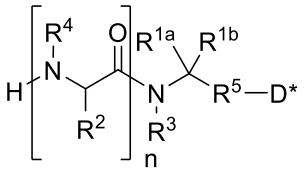
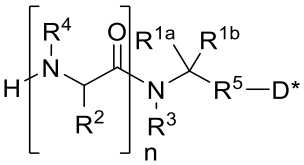
glucocorticoid receptor signalling; and/or dyslipidemia, a metabolic disease, inflammation, or a neurodegenerative disease, in a subject.

[0009] In one example, provided are compounds having the structure of Formula I:



or a pharmaceutically acceptable salt thereof, wherein **R^{1a}** and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; **R^{2}** is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^{2}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 4-, 5-, or 6-membered heterocyclyl; **R^{3}** is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^{3}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{1a}** or **R^{2}** to form the 3-, 4-, 5-, 6-, 7-, or 8 membered heterocyclyl; **R^{4}** is hydrogen or alkyl; **R^{5}** is oxygen, N**R^{6}**, or sulfur; **R^{6}** is hydrogen or alkyl; **D*** is acyl, or a residue of a biologically active compound comprising hydroxyl, amino, or thiol; and **n** is zero, one, two, three, four, five, or six.

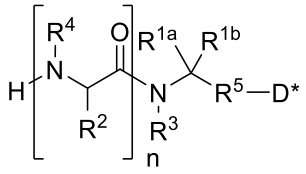
[0009a] In one aspect, provided is a compound having the following structure



or a pharmaceutically acceptable salt thereof, wherein **R^{1a}** and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; **R^{2}** is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^{2}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 4-, 5-, or 6-membered heterocyclyl; **R^{3}** is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^{3}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{1a}** or **R^{2}** to form the 3-, 4-, 5-, 6-, 7-, or 8-

membered heterocyclyl; **R^4** is hydrogen or alkyl; **R^5** is oxygen, N**R^6**, or sulfur within D*; **R^6** is hydrogen or alkyl; **D*** is a residue of an anti-inflammatory biologically active compound comprising a hydroxyl, amino, or thiol for conjugation to -CR^{1a}R^{1b}-, wherein the residue is a steroid or an LXR agonist; and **n** is zero, one, two, three, four, five, or six.

[0010] In one example, provided are compounds having the structure of Formula I:

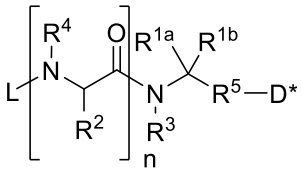


(I)

or a pharmaceutically acceptable salt thereof, wherein **R^{1a}** and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^3** to form a 4-, 5-, or 6-membered heterocyclyl; **R^2** is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^2** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^3** to form a 4-, 5-, or 6-membered heterocyclyl; **R^3** is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^3** is alkylene or heteroalkylene, the alkylene or heteroalkylene is

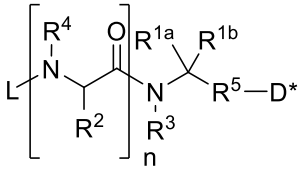
further bonded to **R^{1a}** or **R^{2}** to form the 4-, 5-, or 6-membered heterocyclyl; **R^{4}** is hydrogen or alkyl; **R^{5}** is oxygen, N**R^{6}**, or sulfur; **R^{6}** is hydrogen or alkyl; **D*** is acyl, or a residue of a biologically active compound comprising hydroxyl, amino, or thiol; and **n** is zero, one, two, three, four, or five.

[0011] In another example, provided are linker-payload compounds having the structure of Formula II:



or a pharmaceutically acceptable salt thereof, wherein **L** is a linker comprising a moiety reactive with an antibody or an antigen binding fragment thereof; **R^{1a}** and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or hetereoalkylene is further bonded to **R^{3}** to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; **R^{2}** is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^{2}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 4-, 5-, or 6-membered heterocyclyl; **R^{3}** is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^{3}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{1a}** or **R^{2}** to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; **R^{4}** is hydrogen or alkyl; **R^{5}** is oxygen, N**R^{6}**, or sulfur; **R^{6}** is hydrogen or alkyl; **D*** is acyl, or a residue of a biologically active compound comprising hydroxyl, amino, or thiol; and **n** is zero, one, two, three, four, five, or six.

[0012] In another example, provided are linker-payloads having the structure of Formula II:

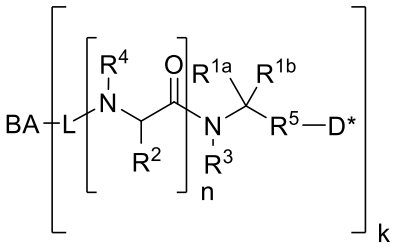


(II)

or a pharmaceutically acceptable salt thereof, wherein **L** is a linker comprising a moiety reactive with an antibody or an antigen binding fragment thereof; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or hetereoalkylene is further bonded to $\mathbf{R^{3}}$ to

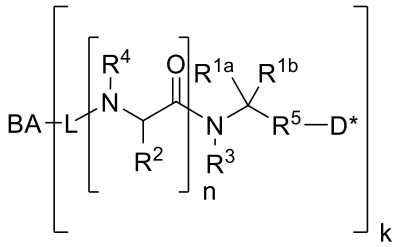
wherein **L** is a linker; **BA** is a binding agent; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^2}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^2}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^3}$ is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when $\mathbf{R^3}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^{1a}}$ or $\mathbf{R^2}$ to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^4}$ is hydrogen or alkyl; $\mathbf{R^5}$ is oxygen, N$\mathbf{R^6}$, or sulfur; $\mathbf{R^6}$ is hydrogen or alkyl; **D*** is a residue of an anti-inflammatory biologically active compound comprising hydroxyl, amino, or thiol; **n** is zero, one, two, three, four, five, or six; and **k** is an integer from one to thirty.

[0015] In another example, provided are compounds having the structure of Formula III:



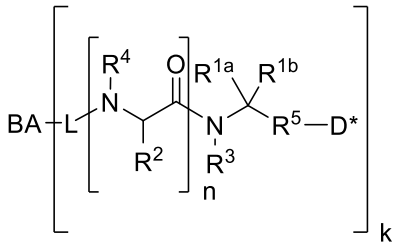
wherein **L** is a linker comprising PAB or PABC; **BA** is a binding agent; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^2}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^2}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^3}$ is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when $\mathbf{R^3}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^{1a}}$ or $\mathbf{R^2}$ to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^4}$ is hydrogen or alkyl; $\mathbf{R^5}$ is oxygen, N$\mathbf{R^6}$, or sulfur; $\mathbf{R^6}$ is hydrogen or alkyl; **D*** is a residue of a biologically active compound comprising hydroxyl, amino, or thiol; **n** is zero, one, two, three, four, five, or six; and **k** is an integer from one to thirty.

[0016] In another example, provided are compounds having the structure of Formula III:



wherein **L** is a linker; **BA** is a binding agent; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^2}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^2}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^3}$ is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when $\mathbf{R^3}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^{1a}}$ or $\mathbf{R^2}$ to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^4}$ is hydrogen or alkyl; $\mathbf{R^5}$ is oxygen, N$\mathbf{R^6}$, or sulfur; $\mathbf{R^6}$ is hydrogen or alkyl; **D*** is a residue of a biologically active compound comprising hydroxyl, amino, or thiol; **n** is zero, one, two, three, four, five, or six; wherein conjugation of **L** to **BA** is selected from the group consisting of a click chemistry residue, an amide residue, and a residue comprising two cysteine residues of a single **BA** that are chemically bonded to **L**; and **k** is an integer from one to thirty.

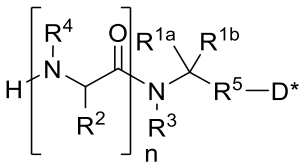
[0017] In another example, provided are compounds having the structure of Formula III:

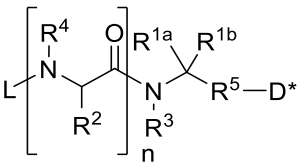


(III)

wherein **L** is a linker; **BA** is a binding agent; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^2}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^2}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^3}$ is hydrogen, alkyl, alkylene, or heteroalkylene,

[0023a] In another aspect, the present disclosure refers to an antibody-drug conjugate comprising an antibody, or an antigen binding fragment thereof, where said antibody or antigen binding fragment thereof is conjugated to a compound having the following structures



or


or a pharmaceutically acceptable salt thereof, wherein **L** is a linker comprising a moiety reactive with an antibody or an antigen binding fragment thereof; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^2}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^2}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^3}$ is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when $\mathbf{R^3}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^{1a}}$ or $\mathbf{R^2}$ to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl; $\mathbf{R^4}$ is hydrogen or alkyl; $\mathbf{R^5}$ is oxygen, N$\mathbf{R^6}$, or sulfur within D*; $\mathbf{R^6}$ is hydrogen or alkyl; **D*** is a residue of an anti-inflammatory biologically active compound comprising a hydroxyl, amino, or thiol for conjugation to -$CR^{1a}R^{1b}$- wherein the residue is a steroid or an LXR agonist; and **n** is zero, one, two, three, four, five, or six.

[0023b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising the compound as disclosed herein, and a pharmaceutically acceptable excipient, carrier, or diluent.

[0023c] In another aspect, the present disclosure refers to compound as disclosed herein or the pharmaceutical composition as disclosed herein for use in therapy.

[0023d] In another aspect, the present disclosure refers to a use of compound as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling in a subject comprising that the compound is to be administered to the subject wherein the disease, disorder, or condition is metabolic, inflammatory, or neurodegenerative.

[0023e] In another aspect, the present disclosure refers to a use of the compound as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for

treating dyslipidemia, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.

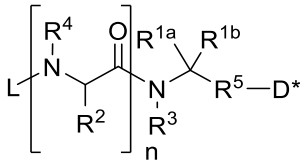
[0023f] In another aspect, the present disclosure refers to a use of the compound as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating dyslipidemia in a subject.

[0023g] In another aspect, the present disclosure refers to a use of the compound as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a metabolic disease in a subject.

[0023h] In another aspect, the present disclosure refers to a use of the compound as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating in a subject.

[0023i] In another aspect, the present disclosure refers to a use of the compound as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a neurodegenerative disease in a subject.

[0023j] In another aspect, the present disclosure refers to a method of preparing an antibody-drug conjugate comprising contacting a binding agent with a compound of the formula:

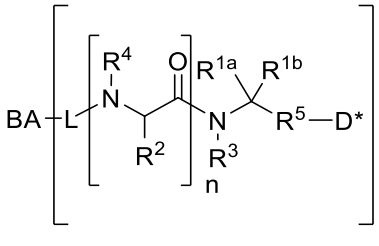


or a pharmaceutically acceptable salt thereof, wherein **L** is a linker comprising a moiety reactive with an antibody or an antigen binding fragment thereof; $\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or hetereoalkylene is further bonded to $\mathbf{R^{3}}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^{2}}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^{2}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^{3}}$ to form a 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^{3}}$ is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{3}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^{1a}}$ or $\mathbf{R^{2}}$ to form the 4-, 5-, or 6-membered heterocyclyl; $\mathbf{R^{4}}$ is hydrogen or alkyl; $\mathbf{R^{5}}$ is oxygen, N$\mathbf{R^{6}}$, or sulfur within D*; $\mathbf{R^{6}}$ is hydrogen or alkyl; **D*** is a residue of an anti-inflammatory biologically active compound comprising a

hydroxyl, amino, or thiol for conjugation to -$CR^{1a}R^{1b}$- wherein the residue is a steroid or an LXR agonist; and **n** is zero, one, two, three, four, five, or six.

WHAT IS CLAIMED IS:

1. A compound having the following structure



wherein

L is a linker;

BA is a binding agent;

R^{1a} and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl;

R^{2} is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^{2}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{3}** to form a 4-, 5-, or 6-membered heterocyclyl;

R^{3} is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^{3}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{1a}** or **R^{2}** to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl;

R^{4} is hydrogen or alkyl;

R^{5} is oxygen, N**R^{6}**, or sulfur within D*;

R^{6} is hydrogen or alkyl;

D* is a residue of an anti-inflammatory biologically active compound comprising a hydroxyl, amino, or thiol for conjugation to -$CR^{1a}R^{1b}$-, wherein the residue is a steroid or an LXR agonist;

n is zero, one, two, three, four, five, or six; and

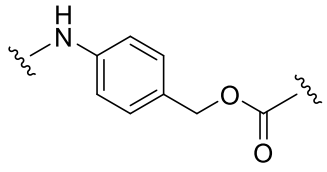
k is an integer from one to thirty.

2. The compound of claim 1, wherein the anti-inflammatory biologically active compound is a steroid or a residue thereof.

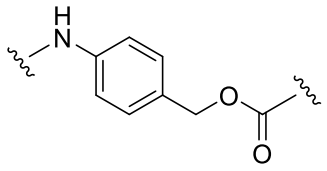
3. The compound of claim 1, wherein the anti-inflammatory biologically active compound is an LXR agonist or a residue thereof.

4. The compound of claim 1, wherein **D*** is a residue of a steroid comprising a hydroxyl or amino for conjugation to -$CR^{1a}R^{1b}$-.

5. The compound of claim 1, wherein

L is a linker comprising 

.

6. The compound of claim 5, wherein **L** is a linker comprising 

, and $\mathbf{R^2}$ is hydrogen.

7. The compound of claim 1wherein conjugation of **L** to **BA** is selected from the group consisting of a click chemistry residue, an amide residue, and a residue comprising two cysteine residues of a single **BA** that are chemically bonded to **L**.

8. The compound of claim 1, wherein

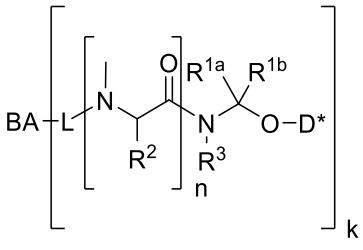
$\mathbf{R^{1a}}$ and $\mathbf{R^{1b}}$ are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when $\mathbf{R^{1a}}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl;

$\mathbf{R^2}$ is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when $\mathbf{R^2}$ is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to $\mathbf{R^3}$ to form a 4-, 5-, or 6-membered heterocyclyl;

R[3] is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R[3]** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R[1a]** or **R[2]** to form the 4-, 5-, or 6-membered heterocyclyl; and

D* is a residue of an anti-inflammatory biologically active compound comprising hydroxyl, amino, or thiol for conjugation to -$CR^{1a}R^{1b}$-, wherein the residue is a steroid or an LXR agonist.

9. The compound of claim 8 having the structure



wherein

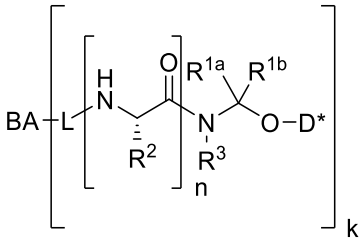
R[1a] and **R[1b]** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, or alkylene, wherein when **R[1a]** is alkylene, the alkylene is further bonded to **R[3]** to form a 4-, 5-, or 6-membered heterocyclyl;

R[2] is hydrogen or an amino acid side chain;

R[3] is hydrogen, alkyl, or alkylene, wherein when **R[3]** is alkylene, the alkylene is further bonded to **R[1a]** to form the 4-, 5-, or 6-membered heterocyclyl; and

D* is a residue of an anti-inflammatory biologically active compound comprising hydroxyl for conjugation to -$CR^{1a}R^{1b}$-, wherein the residue is a steroid or an LXR agonist.

10. The compound of claim 8 having the following structure

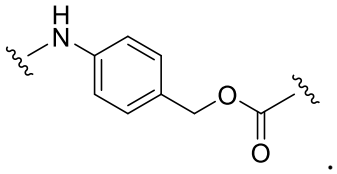


wherein

R[1a] and **R[1b]** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, or alkylene, wherein when **R[1a]** is alkylene, the alkylene is further bonded to **R[3]** to form a 4-, 5-, or 6-membered heterocyclyl;

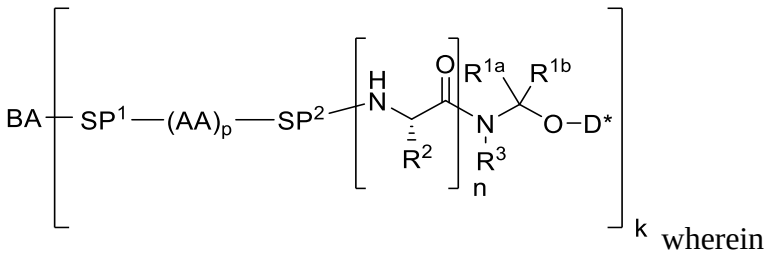
R^2 is hydrogen or an amino acid side chain;
R^3 is hydrogen, alkyl, or alkylene, wherein when **R^3** is alkylene, the alkylene is further bonded to **R^{1a}** to form the 4-, 5-, or 6-membered heterocyclyl; and
D* is a residue of an anti-inflammatory biologically active compound comprising a hydroxyl for conjugation to -$CR^{1a}R^{1b}$-, wherein the residue is a steroid or an LXR agonist.

11. The compound of any one of claims 1-4 and 7-10, wherein the linker comprises



.

12. The compound of claim 8, wherein the compound is

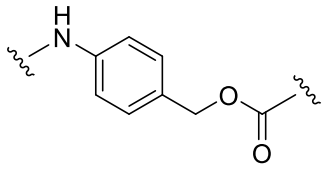


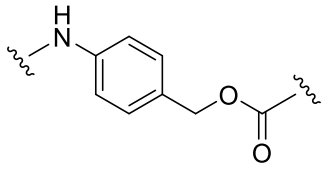
wherein
SP^1 and **SP^2**, when present, are spacer groups wherein **SP^1** further comprises a moiety reactive with an antibody or an antigen binding fragment thereof;
each **AA** is an amino acid; and
p is an integer from 1 to 10.

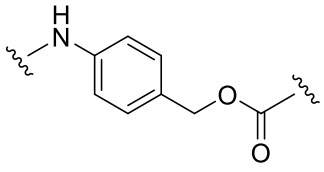
13. The compound of claim 12, wherein **SP^1** comprises a reactive group that comprises an alkyne.

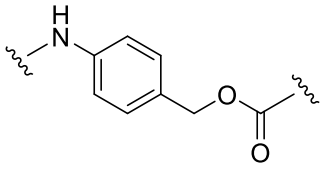
14. The compound of claim 13, wherein the alkyne is capable of participating in a 1,3-cycloaddition reaction.

15. The compound of claim 14, wherein the alkyne is capable of participating in a 1,3-cycloaddition reaction with the binding agent, wherein the binding agent is an azido-functionalized binding agent.

16. The compound of claim 12, wherein **SP²** comprises .

17. The compound of claim 12, wherein **SP²** comprises , and **R²** is hydrogen or alkyl.

18. The compound of claim 15, wherein the alkyne is capable of participating in a 1,3-cycloaddition reaction with the binding agent, the binding agent is an azido-functionalized binding agent, and **SP²** comprises .

19. The compound of claim 15, wherein the alkyne is capable of participating in a 1,3-cycloaddition reaction with the binding agent, the binding agent is an azido-functionalized binding agent, **SP²** comprises , and **R²** is hydrogen or alkyl.

20. The compound of claim 12, wherein the binding agent is an antibody modified with a primary amine compound according to the Formula H_2N-**LL**-**X**, wherein **LL** is a divalent linker selected from the group consisting of

a divalent polyethylene glycol (PEG) group;

–$(CH_2)_{\mathbf{n}}$–;

–$(CH_2CH_2O)_{\mathbf{n}}$-$(CH_2)_p$–;

–$(CH_2)_{\mathbf{n}}$-N(H)C(O)-$(CH_2)_{\mathbf{m}}$–;

–$(CH_2CH_2O)_{\mathbf{n}}$-N(H)C(O)-$(CH_2CH_2O)_{\mathbf{m}}$-$(CH_2)_{\mathbf{p}}$–;

–$(CH_2)_{\mathbf{n}}$-C(O)N(H)-$(CH_2)_{\mathbf{m}}$–;

–$(CH_2CH_2O)_{\mathbf{n}}$-C(O)N(H)-$(CH_2CH_2O)_{\mathbf{m}}$-$(CH_2)_{\mathbf{p}}$–;

–$(CH_2)_{\mathbf{n}}$-N(H)C(O)-$(CH_2CH_2O)_{\mathbf{m}}$-$(CH_2)_{\mathbf{p}}$–;

–$(CH_2CH_2O)_{\mathbf{n}}$-N(H)C(O)-$(CH_2)_{\mathbf{m}}$–;

–$(CH_2)_{\mathbf{n}}$-C(O)N(H)-$(CH_2CH_2O)_{\mathbf{m}}$-$(CH_2)_{\mathbf{p}}$–; and

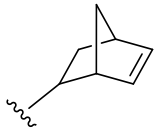
–$(CH_2CH_2O)_{\mathbf{n}}$-C(O)N(H)-$(CH_2)_{\mathbf{m}}$–,

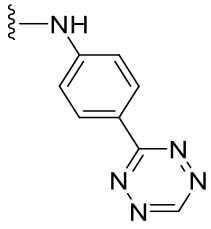
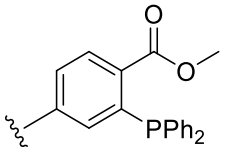
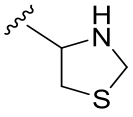
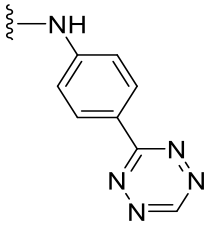
wherein

n is an integer selected from 1 to 12;

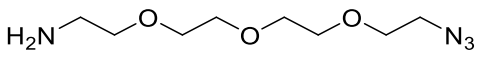
m is an integer selected from 0 to 12;

p is an integer selected from 0 to 2; and

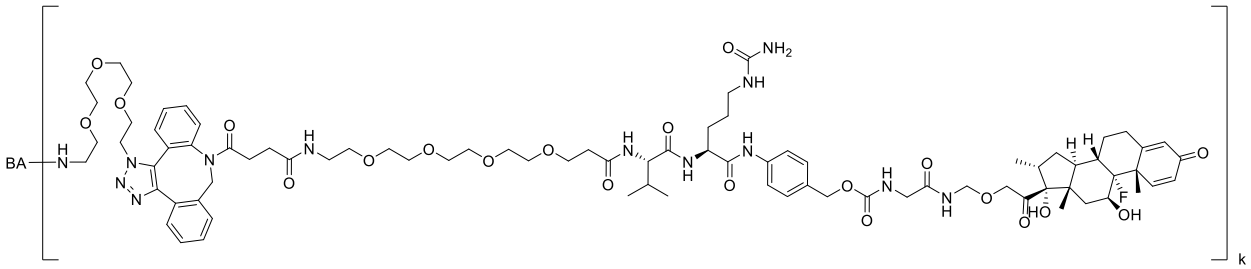
X is selected from the group consisting of –SH, $–N_3$, –C≡CH, –C(O)H, tetrazole, ,

, , , and .

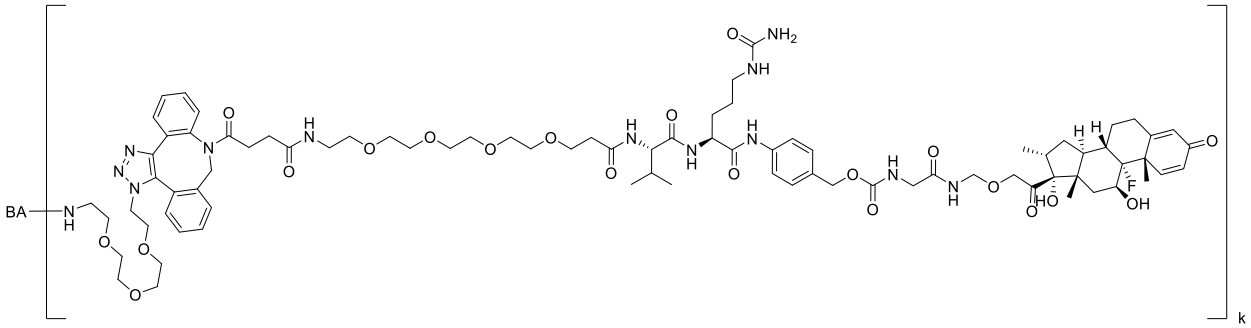
21. The compound of claim 20, wherein the binding agent is an antibody modified with a primary amine having the following structure

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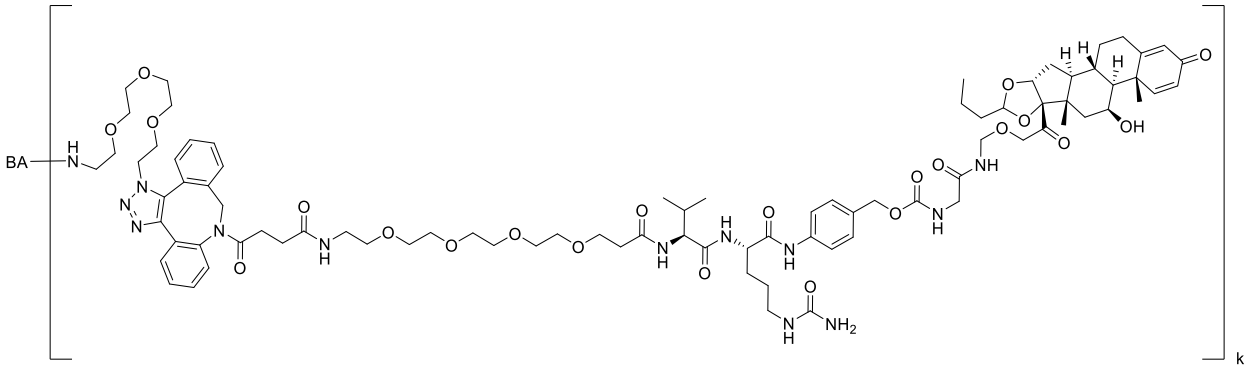
22. The compound of claim 21, wherein the compound is selected from the group consisting of


