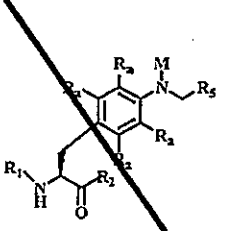
WHAT IS CLAIMED IS:

1. A compound or salt thereof selected from the group consisting of: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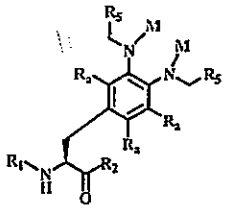
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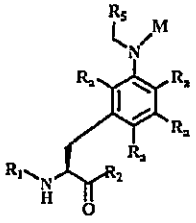
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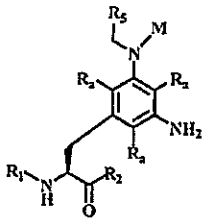
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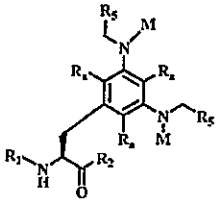

;

wherein each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

M is H or $-CH_2R_5$; or the M-N-C(R_5) moiety may form a 4 to 7 membered ring structure;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_5 is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -C(O)R", -C(O)OR", $-C(O)N(R")_2$, $-C(O)NHCH(R")_2$, -(alkylene or substituted alkylene)-$N(R")_2$, -(alkenylene or substituted alkenylene)-$N(R")_2$, -(alkylene or substituted alkylene)-(aryl or substituted aryl), -(alkenylene or substituted alkenylene)-(aryl or substituted aryl), -(alkylene or substituted alkylene)-$ON(R")_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, or -C(O)OR';

or R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; a polymer; a water-soluble polymer; a derivative of polyethylene glycol; a photocrosslinker; a cytotoxic compound; a drug; an affinity label; a photoaffinity label; a reactive compound; a resin; a second protein or polypeptide or polypeptide analog; an antibody or antibody fragment; a metal chelator; a cofactor; a fatty acid; a carbohydrate; a polynucleotide; a DNA; a RNA; an antisense polynucleotide; a saccharide, a water-soluble dendrimer, a cyclodextrin, a

biomaterial; a nanoparticle; a spin label; a fluorophore, a metal-containing moiety; a radioactive moiety; a novel functional group; a group that covalently or noncovalently interacts with other molecules; a photocaged moiety; an actinic radiation excitable moiety; a ligand; a photoisomerizable moiety; biotin; a biotin analogue; a moiety incorporating a heavy atom; a chemically cleavable group; a photocleavable group; an elongated side chain; a carbon-linked sugar; a redox-active agent; an amino thioacid; a toxic moiety; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; an electron dense group; a magnetic group; an intercalating group; a chromophore; an energy transfer agent; a biologically active agent; a detectable label; a small molecule; an inhibitory ribonucleic acid; a radionucleotide; a neutron-capture agent; a derivative of biotin; quantum dot(s); a nanotransmitter; a radiotransmitter; an abzyme, an activated complex activator, a virus, an adjuvant, an aglycan, an allergan, an angiostatin, an antihormone, an antioxidant, an aptamer, a guide RNA, a saponin, a shuttle vector, a macromolecule, a mimotope, a receptor, a reverse micelle, and any combination thereof; and L is optional, and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, $-S(O)_kN(R')-$, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, $-N(R')S(O)_kN(R')-$, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, $-C(R')_2-N=N-$, and $-C(R')_2-N(R')-N(R')-$;

or R_5 and any R_a optionally form a cycloalkyl or a heterocycloalkyl; and

each R' is independently H, alkyl, or substituted alkyl.

2. The compound of claim 1, wherein R_1 is H and R_2 is OH.

3. The compound of claim 1, wherein R_a is a halogen.

4. The compound of claim 1, wherein both R_1 and R_2 are polypeptides.

5. The compound of claim 1, wherein X is a biologically active agent selected from the group consisting of a peptide, protein, enzyme, antibody, drug, dye, lipid, nucleosides, oligonucleotide, cell, virus, liposome, microparticle, and micelle.

6. The compound of claim 5, wherein X is a drug selected from the group consisting of an antibiotic, fungicide, anti-viral agent, anti-inflammatory agent, anti-tumor agent, cardiovascular agent, anti-anxiety agent, hormone, growth factor, and steroidal agent.

7. The compound of claim 5, wherein X is an enzyme selected from the group consisting of horseradish peroxidase, alkaline phosphatase, β-galactosidase, and glucose oxidase.

8. The compound of claim 1, wherein X is a detectable label selected from the group consisting of a fluorescent, phosphorescent, chemiluminescent, chelating, electron dense, magnetic, intercalating, radioactive, chromophoric, and energy transfer moiety.

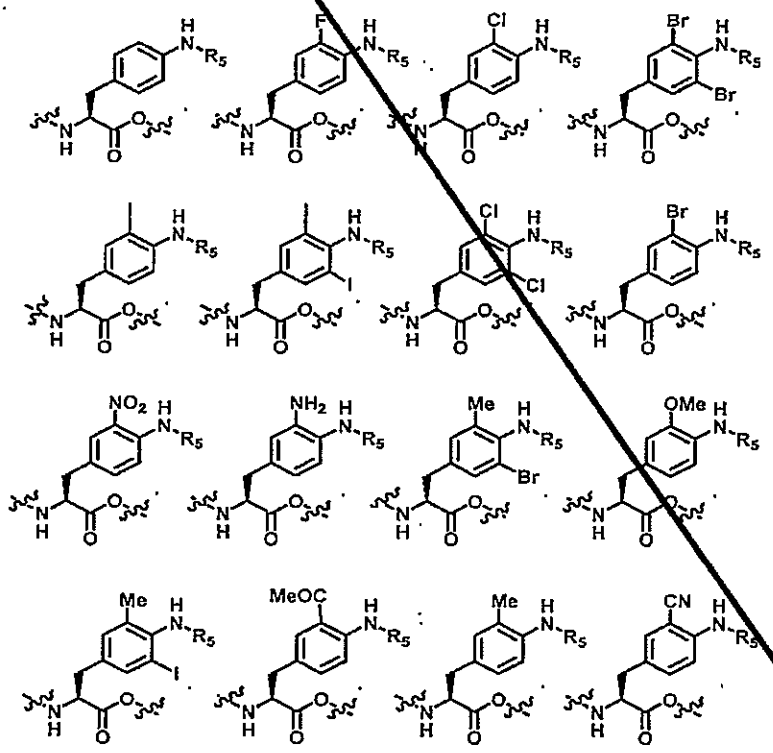
9. The compound of claim 1, wherein X is a polymer comprising alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkaryl, substituted alkaryl, aralkyl, or substituted aralkyl.

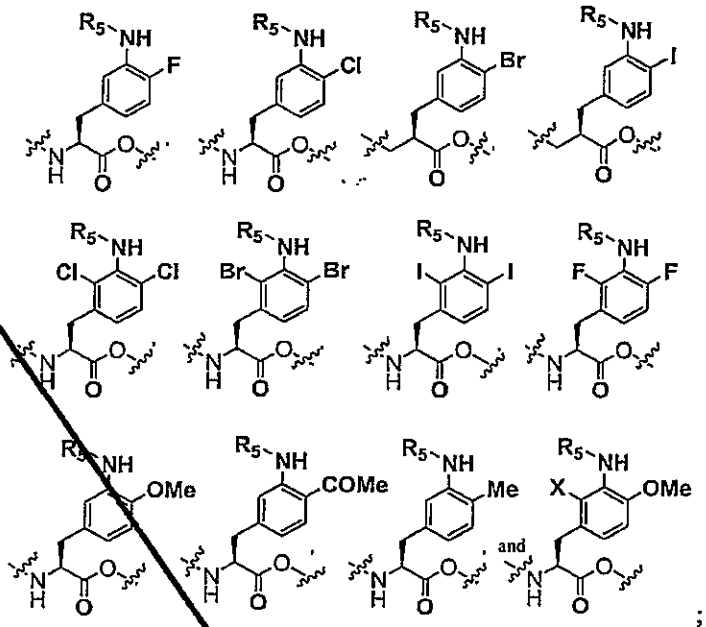
10. The compound of claim 9, wherein the polymer comprises polyalkylene oxide or substituted polyalkylene oxide.

