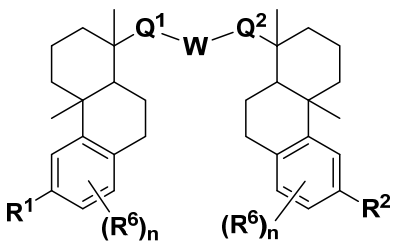
atherosclerosis and stabilizing established atherosclerotic lesions; and (iii) reducing lesion macrophage content by apoptosis.

[0004] The therapeutic potential of small molecule LXR modulators is limited by, for example, undesired modulation of LXR at non-target cells and/or low bioavailability. Modulation of LXR at non-target cells can lead to undesirable side effects, and low bioavailability may manifest for myriad reasons including, without limitation, low solubility that further exacerbates poor therapeutic windows for treatment. The development of ADCs comprising LXR modulators would allow for target-specific modulation of LXR, thereby avoiding side-effects caused by off-target modulation of LXR. Furthermore, such ADCs would provide improved modulation of biological targets, improved bioavailability, and improved therapeutic window. Therefore, there is a continuing need for effective treatments of, for example, metabolic diseases using small molecule ADCs of LXR modulators.

SUMMARY

[0005] Provided herein are compounds useful, for example, for the treatment of metabolic diseases including, without limitation, dyslipidemia. Also provided herein are compounds useful, for example, for the treatment of inflammation or a neurodegenerative disease.

[0006] ~~In one aspect, p~~Provided herein are compounds of Formula I:



(I)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

each of $\mathbf{Q^1}$ and $\mathbf{Q^2}$ is independently $–CH_2–$, –C(O)–, –C(H)(OH)–, $–C(OH)_2–$, $–SO_2–$, –SO–, $–PO(OR^3)–$, $–PO(NR^3NR^4)–$, $–NR^3–$, or –N=;

W is $–CH_2–$, –N(H)–, or –O–;

$\mathbf{R^1}$ is $–N(H)\mathbf{R^4}$ or $–N(\mathbf{R^5})_2$;

$\mathbf{R^2}$ is $–N(H)\mathbf{R^4}$;

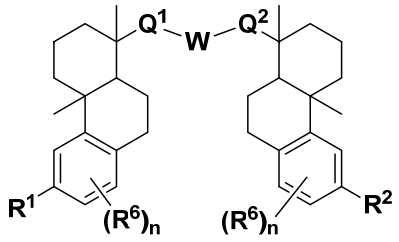
each **R**^{4} is, independently in each instance, hydrogen, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, substituted alkyl, acyl, or substituted acyl;

R^{5} is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and
–CH_2OH, or at least one primary or secondary nitrogen;

each **R**^{6} is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG_{n1}, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve; and

each **R**^{3} is independently hydrogen, alkyl, or aryl.

[0006a] In one aspect, provide herein is a compound of Formula I



(I)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

each of **Q**^{1} and **Q**^{2} is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O**R**^{3})–, –PO(N**R**^{3}N**R**^{4})–, –N**R**^{3}–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

R^{1} is –N(H)**R**^{4} or –N(**R**^{5})$_2$;

R^{2} is –N(H)**R**^{4};

each **R**^{4} is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, substituted alkyl, acyl, or substituted acyl;

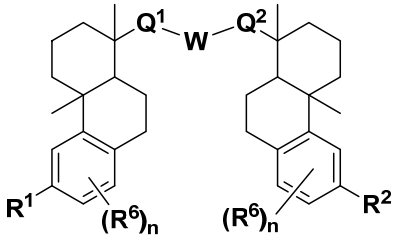
R^{5} is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms

selected from nitrogen and oxygen, and when substituted includes at least one –OH and –CH_2OH, or at least one primary or secondary nitrogen;

each $\mathbf{R^6}$ is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG_{n1}, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve; and

each R^3 is independently hydrogen, alkyl, or aryl.

[0007] In one example, provided herein are compounds according to Formula I:



(I)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

each of $\mathbf{Q^1}$ and $\mathbf{Q^2}$ is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O$\mathbf{R^3}$)–, –PO(N$\mathbf{R^3}$N$\mathbf{R^4}$)–, –N$\mathbf{R^3}$–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

$\mathbf{R^1}$ is –N(H)$\mathbf{R^4}$ or –N($\mathbf{R^5}$)$_2$;

$\mathbf{R^2}$ is –N(H)$\mathbf{R^4}$;

each $\mathbf{R^4}$ is, independently in each instance, hydrogen, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, or alkyl;

$\mathbf{R^5}$ is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and

–CH_2OH, or at least one primary or secondary nitrogen;

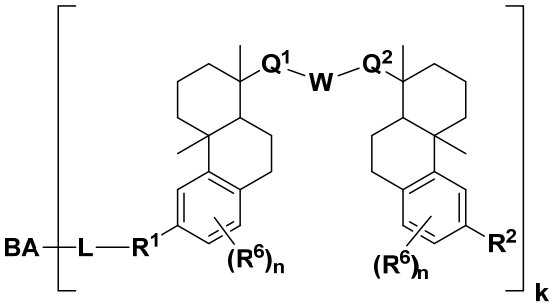
each **R^6** is independently halo, C$_{1-6}$ alkyl, C$_{1-6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG$_{\mathbf{n1}}$, wherein each **n** is an integer from 0-14, and each **n1** is an integer from 1-12; and

each **R^3** is independently hydrogen, alkyl, or aryl.

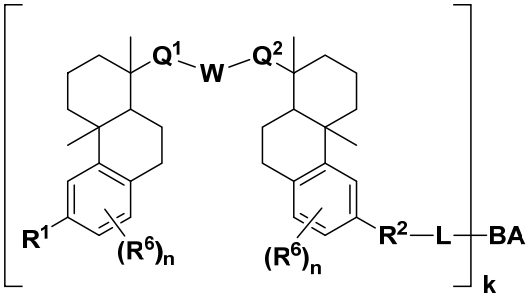
[0008] In another aspect, provided herein is a linker-payload comprising a compound as disclosed herein bonded to a linker In another example, set forth herein is a linker-payload having a compound according to Formula I, above, bonded to a linker.

[0009] In another aspect, provided herein is an antibody-drug conjugate comprising the compound or linker-payload as disclosed herein bonded to an antibody or an antigen binding fragment thereof. In another example, set forth herein is an antibody-drug conjugate having a compound of Formula I or linker-payload, above, bonded to an antibody or an antigen binding fragment thereof.

[0009a] In one aspect, provided herein is a compound of Formula A, B, C, or D



(**A**)



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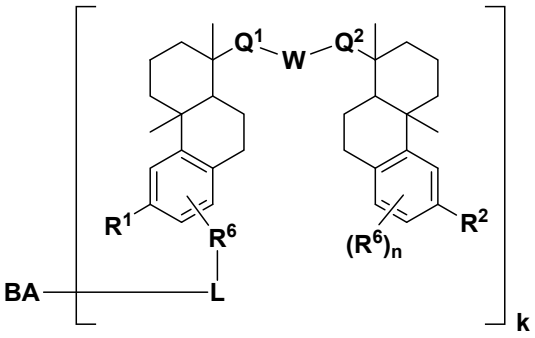
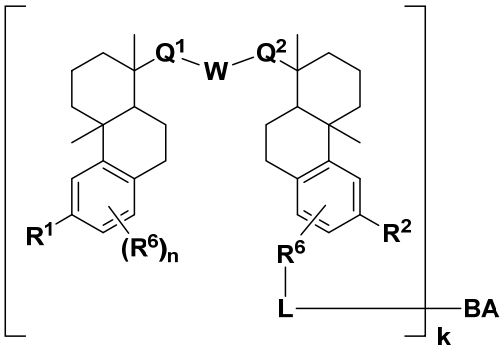


(**C**)



(**D**)

or a pharmaceutically acceptable salt, or stereoisomeric form thereof, wherein

L is a linker;

BA is an antibody or antigen binding fragment thereof;

k is an integer from one to thirty;

each of $\mathbf{Q^1}$ and $\mathbf{Q^2}$ is independently $–CH_2–$, –C(O)–, –C(H)(OH)–, $–C(OH)_2–$, $–SO_2–$, –SO–, $–PO(O\mathbf{R^3})–$, $–PO(N\mathbf{R^3}N\mathbf{R^4})–$, $–N\mathbf{R^3}–$, or –N=;

W is $–CH_2–$, –N(H)–, or –O–;

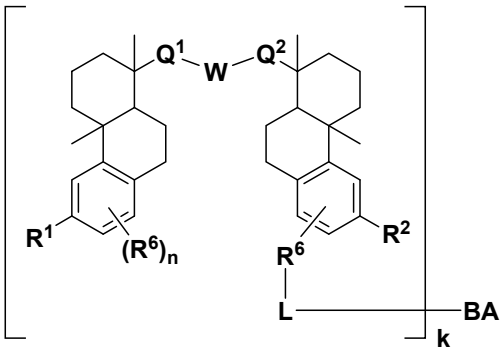
$\mathbf{R^1}$ is $–N(H)\mathbf{R^4}$, $–N(H)\mathbf{R^4}–$, –N(H)–, $–N(\mathbf{R^5})_2$, or $–N(\mathbf{R^5})_2–$;

$\mathbf{R^2}$ is $–N(H)\mathbf{R^4}$, $–N(H)\mathbf{R^4}–$, or –N(H)–;

each $\mathbf{R^4}$ is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, substituted alkyl, acyl, substituted acyl, or -alkylene-;

$\mathbf{R^5}$ is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and

$–CH_2OH$, or at least one primary or secondary nitrogen;



(**D**)

or a pharmaceutically acceptable salt, or stereoisomeric form thereof, wherein

L is a linker;

BA is a binding agent;

k is an integer from 1 to 30;

each of $\mathbf{Q^1}$ and $\mathbf{Q^2}$ is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O$\mathbf{R^3}$)–, –PO(N$\mathbf{R^3}$N$\mathbf{R^4}$)–, –N$\mathbf{R^3}$–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

$\mathbf{R^1}$ is –N(H)$\mathbf{R^4}$, –N(H)$\mathbf{R^4}$–, –N(H)–, –N($\mathbf{R^5}$)$_2$, or –N($\mathbf{R^5}$)$_2$–;

$\mathbf{R^2}$ is –N(H)$\mathbf{R^4}$, –N(H)$\mathbf{R^4}$–, or –N(H)–;

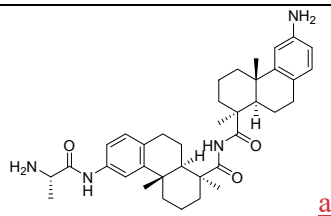
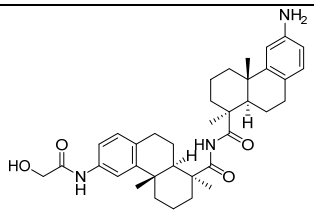
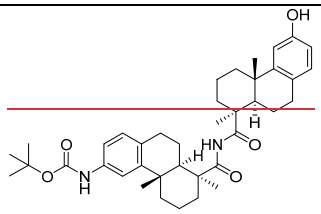
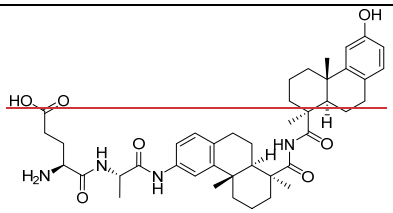
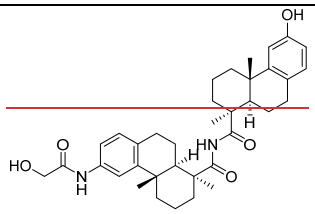
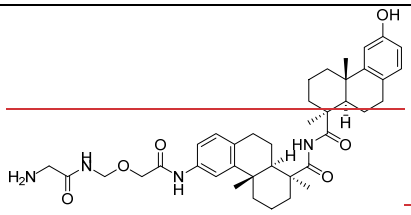
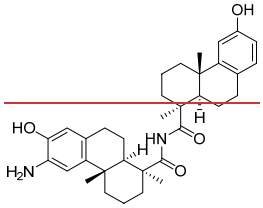
each $\mathbf{R^4}$ is, independently in each instance, hydrogen, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, or -alkylene-;

$\mathbf{R^5}$ is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and –CH_2OH, or at least one primary or secondary nitrogen;

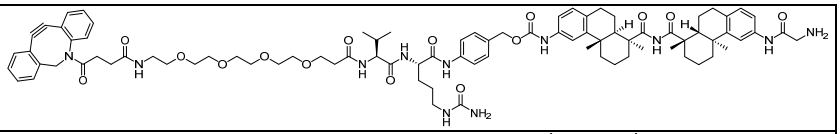
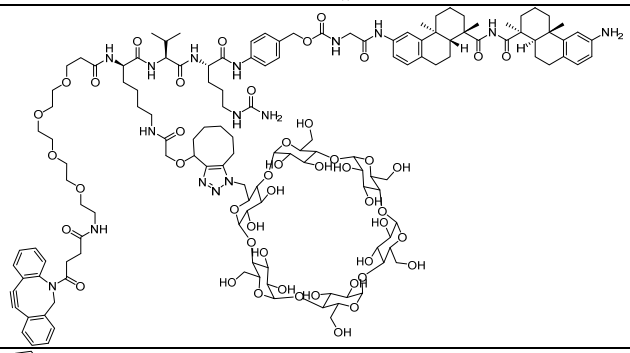
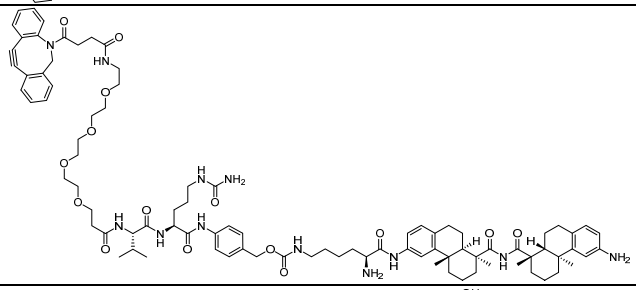
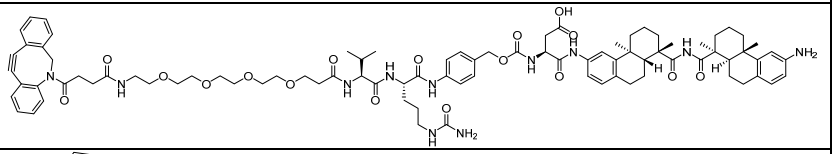
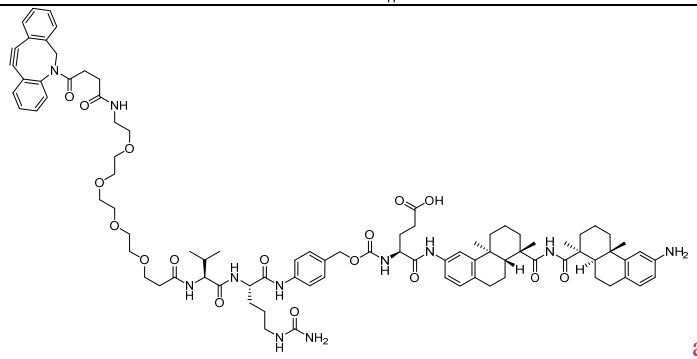
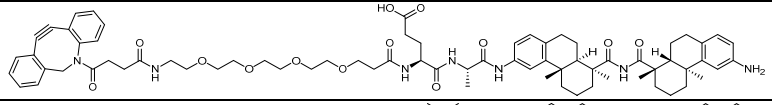
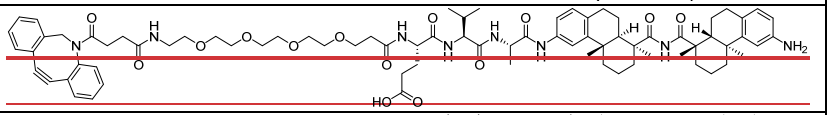
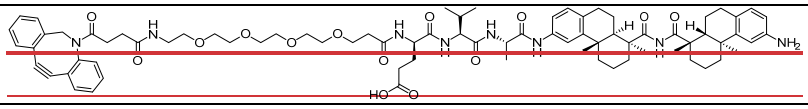
each $\mathbf{R^6}$ is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkylene, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-$PEG_{\mathbf{n1}}$, wherein each **n** is an integer from 0-14, and each **n1** is an integer from 1-12; and

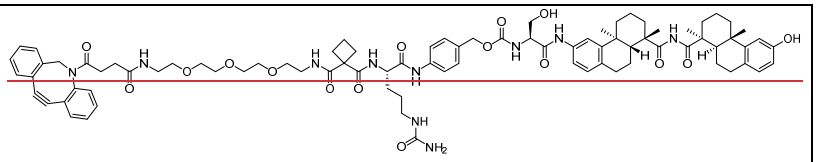
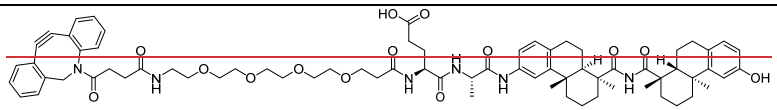
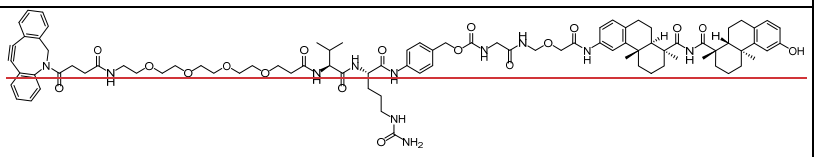
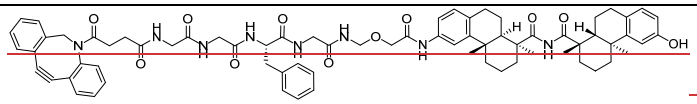
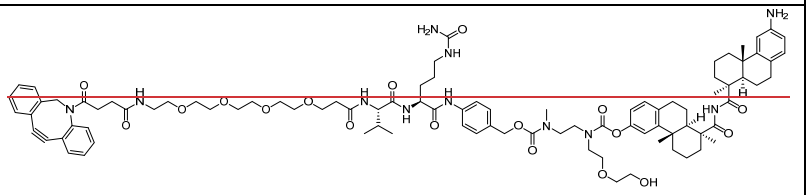
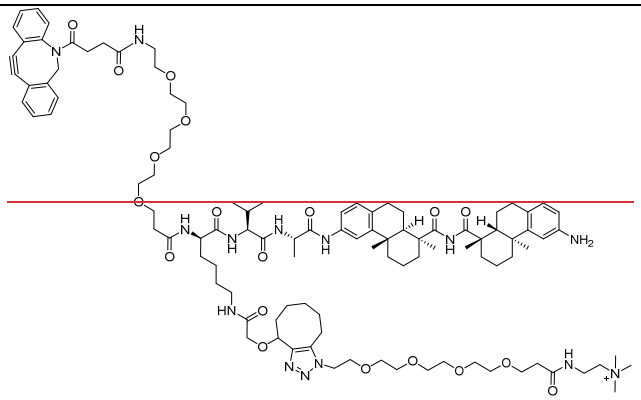
each $\mathbf{R^3}$ is independently hydrogen, alkyl, or aryl.

[0012] In another aspect, disclosed herein is a pharmaceutical composition comprising a compound~~, linker payload,~~ or antibody-drug conjugate as described herein and a pharmaceutically acceptable excipient, carrier, or diluent. In another example, set forth herein is a pharmaceutical composition, including a compound, linker-payload, or antibody-drug conjugate described herein and a pharmaceutically acceptable excipient, carrier, or diluent.

P13	 and
P14	
~~P15~~	
~~P16~~	
~~P17~~	
~~P18~~	 ~~and~~
~~P19~~	

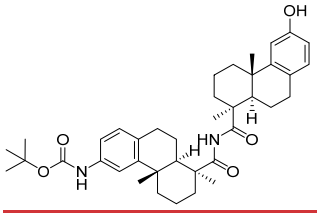
or a pharmaceutically acceptable salt thereof.

LP7	
LP8	
LP9	
LP10	
LP11	 and
LP12	
~~LP13~~	
~~LP14~~	

~~LP15~~	
~~LP16~~	
~~LP17~~	
~~LP18~~	 ~~and~~
~~LP19~~	
~~LP20~~	

or a salt thereof.

[0012e] In another aspect, as disclosed herein is a compound selected from the group consisting of



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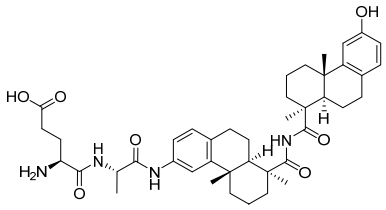

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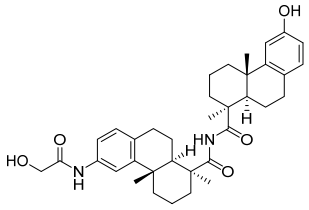

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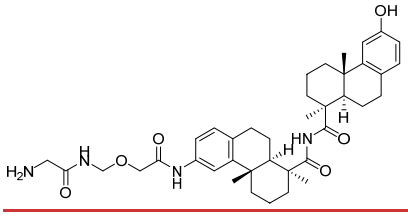

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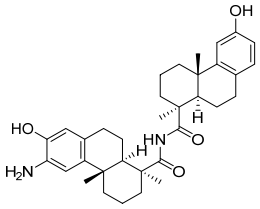
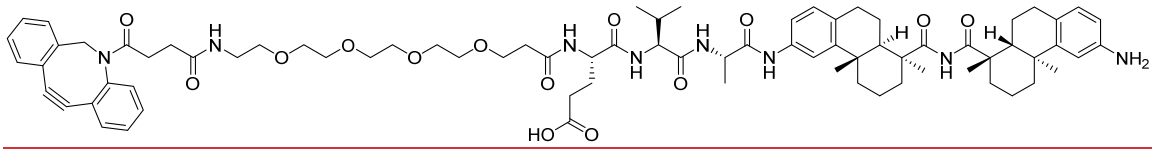


P19.

[0012f] In another aspect, as disclosed herein is a linker-payload selected from the group consisting of



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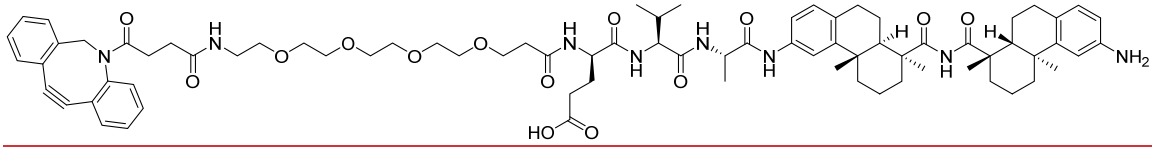

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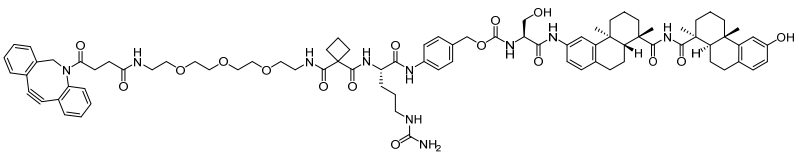

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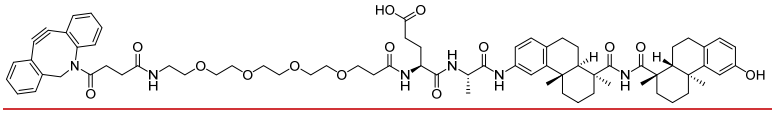

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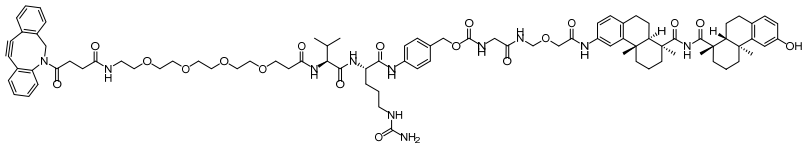
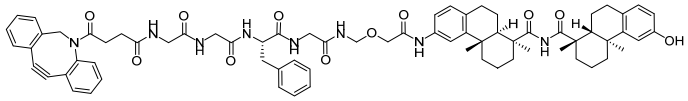
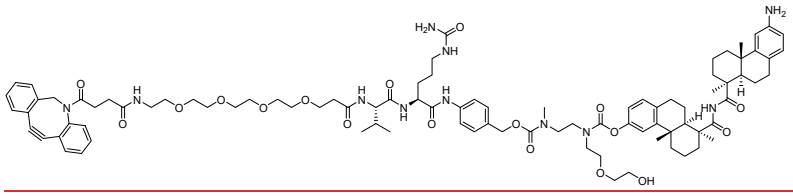


LP17;

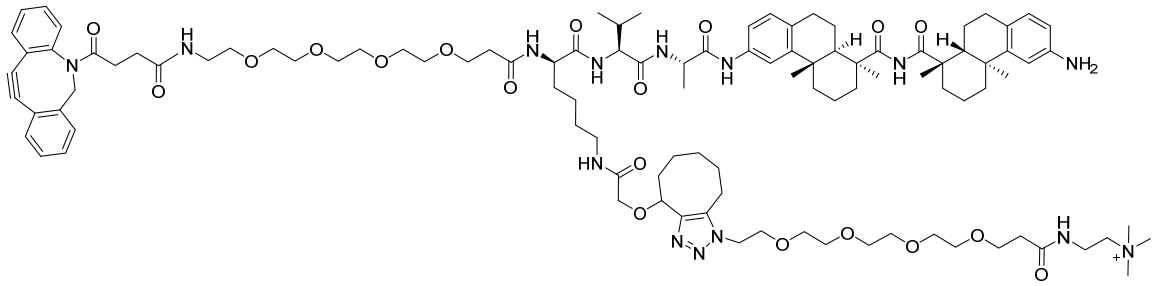


LP18;



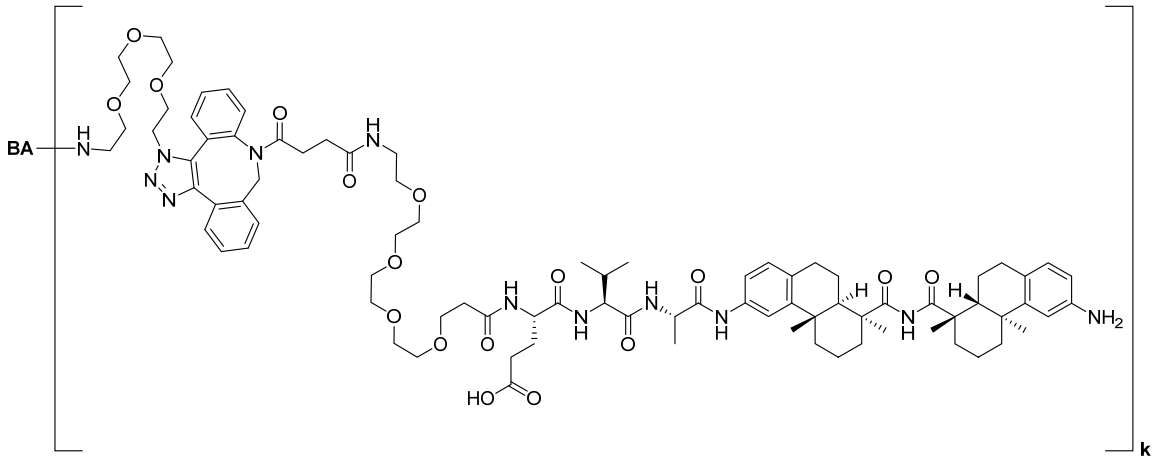
LP19;

and

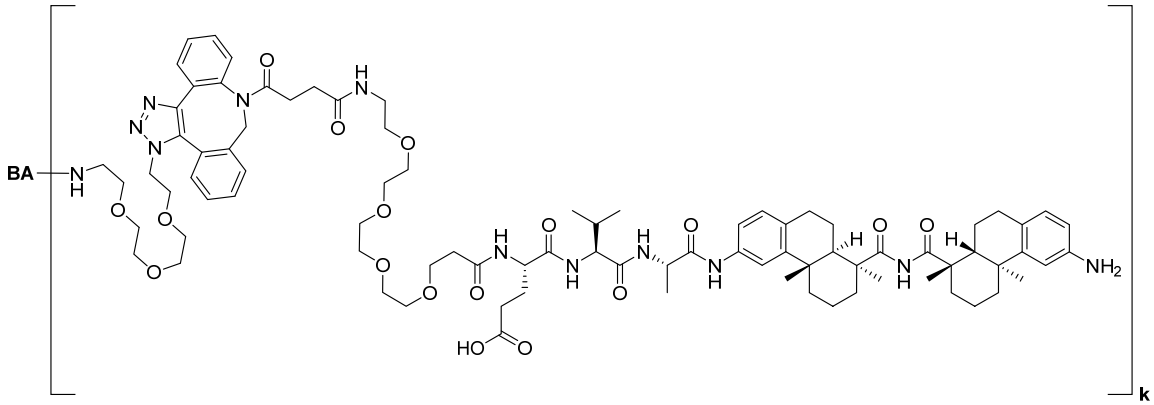


LP20.

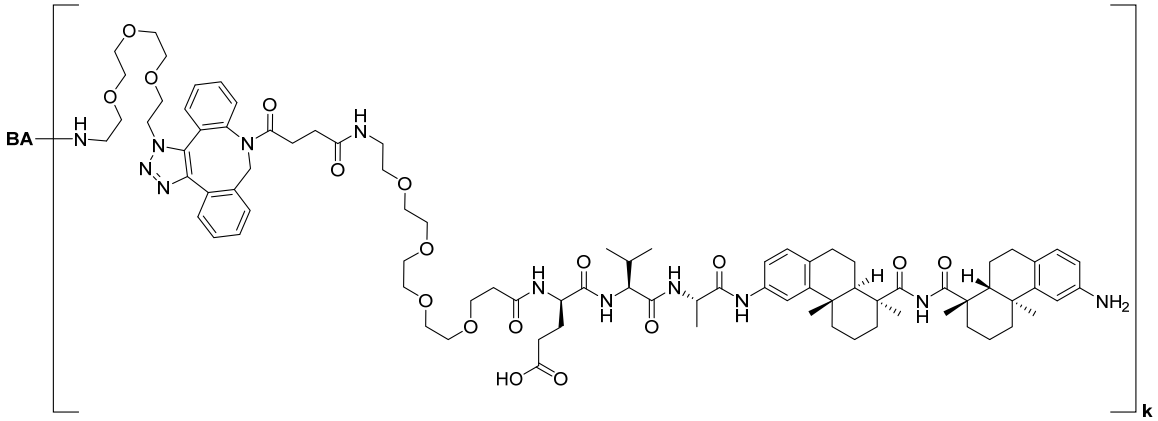
[0012g] In another aspect, as disclosed herein is an antibody-drug conjugate compound selected from the group consisting of



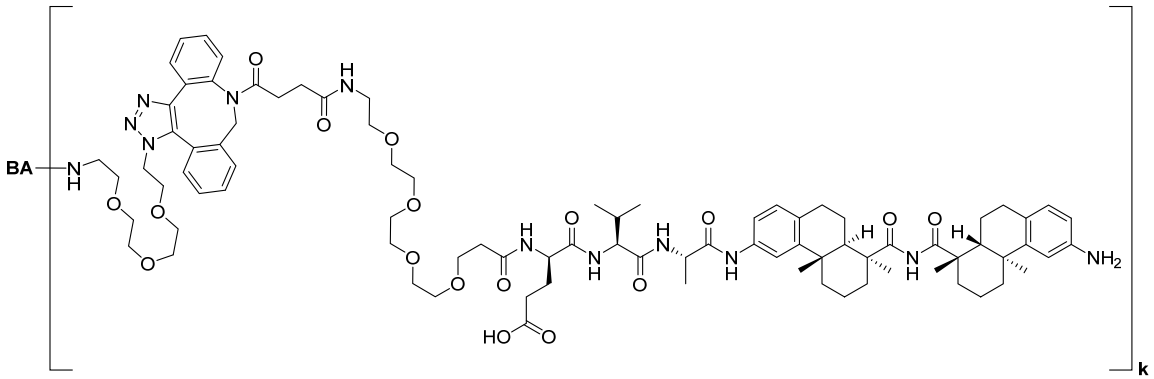
;


BA
HO
NH2
k

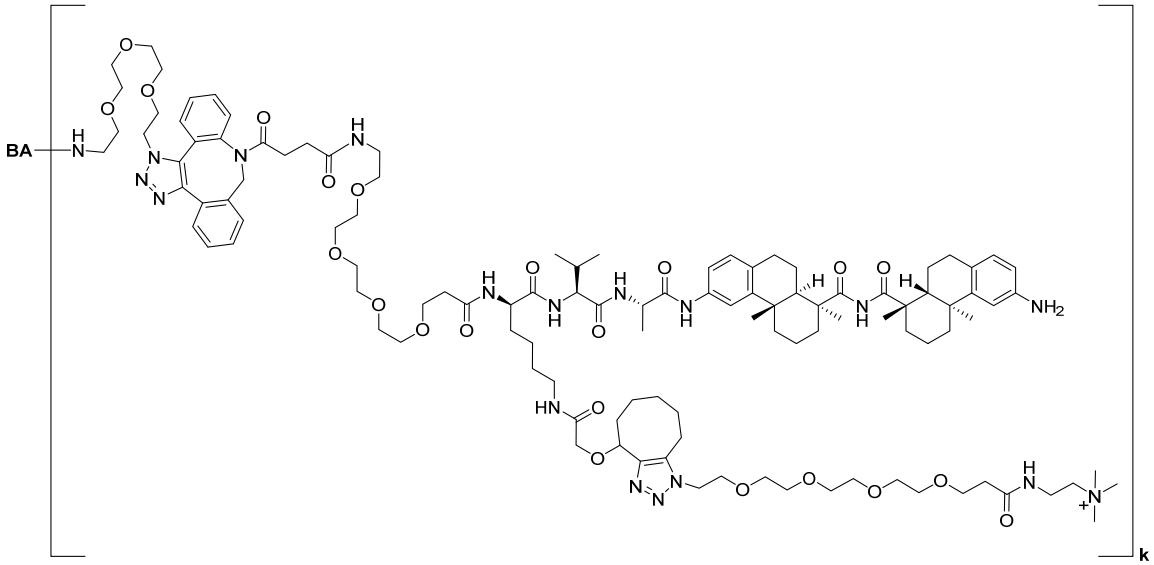
;


BA
HO
NH2
k

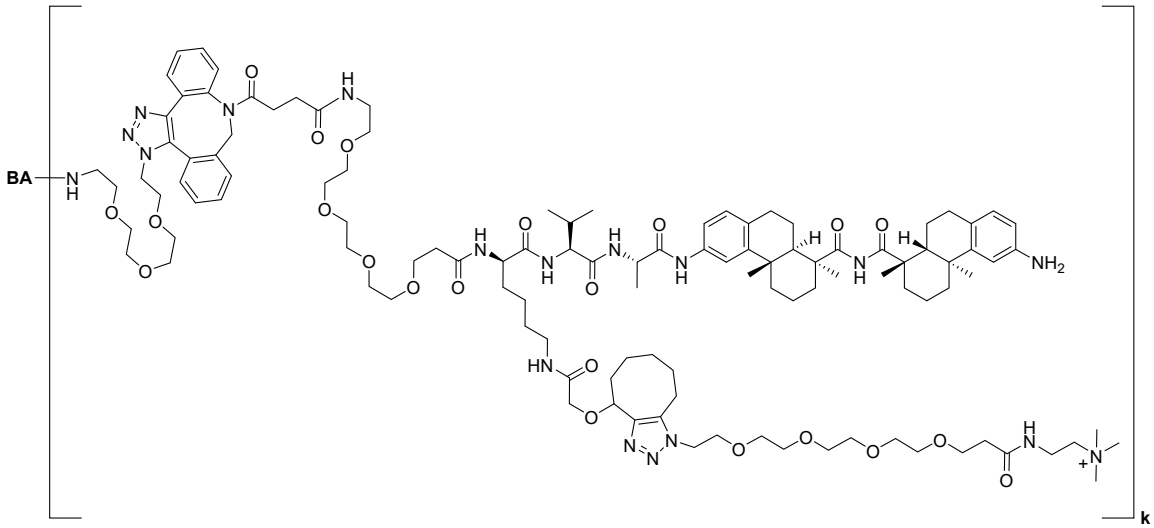
;


BA
HO
NH2
k

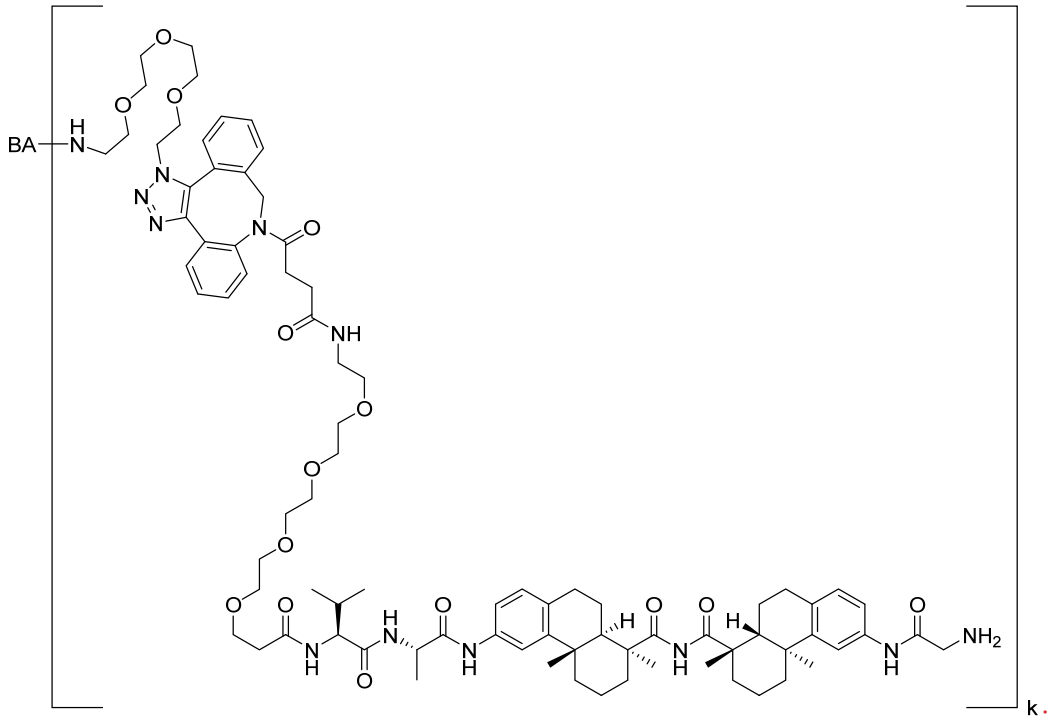
;