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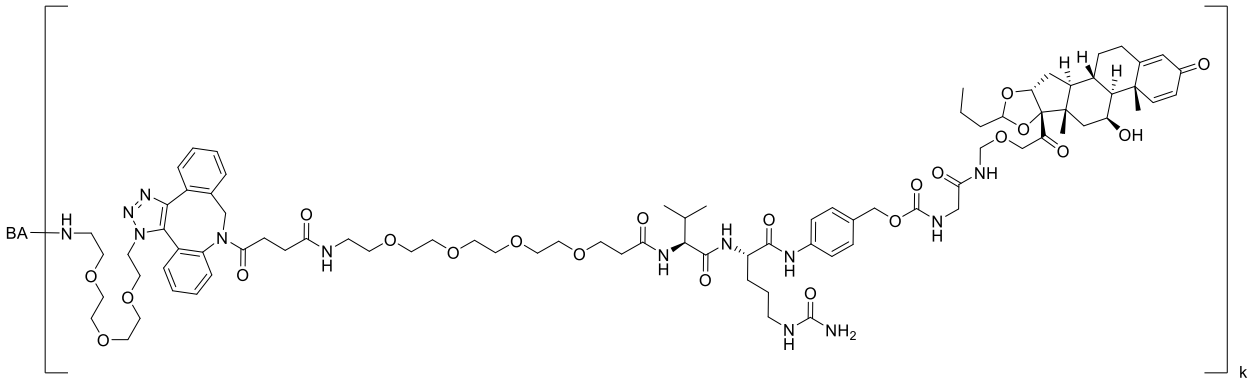
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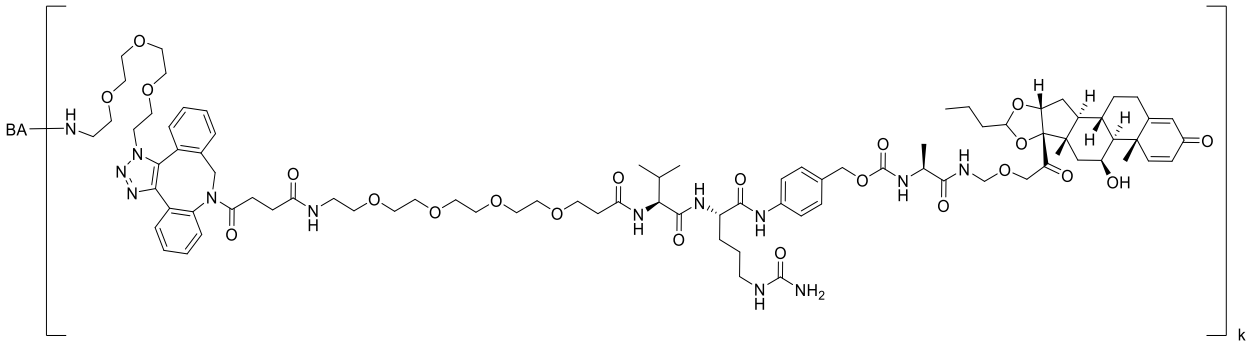
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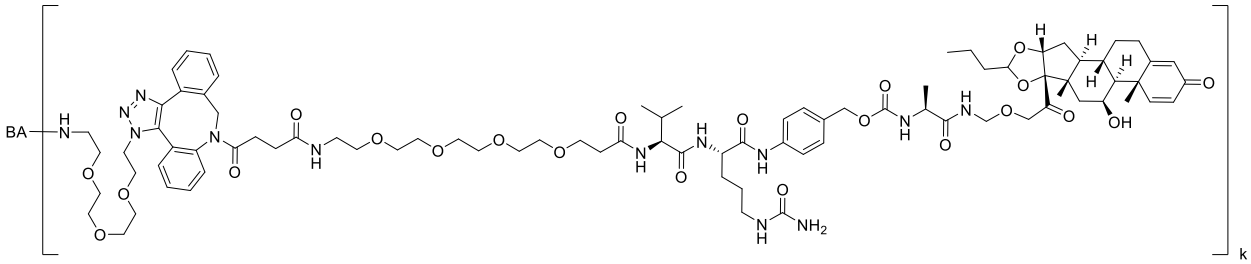
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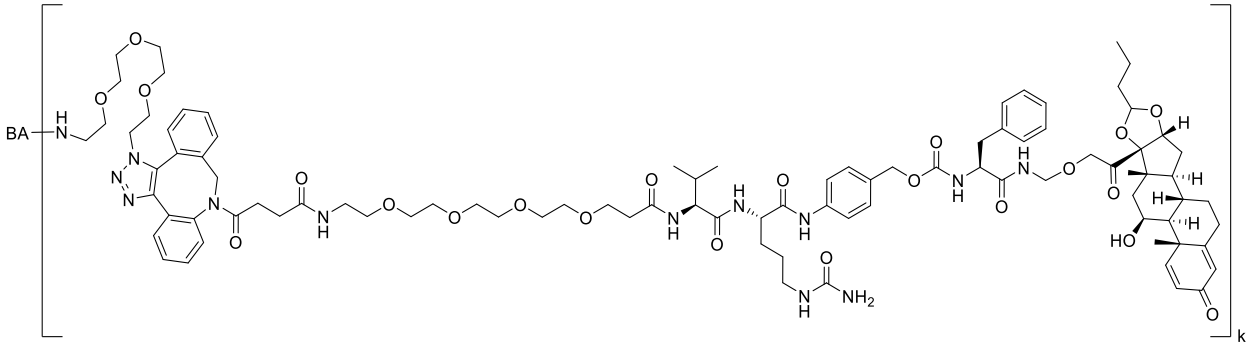
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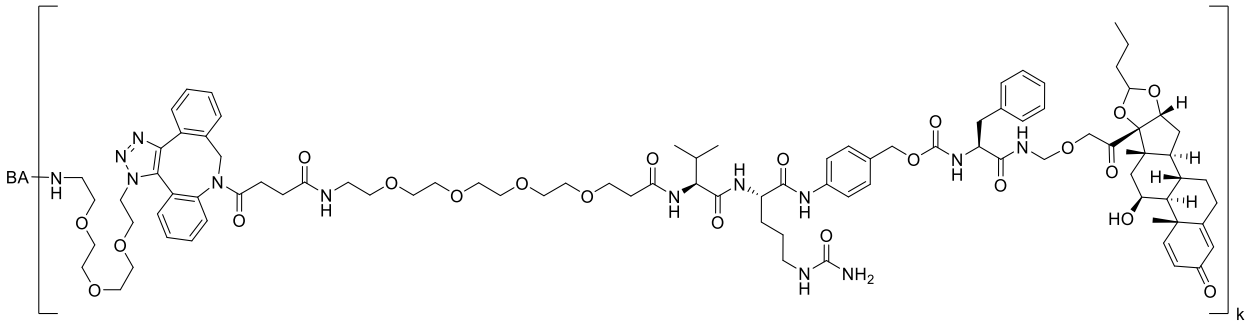
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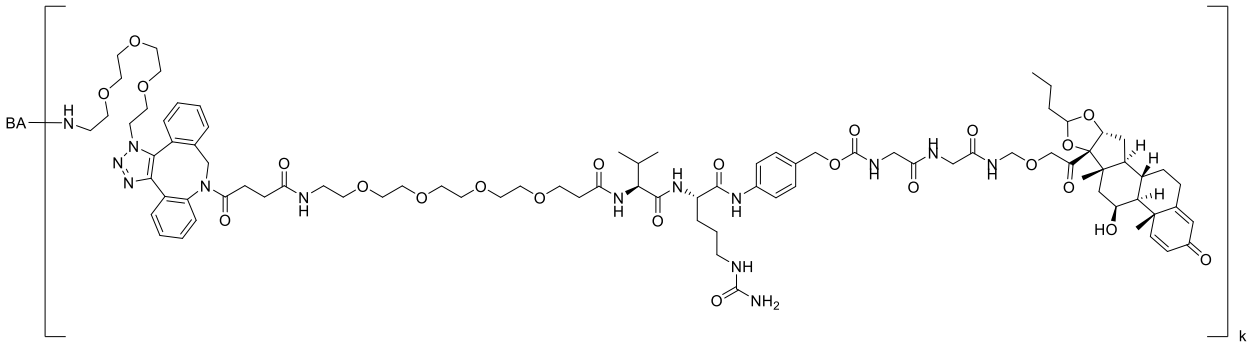
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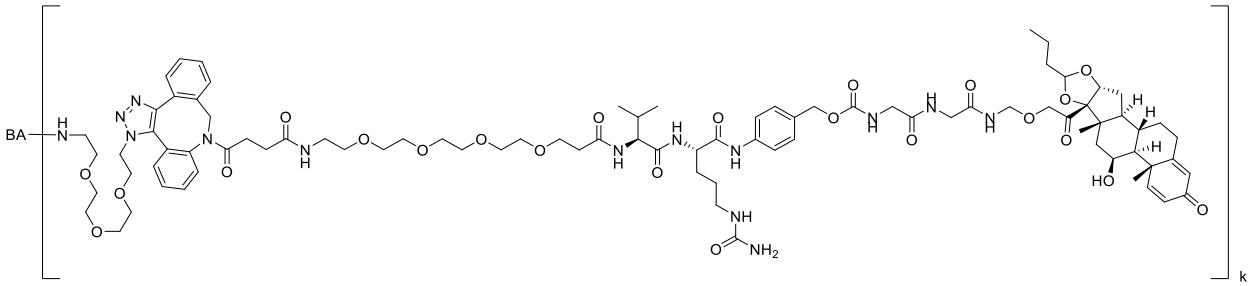
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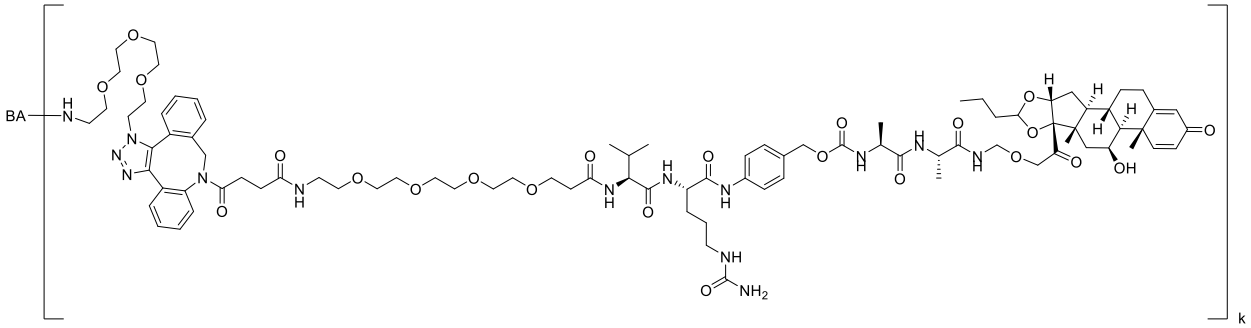
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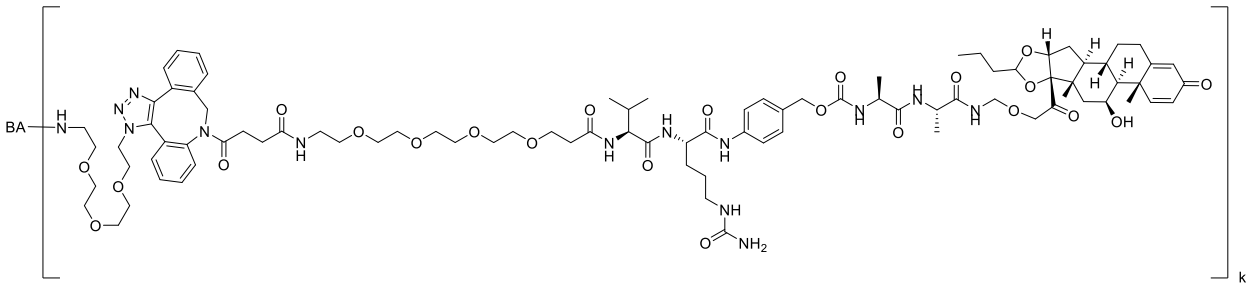
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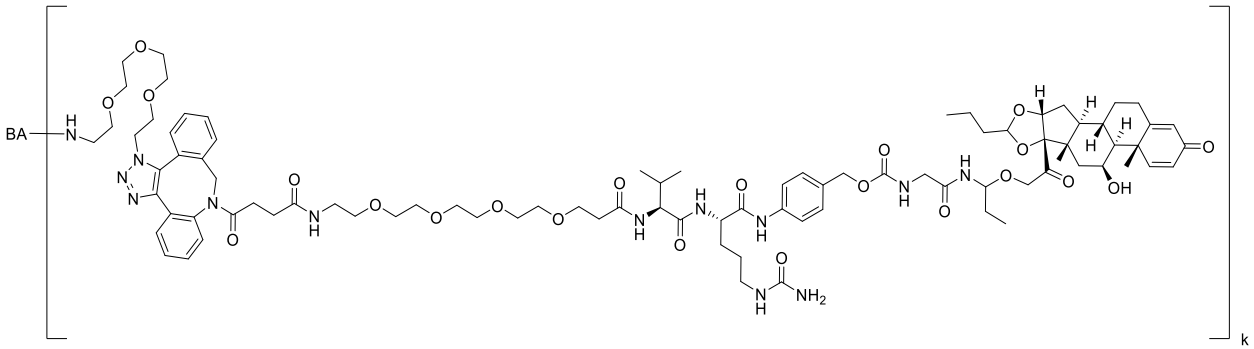
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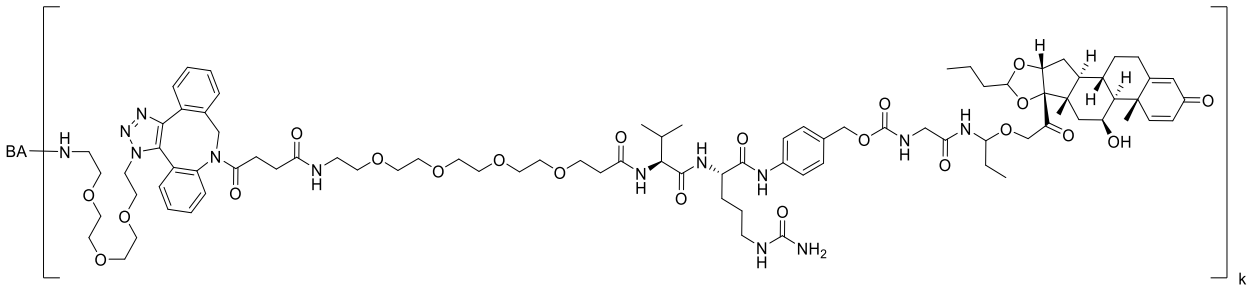
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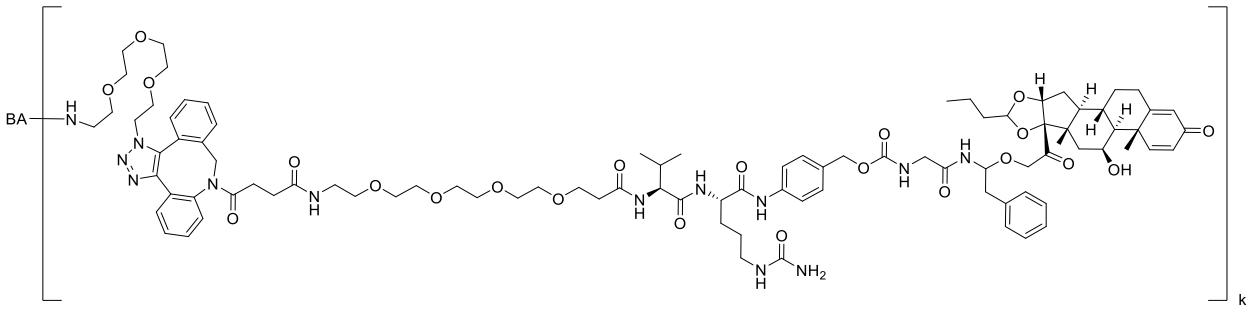
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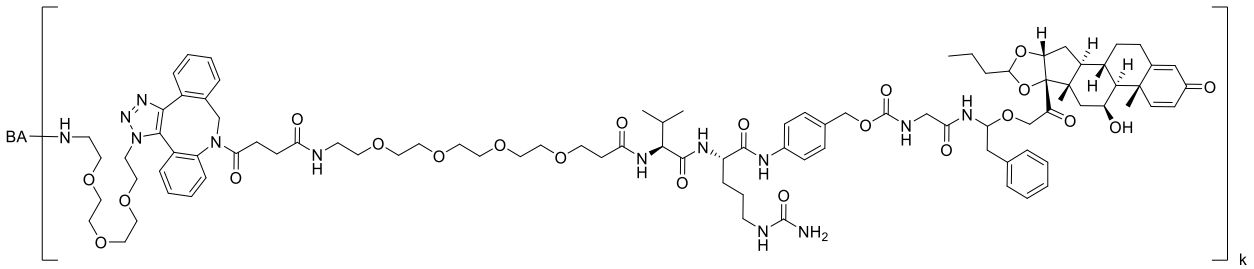
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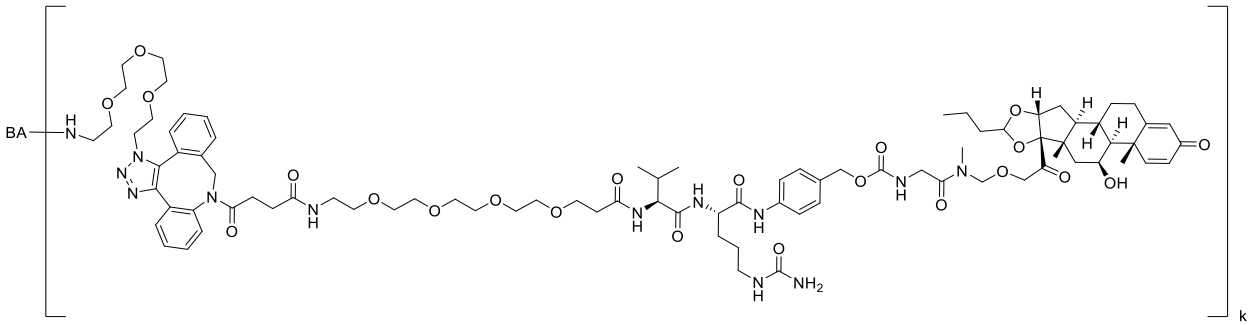
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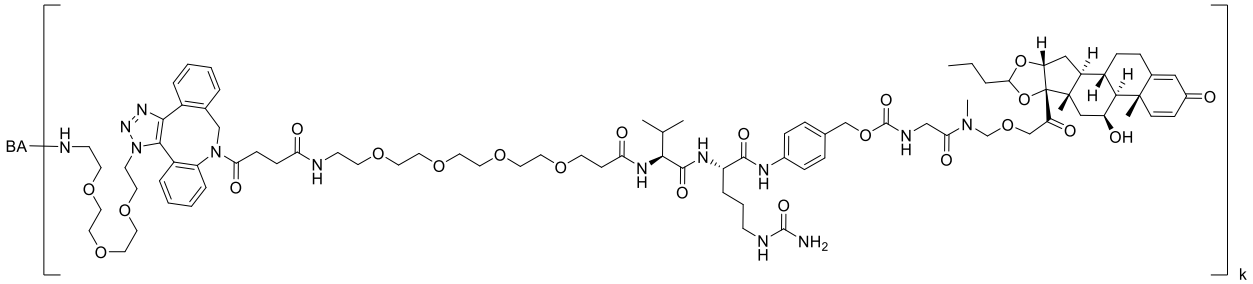
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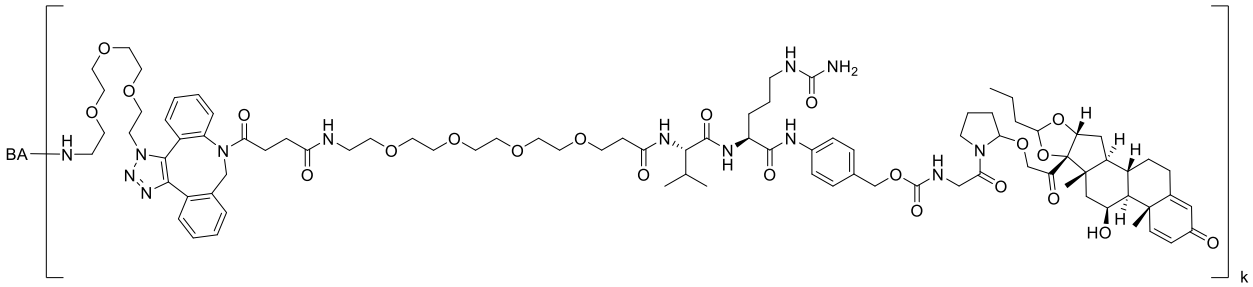
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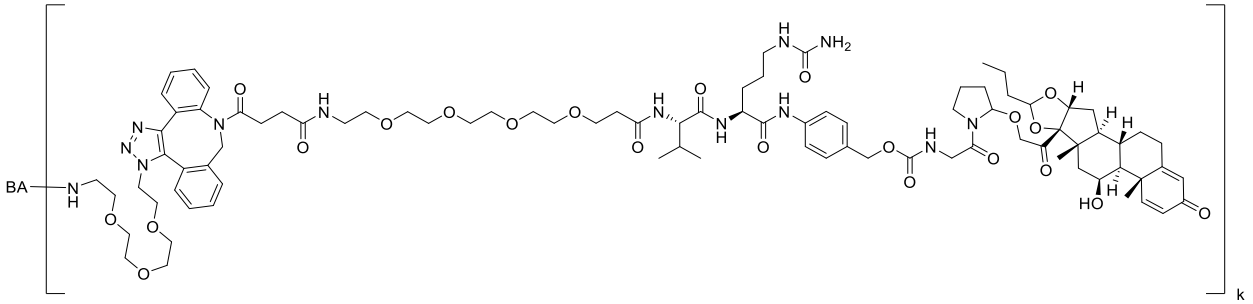
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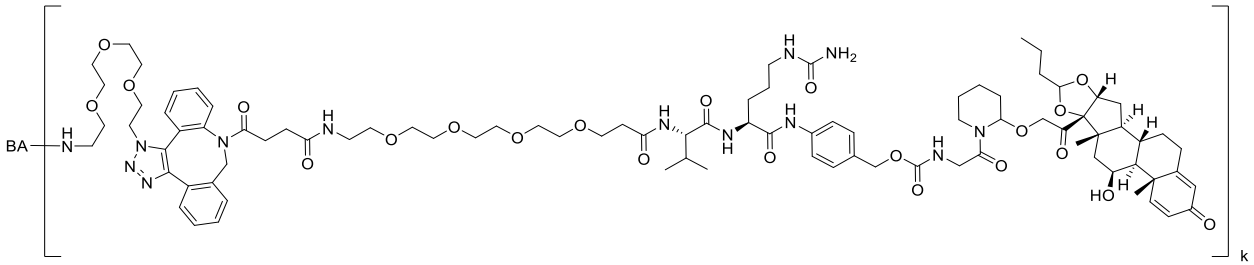
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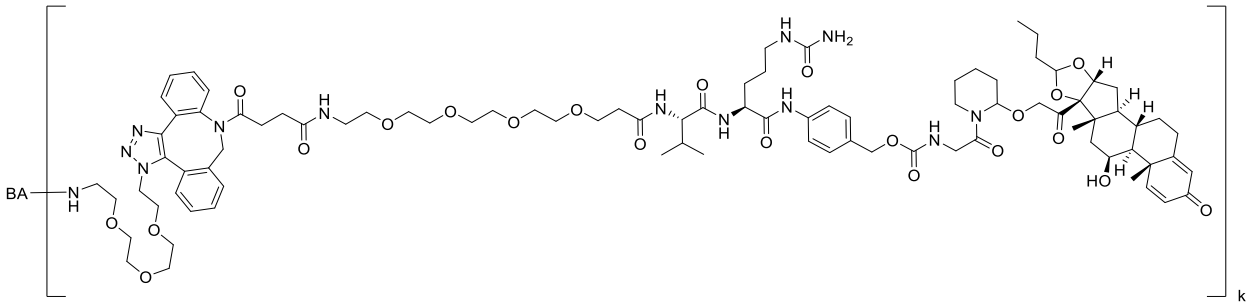
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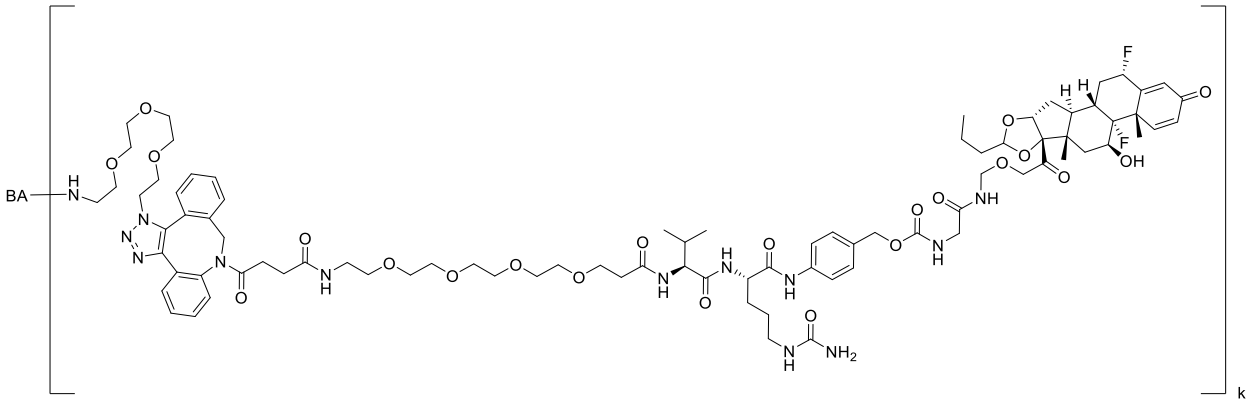
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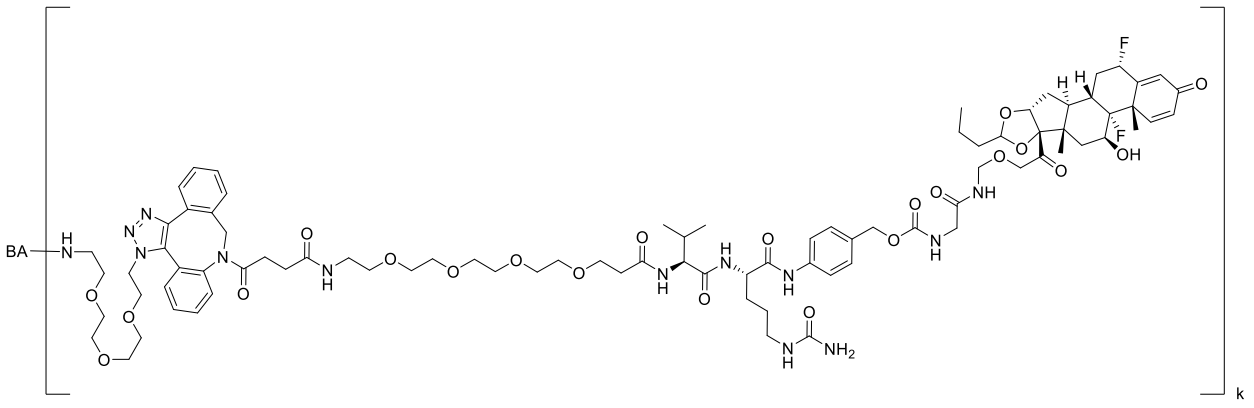
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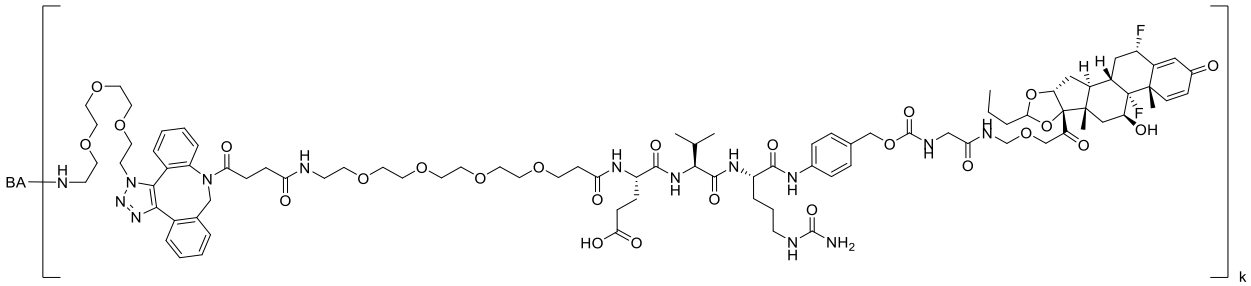
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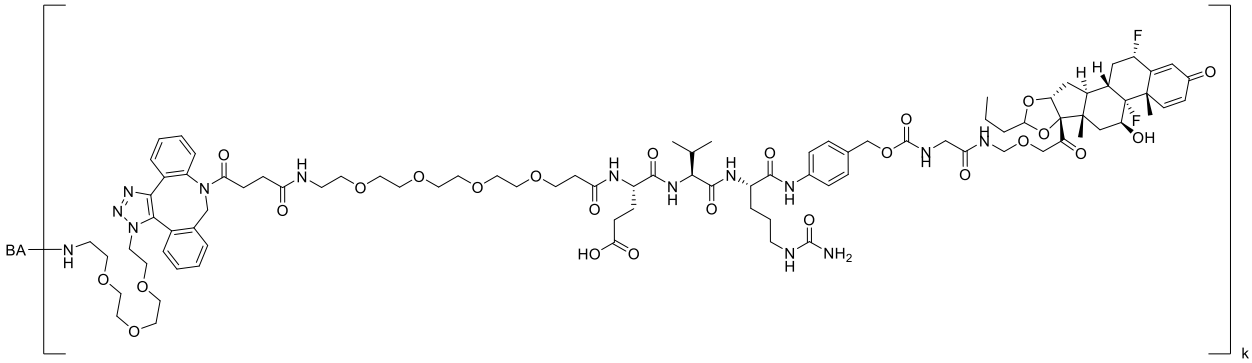
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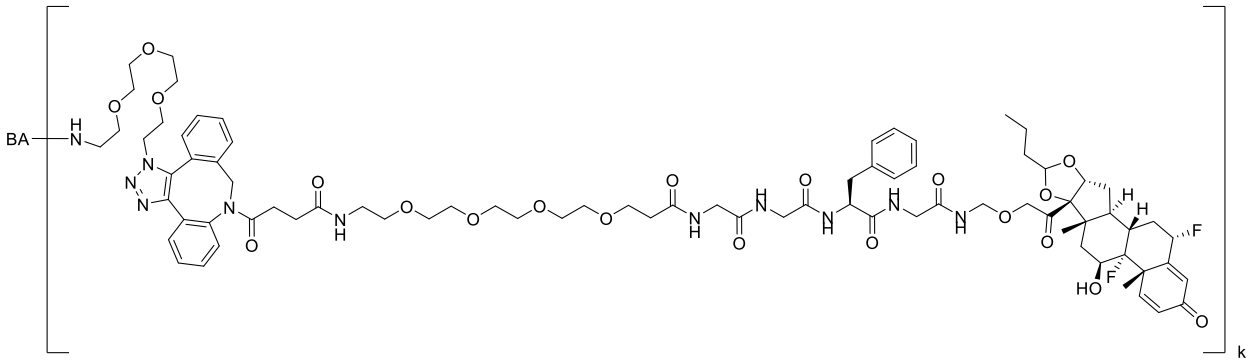
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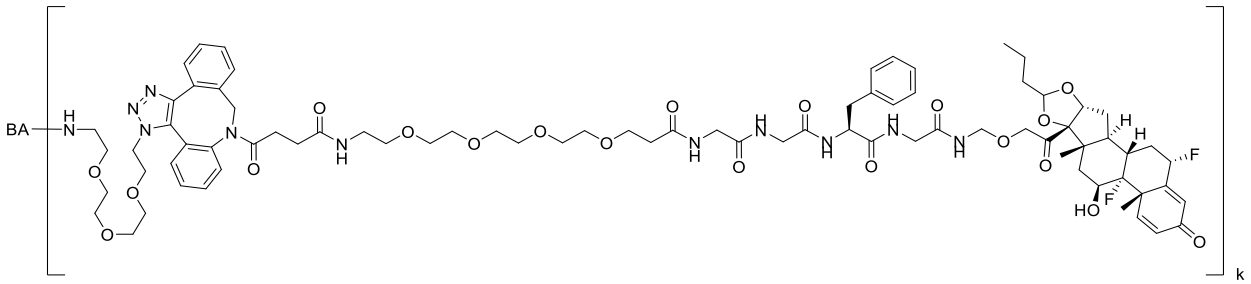
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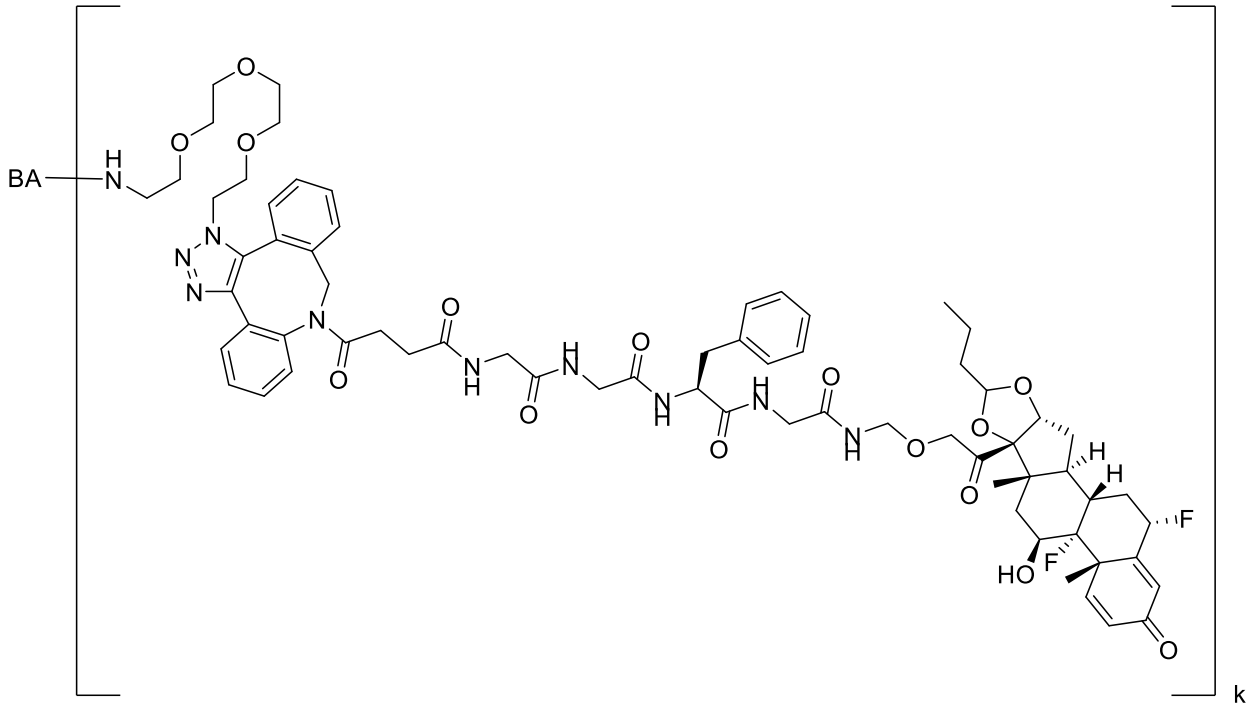
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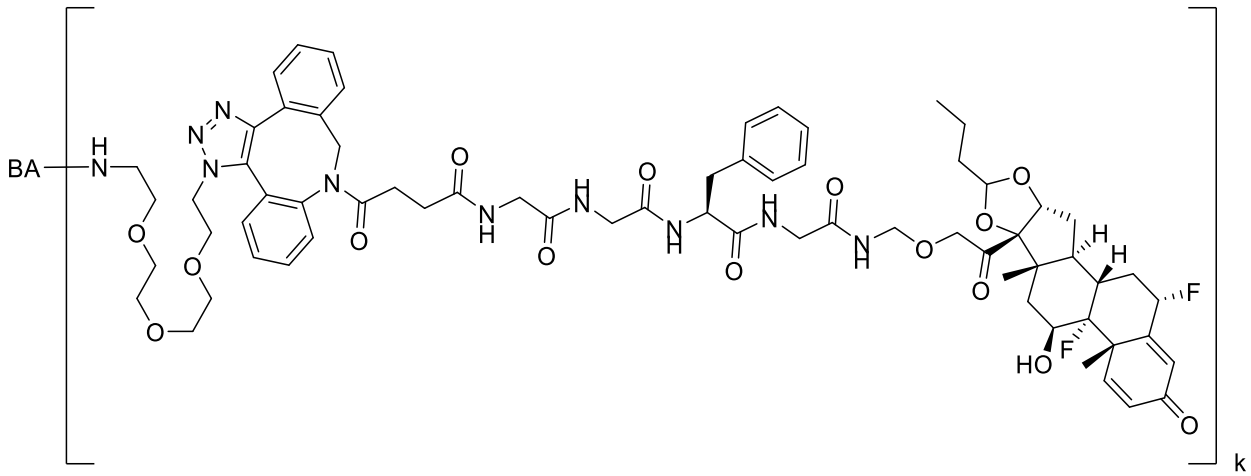
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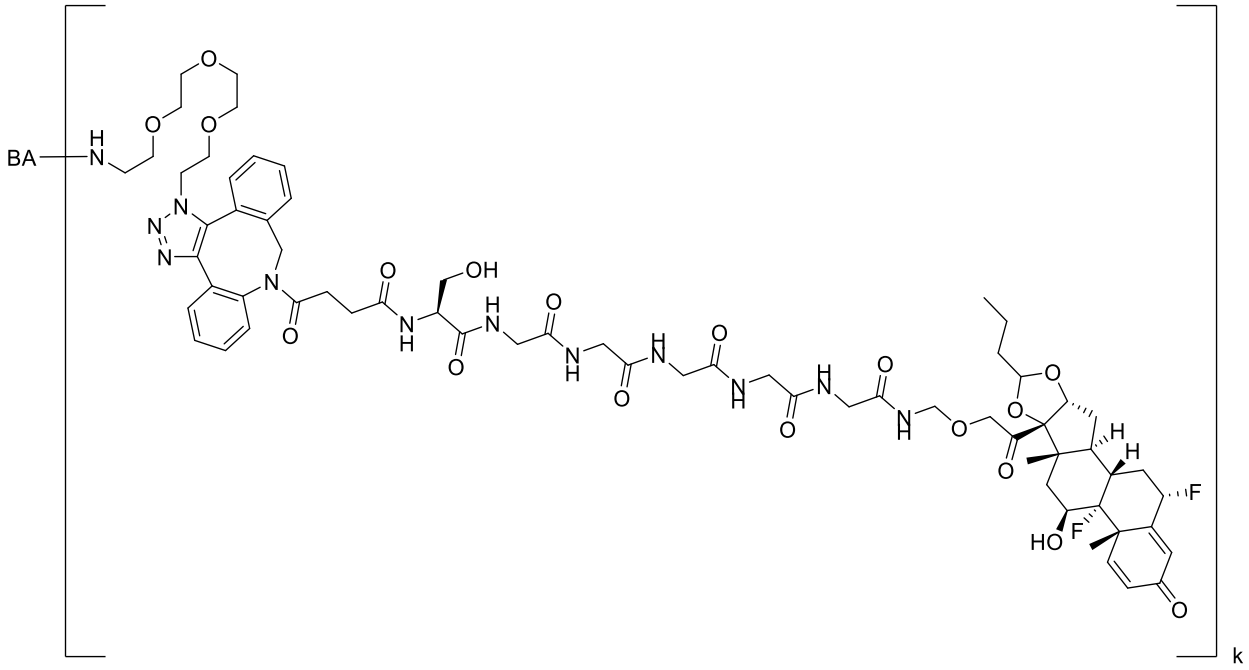
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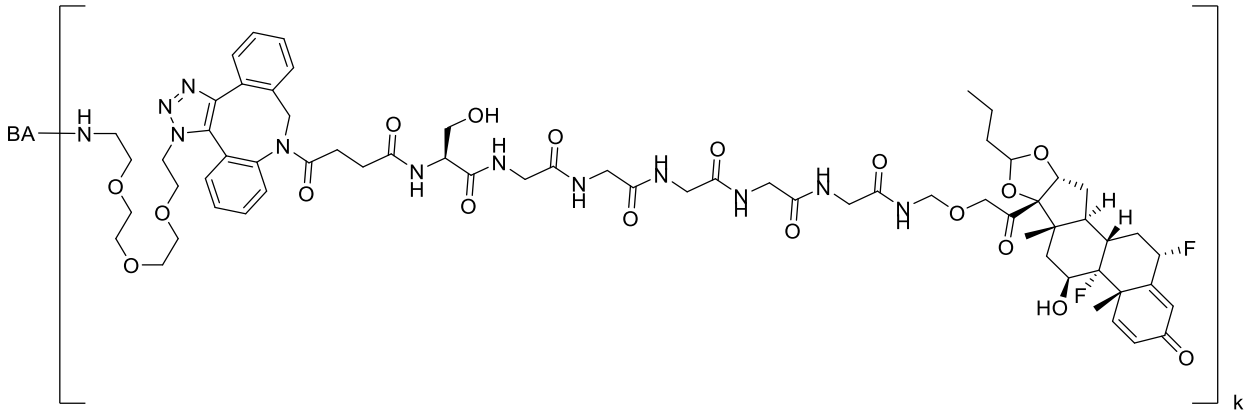
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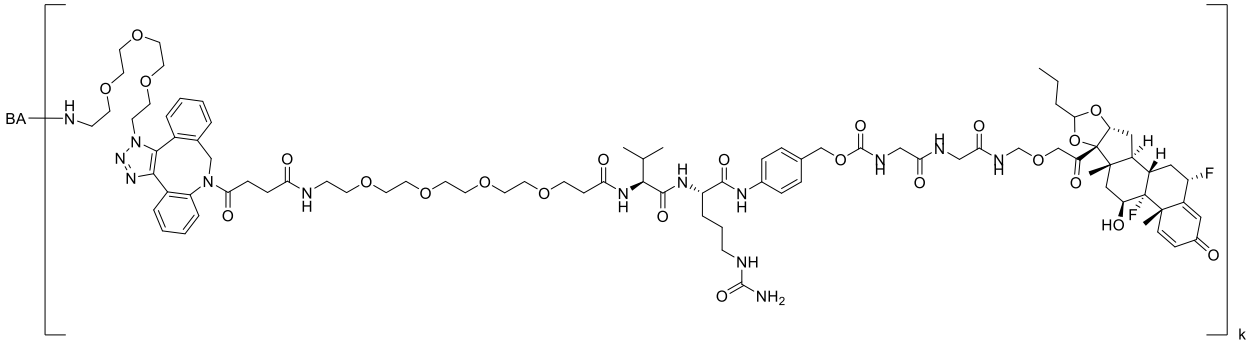
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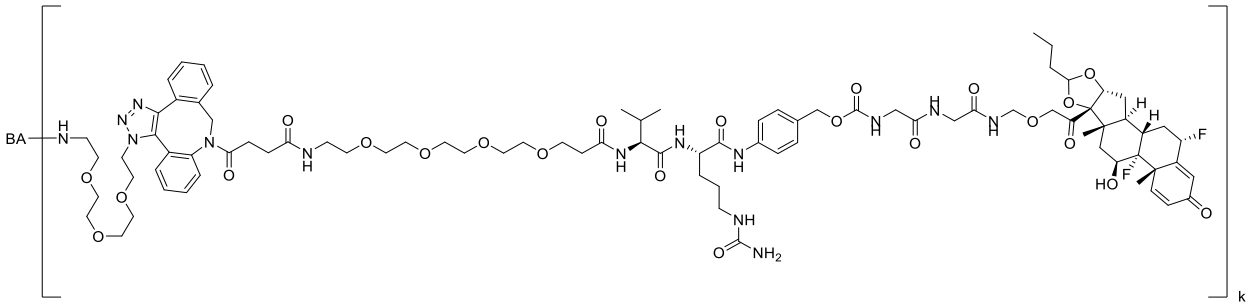
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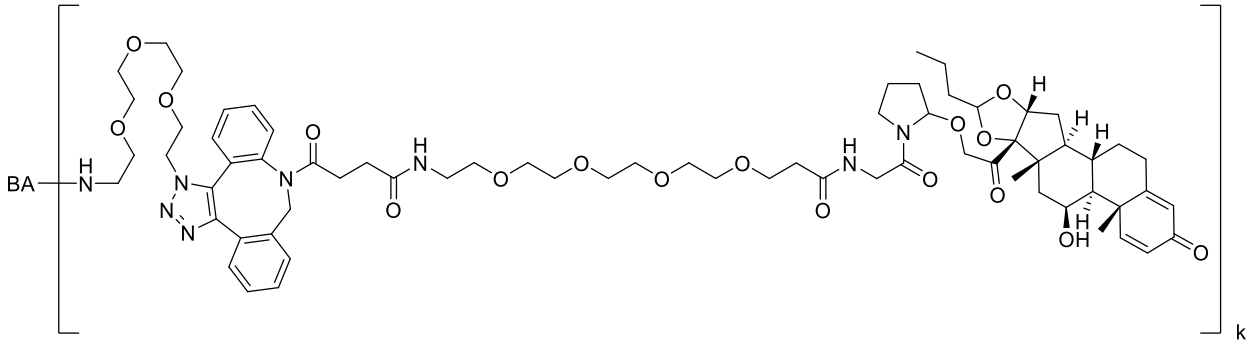
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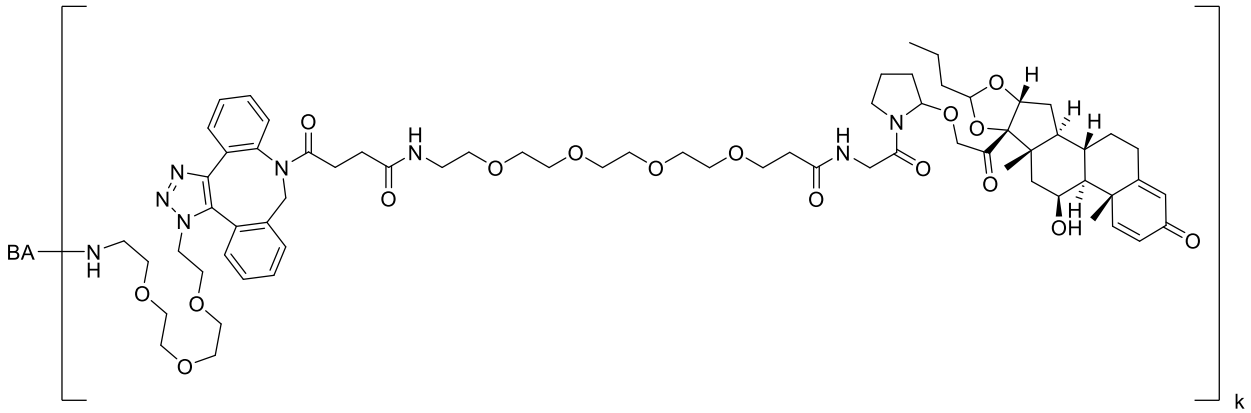
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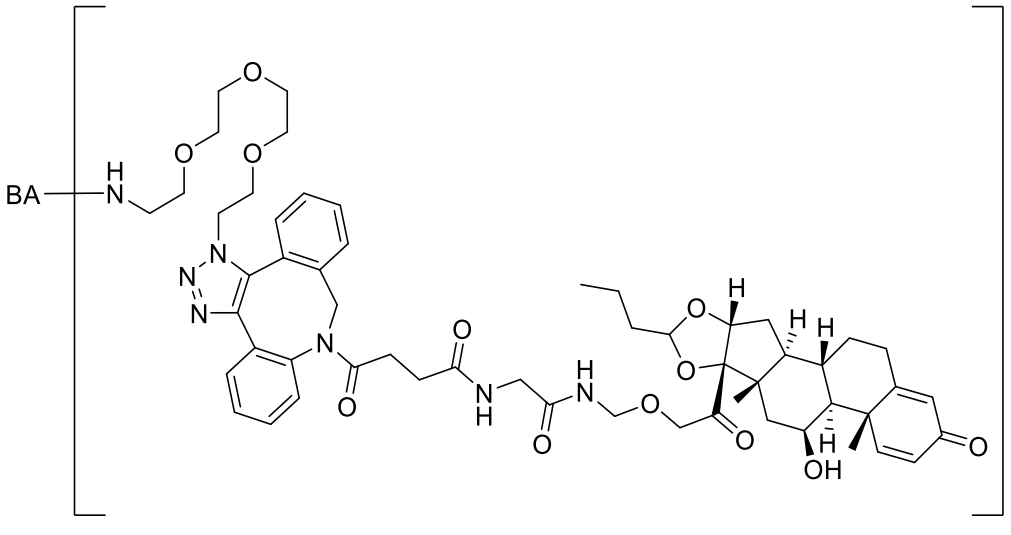
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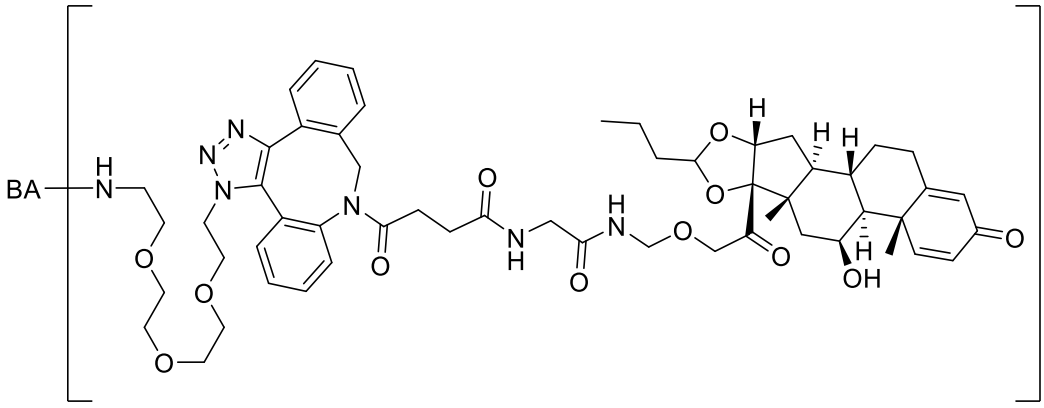
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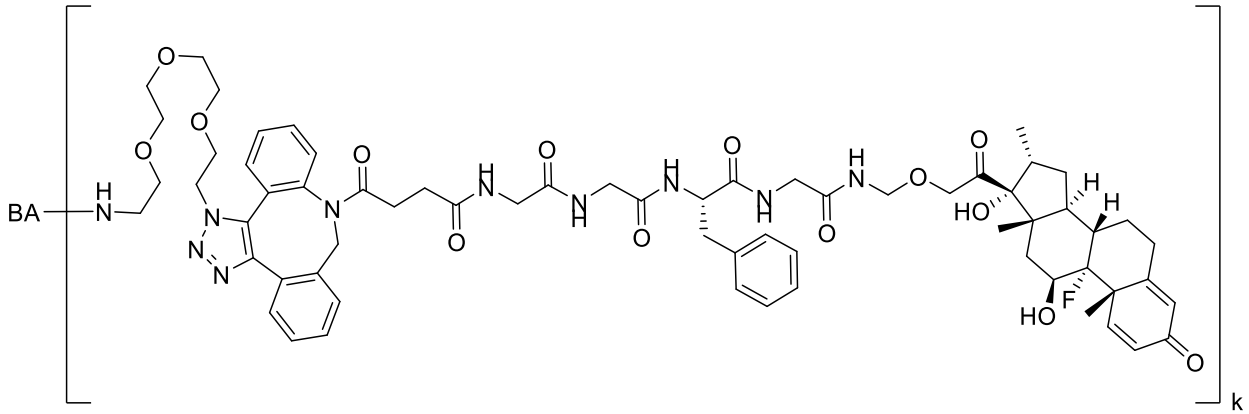
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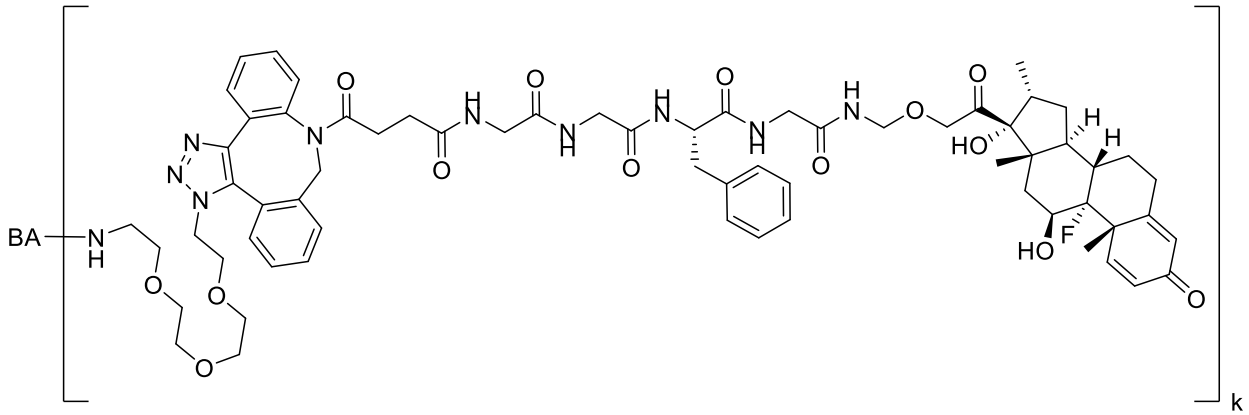
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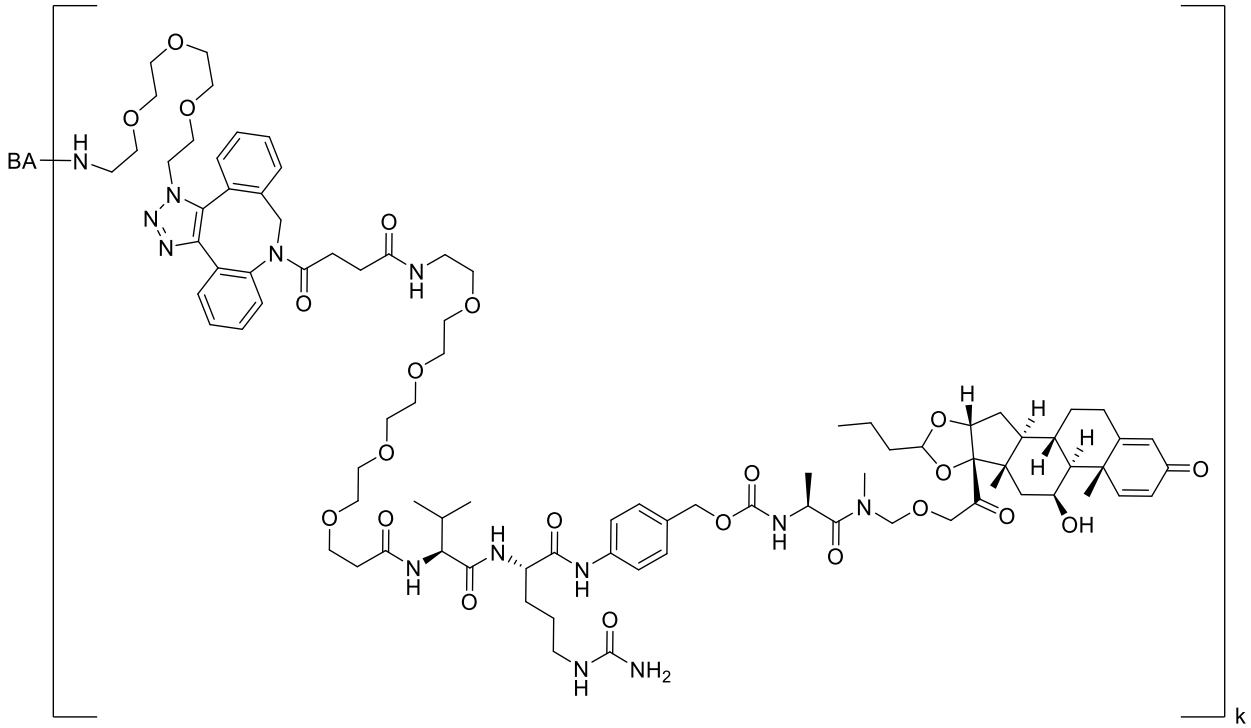
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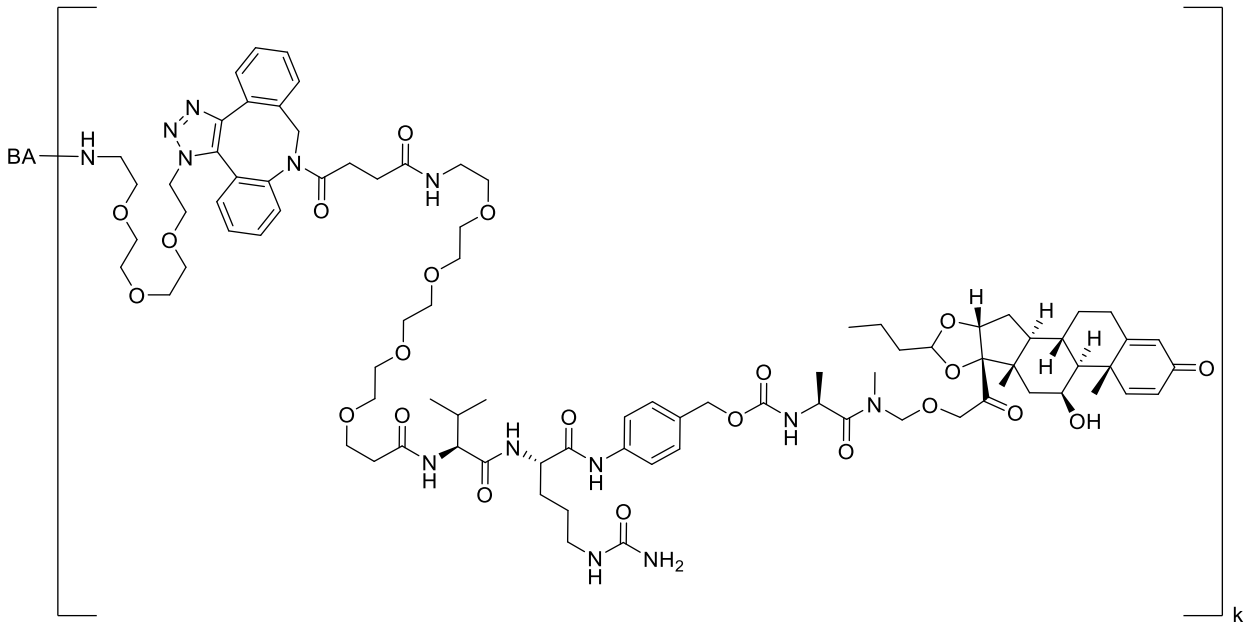
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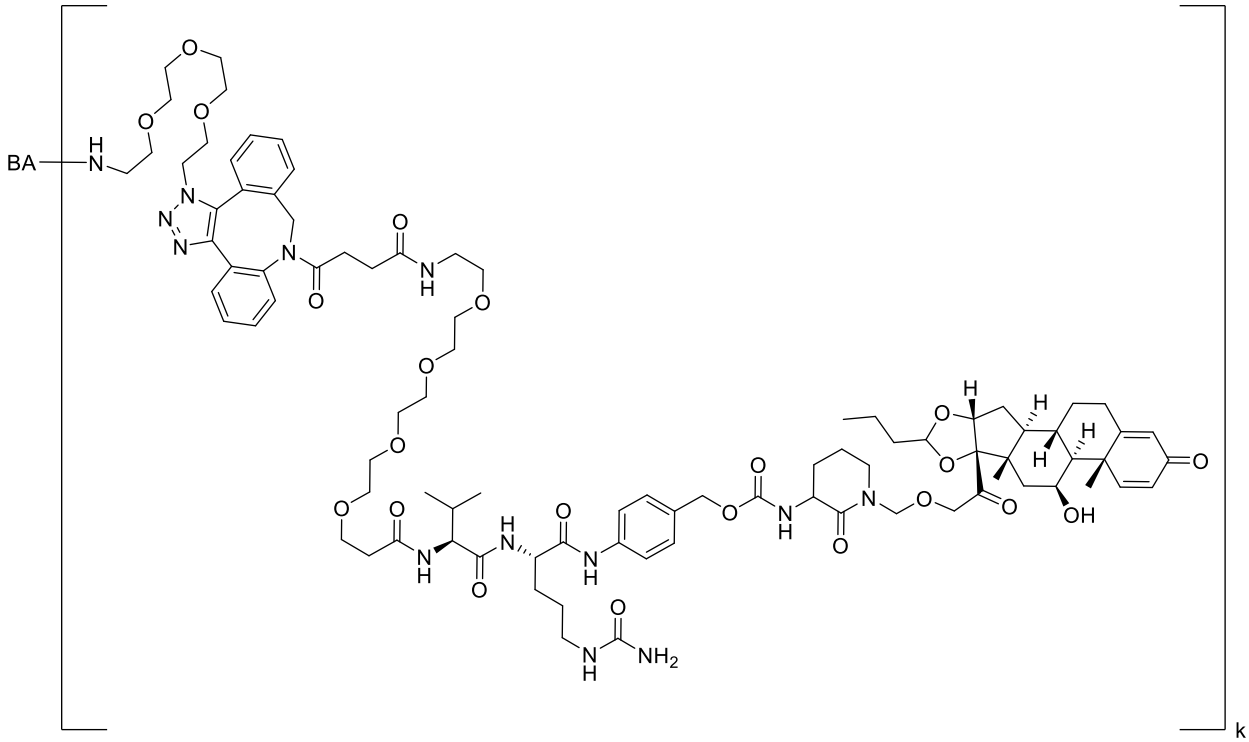
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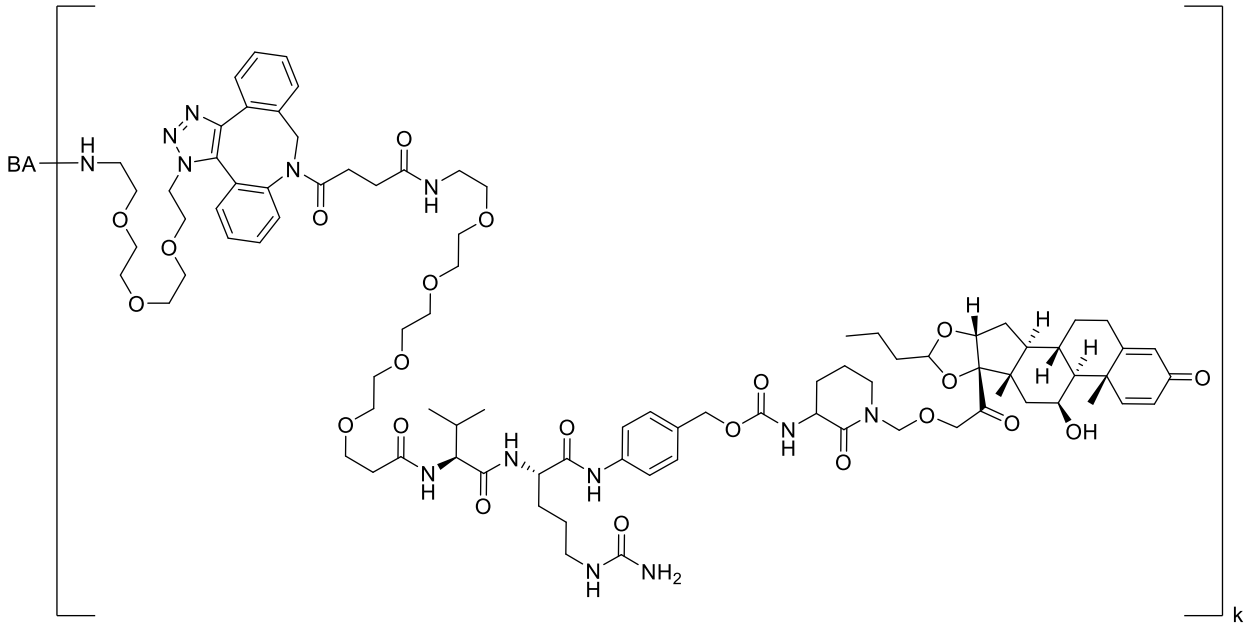