11. The compound of claim 9, wherein the polymer comprises –[(alkylene or substituted alkylene)-O-(hydrogen, alkyl, or substituted alkyl)]$_x$, wherein x is from 20–10,000.

12. The compound of claim 9, wherein the polymer is m-PEG having a molecular weight ranging from about 2 to about 40 KDa.

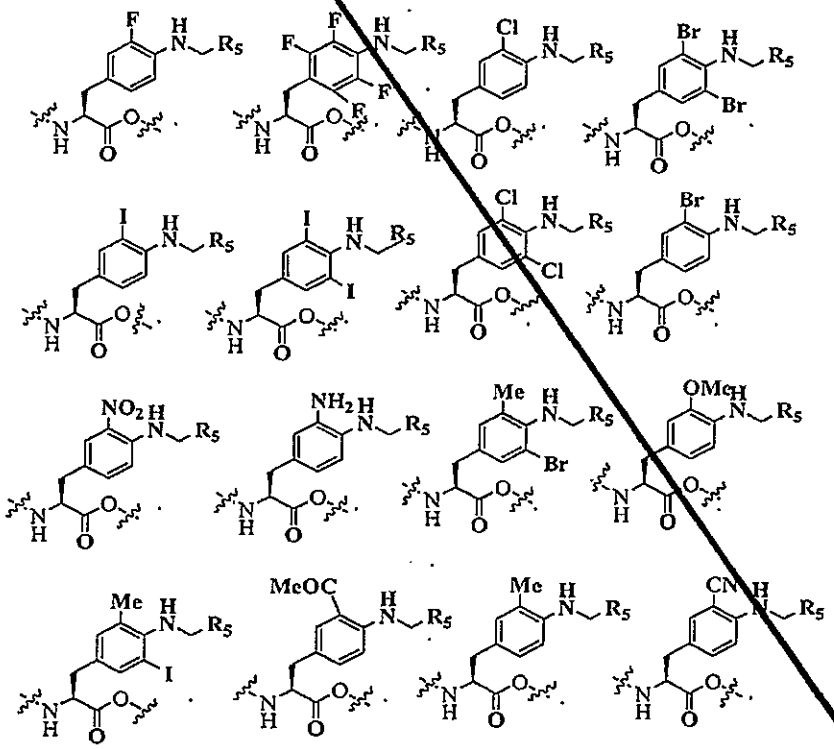
13. A polypeptide, or salt thereof, containing at least one compound of claim 1 selected from the group:

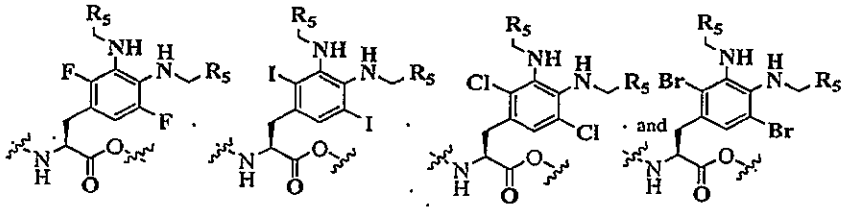




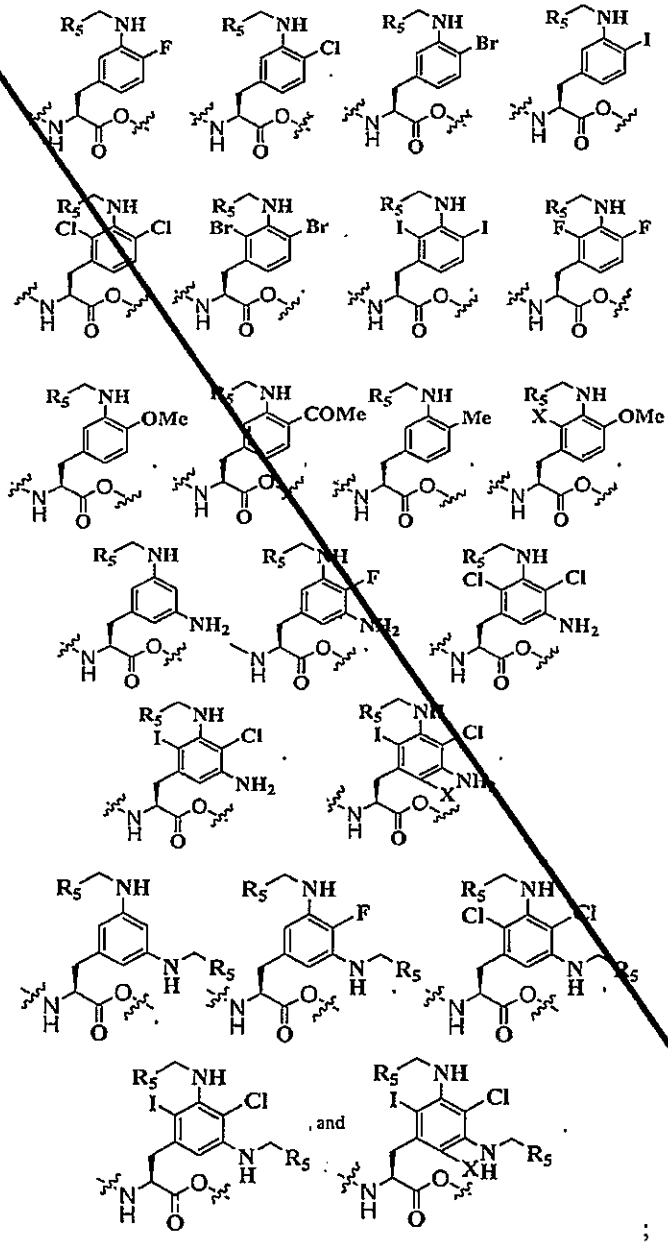
wherein X is a halogen.

14. A polypeptide, or salt thereof, containing at least one compound of claim 1 selected from the group:



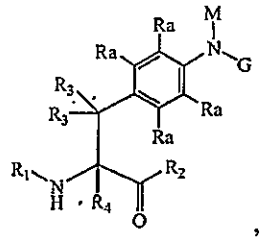


15. A polypeptide, or salt thereof, containing at least one compound of claim 1 selected from the group:



wherein X is a halogen.

