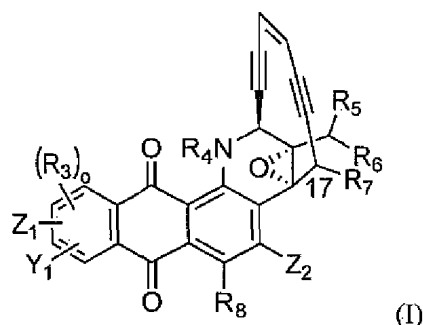


CLAIMS

1. A compound of the formula:



wherein:

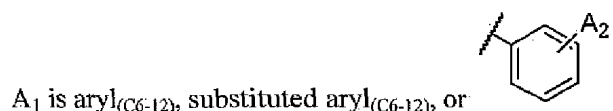
5 Y_1 is $-(CH_2)_mNR_1R_2$;

wherein:

m is 1, 2, 3, 4, 5, or 6; and

10 R_1 and R_2 are each independently selected from hydrogen, hydroxy, alkyl_(C1-12), substituted alkyl_(C1-12), alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), aryl_(C6-12), substituted aryl_(C6-12), aralkyl_(C7-12), substituted aralkyl_(C7-12), heteroaryl_(C1-12), substituted heteroaryl_(C1-12), heterocycloalkyl_(C2-12), substituted heterocycloalkyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12); a monovalent amine protecting group, $-C(O)O(CH_2)_nS-A_1$, $-C(O)O(CH_2)_nS(O)-A_1$, or $-C(O)O(CH_2)_nS(O)_2-A_1$,

wherein:



wherein:

20 A_2 is alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkoxy_(C1-12), substituted alkoxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12), dialkylamino_(C2-12), or substituted dialkylamino_(C2-12); wherein A_2 is not $-CO_2H$, $-CO_2CH_3$, $-OCH_3$, $-OCH_2CH_3$, $-C(O)CH_3$, $-NHCH_3$, $-NHCH_2CH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, and $-OC(O)CH_3$; and

n is 1, 2, 3, 4, or 5; or

30 R_1 and R_2 are taken together and are divalent amine protecting group, alkanediyl_(C1-12), alkylaminodiyl_(C1-8), alkoxydiyl_(C1-8); or a substituted version of either of these groups; or

Z_1 is absent or hydrogen;

R_3 and Z_2 are each independently selected from hydrogen, hydroxy, halo, amino, cyano, nitro, phosphate, or mercapto, or

alkyl_(C1-12), alkenyl_(C2-12), alkynyl_(C2-12), aryl_(C6-12), aralkyl_(C7-12), heteroaryl_(C1-12), heterocycloalkyl_(C2-12), acyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), amido_(C1-12), or a substituted version of any of these groups;

o is 1, 2, or 3;

R_4 is hydrogen, alkyl_(C1-12), a monovalent amine protecting group, or substituted alkyl_(C1-12);

R_5 , R_6 , and R_7 are each independently hydrogen, hydroxy, amino, mercapto, $-OX_1$, $-NX_2X_3$, or $-SX_4$; or

alkyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups;

wherein:

X_1 is a hydroxy protecting group;

X_2 and X_3 are independently selected from hydrogen, a monovalent amine protecting group, or when X_2 and X_3 are taken together form a divalent amine protecting group; and

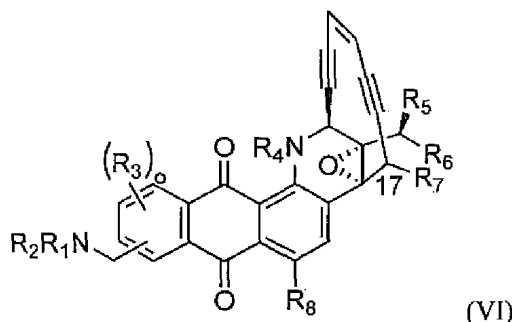
X_4 is a thiol protecting group;

R_8 is hydroxy, amino, or mercapto; or

alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups; and

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein the formula is further defined as:



wherein:

R_1 and R_2 are each independently selected from hydrogen, hydroxy,

alkyl_(C1-12), substituted alkyl_(C1-12), alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), aryl_(C6-12), substituted aryl_(C6-12), aralkyl_(C7-12), substituted aralkyl_(C7-12), heteroaryl_(C1-12), substituted heteroaryl_(C1-12), heterocycloalkyl_(C2-12), substituted heterocycloalkyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12),

substituted acyloxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12); a monovalent amine protecting group, $-C(O)O(CH_2)_nS-A_1$, $-C(O)O(CH_2)_nS(O)-A_1$, or $-C(O)O(CH_2)_nS(O)_2-A_1$,

wherein:

5 A_1 is aryl_(C6-12) or substituted aryl_(C6-12); and

n is 1, 2, 3, 4, or 5;

R_3 is hydrogen, hydroxy, halo, or alkoxy_(C1-12) or substituted alkoxy_(C1-12);

o is 1, 2, or 3;

R_4 is hydrogen, a monovalent amine protecting group, alkyl_(C1-12), or substituted alkyl_(C1-12);

10 R_5 , R_6 , and R_7 are each independently hydrogen, hydroxy, amino, mercapto, $-OX_1$, $-NX_2X_3$, or $-SX_4$; or

alkyl_(C1-12) or substituted alkyl_(C1-12);

wherein:

X_1 is a hydroxy protecting group;

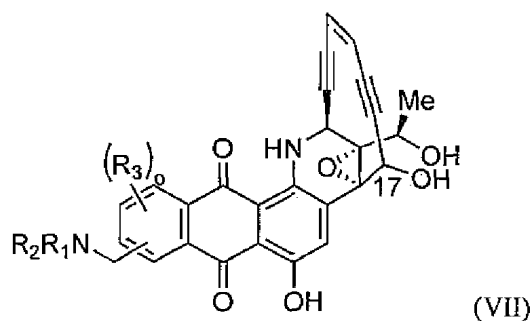
15 X_2 and X_3 are independently selected from hydrogen, a monovalent amine protecting group, or when X_2 and X_3 are taken together form a divalent amine protecting group; and

X_4 is a thiol protecting group; and

R_8 is hydroxy, amino, or mercapto; or

20 a pharmaceutically acceptable salt thereof.

