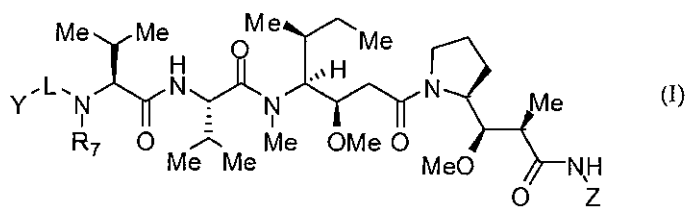


CLAIMS

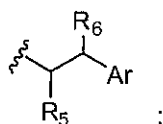
WHAT IS CLAIMED IS:

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



wherein:

Z has the structure of:



R₅ is H, COR₈, C₁-C₆alkyl, or thiazole;

R₈ is OH or -NH-(alkylene-O)_n-NH₂;

R₆ is OH or H;

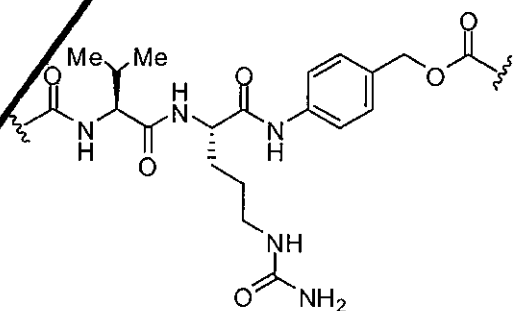
Ar is phenyl or pyridine;

R₇ is C₁-C₆alkyl or hydrogen;

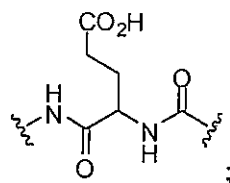
Y and V are each selected from the group consisting of an hydroxylamine, methyl, aldehyde, protected aldehyde, ketone, protected ketone, thioester, ester, dicarbonyl, hydrazine, amidine, imine, diamine, azide, keto-amine, keto-alkyne, alkyne, cycloalkyne, and ene-dione;

L is a linker selected from the group consisting of -alkylene-, -alkylene-C(O)-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -alkylene-C(O)-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, and -(alkylene-O)_n-alkylene-U-alkylene-;

W has the structure of:

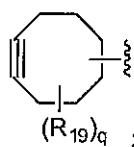


U has the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $-NH-(alkylene-O)_n-NH_2$; and each n, n', n'', n''' and n'''' are independently integers greater than or equal to one.

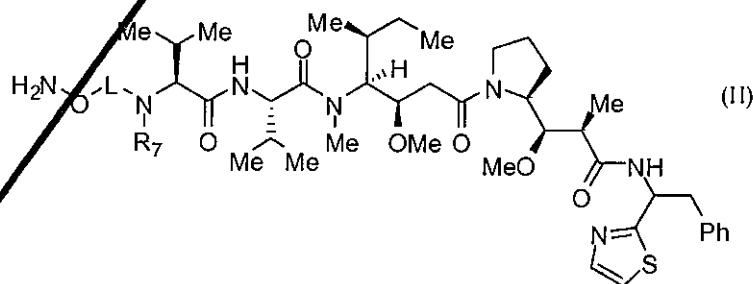
2. The compound of claim 1, wherein R_5 is thiazole.
3. The compound of claim 1, wherein R_6 is H.
4. The compound of claim 1, wherein Ar is phenyl.
5. The compound of claim 1, wherein R_7 is methyl.
6. The compound of claim 1, where n is an integer from 0 to 20.
7. The compound of claim 1, where n is 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

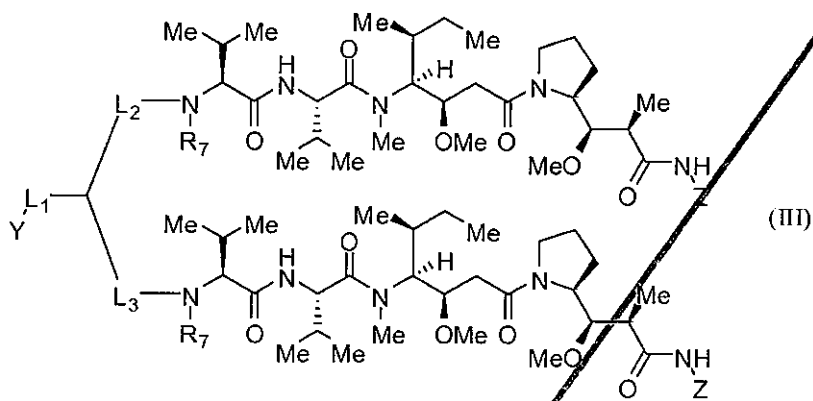
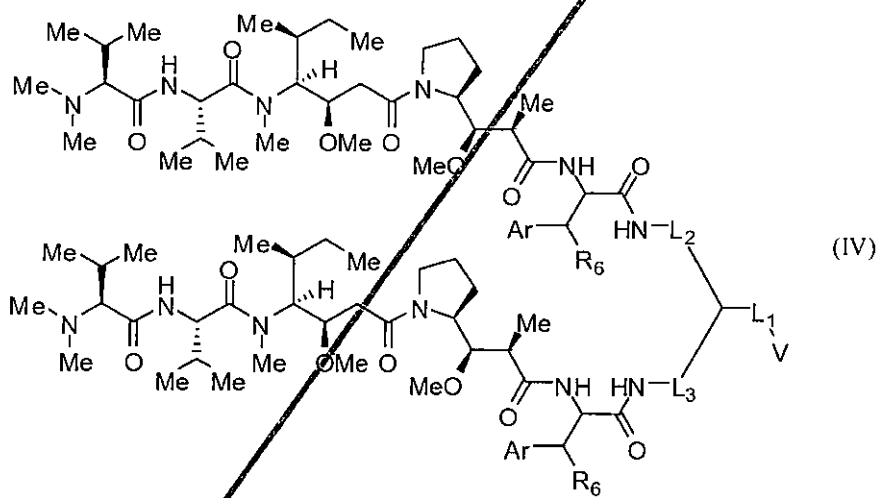
q is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11.

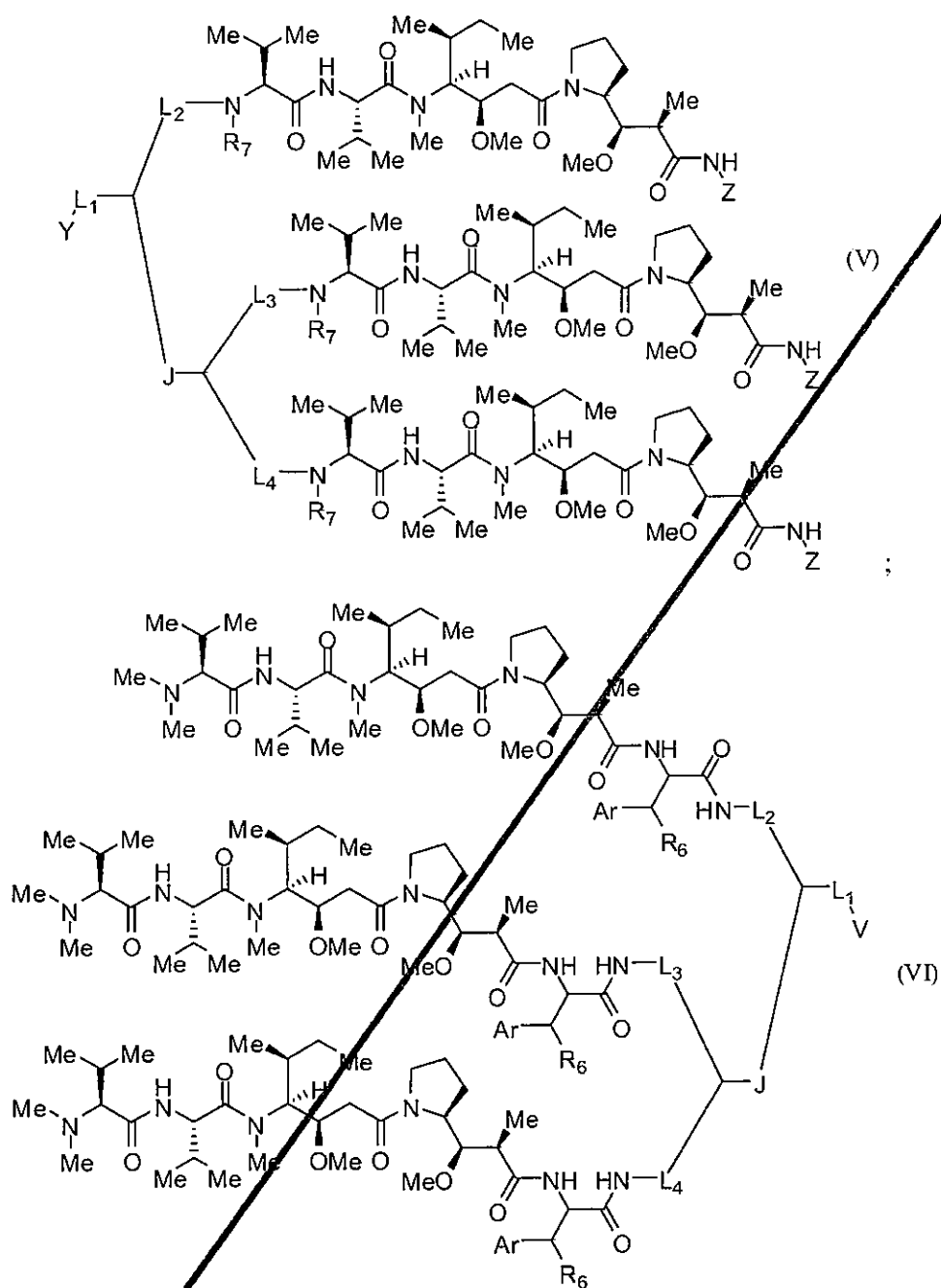
11. The compound of claim 1, wherein Y is azide.
12. The compound of claim 1, comprising Formula (II):



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

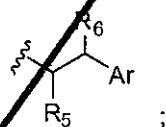
18. The compound of claim 17, wherein each alkylene is $-\text{CH}_2\text{CH}_2-$, n is equal to 4, and R_7 is methyl.
19. The compound of claim 12, wherein L is $-(\text{alkylene}-\text{O})_n-(\text{CH}_2)_n-\text{NHC(O)}-(\text{CH}_2)_n-\text{C}(\text{Me})_2-\text{S}-\text{S}-(\text{CH}_2)_n-\text{NHC(O)}-(\text{alkylene}-\text{O})_n-\text{alkylene}-$.
20. The compound of claim 19, wherein each alkylene is $-\text{CH}_2\text{CH}_2-$, n is equal to 1, n' is equal to 2, n'' is equal to 1, n''' is equal to 2, n'''' is equal to 4, and R_7 is methyl.
21. A compound, or salt thereof, comprising Formula (III), (IV), (V) or (VI):





wherein:

Z has the structure of:



R₅ is H, COR₈, C₁-C₆alkyl, or thiazole;

R₈ is OH;

R₆ is OH or H;

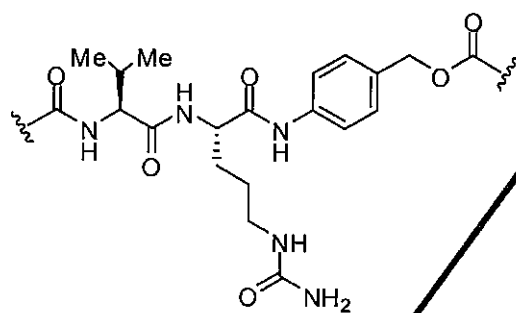
Ar is phenyl or pyridine;

R₇ is C₁-C₆alkyl or hydrogen;

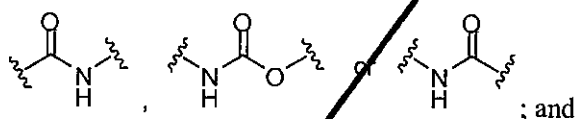
Y and V are each selected from the group consisting of an hydroxylamine, methyl, aldehyde, protected aldehyde, ketone, protected ketone, thiocster, ester, dicarbonyl, hydrazine, amidine, imine, diamine, azide, keto-amine, keto-alkyne, alkyne, cycloalkyne, and ene-dione;

L₁, L₂, L₃, and L₄ are each linkers independently selected from the group consisting of a bond, -alkylene-, -(alkylene-O)_n-alkylene-J-, -alkylene'-J-(alkylene-O)_n-alkylene-, -J-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-J-(alkylene-O)_n'-alkylene-J'-, -(alkylene-O)_n-alkylene-J-alkylene'-, -W-, -alkylene-W-, alkylene'-J-(alkylene-NMe)_n-alkylene-W-, -J-(alkylene-NMe)_n-alkylene-W-, -J-alkylene-NMe-alkylene'-NMe-alkylene"-W-, and -alkylene-J-alkylene'-NMe-alkylene"-NMe-alkylene"-W-;

