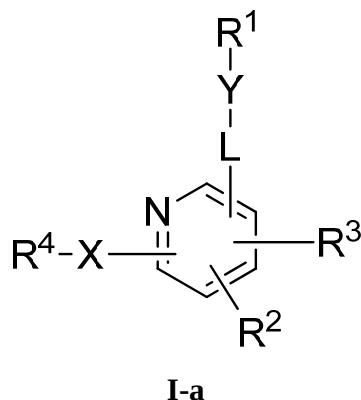


CLAIMS

1. A compound of formula **I-a**,



or a pharmaceutically acceptable salt thereof, wherein:

R² is -CN, or -NRC(O)R₁;

R³ is -H;

each R is independently hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or

two R groups on the same atom are taken together with the atom to which they are attached to form a C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

L is a divalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered

monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or L is a divalent group selected from C₁₋₆ aliphatic-C₃₋₁₀ aryl, C₁₋₆ aliphatic-3-8 membered saturated or partially unsaturated carbocyclic ring, C₁₋₆ aliphatic-3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a C₁₋₆ aliphatic-5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

Y is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or Y is absent;

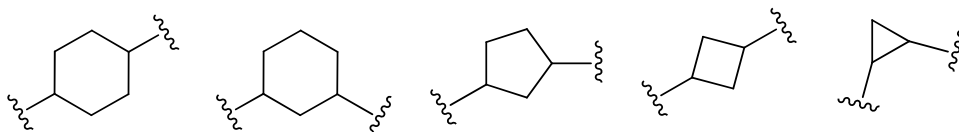
R¹ is C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

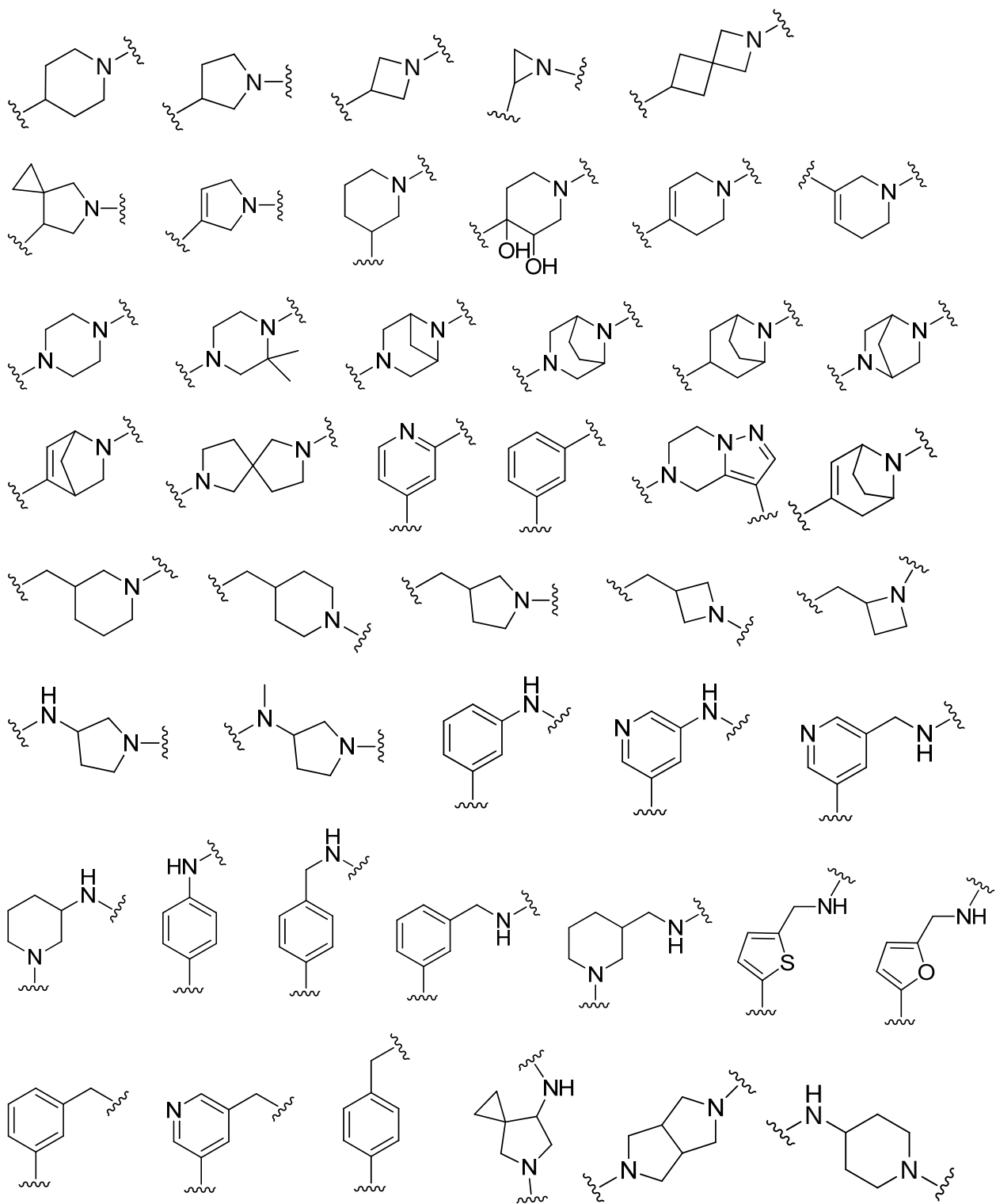
X is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or X is absent; and