3. The compound of claim 1, wherein the formula is further defined as:



wherein:

R_1 and R_2 are each independently selected from hydrogen, hydroxy,

25 alkyl_(C1-12), substituted alkyl_(C1-12), aryl_(C6-12), substituted aryl_(C6-12), aralkyl_(C7-12), substituted aralkyl_(C7-12), acyl_(C1-12), substituted acyl_(C1-12), a monovalent amine protecting group, $-C(O)O(CH_2)_nS-C_6H_5$, $-C(O)O(CH_2)_nS(O)-C_6H_5$, or $-C(O)O(CH_2)_nS(O)_2-C_6H_5$,

a monovalent amine protecting group, or R_1 and R_2 are taken together and form a divalent amine protecting group, or

alkyl_(C1-12), aryl_(C6-12), aralkyl_(C7-12), acyl_(C1-12), or a substituted version of any of these groups;

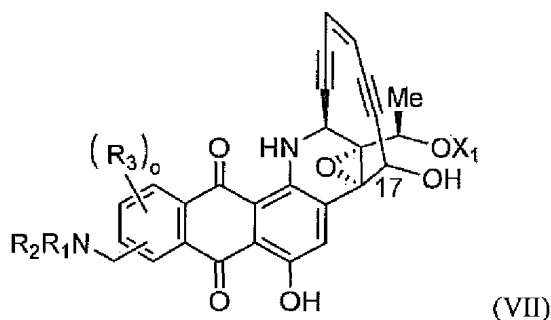
R₃ is hydrogen, hydroxy, halo, or

alkoxy_(C1-12) or substituted alkoxy_(C1-12); and

o is 1, 2, or 3; or

5 a pharmaceutically acceptable salt thereof.

4. The compound of claim 1, wherein the formula is further defined as:



wherein:

X₁ is a hydroxy protecting group;

10 R₁ and R₂ are each independently selected from hydrogen, alkyl_(C1-12), or substituted alkyl_(C1-12); and

R₃ is hydrogen, alkoxy_(C1-12), or substituted alkoxy_(C1-12); and

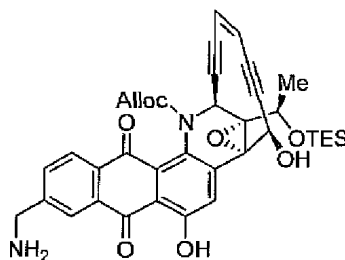
o is 2;

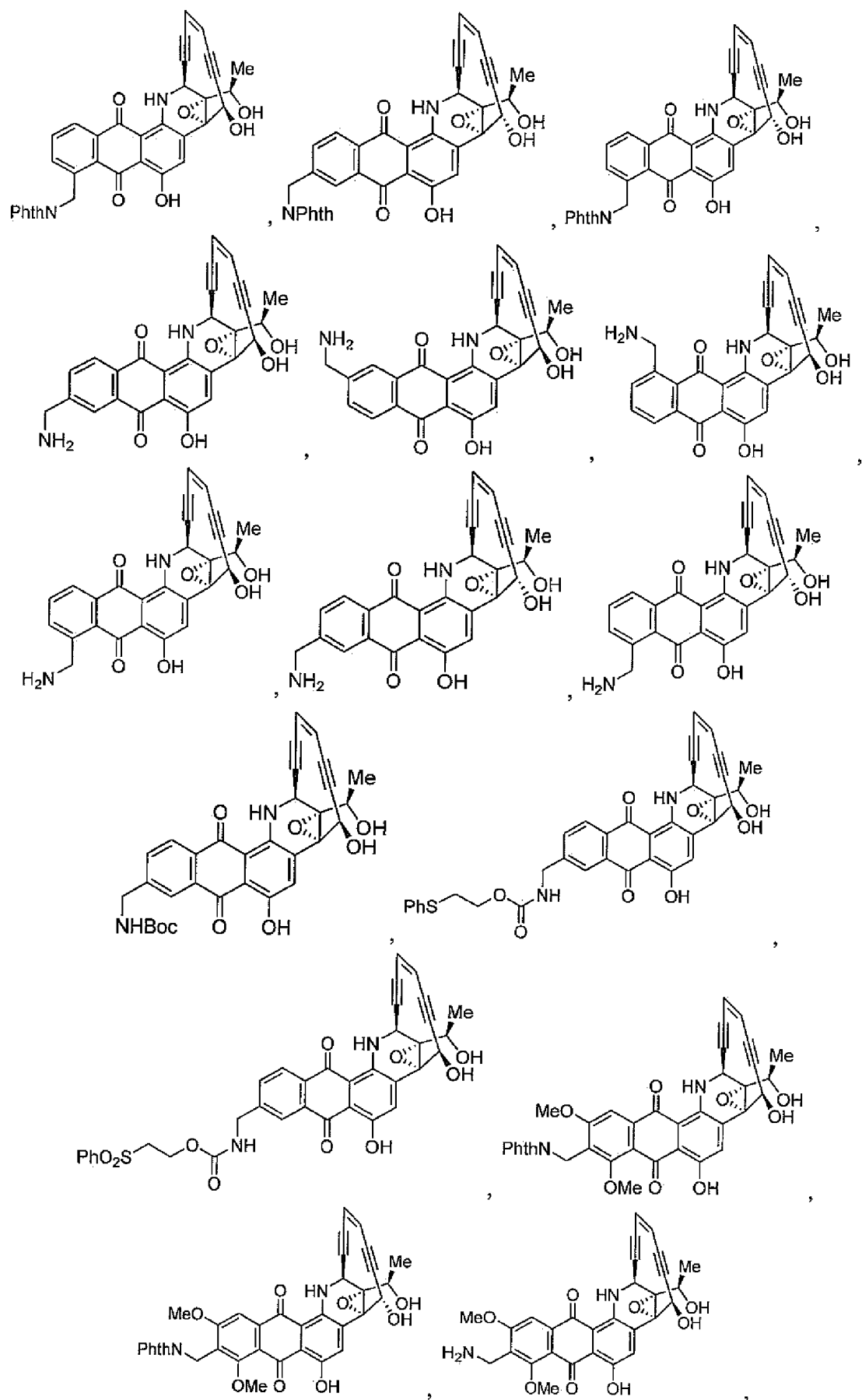
or a pharmaceutically acceptable salt thereof.

