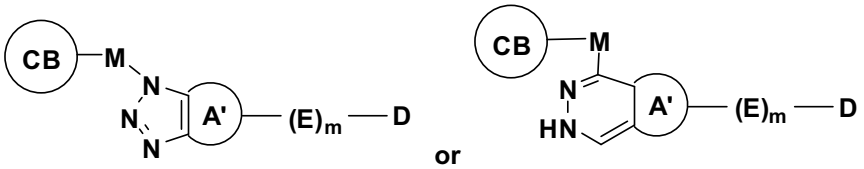
WHAT IS CLAIMED IS

1. An isolated conjugate of Formula III or Formula III'



Formula III **Formula III'**

wherein:

CB is a cell-binding agent;

M is a non-natural amino acid;

A' is a carbocyclyl or heterocyclyl

D is a payload;

Each E is independently selected from the group consisting of -CO-, -CR^1R^2-, -NR^3-, -S-S-, -S-, -SO-, -SO_2-, -O-, -CR^3=N-NR^3-, -CR^3=N-O-, -CR^3=N-NR^3-CO-, -N=N-CO-, alkyl, C3-C8 carbocyclyl, -O-$(CR^1R^2)_a$-, aryl, -$(CR^1R^2)_a$-aryl, heteroaryl, -$(CR^1R^2)_a$-heteroaryl, -$(CR^1R^2)_a$-C3-C8 carbocyclyl, heterocyclyl, -$(CR^1R^2)_a$-heterocyclyl, -$(CH_2CH_2O)_a$-, -$(CH_2CH_2O)_a$-$(CH_2)_b$, —$(CH_2)_a$C(O)-, amino acid, and peptide;

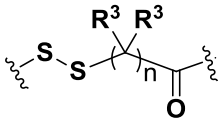
R^1 and R^2 are each independently selected from the group consisting of H, F, Cl, Br, I, OH, -$N(R^3)_2$, -$N(R^3)_3^+$, C1-C8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, -SO_2R^3, -$S(=O)R^3$, -SR^3, -$SO_2N(R^3)_2$, -$C(=O)R^3$, -CO_2R^3, -$C(=O)N(R^3)_2$, —CN, —N_3, —NO_2, C1-C8 alkoxy, polyethyleneoxy, phosphonate, phosphate, C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, aryl, heteroaryl, C3-C8 carbocyclyl, and C1-C20 heterocyclyl; or, when taken together, R^1 and R^2 form a carbonyl (=O), or spiro carbocyclic ring of 3 to 7 carbon atoms; and,

R^3 is selected from the group consisting of H, C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, C6-C20 aryl, C6-C20 heteroaryl, C3-C8 carbocyclyl, and C1-C20 heterocyclyl;

alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocyclyl, and heterocyclyl are optionally independently substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, —$N(R^3)_2$, —$N(R^3)_3^+$, C1-C8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C1-C8 alkylsulfonate, C1-C8 alkylamino, 4-dialkylaminopyridinium, C1-C8 alkylhydroxyl, C1-C8 alkylthiol, -SO_2R, -$S(=O)R^3$, —SR^3, —$SO_2N(R^3)_2$, -$C(=O)R^3$, -CO_2R^3, -$C(=O)N(R^3)_2$, —CN, —N_3, —NO_2, C1-C8 alkoxy, C1-C8 trifluoroalkyl, C1-C8 alkyl, C3-C12 carbocycle, C6-C20 aryl, C6-C20 heteroaryl, C3-C8 carbocyclyl, C2-C20 heterocyclyl, polyethyleneoxy, phosphonate, and phosphate;

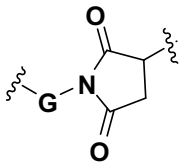
m is an integer from 1 to 100; and,
a and b are each an integer from 1 to 100.

2. An isolated conjugate according to claim 1, wherein each E is independently selected from the group consisting of -$(CH_2CH_2O)_a$-, -$(CH_2)_aC(O)NR^3$-, -$(CH_2)_aNR^3C(O)$-, -$(CH_2)_aC(O)NR^3(CH_2)_b$-, -$(CH_2)_aC(O)NR^3(CH_2CH_2O)_b$-, -$(CH_2)_aC(O)NR^3(CH_2CH_2O)_b(CH_2)_c$-, -$(CH_2CH_2O)_aC(O)NR^3(CH_2CH_2O)_b$-, -$(CH_2CH_2O)_aC(O)NR^3(CH_2CH_2O)_b$, -$(CH_2CH_2O)_aC(O)NR^3(CH_2)_b$-, -$(CH_2CH_2O)_a$-$(CH_2)_b$, —$(CH_2)_aC(O)$-, -$CR^3$=N-$NR^3$-, -$CR^3$=N-O-, -$CR^3$=N-$NR^3$-CO-, -N=N-CO-, -S-, -SO-, -SO_2-, dipeptide, tripeptide;



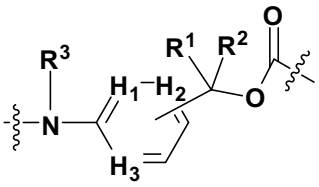
; and,

E1



E2

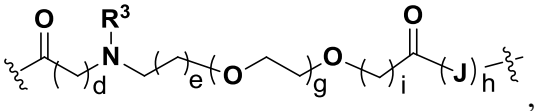
wherein G is selected from the group consisting of alkyl, aryl, carbocyclyl, and heterocyclyl; and,



G1

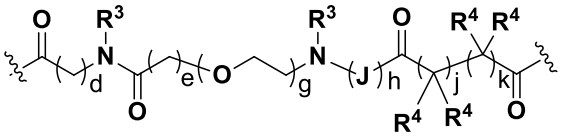
wherein H_1, H_2, and H_3 are each independently selected from N or CR^1.

