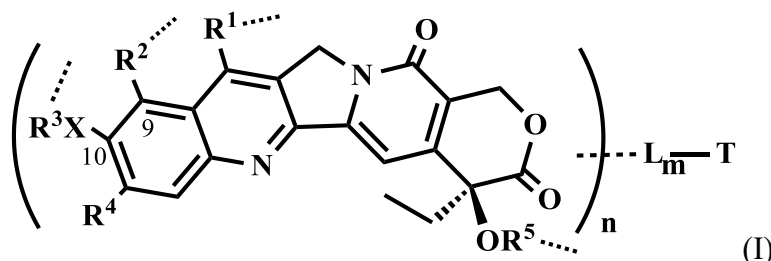


CLAIMS

What is claimed is:

1. A cell surface-binding molecule - camptothecin conjugate having the Formula (I) illustrated below:



or their pharmaceutically acceptable salts, hydrates, or hydrated salts; or the polymorphic crystalline structures of these compounds; or their isotopes, optical isomers, racemates, diastereomers or enantiomers thereof;

wherein T is a cell-binding agent/ molecule; L is a releasable linker; ----- is a linkage bond that L connects to an atom of R¹, R², R³ or R⁵ independently inside the bracket independently; n is 1-30 and m is 1-10;

when R¹ does not bind L, R¹ is H; linear or branched C₁-C₆ of alkyl, alkyl alcohol, or alkyl amine (including primary, secondary, tertiary amine, or quaternary ammonium), when R¹ bind L, R¹ is linear or branched C₁-C₆ of alkyl, alkyleneoxy, or alkylene amino (including primary, secondary, or tertiary amine);

when R² does not bind L, R² is H; linear or branched C₁-C₆ of alkyl alkyl alcohol, or alkyl amine (including primary, secondary, tertiary amine, or quaternary ammonium), when R² binds L, R² is NH, NR⁶, N⁺R⁶R^{6'}, alkylene amino (including primary, secondary, or tertiary amine) or aminoalkylene; or R³ is absent, and R² and X join together to form a 5-, 6- or 7-member heterocyclic ring;

when R³ does not bind L, R³ is H, C(O)R⁶, linear or branched C₁-C₆ of alkyl, alkyl alcohol, or alkyl amine (including primary, secondary, tertiary amine, or tertiary amine); when R³ binds L, R³ is linear or branched C₁-C₆ of alkylene; or when R² and X join together to form a 5-, 6- or 7-member heterocyclic, R³ is absent;

R⁴ is halo (F, Cl, Br, or I), CN, NO₂, SO₃H, OR⁶, SR⁶, S(O₂)R⁶, NHR⁶, N(R⁶)(R^{6'}), C(O)XR⁶, or N⁺(R⁶)(R^{6'})(R^{6''});

X is NH or O;

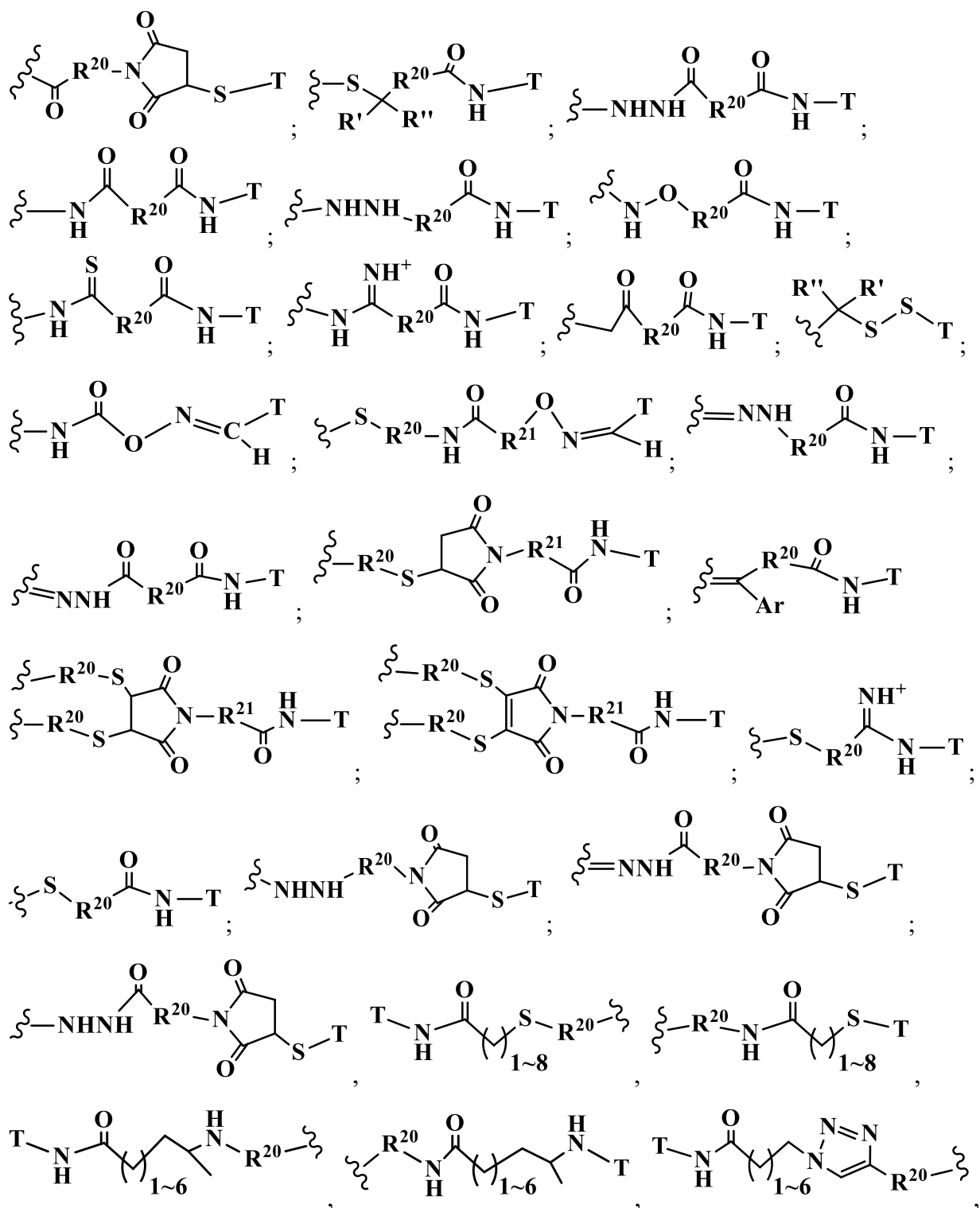
when R⁵ does not bind L, R⁵ is H or linear or branched C₁-C₆ of alkyl; when R⁵ binds L, R⁵ is C(O)O, C(O)NH, or linear or branched C₁-C₆ of alkylene;

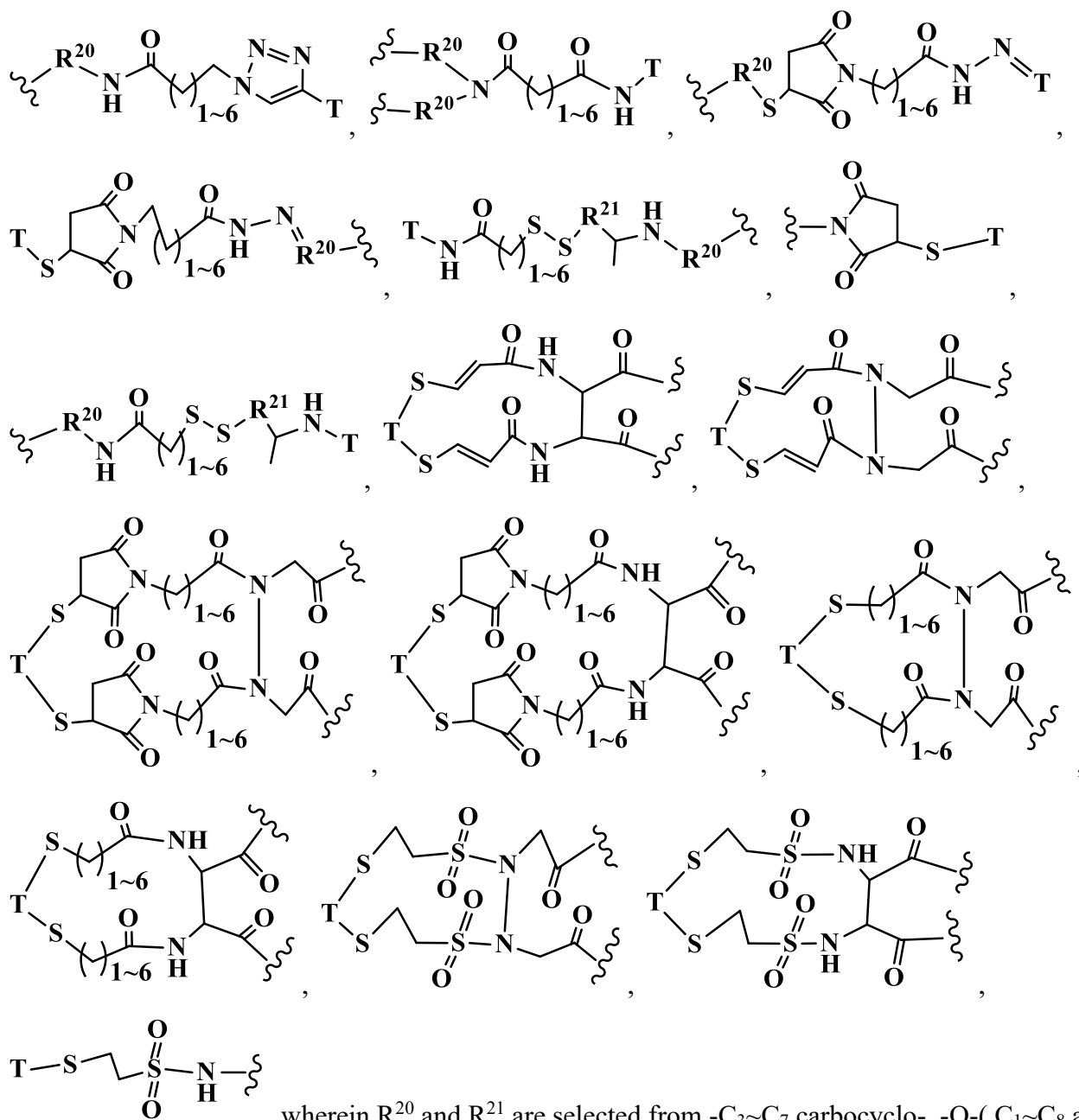
R⁶, R^{6'}, and R^{6''} are independently H, C₁-C₆ of alkyl;

The cell-binding agent/ molecule T is an antibody,

L has the formula of: $-\text{W}_w-(\text{Aa})_r-\text{V}_v-$, wherein: -W- is a Stretcher unit; w is 0 or 1; each -Aa- is independently an Amino Acid unit; r is independently an integer ranging from 0 to 12; -V- is a Spacer unit; and v is 0, 1 or 2.

The Stretcher unit (-W-), when present, links a targeted binding molecular unit (T) to an amino acid unit (-Aa-), or links to V when an Aa is not present. W linked to T has one of the structures below:

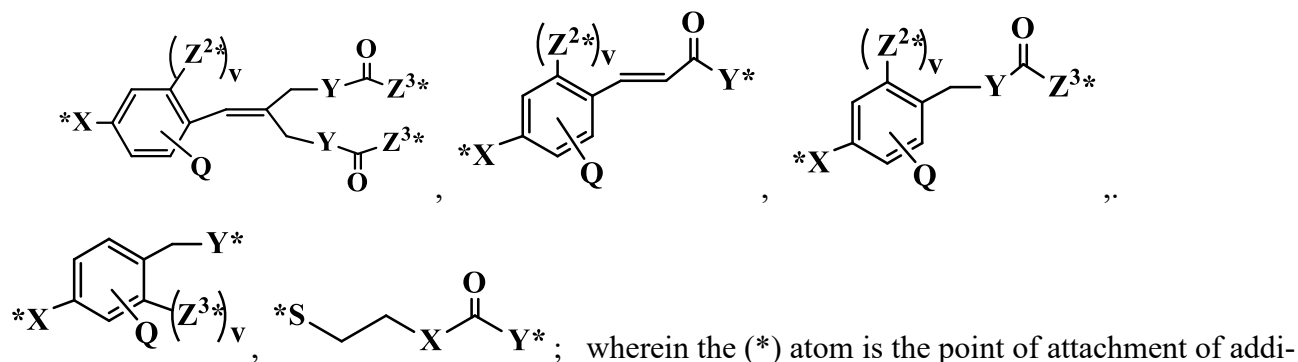




, wherein R²⁰ and R²¹ are selected from -C₃~C₇ carbocyclo-, -O-(C₁~C₈ alkylene)-, -arylene-, -C₁~C₈ alkylene-arylene-, -arylene-, -C₁~C₈ alkylene-, -C₁~C₈ alkylene-(C₃~C₈ carbocyclo)-, -(C₃~C₇ carbocyclo)-C₁~C₉ alkylene-, -C₃~C₈ heterocyclo-, -C₁~C₈ alkylene-(C₃~C₈ heterocyclo)-, -(C₃~C₈ heterocyclo)-C₁~C₉ alkylene-, -(CH₂CH₂O)_k-, -(CH(CH₃)CH₂O)_k-, and -(CH₂CH₂O)_k-CH₂-; k is an integer ranging from 1-20; R' and R'' are independently H or CH₃.

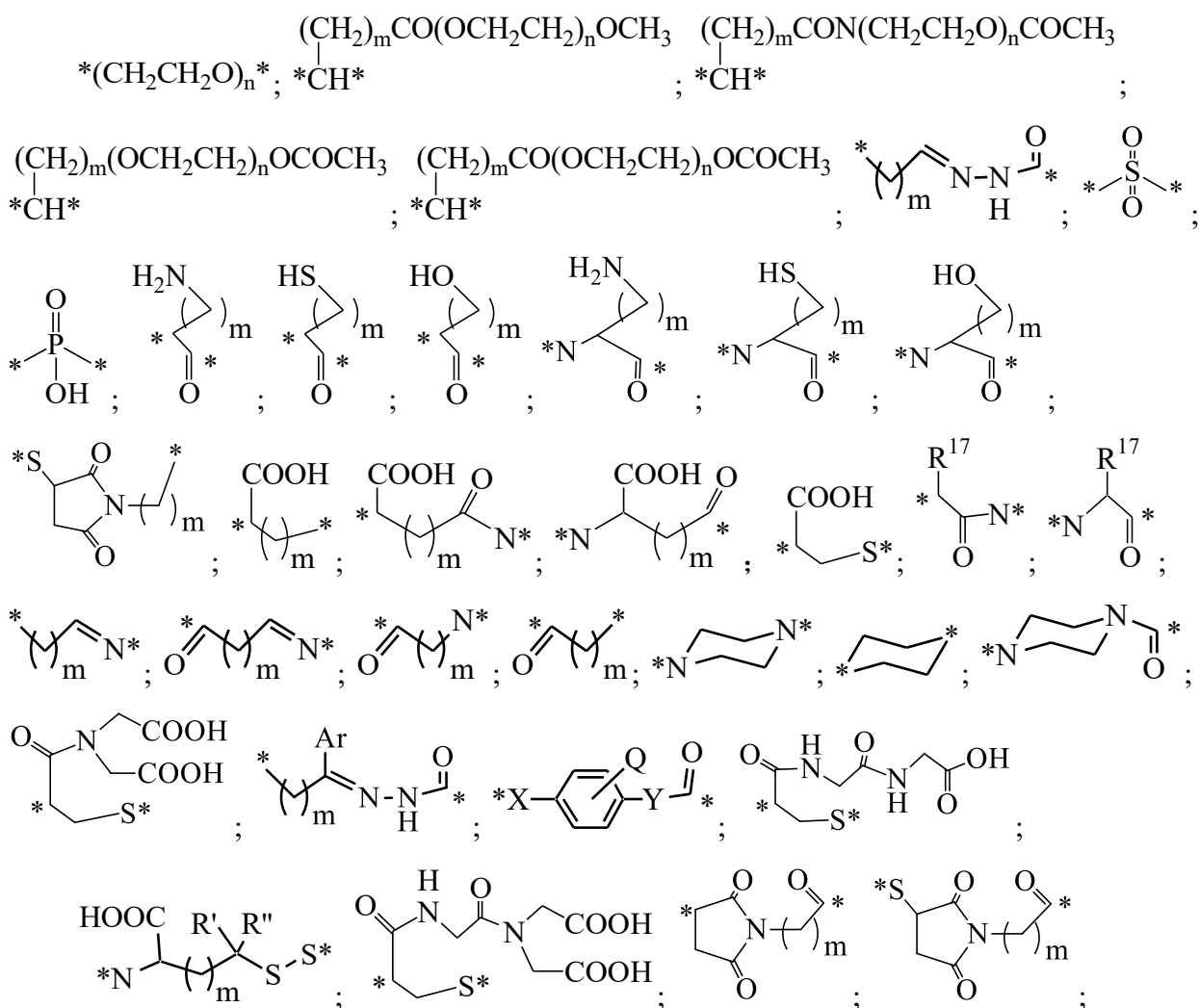
-(Aa)_r- is a natural or unnatural amino acid, the same or different amino acid sequences of dipeptide, tripeptide, tetrapeptide, pentapeptide, hexapeptide, heptapeptide, octapeptide, nonapeptide, decapeptide, undecapeptide or dodecapeptide unit, and r is an integer ranging from 0 to 12.

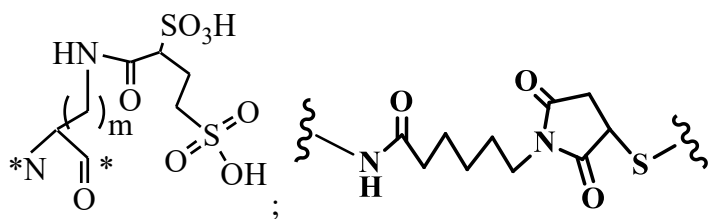
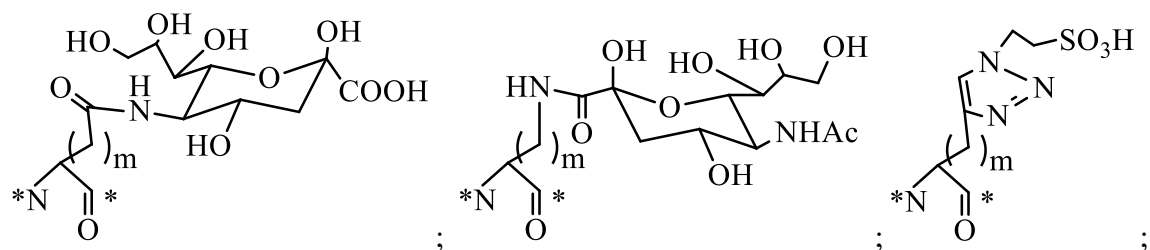
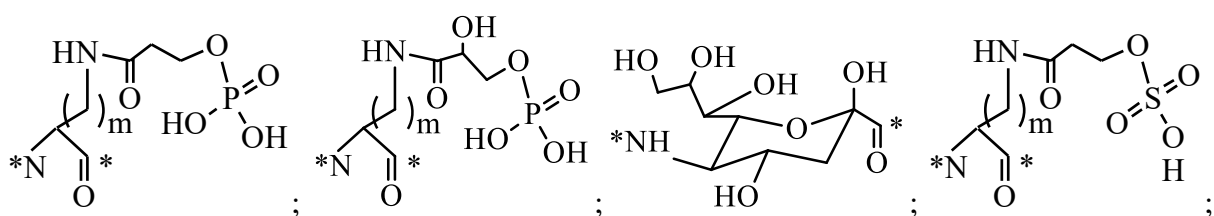
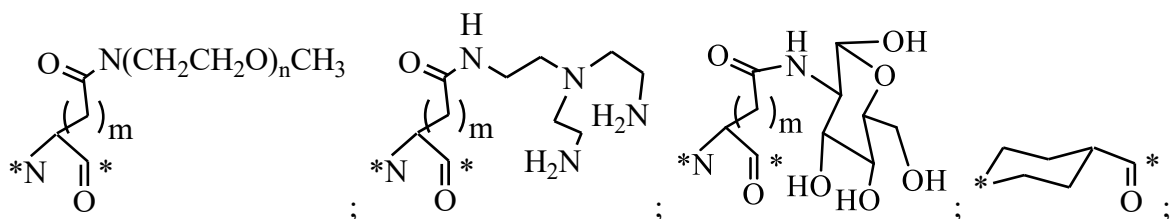
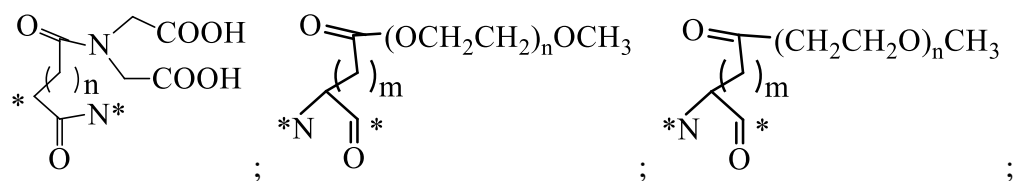
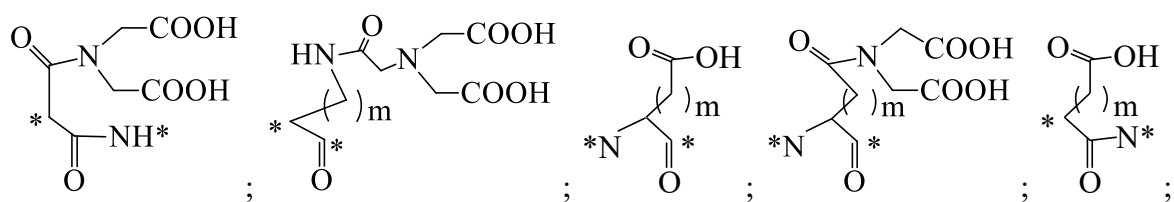
The Spacer unit (-V-) is either a self-immolative or a non self-immolative unit. The self-immolative unit includes para-aminobenzyl-carbamoyl (PAB) group, beta-glucuronide, and ortho or para-aminobenzylacetals; or one of the following structures:



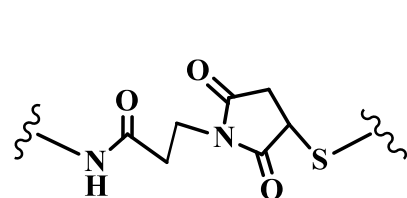
tional spacer or releasable linker units, amino acids (Aa)_r, camptothecin, and/or the binding molecule (T); X, Y and Z³ are independently NH, O, or S; Z² is NH, O or S independently; v is 0 or 1; Q is independently H, OH, C₁~C₆ alkyl, F, Cl, Br, I, OR¹⁷, or SR¹⁷, NR¹⁷R¹⁸, N=NR¹⁷, N=R¹⁷, NR¹⁷R¹⁸, NO₂, SOR¹⁷R¹⁸, SO₂R¹⁷, SO₃R¹⁷, OSO₃R¹⁷, PR¹⁷R¹⁸, POR¹⁷R¹⁸, PO₂R¹⁷R¹⁸, OPO(OR¹⁷)(OR¹⁸), or OCH₂PO(OR¹⁷)(OR¹⁸), wherein R¹⁷, R¹⁸ are independently H, C₁~C₈ of alkyl; C₂~C₈ of alkenyl, alkynyl, heteroalkyl; C₃~C₈ of aryl, heterocyclic, carbocyclic, cycloalkyl, heterocycloalkyl, heteroaralkyl, or alkylcarbonyl;

The non-self-immolative spacer linker units (-V-) include:

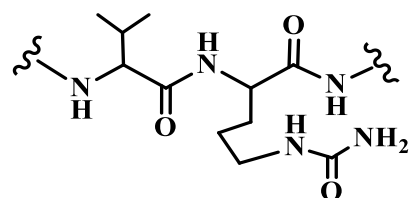




6-maleimidocaproyl (MC),

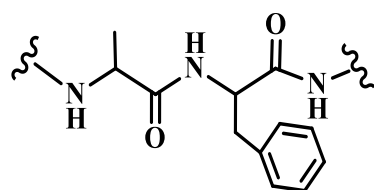


maleimido propanoyl (MP),

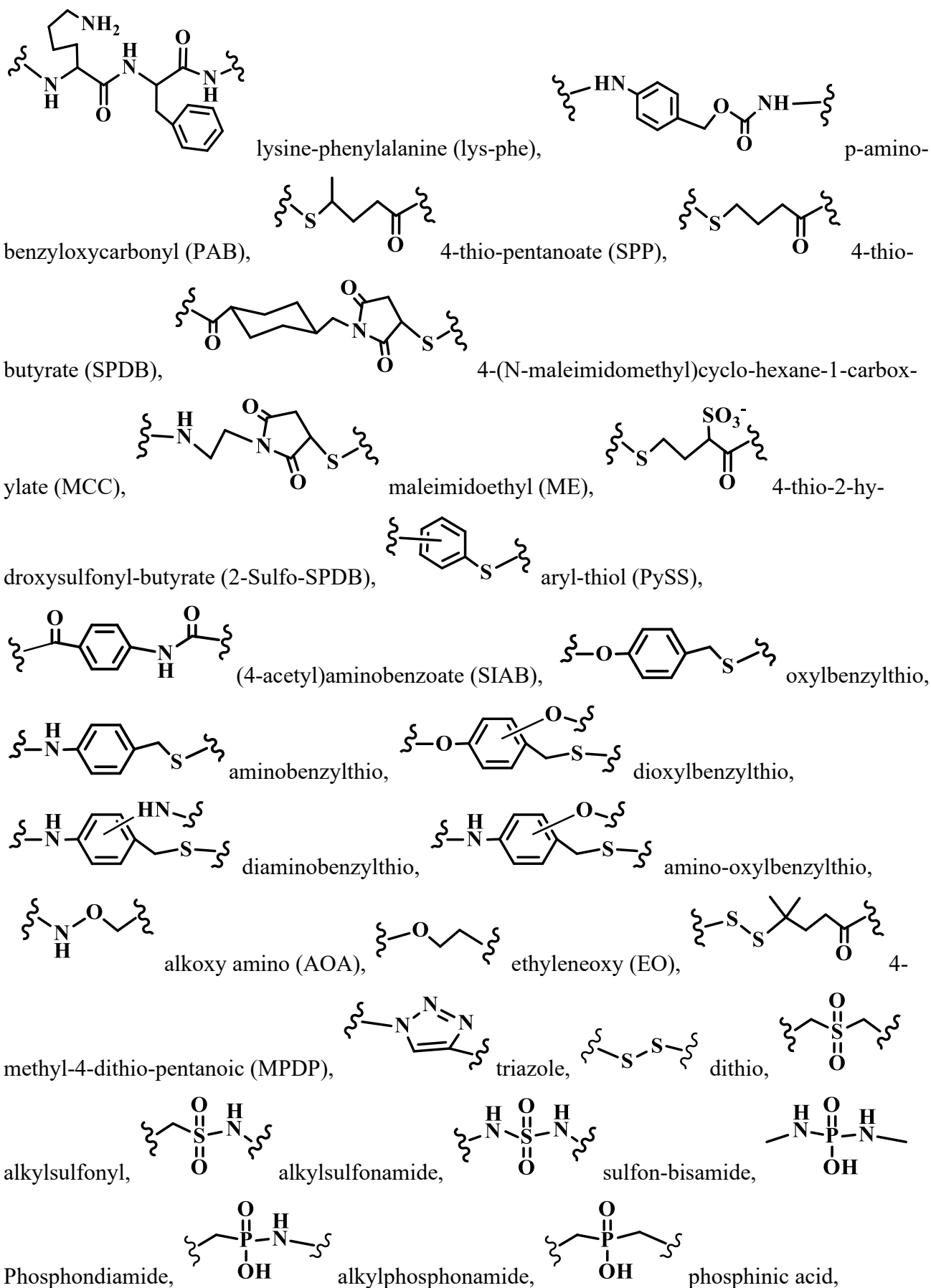


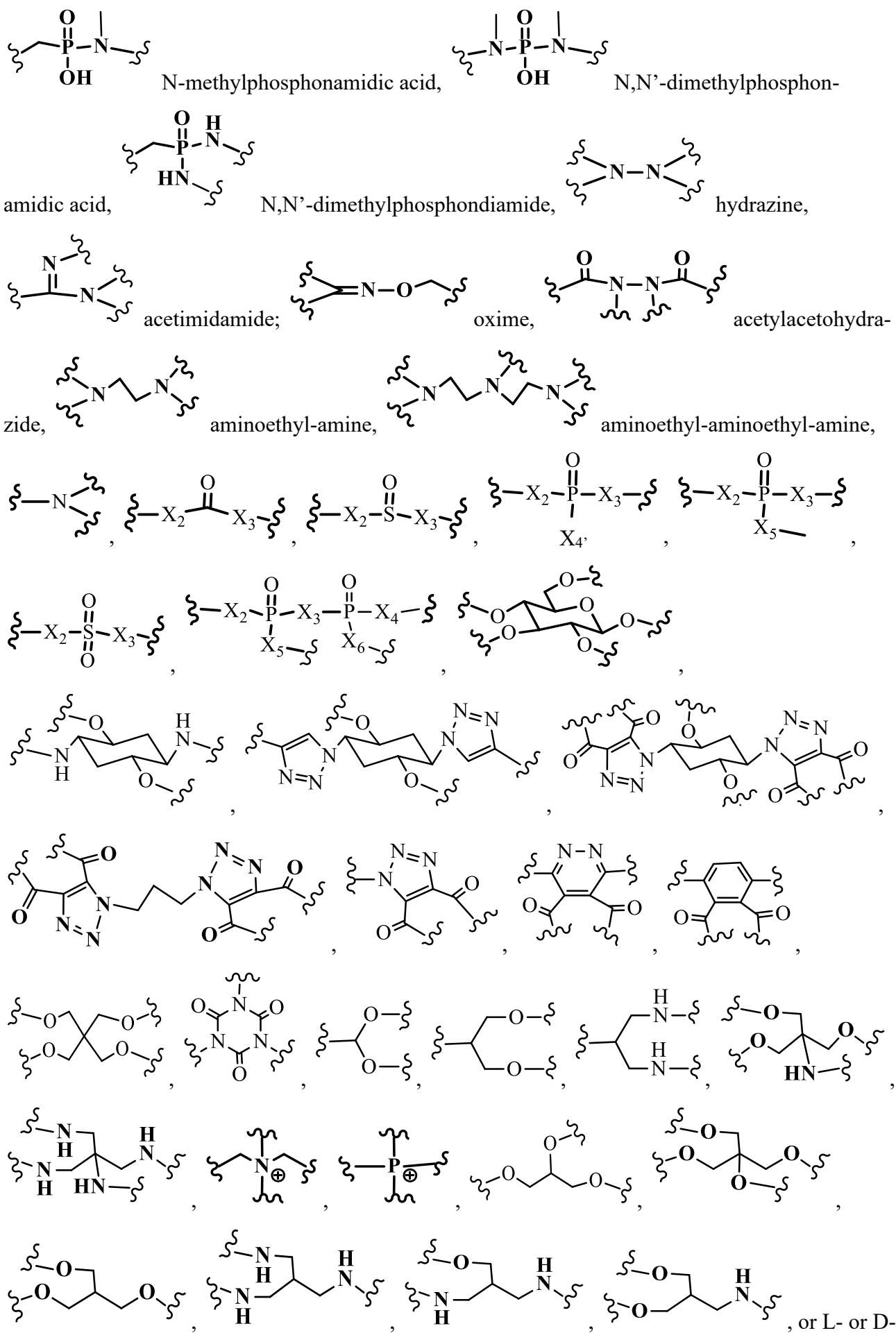
valine-

citrulline (val-cit),



alanine-phenylalanine (ala-phe),



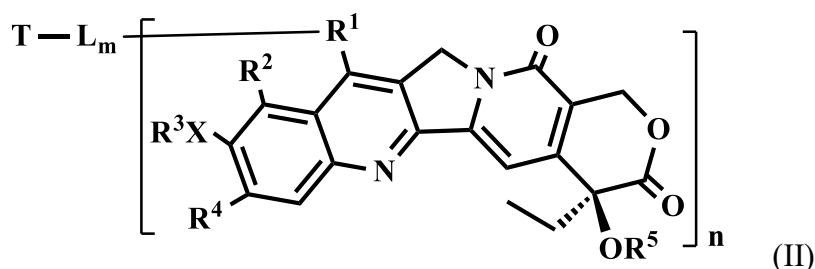


, natural or unnatural peptides containing 1-20 the same or different amino acids; wherein “*” and “ ζ ” are the points of attachment of additional spacer or releaseable linkers, the camptothecin, and/or the binding molecules; m is 1~10; n is 1~20; X₂, X₃, X₄, X₅, or X₆, are independently selected from NH; NHNH; N(R₁₂); N(R₁₂)N(R_{12'}); O; S; C₁-C₆ of alkylene; C₂-C₆ of heteroalkylene, alkylcycloalkylene, heterocycloalkylene; C₃-C₈ of arylene, Ar-alkylene, heterocyclic, carbocyclic, cycloalkylene, heteroarylene;

X₄ is selected from C₁-C₆ of alkyl; C₂-C₆ of heteroalkyl, alkylcycloalkyl, heterocycloalkyl; C₃-C₈ of aryl, Ar-alkyl, heterocyclic, carbocyclic, cycloalkyl, heteroaryl; CH₂OR₁₂, CH₂SR₁₂, CH₂NHR₁₂, or 1~8 amino acids; wherein R₁₂ and R_{12'} are independently H; C₁-C₈ of alkyl; C₂-C₈ of hetero-alkyl, alkylcycloalkyl, heterocycloalkyl; C₃-C₈ of aryl, Ar-alkyl, heterocyclic, carbocyclic, cycloalkyl, heteroalkylcycloalkyl, alkylcarbonyl, heteroaryl; or 1-8 carbon atoms of esters, ether, or amide; or polyethyleneoxy unit of formula (OCH₂CH₂)_p or (OCH₂CH(CH₃))_p, wherein p is an integer from 0 to 1000;

Ar is aryl.

2. A conjugate of camptothecin according to claim 1, having Formula (II):



wherein T is a cell-binding agent/ molecule; L is a releasable linker; n is 1-30 and m is 1-10;

R¹ is C₁-C₆ of alkylene, alkyleneoxyl, alkylene amino (including primary, secondary, or tertiary amino);

R² is H, linear or branched C₁-C₆ of alkyl, alkyl alcohol, alkyl amine (including primary, secondary, tertiary amine, or quaternary ammonium);

R³ is H, R⁶C(O), or linear or branched C₁-C₆ of alkyl, alkyl alcohol, or alkyl amine (including primary, secondary, tertiary amine, or quaternary ammonium);

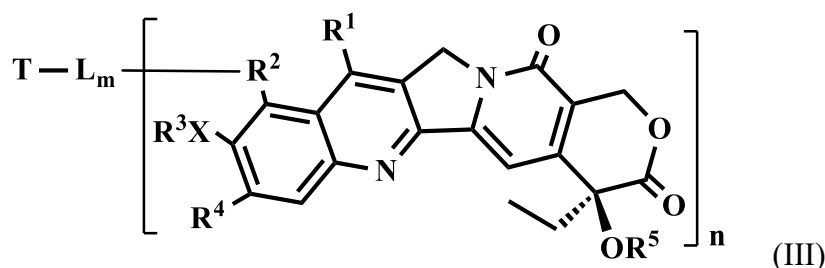
R⁴ is halo (F, Cl, Br, or I), CN, NO₂, SO₃H, OR⁶, SR⁶, S(O₂)R⁶, NHR⁶, N(R⁶)(R^{6'}), C(O)XR⁶, or N⁺(R⁶)(R^{6'})(R^{6''});

X is NH or O;

R⁵ is H, linear or branched C₁-C₆ of alkyl;

R⁶, R^{6'}, and R^{6''} are independently H, C₁-C₆ of alky;

3. A conjugate of camptothecin according to claim 1, having Formula (III):



Wherein T is a cell-binding agent/ molecule; L is a releasable linker; n is 1-30 and m is 1-10;

R^1 is H, linear or branched C_1 - C_6 of alkyl, alkyloxy, alkylamine (including primary, secondary, tertiary amine, or quaternary ammonium);

R^2 is NH, NR^6 , $N^+R^6R^{6'}$, C_1 - C_6 of alkylene, alkyleneoxy alkyleneamino (including primary, secondary, or tertiary amine), or aminoalkylene; or R^3 is absent, and R^2 and X join together to form a 5-, 6- or 7-member heterocyclic ring;

R^3 is H, $R^6C(O)$, linear or branched C_1 - C_6 of alkyl, alkyl alcohol, or alkylamine (including primary, secondary, tertiary amine, or quaternary ammonium); or when R^2 and X join together to form a 5-, 6- or 7-member heterocyclic, R^3 is absent;

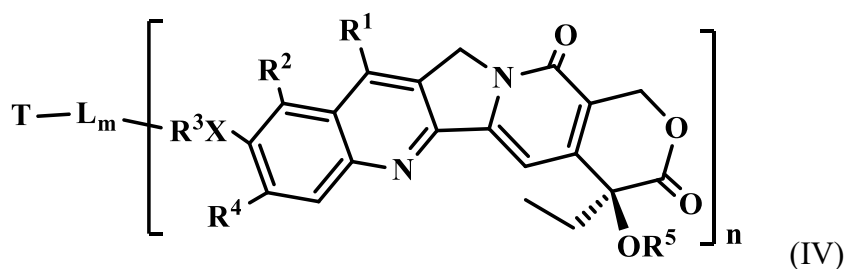
R^4 is halo (F, Cl, Br, or I), CN, NO_2 , SO_3H , OR^6 , SR^6 , $S(O_2)R^6$, NHR^6 , $N(R^6)(R^{6'})$, $C(O)XR^6$, or $N^+(R^6)(R^{6'})(R^{6''})$;

X is NH or O;

R^5 is H, linear or branched C_1 - C_6 of alkyl;

R^6 , $R^{6'}$, and $R^{6''}$ are independently H, C_1 - C_6 of alkyl;

4. A conjugate of camptothecin analogs having Formula (IV):



Wherein T is a cell-binding agent/ molecule; L is a releasable linker; n is 1-30 and m is 1-10;

R^1 and R^2 are independently H, C_1 - C_6 of alkyl, alkyloxy, alkyl amino (including primary, secondary, tertiary amino, or quaternary ammonium);

R^3 is C_1 - C_6 of alkylene,

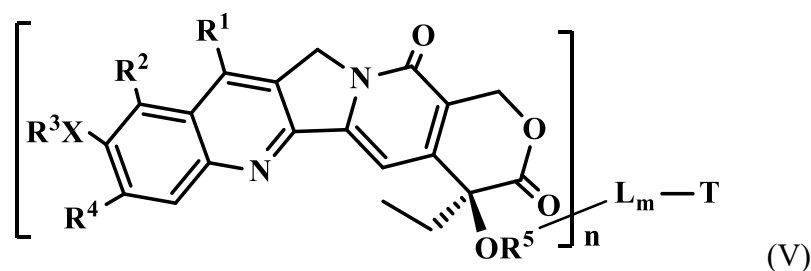
R^4 is halo (F, Cl, Br, or I), CN, NO_2 , SO_3H , OR^6 , SR^6 , $S(O_2)R^6$, $NH(R^6)$, $N(R^6)(R^{6'})$, $C(O)XR^6$, or $N^+(R^6)(R^{6'})(R^{6''})$;

X is NH or O;

R⁵ is H, linear or branched C₁-C₆ of alkyl;

R⁶, R^{6'}, and R^{6''} are independently H, C₁-C₆ of alkyl;

5. A conjugate of camptothecin analogs having Formula (V):



Wherein T is a cell-binding agent/ molecule; L is a releasable linker; n is 1-30 and m is 1-10;

R¹ and R² are independently H, linear or branched C₁-C₆ of alkyl, alkyloxy, alkylamine (including primary, secondary, tertiary amine, or quaternary ammonium);

R³ is H, R⁶C(O), linear or branched C₁-C₆ of alkyl, alkyl alcohol, or alkylamine (including primary, secondary, tertiary amine, or quaternary ammonium);

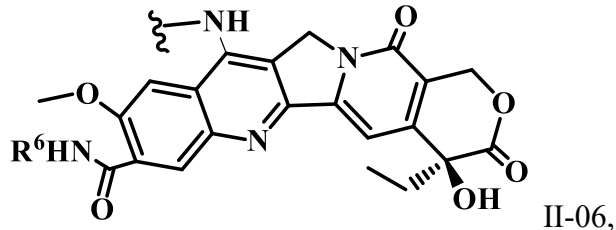
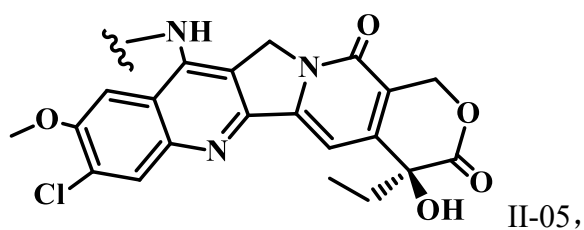
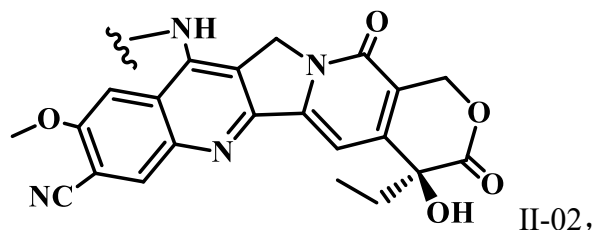
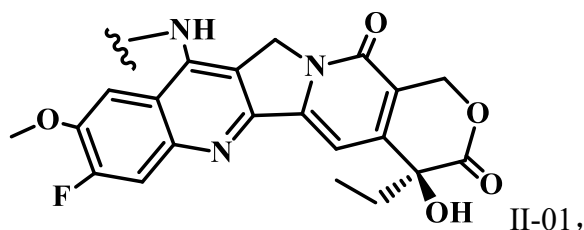
R⁴ is halo (F, Cl, Br, or I), CN, NO₂, SO₃H, OR⁶, SR⁶, S(O₂)R⁶, NH(R⁶), N(R⁶)(R^{6'}), C(O)XR⁶, or N⁺(R⁶)(R^{6'})(R^{6''});

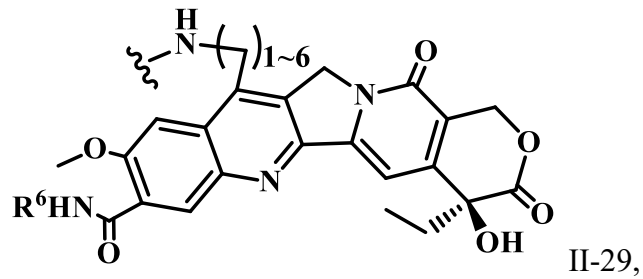
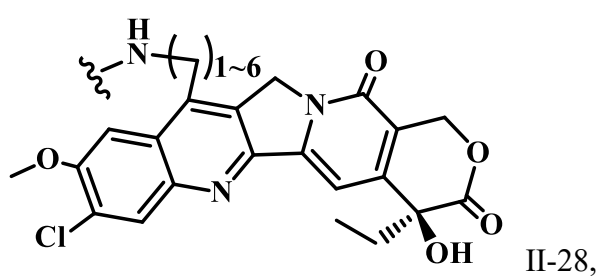
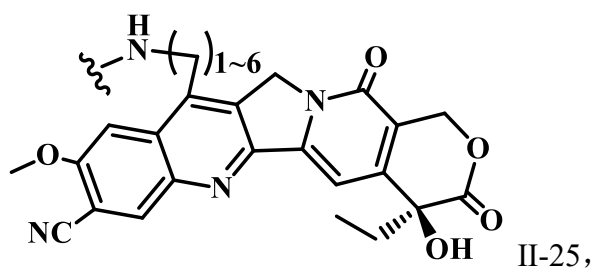
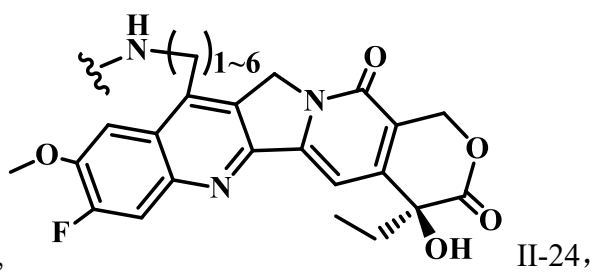
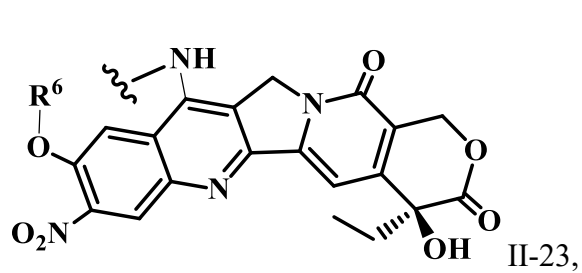
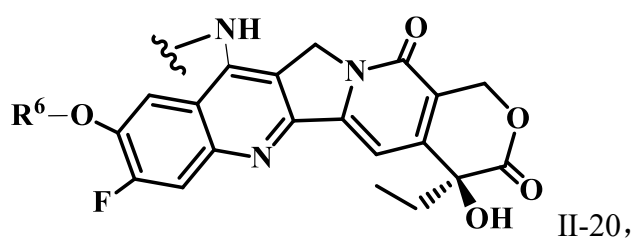
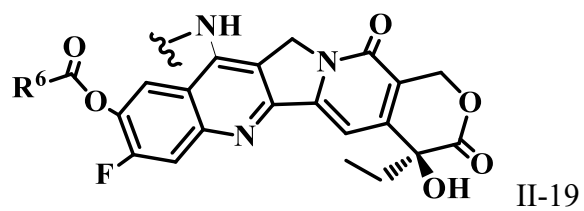
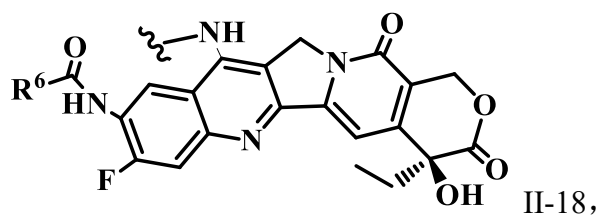
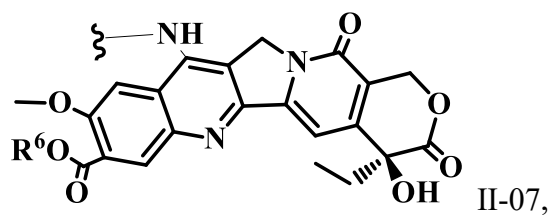
X is NH or O;

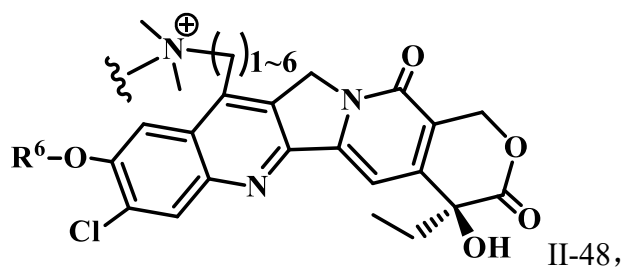
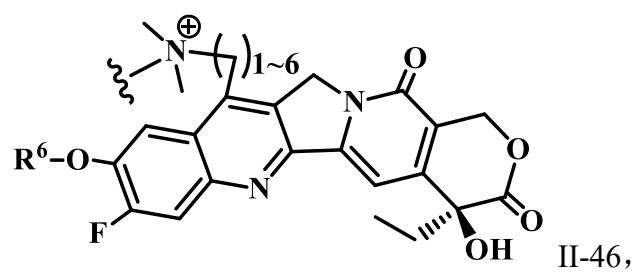
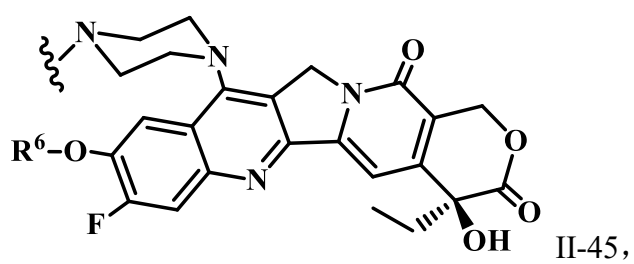
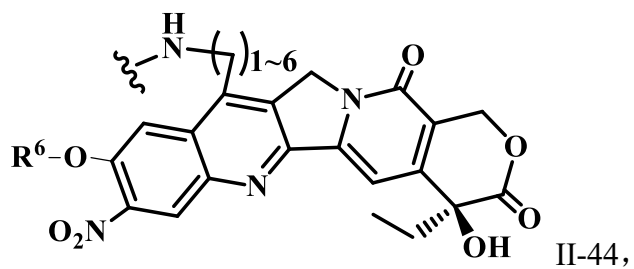
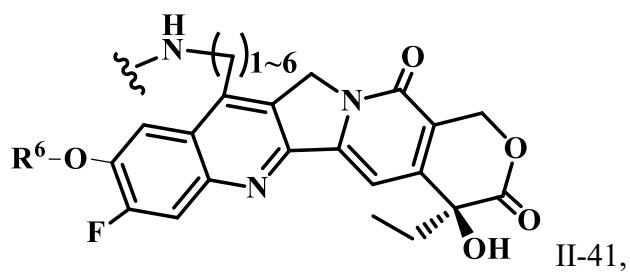
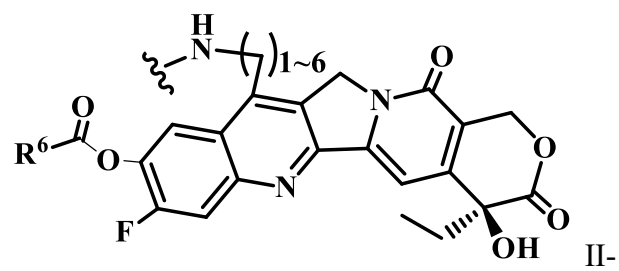
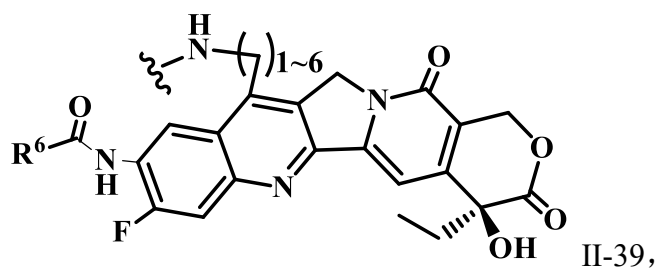
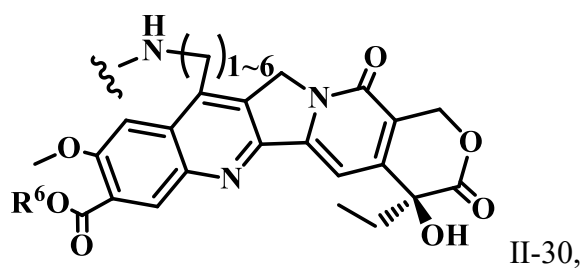
R⁵ is C(O)O, C(O)NH, R⁶C(O), or linear or branched C₁-C₆ of alkylene;

