CLAIMS

1. A Ligand-Functional Agent Conjugate comprising:

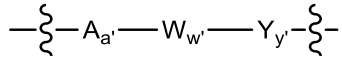
a Ligand unit and at least one Functional Agent selected from the group consisting of a Drug unit, Detection Unit, and Stability unit, wherein the Ligand unit and each of the Functional Agent(s) are joined by a self-stabilizing linker assembly comprising a succinimide ring or a hydrolyzed succinimide or a dilactam directly conjugated to the Ligand unit via a thioether linkage; or wherein the Ligand unit and each of the Functional Agent(s) are joined by a self-stabilizing linker assembly comprising a succinimide ring, a maleimide ring, a hydrolyzed succinimide ring or a hydrolyzed maleimide ring wherein the succinimide ring, maleimide ring, hydrolyzed succinimide ring or hydrolyzed maleimide ring is directly conjugated to the Ligand unit via one or two thioether linkages; and a base and an electron withdrawing group operably linked to stabilize the conjugate in plasma relative to a Ligand-Functional Agent Conjugate lacking the self-stabilizing linker assembly.

2. A Ligand-Functional Agent Conjugate of claim **1**, comprising:

a Ligand unit and at least one Functional Agent selected from the group consisting of a Drug unit, a Detection Unit, and a Stability Unit, wherein the Ligand unit and each of the Functional Agent(s) are joined by a self-stabilizing linker assembly comprising a succinimide ring or a hydrolyzed succinimide or a dilactam directly conjugated to the Ligand unit via a thioether linkage; and a base and an electron withdrawing group operably linked to stabilize the conjugate in plasma relative to a Ligand-Functional Agent Conjugate lacking the self-stabilizing linker assembly.

3. A Ligand-Functional Agent Conjugate of claim **1** or claim **2**, wherein the Ligand-Functional Agent is a Ligand-Drug Conjugate comprising a Drug unit as the Functional Agent and the Ligand-Drug conjugate further comprises a linker assembly which joins each Drug to a self-stabilizing linker assembly.

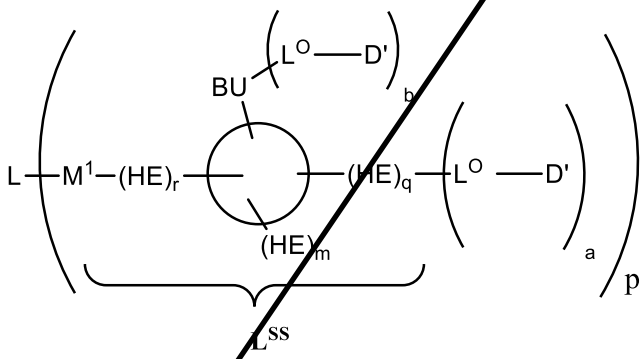
4. A Ligand-Functional Agent Conjugate of claim **3**, wherein the linker assembly has the formula:



wherein -A- is an optional Stretcher unit, the subscript a' is 0 or 1; -W- is an optional Cleavable unit, the subscript w' is 0 or 1; and -Y- is an optional Spacer unit, and the subscript y' is 0 or 1; and the wavy lines indicate the points of attachment to the self-stabilizing linker assembly and the Drug unit.

5. A Ligand-Functional Agent Conjugate of claim **4**, wherein the subscript w' is 1, and W is a dipeptide, tripeptide or tetrapeptide.

6. A Ligand-Functional Agent Conjugate of claim **1**, having the formula:



or a salt thereof, wherein

L is a Ligand unit;

D' is a Drug unit, a Detection unit, or a Stability unit;

L^O is an optional secondary linker assembly; and

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with BU forms a dilactam;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

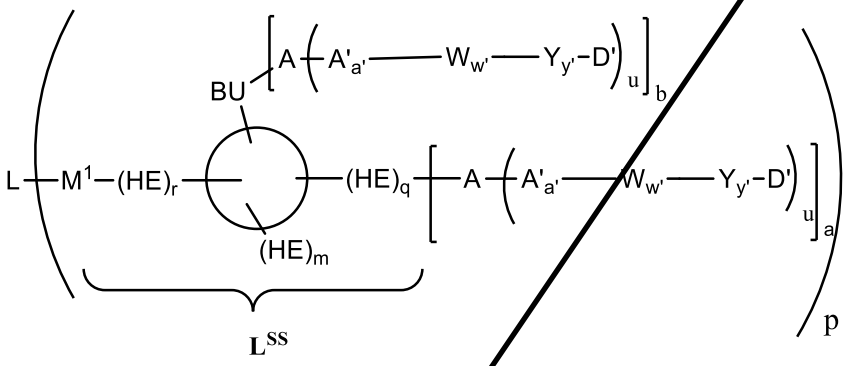
the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1; and

the subscript p ranges from 1 to 20.

7. A Ligand-Functional Agent Conjugate of claim **1** or **2,** having the formula:



or a salt thereof, wherein

L is a Ligand unit;

D' is a Drug unit, a Detection unit, or a Stability unit;

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with BU forms a dilactam;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

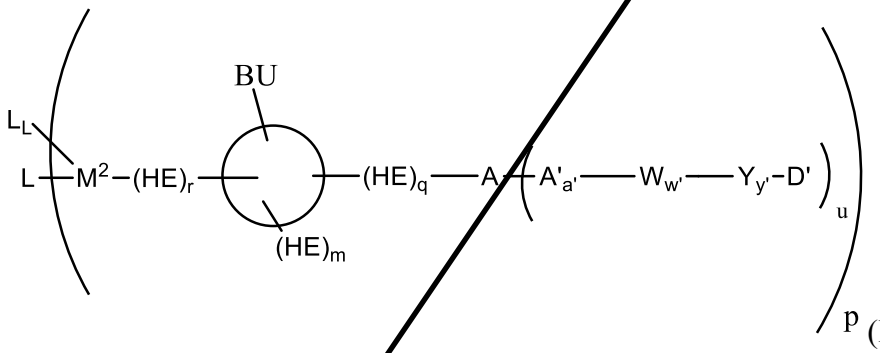
A is a Stretcher unit,

A' is an optional Stretcher unit component at the terminus of A;

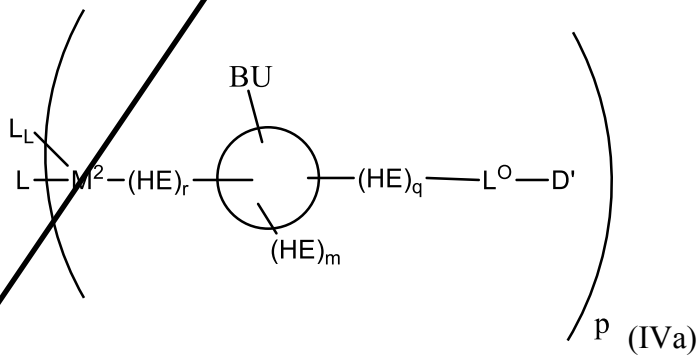
a' is 0 or 1; and

u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

8. A Ligand-Functional Agent Conjugate of claim **2**, represented by Formula IV or IVa:



(IV)



(IVa)

or a pharmaceutically acceptable salt thereof; wherein

L is a Ligand unit

L_L is a Ligand unit that can be present or absent, wherein L and L_L can be the same or different Ligand units;

D' is a Drug unit, a Detection unit, or a Stability unit;

L^O is an optional secondary linker assembly;

M^2 is a maleimide ring, a hydrolyzed maleimide, a succinimide ring, or a hydrolyzed succinimide conjugated to at least one of L or L_L via a thioether linkage; and

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

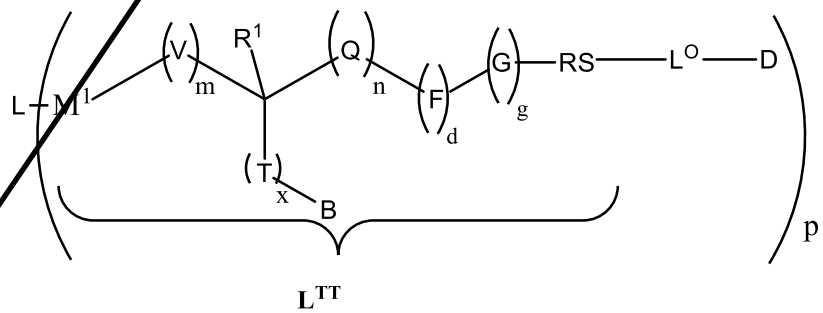
-A- is an optional Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

