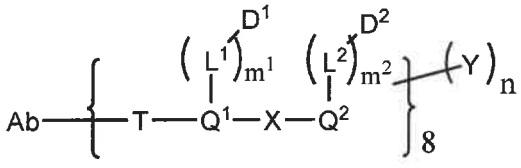
CLAIMS:

1. A multi-drug antibody drug conjugate (MD-ADC) comprising an antibody and eight covalently attached Linking Assembly Units (LA), each having two different Drug Units, D^1 and D^2, attached, wherein each of said eight covalently attached Linking Assembly Units is attached to a thiol produced by reduction of interchain disulfide linkages in said antibody, and wherein each of said covalently attached Linking Assembly Units has from two to four total Drug Units, attached thereto and an optional Partitioning Agent (Y).

2. The antibody drug conjugate of claim **1**, having the formula (I):



(I)

wherein

Ab is an antibody that is a non-engineered antibody;

T is a Tethering Group attached to a thiol produced by reduction of the antibody's interchain disulfide linkages;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

X is an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

L^2 is an Optional Linking Group joining D^2 to Q^2;

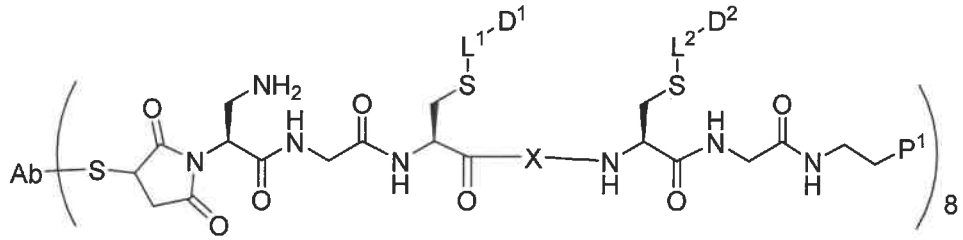
subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X, Q^2, L^1 or L^2; and

subscript n is 0 or 1.

3. The antibody drug conjugate of claim 2, wherein X is an amino acid or a di- or tri-peptide; and wherein each of L^1 and L^2 are independently selected from maleimido-caproyl (mc), maleimido-caproyl-valine-citrulline (mc-vc), maleimido-caproyl-valine-citrulline-paraaminobenzyloxycarbonyl (mc-vc-PABC) and maleimidodiaminopropionyl-valine-citrulline (MDPr-vc)..

4. The antibody drug conjugate of claim 2, having the structure:



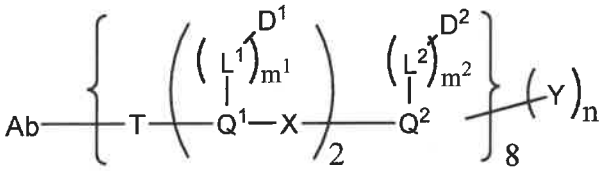
wherein P^1 is a polyethylene glycol group.

5. The antibody drug conjugate of claim 4, wherein each of L^1 and L^2 is independently selected from the group consisting of maleimido-caproyl (mc), maleimido-caproyl-valine-citrulline (mc-vc), and maleimido-caproyl-valine-citrulline-paraaminobenzyloxycarbonyl (mc-vc-PABC).

6. The antibody drug conjugate of claim 4, wherein D^1 and D^2 are independently selected from the group consisting of MMAE, Auristatin T, MMAF and Dolastatin 10; or wherein D^1 and D^2 are independently selected from the group consisting of MMAE, camptothecin, Superdox, Dolastatin 10, Vinblastine and Ciprofloxacin.

7. The multi-drug antibody drug conjugate (MD-ADC) of claim **1**, comprising an antibody and eight covalently attached Linking Assembly Units (LA), wherein each of said eight covalently attached LA Units is attached to a thiol produced by reduction of interchain disulfide linkages in said antibody, and wherein each of said covalently attached LA Units has a total of three Drug Units, D^1 and D^2, attached thereto, wherein the molar ratio of D^1 to D^2 is 2:1.

