B	B
S24-9-16	B	B	C	B	B	B	A	B	B	B	A	C	B	B	B
S24-9-17	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S24-9-18	B	B	B	B	B	B	B	B	B	B	C	B	B	B	B
S24-9-19	B	B	B	B	B	B	A	B	B	A	A	B	B	B	B
S24-9-20	B	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S24-9-21	B	B	B	B	B	B	A	B	B	A	B	B	B	B	B
S24-9-24	B	B	C	B	B	C	A	B	B	B	A	C	B	B	B
S24-9-3	C	B	C	A	B	B	A	B	B	B	C	C	B	B	B
S24-9-4	C	B	C	B	B	C	A	B	B	B	C	B	A	B	B
S24-9-5	B	B	B	B	B	B	A	B	B	B	A	B	B	B	B
S24-9-6	B	B	C	B	B	C	A	B	B	B	A	B	A	B	B
S24-9-7	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S24-9-8	B	B	C	B	B	B	B	B	B	B	C	B	B	B	B
S24-9-9	B	B	B	B	B	B	A	B	B	B	A	C	B	B	B
S25-11-208	A	B	C	A	B	C	A	B	B	B	A	B	A	B	B
S27-9-1	C	B	C	B	B	C	B	B	B	B	A	C	B	B	B

FIG. 8B

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S27-9-2	C	B	C	B	B	B	A	B	B	B	A	C	B	B	B
S27-9-4	C	B	B	B	B	B	B	B	B	B	A	C	B	B	B
S33-8-1	C	B	C	B	B	B	A	B	B	B	C	C	B	B	B
S33-8-2	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C
S33-8-3	C	B	C	B	B	C	B	B	B	B	C	C	B	B	B
S6-4-2	C	B	C	B	C	C	B	C	B	C	C	C	C	C	C
Sancycline	0.5	1		4	8	8	0.25	8	8	32	0.25	33	8	8	32
Minocycline	0.063	0.063	8	0.031	1	16	0.016	2	0.5	8	0.063	16	2	1	8
Tigecycline	0.063	0.063	0.125	0.063	0.03	0.063	0.016	0.016	0.03	0.5	0.25	8	0.25	0.125	1

FIG. 8C

SUBSTITUTE SHEET (RULE 26)

Compound	SA101 29213	SA100 13709	SA161 MRSA, tetM	SA158 tetK	EF103 29212	EF159 tetM	SP106 49619	SP160 tetM	EC107 25922	EC155 tetA	AB110 19606	PA111 27853	EC108 13047	KP109 13883	KP153 tetA
S1-14-115	C	C	C	B	C	C	C	C	B	B	C	C	C	C	B
S1-14-116	C	C	C	B	C	C	B	C	C	C	C	C	C	C	C
S1-14-117	B	B	C	B	B	C	A	B	C	B	A	B	B	B	B
S1-14-118	C	B	B	B	B	B	C	C	B	B	C	C	C	B	C
S1-14-119	C	C	C	B	C	C	C	C	C	B	C	C	C	C	B
S1-14-120	C	B	C	A	B	B	A	B	B	B	A	B	B	B	A
S1-14-121	C	B	C	B	B	C	B	B	B	B	C	C	B	B	B
S1-14-122	C	B	B	B	B	B	B	B	B	B	B	B	B	B	B
S1-14-123	C	B	C	B	B	C	B	B	B	B	C	B	B	B	B
S1-14-124	C	B	C	B	B	C	A	B	B	B	C	B	A	B	B
S1-14-125	C	B	B	A	B	B	A	B	B	B	A	C	B	A	B
S1-14-126	C	B	B	B	B	B	B	B	B	B	C	C	B	B	B
S1-14-127	B	B	B	B	B	B	B	B	B	B	B	C	B	B	B
S1-14-128	C	B	B	A	B	B	A	B	B	B	A	B	B	B	B
S1-14-129	C	B	C	B	B	B	B	C	C	C	C	C	C	C	B
S1-14-131	C	B	B	B	B	C	B	B	B	B	C	B	B	B	B
S1-14-132	C	B	C	B	B	B	A	B	B	B	A	C	B	B	B
S1-14-135	B	B	B	B	B	B	B	B	B	B	A	C	B	B	B
S1-14-137	C	B	C	B	B	C	B	B	B	B	C	C	B	B	B
S114-138	B	B	C	B	B	C	A	B	B	C	C	B	B	B	B
S114-139	B	B	C	B	B	C	A	B	B	B	C	B	B	B	B
S1-14-140	C	B	C	B	B	C	B	B	B	B	C	C	C	B	B
S1-14-141	C	B	C	B	B	B	C	B	B	B	C	C	C	B	B
S1-14-142	C	B	C	B	B	B	B	B	C	B	B	C	C	B	B
S1-14-143	C	B	C	B	C	B	C	B	C	C	C	C	C	B	B
S1-14-144	C	B	C	B	B	C	A	B	B	B	A	C	B	C	B
S1-14-145	C	B	C	B	B	B	A	B	B	B	A	C	B	B	B
S1-14-146	C	B	B	B	B	B	C	C	C	C	C	C	C	B	B
S1-14-147	B	B	C	B	B	C	A	B	B	C	A	C	B	C	B
S1-14-148	B	B	C	B	B	B	A	B	B	B	A	C	B	B	B
S1-14-149	C	B	C	B	B	C	A	B	B	B	A	C	B	B	B
S15-13-180	B	B	B	B	B	B	B	B	B	B	A	C	B	B	B

FIG. 8D

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	BC2 40	SM2 56	AB2 50
S1-14-130	C	B	C	B	A	C	A	B	B	A	B	B	B	B	B	B	C	A	C	C	A
S1-14-133	B	B	C	B	A	B	NT	C	B	NT	B	B	B	C	NT	B	A	A	C	C	A
S1-14-134	B	B	B	B	A	B	NT	B	B	A	B	B	B	B	NT	B	C	C	A	A	C
S1-14-136	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-116	C	B	B	B	A	B	B	C	B	C	C	B	B	C	C	B	C	C	C	C	C
S15-13-117	B	B	B	B	A	B	A	B	A	A	A	B	B	B	B	B	C	B	C	C	A
S15-13-118	C	B	B	B	B	B	C	C	C	C	C	C	B	C	C	C	C	C	C	C	C
S15-13-119	C	B	B	B	A	B	A	B	B	A	A	B	B	B	A	B	C	A	C	C	A
S15-13-120	B	B	B	B	A	C	A	B	A	A	A	B	B	C	A	A	B	A	C	C	A
S15-13-123	C	C	B	B	B	B	B	B	B	C	C	B	B	C	C	C	C	C	C	C	C
S15-13-124	C	C	B	B	B	B	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C
S15-13-125	B	B	B	B	A	C	A	B	A	A	B	B	C	B	C	B	C	A	C	C	C
S15-13-126	C	C	B	B	B	B	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C
S15-13-127	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-128	C	C	B	B	B	B	B	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S15-13-131	C	B	B	B	A	B	A	B	A	A	A	B	B	B	B	B	C	A	C	C	A
S15-13-132	C	C	B	B	A	B	B	C	B	C	C	B	B	B	C	C	C	C	C	C	C
S15-13-168	C	B	C	B	A	B	A	B	A	A	A	B	B	B	C	B	C	A	C	C	A
S15-13-169	C	B	B	B	A	B	A	B	B	A	C	B	B	B	C	C	C	A	C	C	A
S15-13-17	B	B	B	A	A	B	B	B	B	C	B	B	B	C	NT	B	C	A	C	C	A
S15-13-174	C	B	B	B	B	C	A	B	B	A	B	B	C	C	C	B	C	B	C	C	A
S15-13-175	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-177	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-178	C	B	C	B	A	B	A	B	A	C	B	B	B	B	C	C	C	B	C	C	A

FIG. 9A

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S15-13-18	B	B	B	B	A	B	B	B	A	A	B	B	B	B	A	A	B	A	A	NT	A
S15-13-19	B	B	C	C	A	B	B	B	A	A	B	B	B	B	A	A	A	A	A	NT	B
S15-13-20	B	B	C	B	A	B	B	B	A	A	B	B	B	B	A	A	A	A	A	NT	B
S15-13-202	B	B	B	B	A	B	B	B	B	C	B	B	B	B	B	C	C	A	A	C	C
S15-13-203	B	B	B	B	A	B	B	B	B	A	B	B	B	A	NT	A	C	A	A	A	A
S15-13-21	C	C	C	B	B	C	A	C	B	A	C	B	C	C	C	C	C	A	C	C	C
S15-13-22	C	C	C	B	B	C	A	C	B	A	C	B	C	C	C	C	C	A	C	C	C
S15-13-223	B	B	B	A	A	B	B	B	A	A	B	A	A	A	A	B	B	A	A	A	C
S15-13-224	B	B	B	B	A	B	B	B	B	A	B	B	B	A	B	B	C	A	A	C	C
S15-13-225	B	B	B	B	A	B	B	B	A	A	B	B	B	A	B	B	C	A	A	NT	C
S15-13-228	C	C	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-229	C	C	C	B	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-23	B	B	B	A	A	B	A	B	B	C	A	B	B	B	B	B	C	A	A	C	A
S15-13-230	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	NT	C
S15-13-24	C	B	B	B	A	B	A	B	B	A	C	B	B	B	C	C	C	A	A	C	C
S15-13-25	C	B	B	B	B	B	B	B	B	C	C	C	B	C	C	C	C	C	C	C	B
S15-13-26	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NT
S15-13-27	C	C	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-28	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-29	B	B	B	A	A	B	A	B	A	A	A	B	B	B	C	B	C	A	A	C	B
S15-13-31	C	C	B	B	B	B	B	B	C	C	C	B	B	B	C	C	C	C	C	C	C
S15-13-32	C	C	B	B	B	B	C	C	C	C	C	B	B	B	C	C	C	C	C	C	C
S15-13-34	C	B	B	B	A	B	B	B	B	A	B	B	B	B	B	B	C	A	A	C	B
S15-13-35	C	B	C	A	A	B	A	B	B	A	A	B	B	B	A	A	C	A	A	C	A

FIG. 9B

SUBSTITUTE SHEET (RULE 26)