9. A Ligand-Functional Agent Conjugate of claim **1**, that is a Ligand-Drug Conjugate having the formula:



L^{TT}

or a pharmaceutically acceptable salt thereof wherein L is a Ligand unit;

D is a Drug unit;

L^O is the optional secondary linker assembly;

L^{TT} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with B forms a dilactam;

V, Q, T, and G are independently selected from $–(C(R^9)(R^{10}))-$;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is $C(E^1)(E^2)$ wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly or Drug unit;

g is 0 to 5;

m is 0 to 5;

n is 0 to 5;

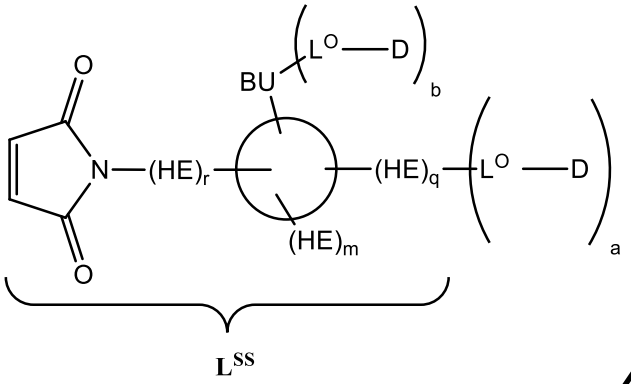
d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS is an electron withdrawing group.

10. A Ligand-Functional Agent Conjugate of claim 9, wherein m is 0, and n is 0.

11. A Drug-Linker Conjugate having the formula:



or a salt thereof, wherein,

D is a Drug unit;

L^O is a an optional secondary linker assembly; and

L^{SS} is the self-stabilizing linker assembly, wherein

BU is a Basic unit;

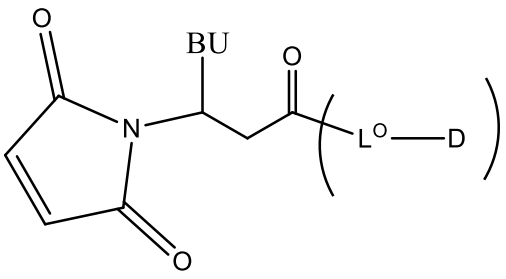
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or Drug unit;

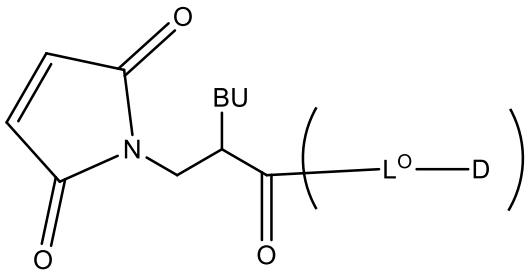
the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene; and

the subscript a and b are each 0 or 1, and the sum of a+b is 1.

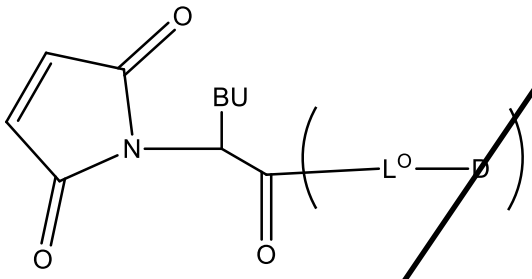
12. A Drug-Linker Conjugate of claim **11**, having the formula:



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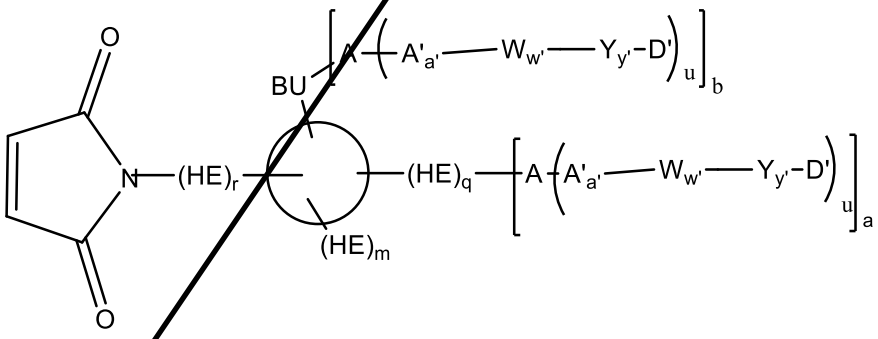


, or



or a salt thereof.

13. A Functional Agent-Linker Conjugate having the formula:



or a salt thereof, wherein

D' is a Drug unit, a Detection unit, or a Stability unit;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

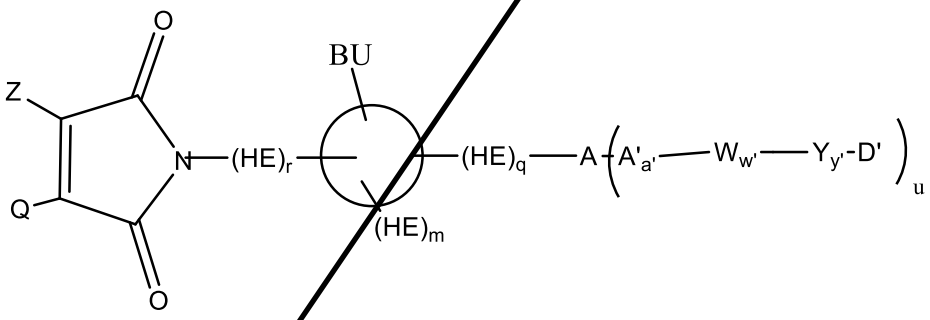
A is a Stretcher unit,

A' is an optional Stretcher unit component at the terminus of A;

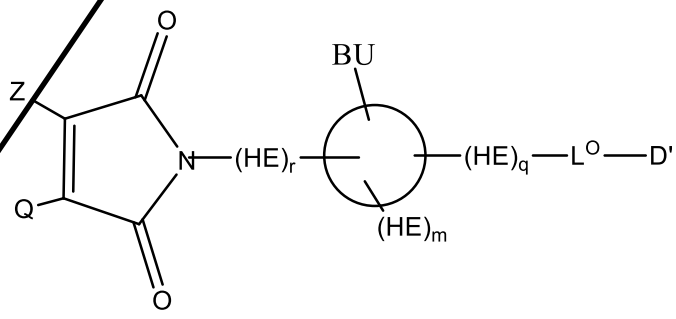
a' is 0 or 1; and

u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

14. A Functional Agent-Linker Conjugate having the formula:



or



or a salt thereof;

wherein

D' is a Drug unit, a Detection unit, or a Stability unit;

L^O is an optional secondary linker assembly;

Q and Z are hydrogen or halogen wherein at least one of Q and Z are halogen;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

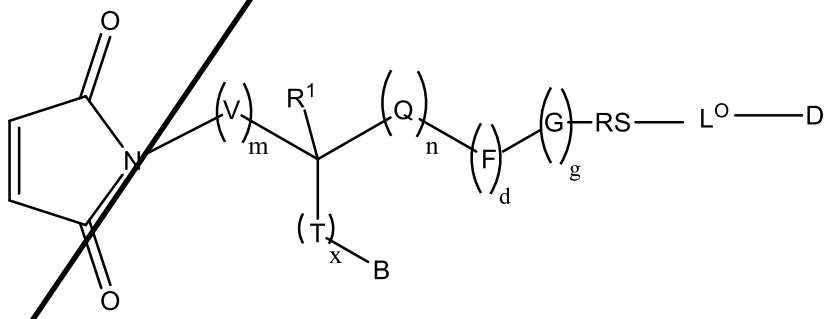
-A- is an optional Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

15. A Drug-Linker having the formula:



or a pharmaceutically acceptable salt thereof wherein

D is a Drug unit;

L^O is the optional secondary linker assembly;

V, Q, T, and G are independently selected from –(C(R^9)(R^{10}))-;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is $C(E^1)(E^2)$ wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly or Drug unit;

g is 0 to 5;

m is 0 to 5;

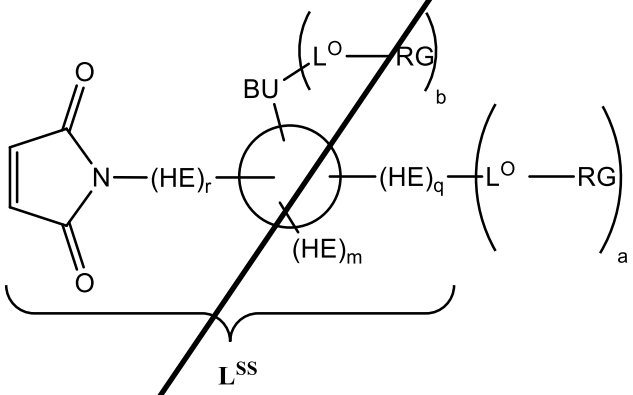
n is 0 to 5;

d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS is an electron withdrawing group.

