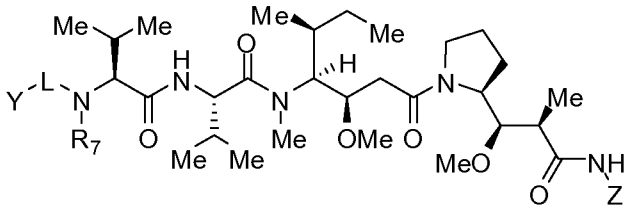
CLAIMS

WHAT IS CLAIMED IS:

1. A compound, or salt thereof, comprising Formula (I):

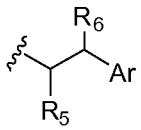


(I)

;

wherein:

Z has the structure of:



;

R_5 is H, COR_8, C_1-C_6alkyl, or thiazole;

R_8 is OH;

R_6 is OH or H;

Ar is phenyl or pyridine;

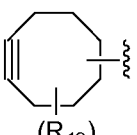
R_7 is C_1-C_6alkyl or hydrogen;

Y is selected from the group consisting of an hydroxylamine, methyl, aldehyde, protected aldehyde, ketone, protected ketone, thioester, ester, dicarbonyl, hydrazine, amidine, imine, diamine, azide, keto-amine, keto-alkyne, alkyne, cycloalkyne, and ene-dione;

L is–alkylene– or –(alkylene–O)$_n$–alkylene–; and

n is an integer greater than or equal to one.

2. The compound of claim 1, wherein R_5 is thiazole.
3. The compound of claim 1, wherein R_6 is H.
4. The compound of claim 1, wherein Ar is phenyl.
5. The compound of claim 1, wherein R_7 is methyl.
6. The compound of claim 1, where n is an integer from 0 to 20.
7. The compound of claim 1, where n is an integer from 0 to 10.
8. The compound of claim 1, where n is an integer from 0 to 5.
9. The compound of claim 1, wherein Y is cyclooctyne.
10. The compound of claim 9, wherein the cyclooctyne has a structure of:



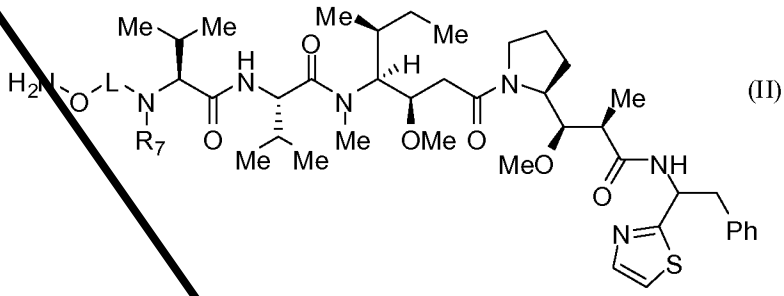
;

each R_{19} is independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, ester, ether, thioether, aminoalkyl, halogen, alkyl ester, aryl ester, amide, aryl amide, alkyl halide, alkyl amine, alkyl sulfonic acid, alkyl nitro, thioester, sulfonyl ester, halosulfonyl, nitrile, alkyl nitrile, and nitro; and

q is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11.

11. The compound of claim 1, wherein Y is azide.

12. The compound of claim 1, comprising Formula (II):



(II)

.

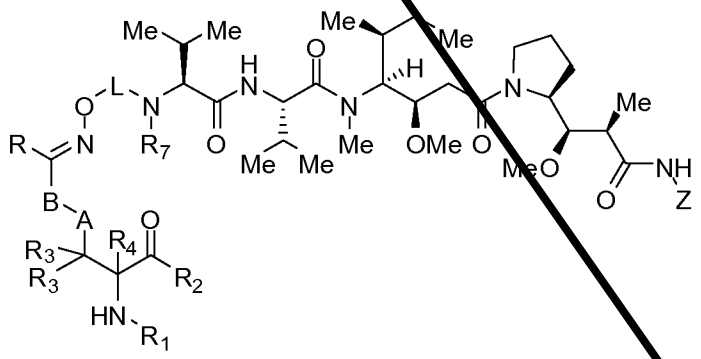
13. The compound of claim 12, wherein L is $-(alkylene-O)_n-alkylene-$.