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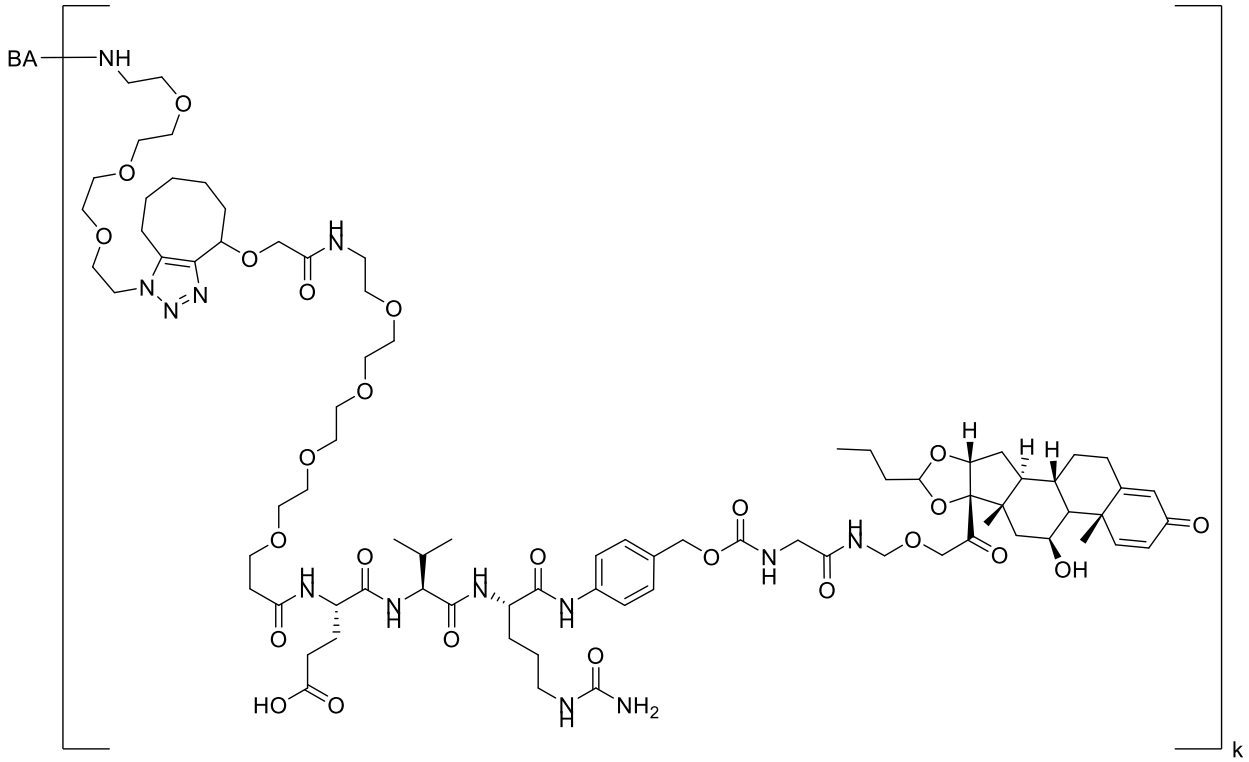