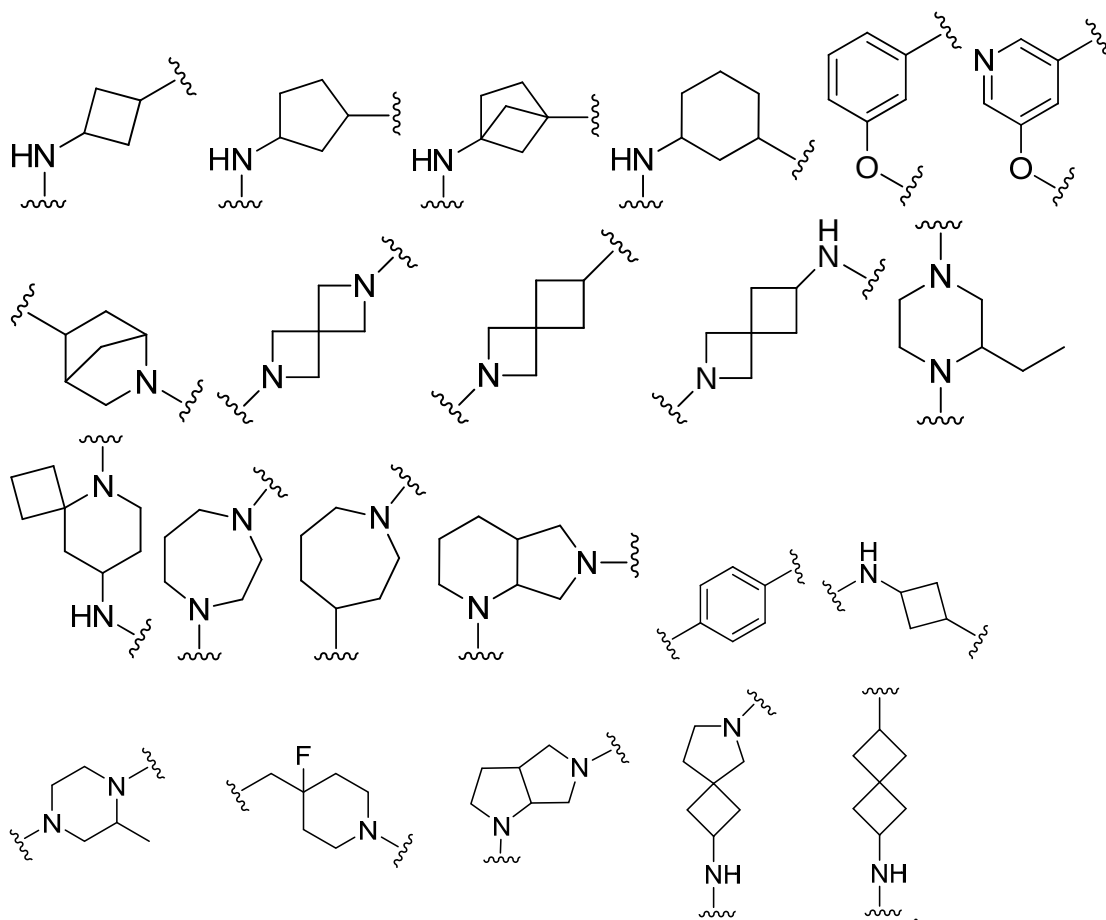
R⁴ is C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted.