16. A compound or salt thereof having the structure;



wherein each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide; and

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

each of R_3 and R_4 is independently H, halogen, lower alkyl, or substituted lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl;

M is H or $-CH_2R_5$;

R_5 is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -C(O)R", -C(O)OR", $-C(O)N(R")_2$, $-C(O)NHCH(R")_2$, -(alkylene or substituted alkylene)-$N(R")_2$, -(alkenylene or substituted alkenylene)-$N(R")_2$, -(alkylene or substituted alkylene)-(aryl or substituted aryl), -(alkenylene or substituted alkenylene)-(aryl or substituted aryl), -(alkylene or substituted alkylene)-$ON(R")_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, or -C(O)OR';

or R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; a polymer; a water-soluble polymer; a derivative of polyethylene glycol; a photocrosslinker; a cytotoxic compound; a drug; an affinity label; a photoaffinity label; a reactive compound; a resin; a second protein or polypeptide or polypeptide analog; an antibody or antibody fragment; a metal chelator; a cofactor; a fatty acid; a carbohydrate; a polynucleotide; a DNA; a RNA; an antisense polynucleotide; a saccharide, a water-soluble dendrimer, a cyclodextrin, a biomaterial; a nanoparticle; a spin label; a fluorophore, a metal-containing moiety; a radioactive moiety; a novel functional group; a group that covalently or noncovalently interacts with other molecules; a photocaged moiety; an actinic radiation excitable moiety; a ligand; a photoisomerizable moiety; biotin; a biotin analogue; a moiety incorporating a heavy atom; a chemically cleavable group; a photocleavable group; an elongated side chain; a carbon-linked sugar; a redox-active agent; an amino thioacid; a toxic moiety; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; an electron dense group; a magnetic group; an intercalating group; a chromophore; an energy transfer agent; a biologically active

agent; a detectable label; a small molecule; an inhibitory ribonucleic acid; a radionucleotide; a neutron-capture agent; a derivative of biotin; quantum dot(s); a nanotransmitter; a radiotransmitter; an abzyme, an activated complex activator, a virus, an adjuvant, an aglycan, an allergan, an angiostatin, an antihormone, an antioxidant, an aptamer, a guide RNA, a saponin, a shuttle vector, a macromolecule, a mimotope, a receptor, a reverse micelle, and any combination thereof; and L is optional, and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, $-S(O)_kN(R')-$, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, $-N(R')S(O)_kN(R')-$, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, $-C(R')_2-N=N-$, and $-C(R')_2-N(R')-N(R')-$;

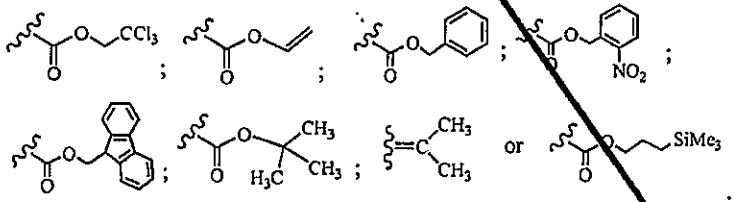
or two R_5 groups optionally form a cycloalkyl or a heterocycloalkyl;

or R_5 and any R_a optionally form a cycloalkyl or a heterocycloalkyl;

with a proviso that when R_1 is H then R_2 is not OH, or when R_2 is OH then R_1 is not H; and

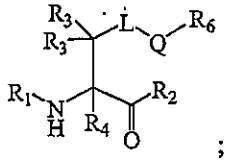
G is an amine protecting group.

17. The compound of claim 16, wherein the amine protecting group is selected from the group consisting of:



18. The compound of claim 16, wherein both R_1 and R_2 are polypeptides.

19. A compound or salt thereof having the structure of:



;

wherein L is optional, and when present is lower alkylene, substituted lower alkylene, lower cycloalkylene, substituted lower cycloalkylene, lower alkenylene, substituted lower alkenylene, alkynylene, lower

heteroalkylene, substituted heteroalkylene, lower heterocycloalkylene, substituted lower heterocycloalkylene, arylene, substituted arylene, heteroarylene, substituted heteroarylene, alkarylene, substituted alkarylene, aralkylene, or substituted aralkylene;

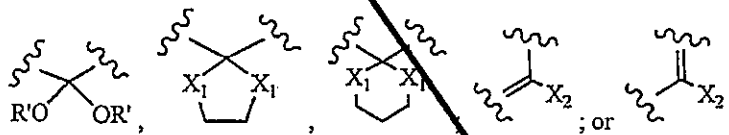
Q is optional, and when present is a linker selected from the group consisting of lower alkylene, substituted lower alkylene, lower alkenylene, substituted lower alkenylene, lower heteroalkylene, substituted lower heteroalkylene, -O-(alkylene or substituted alkylene)-, -S-(alkylene or substituted alkylene)-, where k is 1, 2, or 3, -S(O)$_k$(alkylene or substituted alkylene)-, -C(O)-(alkylene or substituted alkylene)-, -C(S)-(alkylene or substituted alkylene)-, -NR'-(alkylene or substituted alkylene)-, -CON(R")-(alkylene or substituted alkylene)-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, and where each R' is independently H, alkyl, or substituted alkyl;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide; and

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

each of R_3 and R_4 is independently H, halogen, lower alkyl, or substituted lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl;

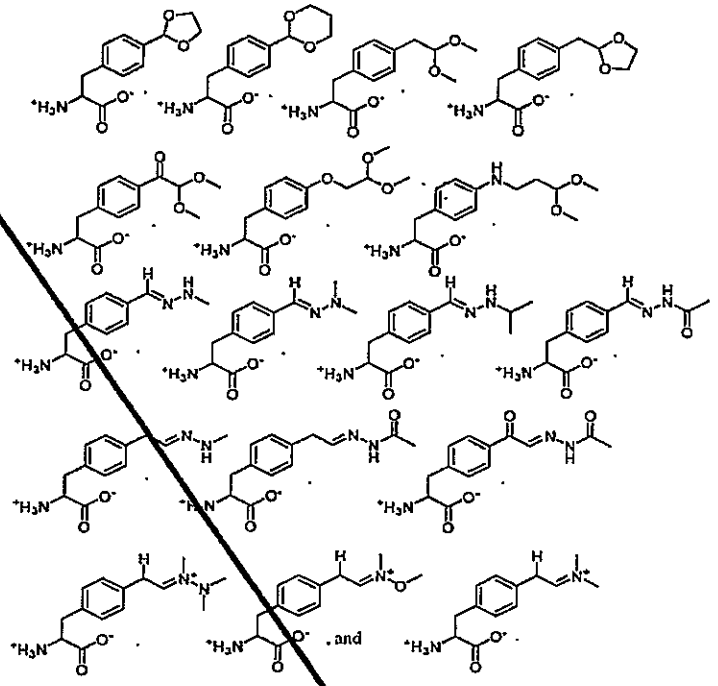
each R_5 is independently selected from the group consisting of H, halogen, alkyl, -NO_2, -CN, substituted alkyl, -N(R')$_2$, -C(O)$_k$R', -C(O)N(R')$_2$, -OR', and -S(O)$_k$R', where k is 1, 2, or 3;

R_6 is a protected aldehyde or a masked aldehyde, wherein the protecting group includes, but is not limited to, , where each X_1 is independently selected from the group consisting of -O-, -S-, -N(H)-, -N(R)-, -N(Ac)-, and –N(OMe)-; X_2 is –OR, -OAc, -SR, -N(R)$_2$, -N(R)(Ac), -N(R)(OMe), or N_3, and where each R' and R is independently H, alkyl, or substituted alkyl.

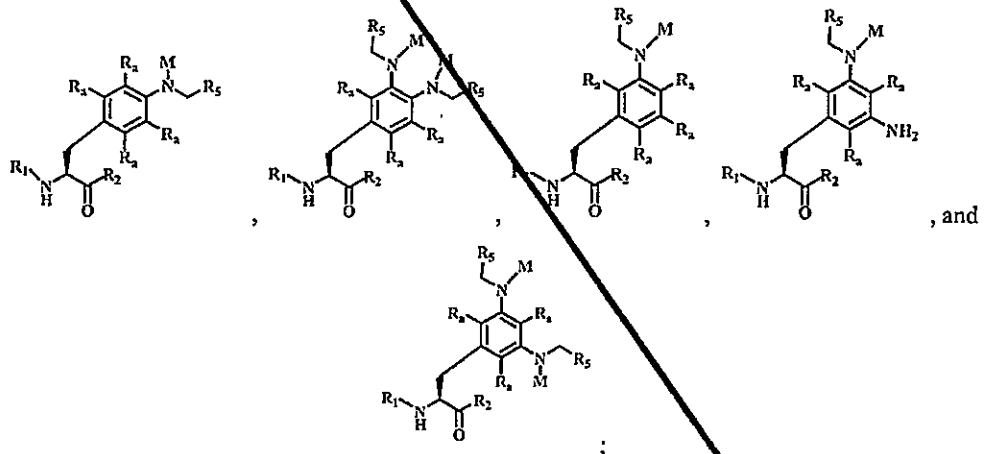
20. The compound of claim 19 wherein X_1 is O.