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S15-13-36	C	B	C	B	A	C	A	B	A	A	A	B	C	B	B	A	C	A	A	C	C
S15-13-37	C	B	C	B	A	B	A	B	B	A	B	B	B	B	C	C	C	B	A	C	C
S15-13-38	C	B	B	B	B	B	B	C	C	C	C	B	B	B	C	C	C	C	A	C	C
S15-13-39	C	B	B	B	B	B	B	C	C	C	C	B	B	C	C	C	C	C	C	C	C
S15-13-40	C	NT	B	B	B	B	B	B	NT	C	C	B	B	B	C	B	NT	NT	C	C	A
S15-13-41	C	NT	C	B	B	C	B	C	NT	A	C	B	C	C	C	B	NT	NT	C	C	C
S15-13-42	B	NT	B	A	A	B	A	B	NT	A	A	B	B	B	B	B	NT	NT	A	C	B
S15-13-43	C	NT	C	A	A	B	A	B	NT	A	A	B	B	B	A	B	NT	NT	A	C	B
S15-13-44	B	NT	C	B	A	C	A	B	NT	A	A	B	B	B	B	A	NT	NT	A	C	C
S15-13-45	C	NT	B	B	B	B	C	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S15-13-46	C	NT	C	C	B	B	C	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S15-13-47	C	NT	B	B	B	B	C	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S15-13-48	C	NT	C	C	B	B	C	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S15-13-81	B	B	C	A	A	B	A	B	A	A	A	B	B	B	A	A	B	A	A	C	A
S15-13-82	B	A	C	A	A	B	A	B	A	A	A	A	B	B	A	B	B	A	A	C	A
S15-13-83	C	C	C	B	A	B	B	B	B	C	C	B	B	B	C	C	C	C	C	C	B
S15-13-84	C	C	C	B	A	C	A	B	B	C	B	B	B	B	C	C	C	A	A	C	C
S15-13-87	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-14-6	C	B	C	B	A	C	A	B	B	A	C	B	B	B	A	A	C	A	C	C	C
S16-10-101	B	B	C	B	A	C	A	B	A	A	C	B	B	B	B	B	C	A	A	C	C
S16-10-102	B	B	C	B	A	C	B	B	B	A	B	B	B	B	NT	B	C	A	C	C	C
S16-10-106	C	B	C	B	A	C	A	B	B	A	B	B	B	B	B	B	C	A	C	C	C
S16-10-107	C	B	C	B	A	C	A	B	B	A	B	B	A	A	B	B	C	A	A	C	C
S16-10-110	C	B	C	B	A	C	B	B	B	A	B	B	B	B	B	B	C	A	C	C	C

FIG. 9C

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S16-10-116	C	B	C	B	A	C	A	B	B	A	C	B	C	C	B	B	C	A	A	C	C
S16-10-117	B	B	B	B	A	B	NT	B	B	NT	B	B	B	B	NT	B	B	A	C	C	B
S16-10-119	C	B	C	B	A	B	A	B	B	C	B	B	B	B	B	B	C	A	C	C	C
S16-10-120	B	B	C	B	A	B	NT	B	B	NT	B	B	B	B	NT	B	C	A	C	C	C
S16-10-121	C	B	C	B	A	C	A	B	B	C	C	B	B	B	C	C	C	A	A	C	C
S16-10-123	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-126	B	B	B	B	A	B	A	B	A	C	A	B	B	B	C	C	C	A	C	C	C
S16-10-129	C	B	C	B	A	C	A	B	B	A	B	B	B	B	B	B	C	A	C	C	C
S16-10-132	B	B	B	A	A	C	A	B	A	A	B	B	B	B	B	B	C	A	A	C	B
S16-10-135	B	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	A	A	C	C
S16-10-136	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	B	C	C	C
S16-10-138	C	B	B	B	A	B	A	B	A	C	C	B	B	B	C	C	C	A	C	C	C
S16-10-139	B	B	C	B	A	C	NT	B	B	NT	B	B	B	B	NT	B	C	A	C	C	C
S16-10-143	C	B	C	B	A	C	A	B	B	A	B	B	B	B	B	A	C	A	A	C	C
S16-10-144	B	B	C	NT	A	C	B	B	B	A	B	B	B	B	NT	B	C	A	A	C	C
S16-10-145	B	B	C	B	A	C	NT	B	B	NT	B	B	B	B	NT	A	B	A	A	C	C
S16-10-146	C	B	C	B	B	C	B	B	B	C	C	B	B	B	NT	C	C	A	C	C	C
S16-10-147	C	B	C	B	A	C	B	B	B	A	C	B	B	B	B	B	C	A	C	C	C
S16-10-148	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S16-10-149	B	B	C	B	A	C	NT	B	B	A	B	B	B	B	NT	B	C	A	C	C	C
S16-10-150	C	B	C	B	A	C	NT	B	B	NT	C	B	B	B	NT	C	C	A	C	C	C
S16-10-151	B	A	C	A	A	C	A	B	A	A	A	B	B	B	B	B	C	A	A	A	C
S16-10-152	B	B	C	B	A	C	A	B	A	A	A	B	B	B	B	B	C	A	A	A	C
S16-10-153	C	C	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	A	C	C

FIG. 9D

SUBSTITUTE SHEET (RULE 26)

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S16-10-154	C	B	C	B	A	B	B	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-155	C	B	C	B	A	C	B	B	B	C	C	B	B	B	C	C	C	A	C	C	C
S16-10-156	C	B	C	B	B	C	B	B	B	C	C	B	C	B	C	C	C	A	C	C	C
S16-10-157	C	B	C	B	B	C	B	B	B	C	C	B	C	C	C	C	C	A	C	C	C
S16-10-158	C	B	C	B	A	C	A	B	A	A	A	B	B	A	C	B	C	A	A	C	C
S16-10-159	C	B	C	B	A	C	B	B	B	C	B	B	B	B	NT	B	C	A	A	C	C
S16-10-160	B	B	B	B	A	B	B	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-161	B	B	C	NT	A	C	B	B	B	A	B	B	B	B	NT	B	C	A	A	C	NT
S16-10-162	B	B	C	B	A	C	A	B	B	A	B	B	B	B	B	B	C	A	C	C	C
S16-10-163	C	C	C	B	A	B	B	B	B	C	C	B	B	B	C	C	C	A	A	C	C
S16-10-164	B	B	C	B	A	C	A	B	A	C	A	B	B	B	C	C	C	A	A	C	C
S16-10-165	B	B	C	B	A	B	C	B	B	C	C	B	B	B	C	C	C	A	C	C	C
S16-10-166	B	B	C	B	A	C	A	B	B	A	B	B	B	B	C	C	C	A	A	C	C
S16-10-167	B	B	C	B	A	C	B	B	B	C	C	B	B	A	C	C	C	A	C	C	C
S16-10-168	C	B	C	B	A	B	B	B	B	C	B	B	B	B	C	C	C	A	A	C	C
S16-10-169	C	C	C	B	B	C	B	B	B	C	C	B	B	B	B	B	C	A	A	C	C
S16-10-170	C	B	C	B	B	C	B	B	B	A	C	B	B	B	C	B	C	A	C	C	C
S16-10-171	C	B	C	B	A	C	B	B	B	A	B	B	B	B	NT	B	C	A	A	C	NT
S16-10-172	C	B	C	B	A	C	A	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-173	C	C	C	B	A	C	A	B	B	C	C	B	B	B	C	C	C	A	A	C	C
S16-10-174	C	B	C	B	A	C	A	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-175	B	B	C	B	A	C	A	B	B	A	B	B	B	B	B	B	C	A	C	C	C
S16-10-176	B	B	C	NT	A	C	B	B	B	C	B	B	B	B	NT	C	C	A	C	C	C
S16-10-177	B	B	C	B	A	C	A	B	B	A	B	B	B	A	B	B	C	A	C	C	C

FIG. 9E

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S16-10-178	C	C	C	B	B	C	B	B	B	C	C	B	B	B	C	B	B	A	C	C	C
S16-10-179	C	B	C	B	A	C	A	B	B	A	B	B	B	B	C	C	C	A	A	C	C
S16-10-28	C	B	C	B	A	C	B	B	B	A	C	B	B	B	B	B	C	A	C	C	C
S16-10-33	C	B	C	B	A	B	A	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S16-10-36	C	B	C	B	B	C	NT	C	B	NT	C	B	C	C	NT	B	C	A	C	C	C
S16-10-37	B	B	C	B	A	C	A	B	B	A	B	B	B	B	A	B	C	A	A	C	C
S16-10-38	C	B	C	B	B	C	B	B	B	C	C	B	B	B	C	B	C	A	C	C	C
S16-10-39	C	B	C	B	B	C	NT	B	B	NT	C	B	C	C	NT	B	C	A	C	C	C
S16-10-40	B	B	C	B	A	C	A	B	A	A	B	B	B	B	C	B	C	A	A	C	C
S16-10-42	B	B	C	B	A	C	NT	B	B	NT	B	B	B	B	NT	B	C	A	C	C	C
S16-10-43	C	B	C	B	A	C	A	B	A	C	B	B	B	B	C	C	C	A	A	C	C
S16-10-45	C	B	C	B	A	C	A	B	B	C	C	B	B	B	C	C	C	A	A	C	C
S16-10-46	C	B	B	B	A	B	A	B	B	C	B	B	B	B	B	B	C	A	A	C	B
S16-10-48	B	B	B	NT	A	B	B	B	A	C	B	B	B	B	NT	B	C	A	A	C	C
S16-10-49	B	B	C	B	A	B	NT	B	B	NT	B	B	B	B	NT	C	C	A	C	C	C
S16-10-52	C	B	C	B	A	C	A	B	B	A	C	B	C	C	C	B	C	A	C	C	C
S16-10-53	C	B	C	B	A	C	A	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-54	B	B	C	B	A	C	A	B	B	C	B	B	B	B	C	C	C	A	A	C	C
S16-10-55	C	B	C	B	B	C	B	B	B	C	C	B	C	B	C	C	C	A	C	C	C
S16-10-61	C	B	C	NT	A	C	B	B	B	C	B	B	B	B	NT	B	C	A	C	C	C
S16-10-64	B	B	B	A	A	B	B	B	A	C	B	B	B	B	NT	C	C	A	A	C	C
S16-10-65	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	B	C	C	C
S16-10-67	B	B	C	B	A	C	B	B	B	C	B	B	B	B	NT	B	C	A	A	C	C
S16-10-69	C	B	C	A	A	B	A	B	A	C	B	B	B	B	C	C	C	A	A	C	C

FIG. 9F

SUBSTITUTE SHEET (RULE 26)