14. The compound of claim 13, wherein each alkylene is $-CH_2CH_2-$, n is equal to 3, and R_7 is methyl.

15. The compound of claim 12, wherein L is –alkylene–.

16. The compound of claim 15, wherein each alkylene is $-CH_2CH_2-$ and R_7 is methyl or hydrogen.

17. A compound comprising Formula (VIII):



(VIII)

;

;

wherein:

A is optional, and when present is lower alkylene, substituted lower alkylene, lower cycloalkylene, substituted lower cycloalkylene, lower alkenylene, substituted lower alkenylene, alkynylene, lower heteroalkylene, substituted heteroalkylene, lower heterocycloalkylene, substituted lower heterocycloalkylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, alkarylene, substituted alkarylene, aralkylene, or substituted aralkylene;

B is optional, and when present is a linker selected from the group consisting of lower alkylene, substituted lower alkylene, lower alkenylene, substituted lower alkenylene, lower

heteroalkylene, substituted lower heteroalkylene, -O-, -O-(alkylene or substituted alkylene)-, -S-, -S-(alkylene or substituted alkylene)-, -$S(O)_k$- where k is 1, 2, or 3, -$S(O)_k$(alkylene or substituted alkylene)-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -N(R')-, -NR'-(alkylene or substituted alkylene)-, -C(O)N(R')-, -CON(R')-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -$S(O)_k$N(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')$S(O)_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -$C(R')_2$-N=N-, and -$C(R')_2$-N(R')-N(R')-, where each R' is independently H, alkyl, or substituted alkyl;

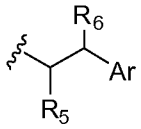
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_3 and R_4 are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl;

Z has the structure of:



;

R_5 is H, COR_8, C_1-C_6alkyl, or thiazole;

R_8 is OH;

R_6 is OH or H;

Ar is phenyl or pyridine;

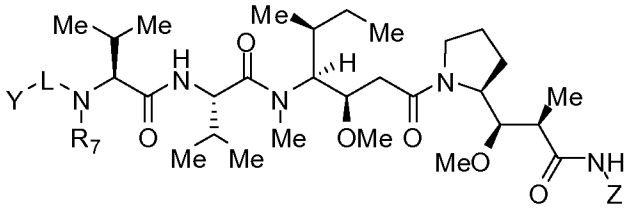
R_7 is C_1-C_6alkyl or hydrogen; and

L is –alkylene– or –(alkylene–O)$_n$–alkylene–; and

n is an integer greater than or equal to one;

or an active metabolite, or a pharmaceutically acceptable prodrug or solvate thereof.

18. The compound of claim 17, wherein R_1 is a polypeptide.
19. The compound of claims 18, wherein the polypeptide is an antibody.
20. The compound of claim 19, wherein the antibody is herceptin.
21. The compound of claim 17, wherein R_2 is a polypeptide.
22. The compound of claims 21, wherein the polypeptide is an antibody.
23. The compound of claim 22, wherein the antibody is herceptin.
24. A method for derivatizing a dolastatin analog comprising Formula (I), the method comprising contacting the dolastatin analog with a reagent of Formula (XXXVII), wherein Formula (I) corresponds to:

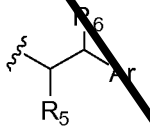


(I)

;

wherein:

Z has the structure of:



;

R_5 is H, COR_8, C_1-C_6alkyl, or thiazole;

R_8 is OH;

R_6 is OH or H;

Ar is phenyl or pyridine;

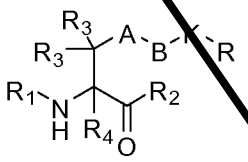
R_7 is C_1-C_6 alkyl or hydrogen;

Y is NH_2–O– or methyl;

L is–alkylene– or –(alkylene–O)$_n$–alkylene–;

n is an integer greater than or equal to one;

wherein Formula (XXXVII) corresponds to:



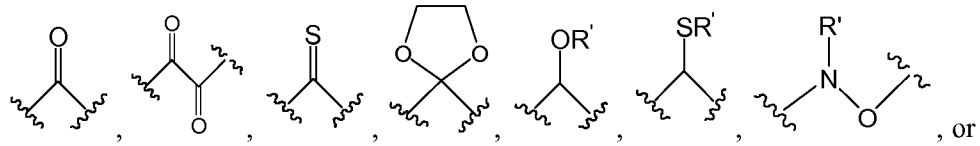
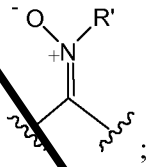
(XXXVII)

wherein:

A is optional, and when present is lower alkylene, substituted lower alkylene, lower alkenylene, substituted lower alkenylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, alkarylene, substituted alkarylene, aralkylene, or substituted aralkylene;

B is optional, and when present is a linker selected from the group consisting of lower alkylene, substituted lower alkylene, lower alkenylene, substituted lower alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -S-, -S-(alkylene or substituted alkylene)-, -S(O)$_k$- where k is 1, 2, or 3, -S(O)$_k$(alkylene or substituted alkylene)-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -N(R')-, -NR'-(alkylene or substituted alkylene)-, -C(O)N(R')-, -CON(R')-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -S(O)$_k$N(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)$_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -C(R')$_2$-N=N-, and -C(R')$_2$-N(R')-N(R')-, where each R' is independently H, alkyl, or substituted alkyl;

each R' is independently H, alkyl, or substituted alkyl;

E is , or ;

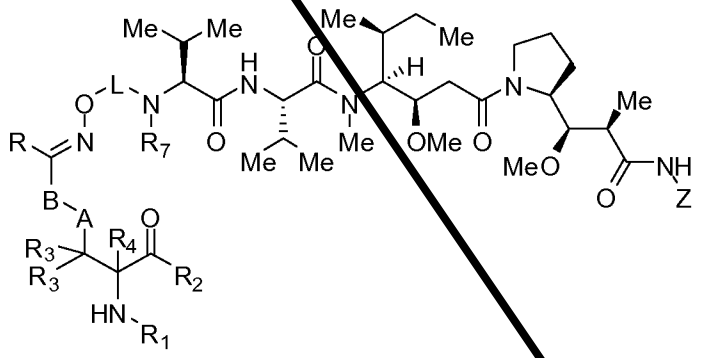
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

R_1 is H, an amino protecting group, resin, at least one amino acid, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, or polynucleotide; and

R_3 and R_4 are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl.

25. The method of claim 24, wherein the derivatized dolastatin analog comprises at least one oxime containing amino acid having the structure of Formula (VIII):

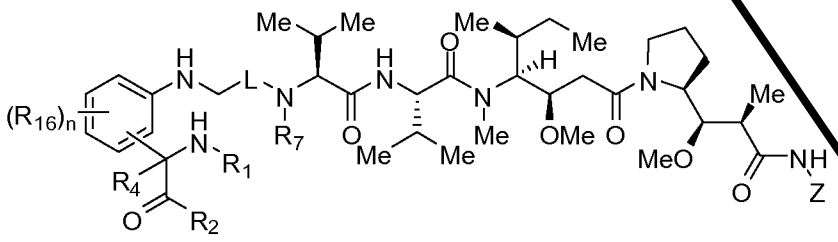


(VIII)

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26. The method of claim 24, wherein the dolastatin analog is contacted with the reagent of Formula (XXXVII) in aqueous solution under mildly acidic conditions.

27. A compound comprising Formula (XXV):

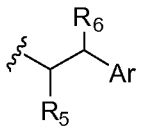


(XXV)

;

wherein:

Z has the structure of:



;

R_5 is H, CO_2H, C_1-C_6alkyl, or thiazole;

R_6 is OH or H;

Ar is phenyl or pyridine;

R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_4 is H, halogen, lower alkyl, or substituted lower alkyl;

