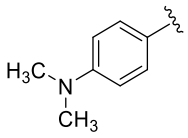
R^4 is not  .

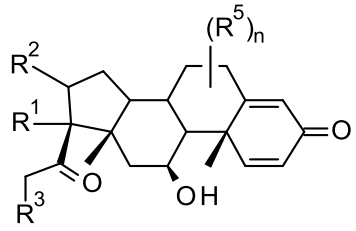
[0006] Provided herein are compounds that are protein-drug conjugates, *e.g.*, antibody-drug conjugates, comprising an antigen-binding protein, *e.g.*, antibody and a compound of Formula (**A**).

[0006a] In another aspect, provided herein is a conjugate compound comprising a binding agent (**BA**) conjugated to a compound as defined herein.

[0007] Provided herein are compounds that are protein-drug conjugates, *e.g.*, antibody-drug conjugates, comprising an antigen-binding protein, *e.g.*, antibody, a compound of Formula (**A**), and a cyclodextrin moiety.

[0007a] In another aspect, provided herein is a conjugate compound comprising a binding agent (**BA**) conjugated to a compound as defined herein and a cyclodextrin (**CD**).

[0007b] In another aspect, provided herein is a conjugate compound comprising a binding agent (**BA**) conjugated to a compound of Formula (**1000**) and a cyclodextrin (**CD**):



1000

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein:

R^1 and R^2 are, independently, -H, alkyl, alkyl-C(O)-O-, -OH, or halo; or

R^1 and R^2 together form ,

wherein R^4 is alkyl, aryl, arylalkyl, alkylene-NR^aR^b, arylene-NR^aR^b, -CH_2 arylene-NR^aR^b, or an N-containing heterocycloalkyl;

R^3 is -OH,

R^5 is, independently in each instance, selected from a substituent in the group consisting of –OH, halo, and alkyl; and each R^5 is positioned on any ring atom; and

R^a and R^b are, independently in each instance, selected from the group consisting of -H and alkyl; or R^a and R^b cyclize to form cycloheteroalkyl with three to six ring atoms, including one hetero atom, which is the N to which they are attached;

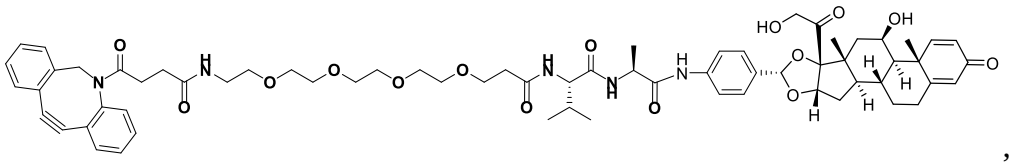
n is an integer from 0-19.

[0007c] In another aspect, provided herein is use of a compound as defined herein or a conjugate compound as defined herein in the manufacture of medicament for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

[0007d] In another aspect, provided herein is an *in vitro* method of delivering a compound as defined herein to a cell comprising contacting said cell with a protein steroid conjugate of said compound, wherein said protein conjugate comprises an antibody or antigen binding fragment thereof that binds a surface antigen of said cell and the compound as defined herein.

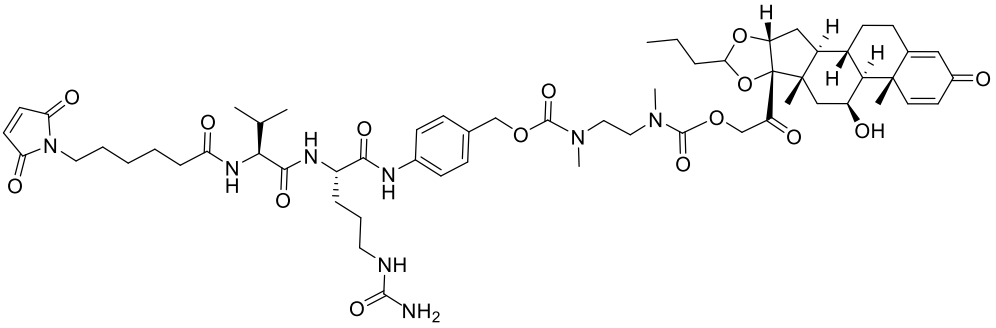
[0007e] In another aspect, provided herein is a linker-payload comprising the compound as defined herein, each linked to a reactive group via a linker.