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S16-10-71	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	A	C	C	C
S16-10-72	C	C	B	B	A	B	A	B	B	C	C	B	B	B	C	C	C	C	A	C	C
S16-10-73	C	C	B	B	B	B	B	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S16-10-74	B	B	B	NT	A	B	B	B	B	C	B	B	B	B	NT	C	C	A	A	C	C
S16-10-75	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	C	C	C	C
S16-10-79	B	B	B	NT	A	B	B	B	B	C	B	B	B	B	NT	C	C	A	A	C	C
S16-10-83	C	B	C	B	A	B	A	B	B	C	C	B	B	B	C	C	C	A	C	C	C
S16-10-86	C	B	C	B	A	C	B	B	B	A	C	B	B	B	B	B	C	A	C	C	C
S16-10-88	C	B	C	B	A	C	NT	B	B	NT	C	B	B	B	NT	B	C	A	C	C	C
S16-10-89	C	B	C	B	A	C	A	B	B	A	C	B	B	B	C	C	C	A	C	C	C
S16-10-91	C	B	C	B	A	C	A	B	B	A	C	B	B	B	C	C	C	A	C	C	C
S16-10-92	B	B	C	B	A	C	A	B	A	A	B	B	B	A	B	C	C	A	A	C	C
S16-10-95	B	B	C	NT	A	C	B	B	B	C	B	B	B	B	NT	B	C	A	C	C	C
S2-4-69	C	C	B	B	B	B	C	B	C	C	C	C	C	C	NT	C	C	C	C	C	C
S24-9-125	B	B	C	B	A	B	A	B	B	A	B	B	B	A	A	B	B	A	A	C	C
S24-9-126	B	NT	C	B	A	B	A	B	NT	A	A	B	B	B	C	C	NT	NT	A	C	C
S24-9-127	B	NT	C	B	A	B	A	B	NT	A	B	B	B	B	B	B	NT	NT	A	C	C
S24-9-128	B	NT	C	B	A	B	A	B	NT	A	A	B	B	B	C	C	NT	NT	A	A	B
S24-9-129	C	NT	B	A	A	B	A	B	NT	C	A	B	B	B	C	C	NT	NT	A	C	B
S24-9-130	B	NT	C	A	A	B	A	B	NT	A	B	B	B	B	B	C	NT	NT	A	A	A
S24-9-131	B	NT	C	B	A	B	A	B	NT	A	A	B	B	B	B	C	NT	NT	A	C	C
S24-9-132	C	NT	B	B	A	B	A	B	NT	C	B	B	B	B	C	C	NT	NT	A	C	C
S24-9-180	C	NT	B	B	B	B	C	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S24-9-2	B	B	C	B	A	C	B	B	B	A	C	B	B	B	NT	B	C	A	C	C	C

FIG. 9G

SUBSTITUTE SHEET (RULE 26)

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	SA1 58 tetK	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	BC2 40	SM2 56
S24-9-22	B	B	C	A	B	NT	B	B	B	NT	B	B	B	B	NT	B	C	A	A	C	C
S24-9-23	B	B	C	A	B	NT	B	B	B	NT	B	B	B	A	NT	A	A	A	A	C	C
S24-9-25	B	B	B	A	B	B	B	A	B	A	B	A	A	A	A	B	B	A	A	C	A
S24-9-26	C	B	C	A	C	B	B	B	B	A	B	B	B	A	A	B	C	A	A	C	C
S24-9-27	B	B	C	A	C	A	B	B	B	C	B	B	C	C	C	C	C	A	A	C	C
S24-9-28	C	NT	C	A	C	B	B	NT	B	A	B	B	C	B	A	A	NT	NT	C	C	C
S24-9-30	C	NT	C	A	C	A	B	NT	B	A	B	B	C	B	A	A	NT	NT	C	C	C
S24-9-31	B	NT	B	A	B	A	B	NT	B	A	B	B	B	B	A	B	NT	NT	C	C	C
S24-9-32	C	NT	C	A	C	A	B	NT	B	A	B	B	B	B	A	B	NT	NT	C	C	C
S24-9-80	B	B	C	A	B	A	B	A	B	A	B	B	B	B	A	B	C	A	C	C	C
S24-9-81	B	B	C	A	B	A	B	B	B	A	B	B	B	B	A	B	C	A	C	C	C
S24-9-82	C	B	C	A	C	A	B	B	B	A	B	B	B	B	A	A	A	A	C	C	C
S24-9-83	C	NT	B	A	B	A	B	NT	B	C	C	B	B	B	C	C	NT	NT	A	C	C
S24-9-84	B	NT	B	A	B	A	B	NT	B	C	B	B	B	B	C	B	NT	NT	A	C	C
S24-9-92	B	NT	C	A	B	A	B	NT	B	B	A	B	B	A	B	A	NT	NT	A	C	C
S24-9-93	C	B	B	A	B	A	B	A	B	C	C	B	B	B	C	C	C	C	A	C	C
S25-11-1	A	A	C	A	B	A	B	A	A	A	A	A	B	A	A	A	A	A	A	C	C
S25-11-10	C	C	B	A	B	B	B	B	B	C	C	B	B	C	C	C	C	C	A	C	C
S25-11-11	C	B	B	B	B	B	B	B	B	C	C	C	B	C	C	C	C	C	A	C	C
S25-11-12	C	B	B	A	B	A	B	B	B	C	B	B	B	B	C	C	C	A	A	C	C
S25-11-13	B	A	B	A	B	A	B	A	A	A	A	B	B	B	A	B	B	A	A	C	C
S25-11-14	B	C	C	A	C	A	B	A	B	A	A	B	B	B	A	A	B	A	A	C	C
S25-11-15	B	C	B	A	C	A	B	A	B	A	A	B	B	B	B	B	B	A	A	C	C
S25-11-16	C	C	B	B	B	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C

FIG. 9H

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S25-11-164	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	B	C	C	A
S25-11-165	A	B	C	A	A	B	A	B	A	C	B	B	B	B	C	C	C	A	A	C	B
S25-11-166	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-168	C	B	B	B	A	B	B	B	B	C	B	B	C	C	C	C	C	C	C	C	NT
S25-11-169	C	B	B	B	B	B	B	B	B	C	B	B	B	B	C	C	C	C	C	C	NT
S25-11-17	C	C	C	B	B	B	A	C	B	C	B	B	C	C	C	C	C	C	C	C	C
S25-11-170	B	A	C	A	A	B	A	B	A	A	A	B	B	B	A	B	C	A	A	C	A
S25-11-171	B	A	B	A	A	B	A	B	A	A	A	B	B	B	C	C	C	B	A	C	B
S25-11-172	B	B	B	B	A	B	A	B	A	C	B	B	B	B	C	C	C	A	C	C	C
S25-11-173	B	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	C	C	C	C
S25-11-174	C	B	B	B	A	B	A	B	B	C	B	B	C	C	C	C	C	C	C	C	C
S25-11-175	B	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	C	C	C	C	C
S25-11-176	A	B	B	A	A	C	A	B	B	C	B	B	B	B	C	B	C	A	C	C	C
S25-11-177	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-178	C	C	B	B	B	B	B	B	B	C	B	B	C	C	C	C	C	C	C	C	C
S25-11-179	C	B	B	B	A	B	B	B	B	C	C	B	B	C	C	C	C	C	C	C	C
S25-11-18	B	B	C	B	A	C	A	B	A	A	A	B	C	C	C	C	C	A	C	C	C
S25-11-180	C	C	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-181	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-182	B	B	B	A	A	B	A	B	A	A	A	A	B	B	A	B	B	A	C	C	C
S25-11-183	B	B	C	A	A	C	A	B	A	A	A	B	B	B	A	A	B	A	C	C	C
S25-11-184	C	B	B	B	B	B	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C
S25-11-185	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-186	C	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C

FIG. 9I

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S25-11-187	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-188	C	B	C	B	A	C	A	B	A	A	B	B	B	B	C	B	C	A	C	C	C
S25-11-189	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-19	B	A	B	A	A	B	A	B	A	A	A	B	B	B	B	B	C	A	A	C	B
S25-11-194	B	A	B	A	A	B	B	B	A	A	B	A	B	B	B	B	C	A	A	A	B
S25-11-195	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-196	C	C	C	B	C	C	B	C	B	A	C	B	C	C	C	C	C	B	C	C	C
S25-11-197	C	C	C	B	B	C	A	C	B	C	C	B	C	C	C	C	C	B	C	C	C
S25-11-198	C	B	B	B	A	B	B	B	C	C	C	B	B	B	C	C	C	C	A	C	B
S25-11-199	C	C	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	NT
S25-11-2	A	A	C	NT	A	B	B	B	A	A	B	A	B	B	NT	A	B	A	A	A	B
S25-11-20	C	B	B	B	A	B	B	C	B	C	C	B	B	C	C	C	C	C	A	C	C
S25-11-200	C	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NT
S25-11-206	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	A	C	C
S25-11-207	C	B	B	B	A	B	A	B	A	C	C	B	B	B	C	C	C	B	A	C	B
S25-11-208	A	A	C	B	NT	C	B	B	NT	NT	NT	B	B	B	NT	NT	NT	NT	NT	NT	NT
S25-11-21	C	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-22	C	B	B	B	A	B	A	B	B	A	A	B	B	B	C	C	C	B	A	C	B
S25-11-23	B	B	C	A	A	B	A	B	A	A	A	A	B	B	A	A	B	A	A	A	C
S25-11-24	C	B	B	A	A	B	A	B	A	A	A	B	B	B	B	B	C	A	A	A	C
S25-11-25	C	C	B	B	A	B	B	B	B	A	C	B	B	B	C	C	C	C	A	C	C
S25-11-26	B	B	C	B	A	C	A	B	A	A	A	B	B	B	A	A	B	A	A	A	B
S25-11-27	B	B	C	B	B	C	A	B	B	A	A	B	B	B	A	A	A	A	C	C	C
S25-11-28	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C

FIG. 9J

SUBSTITUTE SHEET (RULE 26)

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S25-11-29	C	B	B	B	B	B	C	C	C	C	C	C	B	C	C	C	C	C	C	C	C
S25-11-3	C	B	B	B	B	B	B	B	B	C	C	B	B	B	C	C	C	C	A	C	B
S25-11-30	C	A	B	A	A	B	A	B	A	A	A	B	B	B	C	C	C	A	A	C	A
S25-11-31	C	C	B	B	B	B	B	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S25-11-32	C	C	C	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-33	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-34	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-35	C	C	B	B	B	B	B	B	B	C	C	B	B	C	C	C	C	C	A	C	C
S25-11-36	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-37	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-4	C	C	B	B	B	B	C	C	B	C	C	B	B	C	C	C	C	C	C	C	C
S25-11-43	B	B	B	NT	A	B	B	B	B	C	B	B	B	B	NT	B	C	C	A	C	A
S25-11-44	C	B	B	B	A	B	B	B	B	C	B	B	B	B	C	C	C	A	A	C	A
S25-11-45	B	B	B	A	A	B	A	B	A	C	B	B	B	B	C	C	C	A	A	C	C
S25-11-46	C	C	B	B	A	B	B	B	B	C	C	B	B	B	C	C	C	B	A	C	C
S25-11-47	C	B	C	B	B	C	B	B	B	A	C	B	C	C	C	C	C	A	C	C	C
S25-11-48	A	A	B	A	A	B	A	B	A	A	A	B	B	B	B	B	B	A	A	A	C
S25-11-5	C	B	B	B	B	B	B	C	B	C	C	B	C	C	C	C	C	C	C	C	A
S25-11-50	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-51	C	B	B	B	A	B	B	B	B	C	B	B	B	B	C	C	C	B	A	C	NT
S25-11-52	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-53	B	B	B	B	A	B	A	B	A	A	A	B	B	B	B	B	C	A	A	A	C
S25-11-54	B	B	C	B	A	B	A	B	A	A	A	B	B	B	A	A	B	A	A	A	B
S25-11-55	B	A	B	A	A	B	A	B	A	A	A	A	B	B	B	B	C	A	A	C	A

