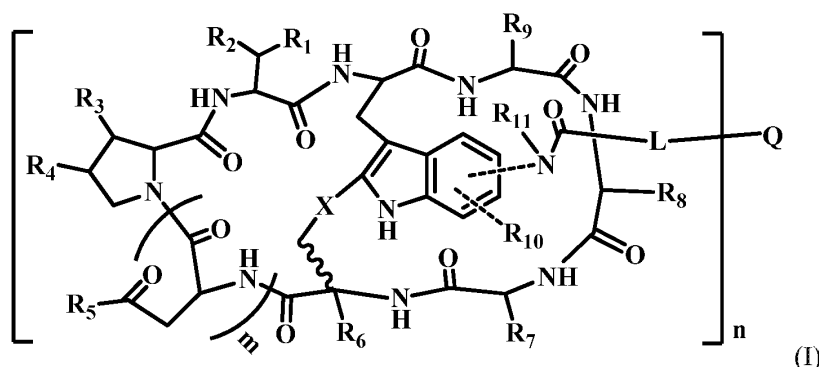


CLAIMS

1. Compounds of Formula (I)



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

Wherein

----- represents a single bond that links any carbon position of the aromatic (indole) ring;

~~~~~ represents an optional single bond or an absent bond.

10 R<sub>1</sub> and R<sub>2</sub> are independently selected from H, OH, CH<sub>2</sub>OH, CH(OH)CH<sub>2</sub>OH, CH(CH<sub>3</sub>)CH<sub>2</sub>OH, CH(OH)CH<sub>3</sub>, C<sub>1</sub>-C<sub>8</sub> alkyl, -OR<sub>12</sub> (ether), C<sub>2</sub>-C<sub>8</sub> alkenyl, alkynyl, heteroalkyl, -OCOR<sub>12</sub> (ester), -OC(=O)OR<sub>12</sub> (carbonate), -OC(=O)NHR<sub>12</sub> (carbamate); C<sub>3</sub>-C<sub>8</sub> aryl, heterocyclic, carbocyclic, cycloalkyl, heterocycloalkyl, heteroaralkyl, alkylcarbonyl.

R<sub>3</sub> and R<sub>4</sub> are independently selected from H, OH, -OR<sub>12</sub> (ether), -OCOR<sub>12</sub> (ester), -OCOCH<sub>3</sub>  
 15 (acetate), -OCOOR<sub>12</sub> (carbonate), -OC(=O)NHR<sub>12</sub> (carbamate), -OP(O)(OR<sub>12</sub>)(OR<sub>12</sub>') (phosphate), OP(O)(NHR<sub>12</sub>)(NHR<sub>12</sub>') (phosphamide), O-SO<sub>3</sub><sup>-</sup>, or O-glycoside;

R<sub>5</sub> is selected from H, OH, NH<sub>2</sub>, NHOH, NHNH<sub>2</sub>, -OR<sub>12</sub>, -NHR<sub>12</sub>, NHNHR<sub>12</sub>, -NR<sub>12</sub>R<sub>12</sub>', N(H)(R<sub>12</sub>)R<sub>13</sub>CO(Aa)<sub>p</sub>, (an amino acid or peptide, wherein Aa is an amino acid or a polypeptide, p represents 0 - 6);

20 R<sub>6</sub> is selected from H, OH, CH<sub>2</sub>OH, CH(OH)CH<sub>2</sub>OH, CH(CH<sub>2</sub>OH)<sub>2</sub>, CH(CH<sub>3</sub>)OH, CH<sub>2</sub>CH<sub>2</sub>OH, PrOH, BuOH, C<sub>1</sub>-C<sub>8</sub> alkyl, -OR<sub>12</sub> (ether), C<sub>2</sub>-C<sub>8</sub> alkenyl, alkynyl, heteroalkyl, -OCOR<sub>12</sub> (ester); C<sub>3</sub>-C<sub>8</sub> aryl, heterocyclic, or carbocyclic.

R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub> are independently selected from H, OH, CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>OH, CH(OH)CH<sub>2</sub>OH, CH<sub>2</sub>CH(OH)CH<sub>2</sub>OH, CH(CH<sub>2</sub>OH)<sub>2</sub>, CH<sub>2</sub>C(OH)(CH<sub>2</sub>OH)<sub>2</sub>,

CH<sub>2</sub>C(OH)(CH<sub>3</sub>)(CH<sub>2</sub>OH), CH<sub>2</sub>C(OH)(CH(CH<sub>3</sub>)<sub>2</sub>)(CH<sub>2</sub>OH), CH<sub>2</sub>CH<sub>2</sub>OH, PrOH, BuOH, CH<sub>2</sub>COOH, CH<sub>2</sub>CH<sub>2</sub>COOH, CH(OH)COOH, CH<sub>2</sub>CONH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CONH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHC(=NH)NH<sub>2</sub>, C<sub>1</sub>~C<sub>8</sub> alkyl, CH<sub>2</sub>Ar, CH<sub>2</sub>SH, CH<sub>2</sub>SR<sub>12</sub>, CH<sub>2</sub>SSR<sub>12</sub>, CH<sub>2</sub>SSAr, CH<sub>2</sub>CH<sub>2</sub>SCH<sub>3</sub>, -OR<sub>12</sub> (ether), C<sub>2</sub>~C<sub>8</sub> alkenyl, alkynyl, heteroalkyl, -OCOR<sub>12</sub> (ester); C<sub>3</sub>~C<sub>8</sub> aryl,

5 heterocyclic, or carbocyclic.

R<sub>10</sub> is selected from H, NH<sub>2</sub>, OH, SH, NO<sub>2</sub>, halogen, -NHOH, -N<sub>3</sub> (azido); -CN (cyano); C<sub>1</sub>~C<sub>8</sub> alkyl, C<sub>2</sub>~C<sub>8</sub> alkenyl, alkynyl, heteroalkyl; C<sub>3</sub>~C<sub>8</sub> aryl, heterocyclic, or carbocyclic; -OR<sub>12</sub> (ether), -OCOR<sub>12</sub> (ester), -OCOCH<sub>3</sub> (acetate), -OC(O)OR<sub>12</sub> (carbonate), -OC(O)CH(R<sub>12</sub>)NHAA (Aa is an amino acid group), -NR<sub>12</sub>R<sub>12</sub>' (amine), -NR<sub>12</sub>COR<sub>12</sub>' (amine), -NR<sub>12</sub>NR<sub>12</sub>'NR<sub>12</sub>' (amine); -OCONR<sub>12</sub>R<sub>12</sub>' (carbamate);  
 10 -NR<sub>12</sub>(C=NH)NR<sub>12</sub>'R<sub>12</sub>' (guanidinium); -NR<sub>12</sub>CO(Aa)<sub>p</sub>, (an amino acid or peptide, wherein Aa is an amino acid or a polypeptide, p represents 0 - 6); -N(R<sub>12</sub>)CONR<sub>12</sub>'R<sub>12</sub>' (urea); -OCSNHR<sub>12</sub> (thiocarbamate); -SH (thiol); -SR<sub>12</sub> (sulfide); -S(O)R<sub>12</sub> (sulfoxide); -S(O<sub>2</sub>)R<sub>12</sub> (sulfone); -SO<sub>3</sub>, HSO<sub>3</sub>, HSO<sub>2</sub>, or a salt of HSO<sub>3</sub><sup>-</sup>, SO<sub>3</sub><sup>2-</sup> or -HSO<sub>2</sub><sup>-</sup> (sulphite); -OSO<sub>3</sub><sup>-</sup>; -N(R<sub>12</sub>)SOOR<sub>12</sub>' (sulfonamide); H<sub>2</sub>S<sub>2</sub>O<sub>5</sub> or a salt of S<sub>2</sub>O<sub>5</sub><sup>2-</sup> (metabisulfite); PO<sub>3</sub>SH<sub>3</sub>, PO<sub>2</sub>S<sub>2</sub>H<sub>2</sub>, POS<sub>3</sub>H<sub>2</sub>, PS<sub>4</sub>H<sub>2</sub> or a salt of PO<sub>3</sub>S<sup>3-</sup>, PO<sub>2</sub>S<sub>2</sub><sup>3-</sup>, POS<sub>3</sub><sup>3-</sup>,  
 15 PS<sub>4</sub><sup>3-</sup> (mono-, di-, tri-, and tetra-thiophosphate); (R<sub>12</sub>O)<sub>2</sub>POSR<sub>12</sub>' (thiophosphate ester); HS<sub>2</sub>O<sub>3</sub> or a salt of S<sub>2</sub>O<sub>3</sub><sup>2-</sup> (thiosulfate); HS<sub>2</sub>O<sub>4</sub> or a salt of S<sub>2</sub>O<sub>4</sub><sup>2-</sup> (dithionite); (P(=S)(OR<sub>12</sub>)(S)(OH) or a salt formed with a cation (phosphorodithioate); -N(R<sub>12</sub>)OR<sub>12</sub>' (hydroxylamine derivative); R<sub>12</sub>C(=O)NOH or a salt formed with a cation (hydroxamic acid); (HOCH<sub>2</sub>SO<sub>2</sub><sup>-</sup>, or its salts (formaldehyde sulfoxylate); -N(R<sub>12</sub>)COR<sub>12</sub>' (amide); R<sub>12</sub>R<sub>12</sub>'R<sub>12</sub>'NPO<sub>3</sub>H (trialkylphosphor-amidate or phosphoramidic acid); or ArAr'Ar''NPO<sub>3</sub>H  
 20 (triarylphosphonium); OP(O)(OM<sub>1</sub>)(OM<sub>2</sub>), OCH<sub>2</sub>OP(O)(OM<sub>1</sub>)(OM<sub>2</sub>), OSO<sub>3</sub>M<sub>1</sub>; O-glycoside (glucoside, galactoside, mannoside, glucuronoside, alloside, fructoside, etc), NH-glycoside, S-glycoside or CH<sub>2</sub>-glycoside; M<sub>1</sub> and M<sub>2</sub> are independently H, Na, K, Ca, Mg, NH<sub>4</sub>, NR<sub>1</sub>'R<sub>2</sub>'R<sub>3</sub>'; R<sub>1</sub>', R<sub>2</sub>' and R<sub>3</sub>' are independently H, C<sub>1</sub>~C<sub>8</sub> alkyl; Ar, Ar', and Ar'' are C<sub>3</sub>~C<sub>8</sub> aryl or heteroaromatic group.

R<sub>11</sub> is H, C<sub>1</sub>~C<sub>8</sub> alkyl; C<sub>2</sub>~C<sub>8</sub> alkenyl, alkynyl, heteroalkyl; C<sub>3</sub>~C<sub>8</sub> aryl, heteroaryl.

25 R<sub>12</sub>, R<sub>12</sub>', and R<sub>12</sub>' are independently selected from H, C<sub>1</sub>~C<sub>8</sub> alkyl; C<sub>2</sub>~C<sub>8</sub> alkenyl, alkynyl, heteroalkyl; C<sub>3</sub>~C<sub>8</sub> aryl, heteroaryl, heterocyclic, or carbocyclic.

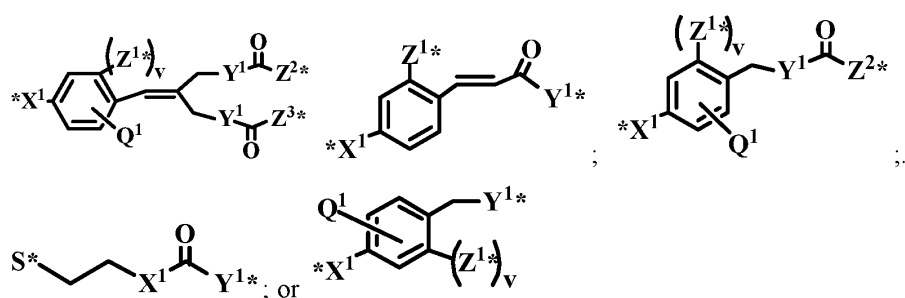
X is S, O, NH, SO, SO<sub>2</sub>, or CH<sub>2</sub>.

m is 0 or 1; n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20.

L is a linker or a linker-cell-binding molecule (Q) covalently bound cluster, or a linker which has a  
 30 functional group on the linker that enables linkage with a cell-binding agent (CBA). L is preferably a releasable linker, which has the formula of: -Ww-(Aa)r-Tt-; or -Ww-(Aa)r-Tt-Q; or Q-Ww-(Aa)r-Tt-; wherein W is a Stretcher unit; w is 0 or 1; Aa is an Amino Acid unit comprising

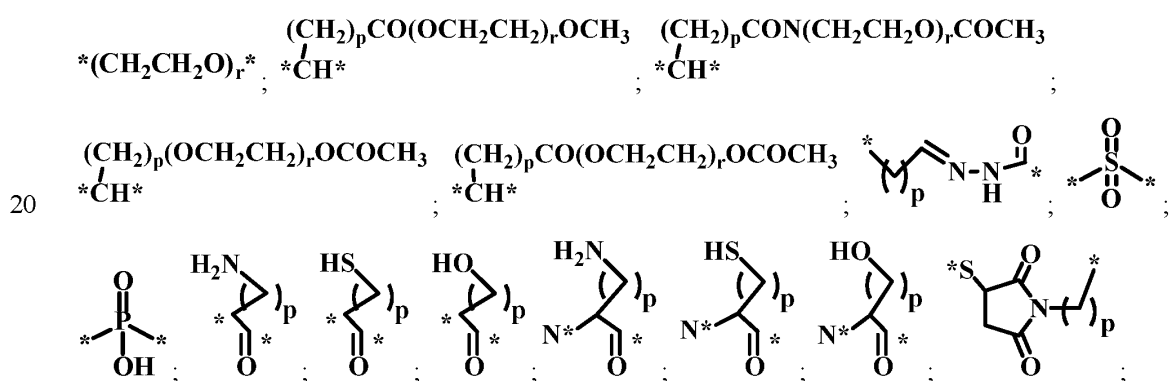
independent amino acids;  $r$  is an integer ranging from 0 to 100. The Stretcher unit  $W$  may contain a self-immolative or a non-self-immolative component, peptidyl units, a hydrazone bond, a disulfide, an ester, an oxime, an amide, or a thioether bond. The self-immolative unit includes, aromatic compounds that are electronically similar to the para-aminobenzylcarbamoyl (PAB) groups, 2-aminoimidazol-5-

5 methanol derivatives, heterocyclic PAB analogs, beta-glucuronide, and ortho or para-aminobenzylacetals. Preferably, the self-immolative linker component has one of the following structures:

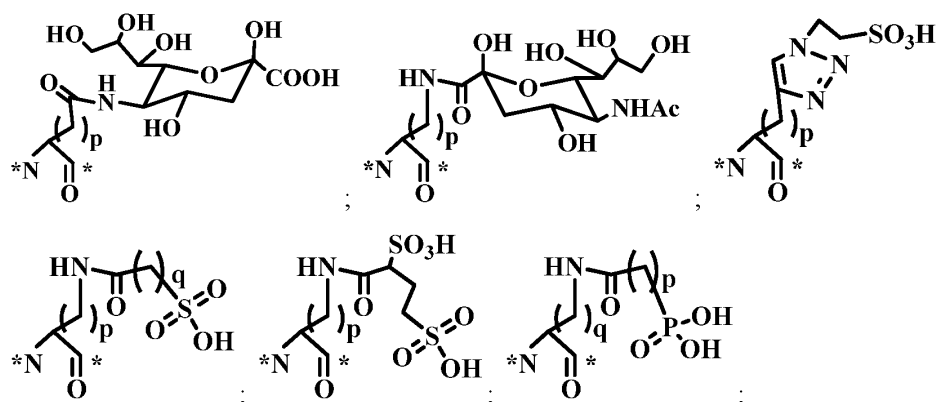


- 10 wherein the (\*) atom is the point of attachment of additional spacer or releasable linker units, or the cytotoxic agent, and/or the binding agent/molecule (CBA);  $X^1$ ,  $Y^1$ ,  $Z^2$  and  $Z^3$  are independently NH, O, or S;  $Z^1$  is independently H, NH, O or S;  $v$  is 0 or 1;  $Q^1$  is independently H, OH,  $C_1\sim C_6$  alkyl,  $(OCH_2CH_2)_nF$ , Cl, Br, I,  $OR_{12}$ ,  $SR_{12}$ ,  $NR_{12}R_{12}'$ ,  $N=NR_{12}$ ,  $N=R_{12}$ ,  $NR_{12}R_{12}'$ ,  $NO_2$ ,  $SOR_{12}R_{12}'$ ,  $SO_2R_{12}$ ,  $SO_3R_{12}$ ,  $OSO_3R_{12}$ ,  $PR_{12}R_{12}'$ ,  $POR_{12}R_{12}'$ ,  $PO_2R_{12}R_{12}'$ ,  $OPO(OR_{12})(OR_{12}')$ , or  $OCH_2PO(OR_{12})(OR_{12}')$
- 15 wherein  $R_{12}$  and  $R_{12}'$  are as defined above; preferably  $R_{12}$  and  $R_{12}'$  are independently selected from H,  $C_1\sim C_8$  alkyl;  $C_2\sim C_8$  alkenyl, alkynyl, heteroalkyl;  $C_3\sim C_8$  aryl, heterocyclic, carbocyclic, cycloalkyl, heterocycloalkyl, heteroaralkyl, alkylcarbonyl; or pharmaceutical cation salts.

The non-self-immolative linker component is one of the following structures:



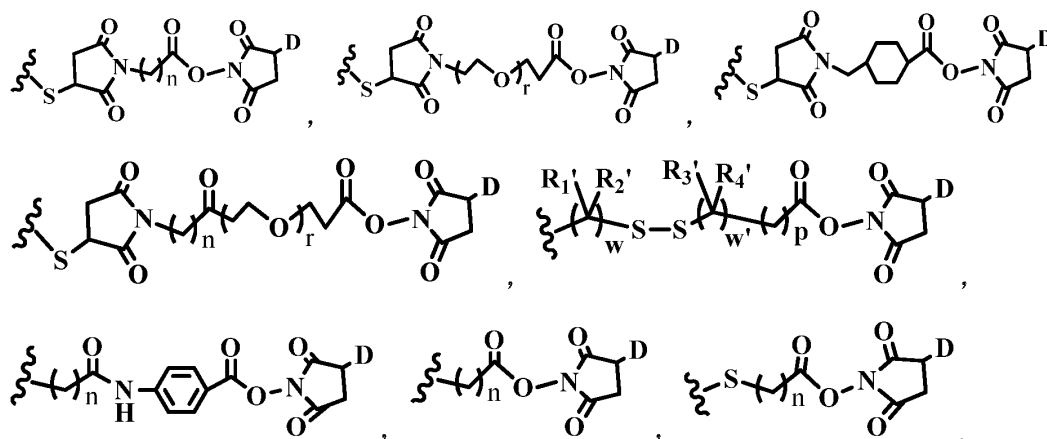


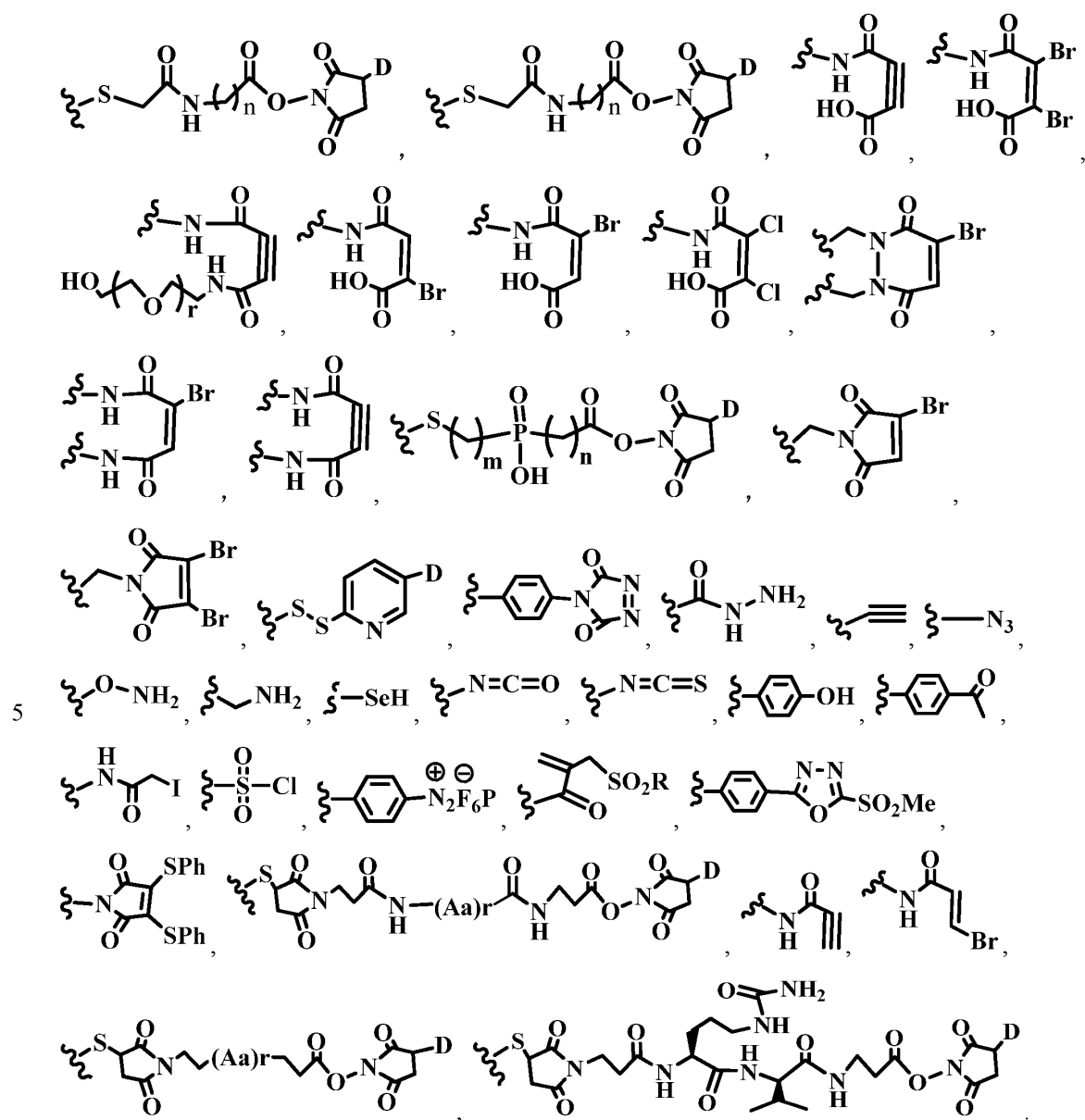


Wherein the (\*) atom is the point of attachment of additional spacer or releasable linkers, the cytotoxic agents, and/or the binding molecules;  $X^1$ ,  $Y^1$ ,  $Q^1$ ,  $R_{12}$ ,  $R_{12}'$  are defined as above;  $r$  is 0~100;  $p$  and  $q$  is independently selected from 0, 1, 2, 3, 4, 5 or 6.

Spacer (T) is a linear, branched or cyclic alkyl, alkenyl, alkynyl or aryl having from 1 to 10 carbon atoms, or T can be a polyethylene glycol ( $-\text{CH}_2\text{CH}_2\text{O}-$ ) spacer;  $t$  is 0, or 1~100. T can also undergo cyclization upon amide bond hydrolysis, such amides include substituted and unsubstituted 4-aminobutyric acid amides, appropriately substituted bicycle [2.2.1] and bicycle [2.2.2] ring systems, and 2-aminophenylpropionic acid amides.

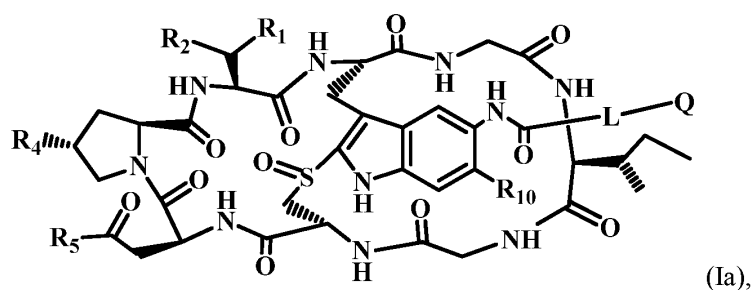
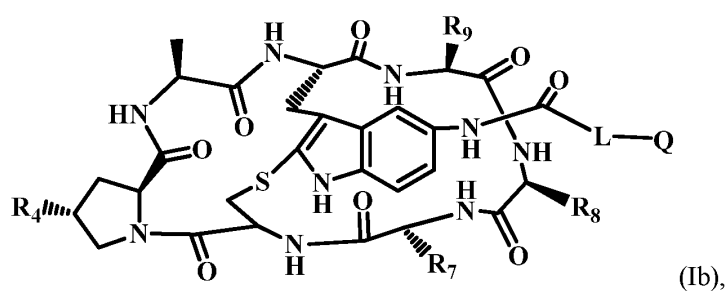
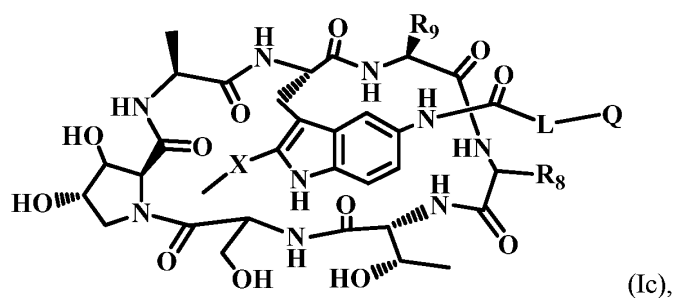
Q is a cell-binding agent/molecule (CBA), or a functional group that enables linkage with a cell-binding agent, or a functional group that enables linkage with a linker attached on a cell-binding agent. The function group is chosen from a thiol, an amine, a hydrazine, an alkoxyamino, a disulfide substituent, a maleimido, a haloacetyl group, a carboxy acid, an *N*-hydroxy succinimide ester, a ketone, an ester, an aldehyde, an alkynyl, an alkenyl, or a protected thiol or disulfide group: SAc, SSR<sub>1</sub> or SSR<sub>2</sub>. Ar is an aromatic group or hetero aromatic group. Q can be one of the following formulas:





Wherein D is H, -NO<sub>2</sub>, SO<sub>3</sub><sup>-</sup>, CN, or F; Aa, r, p, q, m, and n are described above); w and w' are 0 or 1  
 10 independently. R<sub>1</sub>', R<sub>2</sub>', R<sub>3</sub>', and R<sub>4</sub>' are independently H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, C<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>OH.

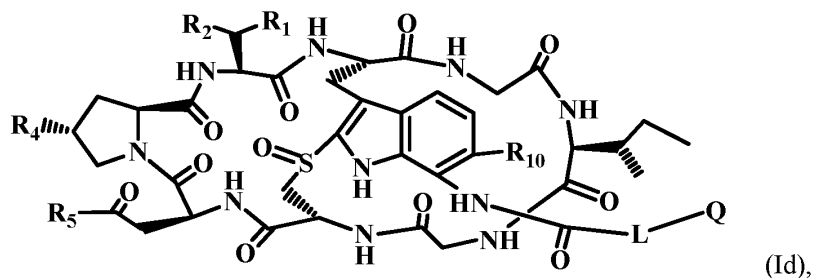
2. A compound according to Claim 1 having the following Formula (Ia) (Ib), and (Ic):



- or a pharmaceutically acceptable salt, hydrates, or hydrated salt, or the polymorphic  
 5 crystalline structure of the compounds thereof,  
 or the optical isomers, racemates, diastereomers or enantiomers.

Wherein  $R_1$ ,  $R_2$ ,  $R_4$ ,  $R_5$ ,  $R_7$ ,  $R_8$ ,  $R_9$ ,  $R_{10}$ ,  $L$  and  $Q$  are defined the same as in Claim 1.

3. A compound according to Claim 1 having the following Formula (Id) :

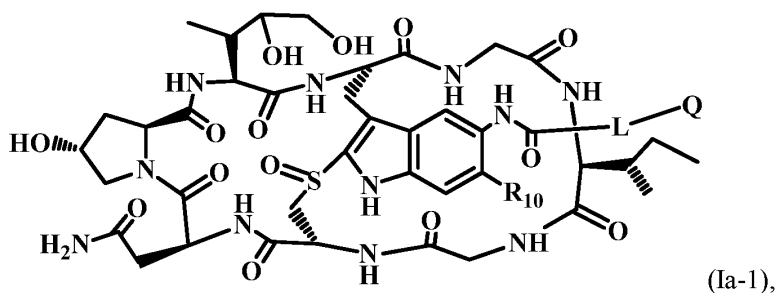
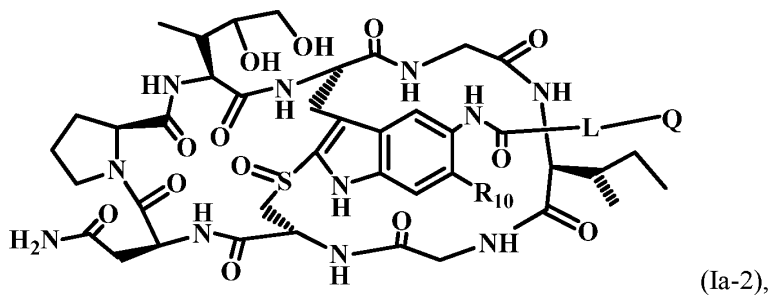
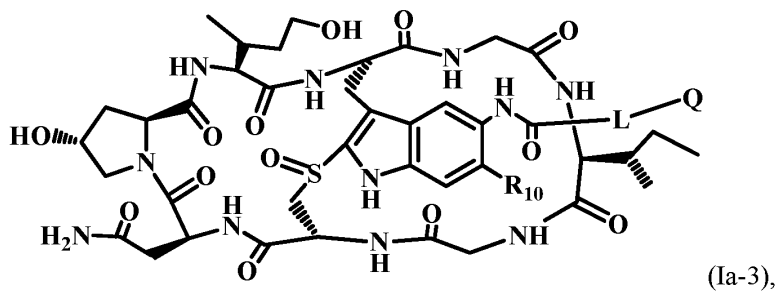
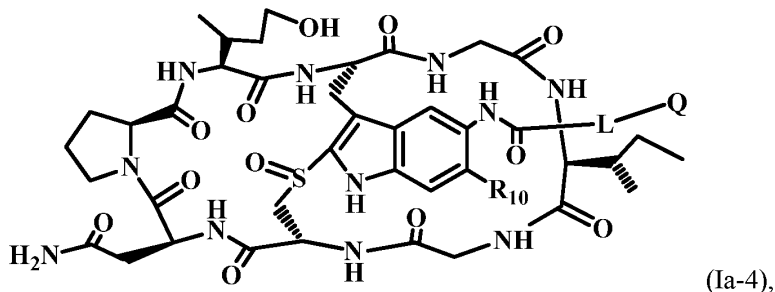


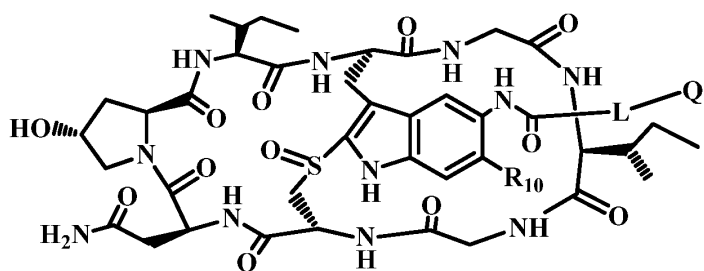
- 10 or a pharmaceutically acceptable salt, hydrates, or hydrated salt, or the polymorphic  
 crystalline structure of the compounds thereof,

or the optical isomers, racemates, diastereomers or enantiomers.

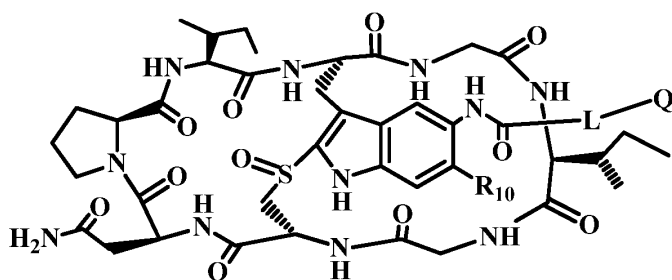
Wherein  $R_1$ ,  $R_2$ ,  $R_4$ ,  $R_5$ ,  $R_{10}$ , L and Q are defined the same as in Claim 1.