2. The compound of claim 1, wherein R² is hydrogen, halogen, -OR, -SR, -CN, -NO₂, -SO₂R, -SOR, -C(O)R, -CO₂R, -C(O)N(R)₂, -NRC(O)R, -NRC(O)N(R)₂, -NRSO₂R, or -N(R)₂, and R³ is hydrogen, halogen, -OR, -SR, -CN, -NO₂, -SO₂R, -SOR, -C(O)R, -CO₂R, -C(O)N(R)₂, -NRC(O)R, -NRC(O)N(R)₂, -NRSO₂R, or -N(R)₂; wherein at least one of R² or R³ is -C(O)N(R)₂.

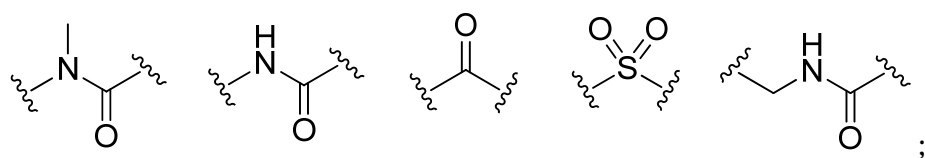
3. The compound of claim 1, wherein L is



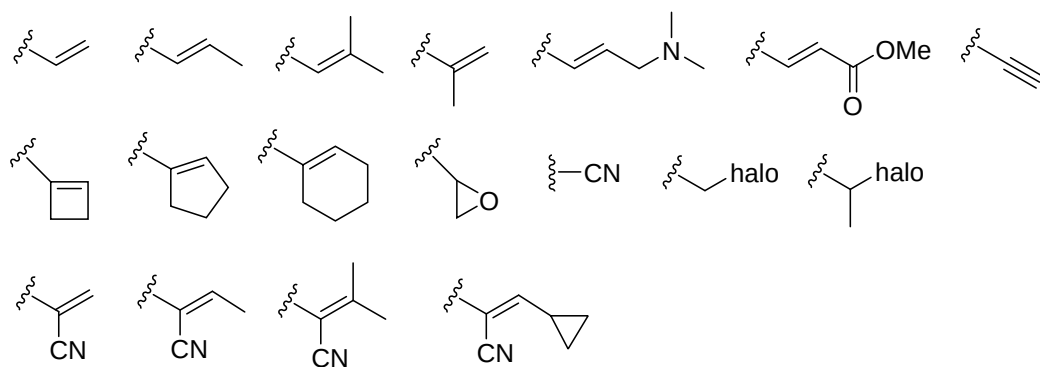




4. The compound of claim 1, wherein Y is

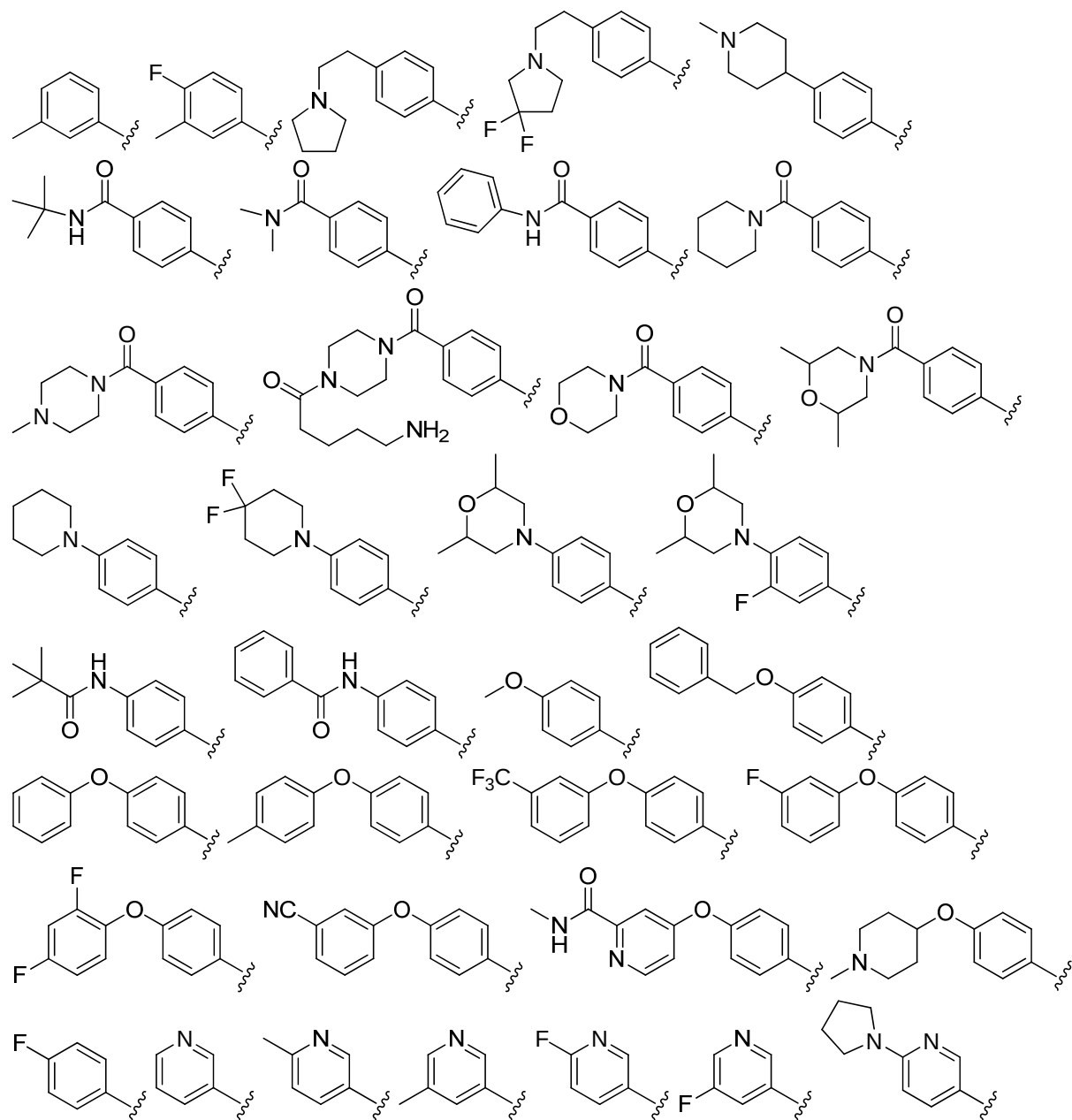


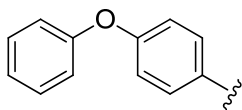
and R¹ is



5. The compound of claim 1, wherein X is O, C(O)NH, -NHC(O), NH, or N(Me); or X is absent.

6. The compound of claim 1, wherein R⁴ is



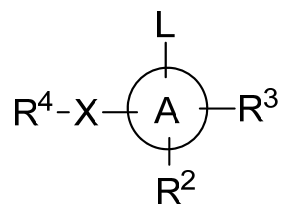


- R⁴ is 

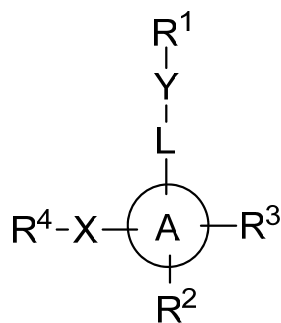
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15. A pharmaceutical composition comprising a compound of claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.
16. A method for inhibiting BTK, or a mutant thereof, activity in a patient or in a biological sample, comprising the step of administering to said patient or contacting said biological sample with a compound of claim 1 or a physiologically acceptable salt thereof.
