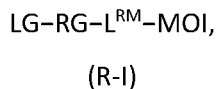


CLAIMS

We claim:

1. A compound having the structure of formula R-I:



or a salt thereof, wherein:

LG is a group comprising a target binding moiety that binds to a target agent,

RG is a reactive group of formula $-\text{L}^{\text{LG}2}-\text{L}^{\text{LG}3}-\text{L}^{\text{LG}4}-\text{L}^{\text{RG}1}-\text{L}^{\text{RG}2}-$, wherein

$\text{L}^{\text{LG}2}$ is $-\text{NH}-\text{C}(\text{O})\text{O}-\text{C}(\text{R}')_2-$, wherein each R' is independently H or C1-C10 alkyl, wherein

R' are optionally connected to form a ring;

$\text{L}^{\text{LG}3}$ is an optionally substituted aryl ring;

$\text{L}^{\text{LG}4}$ is $-\text{NH}-$ or $-\text{O}-$;

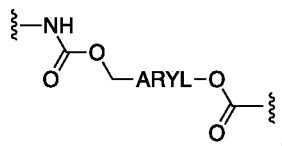
$\text{L}^{\text{RG}1}$ is $-\text{C}(\text{O})-$, $-\text{S}(\text{O})-$, $-\text{OS}(\text{O})_2-$, or $-\text{OP}(\text{O})(\text{OR})_2-$; and

$\text{L}^{\text{RG}2}$ is a covalent bond or $[-\text{C}(\text{R}'')_2\text{C}(\text{R}'')=\text{C}(\text{R}'')]\text{C}(\text{O})-$, wherein each R'' is independently H or C1-C10 alkyl, wherein any two R'' are optionally connected to form a ring;

L^{RM} is a linker; and

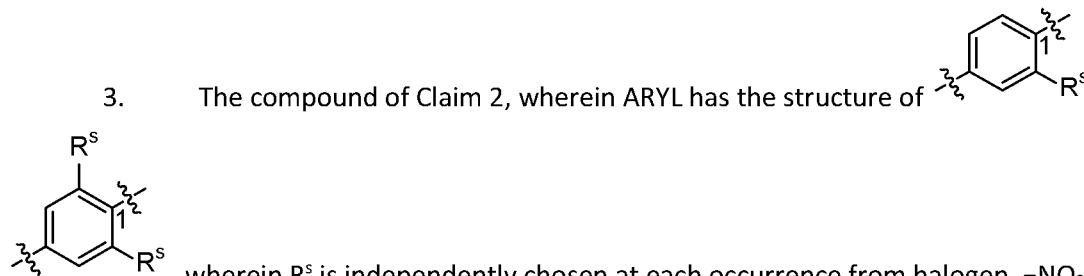
MOI is a moiety of interest.

2. The compound of Claim 1, wherein RG is or comprises a reactive group having the following formula:



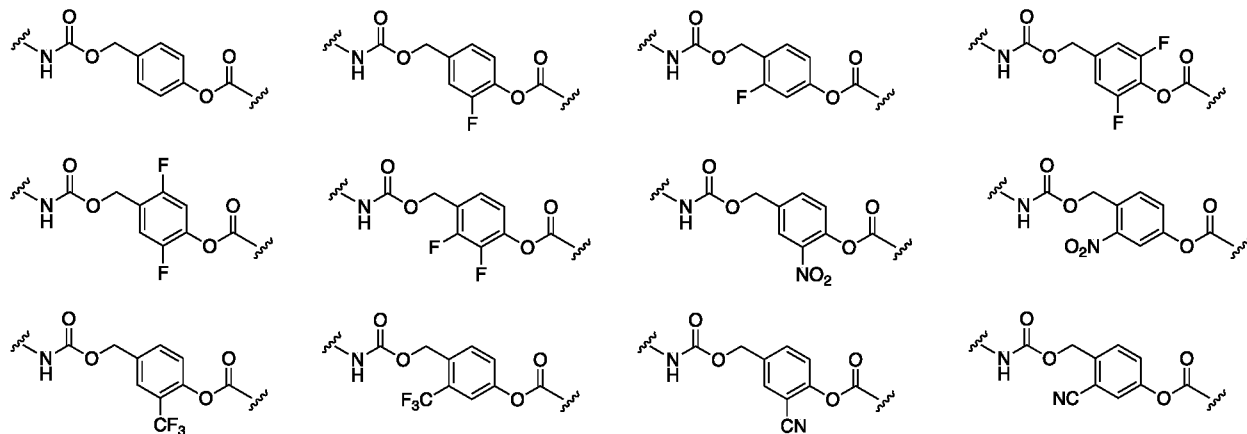
wherein ARYL is a substituted or unsubstituted para-phenylene ring.