BA
NH2
k

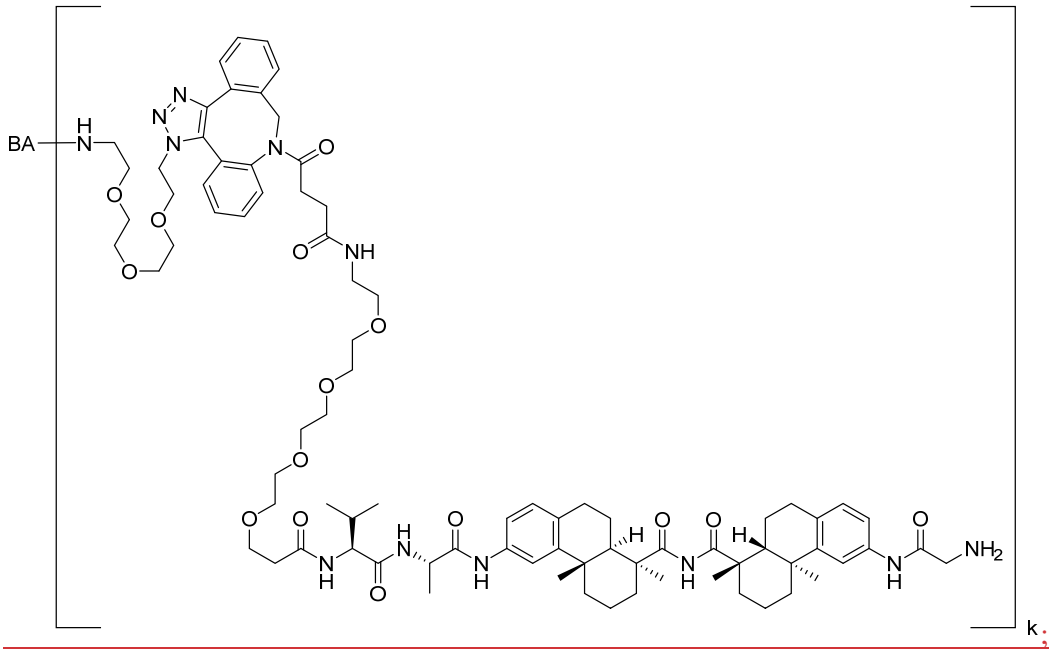
;


BA
NH2
k

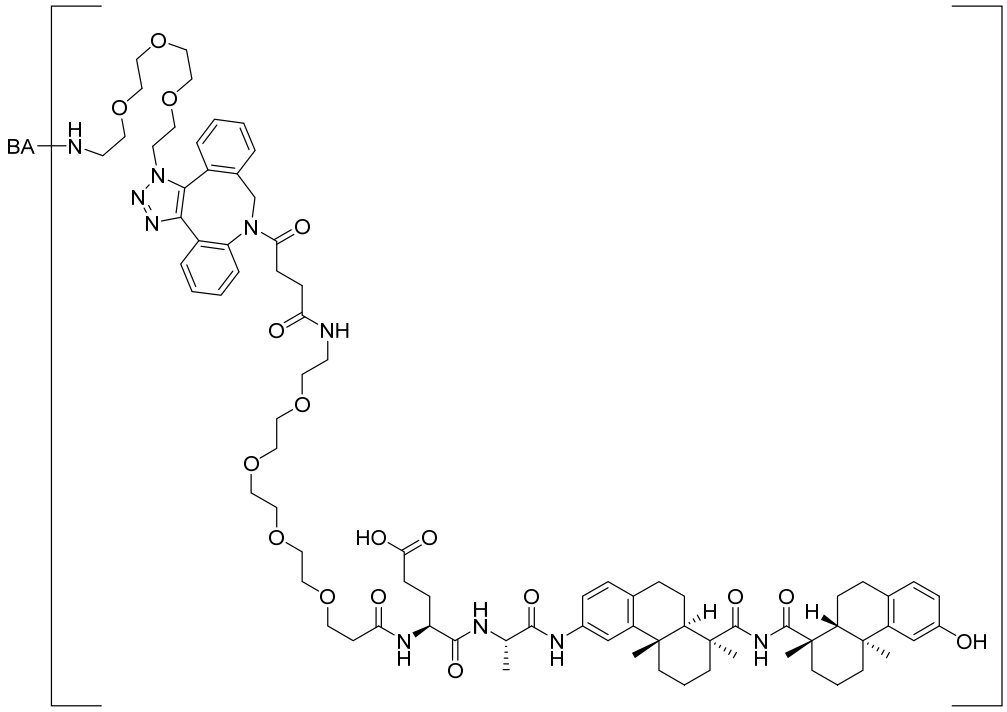
;



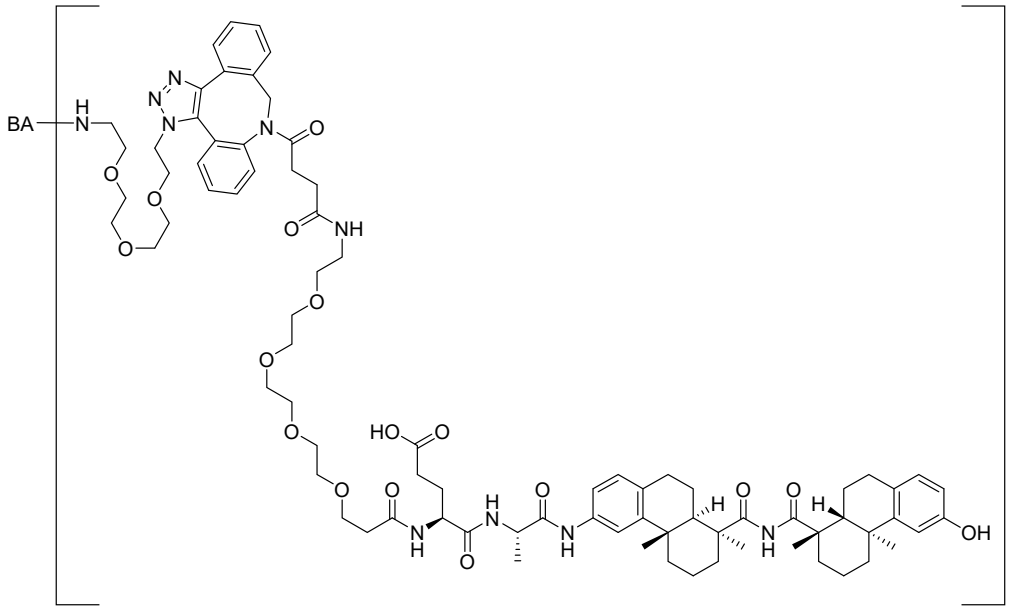
k;



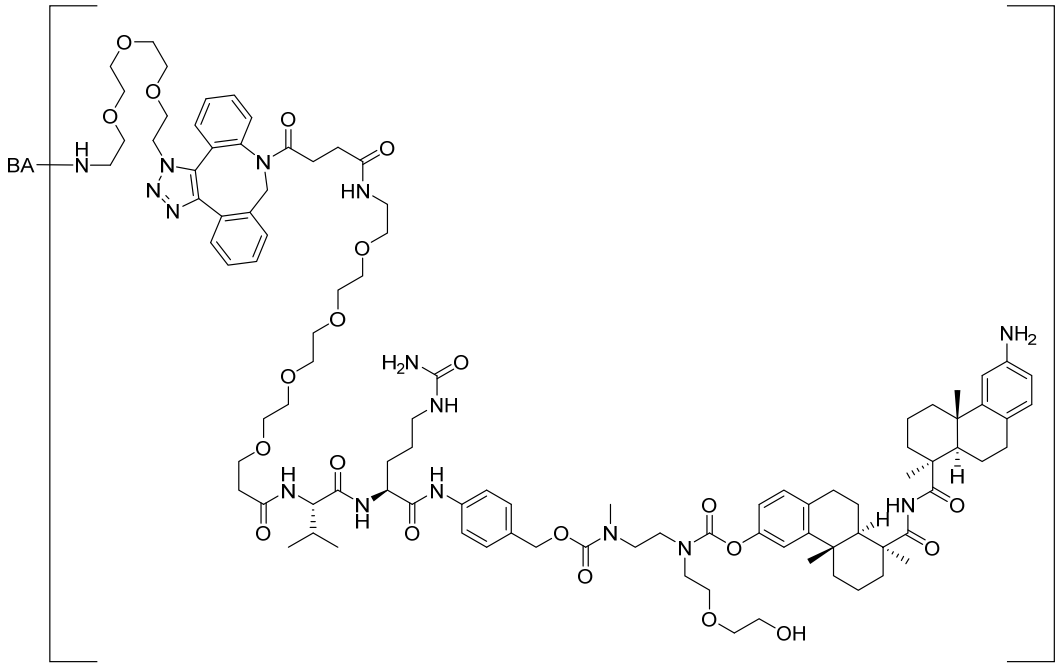
k;



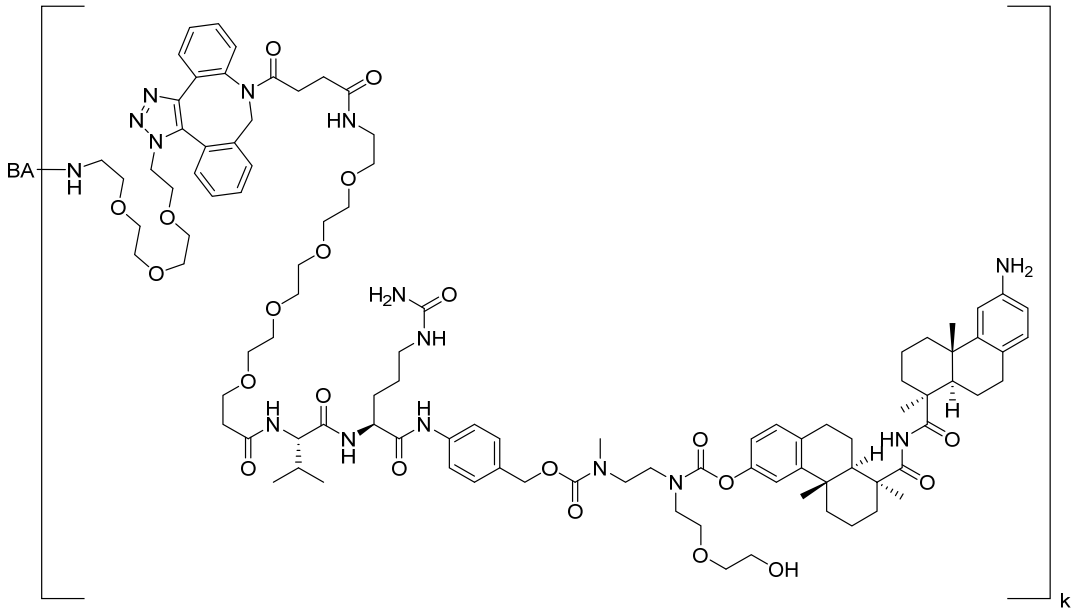
k;



k;



; and

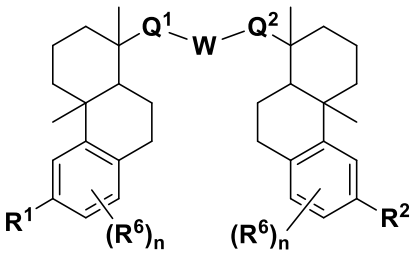


wherein **BA** is an antibody or antigen binding fragment thereof; and **k** is an integer from one to thirty.

[0013] In another example, set forth herein is a method for the treatment of dyslipidemia, a metabolic disease, inflammation, or a neurodegenerative disease in a subject including the

WHAT IS CLAIMED IS:

1. A compound of Formula I



(I)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

each of **Q**^{1} and **Q**^{2} is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O**R**^{3})–, –PO(N**R**^{3}N**R**^{4})–, –N**R**^{3}–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

R^{1} is –N(H)**R**^{4} or –N(**R**^{5})$_2$;

R^{2} is –N(H)**R**^{4};

each **R**^{4} is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, substituted alkyl, acyl, or substituted acyl;

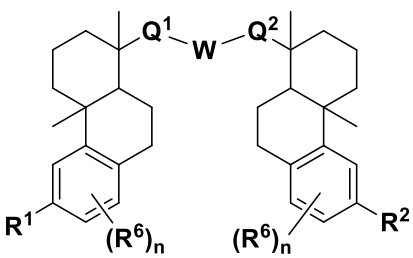
R^{5} is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and

–CH_2OH, or at least one primary or secondary nitrogen;

each **R**^{6} is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG$_{\mathbf{n1}}$, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve; and

each **R**^{3} is independently hydrogen, alkyl, or aryl.

2. The compound of claim 1, according to Formula I



(I)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

each of **Q^1** and **Q^2** is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O**R^3**)–, –PO(N**R^3**N**R^4**)–, –N**R^3**–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

R^1 is –N(H)**R^4** or –N(**R^5**)$_2$;

R^2 is –N(H)**R^4**;

each **R^4** is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, or alkyl;

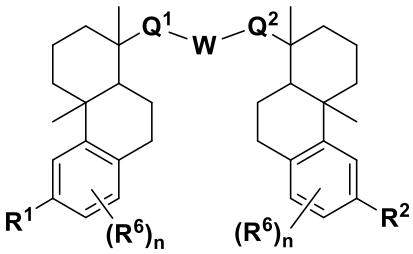
R^5 is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and

–CH_2OH, or at least one primary or secondary nitrogen;

each **R^6** is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG$_{\mathbf{n1}}$, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve; and

each **R^3** is independently hydrogen, alkyl, or aryl.

3. The compound of claim 1, according to Formula I



(I)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

each of **Q^1** and **Q^2** is independently –CH_2–, –C(O)–, –C(H)(OH)–, or –$C(OH)_2$–;

W is –CH_2–, –N(H)–, or –O–;

R^1 is –N(H)**R^4** or –N(**R^5**)$_2$;

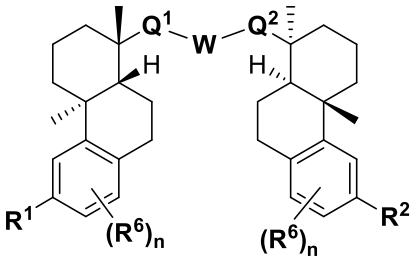
R^2 is –N(H)**R^4**;

each **R**^{4} is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, or alkyl;

R^{5} is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and –CH_2OH, or at least one primary or secondary nitrogen; and

each **R**^{6} is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG$_{\mathbf{n1}}$, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve.

4. The compound of claim 3, according to Formula II



(II)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof.

5. The compound of any preceding claim wherein **Q**^{1} is –CH_2– and **Q**^{2} is –C(O)–.

6. The compound of any preceding claim wherein **Q**^{1} is –C(H)(OH)– and **Q**^{2} is –C(O)–.

7. The compound of any preceding claim wherein **Q**^{1} is –C(O)– and **Q**^{2} is –C(O)–.

8. The compound of any preceding claim wherein **Q**^{1} is –C(O)– and **Q**^{2} is –CH_2–.

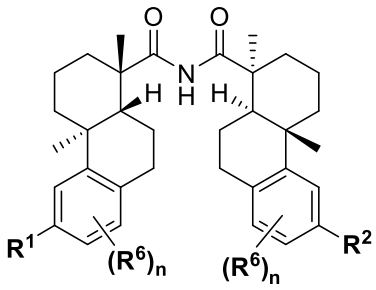
9. The compound of any preceding claim wherein **Q**^{1} is –C(O)– and **Q**^{2} is –C(H)(OH)–.

10. The compound of any preceding claim wherein **W** is –CH_2–.

11. The compound of any preceding claim wherein **W** is –O–.

12. The compound of any preceding claim wherein **W** is –NH–.

13. The compound of any preceding claim according to Formula III



(III)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof.

14. The compound of any one of claims 1-13, wherein $\mathbf{R^1}$ is –N(H)$\mathbf{R^4}$.

15. The compound of any one of claims 1-13, wherein $\mathbf{R^1}$ is –N($\mathbf{R^5}$)$_2$.

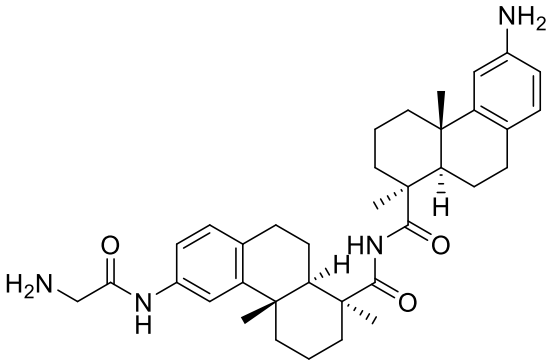
16. The compound of claim 14, wherein $\mathbf{R^1}$ is –NH_2; and

each $\mathbf{R^4}$ is, independently in each instance, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, or alkyl.

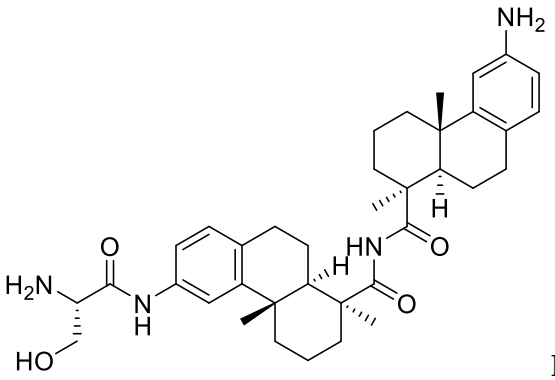
17. The compound of claim 16, wherein each $\mathbf{R^4}$ is, independently in each instance, an amino acid residue; and

the amino acid residue is selected from the group consisting of alanine, isoleucine, leucine, methionine, phenylalanine, tryptophan, tyrosine, valine, serine, threonine, asparagine, glutamine, cysteine, selenocysteine, glycine, proline, arginine, histidine, lysine, aspartic acid, and glutamic acid.

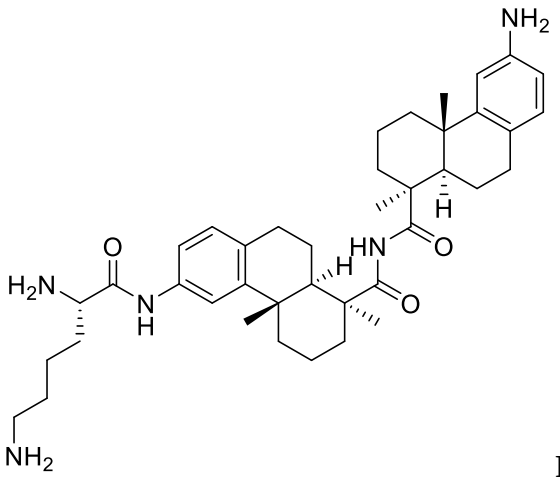
18. The compound of claim 17, selected from the group consisting of



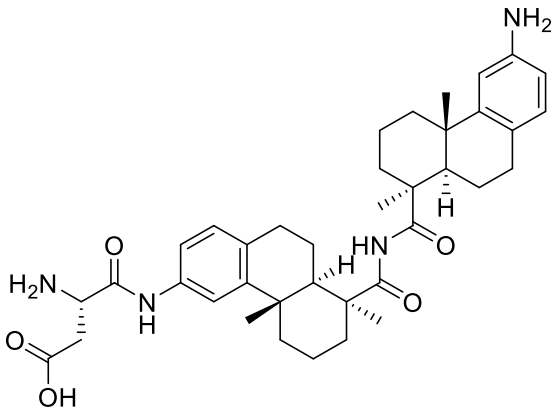
P4;



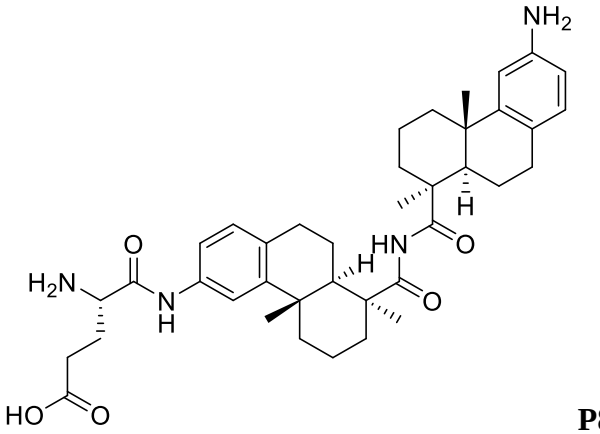
P5;



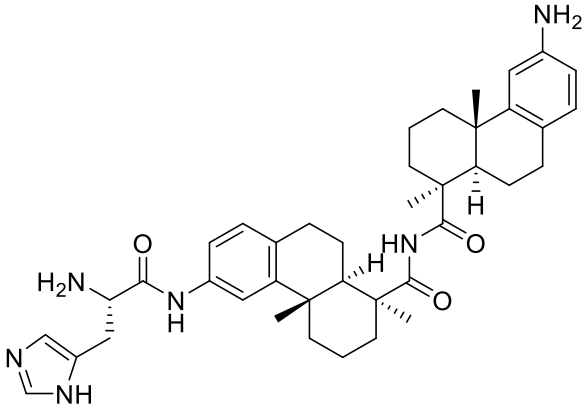
P6;



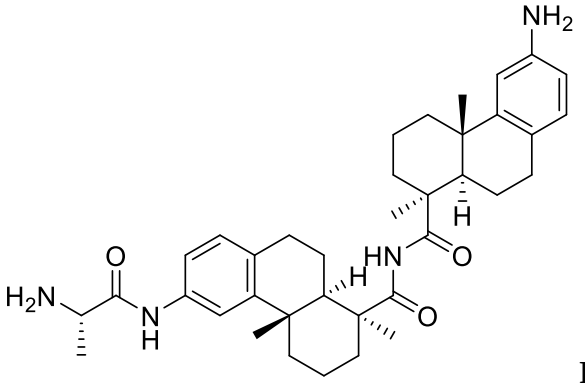
P7;



P8;



P9; and

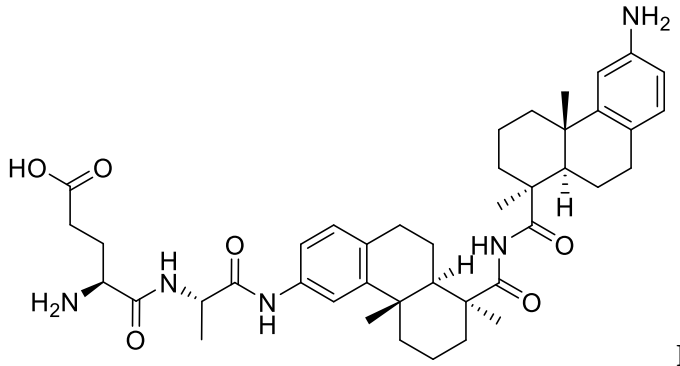


P13; or

a pharmaceutically acceptable salt or solvate thereof.

19. The compound of claim 16, wherein each $\mathbf{R^4}$ is, independently in each instance, a peptide residue, wherein the peptide residue comprises an amino acid selected from the group consisting of alanine, isoleucine, leucine, methionine, phenylalanine, tryptophan, tyrosine, valine, serine, threonine, asparagine, glutamine, cysteine, selenocysteine, glycine, proline, arginine, histidine, lysine, aspartic acid, and glutamic acid, and the residues thereof.

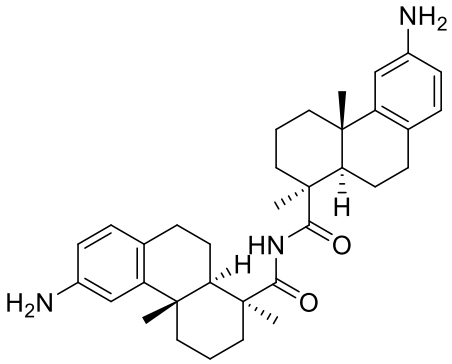
20. The compound of claim 19, wherein the compound is



P12; or

a pharmaceutically acceptable salt or solvate thereof.

21. The compound of claim 14, wherein the compound is



P2; or

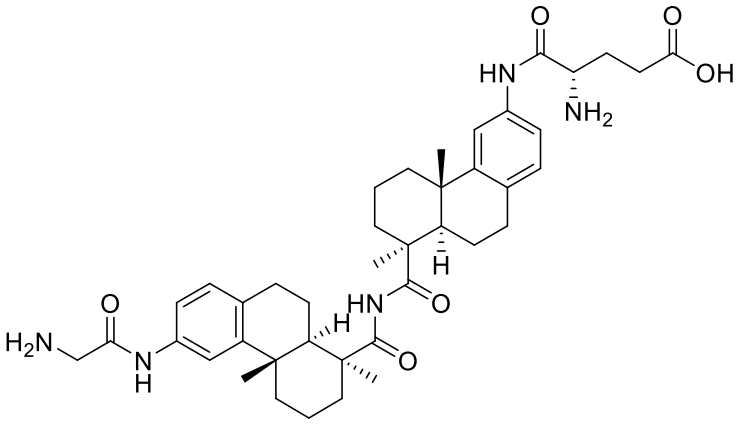
a pharmaceutically acceptable salt or solvate thereof.

22. The compound of any one of claims 1-13, wherein $\mathbf{R^1}$ and $\mathbf{R^2}$ are –N(H)$\mathbf{R^4}$.

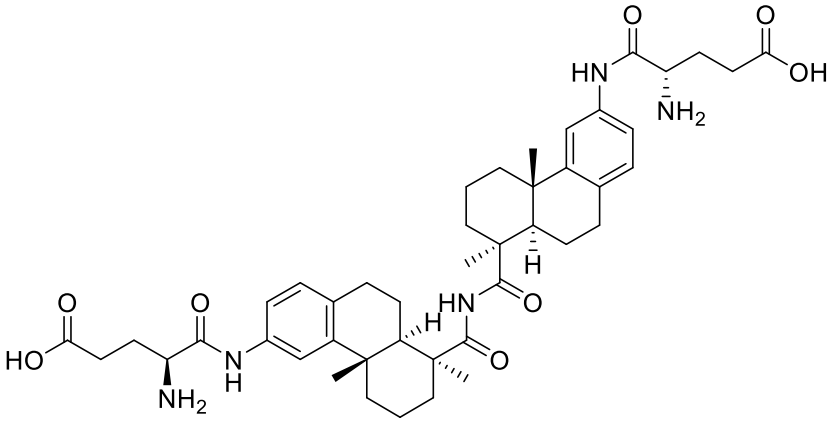
23. The compound of claim 22, wherein each $\mathbf{R^4}$ is, independently in each instance, an amino acid residue; wherein

the amino acid is selected from the group consisting of alanine, isoleucine, leucine, methionine, phenylalanine, tryptophan, tyrosine, valine, serine, threonine, asparagine, glutamine, cysteine, selenocysteine, glycine, proline, arginine, histidine, lysine, aspartic acid, and glutamic acid, and the residues thereof.

24. The compound of claim 23, where the compound is selected from the group consisting of



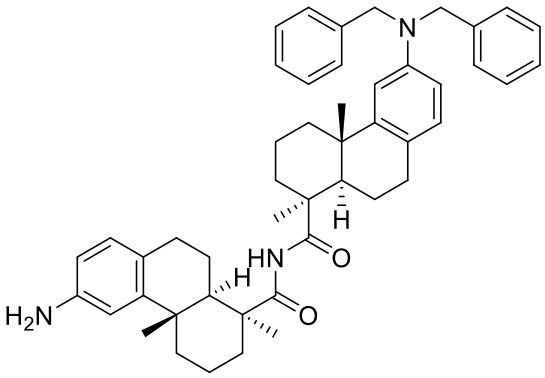
P10; and



P11; or

a pharmaceutically acceptable salts or solvates thereof.

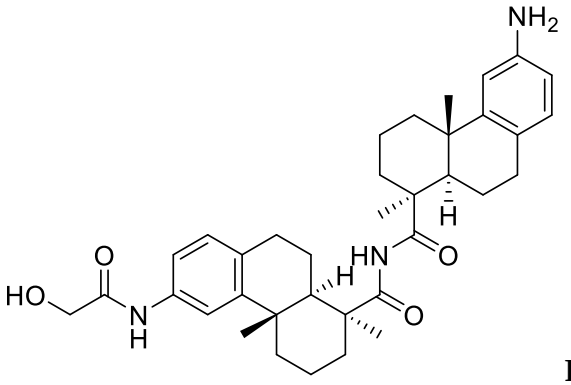
25. The compound of claim 15, wherein the compound is



P3; or

a pharmaceutically acceptable salt or solvate thereof.

26. The compound of claim 22, wherein the compound is

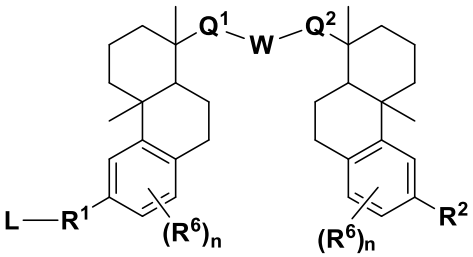


P14; or

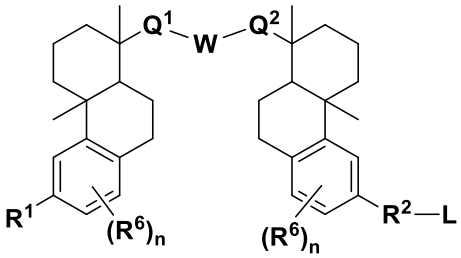
a pharmaceutically acceptable salt or solvate thereof.

27. A linker-payload comprising the compound of any preceding claim bonded to a linker.

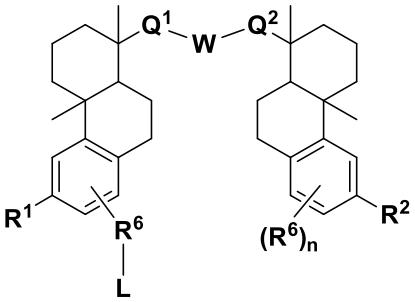
28. The linker-payload of any preceding claim having a Formula **LPa**, **LPb**, **LPc**, or **LPd**



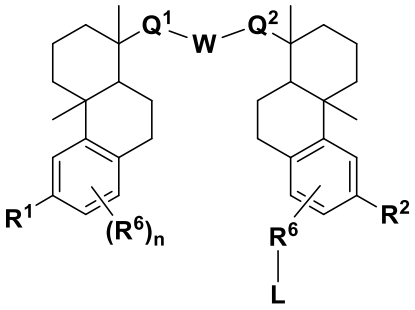
(**LPa**)



(**LPb**)



(**LPc**)



(**LPd**)

or a pharmaceutically acceptable salt, solvate, or stereoisomeric form thereof, wherein

L is a linker;

each of **Q**^{1} and **Q**^{2} is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O**R**^{3})–, –PO(N**R**^{3}N**R**^{4})–, –N**R**^{3}–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

R^{1} is –N(H)**R**^{4}, –N(H)**R**^{4}–, –N(H)–, –N(**R**^{5})$_2$, or –N(**R**^{5})$_2$–;

R^{2} is –N(H)**R**^{4}, –N(H)**R**^{4}–, or –N(H)–;

each **R**^{4} is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, substituted alkyl, acyl, substituted acyl, or -alkylene-;

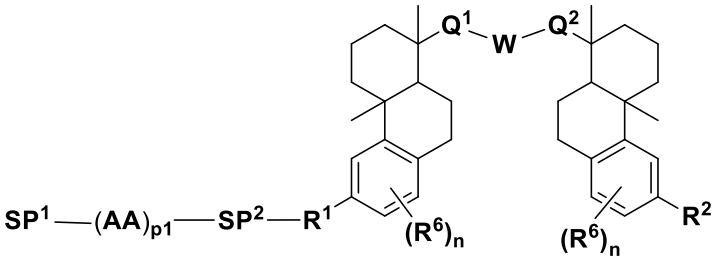
R^{5} is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and
–CH_2OH, or at least one primary or secondary nitrogen;

each **R**^{6} is independently halo, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ alkylene, $C_{1\text{-}6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG$_{\mathbf{n1}}$, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve; and

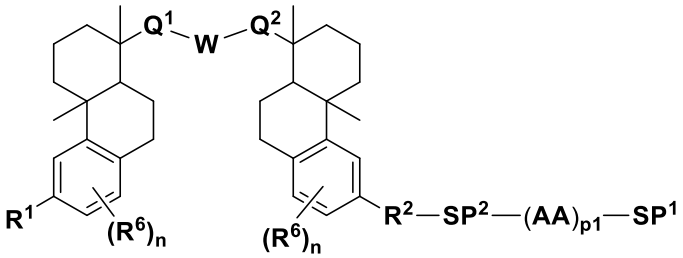
each **R**^{3} is independently hydrogen, alkyl, or aryl.

29. The linker-payload of claim 28, wherein each **R**^{4} is, independently in each instance, hydrogen, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, or -alkylene-.

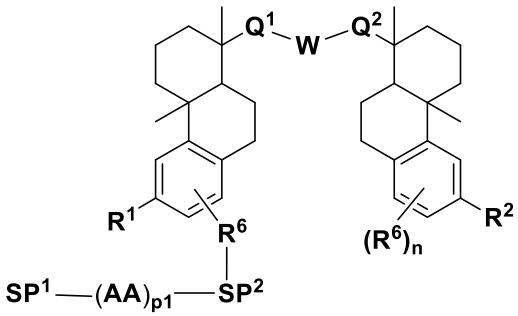
30. The linker-payload of claim 28, having the Formula **LPa'**, **LPb'**, **LPc'**, or **LPd'**



(**LPa'**)

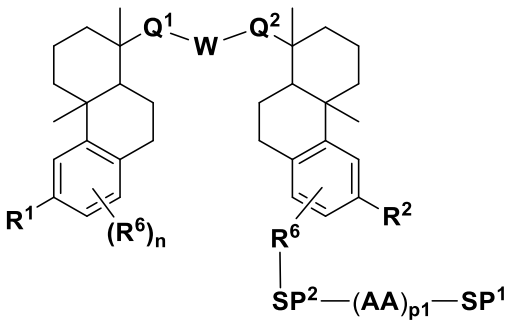


(**LPb'**)



or

(**LPc'**)



(**LPd'**)

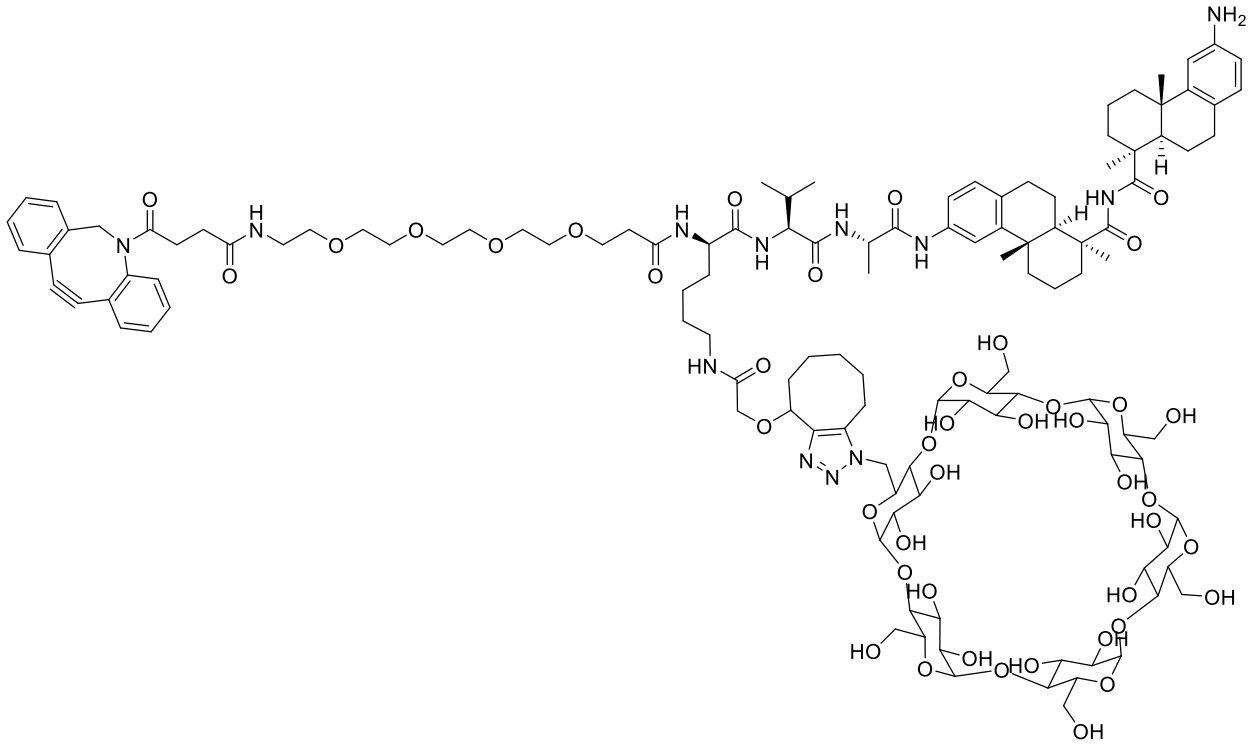
wherein **SP¹** and **SP²**, when present, are spacer groups;

each **AA** is an amino acid residue; and

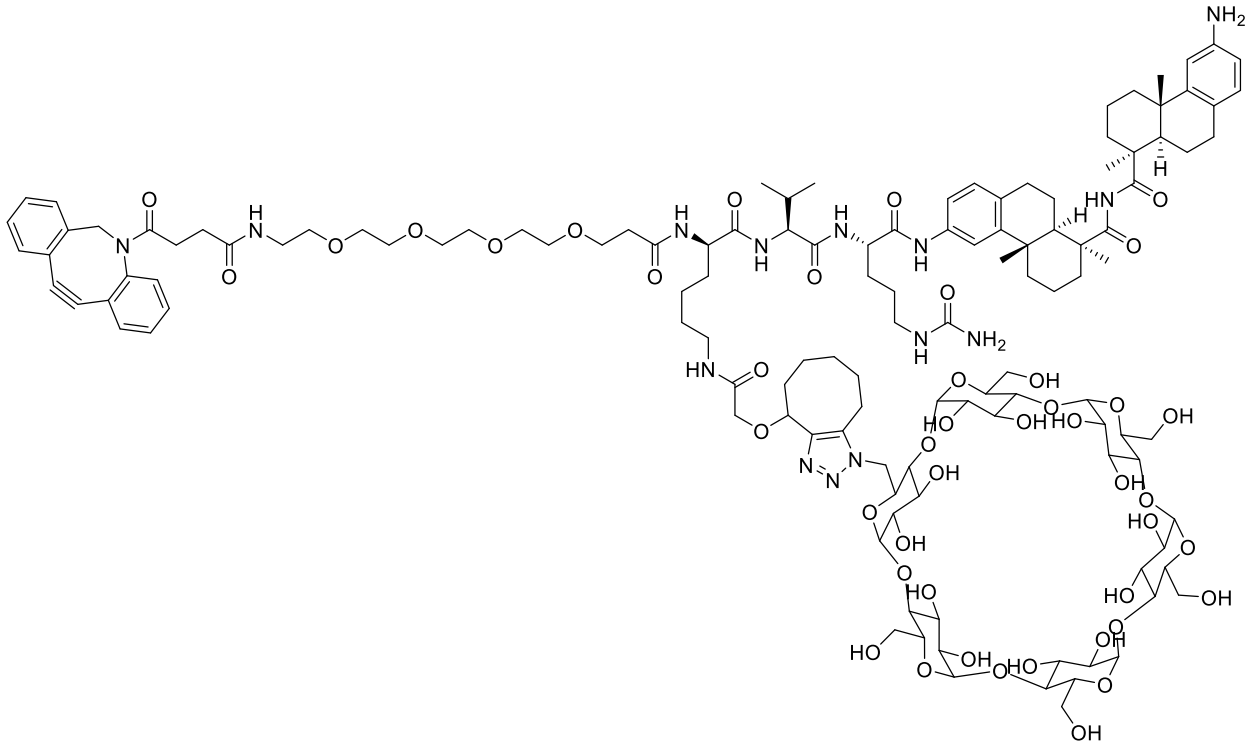
p1 is an integer from one to ten.