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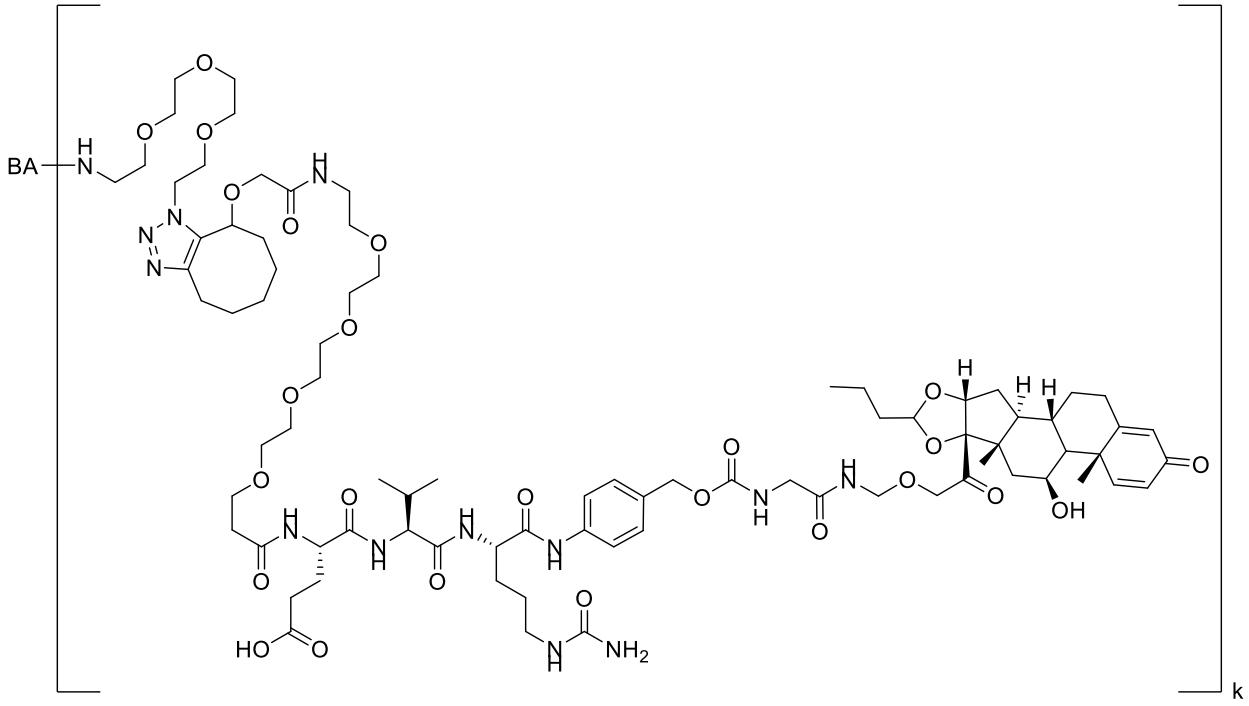

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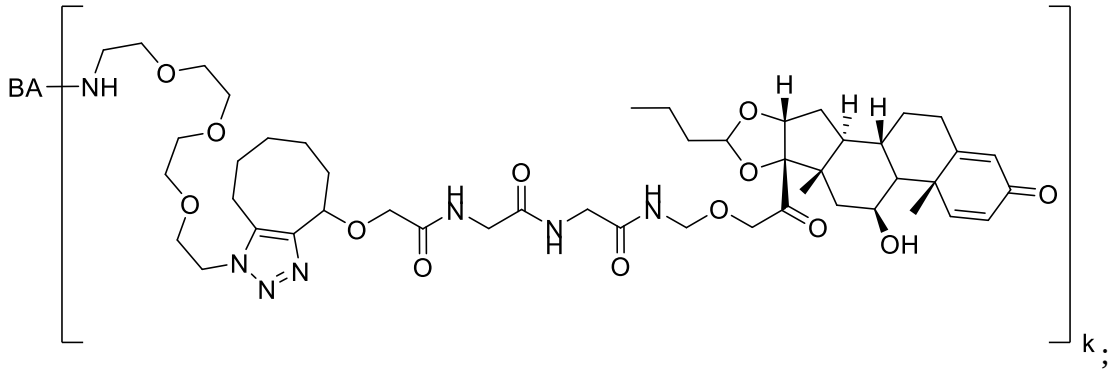
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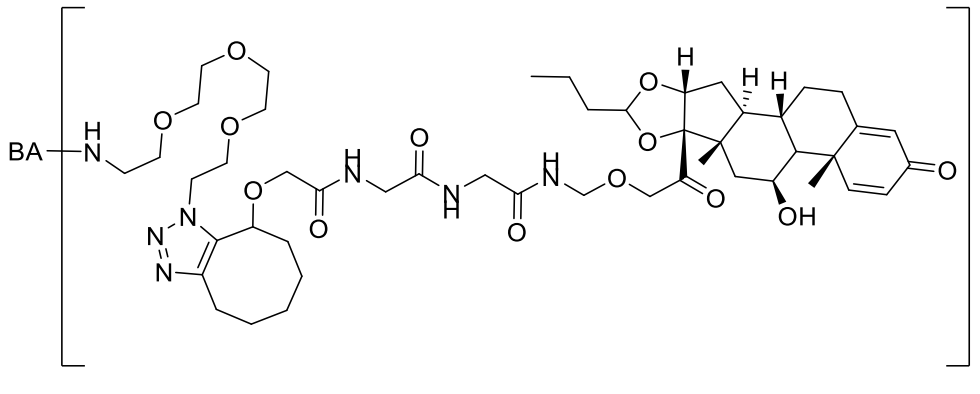

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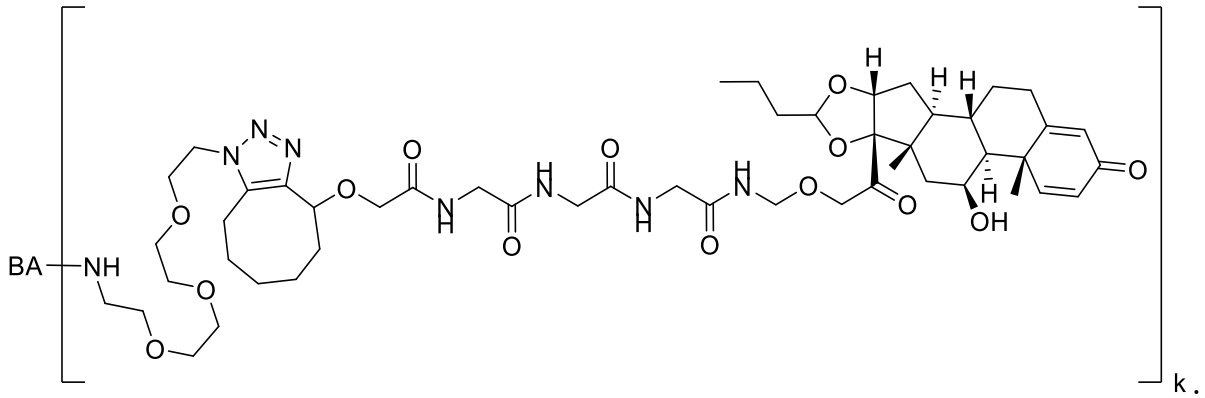
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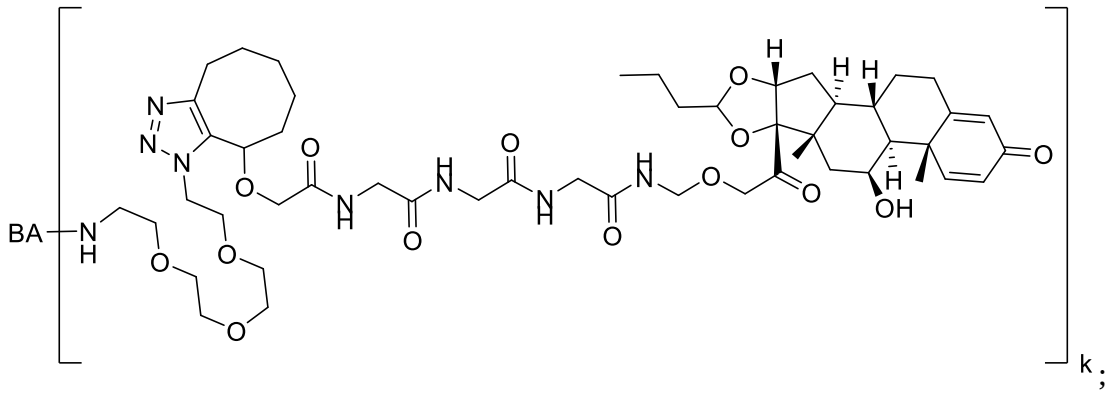

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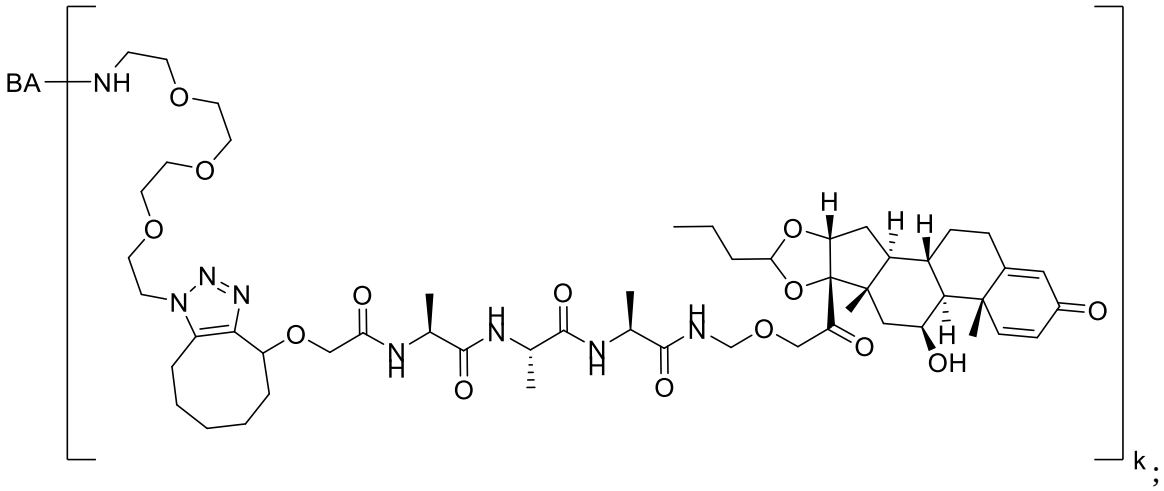
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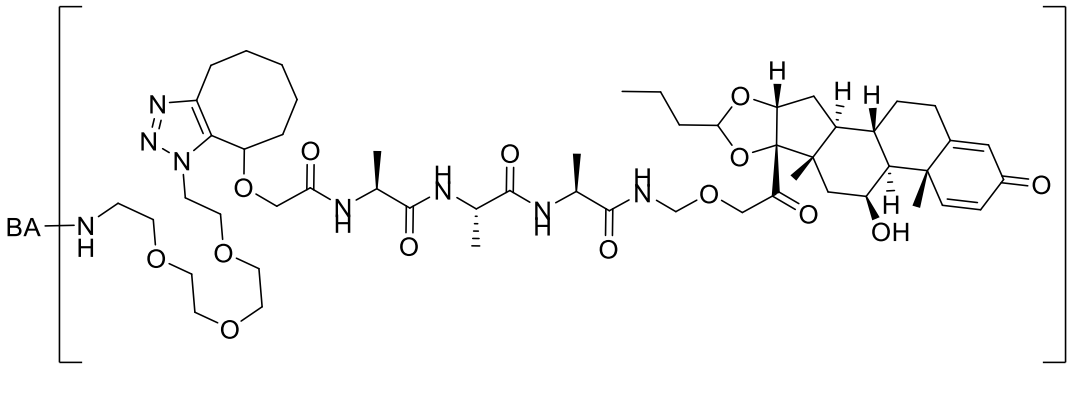