W has the structure of:

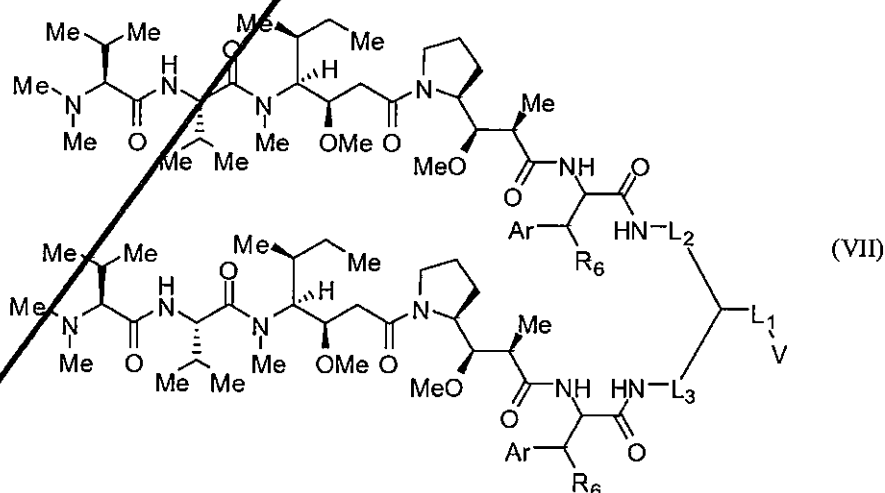


each J and J' independently have the structure of:

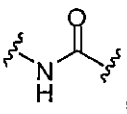
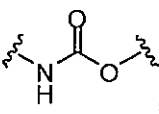


each n and n' are independently integers greater than or equal to one.

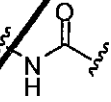
22. The compound of claim 21, comprising Formula (VII):



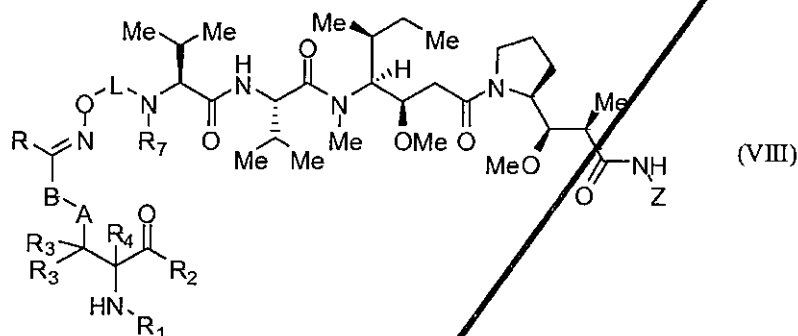
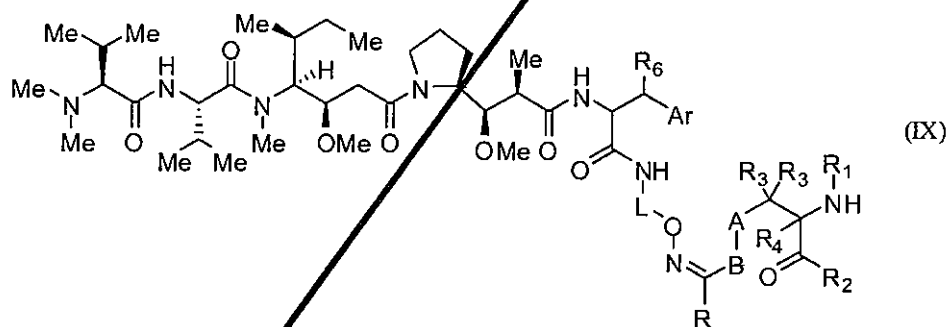
23. The compound of claim 22, wherein L₁ is -(alkylene-O)_n-alkylene-J-, L₂ is -alkylene'-J'-(alkylene-O)_n'-alkylene-, L₃ is -J''-(alkylene-O)_n''-alkylene-, alkylene is -CH₂CH₂-, alkylene' is -(CH₂)₄-, n is

1, n' and n'' are 3, J has the structure of , J' and J'' have the structure of , and R₇ is methyl.

24. The compound of claim 22, comprising Formula (IV) wherein L₁ is -J-(alkylene-O)_n-alkylene-, L₂ is -(alkylene-O)_n-alkylene-J'-alkylene'-, L₃ is -(alkylene-O)_n-alkylene-J'', alkylene is -CH₂CH₂-,

alkylene' is -(CH₂)₄-, n is 1, n' and n'' are 4, and J, J' and J'' have the structure of .

25. A compound comprising Formula (VIII) or (IX):



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)_kN(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)_kN(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;

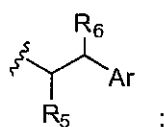
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

R₁ is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₂ is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₃ and R₄ are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R₃ and R₄ or two R₃ groups optionally form a cycloalkyl or a heterocycloalkyl;

Z has the structure of:



R₅ is H, COR₈, C₁-C₆alkyl, or thiazole;

R₈ is OH;

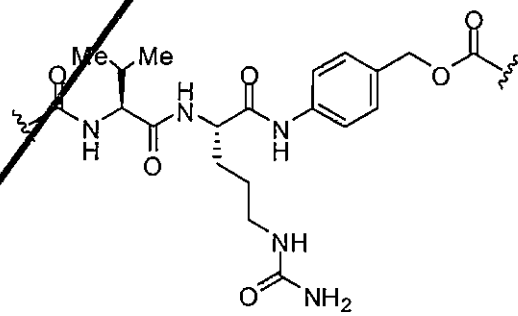
R₆ is OH or H;

Ar is phenyl or pyridine;

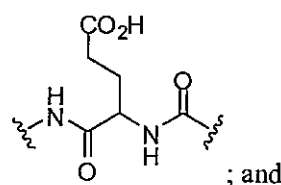
R₇ is C₁-C₆alkyl or hydrogen;

L is a linker selected from the group consisting of -alkylene-, -alkylene-C(O)-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -alkylene-C(O)-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, and -(alkylene-O)_n-alkylene-U-alkylene-;

W has the structure of:

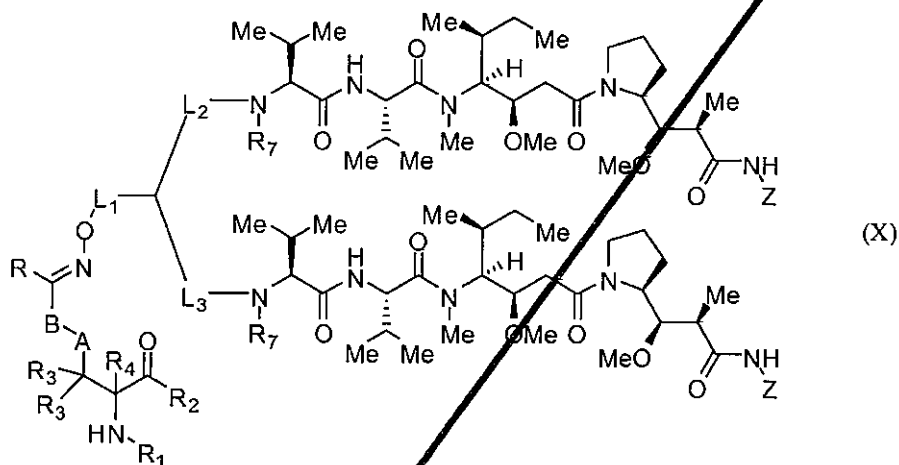
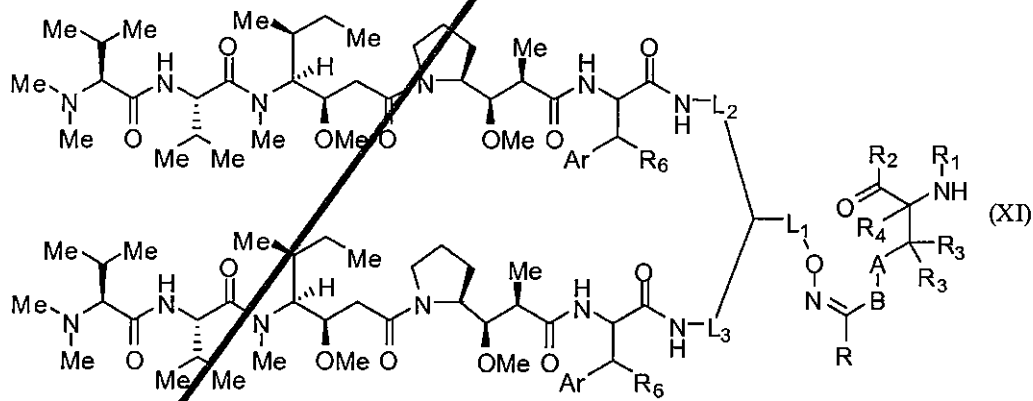


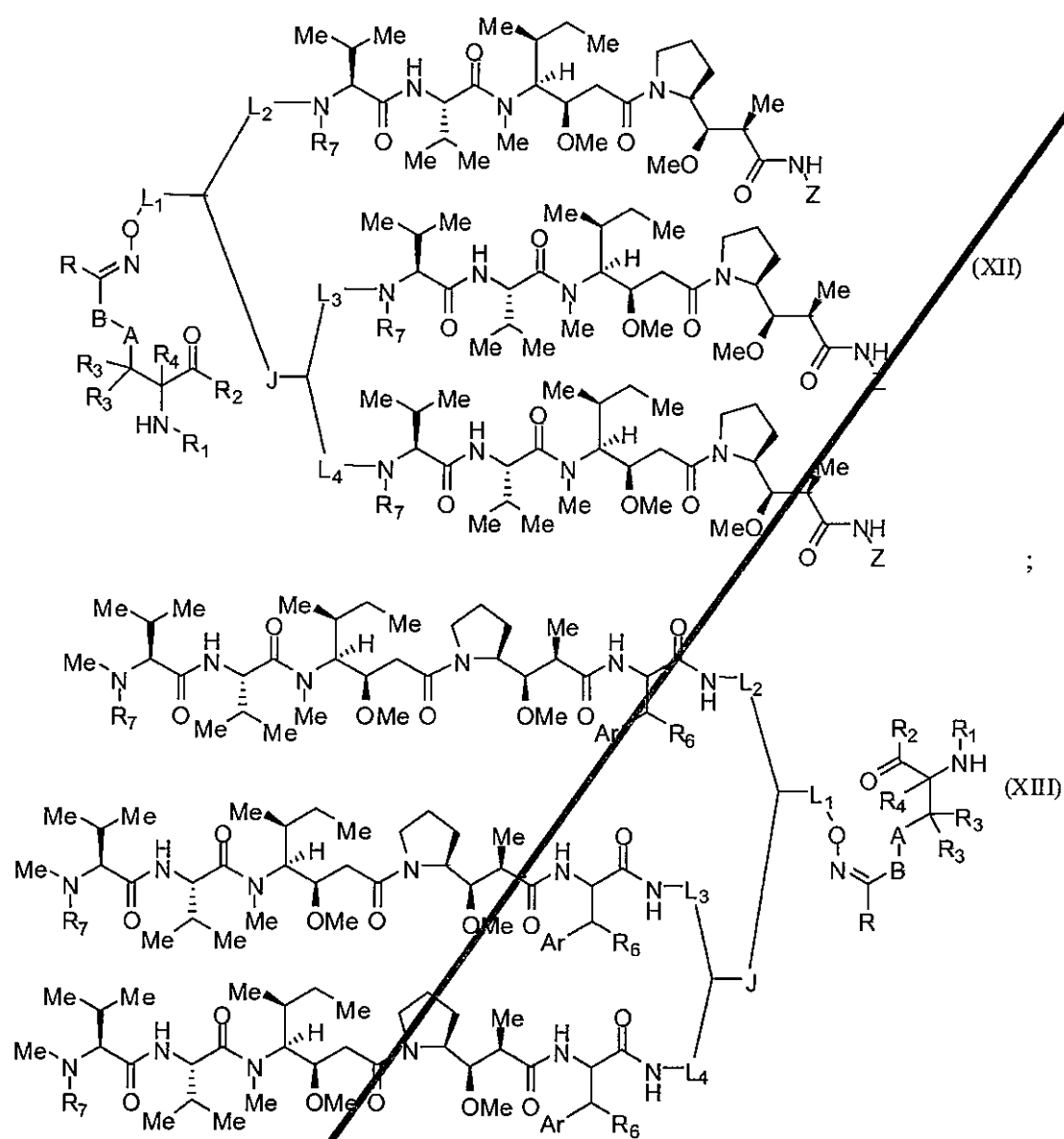
U has the structure of:



; and

- each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one;
 or an active metabolite, or a pharmaceutically acceptable prodrug or solvate thereof.
26. The compound of claim 25, wherein R_1 is a polypeptide.
 27. The compound of claims 26, wherein the polypeptide is an antibody.
 28. The compound of claim 27, wherein the antibody is herceptin.
 29. The compound of claim 25, wherein R_2 is a polypeptide.
 30. The compound of claims 29, wherein the polypeptide is an antibody.
 31. The compound of claim 30, wherein the antibody is herceptin.
 32. The compound, or salt thereof, comprising Formula (X), (XI), (XII) or (XIII).





