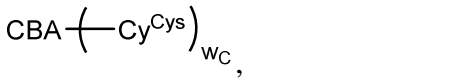
CLAIMS

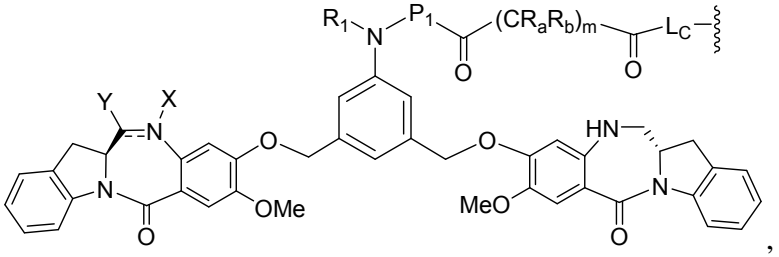
1. A pharmaceutical composition comprising an immunoconjugate and 0.1 mM to 20 mM methionine, wherein the immunoconjugate is represented by the following formula:



CBA is an antibody or antigen-binding fragment thereof;

W_C is 1 or 2; and

Cy^{Cys} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

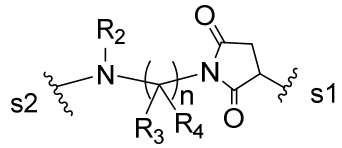
the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a $(C_1$-$C_4)$alkyl; and when it is a single bond, X is -H or an amine protecting moiety, Y is -OH or $-SO_3H$;

R_1 is -H or a $(C_1$-$C_3)$alkyl;

P_1 is an amino acid residue or a peptide containing 2 to 5 amino acid residues;

R_a and R_b, for each occurrence, are independently -H, $(C_1$-$C_3)$alkyl, or a charged substituent or an ionizable group Q;

m is an integer from 1 to 6;

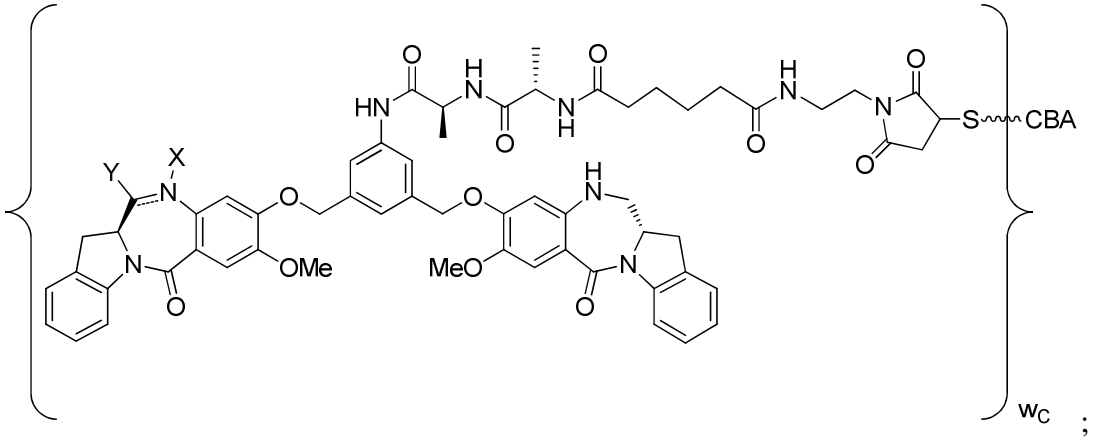
L_C is represented by , s1 is the site covalently linked to CBA, and s2 is the site covalently linked to the -C(=O)- group on Cy^{Cys}; wherein:

R_2 is -H or a $(C_1$-$C_3)$alkyl

R_3 and R_4, for each occurrence, are independently -H or a $(C_1$-$C_3)$alkyl; and

n is an integer between 1 and 10.

2. The pharmaceutical composition of claim 1, wherein the immunoconjugate is represented by the following formula:



;

or a pharmaceutically acceptable salt thereof, wherein the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H, and when it is a single bond, X is -H, and Y is -OH or $-SO_3H$.