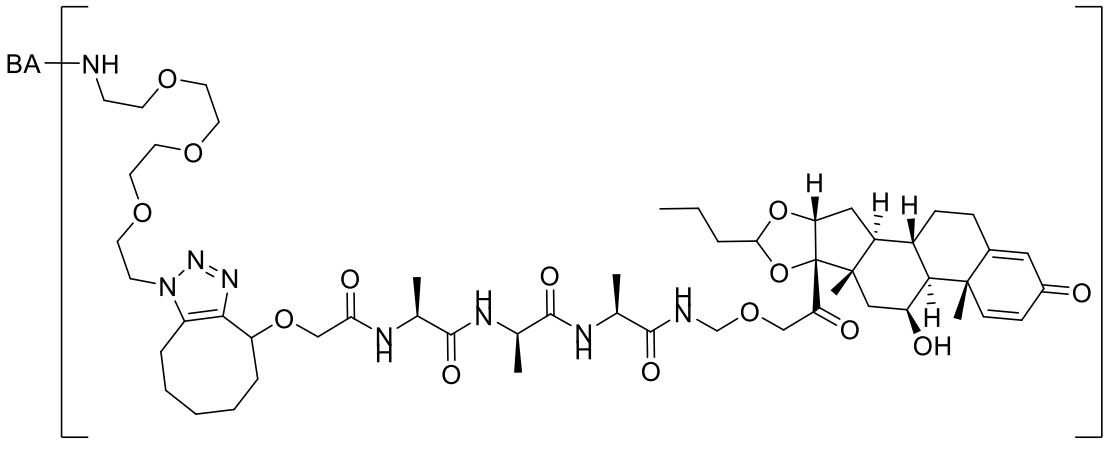


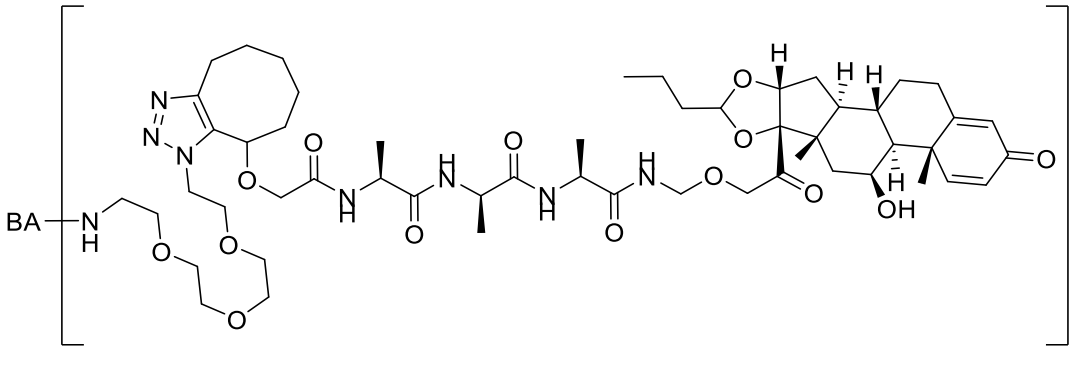


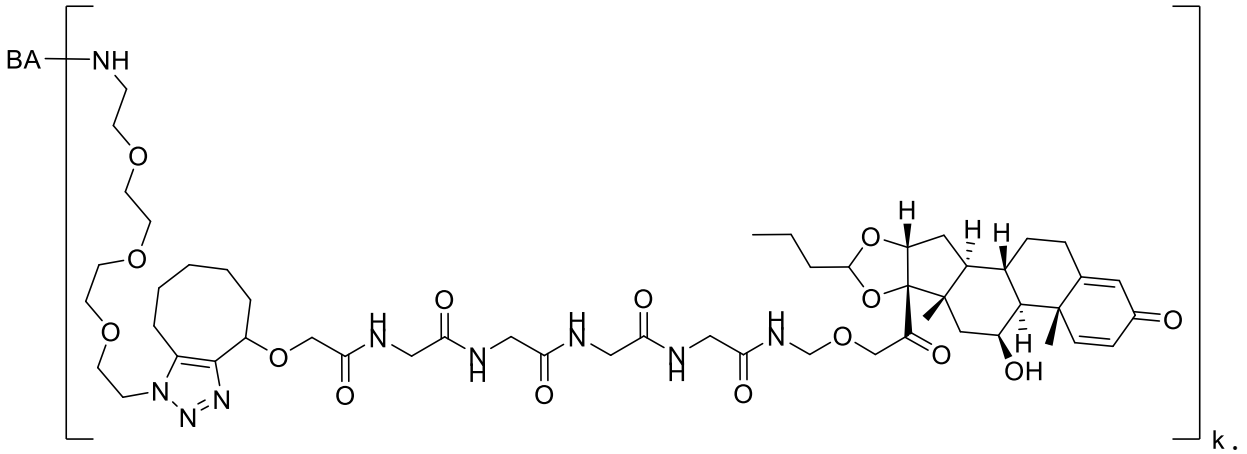


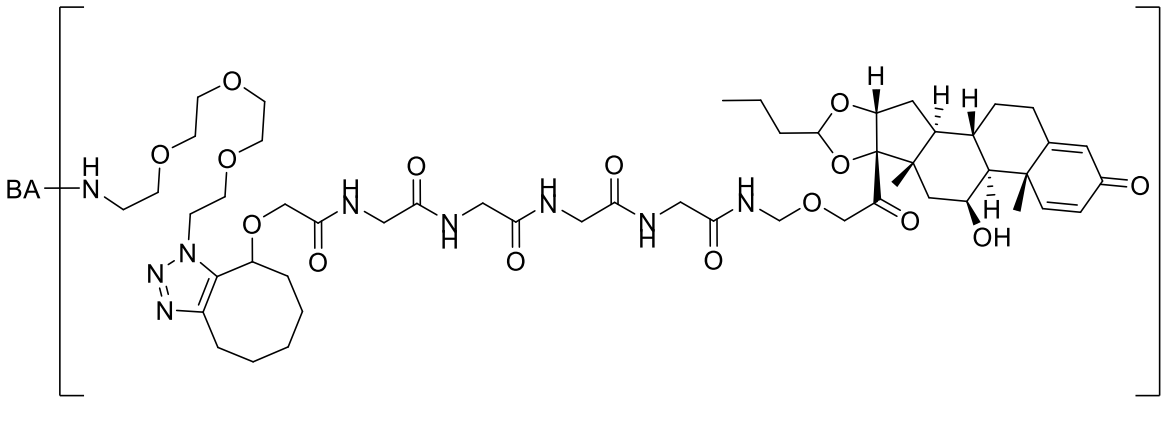


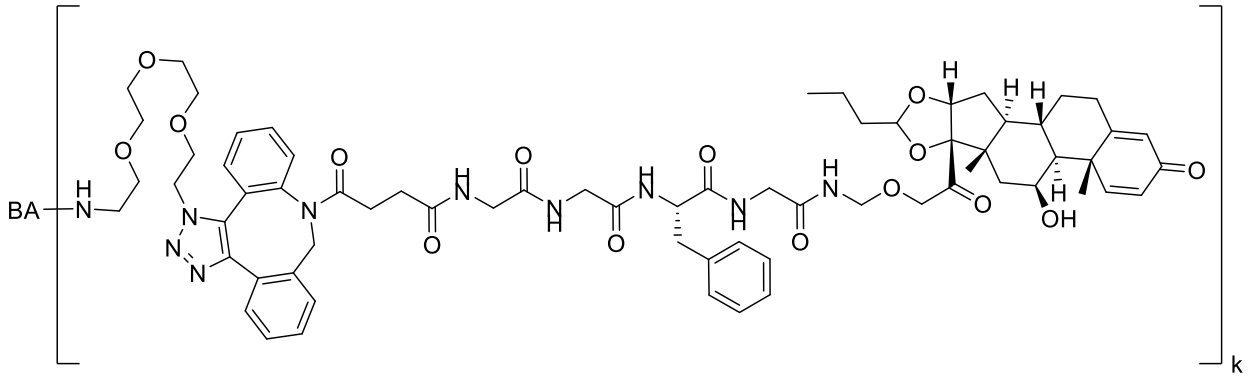




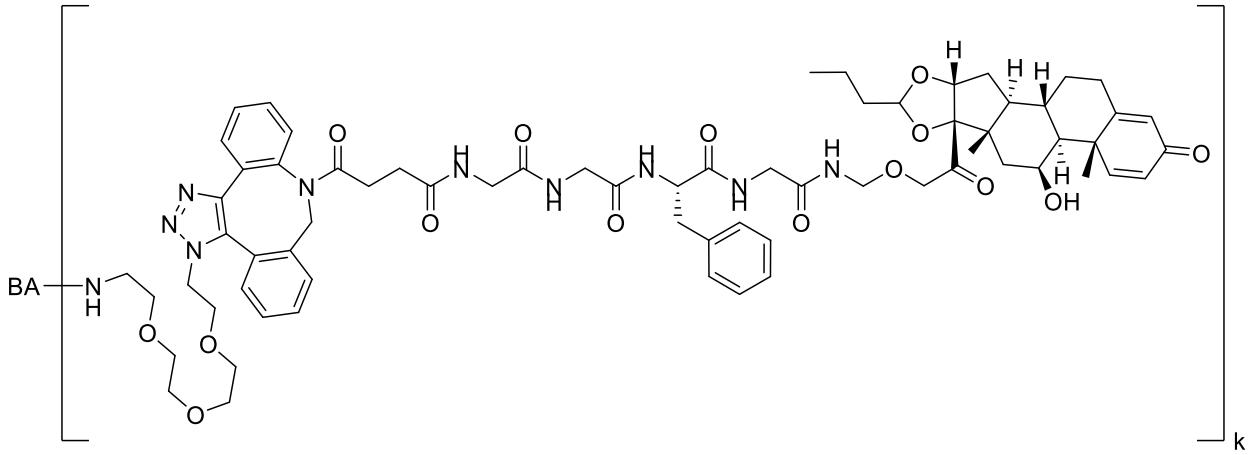




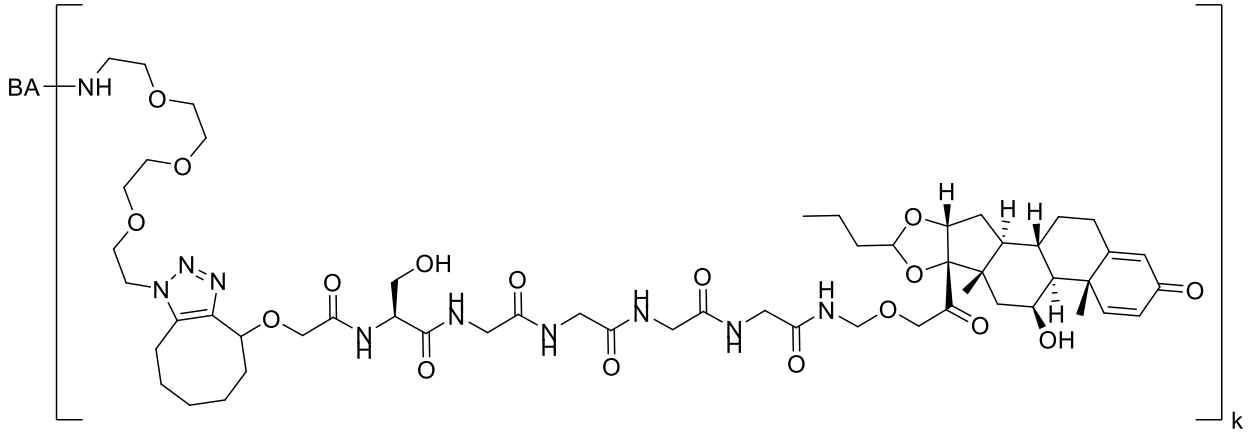




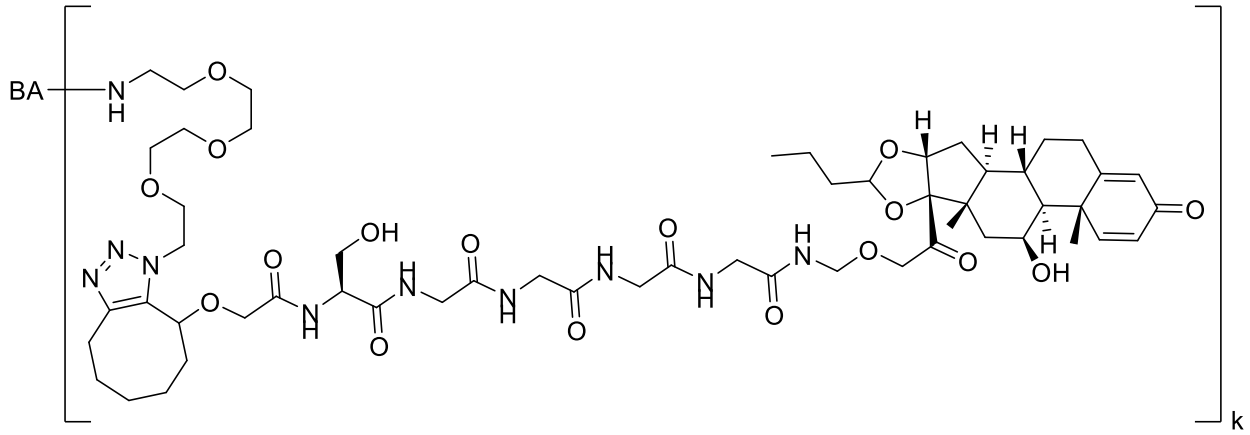
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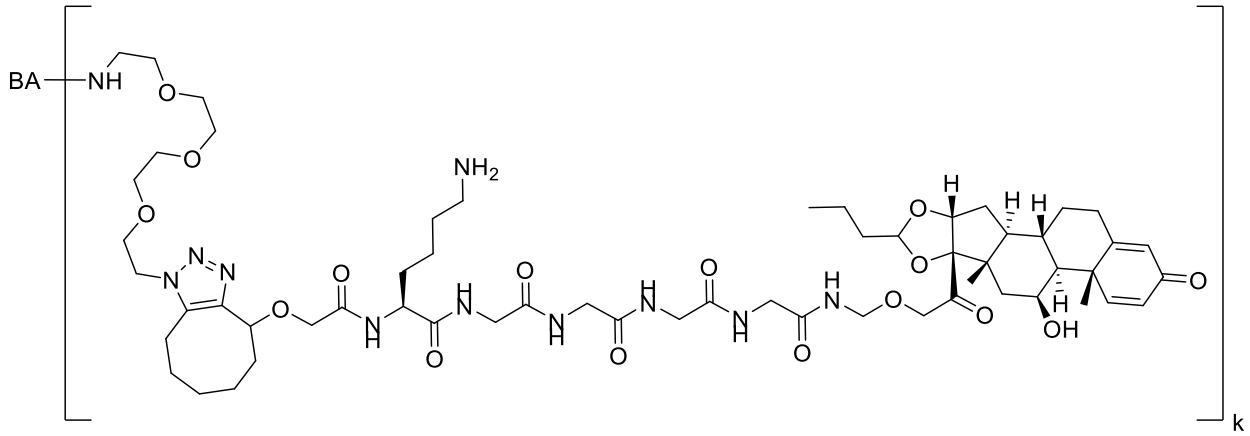
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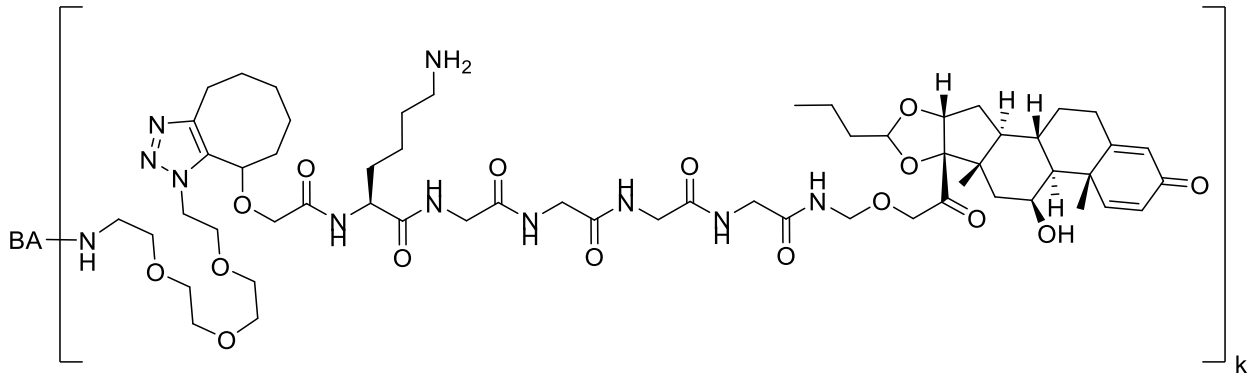
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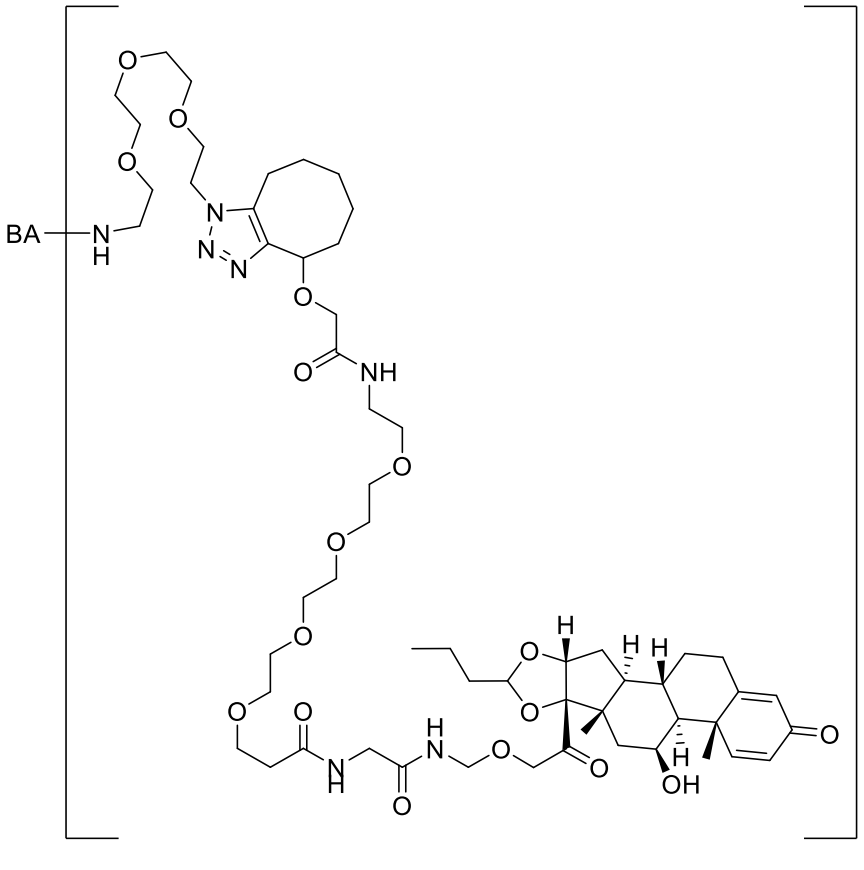
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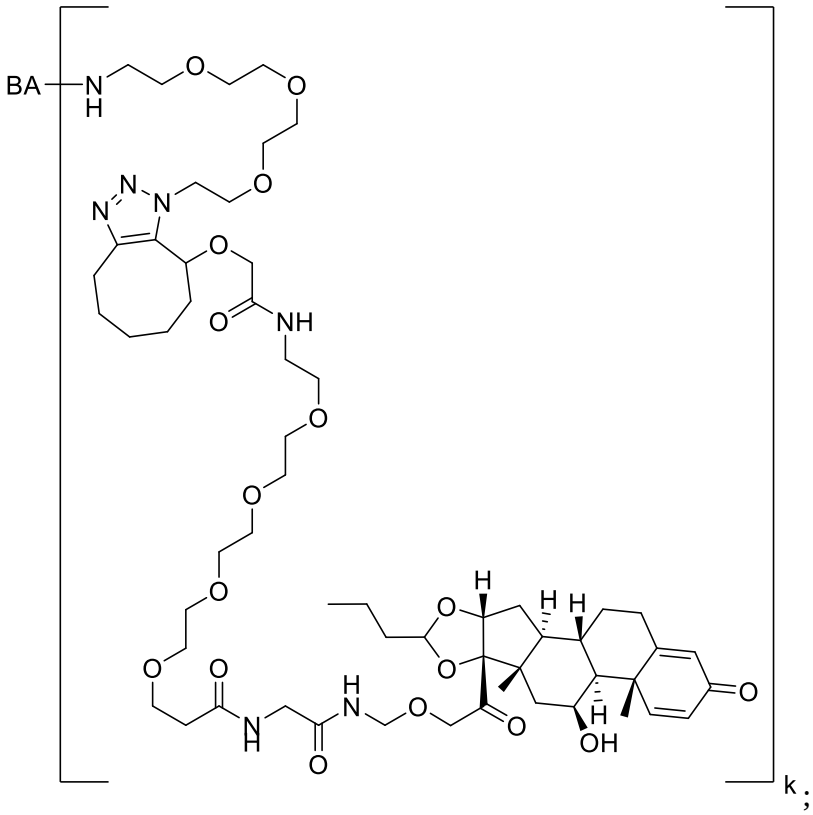


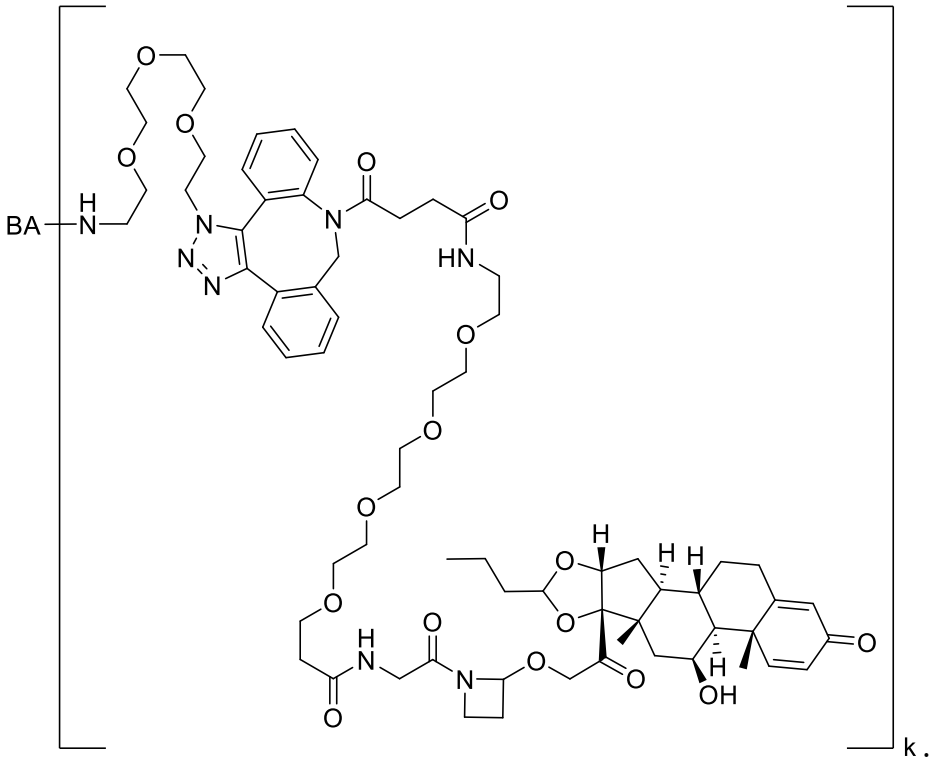
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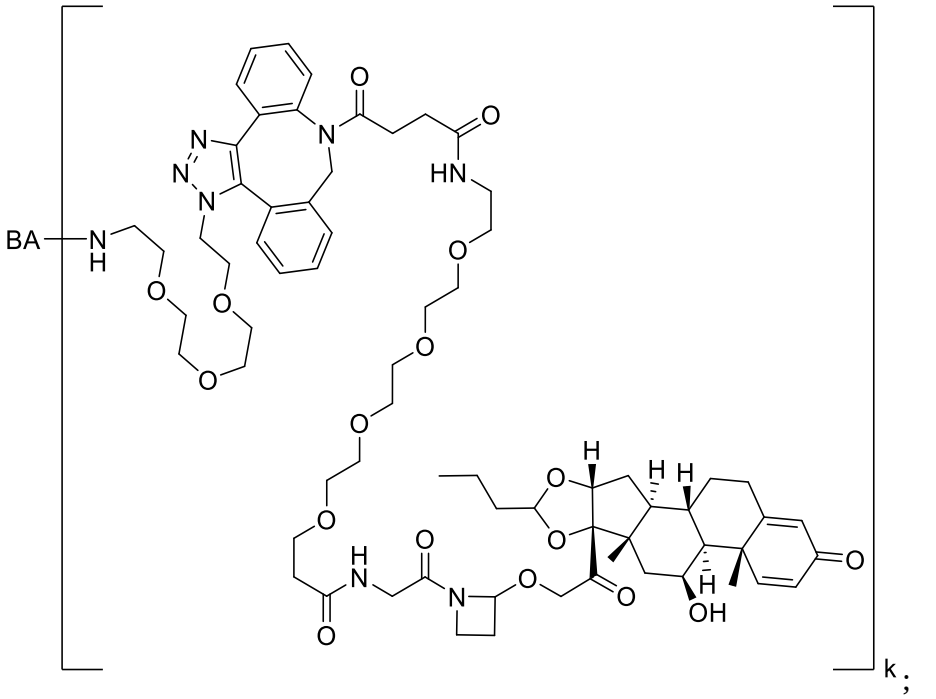
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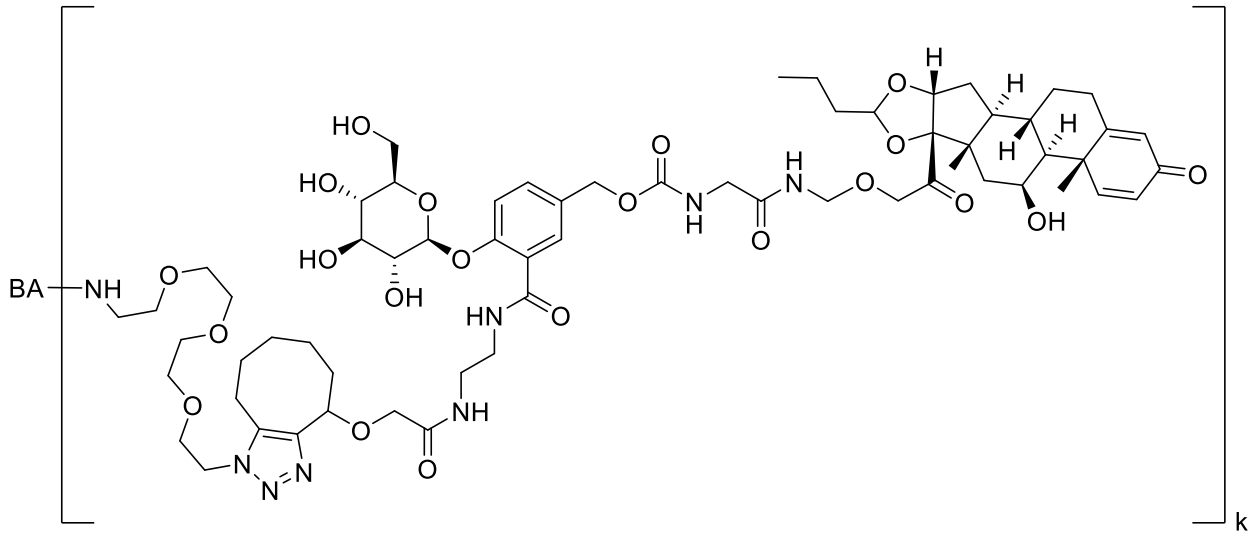

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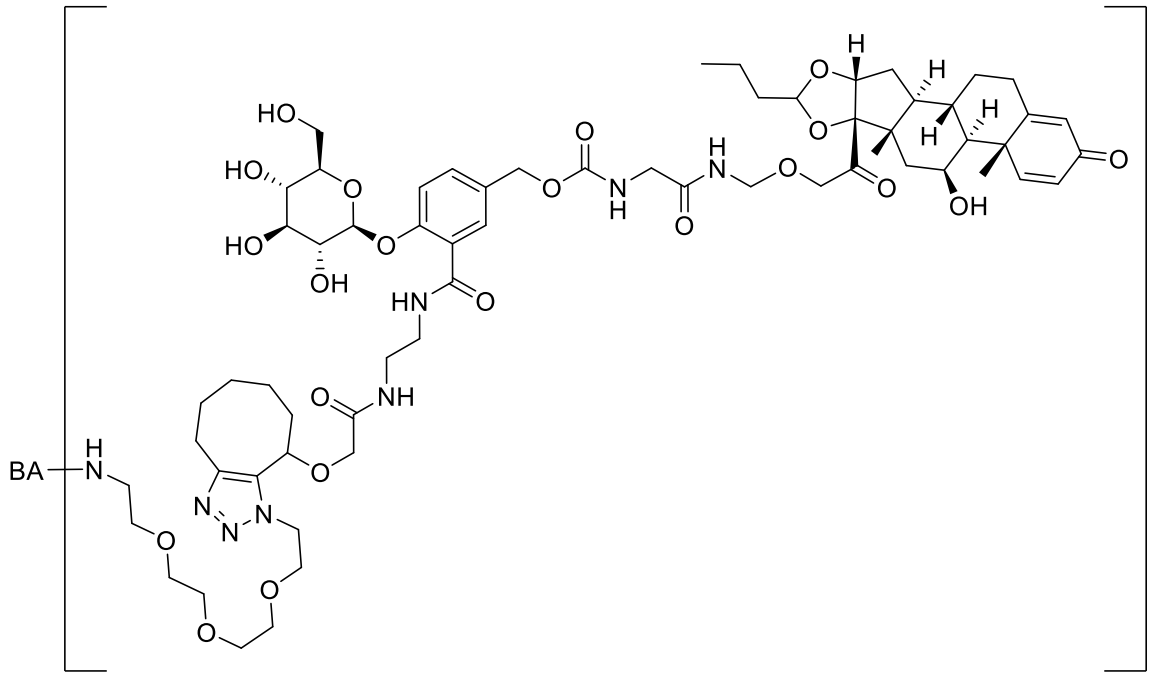
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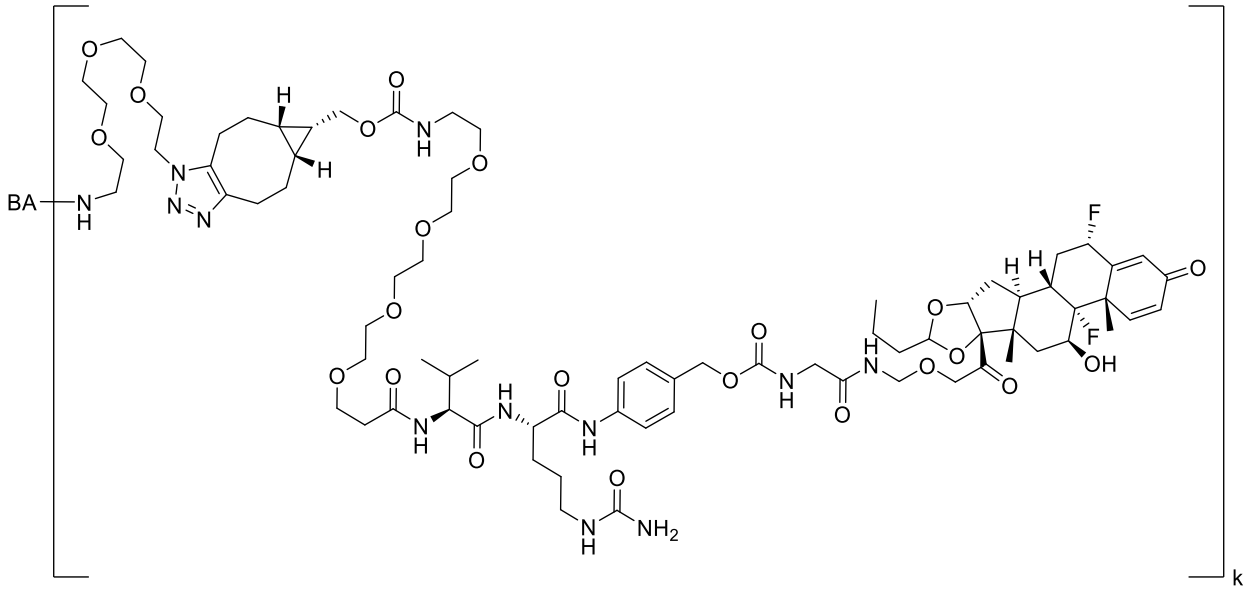
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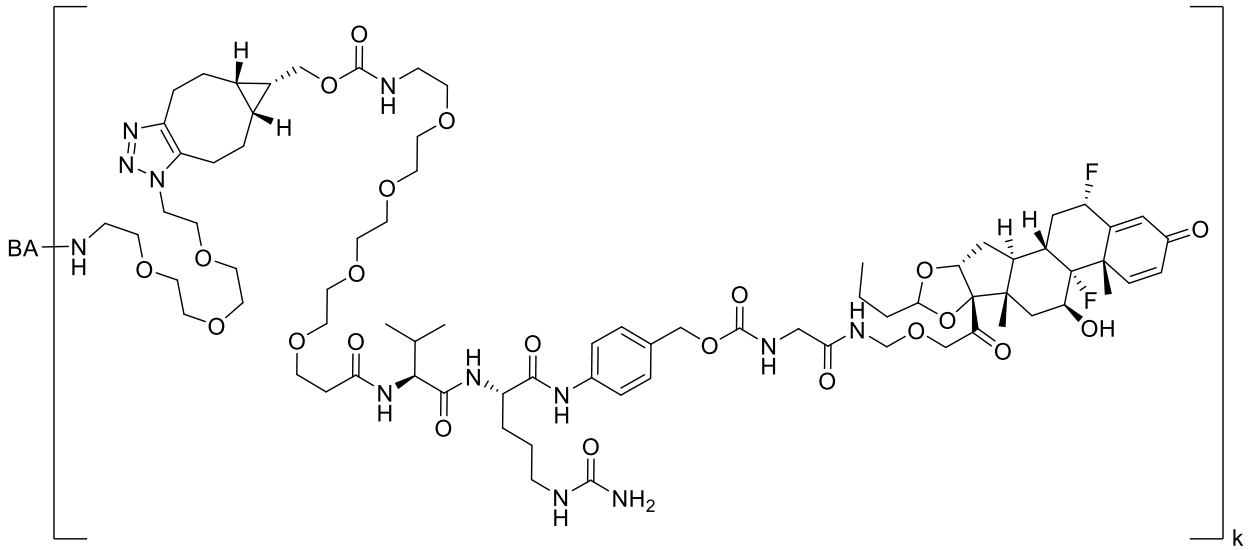
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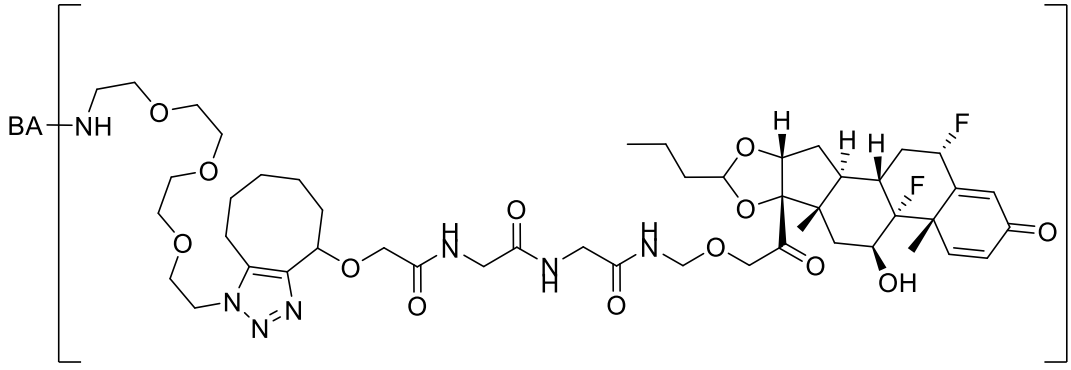
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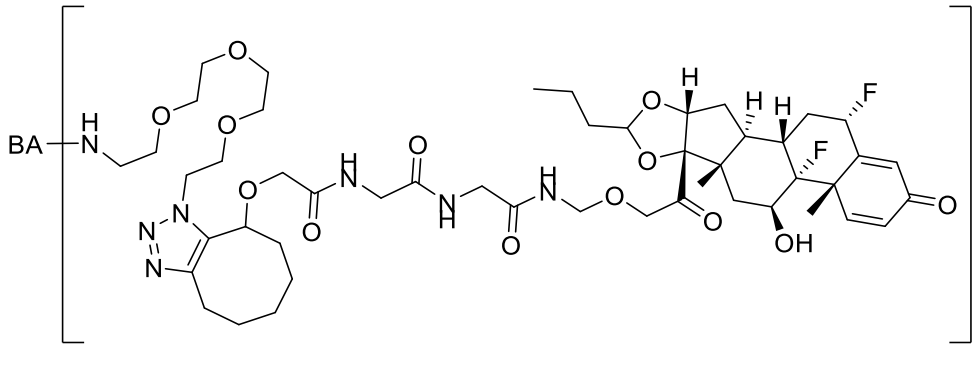
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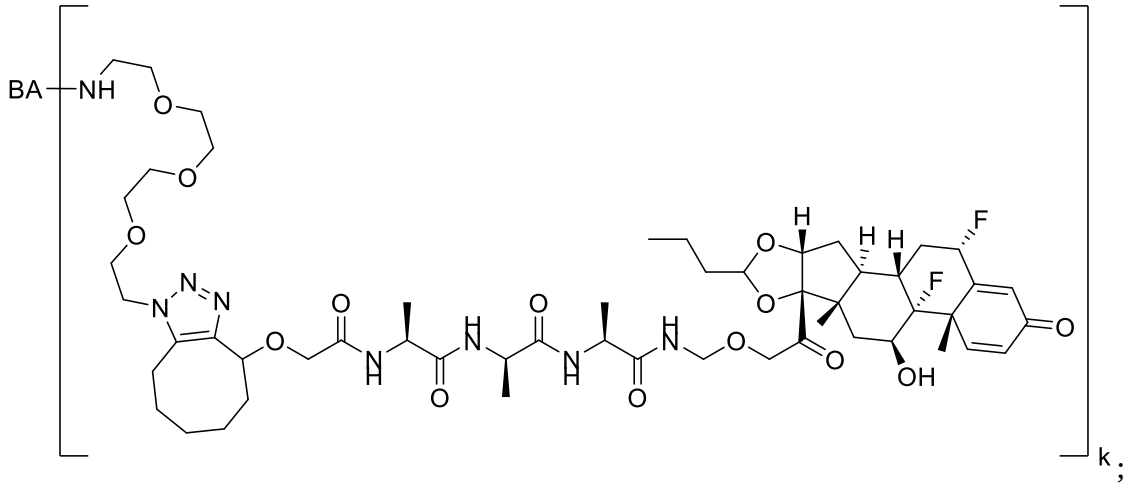