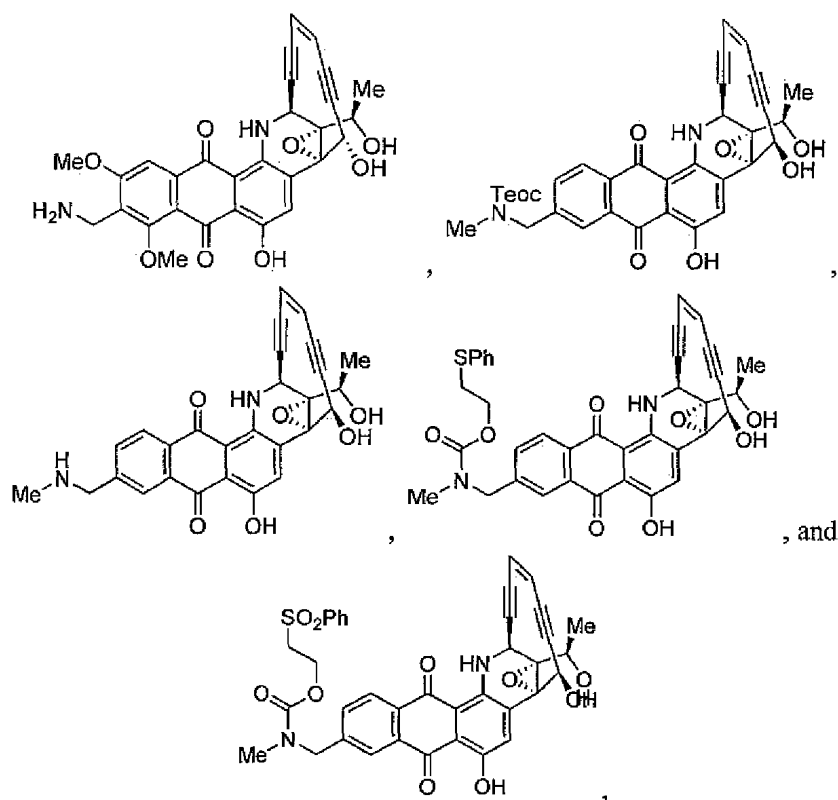
15 5. The compound of claim 1, wherein Z₁ is hydrogen, m is 1, 2, or 3, R₁ or R₂ is hydrogen, R₁ or R₂ is alkyl_(C1-12) or substituted alkyl_(C1-12), R₁ or R₂ is a monovalent amine protecting group, R₁ or R₂ is -C(O)O(CH₂)₂SC₆H₅ or -C(O)O(CH₂)₂S(O)₂C₆H₅, R₁ is taken together with R₂ and is a divalent amine protecting group, R₃ is hydrogen, R₃ is alkoxy_(C1-12), R₄ is hydrogen, R₄ is a monovalent amine protecting group.

20 6. The compound of claim 1, wherein R₅ is alkyl_(C1-12), R₆, R₇, or R₈ is hydroxy, carbon atom 17 is in the R configuration, or carbon atom 17 is in the S configuration.

7. The compound of claim 1, wherein the compound is further defined as:

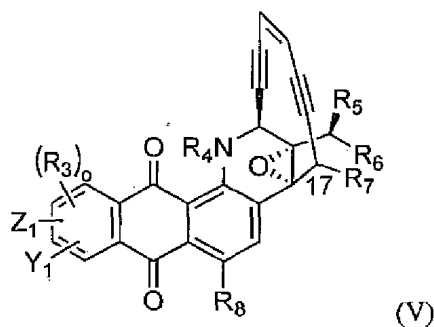






or a pharmaceutically acceptable salt thereof.

- 5 8. A method of preparing a compound of the formula:



wherein:

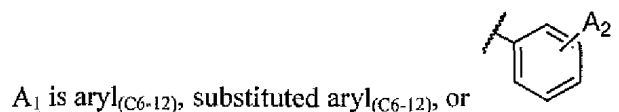
Y_1 is $-(CH_2)_mNR_1R_2$;

wherein:

- 10 m is 1, 2, 3, 4, 5, or 6; and

- 15 R_1 and R_2 are each independently selected from hydrogen, hydroxy, alkyl_(C1-12), substituted alkyl_(C1-12), alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), aryl_(C6-12), substituted aryl_(C6-12), aralkyl_(C7-12), substituted aralkyl_(C7-12), heteroaryl_(C1-12), substituted heteroaryl_(C1-12), heterocycloalkyl_(C2-12), substituted heterocycloalkyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12); a monovalent amine protecting group, $-C(O)O(CH_2)_nS-A_1$, $-C(O)O(CH_2)_nS(O)-A_1$, or $-C(O)O(CH_2)_nS(O)_2-A_1$,

wherein:



wherein:

A_2 is alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkoxy_(C1-12), substituted alkoxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12), dialkylamino_(C2-12), or substituted dialkylamino_(C2-12), wherein A_2 is not $-\text{CO}_2\text{H}$, $-\text{CO}_2\text{CH}_3$, $-\text{OCH}_3$, $-\text{OCH}_2\text{CH}_3$, $-\text{C}(\text{O})\text{CH}_3$, $-\text{NHCH}_3$, $-\text{NHCH}_2\text{CH}_3$, $-\text{N}(\text{CH}_3)_2$, $-\text{C}(\text{O})\text{NH}_2$, and $-\text{OC}(\text{O})\text{CH}_3$; and

n is 1, 2, 3, 4, or 5; or

R_1 and R_2 are taken together and are divalent amine protecting group, alkanediyl_(C1-12), alkylaminodiyl_(C1-8), alkoxydiyl_(C1-8); or a substituted version of either of these groups; or

Z_1 is absent or hydrogen;

R_3 is hydrogen, hydroxy, halo, amino, cyano, nitro, phosphate, or mercapto, or

alkyl_(C1-12), alkenyl_(C2-12), alkynyl_(C2-12), aryl_(C6-12), aralkyl_(C7-12), heteroaryl_(C1-12), heterocycloalkyl_(C2-12), acyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), amido_(C1-12), or a substituted version of any of these groups;

o is 1, 2, or 3;

R_4 is hydrogen, alkyl_(C1-12), a monovalent amine protecting group, or substituted alkyl_(C1-12);

R_5 , R_6 , and R_7 are each independently hydrogen, hydroxy, amino, mercapto, $-\text{OX}_1$, $-\text{NX}_2\text{X}_3$, or $-\text{SX}_4$; or

alkyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups;

wherein:

X_1 is a hydroxy protecting group;

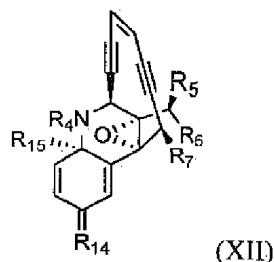
X_2 and X_3 are independently selected from hydrogen, a monovalent amine protecting group, or when X_2 and X_3 are taken together form a divalent amine protecting group;

X_4 is a thiol protecting group;

R_8 is hydroxy, amino, or mercapto; or

alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups; and

by carrying out a reaction comprising admixing a compound of the formula:



wherein:

R₄ is hydrogen, alkyl_(C1-12), a monovalent amine protecting group, or substituted alkyl_(C1-12);

5 R₅, R₆, and R₇ are each independently hydrogen, hydroxy, amino, mercapto, -OX₁, -NX₂X₃, or -SX₄; or

alkyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups;

wherein:

10 X₁ is a hydroxy protecting group;

X₂ and X₃ are independently selected from hydrogen, a monovalent amine protecting group, or when X₂ and X₃ are taken together form a divalent amine protecting group; and

X₄ is a thiol protecting group; and

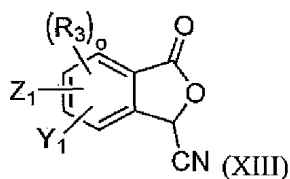
15 R₁₄ is -O-, -S-, or -NR_{15'}-;

wherein:

R_{15'} is hydrogen, alkyl_(C1-6), or substituted alkyl_(C1-6); and

20 R₁₅ is cyano, alkoxy_(C1-12), substituted alkoxy_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkylthio_(C1-12), substituted alkylthio_(C1-12), alkylsulfonyl_(C1-12), substituted alkylsulfonyl_(C1-12), arylsulfonyl_(C1-12), substituted arylsulfonyl_(C1-12), alkylsulfonyloxy_(C1-12), substituted alkylsulfonyloxy_(C1-12), arylsulfonyloxy_(C1-12), or substituted arylsulfonyloxy_(C1-12);

with a compound of the formula:



25 wherein:

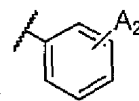
Y₁ is -(CH₂)_mNR₁R₂, or is taken with Z₁ as described below;

wherein:

m is 1, 2, 3, 4, 5, or 6; and

R_1 and R_2 are each independently selected from hydrogen, hydroxy, alkyl_(C1-12), substituted alkyl_(C1-12), alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), aryl_(C6-12), substituted aryl_(C6-12), aralkyl_(C7-12), substituted aralkyl_(C7-12), heteroaryl_(C1-12), substituted heteroaryl_(C1-12), heterocycloalkyl_(C2-12), substituted heterocycloalkyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12); a monovalent amine protecting group, $-C(O)O(CH_2)_nS-A_1$, $-C(O)O(CH_2)_nS(O)-A_1$, or $-C(O)O(CH_2)_nS(O)_2-A_1$,

wherein:



A_1 is aryl_(C6-12), substituted aryl_(C6-12), or

wherein:

A_2 is alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkoxy_(C1-12), substituted alkoxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12), dialkylamino_(C2-12), or substituted dialkylamino_(C2-12), wherein A_2 is not $-CO_2H$, $-CO_2CH_3$, $-OCH_3$, $-OCH_2CH_3$, $-C(O)CH_3$, $-NHCH_3$, $-NHCH_2CH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, and $-OC(O)CH_3$; and

n is 1, 2, 3, 4, or 5; or

R_1 and R_2 are taken together and are divalent amine protecting group, alkanediyl_(C1-12), alkylaminodiyl_(C1-8); alkoxydiyl_(C1-8); or a substituted version of either of these groups; or

Z_1 is absent or hydrogen;

R_3 is hydrogen, hydroxy, halo, amino, cyano, nitro, phosphate, or mercapto, or

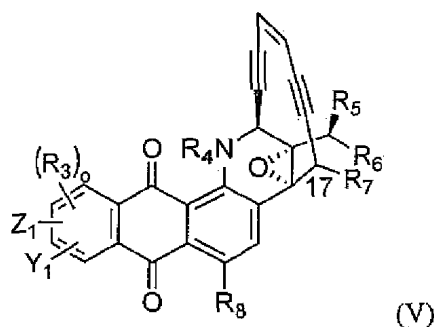
alkyl_(C1-12), alkenyl_(C2-12), alkynyl_(C2-12), aryl_(C6-12), aralkyl_(C7-12), heteroaryl_(C1-12), heterocycloalkyl_(C2-12), acyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), amido_(C1-12), or a substituted version of any of these groups; and

o is 1 or 2;

in the presence of a strong non-nucleophilic base in a solvent under conditions sufficient to cause a reaction.