3. The compound of Claim 2, wherein ARYL has the structure of

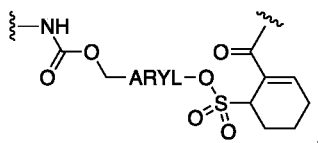


or , wherein R^{S} is independently chosen at each occurrence from halogen, $-\text{NO}_2$, $-\text{F}$, $-\text{L}-\text{R}'$, $-\text{C}(\text{O})-\text{L}-\text{R}'$, $-\text{S}(\text{O})-\text{L}-\text{R}'$, $-\text{S}(\text{O})_2-\text{L}-\text{R}'$, and $-\text{P}(\text{O})(-\text{L}-\text{R}')_2$, and R' is H or C₁-C₆alkyl.

4. The compound of Claim 2 or 3, wherein the reactive group is or comprises has one of the following formulae:



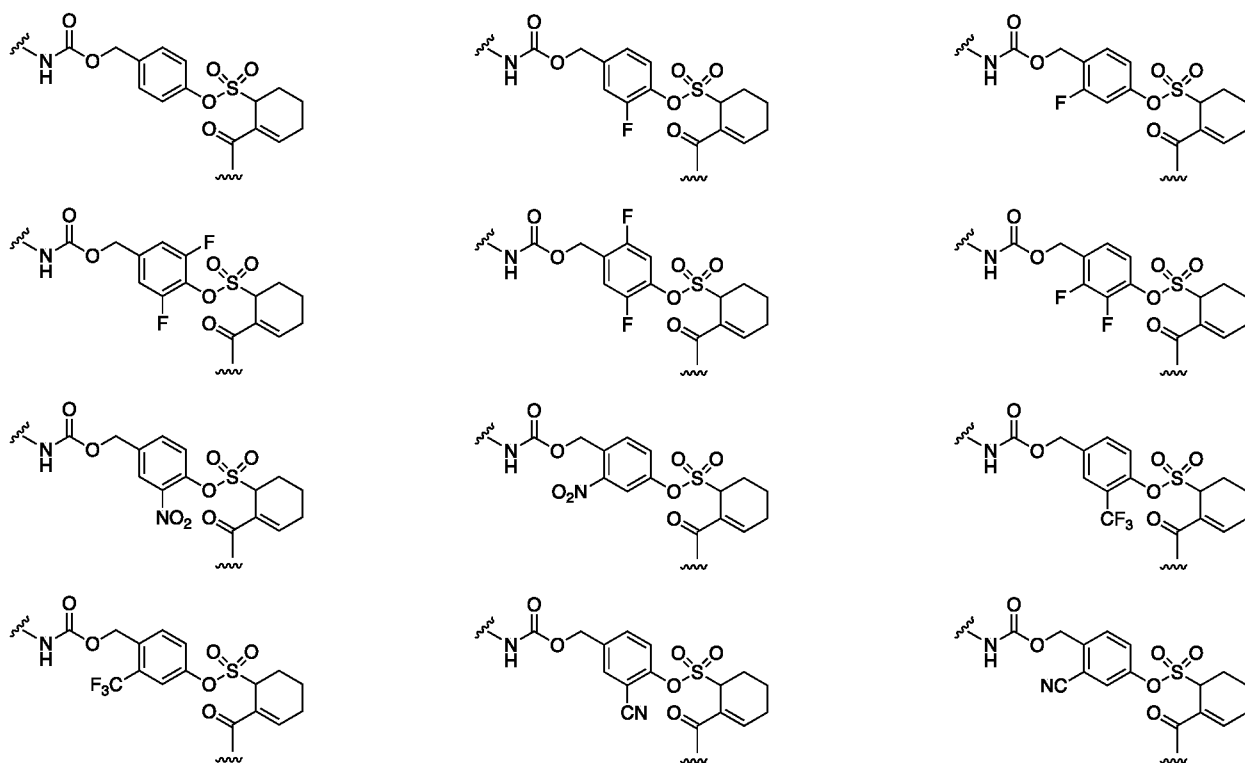
5. The compound of Claim 1, wherein RG is or comprises a reactive group having the following formula:



wherein ARYL is a substituted or unsubstituted para-phenylene ring.

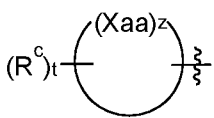
6. The compound of Claim 5, wherein ARYL has the structure of or , wherein R^S is independently chosen at each occurrence from halogen, -NO₂, -F, -L-R', -C(O)-L-R', -S(O)-L-R', -S(O)₂-L-R', and -P(O)(-L-R')₂, and R' is H or C₁-C₆alkyl.

7. The compound of Claim 5 or 6, wherein the reactive group is or comprises has one of the following formulae:



8. The compound of Claim 1, wherein

LG is $R^{LG}-L^{LG}$;

R^{LG} is $(R^c)_t$ —, $R^c-(Xaa)_z$ -, a nucleic acid moiety, or a small molecule moiety;

each Xaa is independently a residue of an amino acid or an amino acid analog;

t is 0-50;

z is 1-50;

each R^c is independently $-L^a-R'$;

each L^a is independently a covalent bond, or an optionally substituted bivalent group selected from C_1 - C_{20} aliphatic or C_1 - C_{20} heteroaliphatic having 1-5 heteroatoms, wherein one or more methylene units of the group are optionally and independently replaced with $-C(R')_2$ -, $-Cy$ -, $-O$ -, $-S$ -, $-S-S$ -, $-N(R')$ -, $-C(O)$ -, $-C(S)$ -, $-C(NR')$ -, $-C(O)N(R')$ -, $-N(R')C(O)N(R')$ -, $-N(R')C(O)O$ -, $-S(O)$ -, $-S(O)_2$ -, $-S(O)_2N(R')$ -, $-C(O)S$ -, or $-C(O)O$ -;

each $-Cy$ - is independently an optionally substituted bivalent monocyclic, bicyclic or polycyclic group wherein each monocyclic ring is independently selected from a C_{3-20} cycloaliphatic ring, a C_{6-20} aryl ring, a 5-20 membered heteroaryl ring having 1-10 heteroatoms, and a 3-20 membered heterocyclyl ring

having 1-10 heteroatoms;

L^{LG} is $-L^{LG1}-$, $-L^{LG1}-L^{LG2}-$, $-L^{LG1}-L^{LG2}-L^{LG3}-$, or $-L^{LG1}-L^{LG2}-L^{LG3}-L^{LG4}-$;