8. The antibody drug conjugate of claim 7, having formula (II):



(II)

wherein

Ab is an antibody that is a non-engineered antibody;

T is a Tethering Group attached to a thiol produced by reduction of the antibody's interchain disulfide linkages;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

each X is independently an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

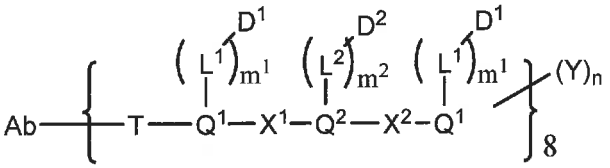
L^2 is an Optional Linking Group joining D^2 to Q^2;

subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X, Q^2, L^1 or L^2; and

subscript n is 0 or 1.; or

having formula (III):



(III)

wherein

Ab is an antibody that is a non-engineered antibody;

T is a Tethering Group attached to a thiol produced by reduction of the antibody's interchain disulfide linkages;

each Q^1 is an independently selected first Attachment Group;

Q^2 is a second Attachment Group;

X^1 and X^2 are each independently an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

each L^1 is an Optional Linking Group joining D^1 to Q^1;

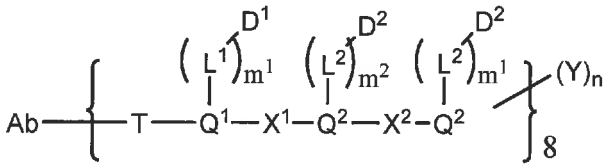
L^2 is an Optional Linking Group joining D^2 to Q^2;

subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X^1, X^2, Q^2, L^1 or L^2; and

subscript n is 0 or 1; or

having formula (IV):



(IV)

wherein

Ab is an antibody that is a non-engineered antibody;

T is a Tethering Group attached to a thiol produced by reduction of the antibody's interchain disulfide linkages;

Q^1 is an independently selected first Attachment Group;

each Q^2 is a second Attachment Group;

X^1 and X^2 are each independently an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

each L^2 is an Optional Linking Group joining D^2 to Q^2;

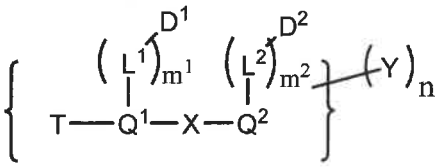
subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X^1, X^2, Q^2, L^1 or L^2; and

subscript n is 0 or 1.

9. The antibody drug conjugate of any one of claims 2 to 8, wherein D^1 and D^2 are a drug pair selected from the group consisting of MMAE/MMAF, MMAE/camptothecin, Superdox/camptothecin, Superdox/MMAE, Dolastatin 10/MMAE, Dolastatin 10/MMAF, Vinblastine/MMAE, and Vinblastine/MMAF.

10. A Drug Linking Assembly Unit having the formula (Ia):



(Ia)

wherein

T is a Tethering Group that can be attached to a thiol produced by reduction of an antibody's interchain disulfide linkage;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

X is an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

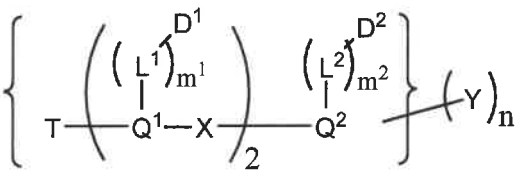
L^2 is an Optional Linking Group joining D^2 to Q^2;

subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X, Q^2, L^1 or L^2; and

subscript n is 0 or 1.

11. A Drug Linking Assembly Unit having the formula (IIa):



(IIa)

wherein

T is a Tethering Group that can be attached to a thiol produced by reduction of an antibody's interchain disulfide linkage;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

each X is independently an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

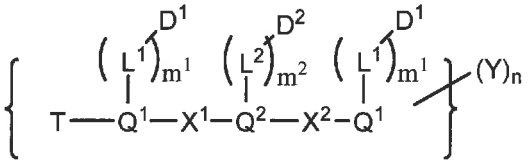
L^2 is an Optional Linking Group joining D^2 to Q^2;

subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X, Q^2, L^1 or L^2; and

subscript n is 0 or 1.

12. A Drug Linking Assembly Unit having the formula (IIIa):



(IIIa)

wherein

T is a Tethering Group that can be attached to a thiol produced by reduction of an antibody's interchain disulfide linkage;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

X^1 and X^2 are each independently an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

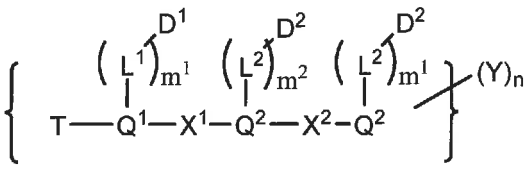
L^2 is an Optional Linking Group joining D^2 to Q^2;

the subscripts m^1 and m^2 are each independently selected from 0 and 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X^1, Q^2, X^2, L^1 or L^2; and

the subscript n is 0 or 1.