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)_kN(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)_kN(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;

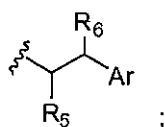
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

R₁ is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₂ is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₃ and R₄ are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R₃ and R₄ or two R₃ groups optionally form a cycloalkyl or a heterocycloalkyl;

Z has the structure of:



R₅ is H, CO₂H, C₁-C₆alkyl, or thiazole;

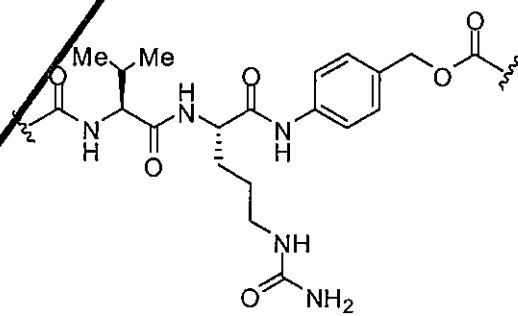
R₆ is OH or H;

Ar is phenyl or pyridine;

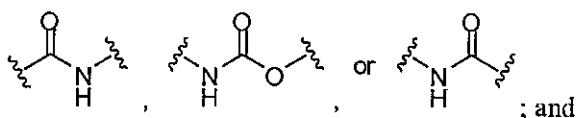
R₇ is C₁-C₆alkyl or hydrogen;

L₁, L₂, L₃, and L₄ are each linkers independently selected from the group consisting of a bond, -alkylene-, -(alkylene-O)_n-alkylene-J-, -alkylene'-J-(alkylene-O)_n-alkylene-, -J-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-J-(alkylene-O)_n'-alkylene-J'-, -(alkylene-O)_n-alkylene-J-alkylene'-, -W-, -alkylene-W-, alkylene'-J-(alkylene-NMe)_n-alkylene-W-, -J-(alkylene-NMe)_n-alkylene-W-, -J-alkylene-NMe-alkylene'-NMe-alkylene"-W-, and -alkylene-J-alkylene'-NMe-alkylene"-NMe-alkylene"-W-;

W has the structure of:

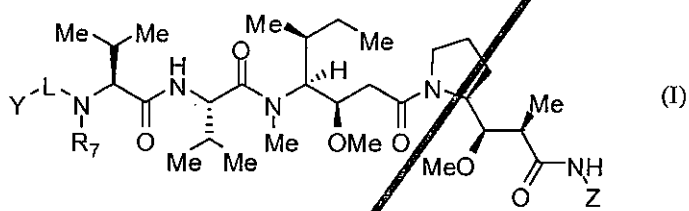
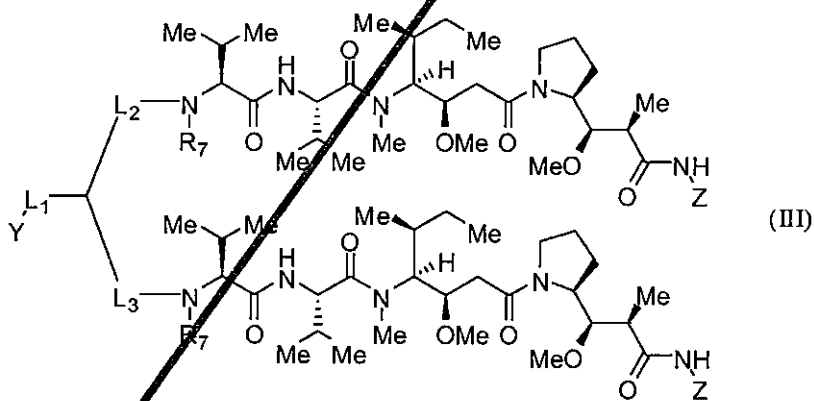
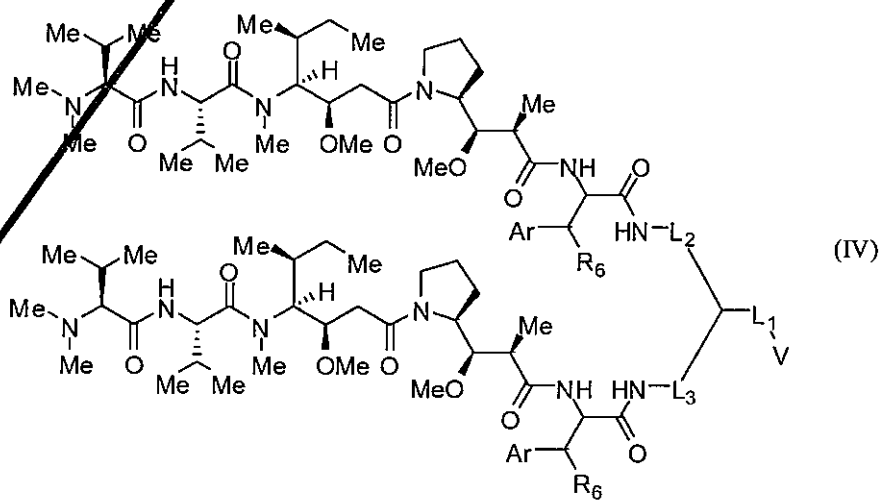


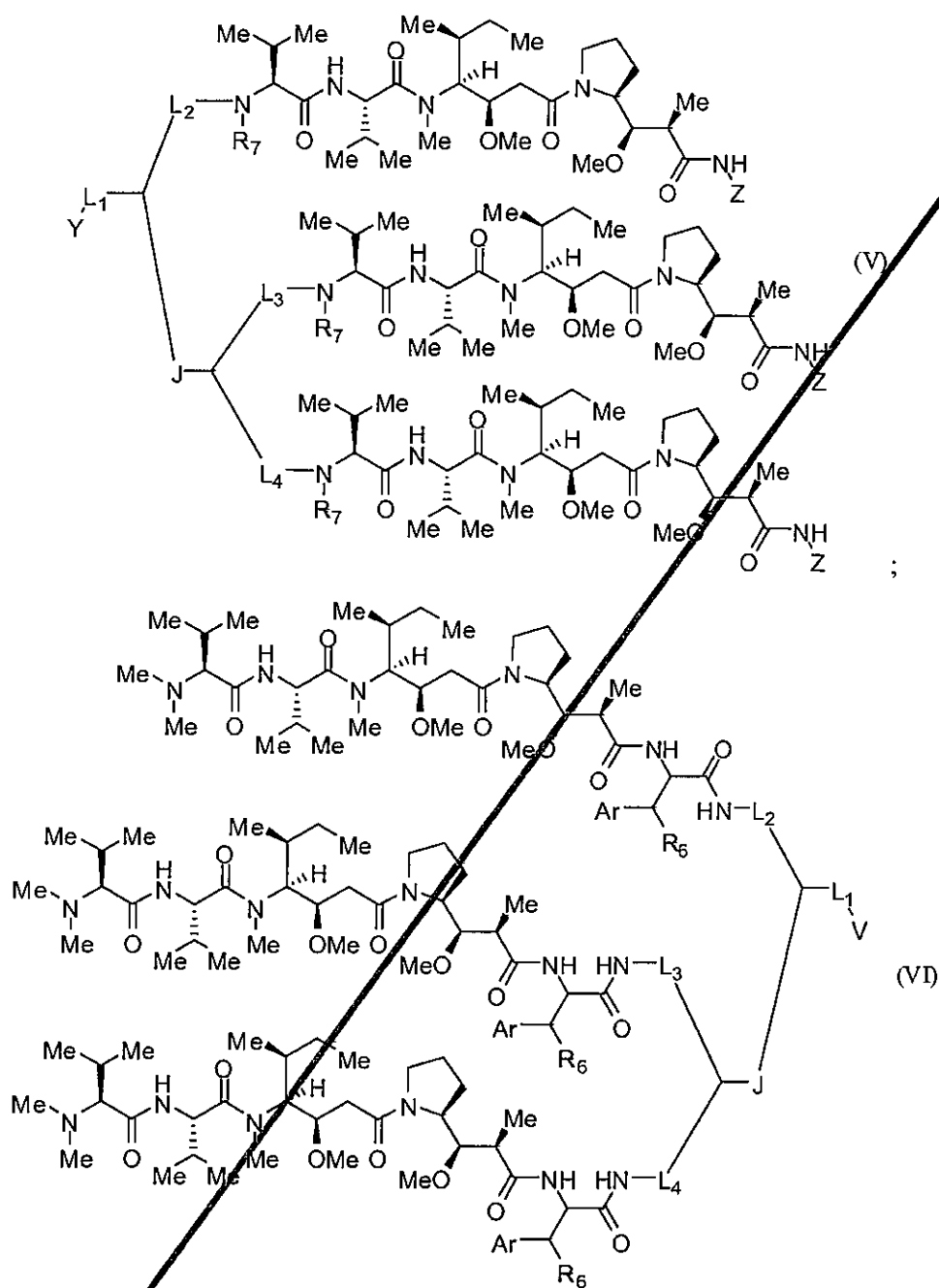
each J and J' independently have the structure of:



each n and n' are independently integers greater than or equal to one.

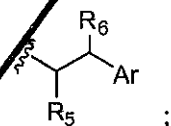
33. The compound of claim 32, wherein R₁ is a polypeptide.
34. The compound of claims 33, wherein the polypeptide is an antibody.
35. The compound of claim 34, wherein the antibody is herceptin.
36. The compound of claim 32, wherein R₂ is a polypeptide.
37. The compound of claims 36, wherein the polypeptide is an antibody.
38. The compound of claim 37, wherein the antibody is herceptin.
39. A method for derivatizing a dolastatin analog comprising Formula (I), (II), (IV), (V), or (VI), the method comprising contacting the dolastatin analog with a reagent of Formula (XXXVII), wherein Formula (I), (III), (IV), (V), or (VI) correspond to:





wherein:

Z has the structure of:



R₅ is H, COR₈, C₁-C₆alkyl, or thiazole;

R₈ is OH or -NH-(alkylene-O)_n-NH₂;

R₆ is OH or H;

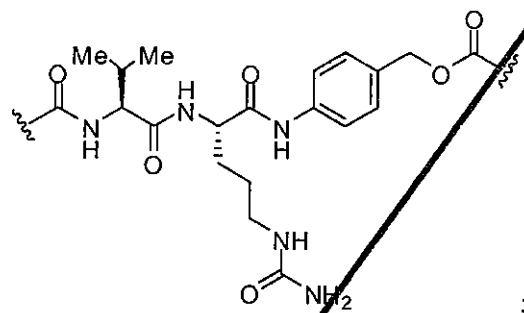
Ar is phenyl or pyridine;

R_7 is C_1 - C_6 alkyl or hydrogen;

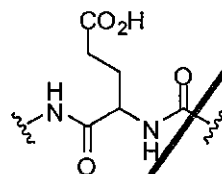
Y is NH_2 -O- or methyl;

L , L_1 , L_2 , L_3 , and L_4 are each linkers selected from the group consisting of a bond, -alkylene-, -alkylene- $C(O)$ -, -(alkylene-O) $_n$ -alkylene-, -(alkylene-O) $_n$ -alkylene- $C(O)$ -, -(alkylene-O) $_n$ -(CH_2) $_n$ -NHC(O)-(CH $_2$) $_n$ -C(Me) $_2$ -S-S-(CH $_2$) $_n$ -NHC(O)-(alkylene-O) $_n$ -alkylene-, -(alkylene-O) $_n$ -alkylene-W-, -alkylene- $C(O)$ -W-, -(alkylene-O) $_n$ -alkylene-J-, -alkylene'-J-(alkylene-O) $_n$ -alkylene-, -(alkylene-O) $_n$ -alkylene-J-alkylene', -J-(alkylene-O) $_n$ -alkylene-, -(alkylene-O) $_n$ -alkylene-J-(alkylene-O) $_n$ -alkylene-J', -W-, -alkylene-W-, alkylene'-J-(alkylene-NMe) $_n$ -alkylene-W-, and J-(alkylene-NMe) $_n$ -alkylene-W-, -(alkylene-O) $_n$ -alkylene-U-alkylene- $C(O)$ -, -(alkylene-O) $_n$ -alkylene-U-alkylene-, -J-alkylene-NMe-alkylene'-NMe-alkylene"-W-, and -alkylene'-J-alkylene'-NMe-alkylene"-NMe-alkylene"-W-;