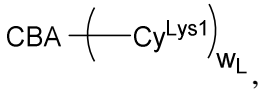
3. The pharmaceutical composition of claim 1 or 2, wherein CBA is an anti-CD123 antibody or antigen-binding fragment thereof comprising:

a) an immunoglobulin heavy chain variable region comprising a CDR1 having an amino acid sequence set forth in SEQ ID NO:4, a CDR2 having an amino acid sequence set forth in SEQ ID NO:5, and a CDR3 having an amino acid sequence set forth in SEQ ID NO:6; and

b) an immunoglobulin light chain variable region comprising a CDR1 having an amino acid sequence set forth in SEQ ID NO:1, a CDR2 having an amino acid sequence set forth in SEQ ID NO:2, and a CDR3 having an amino acid sequence set forth in SEQ ID NO:3.

4. The pharmaceutical composition of claim 3, wherein the antibody or antigen-binding fragment thereof comprises a V_H sequence of SEQ ID NO:7 and a V_L sequence of SEQ ID NO:9.

5. A pharmaceutical composition comprising an immunoconjugate and 0.1 mM to 20 mM methionine, wherein the immunoconjugate is represented by the following formula:

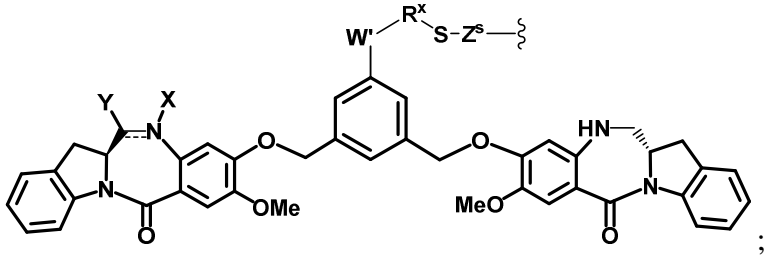


wherein:

CBA is an antibody or antigen-binding fragment thereof;

W_L is an integer from 1 to 20; and

Cy^{Lys1} is represented by the following formula:



;

or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a $(C_1$-$C_4)$alkyl; and when it is a single bond, X is -H or an amine protecting moiety, and Y is -OH or $-SO_3H$;

R^x is independently a $(C_1$-$C_6)$alkyl;

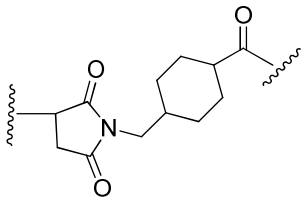
W' is $-NR^e$,

R^e is $-(CH_2$-CH_2-$O)_{n1}$-R^k;

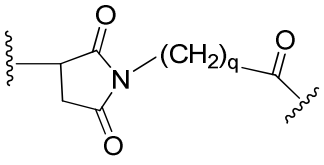
n1 is an integer from 2 to 6;

R^k is -H or -Me;

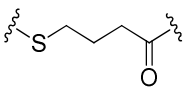
Z^s is selected from any one of the following formulas:



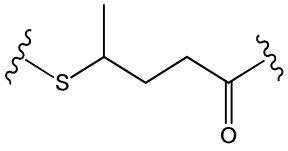
(b1);



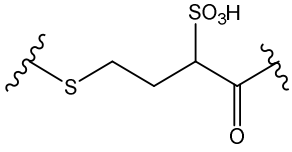
(b2);



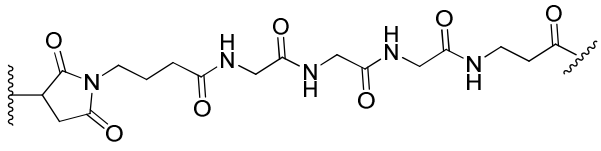
(b3);



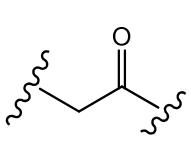
(b4);



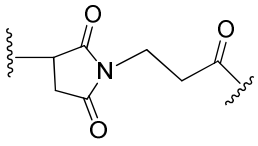
(b5),



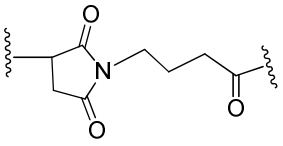
(b6),



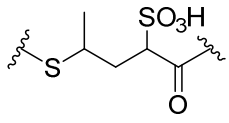
(b7);



(b8);