9. The method of claim 8, wherein Y_1 is not $-NH_2$, $-NHMe$, or $-NHCH_2CH_2NH_2$, the base is lithium bis(trimethylsilyl)amide, sodium bis(trimethylsilyl)amide, potassium bis(trimethylsilyl)amide, lithium diisopropyl amide, sodium diisopropyl amide, potassium diisopropyl amide, lithium tetramethylpiperidide, lithium t-butoxide, sodium t-butoxide, or potassium t-butoxide, lithium hydride, sodium hydride, or potassium hydride preferably wherein the base is lithium bis(trimethylsilyl)amide, the solvent is tetrahydrofuran, the method further comprises admixing the compound of formula IV with the base before contacting the compound of formula III with the compound of formula IV, the compound of formula III is dissolved in THF and added via cannula, the method further comprising

dissolving the compound of formula I or formula II in an organic solvent and reacting the compound of the formula:



wherein:

5 Y_1 is $-O(CH_2)_m Y'$, $-NH(CH_2)_m Y'$, $-S(CH_2)_m Y'$, or $-(CH_2)_m NR_1 R_2$, or is taken together with Z_1 as described below;

wherein:

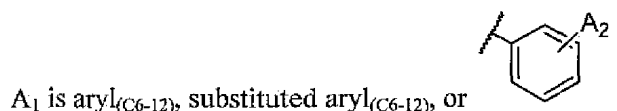
10 Y' is hydroxy, halo, mercapto, $alkyl_{(C1-12)}$, substituted $alkyl_{(C1-12)}$, $alkenyl_{(C2-12)}$, substituted $alkenyl_{(C2-12)}$, $alkynyl_{(C2-12)}$, substituted $alkynyl_{(C2-12)}$, $acyl_{(C1-12)}$, substituted $acyl_{(C1-12)}$, $acyloxy_{(C1-12)}$, substituted $acyloxy_{(C1-12)}$, $alkylamino_{(C1-12)}$, or substituted $alkylamino_{(C1-12)}$;

m is 1, 2, 3, 4, 5, or 6; and

15 R_1 and R_2 are each independently selected from hydrogen, hydroxy, $alkyl_{(C1-12)}$, substituted $alkyl_{(C1-12)}$, $alkenyl_{(C2-12)}$, substituted $alkenyl_{(C2-12)}$, $alkynyl_{(C2-12)}$, substituted $alkynyl_{(C2-12)}$, $aryl_{(C6-12)}$, substituted $aryl_{(C6-12)}$, $aralkyl_{(C7-12)}$, substituted $aralkyl_{(C7-12)}$, $heteroaryl_{(C1-12)}$, substituted $heteroaryl_{(C1-12)}$, $heterocycloalkyl_{(C2-12)}$, substituted $heterocycloalkyl_{(C2-12)}$, $acyl_{(C1-12)}$, substituted $acyl_{(C1-12)}$, $acyloxy_{(C1-12)}$, substituted $acyloxy_{(C1-12)}$, $alkylamino_{(C1-12)}$, substituted $alkylamino_{(C1-12)}$; a monovalent amine protecting group, $-C(O)O(CH_2)_n S-A_1$, $-C(O)O(CH_2)_n S(O)-A_1$, or $-C(O)O(CH_2)_n S(O)_2-A_1$,

20

wherein:



wherein:

25 A_2 is $alkenyl_{(C2-12)}$, substituted $alkenyl_{(C2-12)}$, $alkynyl_{(C2-12)}$, substituted $alkynyl_{(C2-12)}$, $acyl_{(C1-12)}$, substituted $acyl_{(C1-12)}$, $acyloxy_{(C1-12)}$, substituted $acyloxy_{(C1-12)}$, $alkoxy_{(C1-12)}$, substituted $alkoxy_{(C1-12)}$, $alkylamino_{(C1-12)}$, substituted $alkylamino_{(C1-12)}$, $dialkylamino_{(C2-12)}$, or substituted $dialkylamino_{(C2-12)}$, wherein A_2 is not $-CO_2H$, $-CO_2CH_3$, $-OCH_3$, $-OCH_2CH_3$, $-C(O)CH_3$, $-NHCH_3$, $-NHCH_2CH_3$, $-N(CH_3)_2$, $-C(O)NH_2$, and $-OC(O)CH_3$; and

30

n is 1, 2, 3, 4, or 5; or

R_1 and R_2 are taken together and are divalent amine protecting group, alkanediyl_(C1-12), alkylaminodiyl_(C1-8); alkoxydiyl_(C1-8); or a substituted version of either of these groups; or

5

Y_1 is taken with Z_1 and is alkylaminodiyl_(C1-8) substituted alkylaminodiyl_(C1-8); -alkanediyl_(C1-6)-NZ₂-alkanediyl_(C1-6), or -substituted alkanediyl_(C1-6)-NZ₂-substituted alkanediyl_(C1-6),

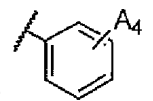
wherein:

Z_2 is hydrogen, an amine protecting group, acyl_(C1-12), substituted acyl_(C1-12), -C(O)O(CH₂)_nS-A₃, or -C(O)O(CH₂)_nS(O)₂-A₃,

10

wherein:

A₃ is aryl_(C6-12), substituted aryl_(C6-12), or



wherein:

15

A₄ is alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkoxy_(C1-12), substituted alkoxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12), dialkylamino_(C2-12), or substituted dialkylamino_(C2-12), wherein A₂ is not -CO₂H, -CO₂CH₃, -OCH₃, -OCH₂CH₃, -C(O)CH₃, -NHCH₃, -NHCH₂CH₃, -N(CH₃)₂, -C(O)NH₂, and -OC(O)CH₃;