3. An isolated conjugate according to claim 1 wherein each E is independently selected from the group consisting of



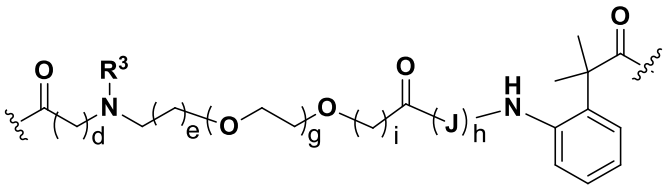
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E3



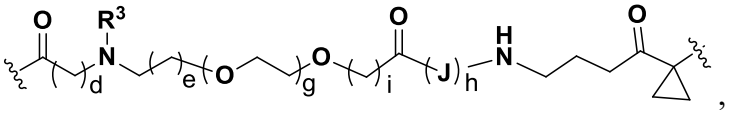
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E4



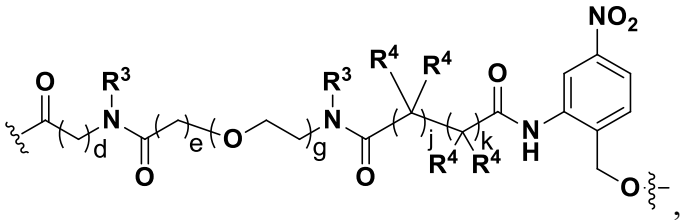
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E5



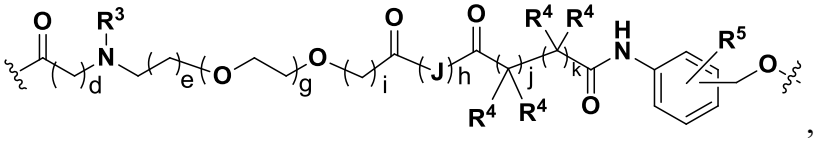
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E6



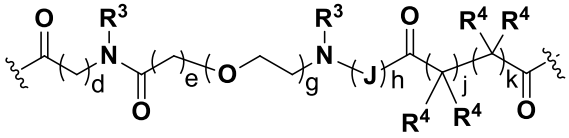
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E7



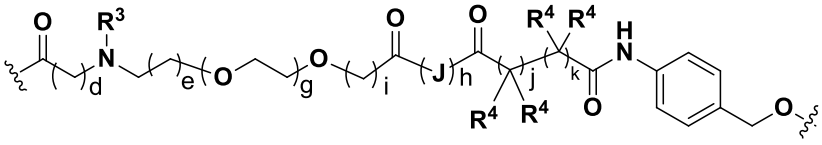
,

E8



; and,

E9



E10

wherein:

J is an amino acid or peptide;

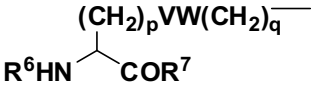
d, e, g, i, j, and k are each independently an integer from 1 to 30;

h is an integer from 0 to 30;

Each R^4 is independently selected from the group consisting of H, alkyl, $-N(R^3)_2$, $-SR^3$, and C1-C8 alkoxy, aryl; and,

R^5 is selected from the group consisting of H, $-N(R^3)_2$, $-SR^3$, C1-C8 alkoxy, aryl, and NO_2.

4. An isolated conjugate according to claim 1, wherein M exhibits the structure



Formula IV

wherein p and q are each an integer from 0-10;

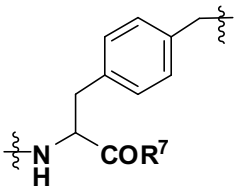
R^6 is is H, amino acid, polypeptide, or a bond;

R^7 is OH, amino acid, polypeptide, or a bond;

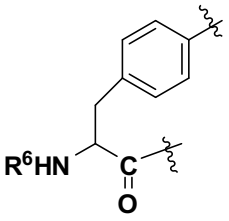
V is an alkyl, aryl, carbocycle, heterocycle, or absent; and,

W is O, N, S, or absent.

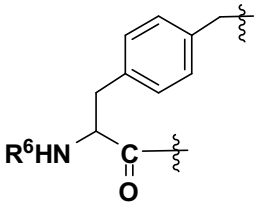
5. An isolated conjugate according to claim 4, wherein M is selected from the group consisting essentially of