16. A Linker having the formula:



or a salt thereof, wherein

RG is a reactive group comprising a reactive site at the terminus of L^O, suitable for attaching a Drug unit;

L^O is an optional secondary linker assembly that is present; and

L^{SS} is the self-stabilizing linker assembly, wherein

BU is a Basic unit;

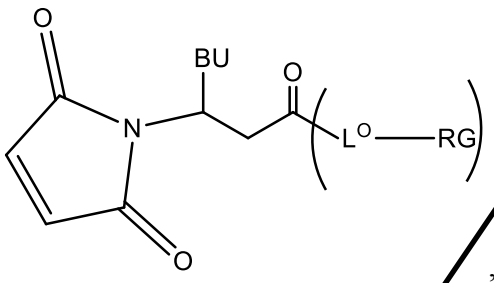
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or Drug unit;

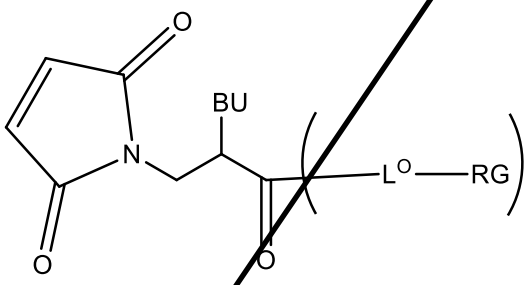
the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene; and

the subscript a and b are each 0 or 1, and the sum of a+b is 1.

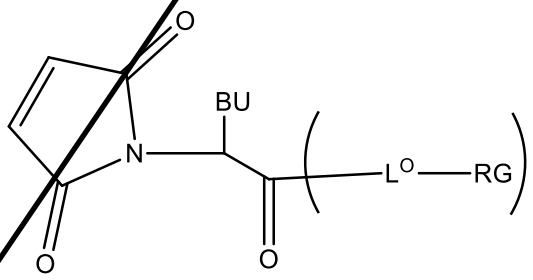
17. A Linker of claim 16, having the formula:



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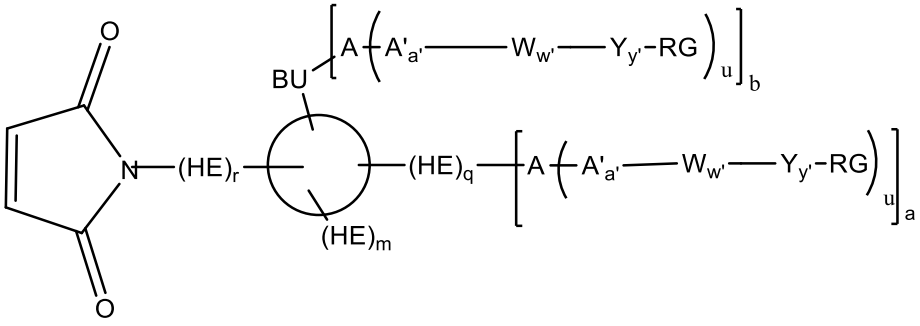
or



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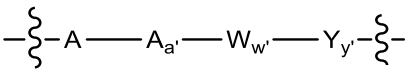
or a salt thereof.

18. A Linker having the formula:



or a salt thereof, wherein

RG is a reactive group comprising a reactive site at the terminus of

 which is suitable for attaching a Drug unit, a Detection unit, or a Stability unit;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or to a Drug unit, a Detection unit, or a Stability unit;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

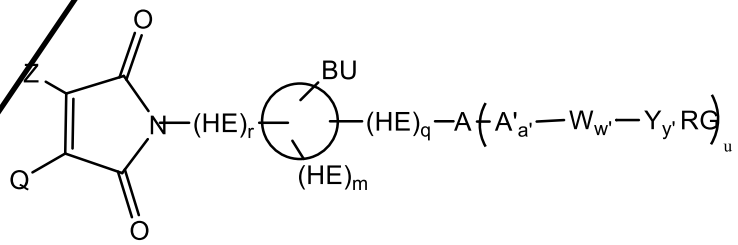
the subscript y' is 0 or 1,

-A- is a Stretcher unit,

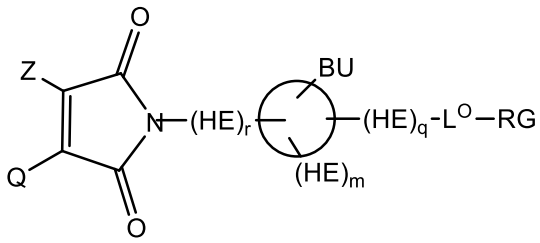
-A'- is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

19. A Linker represented by a formula selected from the group consisting of:

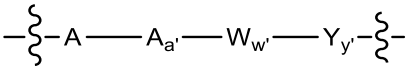


and



or a salt thereof; wherein

RG is a reactive group (comprising a reactive site) at the terminus of L^O or



which is suitable for attaching a Drug unit, Detection unit or Stability unit;

L^O is an optional secondary linker assembly that is present;

Q and Z are hydrogen or halogen wherein at least one of Q and Z are halogen;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or RG;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

W- is an optional Cleavable unit;

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1;

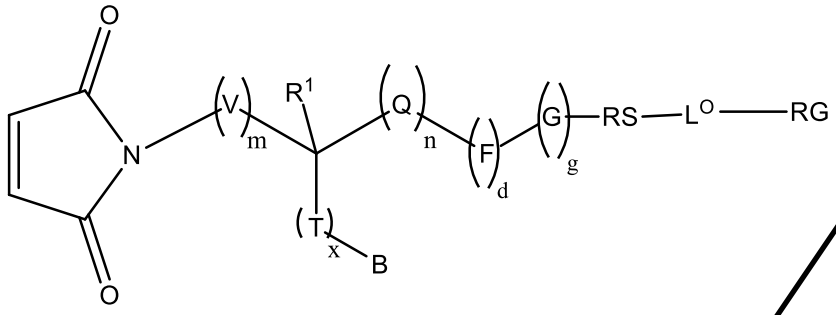
A is an optional Stretcher unit,

A' is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

20. A Linker having the formula



or a pharmaceutically acceptable salt thereof, wherein

L^O is the optional secondary linker assembly that is present;

RG is a reactive group comprising a reactive site at the terminus of L^O which is suitable for attaching a Drug unit;

M^1 is a succinimide ring or hydrolyzed succinimide or together with B forms a dilactam;

V, Q, T, and G are independently selected from $-(C(R^9)(R^{10}))-$;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is $C(E^1)(E^2)$ wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly;

g is 0 to 5;

m is 0 to 5;

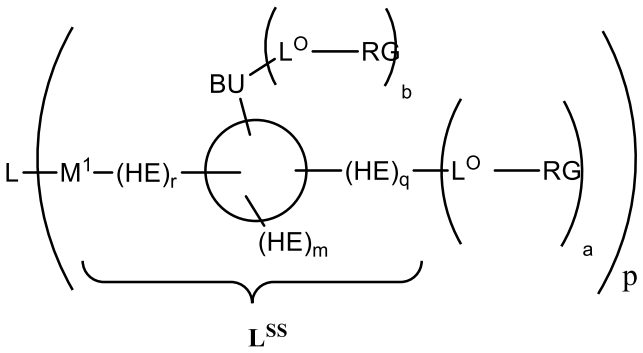
n is 0 to 5;

d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS is an electron withdrawing group.