31. The linker-payload of any preceding claim wherein the linker **L** or spacer $\mathbf{SP^2}$ is bonded to an aryl nitrogen, or an amino acid residue alone or within a peptide.

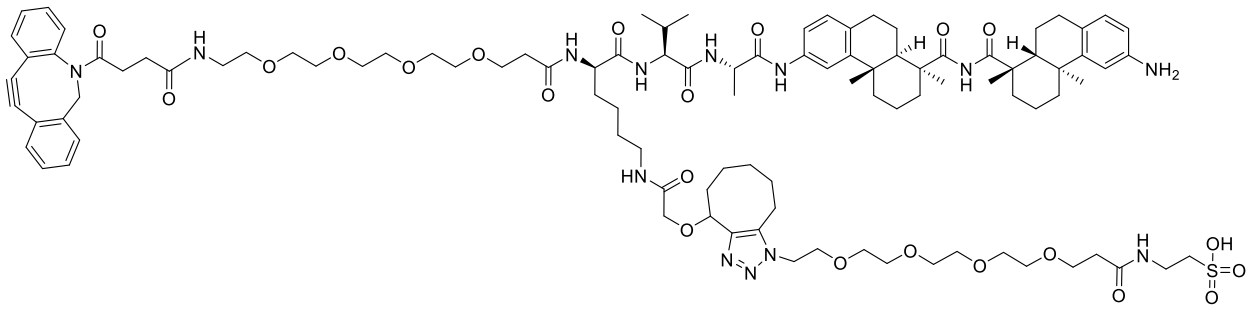
32. The linker-payload of any one of claims 27-31, selected from the group consisting of



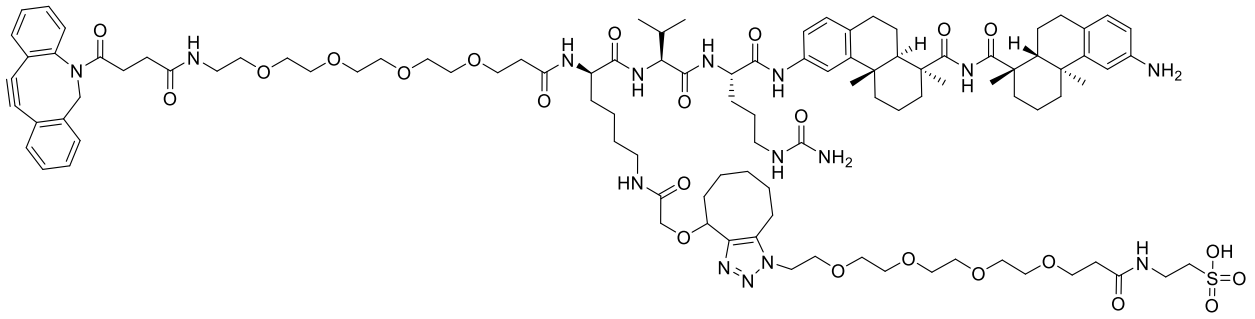
LP1;



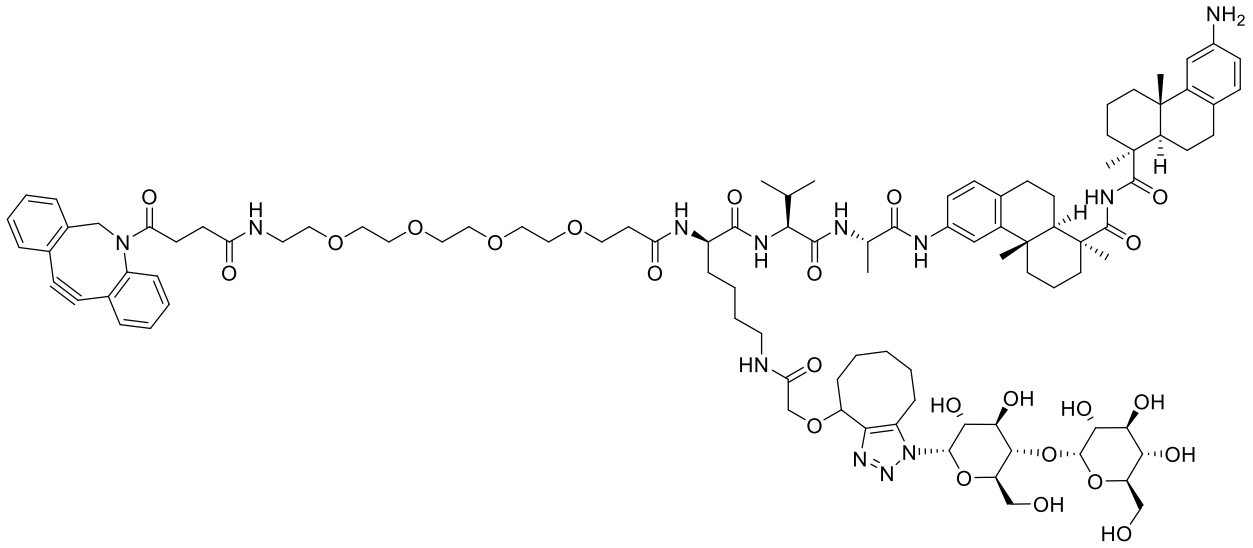
LP2;



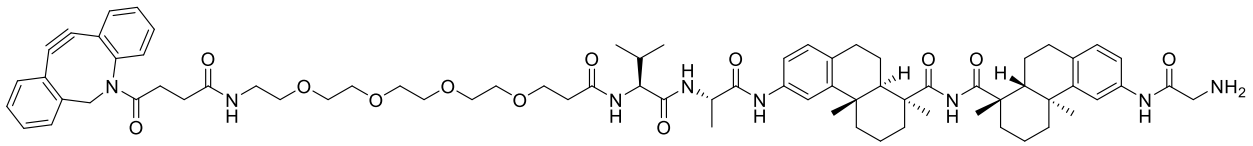
LP3;



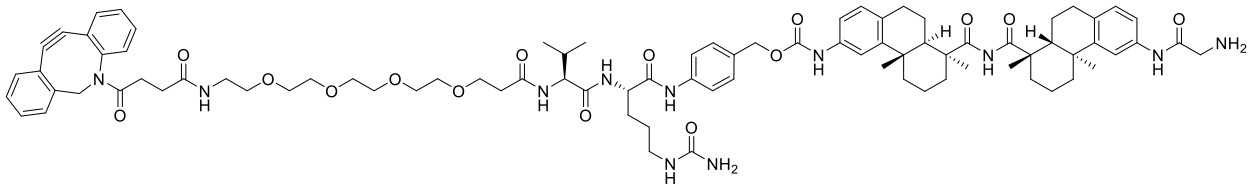
LP4;



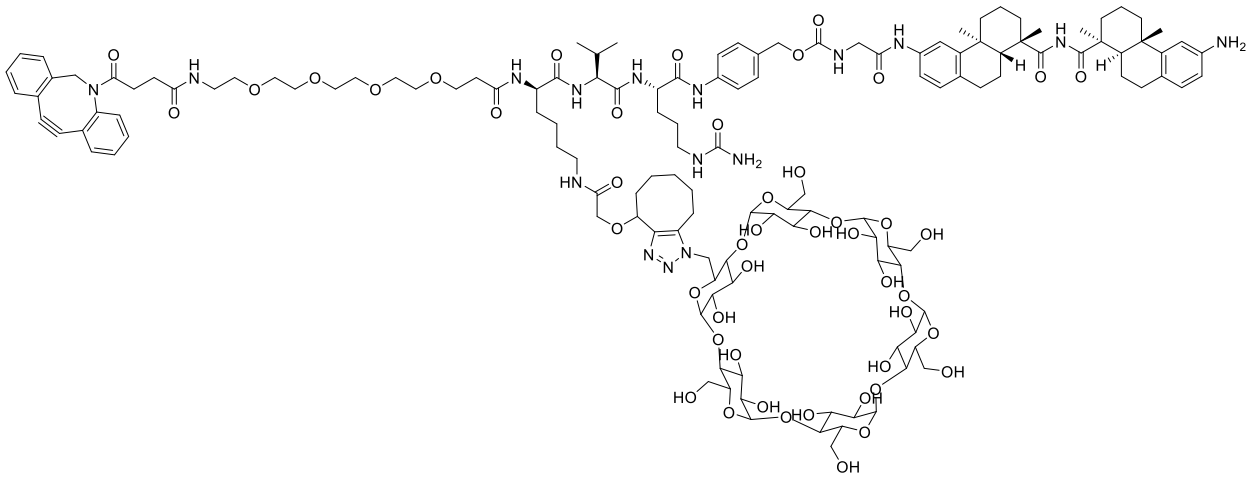
LP5;



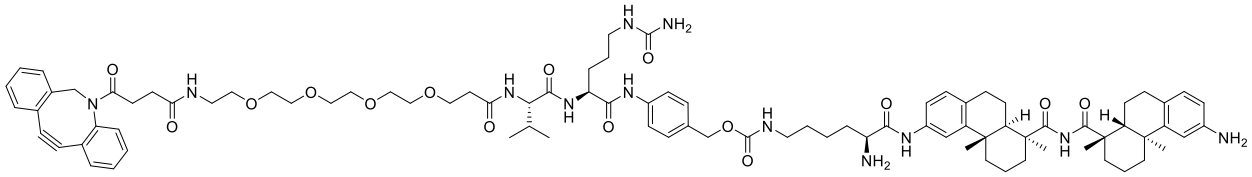
LP6;



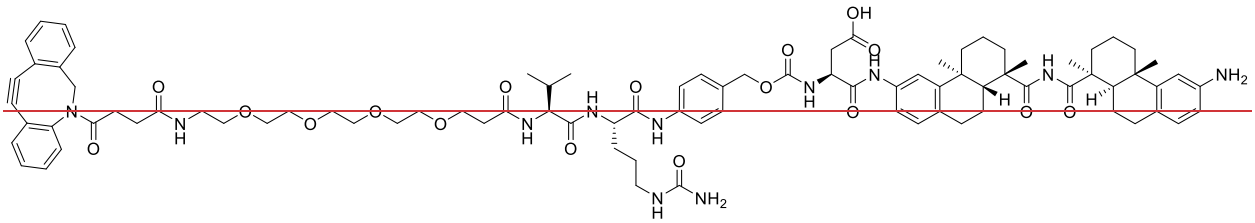
LP7;

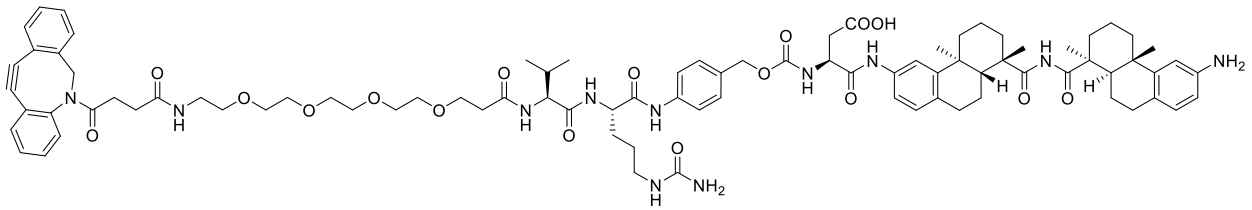


LP8;

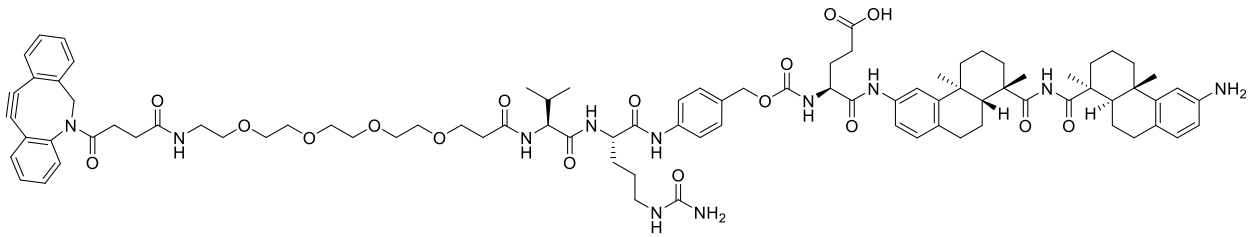


LP9;

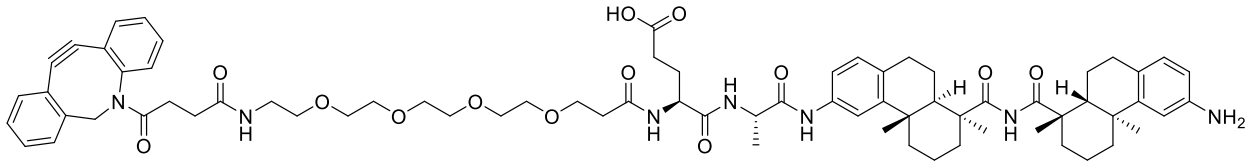




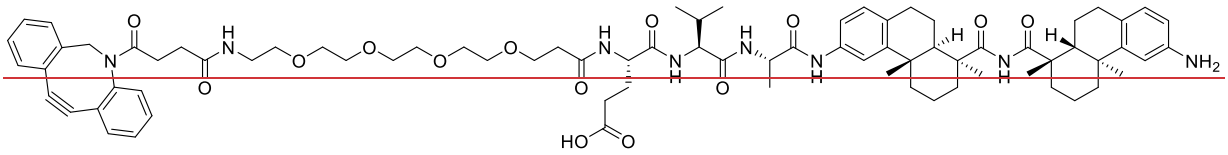
LP10;



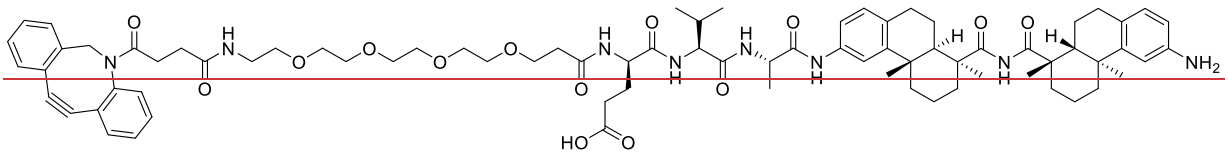
LP11; and



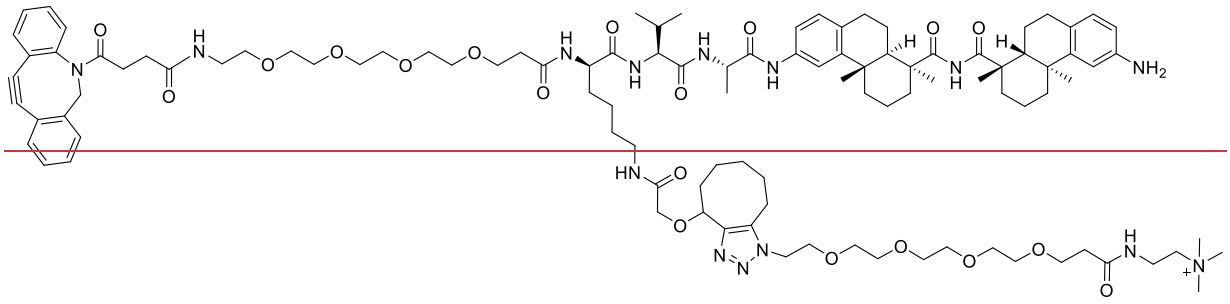
LP12;



~~**LP13;**~~



~~**LP14**; and~~

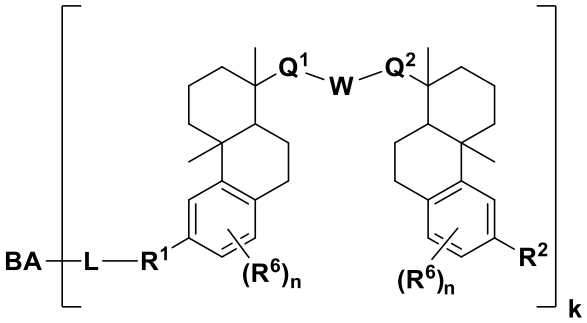


~~LP20;~~ or

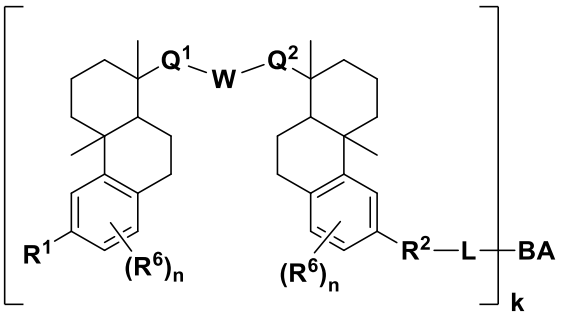
a pharmaceutically acceptable salt or solvate thereof.

33. An antibody-drug-conjugate comprising the compound or linker-payload of any preceding claim or claims 57 or 59 bonded to an antibody, or an antigen binding fragment thereof.

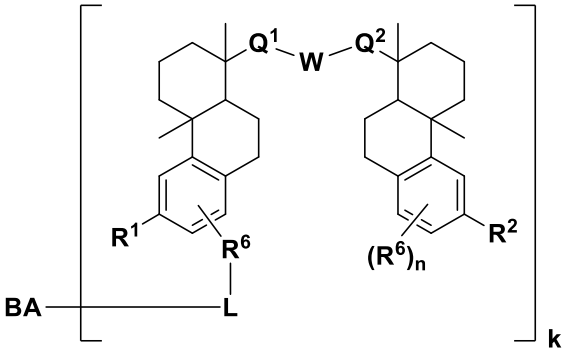
34. A compound of Formula **A**, **B**, **C**, or **D**



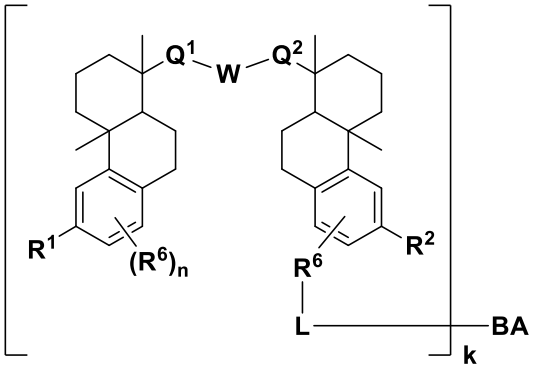
(**A**)



(**B**)



(**C**)



(**D**)

or a pharmaceutically acceptable salt, or stereoisomeric form thereof, wherein

L is a linker;

BA is an antibody or antigen binding fragment thereof;

k is an integer from one to thirty;

each of $\mathbf{Q^1}$ and $\mathbf{Q^2}$ is independently –CH_2–, –C(O)–, –C(H)(OH)–, –$C(OH)_2$– , –SO_2–, –SO–, –PO(O$\mathbf{R^3}$)–, –PO(N$\mathbf{R^3}$N$\mathbf{R^4}$)–, –N$\mathbf{R^3}$–, or –N=;

W is –CH_2–, –N(H)–, or –O–;

$\mathbf{R^1}$ is –N(H)$\mathbf{R^4}$, –N(H)$\mathbf{R^4}$–, –N(H)–, –N($\mathbf{R^5}$)$_2$, or –N($\mathbf{R^5}$)$_2$–;

$\mathbf{R^2}$ is –N(H)$\mathbf{R^4}$, –N(H)$\mathbf{R^4}$–, or –N(H)–;

each $\mathbf{R^4}$ is, independently in each instance, hydrogen, an amino acid residue, an O-amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, substituted alkyl, acyl, substituted acyl, or -alkylene-;

$\mathbf{R^5}$ is alkyl, aryl, arylalkyl, heterocycloalkyl, or substituted heterocycloalkyl, wherein each heterocycloalkyl or substituted heterocycloalkyl comprises one, two, or three heteroatoms selected from nitrogen and oxygen, and when substituted includes at least one –OH and

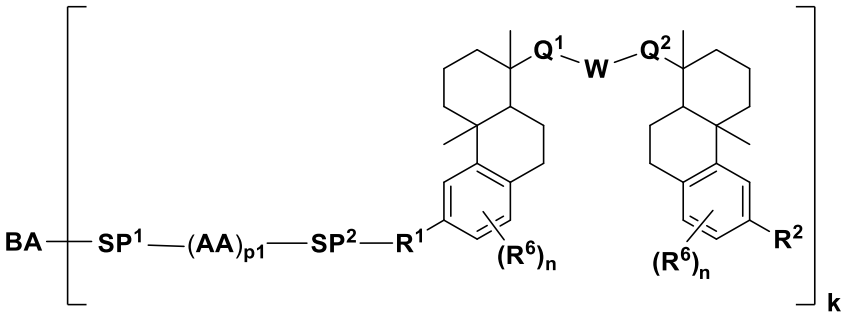
–CH_2OH, or at least one primary or secondary nitrogen;

each **R^6** is independently halo, C$_{1-6}$ alkyl, C$_{1-6}$ alkylene, C$_{1-6}$ alkoxy, –CN, O-glucose, O-amino acid residue, or O-PEG$_{\mathbf{n1}}$, wherein each **n** is an integer from zero to fourteen, and each **n1** is an integer from one to twelve; and

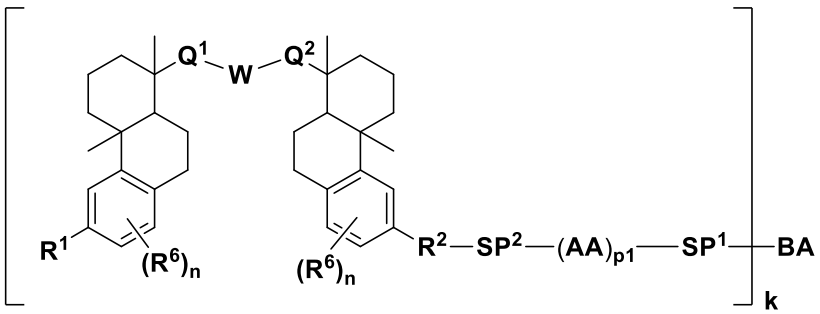
each **R^3** is independently hydrogen, alkyl, or aryl.

35. The compound of claim 34, wherein each **R^4** is, independently in each instance, hydrogen, an amino acid residue, an *N*-alkyl amino acid residue, a peptide residue, a biodegradable moiety, alkyl, or -alkylene-.

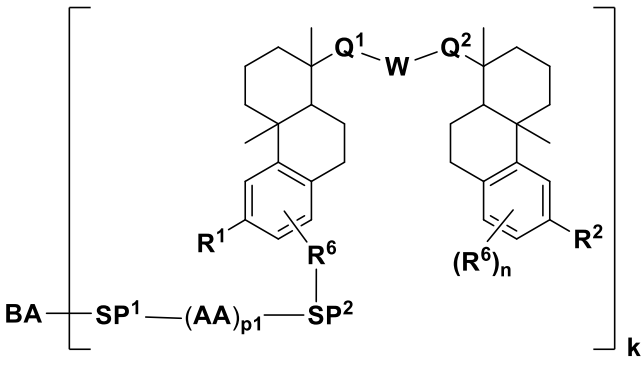
36. The compound of claim 34, having the Formula **A'**, **B'**, **C'**, or **D'**



(**A'**)

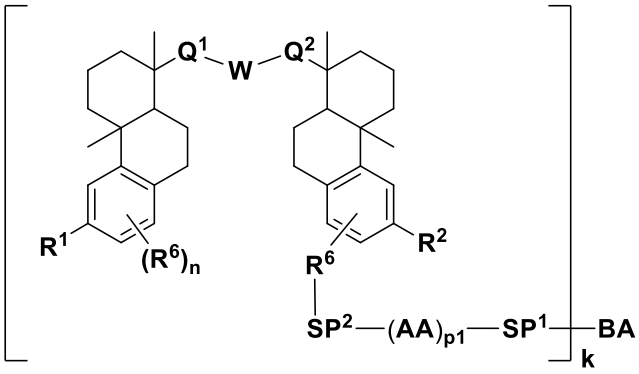


(**B'**)



or

(**C'**)



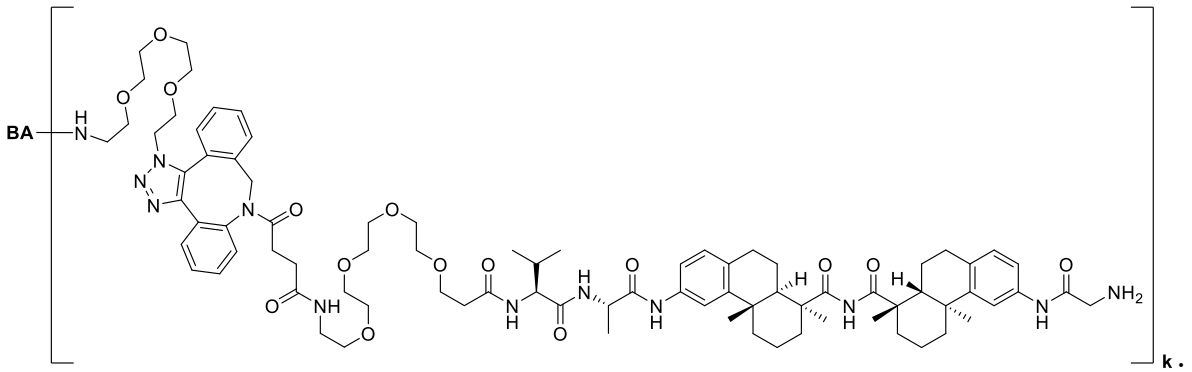
(**D'**)

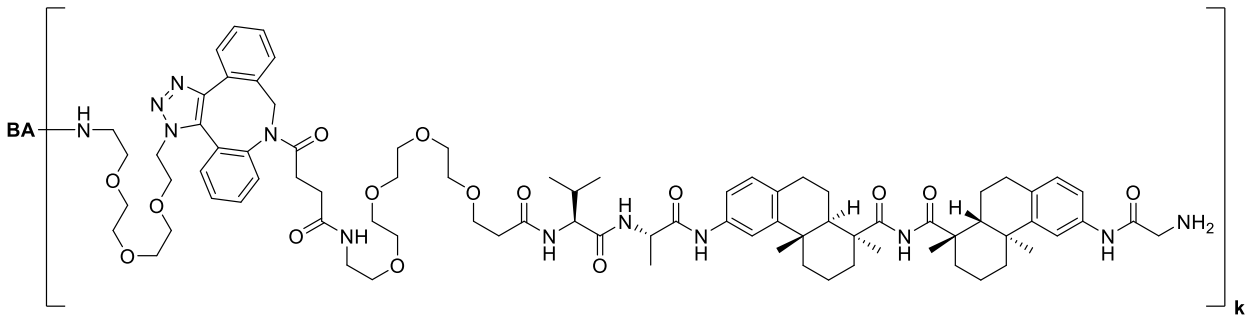
wherein **SP1** and **SP2**, when present, are spacer groups;

each **AA** is an amino acid residue; and

p1 is an integer from one to ten.

37. The compound of claim 36, wherein the compound is selected from the group consisting of





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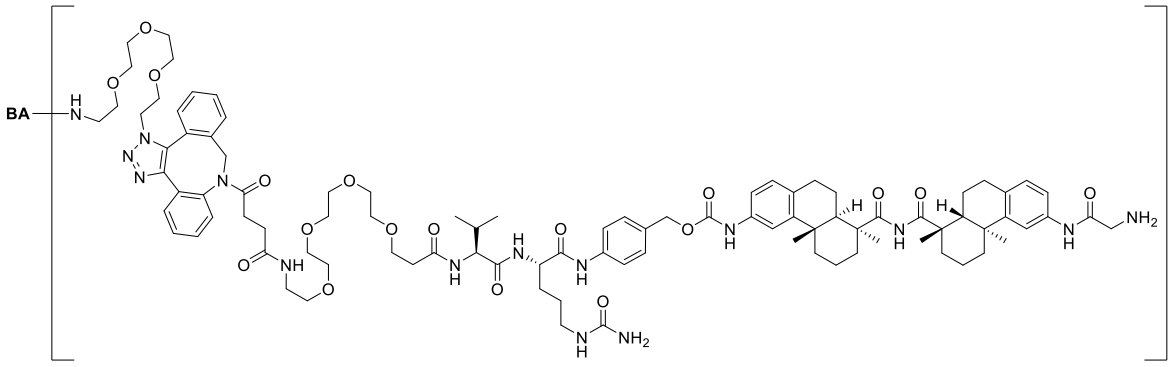
BA
k

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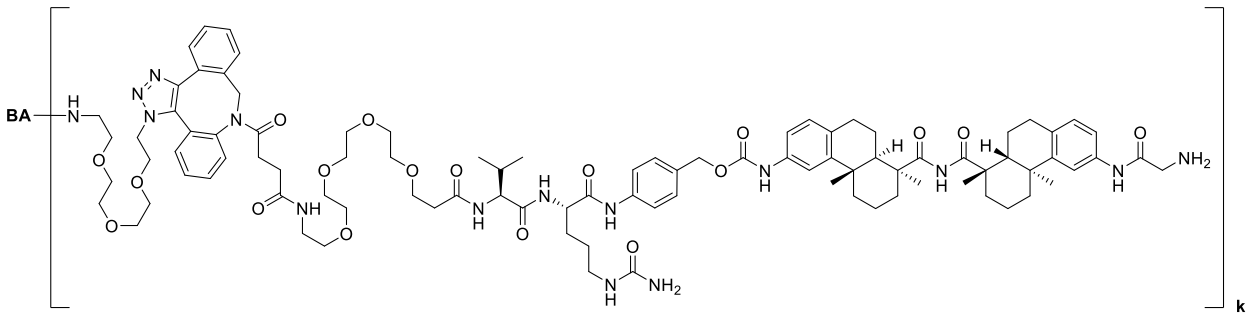
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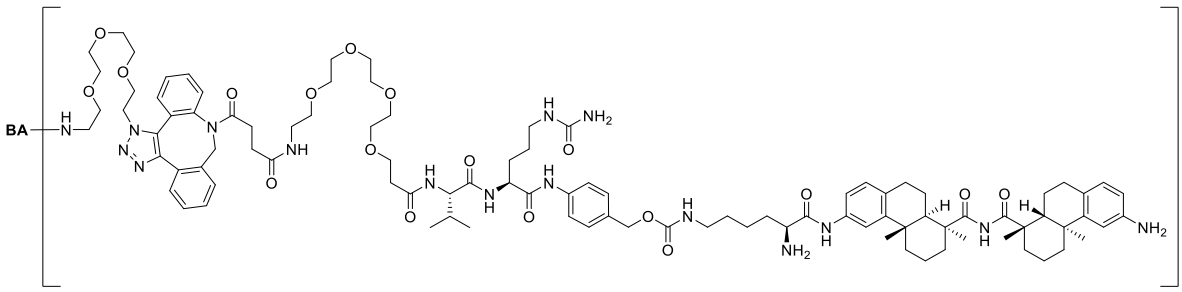
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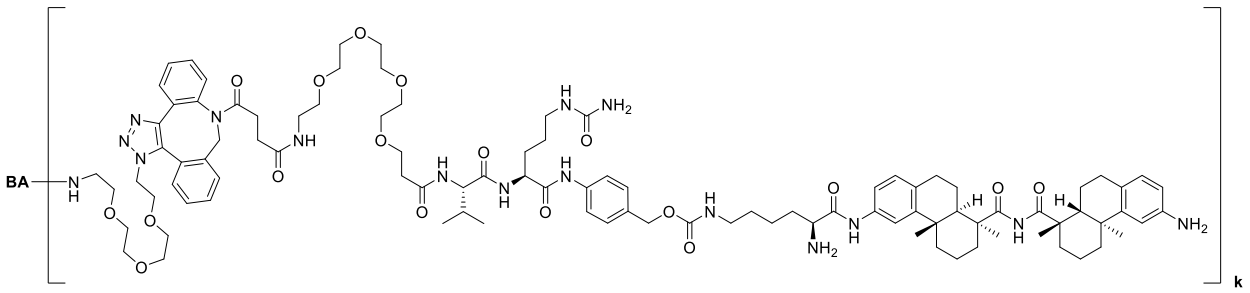
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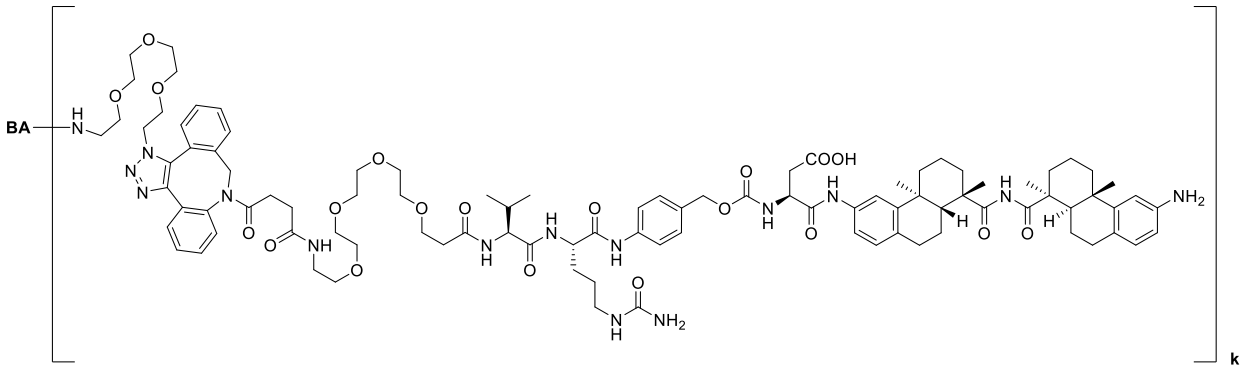
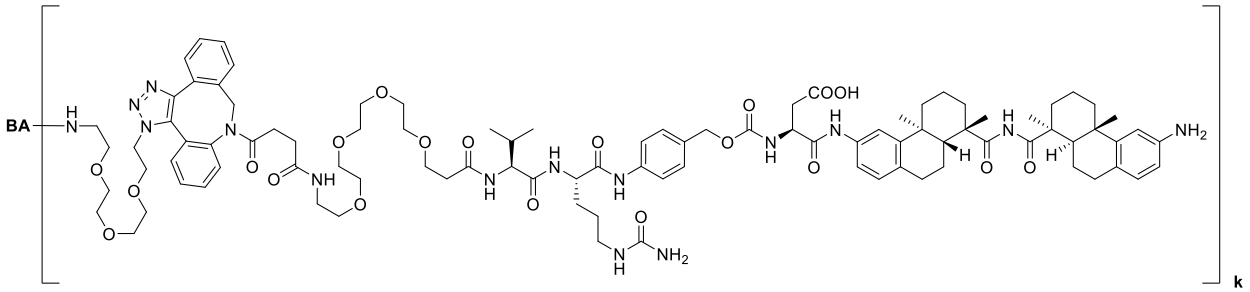

BA
COOH
NH2
k

;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COOH
NH2
k

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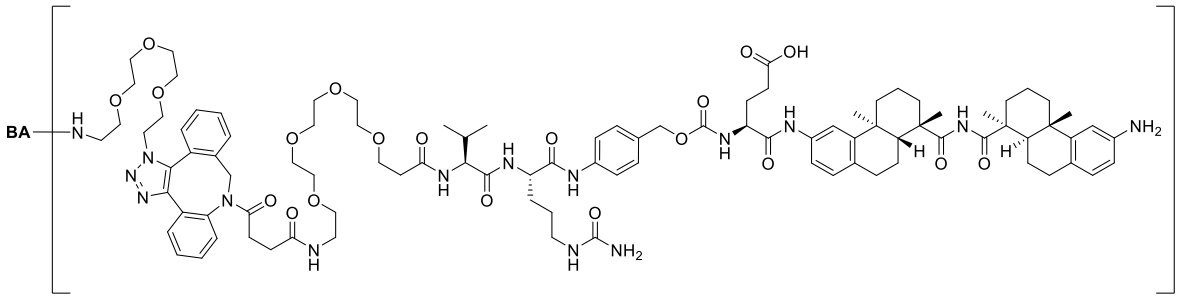
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NH2
k

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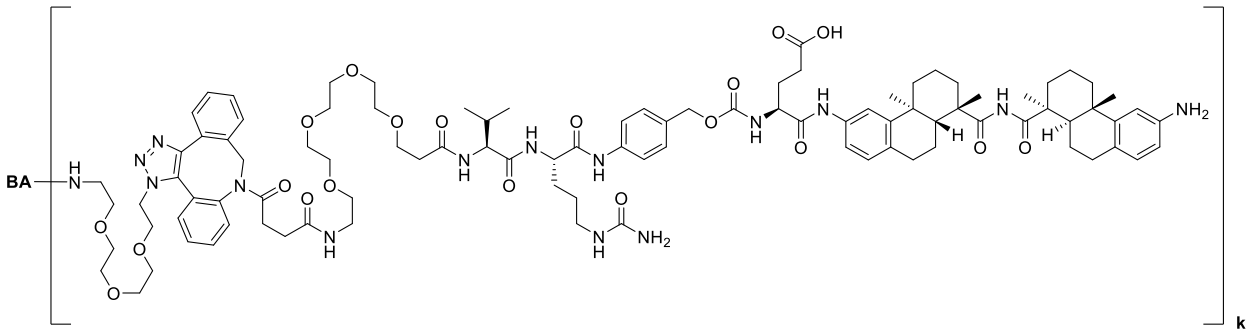
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OH
NH2
k

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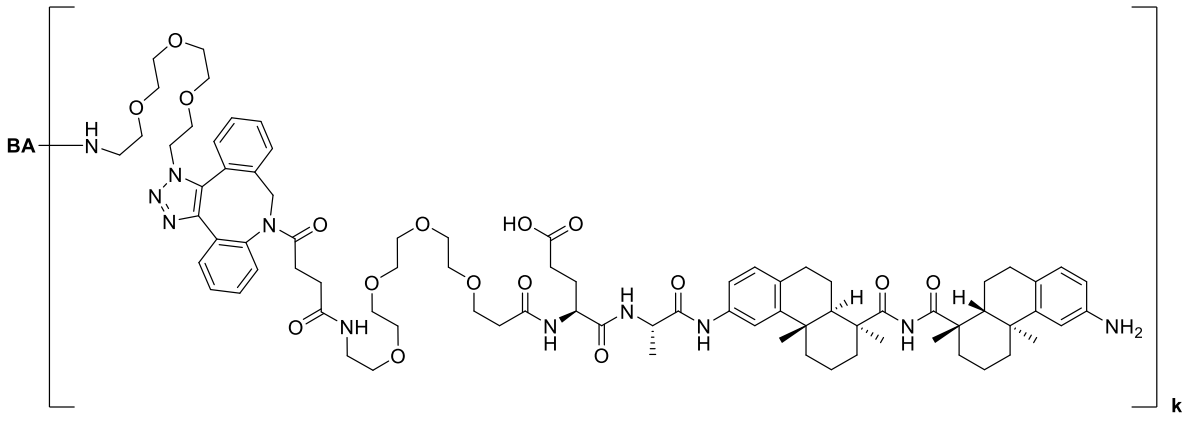