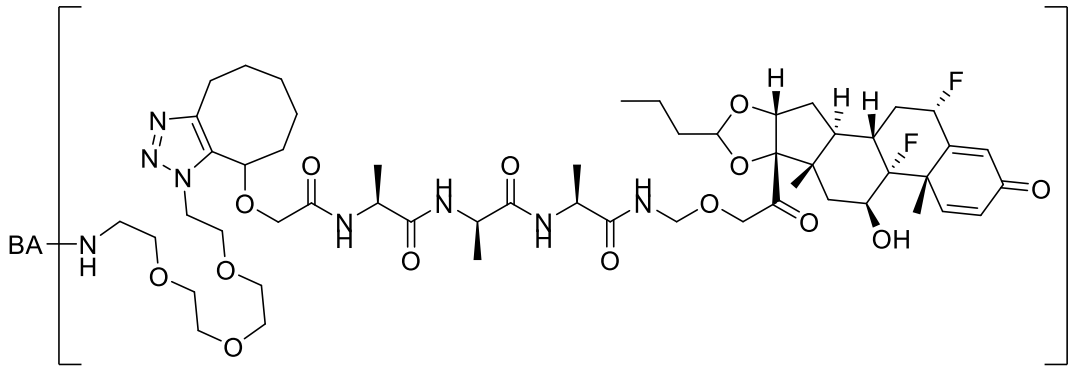
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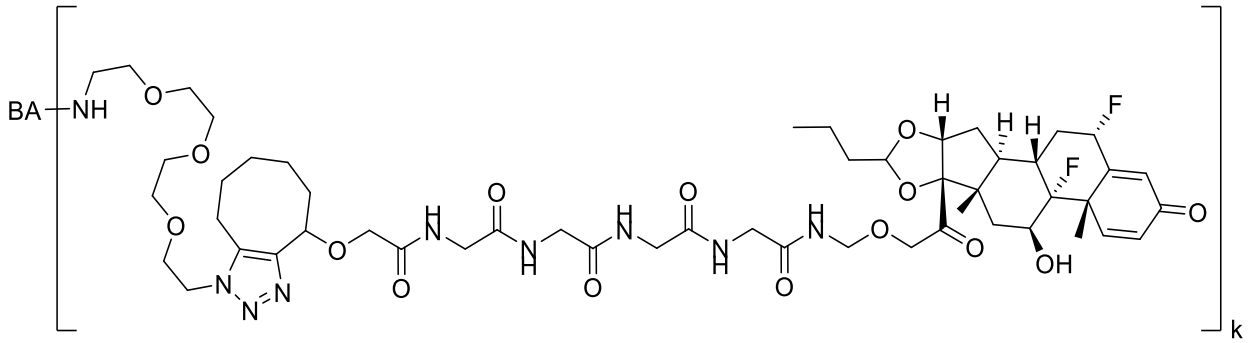


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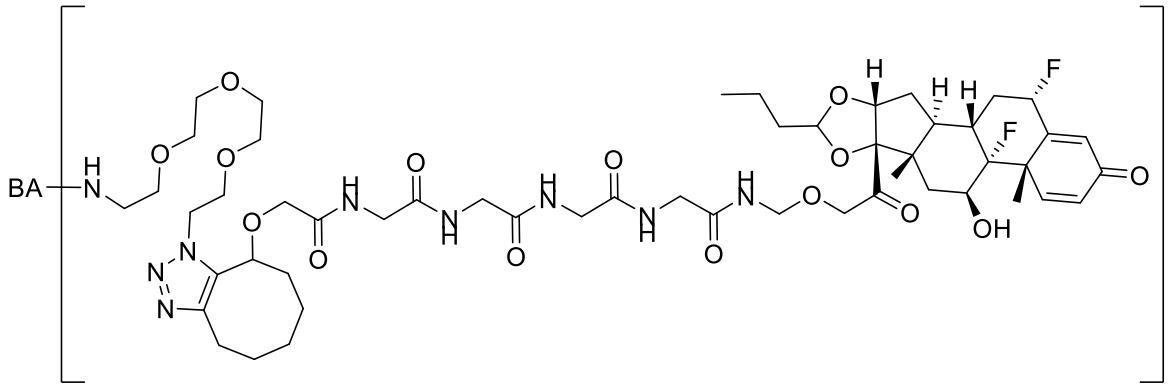




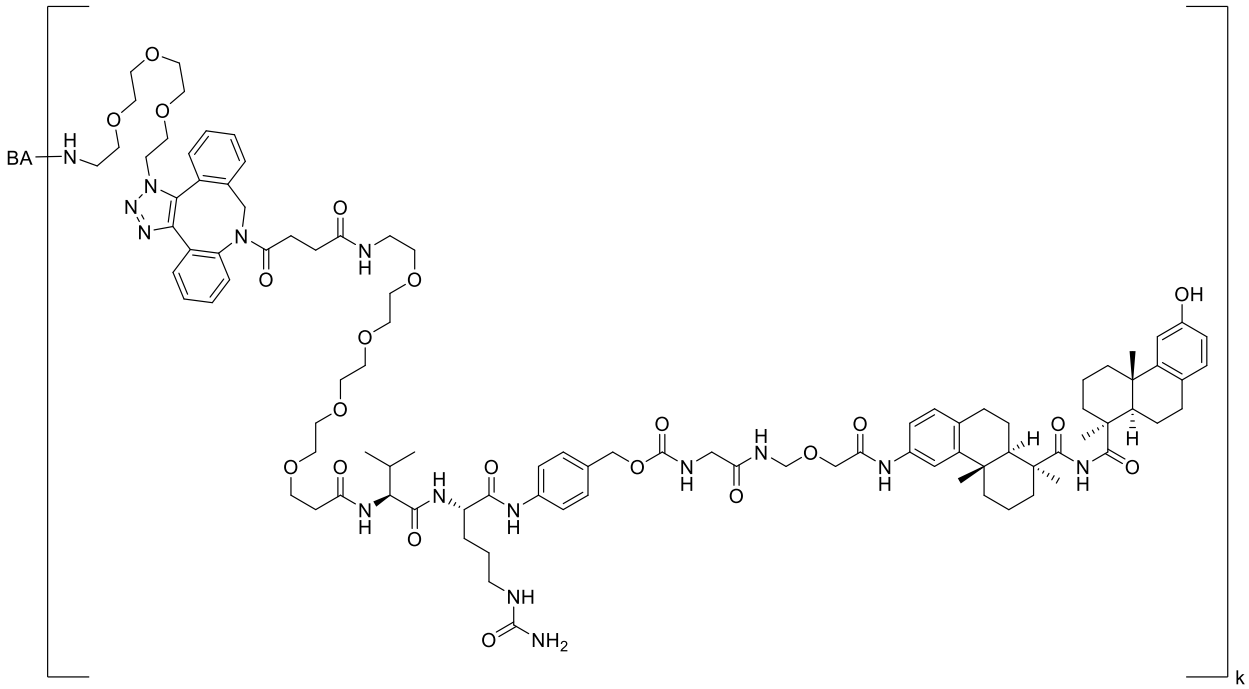


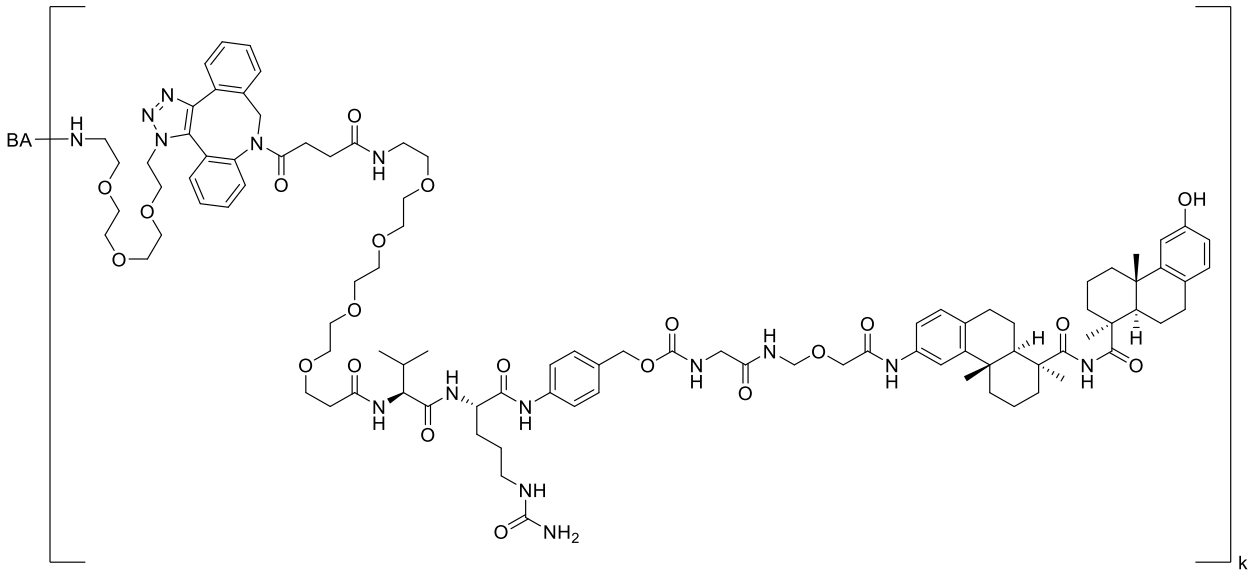


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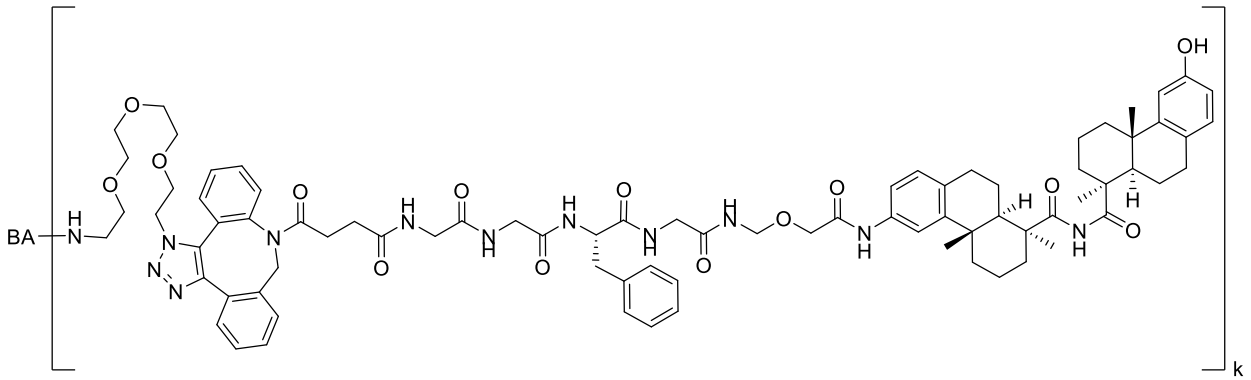


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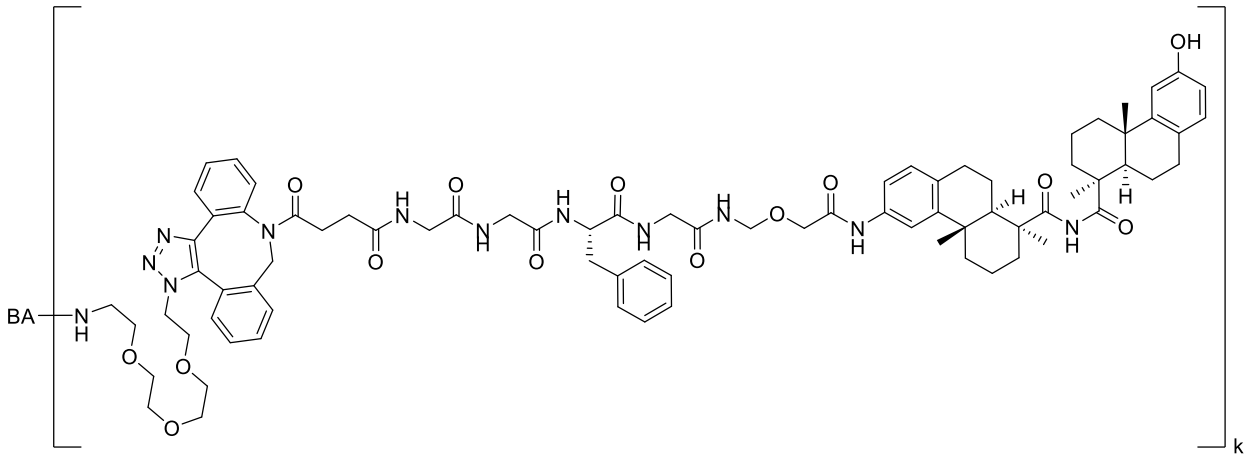

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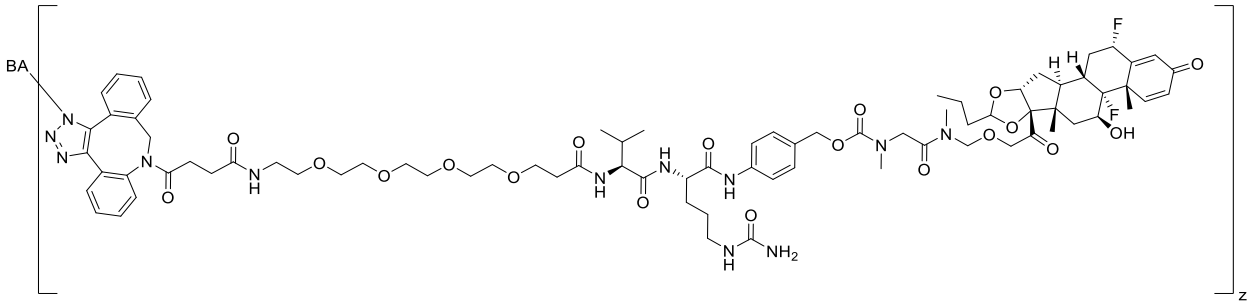
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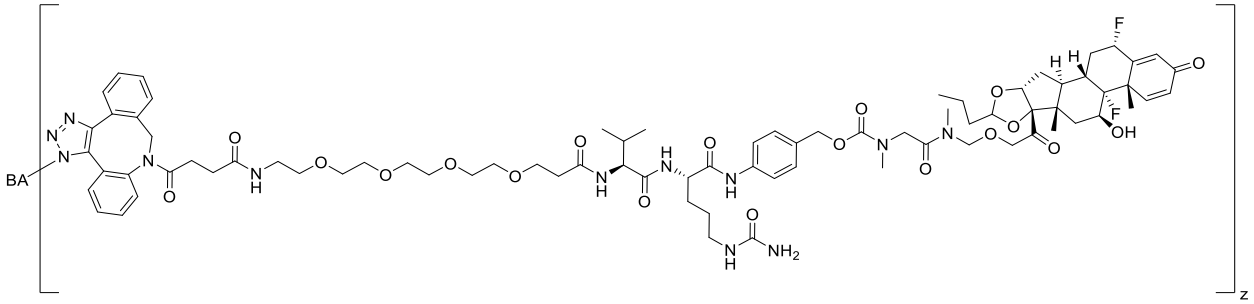
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wherein **k** is 1, 2, 3, or 4.

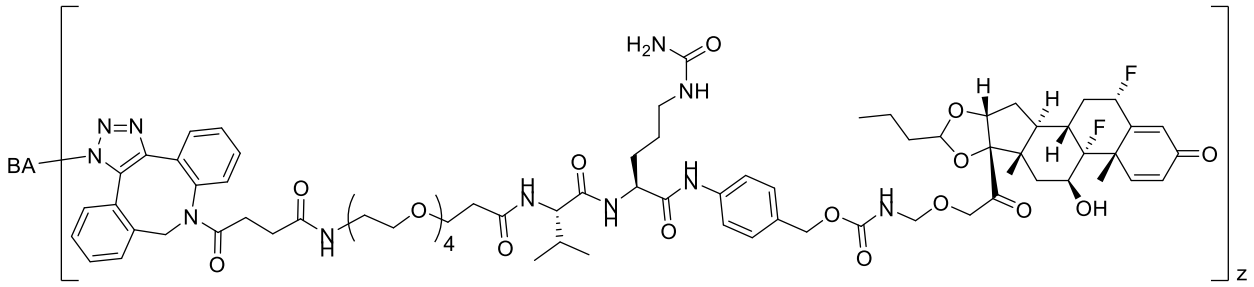
23. The compound of claim 1, wherein the compound is selected from the group consisting of



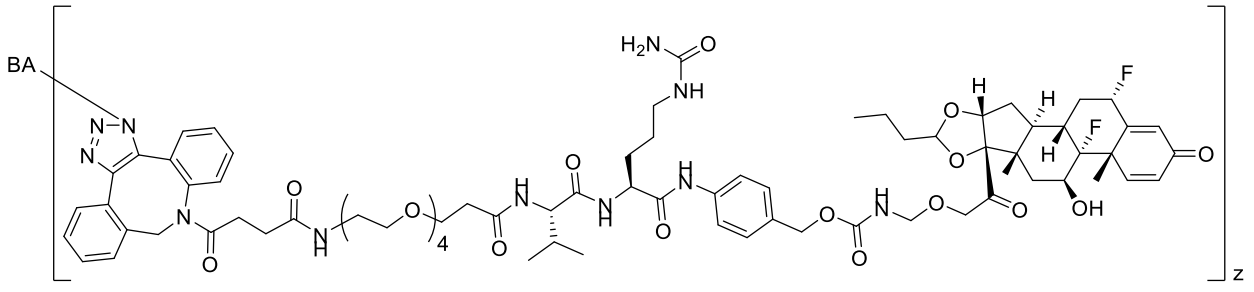
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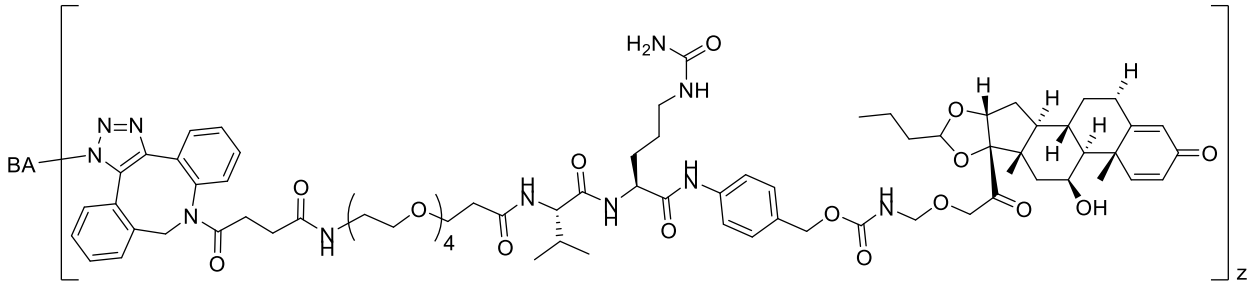
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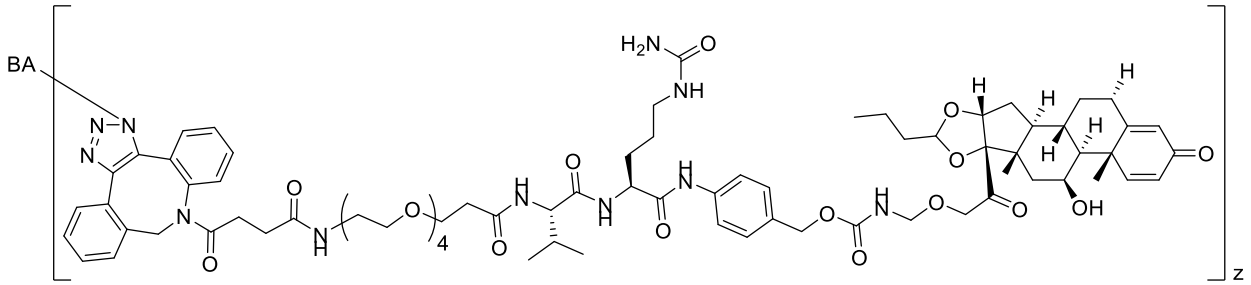
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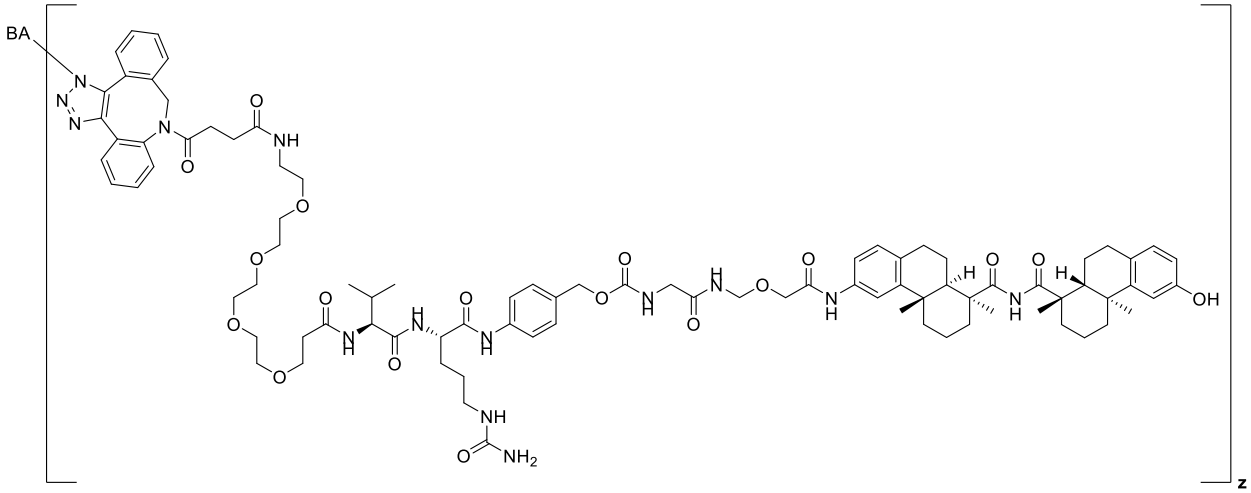


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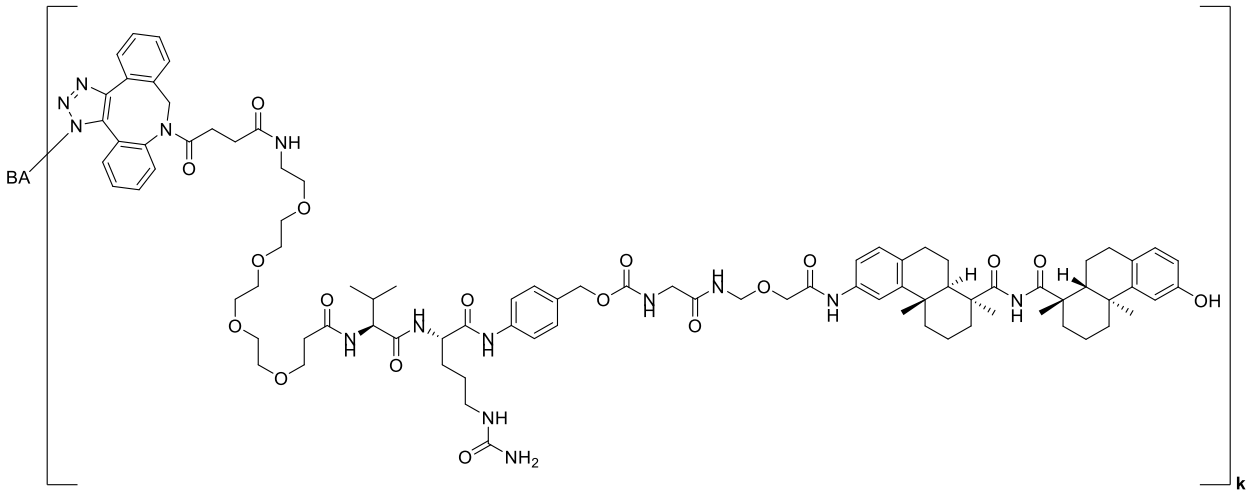


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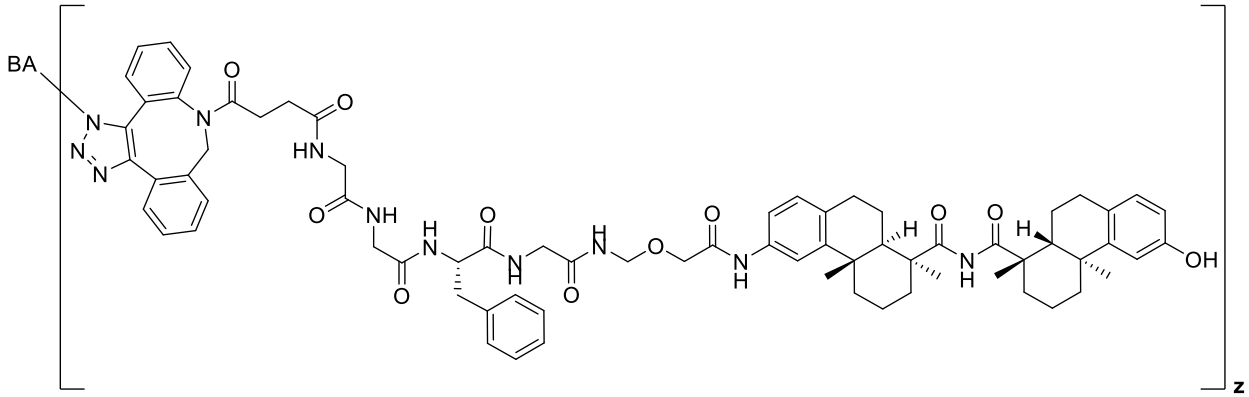




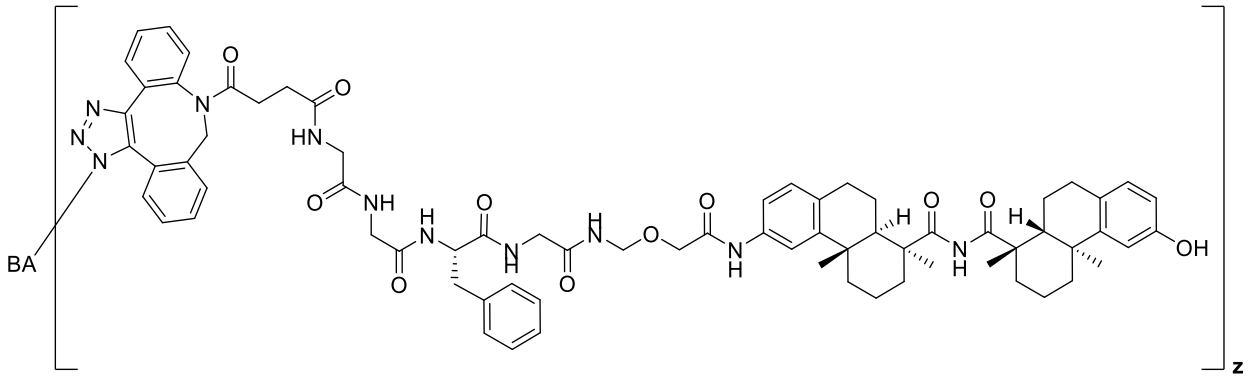
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; wherein **z** is 1, 2, 3, or 4.