21. The compound of claim 19 wherein both R_1 and R_2 are polypeptides.

22. A polypeptide containing at least one compound of claim 19 selected from the group:



23. A method of making a compound containing at least one non-natural amino acid selected from the group consisting of:



wherein the compound is formed by a reductive alkylation of an aromatic amino moiety on at least one non-natural amino acid with at least one reactant comprising at least one aldehyde moiety;

each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

M is H or $-CH_2R_5$; or the M-N-$C(R_5)$ moiety may form a 4 to 7 membered ring structure;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_5 is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -C(O)R", -C(O)OR", -C(O)N(R")$_2$, -C(O)NHCH(R")$_2$, -(alkylene or substituted alkylene)-N(R")$_2$, -(alkenylene or substituted alkenylene)-N(R")$_2$, -(alkylene or substituted alkylene)-(aryl or substituted aryl), -(alkenylene or substituted alkenylene)-(aryl or substituted aryl), -(alkylene or substituted alkylene)-ON(R")$_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, or -C(O)OR';

or R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; a polymer; a water-soluble polymer; a derivative of polyethylene glycol; a photocrosslinker; a cytotoxic compound; a drug; an affinity label; a photoaffinity label; a reactive compound; a resin; a second protein or polypeptide or polypeptide analog; an antibody or antibody fragment; a metal chelator; a cofactor; a fatty acid; a carbohydrate; a polynucleotide; a DNA; a RNA; an antisense polynucleotide; a saccharide, a water-soluble dendrimer, a cyclodextrin, a biomaterial; a nanoparticle; a spin label; a fluorophore, a metal-containing moiety; a radioactive moiety; a novel functional group; a group that covalently or noncovalently interacts with other molecules; a photocaged moiety; an actinic radiation excitable moiety; a ligand; a photoisomerizable moiety; biotin; a biotin analogue; a moiety incorporating a heavy atom; a chemically cleavable group; a photocleavable group; an elongated side chain; a carbon-linked sugar; a redox-active agent; an amino thioacid; a toxic moiety; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; an electron dense group; a magnetic group; an intercalating group; a chromophore; an energy transfer agent; a biologically active agent; a detectable label; a small molecule; an inhibitory ribonucleic acid; a radionucleotide; a neutron-capture agent; a derivative of biotin; quantum dot(s); a nanotransmitter; a radiotransmitter; an abzyme, an activated complex activator, a virus, an adjuvant, an aglycan, an allergan, an angiostatin, an antihormone, an antioxidant, an aptamer, a guide RNA, a saponin, a shuttle vector, a macromolecule, a mimotope, a receptor, a reverse micelle, and any combination thereof; and L is optional, and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, -S(O)$_k$- where k is 1, 2, or 3, -S(O)$_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or

substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, -$S(O)_kN(R')$-, -$N(R')C(O)N(R')$-, -$N(R')C(S)N(R')$-, -$N(R')S(O)_kN(R')$-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -$C(R')_2$-N=N-, and -$C(R')_2$-N(R')-N(R')-;

or R_5 and any R_a optionally form a cycloalkyl or a heterocycloalkyl; and

each R' is independently H, alkyl, or substituted alkyl.

24. The method of claim 23, wherein R_1 and R_2 of the at least one non-natural amino acid is H and OH respectively.

25. The method of claim 23, wherein R_a of the at least one non-natural amino acid is a halogen.

26. The method of claim 23, wherein both R_1 and R_2 of the at least one non-natural amino acid are polypeptides.

27. The method of claim 23, wherein X of the at least one non-natural amino acid is a biologically active agent selected from the group consisting of a peptide, protein, enzyme, antibody, drug, dye, lipid, nucleosides, oligonucleotide, cell, virus, liposome, microparticle, and micelle.

28. The method of claim 27, wherein X of the at least one non-natural amino acid is a drug selected from the group consisting of an antibiotic, fungicide, anti-viral agent, anti-inflammatory agent, anti-tumor agent, cardiovascular agent, anti-anxiety agent, hormone, growth factor, and steroidal agent.

29. The method of claim 27, wherein X of the at least one non-natural amino acid is an enzyme selected from the group consisting of horseradish peroxidase, alkaline phosphatase, β-galactosidase, and glucose oxidase.

30. The method of claim 23, wherein X of the at least one non-natural amino acid is a detectable label selected from the group consisting of a fluorescent, phosphorescent, chemiluminescent, chelating, electron dense, magnetic, intercalating, radioactive, chromophoric, and energy transfer moiety.

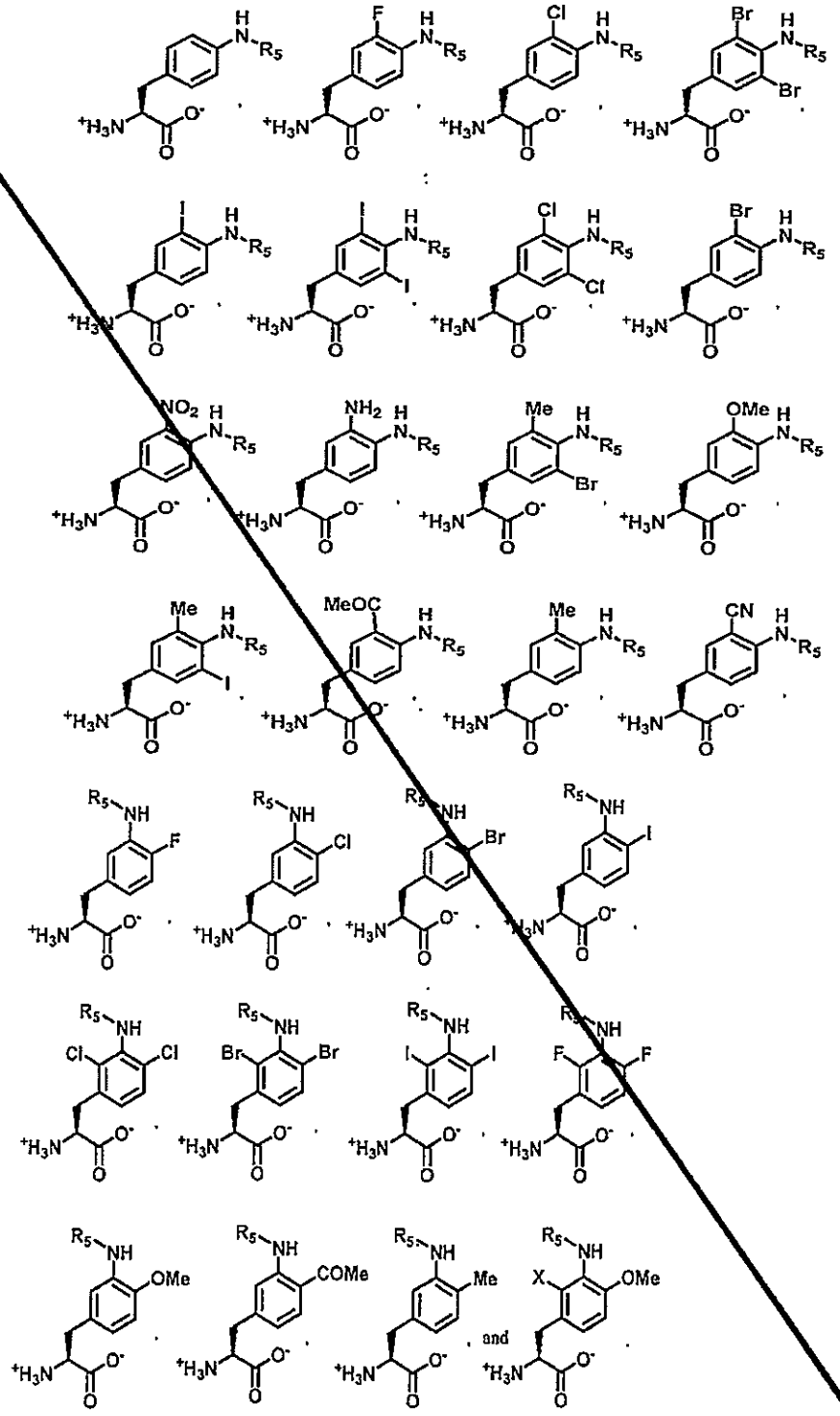
31. The method of claim 23, wherein X of the non-natural amino acid is a polymer comprising alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkaryl, substituted alkaryl, aralkyl, or substituted aralkyl.