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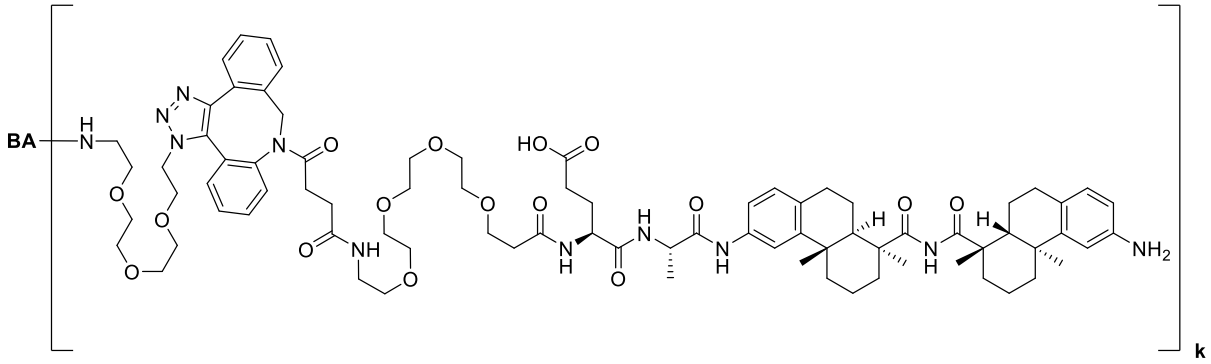
and



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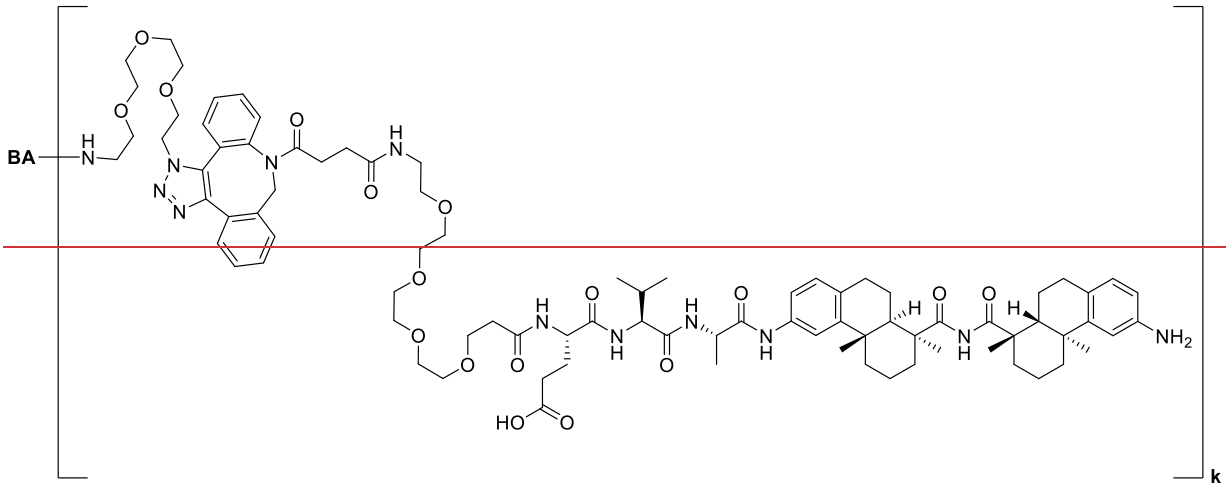

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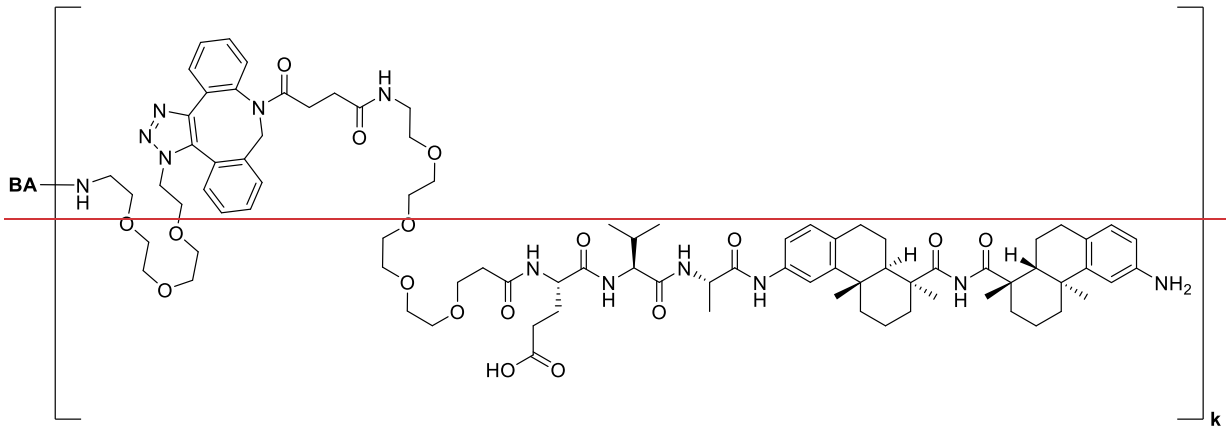

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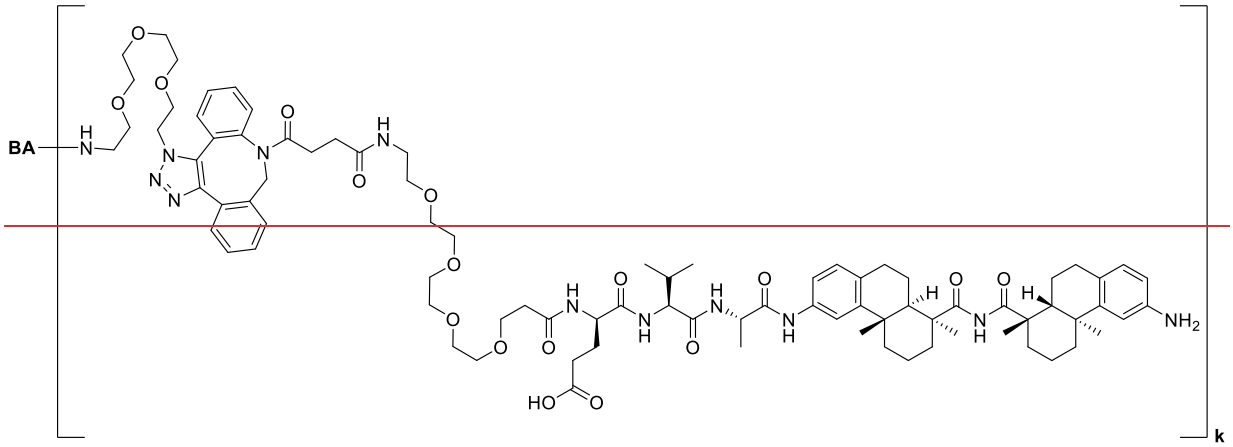
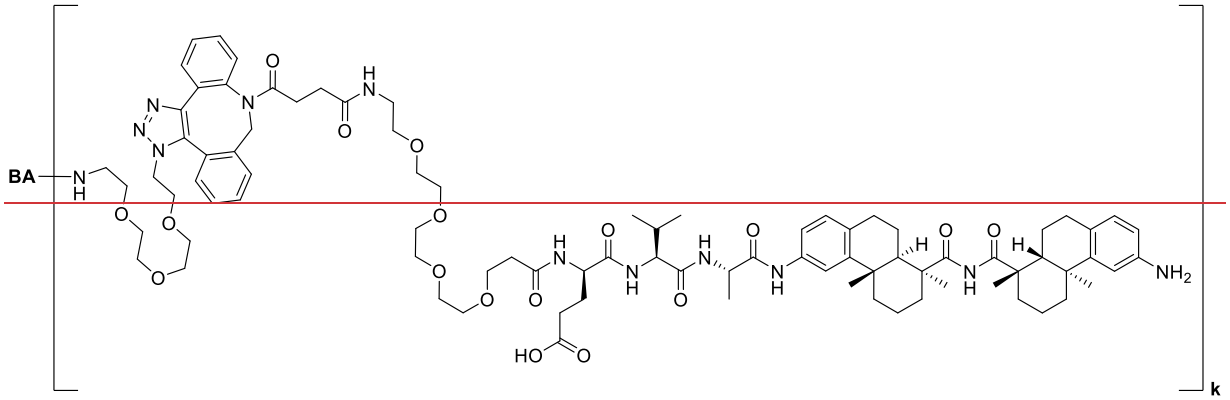


~~; and~~



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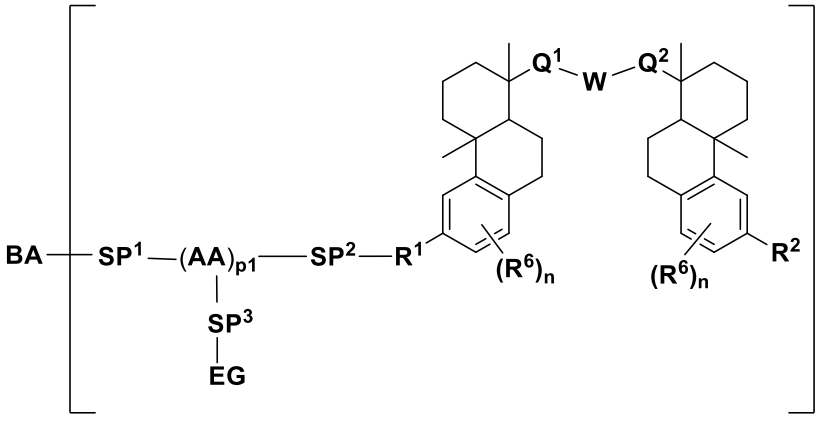
38. The compound, as in claim 34, of the Formula (**A''**)



or

(**A''**)

a pharmaceutically acceptable salt, or stereoisomeric form thereof, or a regioisomer thereof, wherein

each **SP^1**, **SP^2**, and **SP^3** is a spacer group, where **SP^3** is linked to one **AA** of (**AA**)$_{p1}$;

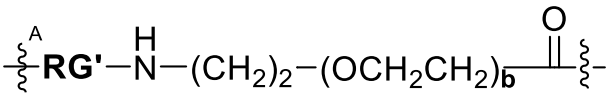
each **AA** is an amino acid residue;

p1 is an integer from one to ten; and

EG is a cyclodextrin or an alkyl, heteroalkyl, alkyleny, or heteroalkylenyl sulfonic acid.

39. The compound of claim 38, wherein

the **SP^1** spacer is



,

wherein **RG'** is a reactive group residue following reaction of a reactive group **RG** with an antibody or antigen binding fragment thereof;;



is a bond, direct or indirect, to the antibody or antigen binding fragment thereof; and

b is an integer from one to four;

the (**AA**)$_{p1}$–**SP^2**– is –NH-lysine-valine-alanine–, –NH-lysine-valine-citrulline–, or

–NH-lysine-valine-citrulline-PABC–;

the **SP^3** spacer is:



wherein **RG'** is a reactive group residue following reaction of a reactive group **RG** with **EG**;

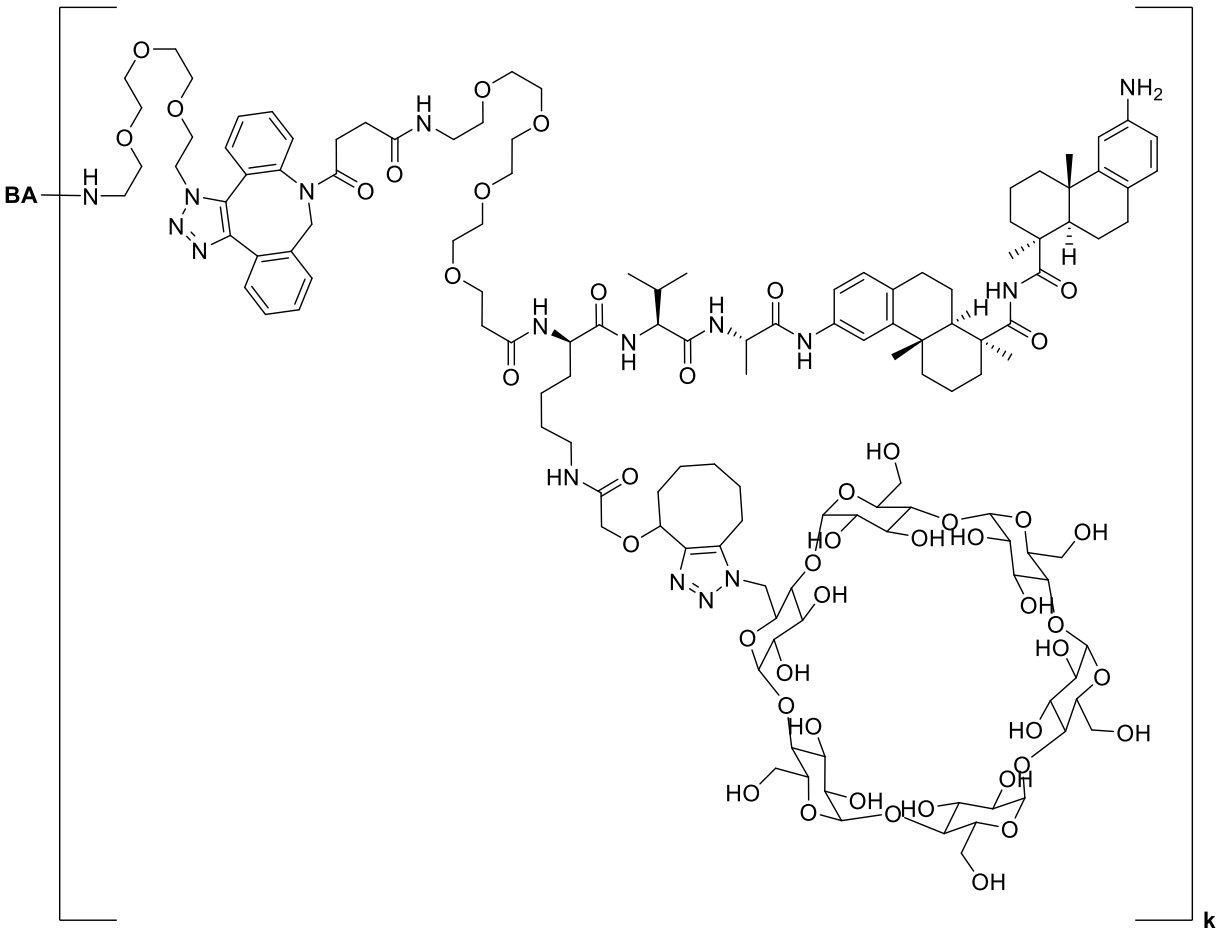


is a bond to EG; and



is a bond to $(\mathbf{AA})_{\mathbf{p1}}$.

40. The compound as in any one of claims 38 or 39, wherein the compound is selected from the group consisting of



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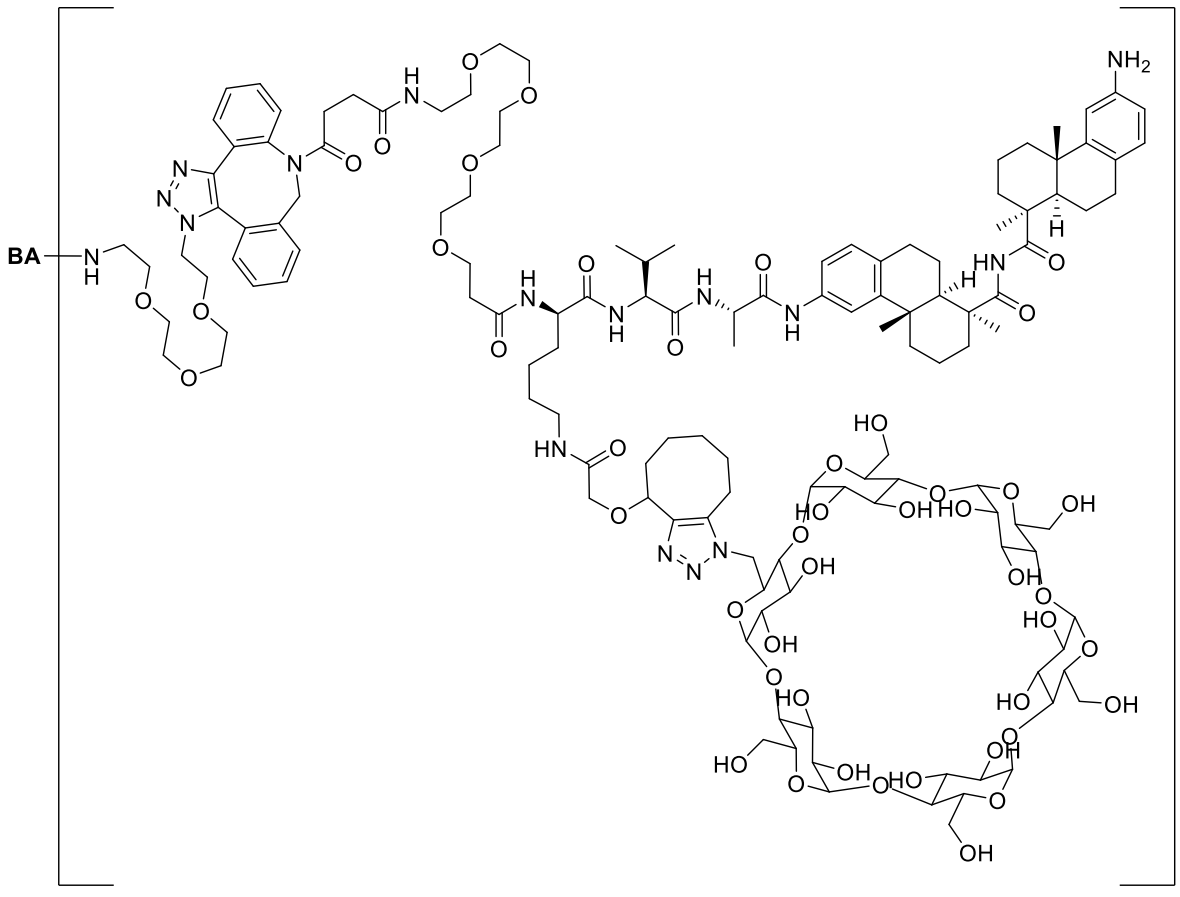
BA
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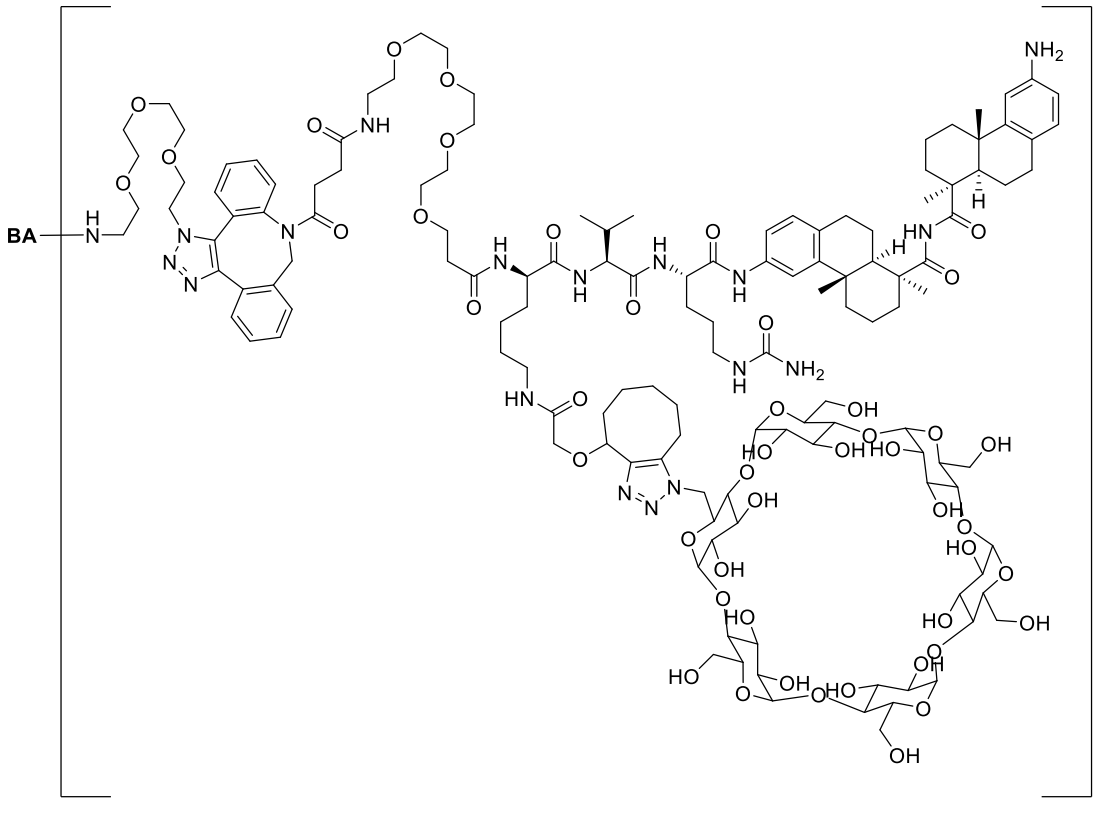
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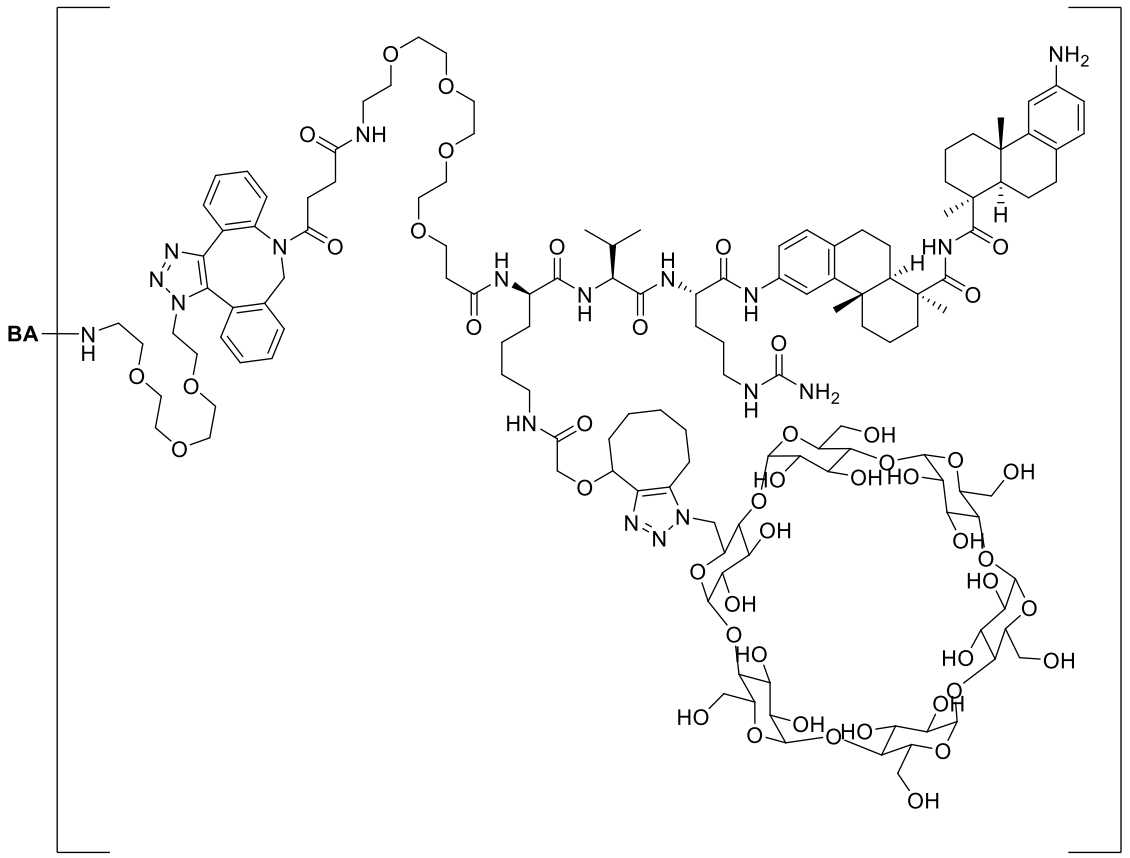

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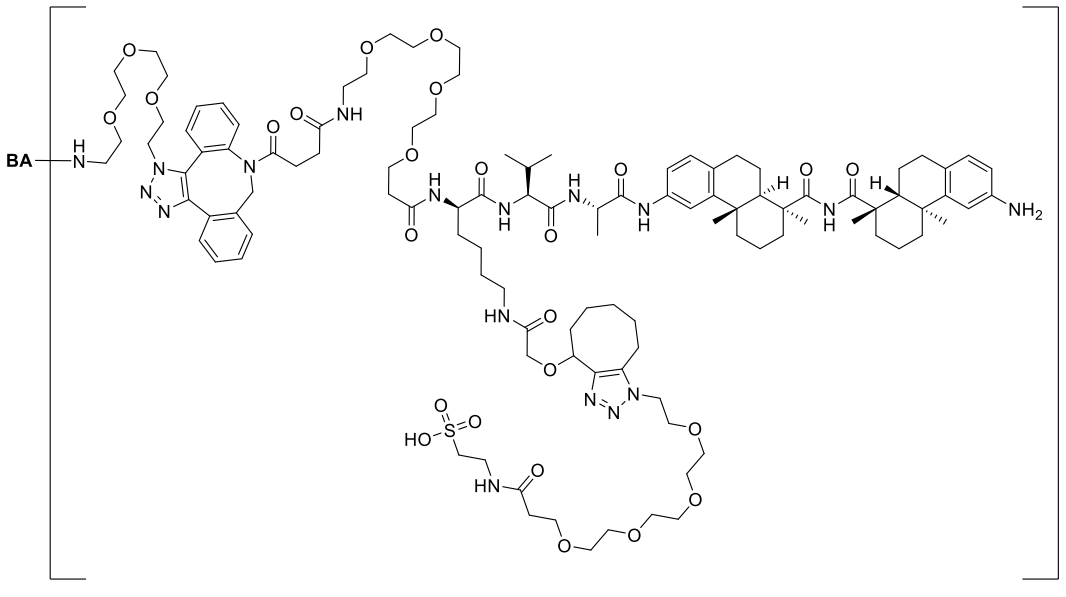

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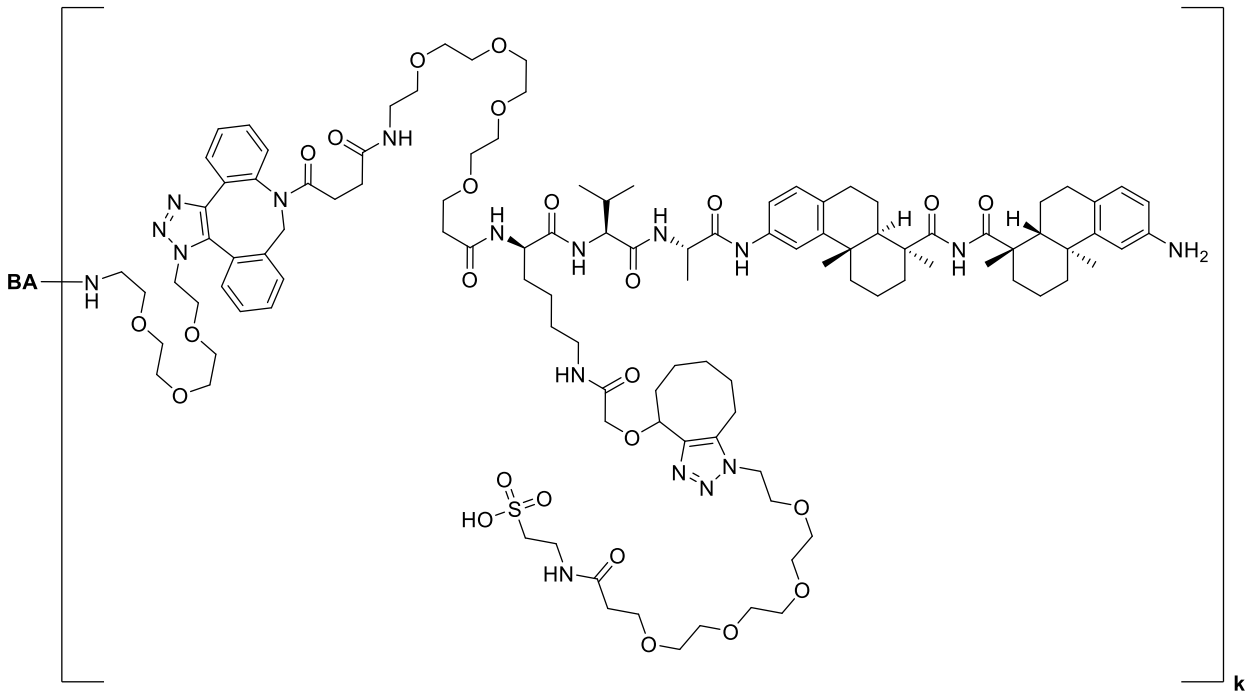
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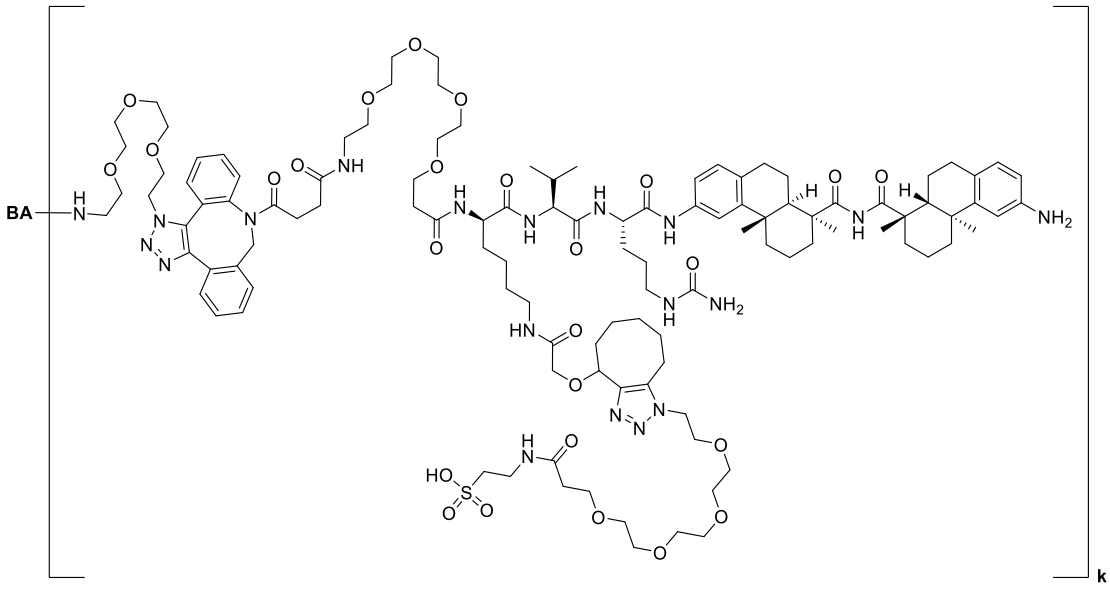
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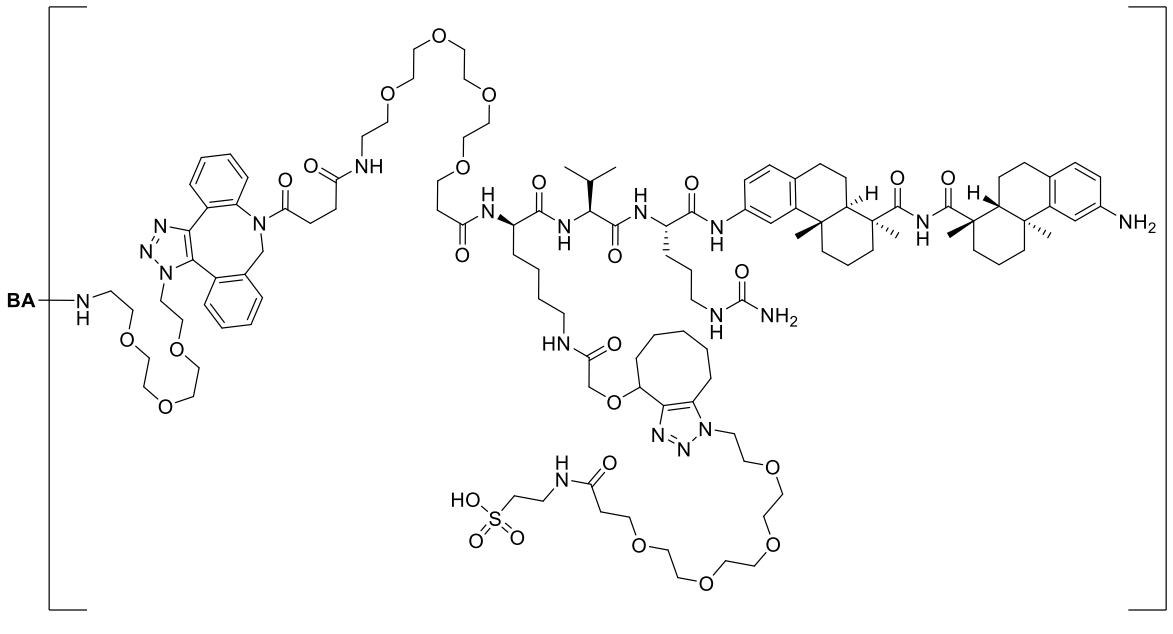
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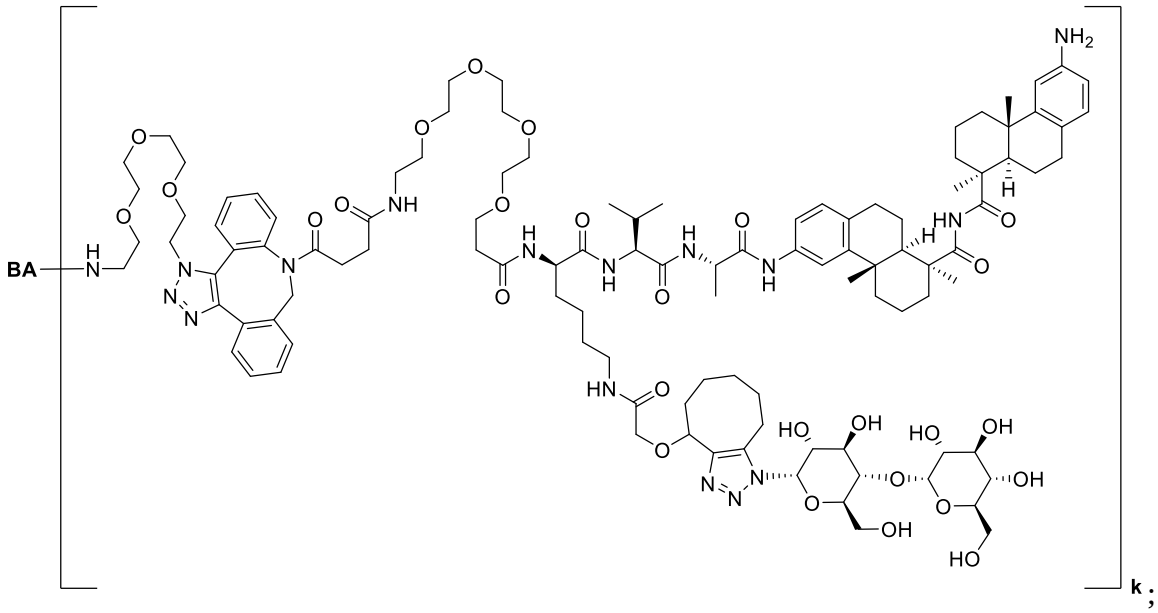
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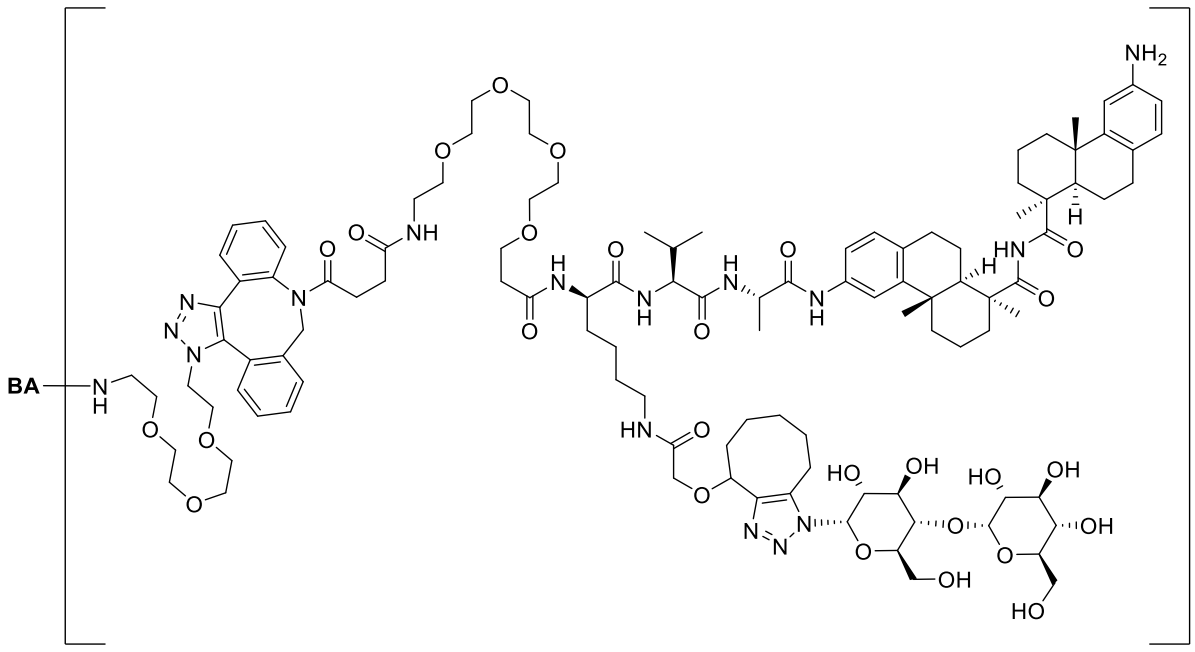
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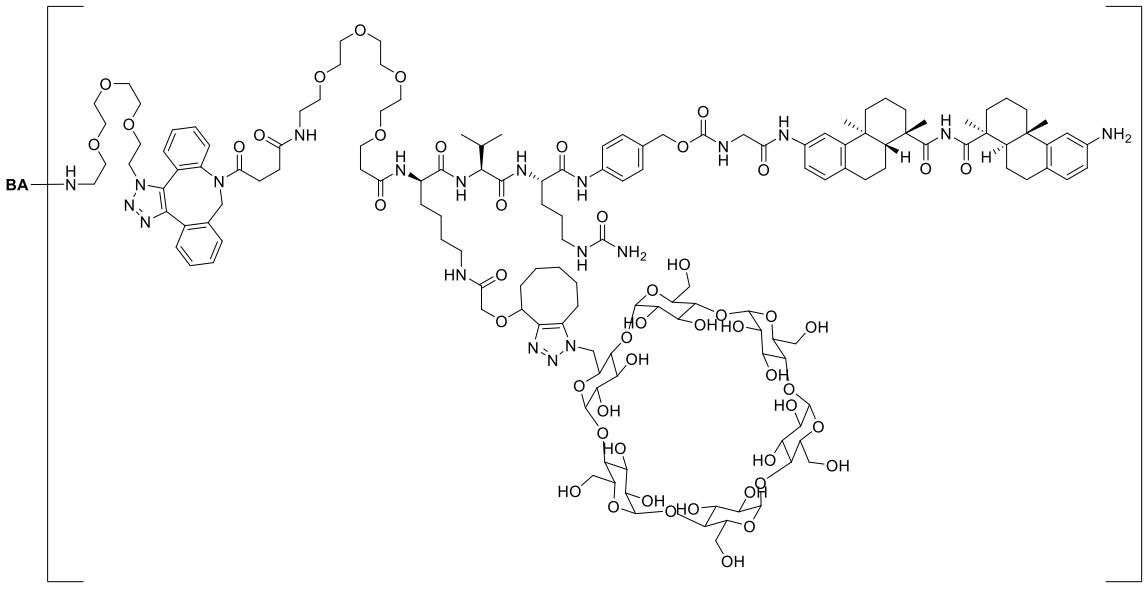
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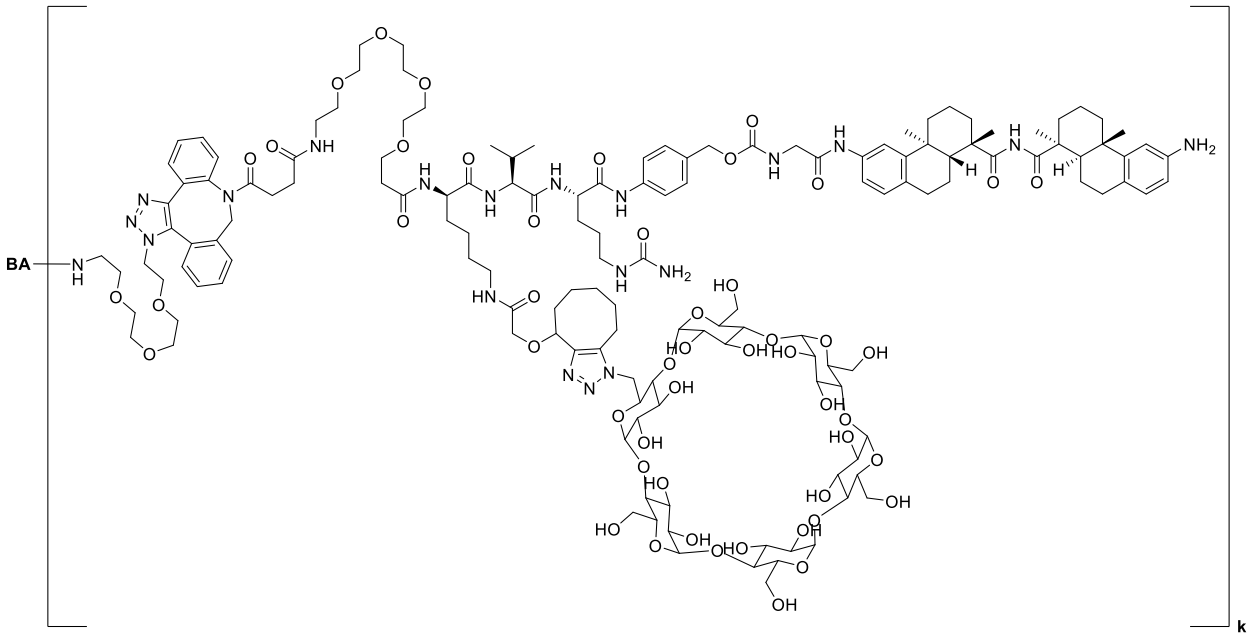