17. A method for treating a BTK-mediated disorder in a patient in need thereof, comprising the step of administering to said patient a compound of claim 1.
18. A method for treating lupus in a subject, comprising the step of administering to said subject a compound of claim 1 or a physiologically acceptable salt thereof.
19. Use of a compound according to claim 1 or physiologically acceptable salts thereof, for the production of a medicament for the prophylactic or therapeutic treatment of a BTK-mediated disorder.
20. A process for manufacturing a compound of formula I according to claim 1, comprising the steps of:

reacting a compound of formula (II):

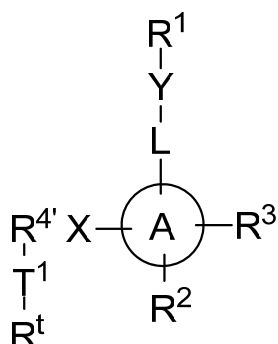


wherein X, X¹, and X², are as defined in claim 1;
with a compound to yield a compound of formula **I**:

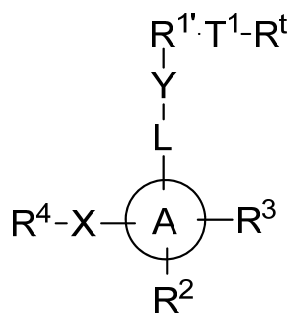


wherein X, R¹, R², R³, R⁴, L and Y are as defined in claim 1.

21. A compound of formula **I-t** or **I-s**



I-t



I-s;

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is pyridine;

R² is -CN, or -NRC(O)R;

R³ is -H;

each R is independently hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or