4. A compound according to Claim 1 having the following Formula (Ia-1), (Ia-2), (Ia-3), (Ia-4), (Ia-5), (Ia-6), (Ia-7), (Ia-8), (Ia-9), (Ia-10), (Ia-11), (Ia-12), (Ia-13), (Ia-14), (Ia-15), (Ia-16), (Ia-17),  
5 (Ia-18), (Ia-19), (Ia-20), (Ia-21), (Ia-22), (Ia-23), (Ia-24), (Ib-1), (Ib-2), (Ib-3), (Ib-4), (Ib-5), (Ib-6), (Ib-7), (Ic-1), (Ic-2), (Ic-3), (Ic-4), (Ic-5), and (Ic-6):

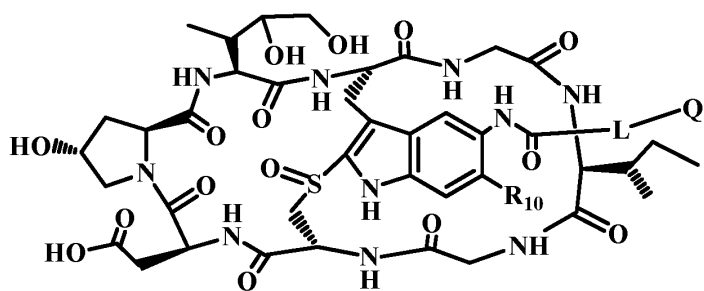




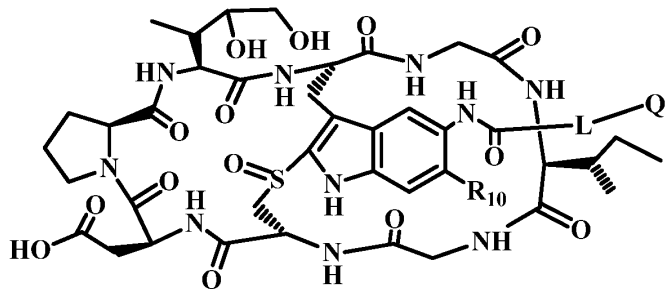
(Ia-5),



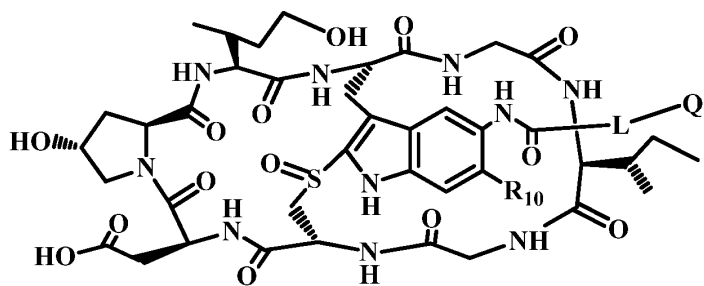
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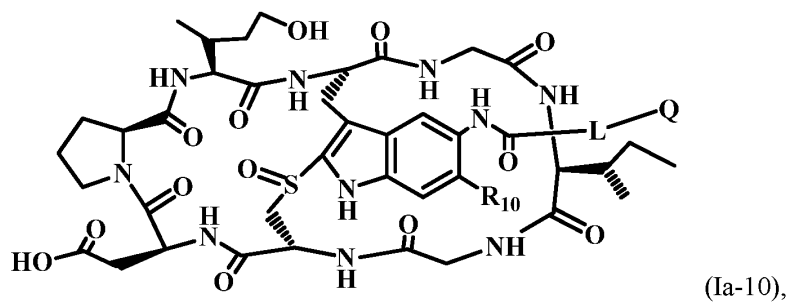
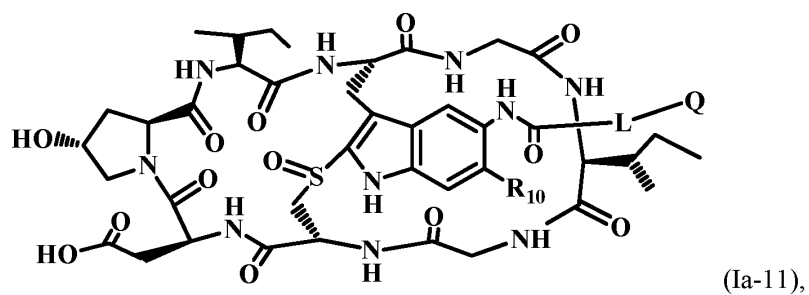
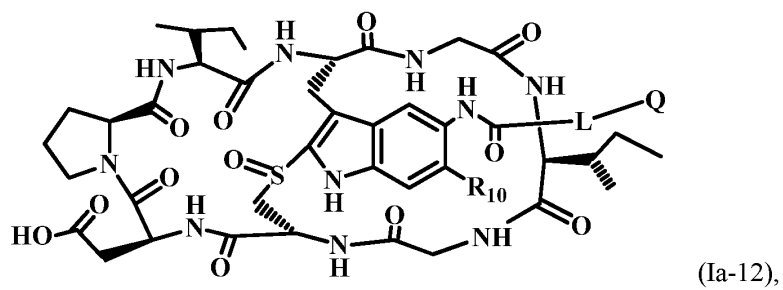
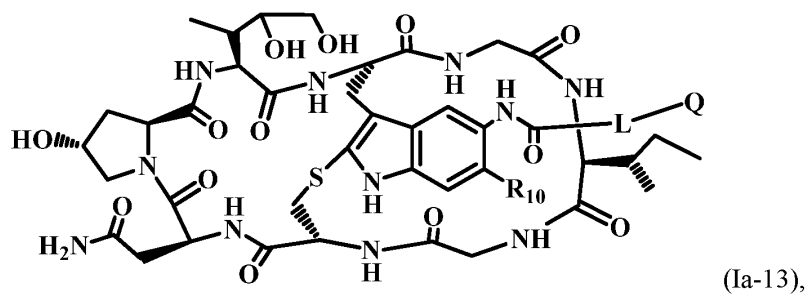
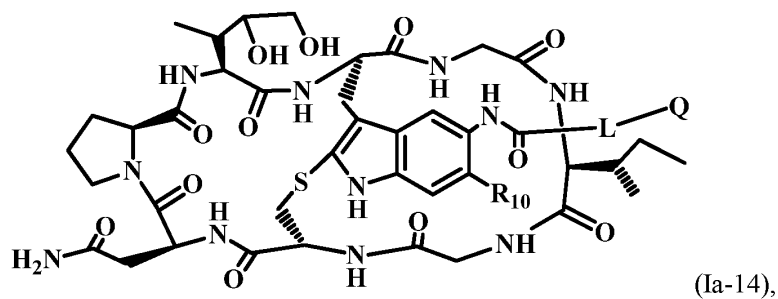
(Ia-7),

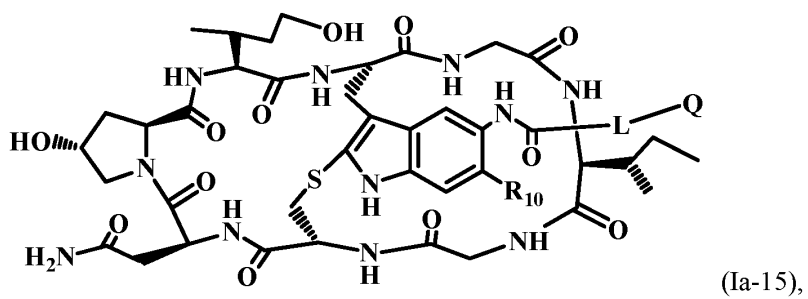
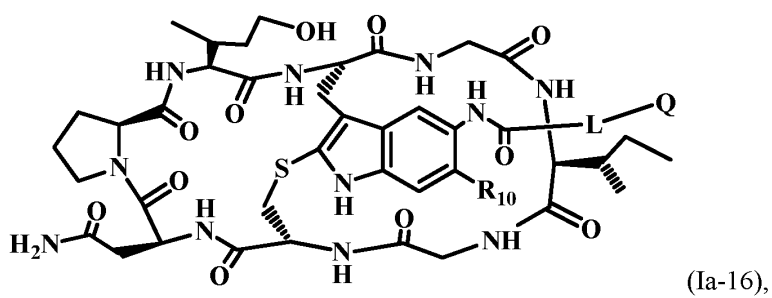
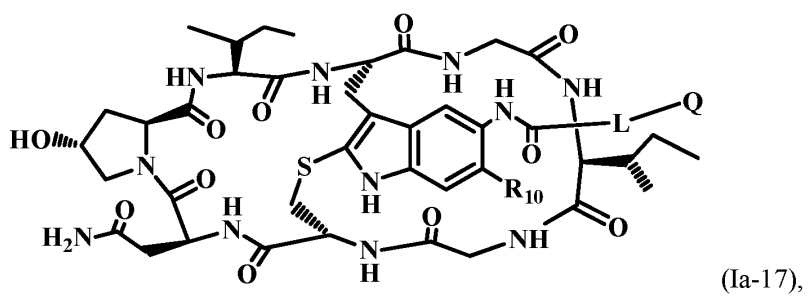
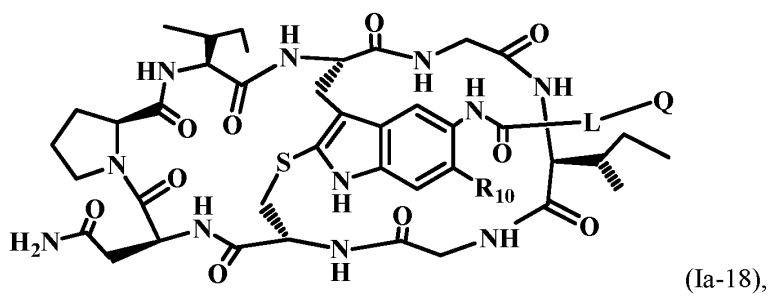
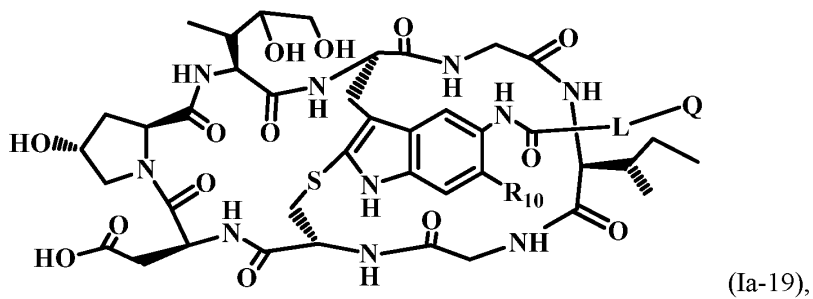


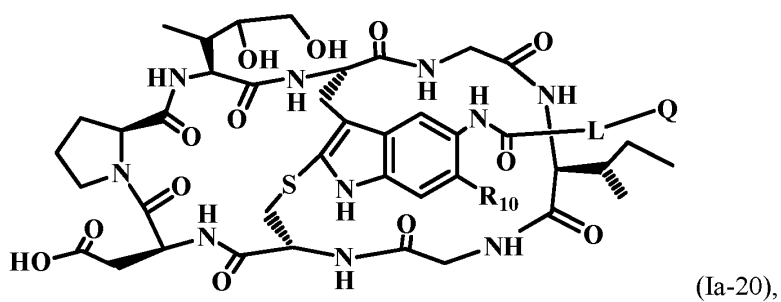
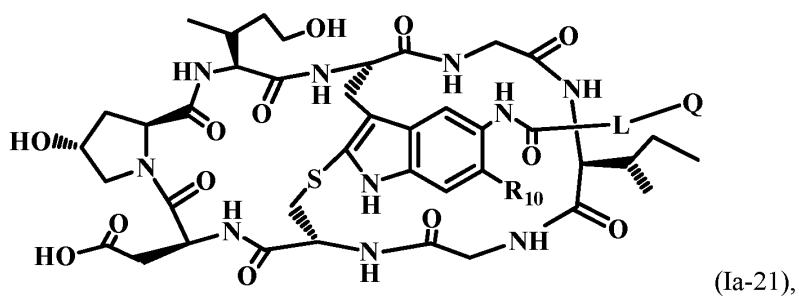
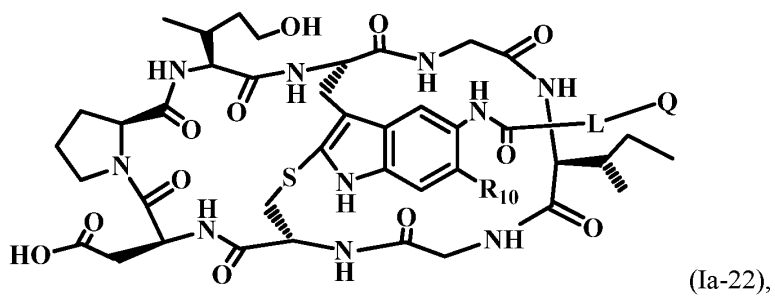
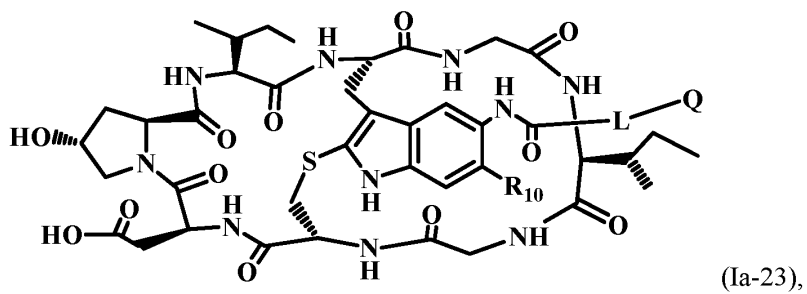
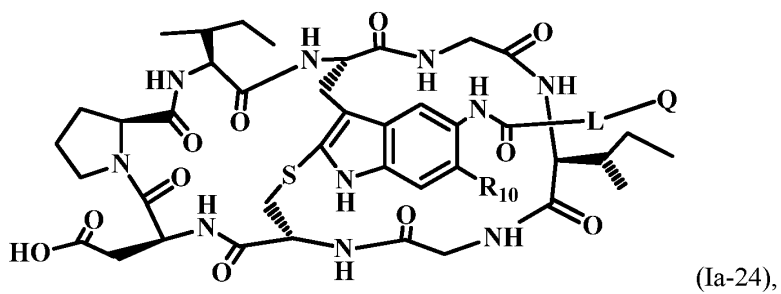
(Ia-8),

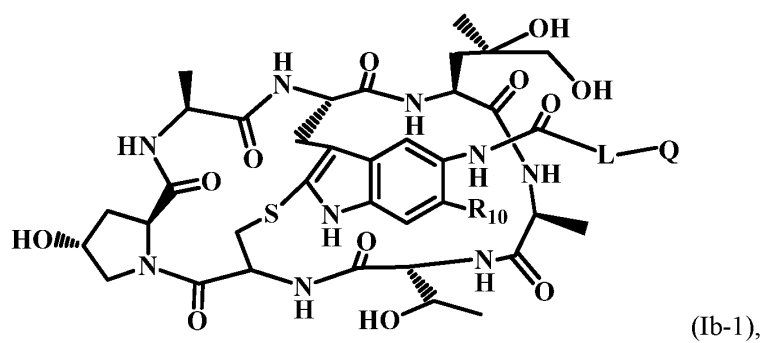
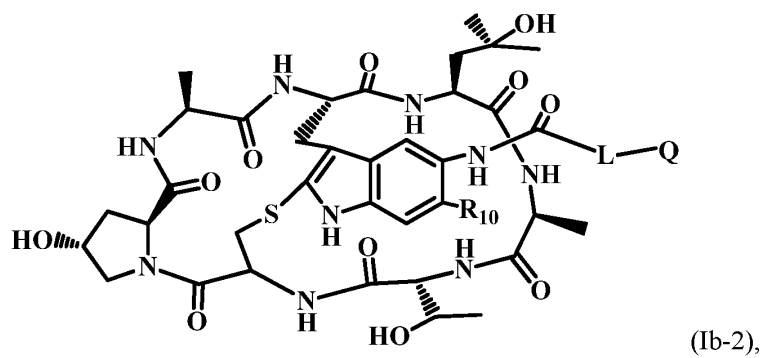
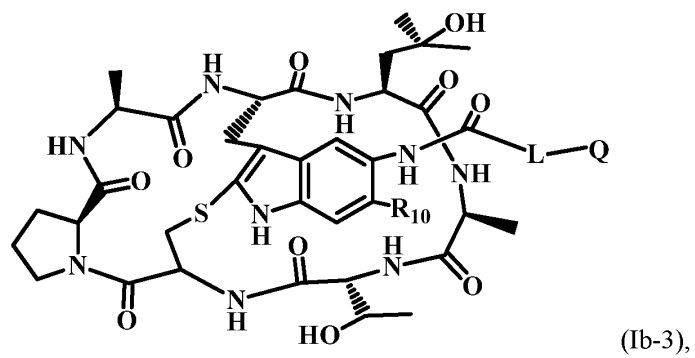
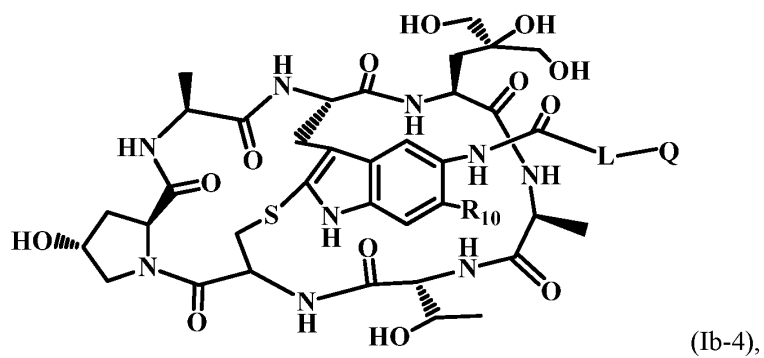


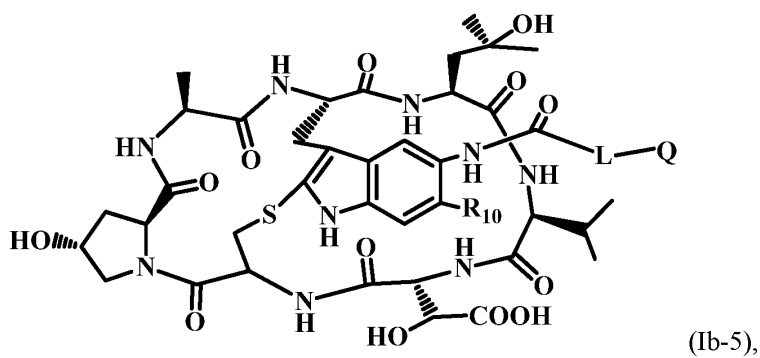
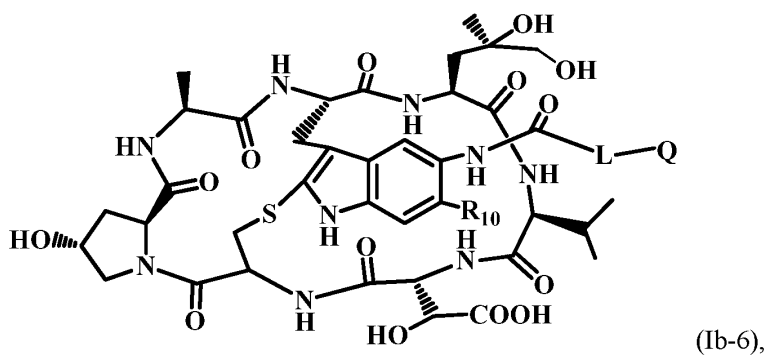
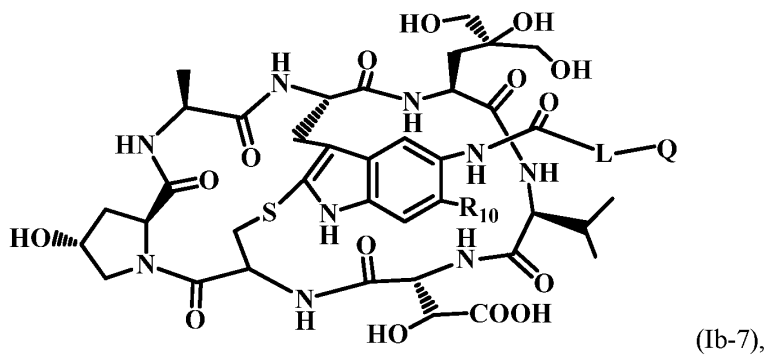
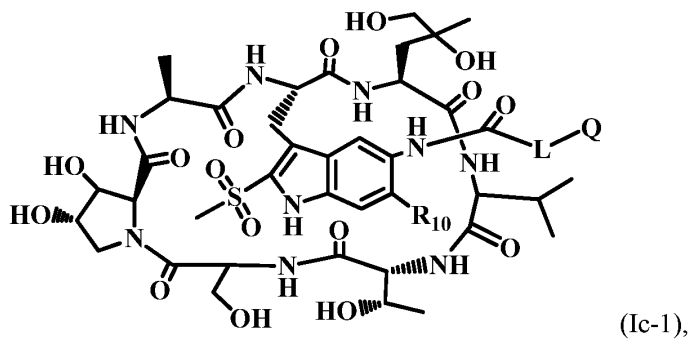
(Ia-9),

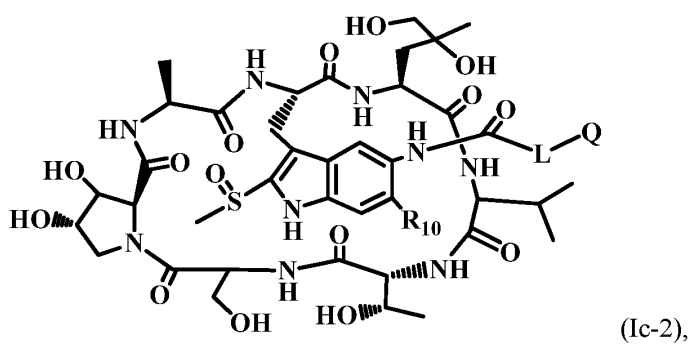
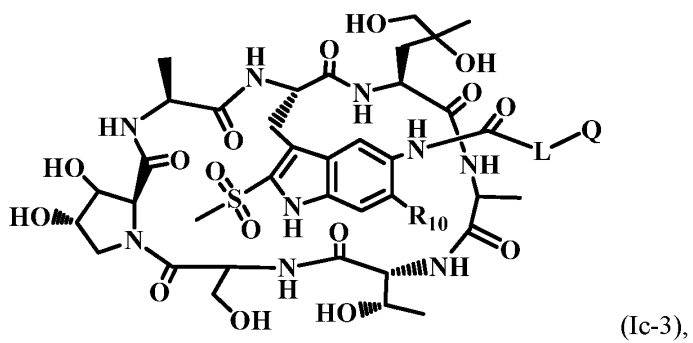
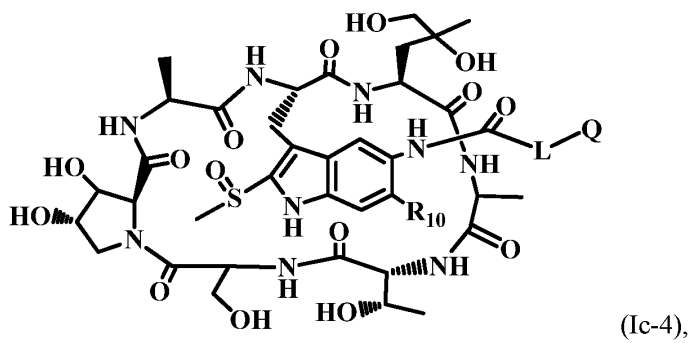
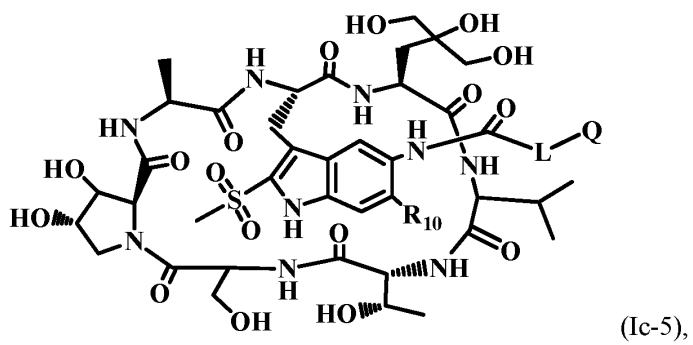


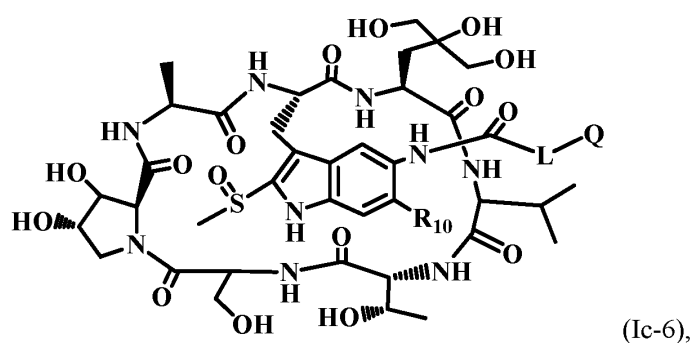










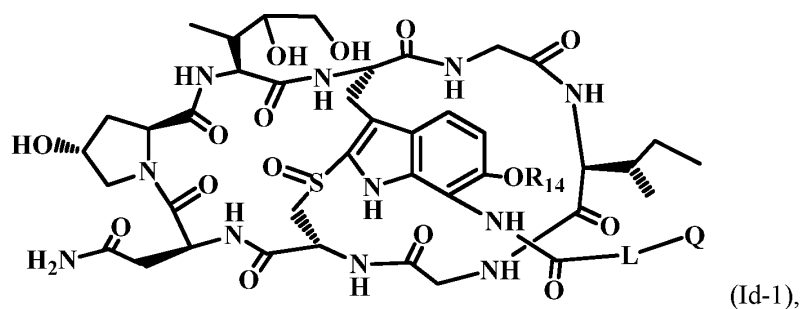
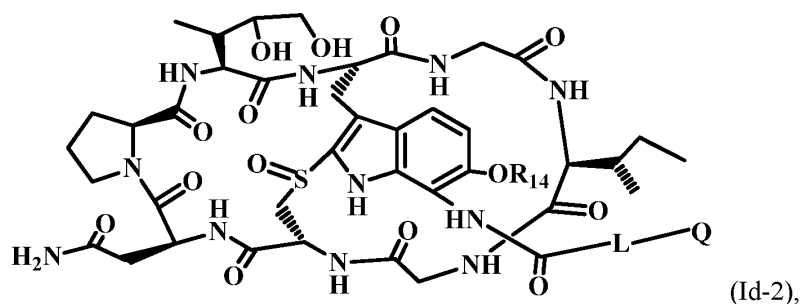


or a pharmaceutically acceptable salt, hydrates, or hydrated salt, or the polymorphic crystalline structure of the compounds thereof,

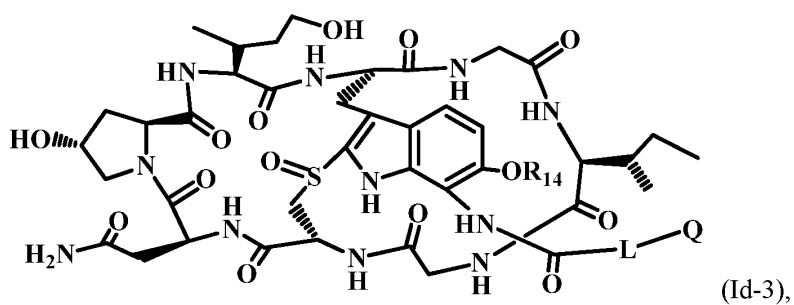
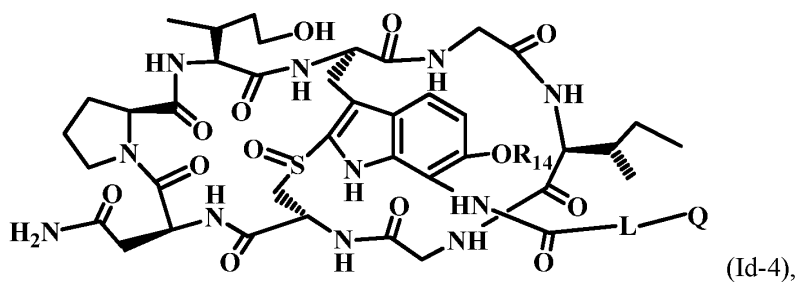
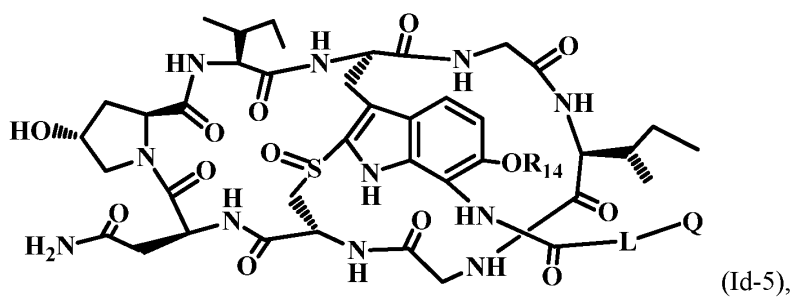
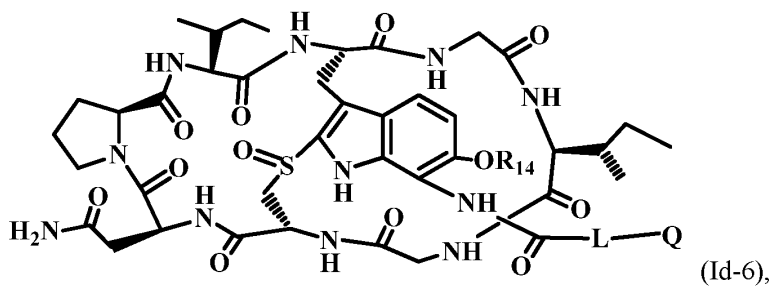
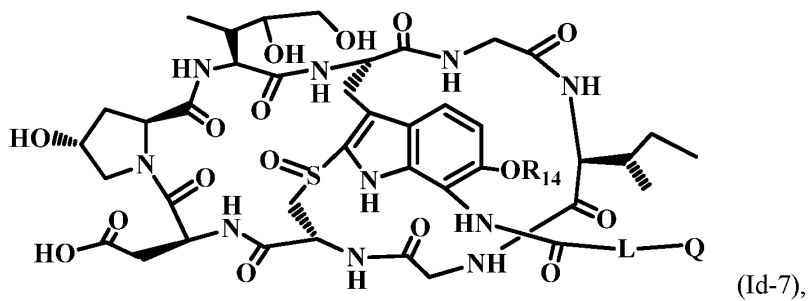
or the optical isomers, racemates, diastereomers or enantiomers.

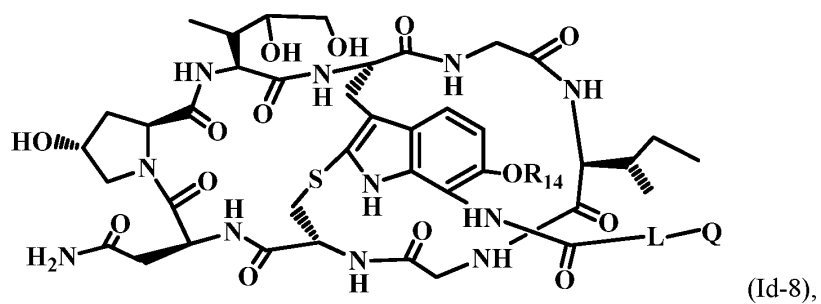
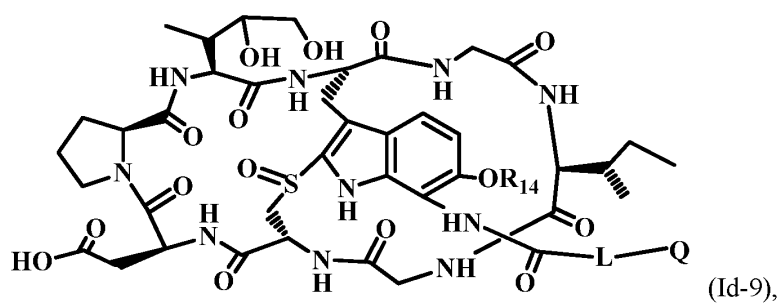
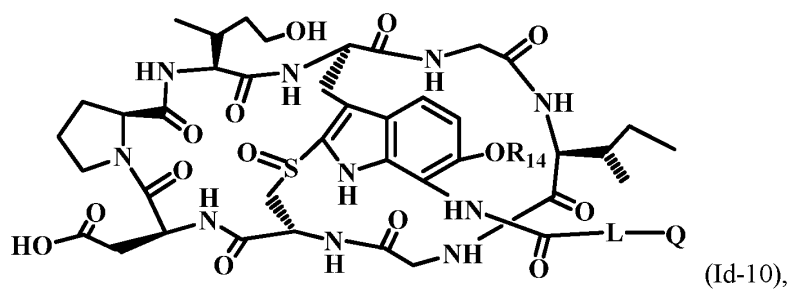
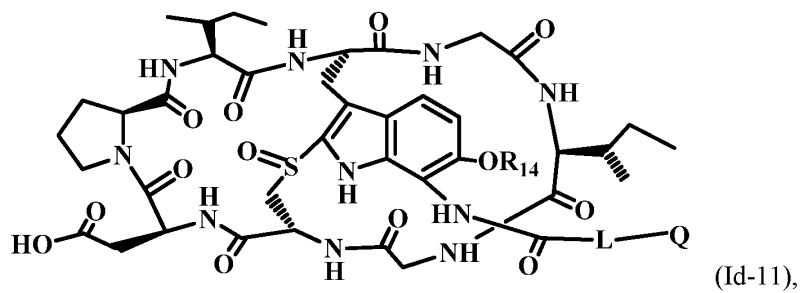
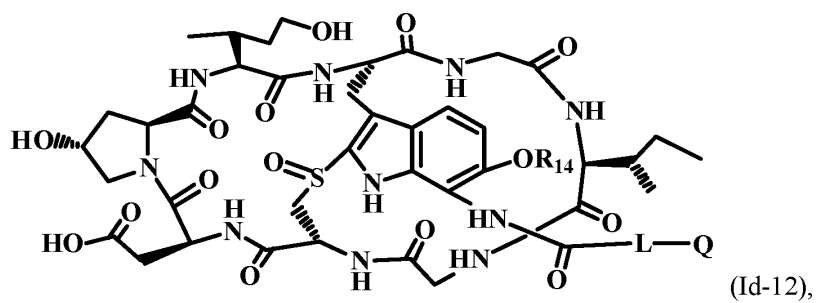
5      Wherein  $R_{10}$ , L and Q are defined the same as in Claim 1.

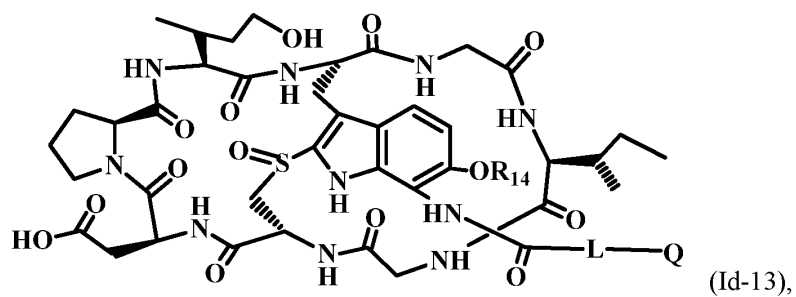
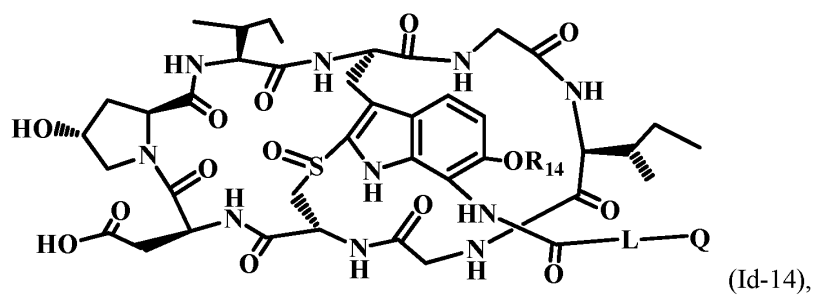
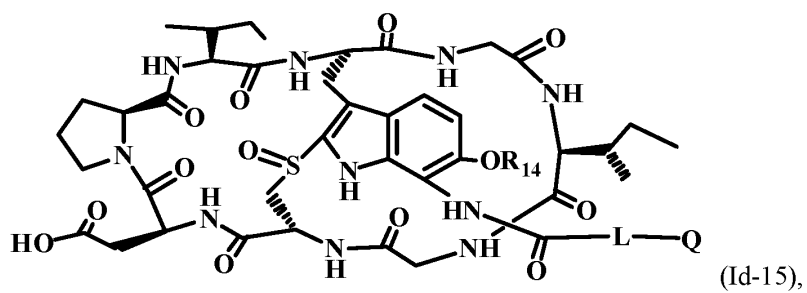
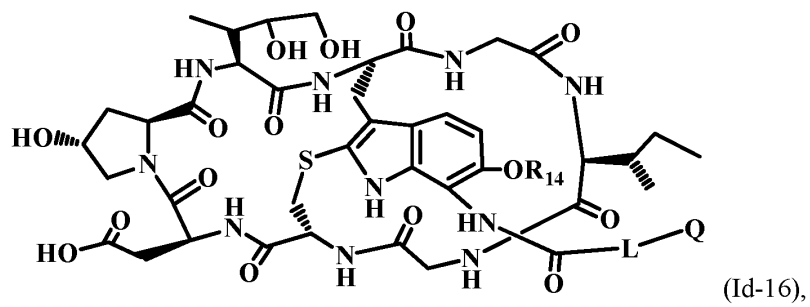
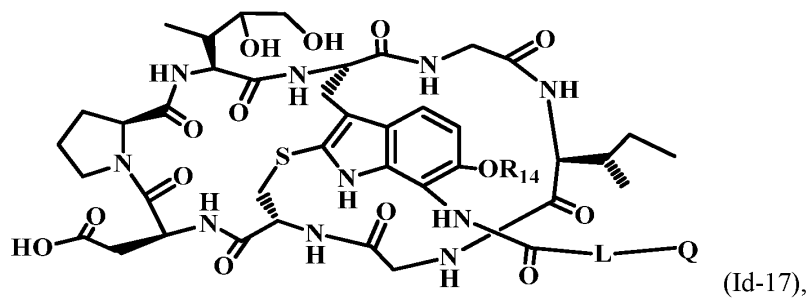
5.    A compound according to Claim 1 having the following Formula (Id-1), (Id-2), (Id-3), (Id-4), (Id-5), (Id-6), (Id-7), (Id-8), (Id-9), (Id-10), (Id-11), (Id-12), (Id-13), (Id-14), (Id-15), (Id-16), (Id-17), (Id-18), (Id-19), (Id-20), and (Id-21):

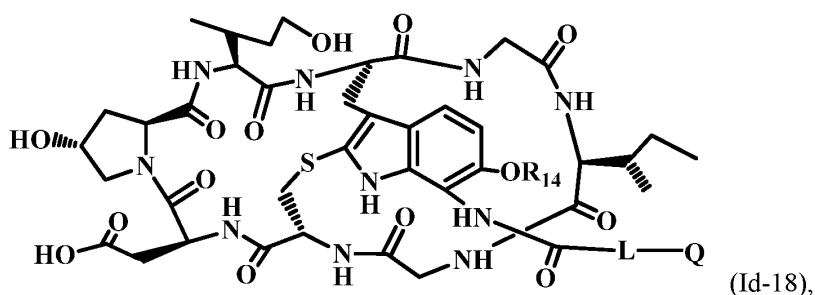
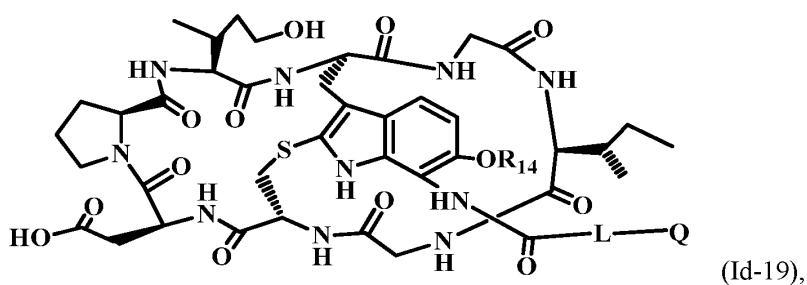
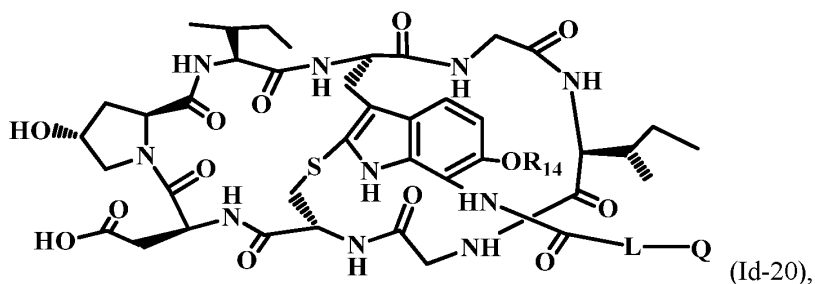
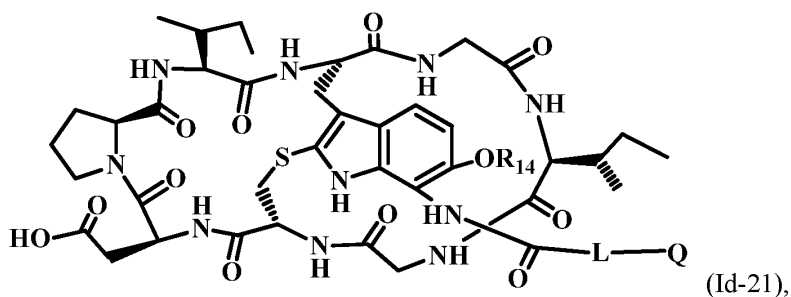


10



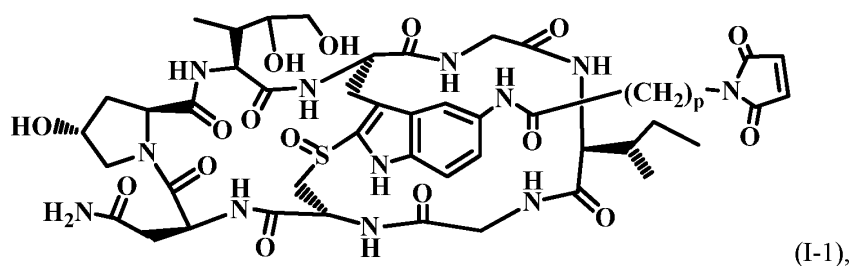
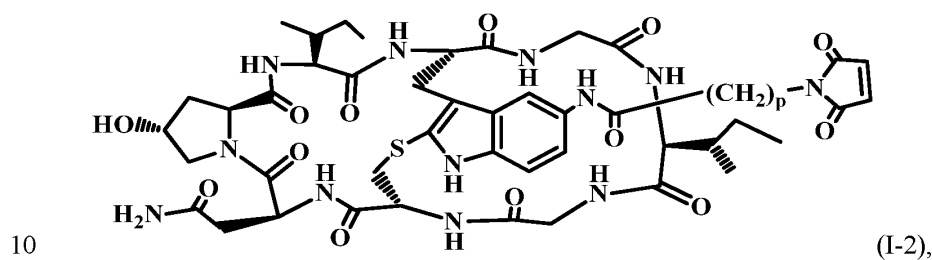
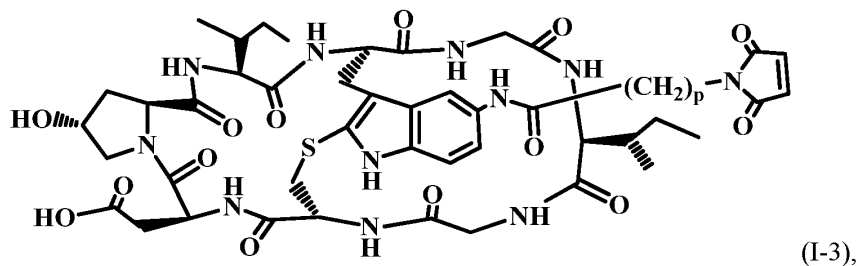
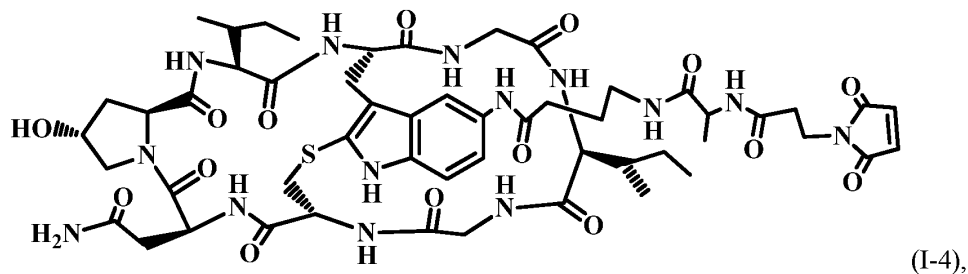


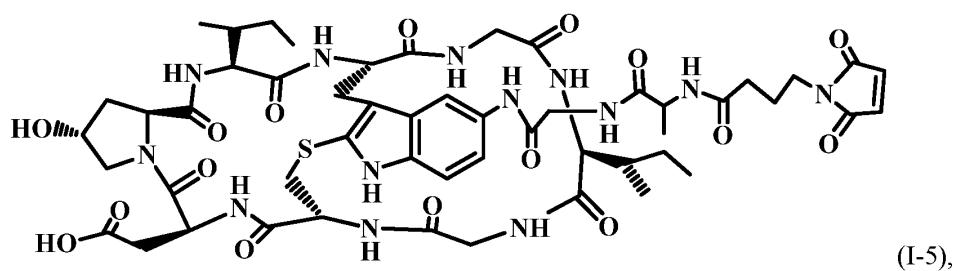
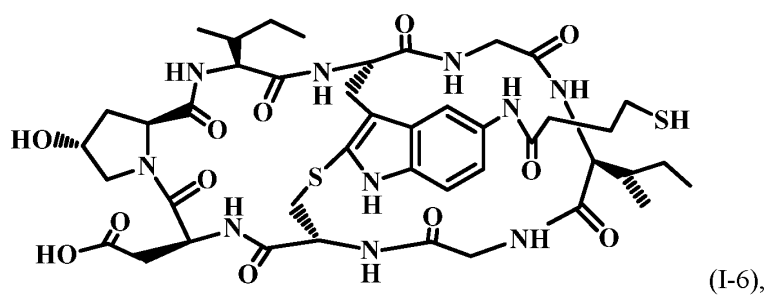
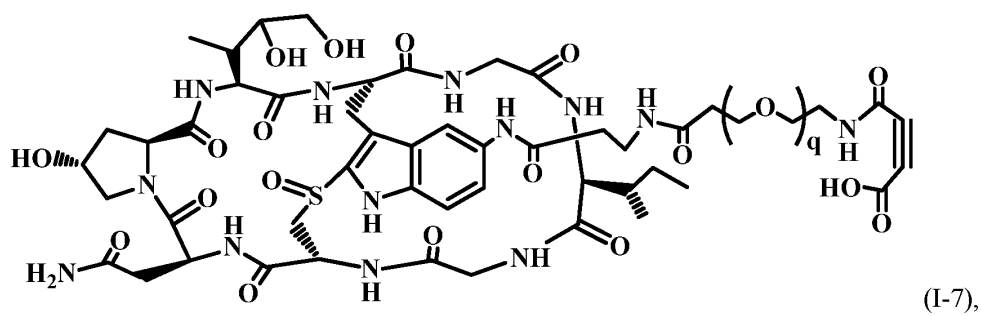
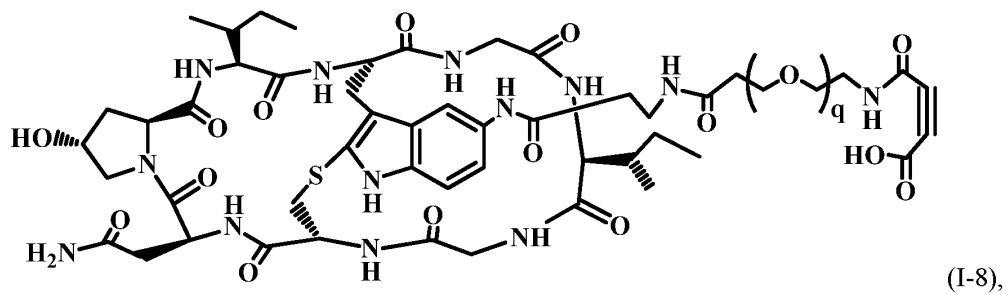
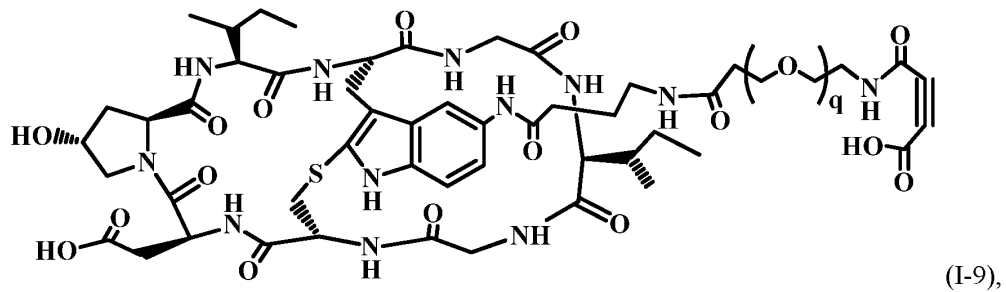


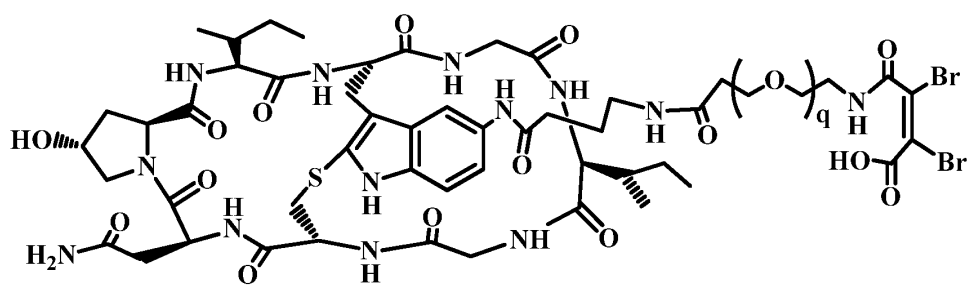


- 5        wherein L and Q are defined the same as in Claim 1. Wherein  $R_{14}$  is H,  $PO_3^{2-}$ ,  $SO_3^-$ ,  $R_{12}$ ,  $-COR_{12}$ ,  $-COCH_3$ ,  $-COOR_{12}$ ,  $-CONR_{12}R_{12}'$ ,  $-C(=O)R_{12}NH(Aa)_t$  (an amino acid or peptide, wherein Aa is an amino acid or a polypeptide, t represents 0 - 100);  $-CSNHR_{12}$  (thiocarbamate);  $-SOR_{12}$  (sulfoxide);  $-SO_2R_{12}$  (sulfone);  $-SO_3^-$ ,  $HSO_3^-$ ,  $HSO_2^-$ , or a salt of  $HSO_3^-$ ,  $SO_3^{2-}$  or  $-HSO_2^-$  (sulphite);  $P(O)(OM_1)(OM_2)$ ,  $CH_2OP(O)(OM_1)(OM_2)$ ,  $SO_3M_1$ ; glycoside (glucoside, galactoside, mannoside, glucuronoside, alloside, fructoside, etc),  $M_1$  and  $M_2$  are independently H, Na, K, Ca, Mg,  $NH_4$ ,  
 10         $NR_1'R_2'R_3'$ ;  $R_1'$ ,  $R_2'$  and  $R_3'$  are independently H,  $C_1-C_8$  alkyl.