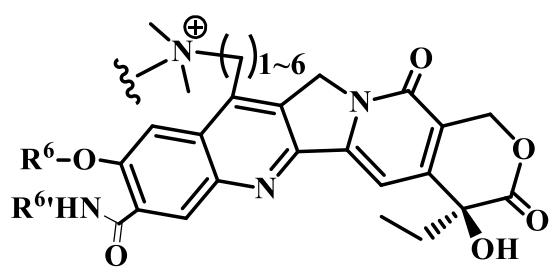
R⁶, R^{6'}, and R^{6''} are independently H, or C₁-C₆ of alkyl,

6. A conjugate according to claim 1, 2, 3, 4, or 5, wherein camptothecin linked to linker L having the structures illustrated below:

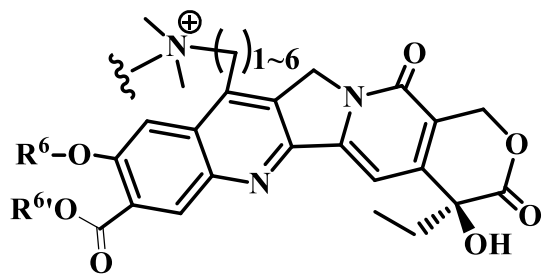




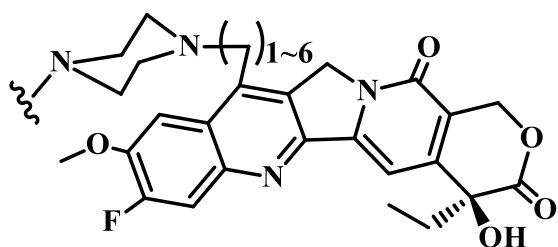




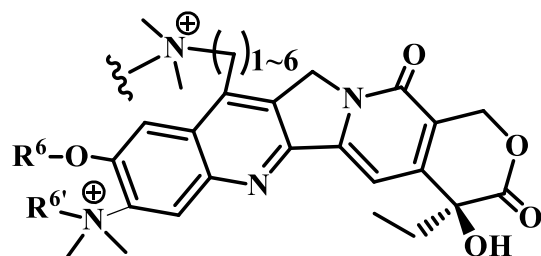
II-49,



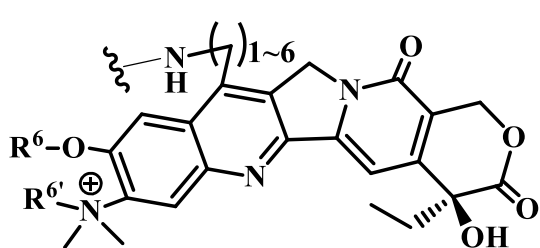
II-50,



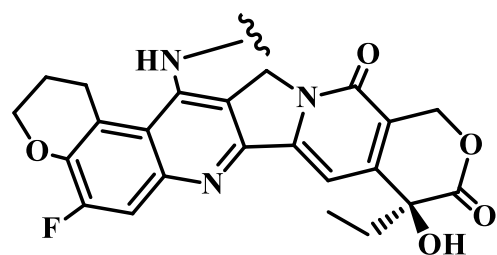
II-51,



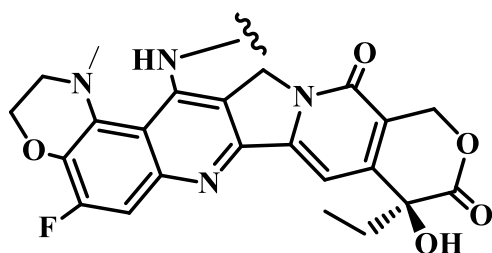
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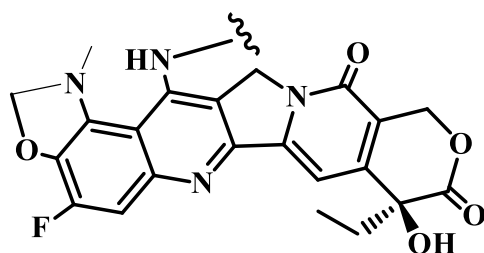
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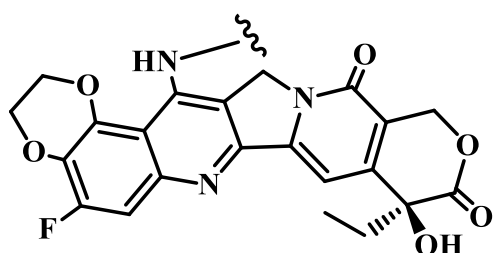
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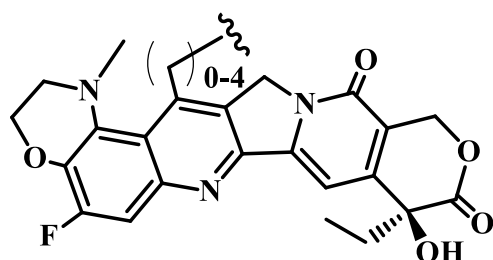
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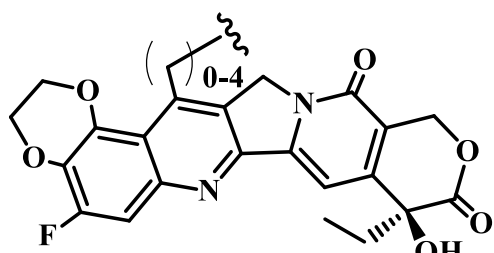
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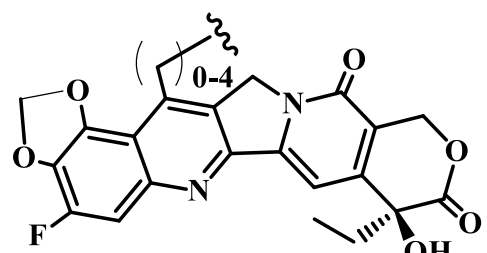
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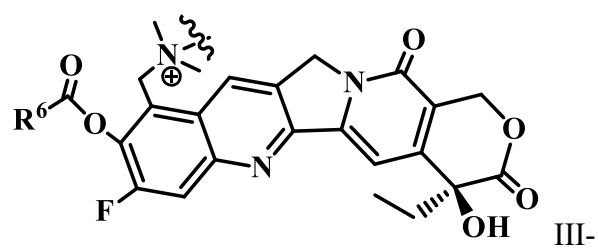
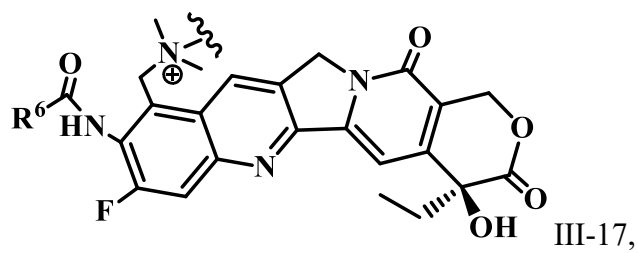
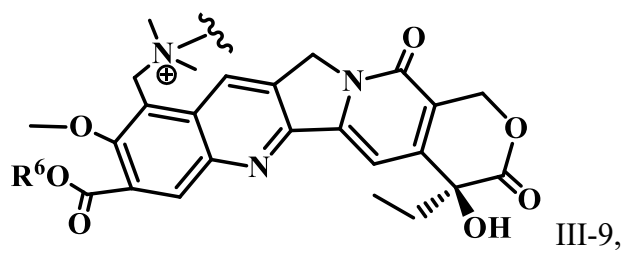
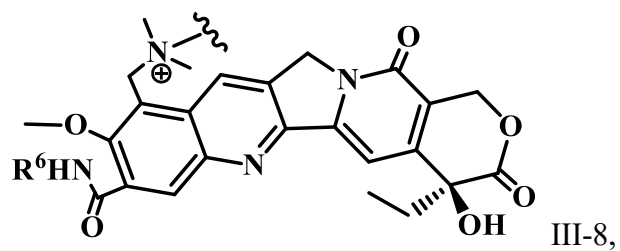
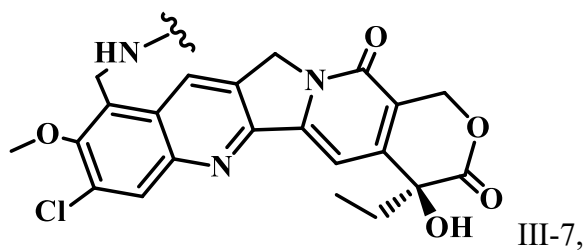
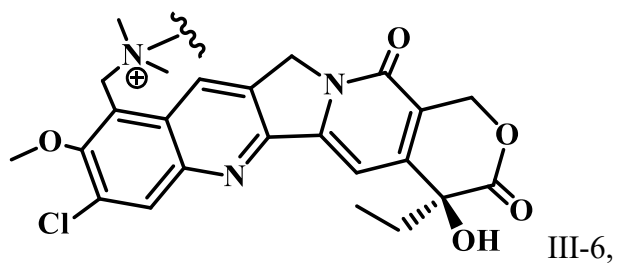
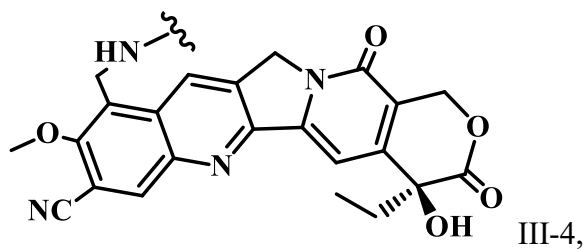
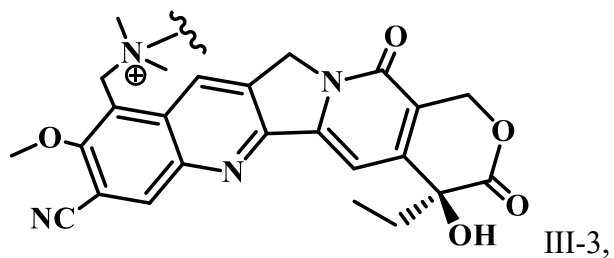
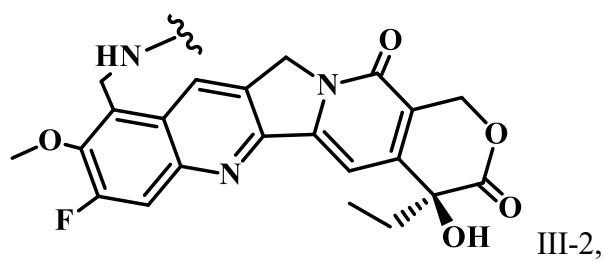
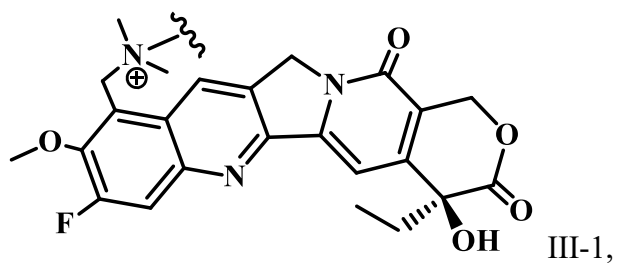
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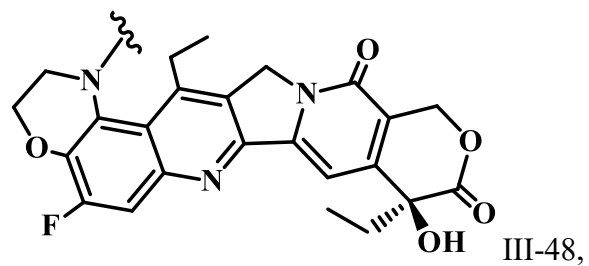
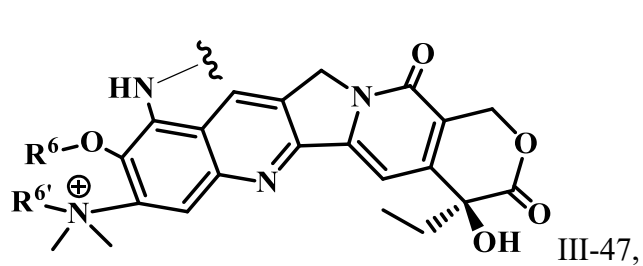
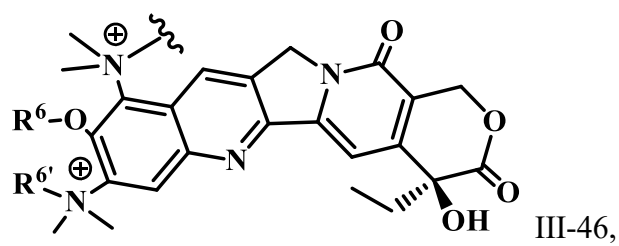
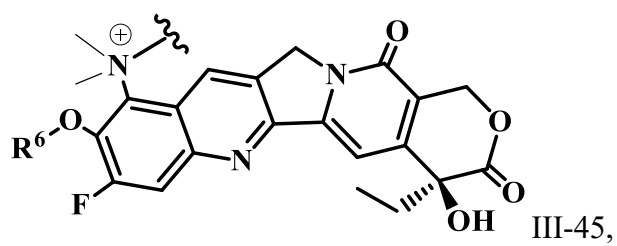
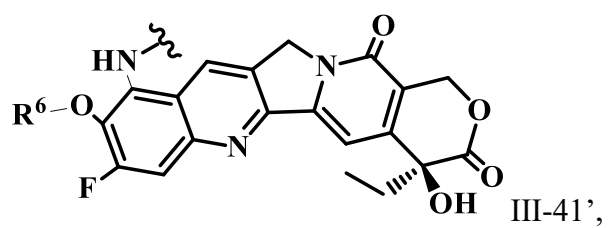
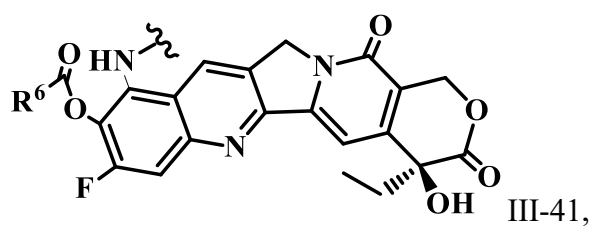
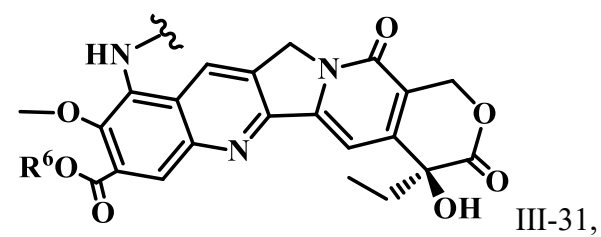
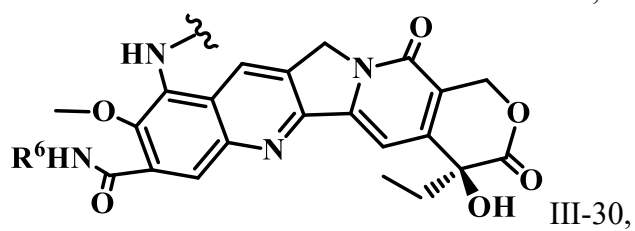
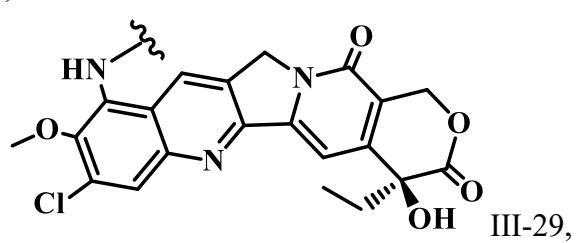
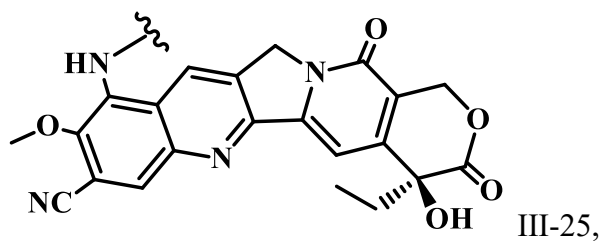
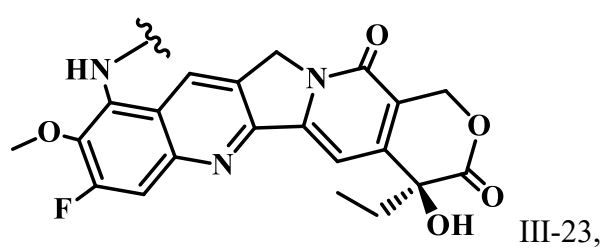
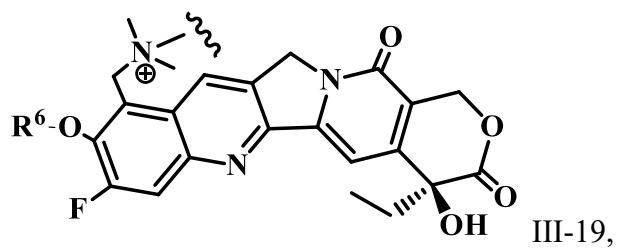


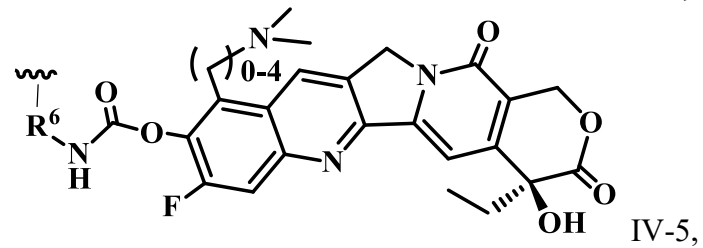
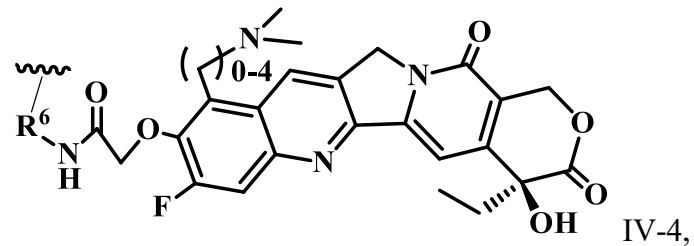
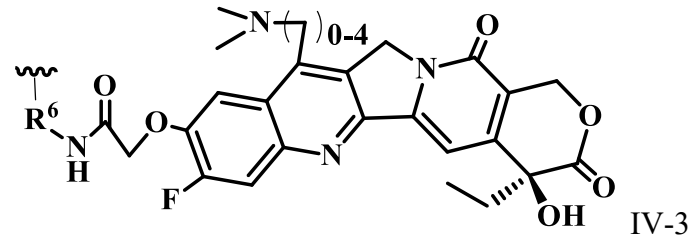
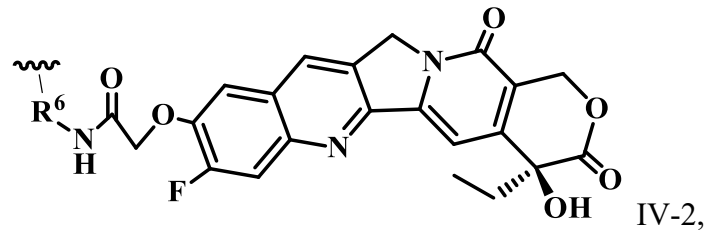
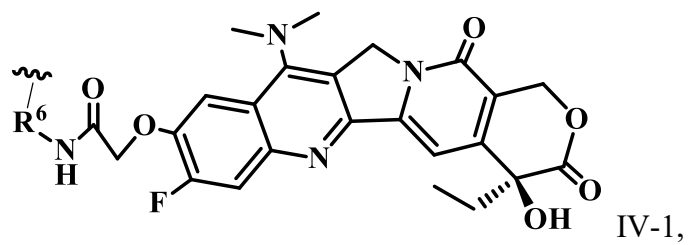
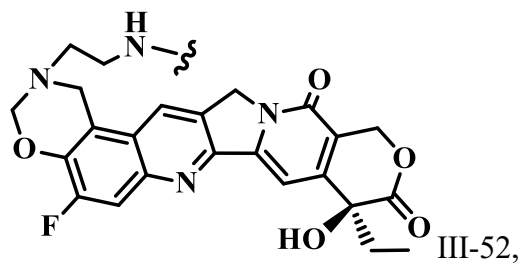
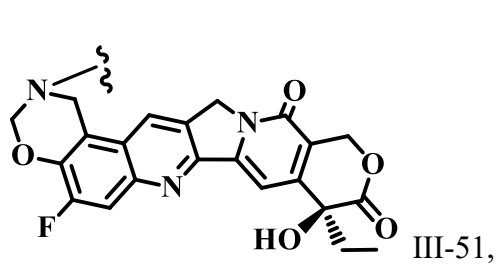
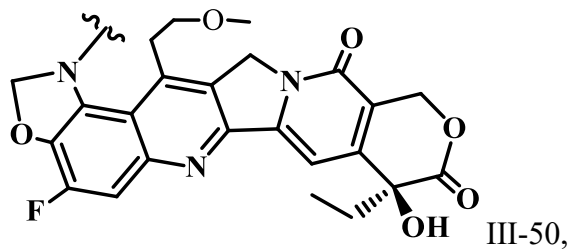
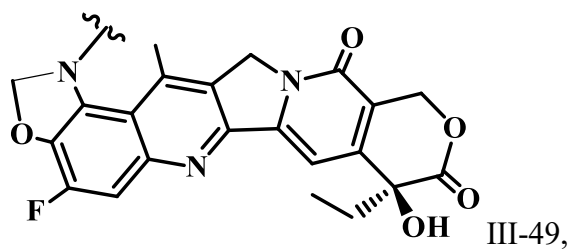
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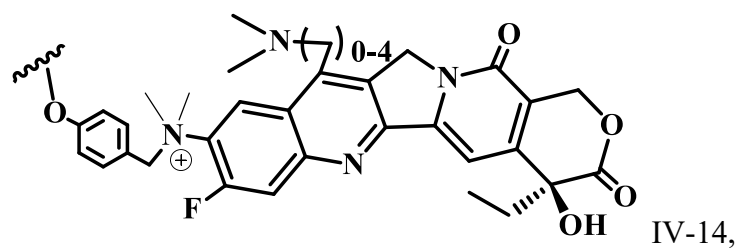
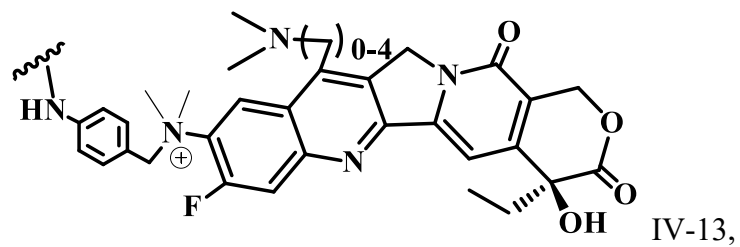
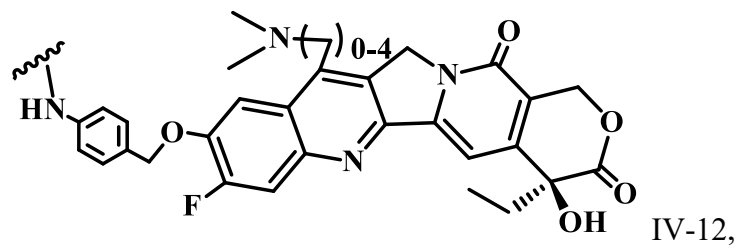
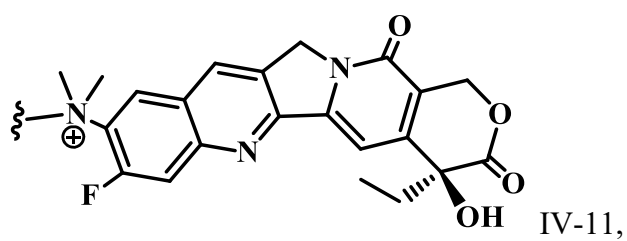
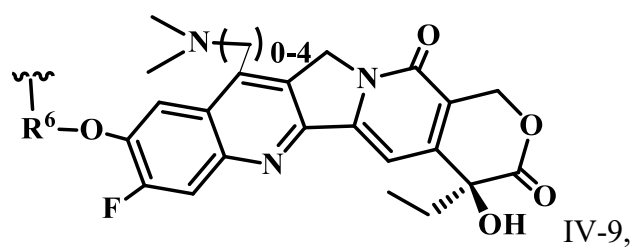
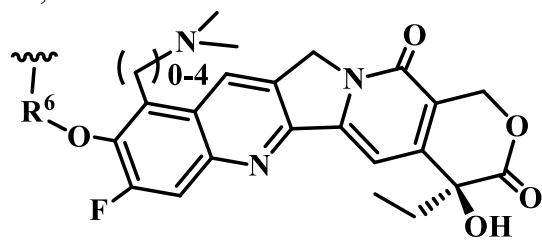
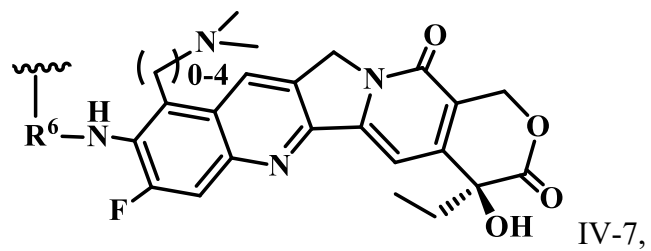
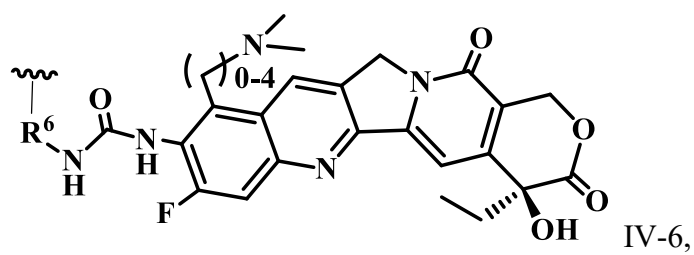


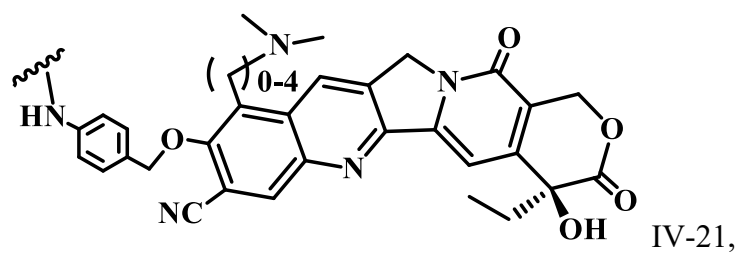
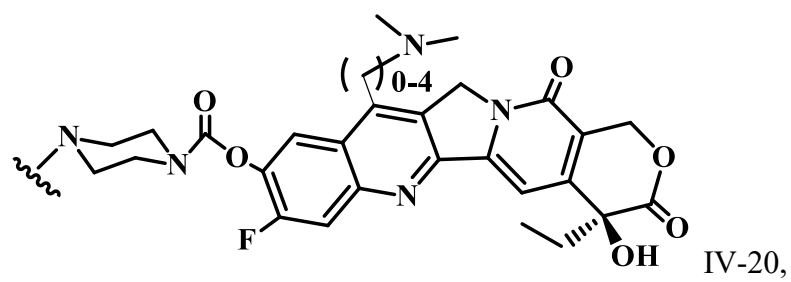
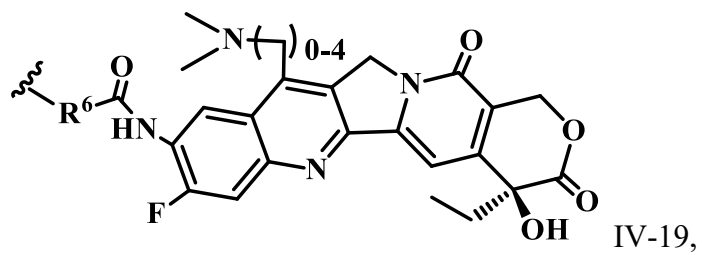
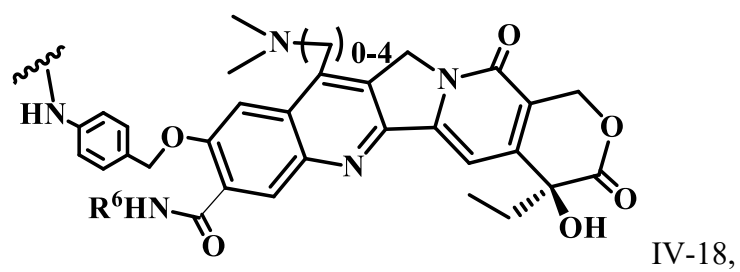
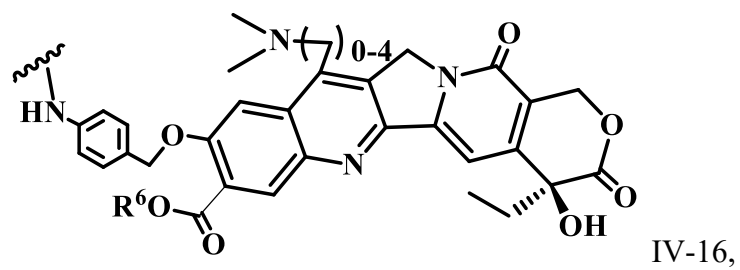
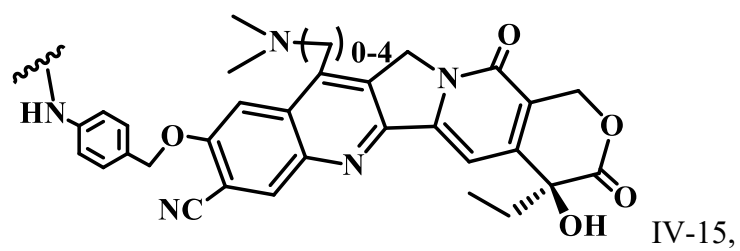
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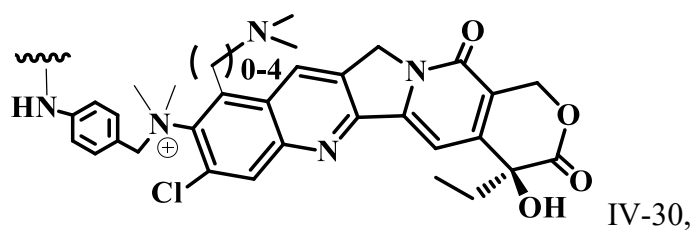
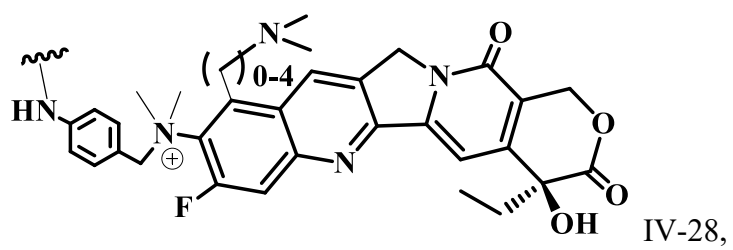
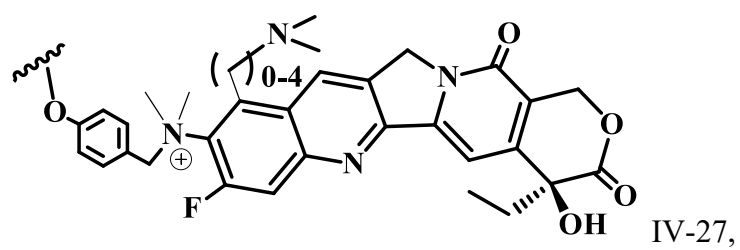
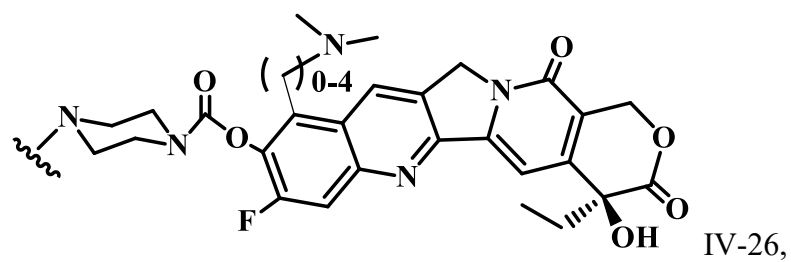
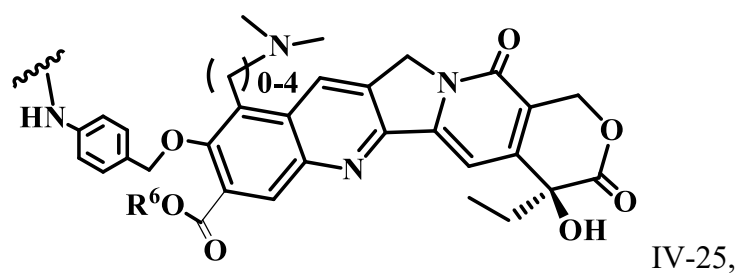
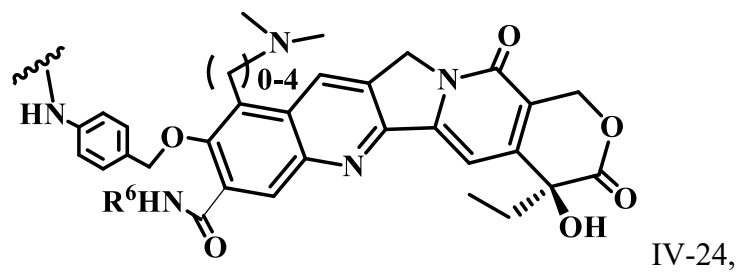
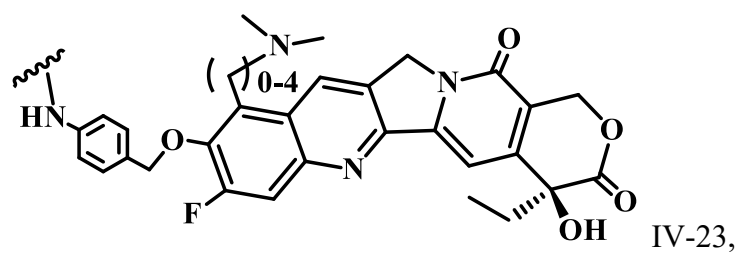


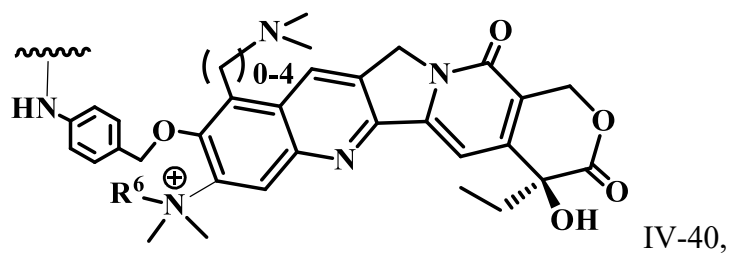
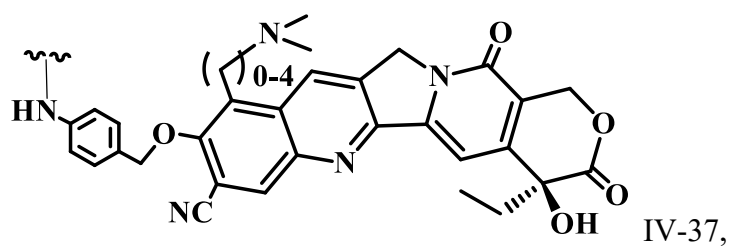
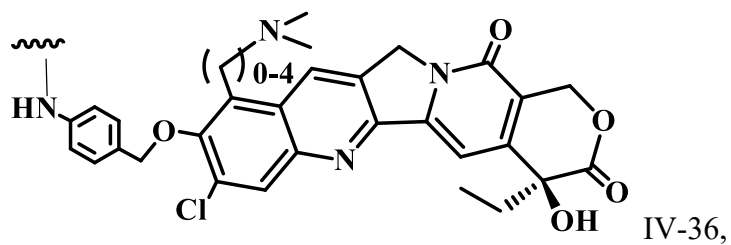
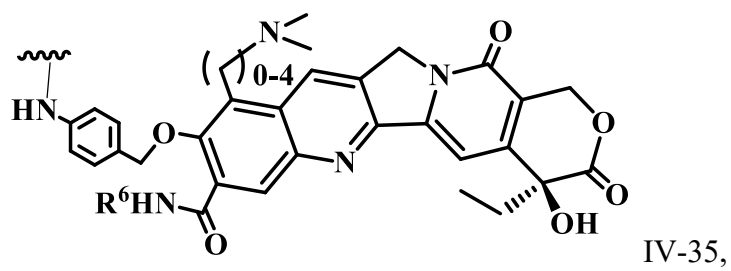
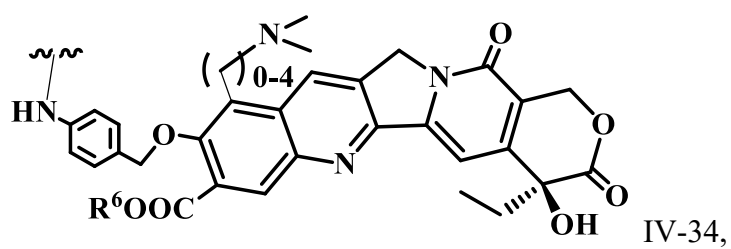
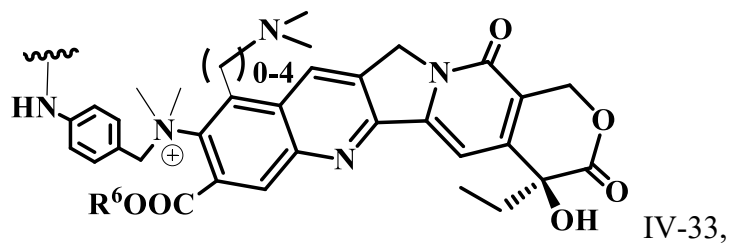
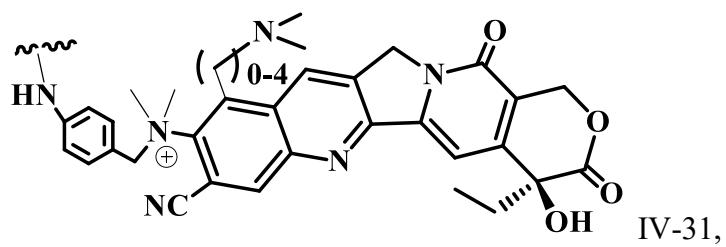


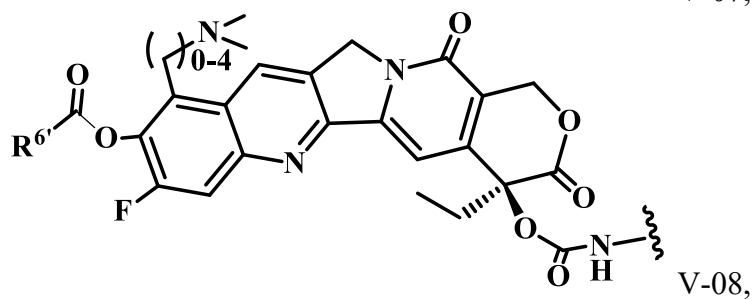
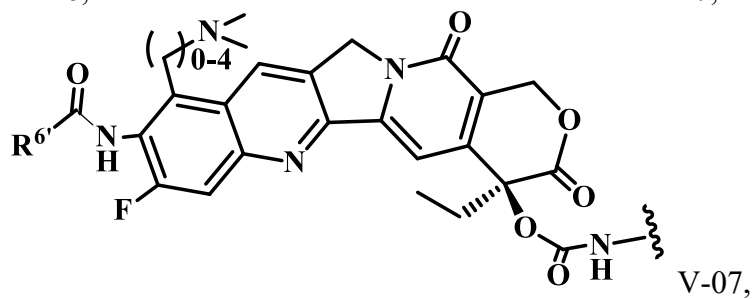
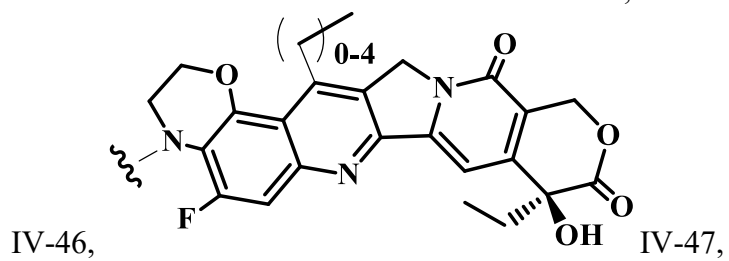
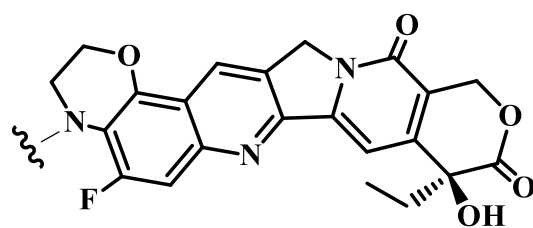
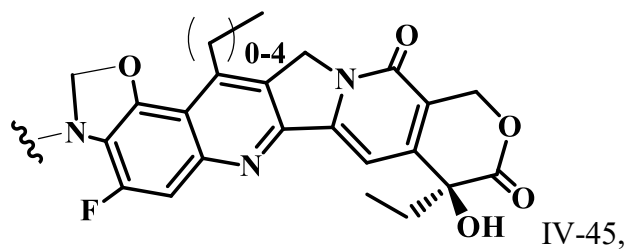
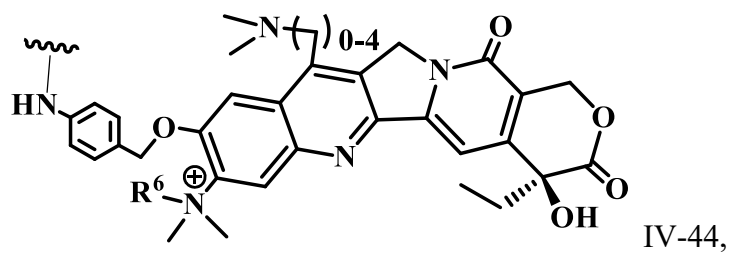
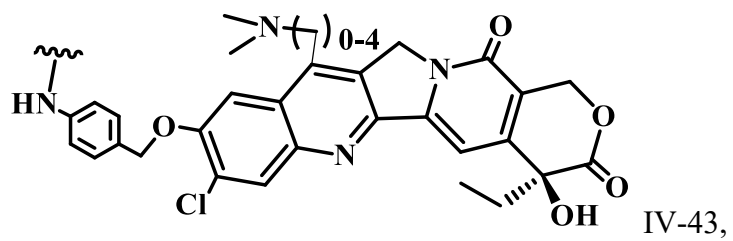
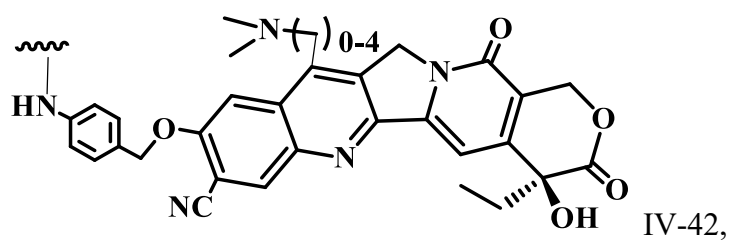


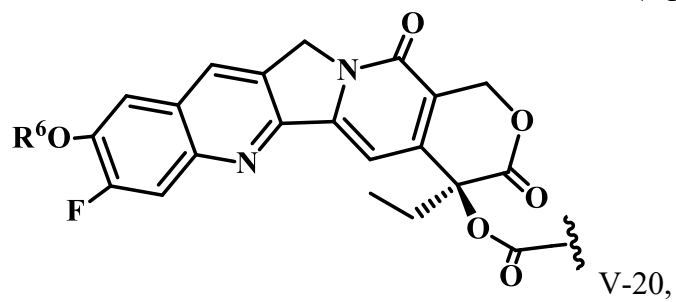
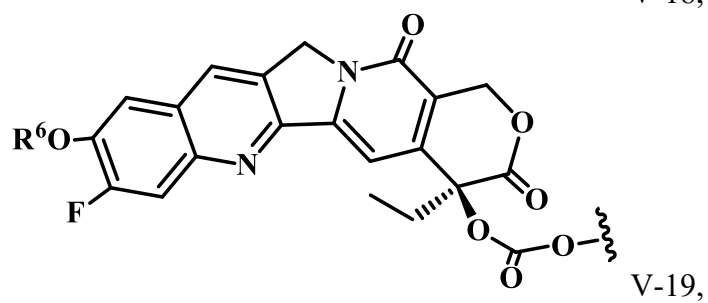
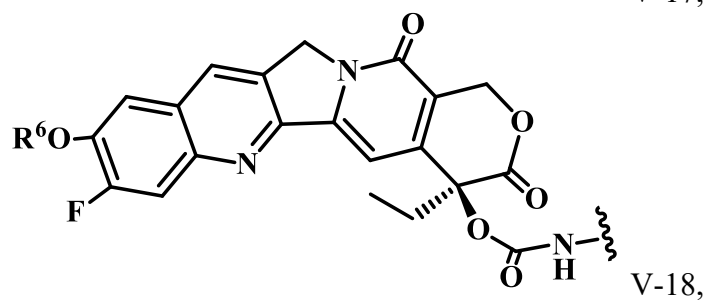
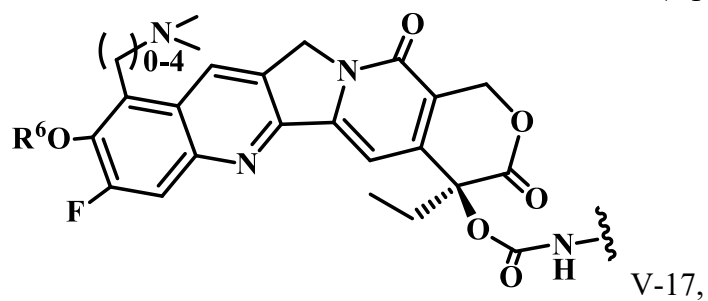
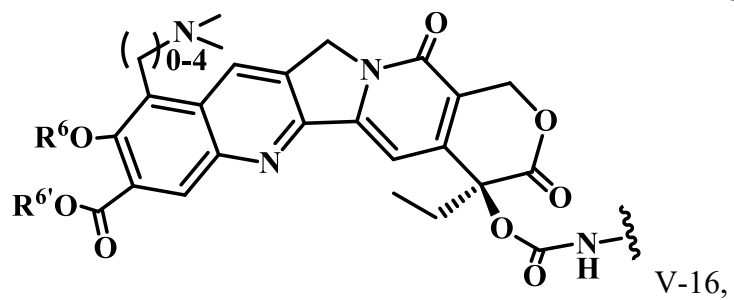
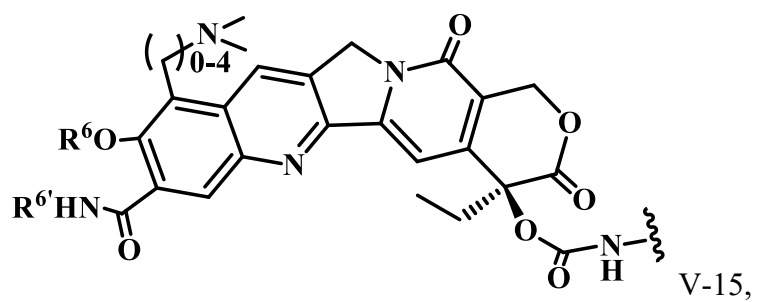