FIG. 9K

SUBSTITUTE SHEET (RULE 26)

Cmpd	SA1 01 292 13	SA1 00 137 09	SP1 93 866 8	SP1 60 tetM	SP1 06 496 19	EF1 59 tetM	SE1 64 122 28	SA1 58 tetK	SA1 61 tetM	SP1 73	PA1 69	PM1 12 356 59	KP1 94 700 603	KP1 53 tetA	EC1 55 tetA	EC1 07 259 22	MC 205 817 6	HI2 62 339 29	AB2 50	SM2 56	BC2 40
S25-11-56	B	B	B	B	A	B	A	B	B	B	C	C	B	B	B	B	A	A	C	C	B
S25-11-57	B	A	A	B	B	C	B	B	C	A	A	B	B	B	B	B	A	A	A	A	A
S25-11-58	B	B	A	B	A	B	A	A	C	A	C	B	A	B	B	B	A	A	A	C	B
S25-11-59	B	A	A	B	A	C	A	A	C	A	C	C	C	C	C	C	B	A	A	C	A
S25-11-6	B	A	A	B	B	B	A	B	C	B	B	B	A	B	B	B	B	B	A	C	A
S25-11-60	B	B	A	B	A	B	A	A	B	A	C	B	B	B	B	B	A	A	A	C	A
S25-11-61	C	B	B	C	B	B	B	B	B	C	C	C	C	C	B	B	B	A	A	C	C
S25-11-62	C	C	C	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-63	B	B	A	B	A	B	A	A	B	A	C	B	B	B	B	B	A	A	A	C	B
S25-11-64	C	B	B	B	A	B	A	B	B	B	C	C	C	B	B	B	B	A	A	C	B
S25-11-65	C	B	B	B	A	B	A	B	B	B	C	C	C	B	B	B	B	A	A	C	C
S25-11-66	C	NT	NT	B	C	B	B	B	B	NT	NT	C	C	C	B	C	C	C	C	C	C
S25-11-67	C	NT	NT	C	C	B	B	B	C	NT	NT	C	C	C	C	C	C	C	C	C	B
S25-11-68	B	B	A	B	A	B	A	A	B	B	A	B	B	B	B	B	A	A	A	C	A
S25-11-69	B	B	A	B	A	B	A	B	B	B	B	C	C	C	B	B	B	A	A	C	B
S25-11-7	C	B	A	B	A	B	A	B	B	A	C	C	C	B	B	B	A	A	A	C	A
S25-11-70	C	NT	NT	C	C	B	B	B	B	NT	NT	C	C	C	C	C	C	C	C	C	B
S25-11-71	C	NT	NT	C	C	B	C	C	C	NT	NT	C	C	C	C	C	C	C	C	C	B
S25-11-72	C	B	B	B	B	B	A	B	B	B	C	C	C	B	B	B	C	A	B	C	B
S25-11-73	C	B	A	B	A	B	A	B	B	B	C	C	C	B	B	B	B	A	A	C	B
S25-11-74	C	C	C	C	C	B	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-75	C	B	B	C	B	C	A	B	C	B	C	C	C	C	C	C	C	B	C	C	B
S25-11-76	C	C	B	B	A	C	B	B	C	C	C	C	C	C	C	C	C	B	C	C	B
S25-11-77	C	NT	NT	B	B	B	B	B	B	NT	NT	C	C	C	C	C	C	C	C	C	B

FIG. 9L

Cmpd	SA1 01 292 13	SA1 00 137 09	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP1 93 866 8	HI2 62 339 29	MC 205 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP1 94 700 603	PM1 12 356 59	PA1 69	PA1 73	AB2 50	SM2 56	BC2 40
S25-11-78	C	NT	B	B	B	B	C	C	NT	C	C	C	C	C	C	C	NT	NT	C	C	C
S25-11-8	B	B	C	A	A	C	A	B	A	A	A	B	B	B	C	C	C	A	A	C	B
S25-11-9	B	B	B	NT	A	B	B	B	A	A	B	B	B	B	NT	B	B	A	A	A	A
S27-9-3	C	C	B	B	B	B	B	B	B	C	C	B	B	B	C	C	C	C	C	NT	C
S27-9-5	B	B	B	B	B	B	NT	B	B	A	B	B	B	B	NT	B	C	A	A	A	C
S27-9-6	C	C	B	B	B	B	B	B	B	C	C	B	B	B	C	C	C	B	C	C	C
S27-9-7	B	B	B	B	A	B	A	B	B	A	A	B	B	B	B	A	C	A	A	C	C
S29-2-1	B	B	B	B	A	B	A	B	B	C	C	B	B	B	A	B	B	A	A	C	C
S29-2-2	B	A	B	A	A	B	A	B	A	C	B	B	B	A	B	B	B	A	A	A	C
S29-2-3	B	B	B	B	A	B	A	B	A	C	B	B	B	B	B	C	C	A	A	C	B
S29-2-4	A	A	B	A	A	B	A	B	A	C	A	B	B	B	B	B	B	A	A	A	C
S30-4-1	C	C	B	B	B	B	C	B	C	C	C	C	C	B	C	C	C	A	C	C	NT
S30-4-2	C	C	C	B	B	C	C	B	B	C	C	B	C	B	C	B	C	A	C	C	NT
S6-4-3	C	B	C	B	A	B	A	B	B	A	C	B	B	A	B	B	C	NT	A	C	C
Sancycline	0.5	1	2	4	4	8	0.25	8	1	0.5	0.125	8	32	32	32	4	32	33	16	1	4
Minocycline	0.06	0.06	8	0.03	0.125	16	0.0155	2	0.0156	1	0.0155	0.5	8	8	32	8	32	16	8	0.5	8
Tigecycline	0.06	0.06	0.125	0.06	0.125	0.06	0.0156	0.0156	0.0156	1	0.0155	0.03	0.5	1	8	1	15	16	8	1	16

FIG. 9M

SUBSTITUTE SHEET (RULE 26)

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	HI26 2 339 29	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	AB2 50	SM2 56	BC2 40
S15-13-121	C	C	C	C	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-129	C	B	C	B	A	B	A	B	B	A	B	B	B	B	NT	C	C	C	A	C	C
S15-13-130	C	B	B	B	B	B	B	B	B	C	B	B	B	B	NT	C	C	C	A	C	C
S15-13-133	C	B	C	C	B	B	C	B	B	C	C	C	C	C	NT	C	C	C	A	C	C
S15-13-134	C	B	B	B	B	B	C	B	B	C	C	C	C	C	C	C	C	C	A	C	C
S15-13-135	C	C	C	C	B	B	C	B	B	C	C	C	C	C	C	C	C	C	A	C	C
S15-13-136	C	B	B	B	A	B	A	B	B	A	B	B	B	C	B	C	C	C	A	C	B
S15-13-142	C	C	C	B	A	C	A	B	B	A	B	B	C	C	A	B	C	C	A	C	C
S15-13-143	C	B	B	B	A	B	A	B	B	A	B	B	B	B	A	B	C	C	A	C	C
S15-13-144	C	B	B	B	A	B	A	B	B	C	B	B	B	B	A	C	C	C	A	C	C
S15-13-145	C	B	C	B	B	B	C	C	C	C	C	C	C	B	C	C	C	C	A	C	C
S15-13-146	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	C	C
S15-13-147	C	C	C	B	A	C	A	B	B	A	A	B	B	B	A	A	A	A	A	C	C
S15-13-148	C	B	B	A	A	B	A	B	B	A	B	B	B	B	A	A	C	B	A	C	B
S15-13-149	B	B	B	A	A	B	A	B	B	A	A	B	B	B	A	A	C	B	A	C	B
S15-13-150	C	B	B	B	A	B	A	B	B	A	B	B	B	B	A	C	C	B	A	C	B
S15-13-151	C	B	B	B	B	B	C	B	B	C	B	B	B	B	C	C	C	B	A	C	B
S15-13-152	C	C	C	B	A	C	A	B	B	A	B	B	B	B	A	A	A	A	A	C	B
S15-13-153	B	B	C	B	A	B	A	B	B	A	A	B	B	A	A	A	C	B	A	C	B
S15-13-154	C	B	B	B	A	B	A	B	B	C	B	B	B	B	B	C	C	B	A	C	B
S15-13-155	C	B	B	B	B	B	B	B	B	C	B	B	C	B	C	C	C	B	A	C	B
S15-13-156	C	B	B	B	A	B	B	B	B	A	B	B	B	B	A	C	C	B	A	C	B
S15-13-157	C	B	B	B	A	B	B	B	B	A	B	B	B	B	B	C	C	B	A	C	B
S15-13-158	C	B	C	B	C	C	C	B	B	C	C	C	C	C	C	C	C	B	A	C	B
S15-13-159	C	B	C	C	C	C	C	B	B	C	C	C	C	C	C	C	C	B	A	C	B
S15-13-160	C	B	B	B	B	B	B	B	B	C	C	B	C	C	C	C	C	B	A	C	B
S15-13-167	B	A	B	B	A	B	A	B	B	C	C	B	B	B	B	C	C	B	A	C	B
S15-13-170	C	B	B	B	A	B	A	B	B	A	B	B	B	B	NT	C	C	B	A	C	B
S15-13-171	C	B	B	B	A	B	B	B	B	C	C	B	B	B	NT	C	C	B	A	C	B

FIG. 10A

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	HI26 2 339 29	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	AB2 50	SM2 56	BC2 40
S15-13-172	C	B	B	B	B	B	C	B	B	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-173	C	B	B	B	B	B	C	B	B	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-176	C	B	B	B	B	B	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-179	C	C	C	B	B	C	A	B	B	A	B	B	B	B	A	A	A	A	C	C	C
S15-13-227	C	C	C	B	A	B	B	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S15-13-30	C	B	B	B	A	B	B	B	B	C	C	B	C	C	C	C	C	C	C	C	C
S15-13-33	C	C	C	C	C	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-49	C	B	B	B	A	B	A	B	B	A	B	B	B	B	NT	B	C	C	A	C	C
S15-13-50	C	B	B	B	A	B	A	B	B	C	C	B	B	B	NT	C	C	C	C	C	C
S15-13-51	C	B	B	B	B	B	B	B	B	C	C	B	B	C	NT	C	C	C	C	C	C
S15-13-52	C	B	B	B	A	B	A	B	B	A	A	B	B	B	NT	B	C	C	A	C	C
S15-13-53	C	C	C	C	B	B	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-54	C	B	B	B	B	B	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-55	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-56	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-57	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	B	C	C	C	C	C
S15-13-58	C	C	C	B	A	B	A	B	B	A	A	B	B	B	A	A	C	B	A	C	C
S15-13-59	C	B	B	B	A	B	A	B	B	A	A	B	B	B	A	B	C	C	A	C	C
S15-13-60	C	B	B	B	A	B	A	B	B	A	B	B	B	B	A	B	C	C	A	C	C
S15-13-61	C	B	B	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-62	C	B	C	B	B	B	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-63	C	C	C	C	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-78	C	B	B	B	A	B	B	B	B	C	C	B	B	B	A	C	C	C	A	C	C
S15-13-85	C	B	B	B	B	B	C	B	B	C	C	C	B	C	C	C	C	C	C	C	C
S15-13-86	C	B	B	B	B	B	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-89	C	B	B	B	B	B	B	B	B	C	C	B	B	B	NT	C	C	C	C	C	C
S15-13-90	C	B	C	B	B	B	C	C	B	C	C	C	C	C	NT	C	C	C	C	C	C
S15-13-91	C	C	C	B	B	C	B	C	C	A	C	B	C	C	NT	C	C	C	C	C	C
S15-13-92	C	C	C	B	B	C	B	C	C	C	C	B	C	C	NT	C	C	C	C	C	C