21. A Ligand-Linker Conjugate having the formula:



or a salt thereof, wherein

L is a Ligand unit;

the subscript ranges from 1 to 32;

L^O is an optional secondary linker assembly that is present;

RG is a reactive group comprising a reactive site at the terminus of L^O which is suitable for attaching a Drug unit;

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide;

BU is a Basic unit;

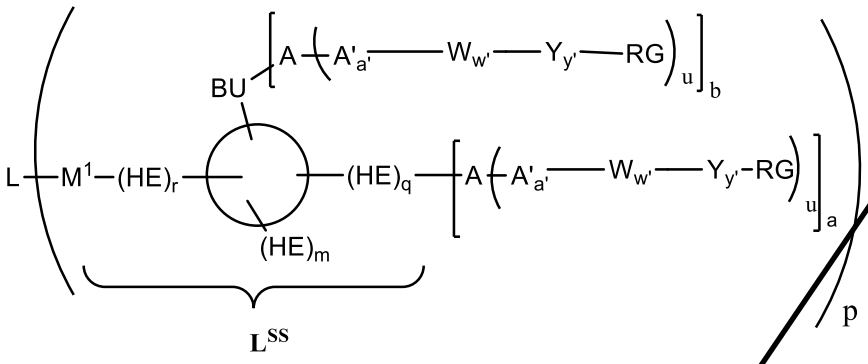
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or Drug unit;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene; and

the subscript a and b are each 0 or 1, and the sum of a+b is 1.

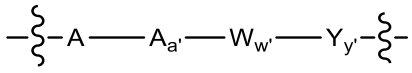
22. A Ligand-Linker Conjugate having the formula:



or a salt thereof, wherein

L is a Ligand unit;

RG is a reactive group comprising a reactive site at the terminus of



which is suitable for attaching a Drug unit, a Detection unit, or a Stability unit;

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with BU forms a dilactam;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

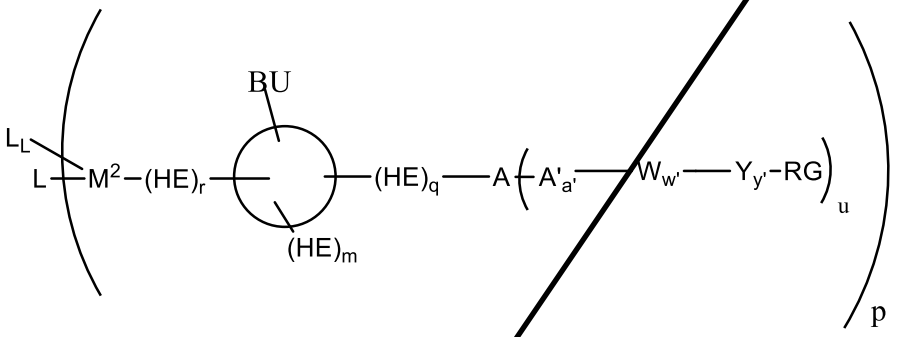
-A- is a Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

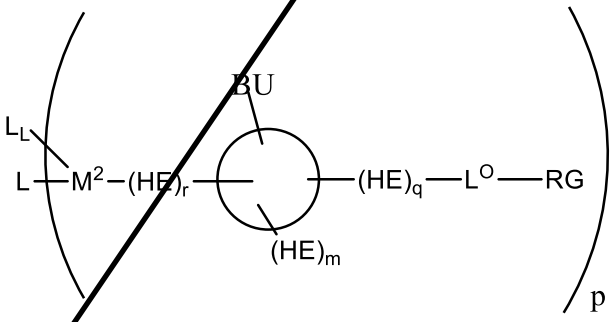
a' is 0 or 1; and

u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

23. Ligand-Linker Conjugate represented by a formula selected from the group consisting of:



and

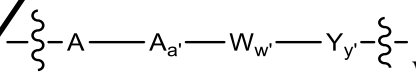


or a pharmaceutically acceptable salt thereof; wherein

L is a Ligand unit;

L_L is a Ligand unit that can be present or absent, wherein L and L_L can be the same or different Ligand units;

RG is a reactive group (comprising a reactive site) at the terminus of L^O or



which is suitable for attaching a Drug unit, Detection unit or Stability unit;

L^O is an optional secondary linker assembly that is present;

M^2 is a maleimide ring, a hydrolyzed maleimide, a succinimide ring, or a hydrolyzed succinimide conjugated to at least one of L or L_L via a thioether linkage; and

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or FA;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

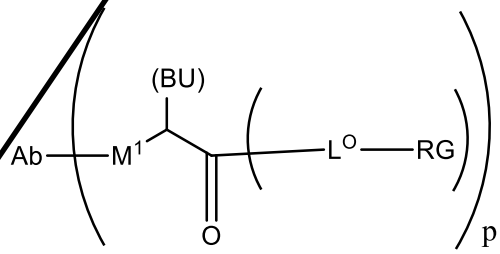
-A- is an optional Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

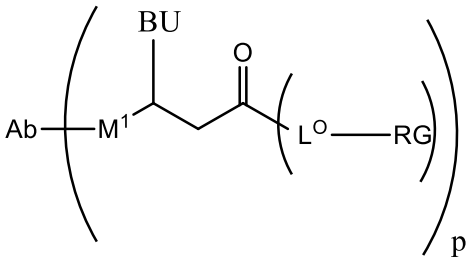
a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

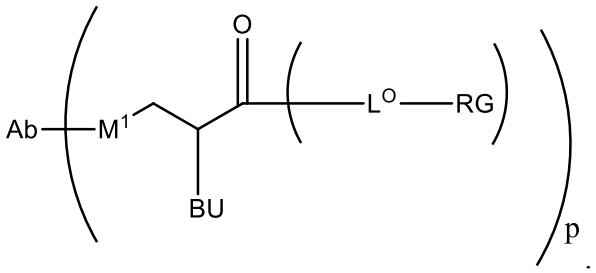
24. A Ligand-Linker Conjugate of claim 21,wherein L is an antibody (Ab) having the formula:



,

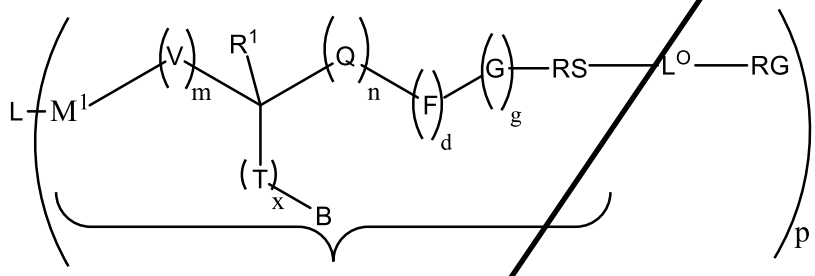


, or



or a salt thereof.

25. A Ligand-Linker Conjugate having the formula



L^{TT}

or a pharmaceutically acceptable salt thereof wherein L is a Ligand unit;

L^O is the optional secondary linker assembly that is present;

RG is a reactive site at the terminus of L^O which is suitable for attaching a Drug unit;

L^{TT} is the self-stabilizing linker assembly, wherein

M^1 is a non-hydrolyzed succinimide or hydrolyzed succinimide or together with B forms a dilactam;

V, Q, T, and G are independently selected from –(C(R^9)(R^{10}))-;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is C(E^1)(E^2) wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly;

g is 0 to 5;

m is 0 to 5;

n is 0 to 5;

d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS acts as an electron withdrawing group.

CLAIMS

1. A Ligand-Functional Agent Conjugate comprising:

a Ligand unit and at least one Functional Agent selected from the group consisting of a Drug unit, Detection Unit, and Stability unit, wherein

the Ligand unit and each of the Functional Agent(s) are joined by a self-stabilizing linker assembly comprising a succinimide ring or a hydrolyzed succinimide or a dilactam directly conjugated to the Ligand unit via a thioether linkage;

or wherein

the Ligand unit and each of the Functional Agent(s) are joined by a self-stabilizing linker assembly comprising a succinimide ring, a maleimide ring, a hydrolyzed succinimide ring or a hydrolyzed maleimide ring wherein the succinimide ring, maleimide ring, hydrolyzed succinimide ring or hydrolyzed maleimide ring is directly conjugated to the Ligand unit via one or two thioether linkages; and

a base and an electron withdrawing group operably linked to stabilize the conjugate in plasma relative to a Ligand-Functional Agent Conjugate lacking the self-stabilizing linker assembly,

in which there are between 2 and 6 intervening atoms between the base of the basic unit and the nitrogen atom of the succinimide (hydrolyzed or non-hydrolyzed) or dilactam and between 2 and 5 intervening atoms between the electron withdrawing group and the nitrogen atom of the succinimide ring (hydrolyzed or non-hydrolyzed) or dilactam.