[0007f] In another aspect, provided herein is a linker-payload selected from the group consisting of:



,

and

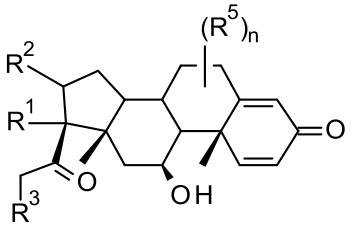


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CLAIMS

What is claimed is:

1. A compound of Formula (**1000**):



1000

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein:

R^1 and R^2 together form ,

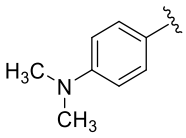
R^3 is -OH,

R^4 is selected from the group consisting of -alkylene-NR^aR^b, -X-arylene-Y-NR^aR^b, and -X-heteroarylene-Y-NR^aR^b; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-;

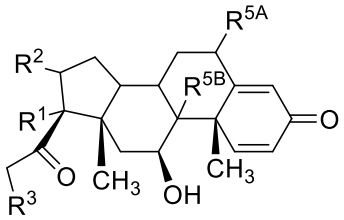
R^5 is, independently in each instance, selected from a substituent in the group consisting of –OH, halo, and alkyl; and each R^5 is positioned on any ring atom; and

R^a and R^b are, independently in each instance, selected from the group consisting of -H and alkyl; or R^a and R^b cyclize to form cycloheteroalkyl with three to six ring atoms, including one hetero atom, which is the N to which they are attached;

n is an integer from 0-19; with the proviso that

R^4 is not .

2. The compound of claim 1, wherein the compound of Formula (**1000**) has the structure of Formula (**A[1]**):

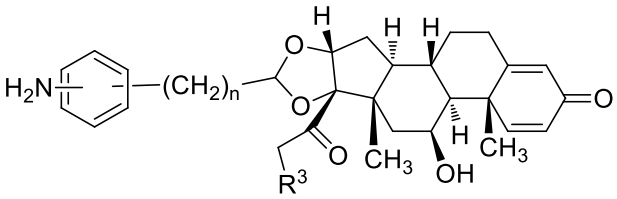


(**A^{1}**)

wherein R^1-R^3 are as defined above and R^{5A} and R^{5B} are each, independently, halo or a hydrogen atom.

3. The compound of claim 2, wherein R^1 and R^2 together form , wherein R^4 is selected from the group consisting of -alkylene-NR^aR^b, -X-arylene-Y-NR^aR^b, and -X-heteroarylene-Y-NR^aR^b; wherein X is absent, -N-, -CH_2-, or -O-; wherein Y is absent or -CH_2-.

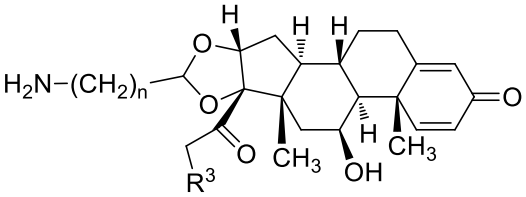
4. The compound of claim 1 according to Formula (**A^{2}**)



(**A^{2}**)

wherein n is an integer from 0 to 4.

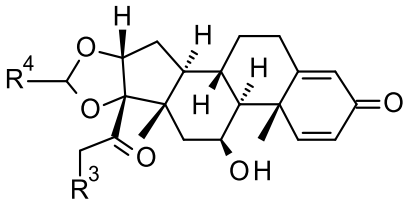
5. The compound of claim 1 according to Formula (**A^{3}**):



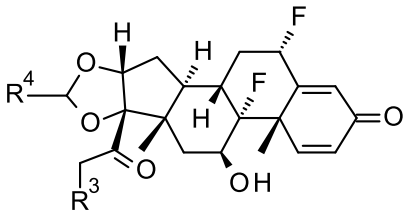
(**A^{3}**)

wherein n is an integer from 1-4.

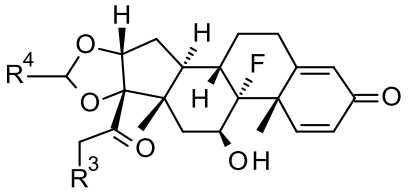
6. The compound of claim 1 according to Formula **1110**, **1120**, **1130**, or **1140**:



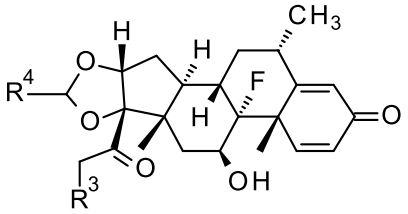
1110



1120

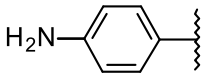


1130

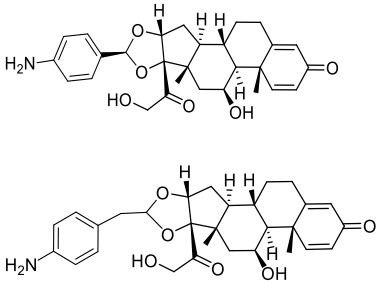


1140

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

7. The compound of claim 6, wherein R^4 is $H_2NCH_2CH_2$- or .

8. The compound of claim 1, wherein the compound is:

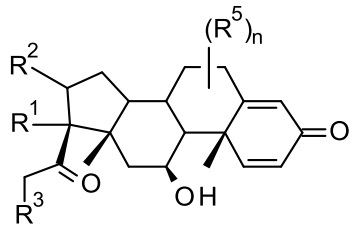


or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

9. A conjugate compound comprising a binding agent (**BA**) conjugated to a compound of any of claims 1-8.

10. A conjugate compound comprising a binding agent (**BA**) conjugated to a compound of any one of claims 1-8 and a cyclodextrin (**CD**).

11. A conjugate compound comprising a binding agent (**BA**) conjugated to a compound of Formula (**1000**) and a cyclodextrin (**CD**):



1000

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof,

wherein:

R^1 and R^2 are, independently, -H, alkyl, alkyl-C(O)-O-, -OH, or halo; or

R^1 and R^2 together form ,

wherein R^4 is alkyl, aryl, arylalkyl, alkylene-NR^aR^b, arylene-NR^aR^b, -CH_2 arylene-NR^aR^b, or an N-containing heterocycloalkyl;

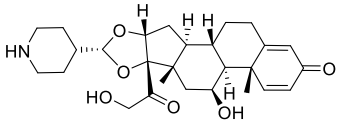
R^3 is -OH,

R^5 is, independently in each instance, selected from a substituent in the group consisting of –OH, halo, and alkyl; and each R^5 is positioned on any ring atom; and

R^a and R^b are, independently in each instance, selected from the group consisting of -H and alkyl; or R^a and R^b cyclize to form cycloheteroalkyl with three to six ring atoms, including one hetero atom, which is the N to which they are attached;

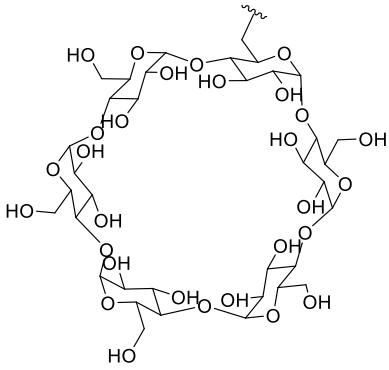
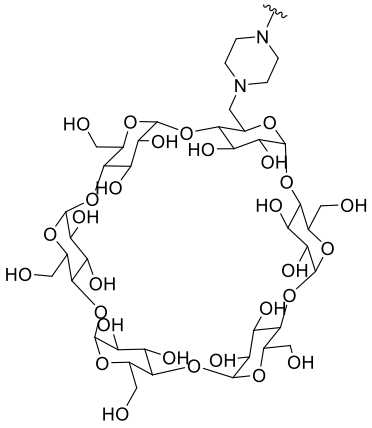
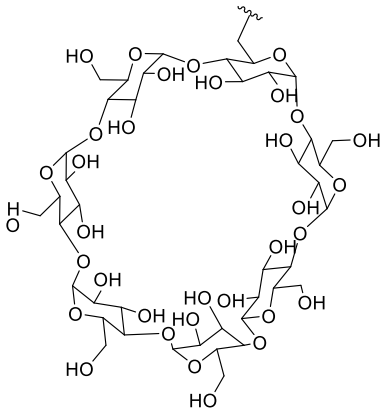
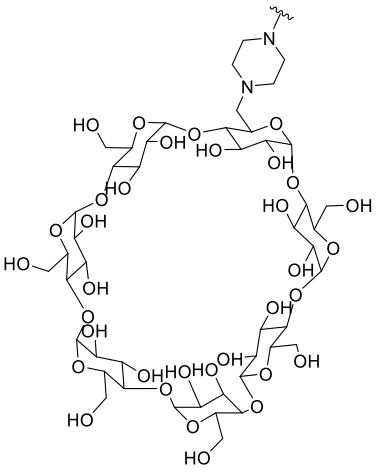
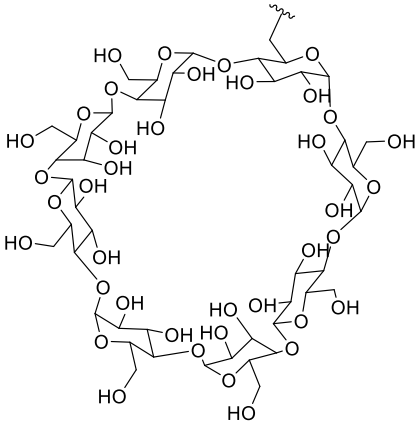
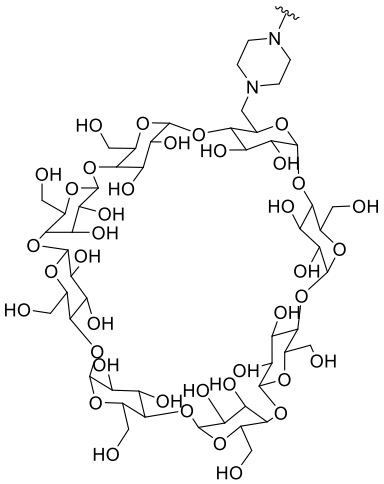
n is an integer from 0-19.