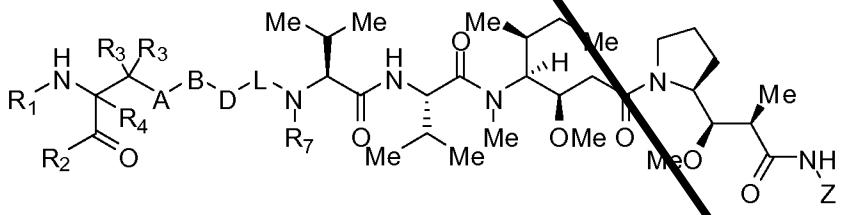
R_7 is C_1-C_6alkyl or hydrogen;

L is–alkylene– or –(alkylene–O)$_n$–alkylene–;

n is an integer greater than or equal to one; and

each R_{16} is independently selected from the group consisting of hydrogen, halogen, alkyl, NO_2, CN, and substituted alkyl.

28. The compound of claim 27, wherein R_1 is a polypeptide.
29. The compound of claims 28, wherein the polypeptide is an antibody.
30. The compound of claim 29, wherein the antibody is herceptin.
31. The compound of claim 27, wherein R_2 is a polypeptide.
32. The compound of claims 31, wherein the polypeptide is an antibody.
33. The compound of claim 32, wherein the antibody is herceptin.
34. A compound comprising Formula (XXXI):

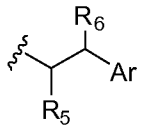


(XXXI)

;

wherein:

Z has the structure of:



;

R_5 is H, CO_2H, C_1-C_6alkyl, or thiazole;

R_6 is OH or H;

Ar is phenyl or pyridine;

R_1 is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

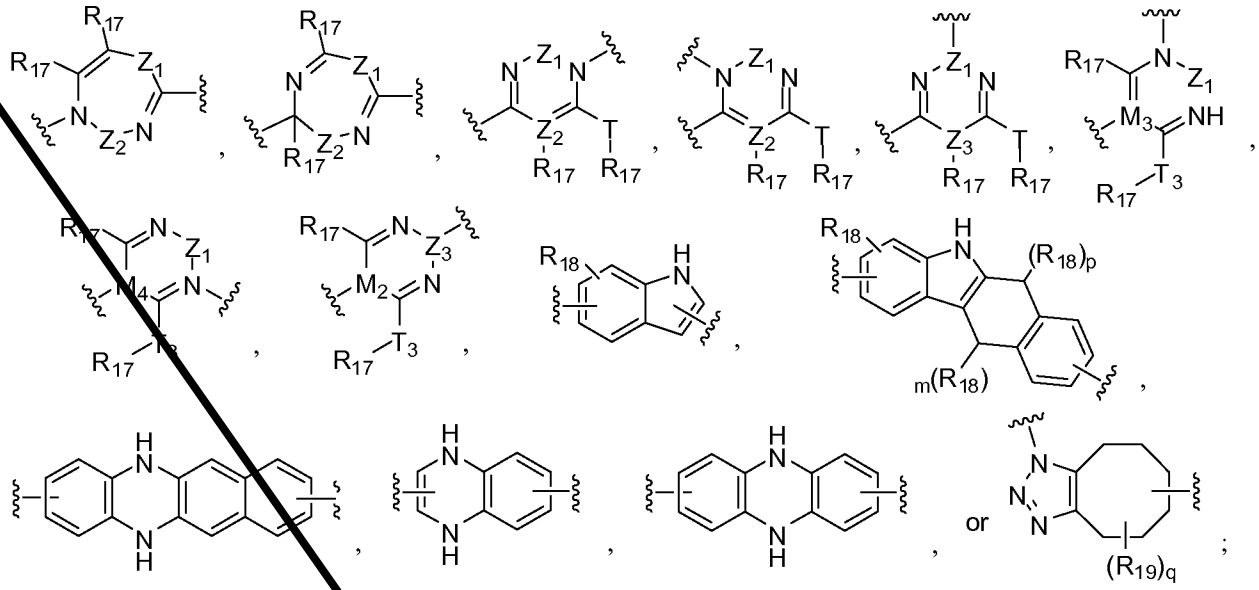
R_4 is H, halogen, lower alkyl, or substituted lower alkyl;

R_7 is C_1-C_6alkyl or hydrogen;

L is–alkylene– or –(alkylene–O)$_n$–alkylene–;

n is an integer greater than or equal to one;