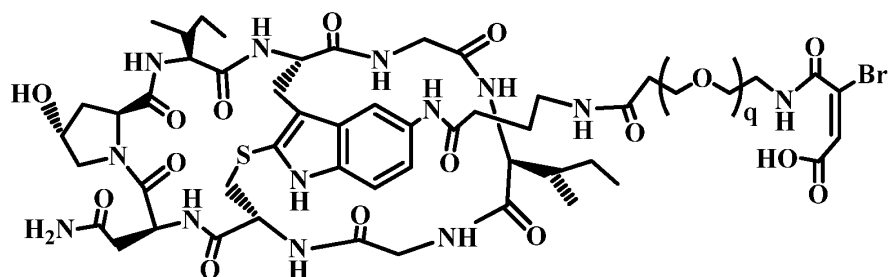
6. A compound according to Claim 1 having the following Formula (I-1), (I-2), (I-3), (I-4), (I-5), (I-6), (I-7), (I-8), (I-9), (I-10), (I-11), (I-12), (I-13), (I-14), (I-15), (I-16), (I-17), (I-18), (I-19), (I-20), (I-21), (I-22), (I-23), (I-24), (I-25), (I-26), (I-27), (I-28), (I-29), (I-30), (I-31), (I-32), (I-33), (I-34), (I-35), (I-36), (I-37), (I-38), (I-39), (I-40), (I-41), (I-42), (I-43), (I-44), (I-45), (I-46), (I-47), (I-48), (I-49), (I-50), (I-51), (I-52), (I-53), (I-54), (I-55), (I-56), (I-57), (I-58), (I-59), (I-60), (I-61), (I-62), (I-63), (I-64), (I-65), (I-66), (I-67), (I-68), (I-69), (I-70), (I-71), (I-72), (I-73), (I-74), (I-75), (I-76), (I-77), (I-78), (I-79), (I-80), (I-81), (I-82), (I-83), (I-84), (I-85), (I-86), (I-87), (I-88), (I-89), (I-90), (I-91), (I-92), (I-93), (I-94), (I-95), (I-96) and (I-97):



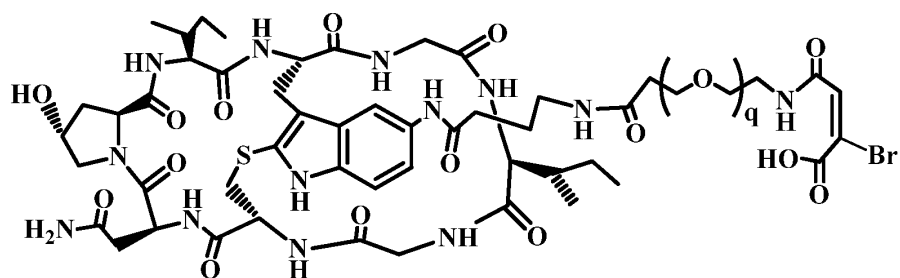




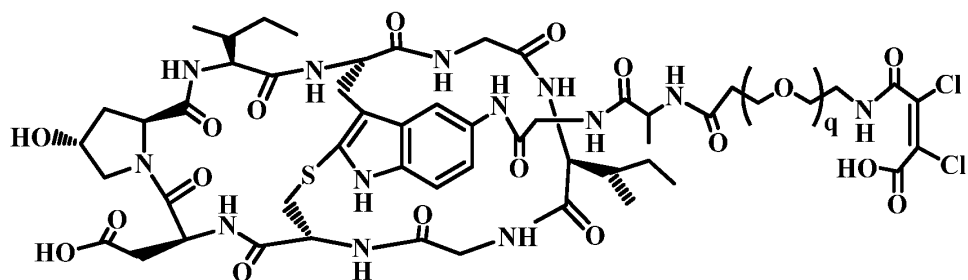
(I-10),



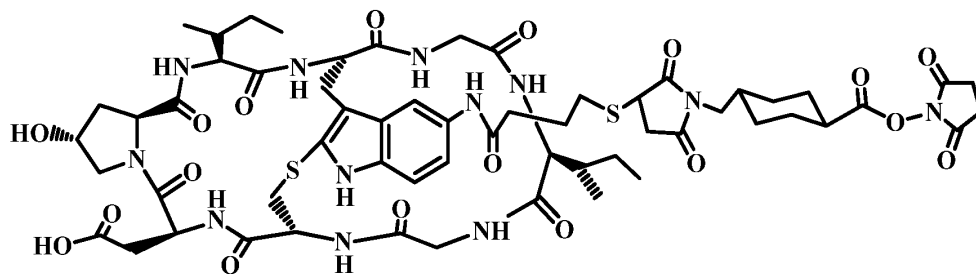
(I-11),



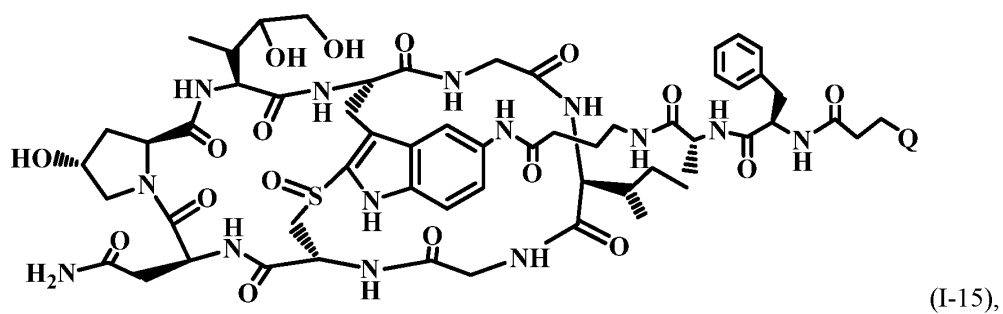
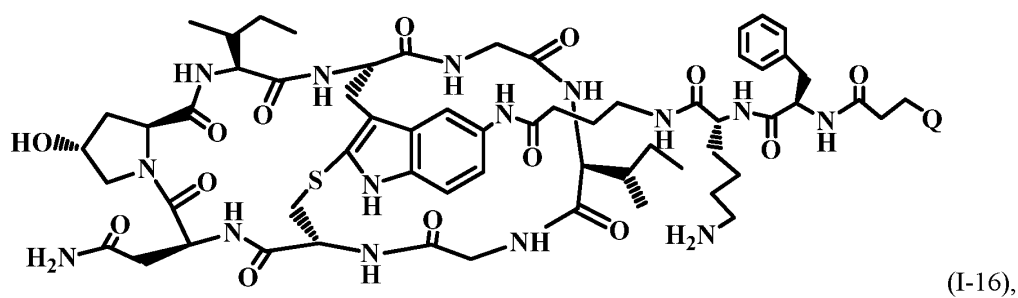
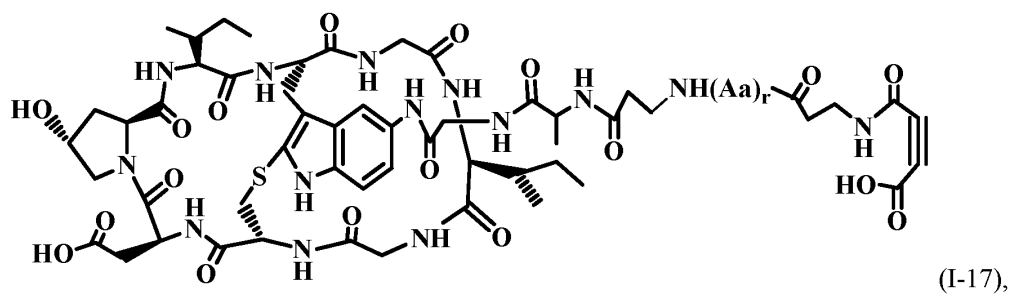
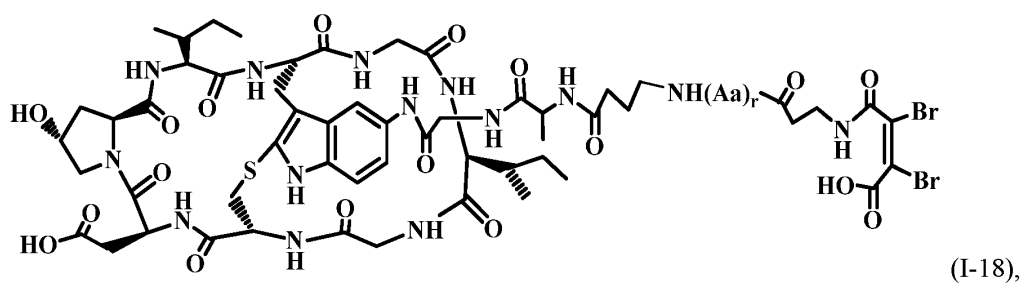
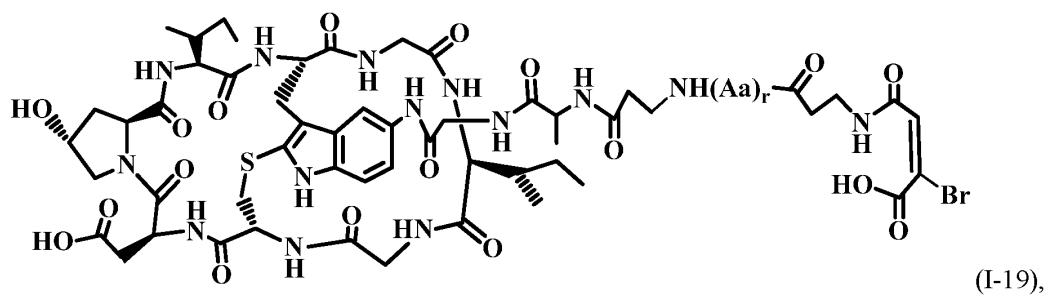
(I-12),

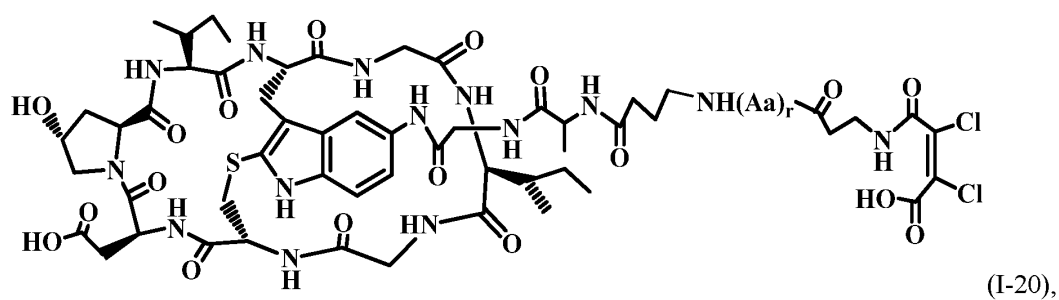
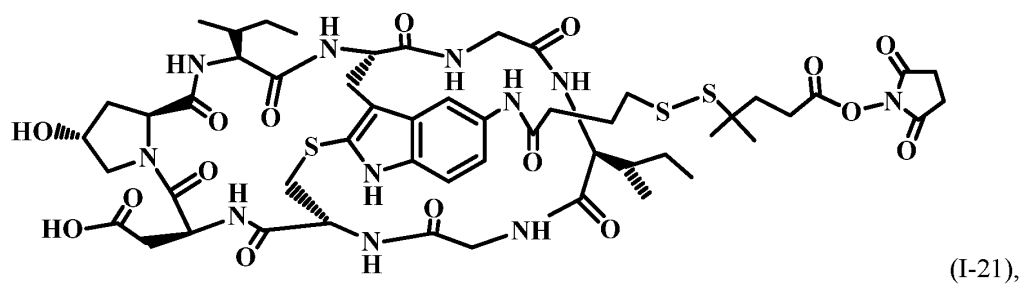
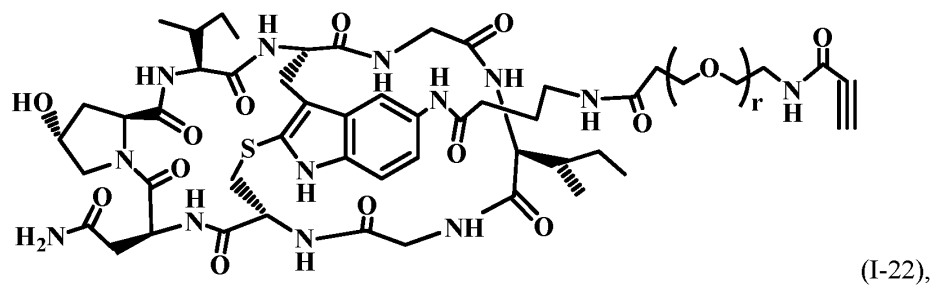
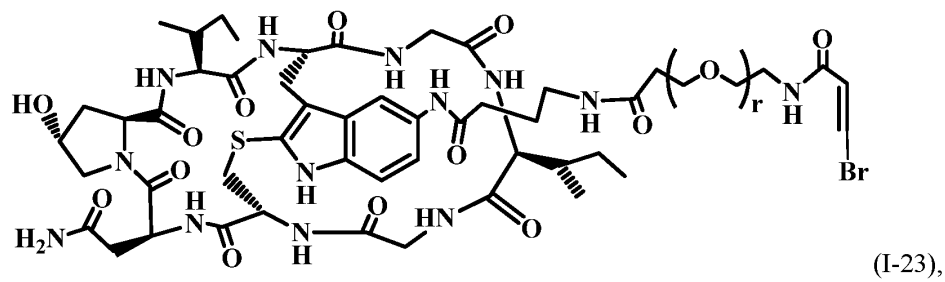
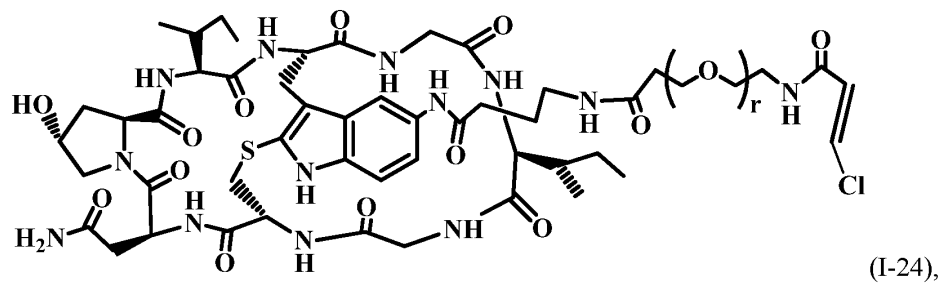


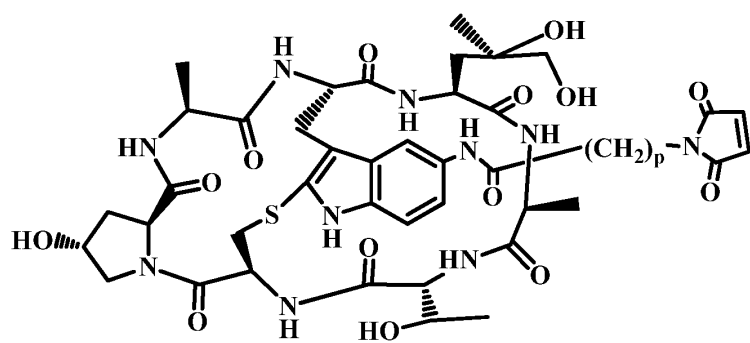
(I-13),



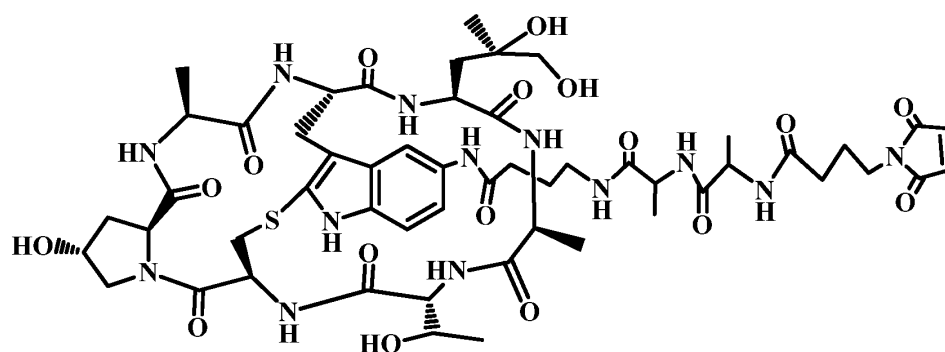
(I-14),



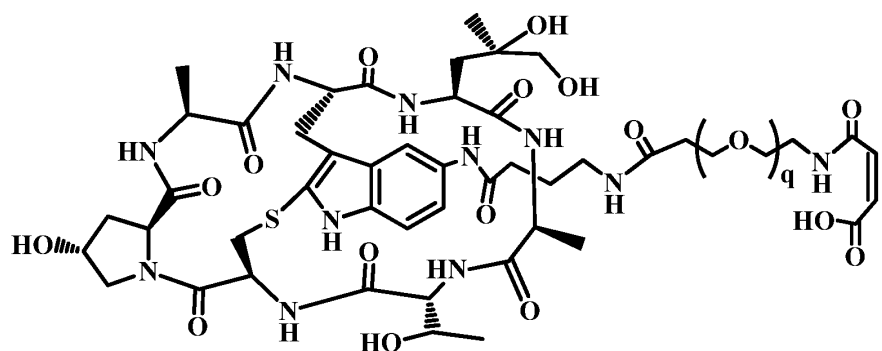




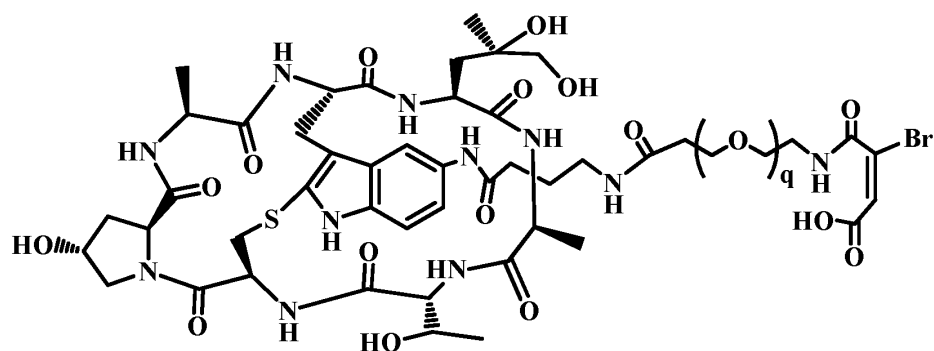
(I-25),



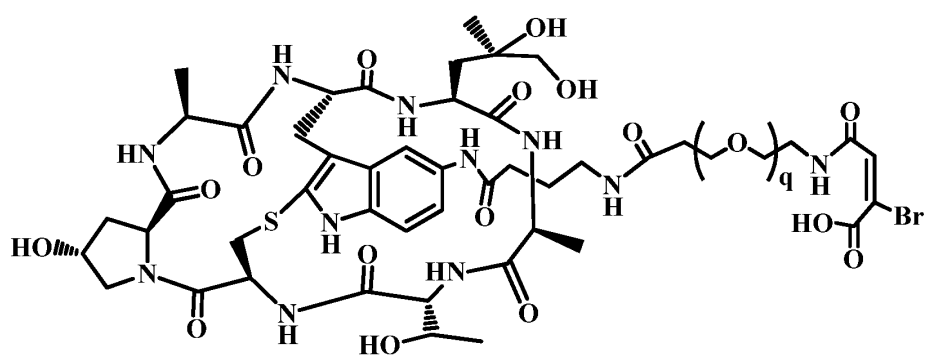
(I-26),



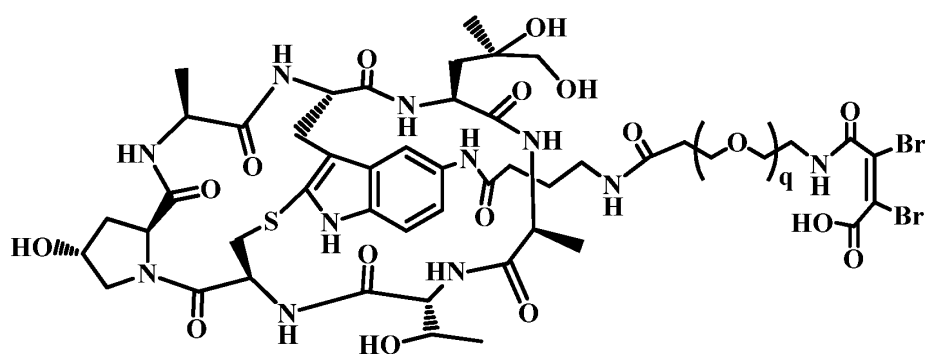
(I-27),



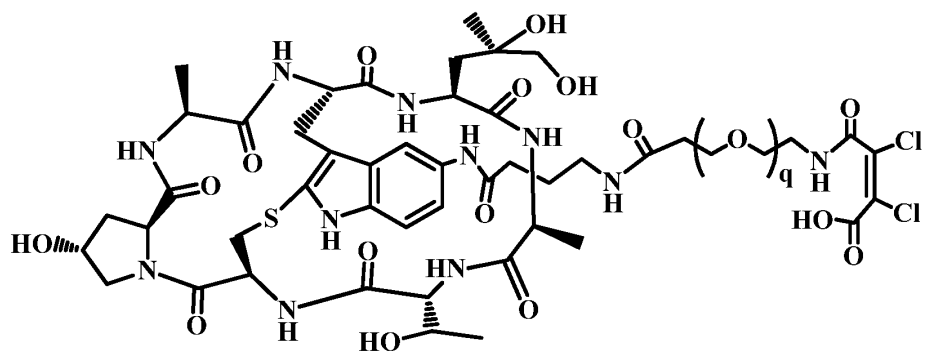
(I-28),



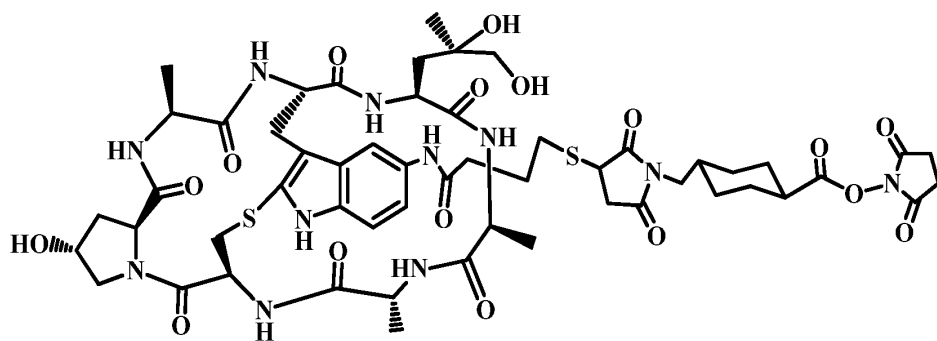
(I-29),



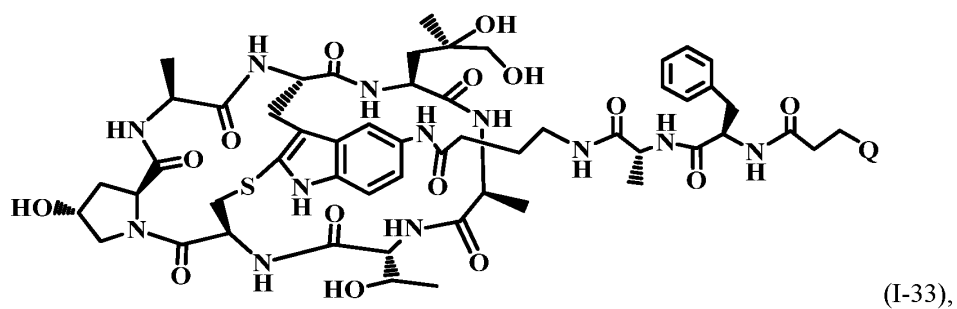
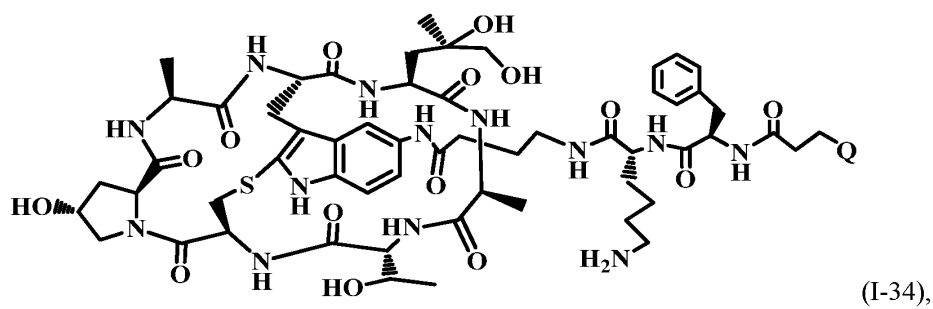
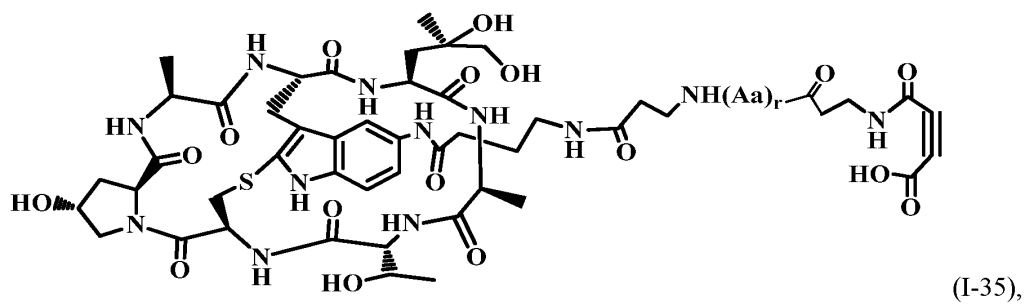
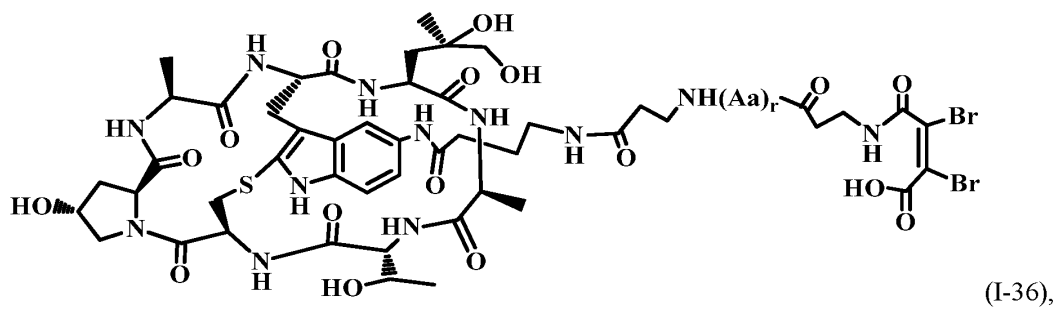
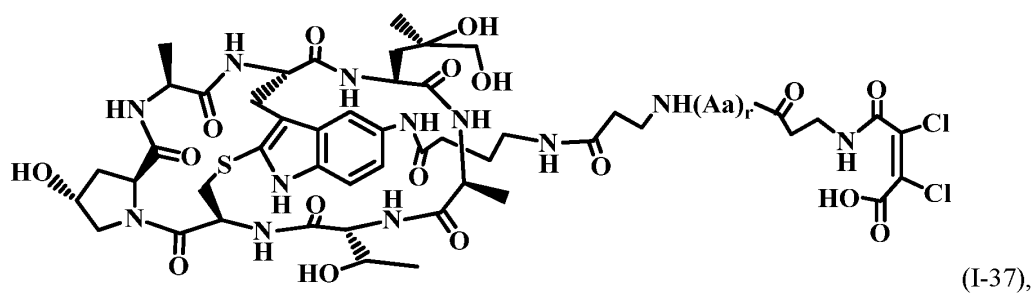
(I-30),

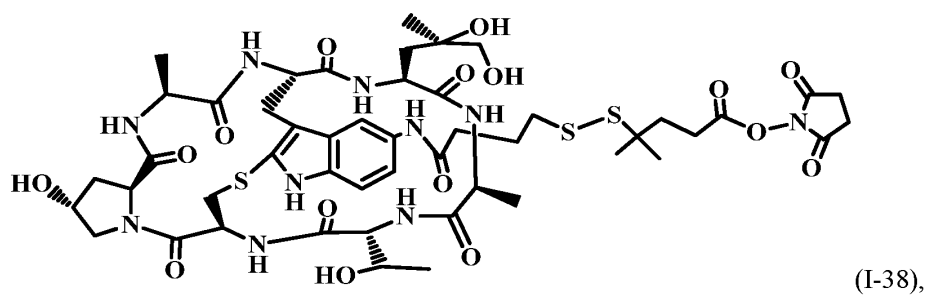
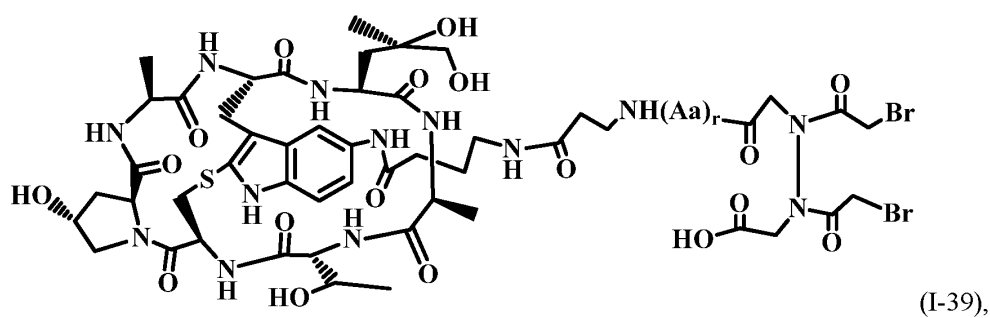
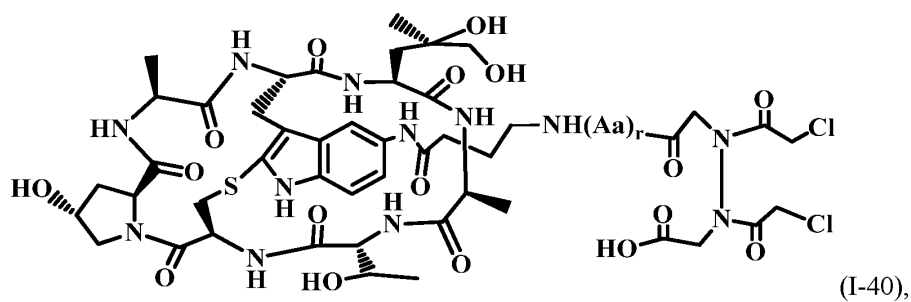
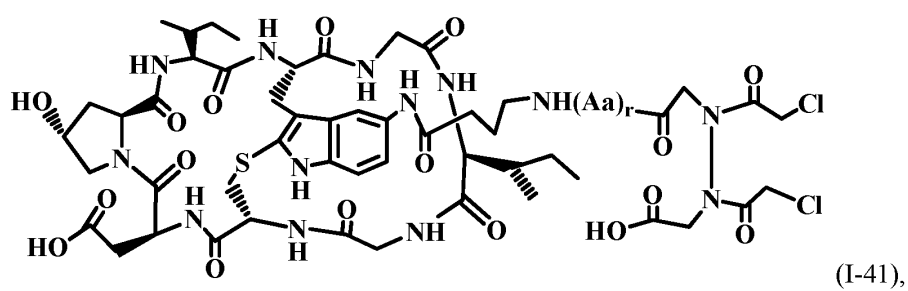
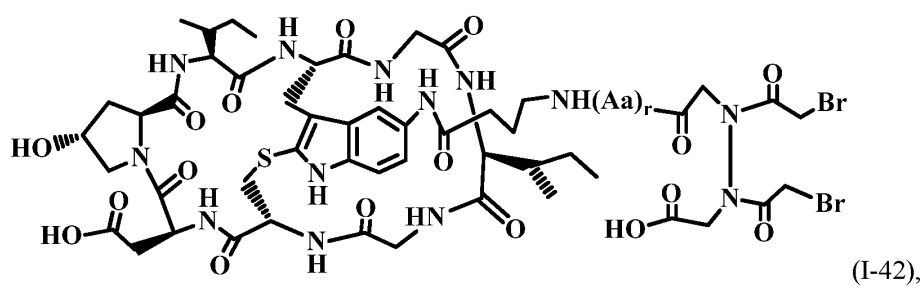


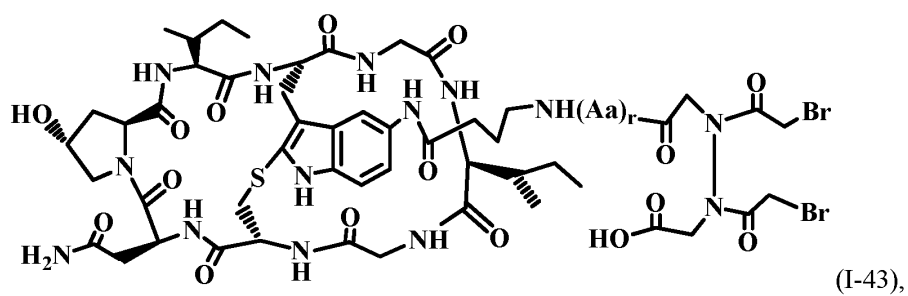
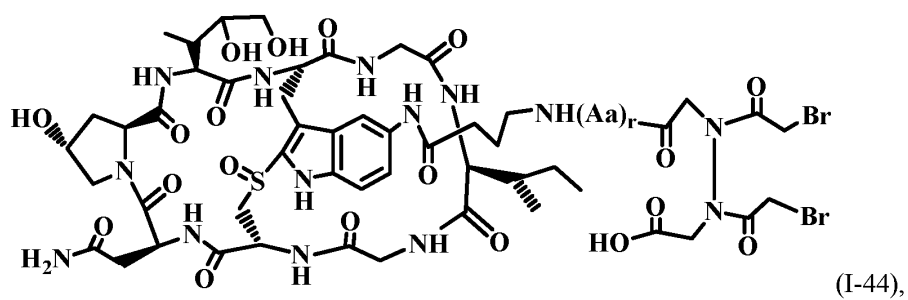
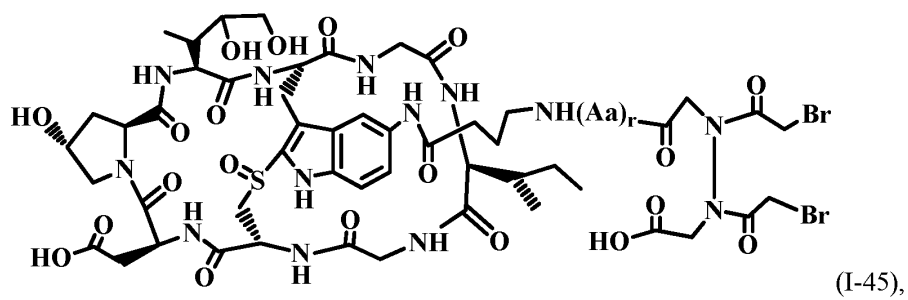
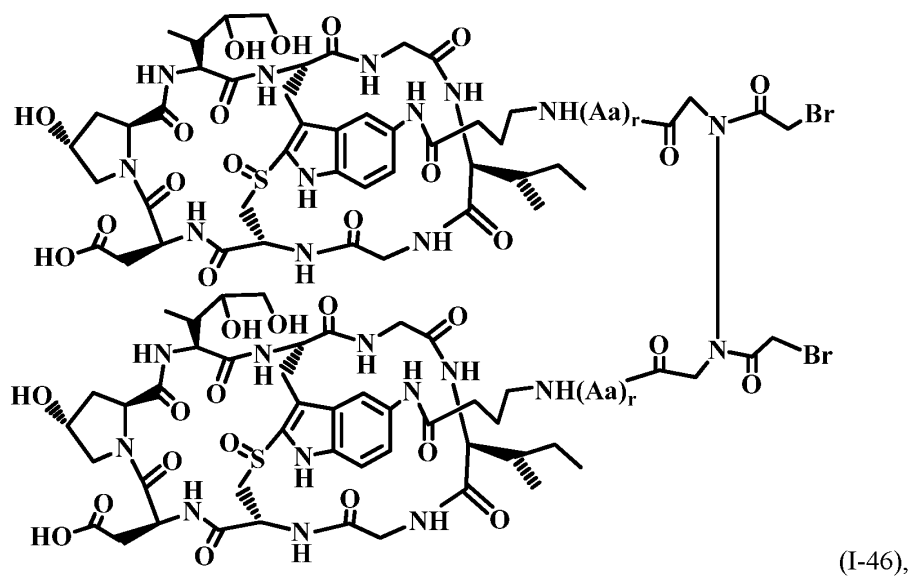
(I-31),

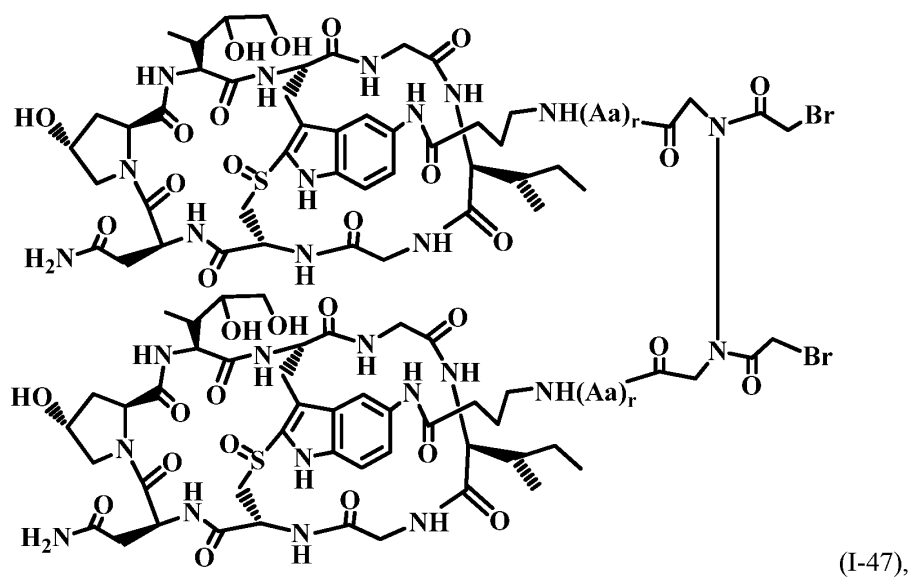
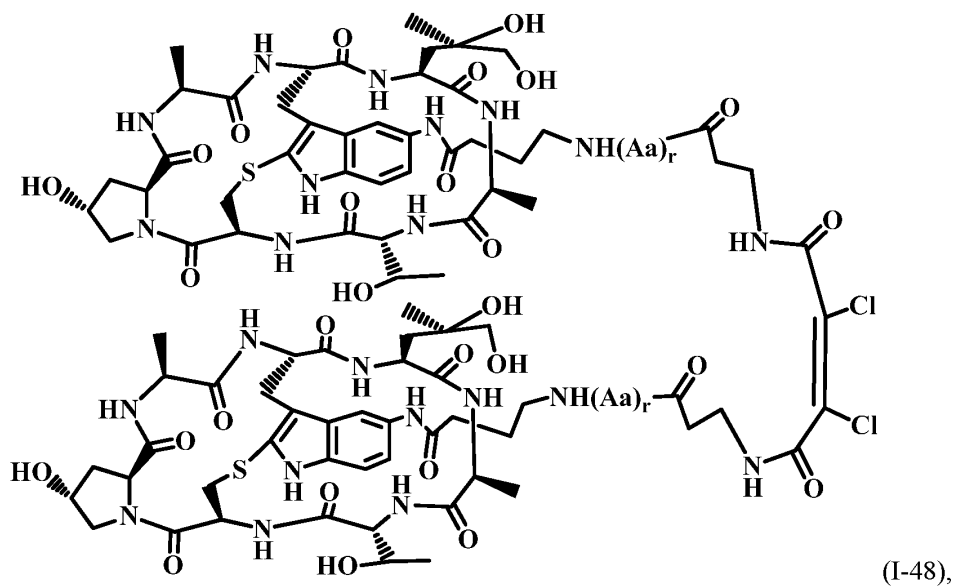
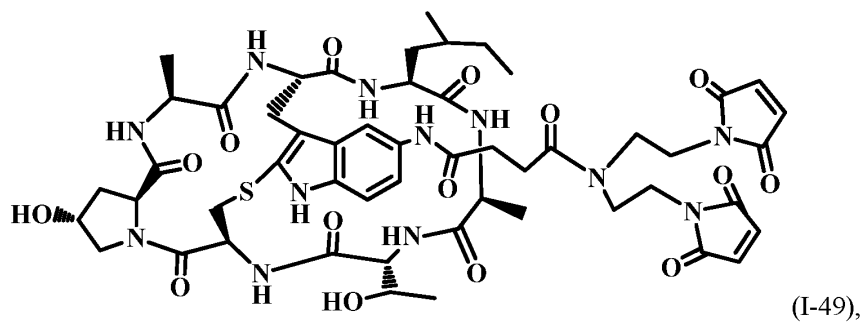


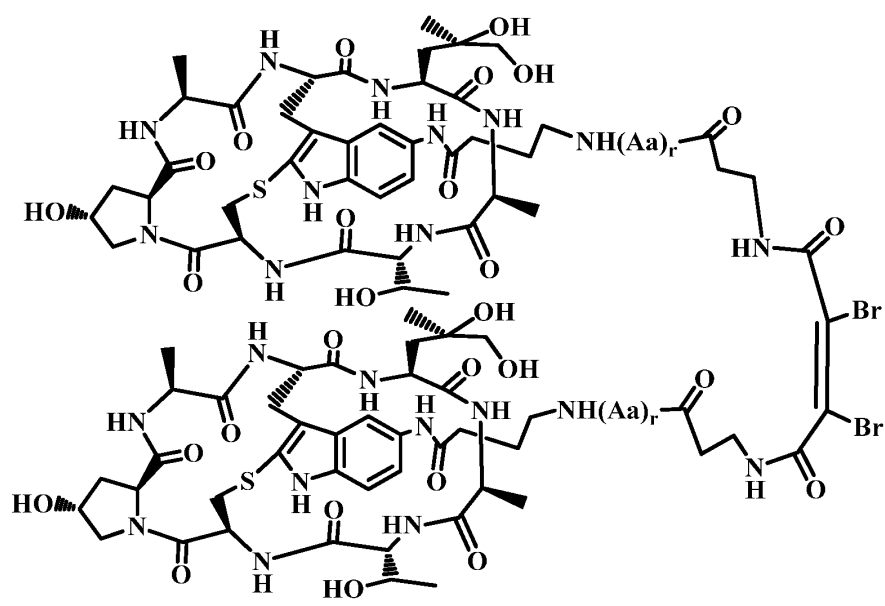
(I-32),



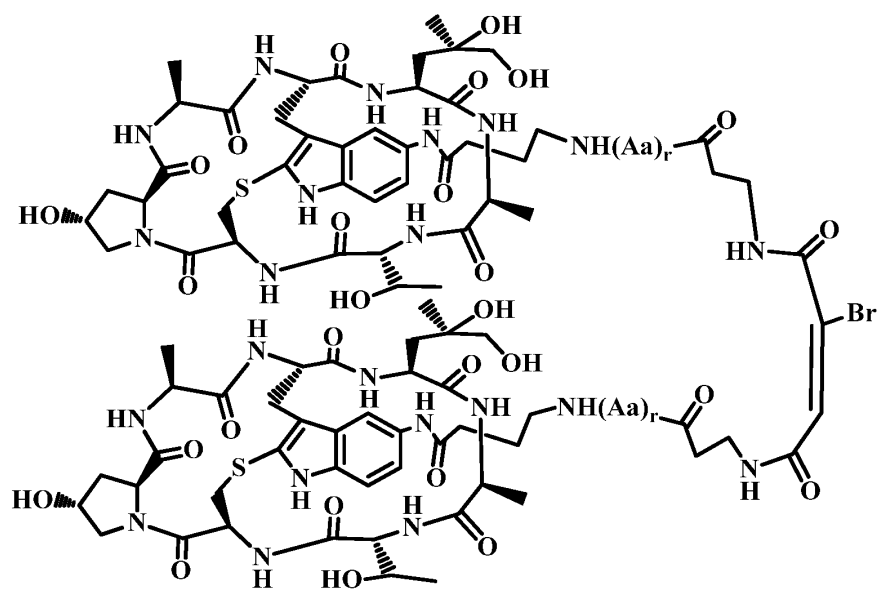




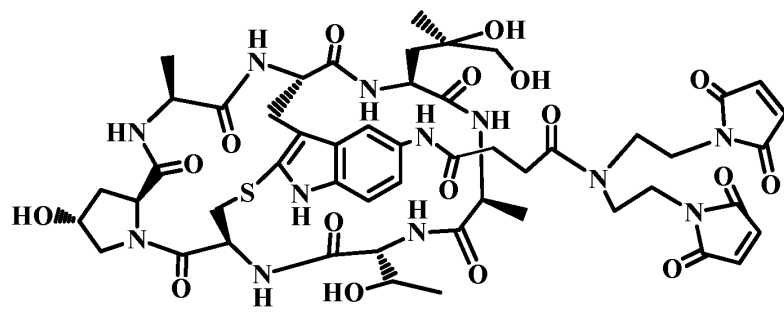




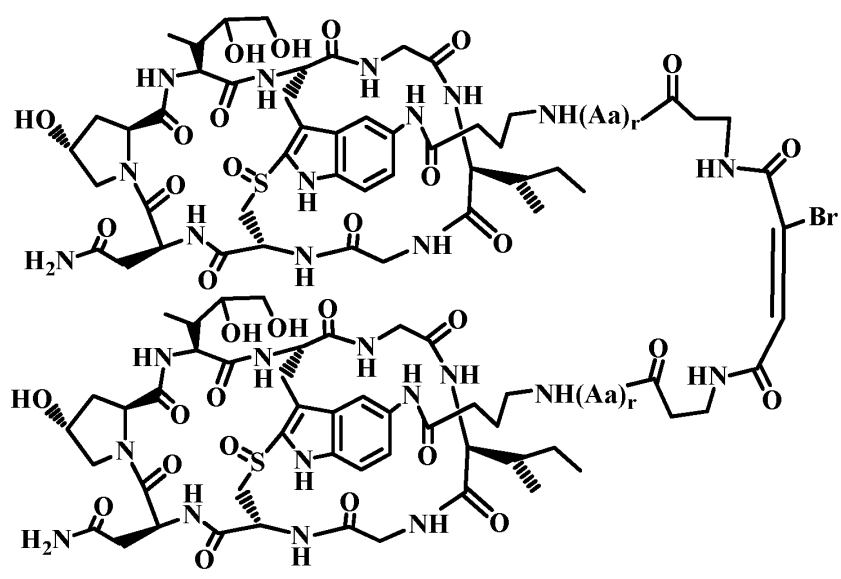
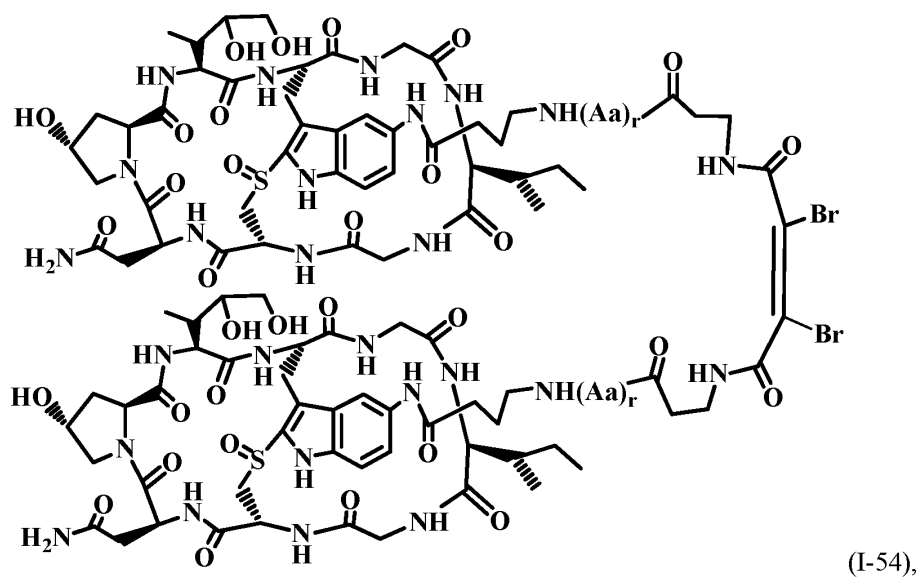
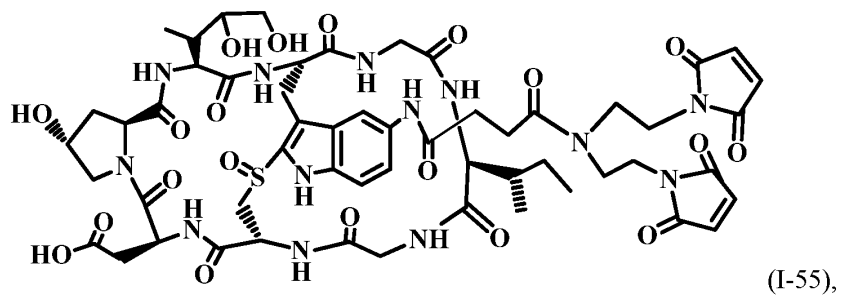