2. A Ligand-Functional Agent Conjugate of claim **1**, comprising:

a Ligand unit and at least one Functional Agent selected from the group consisting of a Drug unit, a Detection Unit, and a Stability Unit, wherein

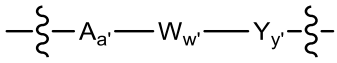
the Ligand unit and each of the Functional Agent(s) are joined by a self-stabilizing linker assembly comprising a succinimide ring or a hydrolyzed succinimide or a dilactam directly conjugated to the Ligand unit via a thioether linkage; and

a base and an electron withdrawing group operably linked to stabilize the conjugate in plasma relative to a Ligand-Functional Agent Conjugate lacking the self-stabilizing linker assembly,

in which there are between 2 and 6 intervening atoms between the base of the basic unit and the nitrogen atom of the succinimide (hydrolyzed or non-hydrolyzed) or dilactam and between 2 and 5 intervening atoms between the electron withdrawing group and the nitrogen atom of the succinimide ring (hydrolyzed or non-hydrolyzed) or dilactam.

3. A Ligand-Functional Agent Conjugate of claim **1** or claim **2**, wherein the Ligand-Functional Agent is a Ligand-Drug Conjugate comprising a Drug unit as the Functional Agent and the Ligand-Drug conjugate further comprises a linker assembly which joins each Drug to a self-stabilizing linker assembly.

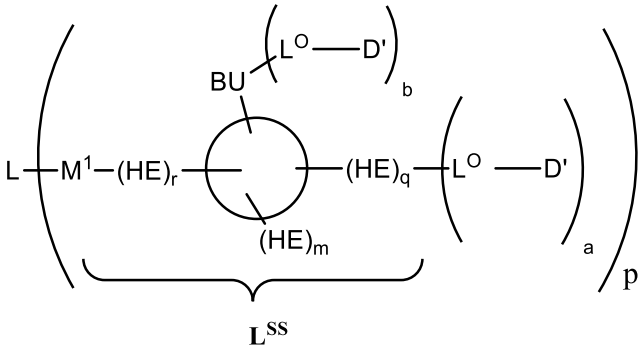
4. A Ligand-Functional Agent Conjugate of claim **3**, wherein the linker assembly has the formula:



wherein -A- is an optional Stretcher unit, the subscript a' is 0 or 1; -W- is an optional Cleavable unit, the subscript w' is 0 or 1; and -Y- is an optional Spacer unit, and the subscript y' is 0 or 1; and the wavy lines indicate the points of attachment to the self-stabilizing linker assembly and the Drug unit.

5. A Ligand-Functional Agent Conjugate of claim **4**, wherein the subscript w' is 1, and W is a dipeptide, tripeptide or tetrapeptide.

6. A Ligand-Functional Agent Conjugate of claim **1**, having the formula:



or a salt thereof, wherein

L is a Ligand unit;

D' is a Drug unit, a Detection unit, or a Stability unit;

L^O is an optional secondary linker assembly; and

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with BU forms a dilactam;

BU is a Basic unit;

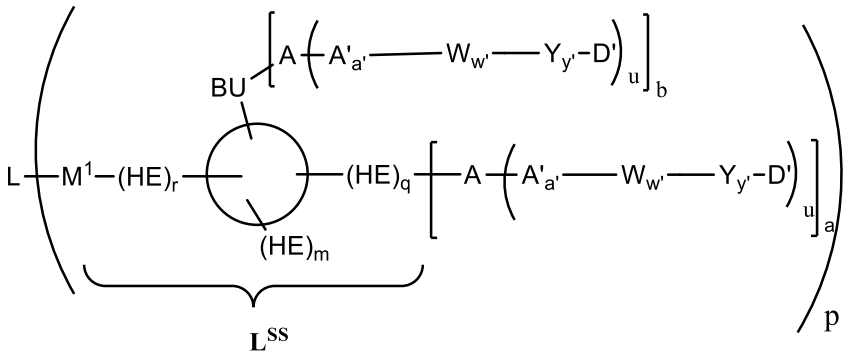
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1; and
the subscript p ranges from 1 to 20.

7. A Ligand-Functional Agent Conjugate of claim **1** or **2,** having the formula:



or a salt thereof, wherein

L is a Ligand unit;

D' is a Drug unit, a Detection unit, or a Stability unit;

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with BU forms a dilactam;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

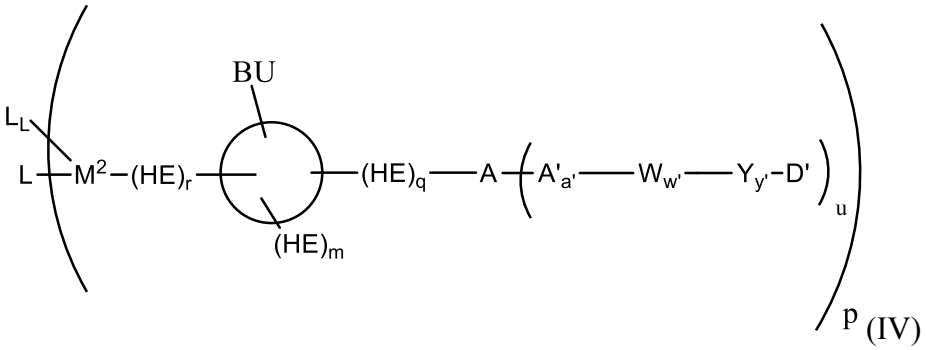
A is a Stretcher unit,

A' is an optional Stretcher unit component at the terminus of A;

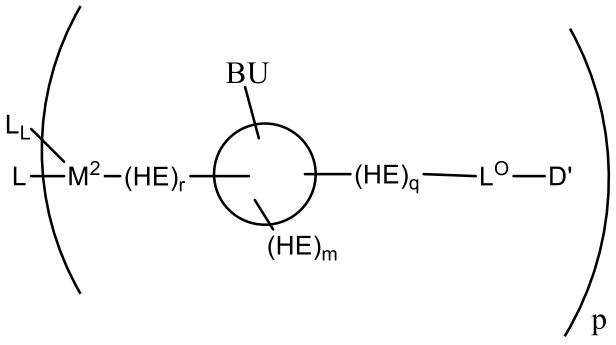
a' is 0 or 1; and

u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

8. A Ligand-Functional Agent Conjugate of claim **2**, represented by Formula IV or IVa:



(IV)



(IVa)

or a pharmaceutically acceptable salt thereof; wherein

L is a Ligand unit

L_L is a Ligand unit that can be present or absent, wherein L and L_L can be the same or different Ligand units;

D' is a Drug unit, a Detection unit, or a Stability unit;

L^O is an optional secondary linker assembly;

M^2 is a maleimide ring, a hydrolyzed maleimide, a succinimide ring, or a hydrolyzed succinimide conjugated to at least one of L or L_L via a thioether linkage; and

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

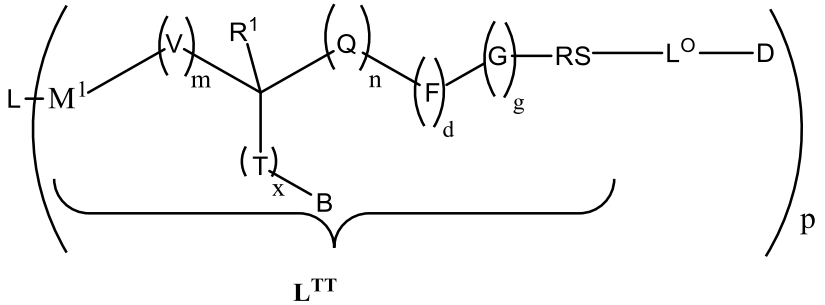
-A- is an optional Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

9. A Ligand-Functional Agent Conjugate of claim **1**, that is a Ligand-Drug Conjugate having the formula:



L^{TT}

or a pharmaceutically acceptable salt thereof wherein L is a Ligand unit;

D is a Drug unit;

L^O is the optional secondary linker assembly;

L^{TT} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with B forms a dilactam;

V, Q, T, and G are independently selected from –(C(R^9)(R^{10}))-;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is $C(E^1)(E^2)$ wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly or Drug unit;

g is 0 to 5;

m is 0 to 5;

n is 0 to 5;

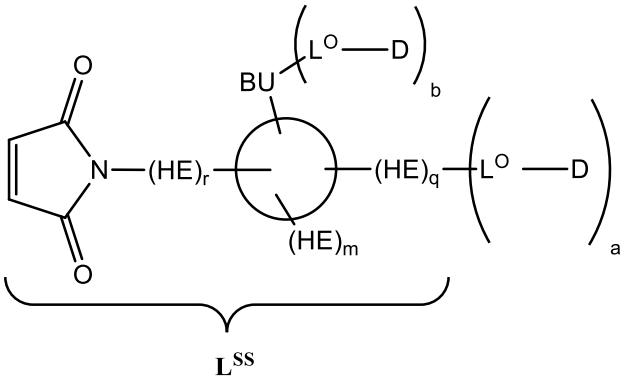
d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS is an electron withdrawing group.