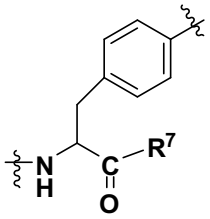
V



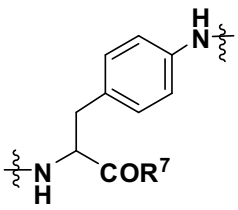
VI



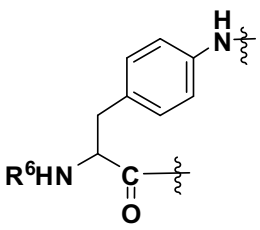
VII



VIII

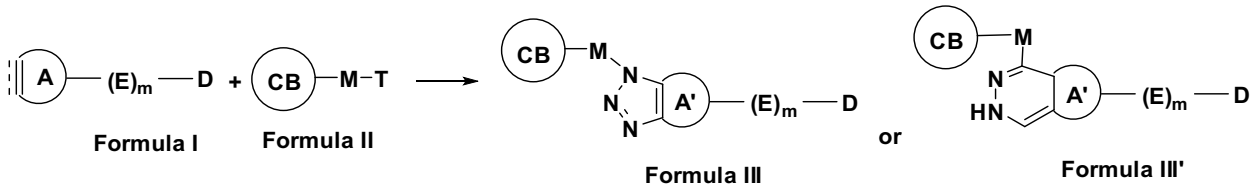


IX



X .

6. An isolated conjugate of Formula III or Formula III' produced by the process of reacting a compound of Formula I with a compound of Formula II



wherein, with reference to Formula I,

A is a strained alkyne ring or a strained alkene ring wherein the ring is carbocyclyl or heterocyclyl;

D is a payload;

Each E is independently selected from the group consisting of -CO-, -CR^1R^2-, -NR^3-, -S-S-, -S-, -SO-, -SO_2-, -O-, -CR^3=N-NR^3-, -CR^3=N-O-, -CR^3=N-NR^3-CO-, -N=N-CO-, alkyl, C3-C8 carbocyclyl, -O-$(CR^1R^2)_a$-, aryl, -$(CR^1R^2)_a$-aryl, heteroaryl, -$(CR^1R^2)_a$-heteroaryl, -$(CR^1R^2)_a$-C3-C8 carbocyclyl, heterocyclyl, -$(CR^1R^2)_a$-heterocyclyl, -$(CH_2CH_2O)_a$-, -$(CH_2CH_2O)_a$-$(CH_2)_b$, —$(CH_2)_a$C(O)-, amino acid, and peptide;

R^1 and R^2 are each independently selected from the group consisting of H, F, Cl, Br, I, OH, -$N(R^3)_2$, -$N(R^3)_3^+$, C1-C8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, -SO_2R^3, -$S(=O)R^3$, -SR^3, -$SO_2N(R^3)_2$, -$C(=O)R^3$, -CO_2R^3, -$C(=O)N(R^3)_2$, —CN, —N_3, —NO_2, C1-C8 alkoxy, polyethyleneoxy, phosphonate, phosphate, C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, aryl, heteroaryl, C3-C8 carbocyclyl, and C1-C20 heterocyclyl; or, when taken together, R^1 and R^2 form a carbonyl (=O), or spiro carbocyclic ring of 3 to 7 carbon atoms; and,

R^3 is selected from the group consisting of H, C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, C6-C20 aryl, C6-C20 heteroaryl, C3-C8 carbocyclyl, and C1-C20 heterocyclyl;

alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocyclyl, and heterocyclyl are optionally independently substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, —$N(R^3)_2$, —$N(R^3)_3^+$, C1-C8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C1-C8 alkylsulfonate, C1-C8 alkylamino, 4-dialkylaminopyridinium, C1-C8 alkylhydroxyl, C1-C8 alkylthiol, -SO_2R, -$S(=O)R^3$, —SR^3, —$SO_2N(R^3)_2$, -$C(=O)R^3$, -CO_2R^3, -$C(=O)N(R^3)_2$, —CN, —N_3, —NO_2, C1-C8 alkoxy, C1-C8 trifluoroalkyl, C1-C8 alkyl, C3-C12 carbocycle, C6-C20 aryl, C6-C20 heteroaryl, C3-C8 carbocyclyl, C2-C20 heterocyclyl, polyethyleneoxy, phosphonate, and phosphate;

m is an integer from 1 to 100;

a and b are each an integer from 1 to 100; and,

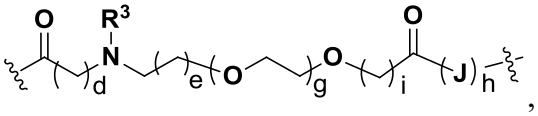
with reference to Formula II,

CB is a cell-binding agent; M is a non-natural amino acid; T is an azide group or a tetrazine group; and,

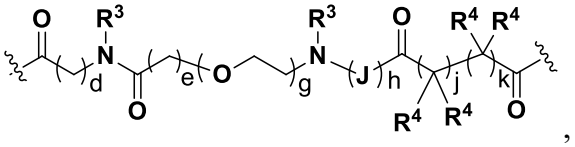
with reference to Formula III and Formula III',

A' is a carbocyclyl or heterocyclyl.