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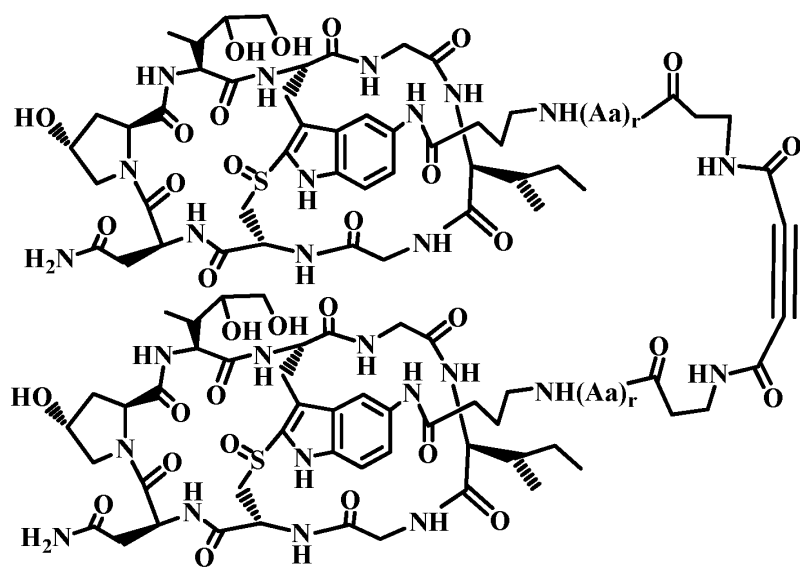
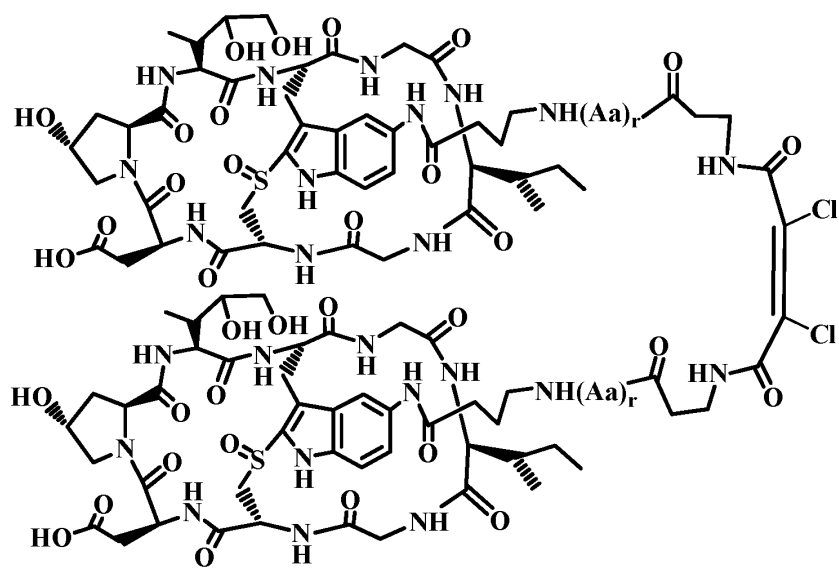
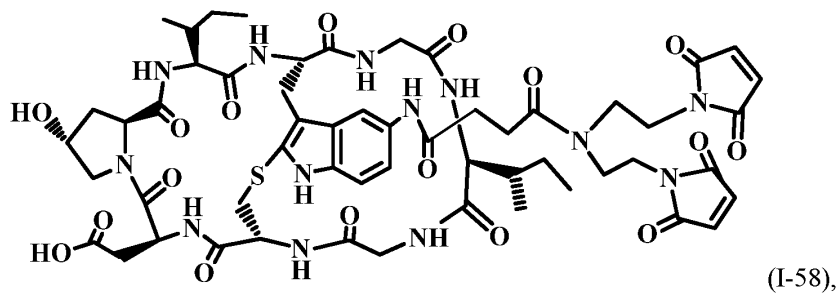


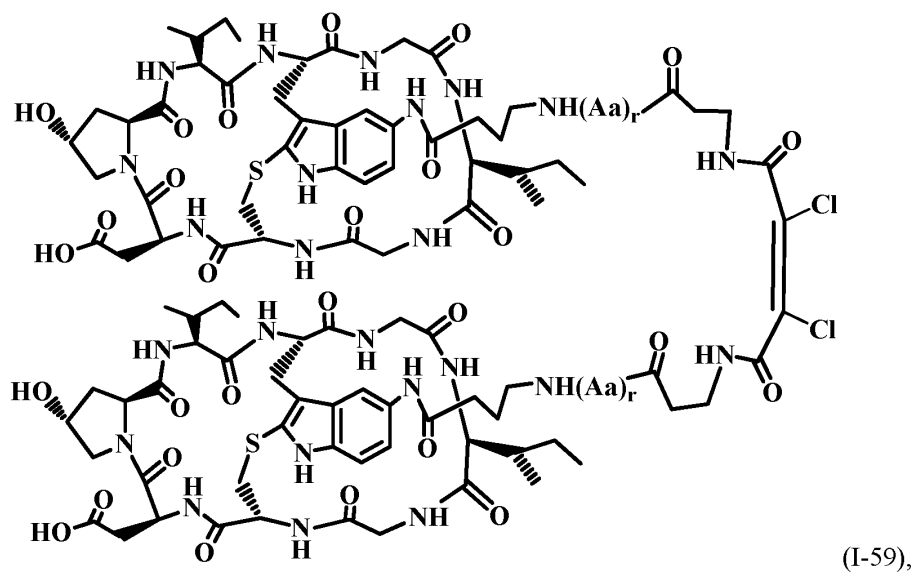
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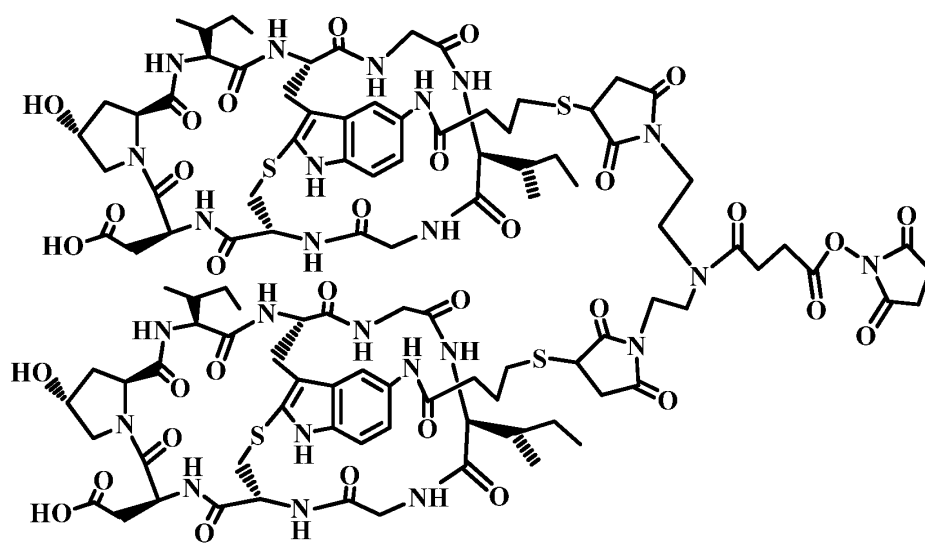
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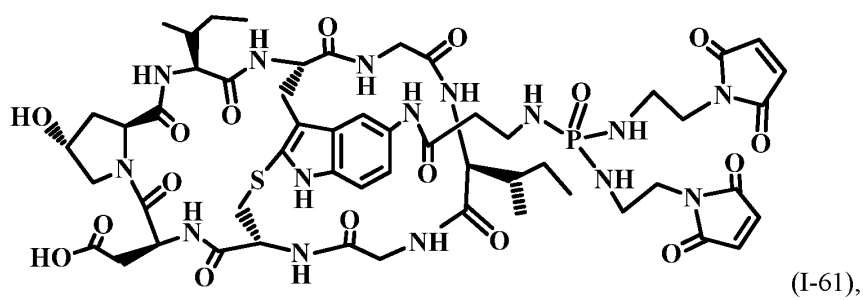




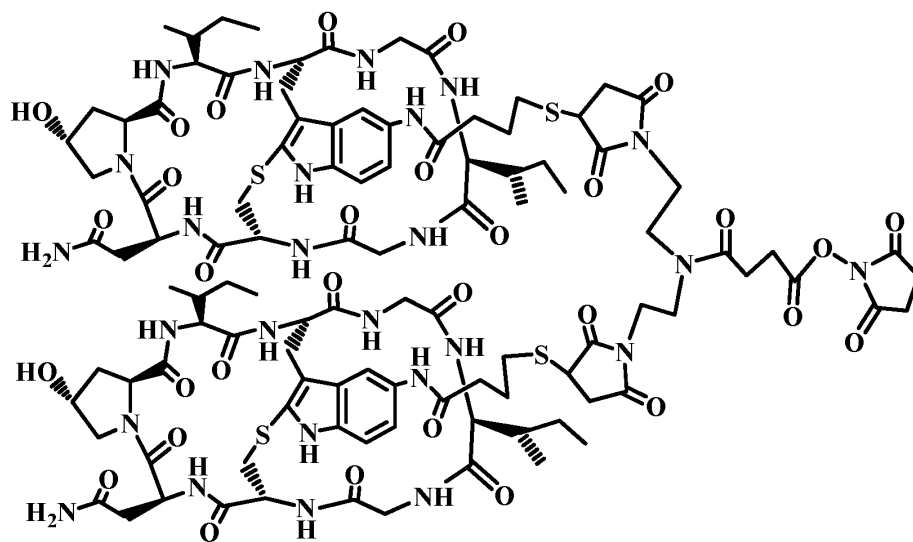
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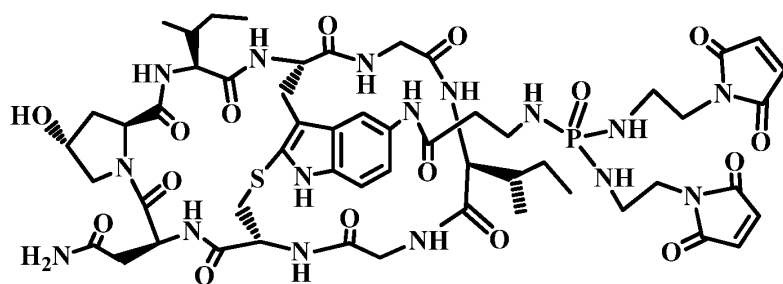
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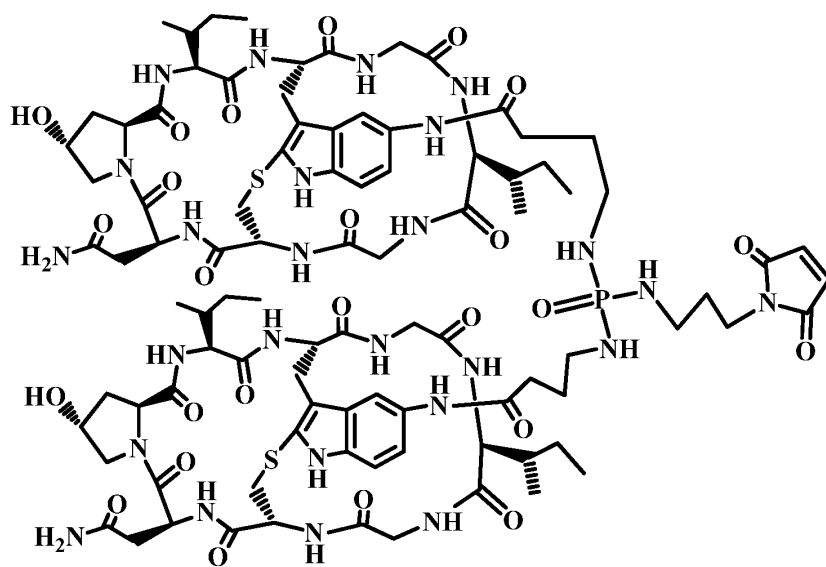
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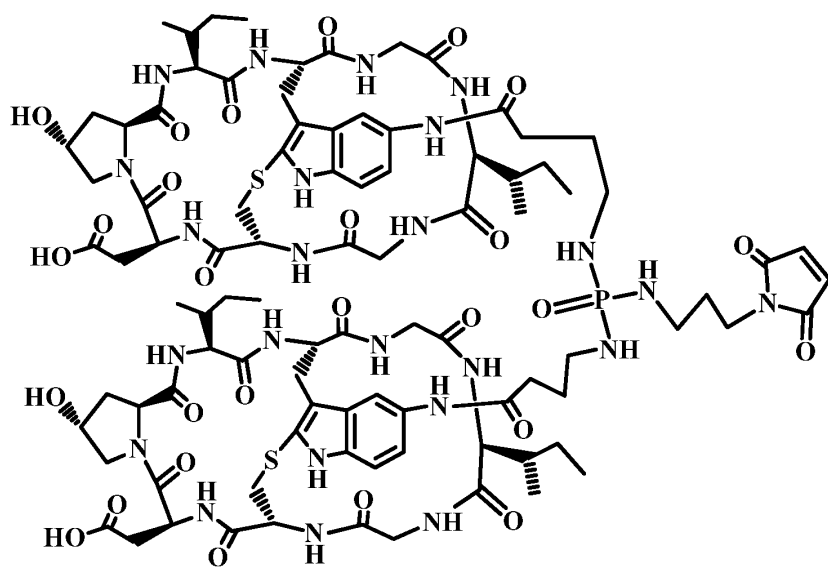
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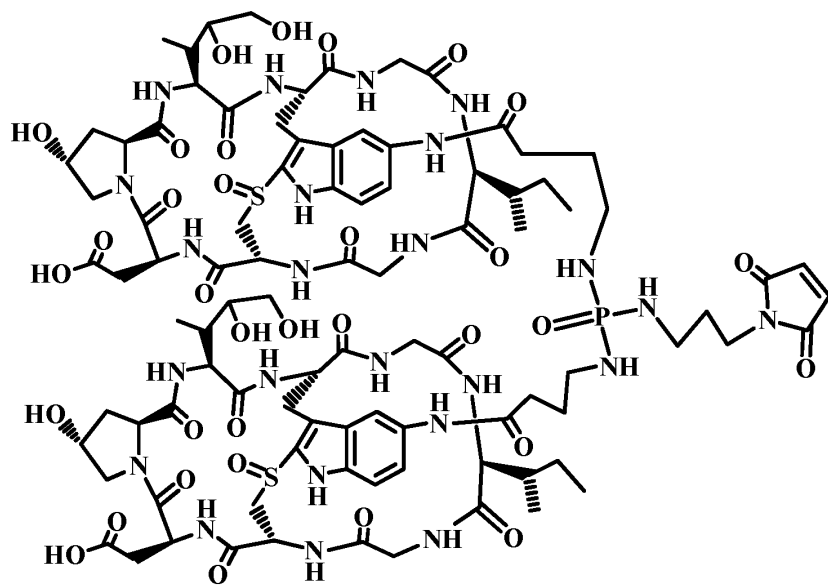
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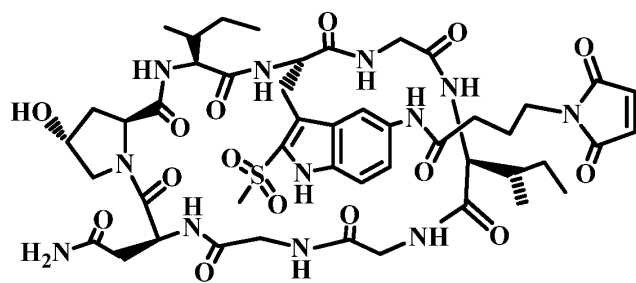
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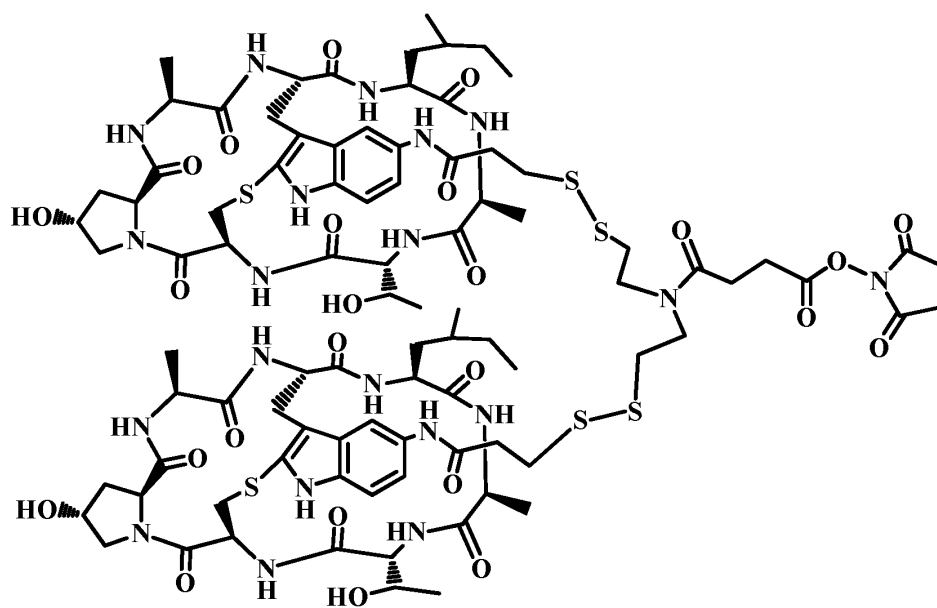
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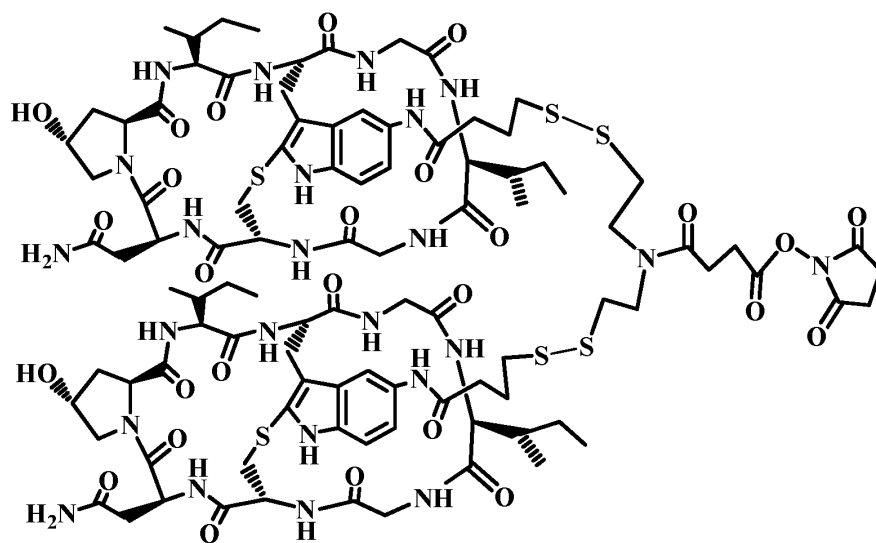
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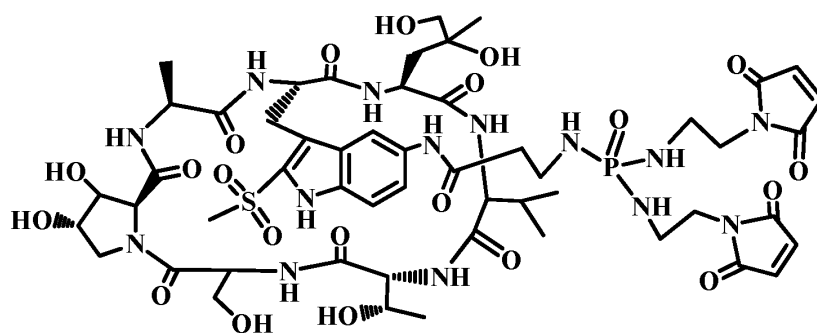
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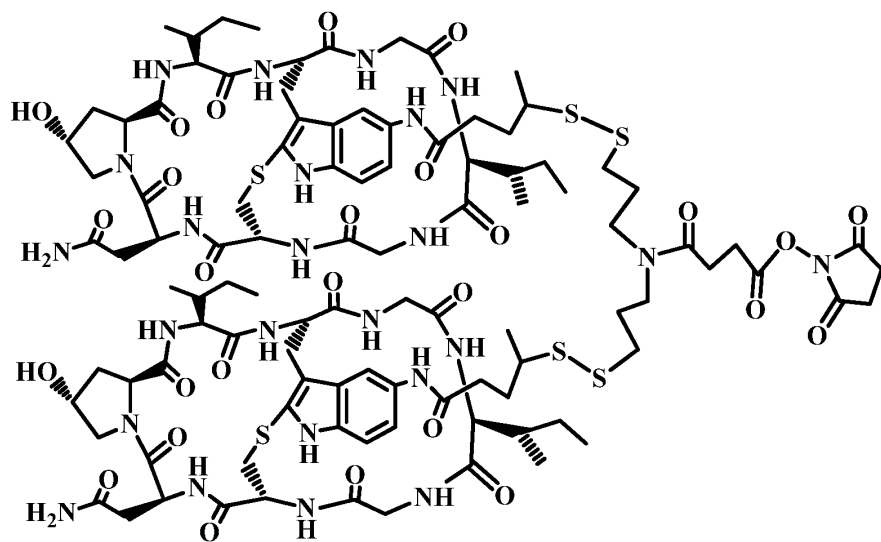
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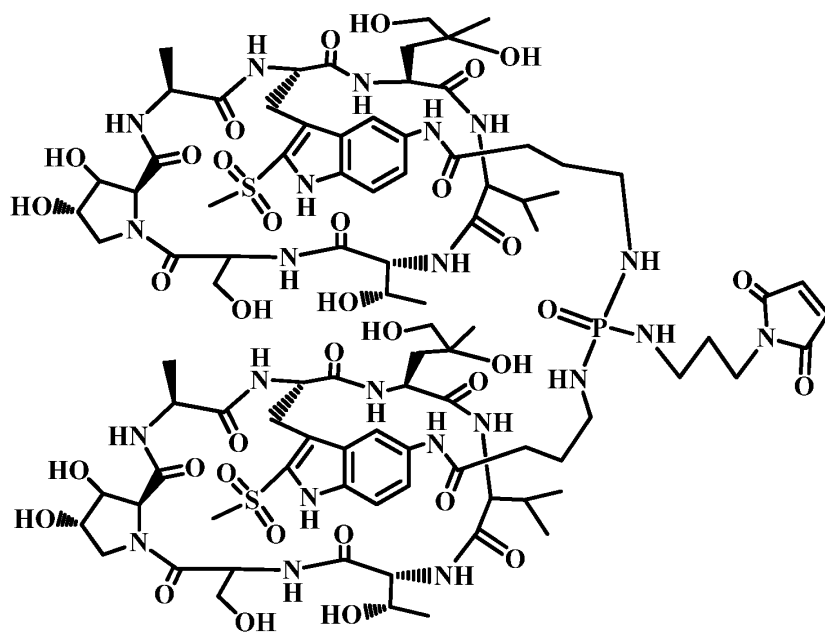
(I-69),



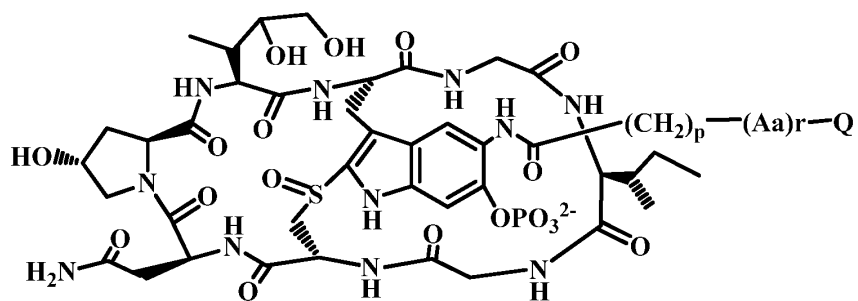
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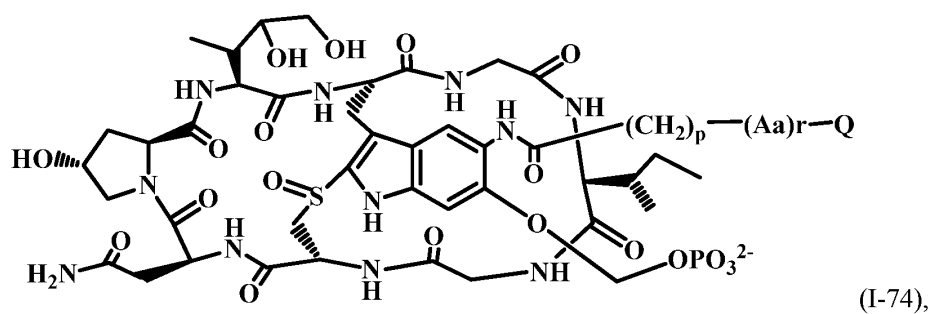
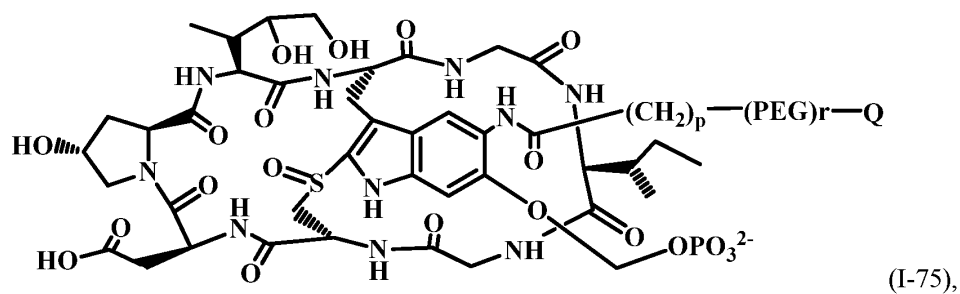
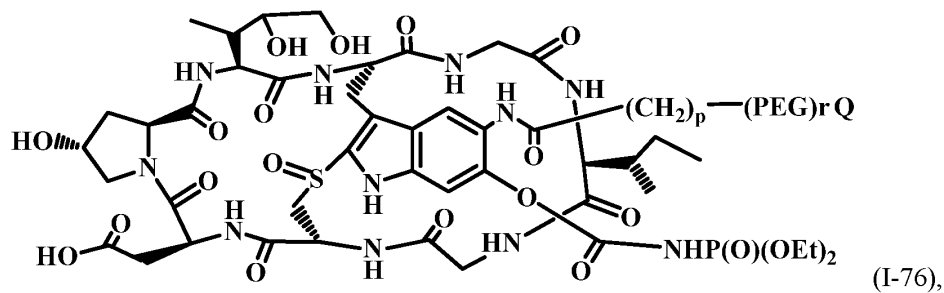
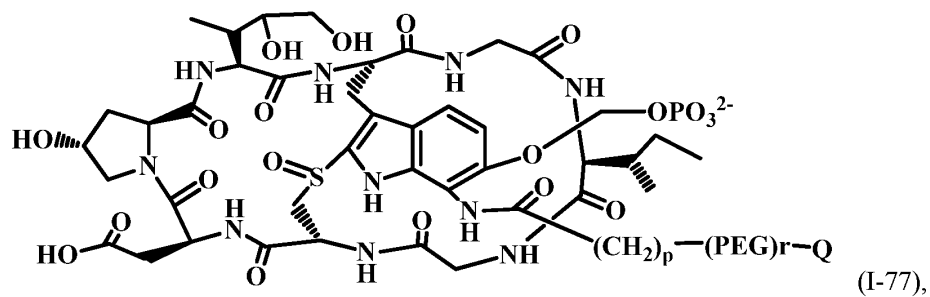
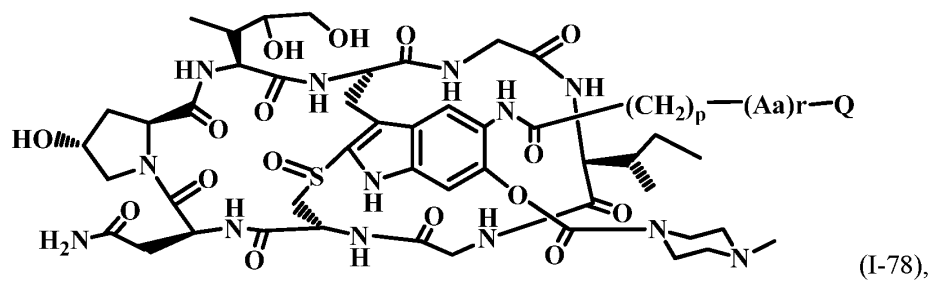
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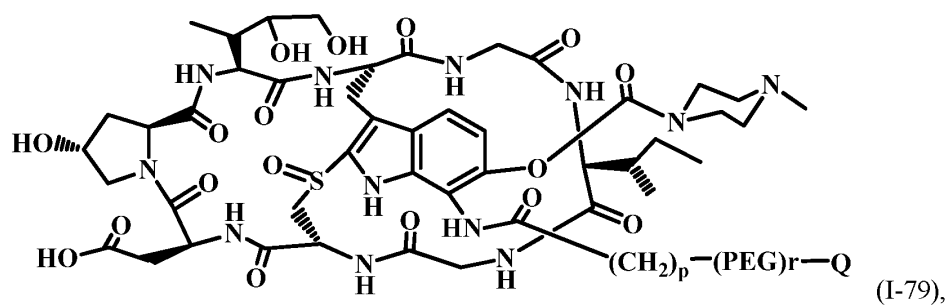
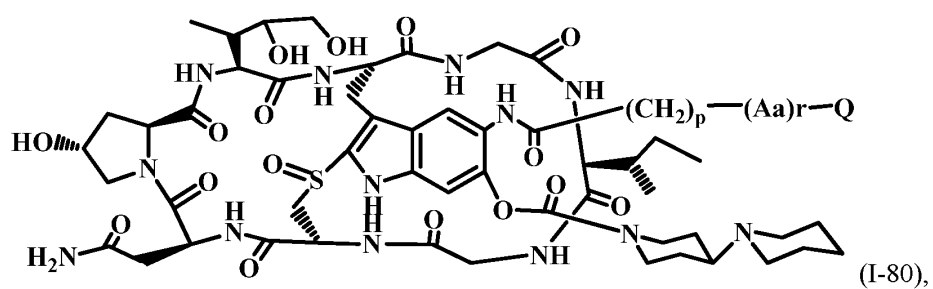
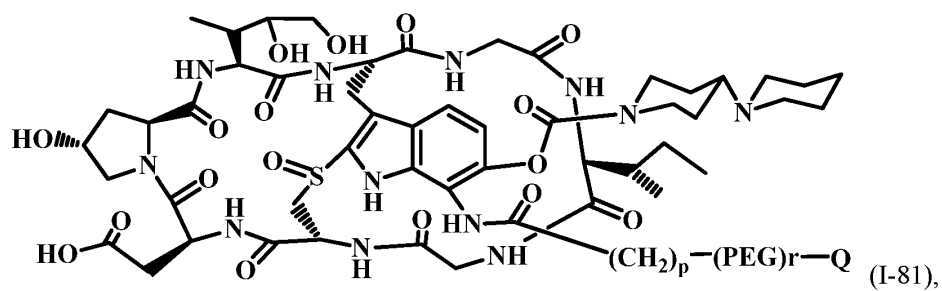
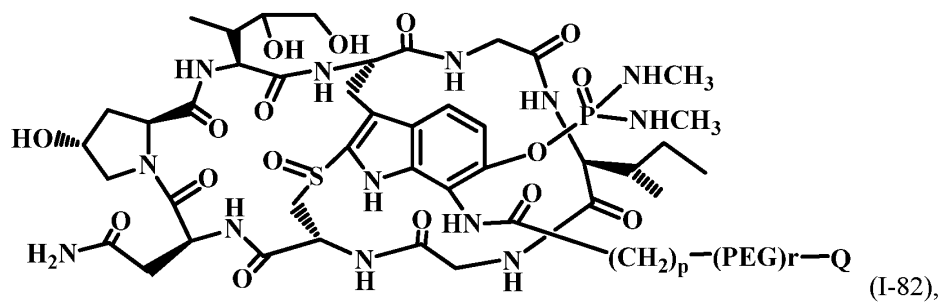
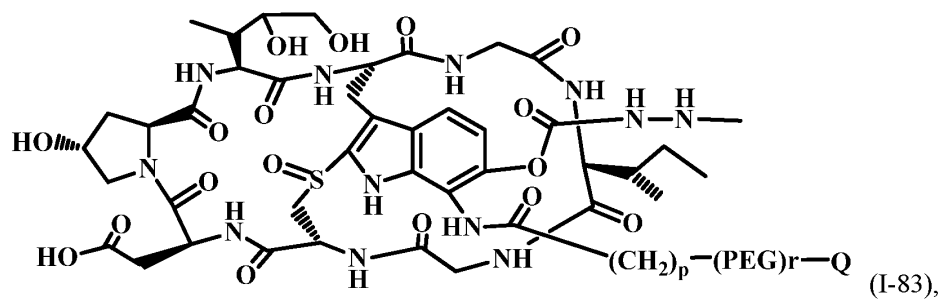


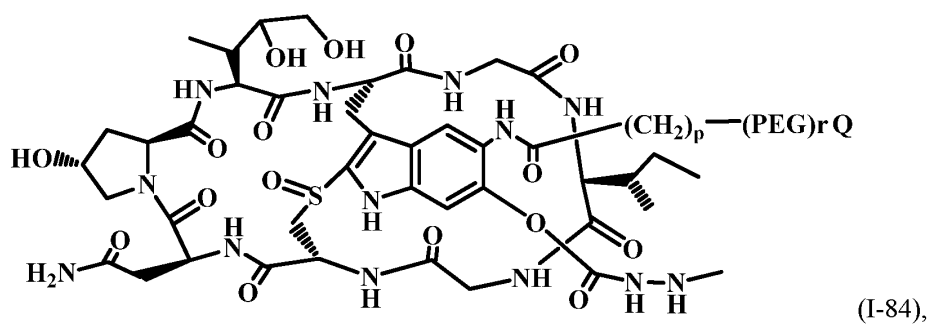
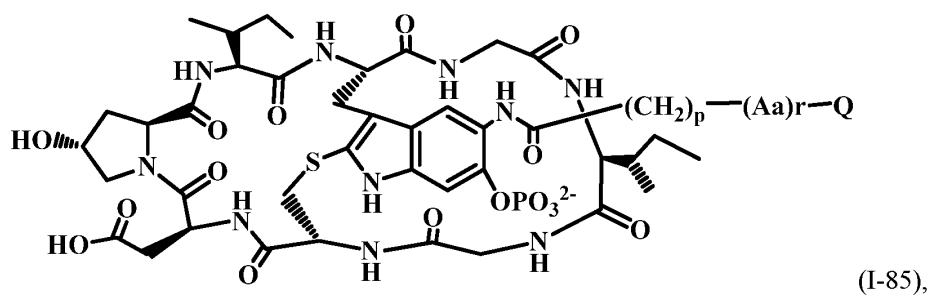
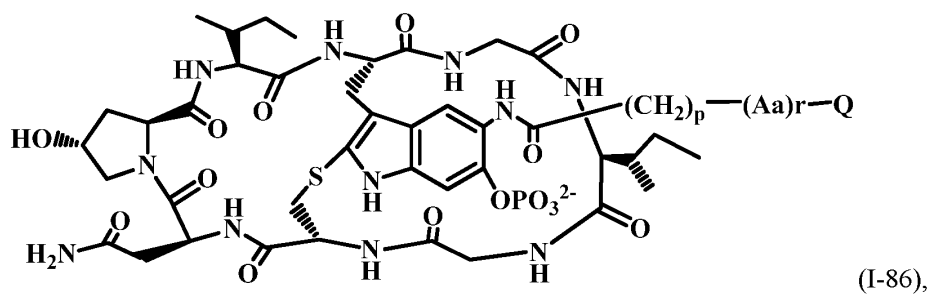
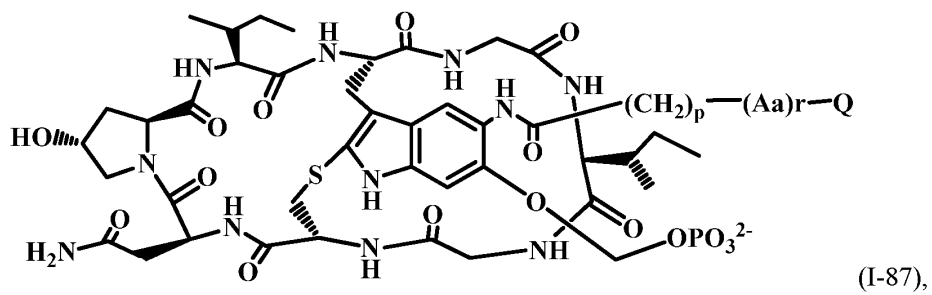
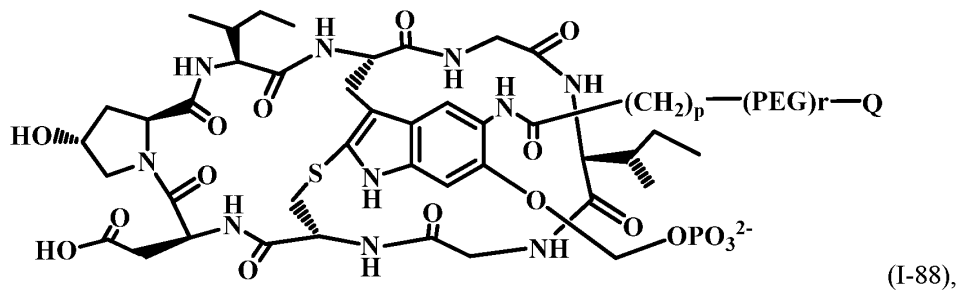
(I-72),

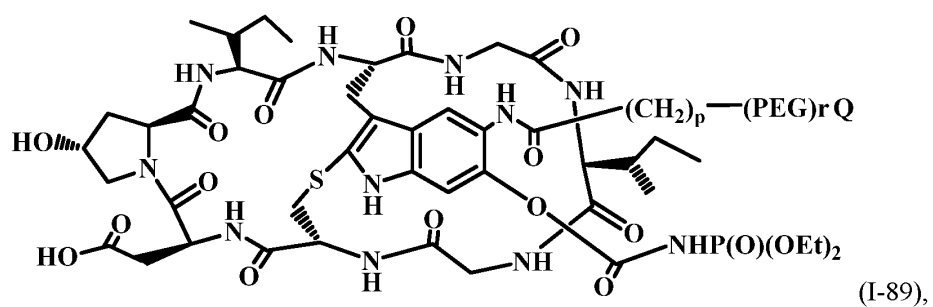
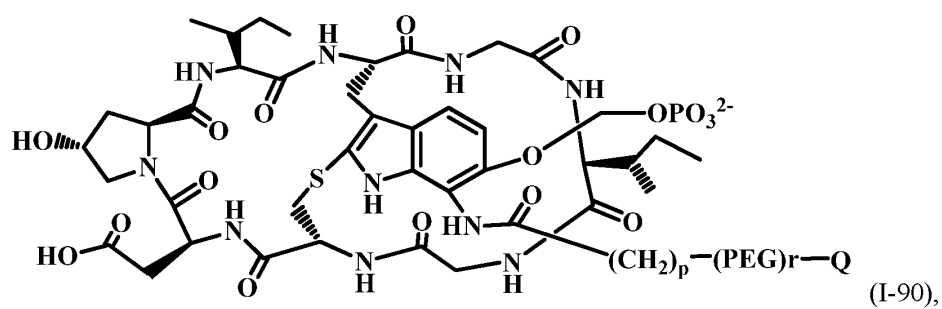
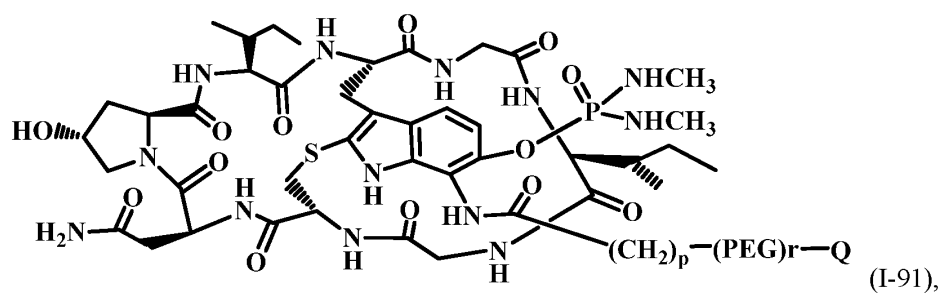
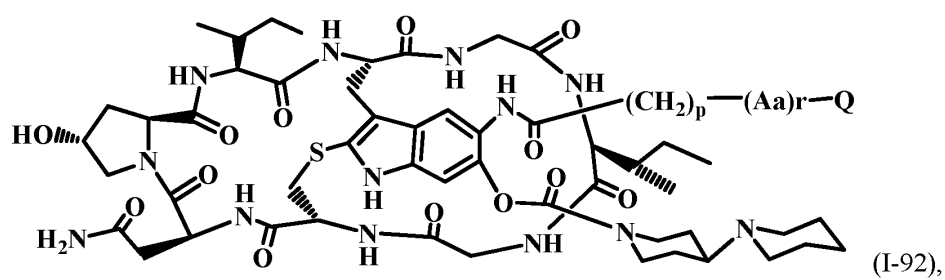
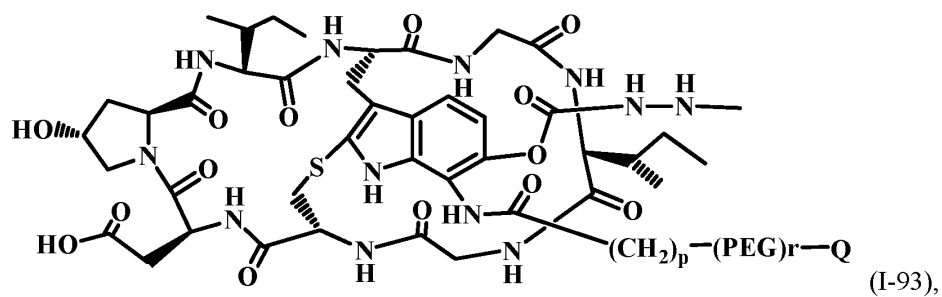


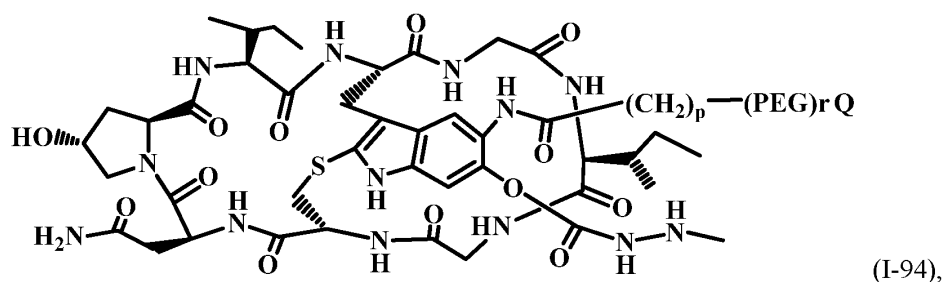
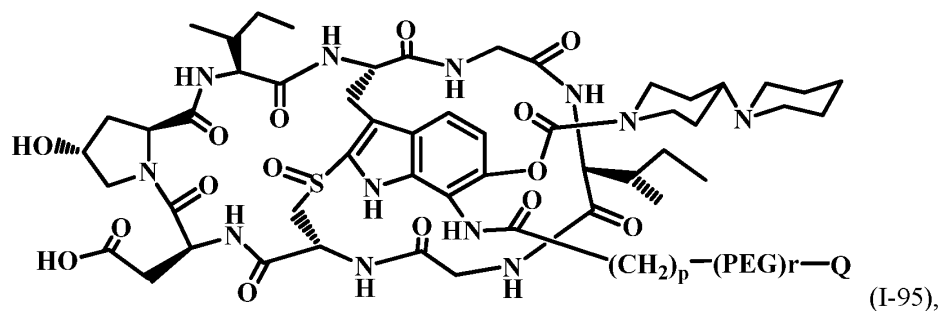
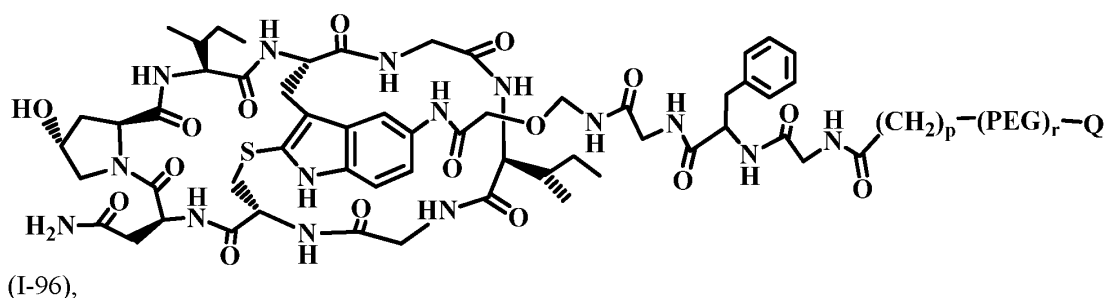
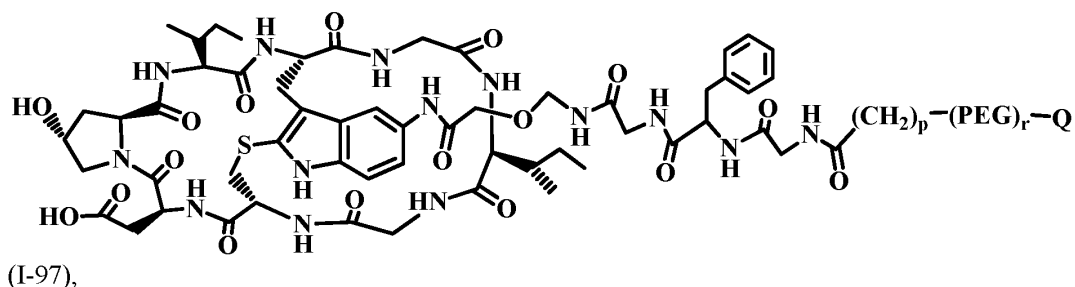
(I-73),









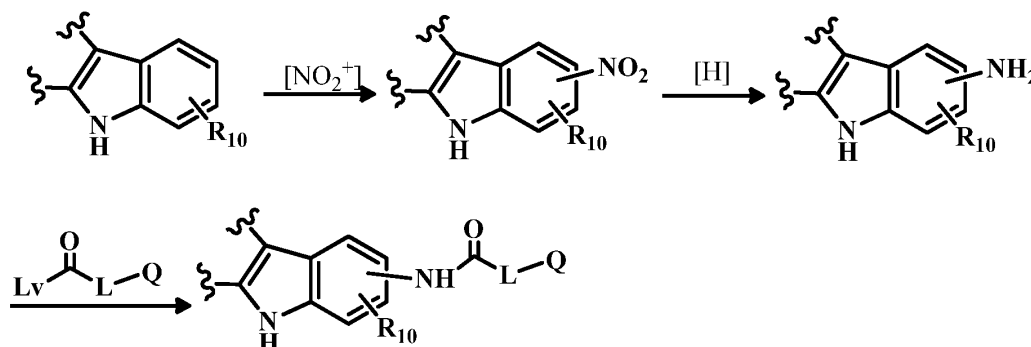


or a pharmaceutically acceptable salt, hydrates, or hydrated salt, or the polymorphic crystalline structure of the compounds thereof, or the optical isomers, racemates, diastereomers or enantiomers.

