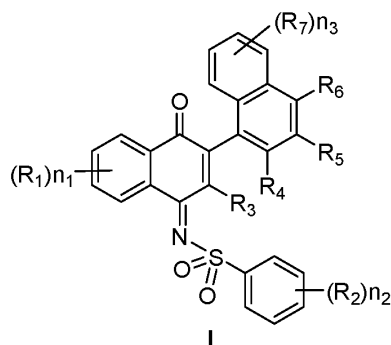


CLAIMS:

1. A compound of Formula I,



or a pharmaceutically acceptable salt thereof, wherein

each occurrence of R_1 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $C(=O)R_a$, $OC(=O)R_a$, $C(=O)OR_a$, NR_bR_c , $NR_bC(=O)R_c$, $C(=O)NR_bR_c$, $NR_bC(=O)OR_c$, $OC(=O)NR_bR_c$, $NR_aC(=O)NR_bR_c$, alkyl, alkenyl, cycloalkyl, optionally substituted aryl, or optionally substituted heterocycle;

n_1 is 0, 1, 2, 3, or 4;

each occurrence of R_2 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $C(=O)R_a$, $OC(=O)R_a$, $C(=O)OR_a$, NR_bR_c , $NR_bC(=O)R_c$, $C(=O)NR_bR_c$, $NR_bC(=O)OR_c$, $OC(=O)NR_bR_c$, $NR_aC(=O)NR_bR_c$, alkyl, alkenyl, cycloalkyl, cycloalkenyl, optionally substituted aryl, optionally substituted aryloxyl, or optionally substituted heterocycle;

n_2 is 0, 1, 2, 3, 4, or 5;

R_3 is hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $OC(=O)R_a$, alkyl, alkenyl, cycloalkyl, or optionally substituted aryl or heteroaryl;

R_4 is hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , NR_bR_c , $OC(=O)R_a$, alkyl, alkenyl, or cycloalkyl;

each occurrence of R_5 , R_6 , and R_7 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $C(=O)R_a$, $OC(=O)R_a$, $C(=O)OR_a$, NR_bR_c , $NR_bC(=O)R_c$, $C(=O)NR_bR_c$,

$\text{NR}_b\text{C}(=\text{O})\text{OR}_c$, $\text{OC}(=\text{O})\text{NR}_b\text{R}_c$, $\text{NR}_a\text{C}(=\text{O})\text{NR}_b\text{R}_c$, alkyl, alkenyl, cycloalkyl, optionally substituted aryl, or optionally substituted heterocycle;

n_3 is 0, 1, 2, 3, or 4; and

each occurrence of R_a , R_b , and R_c is independently hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, heterocycle, or aryl; or said R_b and R_c together with the nitrogen atom to which they are bonded optionally form a heterocycle comprising 1-4 heteroatoms.

2. The compound of claim 1, wherein each occurrence of R_1 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , or SR_a .

3. The compound of claim 1, wherein each occurrence of R_1 is independently $\text{C}(=\text{O})\text{R}_a$, $\text{OC}(=\text{O})\text{R}_a$, $\text{C}(=\text{O})\text{OR}_a$, NR_aR_b , $\text{NR}_b\text{C}(=\text{O})\text{R}_a$, $\text{C}(=\text{O})\text{NR}_b\text{R}_c$, $\text{NR}_b\text{C}(=\text{O})\text{OR}_a$, $\text{OC}(=\text{O})\text{NR}_b\text{R}_c$, or $\text{NR}_a\text{C}(=\text{O})\text{NR}_b\text{R}_c$.

4. The compound of claim 1, wherein each occurrence of R_1 is independently alkyl, alkenyl, cycloalkyl, optionally substituted aryl, or optionally substituted heterocycle.

5. The compound of claim 1, wherein R_1 is H.

6. The compound of any one of the preceding claims, wherein n_1 is 0, 1, or 2.

7. The compound of any one of the preceding claims, wherein n_1 is 1.

8. The compound of any one of claims 1-6, wherein n_1 is 0.

9. The compound of any one of the preceding claims, wherein each occurrence of R_2 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , or SR_a .

10. The compound of any one of claims 1-8, wherein each occurrence of R_2 is independently $\text{C}(=\text{O})\text{R}_a$, $\text{OC}(=\text{O})\text{R}_a$, $\text{C}(=\text{O})\text{OR}_a$, NR_aR_b , $\text{NR}_b\text{C}(=\text{O})\text{R}_a$, $\text{C}(=\text{O})\text{NR}_b\text{R}_c$, $\text{NR}_b\text{C}(=\text{O})\text{OR}_a$, $\text{OC}(=\text{O})\text{NR}_b\text{R}_c$, or $\text{NR}_a\text{C}(=\text{O})\text{NR}_b\text{R}_c$.