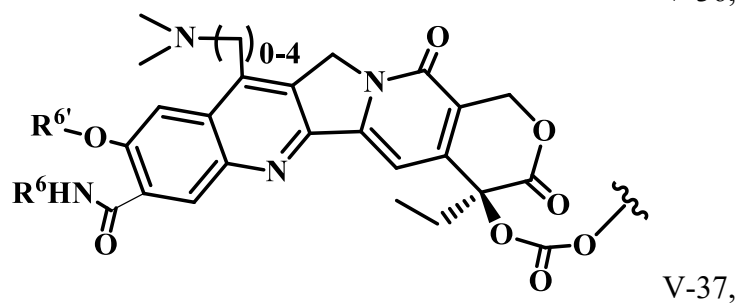
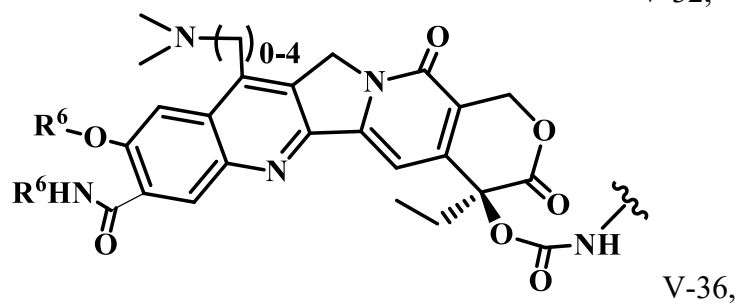
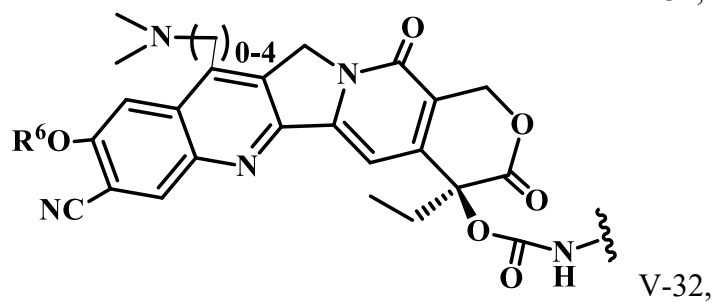
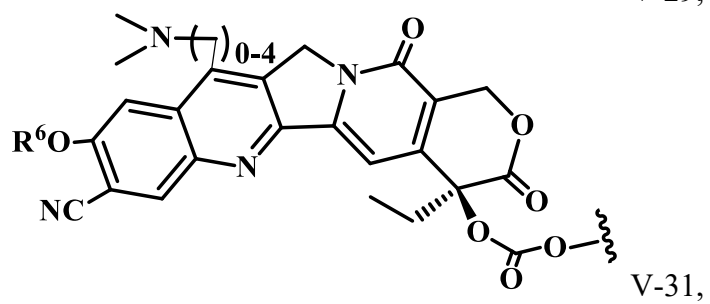
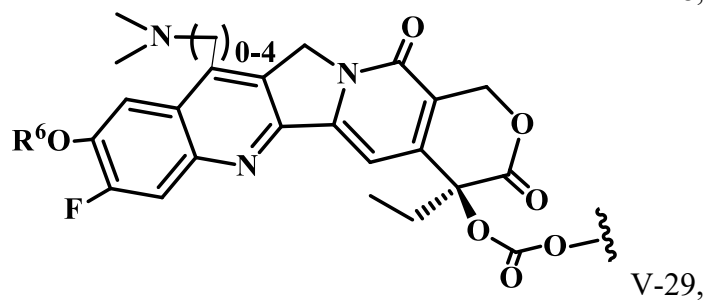
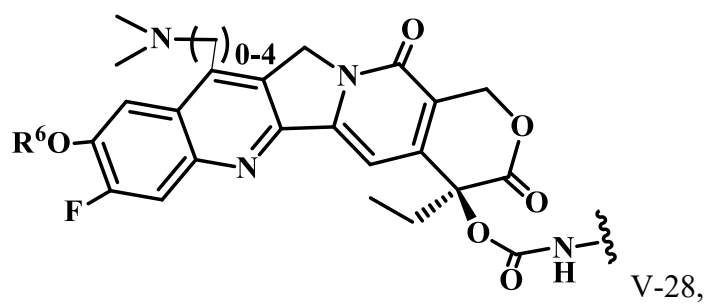


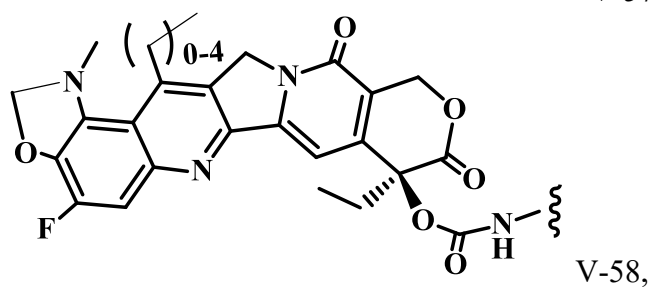
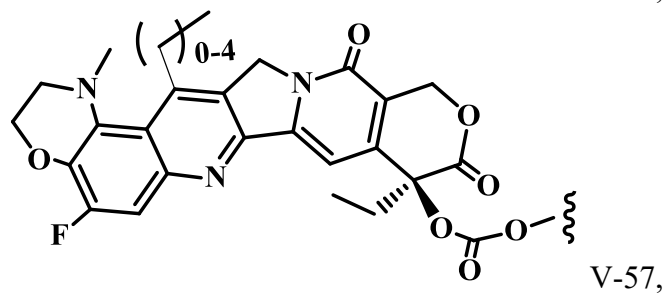
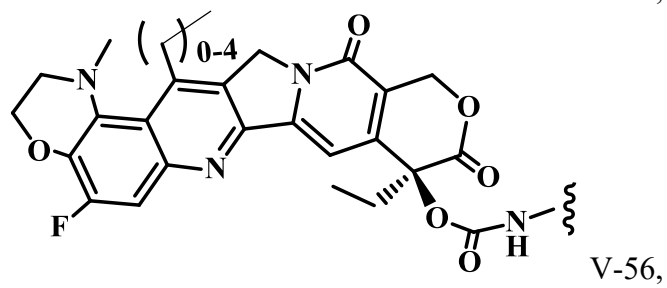
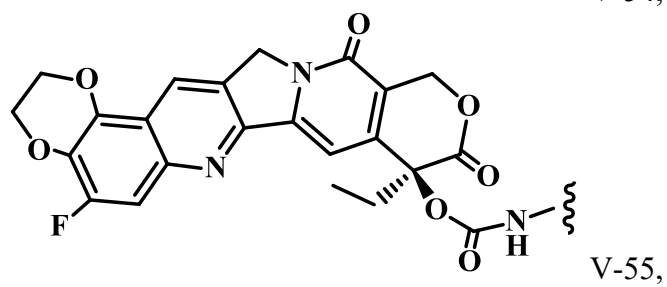
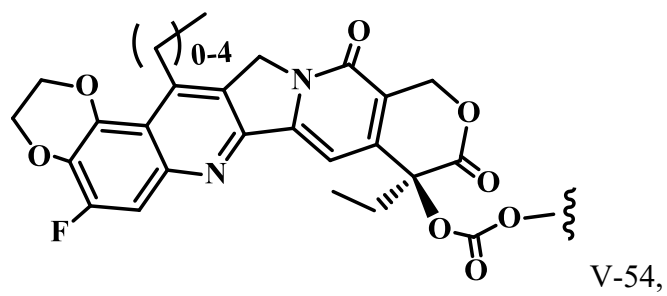
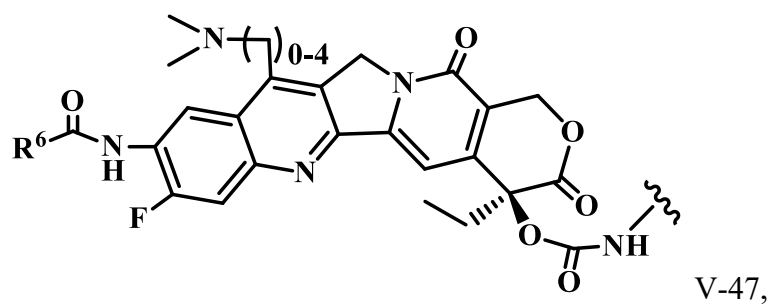


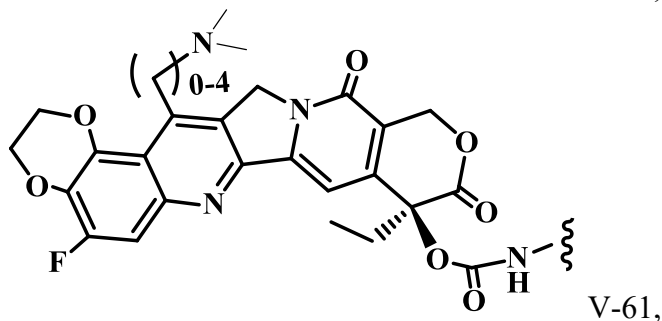
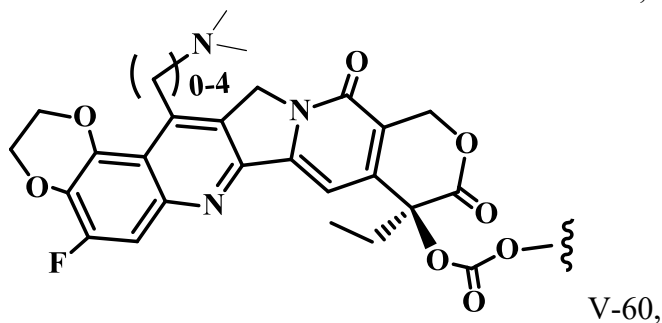
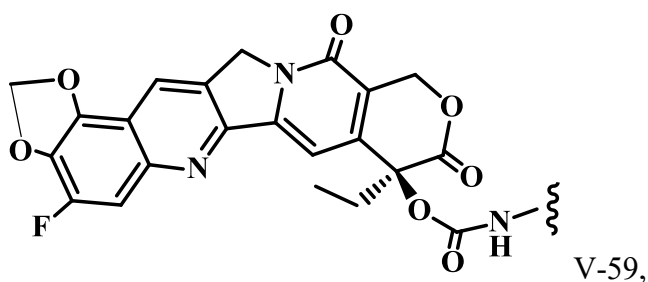










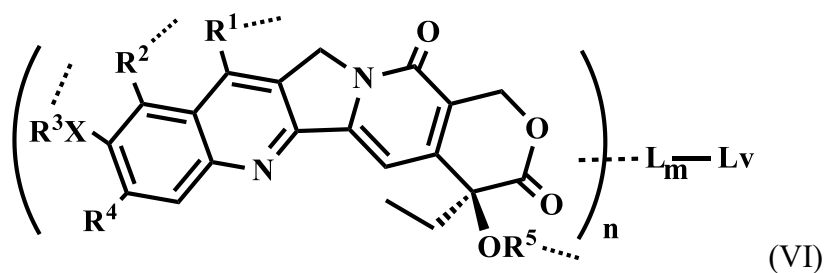


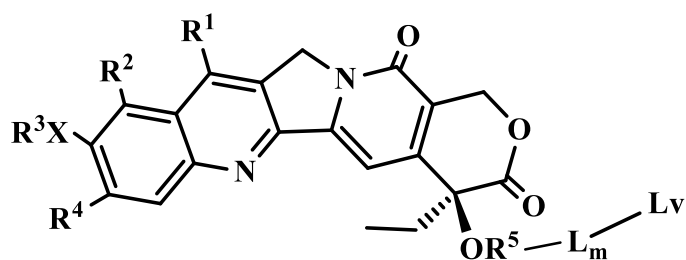
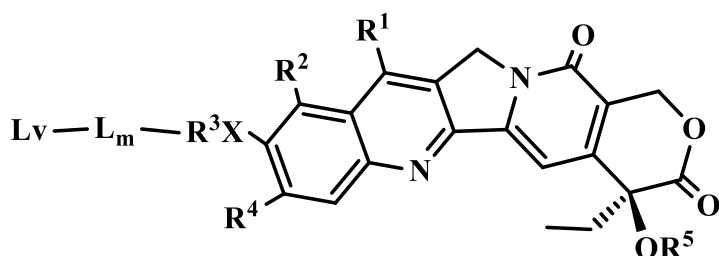
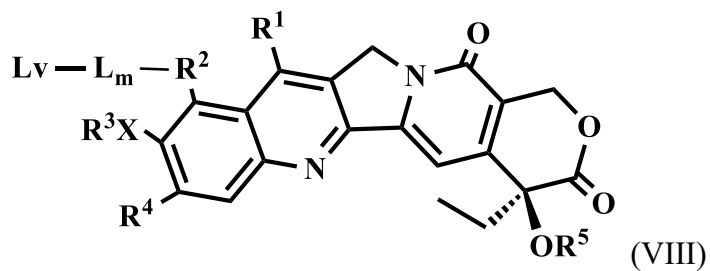
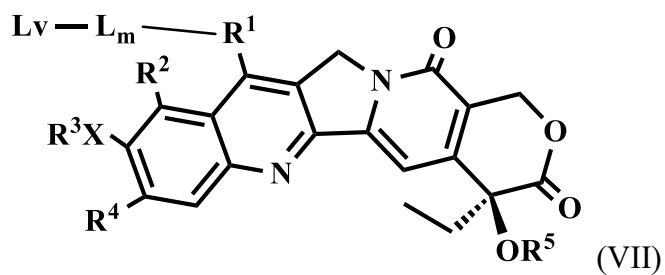
or their pharmaceutically acceptable salts, hydrates, or hydrated salts; or the polymorphic crystalline structures of these compounds; or their isotope, optical isomers, racemates, diastereomers or enantiomers;

wherein “ ζ ” is the site linked to linker L;

wherein R^6 , and $R^{6'}$ are independently H, C_1 - C_6 of alkyl;

7. The method of producing conjugates of camptothecin of Formula (I), (II), (III), (IV), and (V), according to claim 1, 2, 3, 4, or 5, comprising coupling reaction of a cell-binding molecule T with a conjugatable compound of Formula (VI), (VII), (VIII), (IX) and (X) respectively:

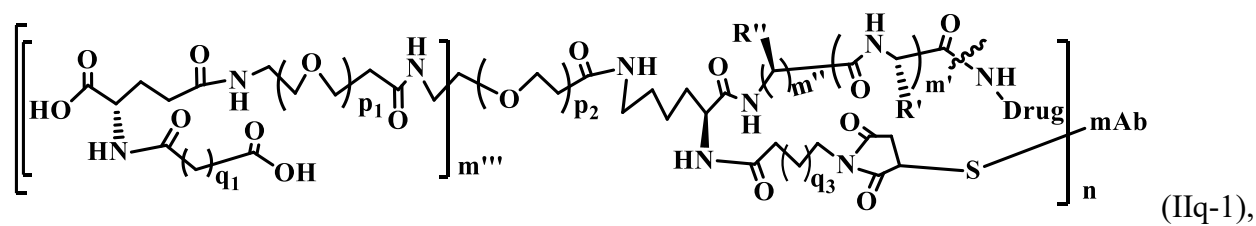


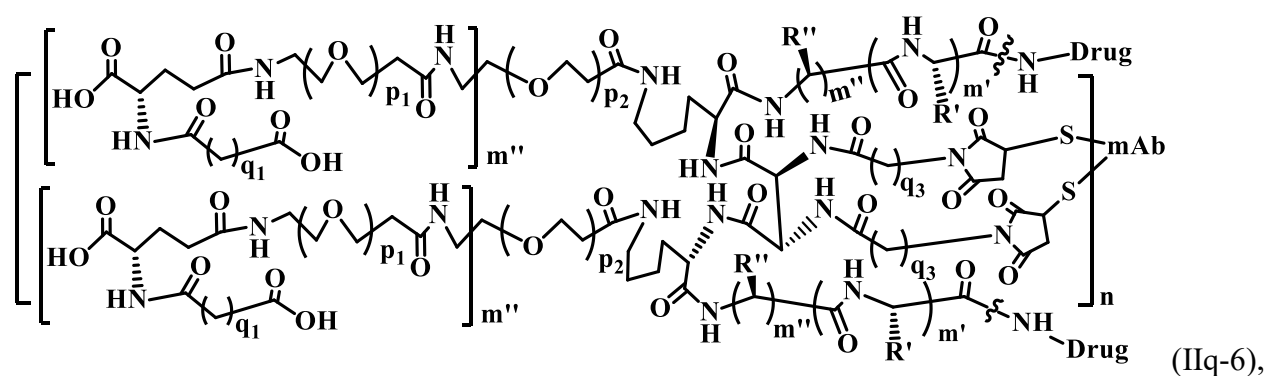
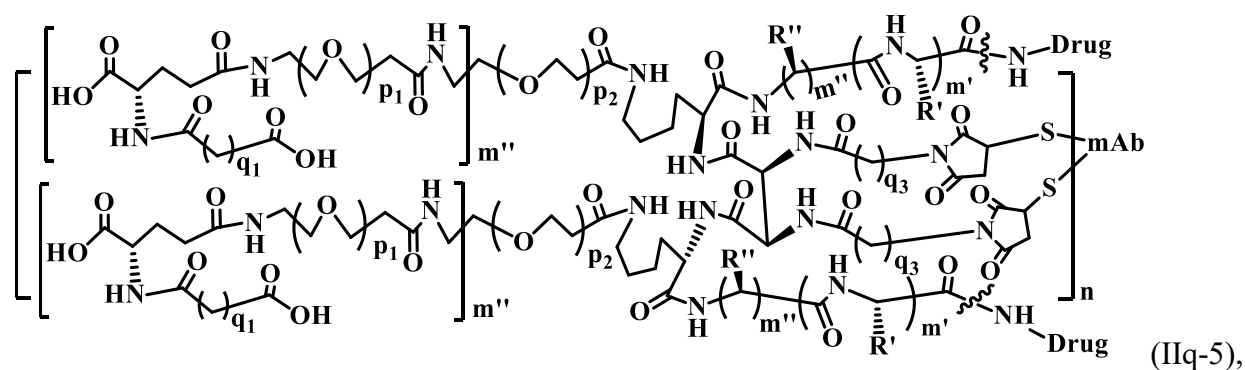
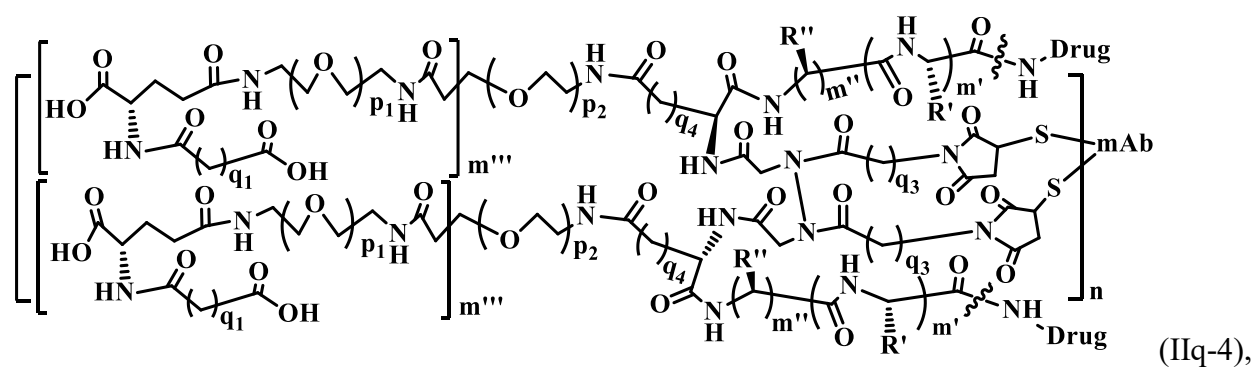
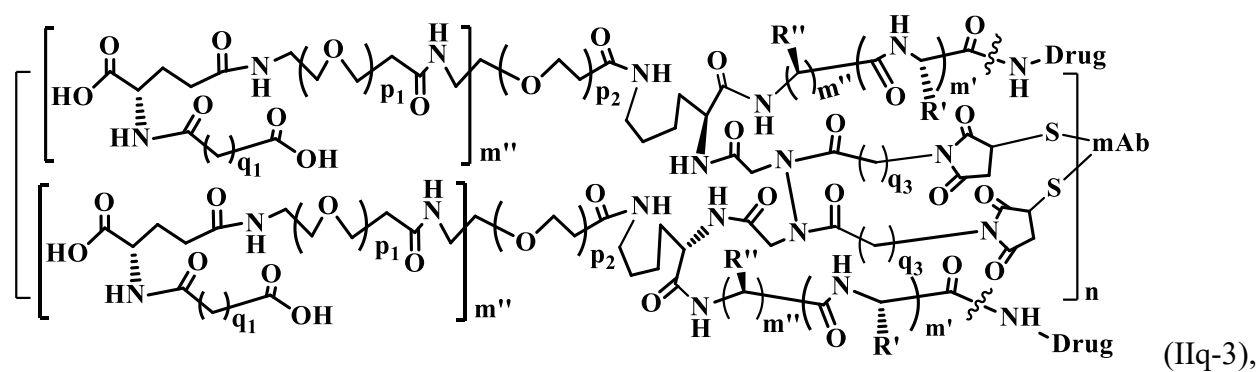
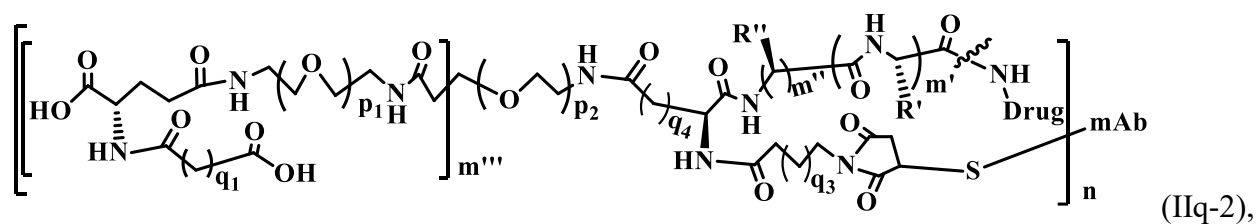


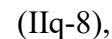
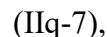
wherein R^1 , R^2 , R^3 , R^4 , R^5 , L , X and m are defined the same as in Formula (I) above;

L_v is a reacting group that can react with a thiol, amine, carboxylic acid, selenol, phenol or hydroxyl group on a cell-binding molecule.

8. A conjugate of camptothecin analogs according to claim 1, 2, 3, or 4, having the formula (IIq-1), (IIq-2), (IIq-3), (IIq-4), (IIq-5), (IIq-6), (IIq-7), (IIq-8) illustrated below:

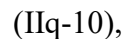
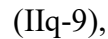


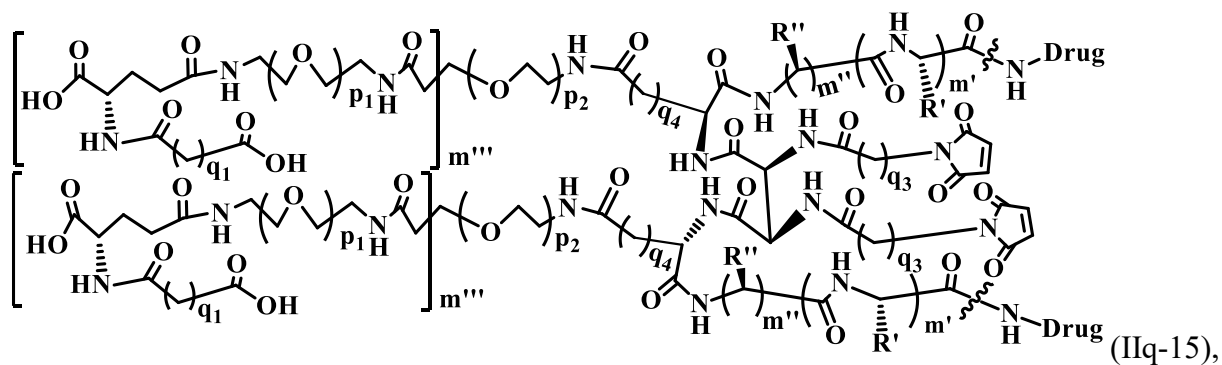
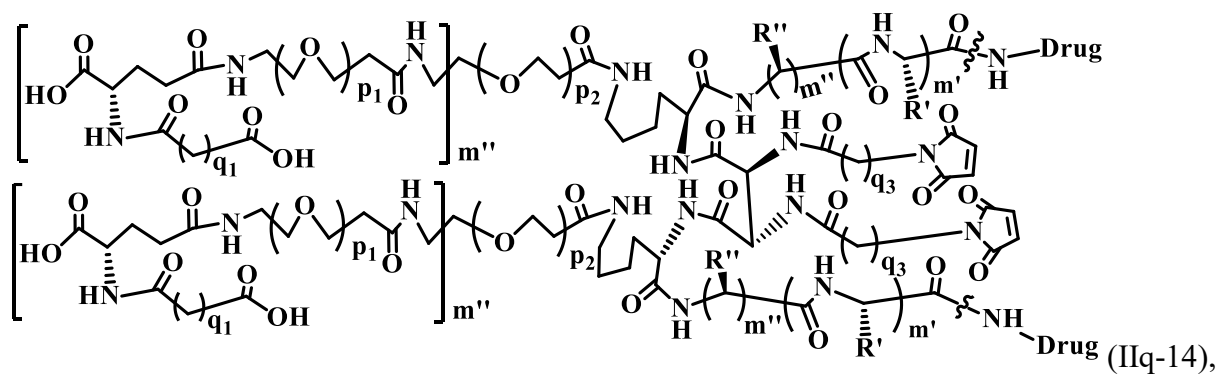
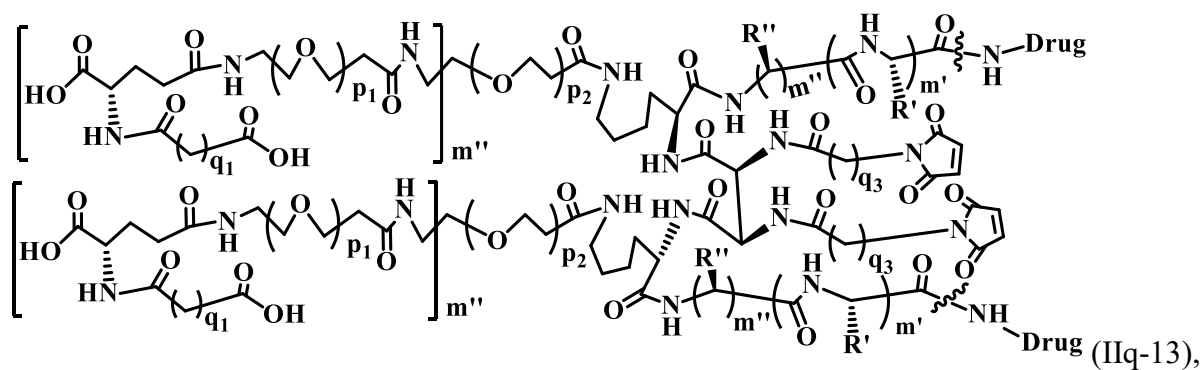
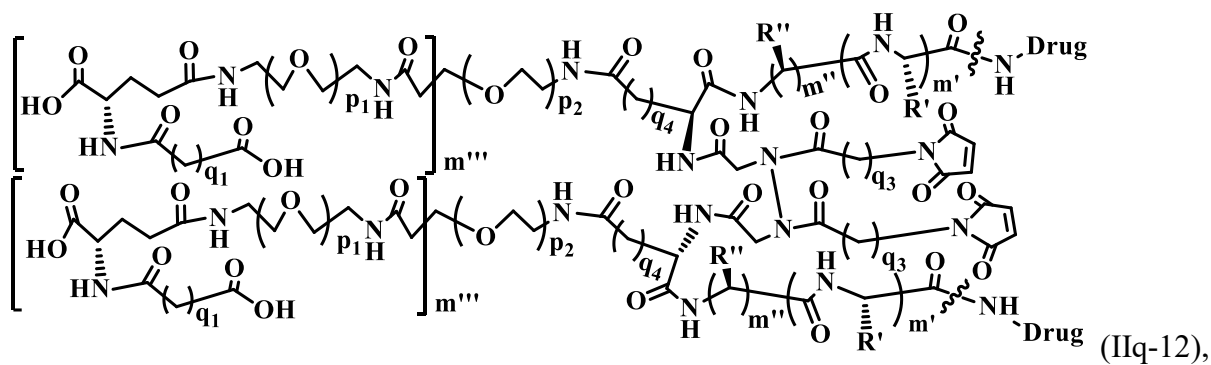
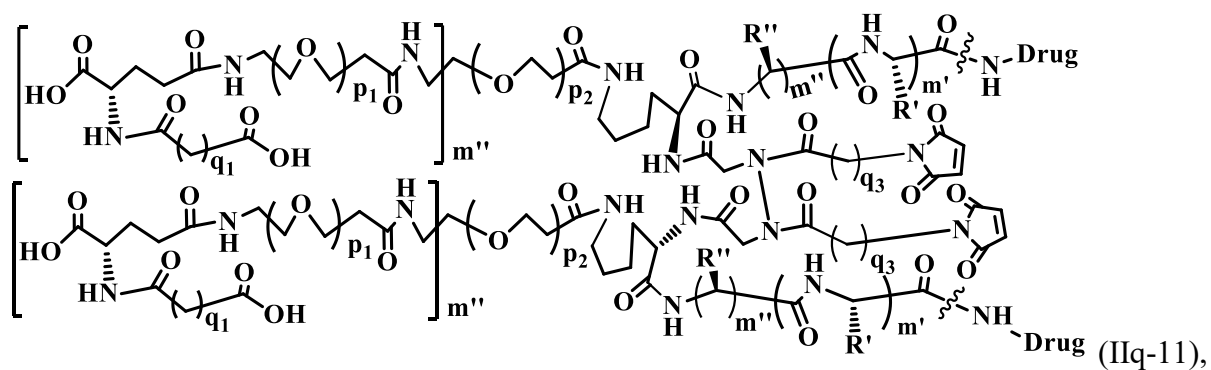


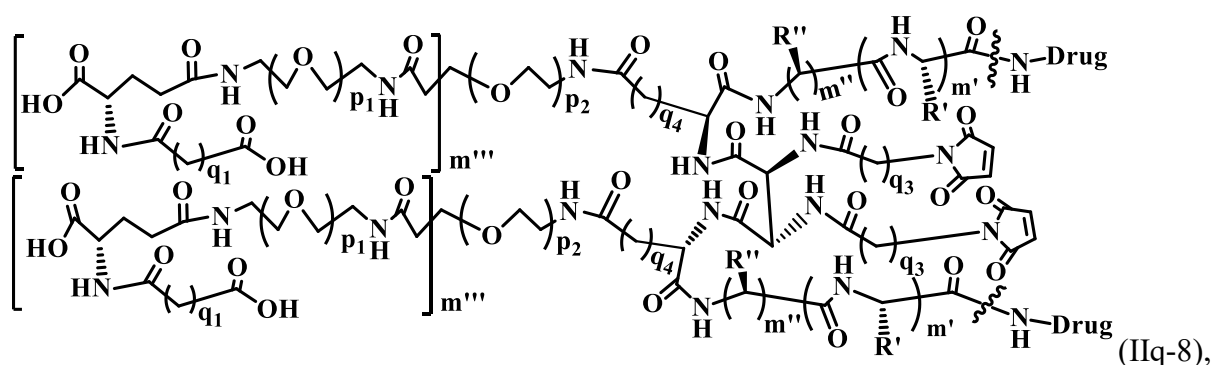


wherein R' and R'' are independently H, Me, Et, *i*Pr, *i*Bu, Bz (CH₂C₆H₅), CH₂COOH, CH₂CH₂COOH, CH₂CONH₂, CH₂CH₂CONH₂, CH₂CH₂CH₂CH₂NH₂, CH₂CH₂SCH₃, CH₂OH, CH₂CH₂CH₂NHC(=NH)NH₂, CH(OH)CH₃, CH₂C₆H₄OH, CH₂C₃N₂H₃; p₁ and p₂ are independently 0 ~ 24; q₁ is 1 ~ 18; q₃ is 0 ~ 6; q₄ is 0 ~ 4; m' and m'' are independently 0 ~ 6; m''' is 0 or 1; and mAb is a cell-binding molecule; NH-Drug here is any one of structures listed claim 6; and  is the site linked to NH-Drug.

9. The method according to claim 7, wherein the conjugatable compound have the formula (IIq-9), (IIq-10), (IIq-11), (IIq-12), (IIq-13), (IIq-14), (IIq-15), (IIq-16) illustrated below:

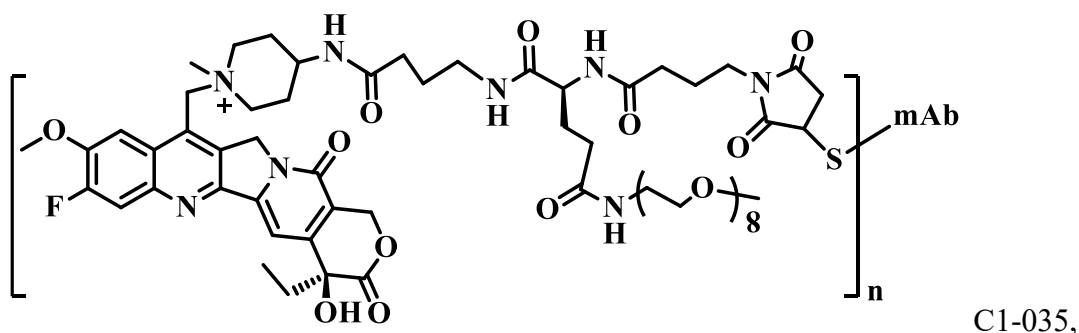
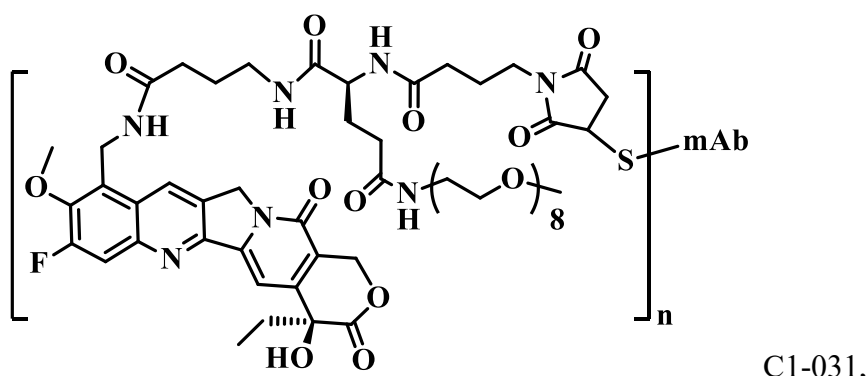
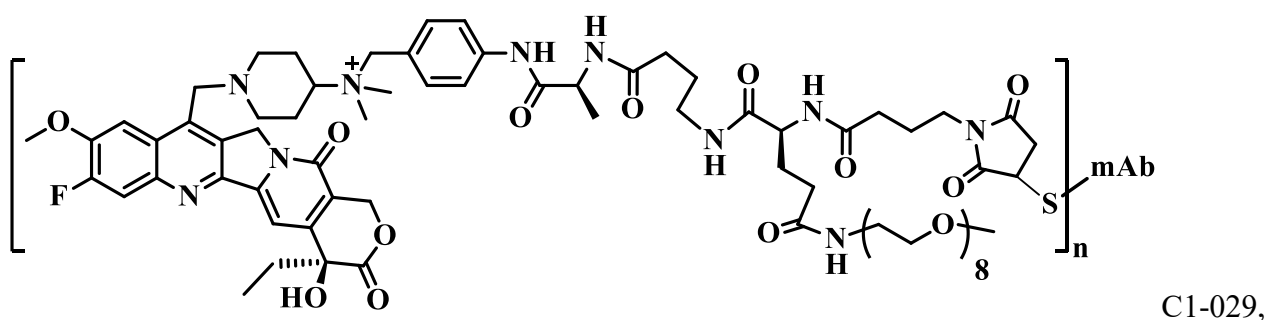


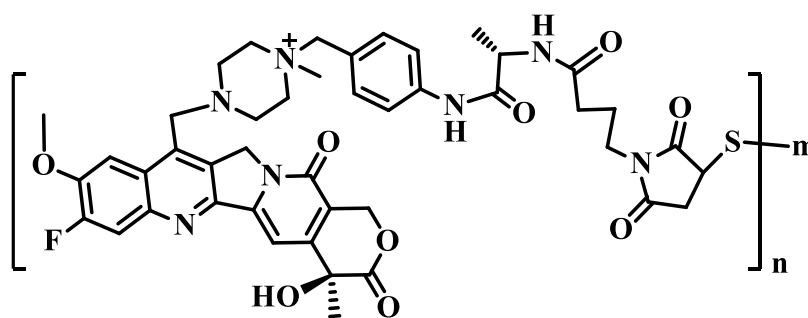




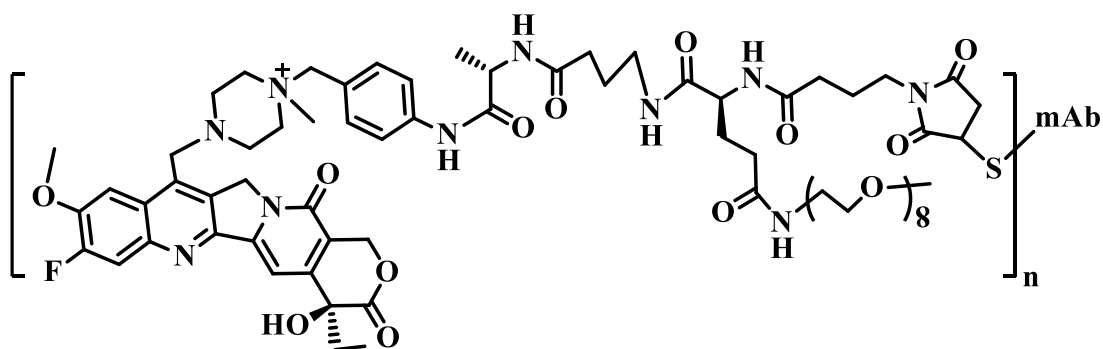
wherein R' and R'' are independently H, Me, Et, ⁱPr, ^tBu, Bz (CH₂C₆H₅), CH₂COOH, CH₂CH₂COOH, CH₂CONH₂, CH₂CH₂CONH₂, CH₂CH₂CH₂CH₂NH₂, CH₂CH₂SCH₃, CH₂OH, CH₂CH₂CH₂NHC(=NH)NH₂, CH(OH)CH₃, CH₂C₆H₄OH, CH₂C₃N₂H₃; p₁ and p₂ are independently 0 ~ 24; q₁ is 1 ~ 18; q₃ is 0 ~ 6; q₄ is 0 ~ 4; m' and m'' are independently 0 ~ 6; m''' is 0 or 1; NH-Drug here is any one of structures listed claim 6; and is the site linked to NH-Drug.

10. A conjugate of camptothecin according to claim 1, 2, 3, 4, or 5, having the structures illustrated below:

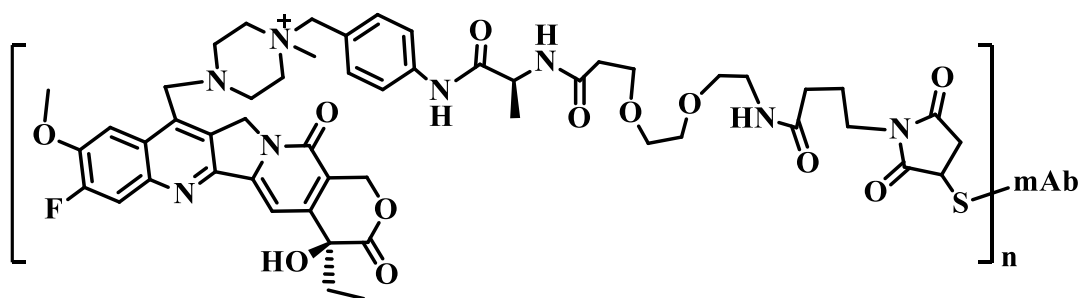




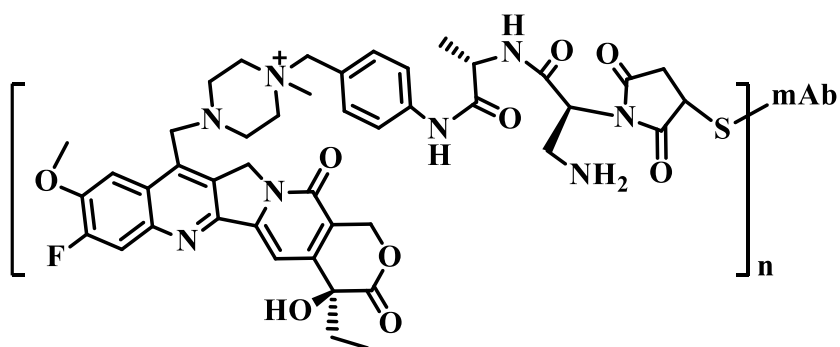
C1-041,



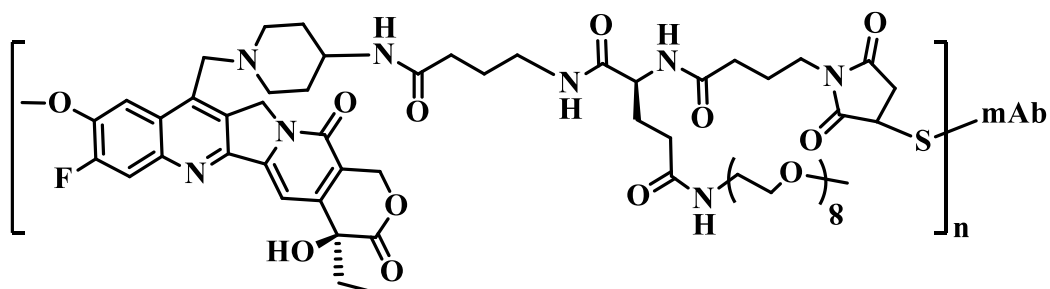
C1-042,



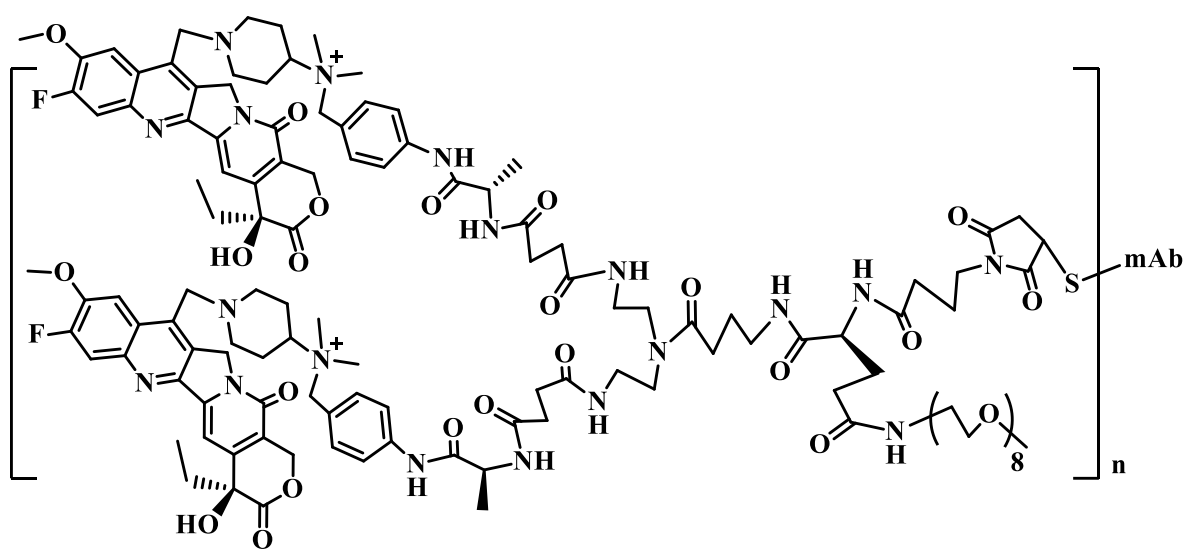
C1-043,



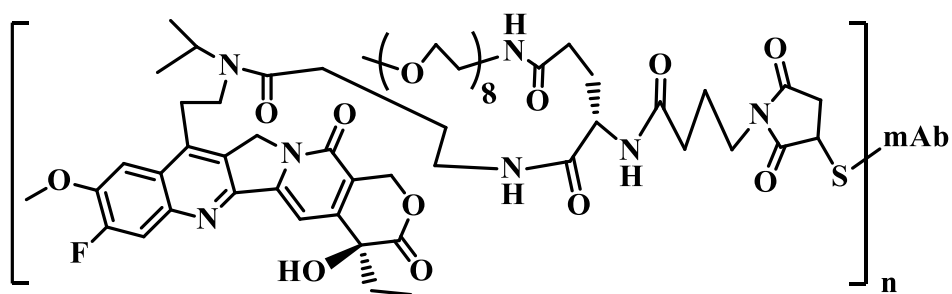
C1-047,



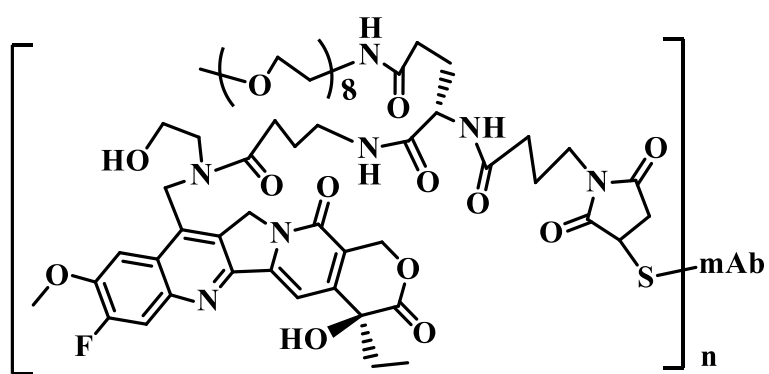
C1-050,



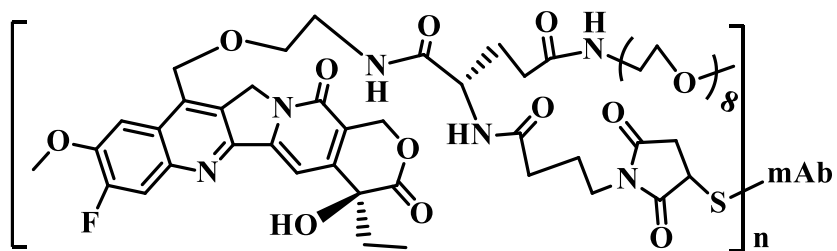
C1-064,



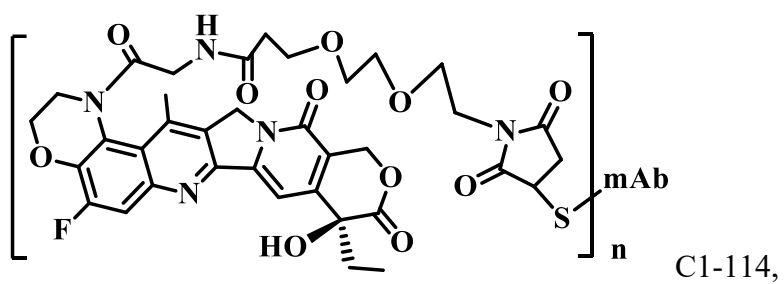
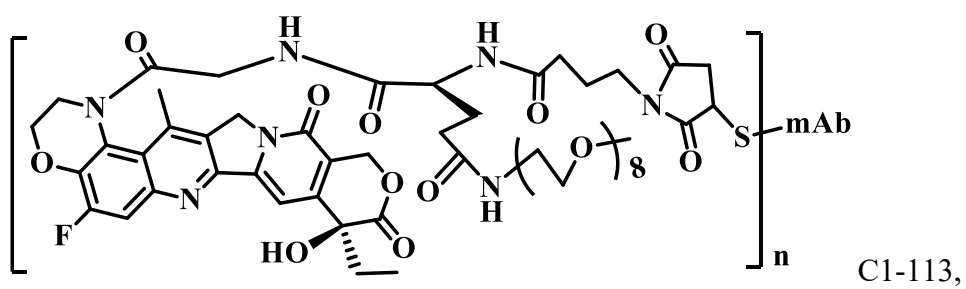
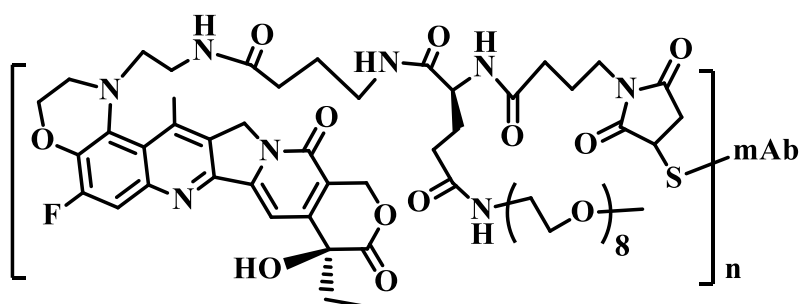
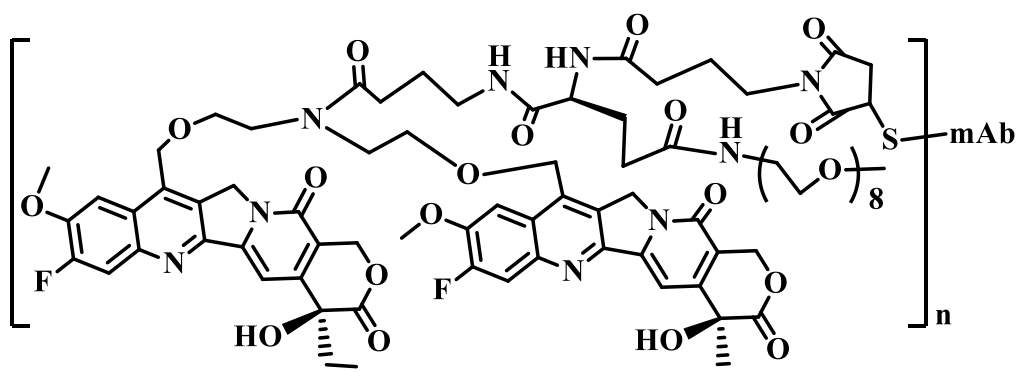
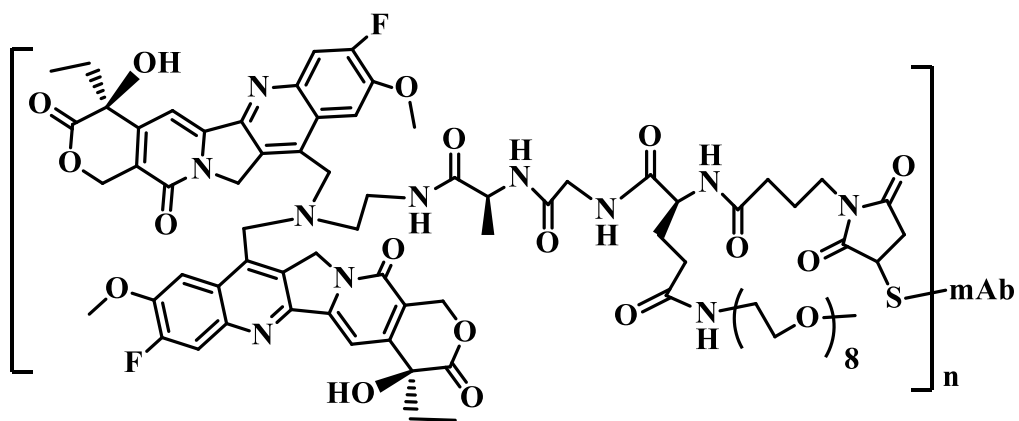
C1-088,