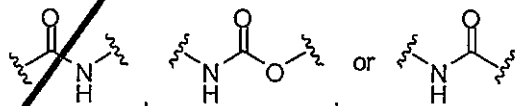
W has the structure of:



U has the structure of:



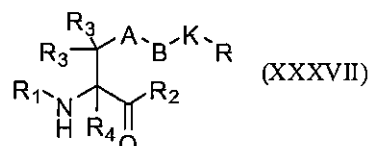
each J and J' independently have the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $-NH-(alkylene-O)_n-NH_2$; and

each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one;

wherein Formula (XXXVII) corresponds to:

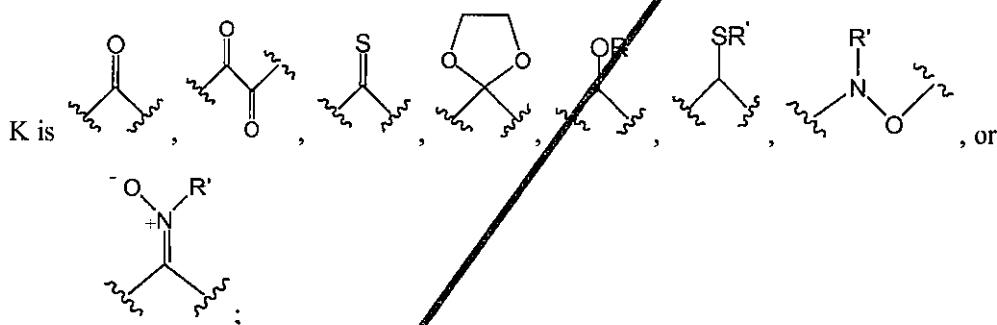


wherein:

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)_kN(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)_kN(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;



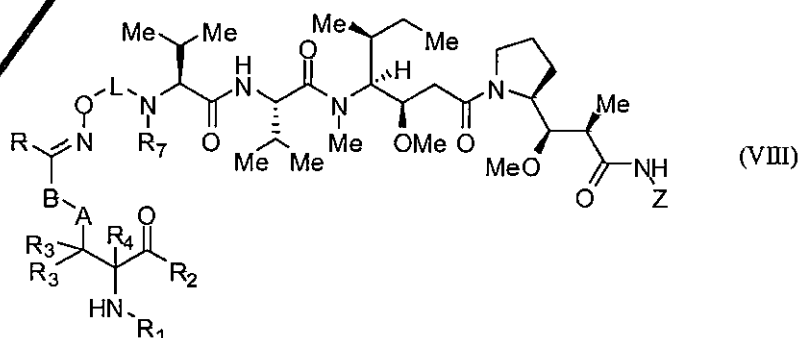
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

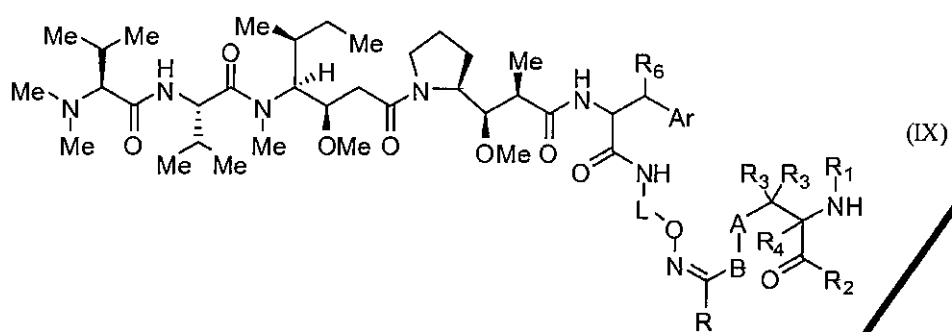
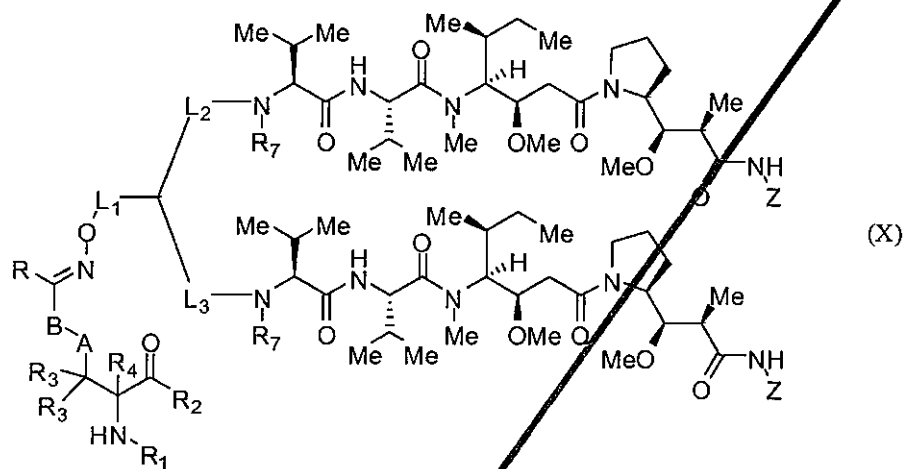
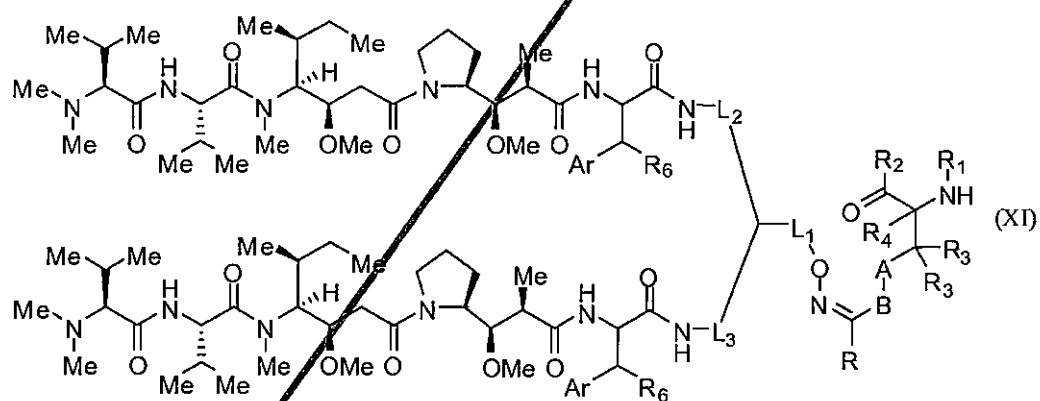
R₁ is H, an amino protecting group, resin, at least one amino acid, or polynucleotide;

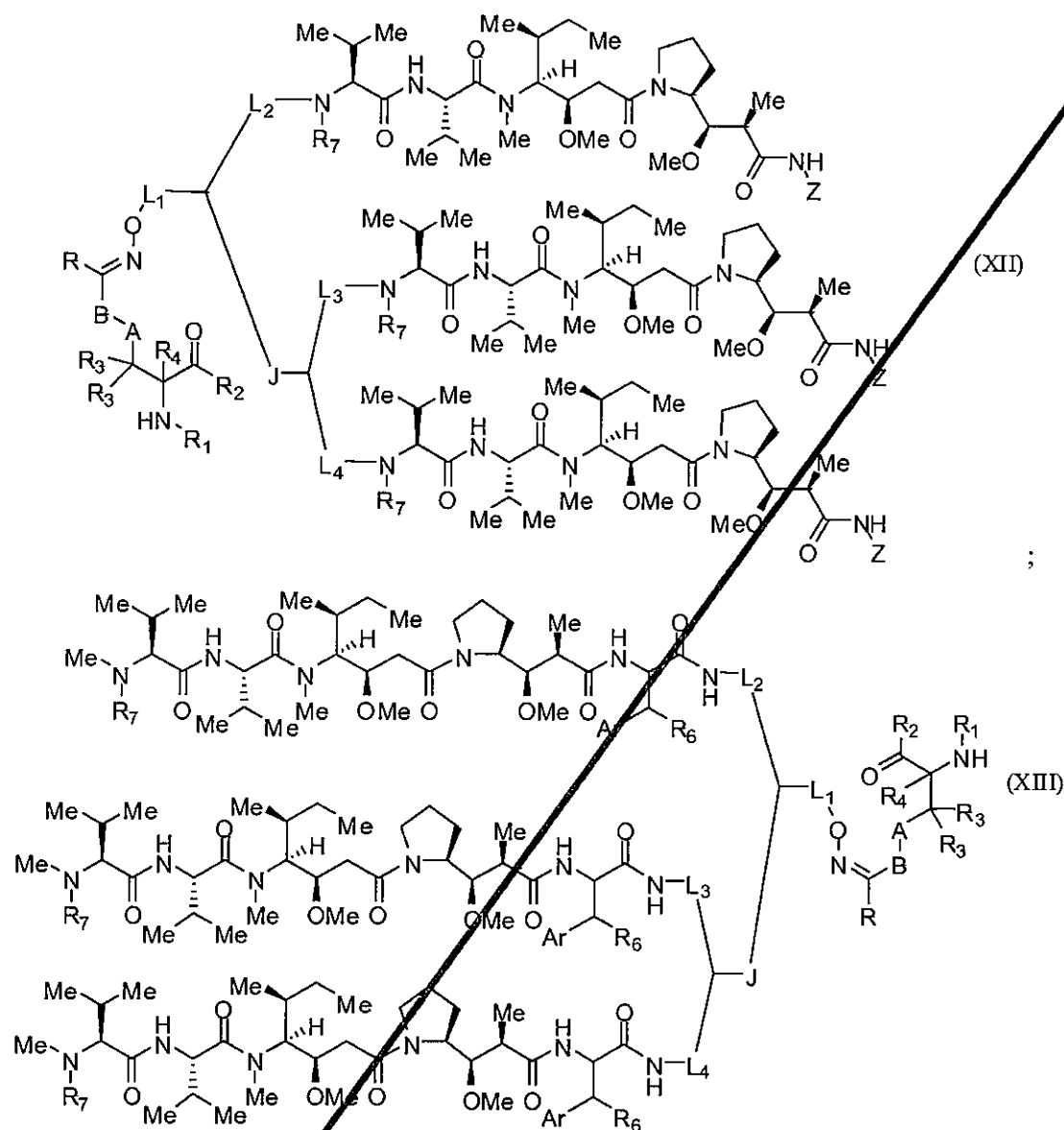
R₂ is OH, an ester protecting group, resin, at least one amino acid, or polynucleotide; and

R₃ and R₄ are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R₃ and R₄ or two R₃ groups optionally form a cycloalkyl or a heterocycloalkyl.