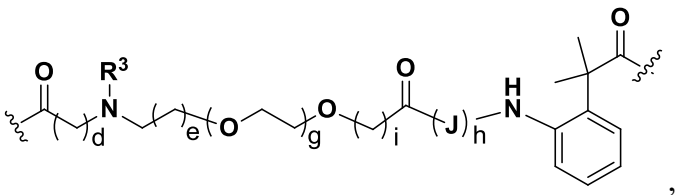
7. An isolated conjugate of Formula III or Formula III' produced by the process according to claim 6 wherein, with reference to Formula I, each E is independently selected from the group consisting of



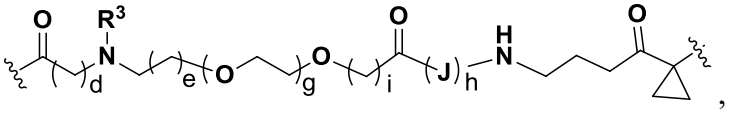
E3



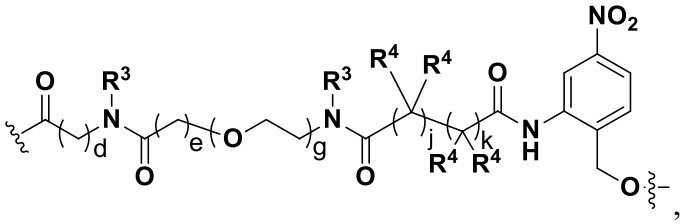
E4



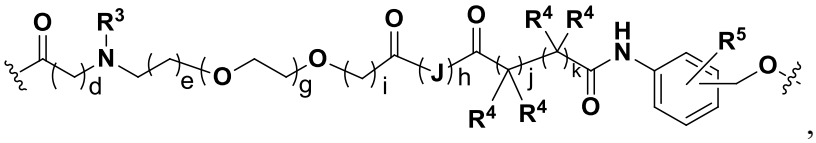
E5



E6

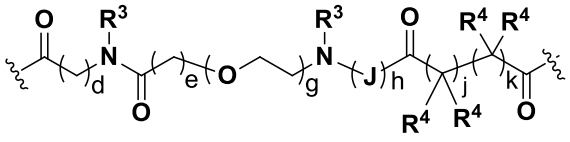


E7



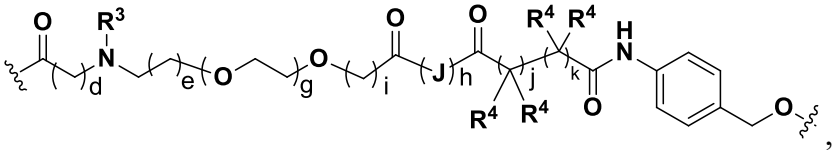
,

E8



; and,

E9



,

E10

wherein J is an amino acid or peptide;

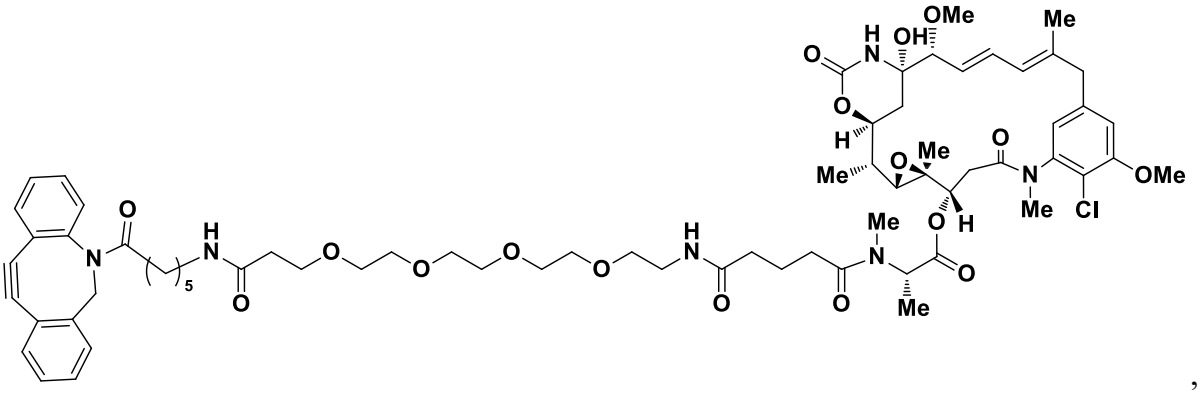
d, e, g, i, j, and k are each independently an integer from 1 to 30;

h is an integer from 0 to 30;

Each R^4 is independently selected from the group consisting of H, alkyl, $-N(R^3)_2$, $-SR^3$, and C1-C8 alkoxy, aryl; and,

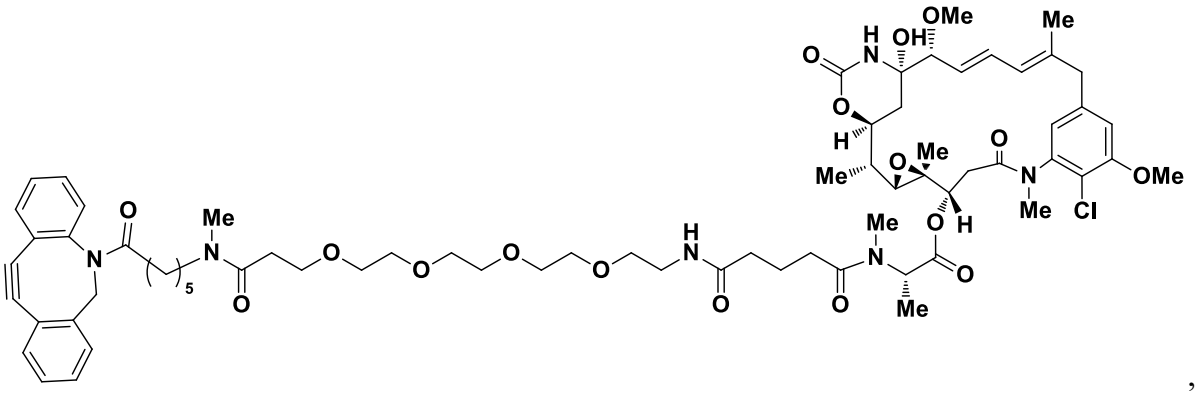
R^5 is selected from the group consisting of H, $-N(R^3)_2$, $-SR^3$, C1-C8 alkoxy, aryl, and NO_2.