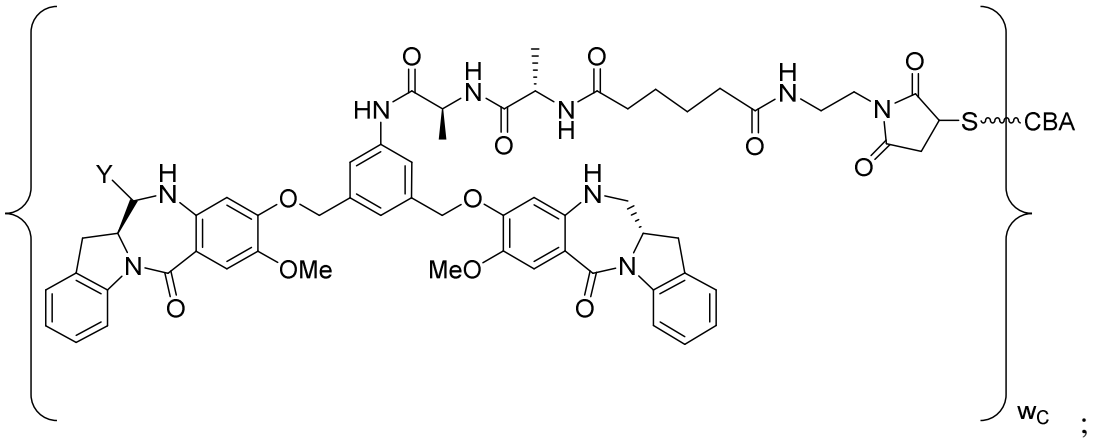
(b9); and



(b10),

or a pharmaceutically acceptable salt thereof, wherein q is an integer from 1 to 5.

6. A pharmaceutical composition comprising 1 mM to 4 mM of methionine and an immunoconjugate represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

Y is -SO_3H or sodium salt thereof;

w_C is 2; and

CBA is an anti-CD123 antibody comprising: a) an immunoglobulin heavy chain having the amino acid sequence set forth in SEQ ID NO:8; and b) an immunoglobulin light chain having the amino acid sequence set forth in SEQ ID NO:10.

7. The pharmaceutical composition of claim 6, wherein the pharmaceutical composition comprises 3 mM methionine.

8. The pharmaceutical composition of claim 6 or 7, wherein the pharmaceutical composition comprises 1 mg/mL to 5 mg/mL, 1 mg/mL to 3 mg/mL, or 1.5 mg/mL to 2.5 mg/mL of the immunoconjugate.

9. The pharmaceutical composition of claim 6, 7 or 8, wherein the pharmaceutical composition further comprises 10 µM to 100 µM, 20 µM to 90 µM, 30 µM to 80 µM, or 40 µM to 60 µM of sodium bisulfite.

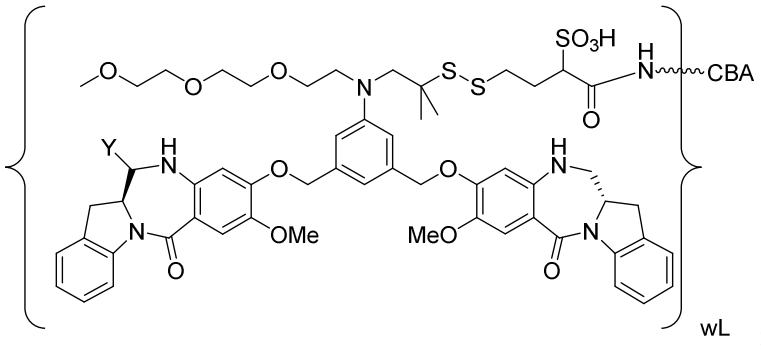
10. The pharmaceutical composition of any one of claims 6-9, wherein the pharmaceutical composition further comprises trehalose, polysorbate 20, and succinate.

11. The pharmaceutical composition of claim 6, wherein the pharmaceutical composition comprises 3mM methionine, 2 mg/mL of the immunoconjugate, 10 mM succinate, 50 µM sodium bisulfite, 7.2% (w/v) trehalose, and 0.01% (w/v) polysorbate 20.

12. The pharmaceutical composition of any one of claims 6-11, wherein the pharmaceutical composition has a pH of 4 to 4.5.

13. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition has a pH of 4.2.

14. A pharmaceutical composition comprising 1 mM to 4 mM of methionine and an immunoconjugate represented by the following formula:



;

or a pharmaceutically acceptable salt thereof, wherein:

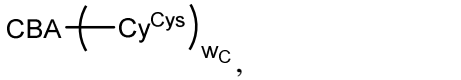
Y is $-SO_3H$ or sodium salt therof;

W_L is an integer from 1 to 10; and

CBA is an anti-CD33 antibody comprising an immunoglobulin heavy chain having the amino acid sequence set forth in SEQ ID NO:18 and an immunoglobulin light chain having the

amino acid sequence set forth in SEQ ID NO:20.