40. The method of claim 39, wherein the derivatized dolastatin analog comprises at least one oxime containing amino acid having the structure of Formula (VIII), (IX), (X), (XI), (XII), or (XIII):

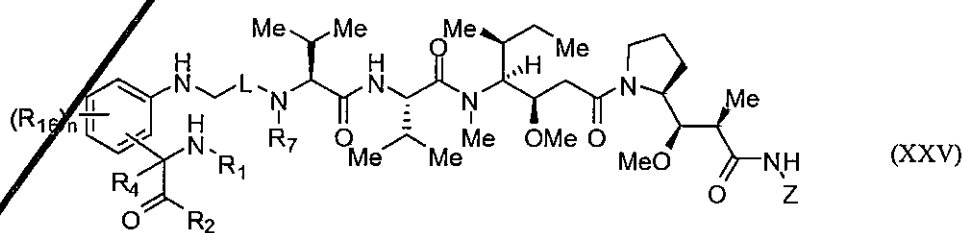


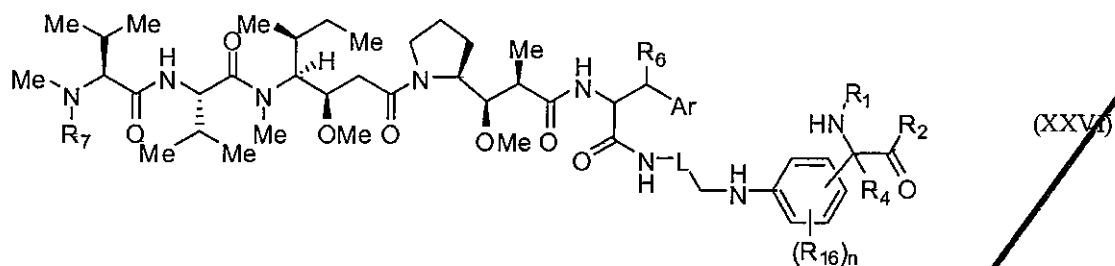
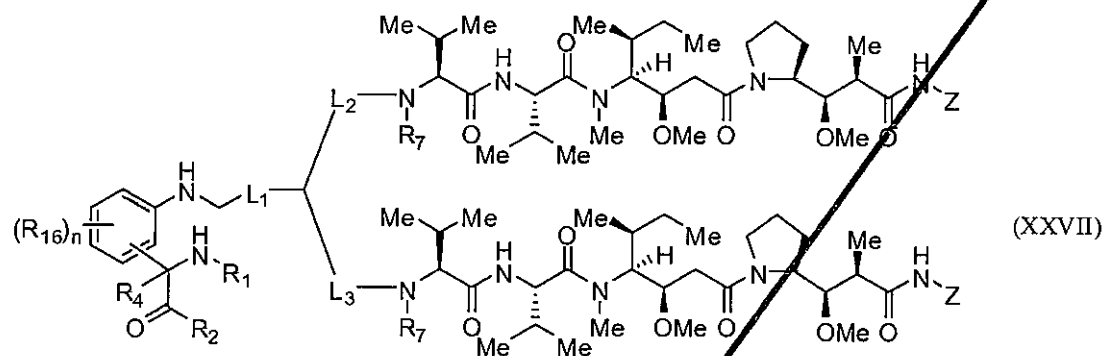
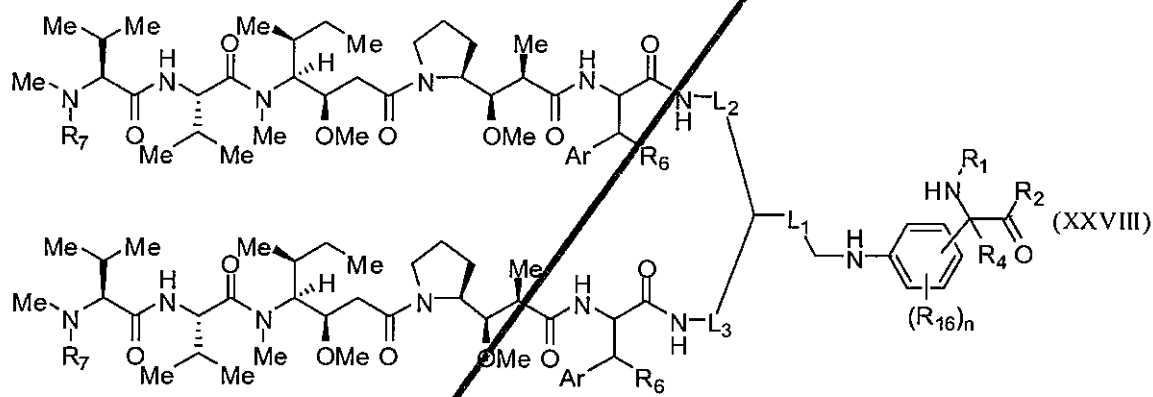
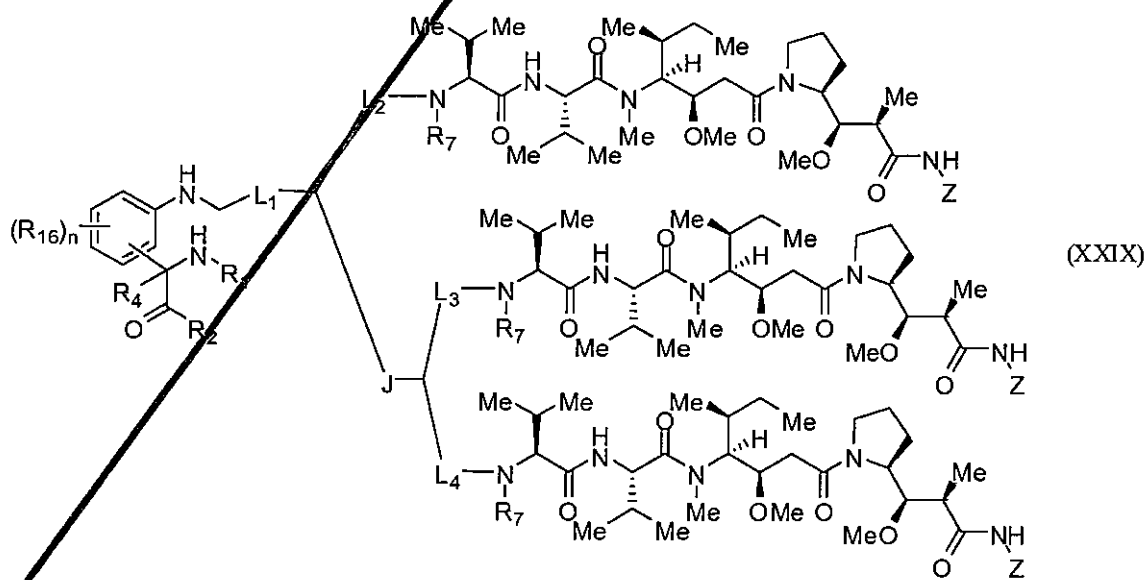


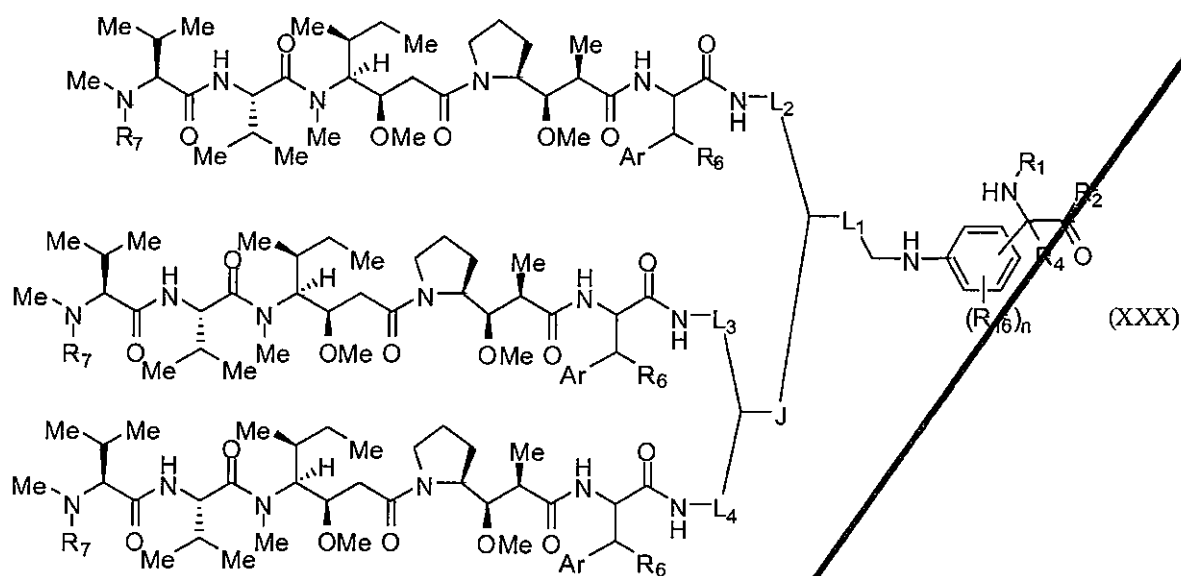


41. The method of claim 39, wherein the dolastatin analog is contacted with the reagent of Formula (XXXVII) in aqueous solution under mildly acidic conditions.

42. A compound comprising Formula (XXV), (XXVI), (XXVII), (XXVIII), (XXIX), or (XXX):

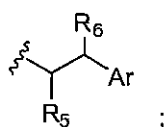






wherein:

Z has the structure of:



R₅ is H, CO₂H, C₁-C₆alkyl, or thiazole;

R₆ is OH or H;

Ar is phenyl or pyridine;

R₁ is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

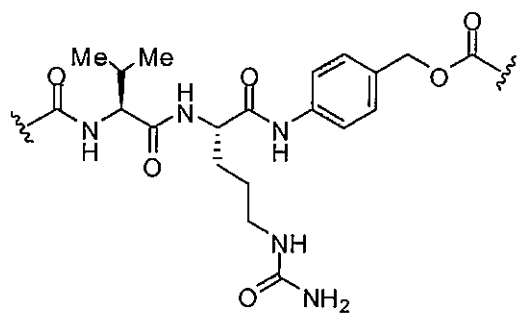
R₂ is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₄ is H, halogen, lower alkyl, or substituted lower alkyl;

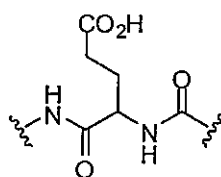
R₇ is C₁-C₆alkyl or hydrogen;

L, L₁, L₂, L₃, and L₄ are each linkers selected from the group consisting of a bond, -alkylene-, -alkylene-C(O)-, -alkylene-J-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-J-, -(alkylene-O)_n-J-alkylene-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -alkylene-C(O)-W-, -(alkylene-O)_n-alkylene-J-, -alkylene'-J-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-J-alkylene', -J-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-J-(alkylene-O)_n-alkylene-J', -W-, -alkylene-W-, alkylene'-J-(alkylene-NMe)_n-alkylene-W-, -J-(alkylene-NMe)_n-alkylene-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, -(alkylene-O)_n-alkylene-U-alkylene-, -J-alkylene-NMe-alkylene'-NMe-alkylene"-W-, and -alkylene-J-alkylene'-NMe-alkylene"-NMe-alkylene"-W-;

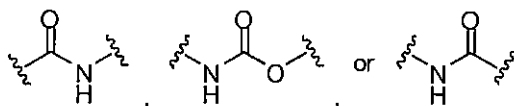
W has the structure of:



U has the structure of:



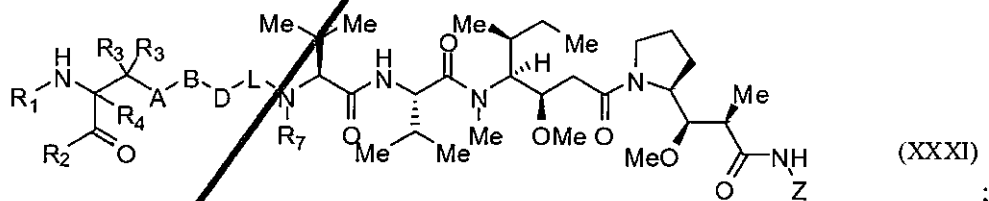
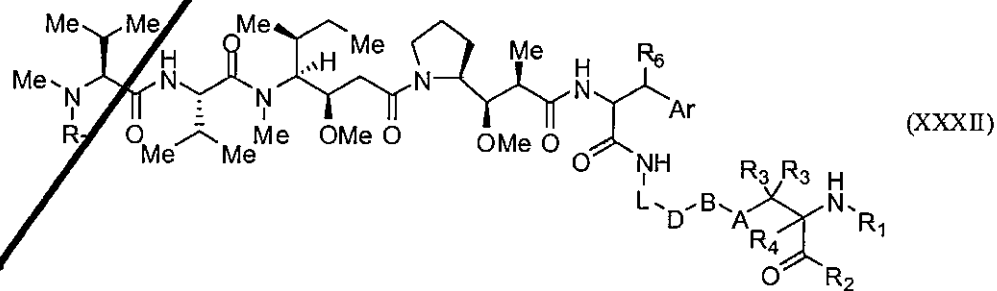
each J and J' independently have the structure of:

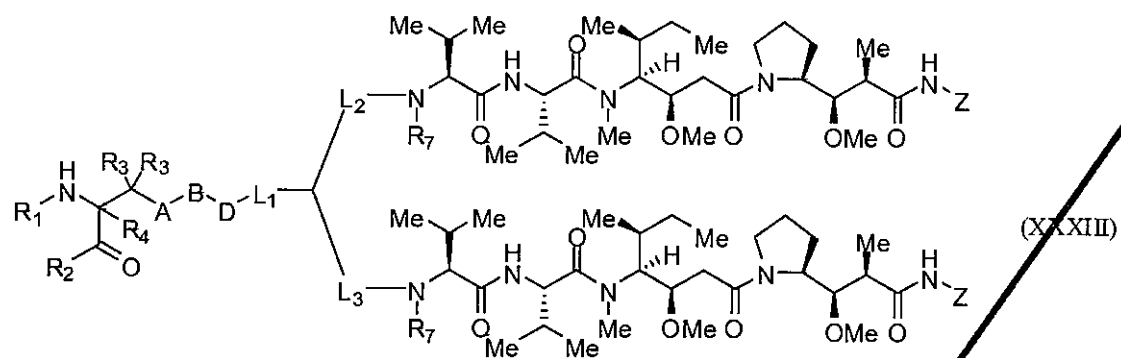
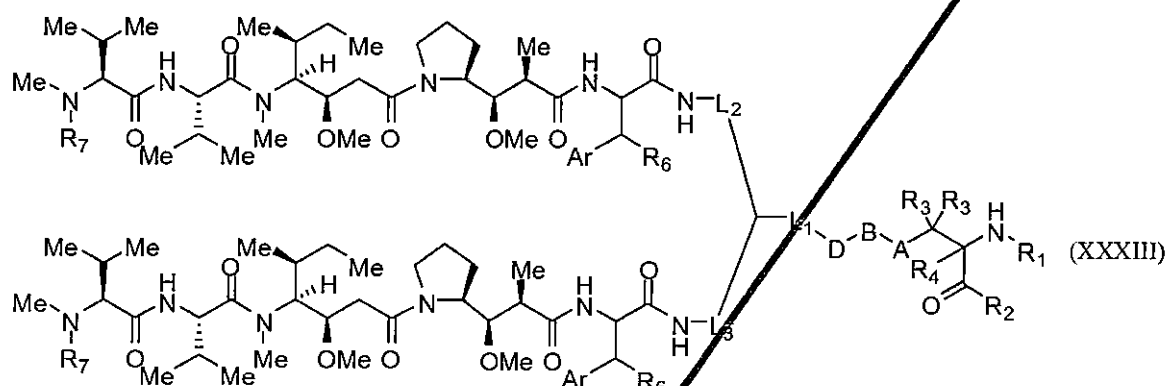
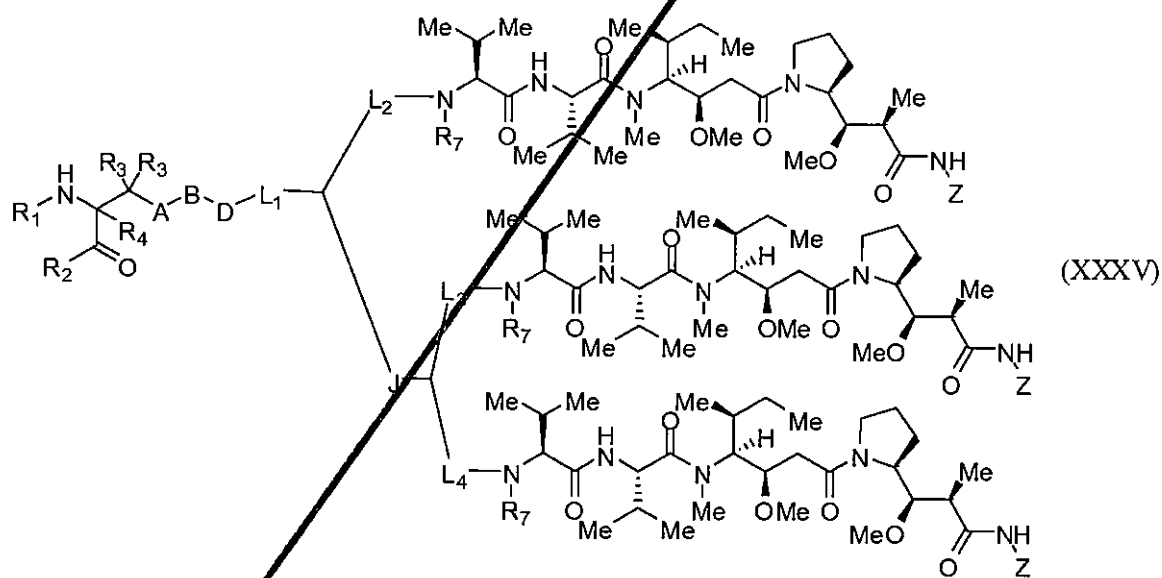


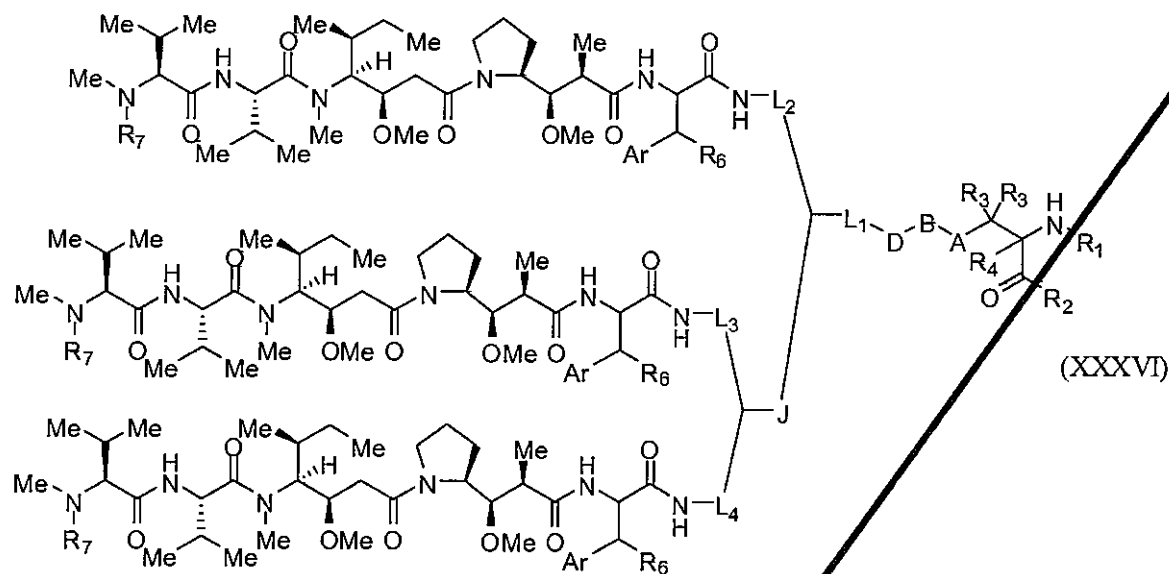
each n and n' are independently integers greater than or equal to one; and

each R₁₆ is independently selected from the group consisting of hydrogen, halogen, alkyl, NO₂, CN, and substituted alkyl.

43. The compound of claim 42, wherein R₁ is a polypeptide.
44. The compound of claims 43, wherein the polypeptide is an antibody.
45. The compound of claim 44, wherein the antibody is herceptin.
46. The compound of claim 42, wherein R₂ is a polypeptide.
47. The compound of claims 46, wherein the polypeptide is an antibody.
48. The compound of claim 47, wherein the antibody is herceptin.
49. A compound comprising Formula (XXXI), (XXXII), (XXXIII), (XXXIV), (XXXV), or (XXXVI):

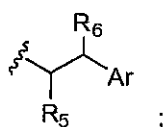






wherein:

Z has the structure of:



R₅ is H, CO₂H, C₁-C₆alkyl, or thiazole;

R₆ is OH or H;

Ar is phenyl or pyridine;

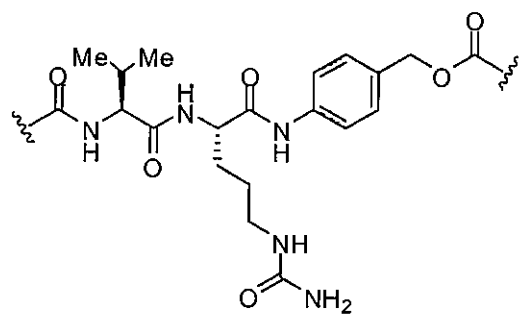
R₁ is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₂ is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

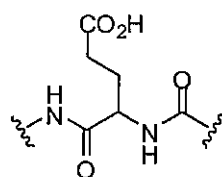
R₄ is H, halogen, lower alkyl, or substituted lower alkyl;

R₇ is C₁-C₆alkyl or hydrogen;

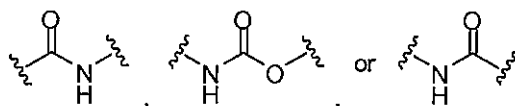
L, L₁, L₂, L₃, and L₄ are each linkers selected from the group consisting of a bond, -alkylene-, -alkylene-C(O)-, -alkylene-J-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-J-, -(alkylene-O)_n-J-alkylene-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -alkylene-C(O)-W-, -(alkylene-O)_n-alkylene-J-, -alkylene'-J-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-J-alkylene', -J-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-J-(alkylene-O)_n-alkylene-J', -W-, -alkylene-W-, alkylene'-J-(alkylene-NMe)_n-alkylene-W-, -J-(alkylene-NMe)_n-alkylene-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, -(alkylene-O)_n-alkylene-U-alkylene-, -J-alkylene-NMe-alkylene'-NMe-alkylene"-W-, and -alkylene-J-alkylene'-NMe-alkylene"-NMe-alkylene"'-W-;



U has the structure of:

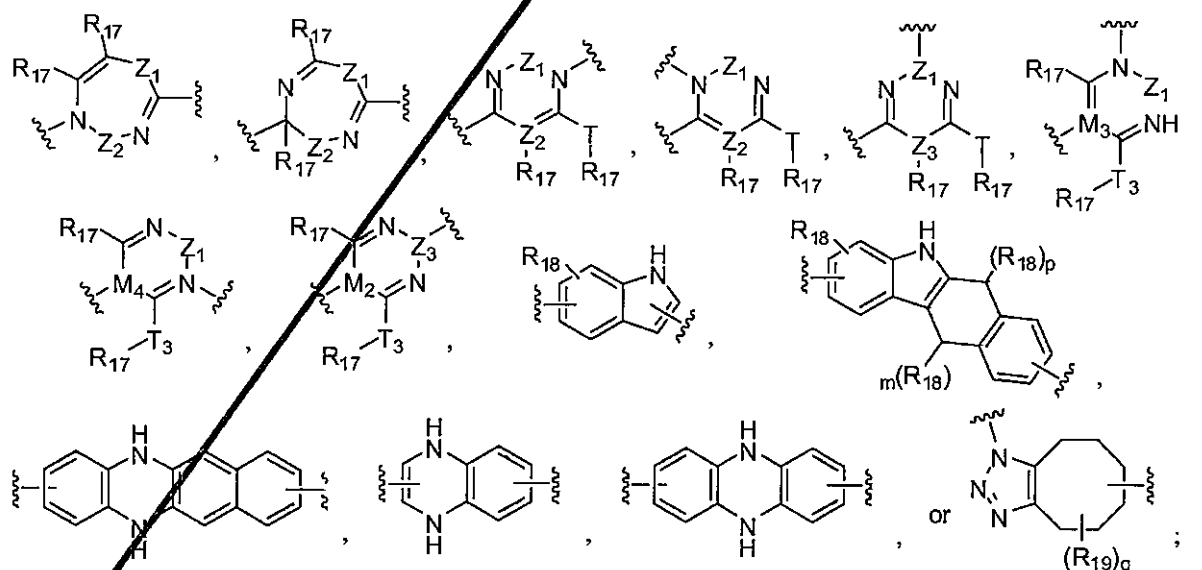


each J and J' independently have the structure of:



each n and n' are independently integers 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)₂R'', 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;

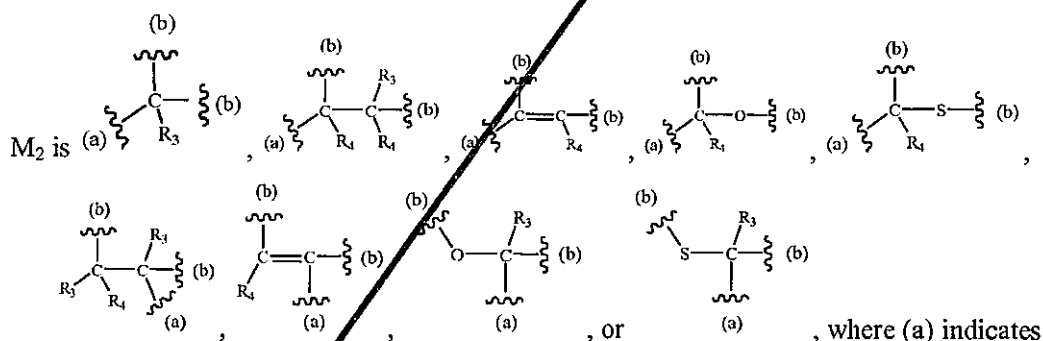
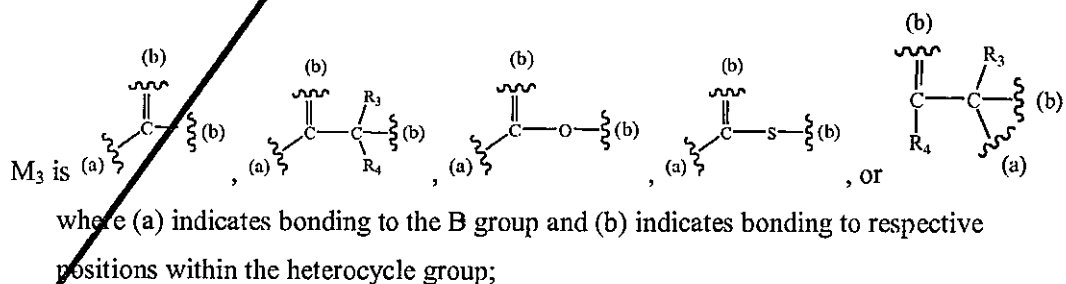
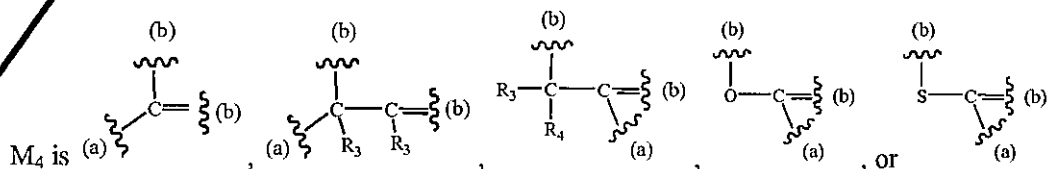
each Z_2 is selected from the group consisting of a bond, $-C(O)-$, $-C(S)-$, optionally substituted C_1-C_3 alkylene, optionally substituted C_1-C_3 alkenylene, and optionally substituted heteroalkyl;