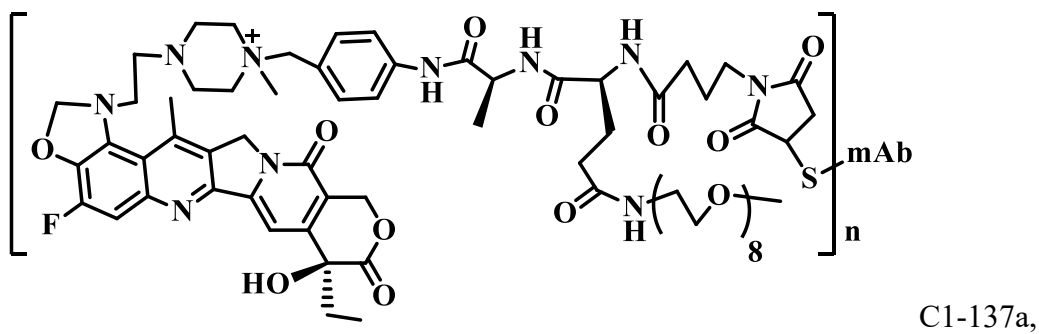
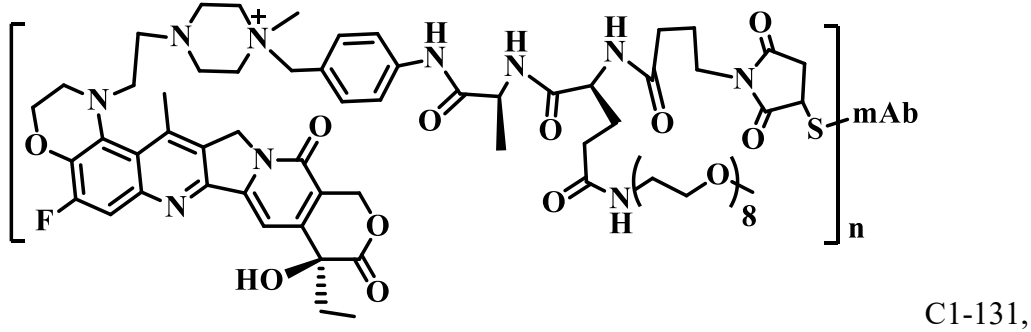
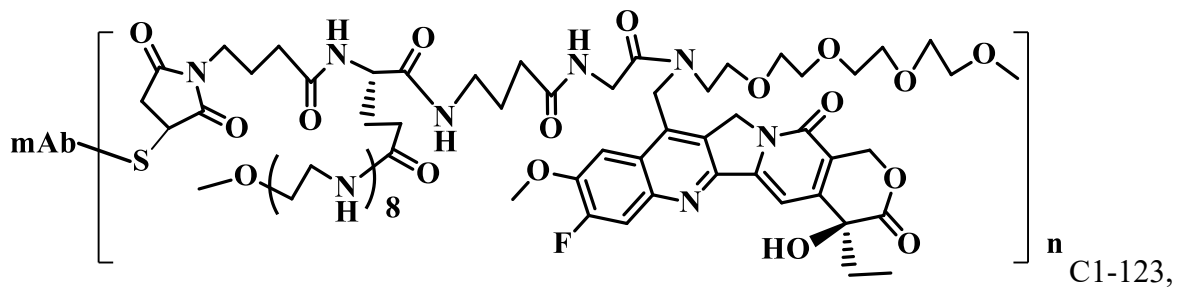
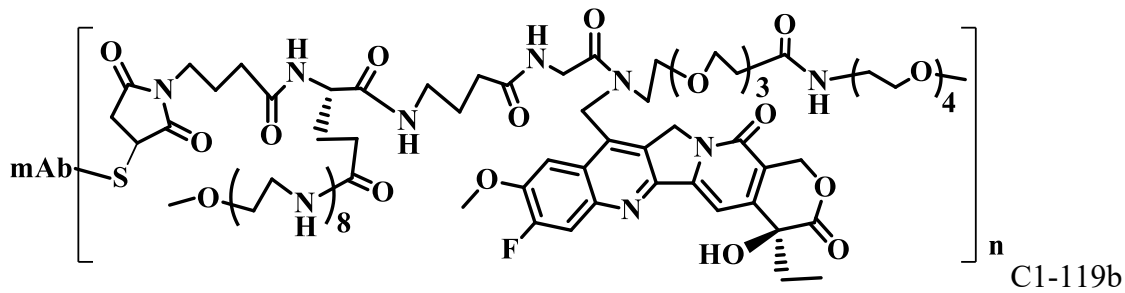
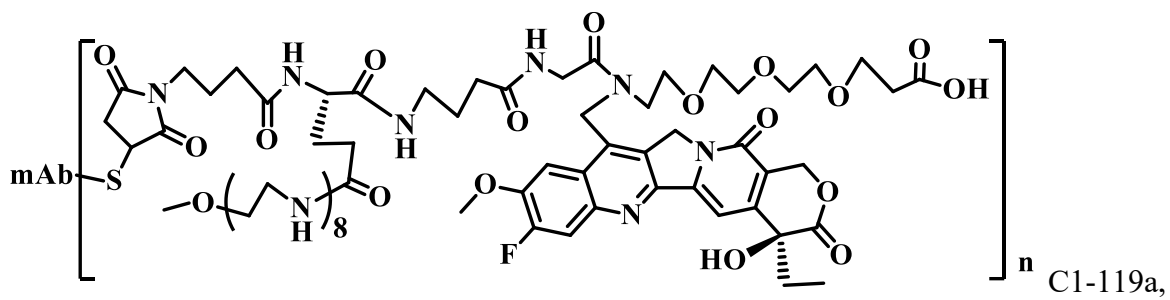


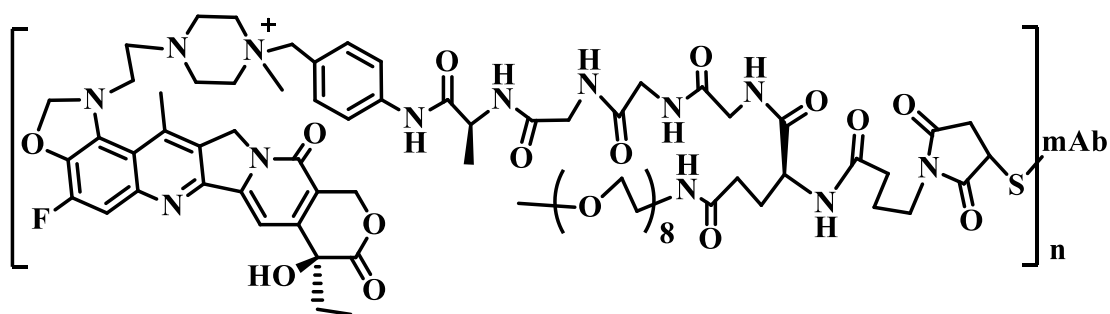
C1-090,



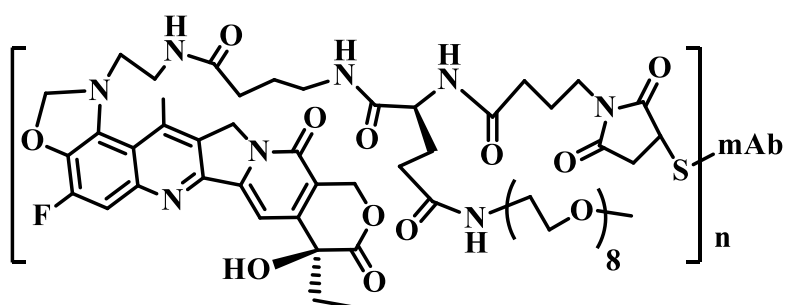
C1-094,



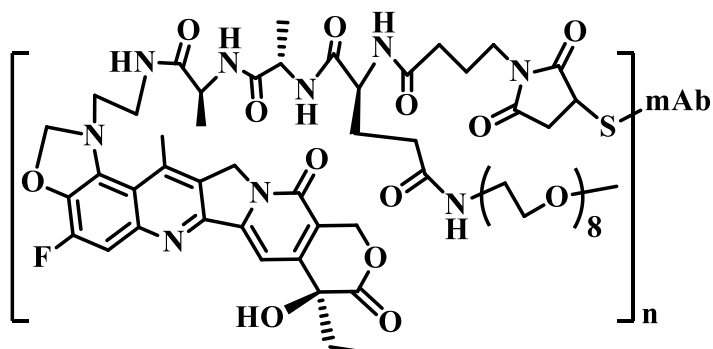




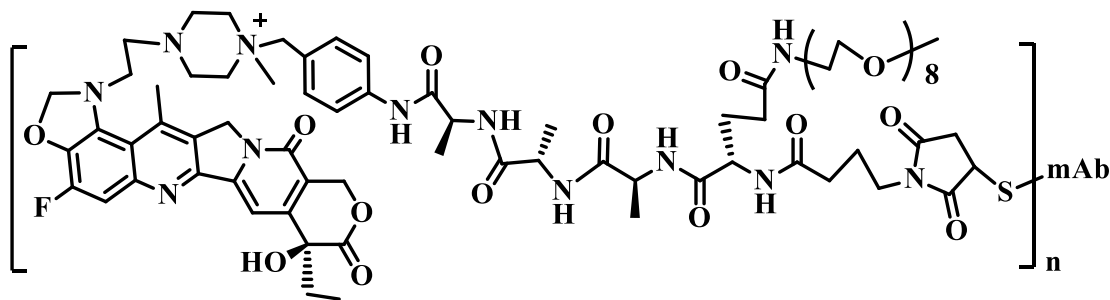
C1-137b,



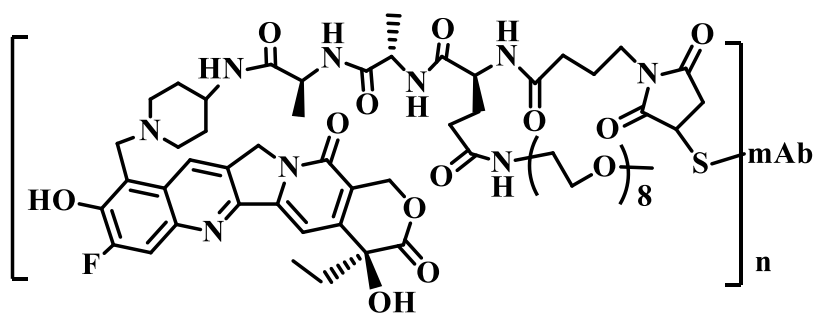
C1-140,



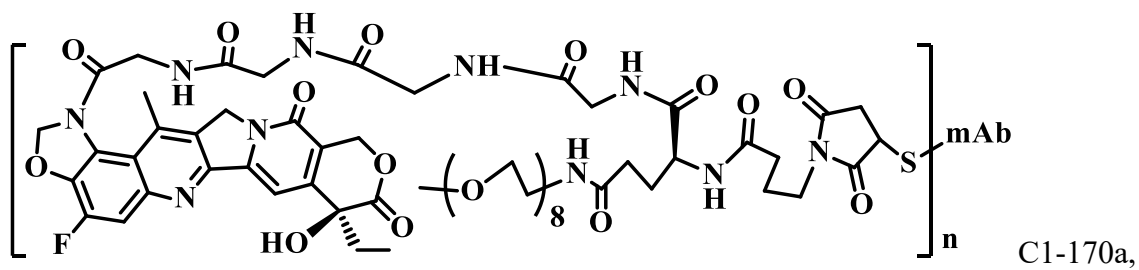
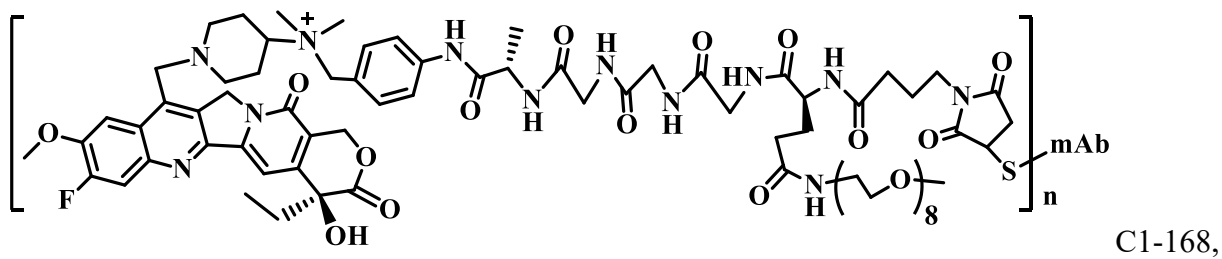
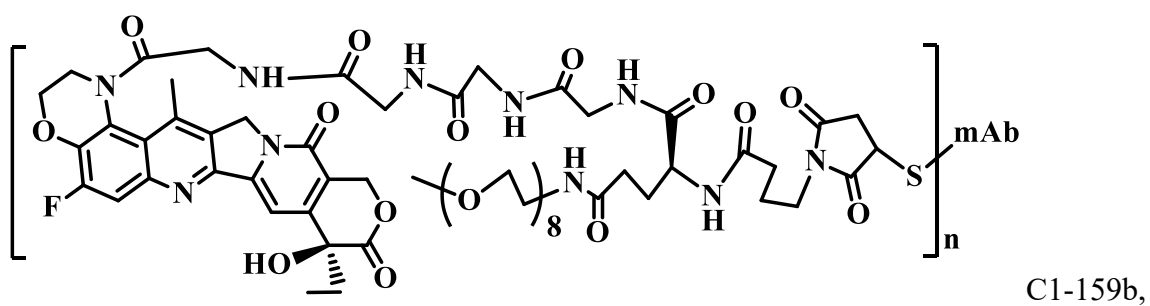
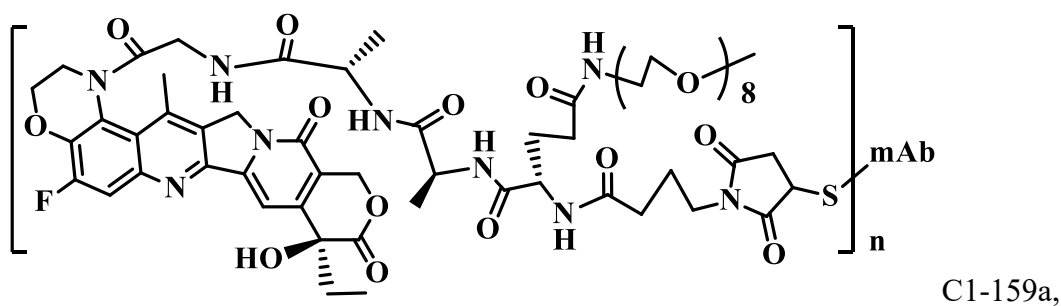
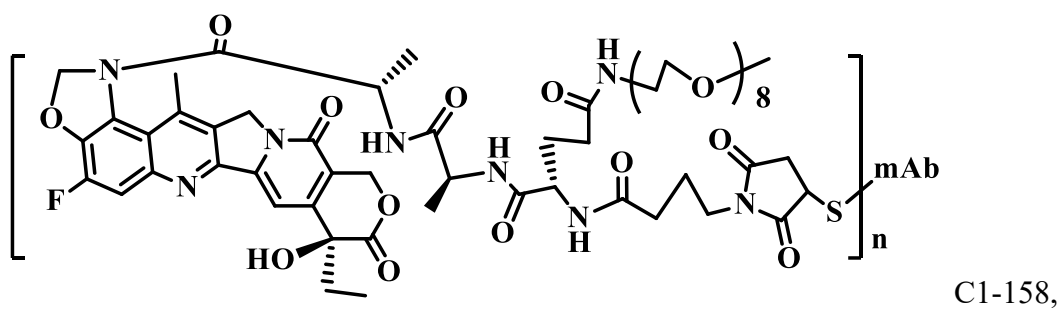
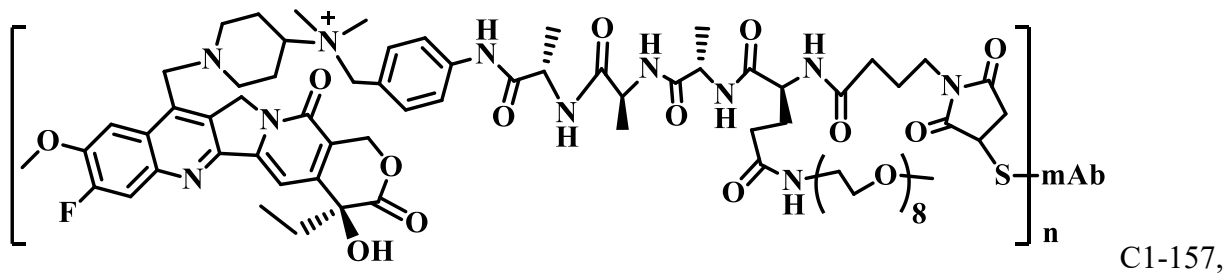
C1-147a

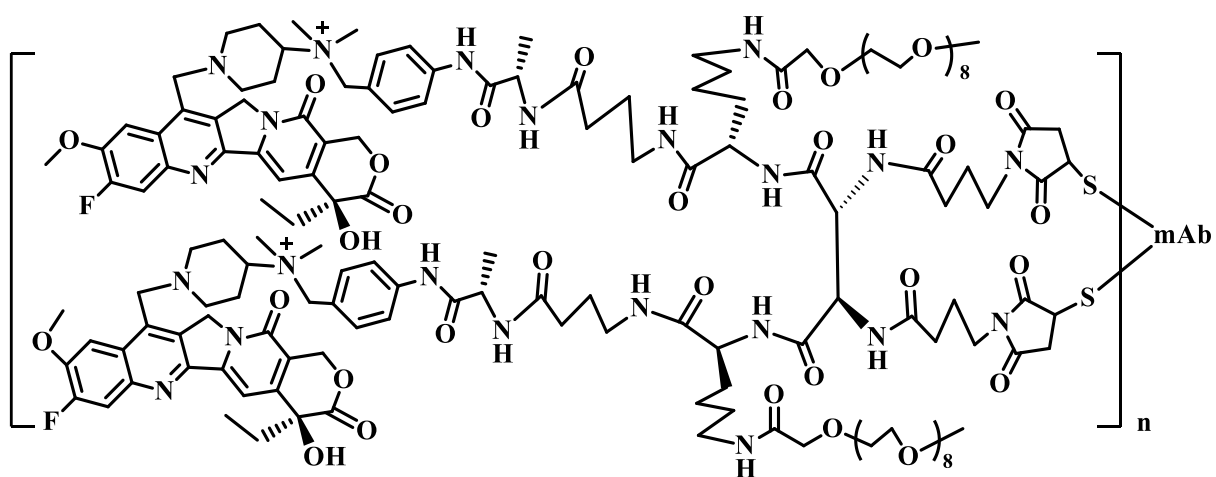
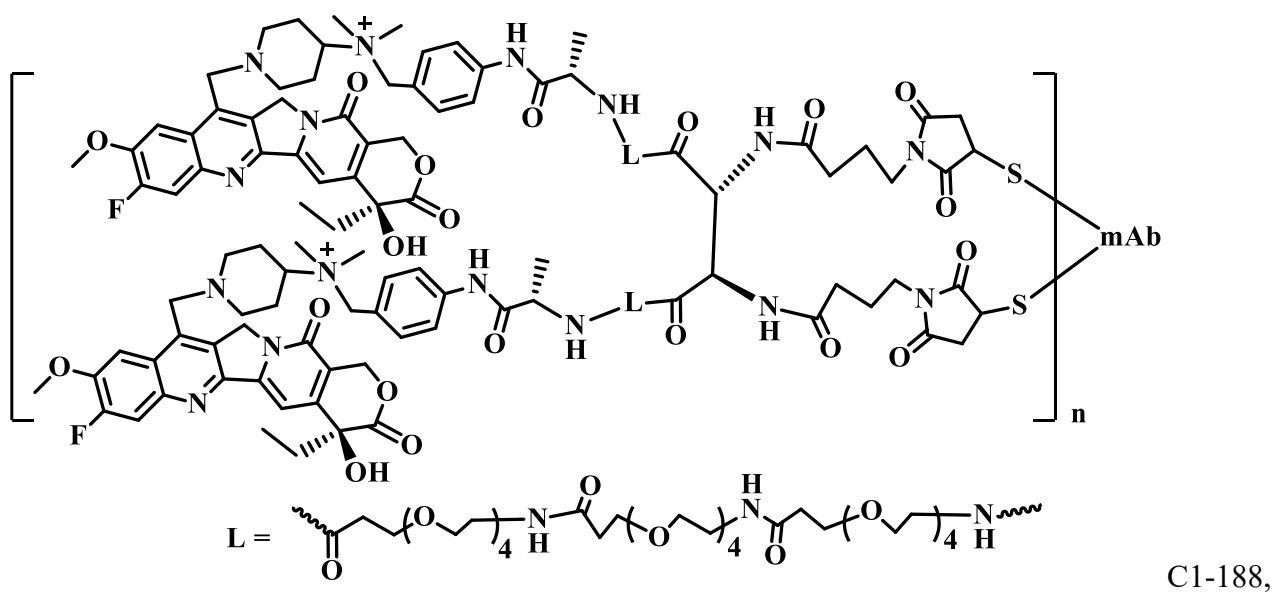
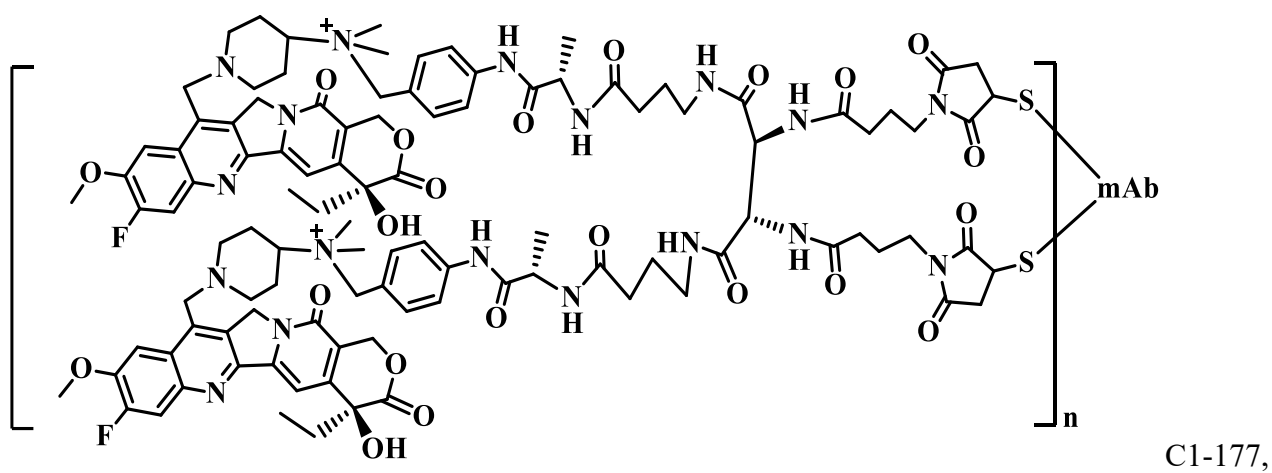
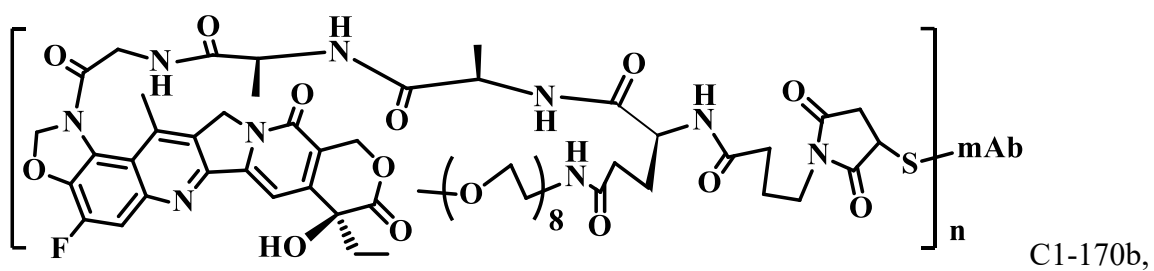


C1-147b,

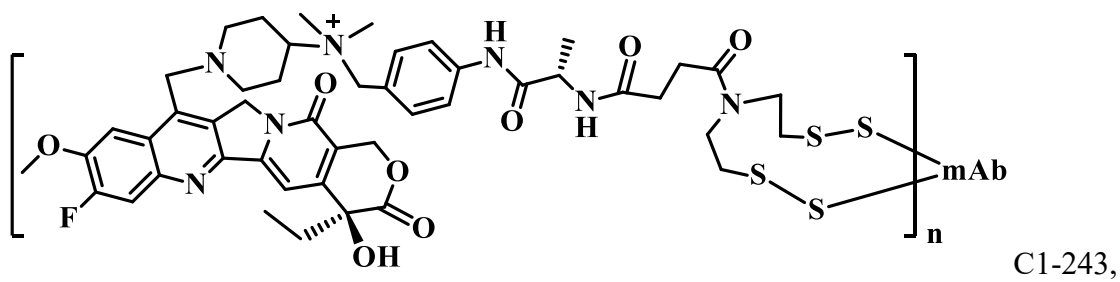
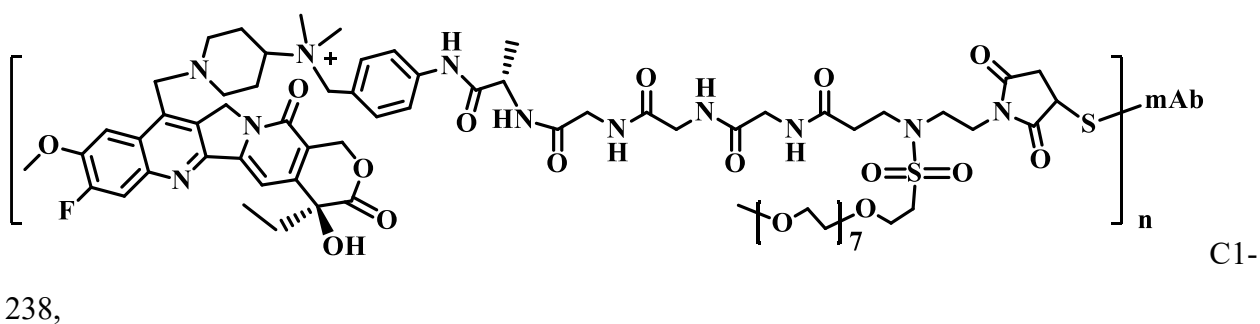
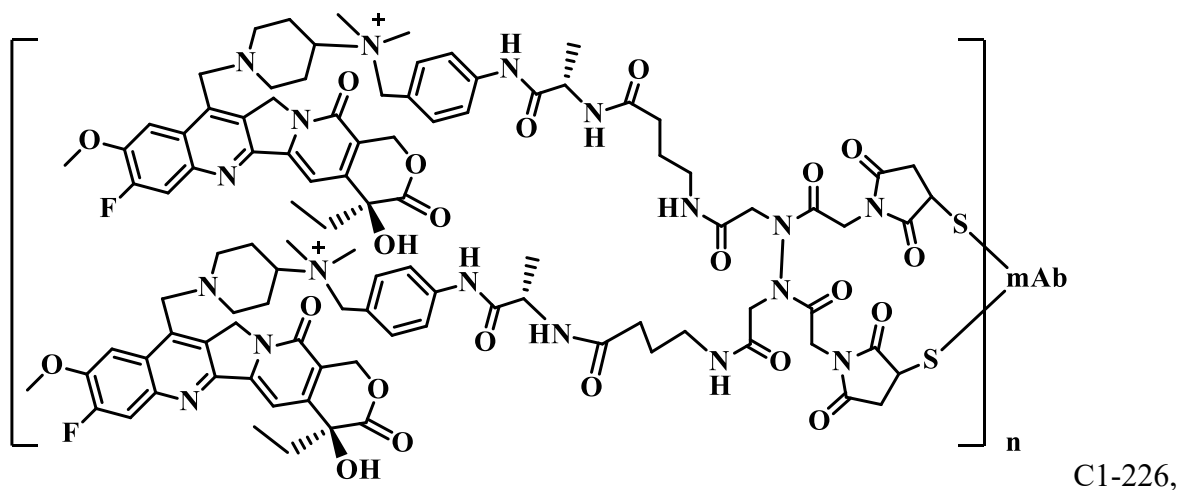
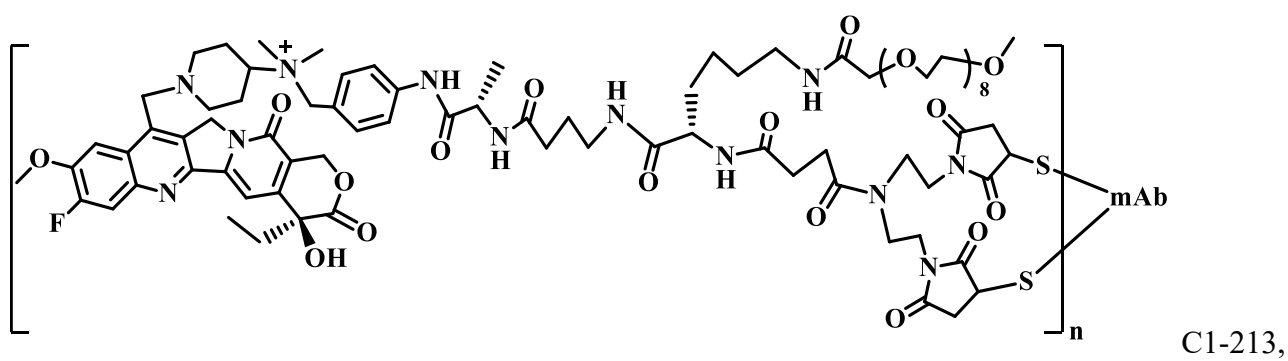
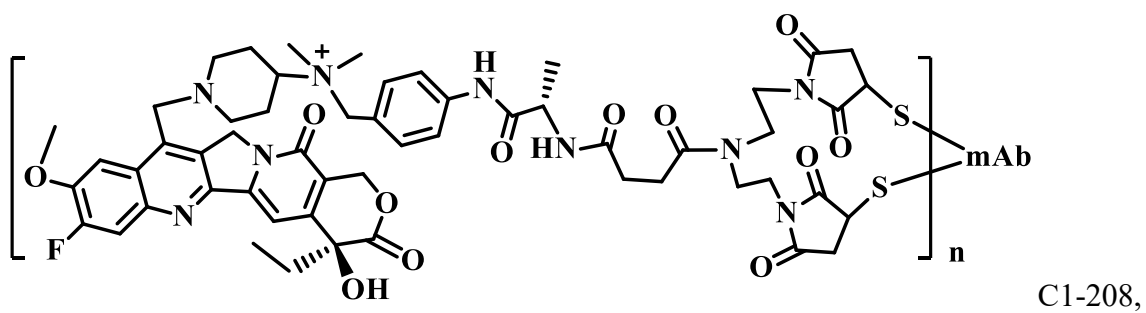


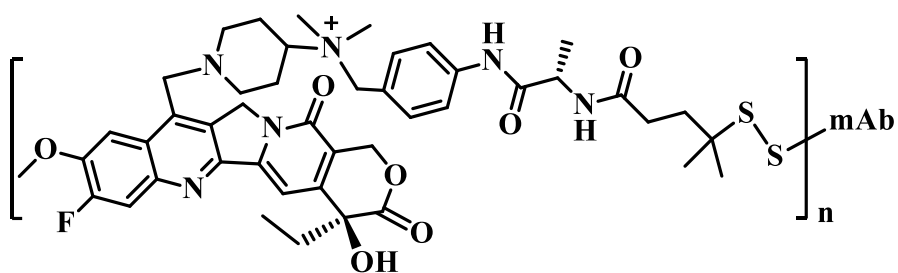
C1-151



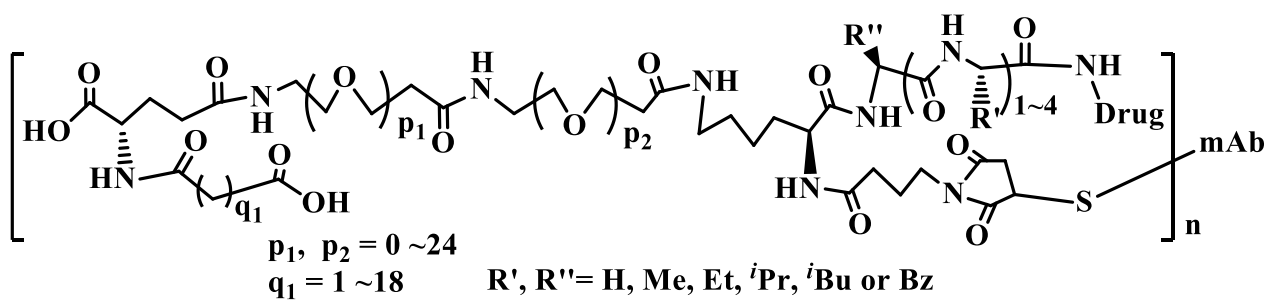


C1-200,

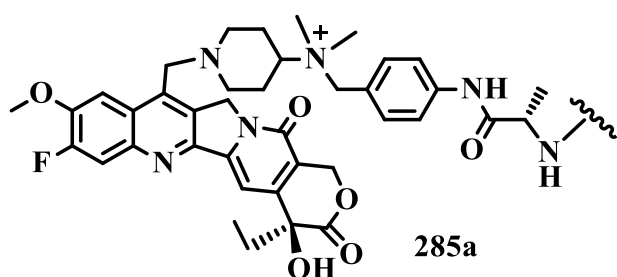




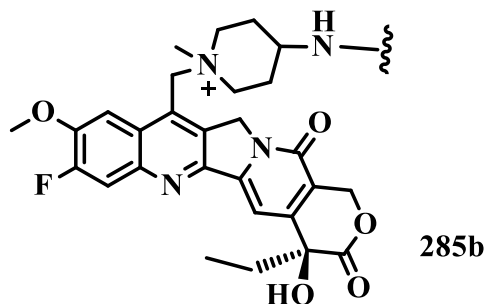
C1-247,



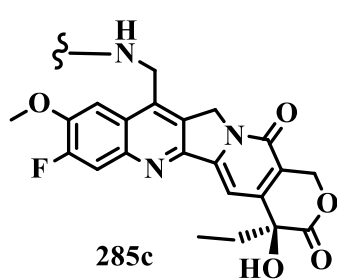
C1-285a ~ C1285z, C1-285a₁-C1285i₁, wherein $\xi - \text{N} - \text{Drug}$ are 285a ~ 285z, 285a₁ ~ 285i₁ illustrated below:



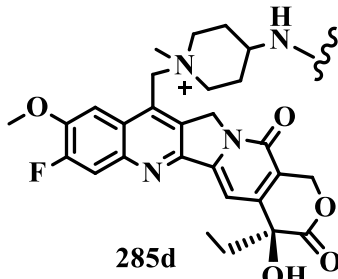
285a



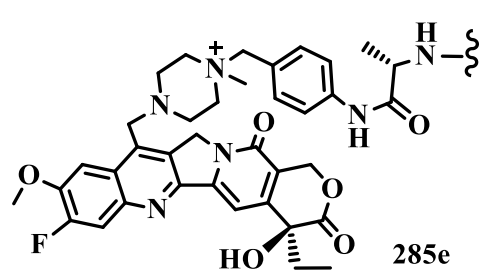
285b



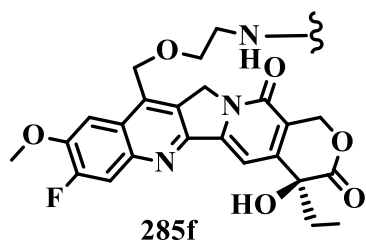
285c



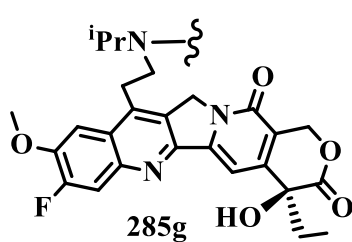
285d



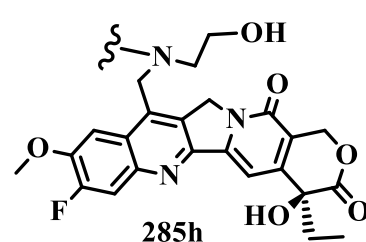
285e



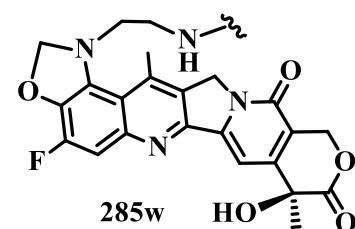
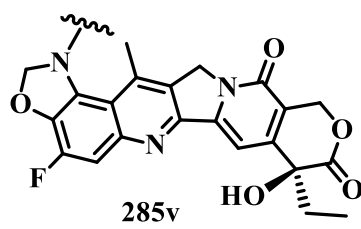
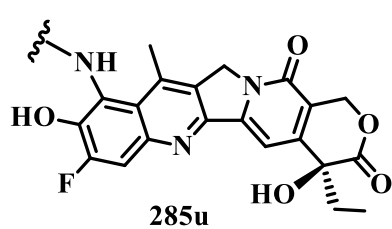
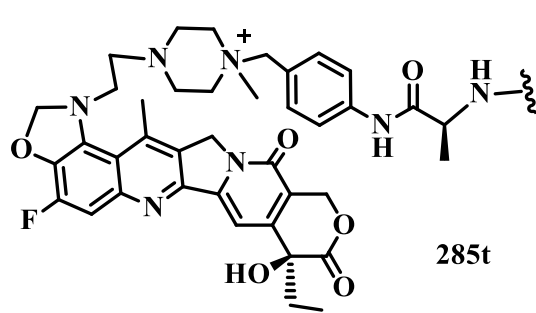
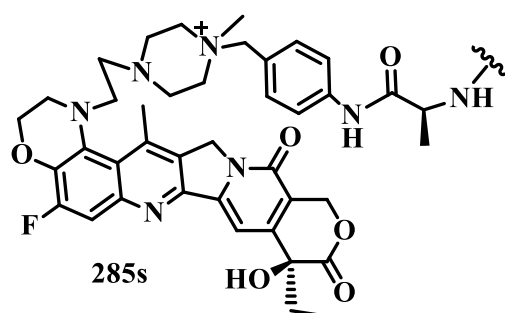
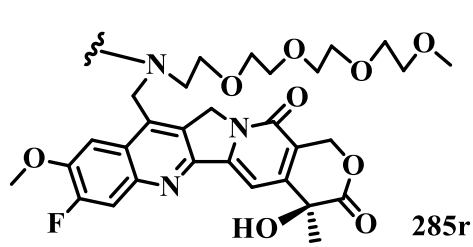
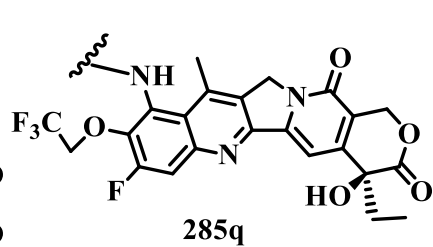
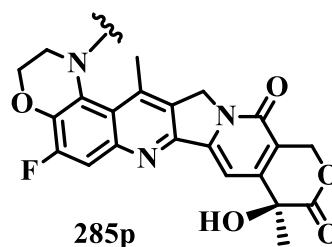
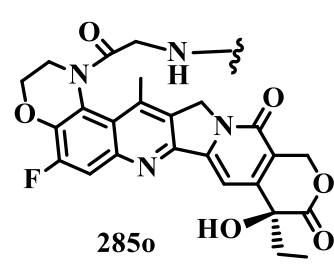
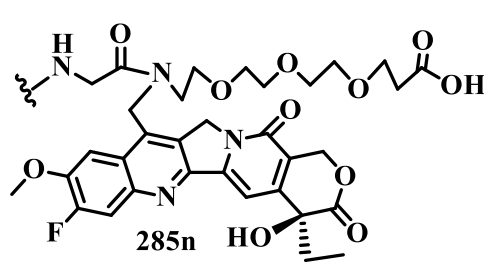
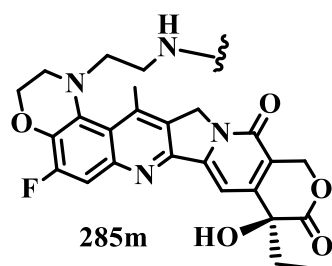
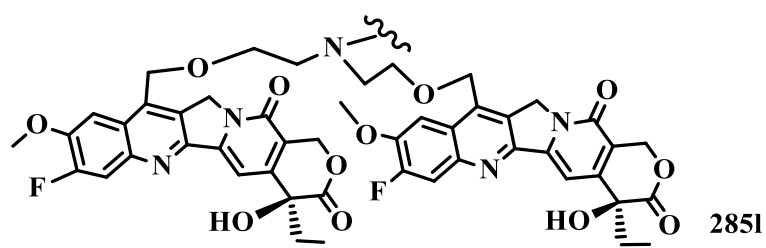
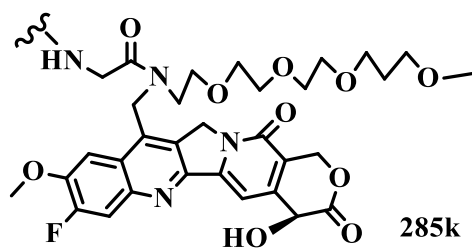
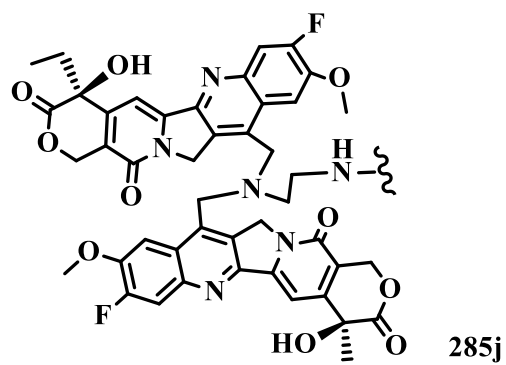
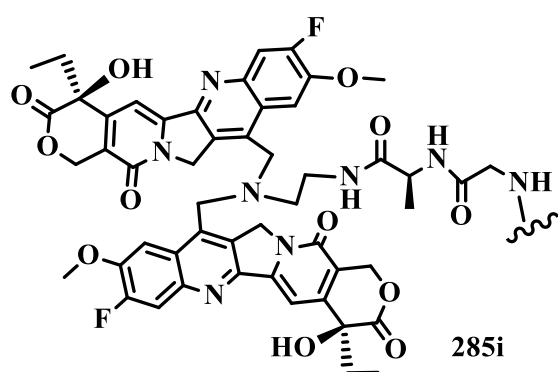
285f

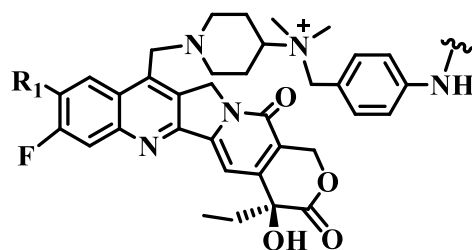
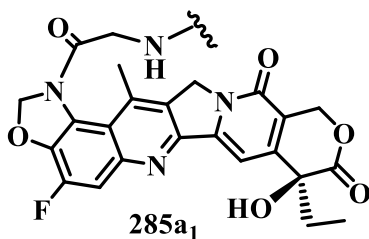
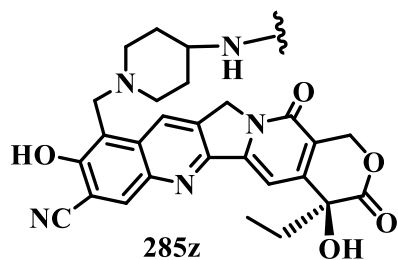
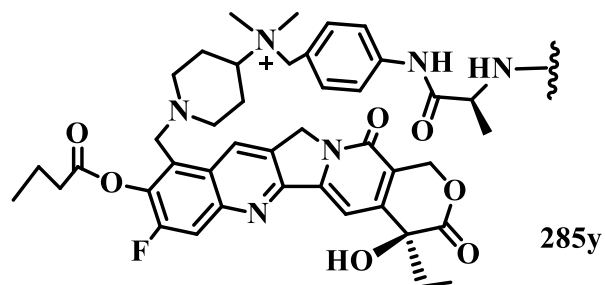
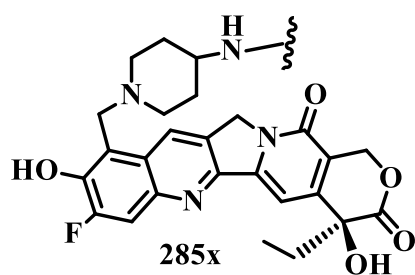