two R groups on the same atom are taken together with the atom to which they are attached to form a C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms

independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

L is a divalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or L is a divalent group selected from C₁₋₆ aliphatic-C₃₋₁₀ aryl, C₁₋₆ aliphatic-3-8 membered saturated or partially unsaturated carbocyclic ring, C₁₋₆ aliphatic-3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a C₁₋₆ aliphatic-5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

Y is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or Y is absent;

R¹ is C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

R^{1'} is a bivalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

X is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or X is absent;

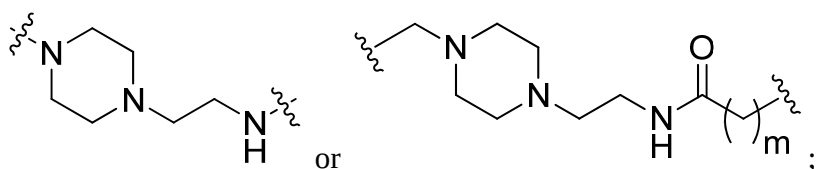
R⁴ is hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

R^{4'} is a bivalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

T¹ is a bivalent tethering moiety; and

R^t is a detectable moiety.

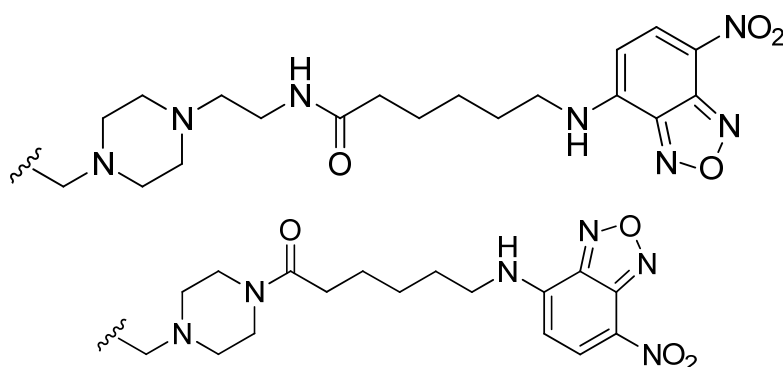
22. The compound of claim 21, wherein -T¹- is