D has the structure of:



each R_{17} is independently selected from the group consisting of H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -(alkylene or substituted alkylene)-ON(R")$_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), -C(O)R", -C(O)$_2$R", or -C(O)N(R")$_2$, wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, alkaryl, substituted alkaryl, aralkyl, or substituted aralkyl;

each Z_1 is a bond, $CR_{17}R_{17}$, O, S, NR', $CR_{17}R_{17}$-$CR_{17}R_{17}$, $CR_{17}R_{17}$-O, O-$CR_{17}R_{17}$, $CR_{17}R_{17}$-S, S-$CR_{17}R_{17}$, $CR_{17}R_{17}$-NR', or NR'-$CR_{17}R_{17}$;

each R' is H, alkyl, or substituted alkyl;

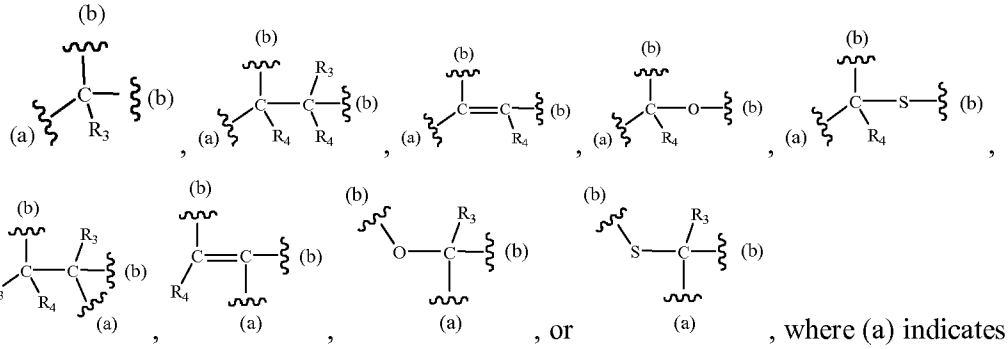
each Z_2 is selected from the group consisting of a bond, -C(O)-, -C(S)-, optionally substituted C_1-C_3 alkylene, optionally substituted C_1-C_3 alkenylene, and optionally substituted heteroalkyl;

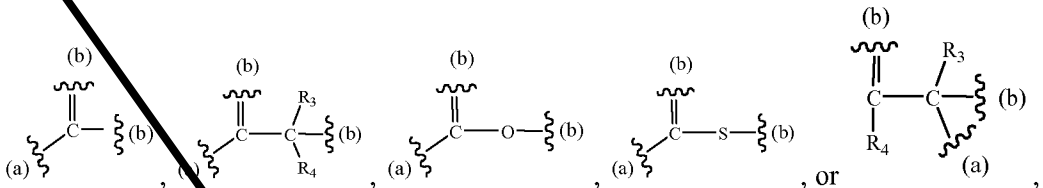
each Z_3 are independently selected from the group consisting of a bond, optionally substituted C_1-C_4 alkylene, optionally substituted C_1-C_4 alkenylene, optionally substituted heteroalkyl, -O-, -S-, -C(O)-, -C(S)-, and -N(R')-;

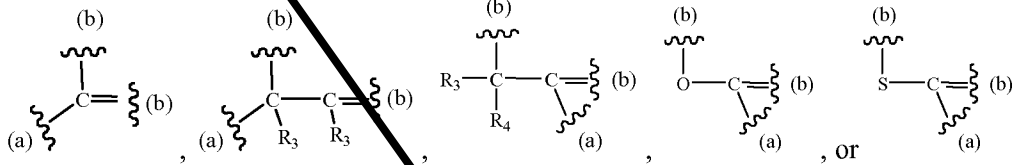
each T_3 is a bond, C(R'')(R''), O, or S; with the proviso that when T_3 is O or S, R'' cannot be halogen;

each R'' is H, halogen, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

m and p are 0, 1, 2, or 3, provided that at least one of m or p is not 0;

M_2 is , where (a) indicates bonding to the B group and (b) indicates bonding to respective positions within the heterocycle group;