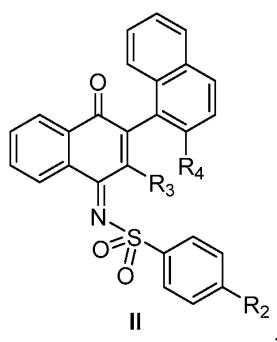
11. The compound of any one of claims 1-8, wherein each occurrence of R_2 is independently alkyl, alkenyl, cycloalkyl, optionally substituted aryl, or optionally substituted heterocycle.

12. The compound of any one of claims 1-9, wherein R_2 is H.

13. The compound of any one of the preceding claims, wherein n_2 is 0, 1, or 2.

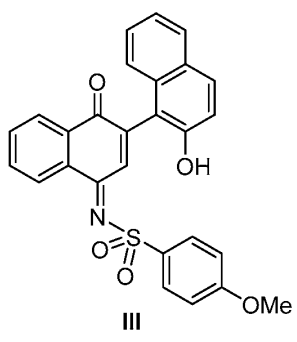
14. The compound of any one of the preceding claims, wherein n_2 is 1.
15. The compound of any one of claims 1-13, wherein n_2 is 0.
16. The compound of any one of the preceding claims, wherein R_3 is hydrogen, halogen, cyano, nitro, or CF_3 .
17. The compound of any one of claims 1-15, wherein R_3 is OCF_3 , OR_a , SR_a , or $OC(=O)R_a$.
18. The compound of any one of claims 1-15, wherein R_3 is alkyl, alkenyl, or cycloalkyl.
19. The compound of any one of claims 1-16, wherein R_3 is H.
20. The compound of any one of the preceding claims, wherein R_4 is hydrogen, halogen, cyano, nitro, or OR_a .
21. The compound of any one of claims 1-19, wherein R_4 is OCF_3 , SR_a , or $OC(=O)R_a$.
22. The compound of any one of claims 1-19, wherein R_4 is alkyl, alkenyl, or cycloalkyl.
23. The compound of any one of claims 1-20, wherein R_4 is OH.
24. The compound of any one of claims 1-20, wherein R_4 is OMe.
25. The compound of any one of the preceding claims, wherein R_5 , R_6 , and R_7 are each independently selected from the group consisting of hydrogen, halogen, cyano, nitro, and CF_3 .
26. The compound of any one of claims 1-24, wherein R_5 , R_6 , and R_7 are each independently selected from the group consisting of OCF_3 , OR_a , and SR_a .
27. The compound of any one of claims 1-24, wherein R_5 , R_6 , and R_7 are each independently selected from the group consisting of OCF_3 and OR_a .
28. The compound of any one of claims 1-24, wherein R_5 , R_6 , and R_7 are each independently selected from the group consisting of $C(=O)R_a$, $OC(=O)R_a$, $C(=O)OR_a$, NR_aR_b , $NR_bC(=O)R_a$, $C(=O)NR_bR_c$, $NR_bC(=O)OR_a$, $OC(=O)NR_bR_c$, and $NR_aC(=O)NR_bR_c$.

29. The compound of any one of claims 1-24, wherein R_5 , R_6 , and R_7 are each independently selected from the group consisting of alkyl, alkenyl, cycloalkyl, optionally substituted aryl, and optionally substituted heterocycle.
30. The compound of any one of claims 1-25, wherein each occurrence of R_5 , R_6 , and R_7 is H.
31. The compound of any one of the preceding claims, wherein n_3 is 0, 1, or 2.
32. The compound of any one of the preceding claims, wherein n_3 is 1.
33. The compound of any one of claims 1-30, wherein n_3 is 0.
34. The compound of any one of the preceding claims, wherein each occurrence of R_a is independently hydrogen, alkyl, heterocycle, or aryl.
35. The compound of claim 33, wherein each occurrence of R_a is independently hydrogen or alkyl.
36. The compound of any one of the preceding claims, wherein each occurrence of R_b and R_c is independently hydrogen, alkyl, heterocycle, or aryl.
37. The compound of claim 35, wherein each occurrence of R_b and R_c is independently hydrogen or alkyl.
38. The compound of any one of claims 1-34, wherein R_b and R_c together with the nitrogen atom to which they are bonded optionally form a heterocycle comprising 1-4 heteroatoms each selected from the group consisting of N, O, and S.
39. The compound of claim 1 having the structure of Formula II:



or a pharmaceutically acceptable salt thereof.