Wherein Aa, r, n, p, q and Q are defined the same as in the Claim 1. PEG is polyethylene glycol with the formula of  $-(OCH_2CH_2)_r$ . Preferably, Q is H,  $C_1$ - $C_8$  of alkyl, alkenyl, alkynyl, aryl, cyclic, cyclohetero, haloalkyl, alkoxy, haloalkoxy alkylamino; halogen;  $-NO_2$ ;  $-CN$ ;  $-SH$ ;  $-SSCH_3$ ;  $-SSAc$ ;  $-SSAr$ ;  $-SS$ -Pyridine;  $-SS$ -Ar( $-NO_2$ );  $-S$ -cell binding agent; or a function group of NHS

ester, pentafluorophenyl ester; alkyloxyamine; aldehyde; ketone; carboxyl acid; hydrazine; amine; or thiolactone; or linked a cell binding agent via Stretcher units (Ww) or via Spacer units (Tt), wherein W, w, T, and t are defined the same as in the Claim 1.

7. The compound according to any one of Claim 1, 2, 3, 4, 5 or 6 are prepared through sequentially aromatic nitration of the indole units, followed by reduction of the nitro group to an amine, and then the produced amine compounds are condensated with a linker having a reactive or a reactable carboxylic group to form an amide linkage as illustrate below:



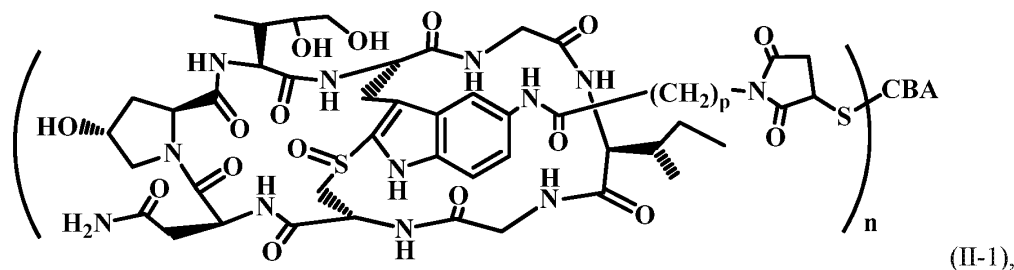
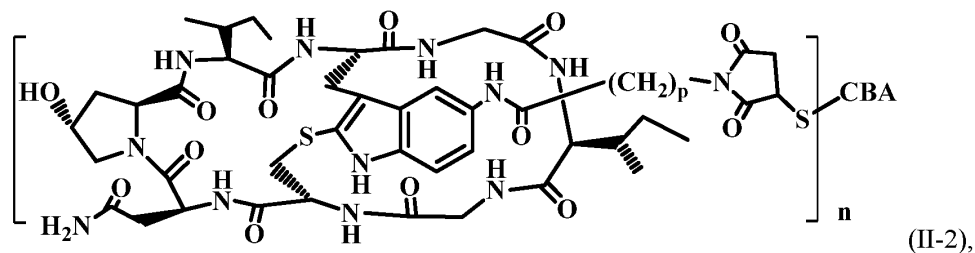
- 10 Wherein  $R_{10}$ , L and Q are defined the same in the Formula (I). Wherein  $L_v$  is leaving group selected from OH, halogen, NHS (N-hydroxyl succinimide), nitrophenol, pentafluorophenol, or a intermediate generated from peptide coupling or from Mitsunobu reaction.

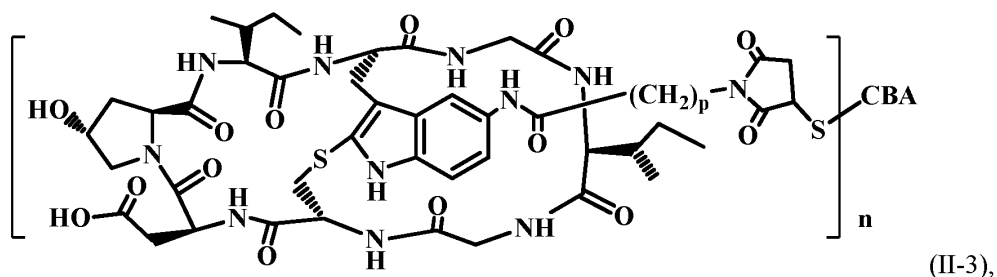
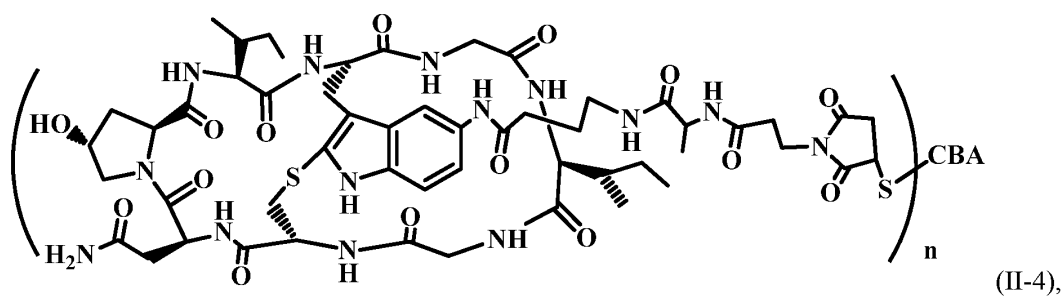
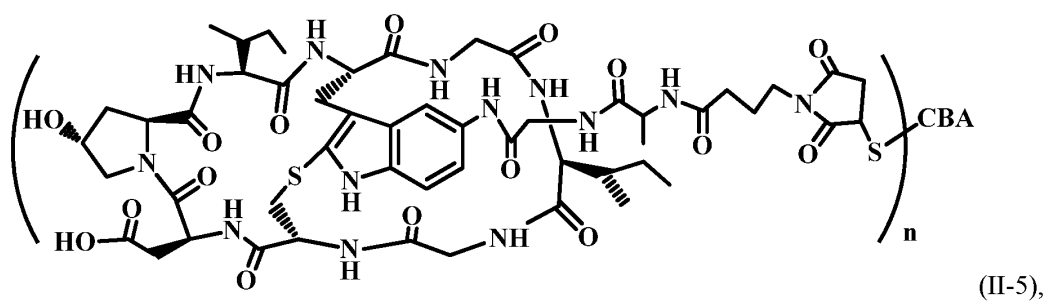
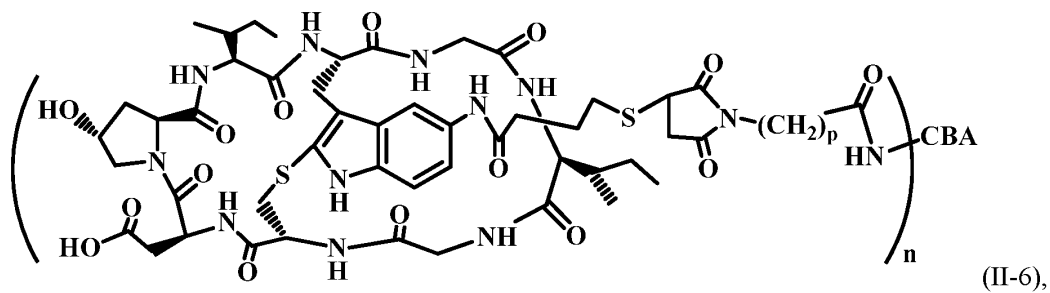
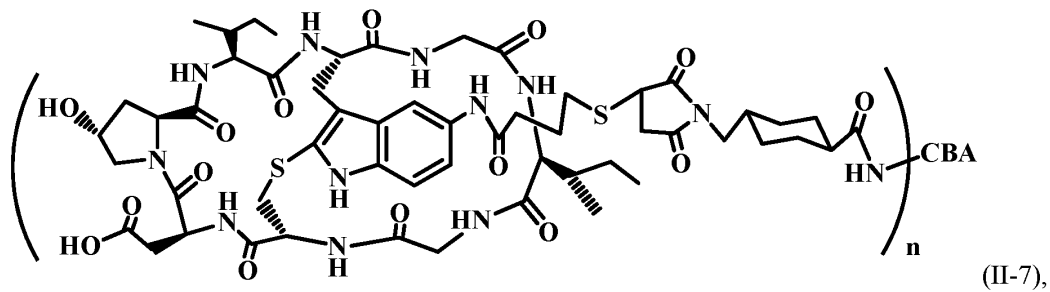
8. The compound according to Claim 1 wherein the linker L can be selected from the group consisting of:  $R_{12}$ ,  $OR_{12}$ ,  $OR_{12}O$ ,  $NHR_{12}$ ,  $NHR_{12}NH$ ,  $NR_{11}R_{12}$ ,  $SR_{12}S$ ,  $OR_{12}NH$ ,  $OR_{12}Ar$ ,  $NHR_{12}Ar$ ,  
 15  $NR_{11}R_{12}NR_{12}'R_{12}''$ ,  $-(CR_{11}R_{12})_p(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(CR_{12}'R_{12}'')_q(Aa)_r(OC$   
 $H_2CH_2)_t$ ,  $-(Aa)_r(CR_{11}R_{12})_p(CR_{12}'R_{12}'')_q-(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(CR_{12}'R_{12}'')_n(OCH_2CH_2)_t(Aa)_r$ ,  
 $-(CR_{11}R_{12})_p(CH=CH)(CR_{12}'R_{12}'')_q(Aa)_r(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(NR_{12}'CO)(Aa)_r(CR_{12}'R_{12}'')_q$ ,  
 $(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(Aa)_r(NHCO)(CR_{12}'R_{12}'')_q-(OCH_2CH_2)_t$ ,  $(CR_{11}R_{12})_p(OCO)(Aa)_r$ ,  
 $(CR_{12}'R_{12}'')_q-(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(OCNR_7)(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(CO)-$   
 20  $(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(NR_{11}CO)(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p$ ,  
 $(OCO)(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p(OCNR_7)(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  
 $(CR_{11}R_{12})_p(CO)(Aa)_r(CR_{12}'R_{12}'')_q(OCH_2CH_2)_b$ ,  $-(CR_{11}R_{12})_p$ -phenyl-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  
 $(CR_{11}R_{12})_p$ -furyl-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -oxazolyl-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -  
 thiazolyl-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -thienyl-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -imidazolyl-CO-  
 25  $(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -morpholino-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -piperazino-CO(Aa) $_r$ ,  
 $(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p$ -N-methylpiperazin-CO(Aa) $_r(CR_{12}'R_{12}'')_q$ ,  $-(CR_{11}R_{12})_p(Aa)_r$ -phenyl-, -

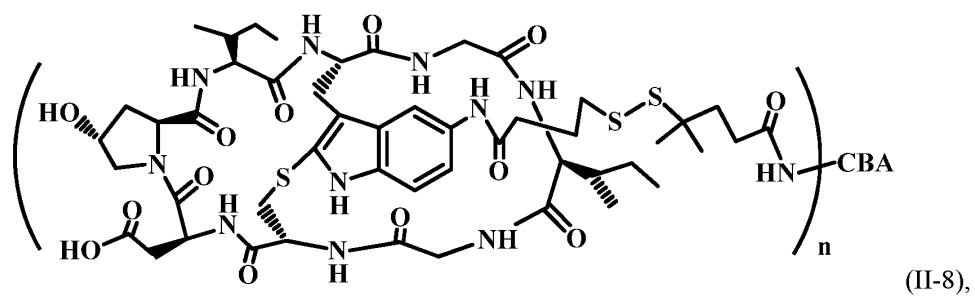
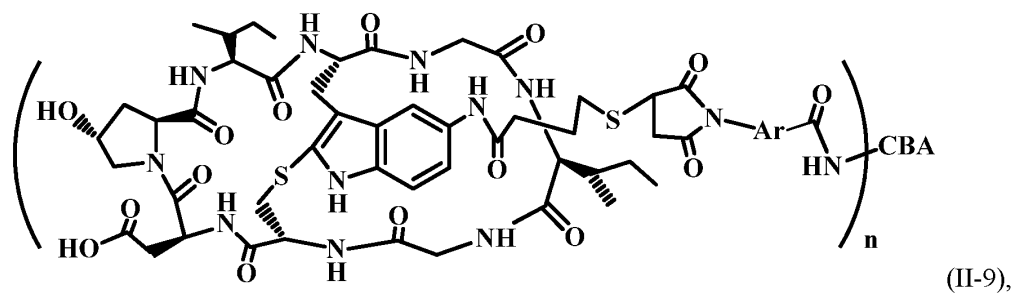
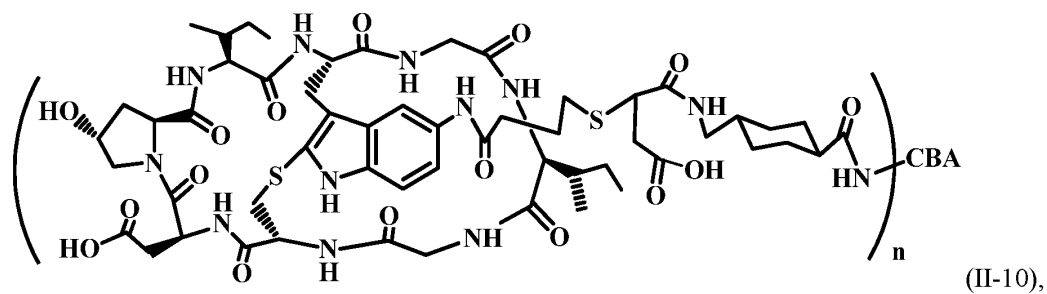
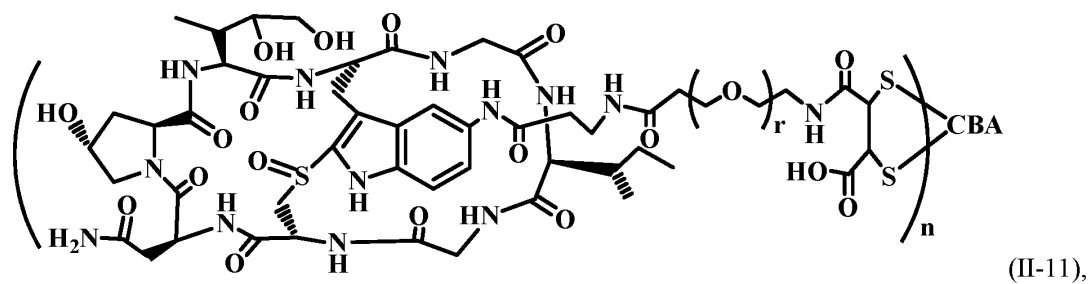
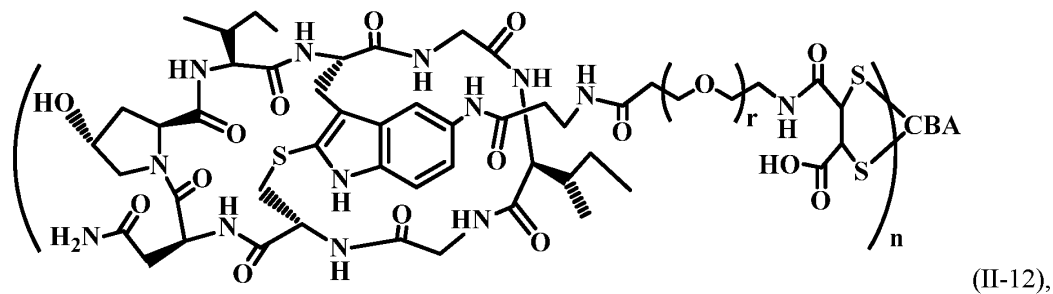
- (CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-(Aa)<sub>r</sub>-furyl-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-oxazolyl(Aa)<sub>r</sub>-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-thiazolyl-(Aa)<sub>r</sub>-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-thienyl-(Aa)<sub>r</sub>-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-imidazolyl(Aa)<sub>r</sub>-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-morpholino-(Aa)<sub>r</sub>-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-piperazino-(Aa)<sub>r</sub>-, -(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-N-methylpiperazino-(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(Aa)<sub>r</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(Aa)<sub>r</sub>(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(CR<sub>7</sub>=CR<sub>8</sub>)(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(Aa)<sub>r</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(NR<sub>7</sub>CO)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(Aa)<sub>r</sub>(NR<sub>7</sub>CO)(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(OCO)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(O CNR<sub>7</sub>)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(CO)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(NR<sub>11</sub>CO)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(OCO)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(OCNR<sub>7</sub>)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>(CO)(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>t</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-phenyl-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-furyl-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-oxazolyl-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-thiazolyl-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-thienyl-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-imidazolyl-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-morpholino-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-piperazino-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-N-methylpiperazino-CO-(Aa)<sub>r</sub>(CR<sub>12</sub>'R<sub>12</sub>'')<sub>q</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-(Aa)<sub>r</sub>-phenyl-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>m</sub>-(Aa)<sub>r</sub>-furyl-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-oxazolyl(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>m</sub>-thiazolyl-(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-thienyl-(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-imidazolyl(Aa)<sub>r</sub>-, -K((CR<sub>11</sub>R<sub>12</sub>)<sub>m</sub>-morpholino-(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>p</sub>-piperazino-(Aa)<sub>r</sub>-, -K(CR<sub>11</sub>R<sub>12</sub>)<sub>m</sub>-N-methylpiperazino-(Aa)<sub>r</sub>.

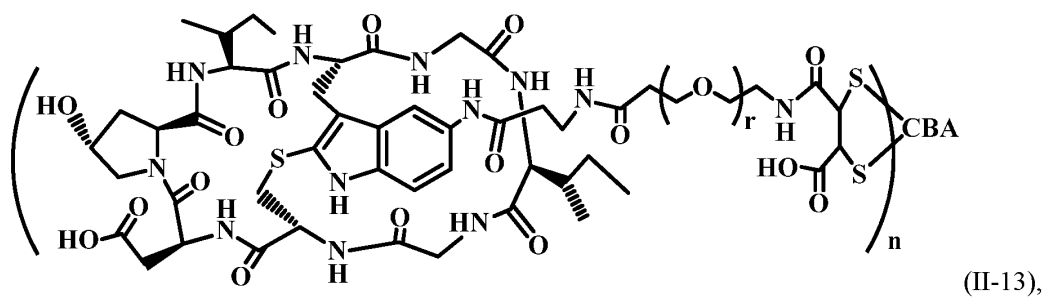
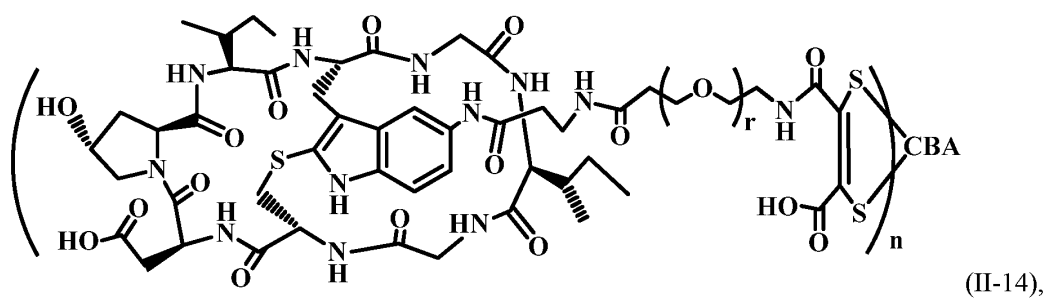
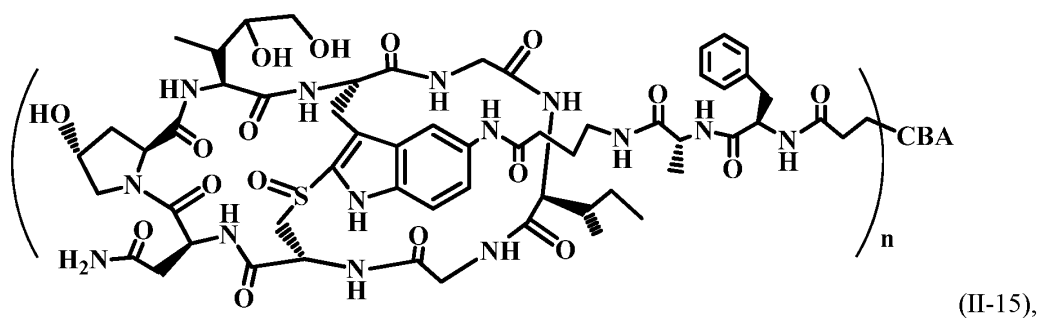
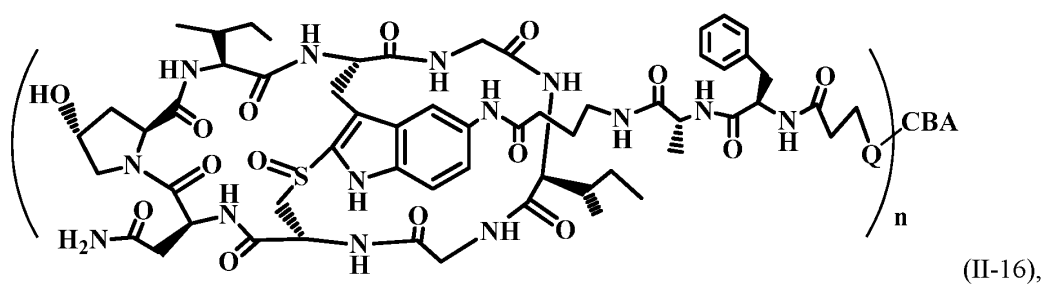
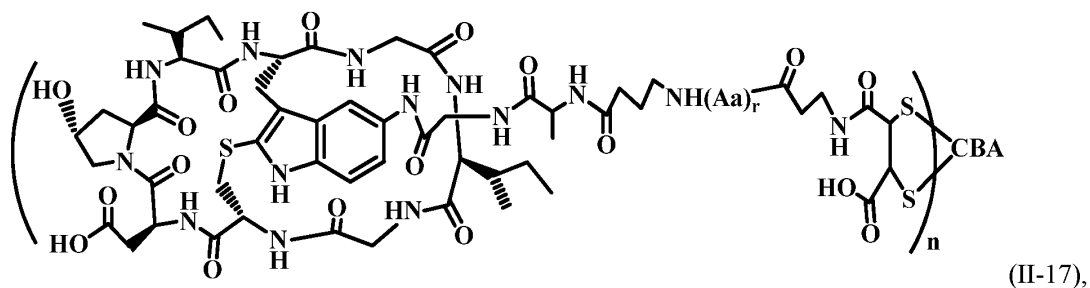
Wherein K is NR<sub>12</sub>, O, S, Se, B, C<sub>3</sub>~C<sub>10</sub> of Ar or Heterocyclic; wherein Aa, r, n, p, q, t, R<sub>7</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>12</sub>', R<sub>12</sub>'' are as defined in Claim 1.