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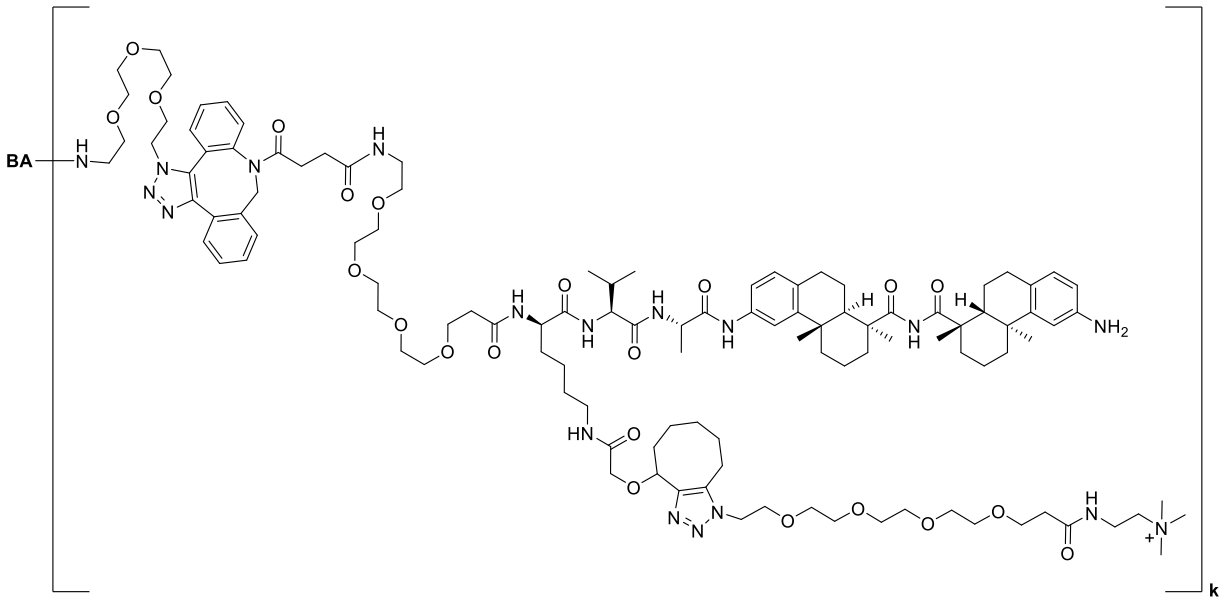

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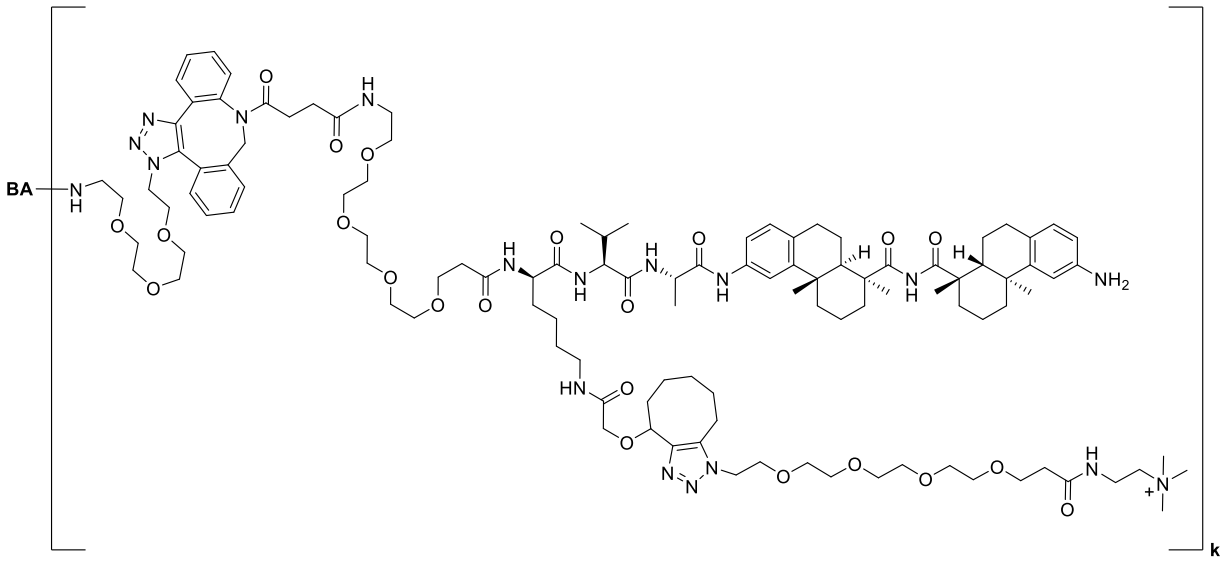

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41. The compound of any one of claims 34-40, wherein **k** is an integer from one to four.

42. The compound of any one of claims 34-41, wherein **BA** is an antibody, or antigen binding fragment thereof that binds HER2.

43. The compound of any one of claims 34-41, wherein **BA** is an antibody, or antigen binding fragment thereof that binds PRLR.

44. The compound of any one of claims 34-41, wherein **BA** is an antibody, or antigen binding fragment thereof that binds MSR1.

45. The compound of any one of claims 34-44, wherein **BA** is an antibody or antigen-binding fragment thereof, and conjugation is through at least one Q295 residue.

46. The compound of any one of claims 34-44, wherein **BA** is an antibody or antigen-binding fragment thereof, and conjugation is through two Q295 residues.

47. The compound of any one of claims 34-46, wherein **BA** is a N297Q antibody or antigen-binding fragment thereof.

48. The compound of any one of claims 34-47, wherein **BA** is a N297Q antibody or antigen-binding fragment thereof, and conjugation is through at least one Q295 and at least one Q297 residue.

49. The compound of any one of claims 34-48, wherein **BA** is a N297Q antibody or antigen-binding fragment thereof, and conjugation is through two Q295 residues and two Q297 residues.

50. A pharmaceutical composition comprising the compound~~, linker-payload,~~ or antibody-drug-conjugate of any one of claims 1-5, 10, 13, 14, 16-~~49~~26, 33-49, 57, or 58, and a pharmaceutically acceptable excipient, carrier, or diluent.

51. A compound or pharmaceutical composition of any one of claims 1-5, 10, 13, 14, 16-~~50~~26, 33-50, 57, or 58, for use in therapy.

52. Use of a compound or pharmaceutical composition of any one of claims 1-5, 10, 13, 14, 16-26, 33-50, 57, or 58, in the manufacture of a medicament for the treatment of dyslipidemia, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.

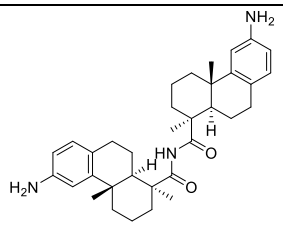
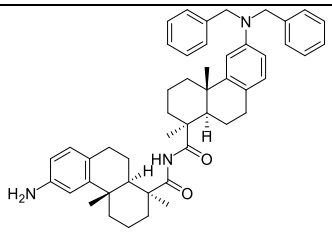
53. Use of a compound or pharmaceutical composition of any one of claims 1-5, 10, 13, 14, 16-26, 33-50, 57, or 58, in the manufacture of a medicament for the treatment of dyslipidemia in a subject.

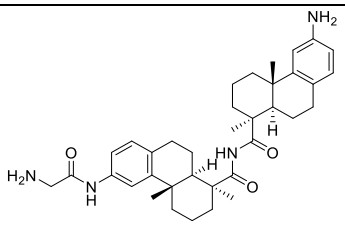
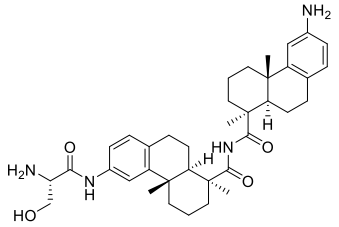
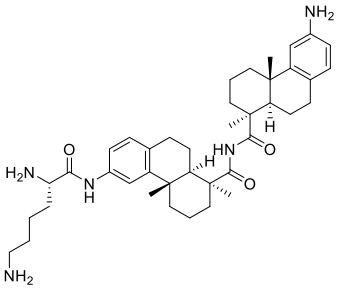
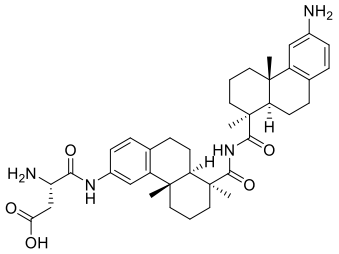
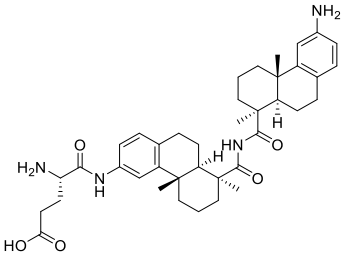
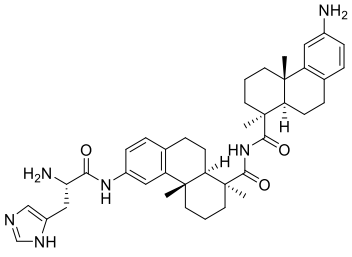
54. Use of a compound or pharmaceutical composition of any one of claims 1-5, 10, 13, 14, 16-26, 33-50, 57, or 58, in the manufacture of a medicament for the treatment of a metabolic disease in a subject.

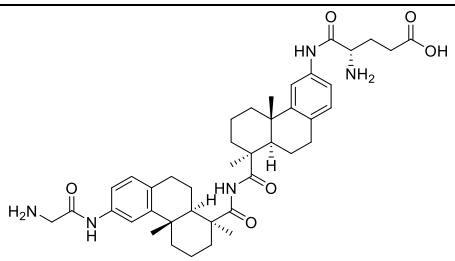
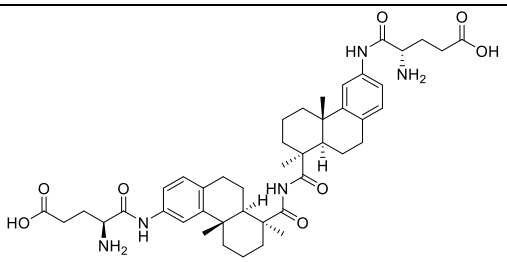
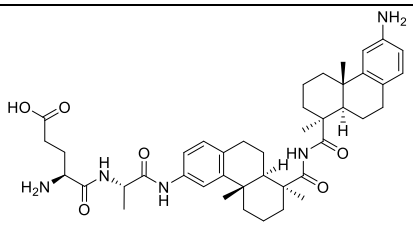
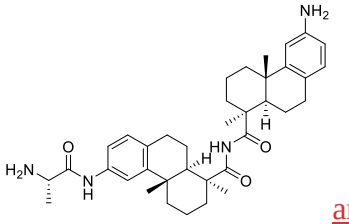
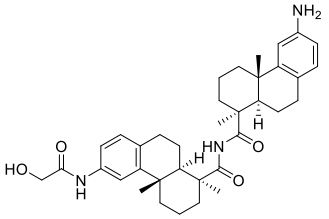
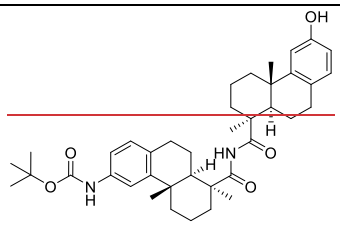
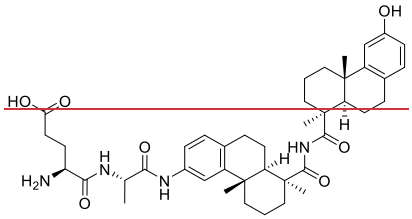
55. Use of a compound or pharmaceutical composition of any one of claims 1-5, 10, 13, 14, 16-26, 33-50, 57, or 58, in the manufacture of a medicament for the treatment of inflammation in a subject.

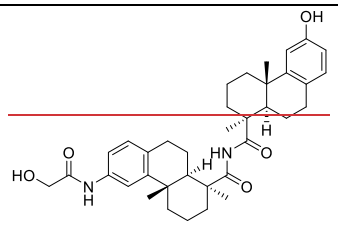
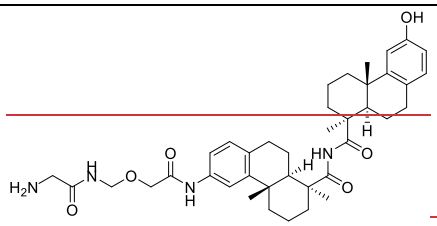
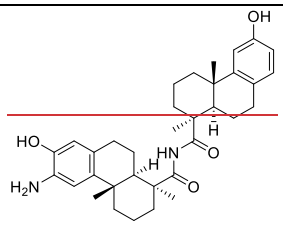
56. Use of a compound or pharmaceutical composition of any one of claims 1-5, 10, 13, 14, 16-26, 33-50, 57, or 58, in the manufacture of a medicament for the treatment of a neurodegenerative disease in a subject.

57. A compound selected from the group consisting of

P2	
P3	

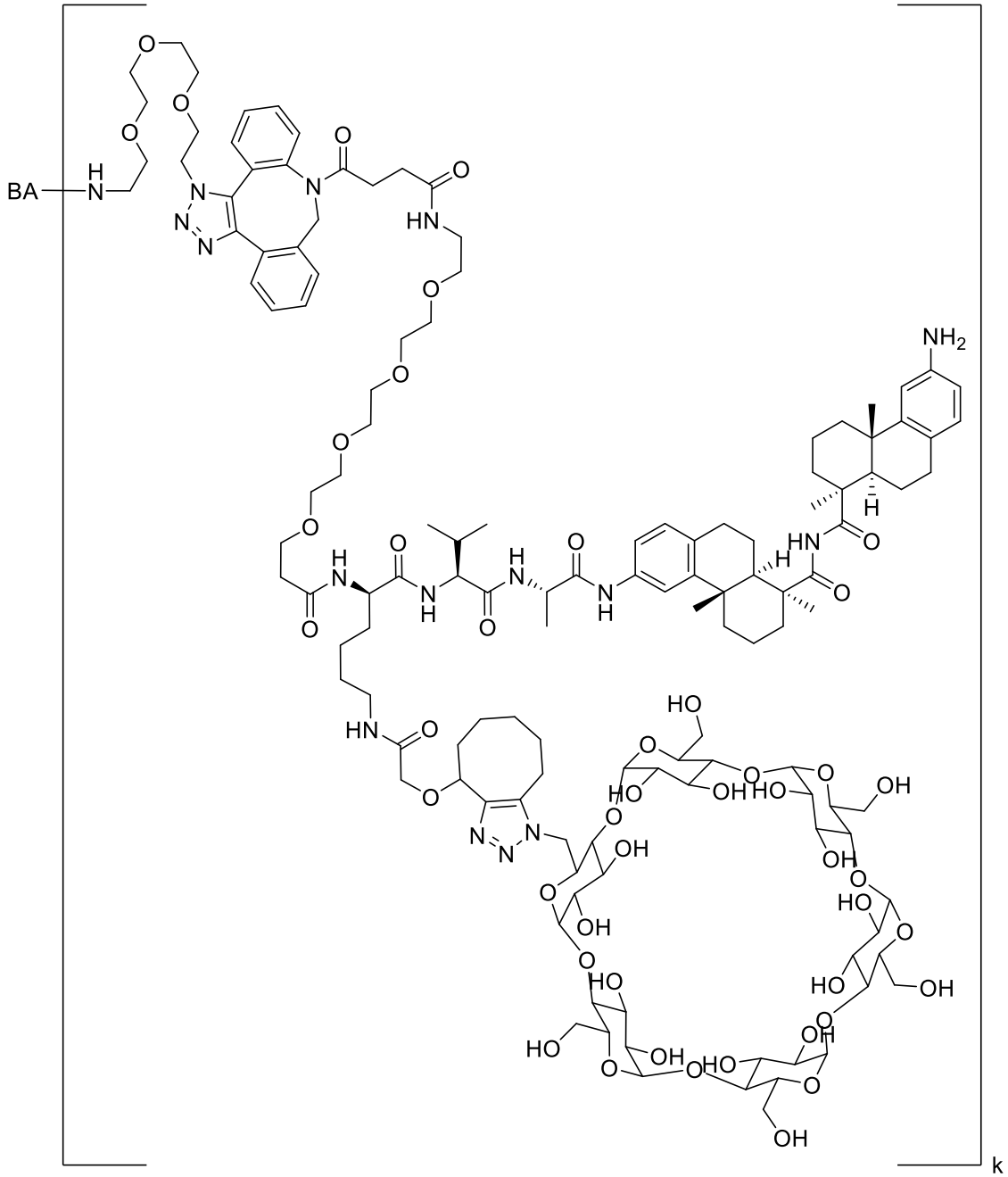
P4	
P5	
P6	
P7	
P8	
P9	

P10	
P11	
P12	
P13	 and
P14	
~~**P15**~~	
~~**P16**~~	

~~P17~~	
~~P18~~	 ~~and~~
~~P19~~	

or a pharmaceutically acceptable salt thereof.

58. The compound of claim 34, selected from the group consisting of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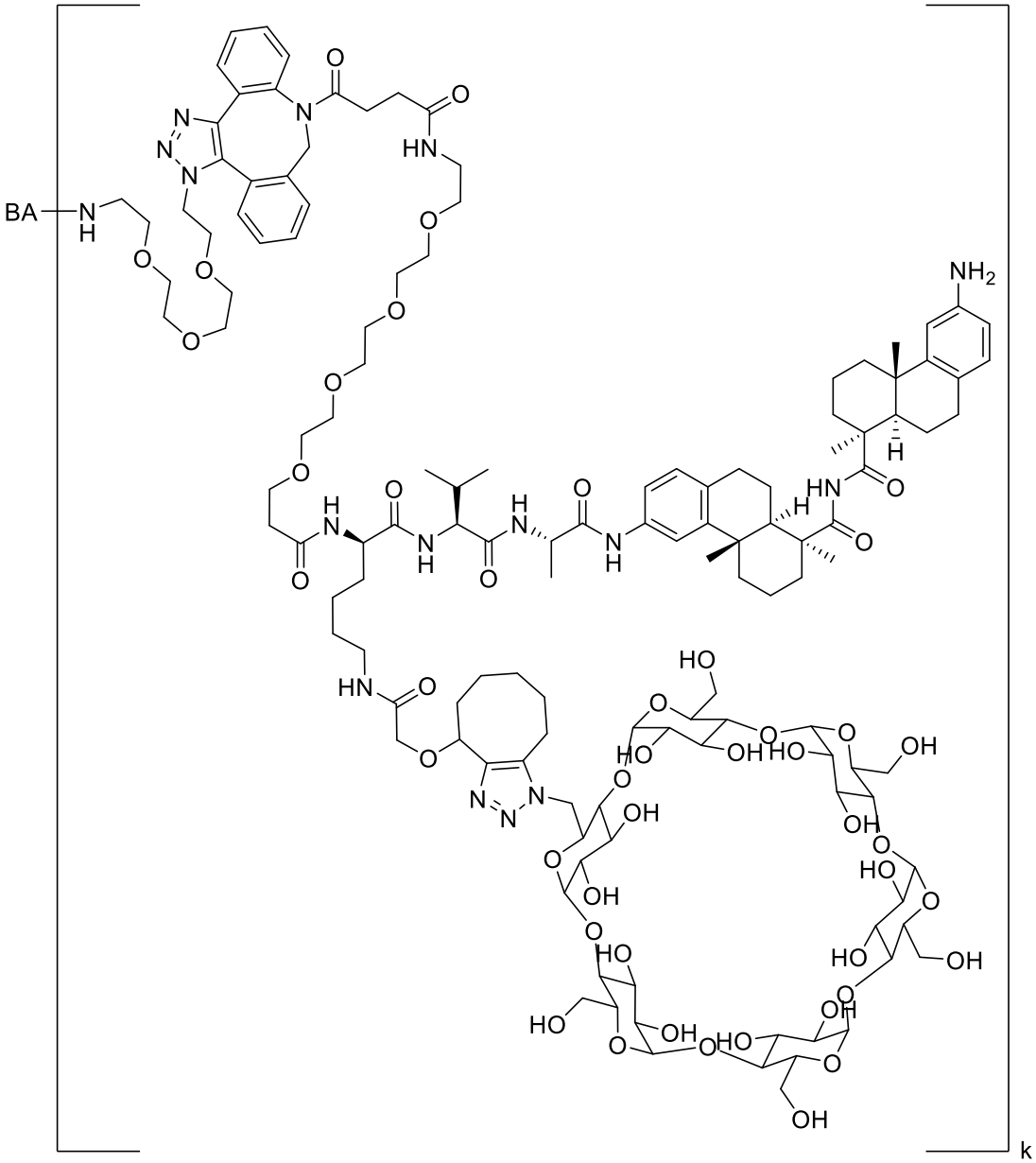

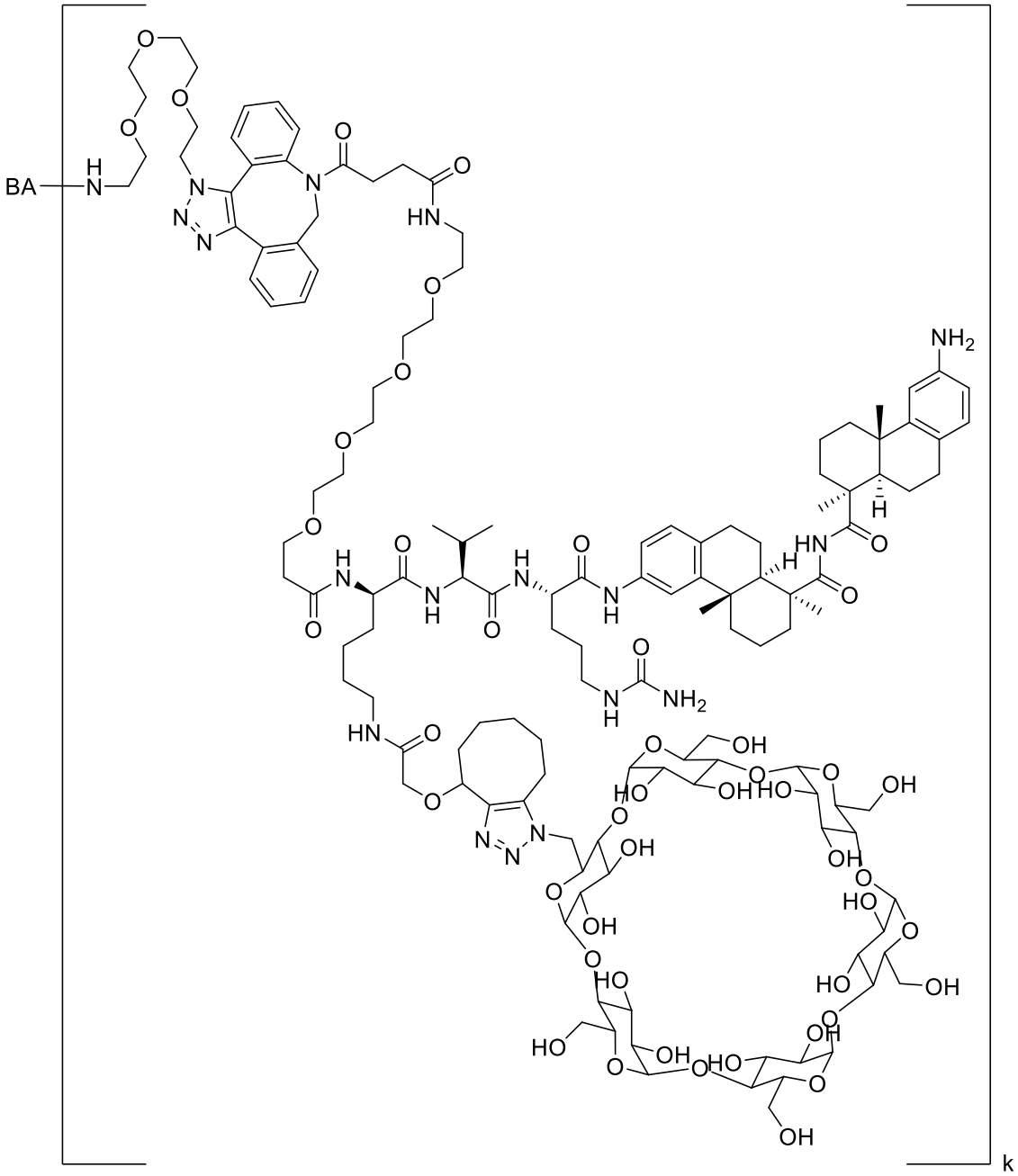
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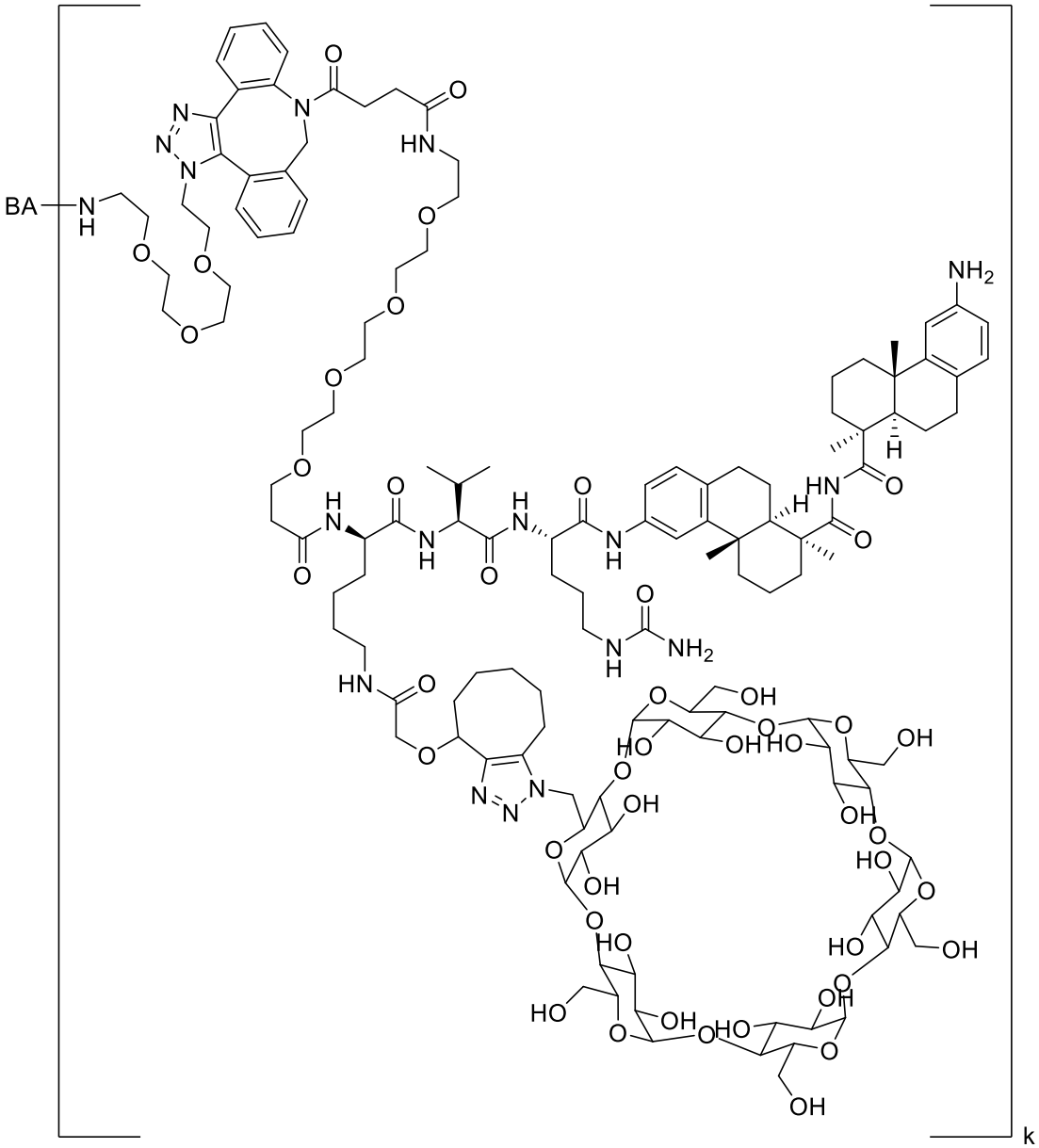
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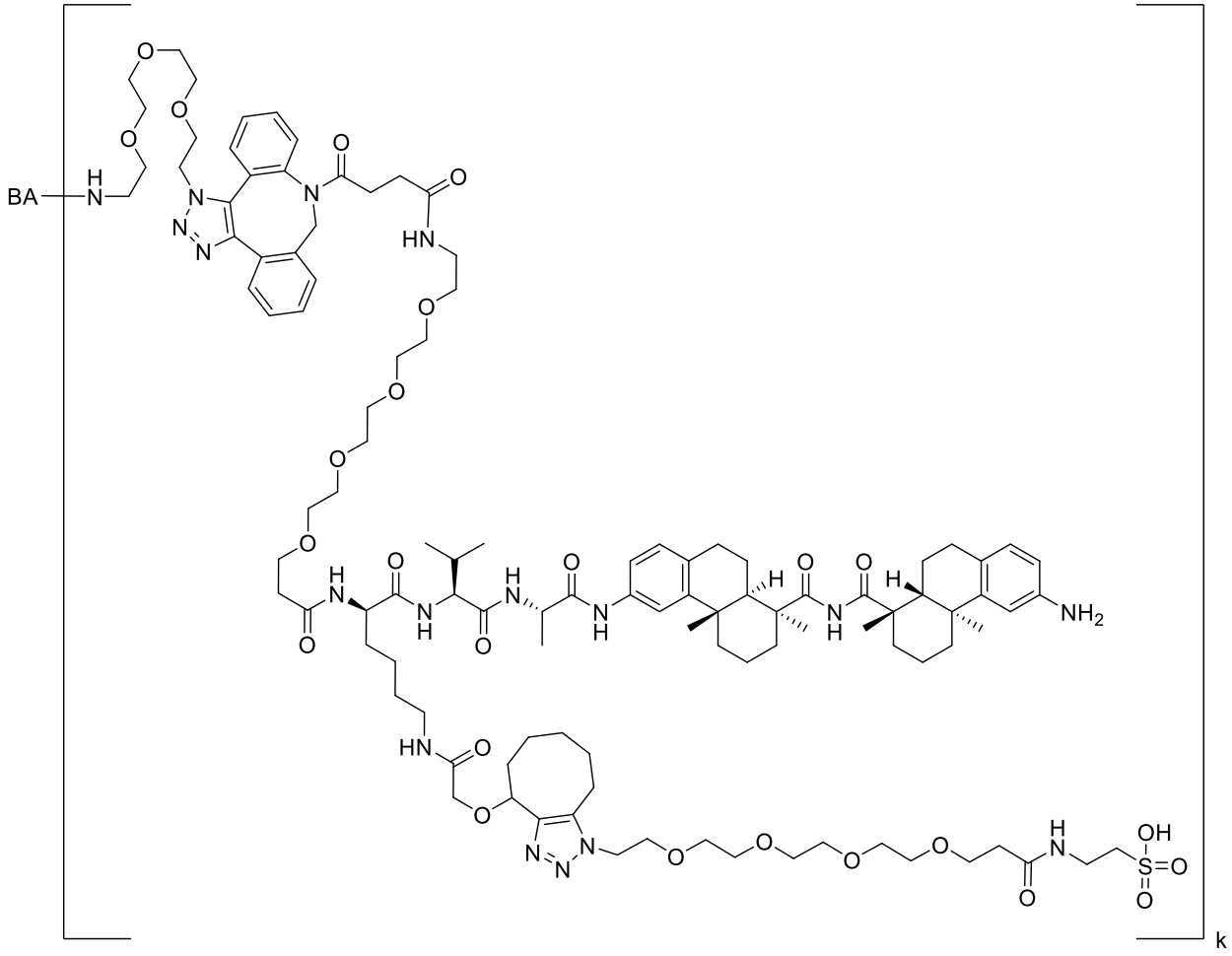
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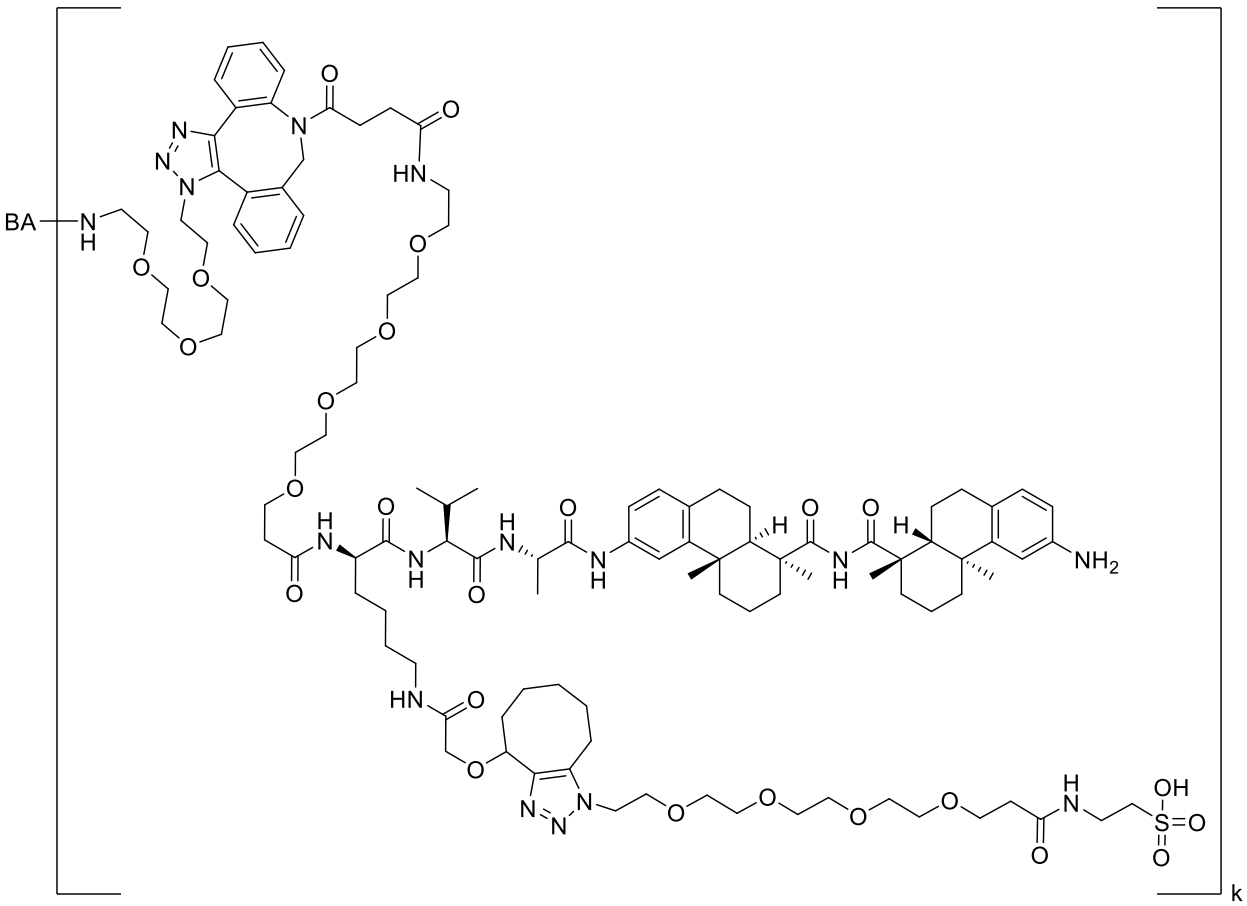
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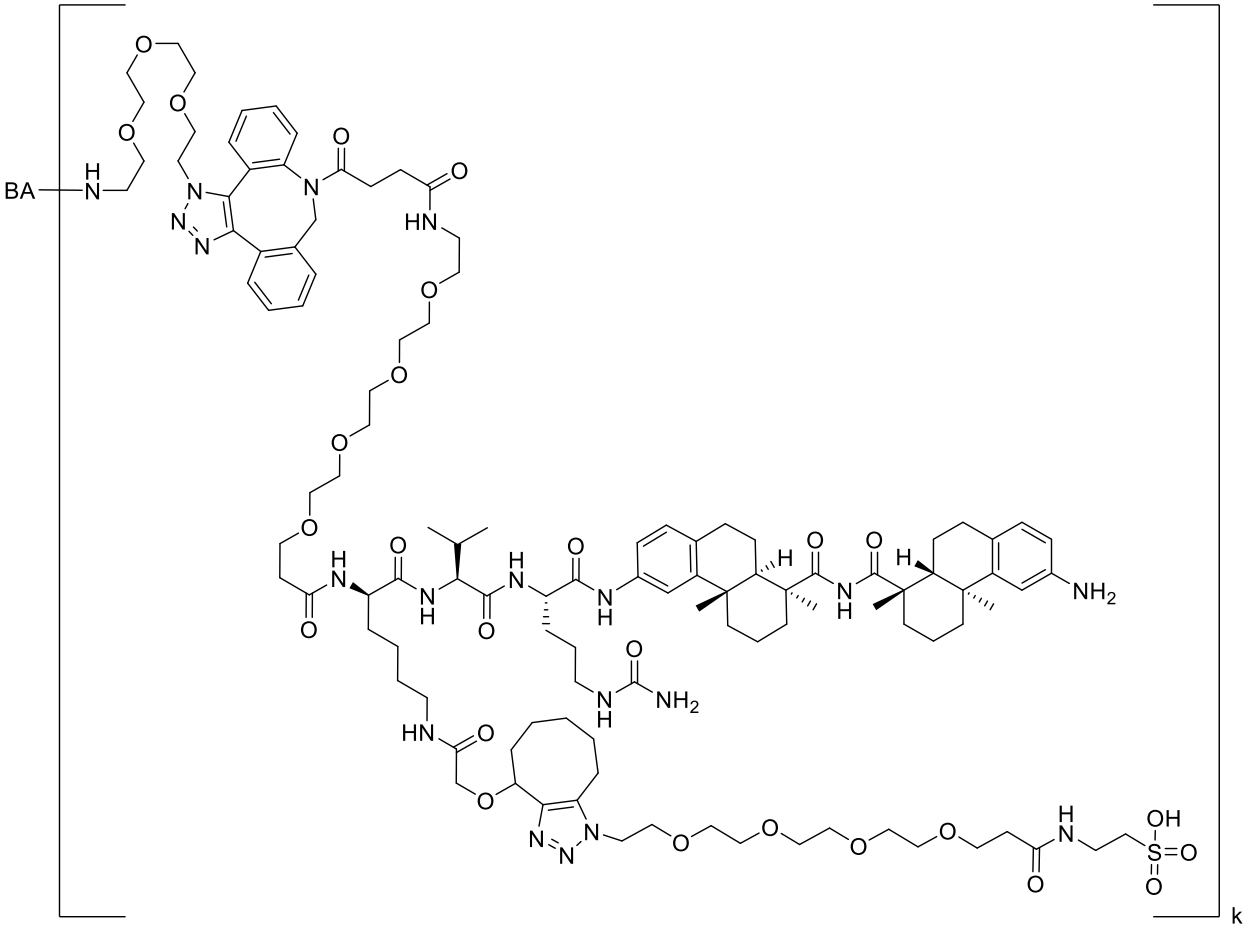
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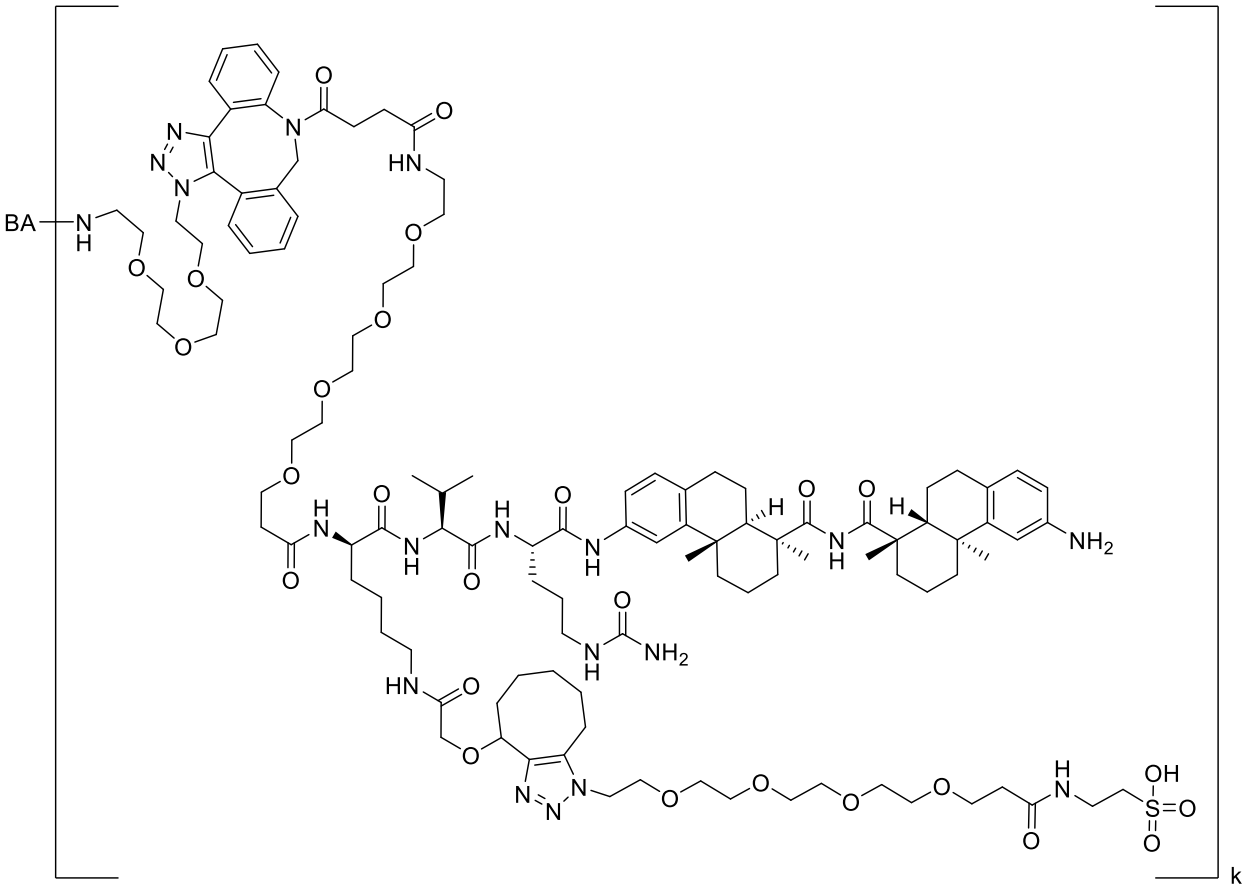
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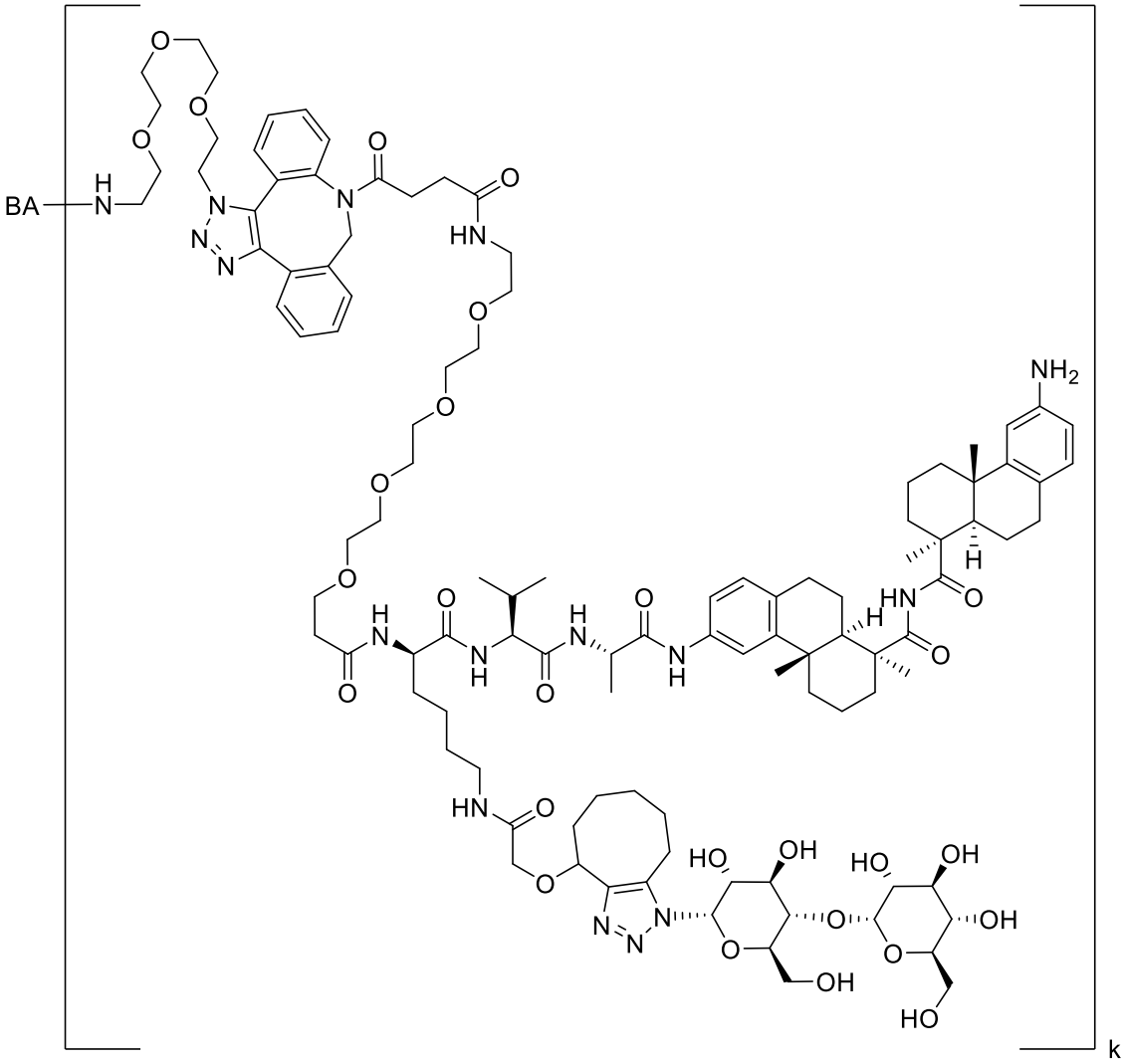
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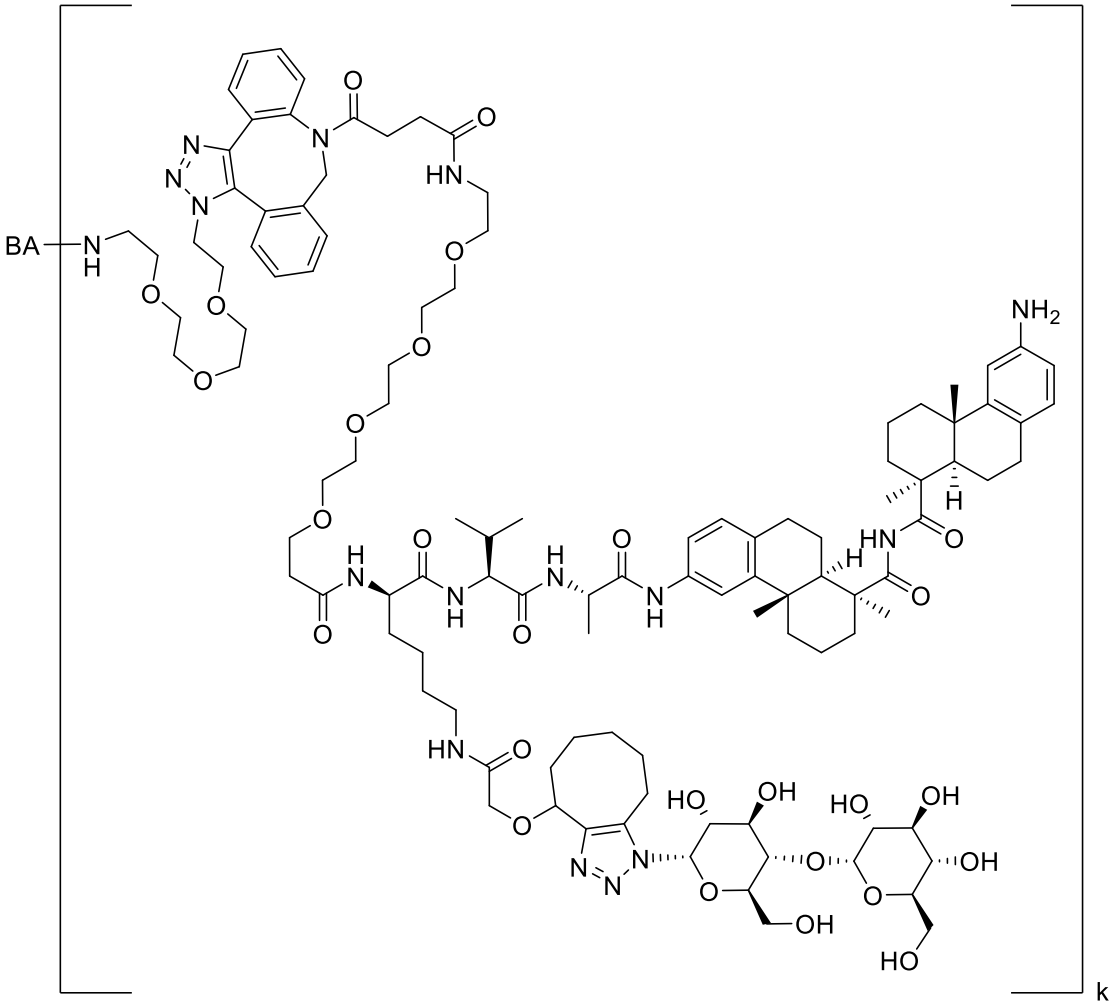