285g



285h



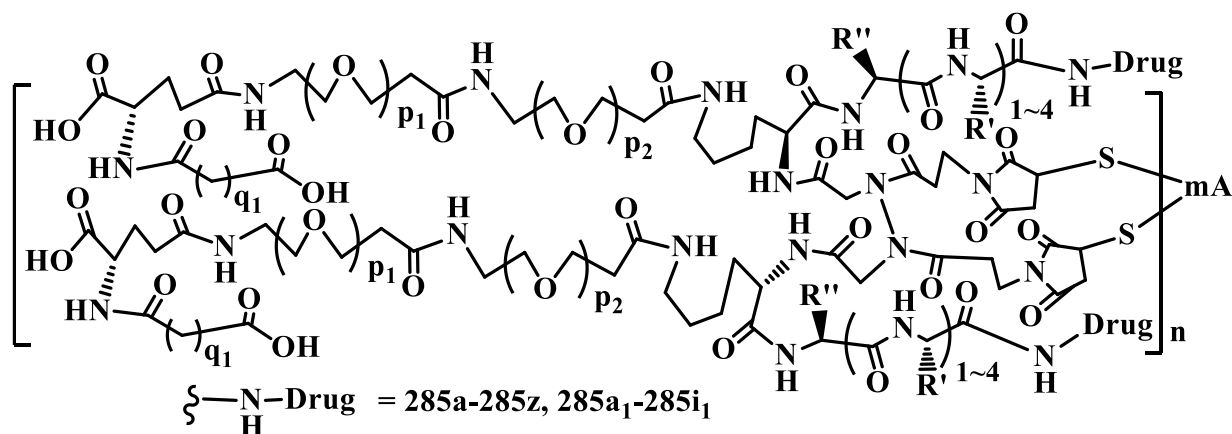


285b₁, R₁ = H 285c₁, R₁ = OH

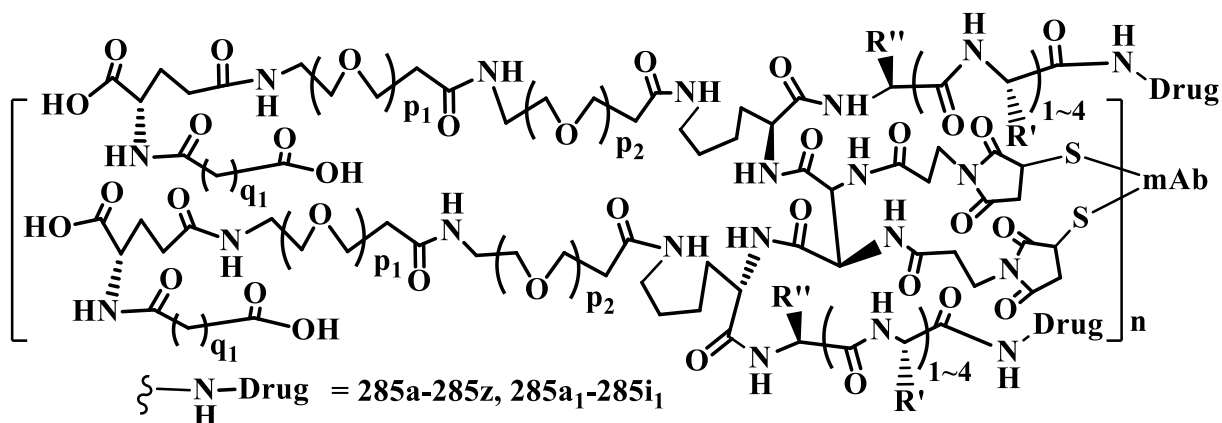
285d₁, R₁ = Ome 285e₁, R₁ = CH₃

285f₁, R₁ = H 285g₁, R₁ = OH 285h₁, R₁ = OMe 285i₁, R₁ = CH₃

ζ = the site linked to C(=O) of the rest part of molecule

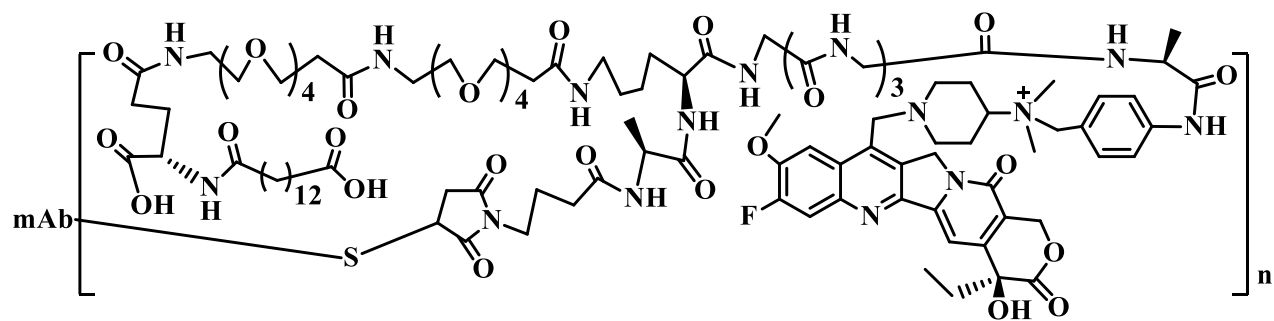
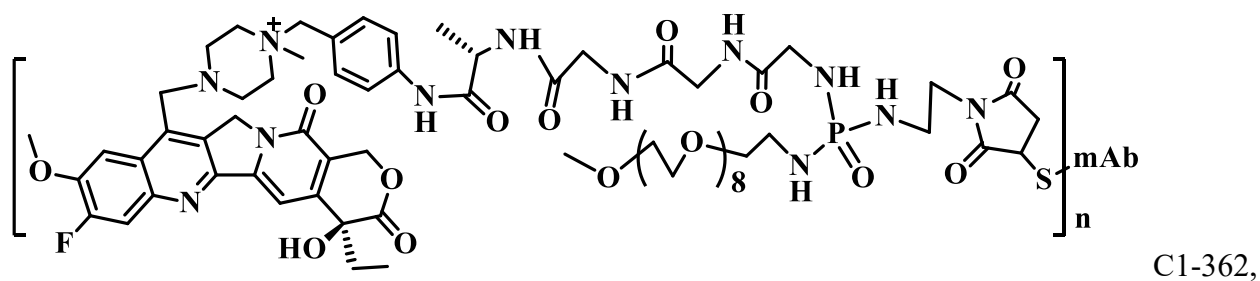
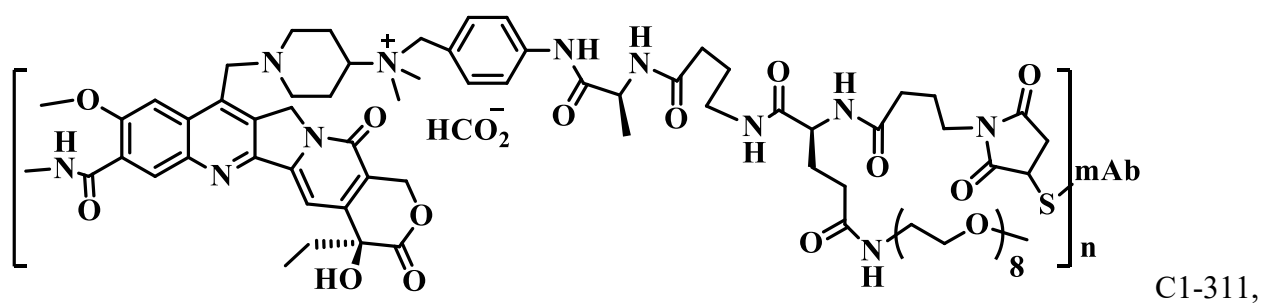
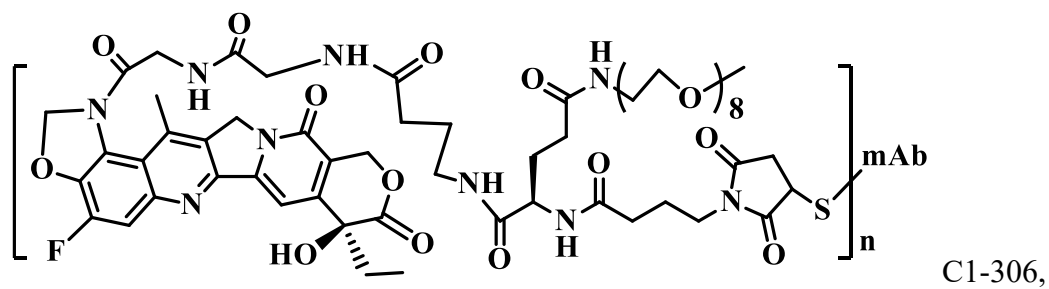
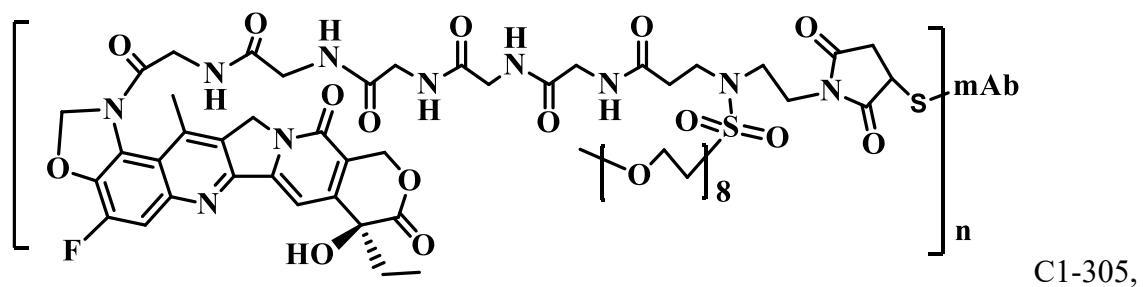


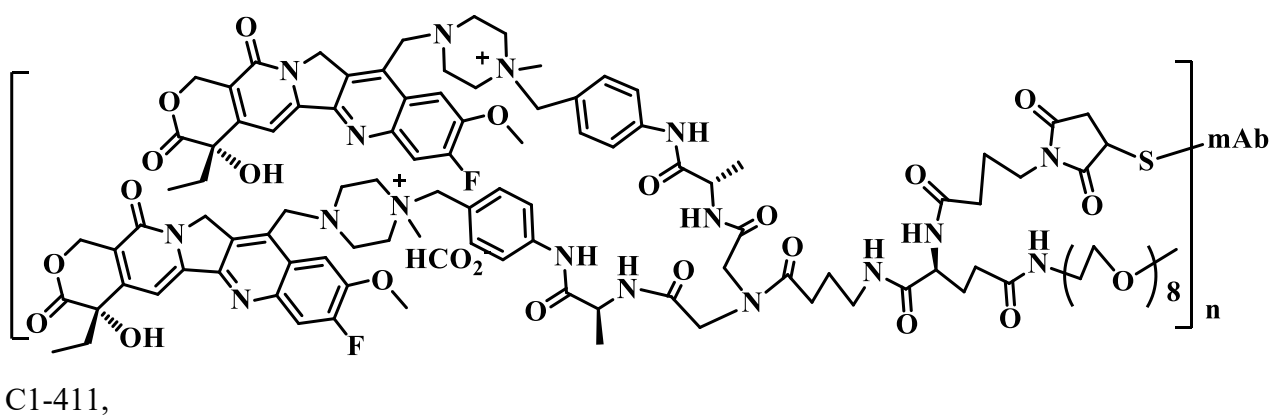
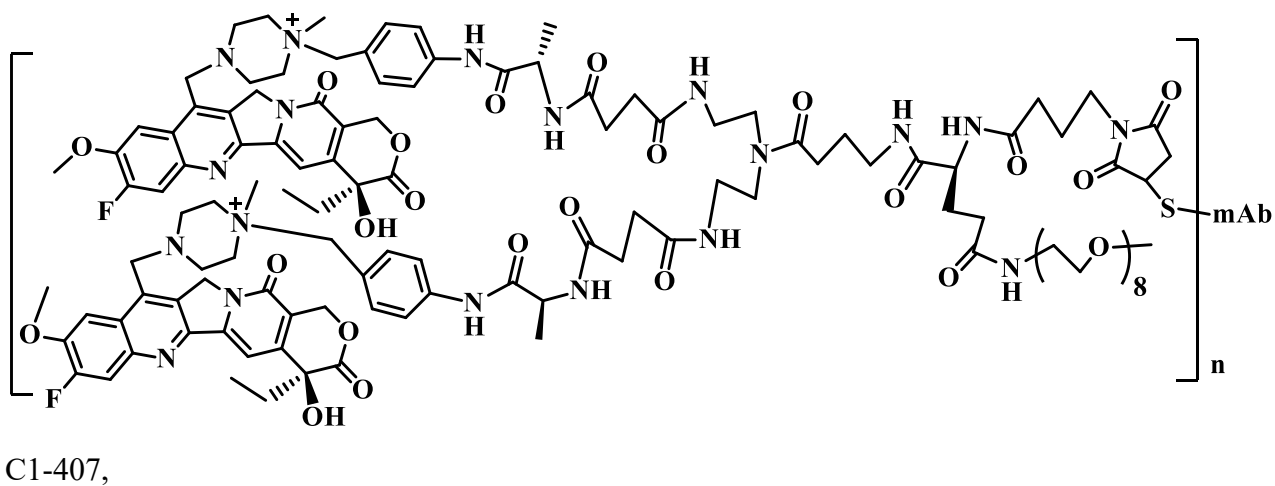
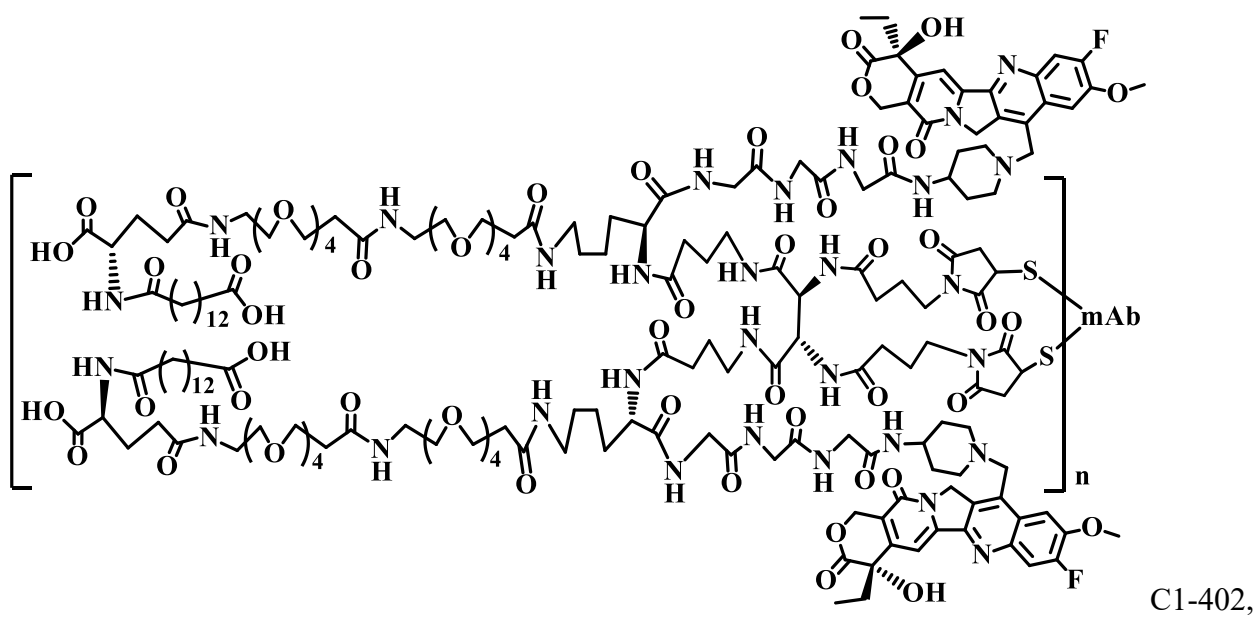
C1-291a ~C1-291z, C1-291a₁ ~C1-291i₁;

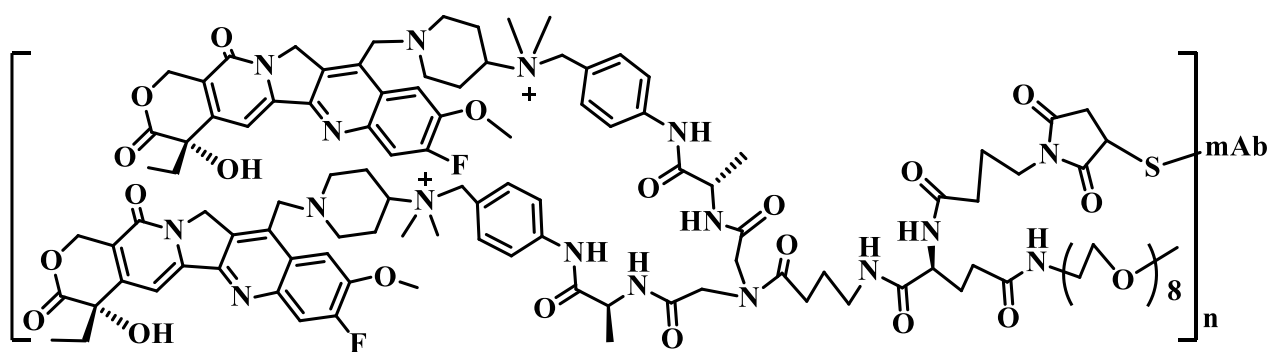


$p_1, p_2 = 0 \sim 24; q_1 = 1 \sim 18$

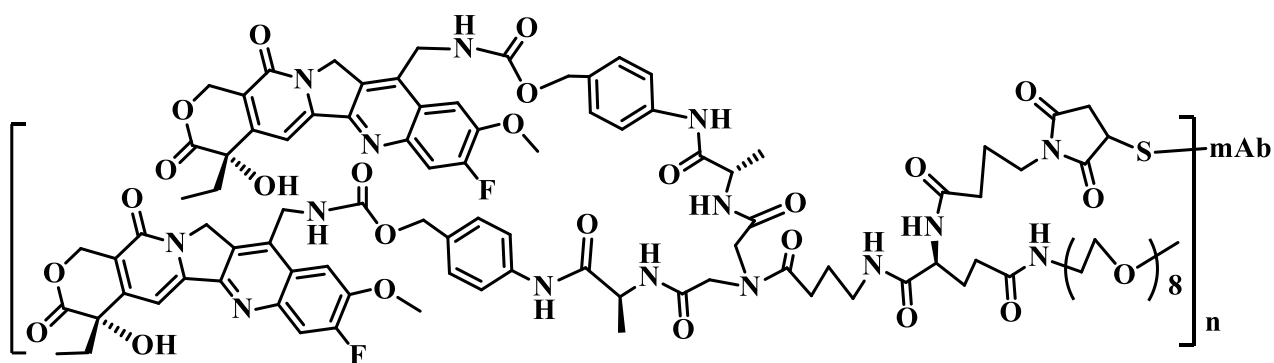
C1-297a ~C1-297z, C1-297a₁ ~C1-297i₁;



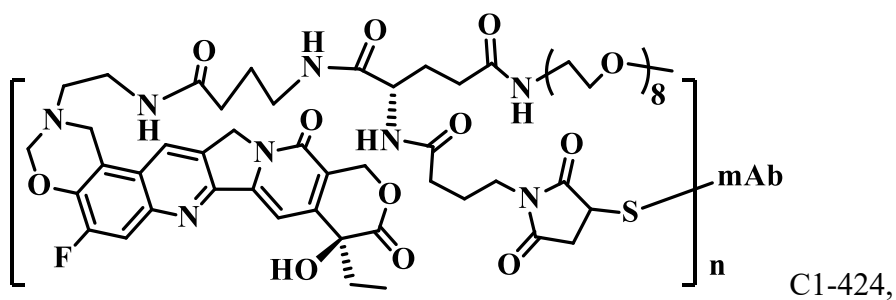




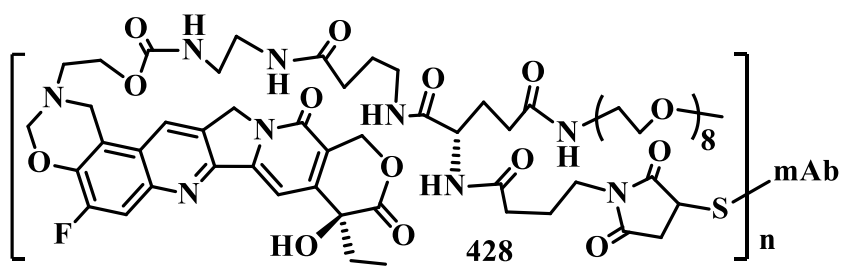
C1-414,



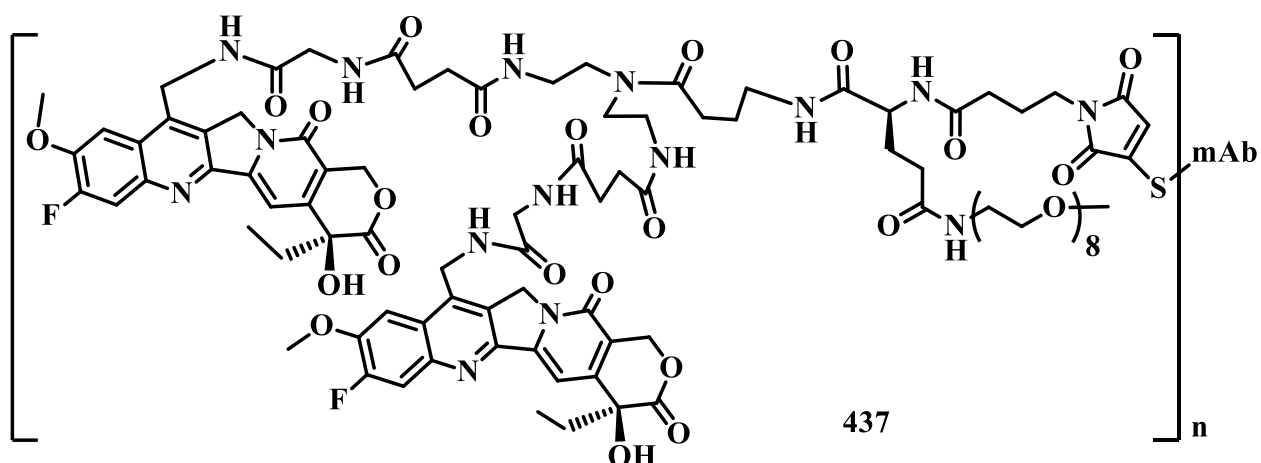
C1-419,



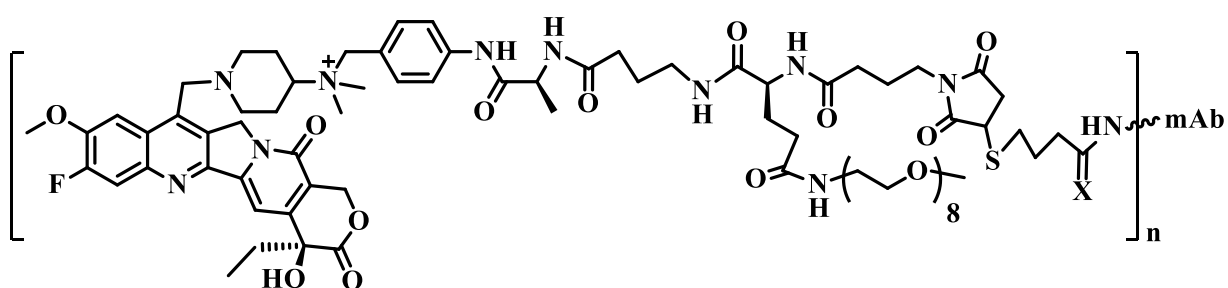
C1-424,



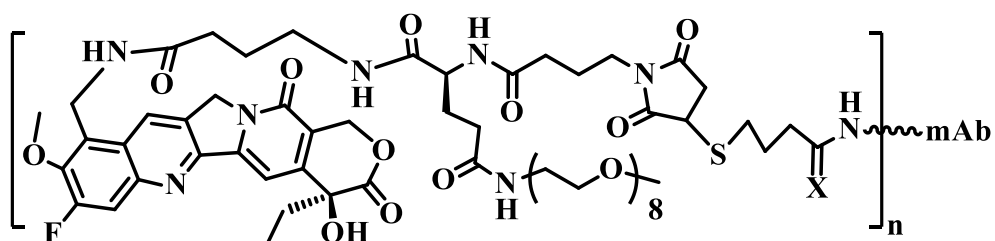
C1-428,



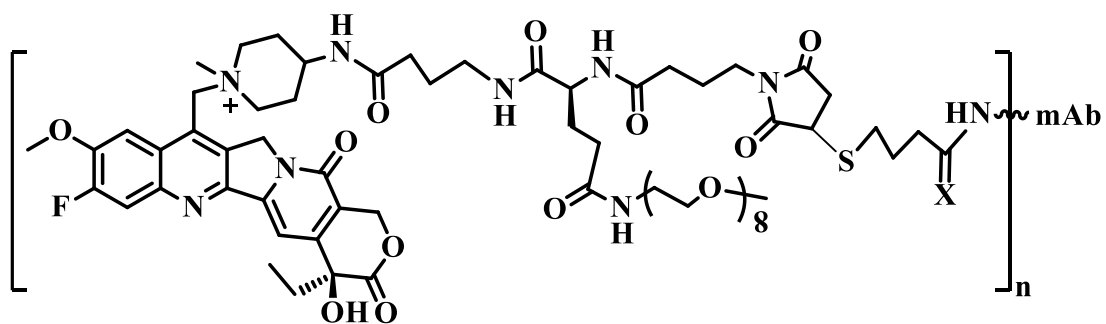
C1-436,



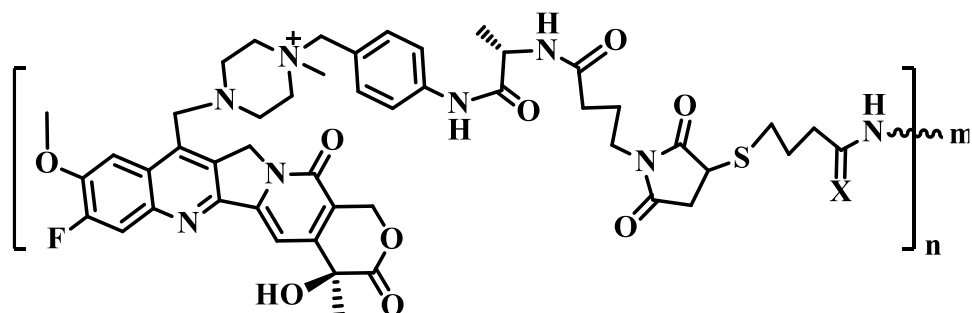
C2-029 (X=NH), C3-029 (X=O);



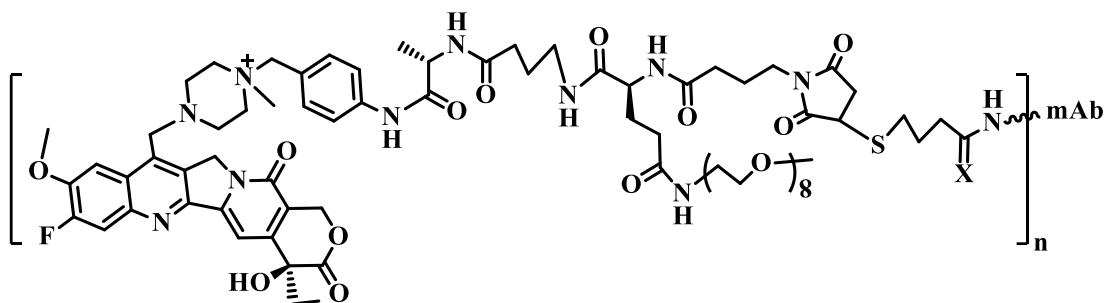
C2-031 (X=NH), C3-031 (X=O);



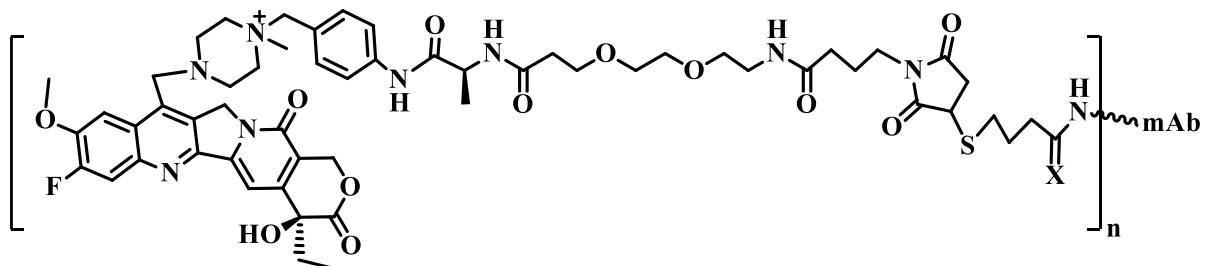
C2-035 (X=NH), C3-035 (X=O);



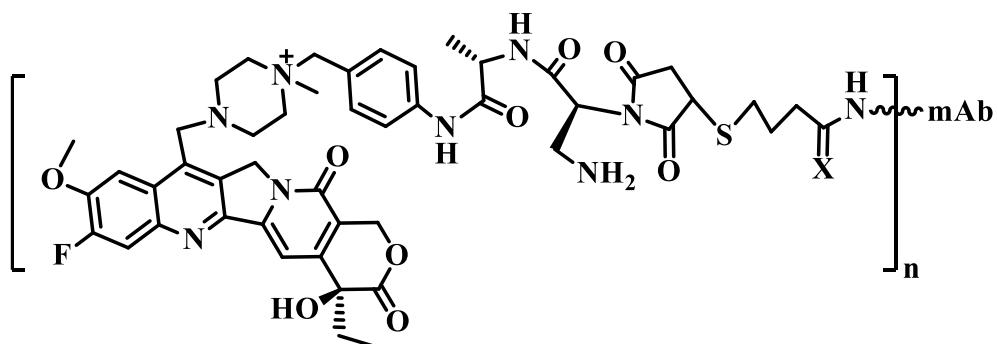
C2-041 (X=NH), C3-041 (X=O);



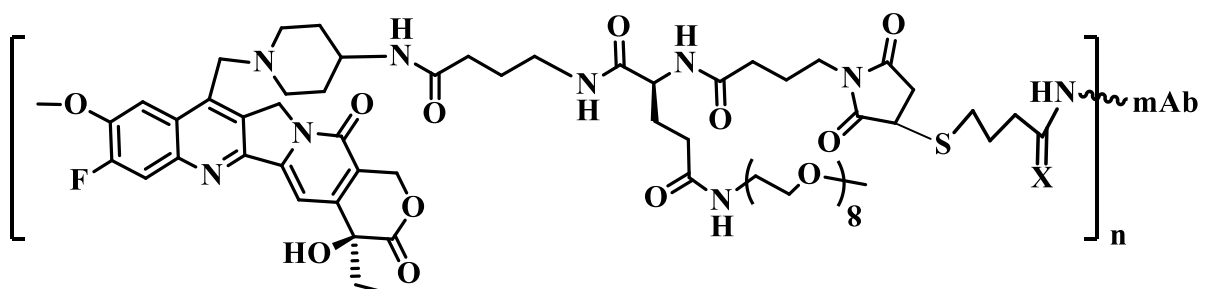
C2-042 (X=NH), C3-042 (X=O);



C2-043 (X=NH), C3-043 (X=O);

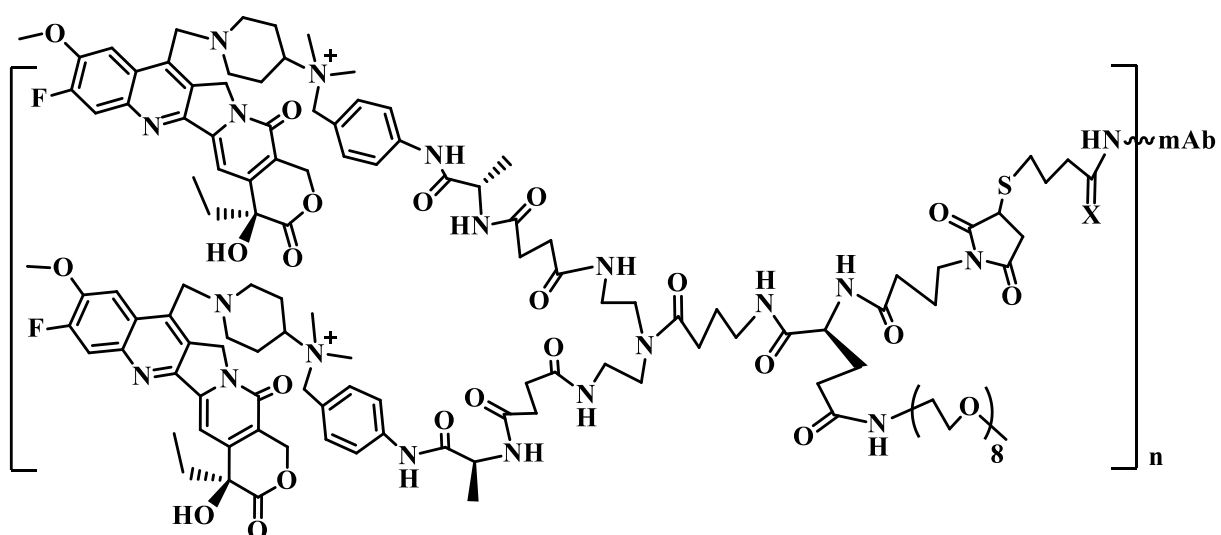


C2-047 (X=NH), C3-047 (X=O);

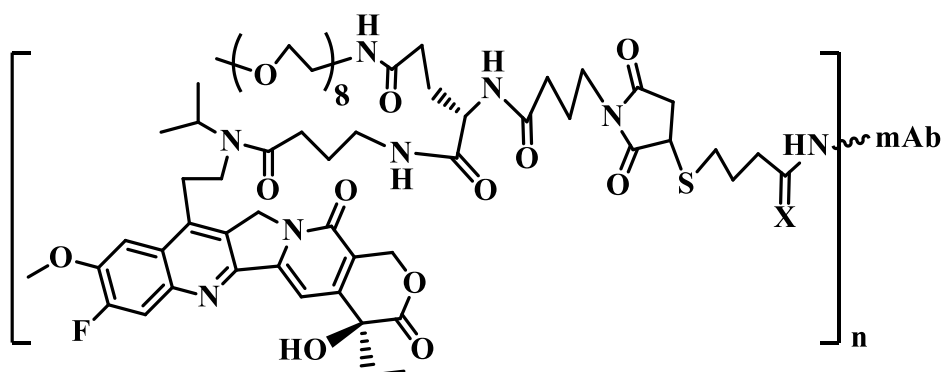


C2-050 (X=NH), C3-050 (X=O);

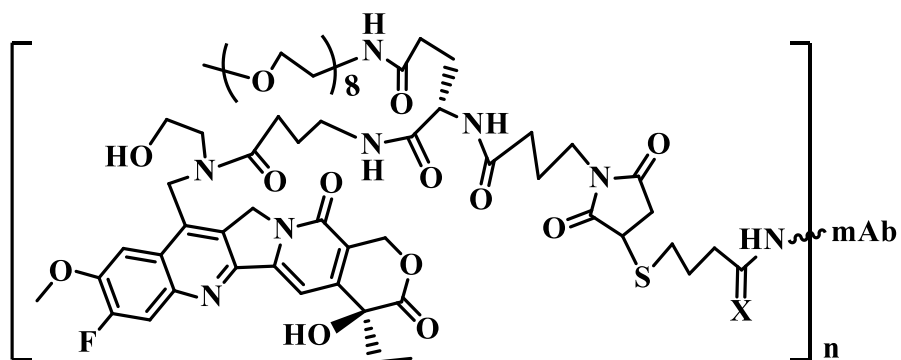
C2-



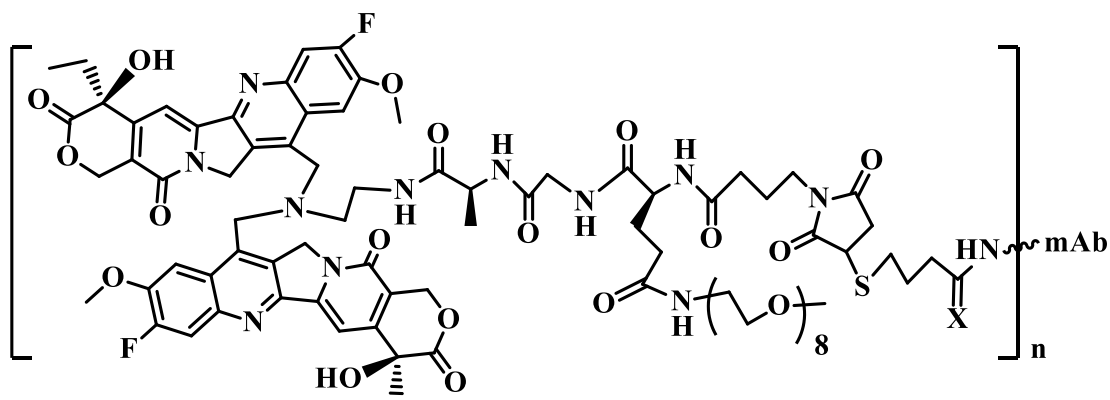
C2-064 (X=NH), C3-064 (X=O);



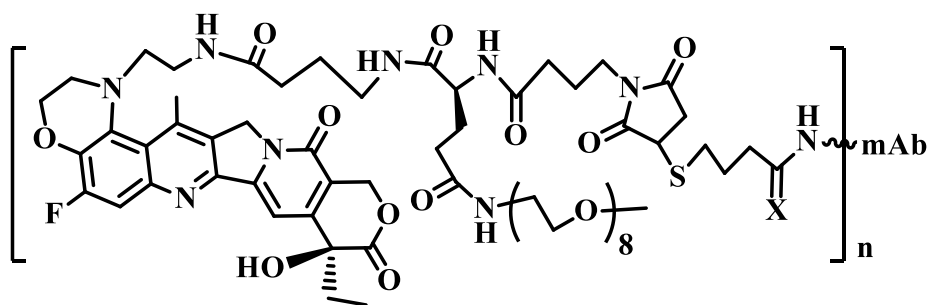
C2-088 (X=NH), C3-088 (X=O);



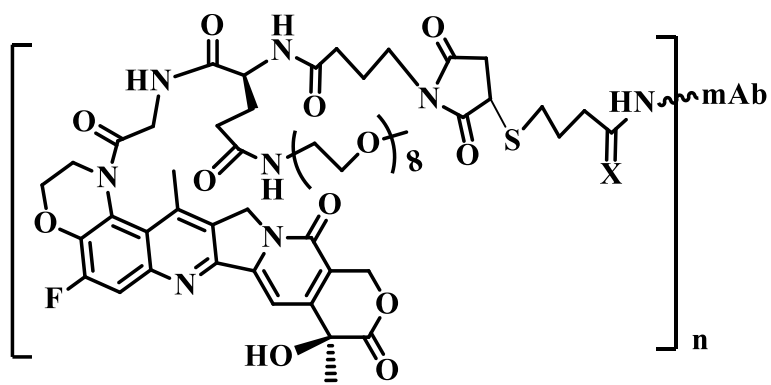
C2-090 (X=NH), C3-090 (X=O);



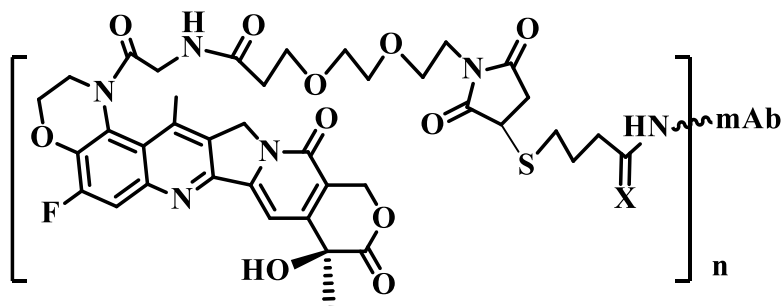
C2-099 (X=NH), C3-099 (X=O);



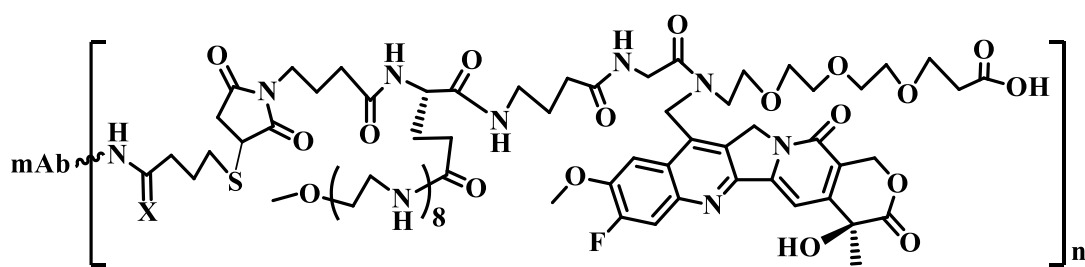
C2-110 (X=NH), C3-110 (X=O);



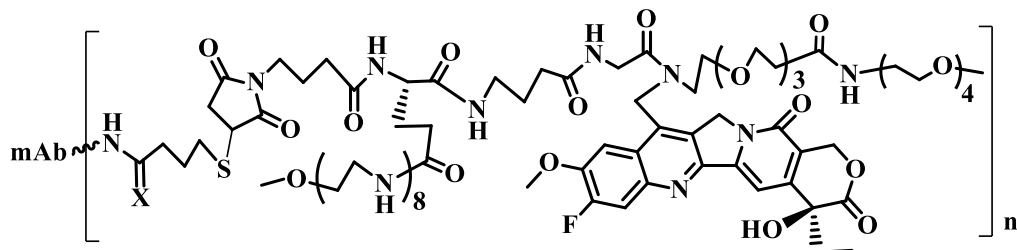
C2-113 (X=NH), C3-113 (X=O);



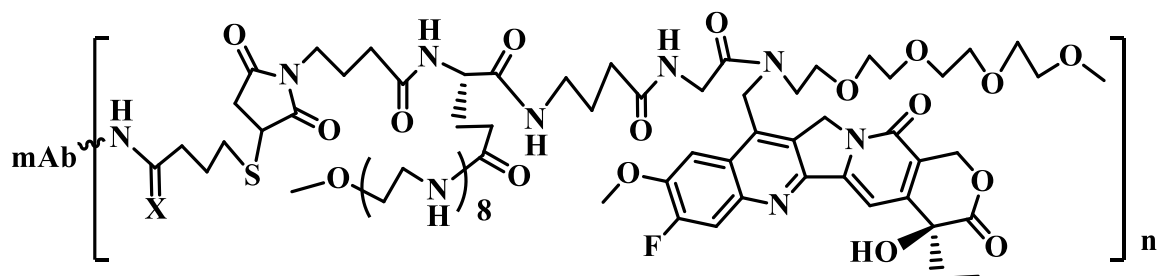
C2-114 (X=NH), C3-114 (X=O);



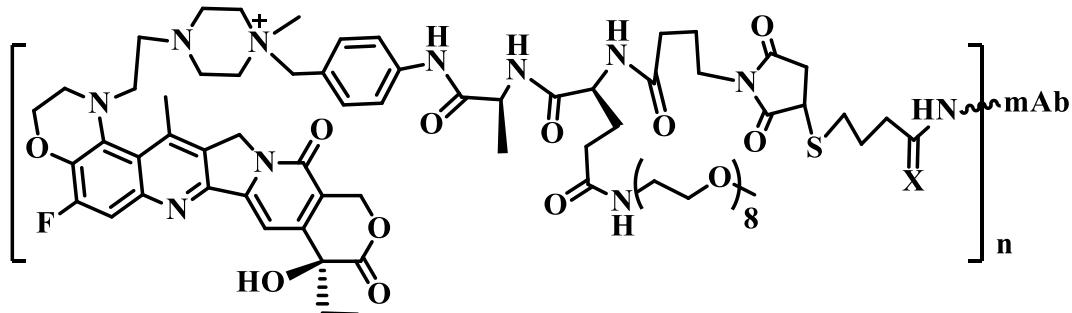
C2-119 (X=NH), C3-119 (X=O);



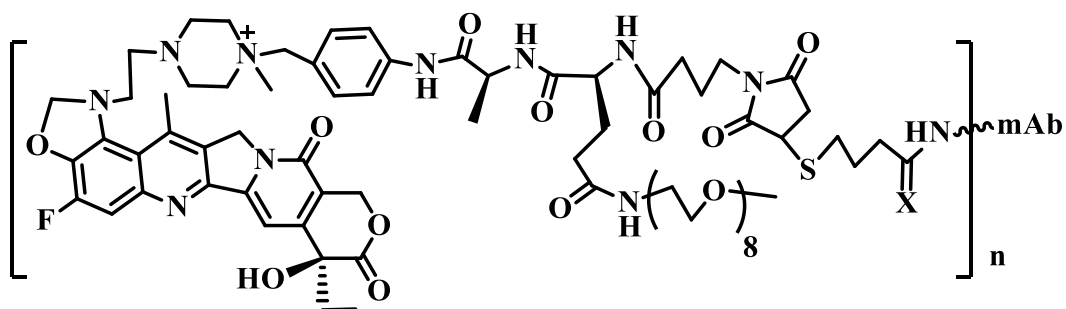
C2-119b (X=NH), C3-119b (X=O);



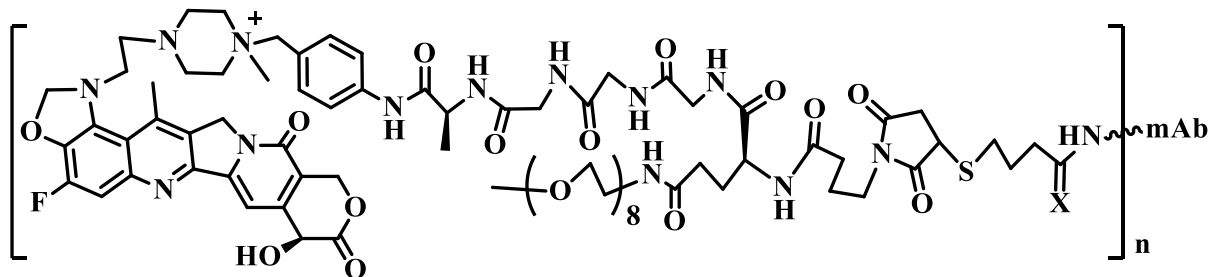
C2-123 (X=NH), C3-123 (X=O);



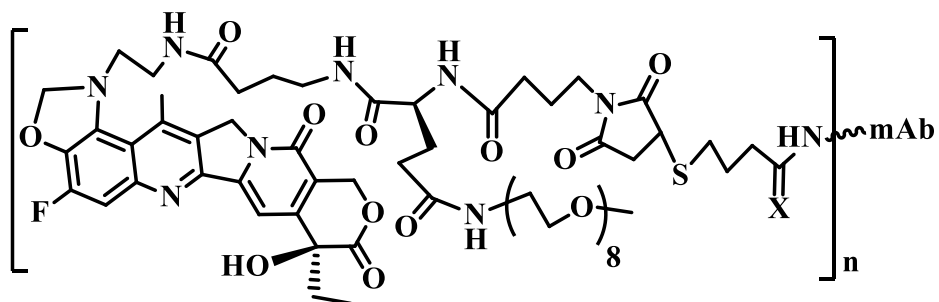
C2-131 (X=NH), C3-131 (X=O);



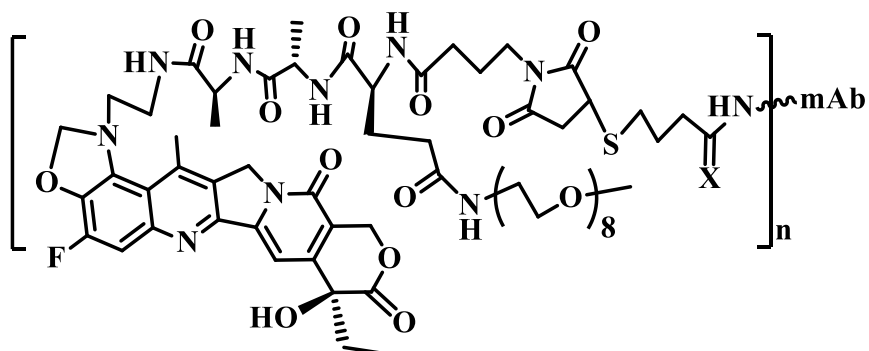
C2-137a (X=NH), C3-137a (X=O);



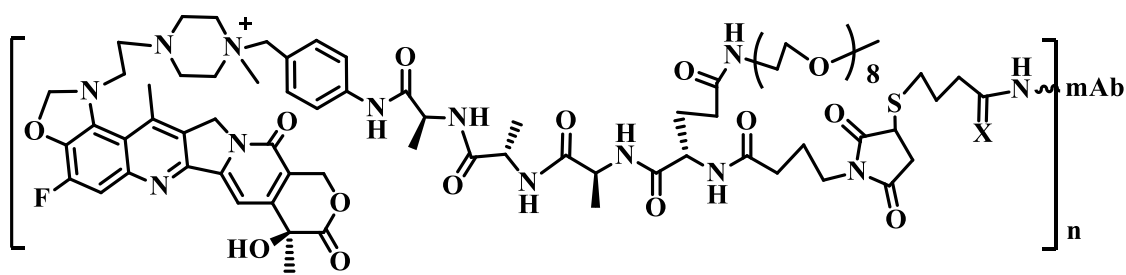
C2-137b (X=NH), C3-137b (X=O);