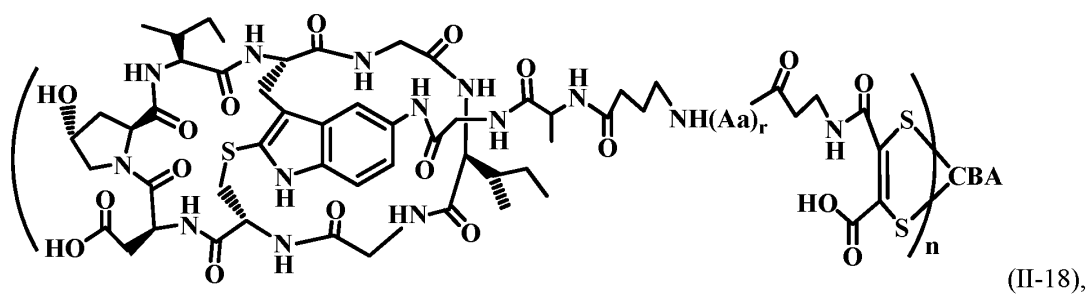
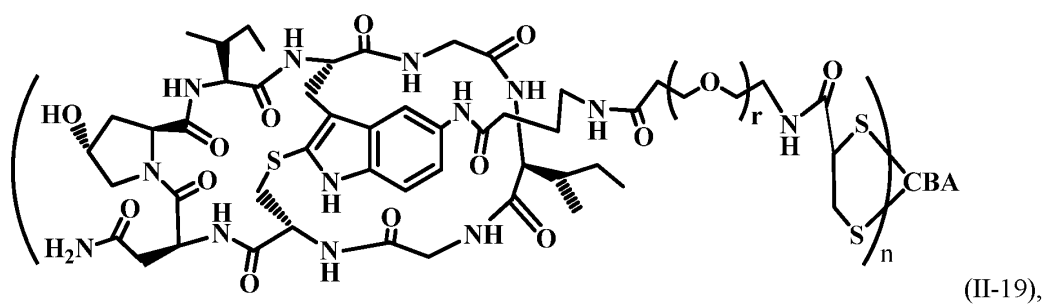
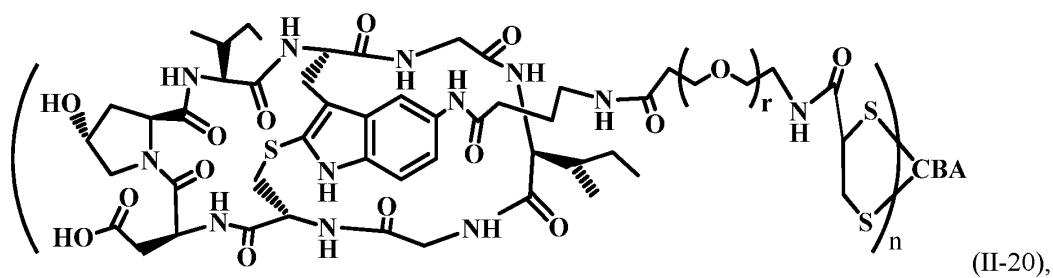
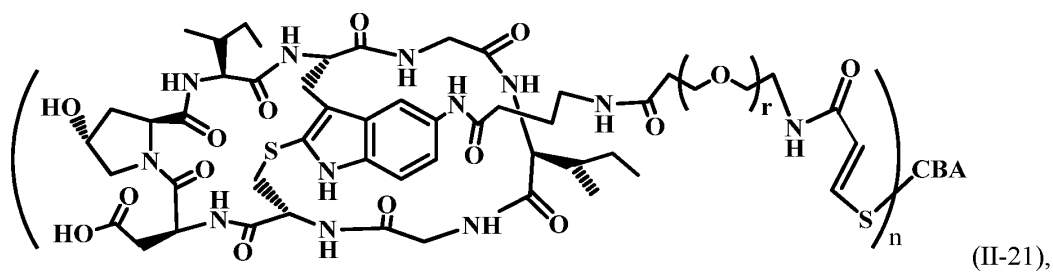
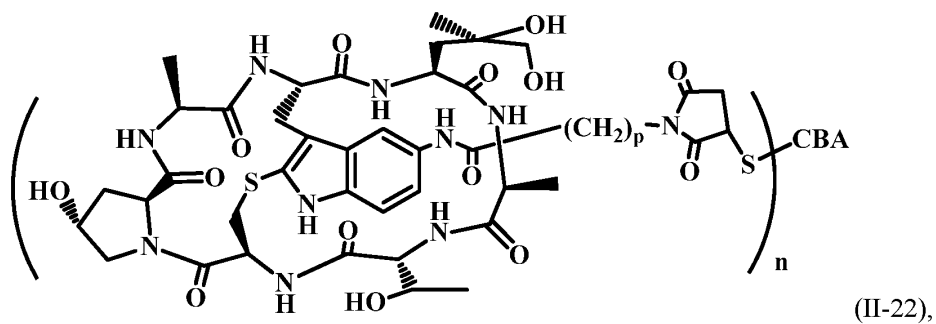
9. A compound according to Claim 1 having the following formula (II-1) - (II-91):

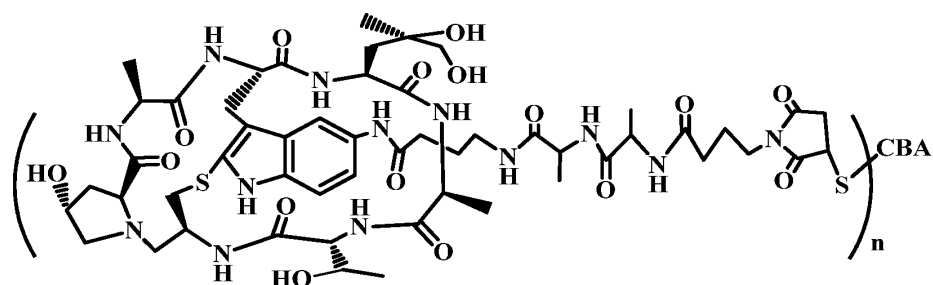




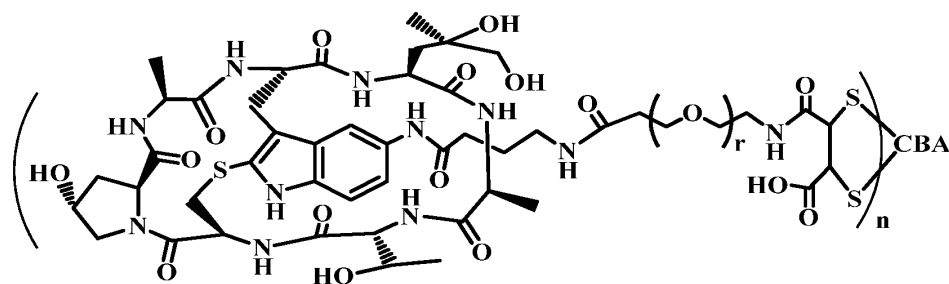




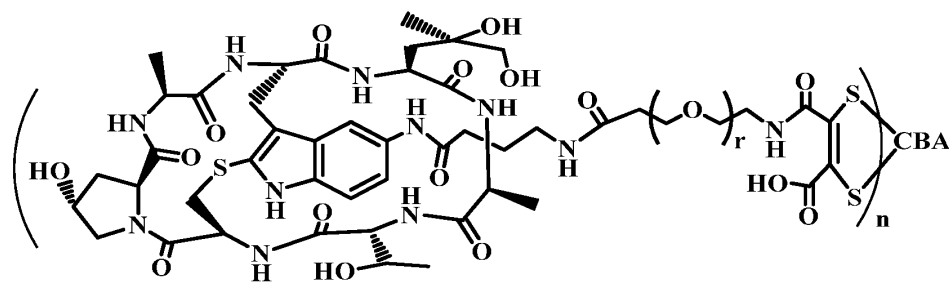




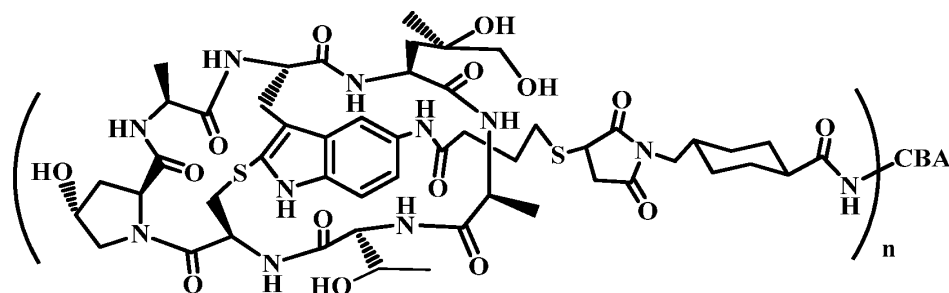
(II-23),



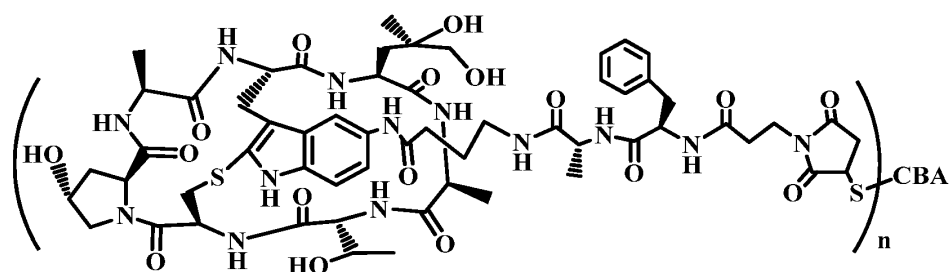
(II-24),



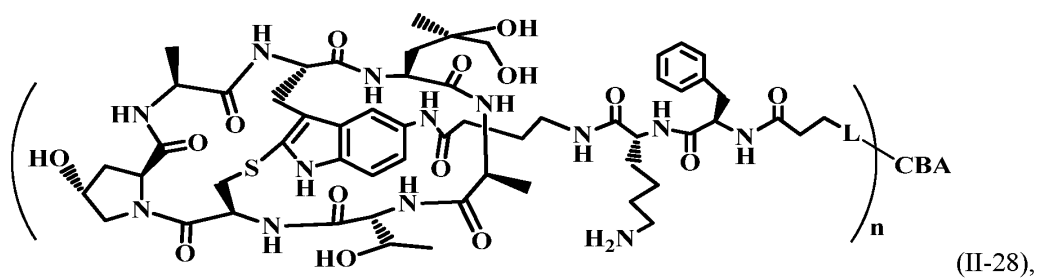
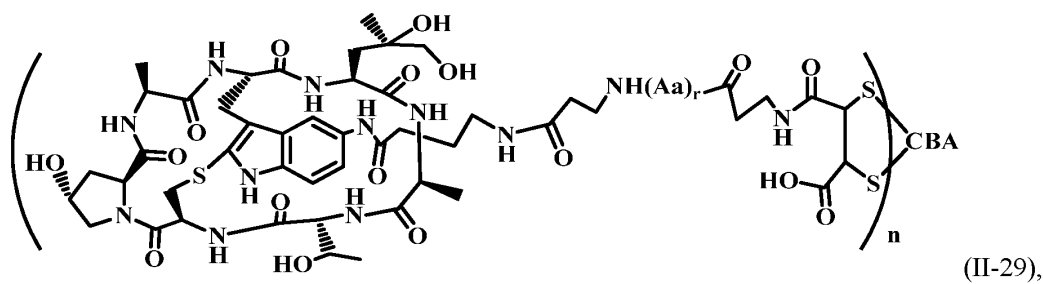
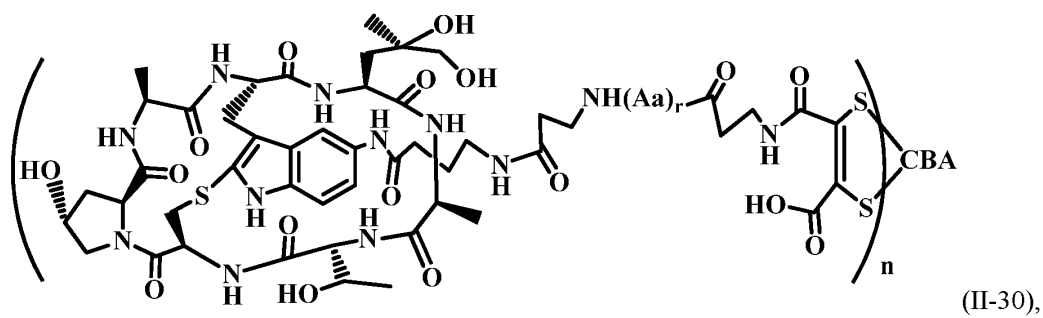
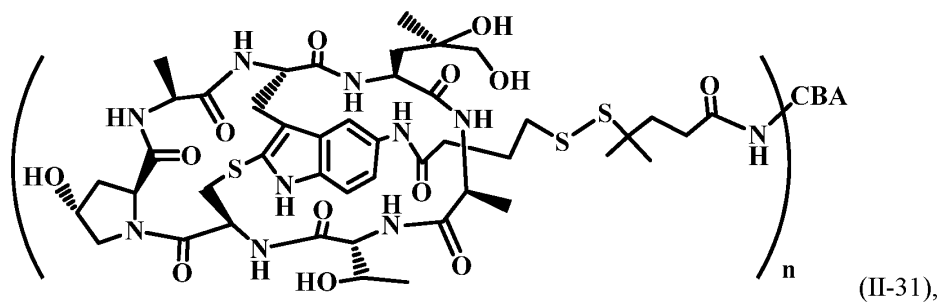
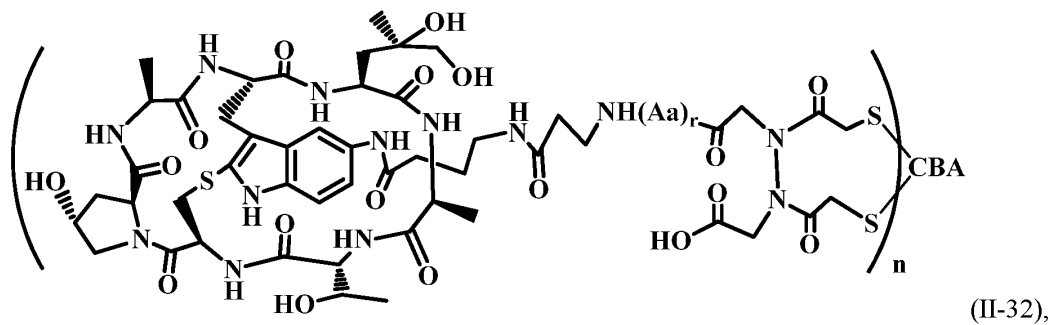
(II-25),

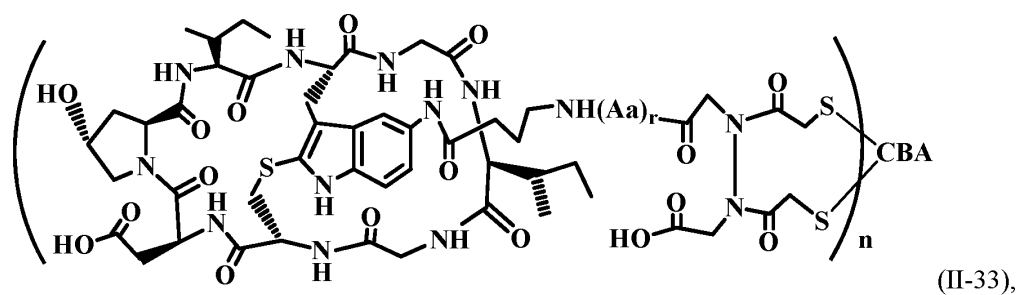
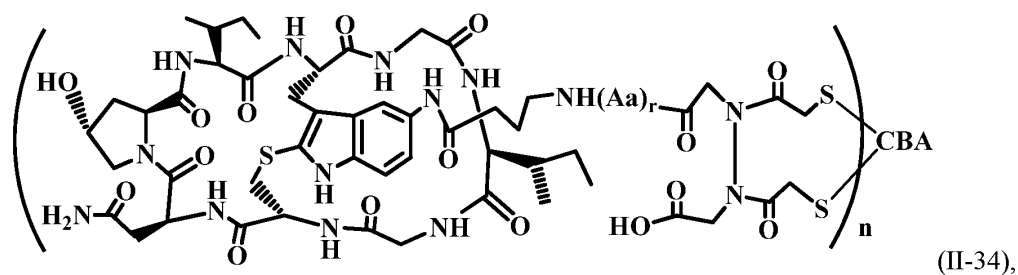
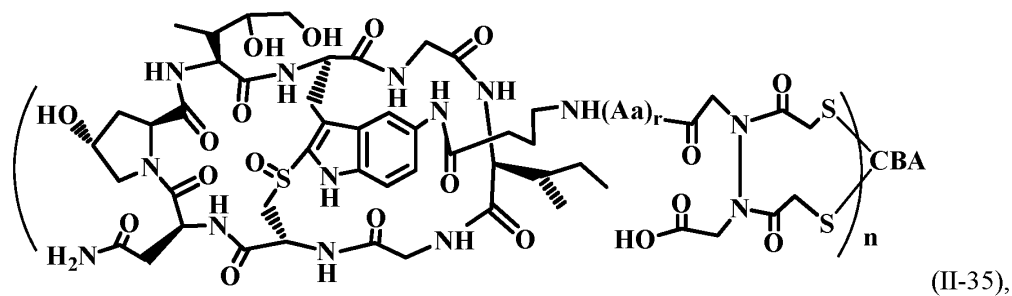
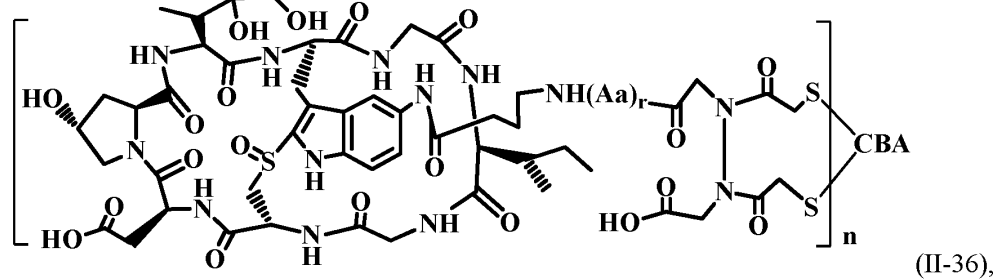
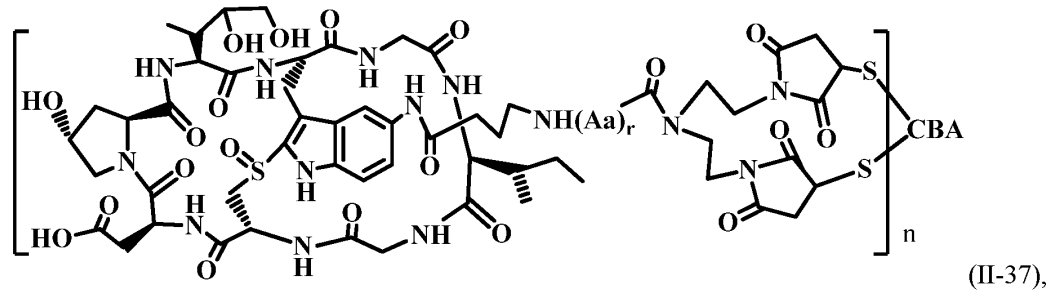


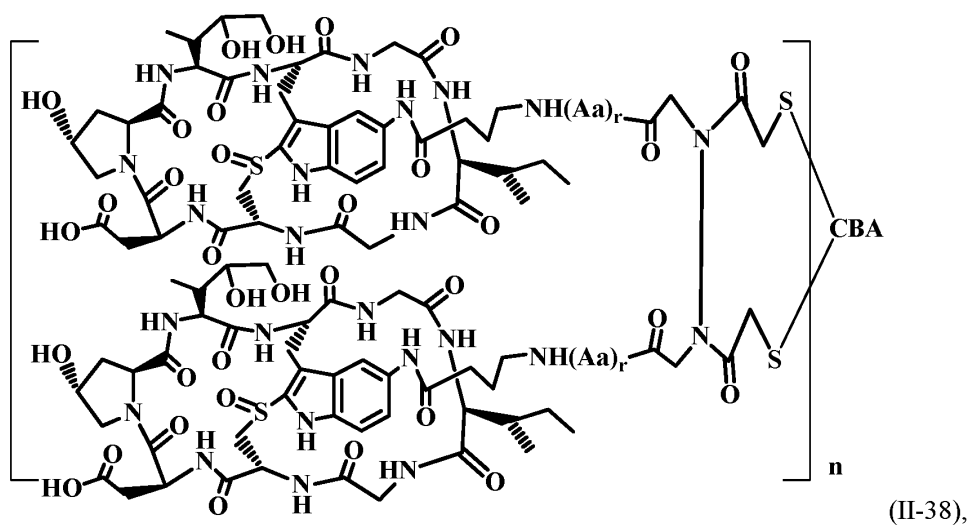
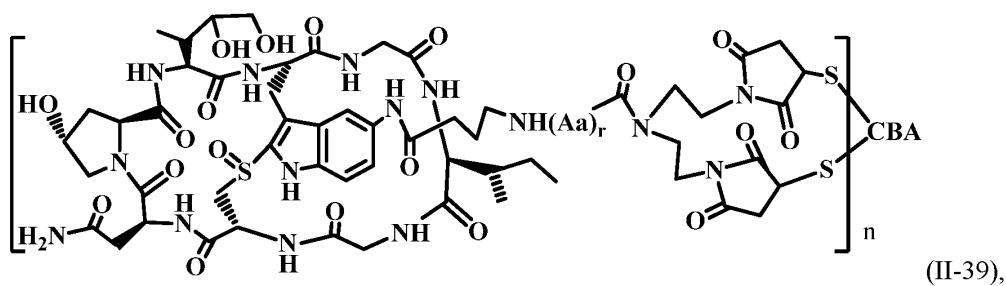
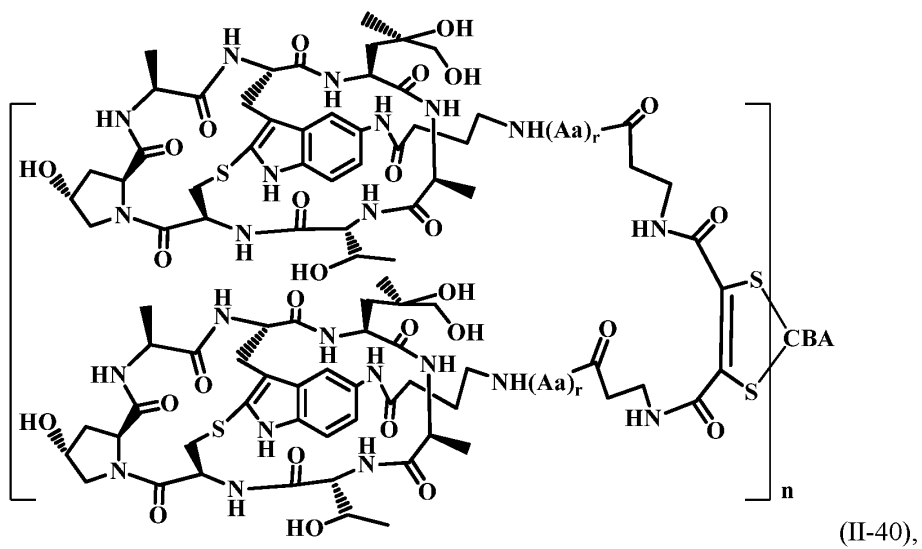
(II-26),

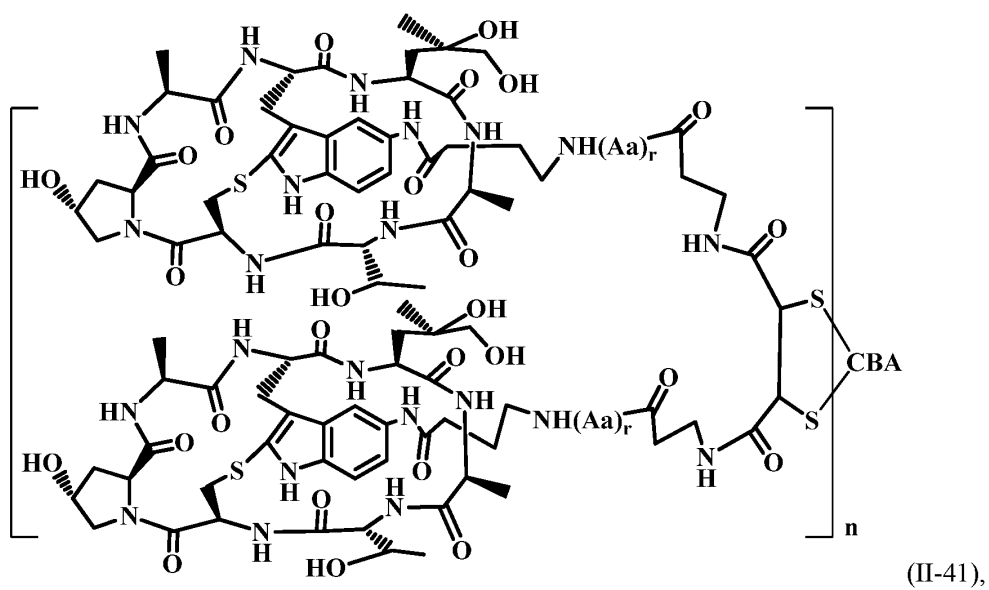
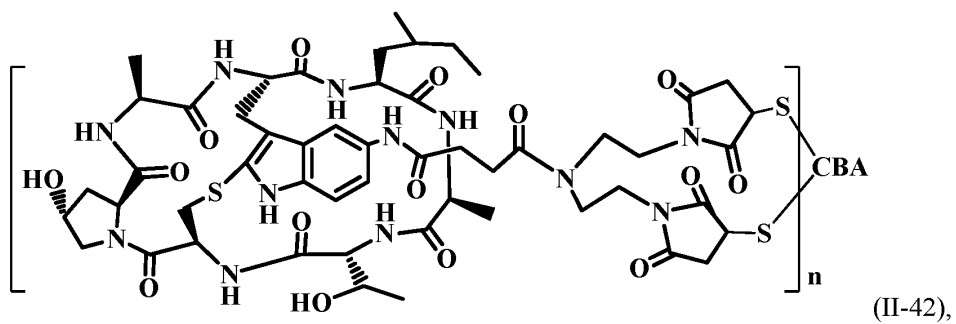
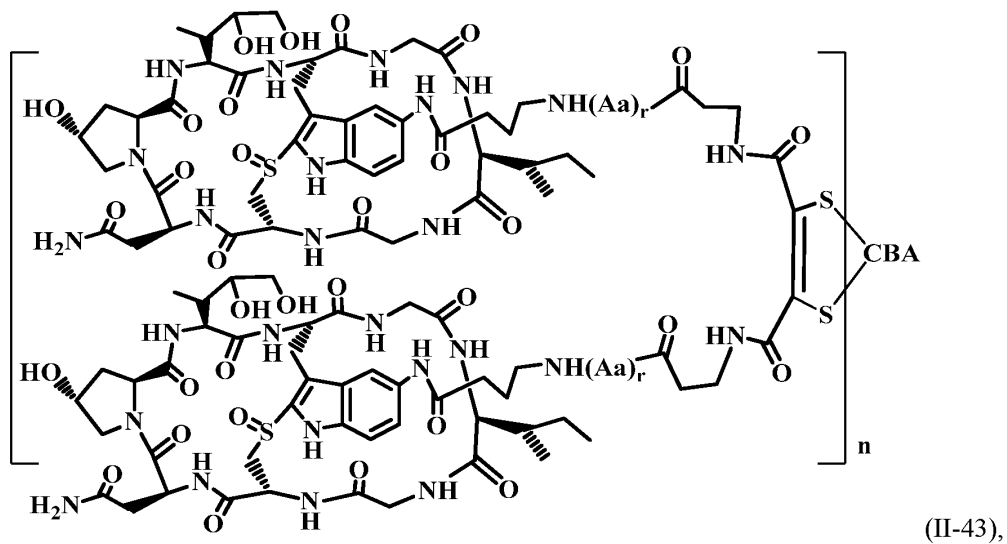


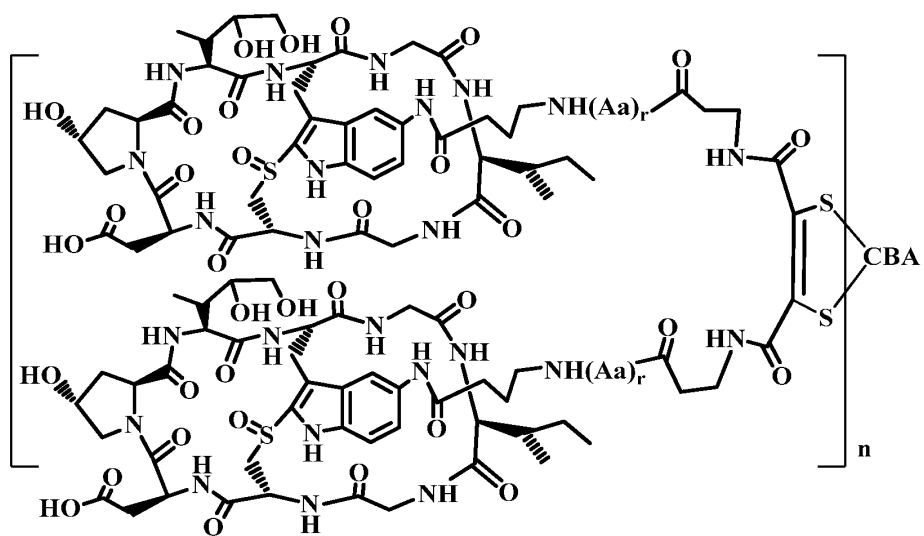
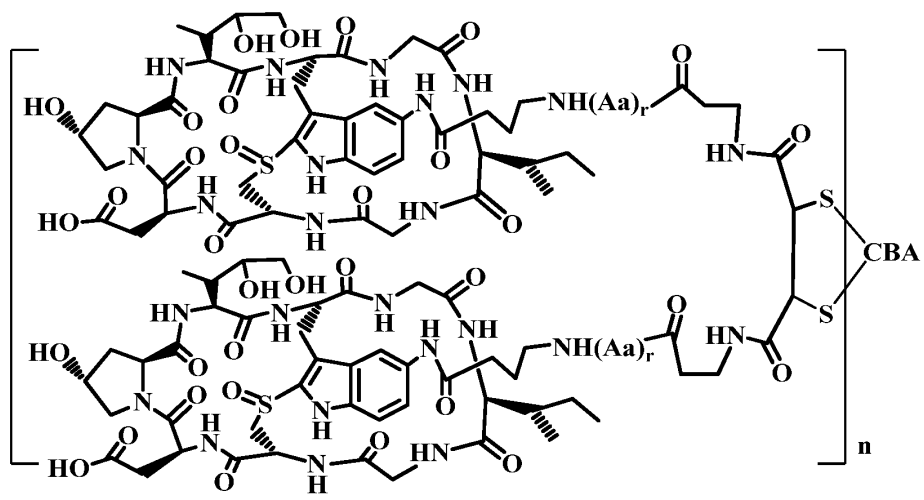
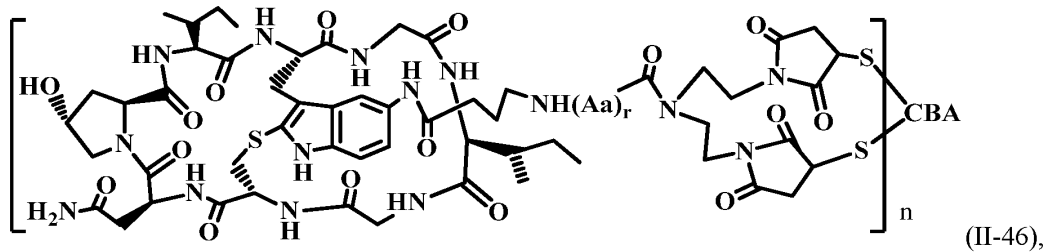
(II-27),

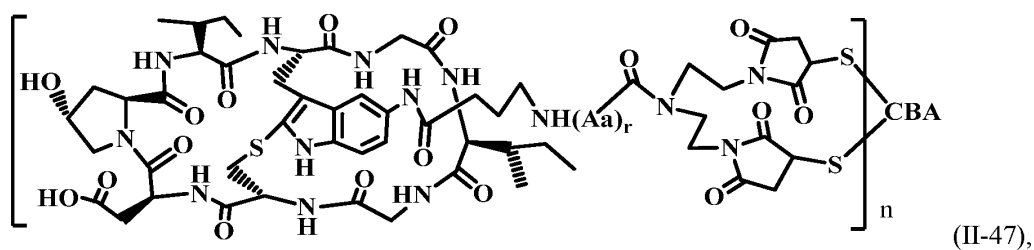
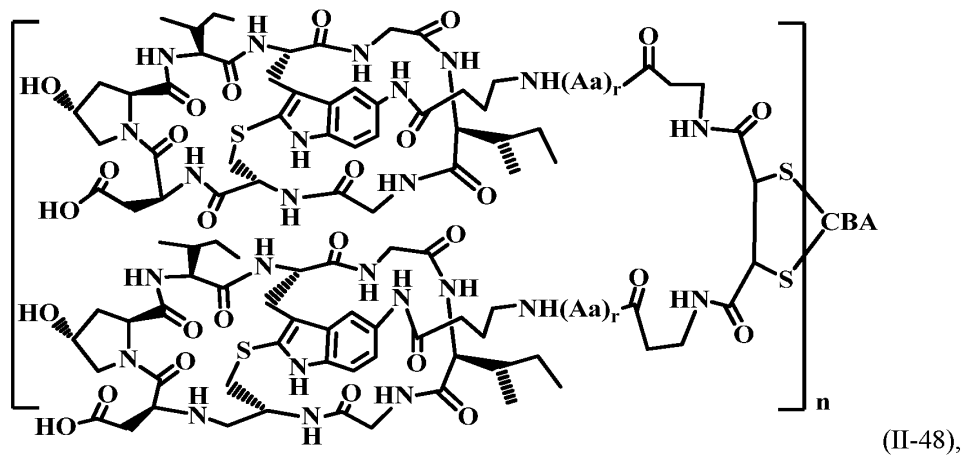
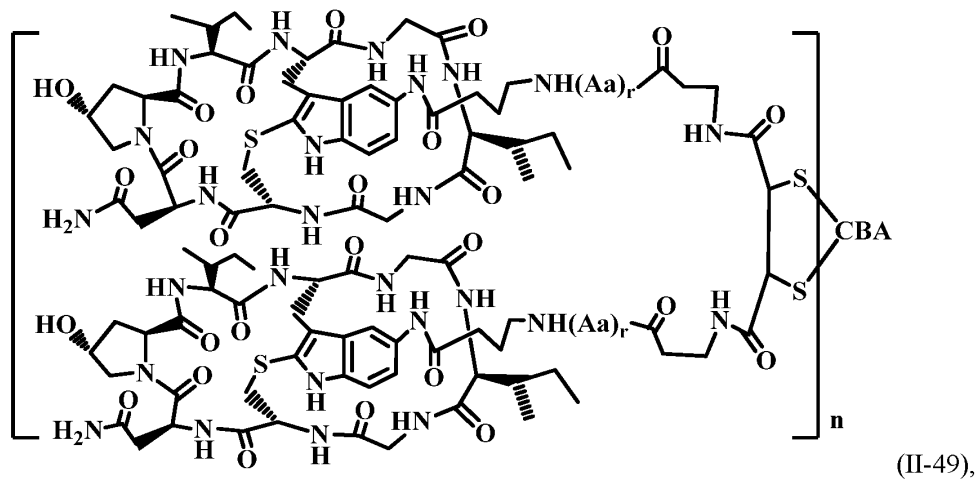
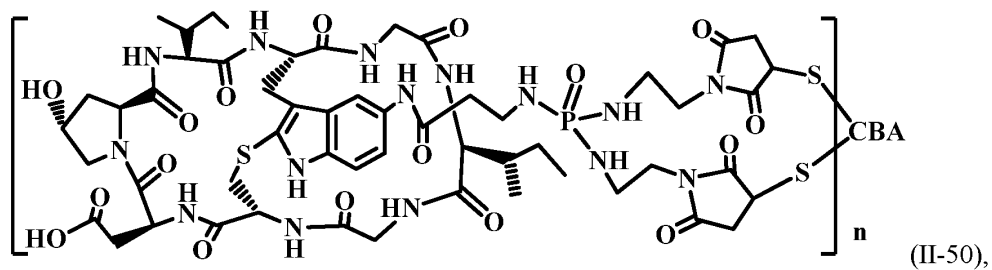


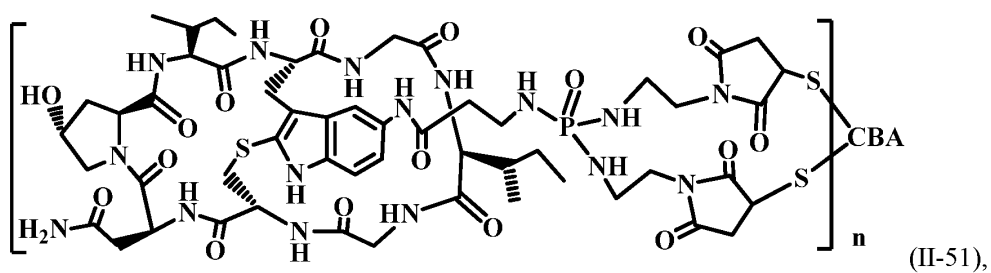
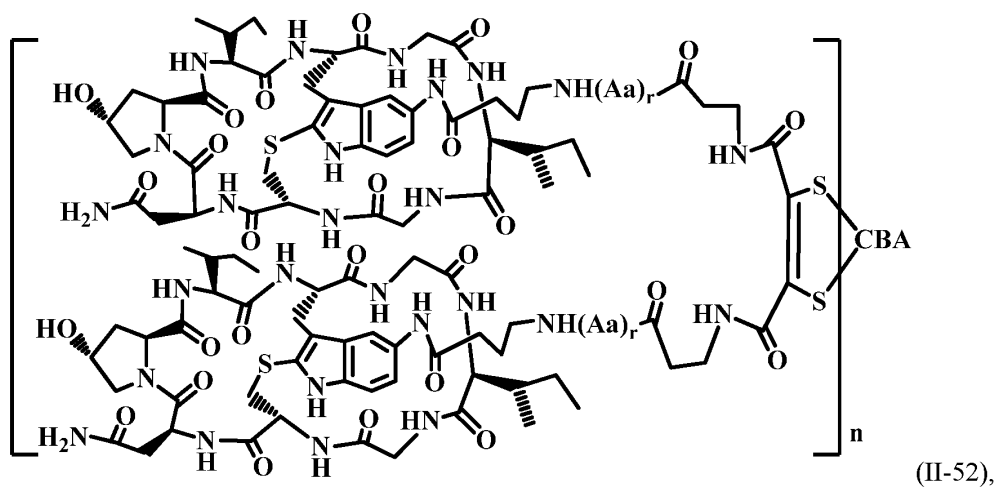
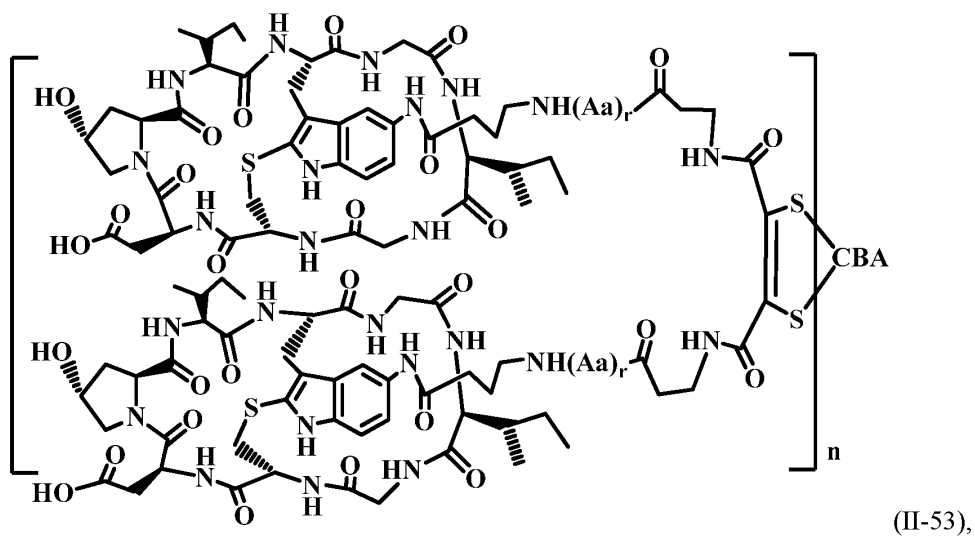


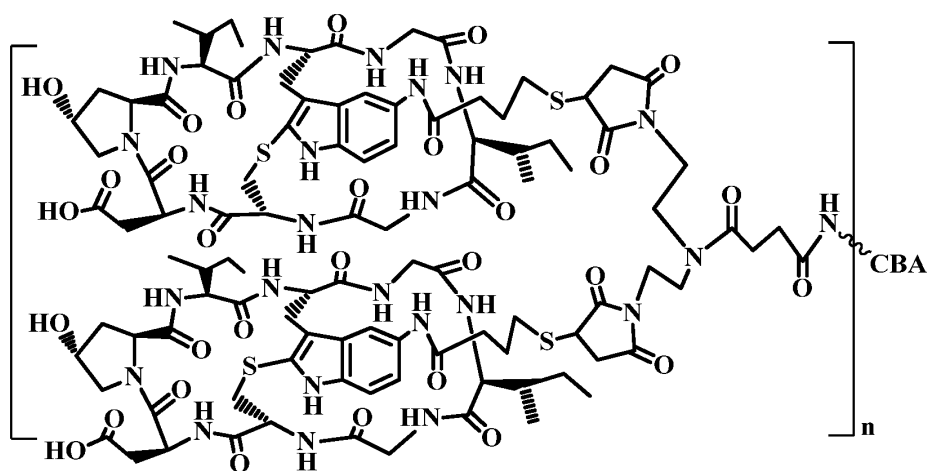
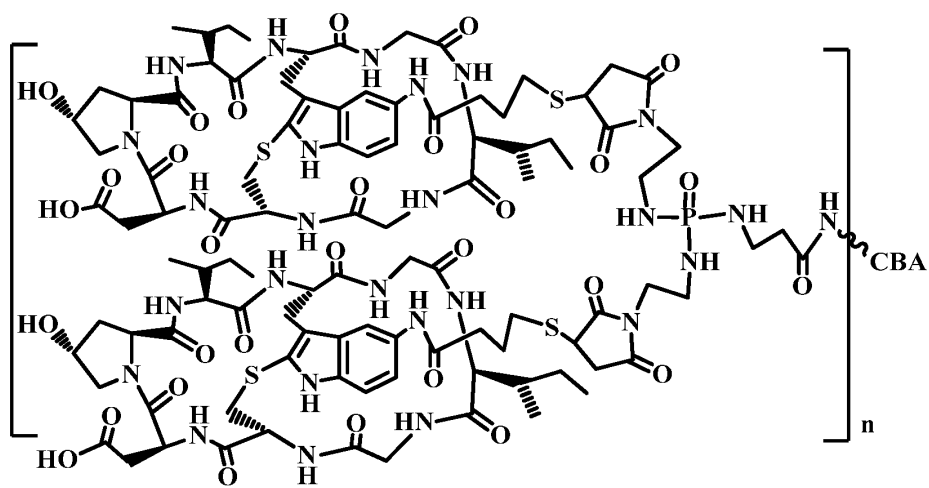
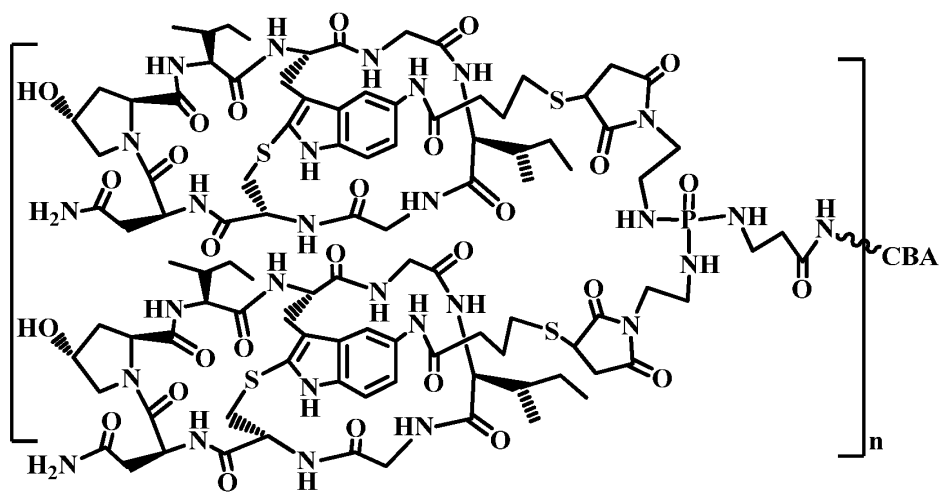


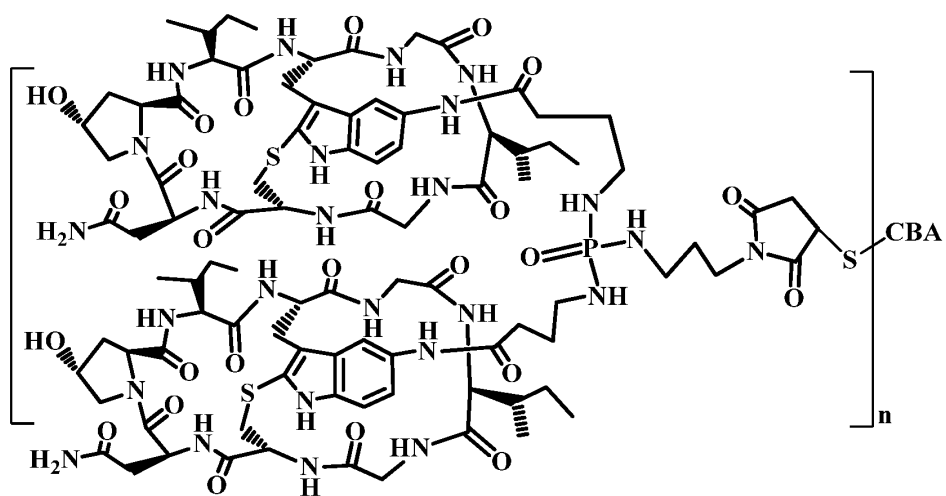
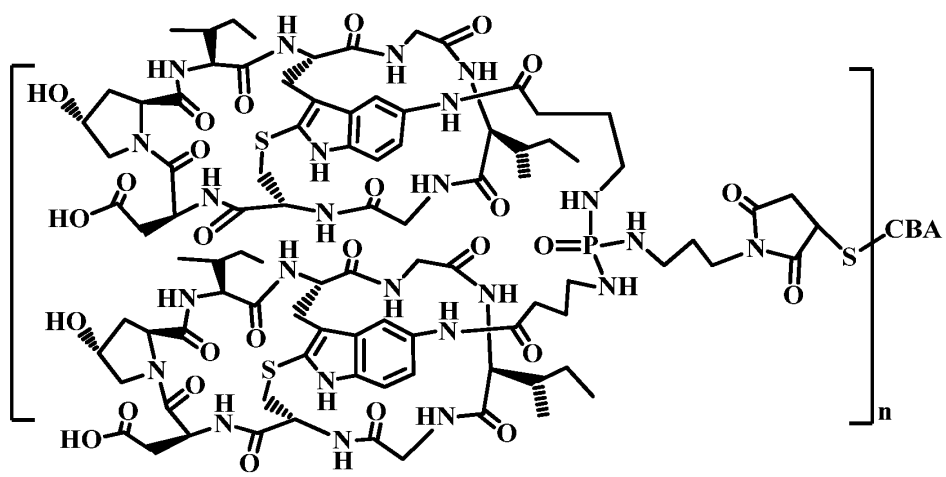
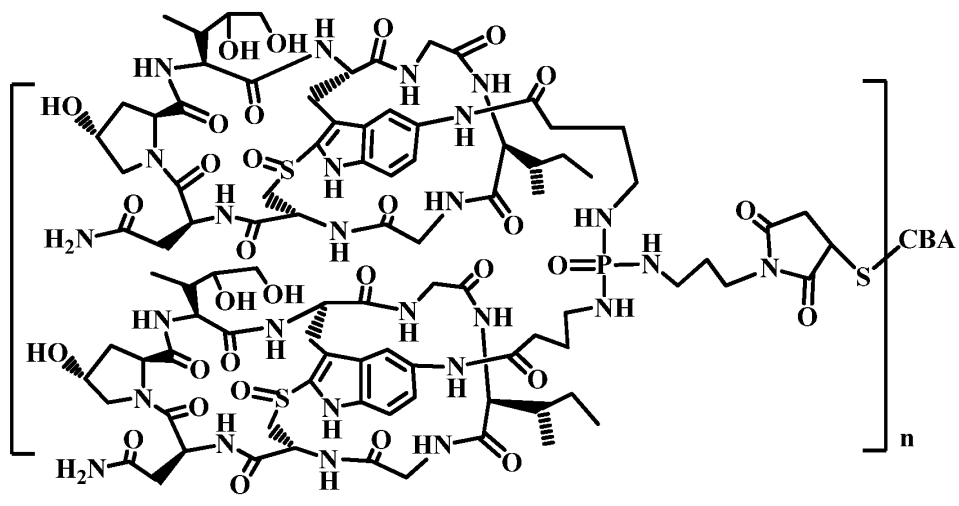


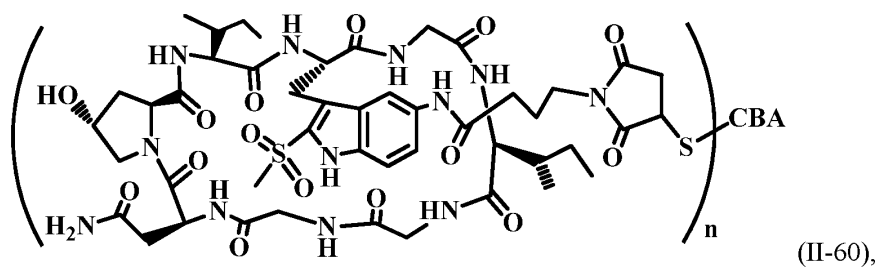
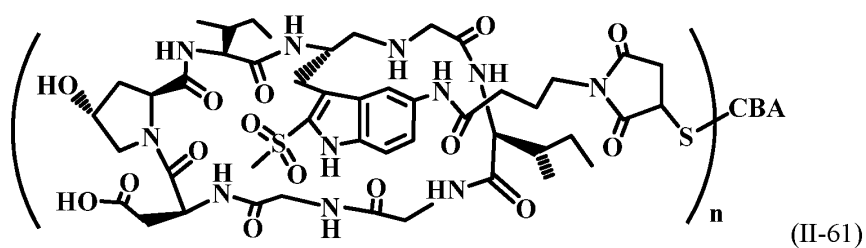
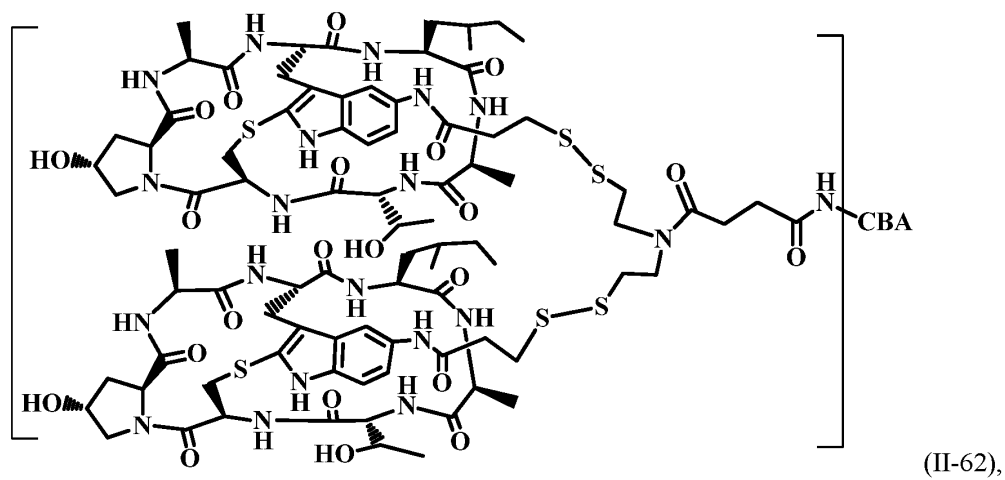
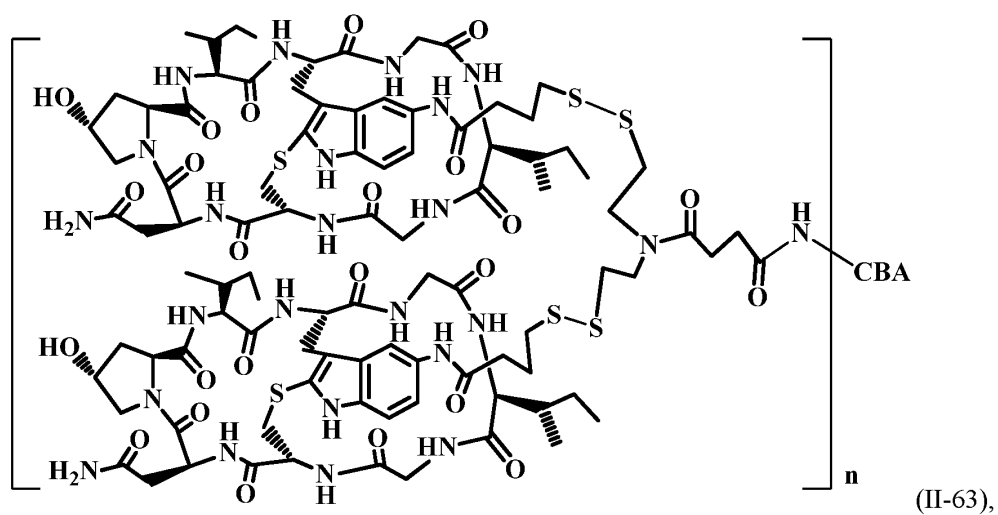


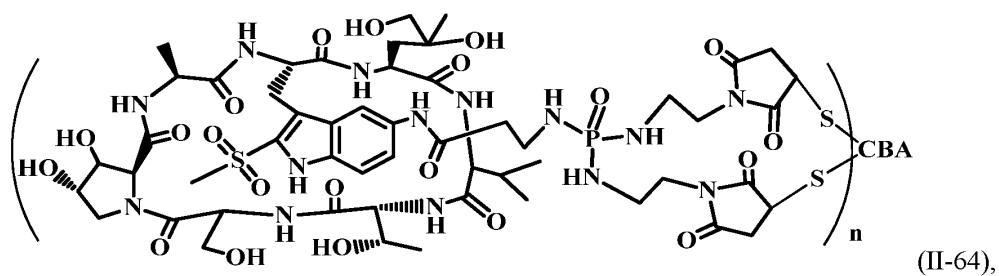
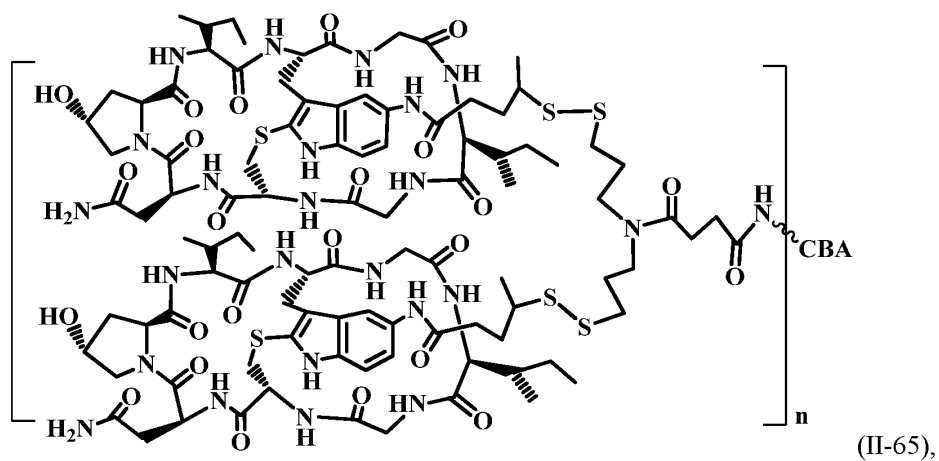
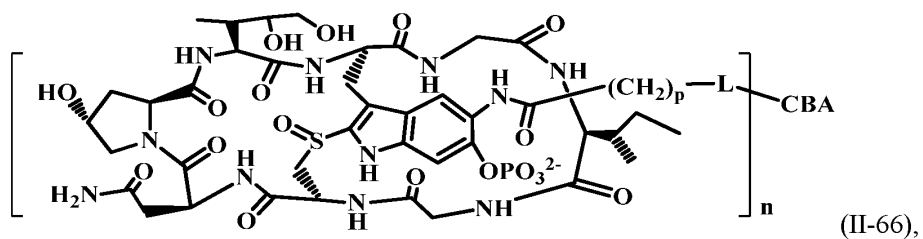
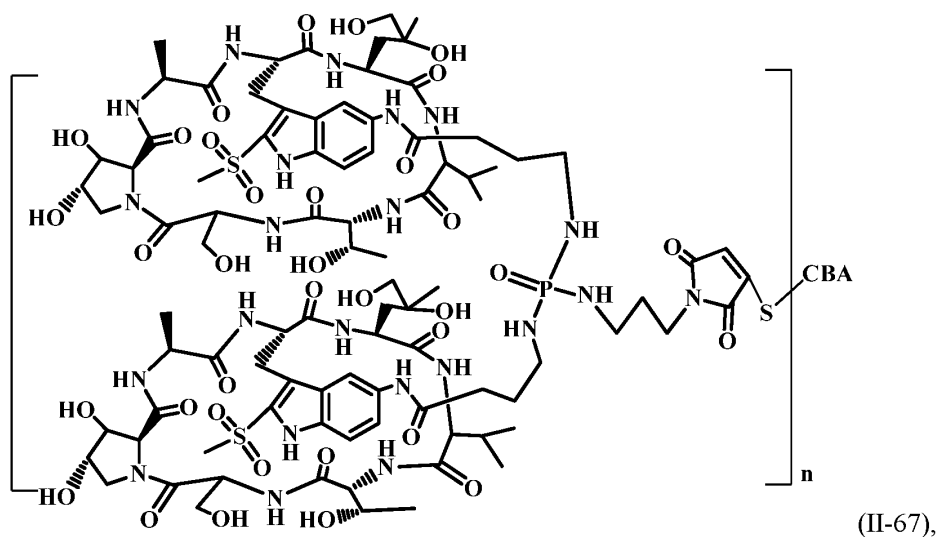


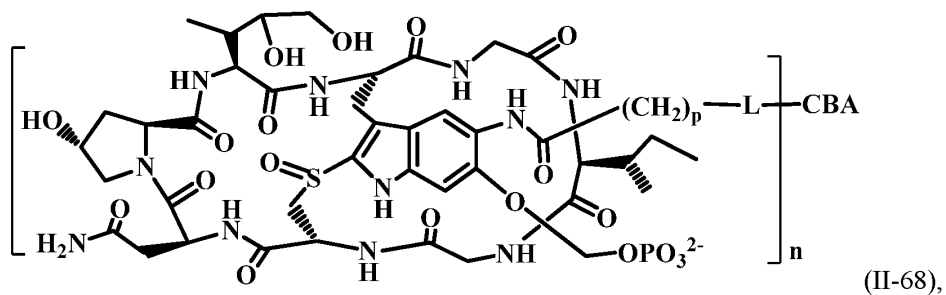
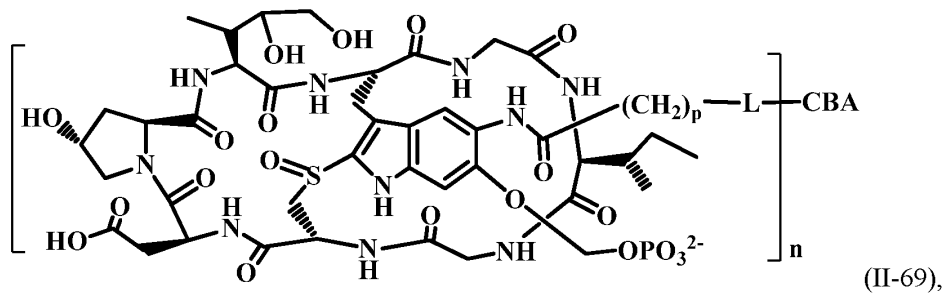
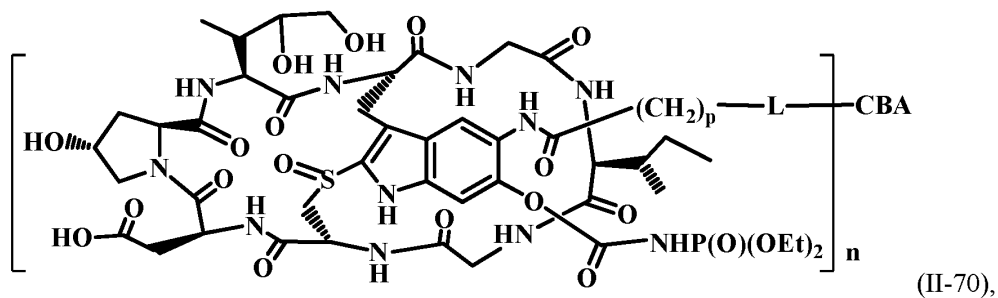
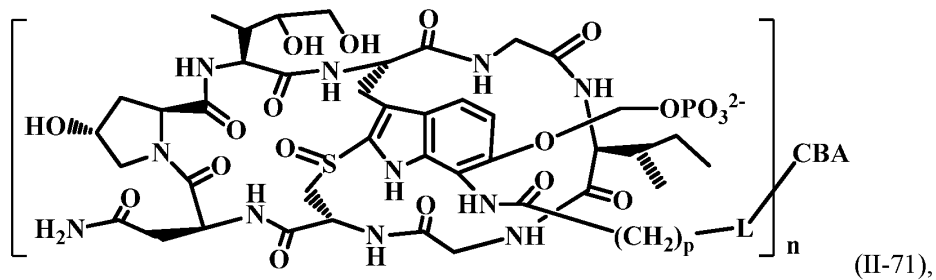
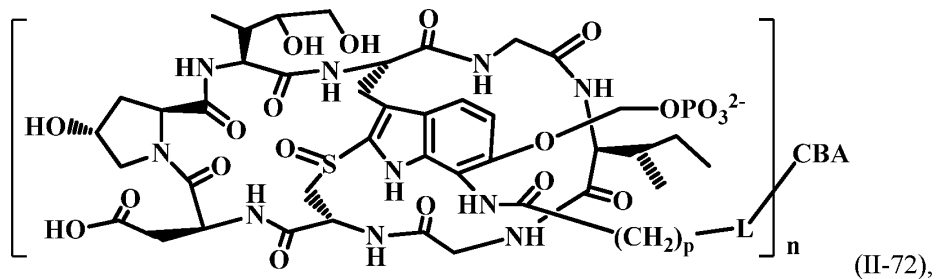


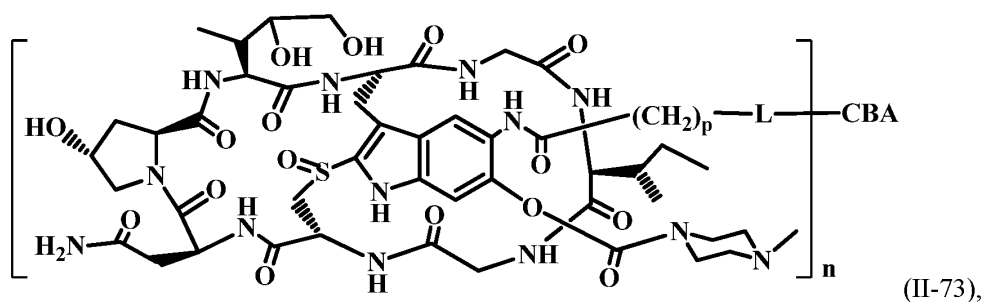
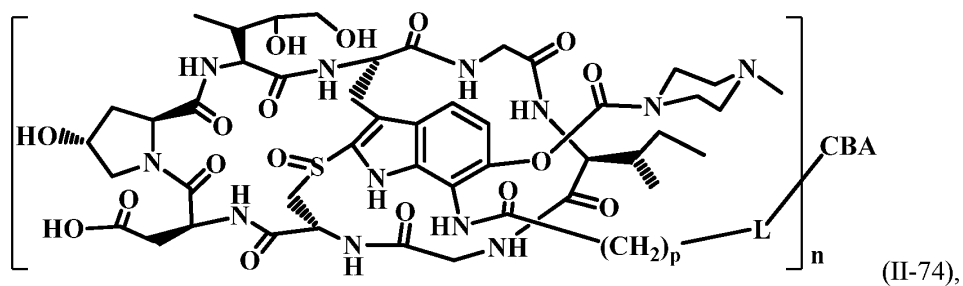
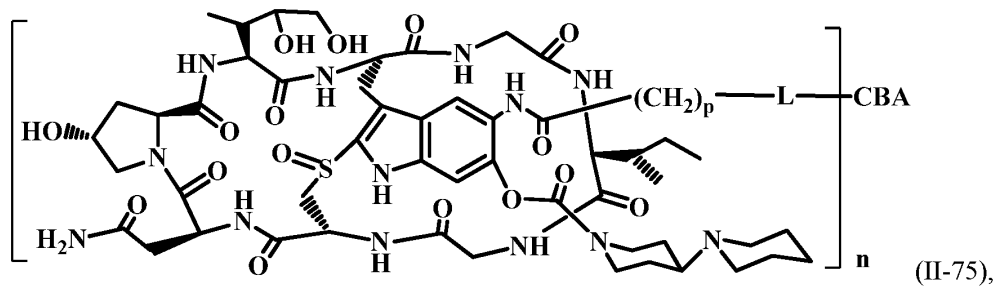
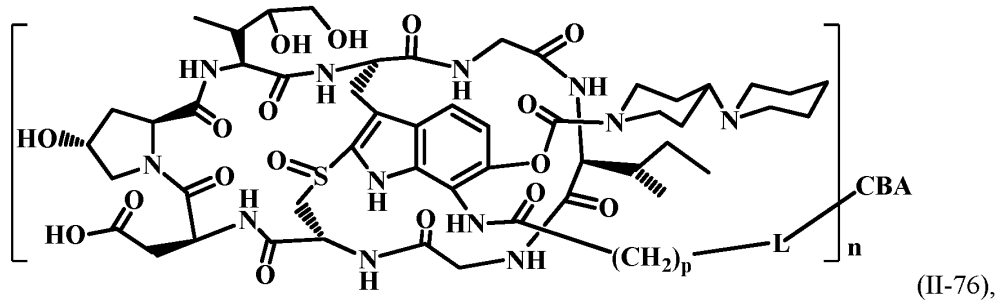
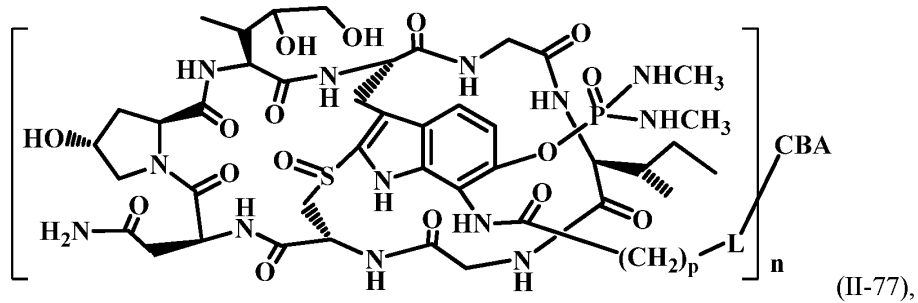


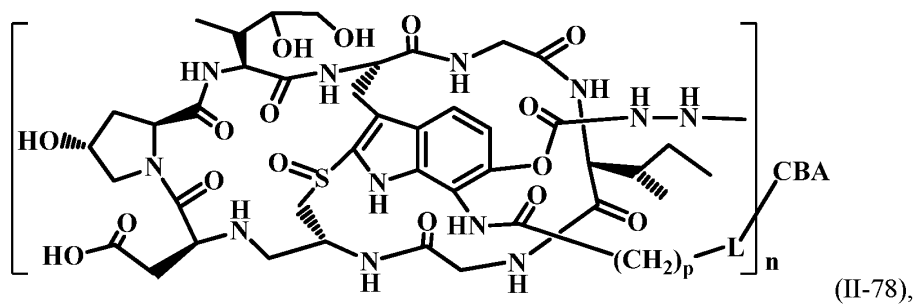
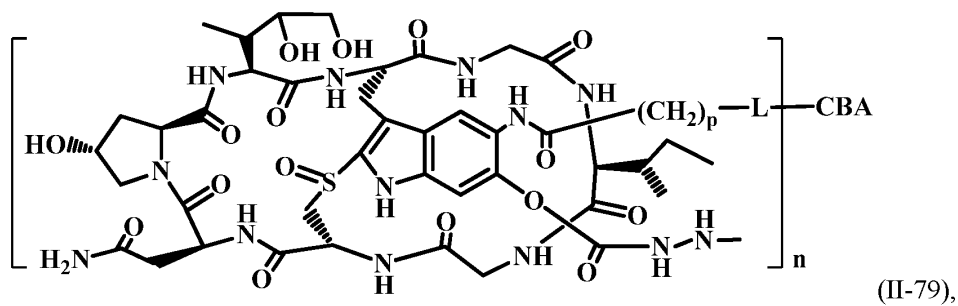
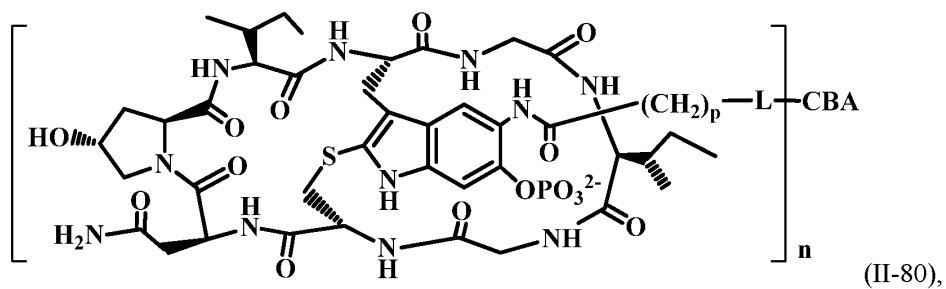
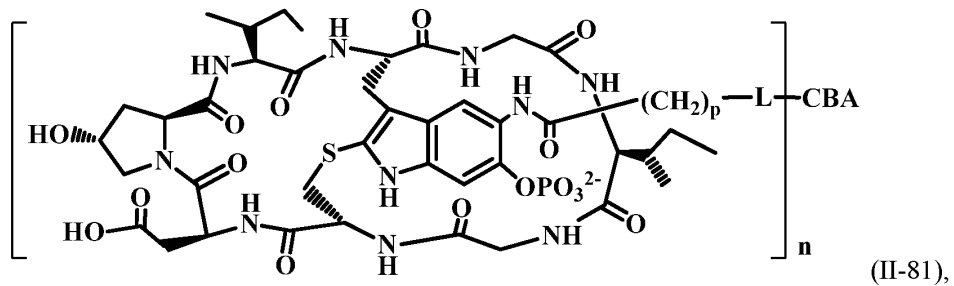
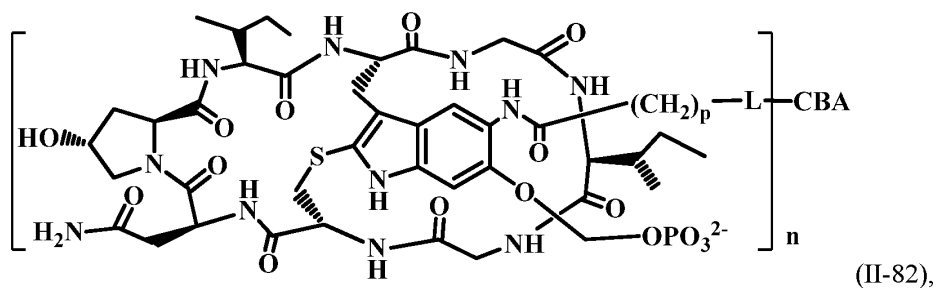


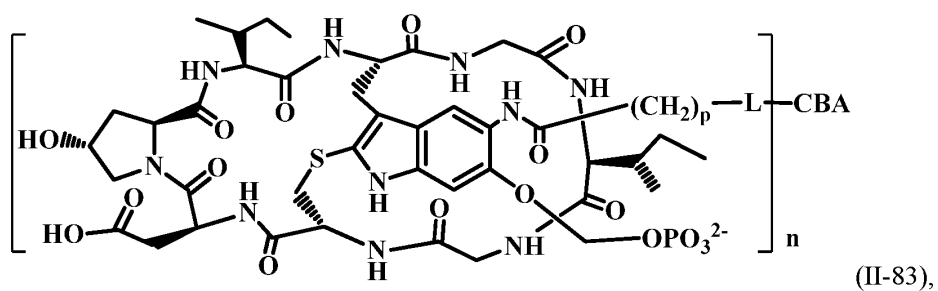
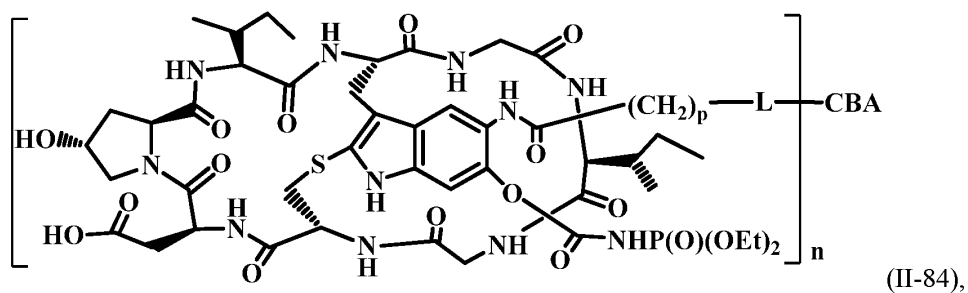
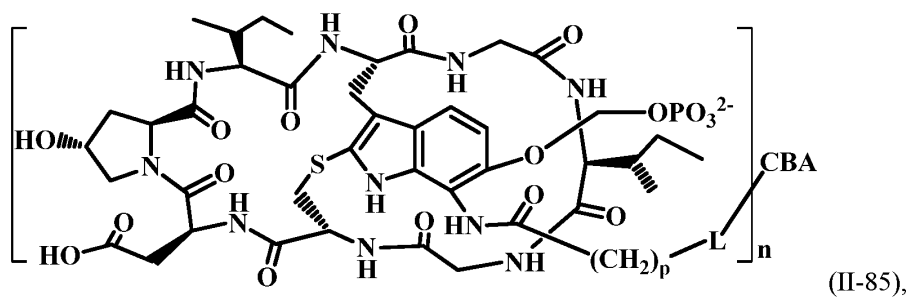
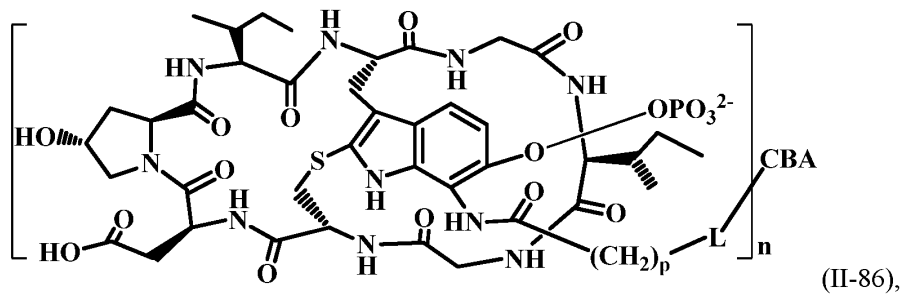
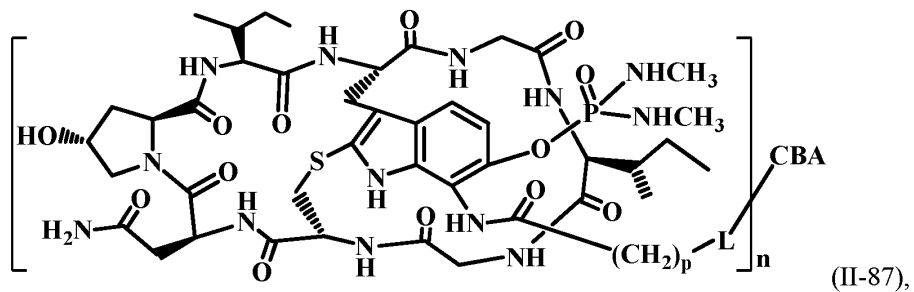


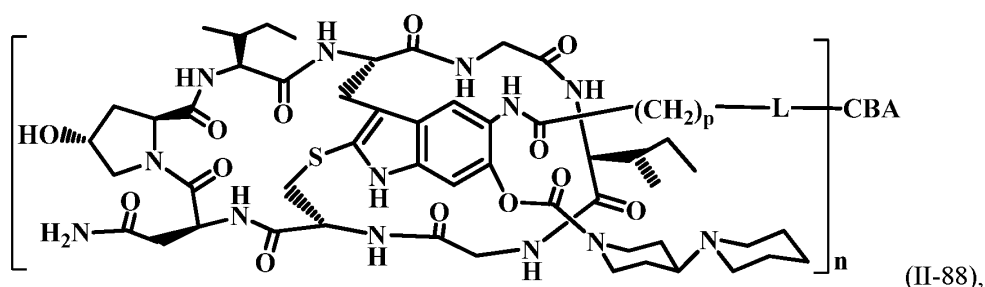
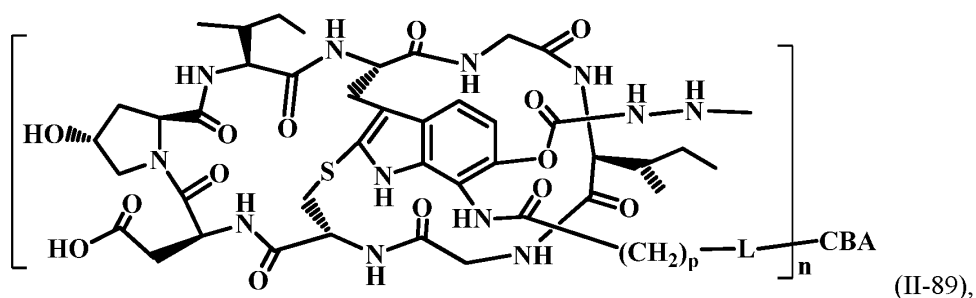
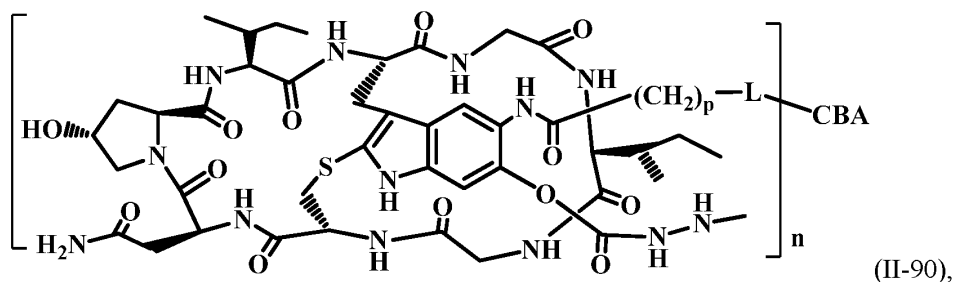
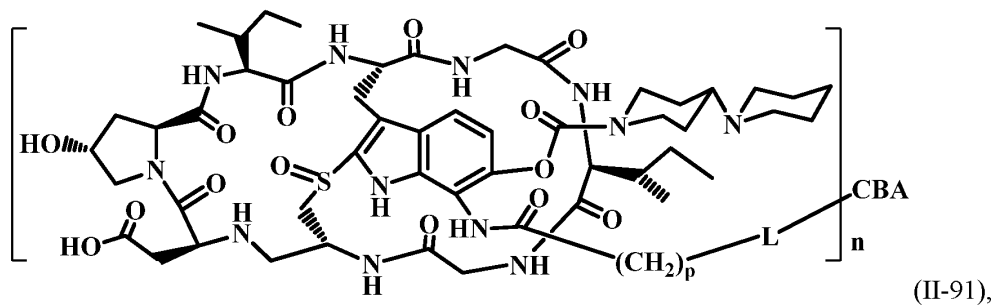










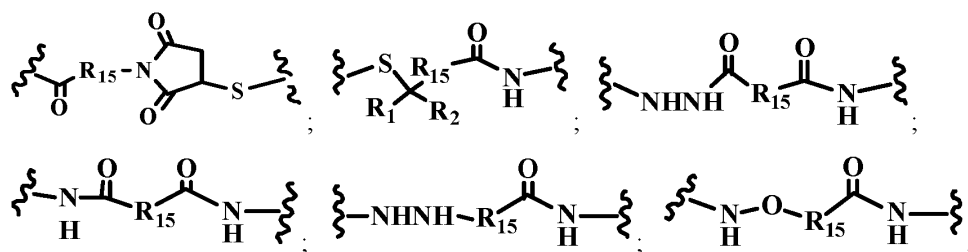


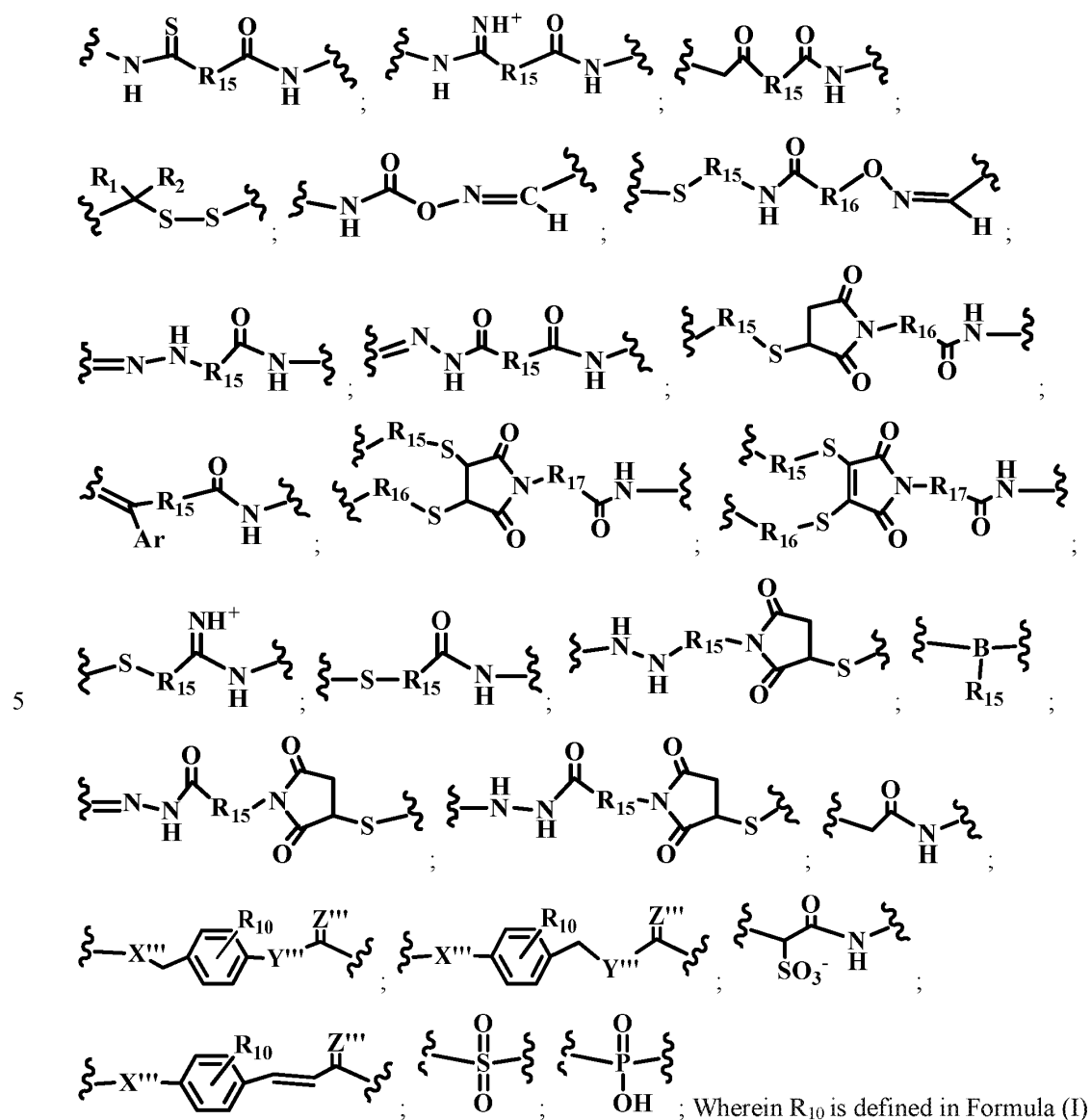
5 wherein Aa, L, m, n, p, Q, r, R<sub>1</sub>, and R<sub>2</sub>, are described above in Claim 1. CBA is a cell-binding agent/molecule.

10 **10.** A cell binding agent (CBA) of any one of claim 1, 2, 3, 4, 5, 6, or 8 is a full-length antibody (polyclonal and monoclonal antibody); a single chain antibody; a diabody, a triabody, a fragments of antibody (Fab, Fab', F(ab')<sub>2</sub>, F<sub>v</sub>, a fragment produced by a Fab expression library, an anti-idiotypic (anti-Id) antibody, CDR's, and an epitope-binding fragment of any of the above which immuno-specifically bind to cancer cell antigens, viral antigens or microbial antigens;