13. A Drug Linking Assembly Unit having the formula (IVa):



(IVa)

wherein

T is a Tethering Group that can be attached to a thiol produced by reduction of an antibody's interchain disulfide linkage;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

X^1 and X^2 are each independently an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

L^2 is an Optional Linking Group joining D^2 to Q^2;

subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X^1, Q^2, X^2, L^1 or L^2; and

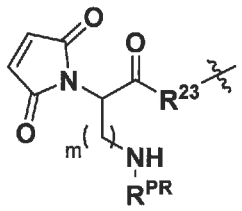
subscript n is 0 or 1.

14. The Drug Linking Assembly Unit of any one of claims 10, 11, 12, or 13, wherein L comprises a maleimido group, and each of X, X^1, X^2, Q^1, and Q^2 is an amino acid; wherein subscript n is 0, Y is absent, and each of L^1 and L^2 is independently selected from the group consisting of maleimido-caproyl (mc), maleimido-caproyl-valine-citrulline (mc-vc), and maleimido-caproyl-valine-citrulline-paraaminobenzyloxycarbonyl (mc-vc-PABC); and wherein T comprises a terminal maleimido group or a self-stabilizing linker.

15. The Drug Linking Assembly Unit of claim 14, wherein subscript n is 0, Y is absent, and each of L^1 and L^2 is independently selected from the group consisting of maleimido-caproyl (mc), maleimido-caproyl-valine-citrulline (mc-vc), and maleimido-

caproyl-valine-citrulline-paraaminobenzyloxycarbonyl (mc-vc-PABC); and wherein T comprises a terminal maleimido group or a self-stabilizing linker.

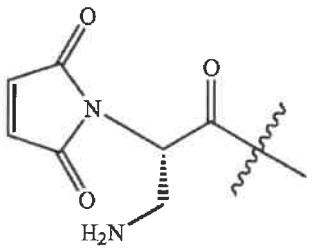
16. The Drug Linking Assembly Unit of any one of claims 10 to 15, wherein T comprises the Formula (VII) of:



(VII),

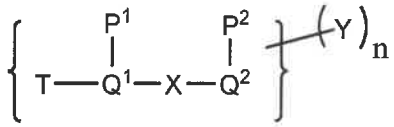
wherein R^{PR} is hydrogen or a protecting group, subscript m is 1 or 2, and R^{23} is -NH-C_{1-5}alkylene-C(=O)-, or a mono, di-, tri-, tetra-, or penta-peptide.

17. The Drug Linking Assembly Unit of claim 16, wherein T comprises the Formula of:



18. The Drug Linking Assembly Unit of claim 16, wherein T is a MDPr-vc linker.

19. An orthogonally protected Linking Assembly Unit having Formula (Ib):



(Ib)

wherein

T is a Tethering Group having a terminal maleimido moiety;

Q^1 is a first Attachment Group comprising a first cysteine moiety or an analogue thereof;

Q^2 is a second Attachment Group comprising a second cysteine moiety or an analogue thereof;

X is an Attachment Group Linker;

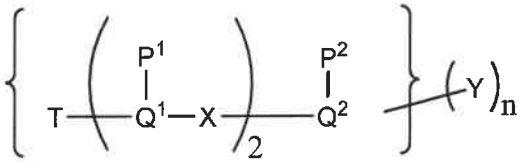
P^1 is a first thiol Protecting Group;

P^2 is a second thiol Protecting Group, and P^1 and P^2 are different;

Y is a Partitioning Agent attached to L, Q^1, X or Q^2; and

subscript n is 0 or 1.

20. An orthogonally protected Linking Assembly Unit having Formula (IIb):



(IIb)

wherein

T is a Tethering Group having a terminal maleimido moiety;

Q^1 is a first Attachment Group comprising a first cysteine moiety or an analogue thereof;

Q^2 is a second Attachment Group comprising a second cysteine moiety or an analogue thereof;

each X is an Attachment Group Linker;

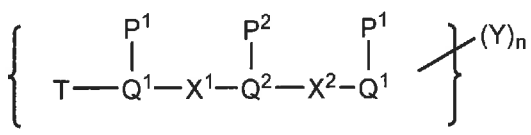
P^1 is a first thiol Protecting Group;

P^2 is a second thiol Protecting Group, and P^1 and P^2 are different;

Y is a Partitioning Agent attached to L, Q^1, X or Q^2; and

subscript n is 0 or 1.