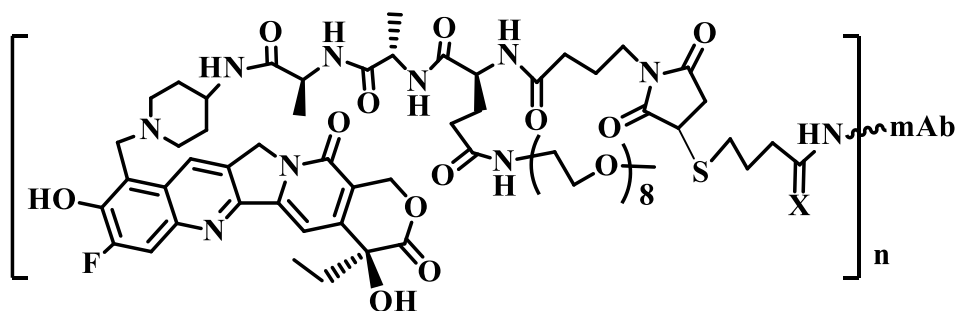
C2-140 (X=NH), C3-140 (X=O);



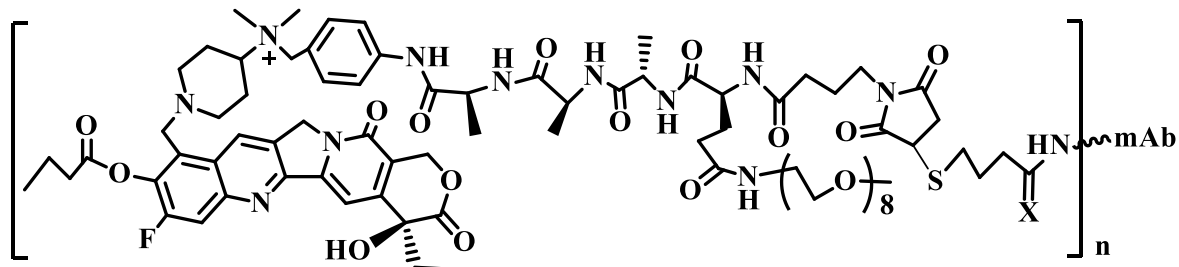
C2-147a (X=NH), C3-147a (X=O);



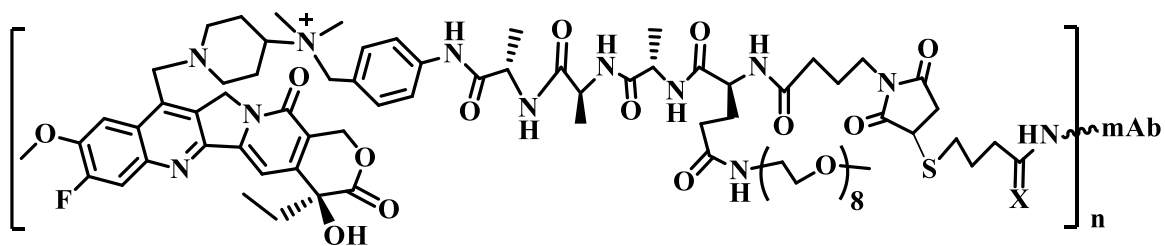
C2-147b (X=NH), C3-147b (X=O);



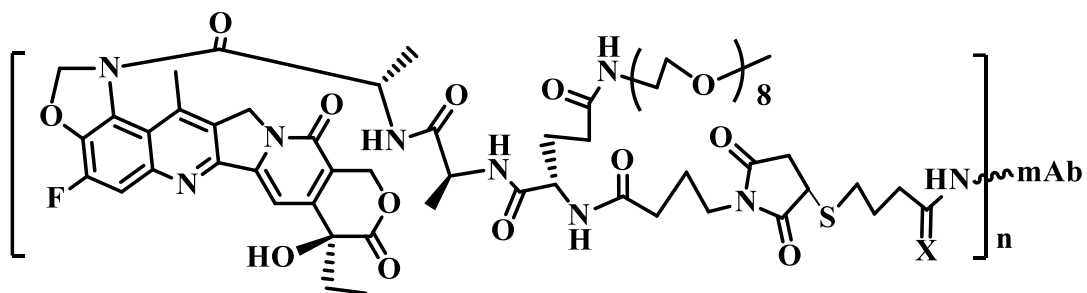
C2-151 (X=NH), C3-151 (X=O);



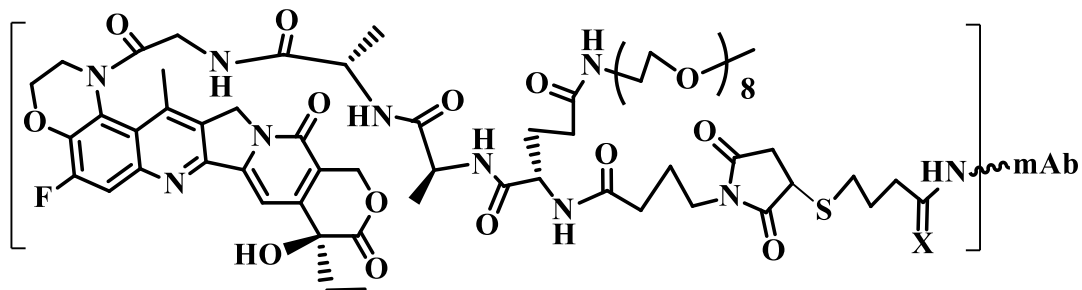
C2-156 (X=NH), C3-156 (X=O);



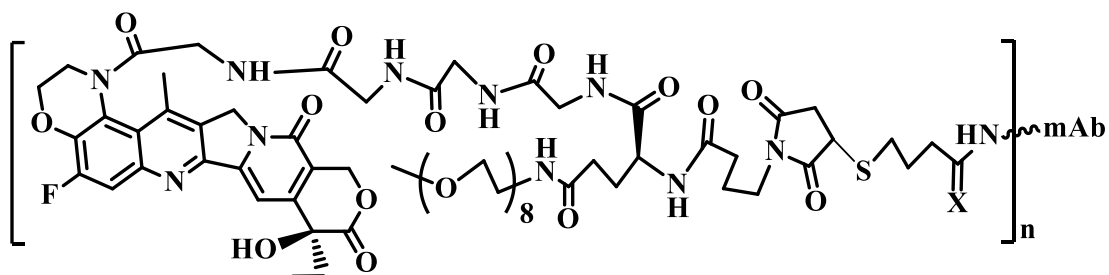
C2-157 (X=NH), C3-157 (X=O);



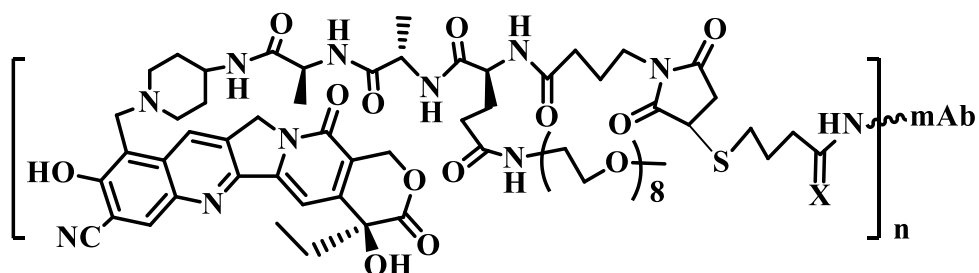
C2-158 (X=NH), C3-158 (X=O);



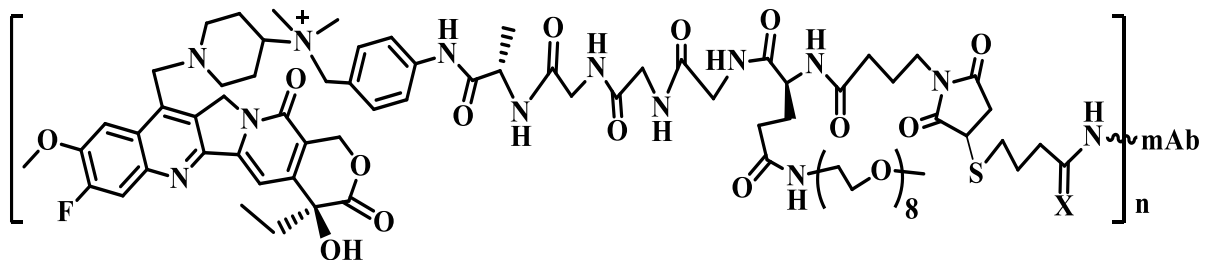
C2-159a (X=NH), C3-159a (X=O);



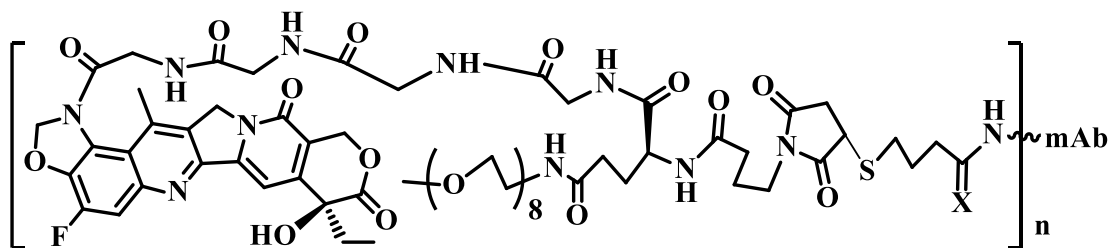
C2-159b (X=NH), C3-159b (X=O);



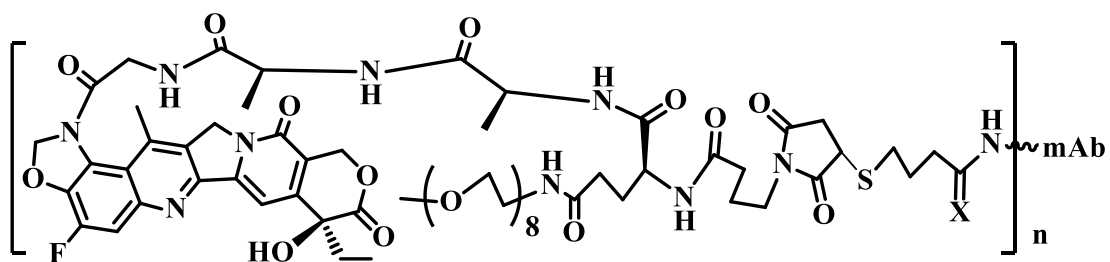
C2-165 (X=NH), C3-165 (X=O);



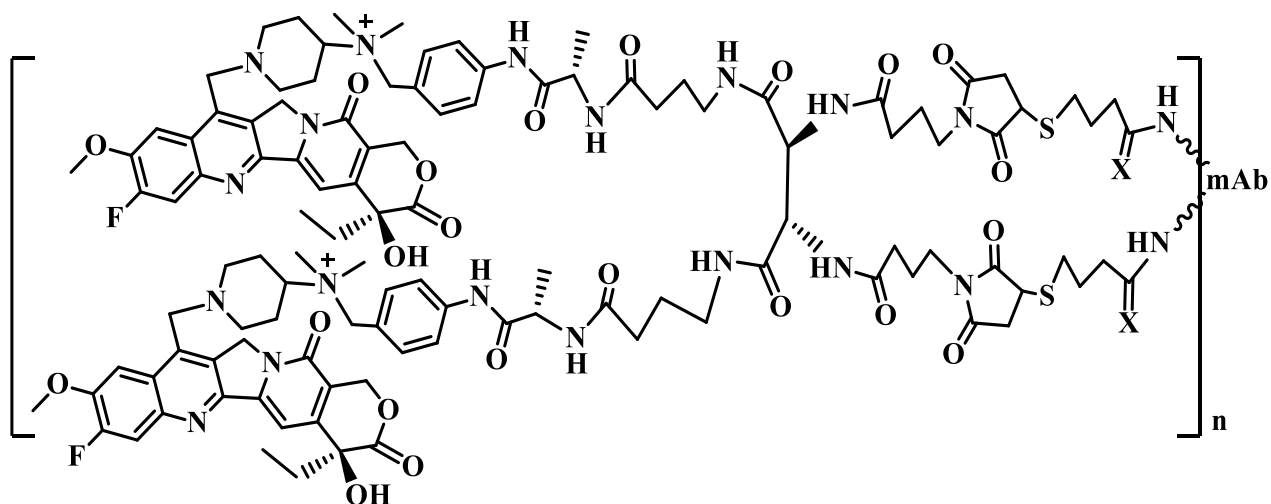
C2-168 (X=NH), C3-168 (X=O);



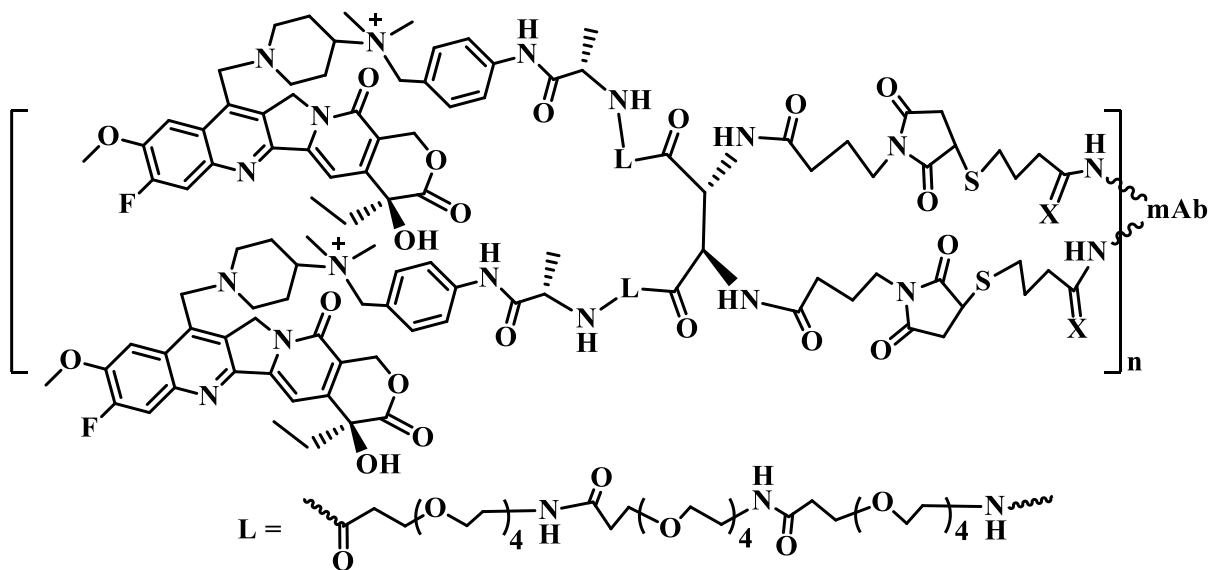
C2-170a (X=NH), C3-170a (X=O);



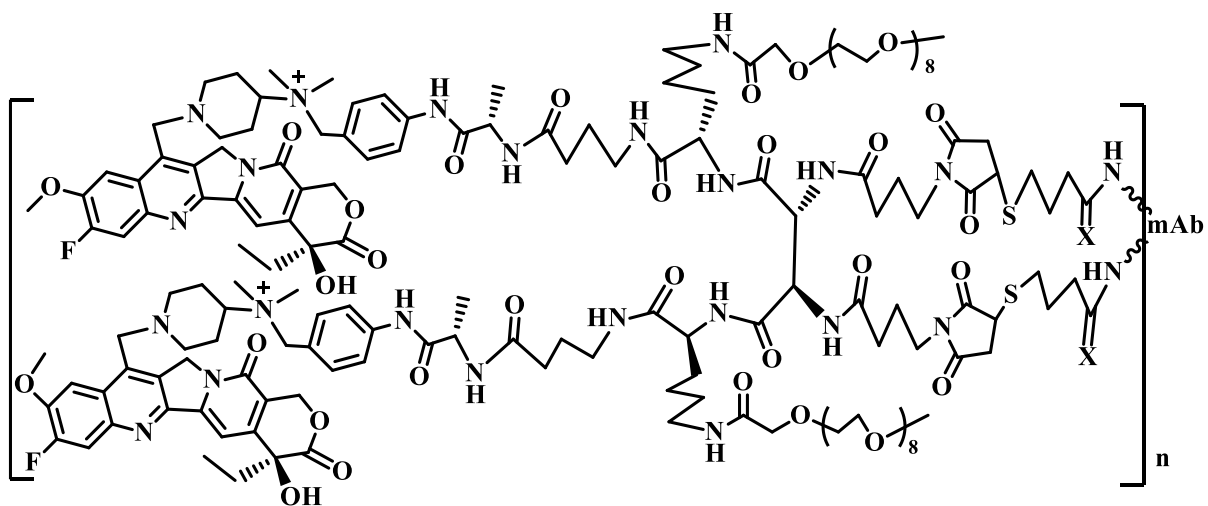
C2-170b (X=NH), C3-170b (X=O);



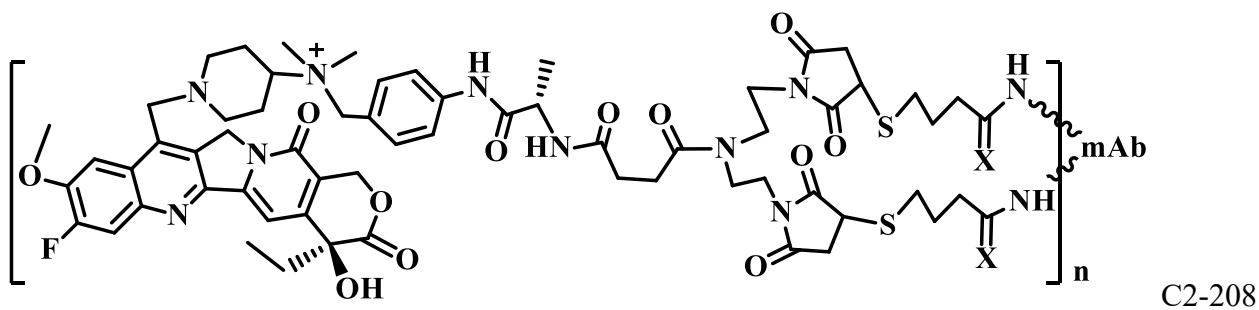
C2-177 (X=NH), C3-177 (X=O);



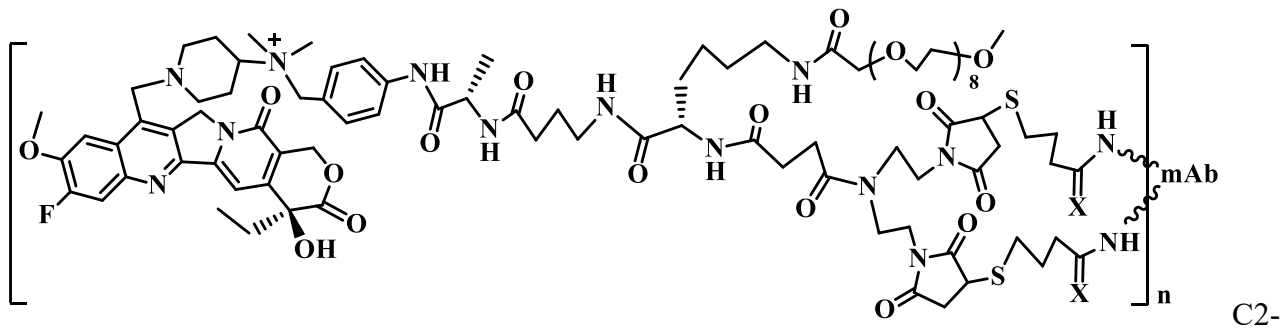
C2-188 (X=NH), C3-188 (X=O);



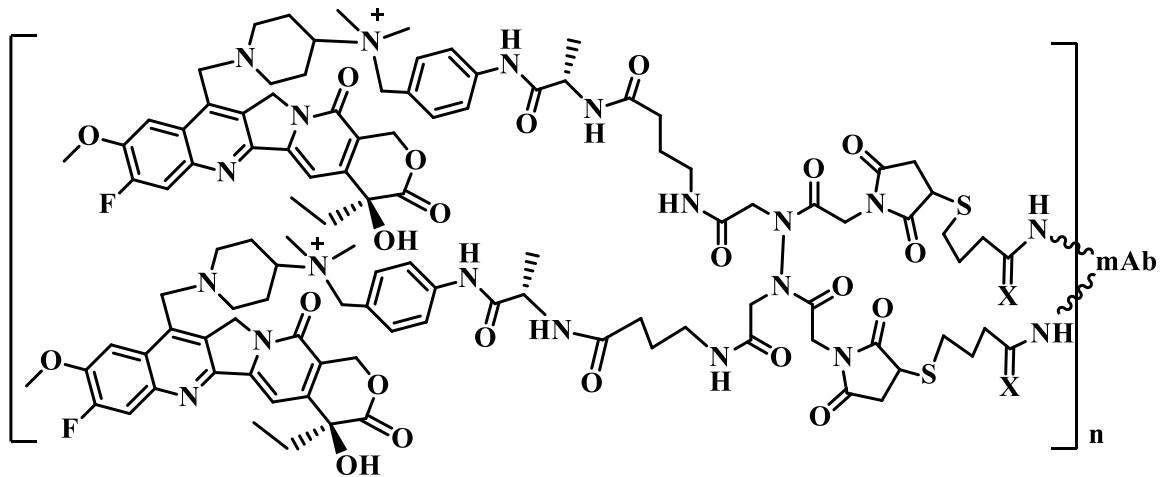
C2-200 (X=NH), C3-200 (X=O);



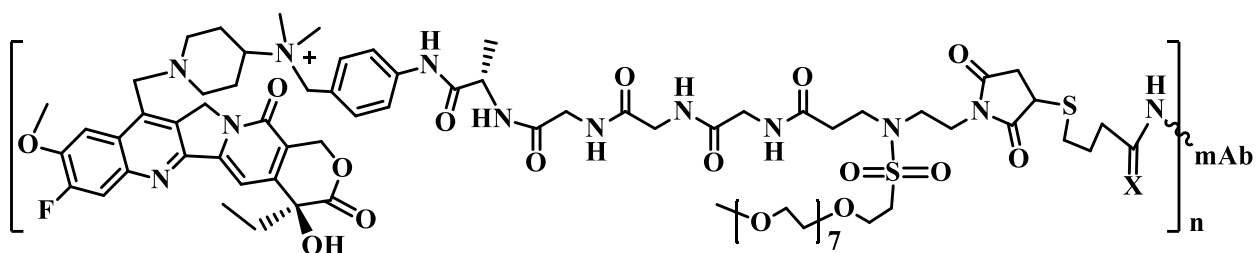
(X=NH), C3-208 (X=O);



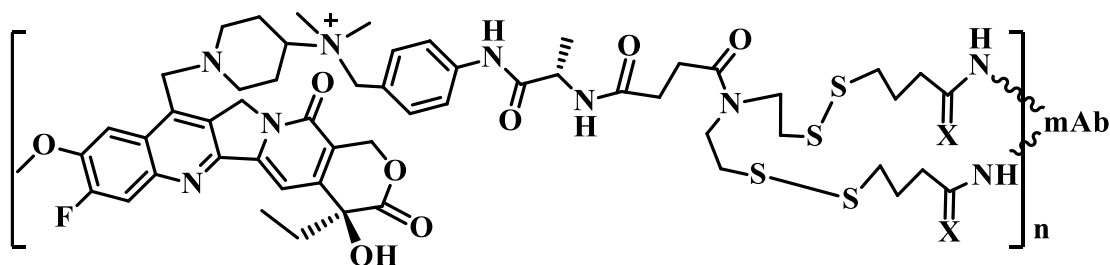
213 (X=NH), C3-213 (X=O);



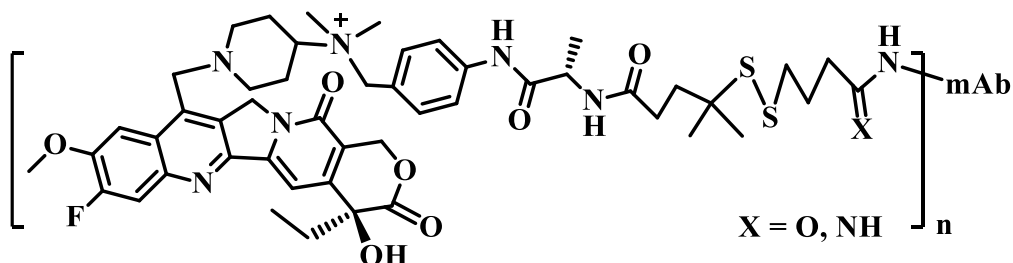
C2-226 (X=NH), C3-226 (X=O);



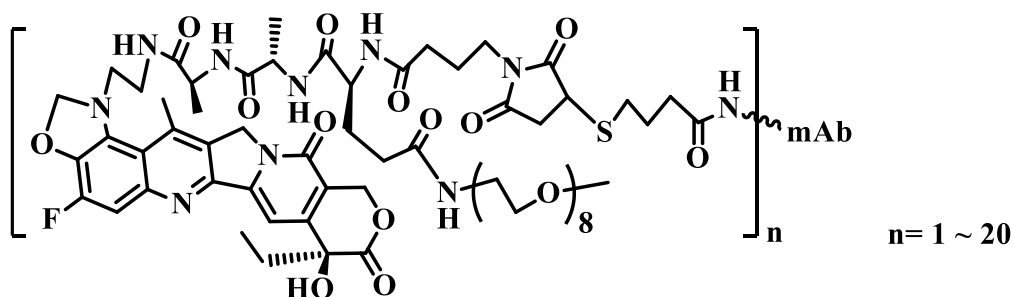
C2-238 (X=NH), C3-238 (X=O);



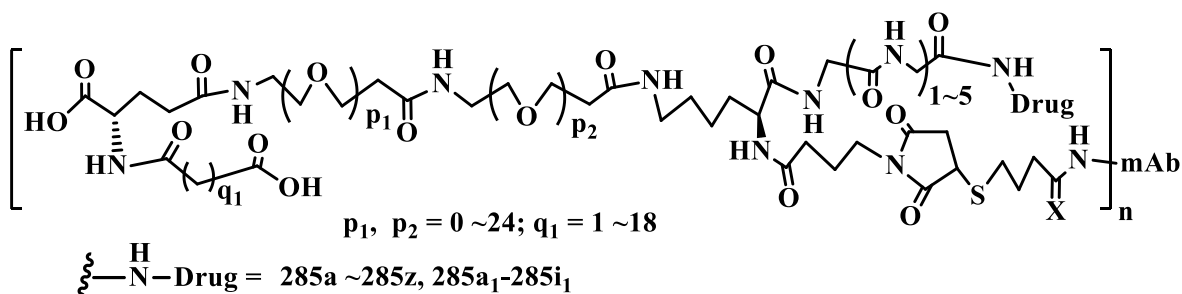
C2-243 (X=NH), C3-243 (X=O);



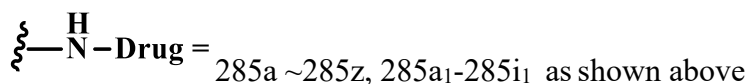
C2-247 (X=NH), C3-247 (X=O);

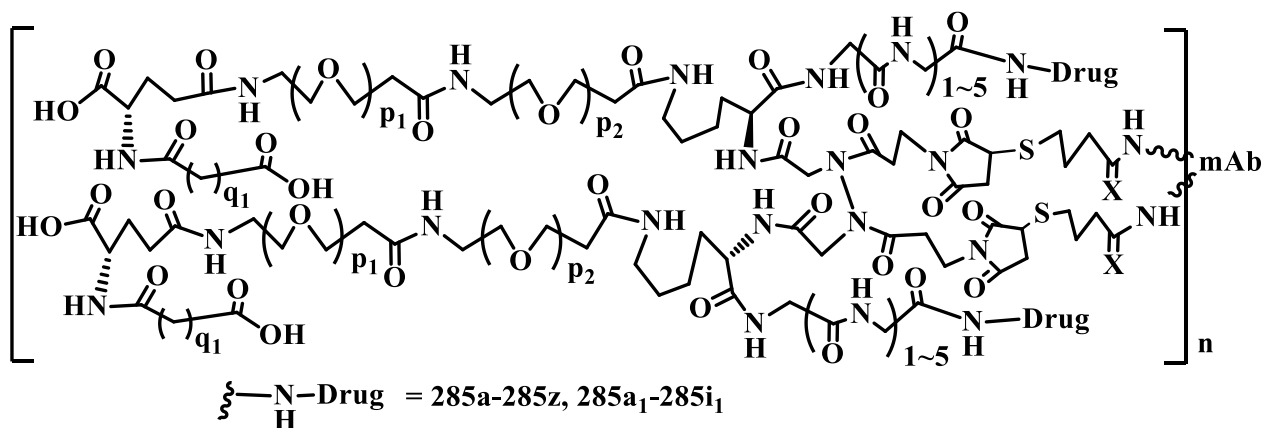


C2-253 (X=NH), C3-253 (X=O);

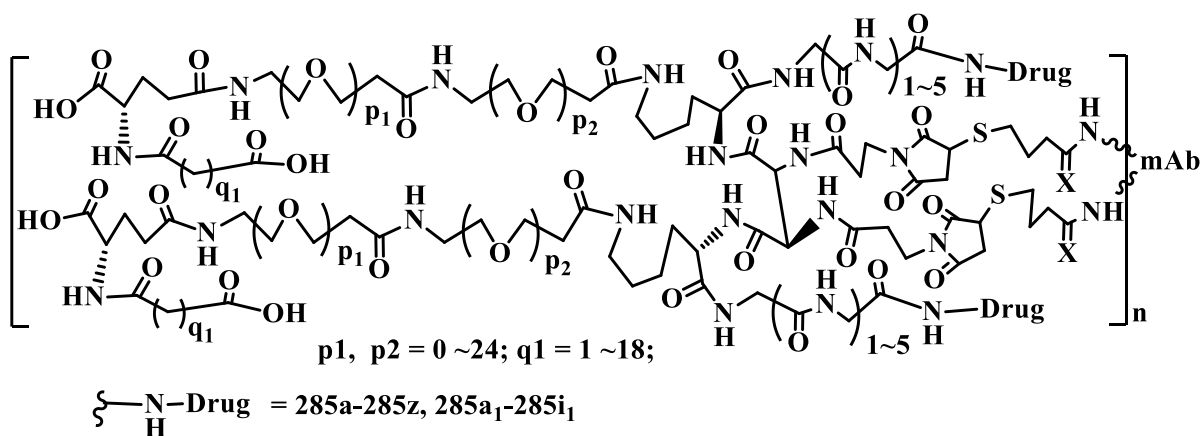


C2-285a ~ C2-285z, X=NH; C2-285a₁-C2-285i₁, X=NH; C3-285a ~ C3-285z, X=O; C3-285a₁-C3-285i₁, X=O;

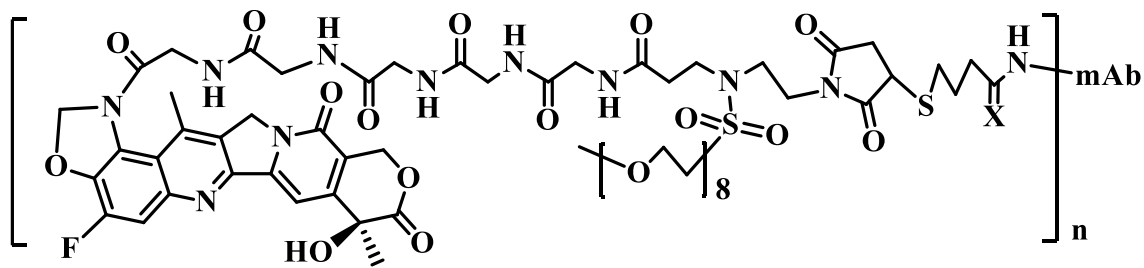




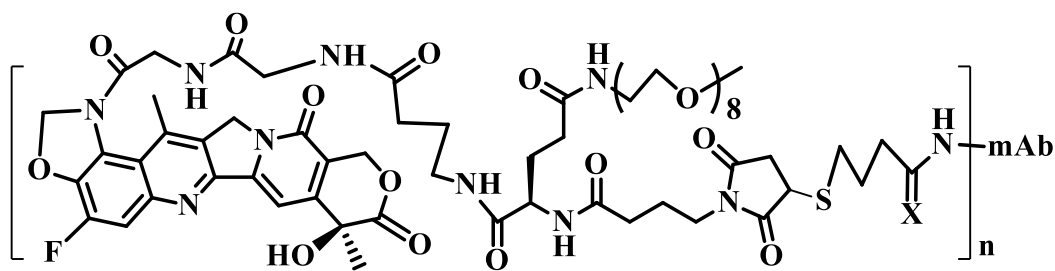
C2-291a ~ C2-291z, X=NH; C2-291a₁-C2-291i₁, X=NH; C3-291a ~ C3-291z, X=O; C3-291a₁-C3-291i₁, X=O;



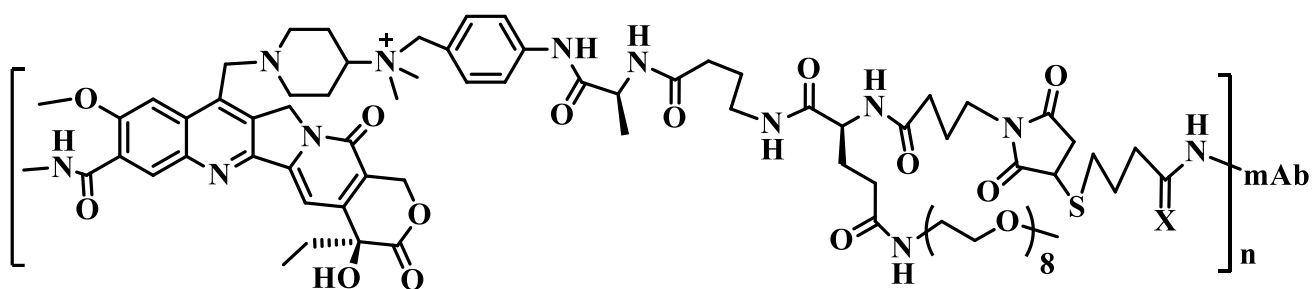
C2-297a ~ C2-297z, X=NH; C2-297a₁-C2-297i₁, X=NH; C3-297a ~ C3-297z, X=O; C3-297a₁-C3-297i₁, X=O; p₁, or p₂ = 0 ~ 24; q₁ = 1 ~ 18;



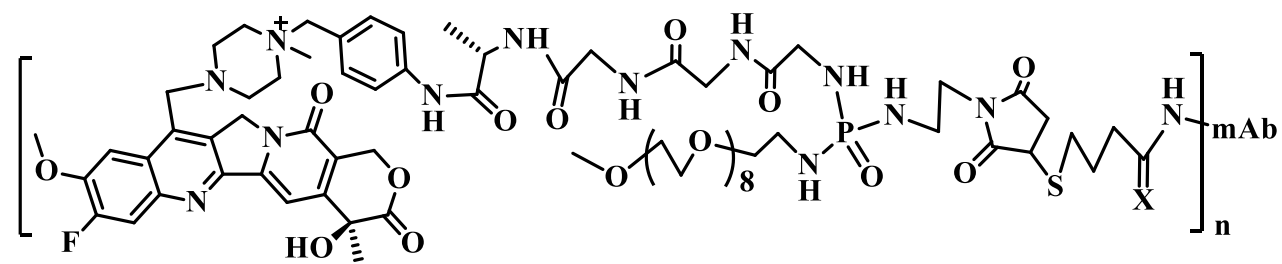
C2-305 (X=NH), C3-305 (X=O);



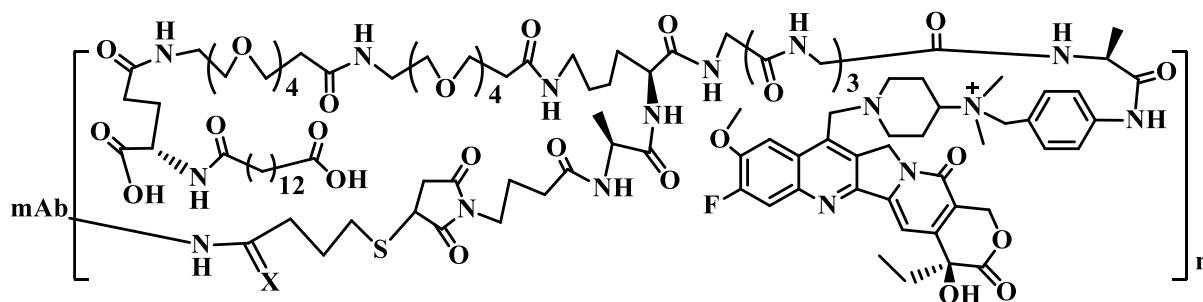
C2-306 (X=NH), C3-306 (X=O);



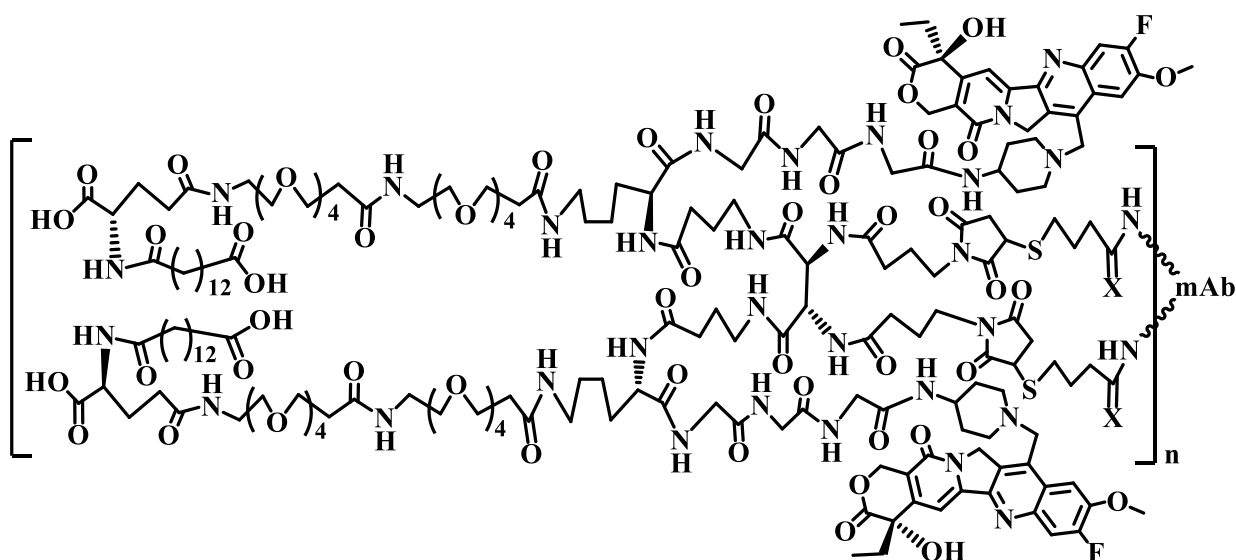
C2-311 (X=NH), C3-311 (X=O);



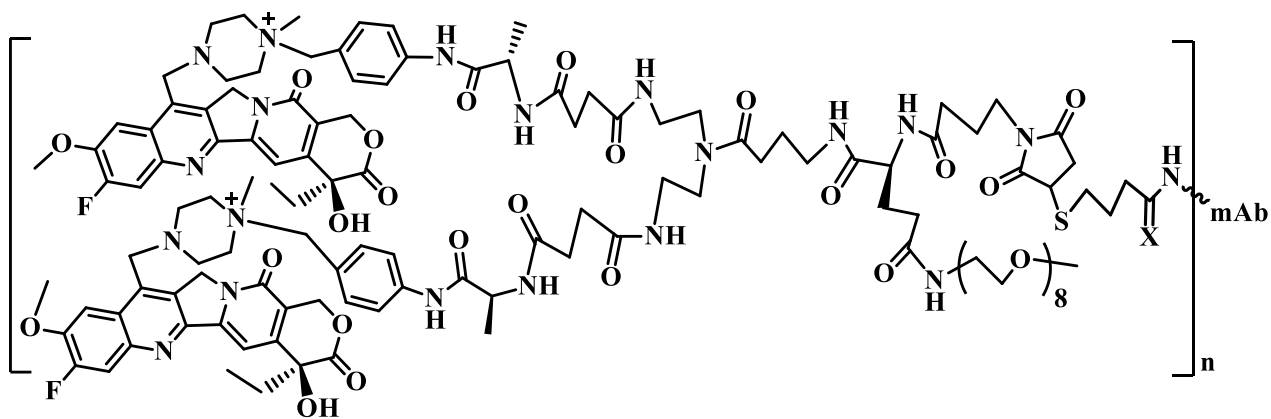
C2-362 (X=NH), C3-362 (X=O);



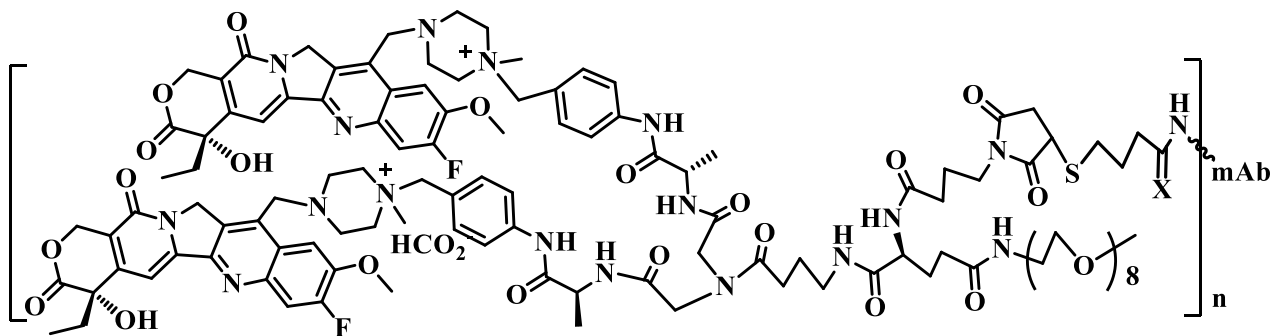
C2-397(X=NH), C3-397 (X=O);



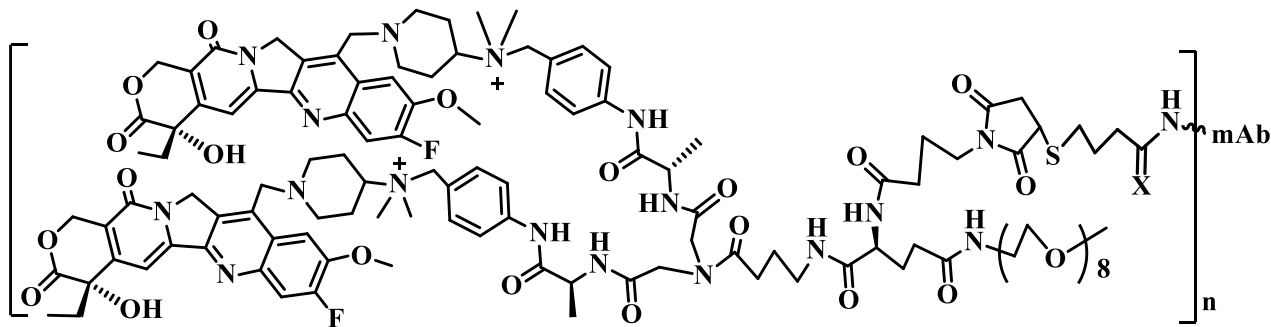
C2-402 (X=NH), C3-402 (X=O);



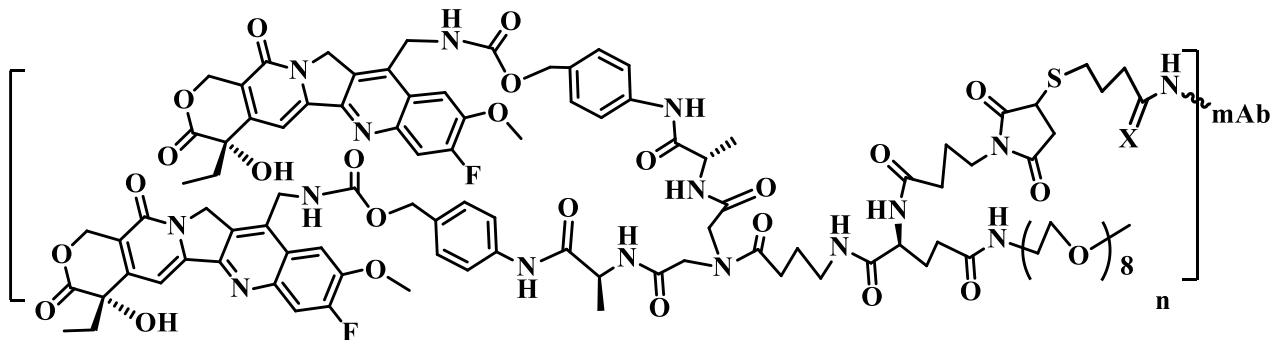
C2-407 (X=NH), C3-407 (X=O);



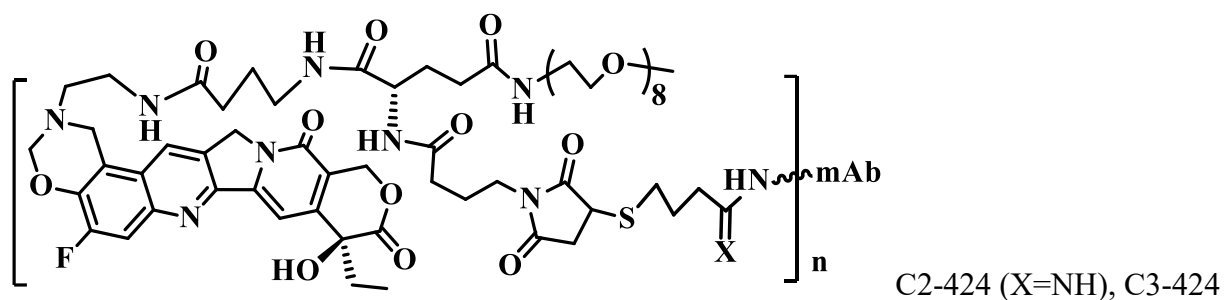
C2-411 (X=NH), C3-411 (X=O);



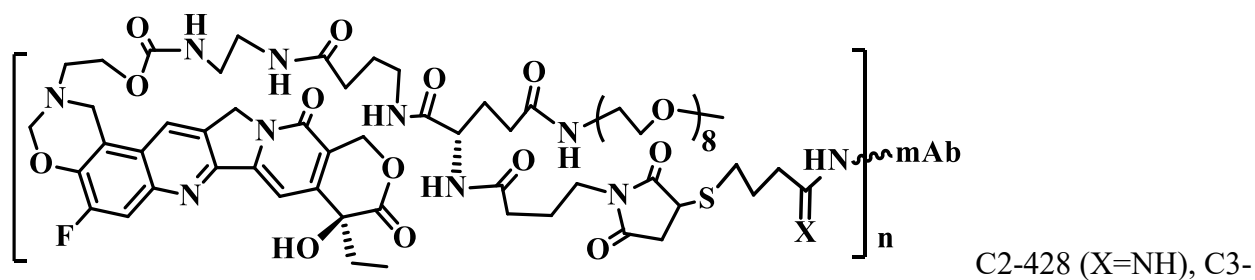
C2-414 (X=NH), C3-414 (X=O);



C2-419 (X=NH), C3-419 (X=O),



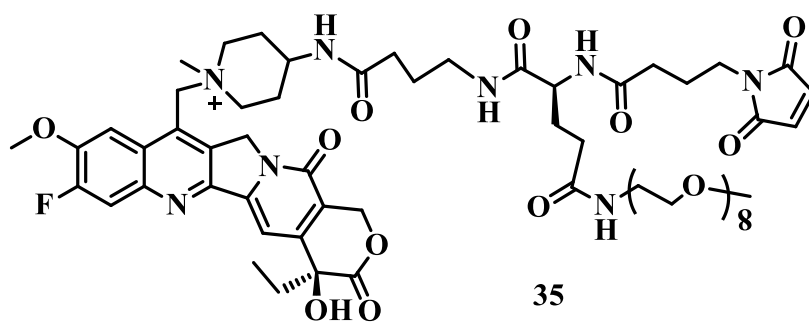
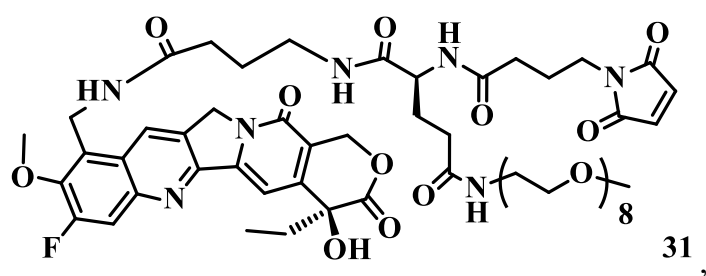
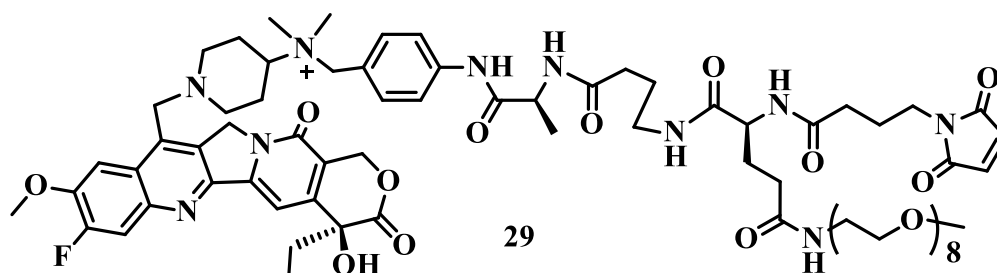
(X=O);