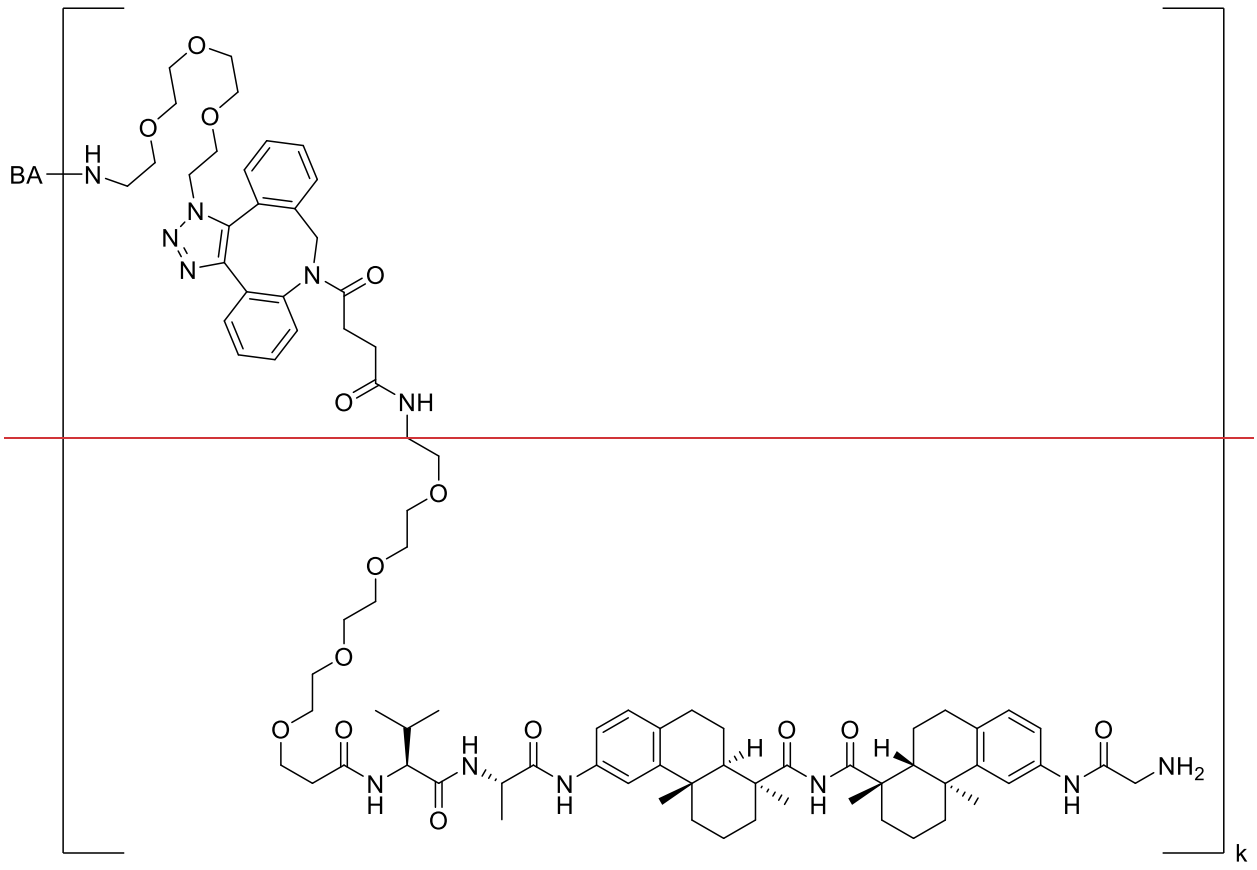

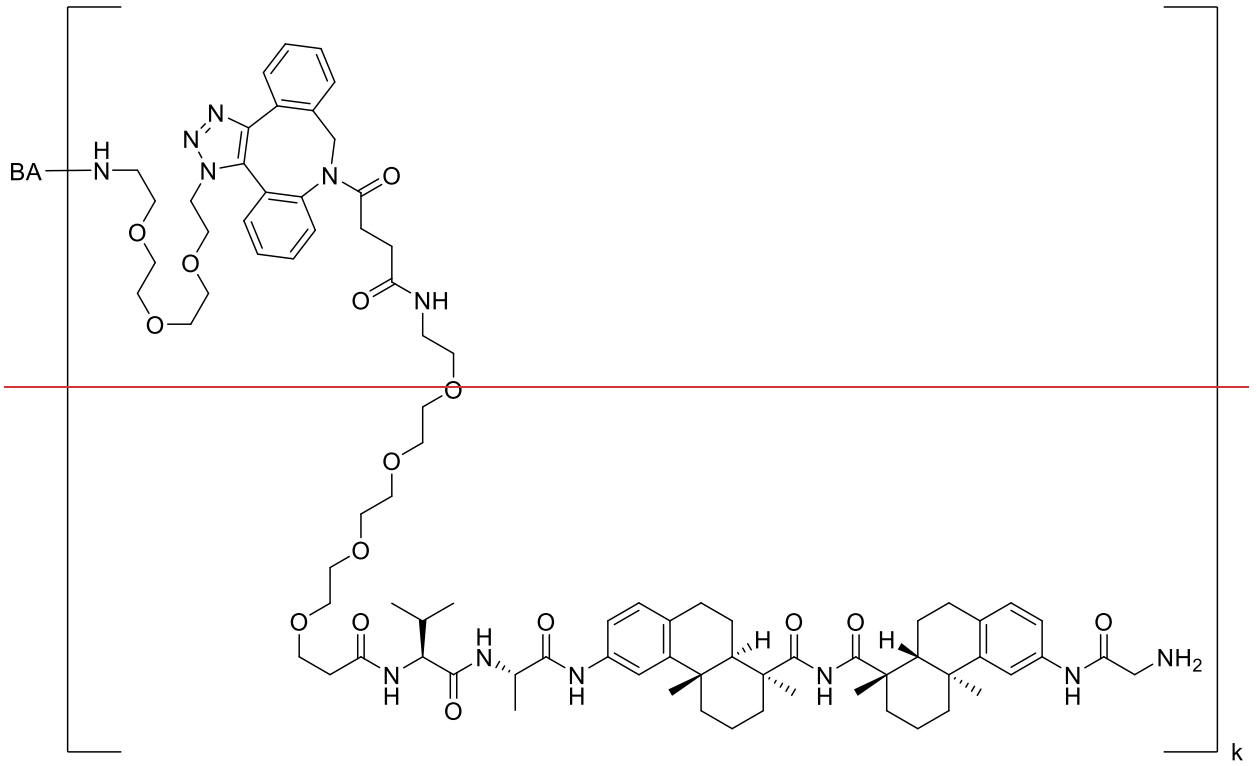

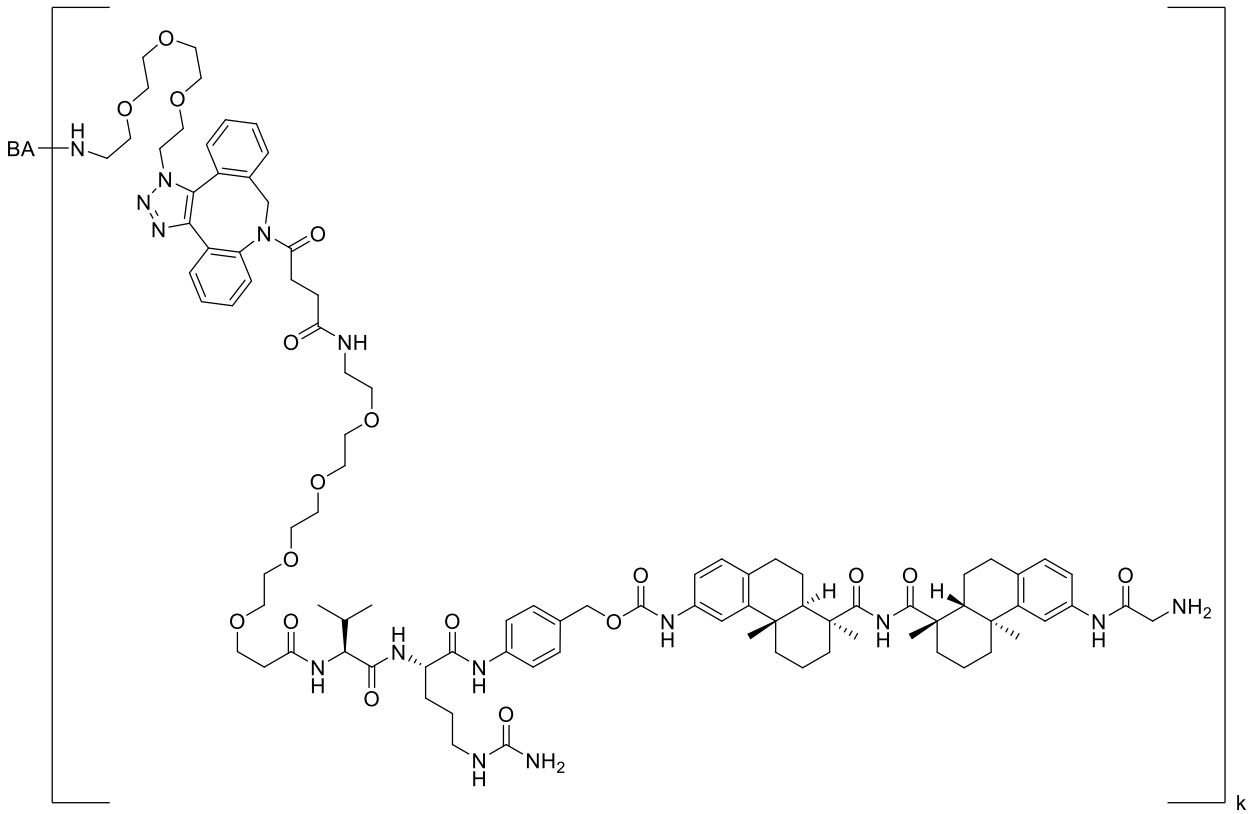
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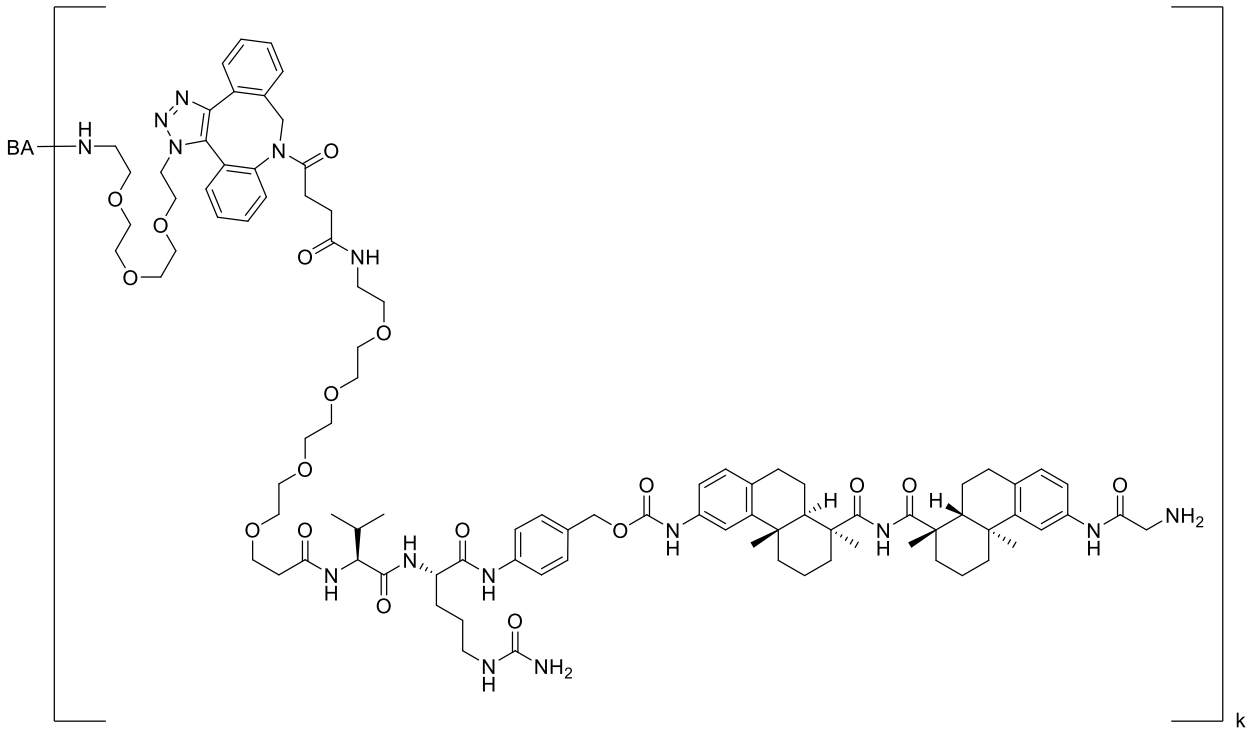
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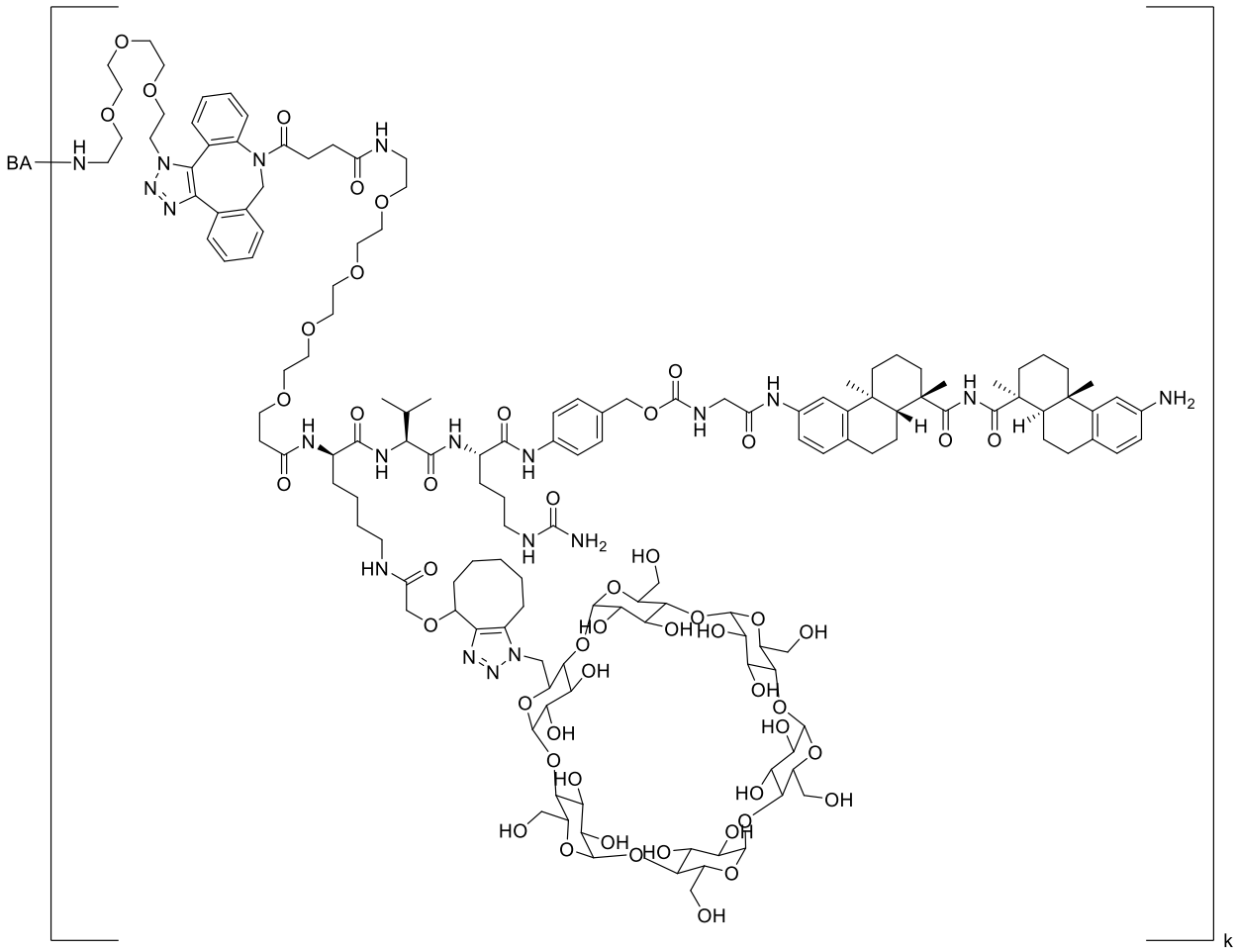
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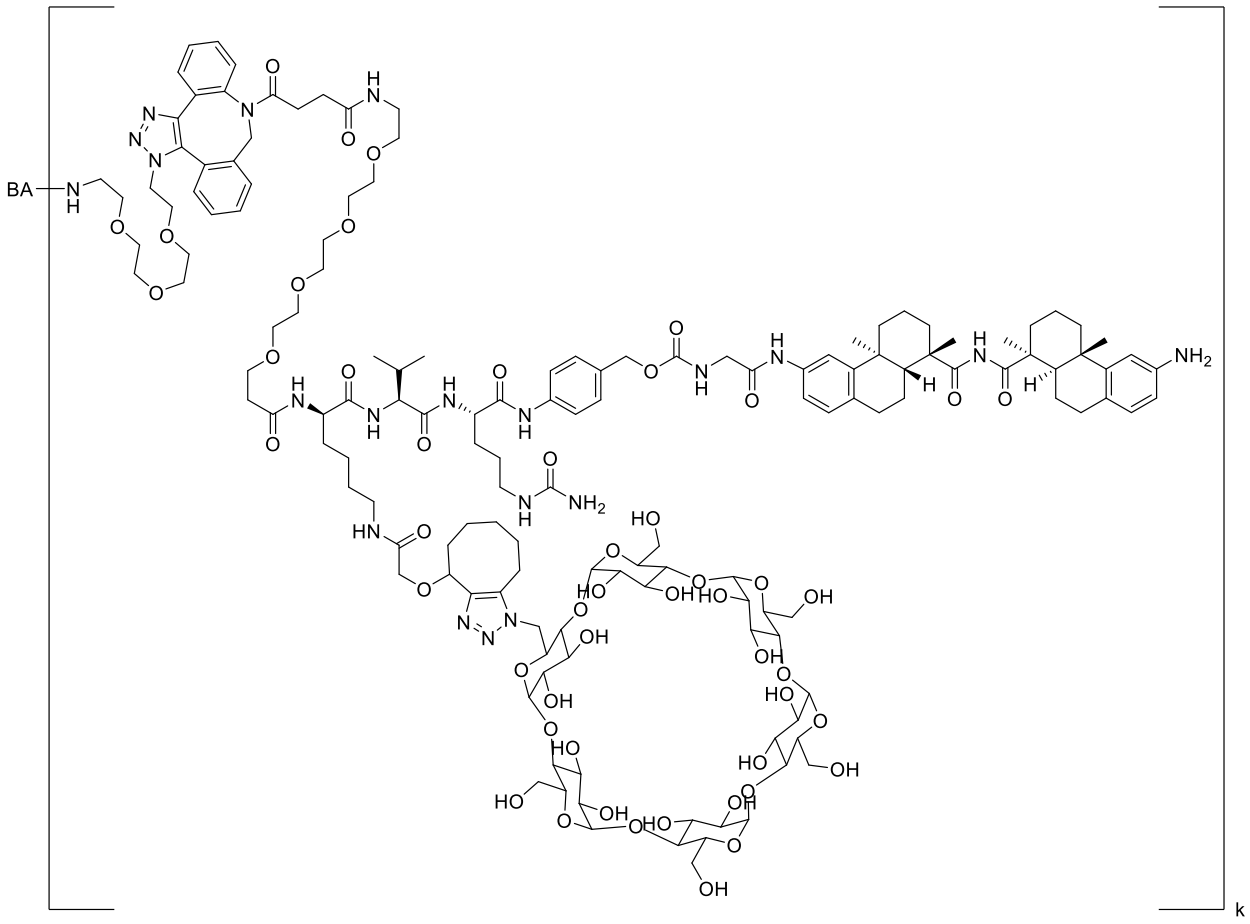
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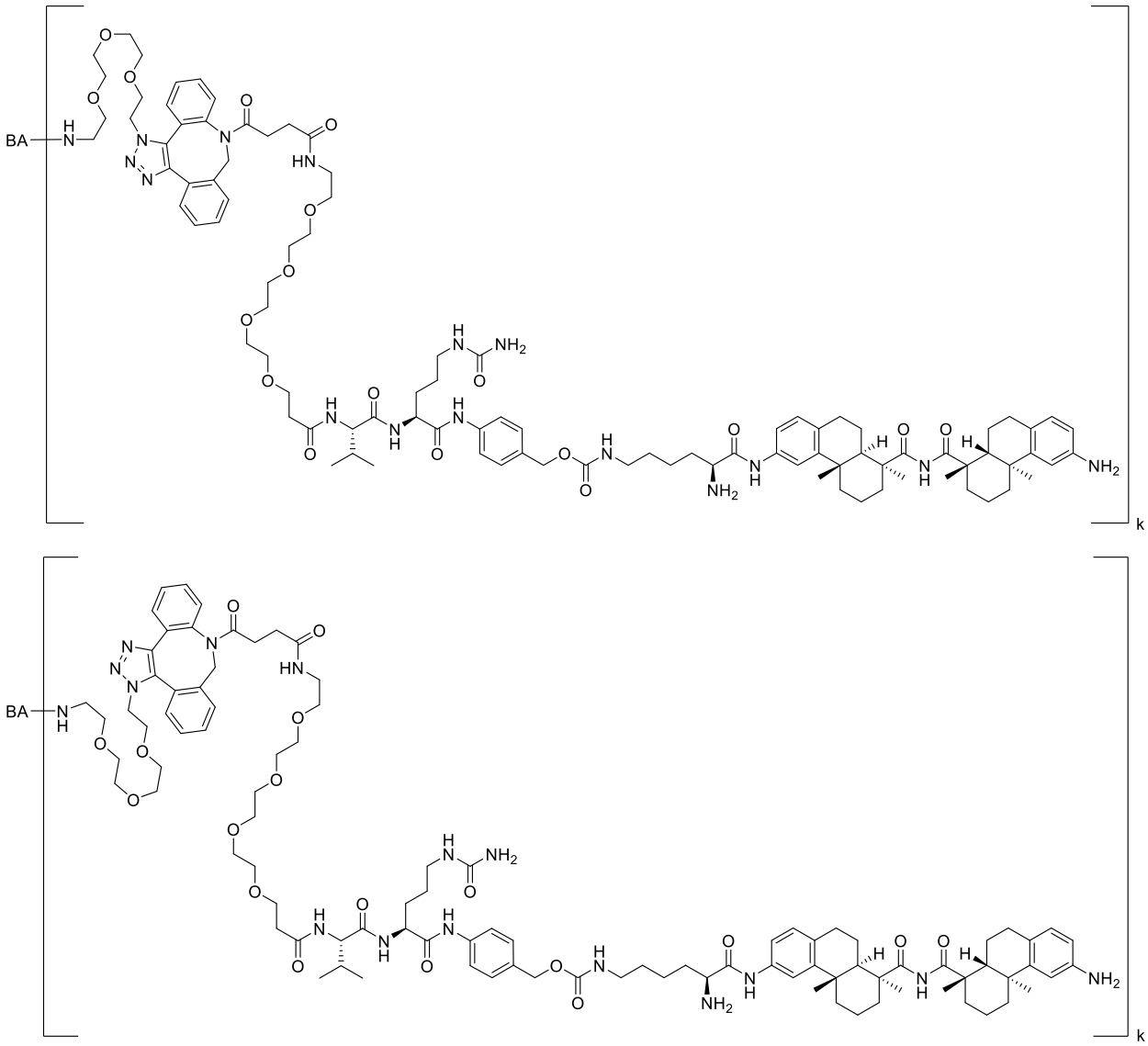