32. The method of claim 31, wherein the polymer comprises polyalkylene oxide or substituted polyalkylene oxide.

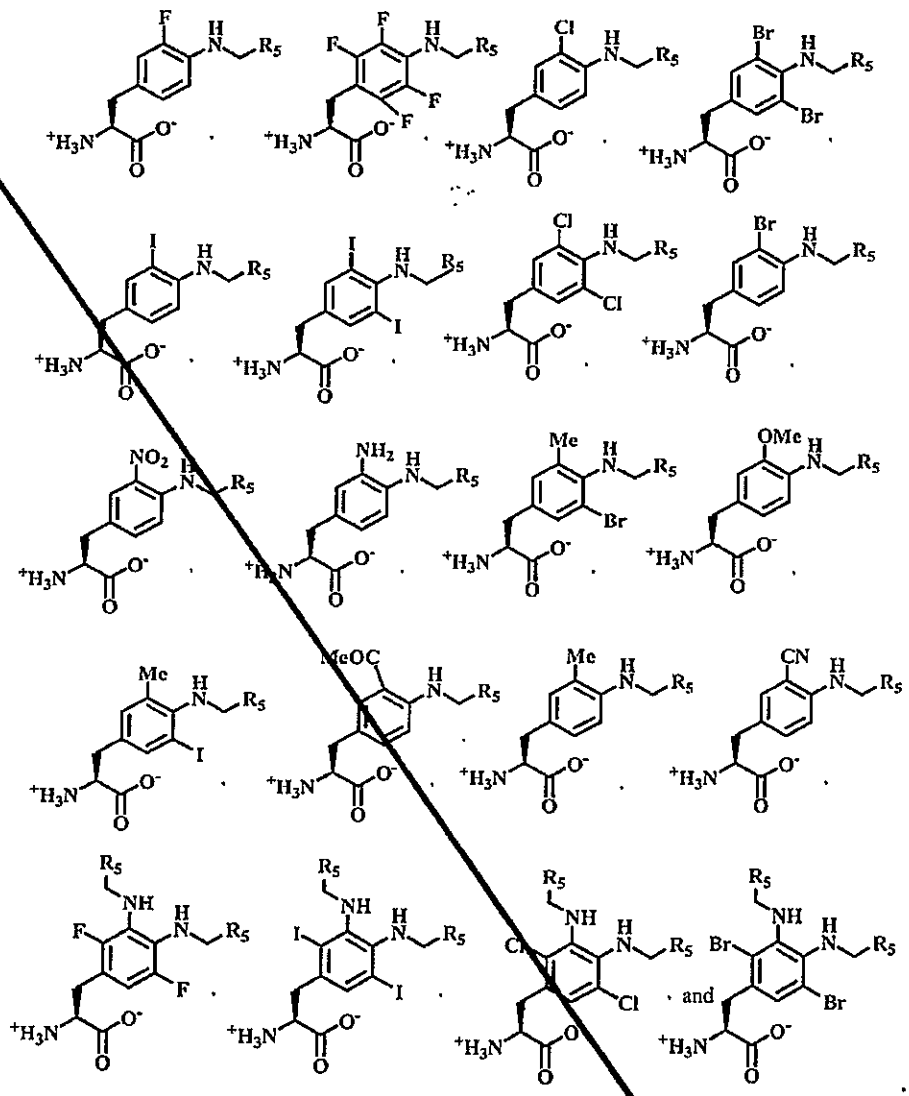
33. The method of claim 31, wherein the polymer comprises –[(alkylene or substituted alkylene)-O-(hydrogen, alkyl, or substituted alkyl)]$_x$, wherein x is from 20–10,000.

34. The method of claim 31, wherein the polymer is m-PEG having a molecular weight ranging from about 2 to about 40 KDa.

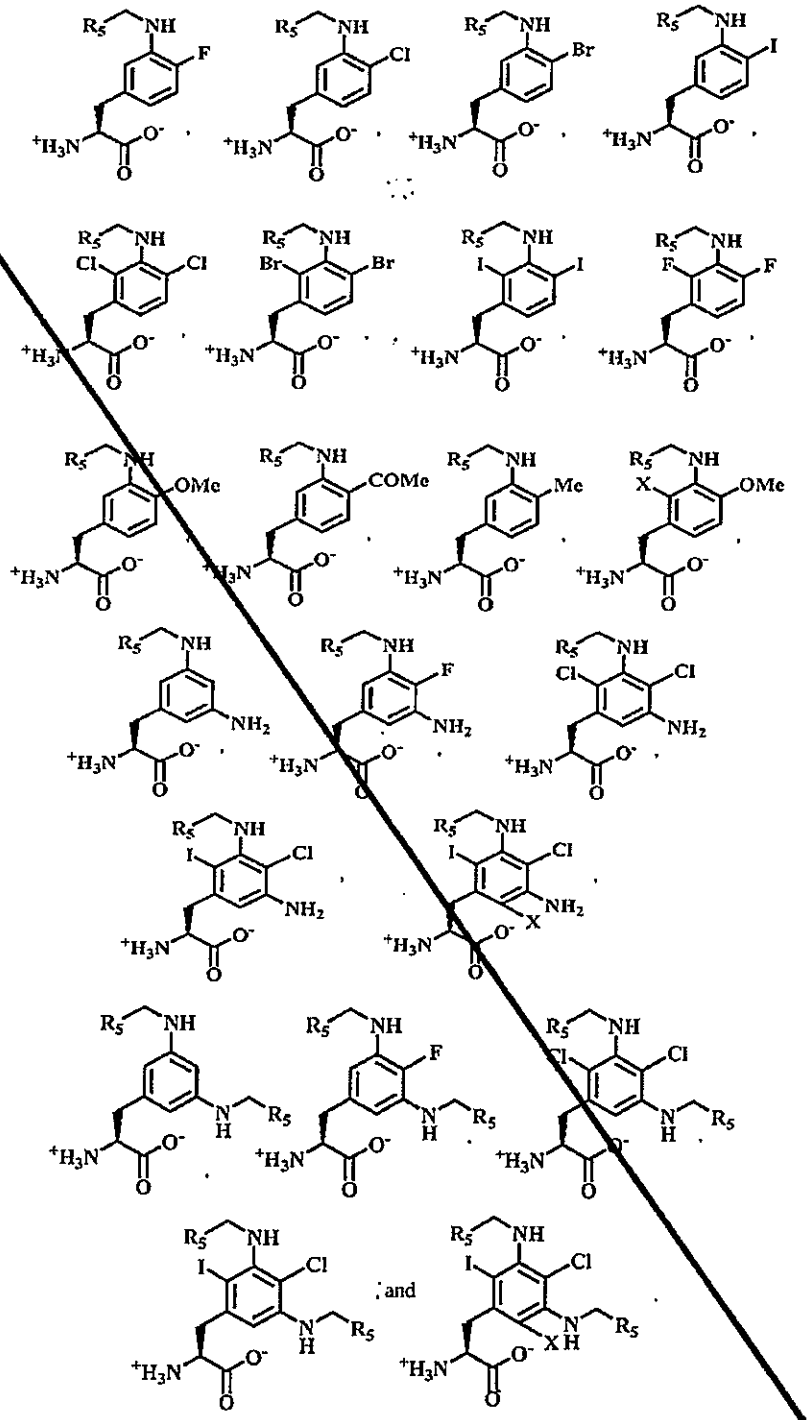
35. The method of claim 23 wherein the at least one non-natural amino acid is selected from a group:



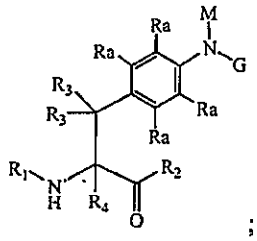
36. The method of claim 23 wherein the at least one non-natural amino acid is selected from a group:



37. The method of claim 23 wherein the at least one non-natural amino acid is selected from a group:



38. A method of making a polypeptide containing at least one non-natural amino acid selected from the group consisting of:



;

wherein the polypeptide is formed by a reductive alkylation of an aromatic amino moiety on at least one non-natural amino acid with at least one reactant comprising at least one aldehyde moiety;

each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide; and

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

each of R_3 and R_4 is independently H, halogen, lower alkyl, or substituted lower alkyl, or R_3 and R_4 or two R_3 groups optionally form a cycloalkyl or a heterocycloalkyl;

M is $-CH_2R_5$;

R_5 is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -C(O)R", -C(O)OR", $-C(O)N(R")_2$, $-C(O)NHCH(R")_2$, -(alkylene or substituted alkylene)-$N(R")_2$, -(alkenylene or substituted alkenylene)-$N(R")_2$, -(alkylene or substituted alkylene)-(aryl or substituted aryl), -(alkenylene or substituted alkenylene)-(aryl or substituted aryl), -(alkylene or substituted alkylene)-$ON(R")_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, or -C(O)OR';

or R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; a polymer; a water-soluble polymer; a derivative of polyethylene glycol; a photocrosslinker; a cytotoxic compound; a drug; an affinity label; a photoaffinity label; a reactive compound; a resin; a second protein or polypeptide or polypeptide analog; an antibody or antibody fragment; a metal chelator; a cofactor; a fatty acid; a carbohydrate; a polynucleotide; a DNA; a RNA; an antisense polynucleotide; a saccharide, a water-soluble dendrimer, a cyclodextrin, a biomaterial; a nanoparticle; a spin label; a fluorophore, a metal-containing moiety; a radioactive moiety; a novel functional group; a group that covalently or noncovalently interacts with other molecules; a photocaged moiety; an actinic radiation excitable moiety; a ligand; a photoisomerizable moiety; biotin; a biotin analogue; a moiety incorporating a heavy atom; a chemically cleavable group; a photocleavable group; an elongated side chain; a carbon-linked sugar; a redox-active agent; an amino thioacid; a toxic moiety; an isotopically labeled moiety; a

biophysical probe; a phosphorescent group; a chemiluminescent group; an electron dense group; a magnetic group; an intercalating group; a chromophore; an energy transfer agent; a biologically active agent; a detectable label; a small molecule; an inhibitory ribonucleic acid; a radionucleotide; a neutron-capture agent; a derivative of biotin; quantum dot(s); a nanotransmitter; a radiotransmitter; an abzyme, an activated complex activator, a virus, an adjuvant, an aglycan, an allergan, an angiostatin, an antihormone, an antioxidant, an aptamer, a guide RNA, a saponin, a shuttle vector, a macromolecule, a mimotope, a receptor, a reverse micelle, and any combination thereof; and L is optional, and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R')-, -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, $-S(O)_kN(R')-$, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, $-N(R')S(O)_kN(R')-$, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, $-C(R')_2-N=N-$, and $-C(R')_2-N(R')-N(R')-$;

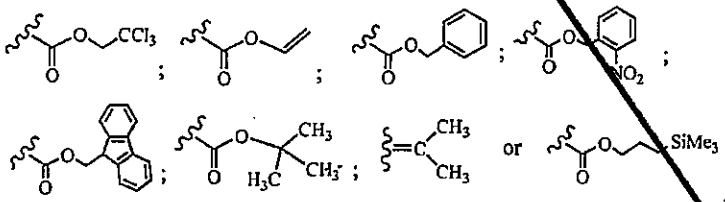
or two R_5 groups optionally form a cycloalkyl or a heterocycloalkyl;

or R_5 and any R_a optionally form a cycloalkyl or a heterocycloalkyl;

with a proviso that when R_1 is H then R_2 is not OH, or when R_2 is OH then R_1 is not H; and

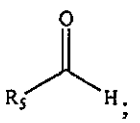
G is an amine protecting group.

39. The method of claim 38 wherein the amine protecting group is selected from the group consisting of:



40. The method of claim 38 wherein both R_1 and R_2 are polypeptides.

41. The method of claims 23 and 38 wherein the at least one aldehyde moiety has the structure corresponding to:



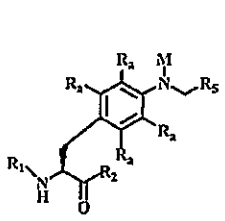
wherein:

R_5 is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -C(O)R", -C(O)OR", -C(O)N(R")$_2$, -C(O)NHCH(R")$_2$, -(alkylene or substituted alkylene)-N(R")$_2$, -(alkenylene or substituted alkenylene)-N(R")$_2$, -(alkylene or substituted alkylene)-(aryl or substituted aryl), -(alkenylene or substituted alkenylene)-(aryl or substituted aryl), -(alkylene or substituted alkylene)-ON(R")$_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, or -C(O)OR';

or R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; a polymer; a water-soluble polymer; a derivative of polyethylene glycol; a photocrosslinker; a cytotoxic compound; a drug; an affinity label; a photoaffinity label; a reactive compound; a resin; a second protein or polypeptide or polypeptide analog; an antibody or antibody fragment; a metal chelator; a cofactor; a fatty acid; a carbohydrate; a polynucleotide; a DNA; a RNA; an antisense polynucleotide; a saccharide, a water-soluble dendrimer, a cyclodextrin, a biomaterial; a nanoparticle; a spin label; a fluorophore, a metal-containing moiety; a radioactive moiety; a novel functional group; a group that covalently or noncovalently interacts with other molecules; a photocaged moiety; an actinic radiation excitable moiety; a ligand; a photoisomerizable moiety; biotin; a biotin analogue; a moiety incorporating a heavy atom; a chemically cleavable group; a photocleavable group; an elongated side chain; a carbon-linked sugar; a redox-active agent; an amino thioacid; a toxic moiety; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; an electron dense group; a magnetic group; an intercalating group; a chromophore; an energy transfer agent; a biologically active agent; a detectable label; a small molecule; an inhibitory ribonucleic acid; a radionucleotide; a neutron-capture agent; a derivative of biotin; quantum dot(s); a nanotransmitter; a radiotransmitter; an abzyme, an activated complex activator, a virus, an adjuvant, an aglycan, an allergan, an angiostatin, an antihormone, an antioxidant, an aptamer, a guide RNA, a saponin, a shuttle vector, a macromolecule, a mimotope, a receptor, a reverse micelle, and any combination thereof; and L is optional, and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-,

-C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, $-S(O)_kN(R')-$, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, $-N(R')S(O)_kN(R')-$, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, $-C(R')_2-N=N-$, and $-C(R')_2-N(R')-N(R')-$.