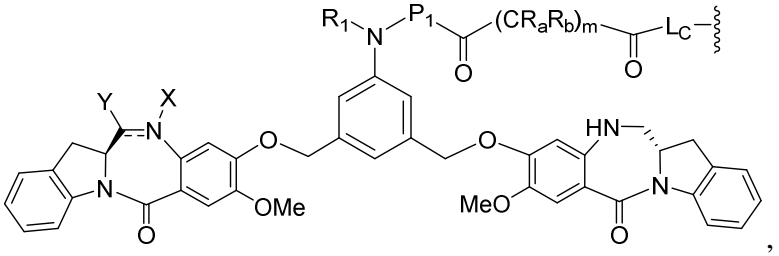
15. A method of reducing the amount of methionine oxidation in an immunoconjugate comprising mixing the immunoconjugate with 0.1 mM to 20 mM methionine to give a pharmaceutical composition comprising the immunoconjugate and methionine, wherein the immunoconjugate is represented by the following formula:



CBA is an antibody or antigen-binding fragment thereof;

W_C is 1 or 2; and

Cy^{Cys} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

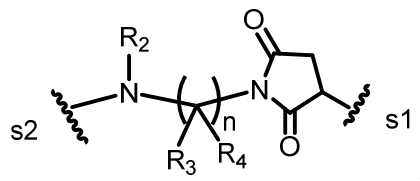
the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a $(C_1$-$C_4)$alkyl; and when it is a single bond, X is -H or an amine protecting moiety, Y is -OH or $-SO_3H$;

R_1 is -H or a $(C_1$-$C_3)$alkyl;

P_1 is an amino acid residue or a peptide containing 2 to 5 amino acid residues;

R_a and R_b, for each occurrence, are independently -H, $(C_1$-$C_3)$alkyl, or a charged substituent or an ionizable group Q;

m is an integer from 1 to 6;

L_C is represented by 

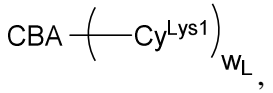
, s1 is the site covalently linked to CBA, and s2 is the site covalently linked to the -C(=O)- group on Cy^{C1}; wherein:

R_2 is -H or a $(C_1$-$C_3)$alkyl

R_3 and R_4, for each occurrence, are independently -H or a $(C_1$-$C_3)$alkyl; and

n is an integer between 1 and 10.

16. A method of reducing the amount of methionine oxidation in an immunoconjugate comprising mixing the immunoconjugate with 0.1 mM to 20 mM methionine to give a pharmaceutical composition comprising the immunoconjugate and methionine, wherein the immunoconjugate is represented by the following formula:

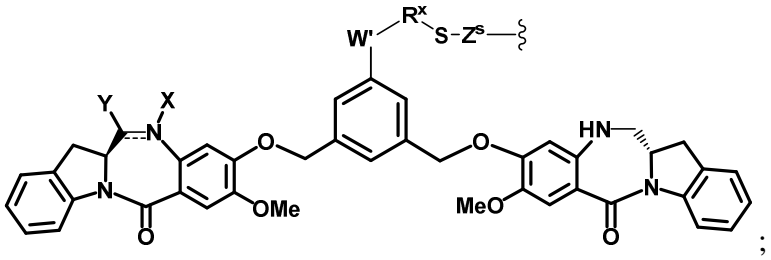


wherein:

CBA is an antibody or antigen-binding fragment thereof;

W_L is an integer from 1 to 20; and

Cy^{Lys1} is represented by the following formula:



;

or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a $(C_1$-$C_4)$alkyl; and when it is a single bond, X is -H or an amine protecting moiety, and Y is -OH or $-SO_3H$;

R^x is independently a $(C_1$-$C_6)$alkyl;

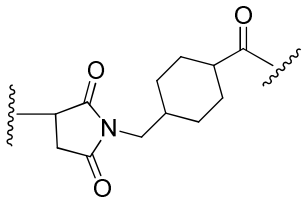
W' is $-NR^e$,

R^e is $-(CH_2$-CH_2-$O)_{n1}$-R^k;

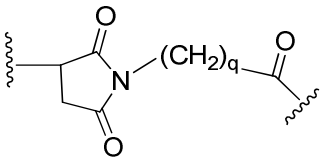
n1 is an integer from 2 to 6;