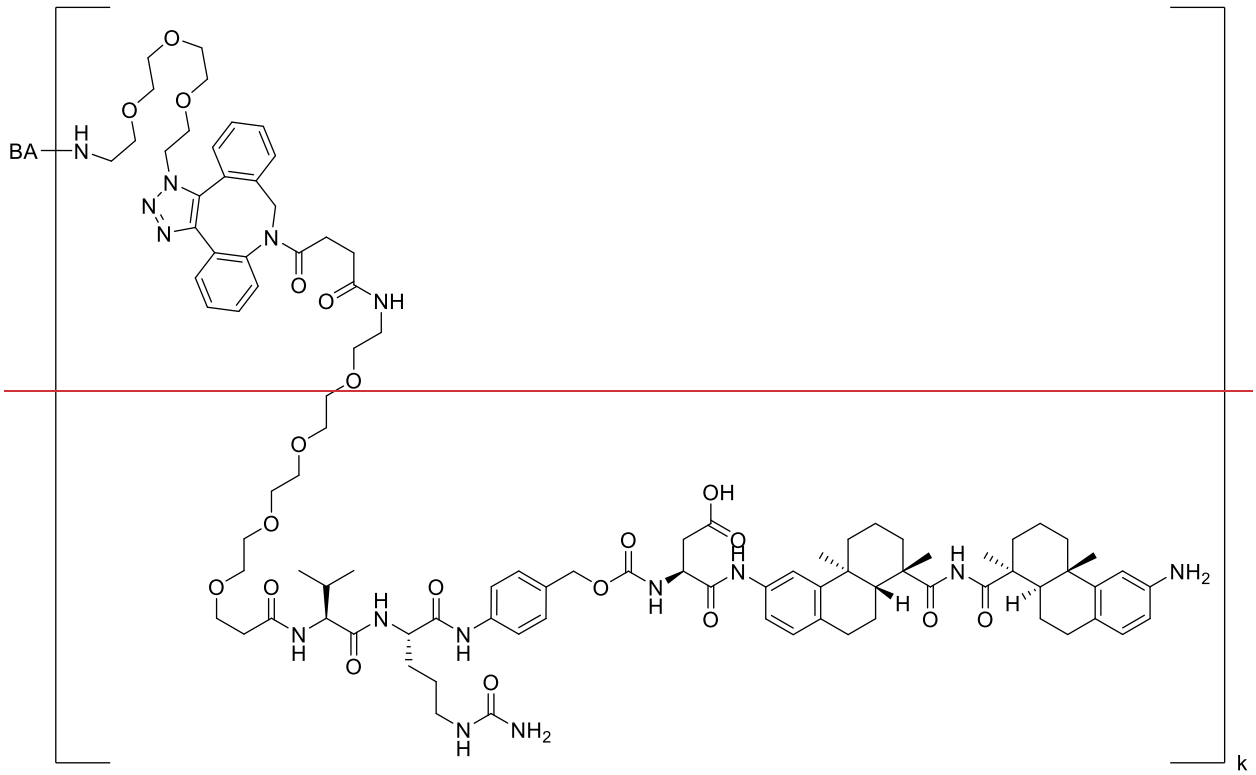
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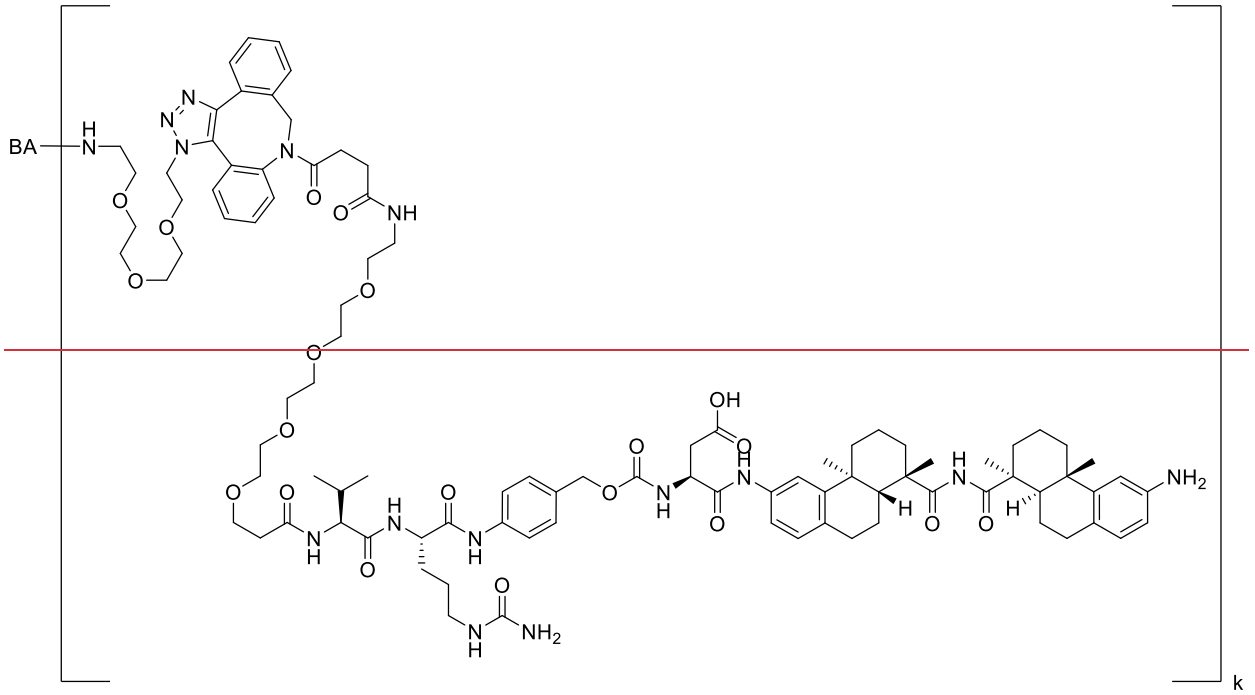
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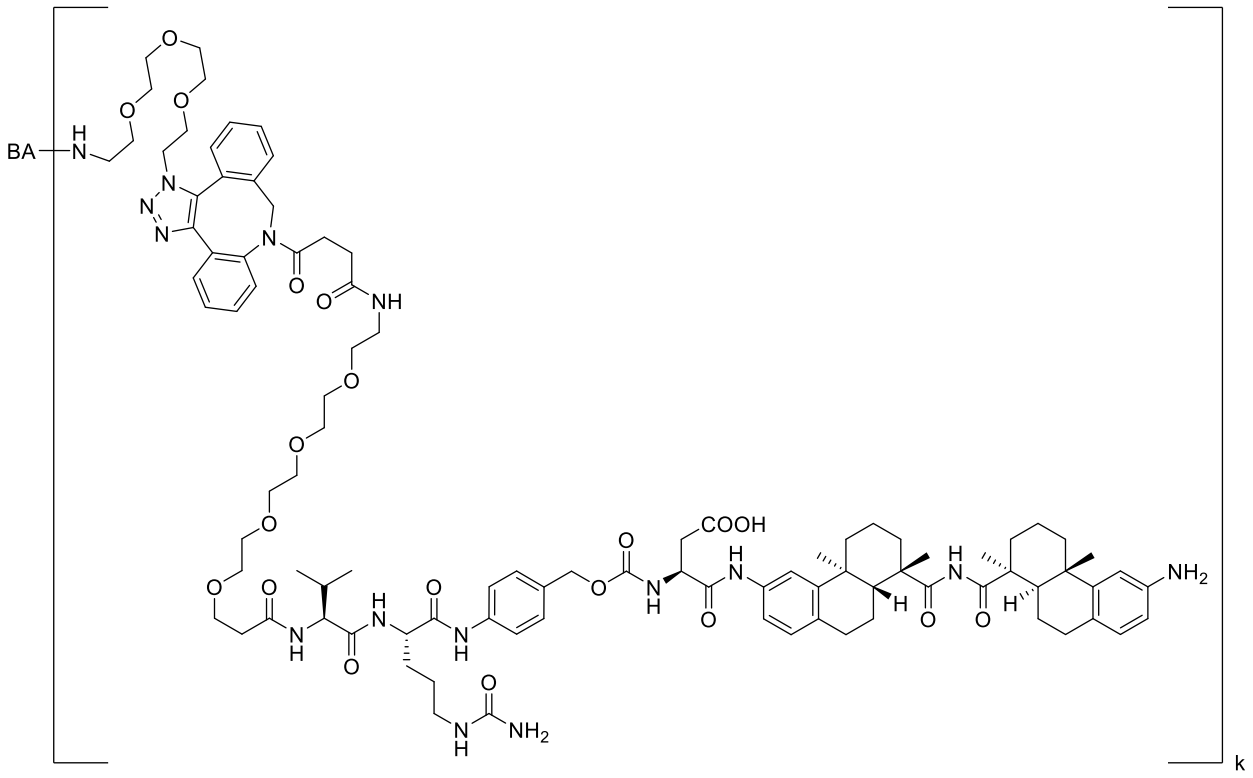
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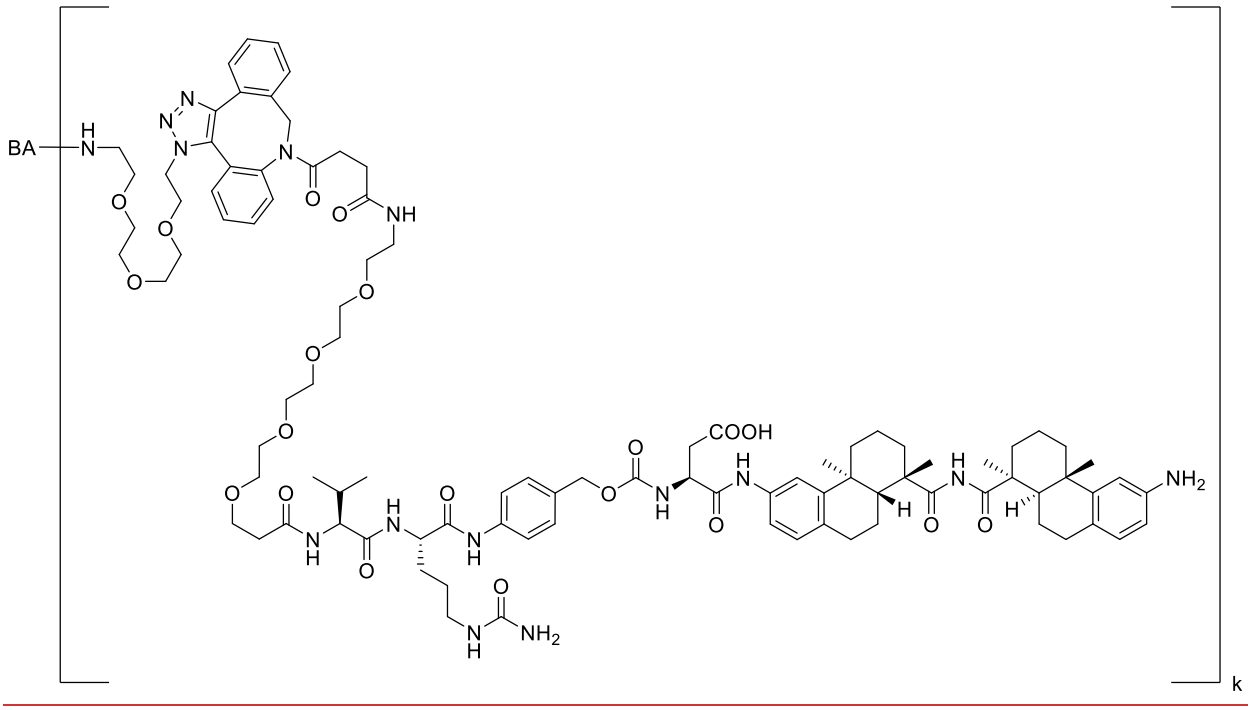
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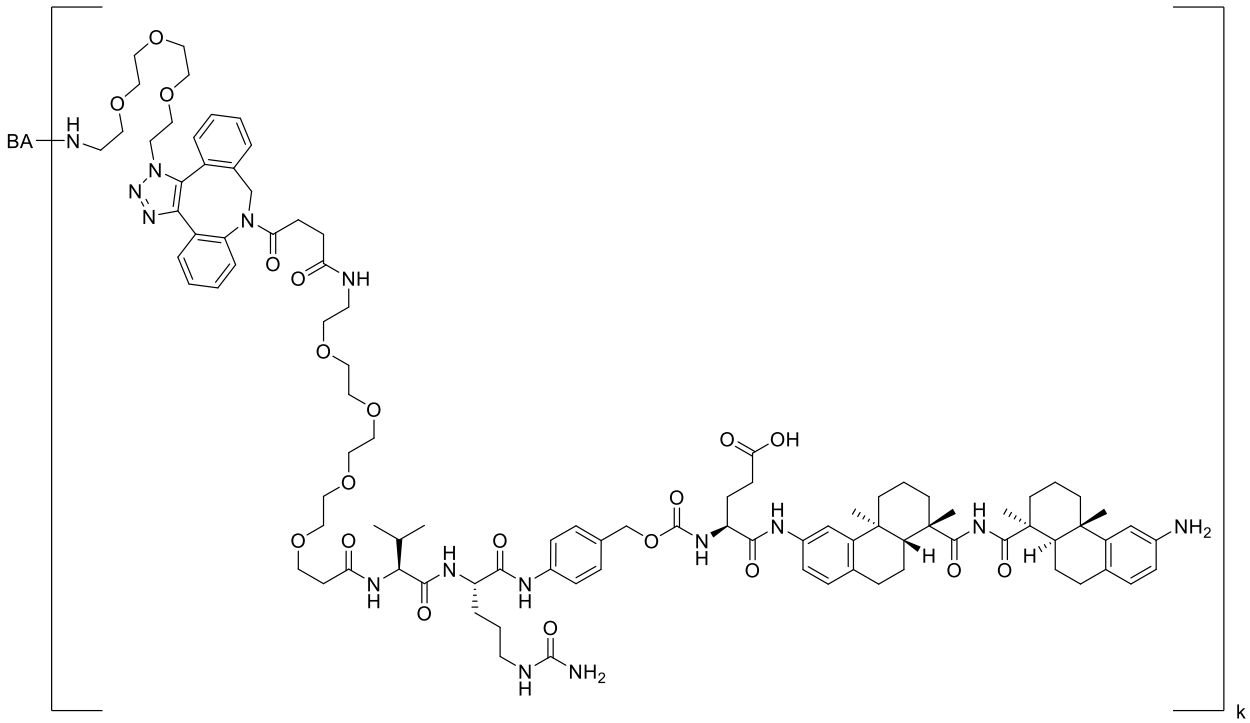
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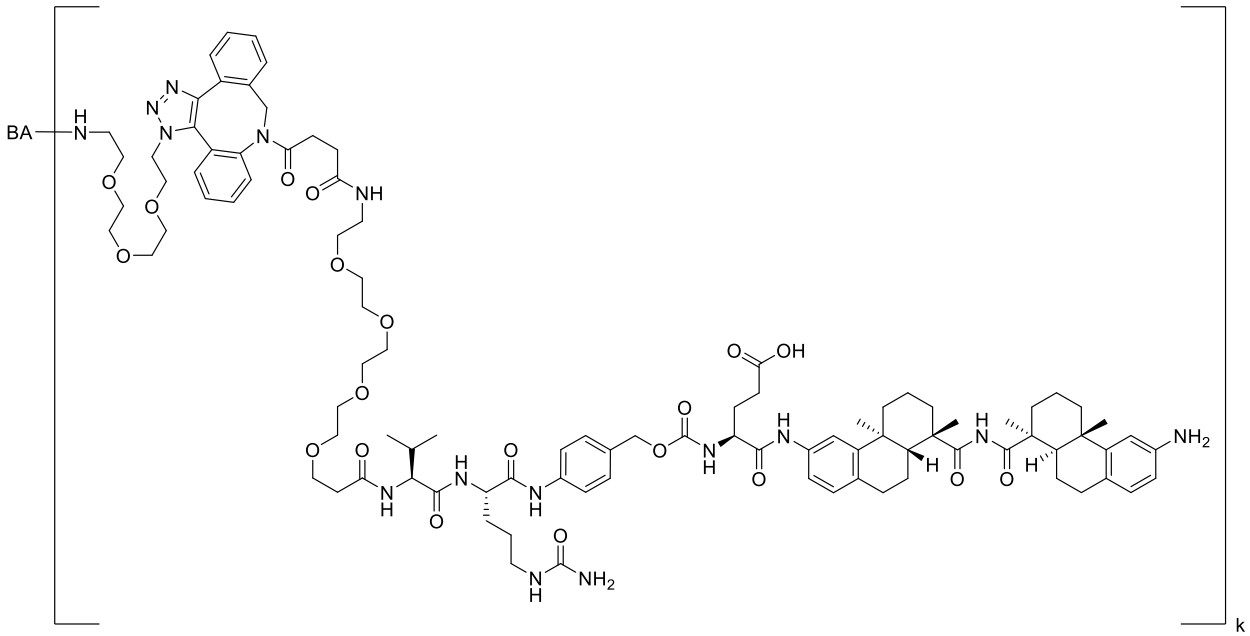
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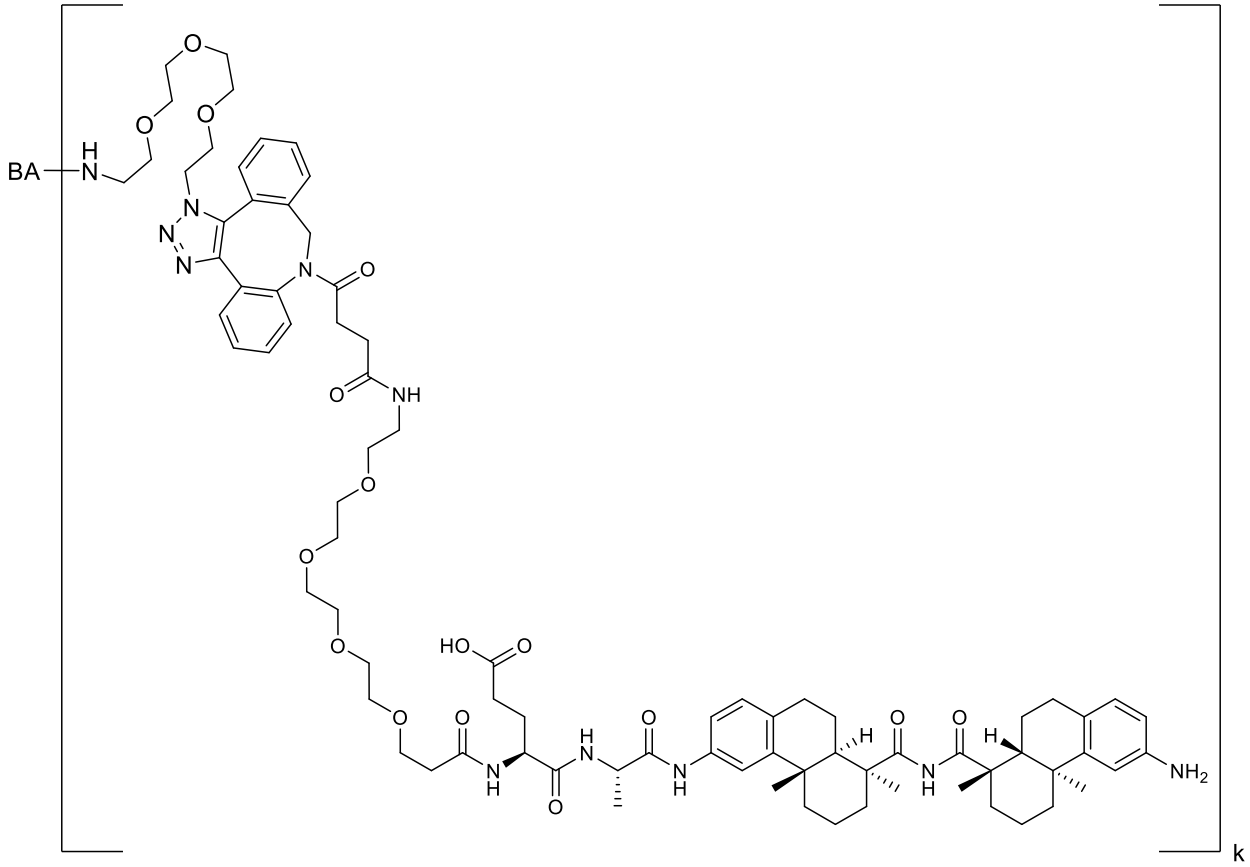
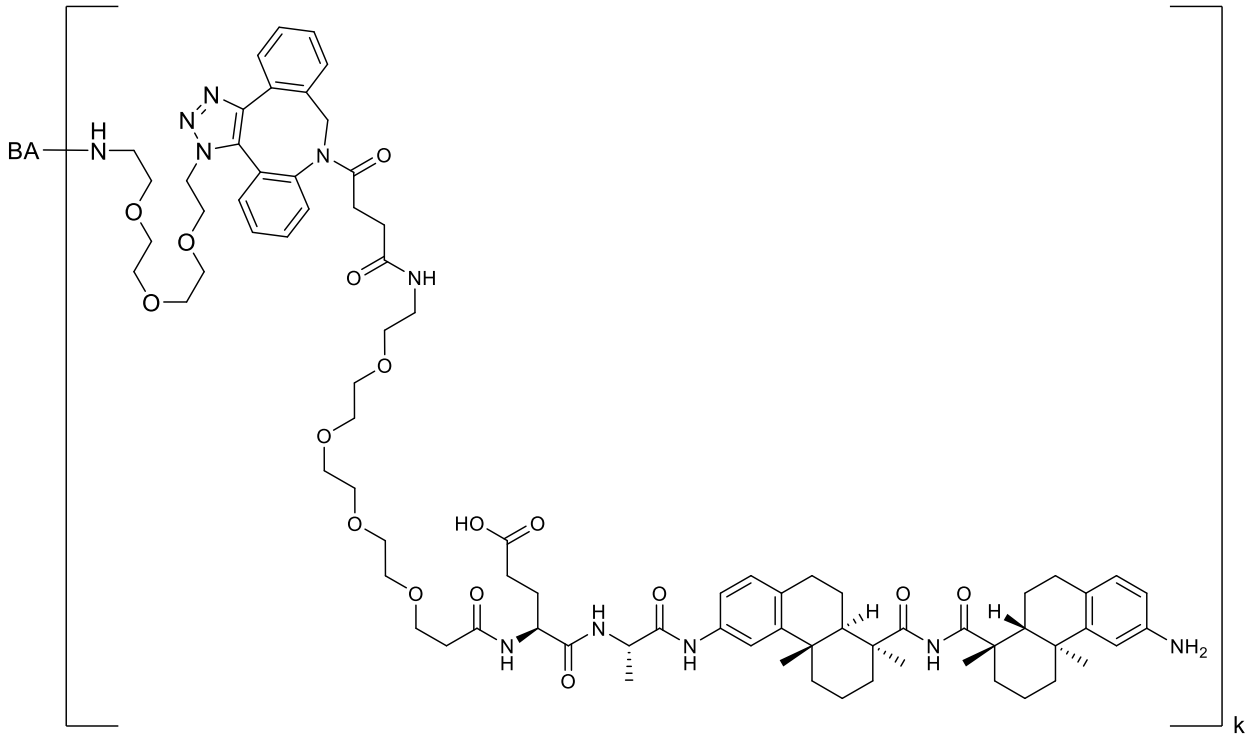
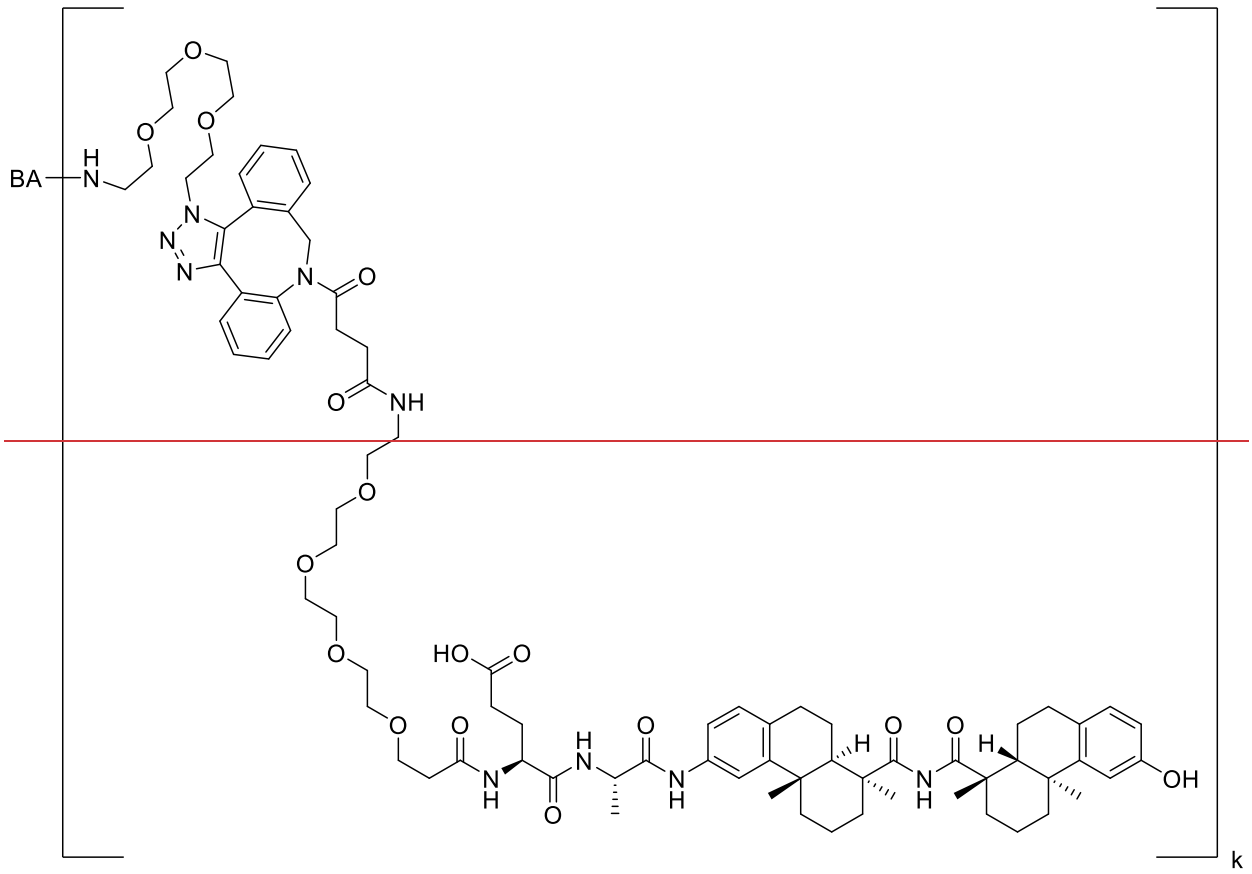
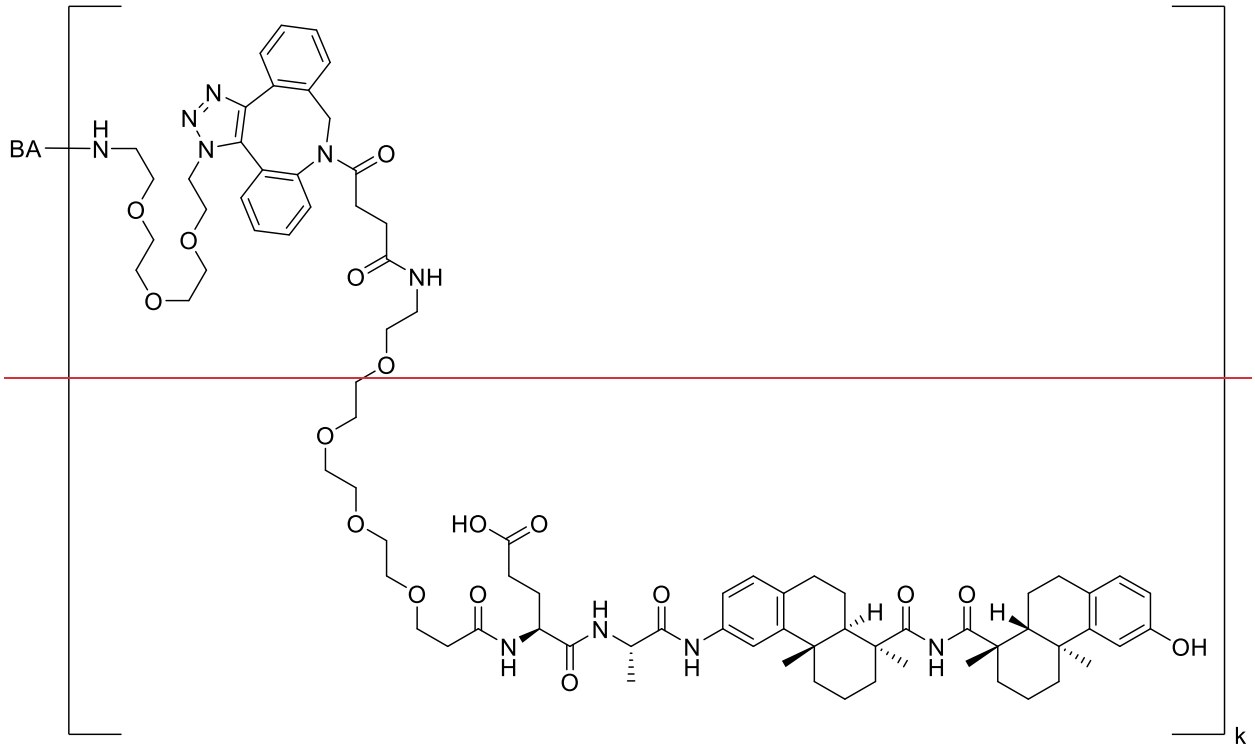
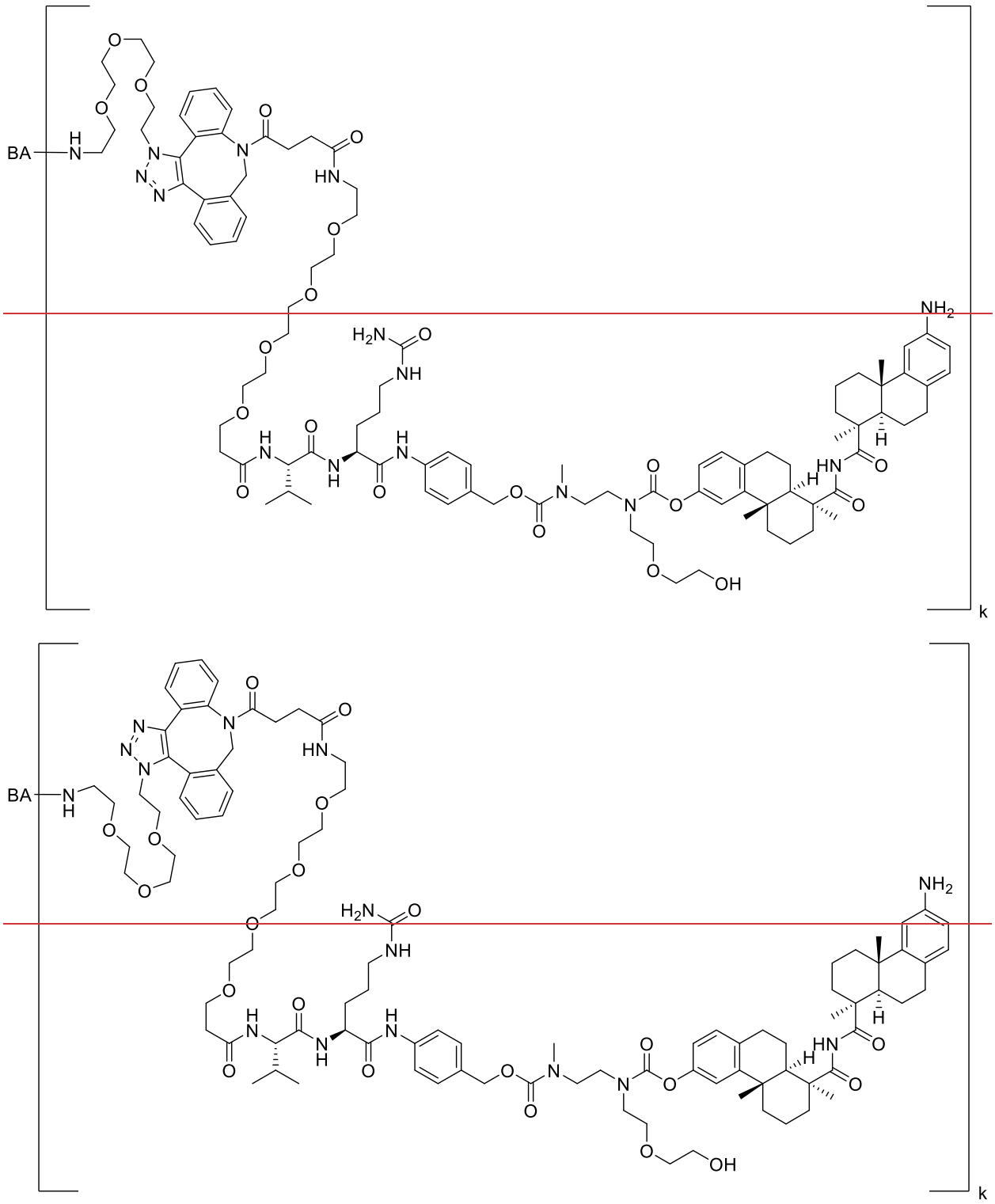
k







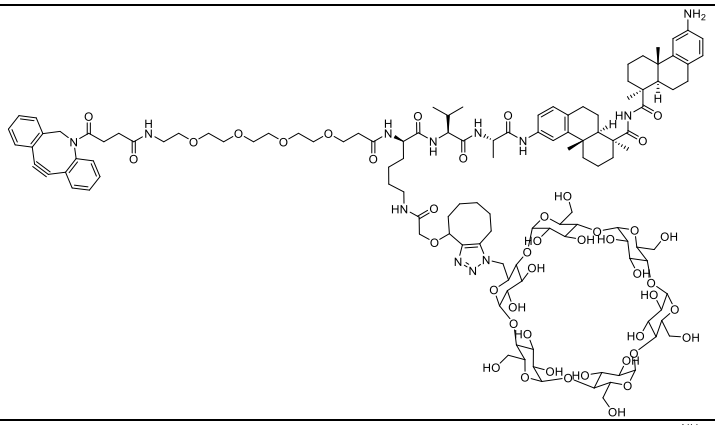
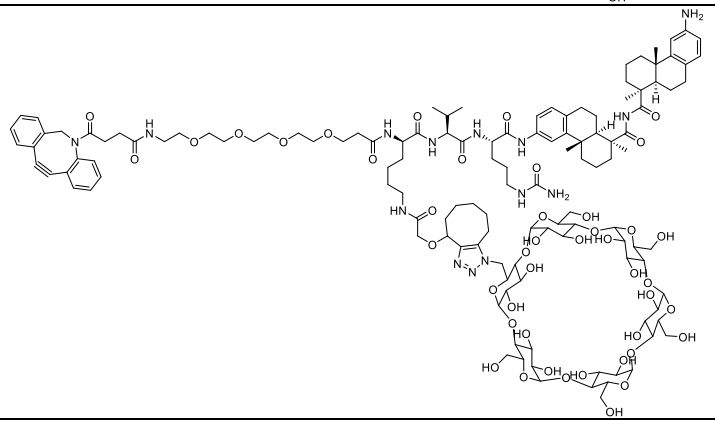
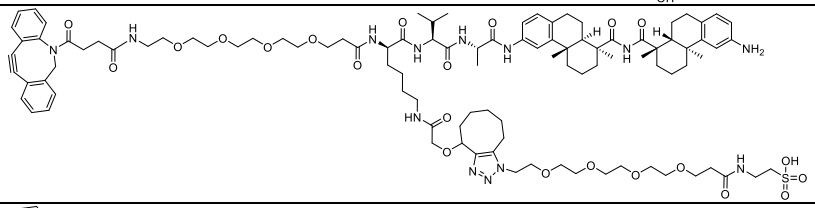
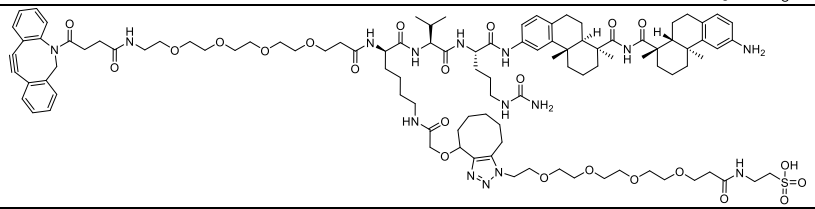
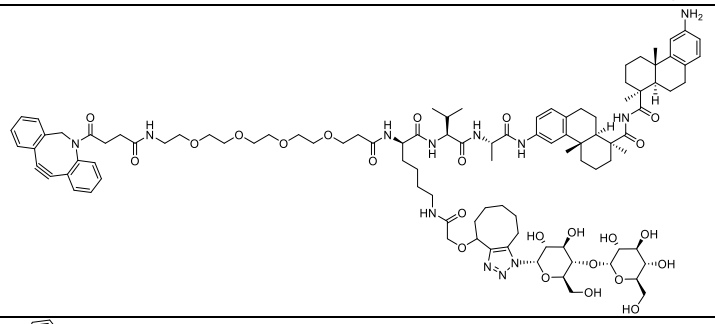
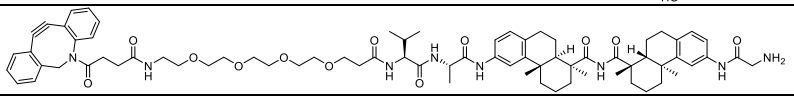
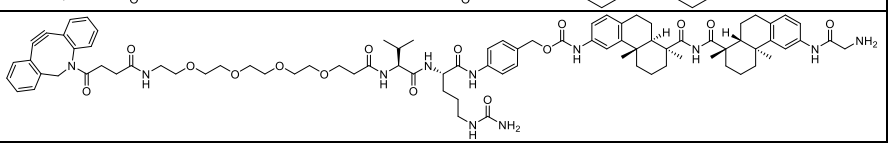


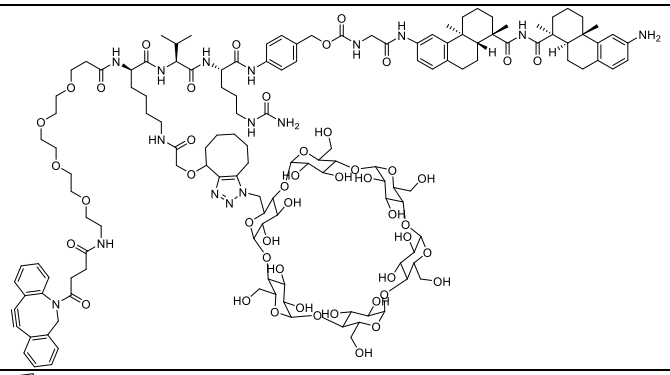
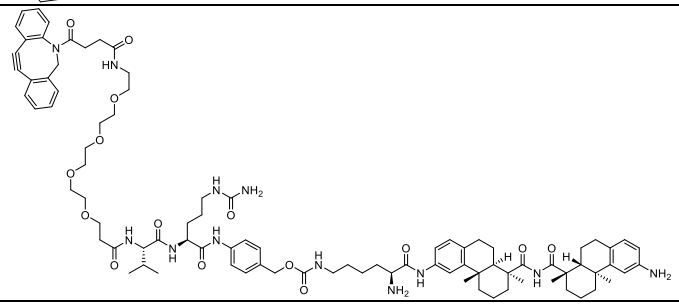
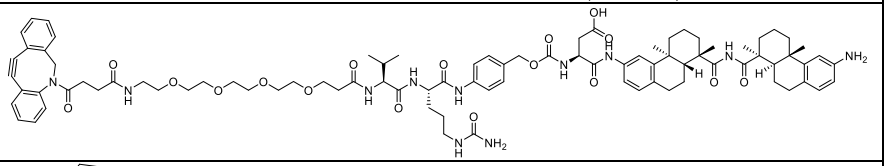
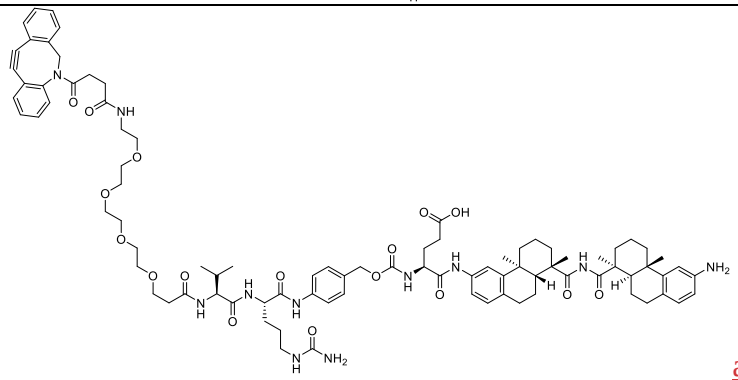
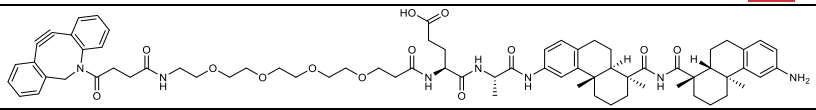
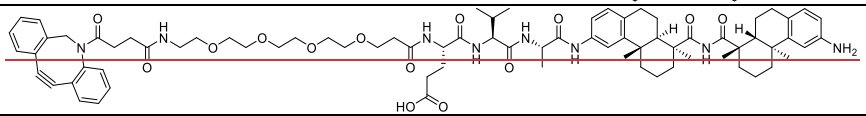
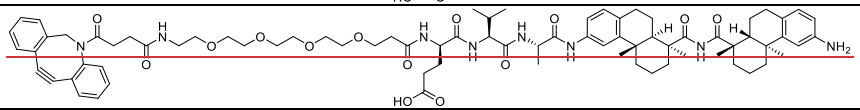
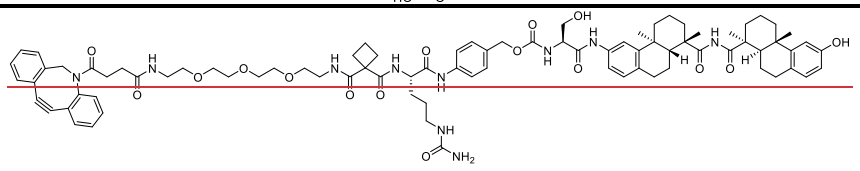
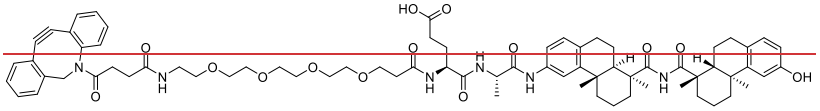


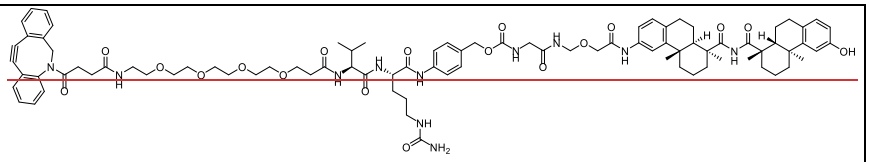
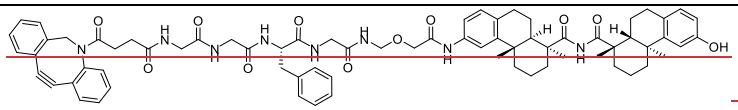
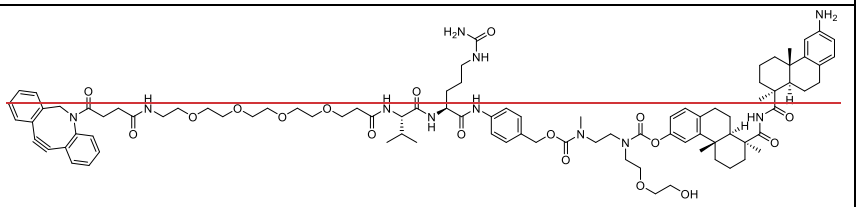
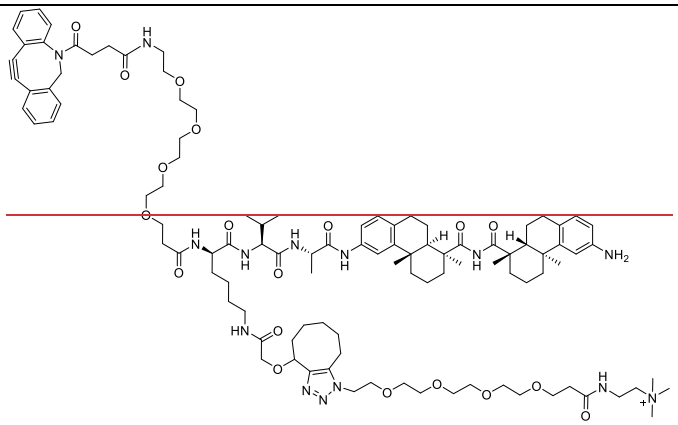
wherein **BA** is an antibody or antigen binding fragment thereof; and

k is an integer from one to four.