42. A method for treating a disorder, condition or disease comprising administering a therapeutically effective amount of a polypeptide comprising at least one non-natural amino acid selected from the group consisting of: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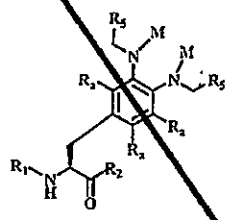
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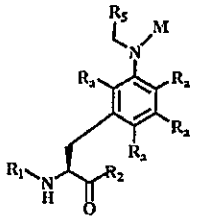
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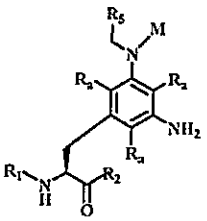
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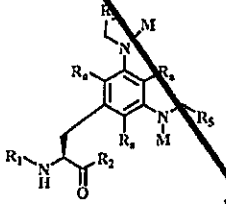

;

wherein each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

M is H or $-CH_2R_5$; or the M-N-$C(R_5)$ moiety may form a 4 to 7 membered ring structure;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_5 is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, alkylalkoxy, substituted alkylalkoxy, polyalkylene oxide, substituted polyalkylene oxide, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, -C(O)R", -C(O)OR", $-C(O)N(R")_2$, $-C(O)NHCH(R")_2$, -(alkylene or substituted alkylene)-$N(R")_2$, -(alkenylene or substituted alkenylene)-$N(R")_2$, -(alkylene or substituted alkylene)-(aryl or substituted aryl), -(alkenylene or substituted alkenylene)-(aryl or substituted aryl),

-(alkylene or substituted alkylene)-ON(R")$_2$, -(alkylene or substituted alkylene)-C(O)SR", -(alkylene or substituted alkylene)-S-S-(aryl or substituted aryl), wherein each R" is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, alkaryl, substituted alkaryl, aralkyl, substituted aralkyl, or -C(O)OR';

or R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; a polymer; a water-soluble polymer; a derivative of polyethylene glycol; a photocrosslinker; a cytotoxic compound; a drug; an affinity label; a photoaffinity label; a reactive compound; a resin; a second protein or polypeptide or polypeptide analog; an antibody or antibody fragment; a metal chelator; a cofactor; a fatty acid; a carbohydrate; a polynucleotide; a DNA; a RNA; an antisense polynucleotide; a saccharide, a water-soluble dendrimer, a cyclodextrin, a biomaterial; a nanoparticle; a spin label; a fluorophore, a metal-containing moiety; a radioactive moiety; a novel functional group; a group that covalently or noncovalently interacts with other molecules; a photocaged moiety; an actinic radiation excitable moiety; a ligand; a photoisomerizable moiety; biotin; a biotin analogue; a moiety incorporating a heavy atom; a chemically cleavable group; a photocleavable group; an elongated side chain; a carbon-linked sugar; a redox-active agent; an amino thioacid; a toxic moiety; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; an electron dense group; a magnetic group; an intercalating group; a chromophore; an energy transfer agent; a biologically active agent; a detectable label; a small molecule; an inhibitory ribonucleic acid; a radionucleotide; a neutron-capture agent; a derivative of biotin; quantum dot(s); a nanotransmitter; a radiotransmitter; an abzyme, an activated complex activator, a virus, an adjuvant, an aglycan, an allergan, an angiostatin, an antihormone, an antioxidant, an aptamer, a guide RNA, a saponin, a shuttle vector, a macromolecule, a mimotope, a receptor, a reverse micelle, and any combination thereof; and L is optional, and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, -S(O)$_k$- where k is 1, 2, or 3, -S(O)$_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')CO-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-S(O)$_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, -S(O)$_k$N(R')-, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)$_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -C(R')$_2$-N=N-, and -C(R')$_2$-N(R')-N(R')-;

or R_5 and any R_a optionally form a cycloalkyl or a heterocycloalkyl; and

each R' is independently H, alkyl, or substituted alkyl.

with a proviso that when R_1 is H then R_2 is not OH, or when R_2 is OH then R_1 is not H.

43. The method of claim 42, further comprising administering a pharmaceutically acceptable carrier with the therapeutically effective amount of the polypeptide.

44. The method of claim 42, wherein R_1 and R_2 are both polypeptides.

45. The method of claim 42, wherein X is a water-soluble polymer.

46. The method of claim 42, wherein X is a derivative of polyethylene glycol.

47. The method of claim 42, wherein X is a cytotoxic compound.

48. The method of claim 42, wherein X is a drug.

49. The method of claim 42, wherein X is a second polypeptide.

50. The method of claim 49, wherein the second polypeptide is a peptide containing a non-natural amino acid polypeptide.

51. The method of claim 42, wherein the polypeptide is a protein homologous to a therapeutic protein selected from the group consisting of alpha-1 antitrypsin, angiostatin, antihemolytic factor, antibody, antibody fragment, apolipoprotein, apoprotein, atrial natriuretic factor, atrial natriuretic polypeptide, atrial peptide, C-X-C chemokine, T39765, NAP-2, ENA-78, gro-a, gro-b, gro-c, IP-10, GCP-2, NAP-4, SDF-1, PF4, MIG, calcitonin, c-kit ligand, cytokine, CC chemokine, monocyte chemoattractant protein-1, monocyte chemoattractant protein-2, monocyte chemoattractant protein-3, monocyte inflammatory protein-1 alpha, monocyte inflammatory protein-i beta, RANTES, I309, R83915, R91733, HCC1, T58847, D31065, T64262, CD40, CD40 ligand, c-kit ligand, collagen, colony stimulating factor (CSF), complement factor 5a, complement inhibitor, complement receptor 1, cytokine, epithelial neutrophil activating peptide-78, MIP-16, MCP-1, epidermal growth factor (EGF), epithelial neutrophil activating peptide, erythropoietin (EPO), exfoliating toxin, Factor IX, Factor VII, Factor VIII, Factor X, fibroblast growth factor (FGF), fibrinogen, fibronectin, four-helical bundle protein, G-CSF, glp-1, GM-CSF, glucocerebrosidase, gonadotropin, growth factor, growth factor receptor, grf, hedgehog protein, hemoglobin, hepatocyte growth factor (hGF), hirudin, human growth hormone (hGH), human serum albumin, ICAM-1, ICAM-1 receptor, LFA-1, LFA-1 receptor, insulin, insulin-like growth factor (IGF), IGF-I, IGF-II, interferon (IFN), IFN-alpha, IFN-beta, IFN-gamma, interleukin (IL), IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, keratinocyte growth factor (KGF), lactoferrin, leukemia inhibitory factor, luciferase, neurturin, neutrophil inhibitory factor (NIF), oncostatin M, osteogenic protein, oncogene product, paracitonin, parathyroid hormone, PD-ECSF, PDGF, peptide hormone, pleiotropin, protein A, protein G, pth, pyrogenic exotoxin A, pyrogenic exotoxin B, pyrogenic exotoxin C, pyy, relaxin, renin, SCF, small biosynthetic protein, soluble complement receptor I, soluble I-CAM 1, soluble interleukin receptor, soluble TNF receptor, somatomedin, somatostatin, somatotropin, streptokinase, superantigens, staphylococcal enterotoxin, SEA, SEB, SEC1, SEC2, SEC3, SED, SEE, steroid hormone receptor, superoxide dismutase, toxic shock syndrome toxin, thymosin alpha 1, tissue plasminogen activator, tumor growth factor (TGF), tumor necrosis factor, tumor necrosis factor alpha, tumor necrosis factor beta, tumor necrosis factor receptor (TNFR), VLA-4 protein, VCAM-1 protein, vascular endothelial growth factor (VEGF), urokinase,

mos, ras, raf, met, p53, tat, fos, myc, jun, myb, rel, estrogen receptor, progesterone receptor, testosterone receptor, aldosterone receptor, LDL receptor, and corticosterone.

52. The method of claim 42, wherein the at least one non-natural acid is incorporated at a specific site within the polypeptide.