24. The compound of claim 8, wherein **BA** is an antibody or antigen-binding fragment thereof.

25. The compound of claim 24, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least one glutamine residue used for conjugation.

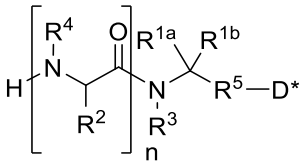
26. The compound of claim 24, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least two glutamine residues used for conjugation.

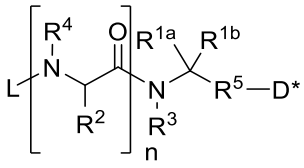
27. The compound of claim 24, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least four glutamine residues used for conjugation.

28. The compound of claim 27, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof, wherein conjugation is at two Q295 residues; and **k** is 2.

29. The compound of claim 27, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof, wherein conjugation is at two Q295 residues and two N297Q residues; and **k** is 4.

30. An antibody-drug conjugate comprising an antibody, or an antigen binding fragment thereof, where said antibody or antigen binding fragment thereof is conjugated to a compound having the following structures



or


or a pharmaceutically acceptable salt thereof, wherein

L is a linker comprising a moiety reactive with an antibody or an antigen binding fragment thereof;

R^{1a} and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^3** to form a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl;

R^2 is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^2** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^3** to form a 4-, 5-, or 6-membered heterocyclyl;

R^3 is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^3** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{1a}** or **R^2** to form the 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl;

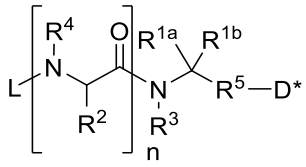
R^4 is hydrogen or alkyl;

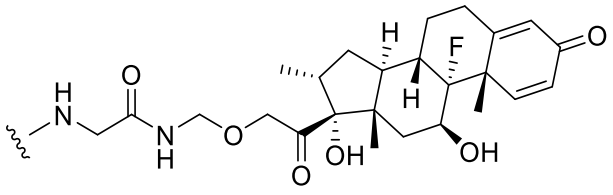
R^5 is oxygen, N**R^6**, or sulfur within D*;

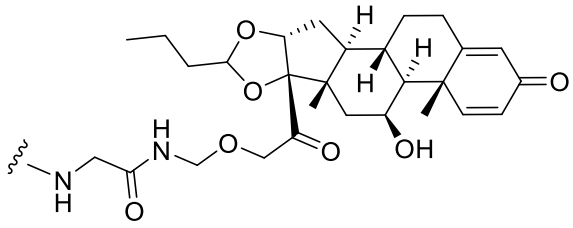
R^6 is hydrogen or alkyl;

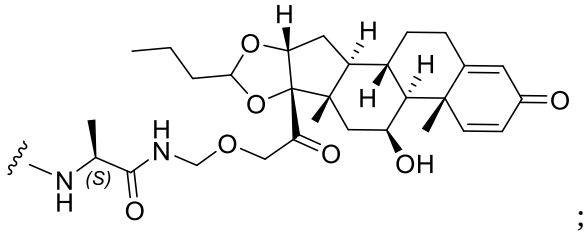
D* is a residue of an anti-inflammatory biologically active compound comprising a hydroxyl, amino, or thiol for conjugation to -CR^{1a}R^{1b}- wherein the residue is a steroid or an LXR agonist; and

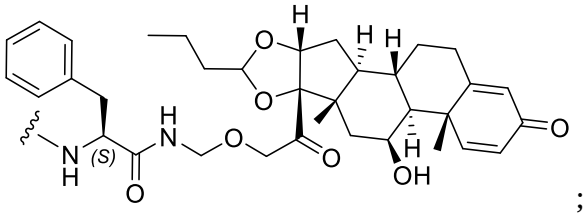
n is zero, one, two, three, four, five, or six.

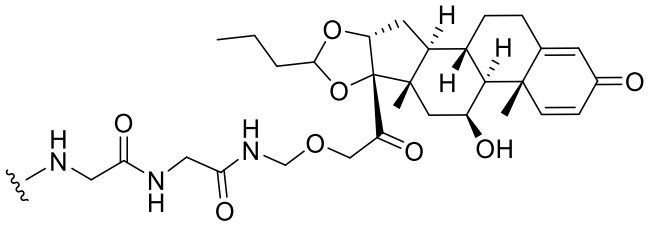
31. The antibody-drug conjugate of claim 30, wherein the antibody or antigen binding fragment thereof is conjugated to  and L is bonded to a moiety selected from the group consisting of

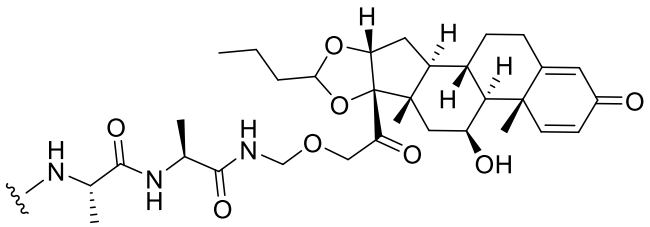

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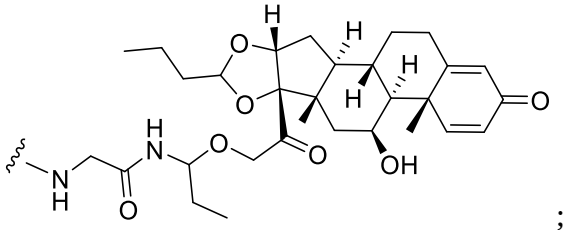

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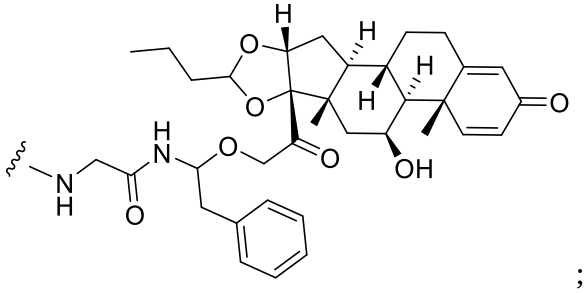

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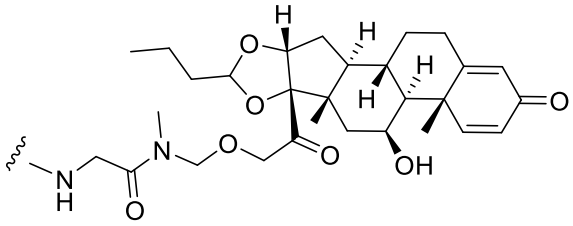

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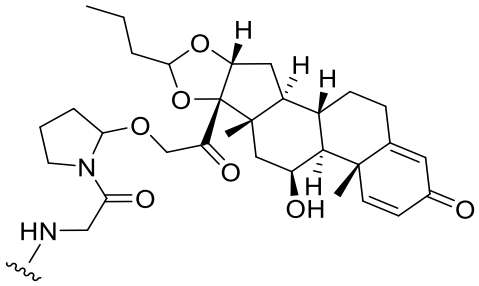

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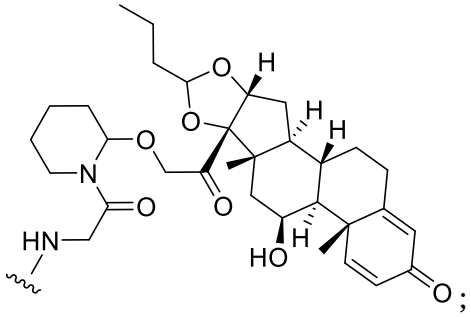

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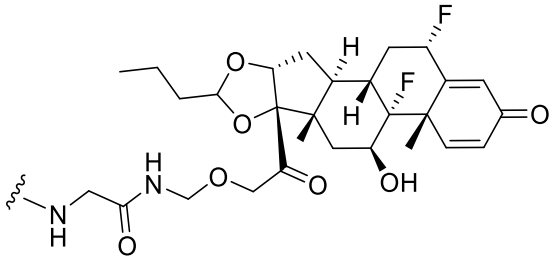

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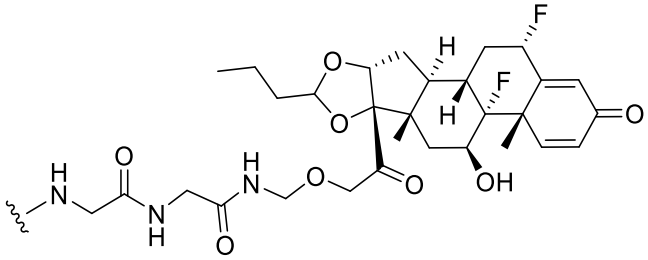

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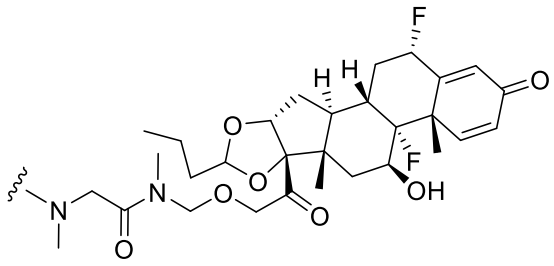

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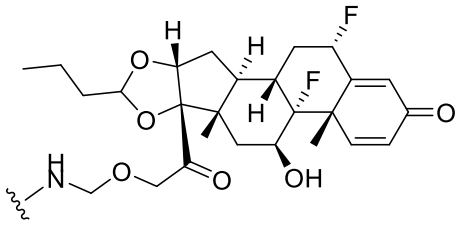

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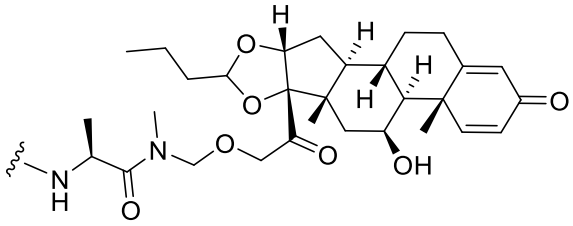

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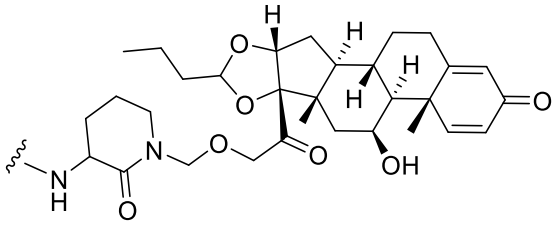

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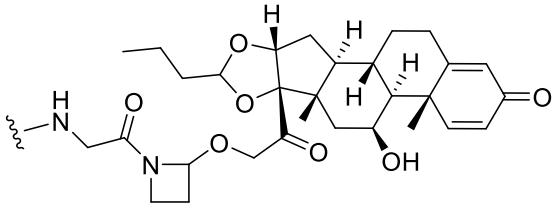

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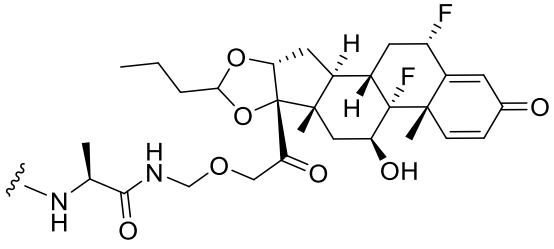

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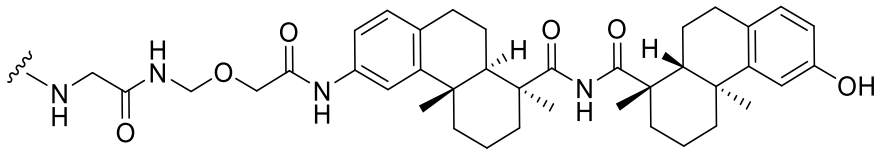

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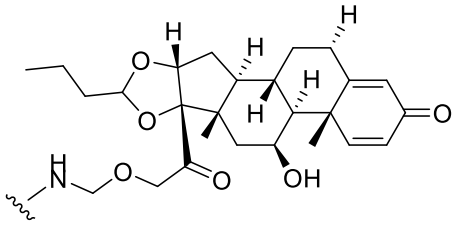

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; and


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32. A pharmaceutical composition comprising the compound of any one of claims 1-31, and a pharmaceutically acceptable excipient, carrier, or diluent.

33. The compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 for use in therapy.

34. Use of the compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 in the manufacture of a medicament for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling in a subject comprising that the compound is to be administered to the subject wherein the disease, disorder, or condition is metabolic, inflammatory, or neurodegenerative.

35. The use of claim 34, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

36. The use of claim 34 or 35, wherein side effects associated with administration of the unconjugated steroid payload of said compound are reduced.

37. Use of the compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 in the manufacture of a medicament for treating dyslipidemia, a metabolic disease, inflammation, or a neurodegenerative disease in a subject.

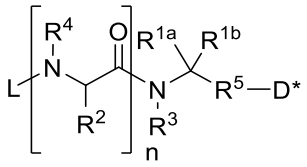
38. Use of the compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 in the manufacture of a medicament for treating dyslipidemia in a subject.

39. Use of the compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 in the manufacture of a medicament for treating a metabolic disease.

40. Use of the compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 in the manufacture of a medicament for treating inflammation in a subject.

41. Use of the compound of any one of claims 1-31 or the pharmaceutical composition of claim 32 in the manufacture of a medicament for treating a neurodegenerative disease in a subject.

42. A method of preparing an antibody-drug conjugate comprising contacting a binding agent with a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein

L is a linker comprising a moiety reactive with an antibody or an antigen binding fragment thereof;

R^{1a} and **R^{1b}** are, independently, hydrogen, alkyl, alkoxy, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, alkylene, or heteroalkylene, wherein when **R^{1a}** is alkylene or heteroalkylene, the alkylene or hetereoalkylene is further bonded to **R^3** to form a 4-, 5-, or 6-membered heterocyclyl;

R^2 is hydrogen, alkylene, heteroalkylene, or an amino acid side chain, wherein when **R^2** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^3** to form a 4-, 5-, or 6-membered heterocyclyl;

R^3 is hydrogen, alkyl, alkylene, or heteroalkylene, wherein when **R^3** is alkylene or heteroalkylene, the alkylene or heteroalkylene is further bonded to **R^{1a}** or **R^2** to form the 4-, 5-, or 6-membered heterocyclyl;

R^4 is hydrogen or alkyl;

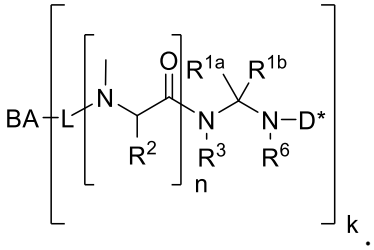
R^5 is oxygen, N**R^6**, or sulfur within D*;

R^6 is hydrogen or alkyl;

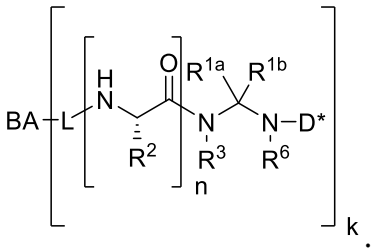
D* is a residue of an anti-inflammatory biologically active compound comprising a hydroxyl, amino, or thiol for conjugation to -$CR^{1a}R^{1b}$- wherein the residue is a steroid or an LXR agonist; and

n is zero, one, two, three, four, five, or six.

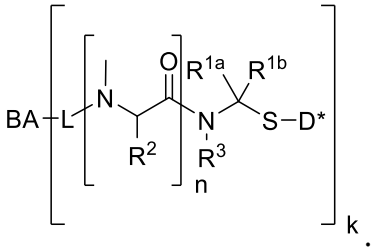
43. The compound of claim 8, having the following structure



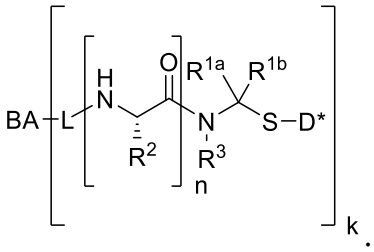
44. The compound of claim 8, having the following structure



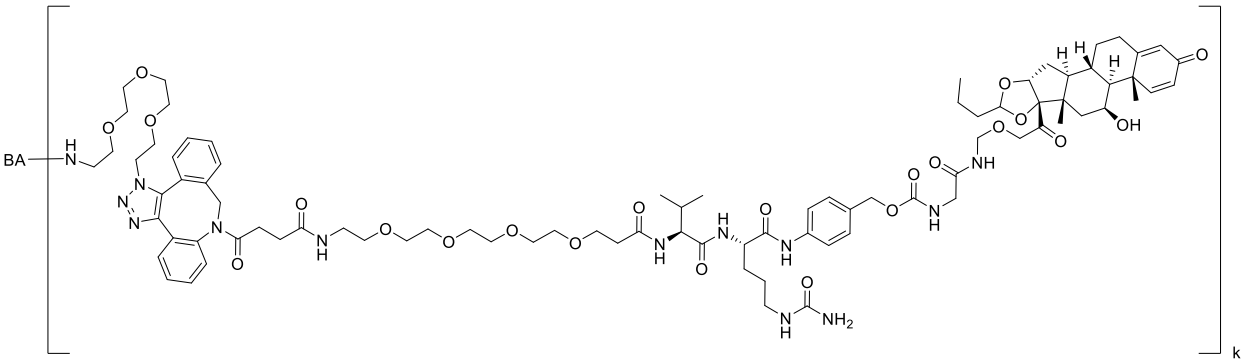
45. The compound of claim 8, having the following structure

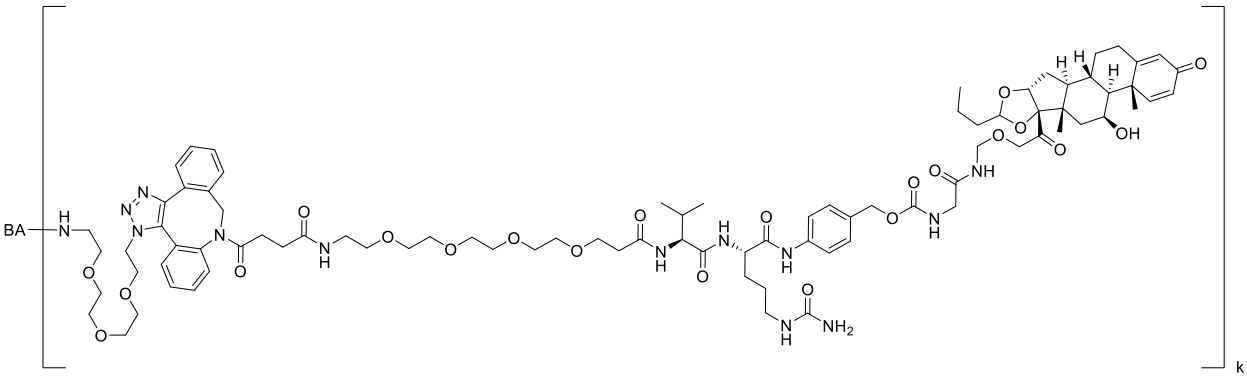


46. The compound of claim 8, having the following structure

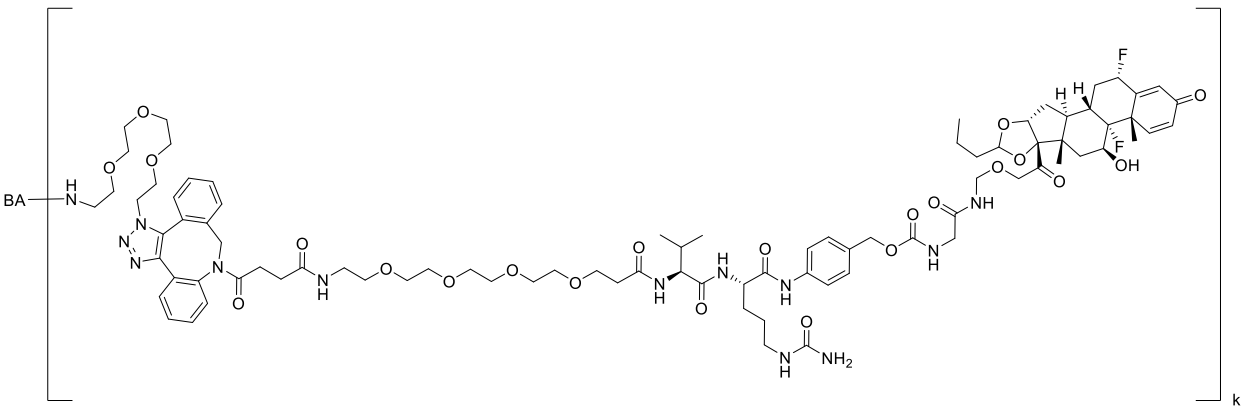


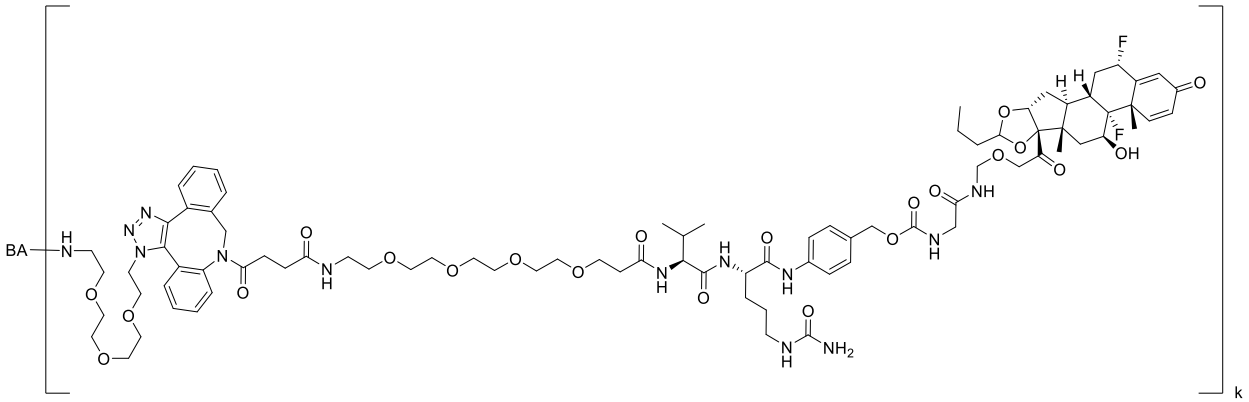
47. The compound of claim 1, selected from the group consisting of



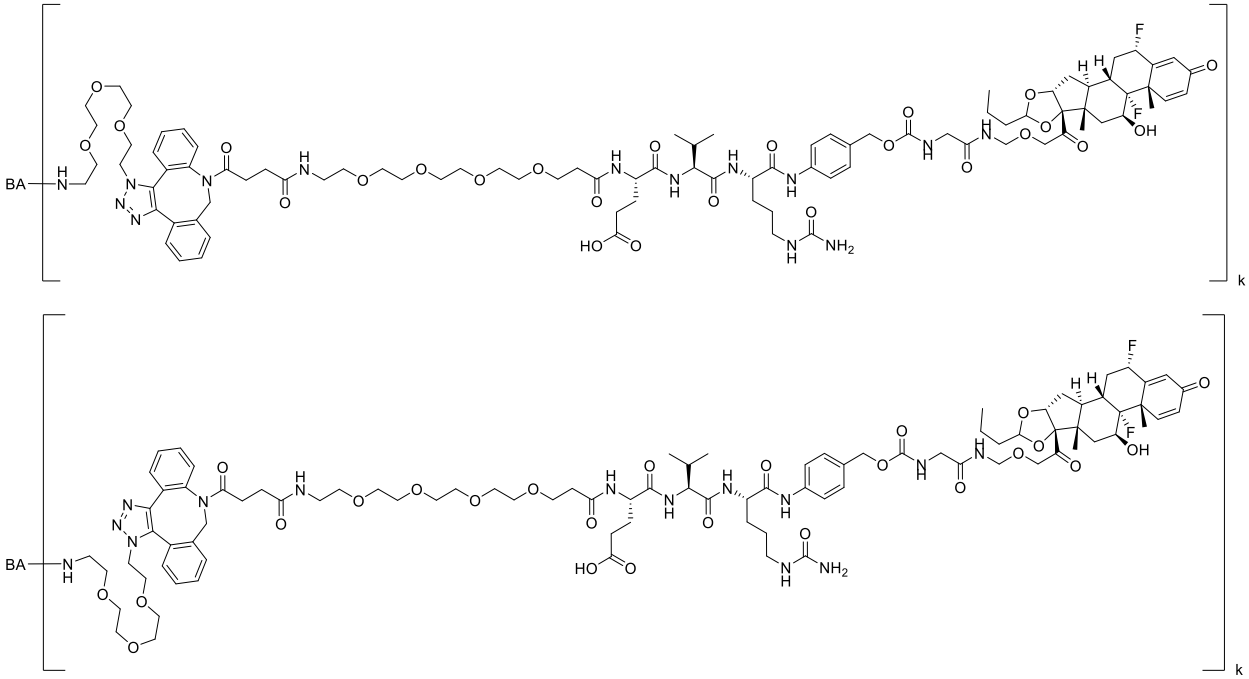


BA-L1-PII-1;