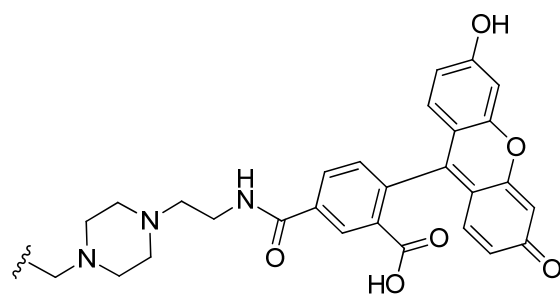
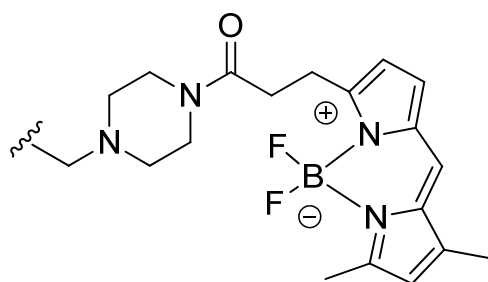
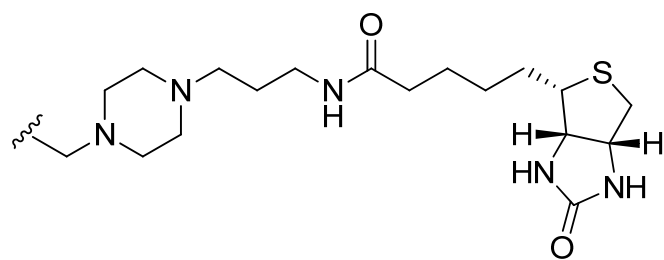
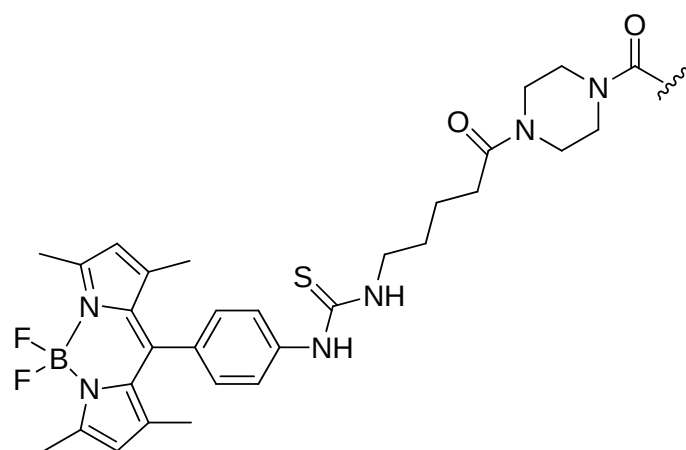
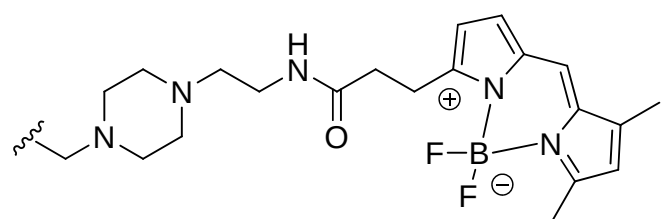


wherein m is 0, 1, 2, 3, 4, 5, 6, or 7.

23. The compound of claim 21, wherein -R^t is quinine, phenylalanine, tyrosine, trptophan, NADH, FMN, EDANS, Lucifer Yellow, pyrene, 4-MU, AMC, DAPI, Hoechst33342, NBD, bimane, Cascade yellow, fluorescein, RH110, TMR, SRh101, naphthofluorescein, SNARF-1, propidium, BODIPY-FL, BODIPY-TR, Cy3, Cy5, Cy7, IRDye 700DX, or resorufin.

24. The compound of claim 23, wherein -T¹-R^t is:







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