each of L^{LG1} , L^{LG2} , L^{LG3} , and L^{LG4} is independently a covalent bond, or a bivalent optionally substituted, linear or branched C_{1-100} group comprising one or more aliphatic moieties, aryl moieties, heteroaliphatic moieties each independently having 1-20 heteroatoms, heteroaromatic moieties each independently having 1-20 heteroatoms, or any combinations of any one or more of such moieties, wherein one or more methylene units of the group are optionally and independently replaced with C_{1-6} alkylene, C_{1-6} alkenylene, a bivalent C_{1-6} heteroaliphatic group having 1-5 heteroatoms, $-C\equiv C-$, $-Cy-$, $-C(R')_2-$, $-O-$, $-S-$, $-S-S-$, $-N(R')-$, $-C(O)-$, $-C(S)-$, $-C(NR')-$, $-C(O)N(R')-$, $-C(O)C(R')_2N(R')-$, $-N(R')C(O)N(R')-$, $-N(R')C(O)O-$, $-S(O)-$, $-S(O)_2-$, $-S(O)_2N(R')-$, $-C(O)S-$, $-C(O)O-$, $-P(O)(OR')-$, $-P(O)(SR')-$, $-P(O)(R')-$, $-P(O)(NR')-$, $-P(S)(OR')-$, $-P(S)(SR')-$, $-P(S)(R')-$, $-P(S)(NR')-$, $-P(R')-$, $-P(OR')-$, $-P(SR')-$, $-P(NR')-$, an amino acid residue, or $-[(O-C(R')_2-C(R')_2)_n]-$, wherein n is 1-20;

each R' is independently $-R$, $-C(O)R$, $-CO_2R$, or $-SO_2R$;

each R is independently $-H$, or an optionally substituted group selected from C_{1-30} aliphatic, C_{1-30} heteroaliphatic having 1-10 heteroatoms, C_{6-30} aryl, C_{6-30} arylaliphatic, C_{6-30} arylheteroaliphatic having 1-10 heteroatoms, 5-30 membered heteroaryl having 1-10 heteroatoms, and 3-30 membered heterocyclyl having 1-10 heteroatoms, or

two R groups are optionally and independently taken together to form a covalent bond, or:

two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms; or

two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms.

9. The compound of Claim 1, wherein LG is or comprises a target binding moiety that binds to a target agent, wherein the target agent is an antibody agent.

10. The compound of Claim 1, wherein LG is or comprises a target binding moiety that binds to a Fc region, and/or R^{LG} is or comprises DCAWXLGELVWCT (SEQ ID NO:2), wherein the two cysteine residues optionally form a disulfide bond, and X is an amino acid residue.

11. The compound of Claim 1, wherein at least one of the following conditions is met:

- (a) the moiety of interest is or comprises a therapeutic agent;
- (b) the moiety of interest is or comprises a moiety that can bind to a protein, nucleic acid or a cell; and/or
- (c) the moiety of interest is or comprises a reactive moiety suitable for a bio-orthogonal reaction.

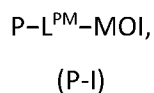
12. The compound of Claim 1, wherein LG is or comprises a target binding moiety having the structure of formula A-1 to A-50 shown in the specification.

13. The compound of Claim 1, wherein MOI is or comprises a therapeutic agent moiety and/or MOI is or comprises an antibody agent.

14. The compound of Claim 1, wherein L^{RM} comprises one or more $-[(CH_2)_n-O]_m-$, wherein each n is independently 1-20, and m is 1-100.

15. The compound of Claim 1, wherein in formula (R-I):
 the target agent is an antibody comprising an IgG heavy chain comprising K246 or K248, and
 the target binding moiety is configured to bind the antibody so as to bring the reactive group in proximity with K246 or K248 of the IgG heavy chain to enable a reaction between K246 or K248 and the reactive group that results in attachment of a moiety comprising L^{RM} -MOI to K246 or K248 and expulsion of the group containing a target binding moiety from the compound.