R^k is -H or -Me;

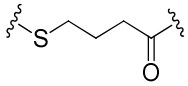
Z^s is selected from any one of the following formulas:



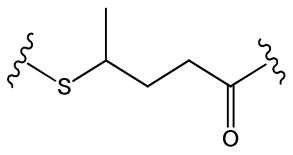
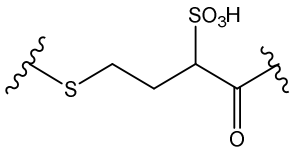
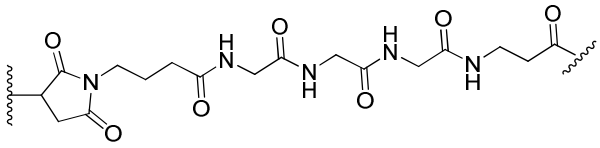
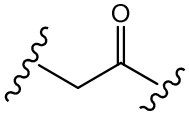
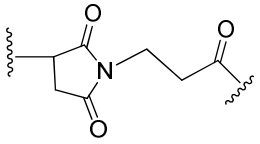
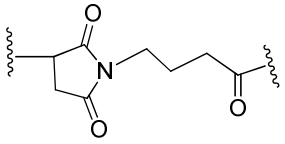
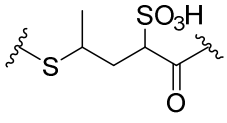
(b1);



(b2);



(b3);

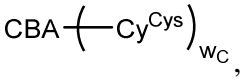

(b4);

(b5),

(b6),

(b7);

(b8);

(b9); and

(b10),

wherein:

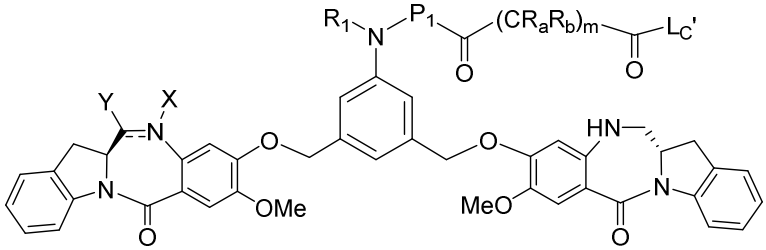
q is an integer from 1 to 5; and

M^+ is $-H^+$ or a cation.

17. A method of preparing an immunoconjugate represented by the following formula:



comprising reacting a CBA with a cytotoxic agent represented by the following formula:

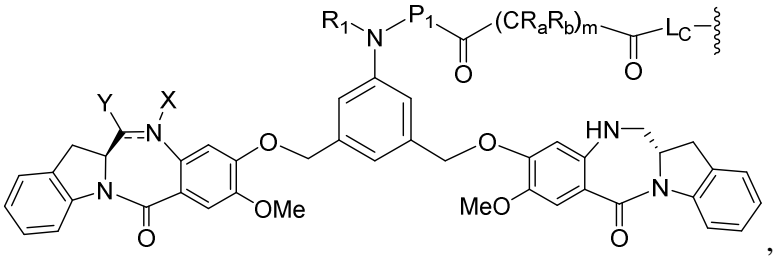


or a pharmaceutically acceptable salt thereof, in the presence of an antioxidant, wherein:

CBA is an antibody or antigen-binding fragment thereof;

W_C is 1 or 2; and

Cy^{Cys} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

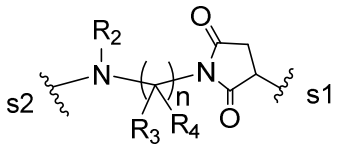
the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C_1-C_4)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, Y is -OH or -SO_3H;

R_1 is -H or a (C_1-C_3)alkyl;

P_1 is an amino acid residue or a peptide containing 2 to 5 amino acid residues;

R_a and R_b, for each occurrence, are independently -H, (C_1-C_3)alkyl, or a charged substituent or an ionizable group Q;

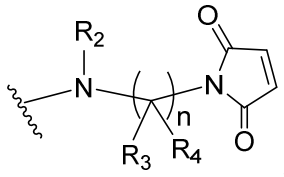
m is an integer from 1 to 6;

L_C is represented by , s1 is the site covalently linked to CBA, and s2 is the site covalently linked to the -C(=O)- group on Cy^{C1};

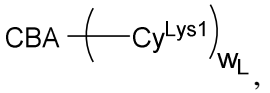
R_2 is -H or a (C_1-C_3)alkyl

R_3 and R_4, for each occurrence, are independently -H or a (C_1-C_3)alkyl; and

n is an integer between 1 and 10; and

L_C' is represented by .