21. An orthogonally protected Linking Assembly Unit having the formula (IIIb):

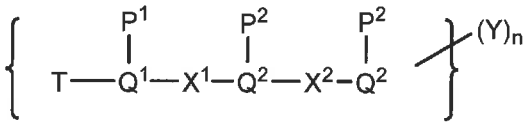


(IIIb)

wherein

T is a Tethering Group having a terminal maleimido moiety;
Q^1 is a first Attachment Group comprising a first cysteine moiety or an analogue thereof;
Q^2 is a second Attachment Group comprising a second cysteine moiety or an analogue thereof;
X^1 and X^2 are each independently an Attachment Group Linker;
P^1 is a first thiol Protecting Group;
P^2 is a second thiol Protecting Group, and P^1 and P^2 are different;
Y is a Partitioning Agent attached to L, Q^1, X or Q^2; and
subscript n is 0 or 1.

22. An orthogonally protected Linking Assembly Unit having the formula (IVb):



(IVb)

wherein
T is a Tethering Group having a terminal maleimido moiety;
Q^1 is a first Attachment Group comprising a first cysteine moiety or an analogue thereof;
Q^2 is a second Attachment Group comprising a second cysteine moiety or an analogue thereof;
X^1 and X^2 are each independently an Attachment Group Linker;
P^1 is a first thiol Protecting Group;
P^2 is a second thiol Protecting Group, and P^1 and P^2 are different;
Y is a Partitioning Agent attached to L, Q^1, X or Q^2; and
subscript n is 0 or 1.

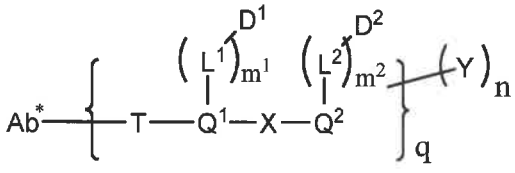
23. The orthogonally protected Linking Assembly Unit of any one of claims 19 to 22, wherein P^1 is selected from the group consisting of –S-isopropyl (SiPr), -S-tert-butyl (StBu), and -S-methyl (SMe); and P^2 is $–CH_2NH-C(O)CH_3$ (acetamidomethyl); or wherein T is MDPr-Val-Cit-; P^1 is selected from the group consisting of –S-isopropyl

(SiPr), -S-tert-butyl (StBu), and -S-methyl (SMe); and P^2 is $-CH_2NH-C(O)CH_3$ (acetamidomethyl); or wherein X is selected from the group consisting of glycine and alanine; T is MDPr-Val-Cit-; P^1 is selected from the group consisting of –S-isopropyl (SiPr), -S-tert-butyl (StBu), and -S-methyl (SMe); and P^2 is $-CH_2NH-C(O)CH_3$ (acetamidomethyl); or wherein T is MDPr-Val-Cit-; Q^1 and Q^2 are each cysteine; X is glycine; P^1 is selected from the group consisting of –S-isopropyl (SiPr), -S-tert-butyl (StBu), and -S-methyl (SMe); and P^2 is $-CH_2NH-C(O)CH_3$ (acetamidomethyl); or wherein T is MDPr-Val-Cit-; Q^1 and Q^2 are each cysteine; X is glycine; P^1 is selected from the group consisting of –S-isopropyl (SiPr), -S-tert-butyl (StBu), and -S-methyl (SMe); P^2 is $-CH_2NH-C(O)CH_3$ (acetamidomethyl); the subscript n is 1 and Y comprises a PEG or cyclodextrin group.

24. An antibody-linker conjugate having 1 to 8 orthogonally protected Linking Assembly Units of any one of claims 19 to23.

25. A multi-drug antibody drug conjugate (MD-ADC) comprising an antibody and one or more covalently attached Linking Assembly Units (LA), each having two different Drug Units, D^1 and D^2, attached, wherein each of said one or more covalently attached Linking Assembly Units are attached to a sulfur atom of an engineered cysteine or derivative thereof in said antibody's heavy chain or light chain or are attached to a thiol produced by reduction of interchain disulfide linkages in said antibody, and wherein each of said covalently attached Linking Assembly Units has from two to four toal Drug Units attached thereto and an optional Partitioning Agent (Y); wherein each of said one or more covalently attached Linking Assembly Units are attached to a sulfur atom of an engineered cysteine or derivative thereof in said antibody's heavy chain or light chain; wherein D^1 and D^2 are a first anticancer agent and a second anticancer agent, respectively; and wherein the first anticancer agent and the second anticancer agent have complementary activity profiles.