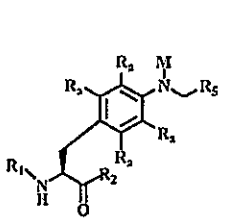
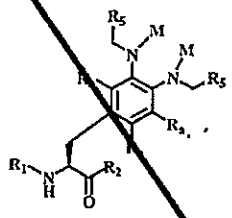
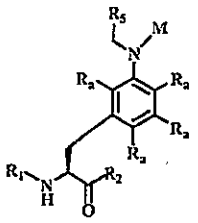
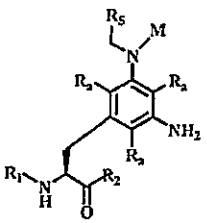
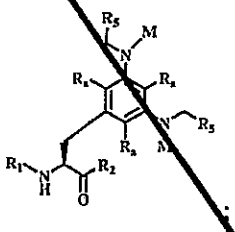
53. The method of claim 42, wherein the non-natural amino acid is incorporated using a translation system.

54. The method of claim 42, wherein the non-natural amino acid is incorporated into the polypeptide using a translation system and a post translation modification system.

55. The method of claim 42, wherein the polypeptide comprising at least one non-natural amino acid is stable for at least 1 month.

56. The method of claim 42, wherein the polypeptide comprising at least one non-natural amino acid is stable for at least 2 weeks.

57. A method for detecting the presence of a polypeptide in a patient, the method comprising administering an effective amount of a homologous non-natural amino acid polypeptide comprising at least one non-natural amino acid selected from the group consisting of:





, and


and detecting an indicator on the polypeptide selected from the group consisting of a label; a dye; an affinity label; a photoaffinity label; a spin label; a second protein or polypeptide or polypeptide analog; a fluorophore; a radioactive moiety; a moiety incorporating a heavy atom; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; biotin, a biotin analogue; an electron dense group; a magnetic group; a chromophore; an energy transfer agent; a detectable label; a radiotransmitter, and any combination of the above;

wherein each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

M is H or $-CH_2R_5$; or the M-N-C(R_5) moiety may form a 4 to 7 membered ring structure;

R_1 is H, an amino protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_2 is OH, an ester protecting group, resin, amino acid, polypeptide, or polynucleotide;

R_5 is L-X, where, X is a selected from the group consisting of a label; a dye; an affinity label; a photoaffinity label; a spin label; a second protein or polypeptide or polypeptide analog; a fluorophore; a radioactive moiety; a moiety incorporating a heavy atom; an isotopically labeled moiety; a biophysical probe; a phosphorescent group; a chemiluminescent group; biotin, a biotin analogue; an electron dense group; a magnetic group; a chromophore; an energy transfer agent; a detectable label; a radiotransmitter, and any combination of the above; and L is optional and when present is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')C(O)-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, $-S(O)_kN(R')-$, -N(R')C(O)N(R')-, -N(R')C(S)N(R')-, $-N(R')S(O)_kN(R')-$, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, $-C(R')_2-N=N-$, and $-C(R')_2-N(R')-N(R')-$;

or R_5 and any R_a optionally form a cycloalkyl or a heterocycloalkyl;

each R' is independently H, alkyl, or substituted alkyl; and

with a proviso that when R_1 is H then R_2 is not OH, or when R_2 is OH then R_1 is not H.

58. The method of claim 57, wherein the at least one non-natural acid is incorporated at a specific site within the polypeptide.

59. The method of claim 57, wherein the non-natural amino acid is incorporated using a translation system.

60. The method of claim 57, wherein the non-natural amino acid is incorporated into the polypeptide using a translation system and a post translation modification system.

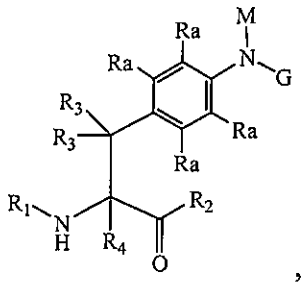
61. The method of claim 57, wherein the at least one non-natural amino acid is stable in aqueous solution for at least 1 month.

62. The method of claim 57, wherein the at least one non-natural amino acid is stable for at least 2 weeks.

63. The method of claim 57, wherein the at least one non-natural amino acid is stable for at least 5 days.

Claims

1. A compound or salt thereof having the structure:



wherein each R_a is independently selected from the group consisting of H, halogen, alkyl, $-NO_2$, -CN, substituted alkyl, $-N(R')_2$, $-C(O)_kR'$, $-C(O)N(R')_2$, -OR', and $-S(O)_kR'$, where k is 1, 2, or 3;

R_1 is H, an amino protecting group, or at least one amino acid; and

R_2 is OH, an ester protecting group, or at least one amino acid;

each of R_3 and R_4 is independently H;

M is $-CH_2R_5$;

R_5 is polyalkylene oxide, substituted polyalkylene oxide;

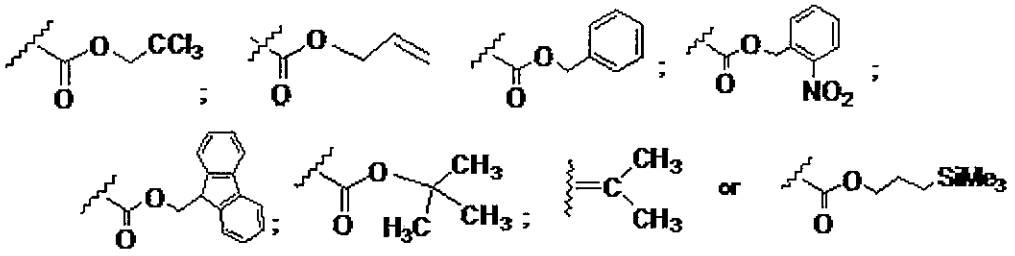
or R_5 is L-X, where, X is polyalkylene oxide or substituted polyalkylene oxide; and L is a linker selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, -O-, -O-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-O-, -C(O)-, -C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)-, -C(O)N(R')-, -C(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-C(O)N(R'), -OC(O)N(R')-, -OC(O)N(R')-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-OC(O)N(R')-, -N(R')C(O)-, -NR'C(O)-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-NR'C(O)-, -S-, -S-(alkylene or substituted alkylene)-, $-S(O)_k-$ where k is 1, 2, or 3, $-S(O)_k$(alkylene or substituted alkylene)-, -C(S)-, -C(S)-(alkylene or substituted alkylene)-, -CSN(R')-, -CSN(R')-(alkylene or substituted alkylene)-, -N(R')C(O)O-, -(alkylene or substituted alkylene)-O-N=CR'-, -(alkylene or substituted alkylene)-C(O)NR'-(alkylene or substituted alkylene)-, -(alkylene or substituted alkylene)-$S(O)_k$-(alkylene or substituted alkylene)-S-, -(alkylene or substituted alkylene)-S-S-, $-S(O)_kN(R')-$,

-N(R')C(O)N(R')-, -N(R')C(S)N(R')-, -N(R')S(O)$_k$N(R')-, -N(R')-N=, -C(R')=N-, -C(R')=N-N(R')-, -C(R')=N-N=, -C(R')$_2$-N=N-, and -C(R')$_2$-N(R')-N(R')-;

each R' is independently H, alkyl, or substituted alkyl;

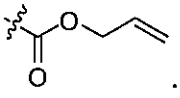
with a proviso that when R_1 is H then R_2 is not OH, or when R_2 is OH then R_1 is not H; and G is an amine protecting group.

2. The compound of claim 16, wherein the amine protecting group is selected from the group consisting of:



3. The compound of claim 1, wherein both R_1 and R_2 are at least one amino acid.

4. The compound of claim 1 wherein R_5 is L-X, where X is polyalkylene oxide.

5. The compound of claim 1 wherein G is .