18. A method of preparing an immunoconjugate represented by the following formula:

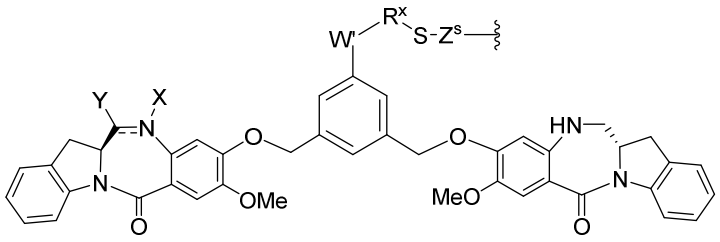
,

wherein:

CBA is an antibody or antigen-binding fragment thereof;

W_L is an integer from 1 to 20; and

Cy^{Lys1} is represented by the following formula:



;

or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a $(C_1$-$C_4)$alkyl; and when it is a single bond, X is -H or an amine protecting moiety, and Y is -OH or $-SO_3H$;

R^x is independently a $(C_1$-$C_6)$alkyl;

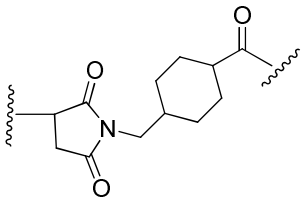
W' is $-NR^e$,

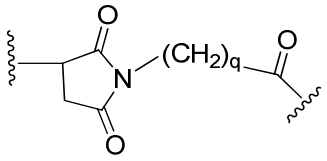
R^e is $-(CH_2$-CH_2-$O)_{n1}$-R^k;

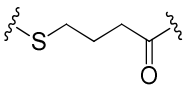
n1 is an integer from 2 to 6;

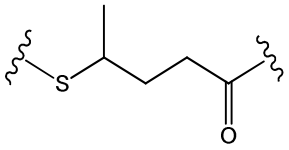
R^k is -H or -Me;

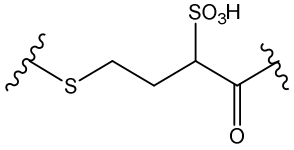
Z^s is selected from any one of the following formulas:

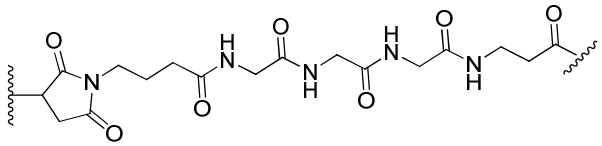


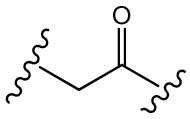
(b1);


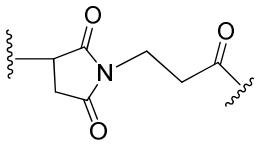
(b2);


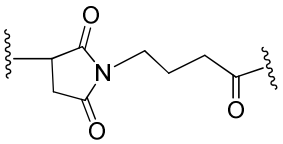
(b3);


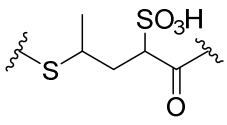
(b4);


(b5),


(b6),


(b7);


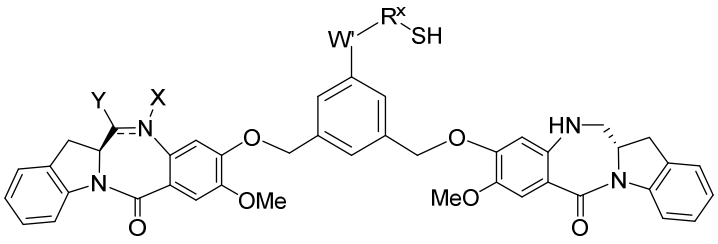
(b8);


(b9); and


(b10),

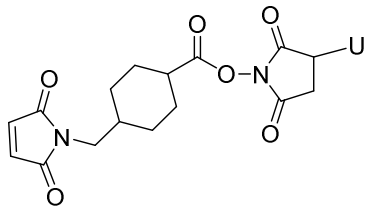
or a pharmaceutically acceptable salt thereof, wherein q is an integer from 1 to 5, comprising the step of:

(a) reacting a cytotoxic agent represented by the following formula:

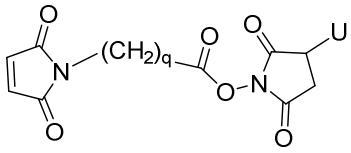


,

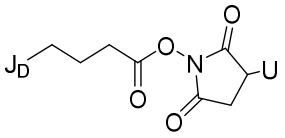
or a pharmaceutically acceptable salt thereof, with a bifunctional crosslinking agent selected from the following:

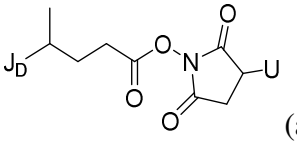


(a1L);

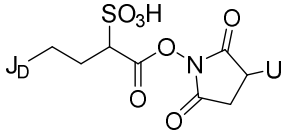


(a2L);



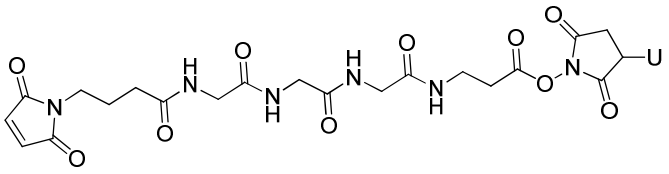


(a3L);

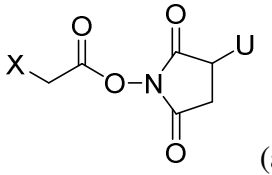


(a4L);

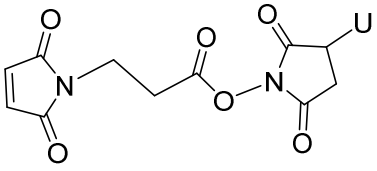
(a5L),



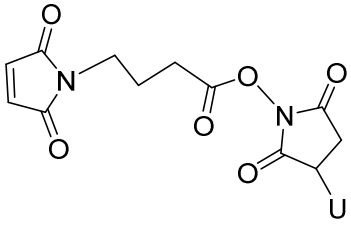
(a6L),

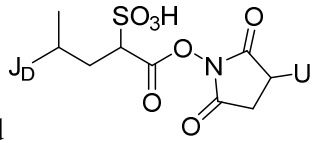


(a7L);



(a8L);





(a9L); and

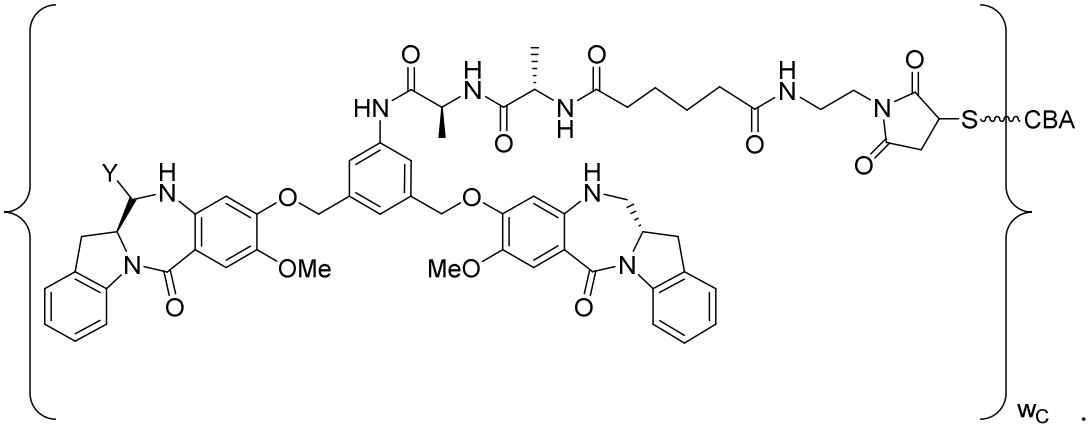
(a10L),

to form a cytotoxic agent-linker compound, wherein X is halogen; J_D –SH, –SSR^d, or –$SC(=O)R^g$; R^d is phenyl, nitrophenyl, dinitrophenyl, carboxynitrophenyl, pyridyl or nitropyridyl; R^g is an alkyl; q is an integer from 1 to 5; and U is –H or SO_3H; and

(b) reacting the CBA with the cytotoxic agent-linker compound in the presence of an