26. The antibody drug conjugate of claim 25, having the formula (I*):



(I*)

wherein

Ab* is an antibody comprising one or more engineered cysteine residues;

T is a Tethering Group attached to a sulfur atom of an engineered cysteine in said antibody's heavy chain or light chain or to a thiol produced by reduction of interchain disulfide linkages in said antibody;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

X is an Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

L^2 is an Optional Linking Group joining D^2 to Q^2;

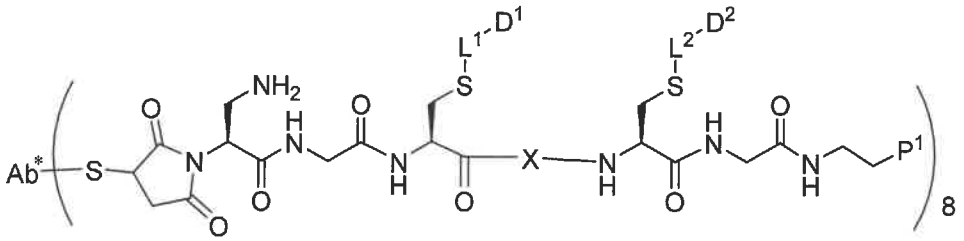
subscripts m^1 and m^2 are each independently 0 or 1;

Y is a Partitioning Agent that is attached to a site on L, Q^1, X, Q^2, L^1 or L^2;

subscript n is 0 or 1; and

subscript q is an integer from 1 to 10.

27. The antibody drug conjugate of claim 26, having the structure:



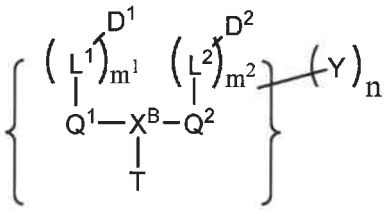
wherein P^1 is a polyethylene glycol group.

28. The antibody drug conjugate of claim 27, wherein each of L^1 and L^2 is independently selected from the group consisting of maleimido-caproyl (mc), maleimido-

caproyl-valine-citrulline (mc-vc), and maleimido-caproyl-valine-citrulline-paraaminobenzyloxycarbonyl (mc-vc-PABC).

28. The antibody drug conjugate of claim 27, wherein D^1 and D^2 are independently selected from the group consisting of MMAE, Auristatin T, MMAF and Dolastatin 10; or , wherein D^1 and D^2 are independently selected from the group consisting of MMAE, camptothecin, Superdox, Dolastatin 10, Vinblastine and Ciprofloxacin.

29. A Drug Linking Assembly Unit having the Formula (XIIIa):



(XIIIa)

wherein

T is a Tethering Group that can be attached to a sulfur atom of an engineered cysteine in said antibody's heavy chain or light chain or to a thiol produced by reduction of an antibody's interchain disulfide linkage;

Q^1 is a first Attachment Group;

Q^2 is a second Attachment Group;

X^B is a branched Attachment Group Linker;

D^1 is a first Drug Unit;

D^2 is a second Drug Unit;

L^1 is an Optional Linking Group joining D^1 to Q^1;

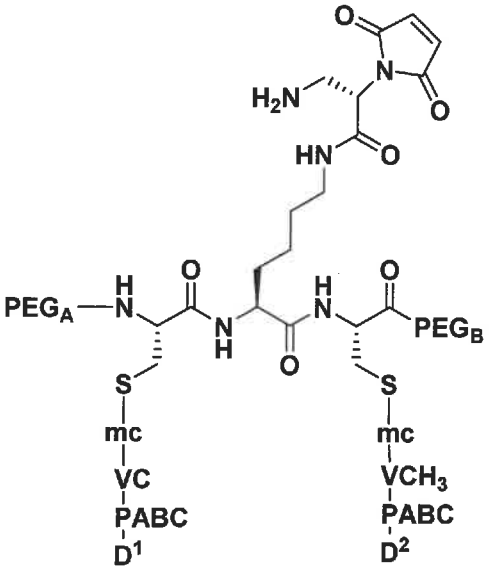
L^2 is an Optional Linking Group joining D^2 to Q^2;