FIG. 10B

SUBSTITUTE SHEET (RULE 26)

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	HI26 2 339 29	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	AB2 50	SM2 56	BC2 40
S15-13-93	C	B	B	A	B	A	B	B	A	A	B	B	B	A	B	C	C	A	A	C
S15-13-94	C	C	C	A	C	A	B	B	A	B	B	B	B	A	B	C	B	A	C	C
S15-13-95	C	C	C	A	C	A	B	B	A	B	B	B	B	A	C	C	C	A	C	C
S15-13-96	C	C	C	A	B	A	B	B	A	A	B	B	B	A	C	C	C	A	C	C
S15-13-97	C	B	B	B	B	C	B	B	C	C	C	B	B	C	C	C	C	A	C	C
S16-10-118	C	B	C	A	B	A	B	B	C	C	C	B	B	NT	C	C	C	C	C	C
S16-10-125	C	C	C	A	C	A	B	B	C	C	B	B	B	A	C	C	C	C	C	C
S16-10-128	C	C	C	B	C	A	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S16-10-130	C	C	C	A	C	A	B	B	A	B	B	B	A	A	C	C	B	C	C	C
S16-10-131	C	C	C	A	C	A	B	B	C	C	B	B	B	A	C	C	C	C	C	C
S16-10-137	C	B	B	A	B	A	B	B	C	C	B	B	C	C	C	C	C	C	C	C
S16-10-31	C	C	C	A	B	A	B	B	C	C	B	B	B	NT	C	C	C	C	C	C
S16-10-44	C	C	C	B	C	B	C	C	C	C	C	B	B	C	C	C	C	C	C	C
S16-10-47	C	C	C	A	C	A	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S16-10-50	C	C	C	B	C	A	B	B	C	C	B	B	B	B	C	C	C	C	C	C
S15-13-227	C	C	C	A	C	A	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S16-10-56	C	C	C	B	C	B	C	C	C	B	C	C	C	B	C	C	C	C	C	C
S16-10-57	C	C	C	B	C	B	C	C	C	C	B	B	B	C	C	C	C	C	C	C
S16-10-58	C	C	C	B	C	B	B	C	C	C	B	B	B	B	C	C	C	C	C	C
S16-10-66	C	B	C	B	B	B	C	C	C	C	C	B	B	C	C	C	C	C	C	C
S16-10-68	C	C	C	B	C	B	B	C	C	B	B	B	B	A	C	C	C	C	C	C
S16-10-76	C	C	C	B	C	B	C	C	C	C	C	B	C	C	C	C	C	C	C	C
S16-10-77	C	C	C	A	C	A	B	B	C	B	B	B	B	A	C	C	C	C	C	C
S16-10-80	C	B	C	A	B	A	B	B	C	A	B	B	B	A	C	C	C	C	C	C
S16-10-81	C	B	B	B	B	B	B	B	C	C	B	B	B	B	C	C	C	C	C	C
S16-10-84	B	C	C	A	C	A	B	B	A	B	B	A	B	NT	C	C	C	C	C	C
S16-10-85	C	C	C	A	C	A	B	B	C	C	B	B	B	NT	C	C	C	C	C	C
S16-10-87	C	C	C	A	C	A	B	B	A	C	B	B	A	A	B	C	C	C	C	C
S16-10-90	C	C	C	A	C	A	B	B	C	B	B	B	B	B	C	C	C	C	C	C
S16-10-93	C	C	C	A	C	A	B	B	A	B	B	B	B	A	C	C	C	C	C	C

FIG. 10C

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	HI26 2 339 29	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	AB2 50	SM2 56	BC2 40
S16-10-96	C	C	C	B	A	C	A	B	B	A	B	B	B	B	NT	C	C	C	A	C	C
S16-10-97	C	B	C	B	A	B	A	B	B	C	C	B	B	B	B	C	C	C	C	C	C
S24-9-100	C	B	B	B	A	B	A	B	B	A	B	B	B	B	A	B	C	B	A	C	B
S24-9-101	C	B	B	B	A	B	A	B	B	A	B	B	B	B	A	B	C	B	A	C	B
S24-9-102	C	B	B	B	A	B	B	B	B	C	C	B	B	B	C	C	C	C	C	C	C
S24-9-103	C	C	C	B	B	C	B	B	B	A	C	B	C	C	A	A	C	B	A	C	C
S24-9-104	C	C	C	B	A	C	A	B	B	A	B	B	B	B	A	A	A	B	A	C	B
S24-9-105	C	C	C	B	A	C	A	B	B	A	B	B	B	B	A	B	C	B	A	C	B
S24-9-106	C	B	C	B	A	B	A	B	B	C	C	B	B	B	B	C	C	C	C	C	C
S24-9-107	C	B	C	B	B	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S24-9-108	C	B	C	B	B	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S24-9-109	B	B	B	B	A	B	A	B	B	A	B	B	B	B	A	A	C	B	A	C	B
S24-9-110	C	B	C	B	A	B	A	B	B	A	A	B	B	B	A	B	C	B	A	C	B
S24-9-111	C	B	C	B	A	B	A	B	B	A	B	B	B	B	A	B	C	B	A	C	B
S24-9-112	C	B	C	B	A	C	B	B	B	A	B	B	C	B	A	A	C	B	A	C	B
S24-9-113	C	B	C	B	A	C	A	B	B	A	B	B	C	C	A	C	C	C	A	C	C
S24-9-115	C	B	C	B	A	C	C	B	B	A	B	B	C	C	A	A	A	B	A	C	B
S24-9-116	C	C	C	B	B	C	B	B	B	A	C	B	C	C	A	B	C	B	A	C	B
S24-9-119	C	C	C	B	B	C	B	B	B	A	C	B	C	C	A	C	A	B	A	C	B
S24-9-120	C	C	C	B	A	C	A	B	B	A	B	B	C	B	A	B	C	B	A	C	B
S24-9-121	C	B	C	B	A	C	A	B	B	A	B	B	B	B	A	B	C	B	A	C	B
S24-9-133	C	C	C	B	B	C	C	C	B	A	C	C	C	C	NT	C	C	C	A	C	C
S24-9-134	C	C	C	B	A	C	A	B	B	A	B	B	C	C	NT	A	C	B	A	C	B
S24-9-136	C	B	C	B	A	C	A	B	B	A	B	B	B	B	NT	B	C	B	A	C	B
S24-9-137	C	C	B	B	A	B	A	B	B	A	B	B	B	B	NT	B	C	B	A	C	B
S24-9-138	B	B	B	B	A	B	A	B	B	C	B	B	B	B	NT	C	C	C	A	C	C
S24-9-139	B	B	B	B	A	B	A	B	B	C	B	B	B	B	NT	C	C	C	A	C	C
S24-9-140	C	C	C	B	A	B	A	B	B	A	B	B	B	B	NT	B	C	B	A	C	B
S24-9-141	C	C	C	B	A	C	A	B	B	A	B	B	B	B	NT	A	A	A	A	C	C

FIG. 10D

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	HI26 2 339 29	SA1 tetM	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	BC2 40	SM2 56	AB2 50
S24-9-142	B	C	C	B	A	C	A	B	B	A	C	B	B	B	B	NT	B	C	B	C	C	A
S24-9-143	C	C	C	B	B	C	B	B	B	A	C	C	B	C	C	NT	A	A	C	C	C	C
S24-9-144	C	C	C	B	A	C	A	B	B	C	C	B	B	B	B	B	C	C	C	C	C	A
S24-9-145	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S24-9-146	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C
S24-9-147	C	C	C	B	B	C	B	C	C	C	C	C	C	C	C	A	B	C	C	C	C	C
S24-9-148	C	C	C	B	A	C	B	B	C	A	C	B	B	C	C	A	C	C	B	C	C	C
S24-9-149	B	C	C	B	A	B	A	B	B	A	C	B	B	B	B	A	C	C	C	C	C	A
S24-9-150	C	C	C	B	A	B	A	B	B	C	C	B	B	B	B	B	C	C	C	C	C	A
S24-9-151	C	C	C	B	A	C	A	B	B	A	C	A	B	B	B	B	A	A	A	C	C	A
S24-9-152	C	C	C	B	A	C	A	B	B	A	C	B	B	B	B	A	B	C	C	C	C	A
S24-9-153	C	C	C	B	A	C	A	B	B	A	C	B	B	B	B	A	B	C	C	C	C	A
S24-9-154	B	C	C	B	A	B	A	B	B	A	C	A	B	B	B	A	B	C	C	C	C	A
S24-9-155	C	C	C	B	A	B	A	B	B	A	C	B	B	B	B	A	B	C	B	C	C	A
S24-9-156	C	C	C	B	A	B	A	B	B	A	C	B	B	B	B	A	B	C	B	C	C	A
S24-9-157	C	C	C	B	A	B	A	B	B	A	C	B	B	B	B	A	B	C	C	C	C	A
S24-9-158	C	C	C	B	B	C	C	C	B	A	C	B	B	C	C	A	C	C	B	C	C	A
S24-9-159	C	C	C	B	A	C	B	B	B	A	C	B	B	B	B	A	C	C	B	C	C	A
S24-9-29	B	C	C	B	A	C	A	B	B	A	C	A	B	B	B	NT	C	C	B	C	C	A
S24-9-33	C	C	C	B	A	C	A	B	B	A	C	B	B	B	B	NT	C	C	B	C	C	A
S24-9-34	C	C	C	B	A	C	A	B	B	A	C	B	B	B	B	NT	C	C	C	C	C	A
S24-9-35	B	C	C	B	A	B	A	B	B	A	C	A	B	B	B	NT	C	C	C	C	C	A
S24-9-36	C	C	C	B	B	C	B	B	B	A	C	C	B	B	B	NT	A	C	C	C	C	A
S24-9-37	C	C	C	B	A	C	A	B	B	A	C	B	B	B	B	NT	A	A	A	C	C	A
S24-9-38	C	C	C	B	A	C	A	B	B	A	C	A	B	B	B	NT	B	C	B	C	C	A
S24-9-39	C	C	C	A	A	C	A	B	B	C	C	A	B	B	B	NT	C	C	C	C	C	A
S24-9-40	C	C	C	B	B	C	C	C	B	A	C	C	C	C	C	NT	C	C	C	C	C	A
S24-9-41	C	B	B	B	A	C	A	B	B	A	C	B	B	B	B	NT	A	A	A	C	C	A
S24-9-42	B	B	C	B	A	C	A	B	B	A	C	A	B	B	B	A	B	C	B	C	C	A
S24-9-43	B	B	C	B	A	C	A	B	B	A	C	A	B	B	B	A	C	C	C	C	C	A