10. A Ligand-Functional Agent Conjugate of claim 9, wherein m is 0, and n is 0.

11. A Drug-Linker Conjugate having the formula:



or a salt thereof, wherein,

D is a Drug unit;

L^O is a an optional secondary linker assembly; and

L^{SS} is the self-stabilizing linker assembly, wherein

BU is a Basic unit;

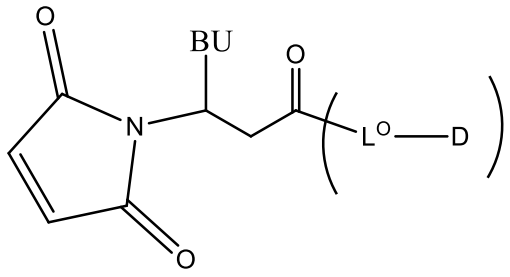
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or Drug unit;

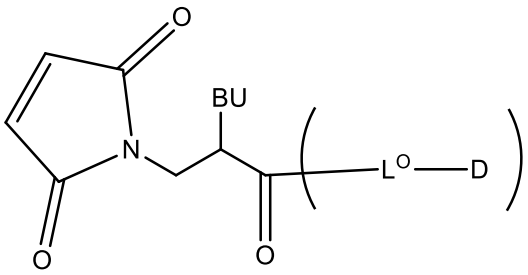
the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene; and

the subscript a and b are each 0 or 1, and the sum of a+b is 1.

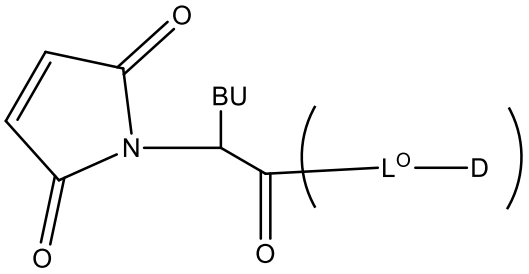
12. A Drug-Linker Conjugate of claim **11**, having the formula:



,

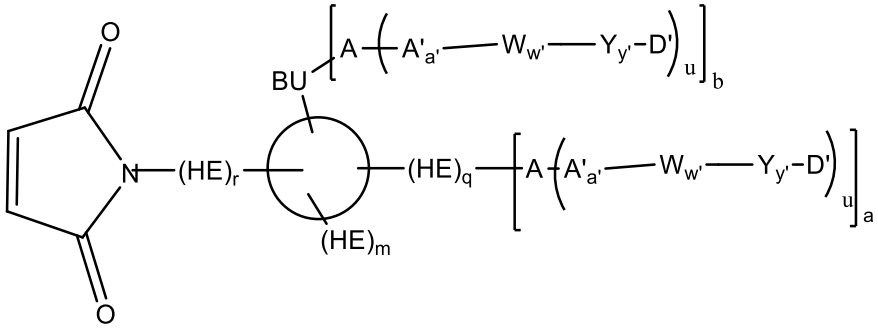


, or



or a salt thereof.

13. A Functional Agent-Linker Conjugate having the formula:



or a salt thereof, wherein

D' is a Drug unit, a Detection unit, or a Stability unit;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

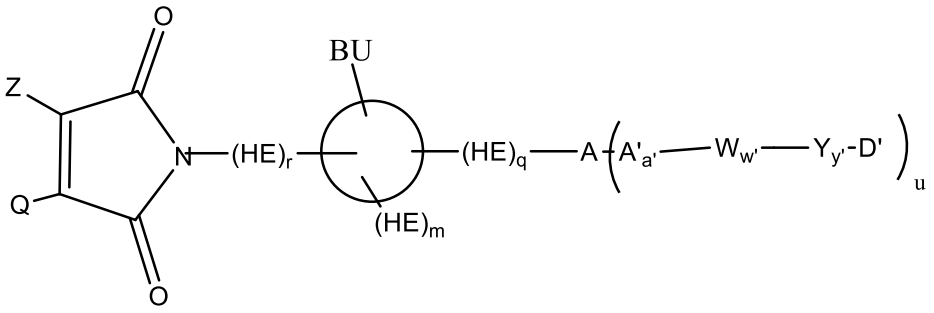
A is a Stretcher unit,

A' is an optional Stretcher unit component at the terminus of A;

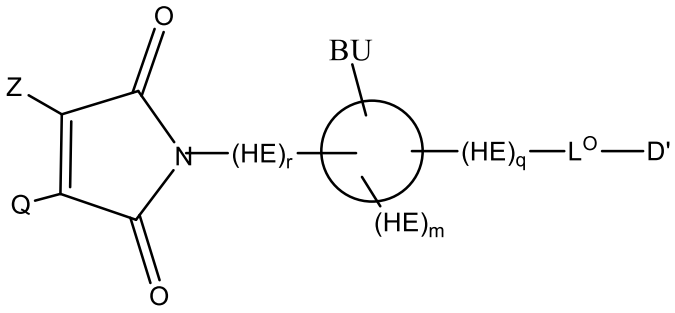
a' is 0 or 1; and

u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

14. A Functional Agent-Linker Conjugate having the formula:



or



or a salt thereof;

wherein

D' is a Drug unit, a Detection unit, or a Stability unit;

L^O is an optional secondary linker assembly;

Q and Z are hydrogen or halogen wherein at least one of Q and Z are halogen;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

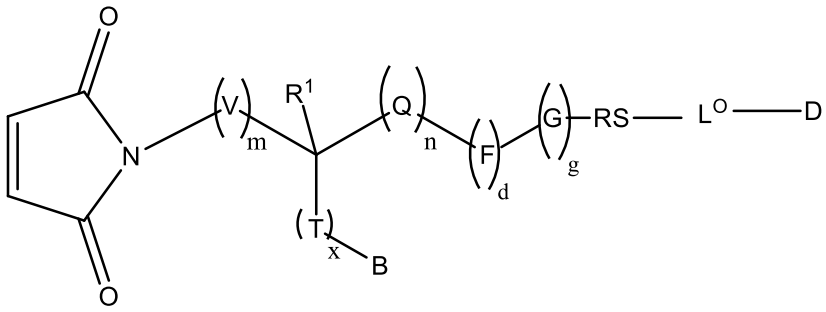
-A- is an optional Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

15. A Drug-Linker having the formula:



or a pharmaceutically acceptable salt thereof wherein

D is a Drug unit;

L^O is the optional secondary linker assembly;

V, Q, T, and G are independently selected from –(C(R^9)(R^{10}))-;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is C(E^1)(E^2) wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly or Drug unit;

g is 0 to 5;

m is 0 to 5;

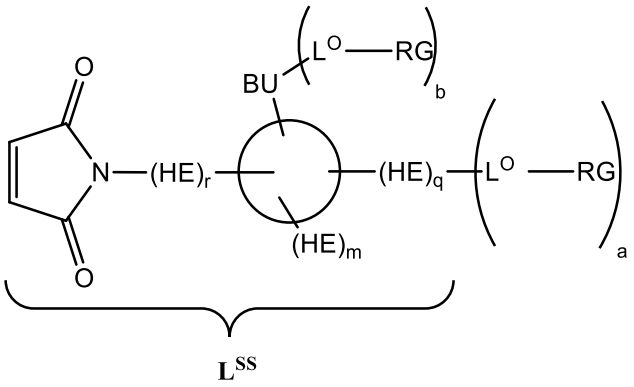
n is 0 to 5;

d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS is an electron withdrawing group.