59. A compound selected from the group consisting of

LP1	
LP2	
LP3	
LP4	
LP5	
LP6	
LP7	

LP8	
LP9	
LP10	
LP11	 and
LP12	
~~**LP13**~~	
~~**LP14**~~	
~~**LP15**~~	
~~**LP16**~~	

~~LP17~~	
~~LP18~~	 ~~and~~
~~LP19~~	
~~LP20~~	

or a salt thereof.

60. The compound of any one of claims 34-36, 38, 39, or 41-49 wherein **BA** is an antibody or antigen-binding fragment thereof, modified with H_2N-**LL**-**X**, wherein **LL** is divalent polyethylene glycol and **X** is $-N_3$.

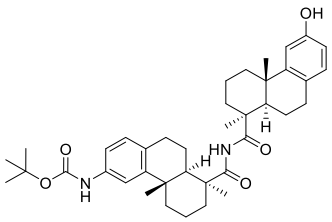
61. The compound of claim 60, wherein **k** is an integer from one to four.

62. The compound of claim 60, wherein **BA** is an antibody or antigen binding fragment thereof that binds HER2, PRLR, or MSR1.

63. The compound of claim 60, wherein **BA** is an antibody or antigen-binding fragment thereof, and conjugation is through at least one Q295 residue; or conjugation is through two Q295 residues.

64. The compound of claim 60, wherein **BA** is a N297Q antibody or antigen-binding fragment thereof; or **BA** is a N297Q antibody or antigen-binding fragment thereof and conjugation is through at least one Q295 and at least one Q297 residue.

65. A compound selected from the group consisting of



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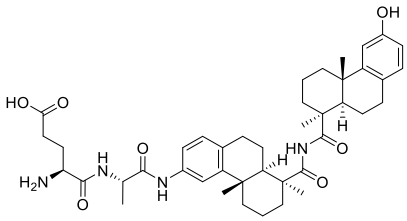
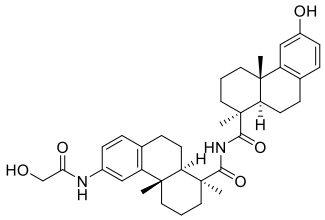


P16;



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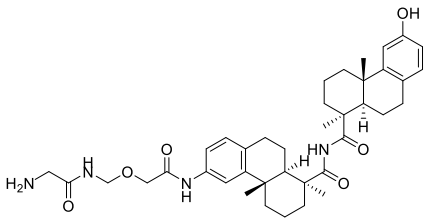
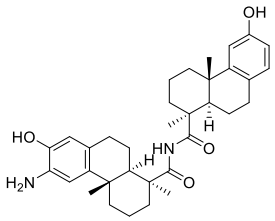
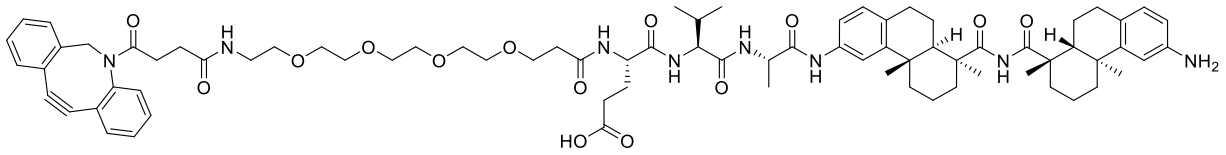


P18; and

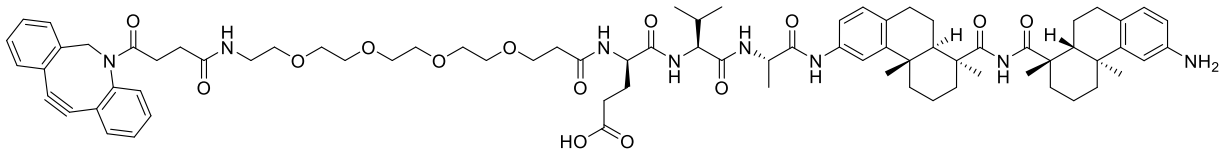


P19.

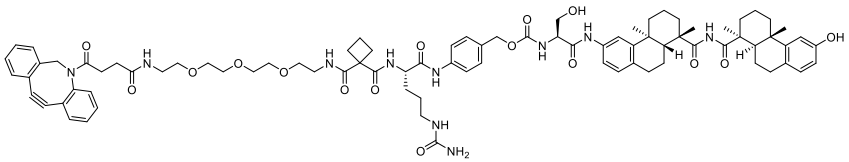
66. A linker-payload selected from the group consisting of



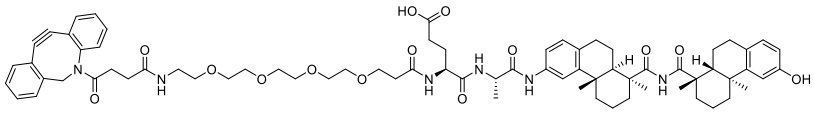
LP13;



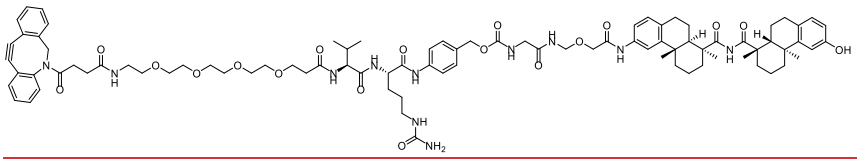
LP14;



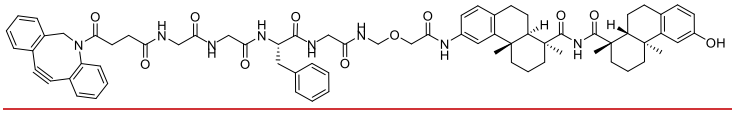
LP15;



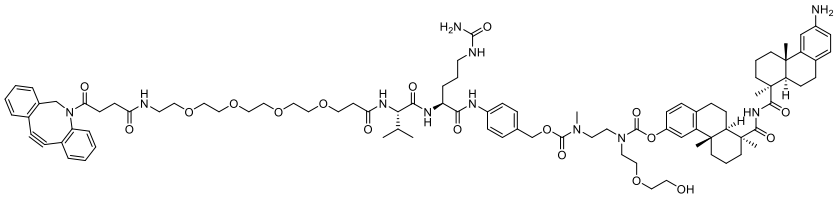
LP16;



LP17;

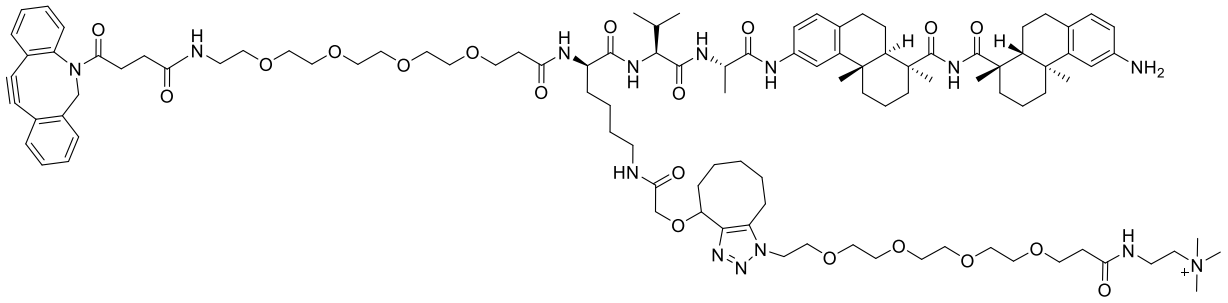


LP18;



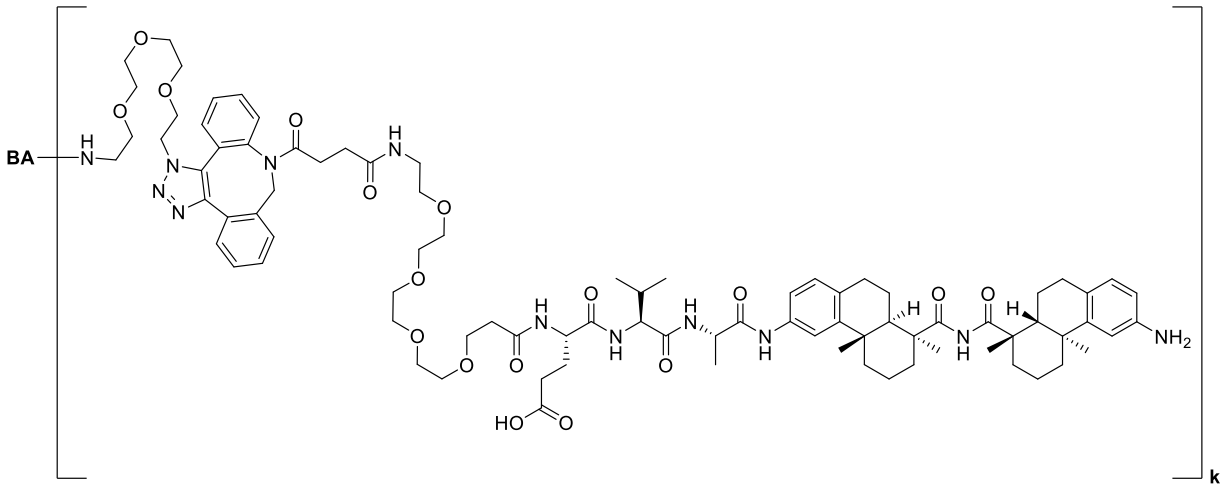
LP19;

and

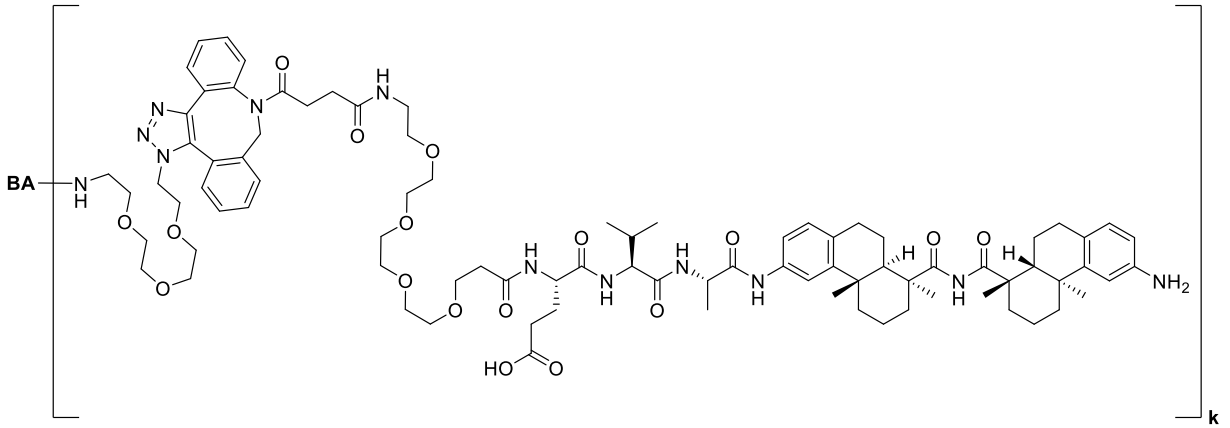


LP20.

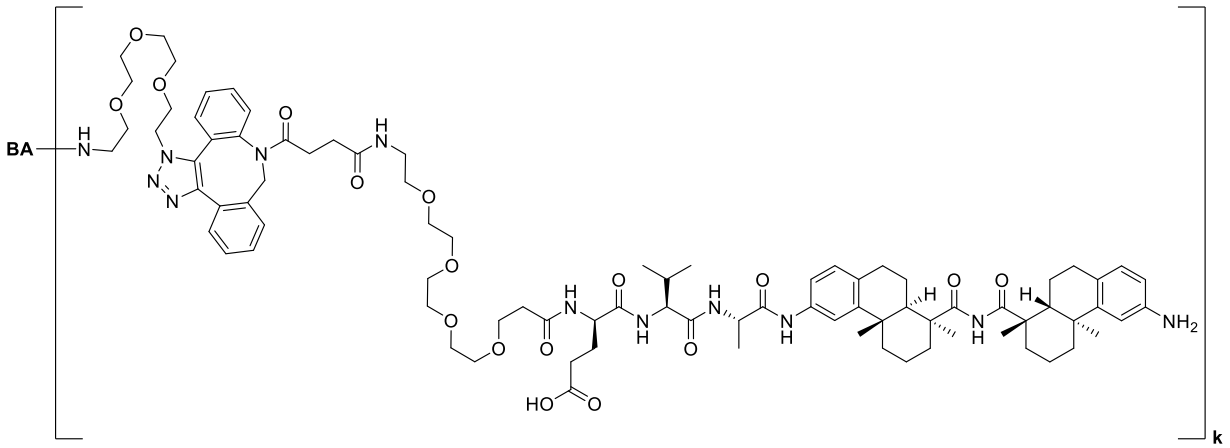
67. An antibody-drug conjugate compound selected from the group consisting of


BA
HO
NH2
k

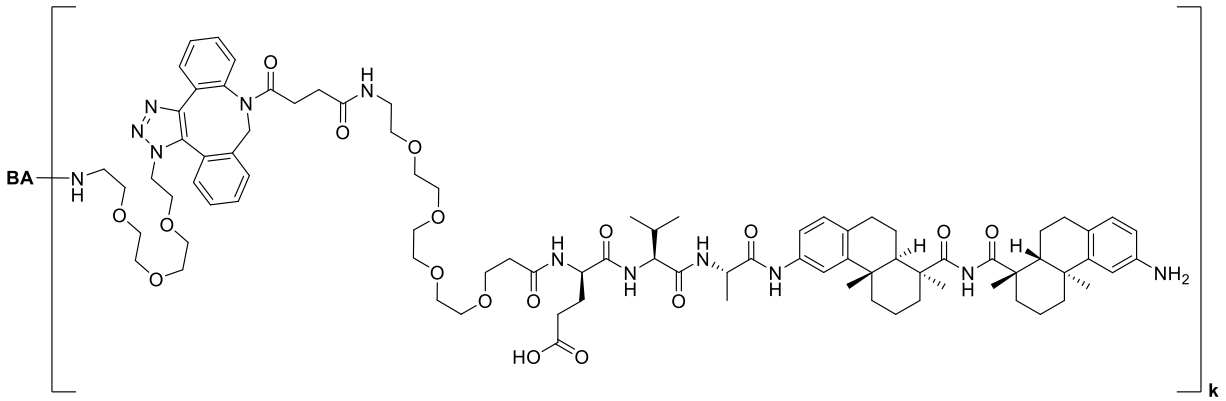
;

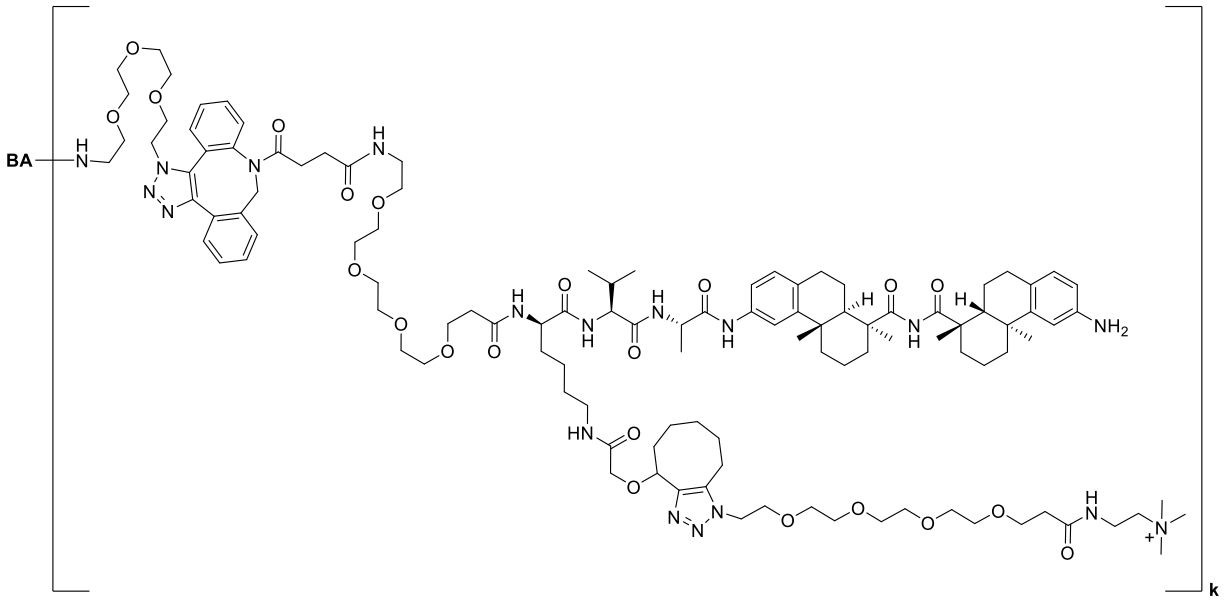

BA
HO
NH2
k

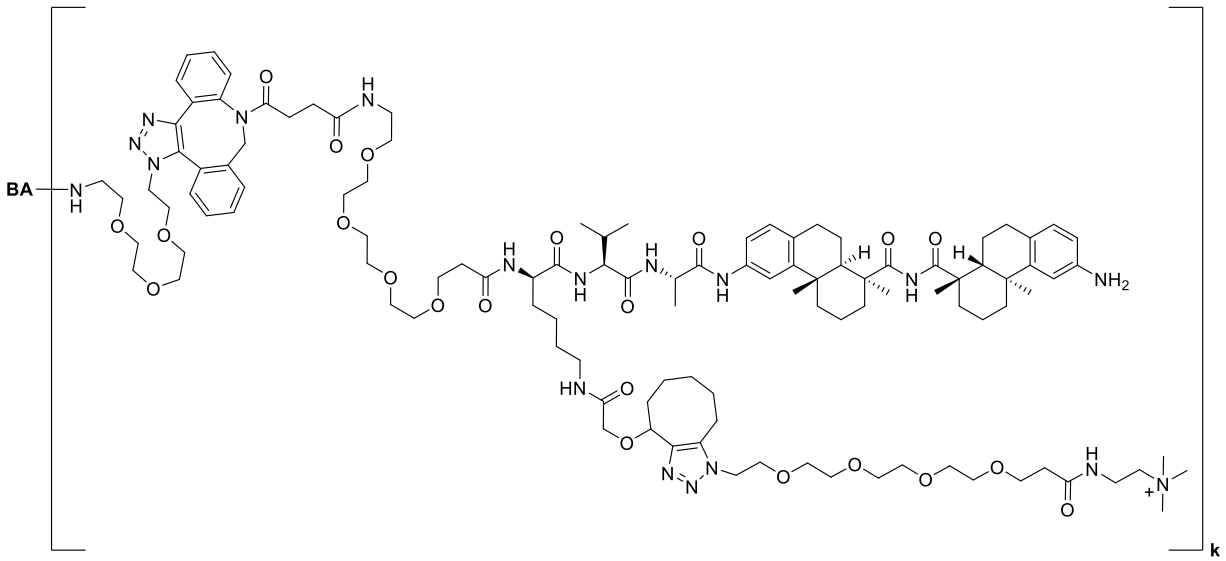
;

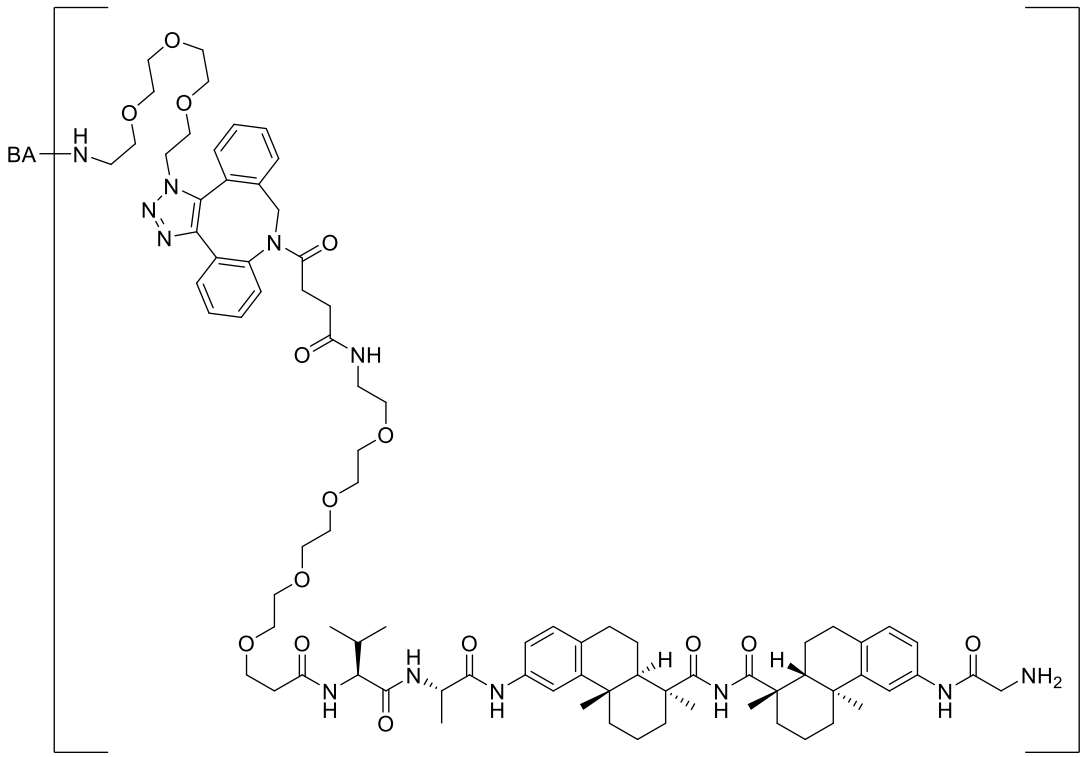

BA
HO
NH2
k

;

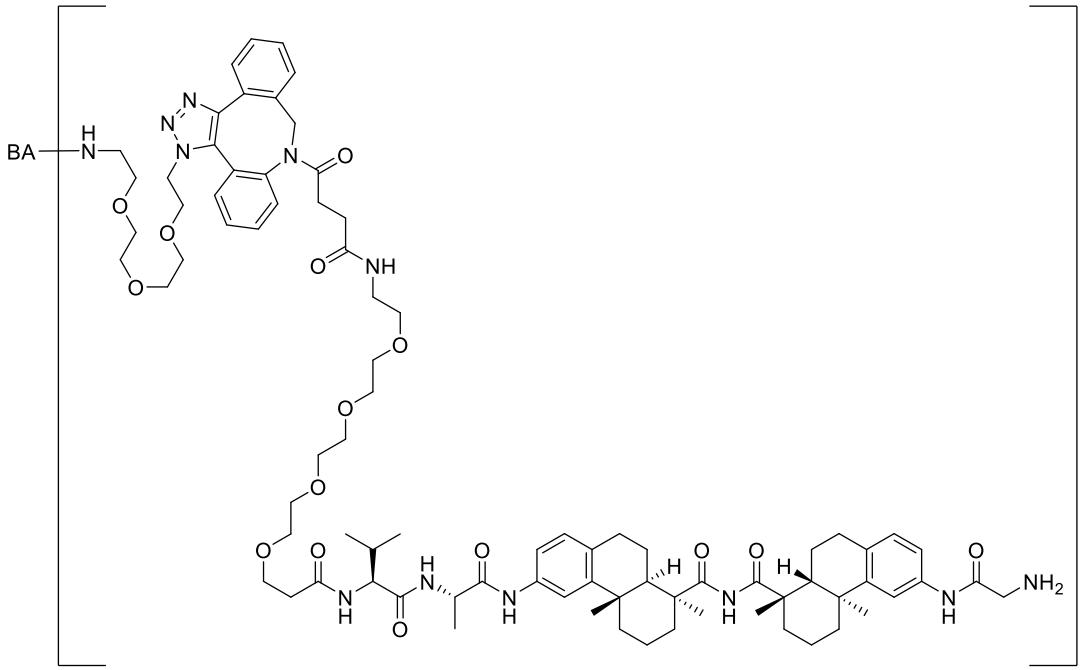

BA
k


BA
k

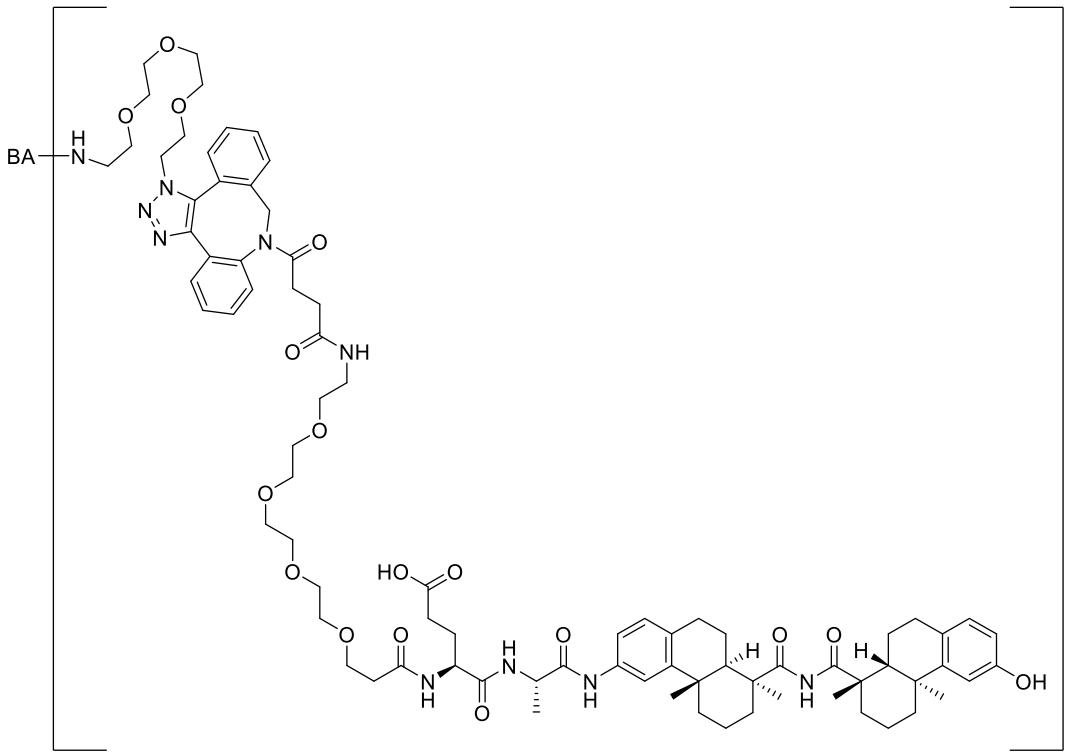

BA
k



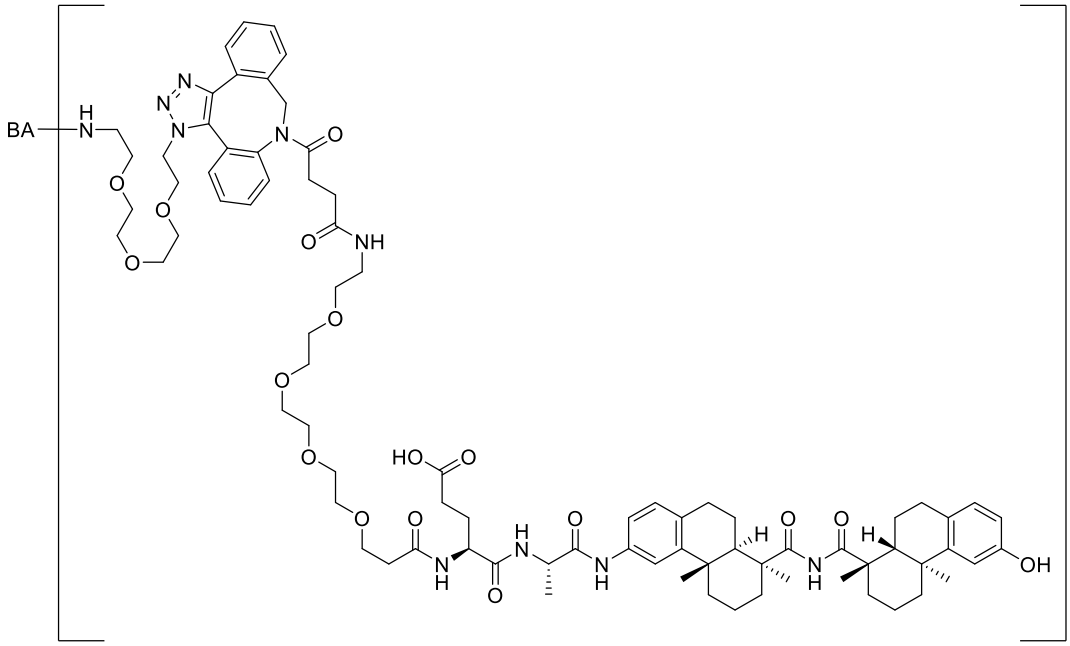
k ;



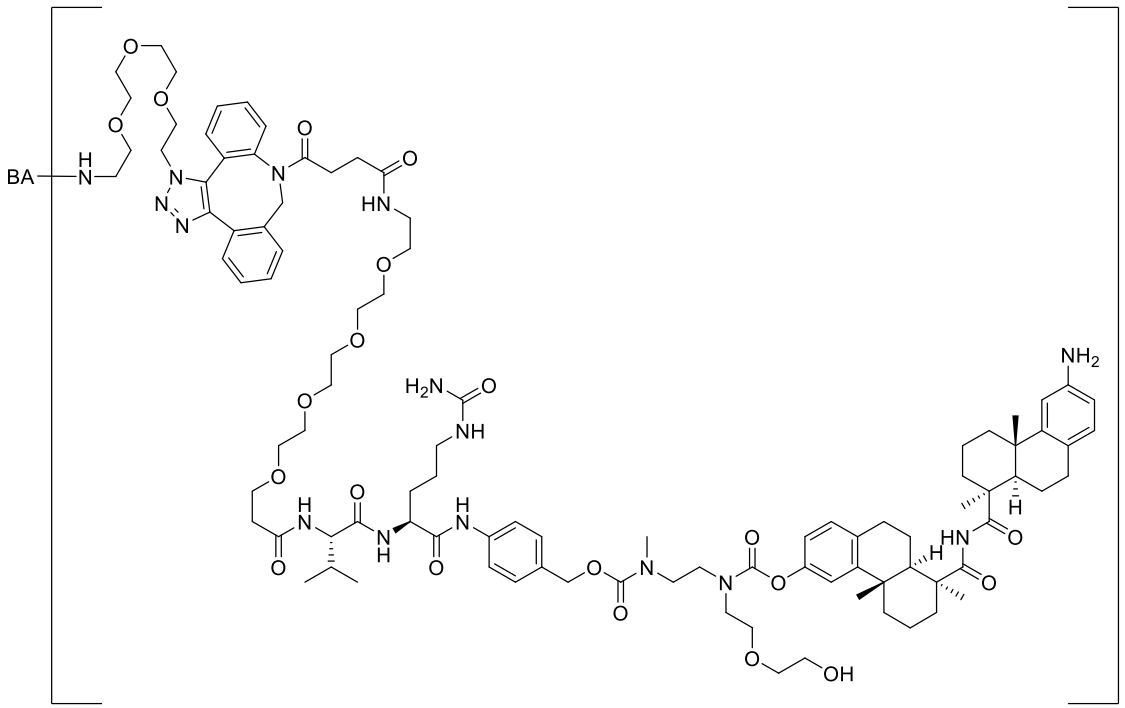
k ;



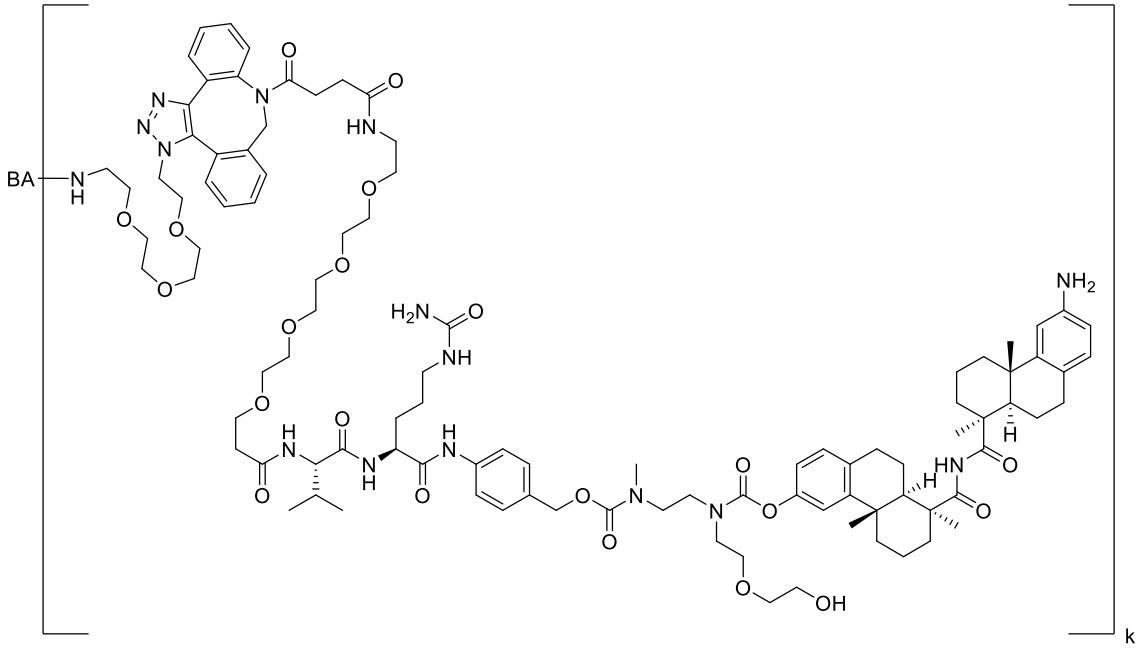
k ;



k ;



; and



wherein **BA** is an antibody or antigen binding fragment thereof; and **k** is an integer from one to thirty.