FIG. 10E

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	S24-9-44	S24-9-45	S24-9-46	S24-9-47	S24-9-48	S24-9-49	S24-9-50	S24-9-51	S24-9-52	S24-9-53	S24-9-54	S24-9-55	S24-9-57	S24-9-66	S24-9-85	S24-9-86	S24-9-87	S24-9-88	S24-9-89	S24-9-90	S24-9-91	S24-9-97	S24-9-98	S24-9-99	S25-11-100	S25-11-101	S25-11-102	S25-11-103	S25-11-104	S25-11-105
SA1 58 tetK	B	B	B	B	B	B	A	A	B	A	B	C	C	C	C	A	B	B	C	C	B	B	C	B	A	A	B	B	C	B	B	C
SE1 64 122 28	A	A	A	A	A	A	A	A	A	A	A	B	B	B	B	A	B	B	A	A	A	A	A	A	A	A	B	B	C	C	C	C
EF1 59 tetM	C	C	C	C	C	C	B	B	B	C	C	C	B	C	B	C	C	B	C	C	C	B	C	B	B	C	C	C	C	C	C	C
SP1 06 496 19	A	A	A	A	A	A	A	A	A	A	A	A	C	B	C	A	B	B	A	A	A	A	B	A	A	A	C	C	C	C	C	C
SP1 60 tetM	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	B	B	C	B	B	B	B	B	B	B	B	B	B	B	B	B	C
SP3 12 tetM	B	B	B	B	B	B	B	B	C	B	B	C	B	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	B	C	B	C
HI26 2 339 29	A	A	A	A	A	A	A	A	C	A	A	A	C	C	C	A	A	A	C	A	A	C	C	A	A	A	C	C	C	C	C	C
MC2 05 817 6	B	B	B	A	A	B	B	B	A	C	C	C	C	A	C	B	C	C	C	B	C	C	B	B	A	A	C	C	C	C	C	C
EC1 07 259 22	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C
EC1 55 tetA	C	B	B	B	B	B	B	B	B	B	B	C	C	C	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C
KP1 53 tetA	C	B	B	B	B	B	B	B	B	B	B	C	C	C	C	B	B	B	B	B	B	B	C	B	B	B	C	C	C	C	C	C
KP4 57	A	A	A	A	A	A	A	A	A	C	A	C	C	C	C	NT	A	NT	NT	A	A	A	C	A	A	A	C	C	C	C	C	C
PM1 12 356 59	B	B	B	C	C	B	B	B	A	C	B	C	C	C	C	B	A	B	C	B	B	C	C	B	C	C	C	C	C	C	C	C
PA5 55	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C
PA5 56	A	B	B	C	C	B	C	C	B	C	C	C	C	C	C	B	A	A	C	B	B	C	C	B	C	C	C	C	C	C	C	C

FIG. 10F

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SE1 64 122 28	SA1 58 tetK	SP3 12 tetM	SP1 60 tetM	SP1 06 496 19	EF1 59 tetM	HI26 2 339 29	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	AB2 50	SM2 56	BC2 40
S25-11-106	C	C	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-106	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-107	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-108	C	C	C	B	B	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-109	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-110	C	B	B	B	B	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-111	C	B	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-112	C	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-113	C	C	C	C	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-114	C	C	C	C	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-115	C	B	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-116	C	C	C	C	B	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-117	C	B	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-118	C	B	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-119	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-120	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C
S25-11-121	C	B	B	B	B	B	B	B	B	A	C	B	B	B	NT	C	C	C	B	C	C
S25-11-122	C	B	B	B	B	B	B	B	B	A	C	B	B	C	NT	C	C	C	B	C	C
S25-11-123	C	B	B	B	B	B	B	B	B	C	C	C	C	C	NT	C	C	C	B	C	C
S25-11-124	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	B	C	C
S25-11-125	C	B	B	A	B	B	C	B	B	A	C	B	B	B	A	C	C	C	B	C	C
S25-11-126	C	B	B	B	B	B	B	B	B	C	C	B	C	C	C	C	C	C	B	C	C
S25-11-127	C	B	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	B	C	C
S25-11-128	C	C	B	C	C	B	C	C	B	C	C	C	C	C	C	C	C	C	B	C	C
S25-11-129	C	B	B	A	B	B	B	B	B	A	B	B	C	B	B	C	C	C	B	C	C
S25-11-130	B	C	C	A	B	B	B	A	B	A	A	B	B	B	A	C	C	C	B	C	C
S25-11-131	C	C	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-132	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-133	C	C	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-38	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C

FIG. 10G

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SA1 58 tetK	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	PM1 12 356 59	KP4 57	KP1 53 tetA	EC1 55 tetA	EC1 07 259 22	MC2 05 817 6	HI26 2 339 29	BC2 40	SM2 56	AB2 50	PA5 56	PA5 55	PA5 56
S25-11-39	C	B	B	B	B	B	C	B	B	C	NT	C	C	B	C	C	C	C	A	C	C	C
S25-11-40	C	B	B	B	B	B	C	C	C	C	NT	C	C	C	C	C	C	C	A	C	C	C
S25-11-41	C	B	B	B	A	B	A	B	B	C	NT	B	B	B	C	A	A	C	A	C	C	C
S25-11-42	C	B	B	B	B	B	C	C	B	C	NT	B	B	C	C	C	C	C	C	C	C	C
S25-11-79	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C	C	C	C	C	C
S25-11-80	C	B	C	B	B	B	C	C	C	C	NT	C	C	C	A	C	C	C	C	C	C	C
S25-11-81	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C	C	C	C	C	C
S25-11-82	C	B	C	B	B	B	B	C	B	C	NT	C	B	B	C	C	C	C	C	C	C	C
S25-11-83	C	C	C	C	C	C	C	B	B	C	NT	C	C	C	C	C	C	C	C	C	C	C
S25-11-84	C	C	C	C	C	C	C	C	C	C	NT	C	C	C	C	C	C	C	C	C	C	C
S25-11-85	B	B	B	B	A	B	A	B	B	B	NT	B	B	B	B	A	A	B	A	B	B	B
S25-11-86	C	B	B	B	A	B	A	B	B	C	NT	B	B	B	B	A	A	B	A	B	B	B
S25-11-87	C	B	B	B	A	B	A	B	B	C	NT	B	B	B	B	A	A	B	A	B	B	B
S25-11-88	C	B	B	B	A	B	B	B	B	C	NT	B	C	C	B	A	A	B	A	B	B	B
S25-11-89	C	C	B	B	B	C	B	B	B	C	C	C	C	C	B	C	C	C	A	B	B	B
S25-11-90	C	B	B	B	B	B	C	B	B	C	C	C	C	C	B	C	C	C	A	B	B	B
S25-11-91	C	B	B	B	A	B	B	B	B	C	C	C	B	B	B	C	C	C	A	B	B	B
S25-11-92	C	B	B	B	A	B	A	B	B	C	C	B	B	B	A	C	C	C	A	B	B	B
S25-11-93	C	B	B	B	A	B	A	B	B	C	C	C	C	B	C	C	C	C	A	B	B	B
S25-11-94	C	B	B	B	A	B	B	B	B	C	C	C	B	B	C	C	C	C	A	B	B	B
S25-11-95	C	C	B	B	B	C	B	B	B	C	C	C	C	C	B	C	C	C	A	B	B	B
S25-11-96	C	C	B	C	C	B	C	B	B	C	C	C	C	C	B	C	C	C	A	B	B	B
S25-11-97	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	B	B	B
S25-11-98	C	B	B	B	A	B	A	B	B	C	A	B	B	B	A	A	C	C	A	B	B	B
S25-11-99	C	B	B	B	B	B	B	B	B	C	C	C	B	B	C	C	C	C	A	B	B	B
S31-7-1	C	B	B	B	A	B	A	B	B	C	B	B	B	B	A	C	C	C	A	B	B	B
S32-6-1-1	C	B	B	B	A	B	A	B	B	C	NT	B	B	B	C	C	C	C	A	B	B	B
S32-6-1-1	C	B	B	B	A	B	A	B	B	C	NT	B	B	B	C	C	C	C	A	B	B	B
S32-6-1-2	C	B	C	B	A	C	A	B	B	C	NT	B	B	B	C	C	C	C	A	B	B	B
S32-6-1-2	C	B	C	B	A	C	A	B	B	C	NT	B	B	B	C	C	C	C	A	B	B	B

FIG. 10H

Compound	SA1 01 292 13	SA1 91	SA1 61 tetM	SE1 64 122 28	EF1 59 tetM	SP1 06 496 19	SP1 60 tetM	SP3 12 tetM	HI26 2 339 29	SA1 58 tetK	MC2 05 817 6	EC1 07 259 22	EC1 55 tetA	KP1 53 tetA	KP4 57	PM1 12 356 59	PA5 55	PA5 56	BC2 40	SM2 56	AB2 50	EC1 26 [illegible] 69 9
S32-6-1-3	C	B	B	A	B	A	B	A	C	B	A	B	B	B	NT	C	NT	NT	C	C	C	C
S32-6-1-3	C	B	B	A	B	A	B	A	C	B	A	B	B	B	NT	C	NT	NT	C	C	C	C
S32-6-1-4	C	B	C	A	C	A	B	B	A	B	C	B	B	B	NT	C	C	C	C	C	C	C
S32-6-1-4	C	B	C	A	C	A	B	B	A	B	C	B	B	B	NT	C	C	C	C	C	C	C
S32-6-1-5	C	B	C	A	C	A	B	B	A	B	B	B	B	B	NT	B	C	B	C	C	C	C
S32-6-1-5	C	B	C	A	C	A	B	B	A	B	B	B	B	B	NT	B	C	B	C	C	C	C
S32-6-1-6	B	B	C	A	C	A	B	B	C	B	B	B	B	B	NT	C	C	C	C	C	C	C
S32-6-1-6	B	B	C	A	C	A	B	B	C	B	B	B	B	B	NT	C	C	C	C	C	C	C
S32-6-1-7	C	A	C	A	C	A	B	A	A	B	A	B	B	B	NT	C	NT	NT	C	C	C	C
S32-6-1-7	C	A	C	A	C	A	B	A	A	B	A	B	B	B	NT	C	NT	NT	C	C	C	C
S32-6-2-1	B	C	C	A	B	A	B	B	A	B	A	B	B	B	NT	C	C	C	C	C	C	C
S32-6-2-1	B	C	C	A	B	A	B	B	A	B	A	B	B	B	NT	C	C	C	C	C	C	C
S32-6-2-2	C	C	C	A	B	A	B	B	C	B	B	B	B	B	NT	C	C	C	C	C	C	C
S32-6-2-2	C	C	C	A	B	A	B	B	C	B	B	B	B	B	NT	C	C	C	C	C	C	C
S32-6-2-3	C	B	C	A	B	A	B	B	C	B	B	B	B	B	NT	C	C	C	C	C	C	C
S32-6-2-3	C	B	C	A	B	A	B	B	C	B	B	B	B	B	NT	C	C	C	C	C	C	C
200	C	C	C	B	C	B	B	B	A	B	B	B	B	B	NT	C	C	C	C	C	C	C
Sancycline	0.5	8	2	4	8	0.25	8	4	0.5	4	0.125	8	32	32	32	4	32	1	4	1	16	0.125
Minocycline	0.06	8	8	0.125	16	0.01 55	2	16	1	0.03	0.01 55	0.5	8	8	32	8	16	0.125	8	0.5	8	0.125
Tigecycline	0.06	0.5	0.125	0.125	0.06	0.01 56	0.01 56	0.01 55	1	0.06	0.01 55	0.03	0.5	1	8	1	16	0.25	0.5	0.125	0.5	0.125