M_3 is , where (a) indicates bonding to the B group and (b) indicates bonding to respective positions within the heterocycle group;

M_4 is , where (a) indicates bonding to the B group and (b) indicates bonding to respective positions within the heterocycle group;

each R_{19} is independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, ester, ether, thioether, aminoalkyl, halogen, alkyl ester, aryl ester, amide, aryl amide, alkyl halide, alkyl amine, alkyl sulfonic acid, alkyl nitro, thioester, sulfonyl ester, halosulfonyl, nitrile, alkyl nitrile, and nitro;

q is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11; and

each R_{16} is independently selected from the group consisting of hydrogen, halogen, alkyl, NO_2, CN, and substituted alkyl.

35. The compound of claim 34, wherein R_1 is a polypeptide.

36. The compound of claims 35, wherein the polypeptide is an antibody.

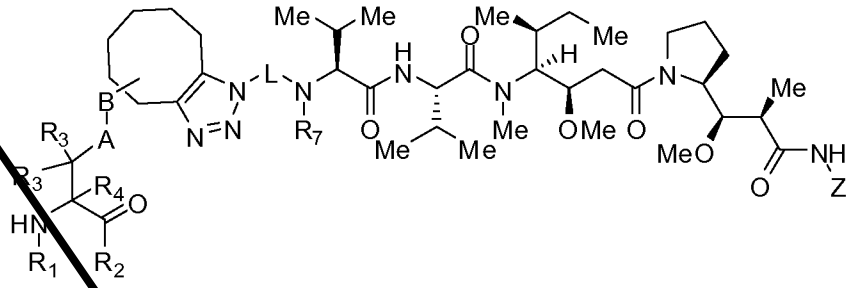
37. The compound of claim 36, wherein the antibody is herceptin.

38. The compound of claim 34, wherein R_2 is a polypeptide.

39. The compound of claims 38, wherein the polypeptide is an antibody.

40. The compound of claim 39, wherein the antibody is herceptin.

41. The compound of claim 34, comprising Formula (XXXI-A):



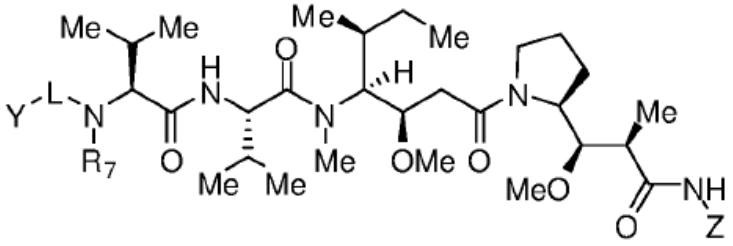
(XXXI-A)

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42. A pharmaceutical composition comprising a compound of any of claims 1-23 and 27-41 and a pharmaceutically acceptable carrier, excipient, or binder.

CLAIMS

1. A compound, or salt thereof, comprising Formula (I):

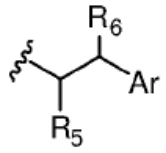


(I)

;

wherein:

Z has the structure of:



;

R_5 is H, COR_8, or , C_1-C_6alkyl,

R_8 is OH;

R_6 is OH or H;

Ar is phenyl or pyridine;

R_7 is C_1-C_6alkyl or hydrogen;

Y is selected from the group consisting of an hydroxylamine, methyl, aldehyde, protected aldehyde, ketone, protected ketone, thioester, ester, dicarbonyl, hydrazine, amidine, imine, diamine, keto-amine, keto-alkyne, alkyne, and ene-dione;

L is–alkylene– or –(alkylene–O)$_n$–alkylene–; and

n is an integer greater than or equal to one.

2. The compound of claim 1, wherein R_6 is H.

3. The compound of claim 1, wherein Ar is phenyl.

4. The compound of claim 1, wherein R_7 is methyl.

5. The compound of claim 1, where n is an integer from 0 to 20.

6. The compound of claim 1, where n is an integer from 0 to 10.

7. The compound of claim 1, where n is an integer from 0 to 5.

8. A pharmaceutical composition comprising a compound of any of claims 1-7 and a pharmaceutically acceptable carrier, excipient, or binder.