8. An isolated conjugate of Formula III or Formula III' produced by the process according to claim 6 wherein each compound of Formula I is independently selected from the group consisting of



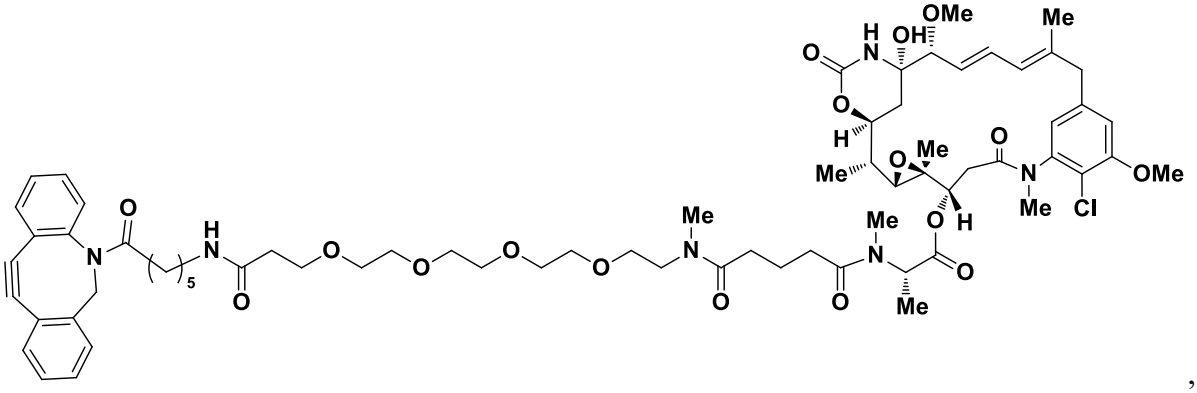
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I1



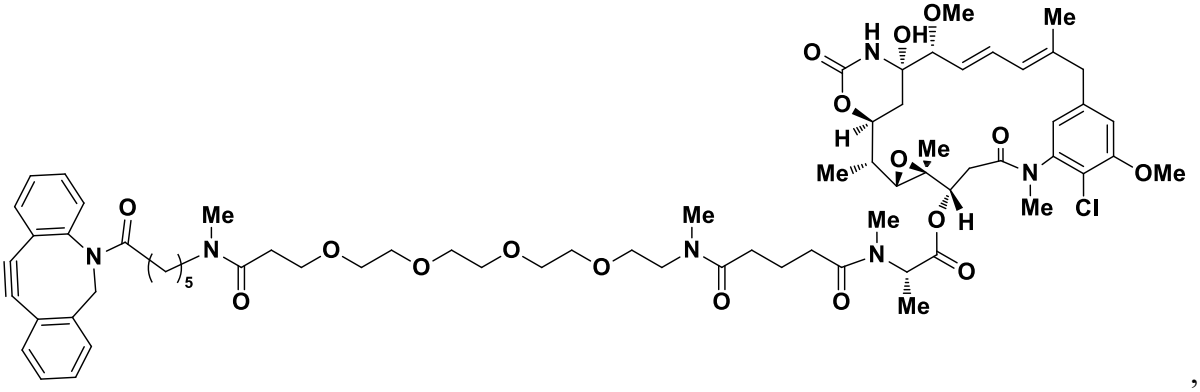
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I2



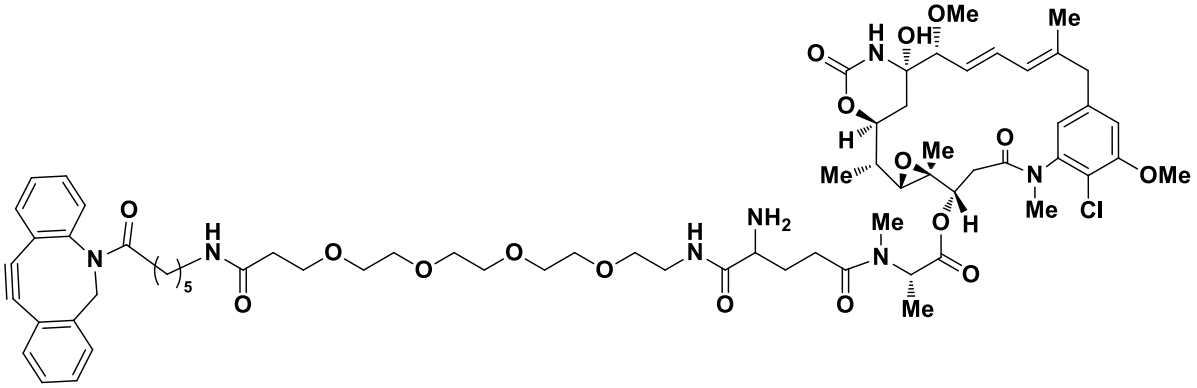
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I3