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;

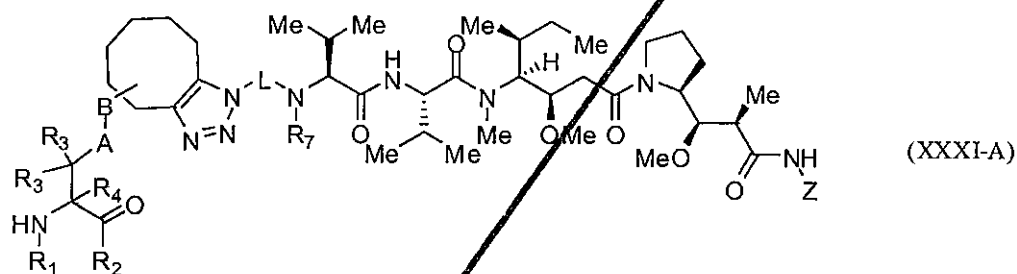


each R_{19} is independently selected from the group consisting of C_1 - C_6 alkyl, C_1 - C_6 alkoxy, ester, ether, thioether, aminoalkyl, halogen, alkyl ester, aryl ester, amide, aryl amide, alkyl halide, alkyl amine, alkyl sulfonic acid, alkyl nitro, thioester, sulfonyl ester, halosulfonyl, nitrile,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

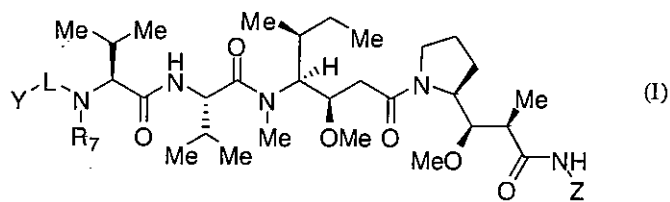
50. The compound of claim 49, wherein R_1 is a polypeptide.
51. The compound of claims 50, wherein the polypeptide is an antibody.
52. The compound of claim 51, wherein the antibody is herceptin.
53. The compound of claim 49, wherein R_2 is a polypeptide.
54. The compound of claims 53, wherein the polypeptide is an antibody.
55. The compound of claim 54, wherein the antibody is herceptin.
56. The compound of claim 49, comprising Formula (XXXI-A):



57. A pharmaceutical composition comprising a compound of any of claims 1-38 and 42-56 and a pharmaceutically acceptable carrier, excipient, or binder.

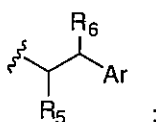
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

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



wherein:

Z has the structure of:



R₅ is thiazole;

R₆ is OH or H;

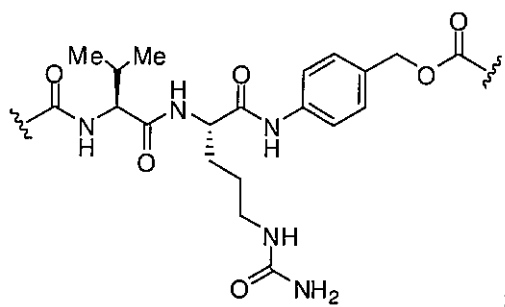
Ar is phenyl or pyridine;

R₇ is C₁-C₆alkyl or hydrogen;

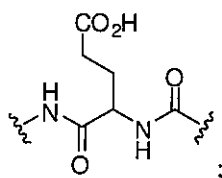
Y is selected from the group consisting of an hydroxylamine, methyl, aldehyde, protected aldehyde, ketone, protected ketone, thioester, ester, dicarbonyl, hydrazine, amidine, imine, diamine, azide, keto-amine, keto-alkyne, alkyne, cycloalkyne, and ene-dione;

L is a linker selected from the group consisting of -alkylene-, -alkylene-C(O)-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -(alkylene-O)_n-(CH₂)_n-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, and -(alkylene-O)_n-alkylene-U-alkylene-;

W has the structure of:



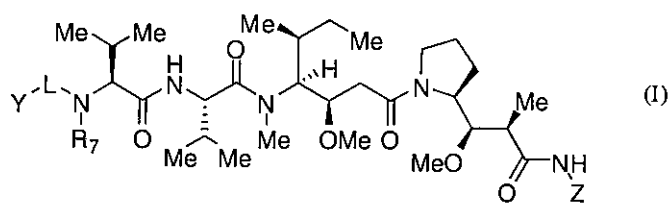
U has the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $-NH-(alkylene-O)_n-NH_2$; and

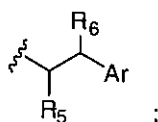
each n, n', n'', n''' and n'''' are independently integers greater than or equal to one.

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



wherein:

Z has the structure of:



R_5 is H, COR_8 , C_1-C_6 alkyl, or thiazole;

R_8 is OH or $-NH-(alkylene-O)_n-NH_2$;

R_6 is OH or H;

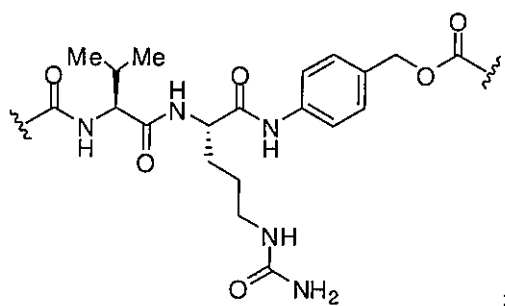
Ar is phenyl or pyridine;

R_7 is C_1-C_6 alkyl or hydrogen;

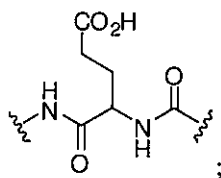
Y is cyclooctyne;

L is a linker selected from the group consisting of $-\text{alkylene}-$, $-\text{alkylene}-\text{C}(\text{O})-$, $-(\text{alkylene}-\text{O})_n-$, $\text{alkylene}-$, $-(\text{alkylene}-\text{O})_n-\text{alkylene}-\text{C}(\text{O})-$, $-(\text{alkylene}-\text{O})_n-(\text{CH}_2)_n-\text{NHC}(\text{O})-(\text{CH}_2)_n-\text{C}(\text{Me})_2-\text{S}-\text{S}-(\text{CH}_2)_n-\text{NHC}(\text{O})-(\text{alkylene}-\text{O})_n-\text{alkylene}-$, $-(\text{alkylene}-\text{O})_n-\text{alkylene}-\text{W}-$, $-(\text{alkylene}-\text{O})_n-(\text{CH}_2)_n-\text{W}-$, $-(\text{alkylene}-\text{O})_n-\text{alkylene}-\text{U}-\text{alkylene}-\text{C}(\text{O})-$, and $-(\text{alkylene}-\text{O})_n-\text{alkylene}-\text{U}-\text{alkylene}-$;

W has the structure of:



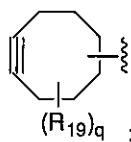
U has the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $-\text{NH}-(\text{alkylene}-\text{O})_n-\text{NH}_2$; and

each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one.

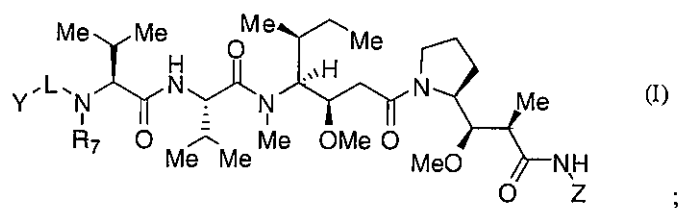
3. The compound of claim 2, wherein the cyclooctyne has a structure of:



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

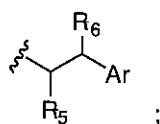
q is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11.

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



wherein:

Z has the structure of:



R₅ is H, COR₈, C₁-C₆alkyl, or thiazole;

R₈ is OH or -NH-(alkylene-O)_n-NH₂;

R₆ is OH or H;

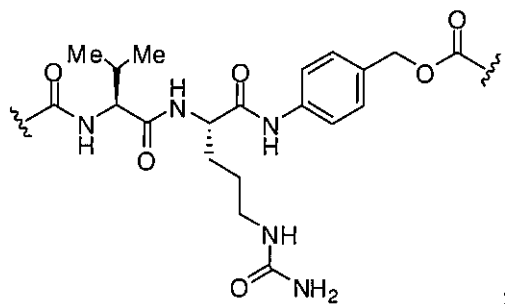
Ar is phenyl or pyridine;

R₇ is C₁-C₆alkyl or hydrogen;

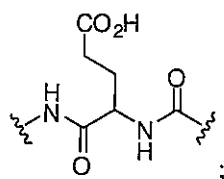
Y is azide;

L is a linker selected from the group consisting of -alkylene-, -alkylene-C(O)-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -(alkylene-O)_n-(CH₂)_n-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, and -(alkylene-O)_n-alkylene-U-alkylene-;

W has the structure of:



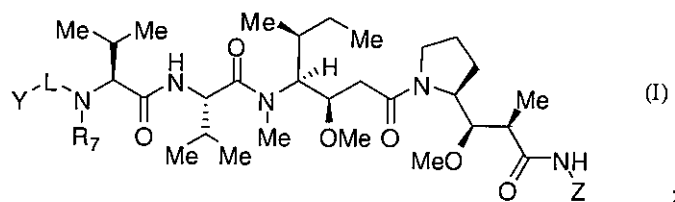
U has the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $-\text{NH}-(\text{alkylene-O})_n-\text{NH}_2$; and

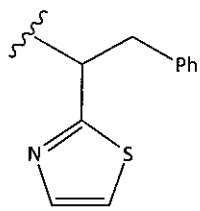
each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one.