12. The conjugate compound of claim 11, wherein the compound is:



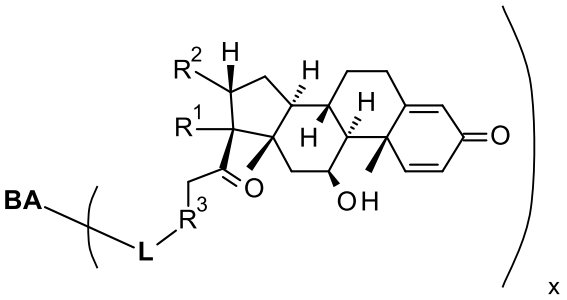
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

13. The conjugate compound of any one of claims 10-12, wherein **CD** is selected from the group consisting of

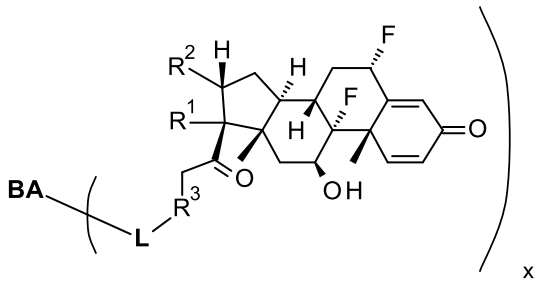

,

,

,

,

, and

, wherein ⁄ indicates the bond through which the CD is linked to the conjugate compound.

14. The conjugate compound of any one of claims 9 to 12, wherein the binding agent (**BA**) is an antibody or antigen binding fragment thereof.

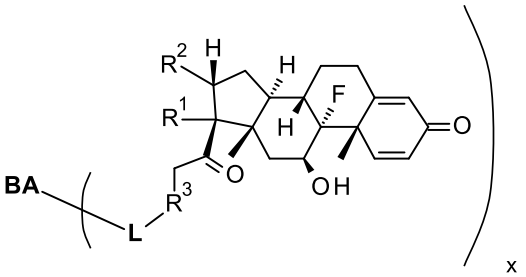
15. The conjugate compound of claim 9 according to Formula **1210**, **1220**, **1230**, or **1240**:



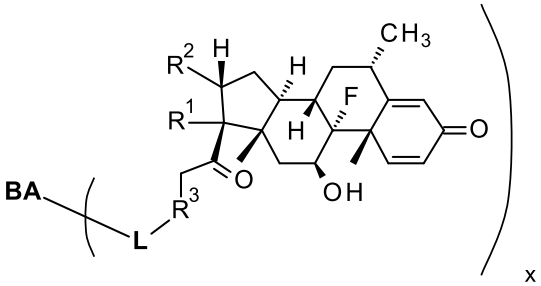
1210



1220



1230



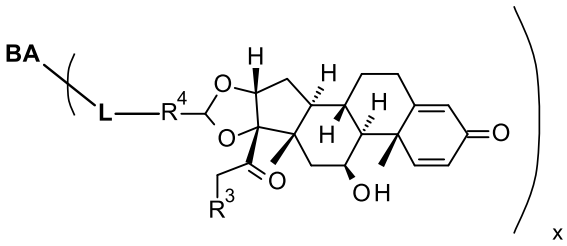
1240

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof;

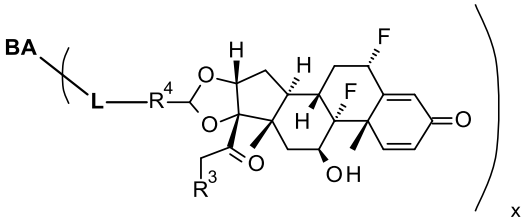
wherein R^3 is covalently bonded to L or BA;

wherein L is an optional linker.