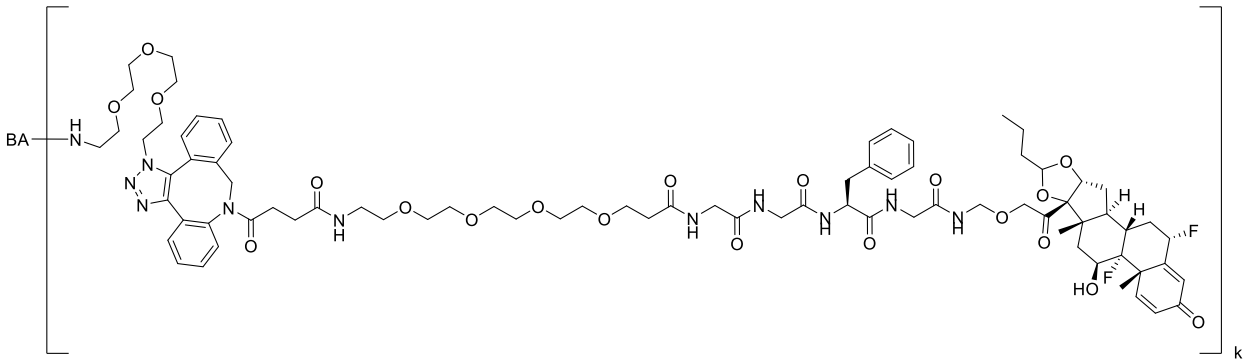


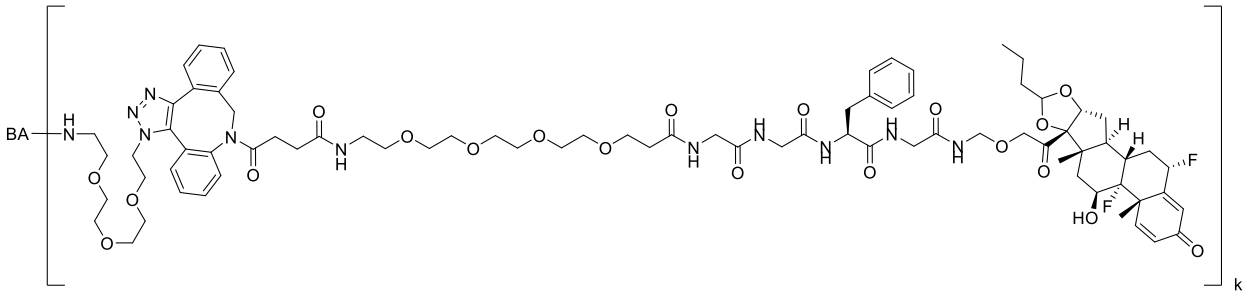


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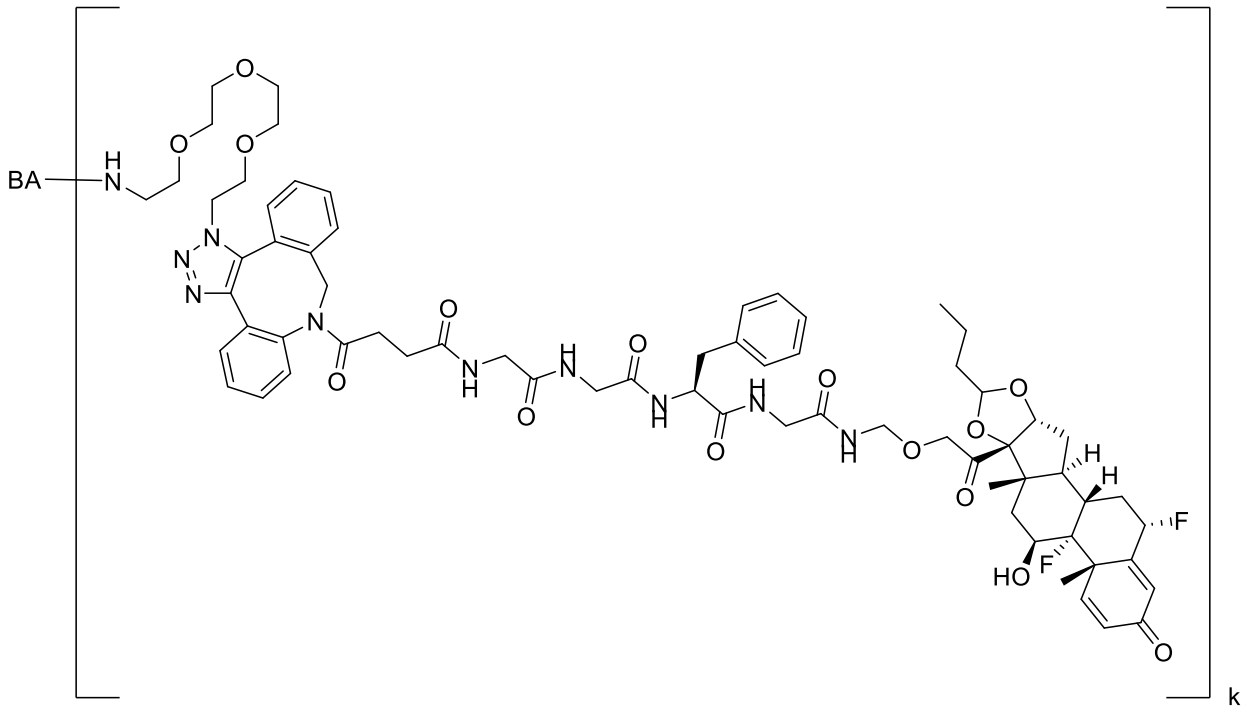


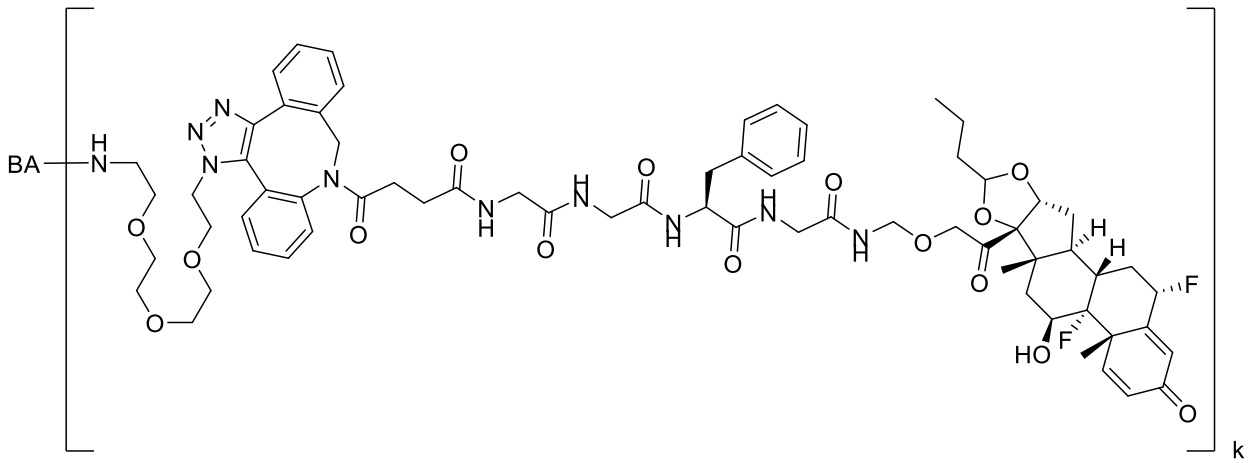
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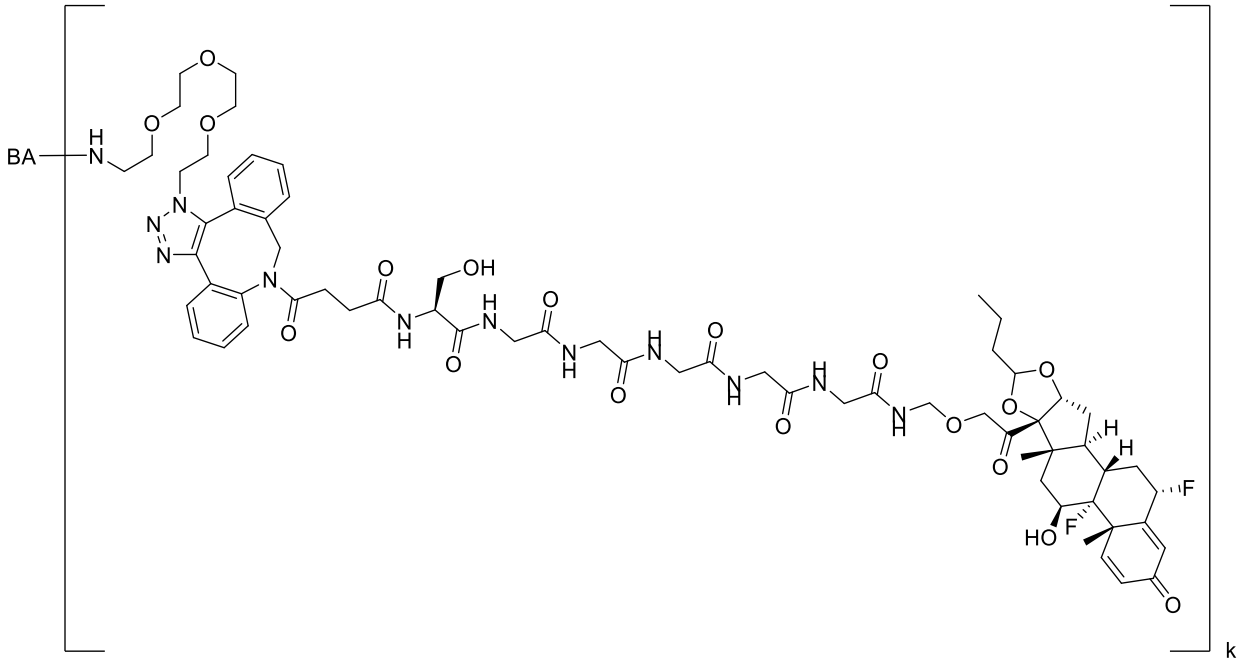


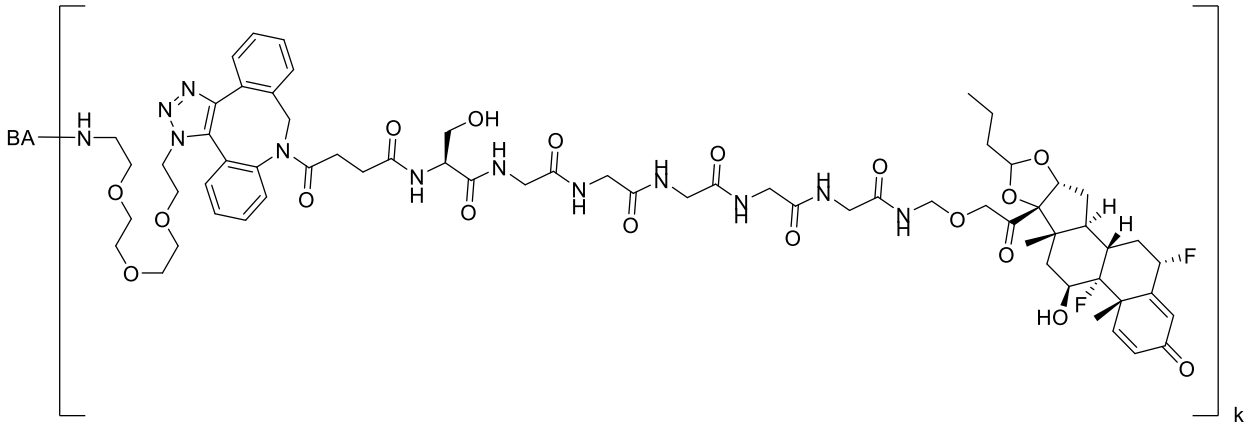
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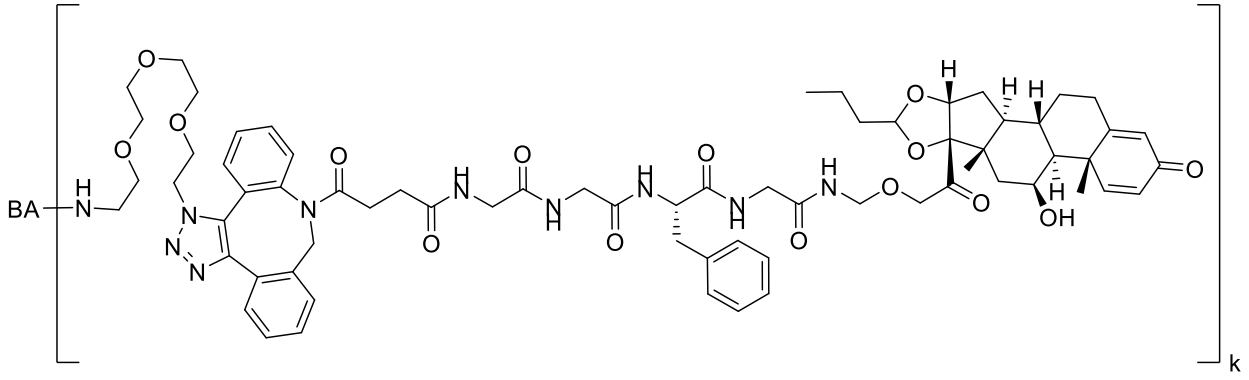


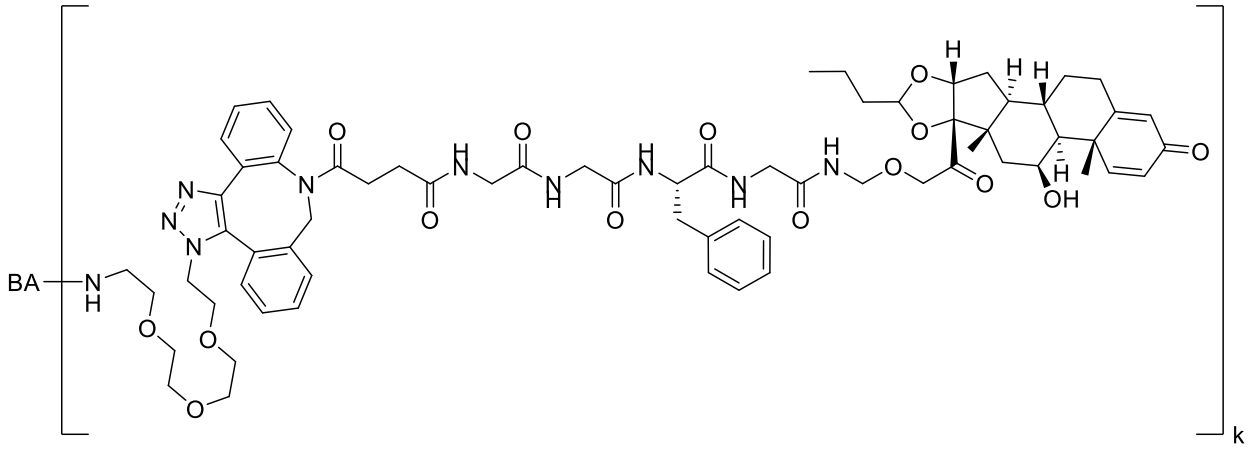
BA-L4-PIII-1;



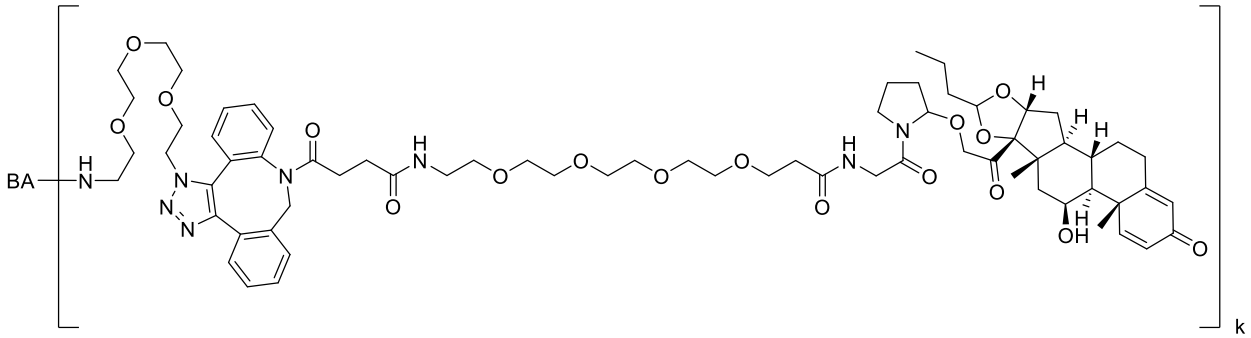


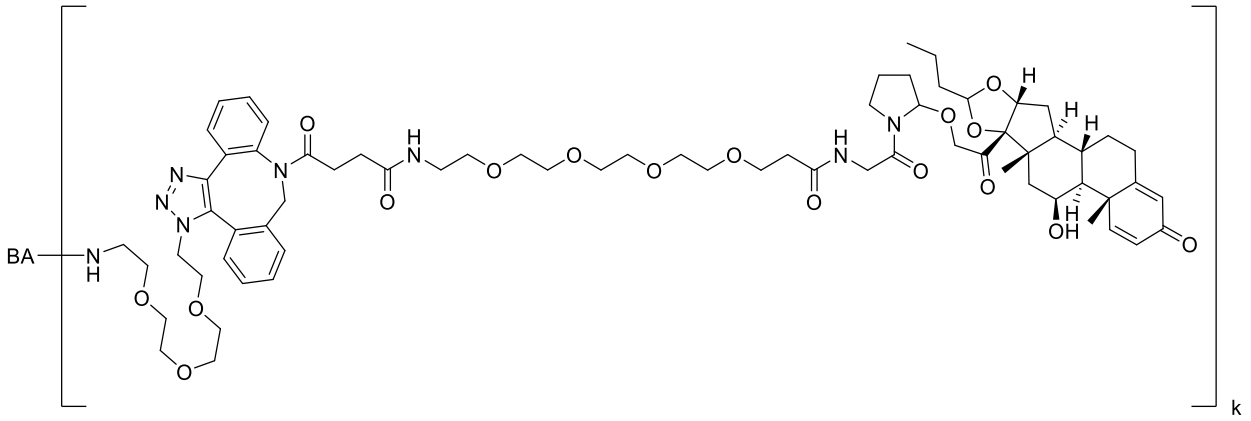
BA-L5-PIII-1;



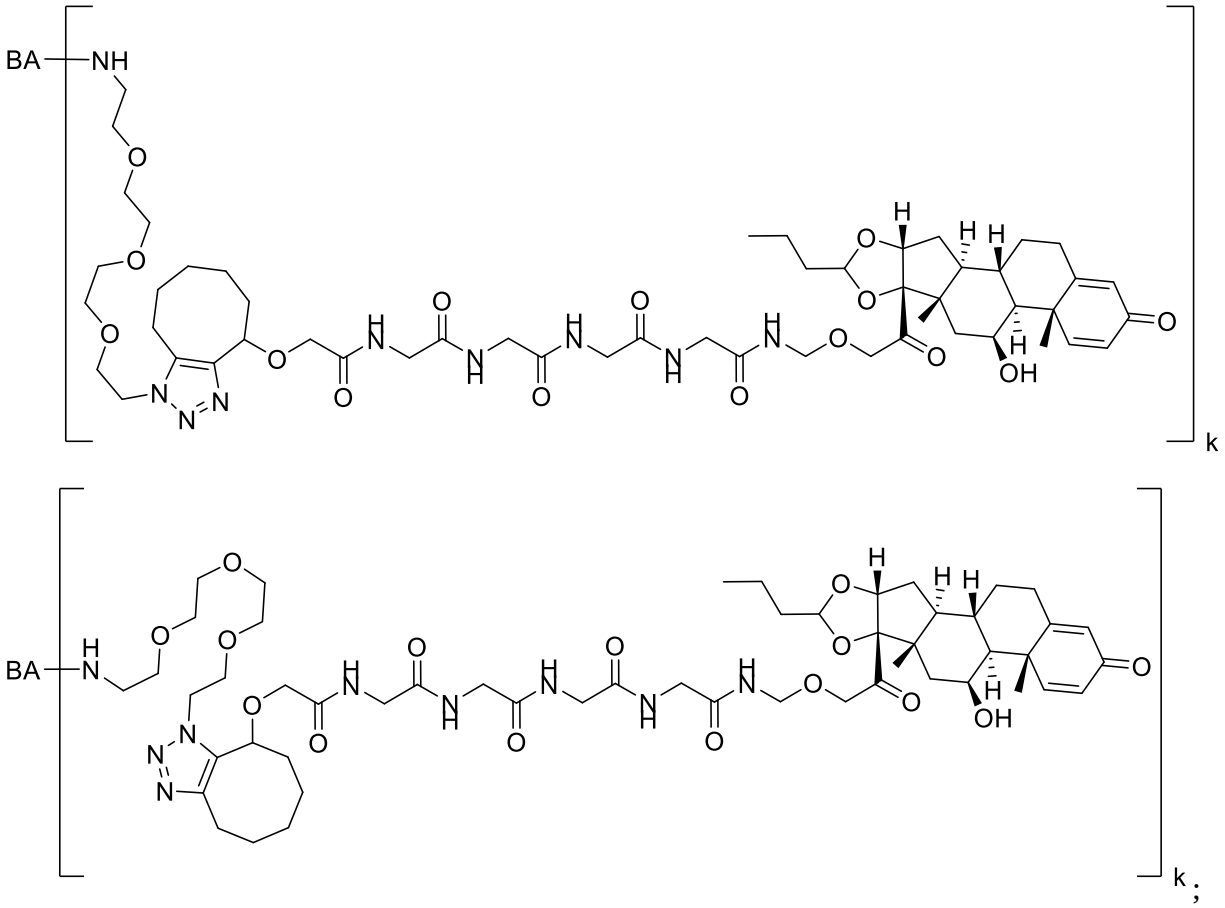


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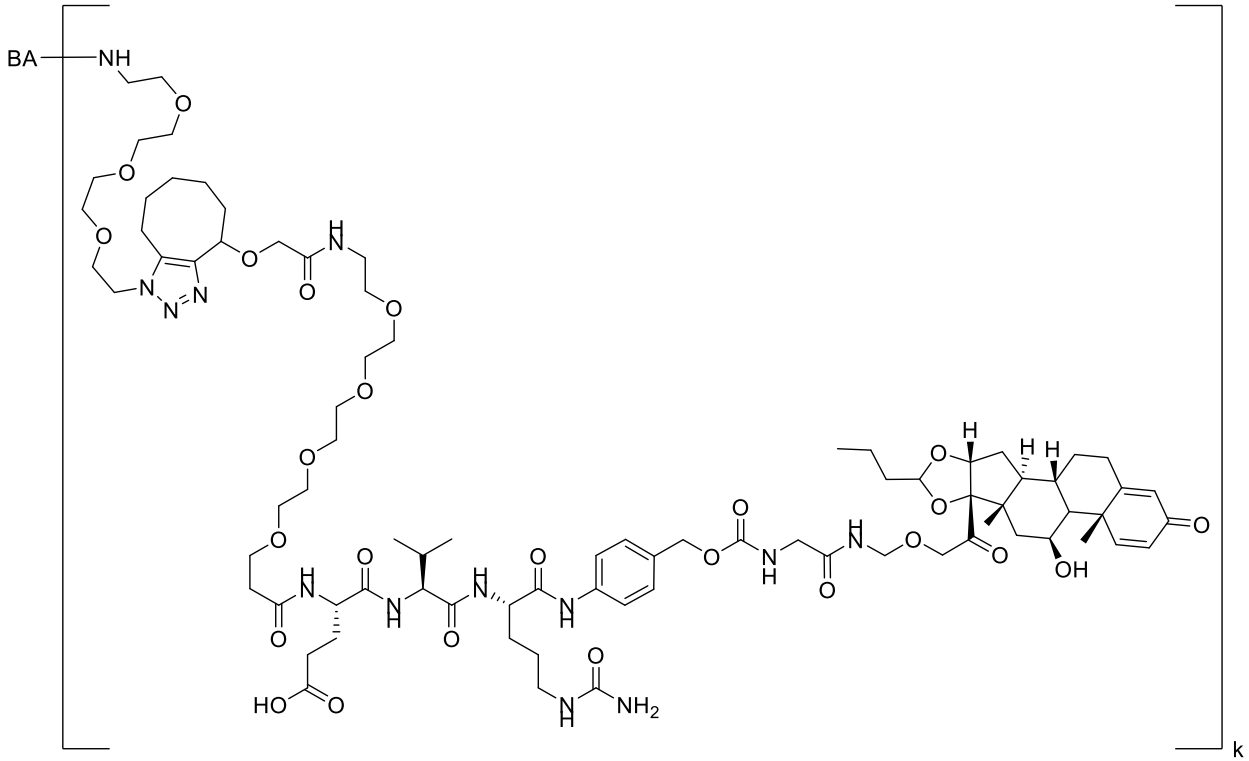


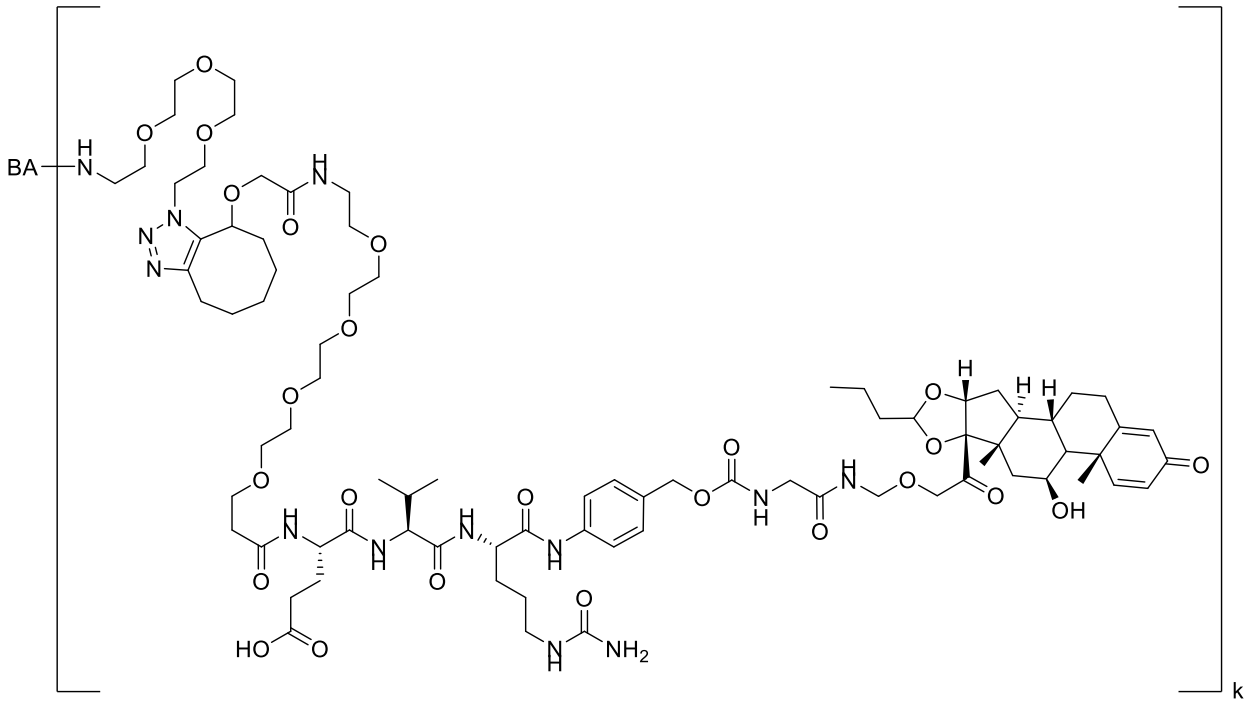


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BA-L13-PII-1; and



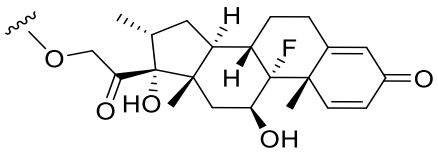
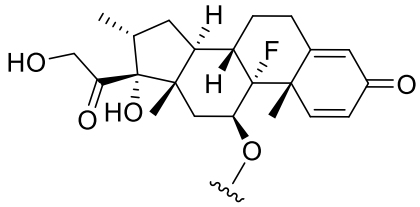
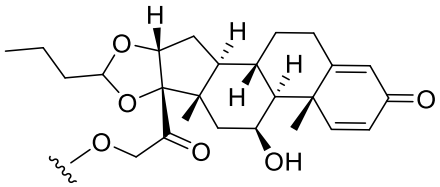
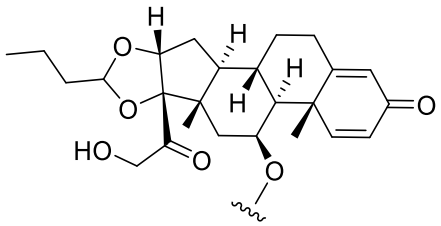
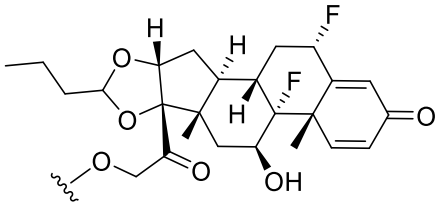
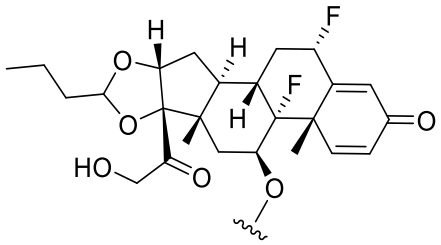
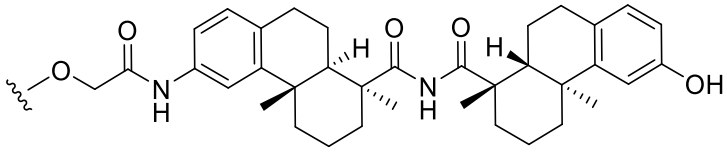
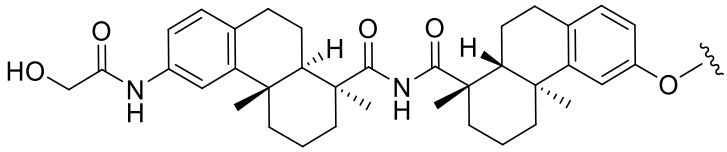


BA-L8-PII-1

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

k is an integer from one to four.

48. The compound of any one of claims 1, 4-21, and 24-29, wherein **R^5-D*** is selected from


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