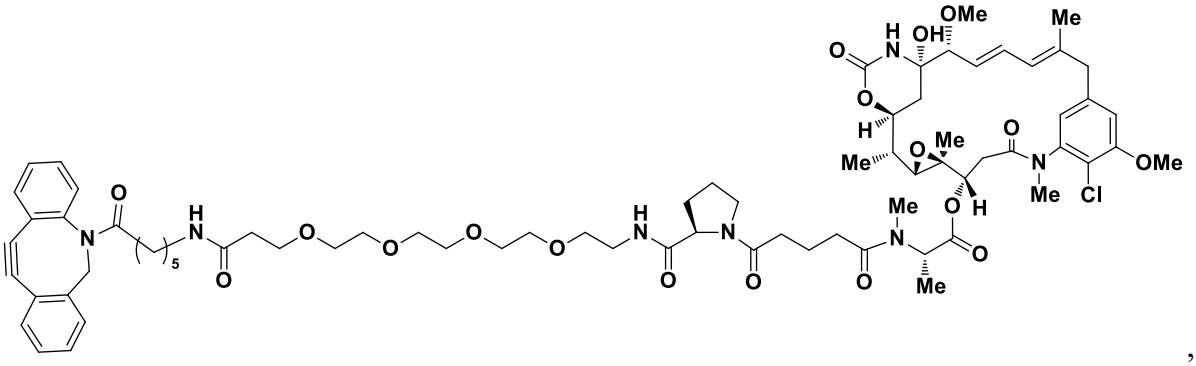
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I4



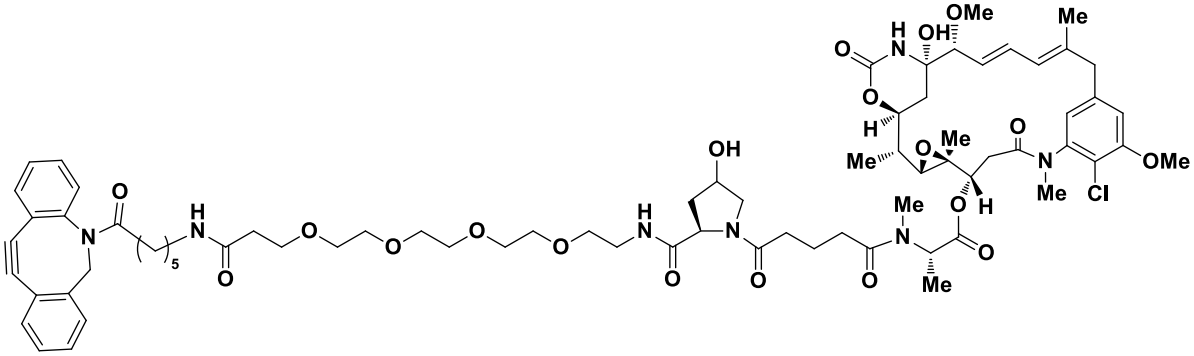
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I5



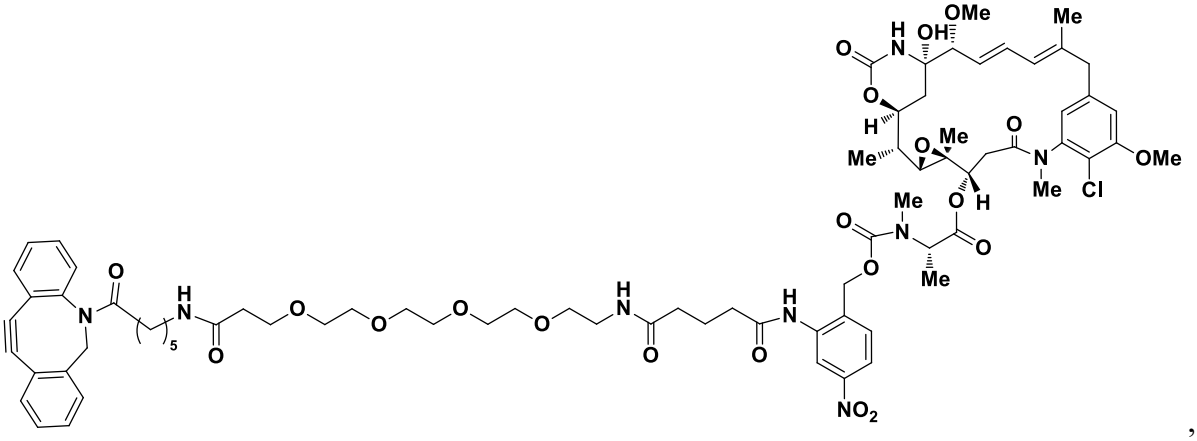
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I6