16. A method of preparing an agent having the structure of P-I:



or a salt thereof, wherein:

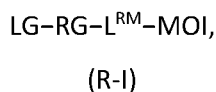
P is a target agent moiety;

L^{PM} is a linker; and

MOI is a moiety of interest.

comprising steps of:

1) contacting a target agent with a reaction partner having the structure of formula R-I:



or a salt thereof, wherein:

LG is a group comprising a target binding moiety that binds to a target agent,

RG is a reactive group of formula $-\text{L}^{\text{LG2}}-\text{L}^{\text{LG3}}-\text{L}^{\text{LG4}}-\text{L}^{\text{RG1}}-\text{L}^{\text{RG2}}-$, wherein

L^{LG2} is $-\text{NH}-\text{C}(\text{O})\text{O}-\text{C}(\text{R}')_2-$, wherein each R' is independently H or C1-C10 alkyl,

wherein R' are optionally connected to form a ring;

L^{LG3} is an optionally substituted aryl ring;

L^{LG4} is $-\text{NH}-$ or $-\text{O}-$;

L^{RG1} is $-\text{C}(\text{O})-$, $-\text{S}(\text{O})-$, $-\text{OS}(\text{O})_2-$, or $-\text{OP}(\text{O})(\text{OR})_2-$; and

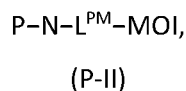
L^{RG2} is a covalent bond or $[-\text{C}(\text{R}'')_2\text{C}(\text{R}'')=\text{C}(\text{R}'')]\text{C}(\text{O})-$, wherein each R'' is independently H or C1-C10 alkyl, wherein any two R'' are optionally connected to form a ring;

L^{RM} is a linker; and

MOI is a moiety of interest; and

2) forming an agent having the structure of formula P-I; or

a method of preparing an agent having the structure of P-II:



wherein:

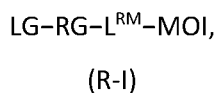
P-N is a protein agent moiety comprising a lysine residue;

L^{PM} is a linker; and

MOI is a moiety of interest;

the method comprising:

contacting P-N with a reaction partner having a structure of formula R-I:



or a salt thereof, wherein:

LG is a group comprising a protein-binding moiety that binds to P-N,

RG is a reactive group of formula $-\text{L}^{\text{LG2}}-\text{L}^{\text{LG3}}-\text{L}^{\text{LG4}}-\text{L}^{\text{RG1}}-\text{L}^{\text{RG2}}-$, wherein

L^{LG2} is $-\text{NH}-\text{C}(\text{O})\text{O}-\text{C}(\text{R}')_2-$, wherein each R' is independently H or C1-C10 alkyl,

wherein R' are optionally connected to form a ring;

L^{LG3} is an optionally substituted aryl ring;

L^{LG4-} is $-NH-$ or $-O-$;

L^{RG1} is $-C(O)-$, $-S(O)-$, $-OS(O)_2-$, or $-OP(O)(OR)_2-$; and

L^{RG2-} is a covalent bond or $[-C(R'')_2C(R'')=C(R'')]C(O)-$, wherein each R'' is independently H or C1-C10 alkyl, wherein any two R'' are optionally connected to form a ring;

L^{RM} is a linker; and

MOI is a moiety of interest.

17. The method of claim 16, wherein a target agent is or comprises an antibody agent.
18. The method of claim 17, wherein a moiety of interest is selectively attached to the antibody agent at K246 or K248 of an IgG1 heavy chain or a corresponding location.
19. The method of claim 17, wherein a moiety of interest is selectively attached to the antibody agent at K251 or K253 of an IgG2 heavy chain or a corresponding location.
20. The method of claim 17, wherein a moiety of interest is selectively attached to the antibody agent at K239 or K241 of an IgG4 heavy chain or a corresponding location.
21. The method of claim 16, wherein the contacting and forming steps are performed in one chemical reaction.
22. A composition comprising one or more compounds of any one of Claims 1-15.
23. A composition comprising:
a first compound having the structure of formula (P-II):
$$P-N-L^{PM}-MOI \quad (P-II)$$

wherein:
P-N is a protein agent moiety comprising a lysine residue;
 L^{PM} is a linker; and
MOI is a moiety of interest; and

a second compound having the structure:



wherein LG is a group comprising a target binding moiety that binds to a target agent.