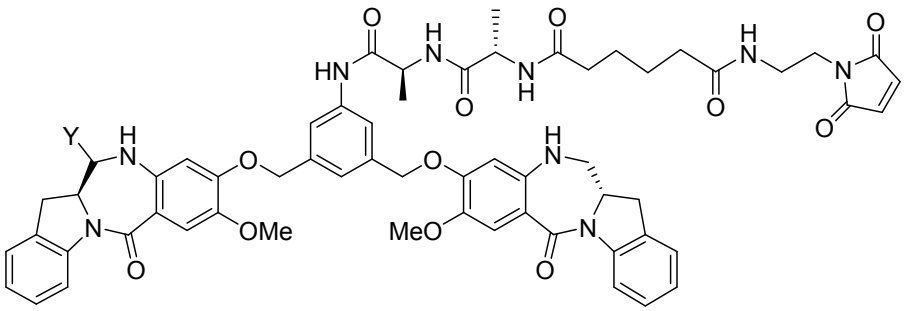
antioxidant to form the immunoconjugate.

19. A method of preparing an immunoconjugate represented by the following formula:



;

or a pharmaceutically acceptable salt thereof, comprising reacting the CBA with a cytotoxic agent represented by the following formula:



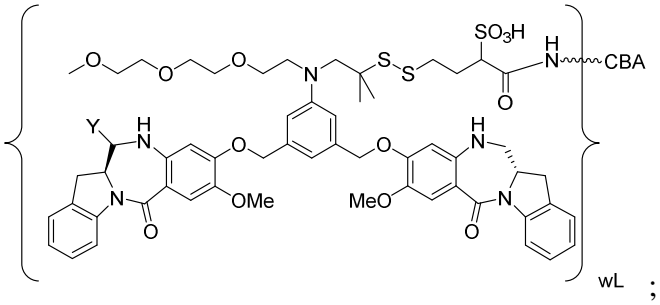
or a pharmaceutically acceptable salt thereof, in the presence of an antioxidant, wherein:

Y is $-SO_3H$ or sodium salt thereof;

W_C is 2; and

CBA is an anti-CD123 antibody comprising: a) an immunoglobulin heavy chain having the amino acid sequence set forth in SEQ ID NO:8; and b) an immunoglobulin light chain having the amino acid sequence set forth in SEQ ID NO:10.

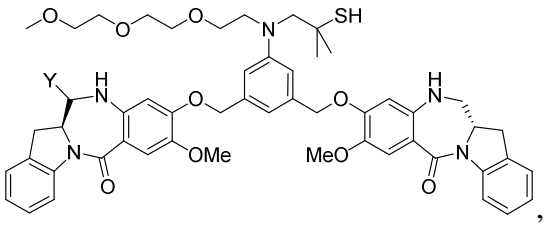
20. A method of preparing an immunoconjugate represented by the following formula:



;

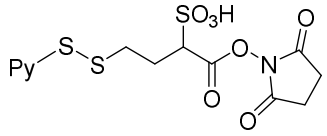
or a pharmaceutically acceptable salt thereof, comprising the steps of:

(a) reacting a cytotoxic agent represented by the following formula:

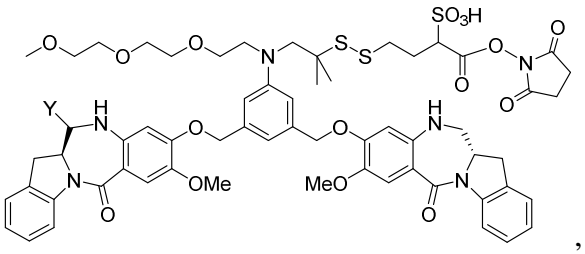


,

or a pharmaceutically acceptable salt thereof, with a bifunctional crosslinking agent sulfo-SPDB presented by the following formula:



to form a cytotoxic agent-linker compound represented by the following formula:



,

or a pharmaceutically acceptable salt thereof; and

(b) reacting the CBA with the cytotoxic agent-linker compound in the presence of an antioxidant to form the immunoconjugate, wherein:

Y is $-SO_3H$;

W_L is an integer from 1 to 10; and

CBA is an anti-CD33 antibody comprising an immunoglobulin heavy chain having the amino acid sequence set forth in SEQ ID NO:18 and an immunoglobulin light chain having the amino acid sequence set forth in SEQ ID NO:20.