20

Z_1 is absent, hydrogen or taken together with Y_1 as defined above;

R_3 is hydrogen, hydroxy, halo, amino, cyano, nitro, phosphate, or mercapto, or

25

alkyl_(C1-12), alkenyl_(C2-12), alkynyl_(C2-12), aryl_(C6-12), aralkyl_(C7-12), heteroaryl_(C1-12), heterocycloalkyl_(C2-12), acyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), amido_(C1-12), or a substituted version of any of these groups;

o is 1 or 2;

R_4 is hydrogen, alkyl_(C1-12), a monovalent amine protecting group, or substituted alkyl_(C1-12);

30

R_5 , R_6 , and R_7 are each independently hydrogen, hydroxy, amino, mercapto, -OX₁, -NX₂X₃, or -SX₄; or

alkyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups;

wherein:

35

X₁ is a hydroxy protecting group;

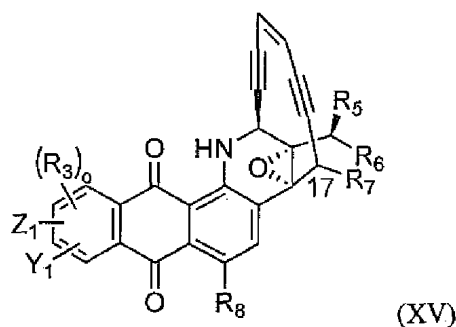
X_2 and X_3 are independently selected from hydrogen, a monovalent amine protecting group, or when X_2 and X_3 are taken together form a divalent amine protecting group;

X_4 is a thiol protecting group;

5 R_8 is hydroxy, amino, or mercapto; or

alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups; and

with a palladium complex in the presence of a base under conditions sufficient to cause a reaction to form a compound of the formula:



wherein:

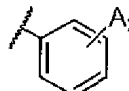
Y_1 is $-(CH_2)_mNR_1R_2$;

wherein:

m is 1, 2, 3, 4, 5, or 6; and

15 R_1 and R_2 are each independently selected from hydrogen, hydroxy, alkyl_(C1-12), substituted alkyl₍₁₋₁₂₎, alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), aryl_(C6-12), substituted aryl_(C6-12), aralkyl_(C7-12), substituted aralkyl_(C7-12), heteroaryl_(C1-12), substituted heteroaryl_(C1-12), heterocycloalkyl_(C2-12), substituted heterocycloalkyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12); a monovalent amine protecting group, $-C(O)O(CH_2)_nS-A_1$, $-C(O)O(CH_2)_nS(O)-A_1$, or $-C(O)O(CH_2)_nS(O)_2-A_1$,

wherein:

25 A_1 is aryl_(C6-12), substituted aryl_(C6-12), or ,

wherein:

30 A_2 is alkenyl_(C2-12), substituted alkenyl_(C2-12), alkynyl_(C2-12), substituted alkynyl_(C2-12), acyl_(C1-12), substituted acyl_(C1-12), acyloxy_(C1-12), substituted acyloxy_(C1-12), alkoxy_(C1-12), substituted alkoxy_(C1-12), alkylamino_(C1-12), substituted alkylamino_(C1-12), dialkylamino_(C2-12), or substituted dialkylamino_(C2-12), wherein A_2 is not $-CO_2H$, $-CO_2CH_3$,

-OCH₃, -OCH₂CH₃, -C(O)CH₃, -NHCH₃, -NHCH₂CH₃,
-N(CH₃)₂, -C(O)NH₂, and -OC(O)CH₃; and

n is 1, 2, 3, 4, or 5; or

5 R₁ and R₂ are taken together and are divalent amine protecting group, alkanediyl_(C1-12), alkylaminodiyl_(C1-8), alkoxydiyl_(C1-8); or a substituted version of either of these groups; or

Z₁ is absent or hydrogen;

R₃ is hydrogen, hydroxy, halo, amino, cyano, nitro, phosphate, or mercapto, or

10 alkyl_(C1-12), alkenyl_(C2-12), alkynyl_(C2-12), aryl_(C6-12), aralkyl_(C7-12), heteroaryl_(C1-12), heterocycloalkyl_(C2-12), acyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), amido_(C1-12), or a substituted version of any of these groups;

o is 1 or 2;

15 R₅, R₆, and R₇ are each independently hydrogen, hydroxy, amino, mercapto, -OX₁, -NX₂X₃, or -SX₄; or

alkyl_(C1-12), alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups;

wherein:

X₁ is a hydroxy protecting group;

20 X₂ and X₃ are independently selected from hydrogen, a monovalent amine protecting group, or when X₂ and X₃ are taken together form a divalent amine protecting group; and

X₄ is a thiol protecting group;

R₈ is hydroxy, amino, or mercapto; or

25 alkoxy_(C1-12), acyloxy_(C1-12), alkylamino_(C1-12), dialkylamino_(C2-12), alkylthio_(C1-12), amido_(C1-12), or a substituted version of any of these groups; and

30 , the palladium complex further comprises a palladium phosphine complex or a palladium salt in the presence of a ligand or other metal complexes or salts preferably wherein the palladium complex is Pd(PPh₃)₄, the base is triethylamine, diisopropylethylamine, ethylenediamine, 1,8-diazabicyclo[5.4.0]undec-7-ene, or morpholine, preferably wherein the base is morpholine, the solvent is tetrahydrofuran, or the method further comprises removing one or more protecting groups.