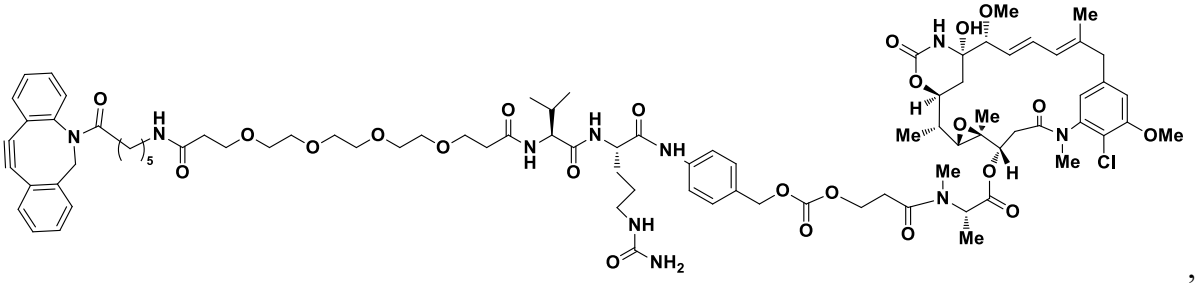
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I7



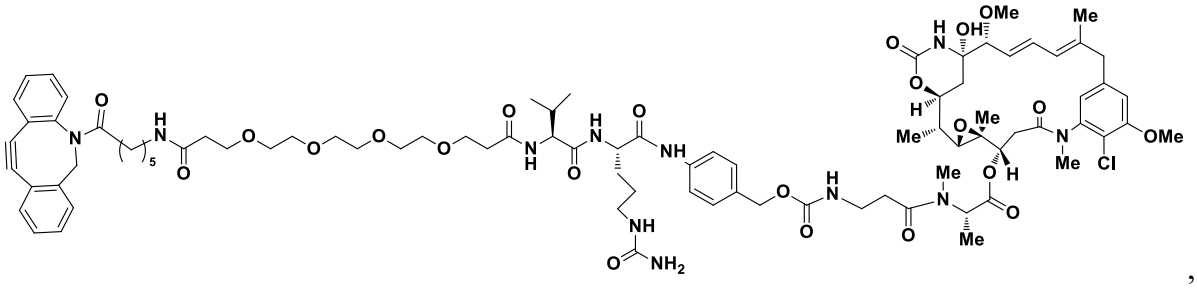
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I8



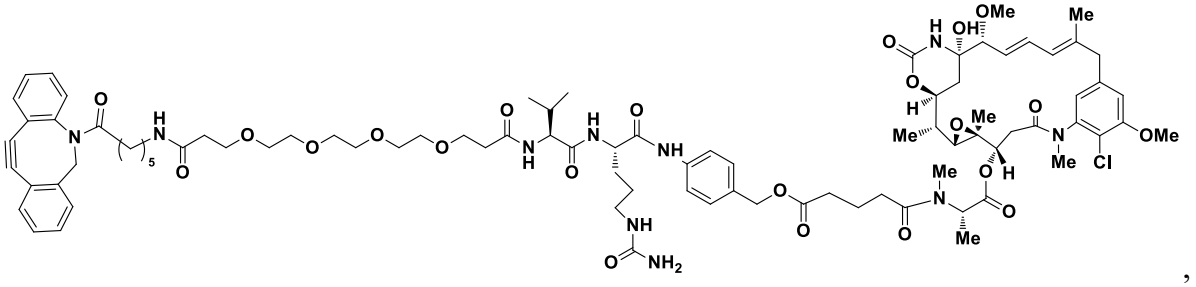
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I9



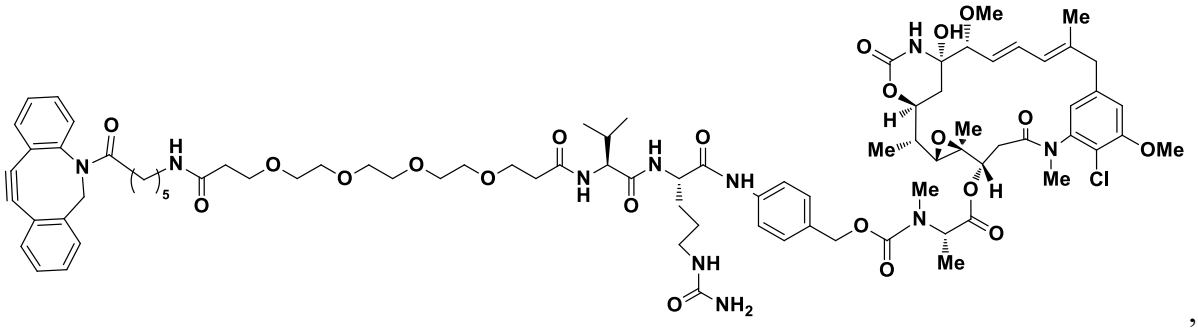
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I10



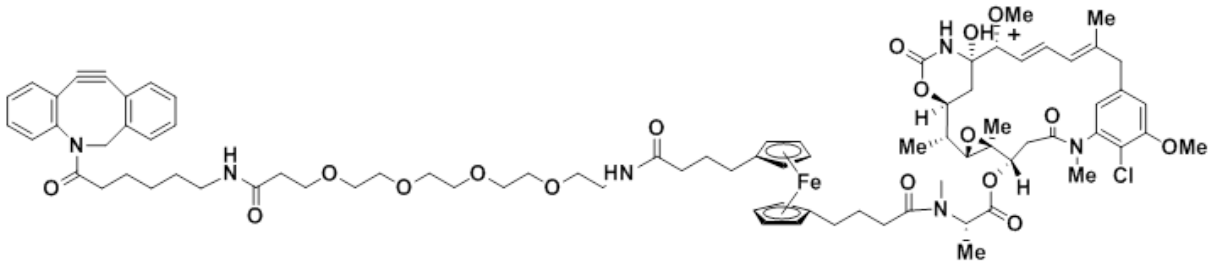
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I11