FIG. 101

Compound	SA101 29213	SA161 tetM	SA158 tetK	EF327 tetM	EF404 tetM	SP160 tetM	SP312 tetM	EC107 25922	EC155 tetA	EC8778 tolC	EC8780 ipxC	EC8782 imp	KP4457 CTX-M-15	PM385	PA5556 BAA-47	PA5556	PA8435151	PA6689	EC6603 tetA	AB2250	SM256	BC2240
S15-13-100	C	C	B	B	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-101	C	B	B	B	B	B	B	B	B	C	B	B	C	C	C	C	C	C	B	A	C	C
S15-13-102	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-103	B	B	B	B	B	B	B	B	B	C	A	A	C	B	C	C	C	B	B	A	A	C
S15-13-104	C	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-105	C	B	B	B	B	B	B	B	B	C	B	B	C	B	C	C	C	C	B	A	C	B
S15-13-106	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-107	C	B	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-108	C	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-109	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-110	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-111	C	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-112	C	C	B	B	B	B	B	B	B	B	B	B	C	B	C	C	C	B	B	A	C	B
S15-13-113	C	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-114	B	C	B	B	B	B	B	B	B	B	B	B	A	A	A	A	B	A	B	A	A	B
S15-13-115	C	B	B	B	B	B	B	B	B	C	A	B	C	B	C	C	B	B	B	A	C	C
S15-13-122	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-137	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-138	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-139	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-140	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-141	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-161	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-162	C	C	C	C	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-163	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-164	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-165	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-166	C	C	C	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-227	C	C	B	B	C	B	B	B	B	C	B	B	C	C	C	C	C	C	B	C	C	C
S15-13-64	C	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C

FIG. 11A

SUBSTITUTE SHEET (RULE 26)

Compound	SA1 01 292 13	SA1 61 tetM	SA1 58 tetK	EF3 27 tetM	EF4 04 tetM	SP1 60 tetM	SP3 12 tetM	EC1 07 259 22	EC1 55 tetA	EC8 78 tolC	EC8 80 ipxC	EC8 82 imp	KP4 57 CTX-M-15	PM 385	PA5 55 BAA -47	PA5 56	PA8 84 351 51	PA6 89	EC6 03 tetA	AB2 50	SM 256	BC2 40
S15-13-65	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-66	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S15-13-67	C	B	B	B	B	B	B	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-68	C	B	C	B	B	B	B	C	C	C	B	B	C	C	C	B	C	C	C	C	C	C
S15-13-69	C	C	C	B	B	B	B	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-70	C	C	C	C	B	C	C	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-71	C	B	B	B	B	B	B	B	B	C	B	B	C	C	C	C	C	C	B	C	C	C
S15-13-72	C	B	B	B	B	B	B	B	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-73	C	C	B	B	C	C	B	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-74	C	B	B	B	B	B	B	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-75	C	B	B	B	B	B	B	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C
S15-13-76	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
S15-13-77	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
S15-13-79	C	C	B	B	C	C	B	B	C	B	A	A	C	C	C	C	C	C	B	B	C	C
S15-13-80	B	B	B	B	B	B	B	C	C	B	A	A	C	C	C	C	C	C	B	B	C	C
S15-13-98	B	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	B	C	C
S15-13-99	C	C	B	C	B	B	B	C	C	B	A	A	C	C	C	C	C	C	B	B	C	C
S15-14-5	C	C	B	C	C	B	B	C	C	B	A	A	B	C	C	C	C	C	B	B	C	C
S16-10-100	C	B	B	B	C	B	B	B	B	A	A	A	B	B	C	B	B	B	B	B	C	C
S16-10-103	C	B	B	C	C	B	B	B	B	A	A	A	B	B	C	B	B	B	B	B	C	C
S16-10-104	C	B	B	C	C	B	B	B	B	B	B	B	B	C	C	B	B	B	B	B	C	C
S16-10-105	C	B	B	C	C	B	B	B	B	B	B	B	C	C	C	C	B	B	B	B	C	C
S16-10-108	C	B	B	C	C	B	B	B	B	B	A	A	B	C	C	B	B	B	B	B	C	C
S16-10-109	C	B	B	C	C	B	C	B	B	B	B	B	C	C	C	C	B	C	B	B	C	C
S16-10-111	C	B	B	C	C	B	B	B	B	B	A	B	B	B	C	B	B	B	B	B	C	C
S16-10-112	C	B	B	C	C	B	B	B	B	B	B	B	B	C	C	B	B	B	B	B	C	C
S16-10-113	C	B	B	C	C	B	B	B	B	C	B	B	C	C	C	B	B	B	B	B	C	C
S16-10-114	C	B	B	C	C	B	B	B	B	B	B	B	C	C	C	B	B	B	B	B	C	C
S16-10-115	C	B	B	C	C	B	B	B	B	B	B	B	C	C	C	B	B	C	B	B	C	C
S16-10-122	C	B	B	C	C	B	B	B	B	B	B	B	C	C	C	B	B	C	B	B	C	C

FIG. 11B

Compound	SA1 01 292 13	SA1 61 tetM	SP1 60 tetM	SP3 12 tetM	EF3 27 tetM	EF4 04 tetM	EC1 07 259 22	EC1 55 tetA	EC8 78 tolC	EC8 80 ipxC	SA1 58 tetK	EC8 82 imp	KP4 57 CTX-M-15	PM 385	PA5 55 BAA -47	PA5 56	PA8 84 351 51	PA6 89	EC6 03 tetA	BC2 40	SM 256	AB2 50
S16-10-124	C	C	B	C	C	C	B	B	C	B	B	B	B	C	C	C	B	B	B	C	C	C
S16-10-127	B	C	B	B	B	B	B	B	C	A	A	A	C	C	C	B	B	B	B	C	C	A
S16-10-133	C	C	B	B	B	B	B	B	C	A	B	A	C	C	C	C	C	C	B	C	C	A
S16-10-134	C	C	C	B	B	C	B	B	C	B	B	B	C	C	C	C	C	C	B	C	C	C
S16-10-140	C	B	B	B	B	B	B	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C
S16-10-141	C	B	B	B	B	B	C	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C
S16-10-142	C	B	B	C	B	B	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C
S16-10-29	B	C	B	B	B	C	B	B	B	A	B	A	A	B	C	A	B	B	B	C	C	A
S16-10-30	C	C	B	B	C	C	B	B	B	A	B	A	B	B	C	B	B	B	B	C	C	A
S16-10-32	C	B	C	B	B	C	B	B	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-34	C	B	C	B	B	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-35	C	B	C	C	B	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-41	C	C	B	C	C	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S15-13-227	C	C	B	C	C	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-60	C	C	B	C	C	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-62	C	C	B	C	C	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-63	C	C	B	C	C	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-70	C	C	B	C	B	C	C	C	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-78	C	B	C	B	B	B	B	B	C	B	B	B	C	C	C	B	C	C	C	C	C	A
S16-10-82	C	B	C	B	B	B	C	B	C	C	B	C	C	C	C	B	C	C	C	C	C	A
S16-10-94	C	C	B	C	B	C	B	B	C	B	B	B	C	C	C	B	C	C	C	C	C	A
S16-10-98	C	C	B	C	B	C	B	B	C	B	B	B	C	C	C	B	C	C	C	C	C	A
S16-10-99	B	C	C	C	B	C	B	B	B	A	B	A	C	C	C	B	B	B	B	C	C	A
S24-9-117	B	C	C	C	C	C	B	C	B	B	B	B	C	C	C	B	C	C	C	C	C	A
S24-9-118	C	C	B	C	C	C	B	C	B	B	B	B	C	C	C	B	C	C	C	C	C	A
S24-9-122	C	C	B	C	B	C	B	B	B	C	B	B	C	C	C	B	B	B	B	C	C	A
S24-9-123	C	C	B	B	B	B	B	B	C	A	B	A	C	C	C	B	C	C	C	C	C	A
S24-9-124	C	C	B	B	B	B	B	B	C	A	B	A	C	C	C	B	C	C	C	C	C	A
S24-9-160	C	C	B	B	B	B	B	B	B	A	B	A	C	C	C	B	C	C	C	C	C	A
S24-9-161	C	B	B	B	B	B	B	B	C	A	B	A	C	C	C	B	C	C	C	C	C	A