16. A Linker having the formula:



or a salt thereof, wherein

RG is a reactive group comprising a reactive site at the terminus of L^O, suitable for attaching a Drug unit;

L^O is an optional secondary linker assembly that is present; and

L^{SS} is the self-stabilizing linker assembly, wherein

BU is a Basic unit;

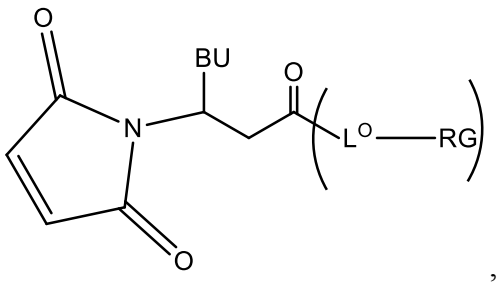
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or Drug unit;

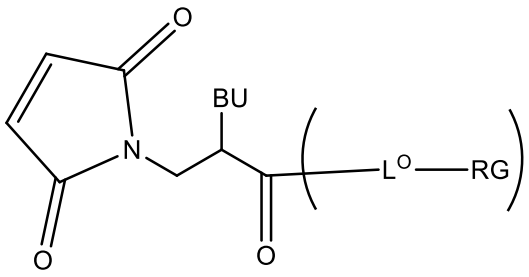
the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene; and

the subscript a and b are each 0 or 1, and the sum of a+b is 1.

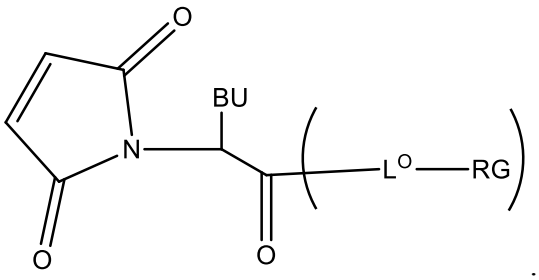
17. A Linker of claim 16, having the formula:



,



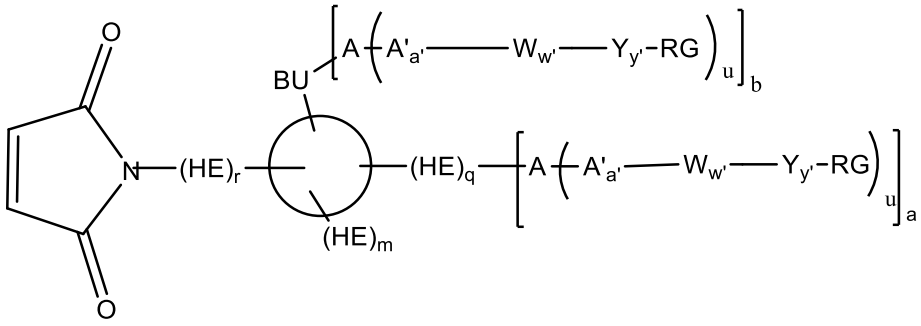
or



.

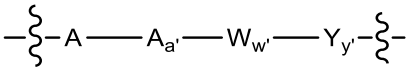
or a salt thereof.

18. A Linker having the formula:



or a salt thereof, wherein

RG is a reactive group comprising a reactive site at the terminus of

 which is suitable for attaching a Drug unit, a Detection unit, or a Stability unit;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or to a Drug unit, a Detection unit, or a Stability unit;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

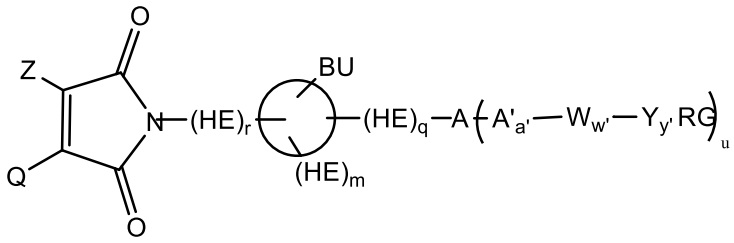
the subscript y' is 0 or 1,

-A- is a Stretcher unit,

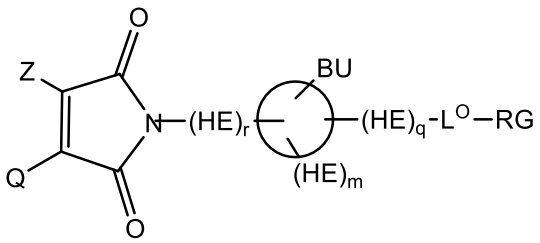
-A'- is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

19. A Linker represented by a formula selected from the group consisting of:

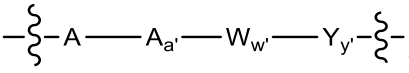


and



or a salt thereof; wherein

RG is a reactive group (comprising a reactive site) at the terminus of L^O or



which is suitable for attaching a Drug unit, Detection unit or Stability unit;

L^O is an optional secondary linker assembly that is present;

Q and Z are hydrogen or halogen wherein at least one of Q and Z are halogen;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or RG;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

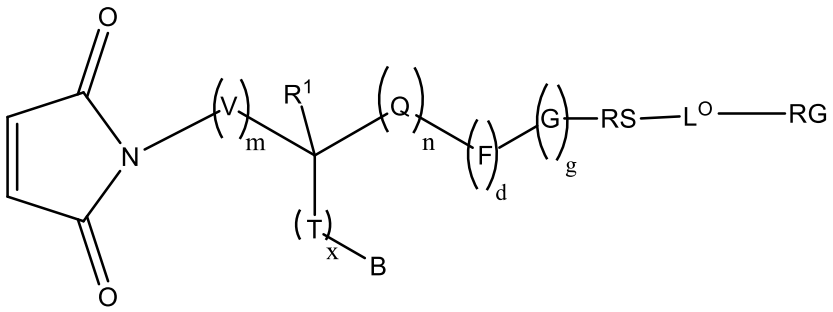
A is an optional Stretcher unit,

A' is an optional Stretcher unit component at the terminus of A;

a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

20. A Linker having the formula



or a pharmaceutically acceptable salt thereof, wherein

L^O is the optional secondary linker assembly that is present;

RG is a reactive group comprising a reactive site at the terminus of L^O which is suitable for attaching a Drug unit;

M^1 is a succinimide ring or hydrolyzed succinimide or together with B forms a dilactam;

V, Q, T, and G are independently selected from $-(C(R^9)(R^{10}))-$;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is $C(E^1)(E^2)$ wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly;

g is 0 to 5;

m is 0 to 5;

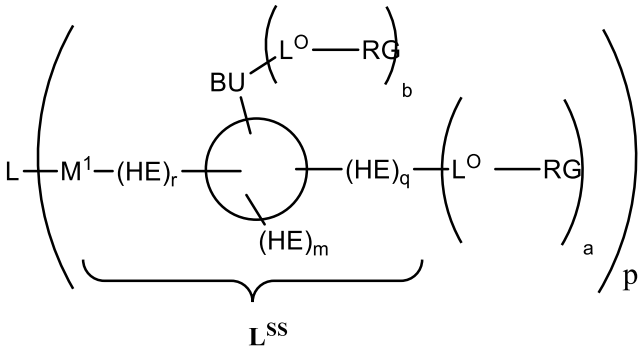
n is 0 to 5;

d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS is an electron withdrawing group.

21. A Ligand-Linker Conjugate having the formula:



or a salt thereof, wherein

L is a Ligand unit;

the subscript ranges from 1 to 32;

L^O is an optional secondary linker assembly that is present;

RG is a reactive group comprising a reactive site at the terminus of L^O which is suitable for attaching a Drug unit;

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide;

BU is a Basic unit;

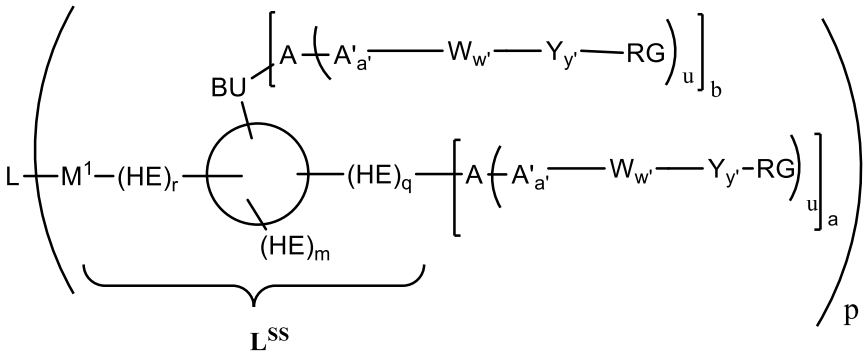
HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or Drug unit;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene; and

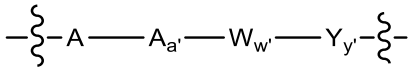
the subscript a and b are each 0 or 1, and the sum of a+b is 1.