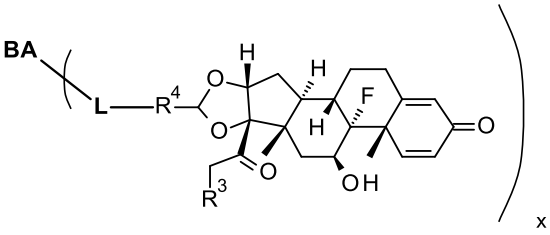
16. The conjugate compound of claim 9 according to Formula **1310**, **1320**, **1330**, or **1340**:



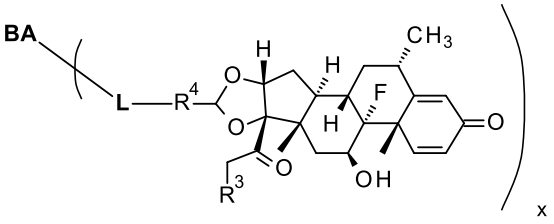
1310



1320



1330



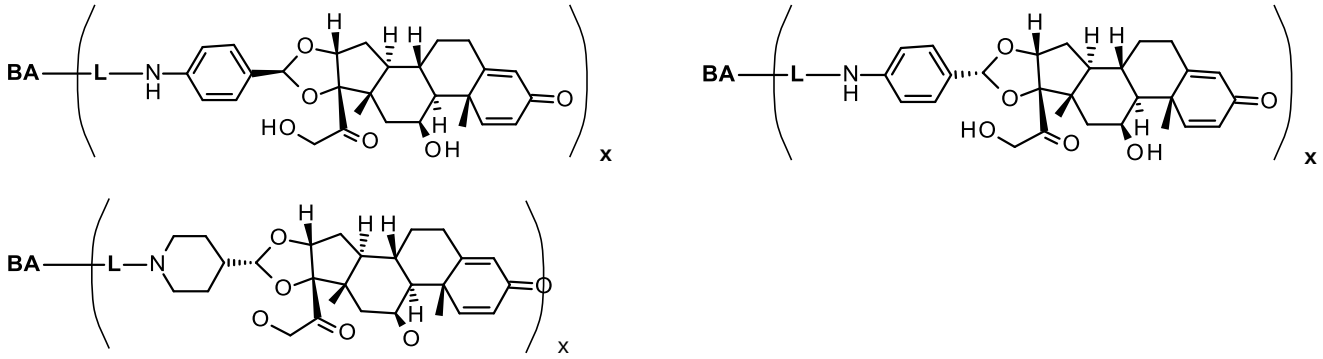
1340

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof;

wherein R^4 is covalently bonded to L or BA;

wherein L is an optional linker.

17. The conjugate compound of claim 9 or 12 selected from the group consisting of:



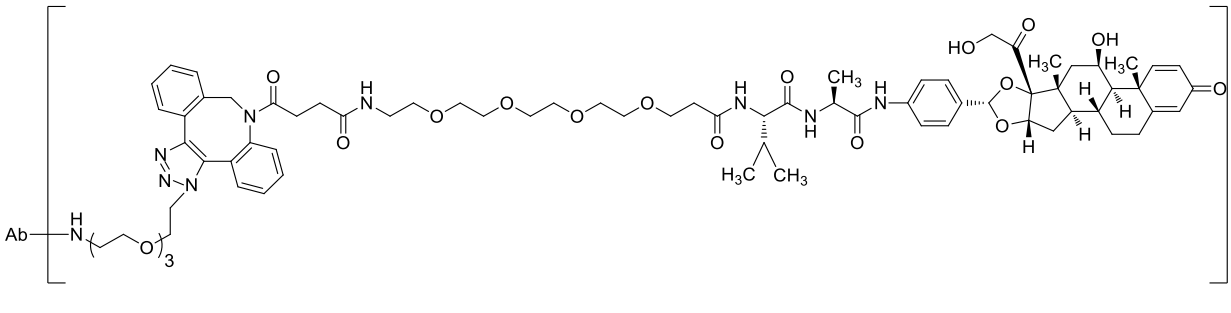
and pharmaceutically acceptable salts, solvates, and stereoisomers thereof;

wherein each L is an optional linker;