24. The composition of Claim 23, further comprising:

a third compound having the formula (R-I):



LG is a group comprising a target binding moiety that binds to a target agent, which is identical to LG in formula (LG-I);

RG is a reactive group of formula $-\text{L}^{\text{LG2}}-\text{L}^{\text{LG3}}-\text{L}^{\text{LG4}}-\text{L}^{\text{RG1}}-\text{L}^{\text{RG2}}-$, wherein

L^{LG2} is $-\text{NH}-\text{C}(\text{O})\text{O}-\text{C}(\text{R}')_2-$, wherein each R' is independently H or C1-C10 alkyl,

wherein R' are optionally connected to form a ring;

L^{LG3} is an optionally substituted aryl ring;

L^{LG4} is $-\text{NH}-$ or $-\text{O}-$;

L^{RG1} is $-\text{C}(\text{O})-$, $-\text{S}(\text{O})-$, $-\text{OS}(\text{O})_2-$, or $-\text{OP}(\text{O})(\text{OR})_2-$; and

L^{RG2} is a covalent bond or $[-\text{C}(\text{R}'')_2\text{C}(\text{R}'')=\text{C}(\text{R}'')]\text{C}(\text{O})-$, wherein each R'' is independently H or C1-C10 alkyl, wherein any two R'' are optionally connected to form a ring;

L^{RM} is a linker, which is identical to in formula (P-II); and

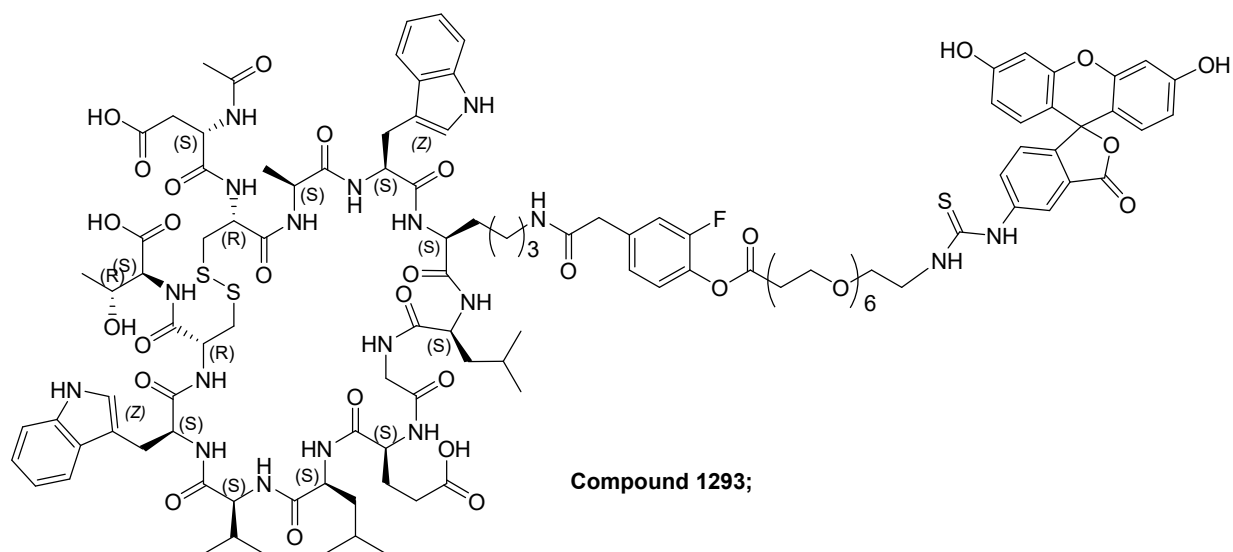
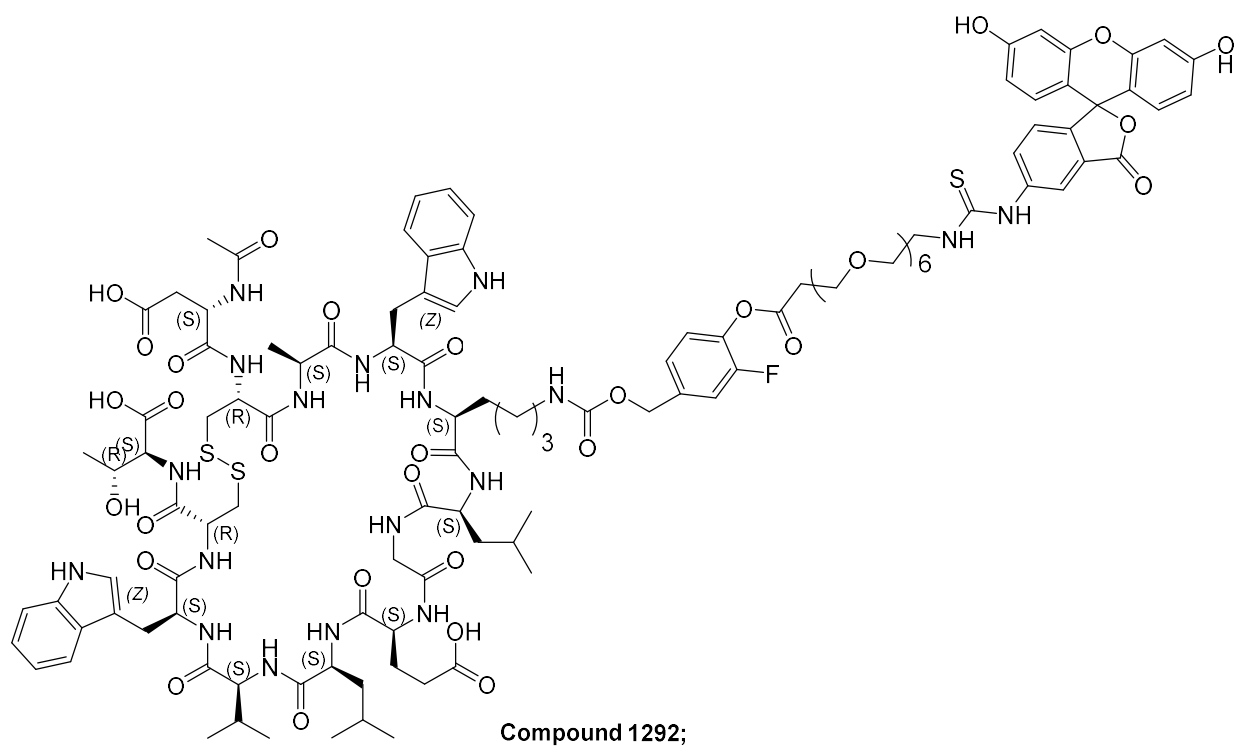
MOI is a moiety of interest;