interferon (type I, II, III); a peptide; a lymphokine IL-2, IL-3, IL-4, IL-6, GM-CSF, interferon-  
 gamma (IFN- $\gamma$ ); a hormone, insulin, TRH (thyrotropin releasing hormone), MSH (melanocyte-  
 stimulating hormone), a steroid hormone, androgens, estrogens, melanocyte-stimulating hormone  
 (MSH); a growth factor and a colony-stimulating factor, an epidermal growth factors (EGF), a  
 5 granulocyte-macrophage colony-stimulating factor (GM-CSF), a transforming growth factors  
 (TGF), TGF $\alpha$ , TGF $\beta$ ; a insulin and insulin like growth factor (IGF-I, IGF-II) G-CSF, M-CSF and  
 GM-CSF; a vaccinia growth factor (VGF); a fibroblast growth factor (FGFs); a smaller molecular  
 weight protein, poly-peptide, peptides and peptide hormones, bombesin, gastrin, gastrin-releasing  
 peptide; a platelet-derived growth factor; an interleukin and a cytokine, interleukin-2 (IL-2),  
 10 interleukin-6 (IL-6), a leukemia inhibitory factor, a granulocyte-macrophage colony-stimulating  
 factor (GM-CSF); a vitamin, folate; an apoprotein and a lycoproteis; transferrin; a sugar-binding  
 protein or a lipoproteins, a lectin; a cell nutrient-transport molecule (transferrin); and a small  
 molecular inhibitor, prostate-specific membrane antigen (PSMA) inhibitor and small molecular  
 tyrosine kinase inhibitors (TKI); peptides, or peptide analogs, proteins including conjugated  
 15 proteins that are able to bind targeted cells; a non-peptides or any other cell binding molecule or  
 substance in forms of bioactive polymer, bioactive dendrimer, nanoparticle, liposome, or viral  
 capsid.

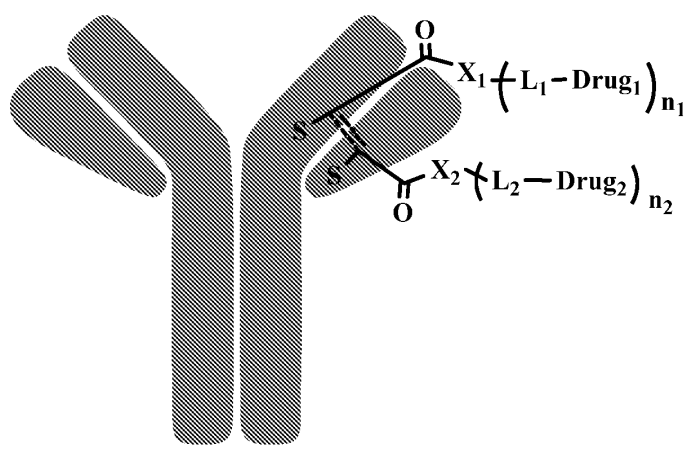
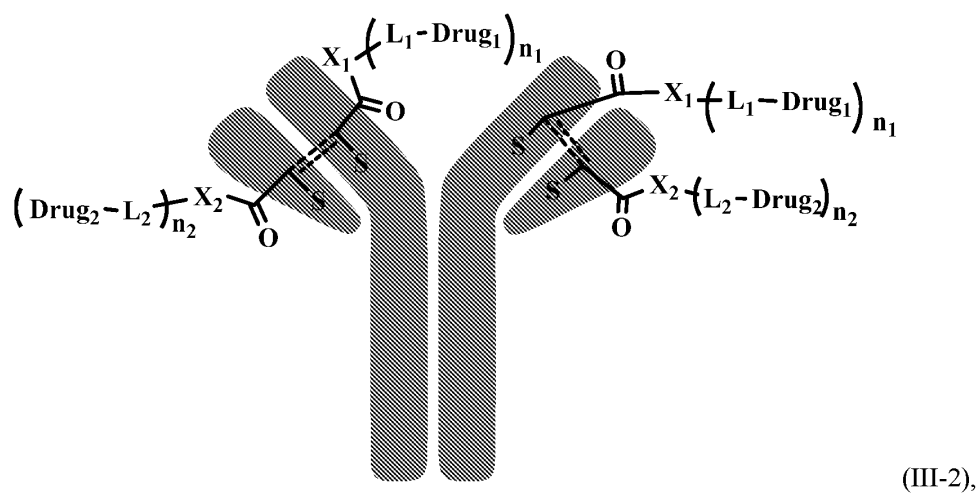
**11.** The linker L according to any one of Claim 1, 2, 3, 4, 5, 6, or 9 can be composed of one  
 or more linker components of 6-maleimidocaproyl ("MC"), maleimidopropanoyl ("MP"), valine-  
 20 citrulline ("val-cit" or "vc"), alanine-phenylalanine ("ala-phe" or "af"), glycine-glycine, a nature  
 peptides containing up to 6 the same or different natural amino acids (dipeptide, tripeptide,  
 tetrapeptide, pentapeptide, hexapeptide), p-aminobenzyloxycarbonyl ("PAB"), N-succinimidyl 4-  
 (2-pyridylthio)pentanoate ("SPP"), N-succinimidyl 4-(N-maleimidomethyl)cyclohexane-1  
 carboxylate ("SMCC"), N-Succinimidyl (4-iodo-acetyl)aminobenzoate ("SIAB"), ethyleneoxy (-  
 25 -CH<sub>2</sub>CH<sub>2</sub>O-) as one or up to 100 repeating units ("EO" or "PEO"), or one or more components  
 that are illustrated below:

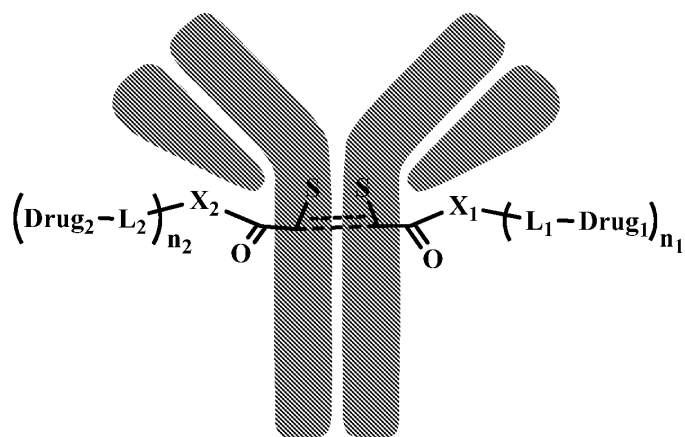




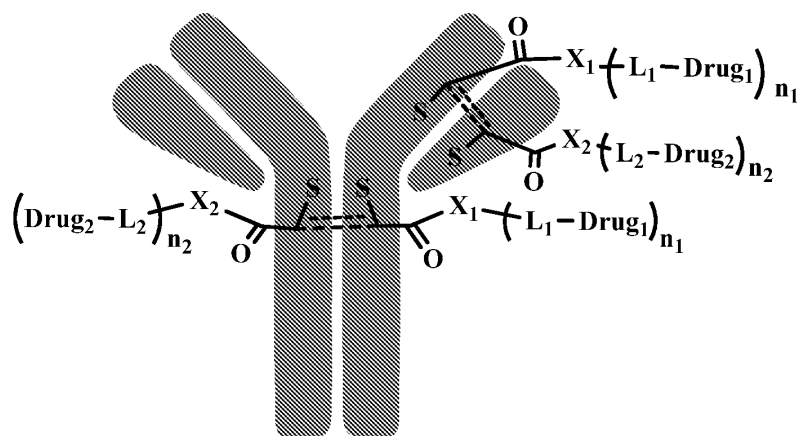
above. Wherein R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub> are independently selected from -C<sub>1</sub>~C<sub>8</sub> alkyl or alkylene-, -C<sub>1</sub>~C<sub>7</sub> carbocyclo-, -O-(C<sub>1</sub>~C<sub>8</sub> alkyl)-, -NH-(C<sub>1</sub>~C<sub>8</sub> alkyl)-, -arylene-, -C<sub>1</sub>~C<sub>8</sub> alkylene-arylene-, -arylene-, -C<sub>1</sub>~C<sub>8</sub> alkylene-, -C<sub>1</sub>~C<sub>8</sub> alkylene-(C<sub>1</sub>~C<sub>8</sub> carbocyclo)-, -(C<sub>3</sub>~C<sub>7</sub> carbocyclo)-C<sub>1</sub>~C<sub>8</sub> alkylene-, -C<sub>3</sub>~C<sub>8</sub> heterocyclo-, -C<sub>1</sub>~C<sub>8</sub> alkylene-(C<sub>3</sub>~C<sub>8</sub> heterocyclo)-, -(C<sub>3</sub>~C<sub>8</sub> heterocyclo)-C<sub>1</sub>~C<sub>9</sub> alkylene-, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>k</sub>-, -(CH(CH<sub>3</sub>)CH<sub>2</sub>O)<sub>k</sub>-, and -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>k</sub>-CH<sub>2</sub>-; k is an integer ranging from 1-50; X'''', Y''' and Z''' are independently selected from NH, O or S.