22. A Ligand-Linker Conjugate having the formula:



or a salt thereof, wherein

L is a Ligand unit;

RG is a reactive group comprising a reactive site at the terminus of  which is suitable for attaching a Drug unit, a Detection unit, or a Stability unit;

L^{SS} is the self-stabilizing linker assembly, wherein

M^1 is a succinimide ring or hydrolyzed succinimide or together with BU forms a dilactam;

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that is C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to the optional secondary linker assembly or D';

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript a and b are each 0 or 1, and the sum of a+b is 1;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

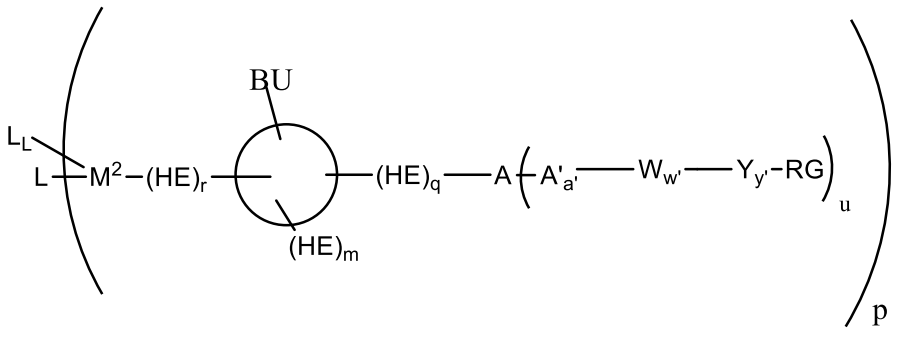
-A- is a Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

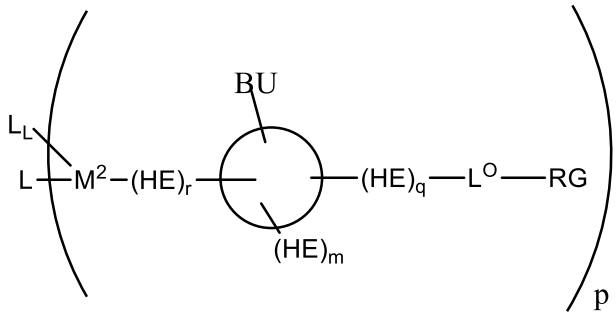
a' is 0 or 1; and

u is from 1 to 20, wherein when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

23. Ligand-Linker Conjugate represented by a formula selected from the group consisting of:



and

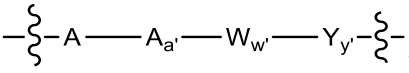


or a pharmaceutically acceptable salt thereof; wherein

L is a Ligand unit;

L_L is a Ligand unit that can be present or absent, wherein L and L_L can be the same or different Ligand units;

RG is a reactive group (comprising a reactive site) at the terminus of L^O or



which is suitable for attaching a Drug unit, Detection unit or Stability unit;

L^O is an optional secondary linker assembly that is present;

M^2 is a maleimide ring, a hydrolyzed maleimide, a succinimide ring, or a hydrolyzed succinimide conjugated to at least one of L or L_L via a thioether linkage; and

BU is a Basic unit;

HE is a hydrolysis enhancer comprising an electron withdrawing group;

the circle represents a scaffold that can be C_{1-8} alkylene, C_{1-8} heteroalkylene comprising 1 to 8 carbon atoms and 1 to 3 heteroatoms selected from the group consisting of O, N, Si and S, C_{6-10} arylene, or C_{4-10} heteroarylene, and optionally comprises a reactive site suitable for attachment to L^O, A, W, Y or FA;

the subscripts m, q and r are each 0 or 1, and the sum of m + q + r is 0, 1 or 2 provided that if m + q + r is 0, the scaffold is a C_{6-10} arylene or C_{4-10} heteroarylene;

the subscript p ranges from 1 to 20;

-W- is an optional Cleavable unit,

the subscript w' is 0 or 1;

-Y- is an optional Spacer unit,

the subscript y' is 0 or 1,

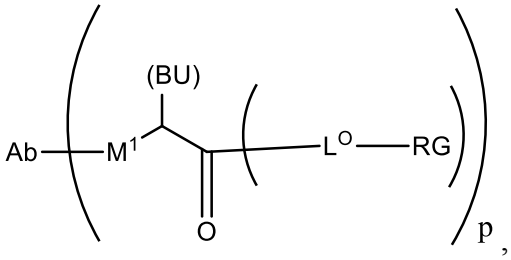
-A- is an optional Stretcher unit,

-A'- is an optional Stretcher unit component at the terminus of A;

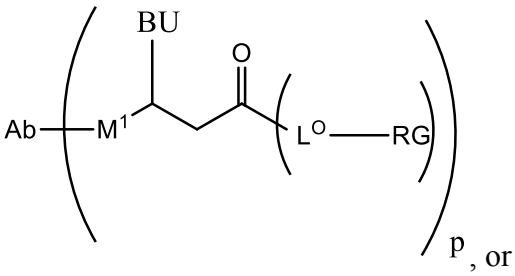
a' is 0 or 1; and

u is from 1 to 20, with the proviso that when u is from 2 to 20, A is present and when u is 1, A can be present or absent.

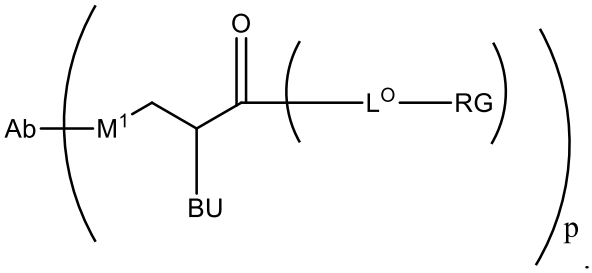
24. A Ligand-Linker Conjugate of claim 21,wherein L is an antibody (Ab) having the formula:



,



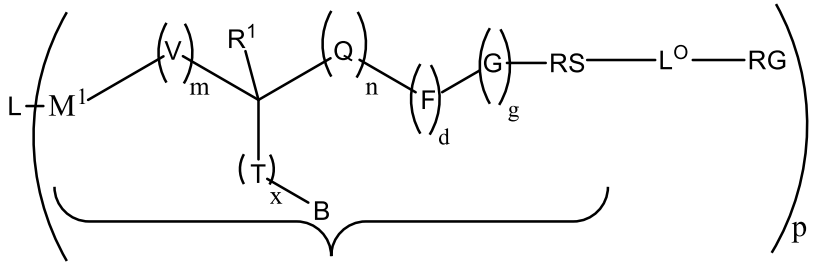
, or



.

or a salt thereof.

25. A Ligand-Linker Conjugate having the formula



L^{TT}

or a pharmaceutically acceptable salt thereof wherein L is a Ligand unit;

L^O is the optional secondary linker assembly that is present;

RG is a reactive site at the terminus of L^O which is suitable for attaching a Drug unit;

L^{TT} is the self-stabilizing linker assembly, wherein

M^1 is a non-hydrolyzed succinimide or hydrolyzed succinimide or together with B forms a dilactam;

V, Q, T, and G are independently selected from –(C(R^9)(R^{10}))-;

R^1 is H or C_{1-3} alkyl;

R^9 and R^{10} are, in each occurrence, independently selected from H or C_{1-3} alkyl;

F is C(E^1)(E^2) wherein E^1 and E^2 are independently selected from hydrogen, an electron withdrawing group, or E^1 and E^2 together are (=O);

RS is a reactive site for conjugation to a component of the optional secondary linker assembly;

g is 0 to 5;

m is 0 to 5;

n is 0 to 5;

d is 0 or 1;

x is 0 to 4, provided that when m is 0, x is 1 to 4;

and B is a base, provided that when d is zero or E^1 and E^2 are hydrogen, RS acts as an electron withdrawing group.