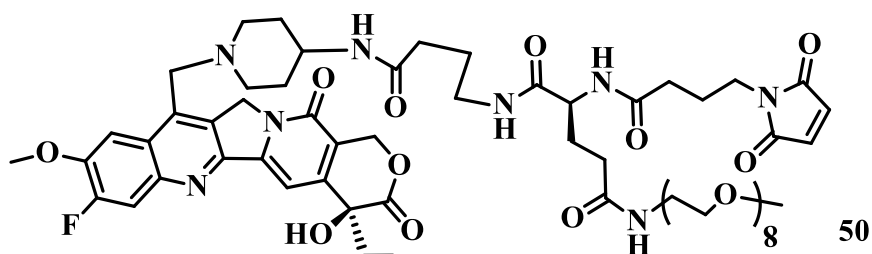
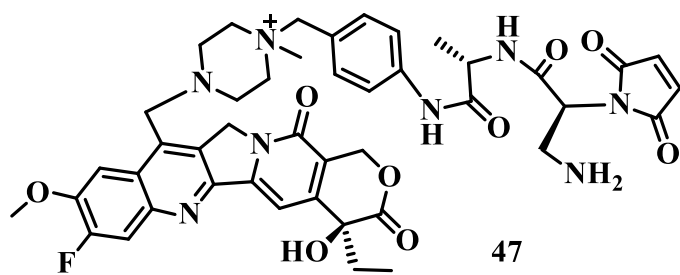
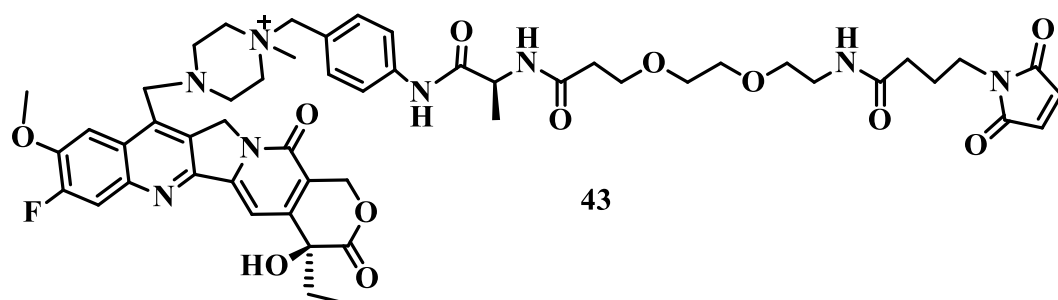
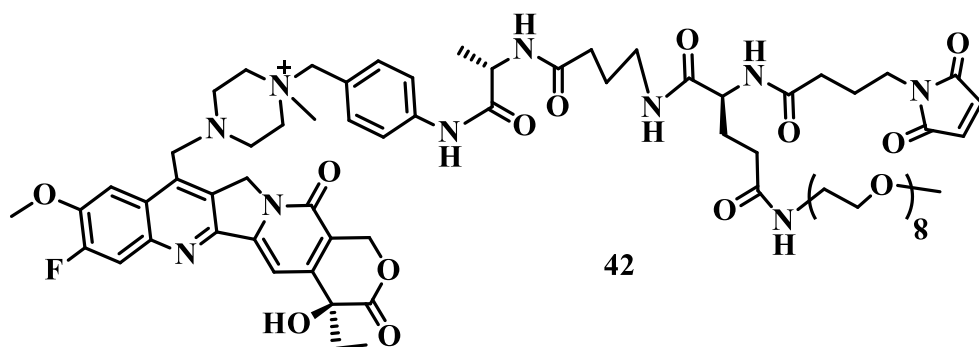
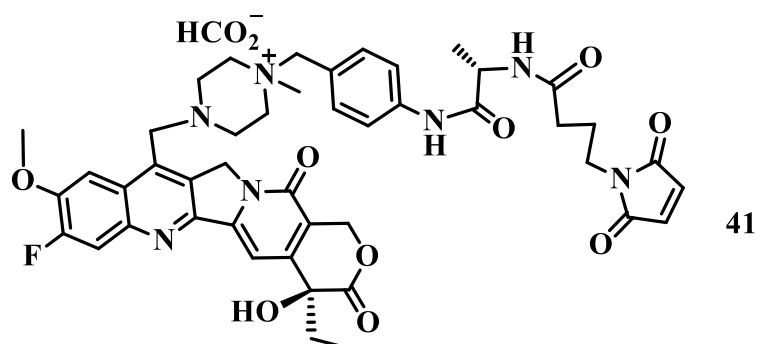


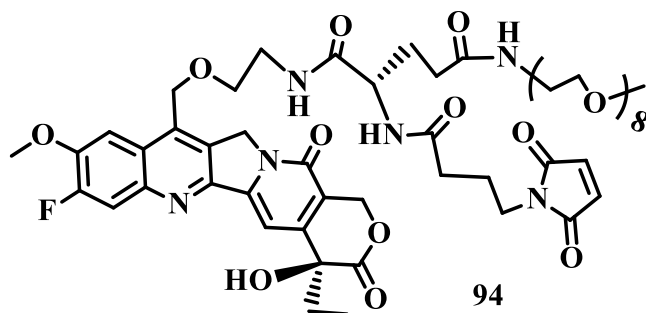
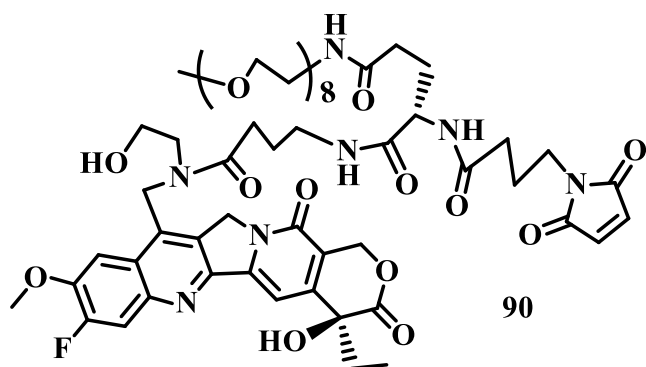
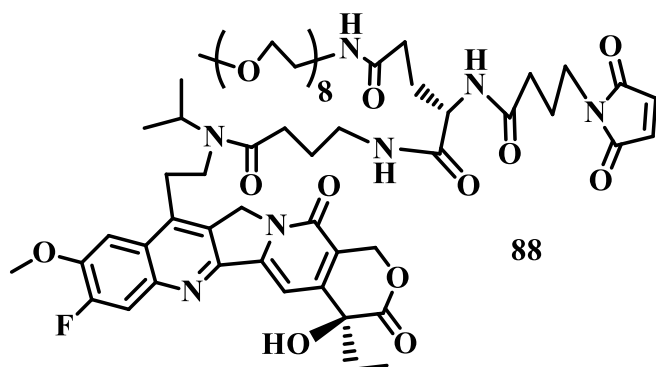
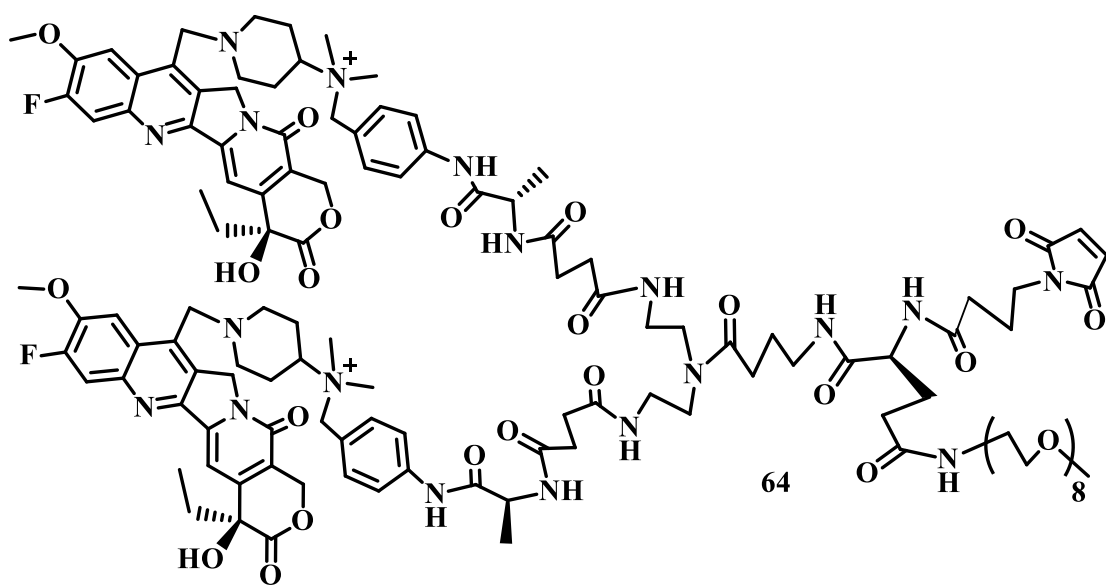
428 (X=O);

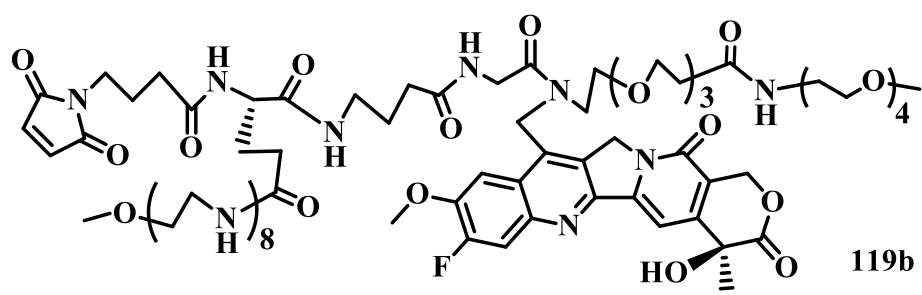
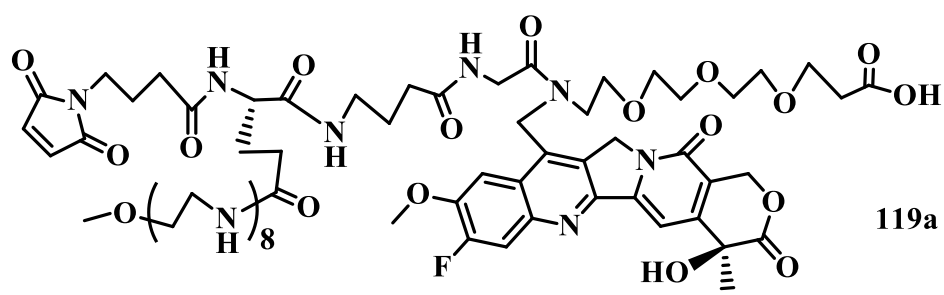
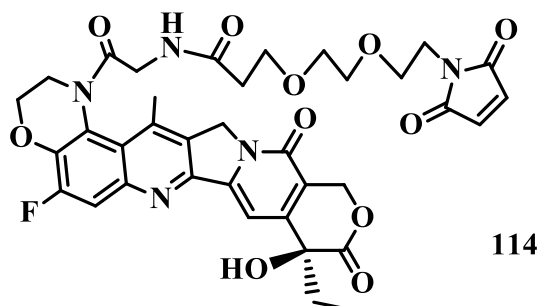
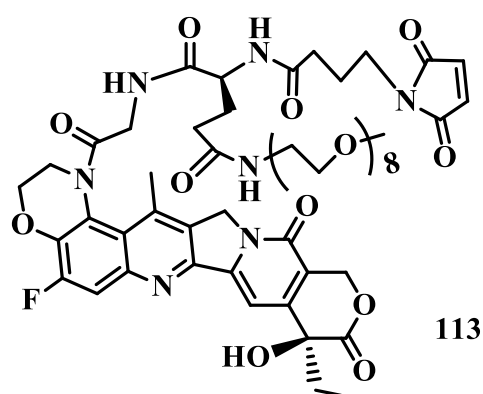
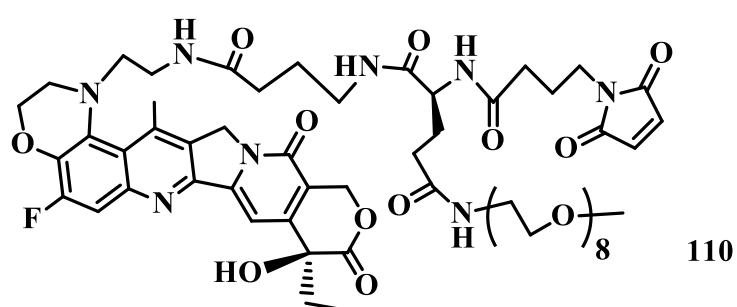
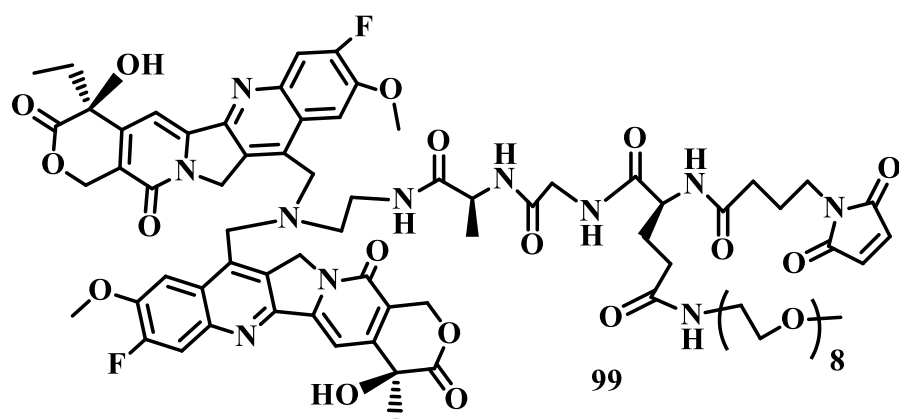
wherein mAb is an antibody.

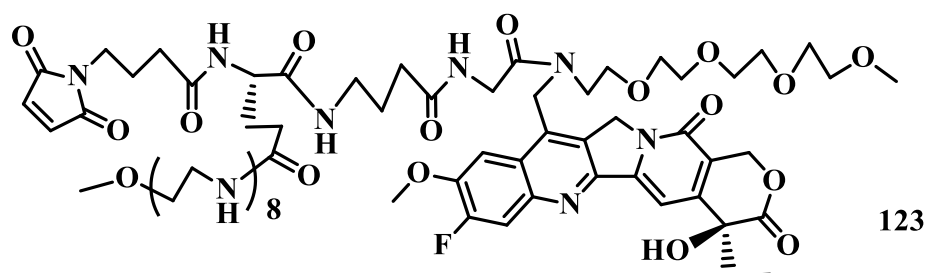
11. The method according to claim 7, wherein the conjugatable compound have the structures of compounds illustrated below:



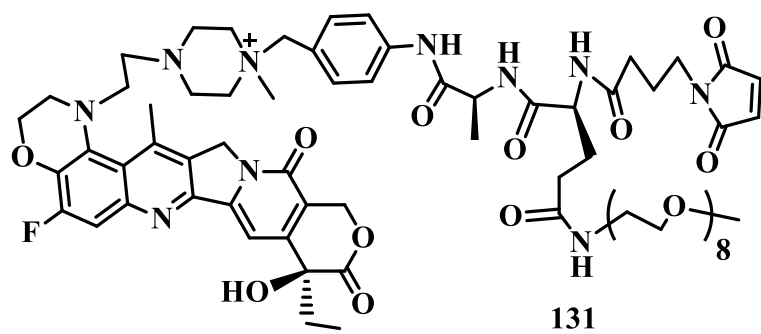




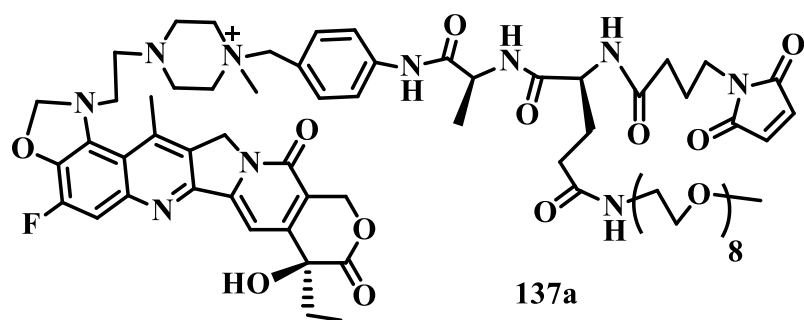




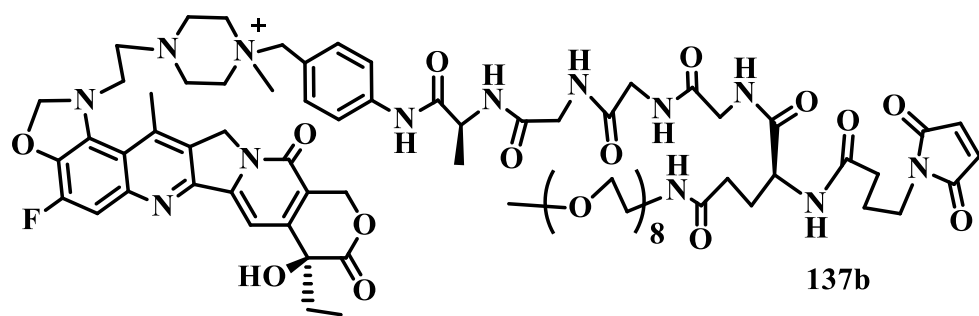
123



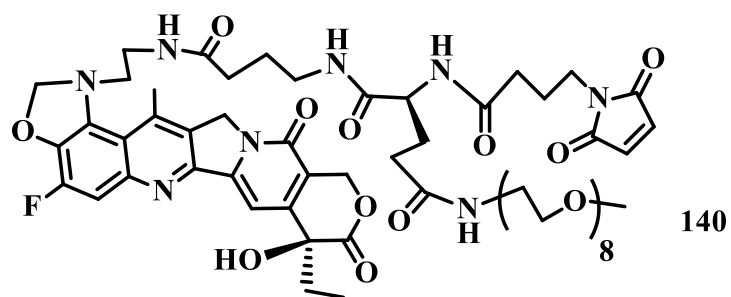
131



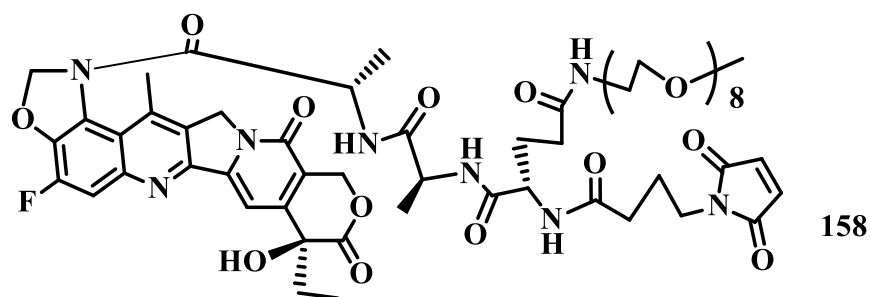
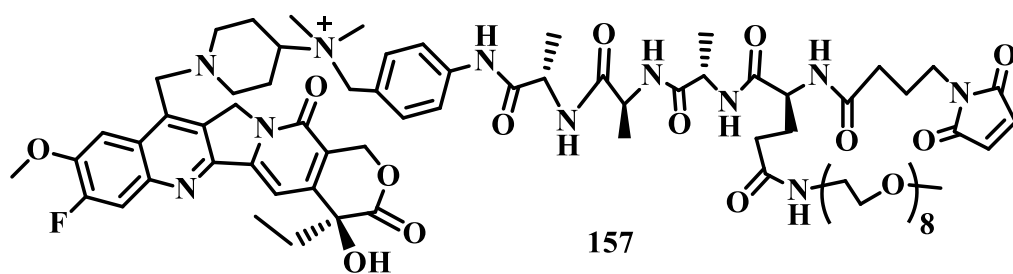
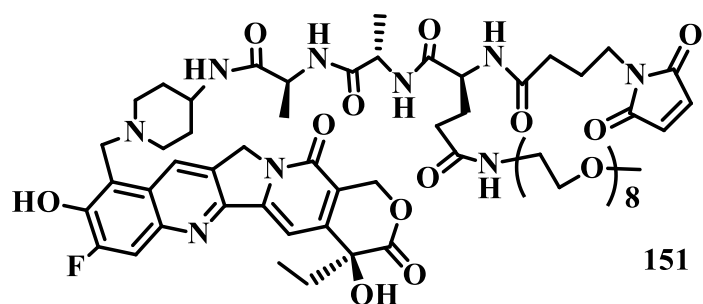
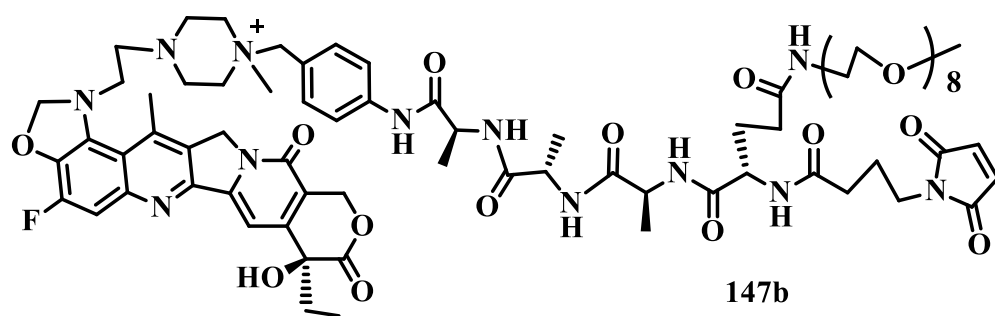
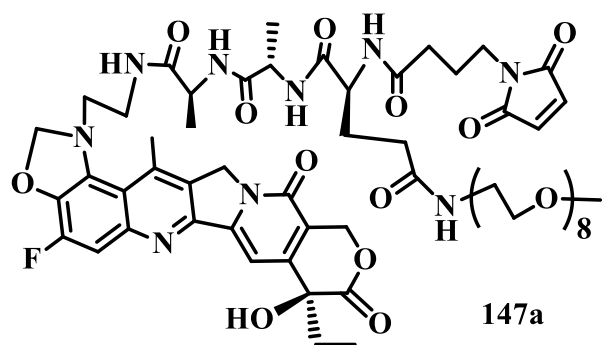
137a

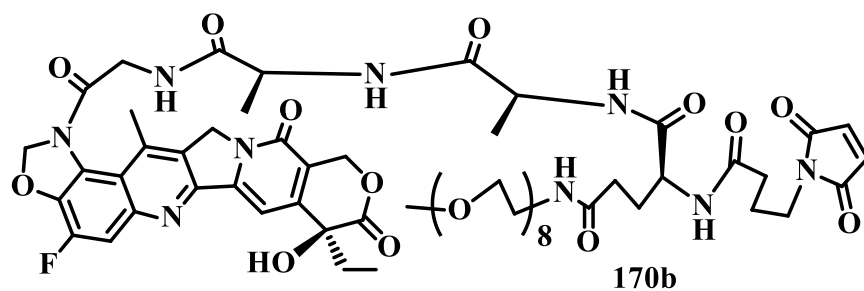
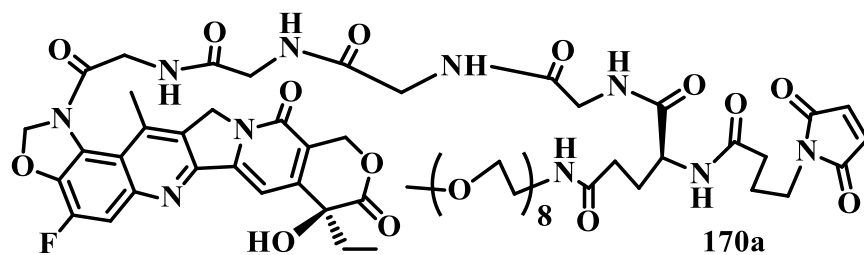
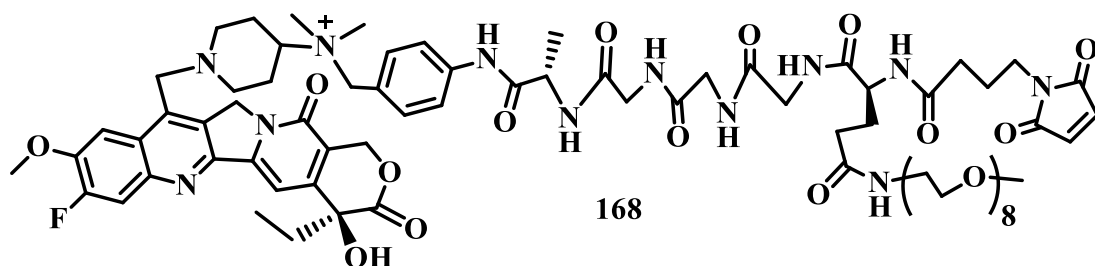
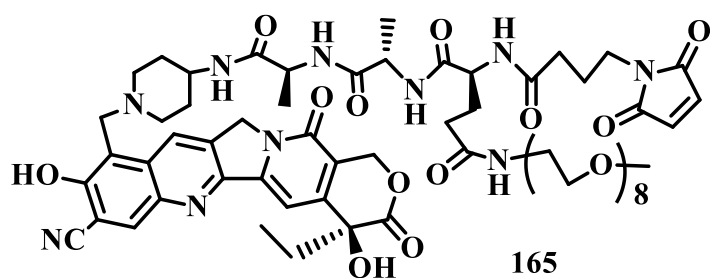
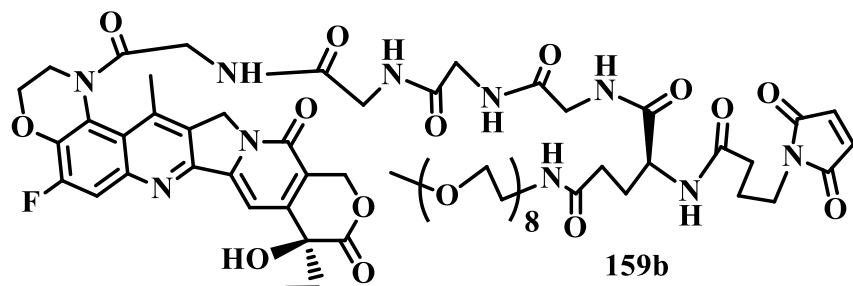
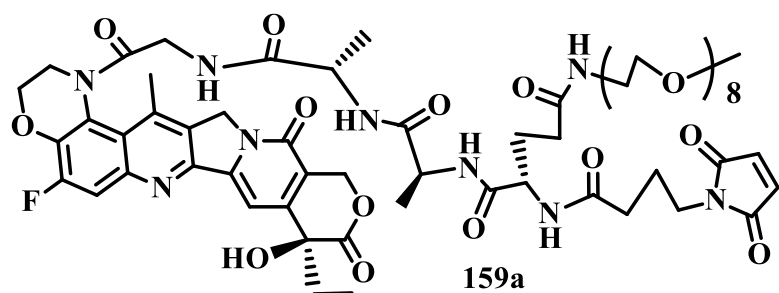


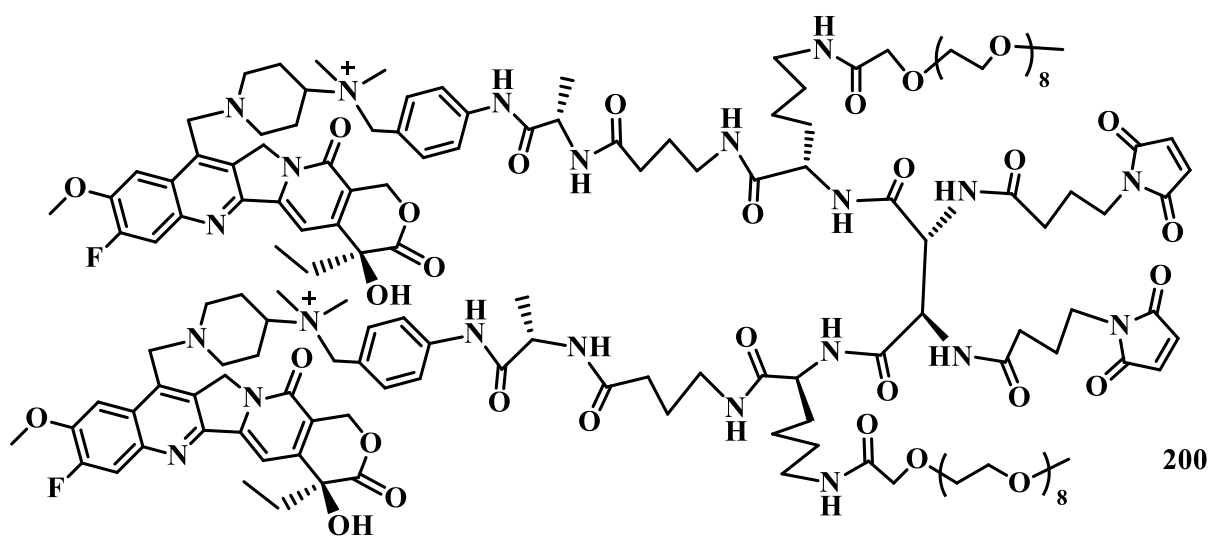
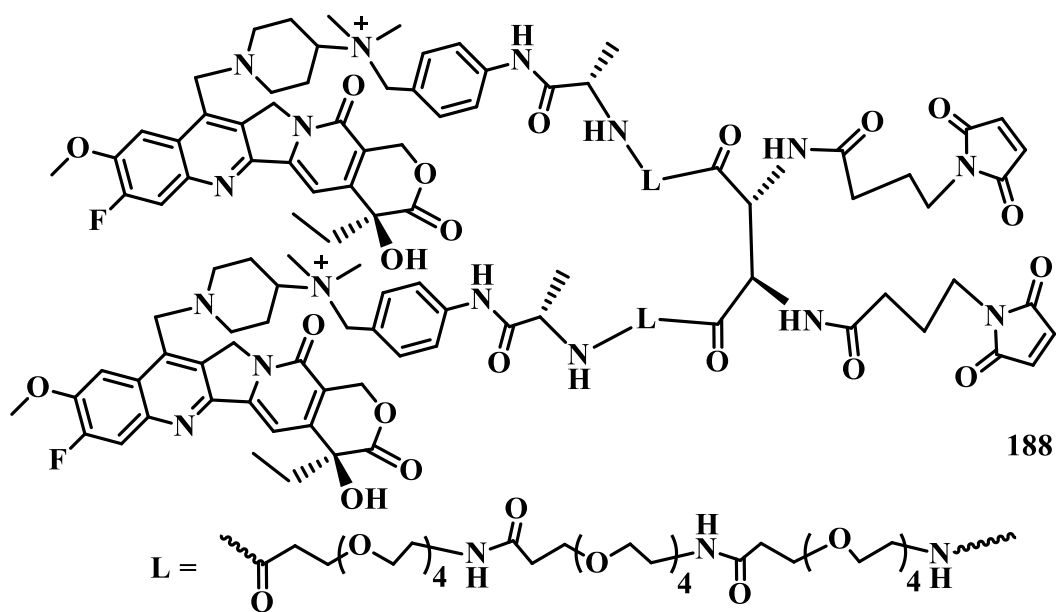
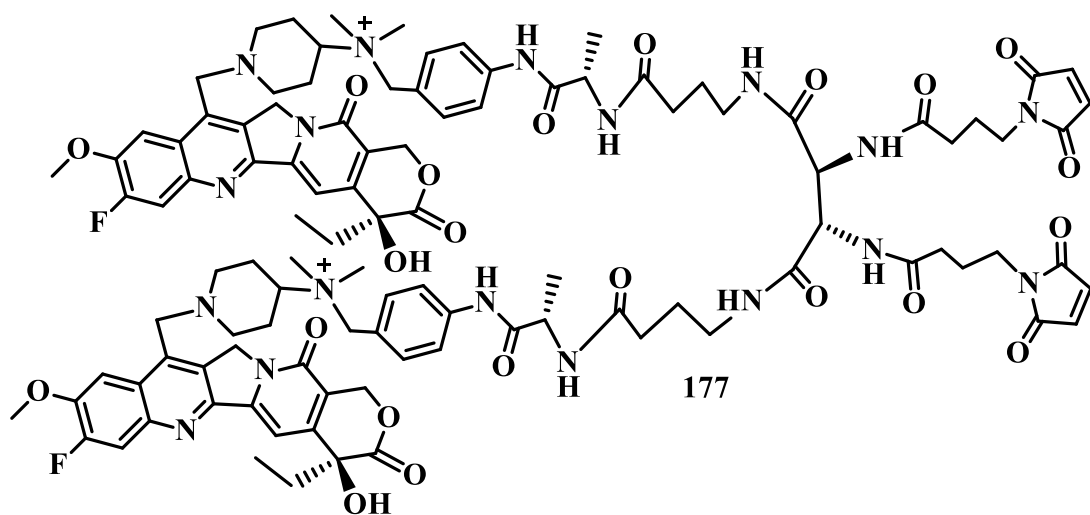
137b

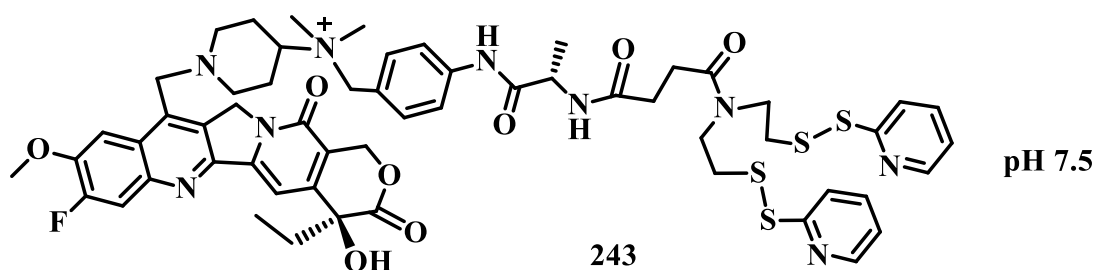
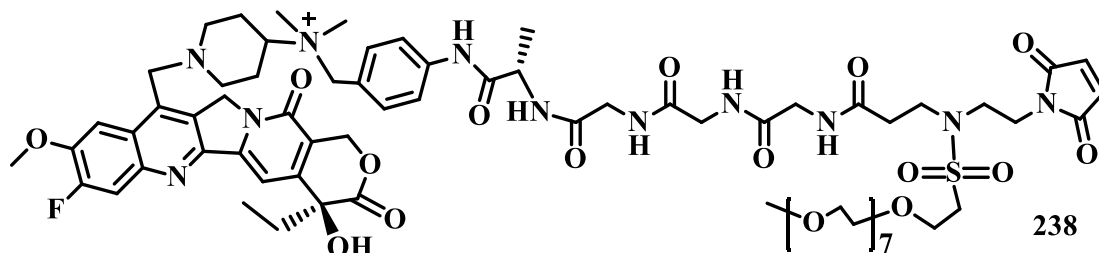
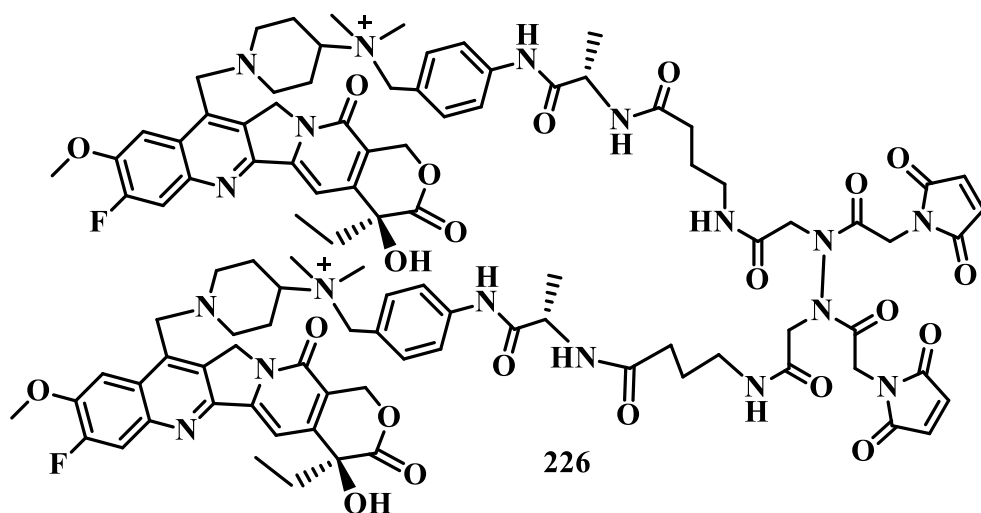
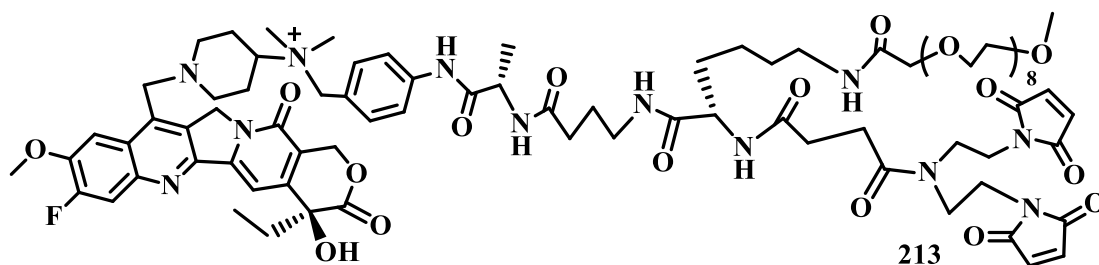
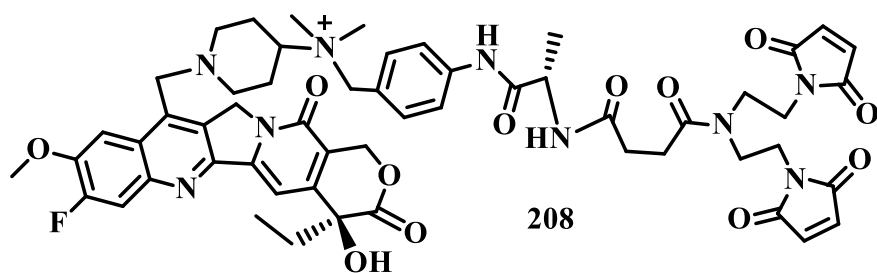


140

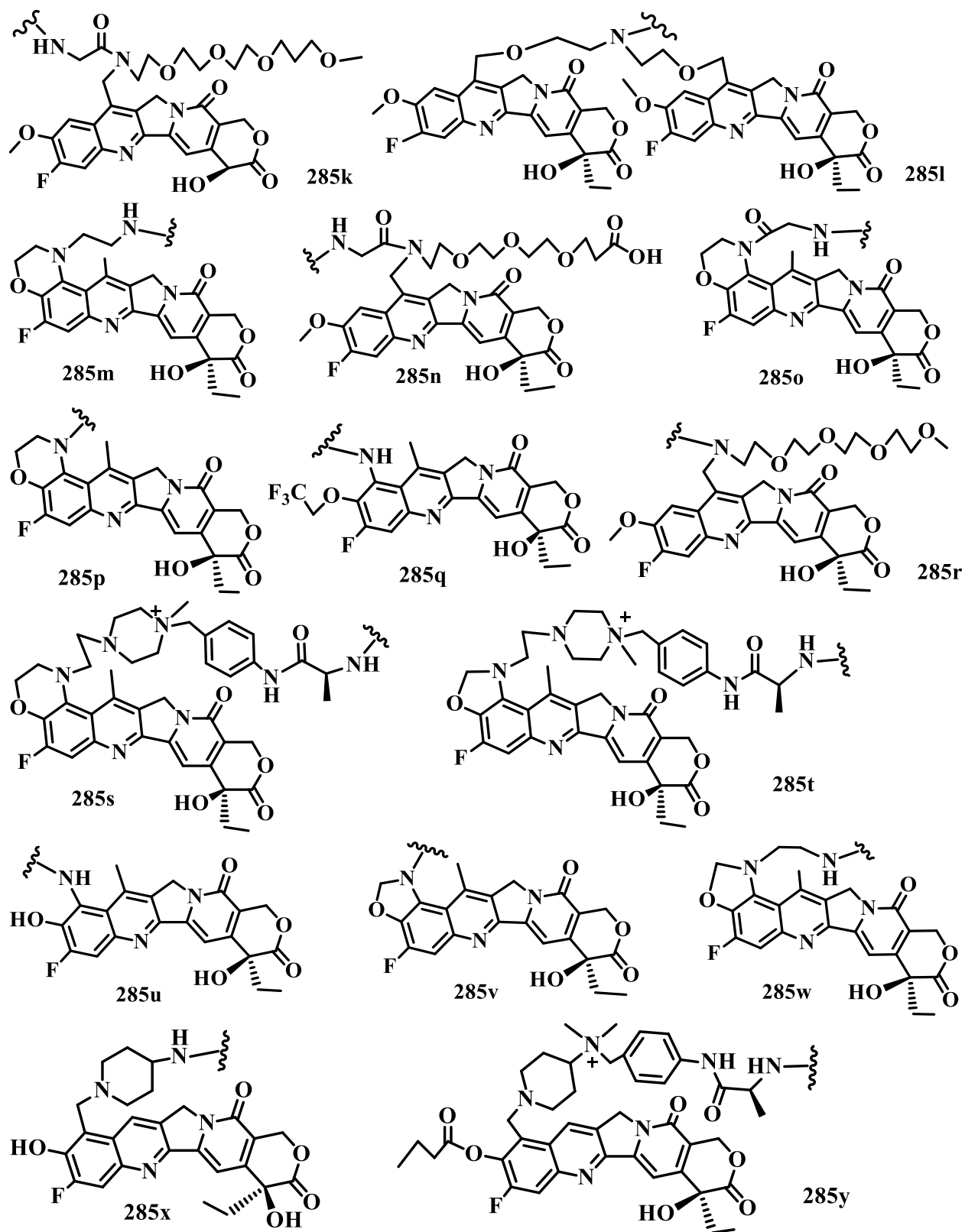


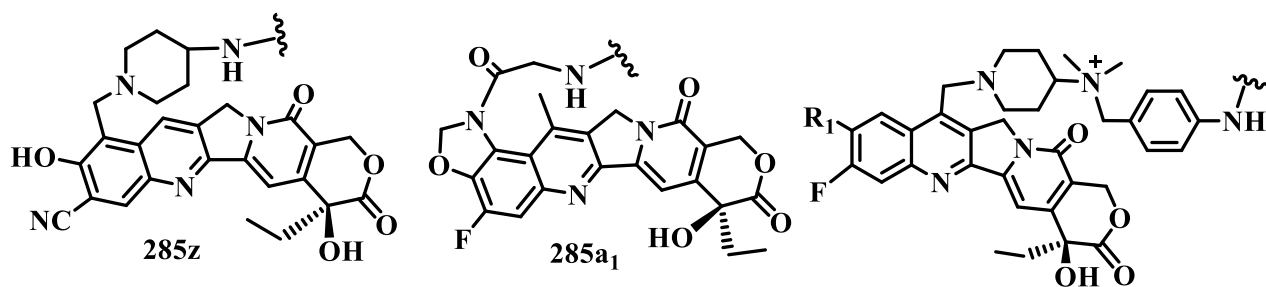










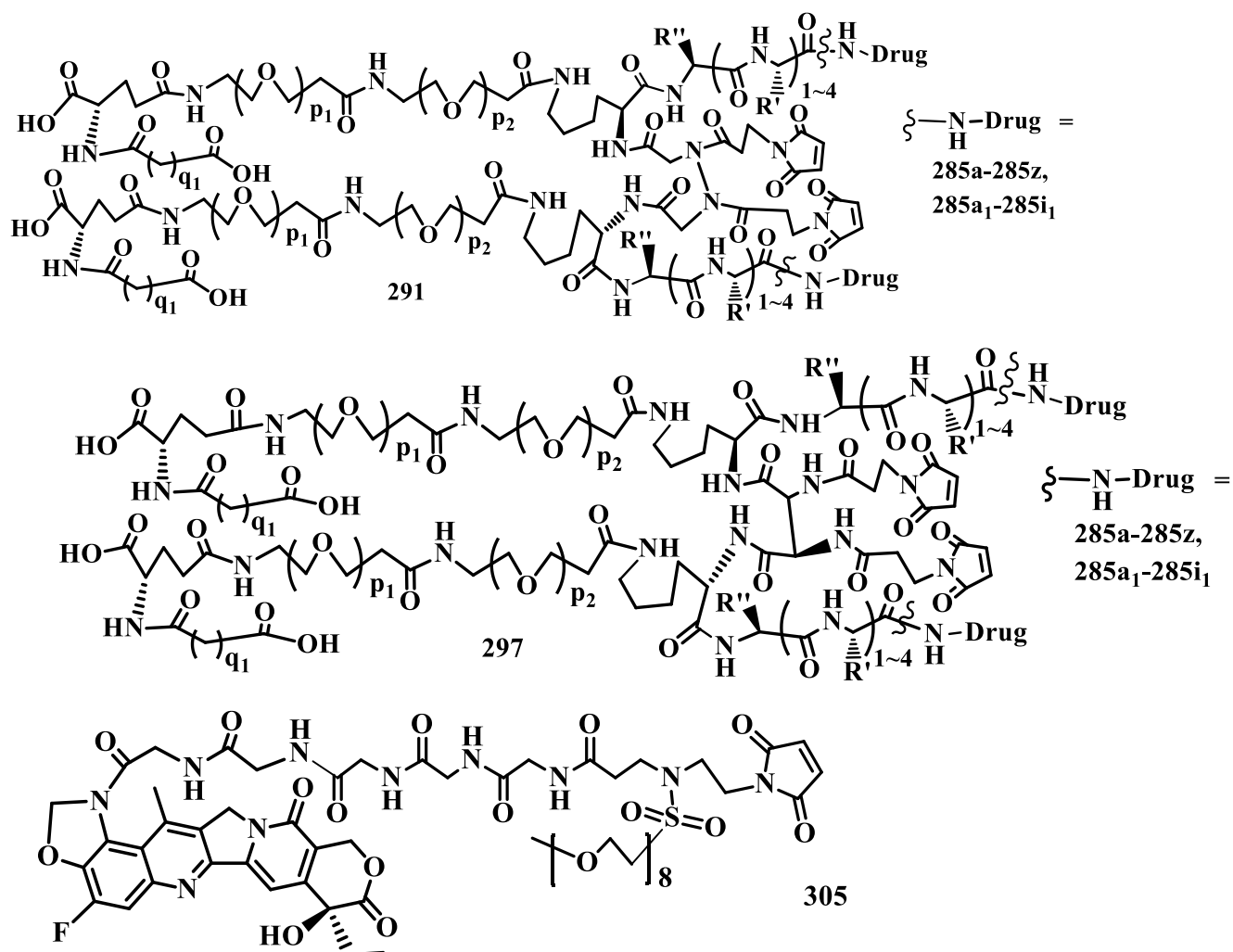


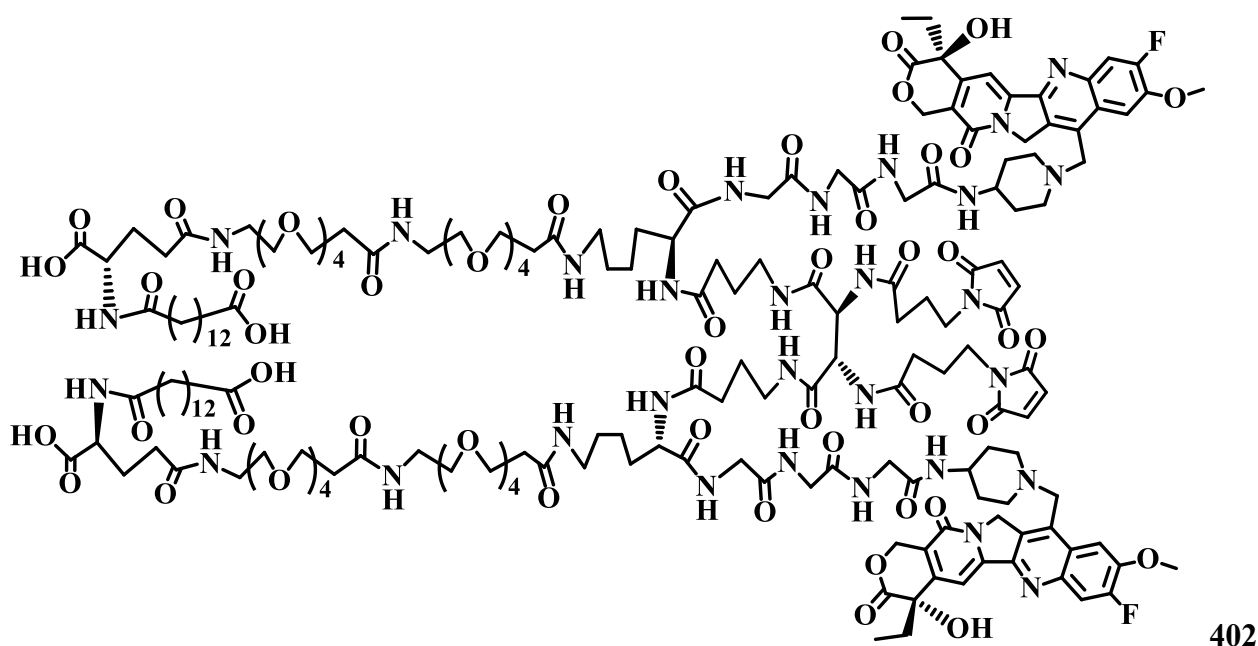
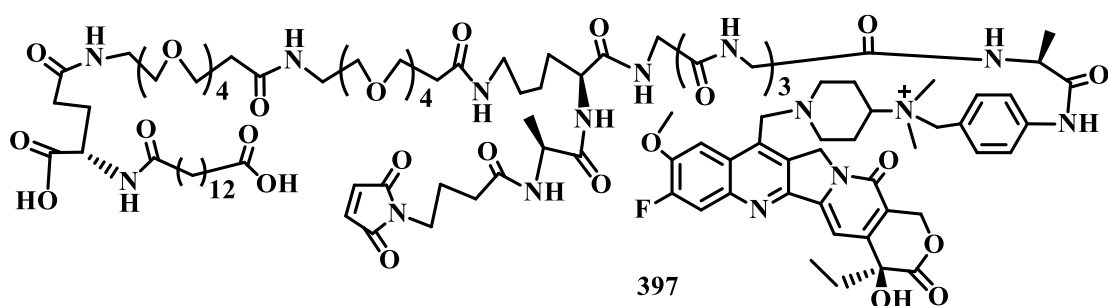
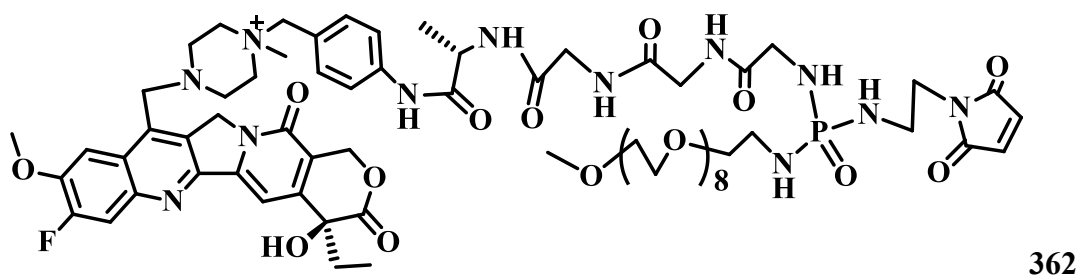
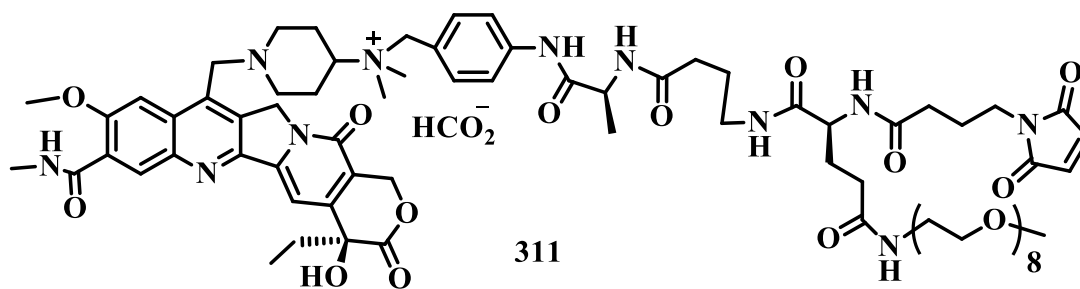
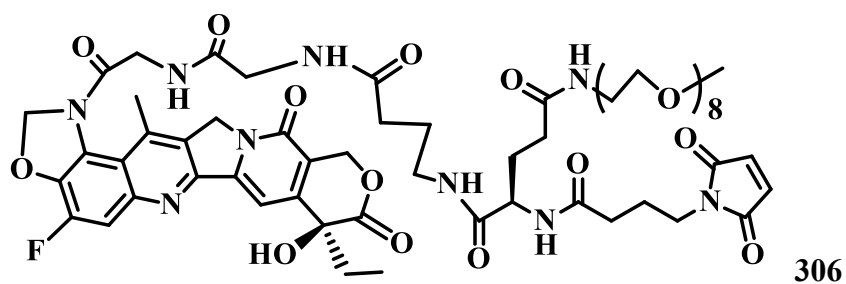
285b1, R1 = H 285c1, R1 = OH