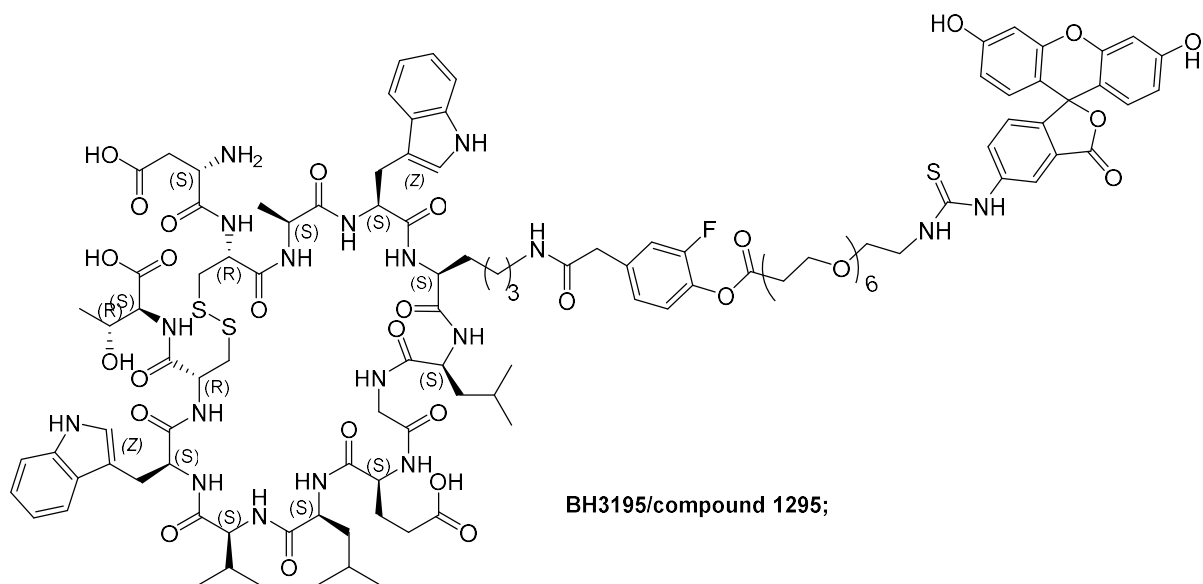
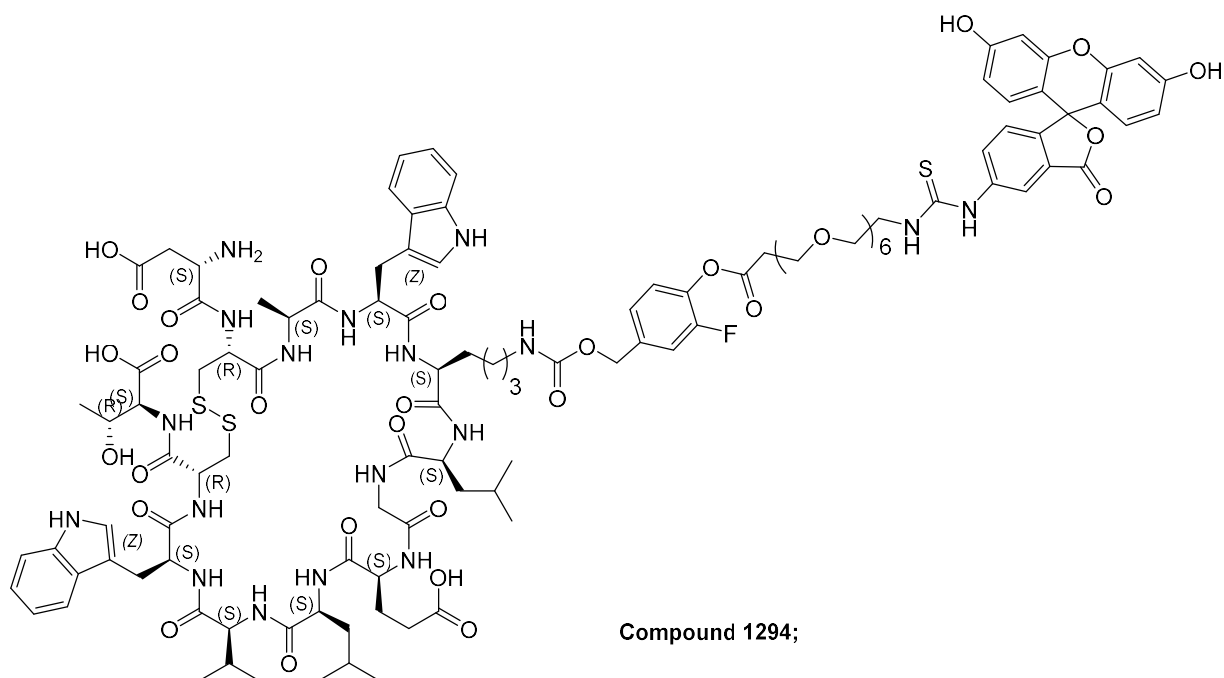
a fourth compound having the formula (R-III):



or a combination thereof.

25. A compound of claim 1, of the formula





26. A compound of claim 1 of the formula