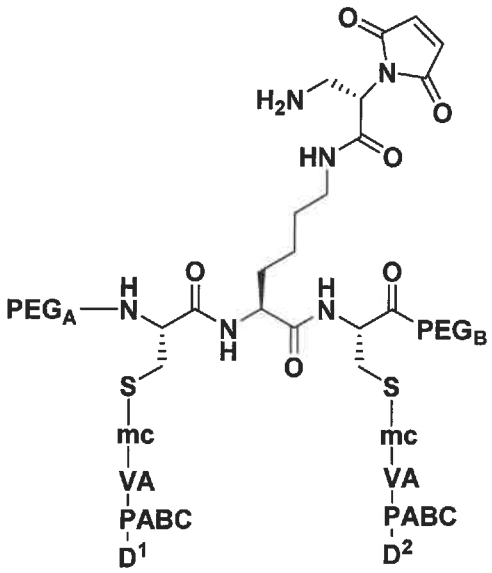
subscripts m^1 and m^2 are each independently 0 or 1;

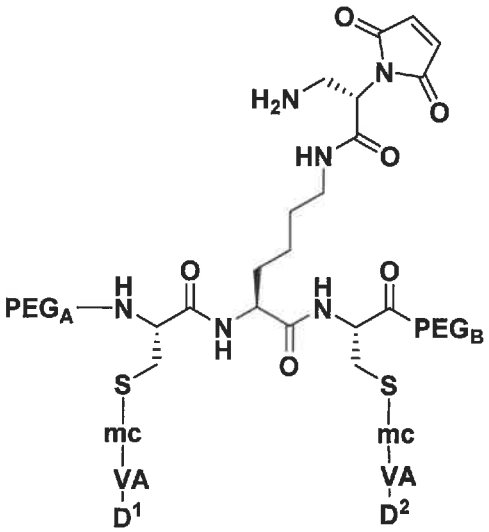
Y is a Partitioning Agent that is attached to a site on L, Q^1, X^B, Q^2, L^1 or L^2; and

subscript n is 0, 1, or 2.

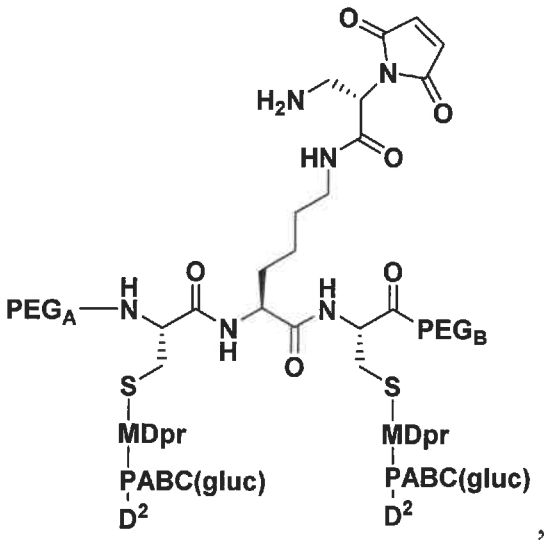
30. The Drug Linking Assembly Unit of claim 29, having the Formula of:



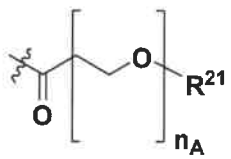




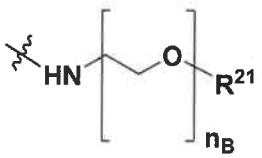
or



,

wherein PEG_A has the structure 

;

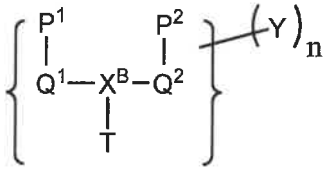
PEG_B has the structure 

;

R^{21} is C_{1-4} alkyl or $-CH_2CH_2CO_2H$; and

Subscripts n_A and n_B are each independently an integer from between 8 and 24.

31. An orthogonally protected Linking Assembly Unit having the formula (XIIIb):



(XIIIb)

wherein

T is a Tethering Group having a terminal maleimido moiety;

Q^1 is a first Attachment Group comprising a first cysteine moiety;

Q^2 is a second Attachment Group comprising a second cysteine moiety;

X^B is a branched Attachment Group Linker;

P^1 is a first thiol Protecting Group;

P^2 is a second thiol Protecting Group, and P^1 and P^2 are different;

Y is a Partitioning Agent attached to L, Q^1, X^B or Q^2; and

subscript n is 0, 1, or 2.