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



wherein:

Z is:

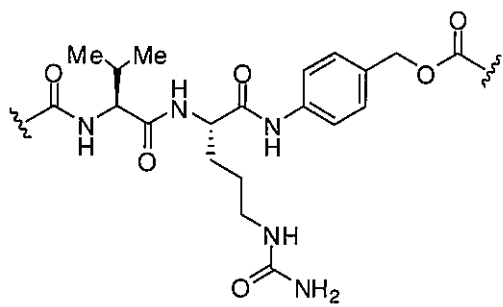


R_7 is $\text{C}_1\text{-C}_6$ alkyl or hydrogen;

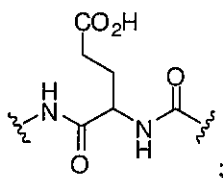
Y is hydroxylamine;

L is a linker selected from the group consisting of $-\text{alkylene}-$, $-\text{alkylene-C(O)}-$, $-(\text{alkylene-O})_n-$, $-\text{alkylene}-$, $-(\text{alkylene-O})_n-\text{alkylene-C(O)}-$, $-(\text{alkylene-O})_n-(\text{CH}_2)_n-\text{NHC(O)}-(\text{CH}_2)_n-$, $\text{C(Me)}_2-\text{S-S}-(\text{CH}_2)_n-\text{NHC(O)}-(\text{alkylene-O})_n-\text{alkylene}-$, $-(\text{alkylene-O})_n-\text{alkylene-W}-$, $-(\text{alkylene-O})_n-(\text{CH}_2)_n-\text{W}-$, $-(\text{alkylene-O})_n-\text{alkylene-U-alkylene-C(O)}-$, and $-(\text{alkylene-O})_n-\text{alkylene-U-alkylene}-$;

W has the structure of:



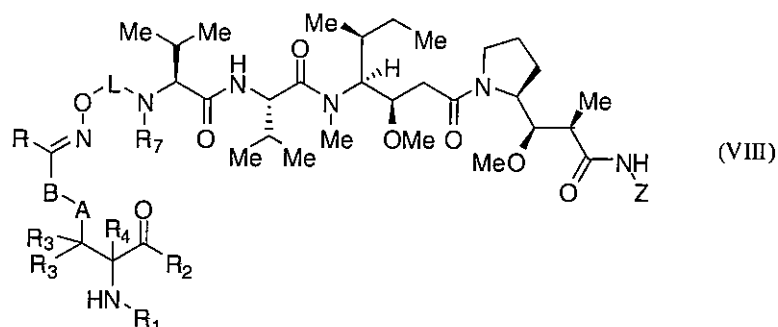
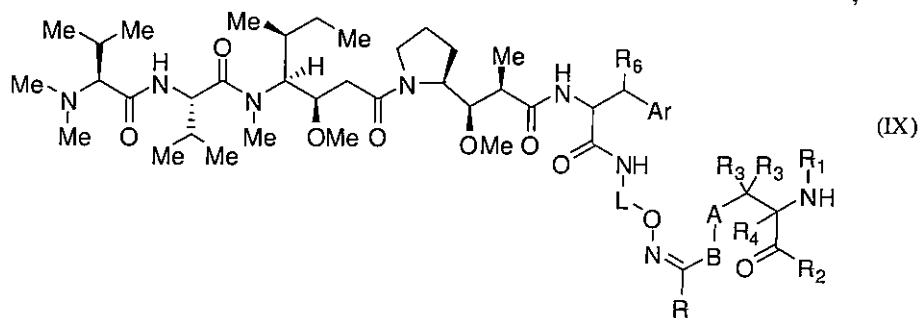
U has the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $-NH-(alkylene-O)_n-NH_2$; and

each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one.

6. The compound of Formula (II) of claim 5, wherein L is $-(alkylene-O)_n-alkylene-$.
7. The compound of claim 6, wherein each alkylene is $-CH_2CH_2-$, n is equal to 3, and R_7 is methyl.
8. The compound of Formula (II) of claim 5, wherein L is $-alkylene-$.
9. The compound of claim 8, wherein each alkylene is $-CH_2CH_2-$ and R_7 is methyl or hydrogen.
10. The compound of Formula (II) of claim 5, wherein L is $-(alkylene-O)_n-alkylene-C(O)-$.
11. The compound of claim 10, wherein each alkylene is $-CH_2CH_2-$, n is equal to 4, and R_7 is methyl.
12. The compound of Formula (II) of claim 5, wherein L is $-(alkylene-O)_n-(CH_2)_{n'}-NHC(O)-(CH_2)_{n''}-C(Me)_2-S-S-(CH_2)_{n'''}-NHC(O)-(alkylene-O)_{n'''}-alkylene-$.
13. The compound of claim 12, wherein each alkylene is $-CH_2CH_2-$, n is equal to 1, n' is equal to 2, n'' is equal to 1, n''' is equal to 2, n'''' is equal to 4, and R_7 is methyl.
14. A compound comprising Formula (VIII) or (IX):



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)_kN(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)_kN(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;

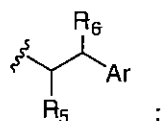
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

R₁ is H, an amino protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₂ is OH, an ester protecting group, resin, at least one amino acid, polypeptide, or polynucleotide;

R₃ and R₄ are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R₃ and R₄ or two R₃ groups optionally form a cycloalkyl or a heterocycloalkyl;

Z has the structure of:



R₅ is H, COR₈, C₁-C₆alkyl, or thiazole;

R₈ is OH;

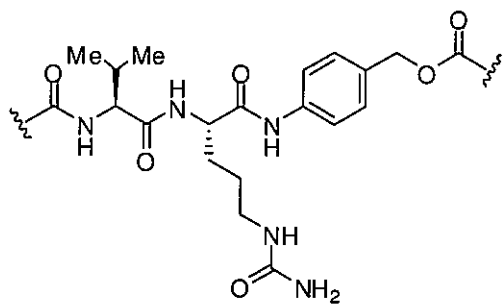
R₆ is OH or H;

Ar is phenyl or pyridine;

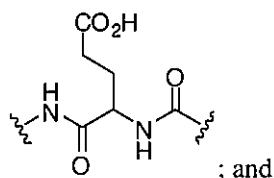
R₇ is C₁-C₆alkyl or hydrogen;

L is a linker selected from the group consisting of -alkylene-, -alkylene-C(O)-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-(CH₂)_n-NHC(O)-(CH₂)_n-C(Me)₂-S-S-(CH₂)_n-NHC(O)-(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-W-, -alkylene-C(O)-W-, -(alkylene-O)_n-alkylene-U-alkylene-C(O)-, and -(alkylene-O)_n-alkylene-U-alkylene-;

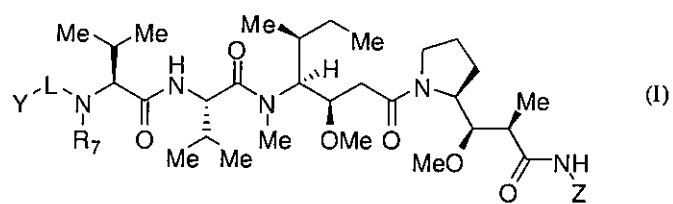
W has the structure of:



U has the structure of:

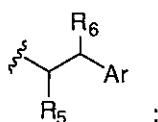


- each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one;
 or an active metabolite, or a pharmaceutically acceptable prodrug or solvate thereof.
15. The compound of claim 14, wherein R_1 is a polypeptide.
 16. The compound of claim 15, wherein the polypeptide is an antibody.
 17. The compound of claim 16, wherein the antibody is trastuzumab.
 18. The compound of claim 14, wherein R_2 is a polypeptide.
 19. The compound of claim 18, wherein the polypeptide is an antibody.
 20. The compound of claim 19, wherein the antibody is trastuzumab.
 21. 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:



wherein:

Z has the structure of:



R_5 is H, COR₈, C₁-C₆alkyl, or thiazole;

R_8 is OH or -NH-(alkylene-O)_n-NH₂;

R_6 is OH or H;

Ar is phenyl or pyridine;

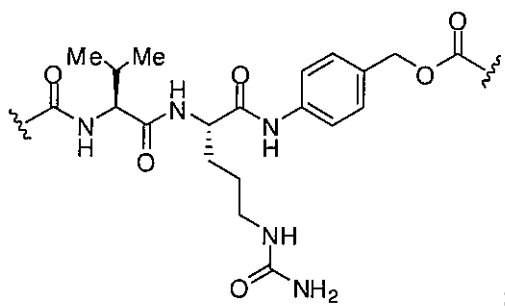
R_7 is C₁-C₆ alkyl or hydrogen;

Y is NH₂-O- or methyl;

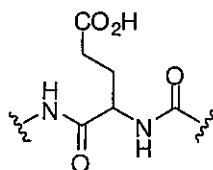
L is a linker selected from the group consisting of a bond, -alkylene-, -alkylene-C(O)-, -(alkylene-O)_n-alkylene-, -(alkylene-O)_n-alkylene-C(O)-, -(alkylene-O)_n-(CH₂)_n-

$\text{NHC(O)-(CH}_2)_n\text{-C(Me)}_2\text{-S-S-(CH}_2)_{n''}\text{-NHC(O)-(alkylene-O)}_n\text{-alkylene-}$, $\text{-(alkylene-O)}_n\text{-alkylene-W-}$, -alkylene-C(O)-W- , $\text{-(alkylene-O)}_n\text{-alkylene-J-}$, -alkylene'-J- , $\text{(alkylene-O)}_n\text{-alkylene-}$, $\text{-(alkylene-O)}_n\text{-alkylene-J-alkylene'}$, $\text{-J-(alkylene-O)}_n\text{-alkylene-}$, $\text{-(alkylene-O)}_n\text{-alkylene-J-(alkylene-O)}_{n'}\text{-alkylene-J'}$, -W- , -alkylene-W- , alkylene'-J- , $\text{(alkylene-NMe)}_n\text{-alkylene-W-}$, and $\text{J-(alkylene-NMe)}_n\text{-alkylene-W-}$, $\text{-(alkylene-O)}_n\text{-alkylene-U-alkylene-C(O)-}$, $\text{-(alkylene-O)}_n\text{-alkylene-U-alkylene-}$; $\text{-J-alkylene-NMe-alkylene'-NMe-alkylene''-W-}$, and $\text{-alkylene-J-alkylene'-NMe-alkylene''-NMe-alkylene'''-W-}$;

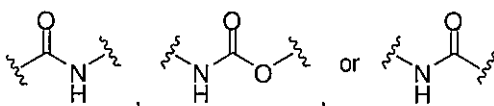
W has the structure of:



U has the structure of:



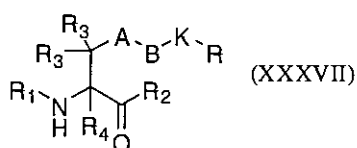
each J and J' independently have the structure of:



or L is absent, Y is methyl, R_5 is COR_8 , and R_8 is $\text{-NH-(alkylene-O)}_n\text{-NH}_2$; and

each n , n' , n'' , n''' and n'''' are independently integers greater than or equal to one;

wherein Formula (XXXVII) corresponds to:

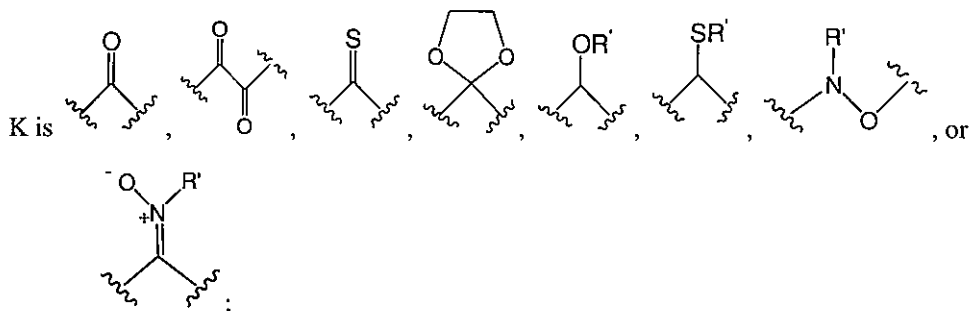


wherein:

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)_kN(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)_kN(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;



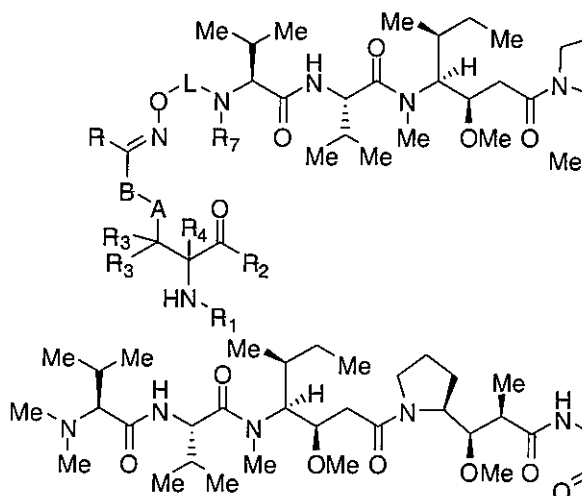
R is H, alkyl, substituted alkyl, cycloalkyl, or substituted cycloalkyl;

R₁ is H, an amino protecting group, resin, at least one amino acid, or polynucleotide;

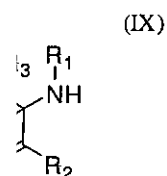
R₂ is OH, an ester protecting group, resin, at least one amino acid, or polynucleotide; and

R₃ and R₄ are each independently H, halogen, lower alkyl, or substituted lower alkyl, or R₃ and R₄ or two R₃ groups optionally form a cycloalkyl or a heterocycloalkyl.

22. The method of claim 21, wherein the derivatized dolastatin analog comprises at least one oxime containing amino acid having the structure of Formula (VIII), or (IX):



(VIII)



(IX)

23. The method of claim 21, wherein the dolastatin analog is compound (XXXVII) in aqueous solution under mildly acidic condition
24. A pharmaceutical composition comprising a compound of a pharmaceutically acceptable carrier, excipient, or binder.
25. A compound according to any one of claims 1, 2, 4, 5 or 14 analog comprising Formula (I) according to claim 21.

reagent of Formula

1 to 20 and a

derivatizing a dolastatin