12. A compound according to any one of Claim 1, 2, 3, 4, 5, 6, or 9 when it is conjugated to an IgG antibody through a bridge linker to a pair of thiols of an IgG antibody, is preferred conjugating via a bridge linker specifically at the pair of thiols (through reduction of the disulfide bonds) between the light chain and heavy chain, or/and the upper disulfide bonds between the two heavy chains, or/and the lower disulfide bonds between the two heavy chains, and having any one of the following specific conjugation structures of (III-1), (III-2), (III-3), (III-4), (III-5), (III-6), (III-7), (III-8), (III-9), (III-10), (III-11), or (III-12):

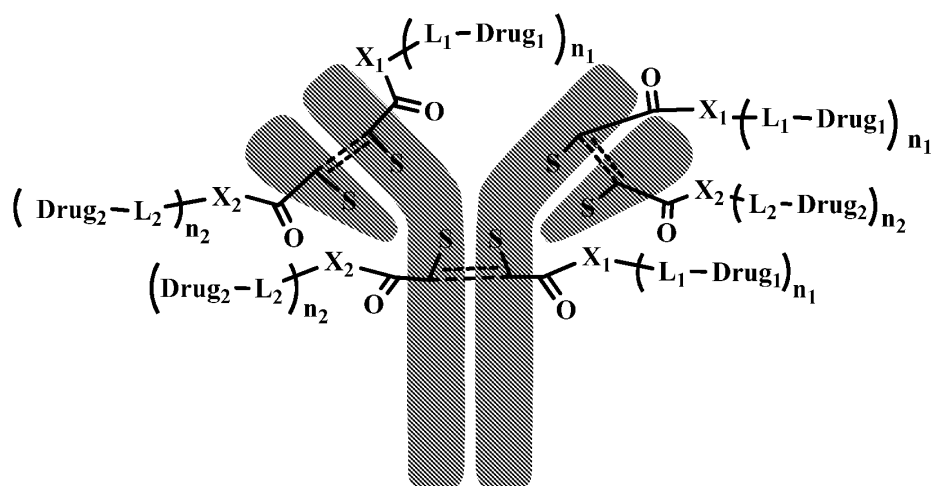




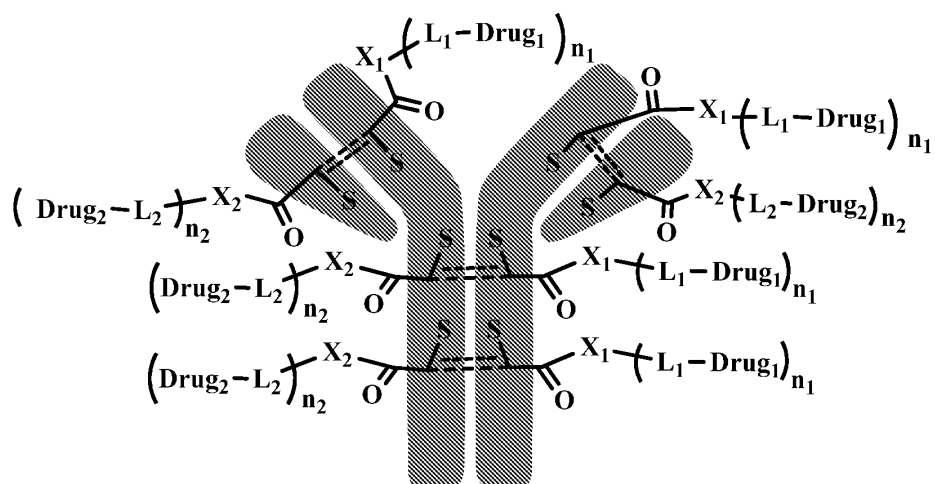
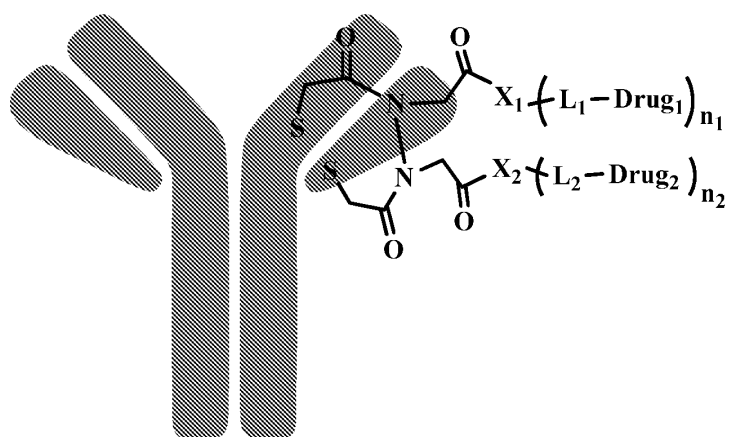
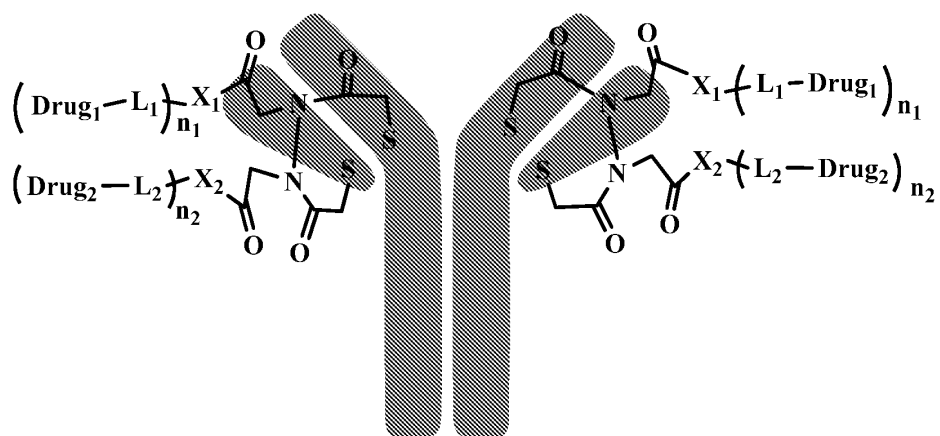
(III-3),

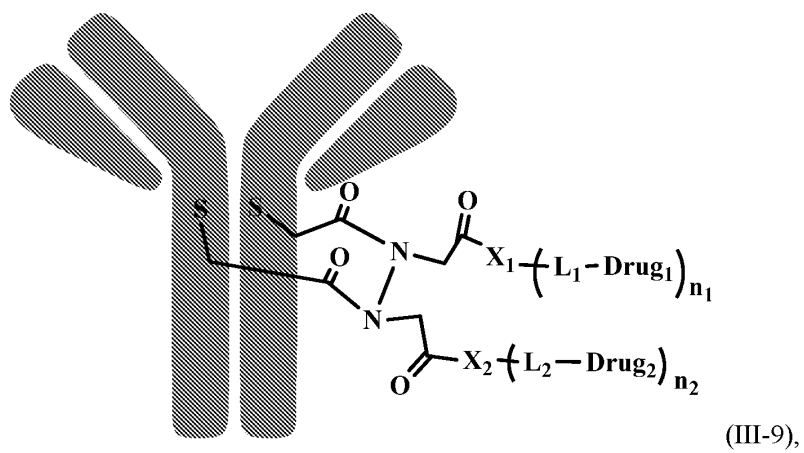
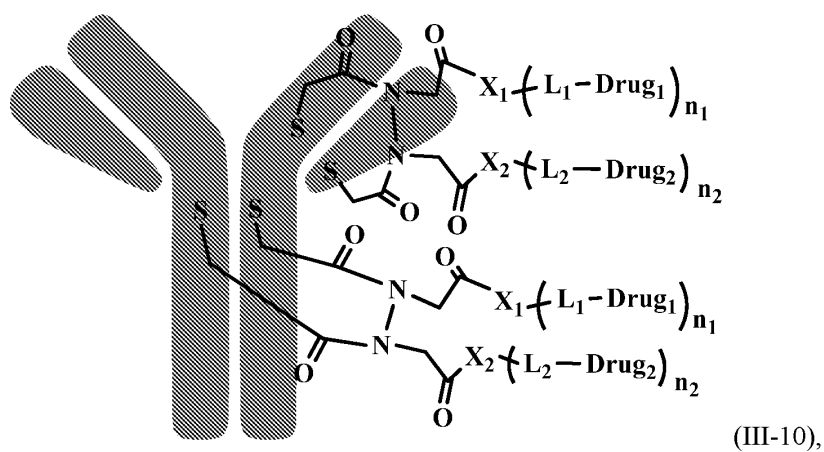
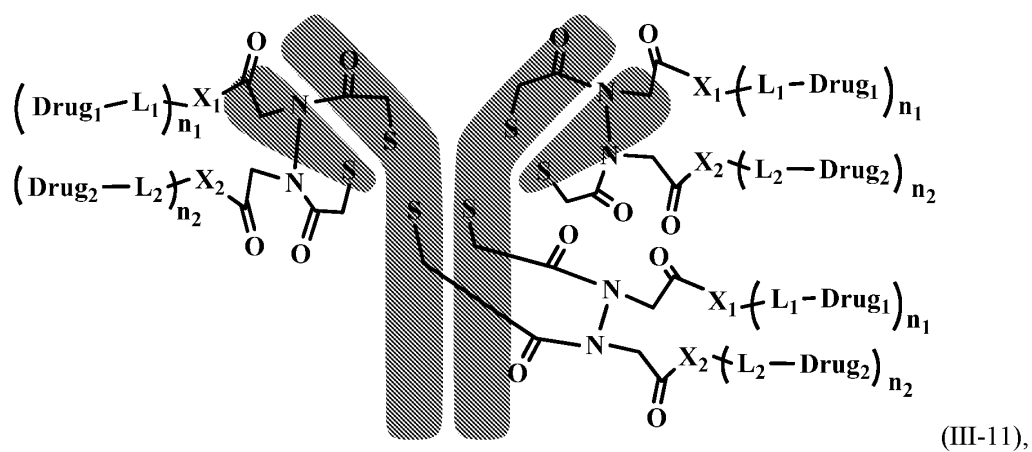


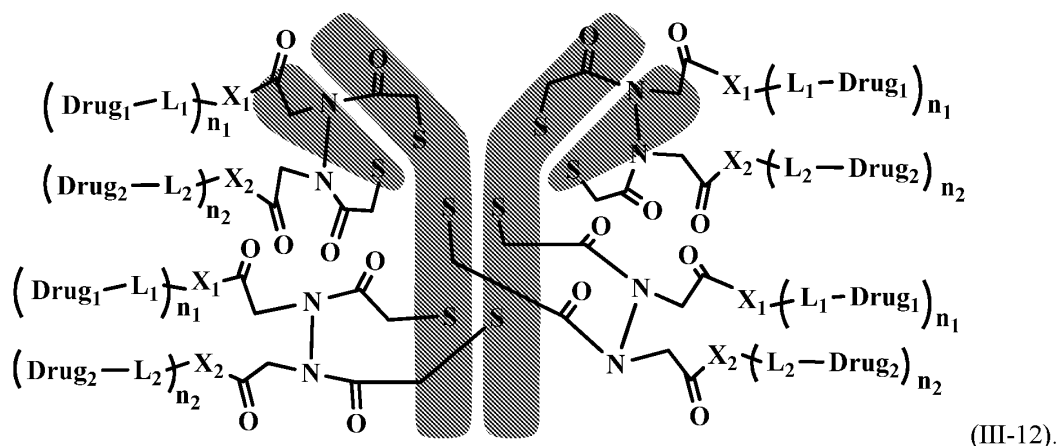
(III-4),



(III-5),

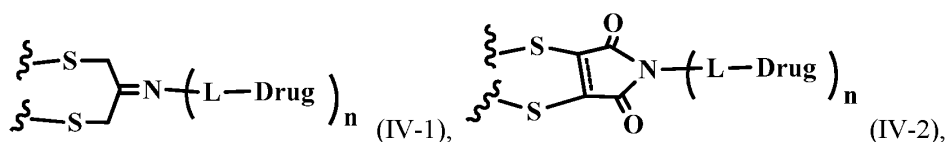


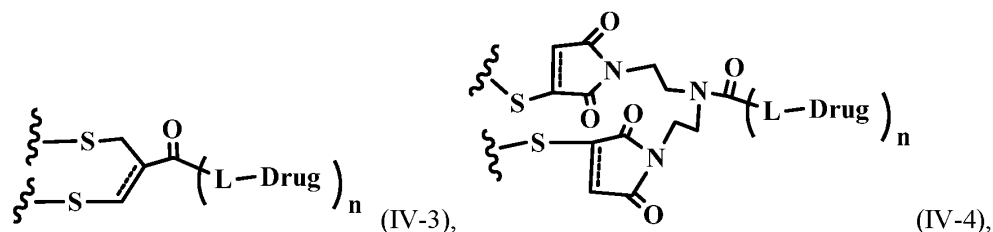
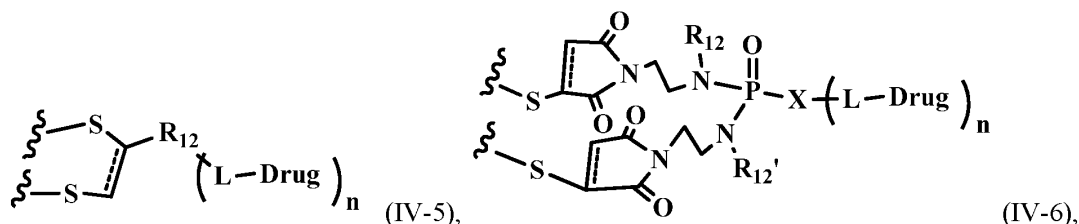




wherein the bold structure  is an IgG antibody, preferably IgG1, IgG2, IgG3 or IgG4 antibody; “**≡**” represents either a single bond or a double bond; L<sub>1</sub> and L<sub>2</sub> are, the same or deferent, independently defined the same as L in Claim 1; X<sub>1</sub> and X<sub>2</sub>, are, the same or deferent, independently selected from NH, N(R<sub>1</sub>), O, S, CH<sub>2</sub>, or Ar, wherein R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl and Ar is aromatic or heteroaromatic ring; wherein Drug<sub>1</sub> and Drug<sub>2</sub> are the same or deferent, a derivative of amanita toxins of any one of Claim 1, 2, 3, 4, 5 or 6; in addition, either Drug<sub>1</sub> or Drug<sub>2</sub> can be absent, but not be absent at the same time. When any single one of either Drug<sub>1</sub> or Drug<sub>2</sub> is a derivative of amanita toxin of any one of Claim 1, 2, 3, 4, 5 or 6, the other one of either Drug<sub>1</sub> or Drug<sub>2</sub> can be selected from (OCH<sub>2</sub>CH<sub>2</sub>)<sub>r</sub>OR<sub>10</sub>, or (OCH<sub>2</sub>CH(CH<sub>3</sub>))<sub>p</sub>OR<sub>10</sub>, or NH(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>10</sub>, or NH(CH<sub>2</sub>CH(CH<sub>3</sub>)O)<sub>p</sub>R<sub>10</sub>, or N[(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>10</sub>][(CH<sub>2</sub>CH<sub>2</sub>O)<sub>r</sub>R<sub>5</sub>], or (OCH<sub>2</sub>CH<sub>2</sub>)<sub>p</sub>COOR<sub>10</sub>, or CH<sub>2</sub>CH<sub>2</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>p</sub>COOR<sub>10</sub>, wherein p, r, R<sub>10</sub> are described the same as in Claim 1. In addition, both Drug<sub>2</sub> and L<sub>2</sub> can be absent when Drug<sub>1</sub> is not absent, thus X<sub>2</sub> is NH<sub>2</sub> or OH.

**13.** A conjugate compound according to any one of Claim 1, 2, 3, 4, 5, 6, or 9 when one compound of any one of Claim 1, 2, 3, 4, 5, 6 or 9 is conjugated to an IgG antibody through a bridge linker, is preferred having any one of the following linkage structures of (IV-1), (IV-2), (IV-3), (IV-4), (IV-5), and (IV-6):





wherein “ $\equiv$ ” represents either a single bond or a double bond; Drug is a derivative of Amanita toxin of Formula (I), (Ia), (Ib), (Ic) or (Id);  $\zeta$  represents the sites on an antibody; L, X, n and R<sub>12</sub> are defined the same as in Formula (I).

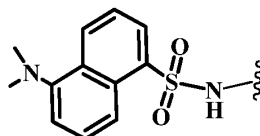
**14.** The pairs of thiols according to Claim 12 or Claim 13 are preferred to be reduced by one or more reducing agent selected from dithiothreitol (DTT), dithioerythritol (DTE), L-glutathione (GSH), tris (2-carboxyethyl) phosphine (TCEP), 2-mercaptoethylamine (β-MEA), or/and beta mercaptoethanol (β-ME, 2-ME). Preferably, the reducing agent is loaded or covalently bonded to a solid polymer or a solid particle. The polymer or the particle is selected from polyethylene, polyacrylate, silican, crossed-linked silica (2-mercaptoethyl)silica, (aminoethyl)silica, (aminopropyl)silica, polyethylene terephthalate, polyethylene glycol, polystyrene, poly(isopropyl acrylate), dextrans (Sephadex, cross-linked dextran), isopropylacrylamide butyl methacrylate copolymer, polysaccharide polymer (agarose, agar, agarpectin, Sepharose).

**15.** The conjugate compound according to Claim 12, when any single one of either Drug<sub>1</sub> or Drug<sub>2</sub> of Formula (III-1), (III-2), (III-3), (III-4), (III-5), (III-6), (III-7), (III-8), (III-9), (III-10), (III-11), or (III-12) is a derivative of Amanita toxin of any one of Claim 1, 2, 3, 4, 5, 6, or 9 the other one of either Drug<sub>1</sub> or Drug<sub>2</sub> can be selected from a protein, an antibody (a monoclonal or polyclonal antibody, antibody dimers, antibody multimers, a bispecific or trispecific antibody, a single chain antibody, an antibody fragment that binds to the target cell), a chromophore molecule, a tubulysin derivative, a maytansinoid, a taxanoid (taxane), a CC-1065 analog, a daunorubicin or doxorubicin compound, a benzodiazepine dimer (e.g., dimers of pyrrolobenzodiazepine (PBD),

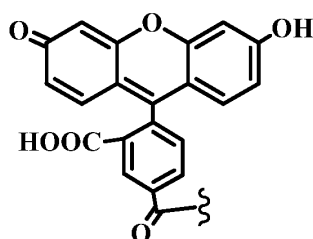
tomaymycin, anthramycin, indolinobenzodiazepines, imidazobenzothiadiazepines, or oxazolidinobenzodiazepines), a calicheamicin, a dolastatin or auristatin derivative (monomethyl auristatin E, MMAE, MMAF, auristatin PYE, auristatin TP, Auristatins 2-AQ, 6-AQ, EB (AEB), and EFP (AEFP)), a duocarmycin, a siRNA, or an enzyme. The preferred structures of some of these function molecules or cytotoxic drugs are illustrated below:



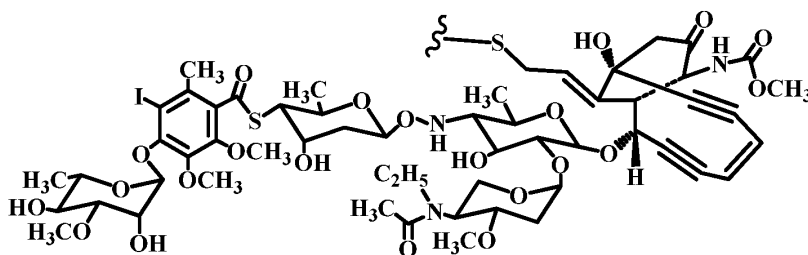
(V-1, an antibody),



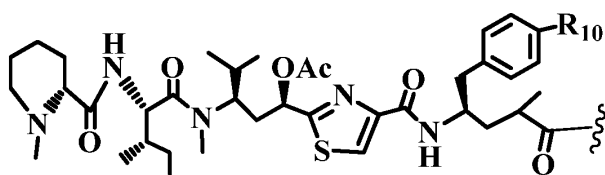
(V-2, a chromophore molecule),



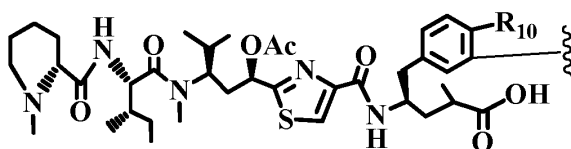
(V-3, a chromophore molecule),



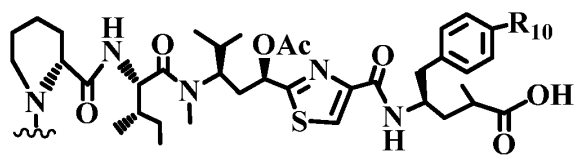
(V-4, a calicheamicin),



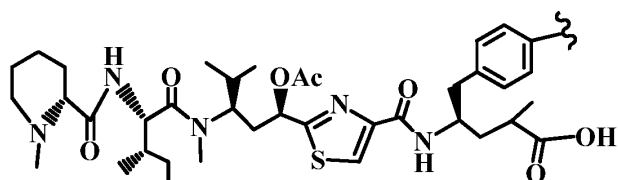
(V-5, a tubulysin derivative),



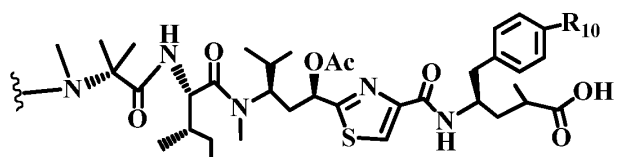
(V-6, a tubulysin derivative),



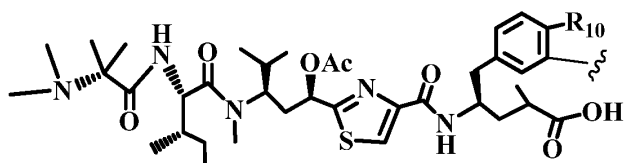
(V-7, a tubulysin derivative),



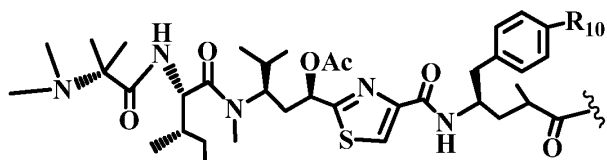
(V-8, a tubulysin derivative),



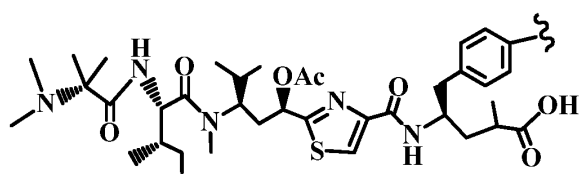
(V-9, a tubulysin derivative),



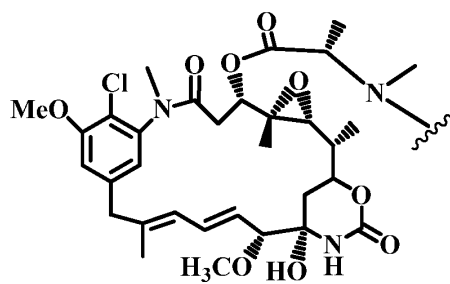
(V-10, a tubulysin derivative),



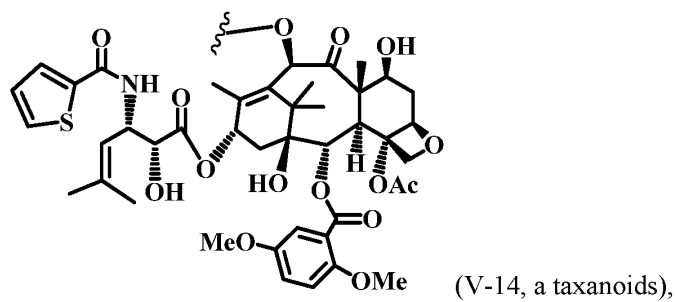
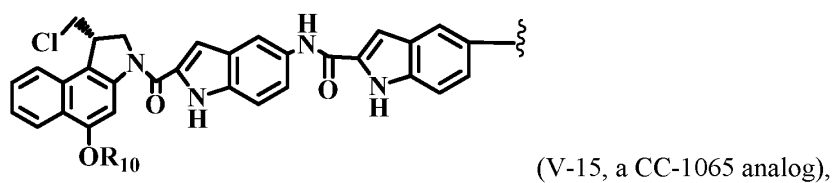
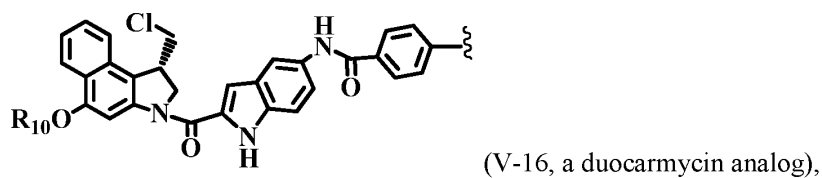
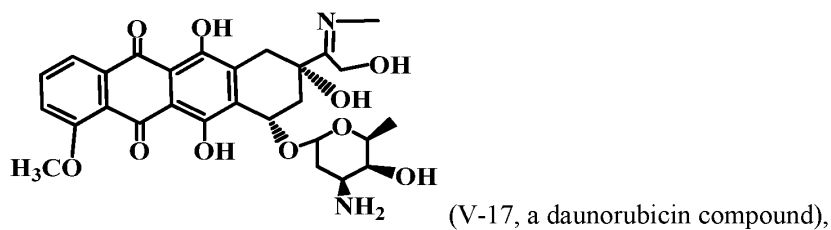
(V-11, a tubulysin derivative),



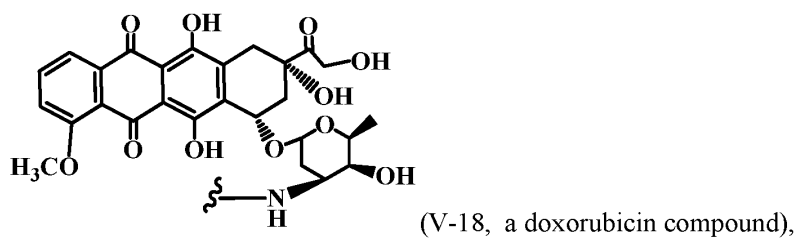
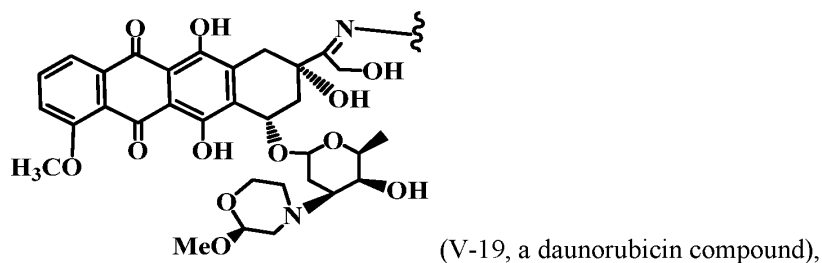
(V-12, a tubulysin derivative),

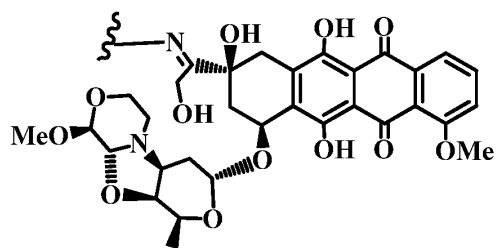


(V-13, a maytansinoid),

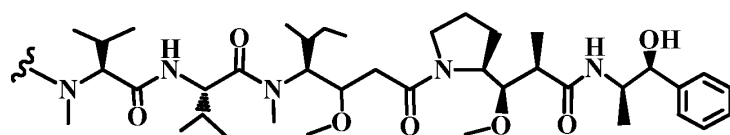


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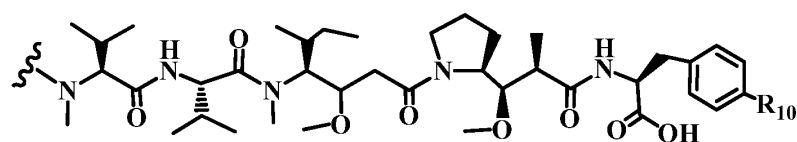




(V-20, a daunorubicin or doxorubicin compound),

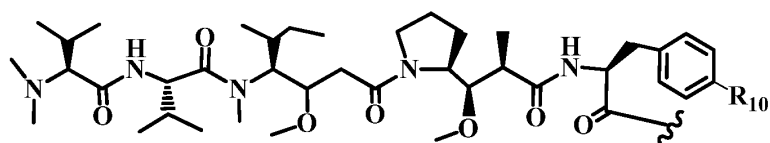


(V-21, an auristatin derivative),



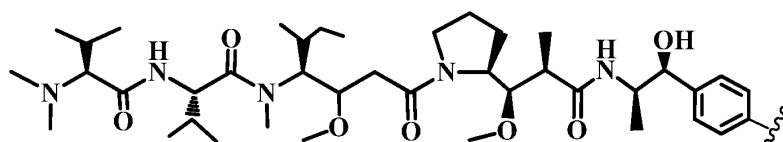
(V-22, an auristatin

derivative),



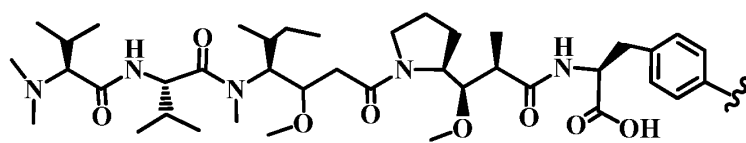
(V-23, an auristatin derivative)

5



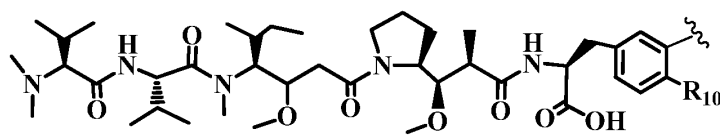
(V-24, a dolastatin or an

auristatin derivative (MMAE))



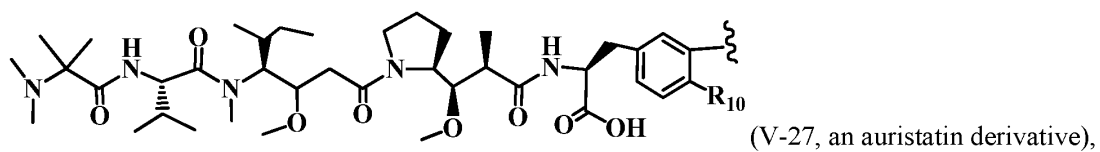
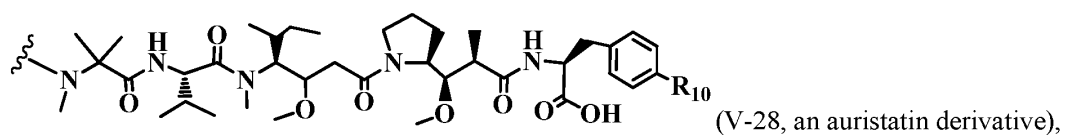
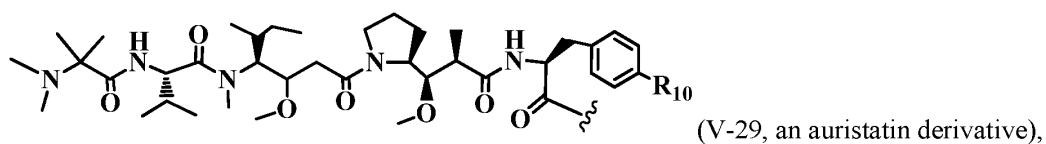
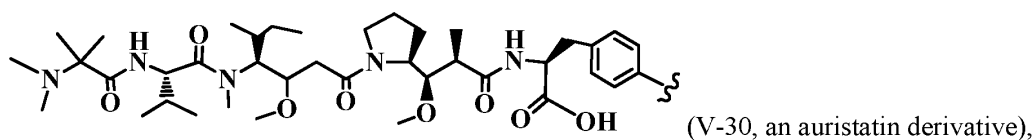
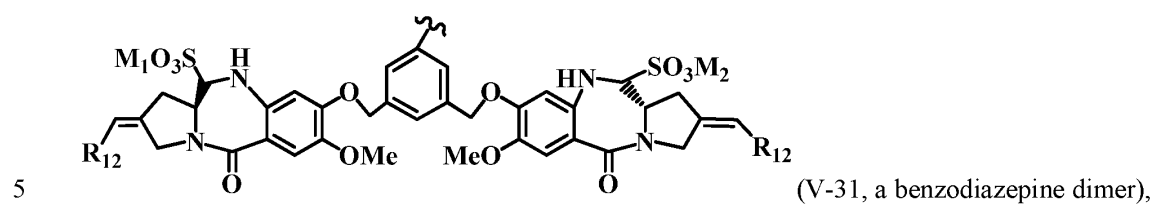
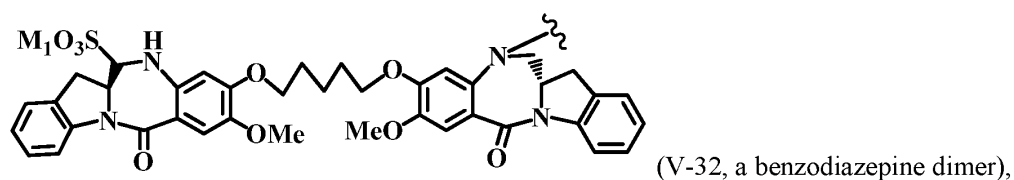
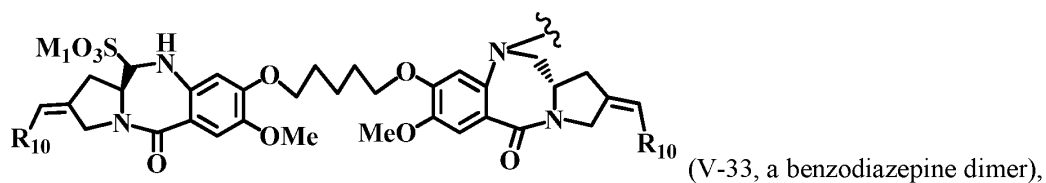
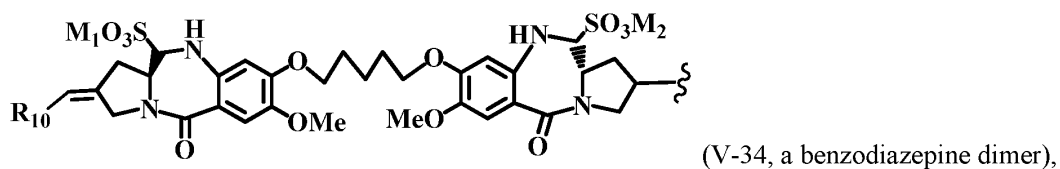
(V-25, a dolastatin or an

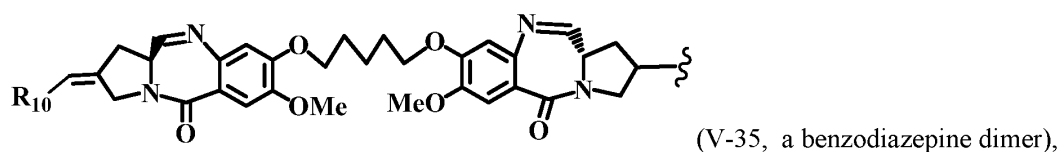
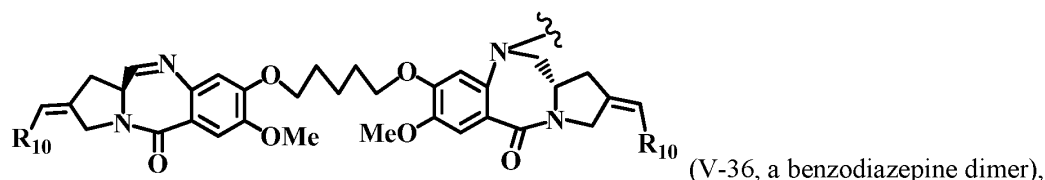
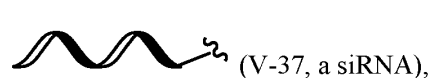
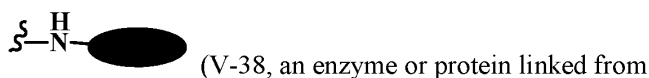
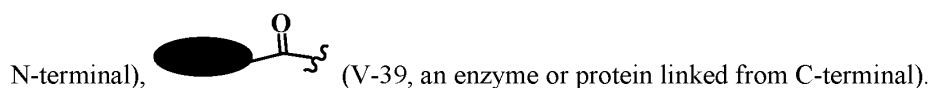
auristatin derivative),



(V-26, an auristatin derivative),

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- 5 wherein R<sub>10</sub> are described in Claim 1 and  is the site to link either linker L<sub>1</sub> or linker L<sub>2</sub> of Claim 11.

16. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of Claim 1, 2, 3, 4, 5, 6, 9, 12, 13, 14 or 15, and a pharmaceutically acceptable excipients selected from one or more components of 0.002% -1% of polysorbate (polysorbate 20, polysorbate 40, polysorbate 60, or polysorbate 80) or sodium lauryl sulfate, triton X-100; and/or 0.01% ~ 10% of binders (disaccharides: sucrose, lactose, trehalose or maltose; or sugar alcohols: xylitol, sorbitol or maltitol, or polyethylene glycol), and 0.01% ~10% of pharmaceutical buffering agents (selected from citrate, succinate acetate, phosphate, or borate) at a certain pH in the range of pH 4.5 -9.5.

17. A compound according to any one of Claim 1, 2, 3, 4, 5, 6, 9, 12, 13, 14, 15, or 16 is used for inhibiting abnormal cell growth or treating a proliferative disorder including cancers, benign or malignant tumors; leukemia and lymphoid malignancies; neuronal, glial, astrocytal, hypothalamic, glandular, macrophagal, epithelial, stromal, blastocoelic, angiogenic and immunologic disorders; inflammatory; autoimmune disorders; destructive disorders; bone disorder; infectious disease; viral disease; fibrotic disease; neurodegenerative disorder; pancreatitis or kidney disease; in a mammal.

18. A pharmaceutical composition according to Claim 16 comprising one or more synergistic drugs of clinic known chemotherapeutic agent, the radiation therapy, immunotherapy agents, autoimmune disorder agents, anti-infectious agents or the other conjugates for synergistically effective treatment or prevention of a cancer, or an autoimmune disease, or an infectious disease.

19. The cell binding agent (CBA) according to any one of Claim 1, 2, 3, 4, 5, 6, 9, 12, 13, 14, or 15, is further preferably an antibody, an antibody fragment, a diabody, a tri(a)body, an epidermal growth factor (EGF), a prostate specific membrane antigen (PSMA) inhibitor, a melanocyte stimulating hormone (MSH), a thyroid stimulating hormone (TSH), a polyclonal antibody, a somatostatin, a folate, a matriptase inhibitor, an estrogen, an estrogen analogue, a designed ankyrin repeat proteins (DARPs), an androgen, and an androgen analogue.

20. A compound according to any one of Claim 1, 2, 3, 4, 5, 6, 9, 12, 13, 14, 15 or 16 further preferably targets cells selected from tumor cells; virus infected cells; microorganism infected cells; parasite infected cells; autoimmune cells; activated cells; myeloid cells; activated T-cells, B cells, or melanocytes; or cells expressing the antigen of CD3, CD4, CD5, CD6, CD7, CD8, CD9, CD10, CD11a, CD11b, CD11c, CD12w, CD14, CD15, CD16, CDw17, CD18, CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD26, CD27, CD28, CD29, CD30, CD31, CD32, CD33, CD34, CD35, CD36, CD37, CD38, CD39, CD40, CD41, CD42, CD43, CD44, CD45, CD46, CD47, CD48, CD49b, CD49c, CD51, CD52, CD53, CD54, CD55, CD56, CD58, CD59, CD61, CD62E, CD62L, CD62P, CD63, CD66, CD68, CD69, CD70, CD72, CD74, CD79, CD79a, CD79b, CD80, CD81, CD82, CD83, CD86, CD87, CD88, CD89, CD90, CD91, CD95, CD96, CD98, CD100, CD103, CD105, CD106, CD109, CD117, CD120, CD125, CD126, CD127, CD133, CD134, CD135, CD137, CD138, CD141, CD142, CD143, CD144, CD147, CD151, CD147, CD152, CD154, CD156, CD158, CD163, CD166, CD168, CD174, CD180, CD184, CDw186, CD194, CD195, CD200, CD200a, CD200b, CD209, CD221, CD227, CD235a, CD240, CD262, CD271, CD274, CD276 (B7-H3), CD303, CD304, CD309, CD326, 4-1BB, 5AC, 5T4 (Trophoblast glycoprotein, TPBG, 5T4, Wnt-Activated Inhibitory Factor 1 or WAI1), 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, CD194), CCR5, CD3E (epsilon), CEA (Carcinoembryonic antigen), CEACAM3, CEACAM5 (carcino-embryonic antigen), CFD (Factor D), Ch4D5, Cholecystokinin 2 (CCK2R), CLDN18 (Claudin-18), Clumping factor A, cMet, CRIPTO, FCSF1R (Colony stimulating factor 1 receptor,

CD115), 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 (CD184), C-X-C chemokine receptor type 4, cyclic ADP ribose hydrolase, Cyclin B1, CYP1B1, Cytomegalovirus, Cytomegalovirus glycoprotein B, Dabigatran, DLL4 (delta-like-  
5 ligand 4), DPP4 (Dipeptidyl-peptidase 4), DR5 (Death 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 (CD105), 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  
10 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 idiotype, GloboH, Glypican 3, N-glycolylneuraminic acid, GM3, GMCSF receptor  $\alpha$ -chain, Growth differentiation factor 8, GP100, GPNMB (Trans-membrane glycoprotein  
15 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),  
20 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), Idiotype, IGF1R (IGF-1, insulin-like growth factor 1 receptor), IGHE, IFN- $\gamma$ , Influenza hemagglutinin, IgE, IgE Fc region, IGHE, IL-1, IL-2 receptor (interleukin 2 receptor), IL-4, IL-5, IL-6, IL-6R (interleukin 6 receptor), IL-9, IL-10, IL-12, IL-13, IL-17, IL-17A, IL-20, IL-22,  
25 IL-23, IL31RA, ILGF2 (Insulin-like growth factor 2), Integrins ( $\alpha$ 4,  $\alpha$ 11b $\beta$ 3,  $\alpha$ v $\beta$ 3,  $\alpha$ 4 $\beta$ 7,  $\alpha$ 5 $\beta$ 1,  $\alpha$ 6 $\beta$ 4,  $\alpha$ 7 $\beta$ 7,  $\alpha$ 11 $\beta$ 3,  $\alpha$ 5 $\beta$ 5,  $\alpha$ v $\beta$ 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  
30 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,
- 5 OX-40, OxLDL (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,CD279), PDGF-R $\alpha$  (Alpha-type platelet-derived growth factor receptor ), PDGFR- $\beta$ , PDL-1, PLAC1, PLAP-like testicular alkaline phosphatase, Platelet-derived growth factor receptor beta, Phosphate-sodium co-transporter, PMEL 17, Polysialic acid,
- 10 Proteinase3 (PR1), Prostatic carcinoma, PS (Phosphatidylserine), Prostatic carcinoma cells, Pseudomonas aeruginosa, PSMA, PSA, PSCA, Rabies virus glycoprotein, RHD (Rh polypeptide 1 (RhPI), CD240), 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
- 15 (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- $\alpha$ , TGF- $\beta$  (Transforming growth factor beta), TGF- $\beta$ 1, TGF- $\beta$ 2 (Transforming growth factor-beta 2), Tie (CD202b), Tie2, TIM-1 (CDX-014), Tn, TNF, TNF- $\alpha$ ,
- 20 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-2, Tyrosinase, VCAM-1 (CD106), VEGF,
- 25 VEGF-A, VEGF-2 (CD309), VEGFR-1, VEGFR2, or vimentin, WT1, XAGE 1, or cells expressing any insulin growth factor receptors, or any epidermal growth factor receptors.
- 21.** A pharmaceutical composition according to Claim 16 or Claim 18 is applied *in vitro*, *in vivo*, or *ex vivo* for treatment of cancer, autoimmune disorders, infectious diseases or viral disease.