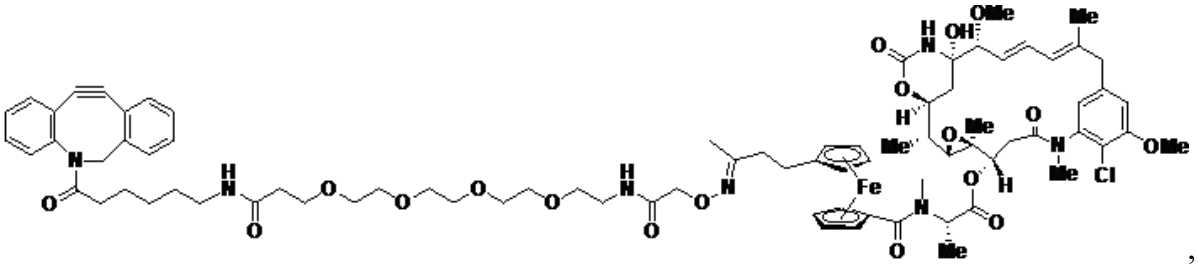
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I12



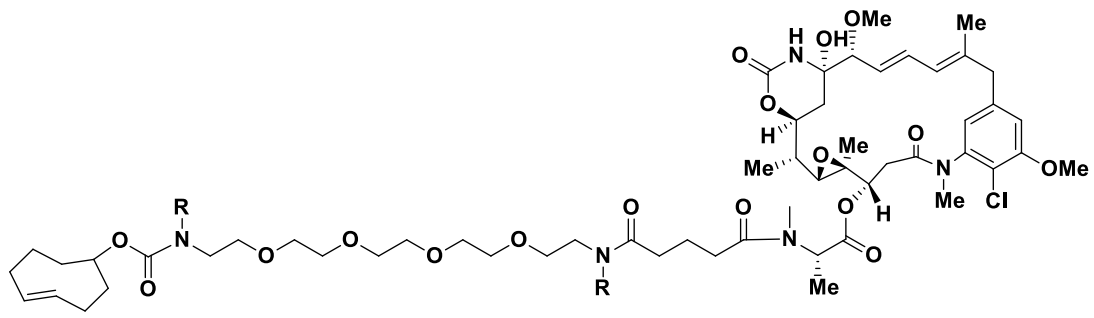
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I13



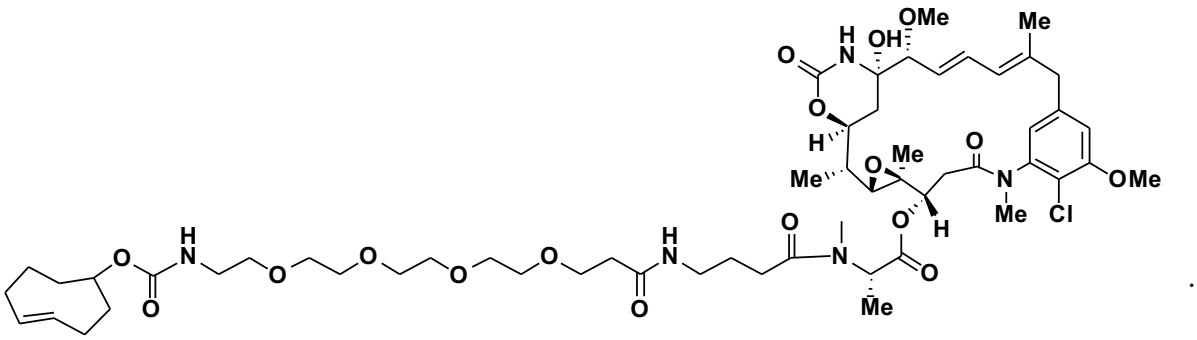
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I14



I15

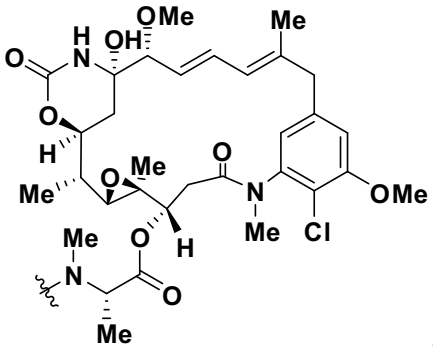
R = H or CH3 (methyl); and,



I16

9. An isolated conjugate according to claim 1 wherein D is a maytansinoid.

10. An isolated conjugate according to claim 9 wherein the maytansinoid is of the structure



C1

11. A pharmaceutical composition comprising an effective amount of a conjugate according to claim 1 and at least one pharmaceutically acceptable excipient.

12. A pharmaceutical composition comprising an effective amount of a conjugate according to claim 9 and at least one pharmaceutically acceptable excipient .

13. A method of treatment of a disorder in a mammal comprising administering an effective amount of a conjugate according to claim 1.

14. A method of treatment of a disorder in a mammal comprising administering an effective amount of a conjugate according to claim 9.