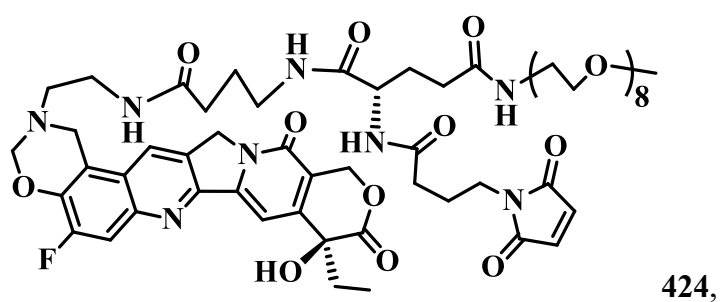
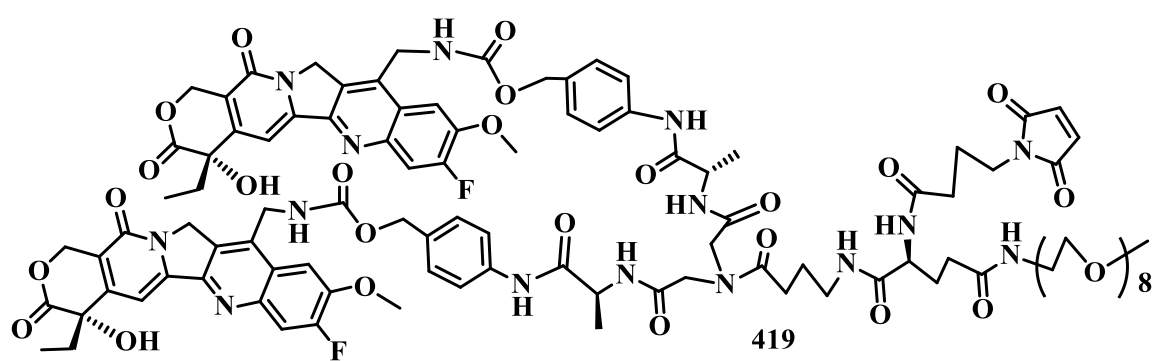
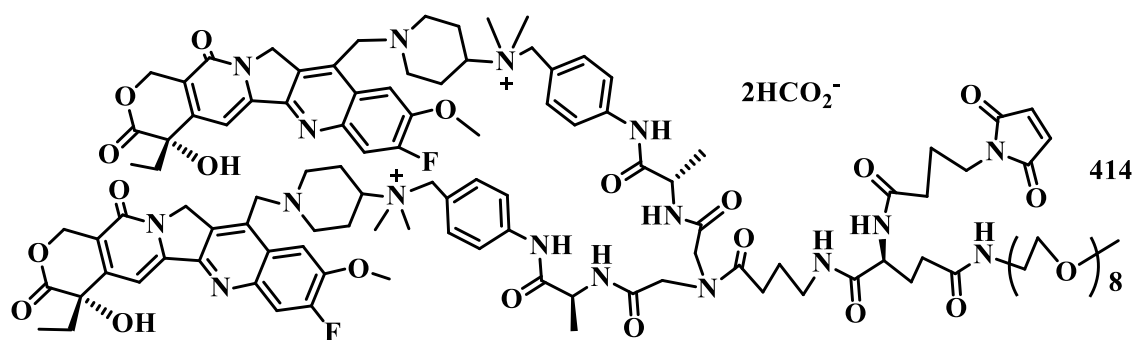
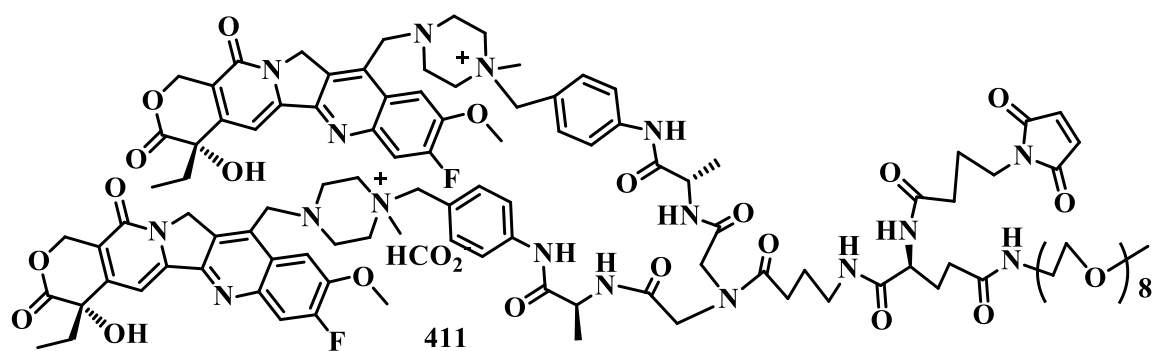
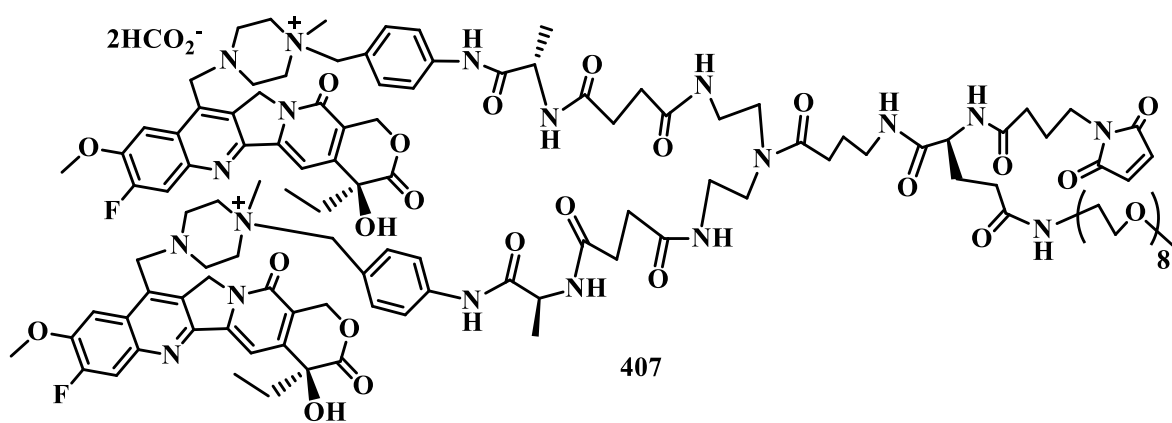
285d1, R1 = Ome 285e1, R1 = CH₃

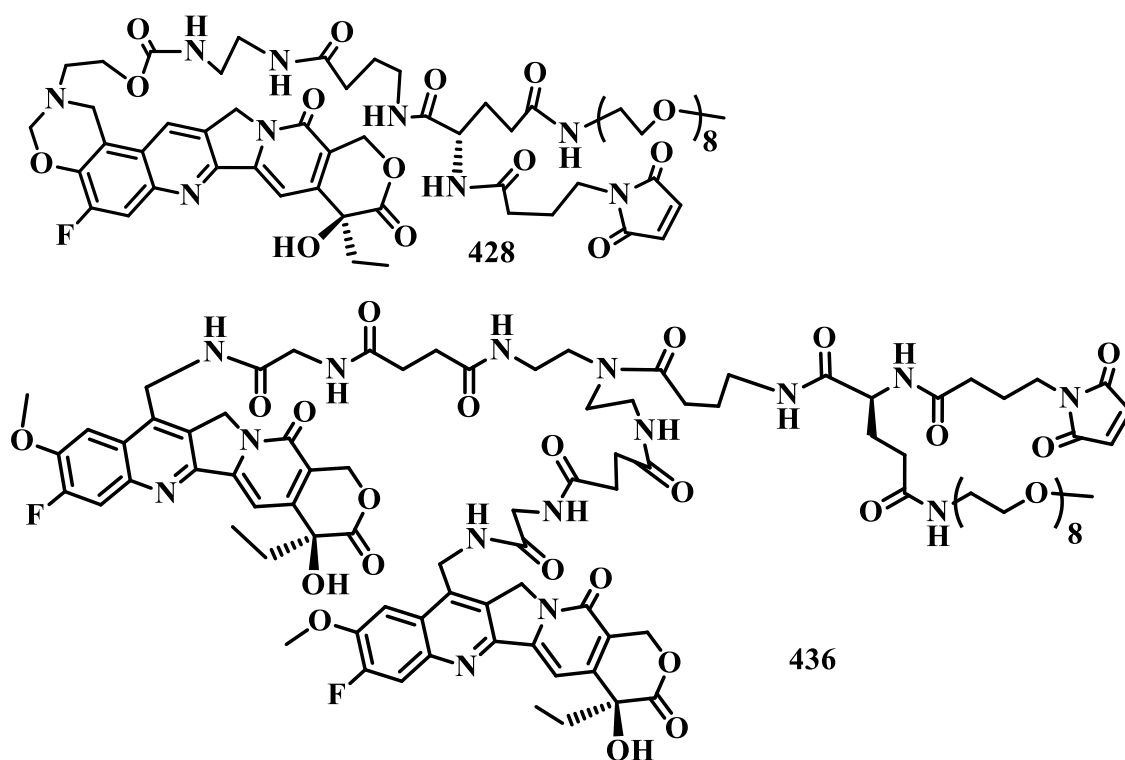
285f1, R1 = H 285g1, R1 = OH 285h1, R1 = OMe 285i1, R1 = CH₃

~ = the site linked to C(=O) of the rest part of molecule









12. The conjugates according to claim 1, 2, 3, 4, 5, 6, 8, or 10, wherein cell-binding molecule is capable of targeting against a tumor cell, a virus infected cell, a microorganism infected cell, a parasite infected cell, an autoimmune disease cell, an activated tumor cells, a myeloid cell, an activated T-cell, an affecting B cell, or a melanocyte, or any cells expressing any one of the following antigens or receptors: CD1, CD1a, CD1b, CD1c, CD1d, CD1e, CD2, CD3, CD3d, CD3e, CD3g, CD4, CD5, CD6, CD7, CD8, CD8a, CD8b, CD9, CD10, CD11a, CD11b, CD11c, CD11d, CD12w, CD13, CD14, CD15, CD16, CD16a, CD16b, CDw17, CD18, CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD26, CD27, CD28, CD29, CD30, CD31, CD32, CD32a, CD32b, CD33, CD34, CD35, CD36, CD37, CD38, CD39, CD40, CD41, CD42, CD42a, CD42b, CD42c, CD42d, CD43, CD44, CD45, CD46, CD47, CD48, CD49b, CD49c, CD49c, CD49d, CD49f, CD50, CD51, CD52, CD53, CD54, CD55, CD56, CD57, CD58, CD59, CD60, CD60a, CD60b, CD60c, CD61, CD62E, CD62L, CD62P, CD63, CD64, CD65, CD65s, CD66, CD66a, CD66b, CD66c, CD66d, CD66e, CD66f, CD67, CD68, CD69, CD70, CD71, CD72, CD73, CD74, CD75, CD75s, CD76, CD77, CD78, CD79, CD79a, CD79b, CD80, CD81, CD82, CD83, CD84, CD85, CD85a, CD85b, CD85c, CD85d, CD85e, CD85f, CD85g, CD85g, CD85i, CD85j, CD85k, CD85m, CD86, CD87, CD88, CD89, CD90, CD91, CD92, CD93, CD94, CD95, CD96, CD97, CD98, CD99, CD100, CD101, CD102, CD103, CD104, CD105, CD106, CD107, CD107a, CD107b, CD108, CD109, CD110, CD111, CD112, CD113, CD114, CD115, CD116, CD117, CD118, CD119, CD120, CD120a, CD120b, CD121, CD121a, CD121b, CD122, CD123, CD123a, CD124, CD125, CD126, CD127, CD128, CD129, CD130, CD131, CD132, CD133, CD134, CD135, CD136, CD137, CD138, CD139,

CD140, CD140a, CD140b, CD141, CD142, CD143, CD144, CD145, CDw145, CD146, CD147, CD148, CD149, CD150, CD151, CD152, CD153, CD154, CD155, CD156, CD156a, CD156b, CD156c, CD156d, CD157, CD158, CD158a, CD158b1, CD158b2, CD158c, CD158d, CD158e1, CD158e2, CD158f2, CD158g, CD158h, CD158i, CD158j, CD158k, CD159, CD159a, CD159b, CD159c, CD160, CD161, CD162, CD163, CD164, CD165, CD166, CD167, CD167a, CD167b, CD168, CD169, CD170, CD171, CD172, CD172a, CD172b, CD172g, CD173, CD174, CD175, CD175s, CD176, CD177, CD178, CD179, CD179a, CD179b, CD180, CD181, CD182, CD183, CD184, CD185, CD186, CDw186, CD187, CD188, CD189, CD190, CD191, CD192, CD193, CD194, CD195, CD196, CD197, CD198, CD199, CDw198, CDw199, CD200, CD201, CD202, CD202(a,b), CD203, CD203c, CD204, CD205, CD206, CD207, CD208, CD209, CD210, CDw210a, CDw210b, CD211, CD212, CD213, CD213a1, CD213a2, CD214, CD215, CD216, CD217, CD218, CD218a, CD218, CD21b9, CD220, CD221, CD222, CD223, CD224, CD225, CD226, CD227, CD228, CD229, CD230, CD231, CD232, CD233, CD234, CD235, CD235a, CD235b, CD236, CD237, CD238, CD239, CD240, CD240ce, CD240d, CD241, CD242, CD243, CD244, CD245, CD246, CD247, CD248, CD249, CD250, CD251, CD252, CD253, CD254, CD255, CD256, CD257, CD258, CD259, CD260, CD261, CD262, CD263, CD264, CD265, CD266, CD267, CD268, CD269, CD270, CD271, CD272, CD273, CD274, CD275, CD276, CD277, CD278, CD279, CD281, CD282, CD283, CD284, CD285, CD286, CD287, CD288, CD289, CD290, CD291, CD292, CD293, CD294, CD295, CD296, CD297, CD298, CD299, CD300, CD300a, CD300b, CD300c, CD301, CD302, CD303, CD304, CD305, CD306, CD307, CD307a, CD307b, CD307c, CD307d, CD307e, CD307f, CD308, CD309, CD310, CD311, CD312, CD313, CD314, CD315, CD316, CD317, CD318, CD319, CD320, CD321, CD322, CD323, CD324, CD325, CD326, CD327, CD328, CD329, CD330, CD331, CD332, CD333, CD334, CD335, CD336, CD337, CD338, CD339, CD340, CD341, CD342, CD343, CD344, CD345, CD346, CD347, CD348, CD349, CD350, CD351, CD352, CD353, CD354, CD355, CD356, CD357, CD358, CD359, CD360, CD361, CD362, CD363, CD364, CD365, CD366, CD367, CD368, CD369, CD370, CD371, CD372, CD373, CD374, CD375, CD376, CD377, CD378, CD379, CD381, CD382, CD383, CD384, CD385, CD386, CD387, CD388, CD389, CRIPTO, CRIPTO, CR, CR1, CRGF, CRIPTO, CXCR5, LY64, TDGF1, 4-1BB, APO2, ASLG659, BMPR1B, 4-1BB, 5AC, 5T4 (trophoblastic glycoprotein, TPBG, 5T4, Wnt-activated inhibitory factor 1 or WAIF1), adenocarcinoma antigen, AGS-5, AGS-22M6, activin receptor-like kinase 1, AFP, AKAP-4, ALK, alpha integrin, alpha v beta6, amino-peptidase N, Amyloid beta, androgen receptor, angiopoietin 2, angiopoietin 3, annexin A1, anthrax toxin protective antigen, anti-transferrin receptor, AOC3 (VAP-1), B7-H3, Bacillus anthracis anthrax, BAFF (B-cell activating factor),

BCMA, B-lymphoma cell, bcr-abl, Bombesin, BORIS, C5, C242 antigen, CA125 (carbohydrate antigen 125, MUC16), CA-IX (or CAIX, carbonic anhydrase 9), CALLA, CanAg, Canis lupus familiaris IL31, carbonic anhydrase IX, cardiac myosin, CCL11(C-C motif chemokine 11), CCR4 (C-C chemokine receptor type 4), CCR5, CD3E (epsilon), CEA (carcinoembryonic antigen), CEACAM3, CEACAM5 (carcino-embryonic antigen), CFD (Factor D), Ch4D5, cholecystokinin 2 (CCK2R), CLDN18 (Claudin-18), CLDN18.2 (Claudin-18.2), clumping factor A, cMet, CRIPTO, FCSF1R (colony stimulating factor 1 receptor), CSF2 (colony stimulating factor 2, granulocyte-macrophage colony-stimulating factor (GM-CSF)), CSP4, CTLA4 (cytotoxic T-lymphocyte-associated protein 4), CTAA16.88 tumor antigen, CXCR4, C-X-C chemokine receptor type 4, cyclic ADP ribose hydrolase, cyclin B1, CYP1B1, cytomegalovirus, cytomegalovirus glycoprotein B, Dabigatran, DLL3 (delta-like-ligand 3), DLL4 (delta-like-ligand 4), DPP4 (dipeptidyl-peptidase 4), DR5 (feath receptor 5), E. coli shiga toxin type-1, E. coli shiga toxin type-2, ED-B, EGFL7 (EGF-like domain-containing protein 7), EGFR, EGFRII, EGFRvIII, endoglin, endothelin B receptor, endotoxin, EpCAM (epithelial cell adhesion molecule), EphA2, Episialin, ERBB2 (epidermal growth factor receptor 2), ERBB3, ERG (TMPRSS2 ETS fusion gene), Escherichia coli, ETV6-AML, FAP (fibroblast activation protein alpha), FCGR1, alpha-Fetoprotein, Fibrin II, beta chain, fibronectin extra domain-B, FOLR (folate receptor), folate receptor alpha, folate hydrolase, Fos-related antigen 1F protein of respiratory syncytial virus, frizzled receptor, fucosyl GM1, GD2 ganglioside, G-28 (a cell surface antigen glycolipid), GD3 idiootype, GloboH, glypican 3, N-glycolylneuraminic acid, GM3, GMCSF receptor α -chain, growth differentiation factor 8, GP100, GPNMB (trans-membrane glycoprotein NMB), GUCY2C (guanylate cyclase 2C, guanylyl cyclase C(GC-C), intestinal guanylate cyclase, guanylate cyclase-C receptor, heat-stable enterotoxin receptor (hSTAR)), heat shock proteins, hemagglutinin, hepatitis B surface antigen, hepatitis B virus, HER1 (human epidermal growth factor receptor 1), HER2, HER2/neu, HER3 (ERBB-3), IgG4, HGF/SF (Hepatocyte growth factor/scatter factor), HHGFR, HIV-1, histone complex, HLA-DR (human leukocyte antigen), HLA-DR10, HLA-DRB, HMWMAA, human chorionic gonadotropin, HNGF, human scatter factor receptor kinase, HPV E6/E7, Hsp90, hTERT, ICAM-1 (Intercellular Adhesion Molecule 1), idiootype, IGF1R (IGF-1, insulin-like growth factor 1 receptor), IGHE, IFN- γ , Influenza hemagglutinin, IgE, IgE Fc region, IGHE, interleukins (comprising IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6R, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-17, IL-17A, IL-18, IL-19, IL-20, IL-21, IL-22, IL-23, IL-27, or IL-28), IL31RA, ILGF2 (insulin-like growth factor 2), Integrins (α 4, α IIb β 3, α v β 3, α 4 β 7, α 5 β 1, α 6 β 4, α 7 β 7, α IIb β 3, α 5 β 5, α v β 5), interferon gamma-induced protein, ITGA2, ITGB2, KIR2D, Kappa Ig, LCK, Le, Legumain, Lewis-Y antigen, LFA-1 (lymphocyte function-associated antigen 1, CD11a), LHRH, LINGO-1, lipoteichoic acid, LIV1A, LMP2, LTA, MAD-CT-1, MAD-CT-2, MAGE-1,

MAGE-2, MAGE-3, MAGE A1, MAGE A3, MAGE 4, MART1, MCP-1, MIF (macrophage migration inhibitory factor, or glycosylation-inhibiting factor (GIF)), MS4A1 (membrane-spanning 4-domains subfamily A member 1), MSLN (mesothelin), MUC1 (Mucin 1, cell surface associated (MUC1) or polymorphic epithelial mucin (PEM)), MUC1-KLH, MUC16 (CA125), MCP1 (monocyte chemotactic protein 1), MelanA/MART1, ML-IAP, MPG, MS4A1 (membrane-spanning 4-domains subfamily A), MYCN, myelin-associated glycoprotein, myostatin, NA17, NARP-1, NCA-90 (granulocyte antigen), Nectin-4 (ASG-22ME), NGF, neural apoptosis-regulated proteinase 1, NOGO-A, Notch receptor, nucleolin, neu oncogene product, NY-BR-1, NY-ESO-1, OX-40, Ox-LDL (oxidized low-density lipoprotein), OY-TES1, P21, p53 nonmutant, P97, Page4, PAP, paratope of anti-(N-glycolylneuraminic acid), PAX3, PAX5, PCSK9, PDCD1 (PD-1, programmed cell death protein 1), PDGF-R α (Alpha-type platelet-derived growth factor receptor), PDGFR- β , PDL-1, PLAC1, PLAP-like testicular alkaline phosphatase, platelet-derived growth factor receptor beta, phosphate-sodium co-transporter, PMEL 17, polysialic acid, proteinase3 (PR1), prostatic carcinoma, PS (Phosphatidylserine), prostatic carcinoma cells, pseudomonas aeruginosa, PSMA, PSA, PSCA, rabies virus glycoprotein, RHD (Rh polypeptide 1 (RhPI)), Rhesus factor, RANKL, RhoC, Ras mutant, RGS5, ROBO4, respiratory syncytial virus, RON, ROR1, Sarcoma translocation breakpoints, SART3, sclerostin, SLAMF7 (SLAM family member 7), Selectin P, SDC1 (Syndecan 1), sLe(a), Somatomedin C, SIP (Sphingosine-1-phosphate), Somatostatin, sperm protein 17, SSX2, STEAP1 (six-transmembrane epithelial antigen of the prostate 1), STEAP2, STn, TAG-72 (tumor associated glycoprotein 72), Survivin, T-cell receptor, T cell transmembrane protein, TEM1 (Tumor endothelial marker 1), TENB2, Tenascin C (TN-C), TGF- α , TGF- β (transforming growth factor beta), TGF- β 1, TGF- β 2 (transforming growth factor-beta 2), Tie (CD202b), Tie2, TIM-1 (CDX-014), Tn, TNF, TNF- α , TNFRSF8, TNFRSF10B (tumor necrosis factor receptor superfamily member 10B), TNFRSF-13B (tumor necrosis factor receptor superfamily member 13B), TPBG (trophoblast glycoprotein), TRAIL-R1 (tumor necrosis apoptosis inducing ligand receptor 1), TRAILR2 (death receptor 5 (DR5)), tumor-associated calcium signal transducer 2, tumor specific glycosylation of MUC1, TWEAK receptor, TYRP1 (glycoprotein 75), TRP-1 (Trop-1), TRP-2 (Trop-2), tyrosinase, VCAM-1, VEGF, VEGF-A, VEGF-2, VEGFR-1, VEGFR2, or vimentin, WT1, XAGE 1, or cells expressing any insulin growth factor receptors, or any epidermal growth factor receptors.

13. The conjugates according to claim **12**, wherein the tumor cell is selected from the group consisting of lymphoma cells, myeloma cells, renal cells, breast cancer cells, prostate cancer cells, ovarian cancer cells, colorectal cancer cells, gastric cancer cells, squamous cancer cells, small-cell lung cancer cells, none small-cell lung cancer cells, testicular cancer cells, or malignant cells.

14. A pharmaceutical composition comprising a therapeutically effective amount of the conjugates of any one of claim **1, 2, 3, 4, 5, 6, 8, 10, 12** or **13**, and a pharmaceutically acceptable salt, carrier, diluent, or excipient therefore, or a combination of the conjugates thereof, for the treatment or prevention of a cancer, or an autoimmune disease, or an infectious disease.

15. Use of the pharmaceutical composition according to claim **14** in the manufacture of a medicament for concurrent administration with a chemotherapeutic agent, a radiation therapy, an immunotherapy agent, an autoimmune disorder agent, an anti-infectious agents, other agents or the other conjugates for treatment or prevention of a cancer, or an autoimmune disease, or an infectious disease.

16. Use of the pharmaceutical composition according to claim **15**, wherein the chemotherapeutic agent is selected from any one or more of:

(1). a). an alkylating agent: selected from nitrogen mustards: chlorambucil, chlornaphazine, cyclophosphamide, dacarbazine, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, mannomustine, mitobronitol, melphalan, mitolactol, pipobroman, novembichin, phenesterine, prednimustine, thiotepa, trofosfamide, uracil mustard; CC-1065 and adozelesin, carzelesin, bizelesin or their synthetic analogues; duocarmycin and its synthetic analogues, KW-2189, CBI-TMI, or CBI dimers; benzodiazepine dimers or pyrrolobenzodiazepine (PBD) dimers, tomaymycin dimers, indolinobenzodiazepine dimers, imidazobenzothiadiazepine dimers, or oxazolidinobenzodiazepine dimers; nitrosoureas: comprising carmustine, lomustine, chlorozotocin, fotemustine, nimustine, ranimustine; alkylsulphonates: including busulfan, treosulfan, improsulfan and piposulfan); triazenes or dacarbazine; platinum containing compounds: comprising carboplatin, cisplatin, and oxaliplatin; aziridines, benzodopa, carboquone, meturedopa, or uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, trietylenephosphoramidate, triethylenethiophosphoramidate and trimethylolomelamine;

b). A plant alkaloid: selected from the group consisting of vinca alkaloids: including vincristine, vinblastine, vindesine, vinorelbine, and navelbin; taxoids: comprising paclitaxel, docetaxol and their analogs, maytansinoids including DM1, DM2, DM3, DM4, DM5, DM6, DM7, maytansine, ansamitocins and their analogs, cryptophycins (including the group of cryptophycin 1 and cryptophycin 8); epothilones, eleutherobin, discodermolide, bryostatins, dolostatins, auristatins, tubulysins, cephalostatins; pancratistatin; a sarcodictyin; spongistatin;

c). A DNA topoisomerase inhibitor: selected from the groups of epipodophyllins: comprising 9-aminocamptothecin, camptothecin, crisnatol, daunomycin, etoposide, etoposide phosphate, irinotecan, mitoxantrone, novantrone, retinoic acids (or retinols), teniposide, topotecan, 9-nitrocamptothecin or RFS 2000; and mitomycins and their analogs;

d). An antimetabolite: selected from the group consisting of [Anti-folate: (DHFR inhibitors: comprising methotrexate, trimetrexate, denopterin, pteropterin, aminopterin (4-aminopteroic acid) or folic acid analogues); IMP dehydrogenase inhibitors: (including mycophenolic acid, tiazofurin, ribavirin, EICAR); ribonucleotide reductase inhibitors (including hydroxyurea, deferoxamine)]; [pyrimidine analogs: uracil analogs (including ancitabine, azacitidine, 6-azauridine, capecitabine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, 5-Fluorouracil, floxuridine, rat- itrexed); cytosine analogs (including cytarabine, cytosine arabinoside, fludarabine); purine analogs (including azathioprine, fludarabine, mercaptopurine, thiamiprine, thioguanine)]; folic acid replenisher, frolic acid;

e). A hormonal therapy: selected from receptor antagonists [anti-estrogen (including megestrol, raloxifene, tamoxifen); LHRH agonists (including goserelin, leuprolide acetate); anti-androgens (including bicalutamide, flutamide, calusterone, dromostanolone propionate, epitioestanol, goserelin, leuprolide, mepitioestane, nilutamide, testolactone, trilostane and other androgens inhibitors)]; retinoids/deltoids [vitamin D3 analogs (including CB 1093, EB 1089 KH 1060, cholecalciferol, ergocalciferol)]; photodynamic therapies (including verteporfin, phthalocyanine, photosensitizer Pc4, demethoxyhypocrellin A); cytokines (comprising interferon-alpha, interferon-gamma, tumor necrosis factor (TNFs), human proteins containing a TNF domain)];

f). A kinase inhibitor, selected from the group consisting of BIBW 2992 (anti-EGFR/Erb2), imatinib, gefitinib, pegaptanib, sorafenib, dasatinib, sunitinib, erlotinib, nilotinib, lapatinib, axitinib, pazopanib, vandetanib, E7080 (anti-VEGFR2), mubritinib, ponatinib, bafetinib, bosutinib, cabozantinib, vismodegib, iniparib, ruxolitinib, CYT387, axitinib, tivozanib, sorafenib, bevacizumab, cetuximab, trastuzumab, ranibizumab, panitumumab, ispinesib;

g). A poly (ADP-ribose) polymerase (PARP) inhibitors selected from the group of olaparib, niraparib, iniparib, talazoparib, veliparib, CEP 9722 (Cephalon's), E7016 (Eisai's), BGB-290 (BeiGene's), or 3-aminobenzamide.

h). An antibiotic, selected from the group consisting of an enediyne antibiotic (selected from the group of calicheamicin, calicheamicin γ 1, δ 1, α 1 or β 1; dynemicin, including dynemicin A and deoxydynemicin; esperamicin, kedarcidin, C-1027, maduropeptin, or neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromomophores), aclacinomycins, actinomycin, anthramycin, azaserine, bleomycins, cactinomycin, carabacin, carminomycin, carzinophilin; chromomycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin, epirubicin, eribulin, esorubicin, idarubicin, marcellomycin, nitomycins, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin;

i). A polyketide (acetogenin), bullatacin and bullatacinone; gemcitabine, epoxomicins and carfilzomib, bortezomib, thalidomide, lenalidomide, pomalidomide, tosedostat, zybrestat, PLX4032, STA-9090, Stimuvax, allovectin-7, Xegeva, Provengé, Yervoy, isoprenylation inhibitors and lovastatin, dopaminergic neurotoxins and 1-methyl-4-phenylpyridinium ion, cell cycle inhibitors (including staurosporine), actinomycins (including actinomycin D, dactinomycin), amanitins, bleomycins (including bleomycin A2, bleomycin B2, peplomycin), anthracyclines (including daunorubicin, doxorubicin (adriamycin), idarubicin, epirubicin, pirarubicin, zorubicin, mtoxantrone, MDR inhibitors or verapamil, Ca^{2+} ATPase inhibitors or thapsigargin, histone deacetylase inhibitors (including vorinostat, romidepsin, panobinostat, valproic acid, mocetinostat (MGCD0103), belinostat, PCI-24781, entinostat, SB939, resminostat, givinostat, AR-42, CUDC-101, sulforaphane, trichostatin A); thapsigargin, celecoxib, glitazones, epigallocatechin gallate, disulfiram, salinosporamide A; anti-adrenals, selected from the group of aminoglutethimide, mitotane, trilostane; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; arabinoside, bestabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; eflornithine (DFMO), elfomithine; elliptinium acetate, etoglucid; gallium nitrate; gacytosine, hydroxyurea; ibandronate, lentinan; lonidamine; mitoguazone; mitoxantrone; mopidamol; nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK[®]; razoxane; rhizoxin; sizofiran; spirogermanium; tenuazonic acid; triaziquone; 2, 2', 2''-trichlorotriethylamine; trichothecenes (including the group of T-2 toxin, verrucarins A, roridin A and anguidine); urethane, siRNA, antisense drugs;

(2). An anti-autoimmune disease agent: cyclosporine, cyclosporine A, aminocaproic acid, azathioprine, bromocriptine, chlorambucil, chloroquine, cyclophosphamide, corticosteroids (including the group consisting of amcinonide, betamethasone, budesonide, hydrocortisone, flunisolide, fluticasone propionate, fluocortolone danazol, dexamethasone, Triamcinolone acetonide, beclomethasone dipropionate), DHEA, enanercept, hydroxychloroquine, infliximab, meloxicam, methotrexate, mofetil, mycophenylate, prednisone, sirolimus, tacrolimus.

(3). An anti-infectious disease agents comprising of:

a). Aminoglycosides: amikacin, astromicin, gentamicin (netilmicin, sisomicin, isepamicin), hygromycin B, kanamycin (amikacin, arbekacin, bekanamycin, dibekacin, tobramycin), neomycin (framycetin, paromomycin, ribostamycin), netilmicin, spectinomycin, streptomycin, tobramycin, verdamicin;

b). Amphenicols: azidamfenicol, chloramphenicol, florfenicol, thiamphenicol;

c). Ansamycins: geldanamycin, herbimycin;

d). Carbapenems: biapenem, doripenem, ertapenem, imipenem, cilastatin, meropenem, panipenem;

e). Cephems: carbacephem (loracarbef), cefacetrile, cefaclor, cefradine, cefadroxil, cefalonium, cefaloridine, cefalotin or cefalothin, cefalexin, cefaloglycin, cefamandole, cefapirin, cefatrizine, cefazaflur, cefazedone, cefazolin, cefbuperazone, cefcapene, cefdaloxime, cefepime, cefminox, cefoxitin, cefprozil, cefroxadine, ceftazidime, cefuroxime, cefixime, cefdinir, cefditoren, cefepime, cefetamet, cefmenoxime, cefodizime, cefonicid, cefoperazone, ceforanide, cefotaxime, cefotiam, cefozopran, cephalixin, cefpimizole, cefpiramide, cefpirome, cefpodoxime, cefprozil, cefquinome, cefsulodin, ceftazidime, ceftazidime, ceftibuten, ceftiolene, ceftizoxime, ceftobiprole, ceftriaxone, cefuroxime, cefuzonam, cephamycin (including cefoxitin, cefotetan, cefmetazole), oxacephem (flomoxef, latamoxef);

f). Glycopeptides: bleomycin, vancomycin (including oritavancin, telavancin), teicoplanin (dalbavancin), ramoplanin;

g). Glycylcyclines: tigecycline;

h). β -Lactamase inhibitors: penam (sulbactam, tazobactam), clavam (clavulanic acid);

i). Lincosamides: clindamycin, lincomycin;

j). Lipopeptides: daptomycin, A54145, calcium-dependent antibiotics (CDA);

k). Macrolides: azithromycin, cethromycin, clarithromycin, dirithromycin, erythromycin, flurithromycin, josamycin, ketolide (telithromycin, cethromycin), midecamycin, miocamycin, oleandomycin, rifamycins (rifampicin, rifampin, rifabutin, rifapentine), rokitamycin, roxithromycin, spectinomycin, spiramycin, tacrolimus (FK506), troleandomycin, telithromycin;

l). Monobactams: aztreonam, tigemonam;

m). Oxazolidinones: linezolid;

n). Penicillins: amoxicillin, ampicillin, pivampicillin, hetacillin, bacampicillin, metampicillin, talampicillin, azidocillin, azlocillin, benzylpenicillin, benzathine benzylpenicillin, benzathine phenoxymethylpenicillin, clometocillin, procaine benzylpenicillin, carbenicillin (carindacillin), cloxacillin, dicloxacillin, epicillin, flucloxacillin, mecillinam (pivmecillinam), mezlocillin, meticillin, nafcillin, oxacillin, penamecillin, penicillin, pheneticillin, phenoxymethylpenicillin, piperacillin, propicillin, sulbenicillin, temocillin, ticarcillin;

o). Polypeptides: bacitracin, colistin, polymyxin B;

p). Quinolones: alatrofloxacin, balofloxacin, ciprofloxacin, clinafloxacin, danofloxacin, difloxacin, enoxacin, enrofloxacin, floxin, garenoxacin, gatifloxacin, gemifloxacin, grepafloxacin, kano trovafloxacin, levofloxacin, lomefloxacin, marbofloxacin, moxifloxacin, nadifloxacin, norfloxacin, orbifloxacin, ofloxacin, pefloxacin, trovafloxacin, grepafloxacin, sitafloxacin, sparfloxacin, temafloxacin, tosufloxacin, trovafloxacin;

q). Streptogramins: pristinamycin, quinupristin/dalfopristin;

r). Sulfonamides: mafenide, prontosil, sulfacetamide, sulfamethizole, sulfanilimide, sulfasalazine, sulfisoxazole, trimethoprim, trimethoprim-sulfamethoxazole (co-trimoxazole);

s). Steroid antibacterials: selected from fusidic acid;

t). Tetracyclines: doxycycline, chlortetracycline, clomocycline, demeclocycline, lymecycline, meclocycline, metacycline, minocycline, oxytetracycline, penimepicycline, rolitetracycline, tetracycline, glycylcyclines (including tigecycline);

u). Other antibiotics: selected from the group consisting of annonacin, arspenamine, bactoprenol inhibitors (Bacitracin), DADAL/AR inhibitors (cycloserine), dictyostatin, discodermolide, eleutherobin, epothilone, ethambutol, etoposide, faropenem, fusidic acid, furazolidone, isoniazid, laulimalide, metronidazole, mupirocin, mycolactone, NAM synthesis inhibitors (fosfomycin), nitrofurantoin, paclitaxel, platensimycin, pyrazinamide, quinupristin/dalfopristin, rifampicin (rifampin), tazobactam tinidazole, uvaricin;

(4). Anti-viral drugs comprising of:

a). Entry/fusion inhibitors: aplaviroc, maraviroc, vicriviroc, *gp41* (enfuvirtide), PRO 140, CD4 (ibalizumab);

b). Integrase inhibitors: raltegravir, elvitegravir, globoidnan A;

c). Maturation inhibitors: bevirimat, vivecon;

d). Neuraminidase inhibitors: oseltamivir, zanamivir, peramivir;

e). Nucleosides & nucleotides: abacavir, aciclovir, adefovir, amdoxovir, apricitabine, brivudine, cidofovir, clevudine, dexelvucitabine, didanosine (ddI), elvucitabine, emtricitabine (FTC), entecavir, famciclovir, fluorouracil (5-FU), 3'-fluoro-substituted 2', 3'-dideoxynucleoside analogues (including the group consisting of 3'-fluoro-2',3'-dideoxythymidine (FLT) and 3'-fluoro-2',3'-dideoxyguanosine (FLG), fomivirsen, ganciclovir, idoxuridine, lamivudine (3TC), l-nucleosides (including the group consisting of β -l-thymidine and β -l-2'-deoxycytidine), penciclovir, racivir, ribavirin, stampidine, stavudine (d4T), taribavirin (viramidine), telbivudine, tenofovir, trifluridine valaciclovir, valganciclovir, zalcitabine (ddC), zidovudine (AZT);

f). Non-nucleosides: amantadine, ateviridine, capravirine, diarylpyrimidines (etravirine, rilpivirine), delavirdine, docosanol, emivirine, efavirenz, foscarnet (phosphonoformic acid), imiquimod, interferon alfa, loviride, lodenosine, methisazone, nevirapine, NOV-205, peginterferon alfa, podophyllotoxin, rifampicin, rimantadine, resiquimod (R-848), tromantadine;

g). Protease inhibitors: amprenavir, atazanavir, boceprevir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, pleconaril, ritonavir, saquinavir, telaprevir (VX-950), tipranavir;

h). Other types of anti-virus drugs: abzyme, arbidol, calanolide a, ceragenin, cyanovirin-n, diarylpyrimidines, epigallocatechin gallate (EGCG), foscarnet, griffithsin, taribavirin (viramidine), hydroxyurea, KP-1461, miltefosine, pleconaril, portmanteau inhibitors, ribavirin, seliciclib.

(5). The pharmaceutically acceptable salts, acids, hydrate or hydrated salt; or a crystalline structure; or an optical isomer, racemate, diastereomer or enantiomer of any of the above drugs.

17. Use of the pharmaceutical composition according to claim **15**, wherein the other agents are selected from one or several of the following drugs: Abatacept, Abemaciclib, Abiraterone acetate, Abraxane, Acetaminophen/hydrocodone, Acalabrutinib, Aducanumab, Adalimumab, ADXS31-142, ADXS-HER2, Afatinib dimaleate, Aldesleukin, Alectinib, Alemtuzumab, Alitretinoin, ado-Trastuzumab emtansine, Amphetamine/ dextroamphetamine, Anastrozole, Aripiprazole, Anthracyclines, Aripiprazole, Atazanavir, Atezolizumab, Atorvastatin, Avelumab, Axicabtagene ciloleucel, Axitinib, Belinostat, BCG Live, Bevacizumab, Bexarotene, Blinatumomab, Bortezomib, Bosutinib, Brentuximab vedotin, Brigatinib, Budesonide, Budesonide/ formoterol, Buprenorphine, Cabazitaxel, Cabozantinib, Capmatinib, Capecitabine, Carfilzomib, chimeric antigen receptor-engineered T (CAR-T) cells, Celecoxib, Ceritinib, Cetuximab, Chidamide, Ciclosporin, Cinacalcet, Crizotinib, Cobimetinib, Cosentyx, CTL019, Dabigatran, Dabrafenib, Dacarbazine, Daclizumab, Dacomotinib, Daptomycin, Daratumumab, Darbepoetin alfa, Darunavir, Dasatinib, Denileukin diftitox, Denosumab, Depakote, Dexlansoprazole, Dexmethylphenidate, Dexamethasone, Dinutuximab, Doxycycline, Duloxetine, Duvelisib, Durvalumab, Elotuzumab, Emtricitabine/Rilpivirine/Tenofovir, Disoproxil fumarate, Emtricitabine/Tenofovir/Efavirenz, Enoxaparin, ensartinib, Enzalutamide, Epoetin alfa, Erlotinib, Esomeprazole, Eszopiclone, Etanercept, Everolimus, Exemestane, Everolimus, Exenatide ER, Ezetimibe, Ezetimibe/simvastatin, Fenofibrate, Filgrastim, Fingolimod, Fluticasone propionate, Fluticasone/salmeterol, Fulvestrant, Gazyva, Gefitinib, Glatiramer, Goserelin acetate, Icotinib, Imatinib, Ibritumomab tiuxetan, Ibrutinib, Idelalisib, Ifosfamide, Infliximab, Imiquimod, ImmuCyst, Immuno BCG, Iniparib, Insulin aspart, Insulin detemir, Insulin glargine, Insulin lispro, Interferon alfa, Interferon alfa-1b, Interferon alfa-2a, Interferon alfa-2b, Interferon beta, Interferon beta 1a, Interferon beta 1b, Interferon gamma-1a, lapatinib, Ipilimumab, Ipratropium bromide/ salbutamol, Ixazomib, Kanuma, Lanreotide acetate, Lenalidomide, Lenaliomide, Lenvatinib mesylate, Letrozole, Levothyroxine, Levothyroxine, Lidocaine, Linezolid, Liraglutide, Lisdexamfetamine, LN-144, Lorlatinib, Memantine, Methylphenidate, Metoprolol, Mekinist, Mericitabine/ Rilpivirine/Tenofovir, Modafinil, Mometasone, Mycidac-C, Necitumumab, Neratinib, Nilotinib, Nivolumab, Ofatumumab, Obinutuzumab, Olaparib, Olmesartan, Olmesartan/ hydrochlorothiazide, Omalizumab, Omega-3 fatty acid ethyl esters, Oncorine, Oseltamivir, Osimertinib, Oxycodone, palbociclib, Palivizumab, Panitumumab, Panobinostat, Pazopanib, Pembrolizumab, PD-1 antibody, PD-L1 antibody, Pemetrexed, Pertuzumab, Pneumococcal conjugate vaccine, Pomalidomide, Pregabalin, ProscarVax, Propranolol, Quetiapine, Rabeprazole, Radium 223 chloride, Raloxifene, Raltegravir, Ramucirumab, Ranibizumab, Regorafenib, Ribociclib, Rituximab, Rivaroxaban,

Romidepsin, Rosuvastatin, Ruxolitinib phosphate, Salbutamol, Savolitinib, Semaglutide, Sevelamer, Sildenafil, Siltuximab, Sipuleucel-T, Sitagliptin, Sitagliptin/metformin, Solifenacin, Solanezumab, Sonidegib, Sorafenib, Sunitinib, Tacrolimus, Tacrimus, Tadalafil, Tamoxifen, Tafenlar, Talimogene laherparepvec, Talazoparib, Telaprevir, Talazoparib, Temozolomide, Temsirolimus, Tenofovir/ emtricitabine, Tenofovir disoproxil fumarate, Testosterone gel, Thalidomide, TICE BCG, Tiotropium bromide, Tisagenlecleucel, Toremifene, Trametinib, Trastuzumab, Trabectedin (ecteinascidin 743), Trametinib, Tremelimumab, Trifluridine/tipiracil, Tretinoin, Uro-BCG, Ustekinumab, Valsartan, Veliparib, Vandetanib, Vemurafenib, Venetoclax, Vorinostat, Ziv-aflibercept, Zostavax, and their pharmaceutically acceptable salts, carriers, diluents, or excipients thereof, or a combination above thereof.