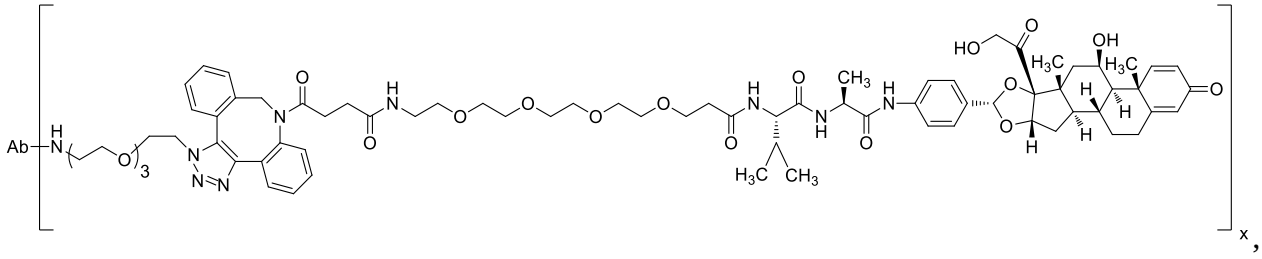
each BA is a binding agent; and

each x is an integer from 1 to 30.

18. The conjugate compound of claim 9 selected from the group consisting of:



or



,

wherein x is an integer from 1 to 30;

Ab is an antibody or antibody binding fragment thereof;

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

19. Use of a compound of any of claims 1-8 or a conjugate compound of any one of claims 9-17 in the manufacture of a medicament for treating a disease, disorder, or condition associated with glucocorticoid receptor signaling, wherein the disease, disorder, or condition, is an inflammatory disease, disorder, or condition.

20. The use of claim 18, wherein the disease, disorder, or condition, is asthma.

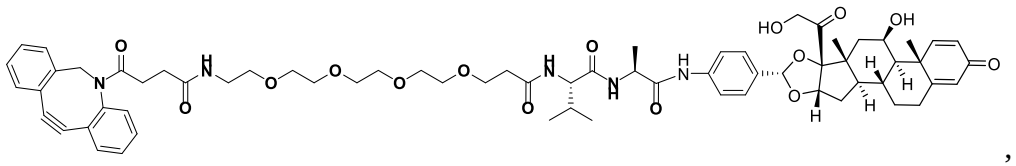
21. The use of claim 19, wherein the compound is a compound of any one of claims 6-8.

22. The use of claim 20, wherein side effects associated with administration of the unconjugated steroid payload of said compound are reduced.

23. An *in vitro* method of delivering a compound of claim 1 to a cell comprising contacting said cell with a protein steroid conjugate of said compound, wherein said protein conjugate comprises an antibody or antigen binding fragment thereof that binds a surface antigen of said cell and the compound of claim 1.

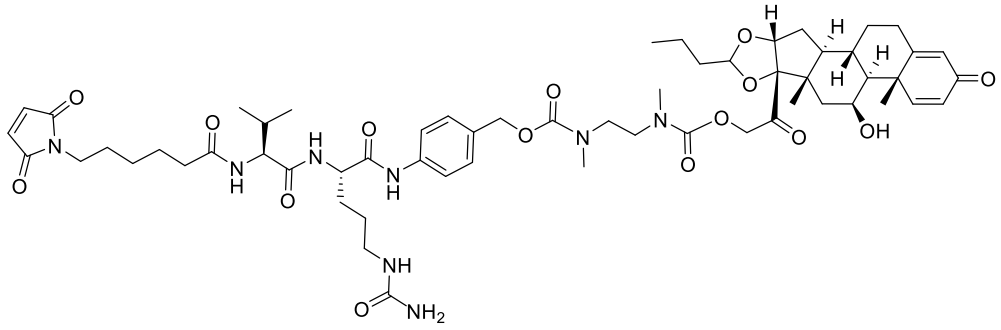
24. A linker-payload comprising the compound of any of claims 1-8 or the conjugate compound of claim 9 or 12, each linked to a reactive group via a linker.

25. A linker-payload selected from the group consisting of:


HO
O
OH
O
H
H
H
H
O
O
O

26. The conjugate compound of claim 11 wherein the binding agent is conjugated to budesonide.

27. The linker-payload of claim 24, wherein the linker-payload is



.

28. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-8 or a conjugate compound of any one of claims 9-17.