FIG. 11C

Compound	SA1 01 292 13	SA1 61 tetM	SA1 58 tetK	SP1 60 tetM	EF4 04 tetM	EF3 27 tetM	EC1 55 tetA	EC1 07 259 22	SP3 12 tetM	PA6 89	PA8 84 351 51	PA5 56	PA5 55 BAA -47	PM 385	KP4 57 CTX-M-15	EC8 82 imp	EC8 80 ipxC	EC8 78 tolC	EC6 03 tetA	AB2 50	SM 256	BC2 40
S24-9-162	C	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	B	C	B	A	C	C
S24-9-163	C	B	B	C	B	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S24-9-164	B	B	A	B	B	B	B	B	B	C	C	C	C	C	C	A	A	B	B	A	C	C
S24-9-165	C	B	A	B	B	B	B	C	B	C	B	C	C	C	C	A	A	B	B	A	C	C
S24-9-166	C	B	B	B	B	B	B	B	B	C	C	C	C	C	C	A	A	C	B	A	C	C
S24-9-167	C	B	B	B	B	B	B	C	B	B	B	B	C	C	C	B	A	C	C	A	C	C
S24-9-168	C	C	A	B	B	B	A	B	B	B	B	B	C	B	C	A	A	B	B	A	C	C
S24-9-169	B	C	B	B	B	B	B	B	B	A	B	B	C	A	A	A	A	B	B	A	C	C
S24-9-170	B	C	B	B	B	B	B	B	B	B	B	B	C	B	B	A	A	B	B	A	C	C
S24-9-171	C	B	B	B	B	B	B	B	B	A	B	A	A	A	B	A	A	B	B	A	C	C
S24-9-172	B	B	B	B	B	B	A	B	B	A	B	B	C	B	A	A	A	B	B	A	C	C
S24-9-173	B	C	B	B	B	B	B	B	B	B	B	B	C	C	C	A	A	B	B	A	C	C
S24-9-174	C	C	B	B	B	B	B	B	B	A	B	A	A	A	A	B	B	B	B	A	C	C
S24-9-175	C	C	B	B	B	B	B	B	B	B	B	C	C	C	C	B	B	B	B	A	C	C
S24-9-179	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	C	C	C	C	C
S24-9-182	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	C	C	C	C	C
S24-9-56	C	B	A	B	B	B	C	C	B	B	C	B	C	C	C	C	C	C	B	A	C	C
S24-9-58	C	B	A	B	B	B	B	B	B	A	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-59	C	B	B	B	B	B	B	B	B	A	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-60	C	A	A	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-61	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-62	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-63	B	C	A	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-64	B	C	A	B	B	B	B	B	B	B	C	B	C	C	C	C	C	C	B	A	C	C
S24-9-65	B	B	A	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-67	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-68	C	C	B	B	B	B	B	C	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-69	C	B	B	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	B	A	C	C
S24-9-70	B	C	A	B	B	B	B	B	B	B	B	B	C	B	B	C	C	C	B	A	C	C
S24-9-71	C	B	B	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	B	A	C	C

FIG. 11D

Compound	SA1 01 292 13	SA1 61 tetM	SA1 58 tetK	EF3 27 tetM	EF4 04 tetM	SP1 60 tetM	SP3 12 tetM	EC1 07 259 22	EC1 55 tetA	EC8 78 tolC	EC8 80 ipxC	EC8 82 imp	KP4 57 CTX-M-15	PM 385	PA5 55 BAA -47	PA5 56	PA8 84 351 51	PA6 89	EC6 03 tetA	AB2 50	SM 256	BC2 40
S24-9-72	C	B	B	B	B	B	B	B	B	C	B	B	C	C	C	C	C	C	B	C	C	C
S24-9-73	C	C	B	B	B	B	B	B	B	B	B	B	B	A	C	B	B	A	B	A	C	C
S24-9-74	C	B	B	B	B	B	B	B	B	B	B	B	B	A	C	B	B	B	B	A	C	B
S24-9-75	B	B	A	B	B	B	B	B	B	A	A	A	B	B	C	C	B	A	B	A	C	B
S24-9-76	C	C	B	C	C	B	C	B	B	B	B	B	B	A	A	A	B	A	B	C	C	C
S24-9-77	C	B	B	B	B	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S24-9-78	C	C	B	C	C	B	B	B	C	C	C	B	B	A	A	A	B	A	C	C	C	C
S24-9-79	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
S24-9-94	C	C	B	C	C	B	C	B	C	B	B	B	C	C	C	B	C	C	C	C	C	C
S24-9-95	C	C	B	C	C	B	C	B	C	B	B	B	C	C	C	B	C	C	C	C	C	C
S24-9-96	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
S25-11-134	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-135	C	C	B	B	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-136	C	C	C	B	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-137	C	C	C	C	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-138	C	C	C	C	C	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-139	C	C	C	B	B	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-140	C	C	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-141	C	C	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-142	C	C	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-143	C	B	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	B	C	C	C	C
S25-11-144	C	C	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-145	C	C	B	C	B	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-146	C	B	B	B	B	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-147	C	B	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-148	C	C	B	B	B	B	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-149	C	B	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-150	C	B	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-151	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-152	C	C	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C

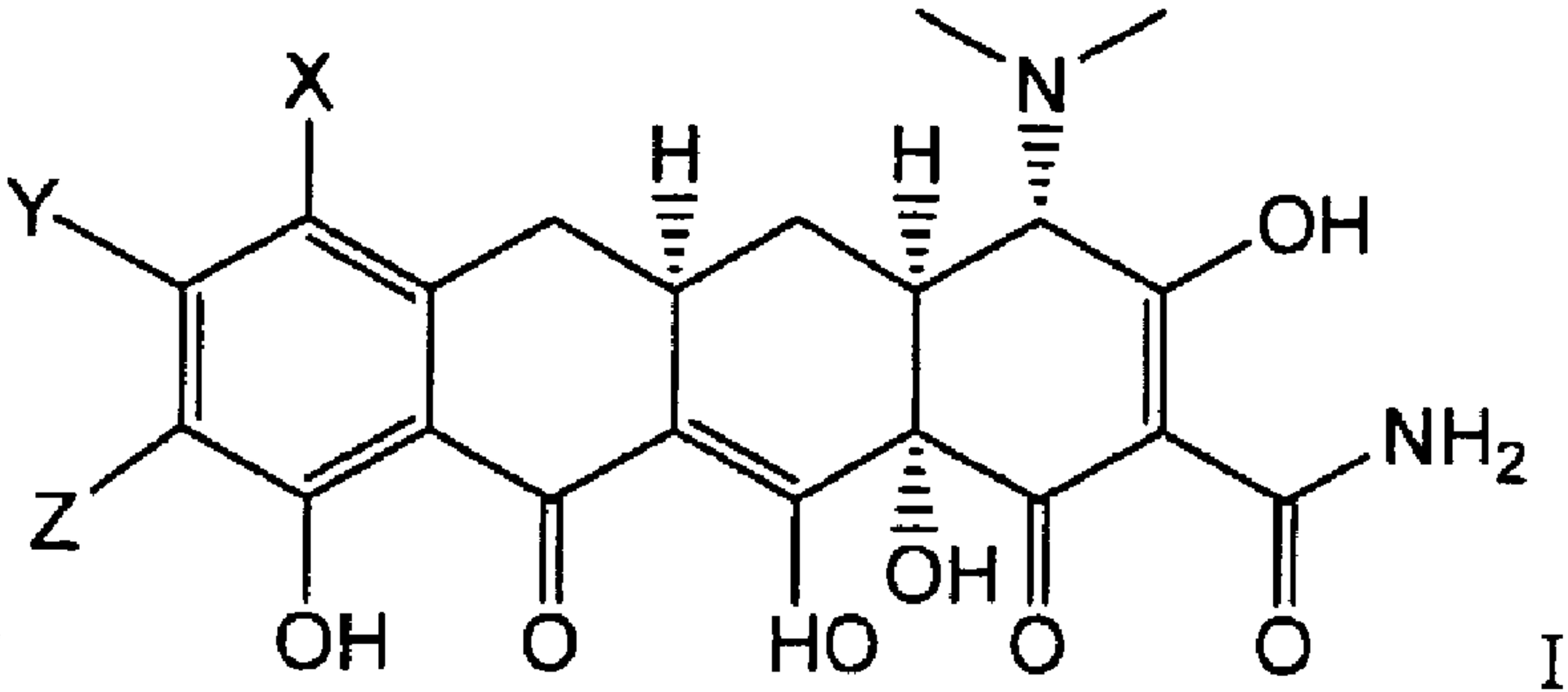
FIG. 11E

Compound	SA1 01 292 13	SA1 61 tetM	SA1 58 tetK	EF3 27 tetM	EF4 04 tetM	SP1 60 tetM	SP3 12 tetM	EC1 07 259 22	EC1 55 tetA	EC8 78 tolC	EC8 80 ipxC	EC8 82 imp	KP4 57 CTX-M-15	PM 385	PA5 55 BAA -47	PA5 56	PA8 84 351 51	PA6 89	BC2 40	SM 256	AB2 50	EC6 03 tetA
S25-11-153	C	C	C	C	B	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-154	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-155	C	C	B	B	B	B	B	B	B	B	B	A	A	A	A	A	A	A	C	C	C	B
S25-11-156	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-157	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-158	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-159	C	C	B	B	B	B	B	C	C	C	C	C	C	C	A	C	C	C	C	C	C	C
S25-11-160	C	C	C	B	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-161	C	C	C	B	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
S25-11-162	C	B	A	B	B	B	B	B	B	B	A	A	C	B	A	C	B	B	C	C	A	B
S25-11-163	C	B	B	B	B	B	B	B	B	C	B	B	C	C	C	C	C	B	C	C	A	B
S25-11-167	C	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	B	C	C	C	C
S25-11-190	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	B	C	C	C	B
S25-11-191	C	C	B	B	B	B	B	C	C	B	C	C	C	C	C	C	C	B	C	C	C	B
S25-11-192	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	B	C	C	C	B
S25-11-193	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	B	C	C	C	B
S25-11-201	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C	C
S25-11-202	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C	C
S25-11-203	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	B	C	C	C	C
S25-11-204	C	B	B	B	B	B	B	C	C	C	C	C	C	C	C	C	C	B	C	C	C	B
S25-11-205	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	C	C	C	B
S25-11-209	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	C	C	C	B
S26-7-1	C	C	B	B	B	B	B	B	B	B	B	B	B	A	C	B	B	A	C	C	B	B
S26-7-2	C	C	B	B	B	B	B	B	C	B	B	B	B	B	C	B	B	B	C	C	B	B
S26-7-3	C	C	B	B	B	B	B	B	C	C	A	A	C	C	C	C	B	B	C	C	B	B
S26-7-4	C	C	B	B	B	B	B	B	B	C	A	A	C	C	C	C	C	B	C	C	B	B
Sancycline	0.5	2	4	4	4	8	4	8	32	1	0.25	0.25	8	8	32	1	4	16	4	1	16	4
Minocycline	0.06	8	0.03	32	8	2	16	0.5	8	0.25	0.01 55	0.01 55	8	16	16	0.12 5	1	8	8	0.5	8	2
Tigecycline	0.06	0.12	0.06	0.06	0.03	0.01	0.01	0.03	0.5	0.03	0.01	0.01	1	4	16	0.25	0.06	1	16	0.5	2	1

FIG. 11F

Compound	SA1 01 292 13	SA1 61 tetM	SA1 58 tetK	EF3 27 tetM	EF4 04 tetM	SP1 60 tetM	SP3 12 tetM	EC1 07 259 22	EC1 55 tetA	EC8 78 tolC	EC8 80 ipxC	EC8 82 imp	KP4 57 CTX-M-15	PM 385	PA5 55 BAA -47	PA5 56	PA8 84 351 51	PA6 89	EC6 03 tetA	AB2 50	SM 256	BC2 40
		5		25	12	55	55			12	55	55					25					

FIG. 11G



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