10. A conjugate of the formula:

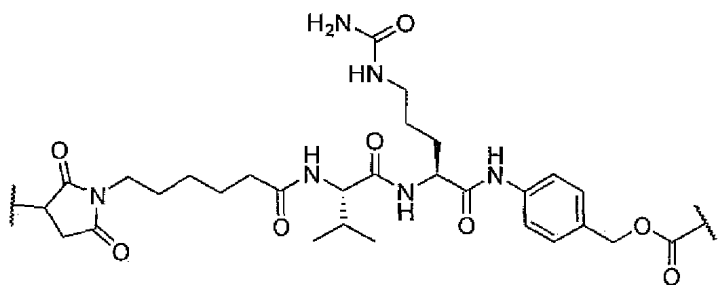
35 (A₅-L)_r-A₆ (XVII)

wherein:

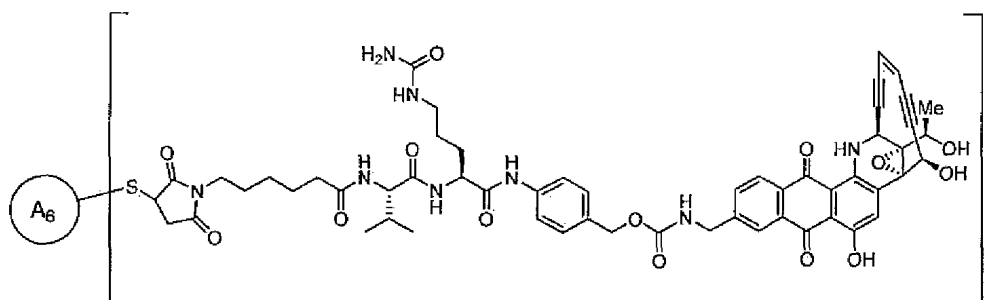
A₅ is a compound of claim 1;

A₆ is a cell targeting moiety.

11. The conjugate of claim 10, wherein L comprises a polypeptide cleavable by an intracellular enzyme.
12. The conjugate of claim 11, wherein the enzyme is cathepsin B.
13. The conjugate of claim 10, wherein L comprises a self-immolating group.
14. The conjugate of claim 10, wherein L is:



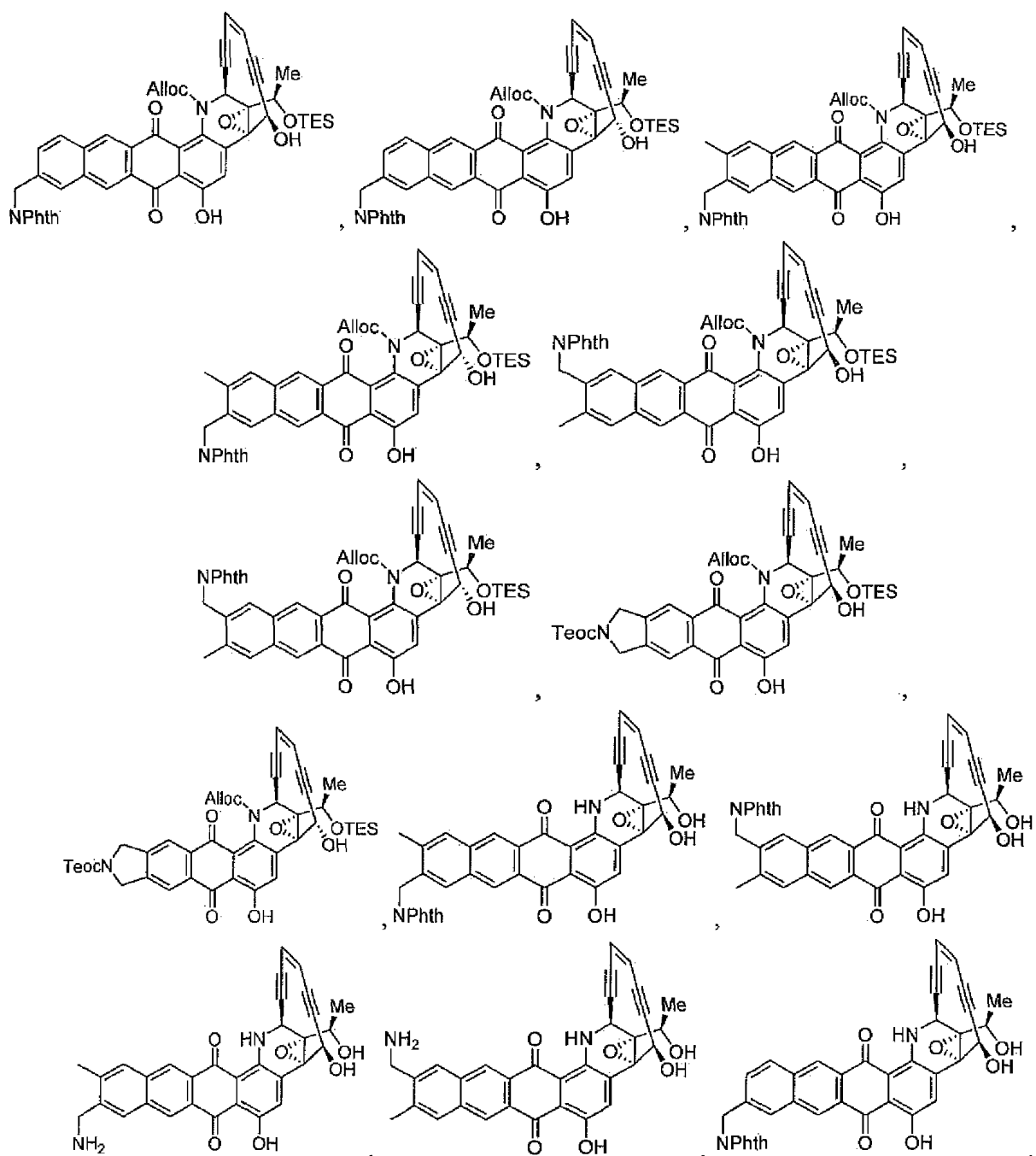
15. The conjugate of claim 10, wherein A₆ is an antibody whose antigen is a tumor associated antigen.
16. The conjugate of claim 15, wherein the antigen is mesothelin, glypican-3, or CD70.
17. The conjugate of claim 10, further comprising a structure of the formula:

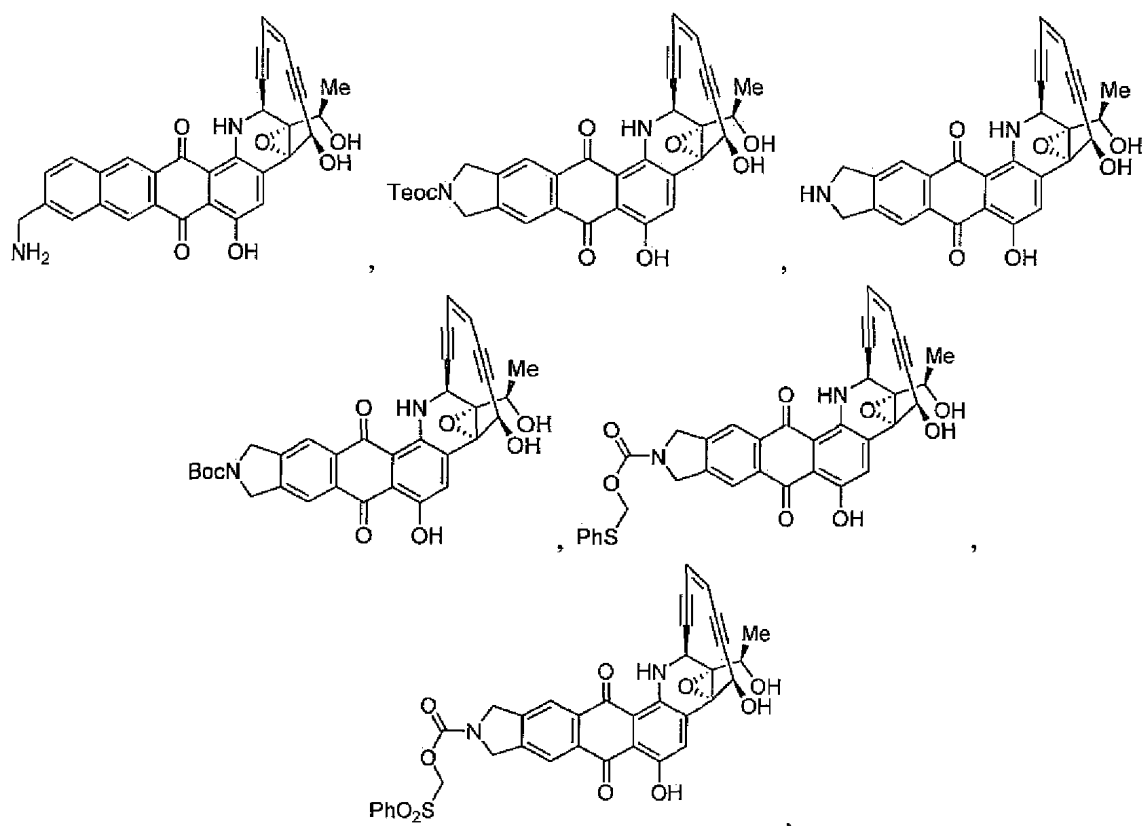


A_6 is an antibody and r is 1, 2, 3, or 4.

18. The conjugate of claim 17, wherein the antibody is an anti-mesothelin, anti-glypican-3, or anti-CD70 antibody.
19. A pharmaceutical composition comprising a compound according to any one of claims 1-7 or conjugate according to any one of claims 10-18 and an excipient.
20. The pharmaceutical composition of claim 19, wherein the compound is formulated for oral, intraadiposal, intraarterial, intraarticular, intracranial, intradermal, intralesional, intramuscular, intranasal, intraocular, intrapericardial, intraperitoneal, intrapleural, intraprostatic, intrarectal, intrathecal, intratracheal, intratumoral, intraumbilical, intravaginal, intravenous, intravesicular, intravitreal, liposomal, local, mucosal, parenteral, rectal, subconjunctival, subcutaneous, sublingual, topical, transbuccal, transdermal, vaginal, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, or via localized perfusion administration.

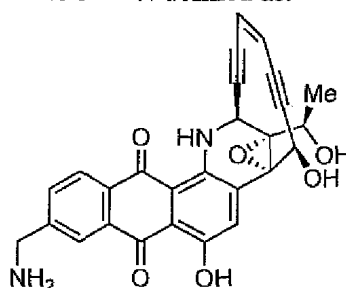
21. Use of a compound or composition of claims 1-7 or 10-20 in the manufacture of a medicament for treating a cancer or a bacterial infection, the use comprising a pharmaceutically effective amount of compound or conjugate of the claims 1-7 or 10-20 to be administered to a patient in need thereof.
22. The use of claim 21, wherein the disease or disorder is cancer, more preferably wherein the cancer is lung cancer, gastric cancer, ovarian cancer, liver cancer, renal cancer, or breast cancer, the cancer exhibit one or more tumor markers, the tumor marker is mesothelin, glypican-3, or CD70, the use comprises a compound of claims 1-7 to be administered, the use comprises a conjugate of claims 10-20 to be administered, the use further comprises a second therapeutic agent to be administered such as wherein the second therapeutic agent is a second chemotherapeutic agent, surgery, a radiotherapy agent, a genetic therapy agent, or an immunotherapy agent, or the disease or disorder is a bacterial infection.
23. A compound of the formula:





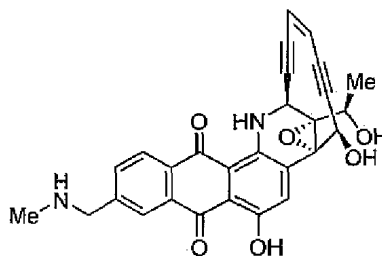
or a pharmaceutically acceptable salt thereof.

- 5 24. The compound according to claim 45 further defined as:



or a pharmaceutically acceptable salt thereof.

- 10 25. The compound according to claim 45 further defined as:



or a pharmaceutically acceptable salt thereof.