40. The compound of claim 39, wherein R_2 is H, OH, alkyl, alkoxy, halogen, NR_bR_c , CF_3 , OCF_3 , or CN.
41. The compound of claim 40, wherein R_2 is NH_2 , OH, OMe, OEt, $OCH_2CH_2CH_3$, or $OCH(CH_3)_2$.
42. The compound of claim 39, wherein R_2 is selected from the group consisting of hydrogen, methyl, ethyl, propyl, tert-butyl, F, Cl, Br, CF_3 , nitro, methoxy, ethoxy, OCF_3 , $-C(=O)Me$, $-C(=O)OMe$, $-NHC(=O)Me$, 1,4-dioxanyl, cyclohexanyl, cyclohexenyl, phenoxy, 2-methoxyphenoxy, 3-methoxyphenoxy, 4-methoxyphenoxy, 2-chlorophenoxy, 3-chlorophenoxy, 4-chlorophenoxy, 2-methylphenoxy, 3-methylphenoxy, and 4-methylphenoxy.
43. The compound of claim 42, wherein R_2 is OMe.
44. The compound of any one of claims 39-43, wherein R_3 is H, OH, alkyl, alkoxy, or halogen.
45. The compound of any one of claims 39-43, wherein R_3 is H.
46. The compound of any one of claims 39-45, wherein R_4 is H, alkyl, OH, NH_2 , alkoxy, halogen, CF_3 , or CN.
47. The compound of any one of claims 39-45, wherein R_4 is H, OH, or alkoxy.
48. The compound of any one of claims 39-45, wherein R_4 is OH.
49. The compound of any one of claims 39-45, wherein R_4 is OMe.
50. The compound of claim 39 having the structure of Formula III,



or a pharmaceutically acceptable salt thereof.

51. The compound of claim 1, selected from the group consisting of the compounds in Table 1a, or a pharmaceutically acceptable salt thereof.
52. The compound of claim 1, selected from the group consisting of the compounds in Table 1b, or a pharmaceutically acceptable salt thereof.
53. A pharmaceutical composition comprising at least one compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.
54. A method of inhibiting STAT3 in a cell, comprising delivering to the cell an effective amount of at least one compound according to any one of claims 1-52 or a pharmaceutically acceptable salt thereof.
55. The method of claim 54, wherein the cell is *in vivo* in a mammal.
56. The method of claim 55, wherein the mammal is a human, a dog, a cat, a horse, a cow, a pig, a sheep, or a goat.
57. The method of claim 56, wherein the cell is a cancer cell.
58. The method of claim 57 further comprising inducing apoptosis in the cancer cell.
59. The method of claim 57 further comprising inhibiting angiogenesis in a tumor, enhancing anti-tumor immune-mediated cytotoxicity, decreasing tumor growth, improving the mammal's survival, inhibiting STAT3 phosphorylation, and/or inhibiting nuclear-to-cytoplasmic translocation of STAT3.
60. The method of claim 56, wherein the human is suffering from, or known, suspected, or at risk for developing a neurodegenerative disease, anaphylaxis, muscle wasting, muscle weakness, cachexia, asthma, ulcerative colitis, non-alcoholic fatty liver disease, fibrosis, steatohepatitis, chagasic cardiomyopathy, scleroderma, a hyperproliferative disease, a viral infection, myelodysplastic syndrome, asthma, psoriasis, inflammatory bowel disease, uveitis, scleritis, multiple sclerosis, graft-versus-host diseases, pancreatitis, pulmonary lymphangiomyomatosis, age-related macular degeneration, amyloidosis, astrogliosis in Alzheimer's or other neurodegenerative disease, or a combination thereof.

61. The method of claim 60, wherein the hyperproliferative disease is selected from the group consisting of head and neck cancer, lung cancer, liver cancer, breast cancer, skin cancer, kidney cancer, testes cancer, colon cancer, rectal cancer, gastric cancer, metastatic melanoma, prostate cancer, ovarian cancer, cervical cancer, bone cancer, spleen cancer, gall bladder cancer, brain cancer, pancreatic cancer, stomach cancer, anal cancer, prostate cancer, multiple myeloma, post-transplant lymphoproliferative disease, restenosis, myelodysplastic syndrome, and leukemia.

62. The method of claim 61, wherein the leukemia is acute myelogenous leukemia.

63. The method of claim 60, wherein the fibrosis is selected from the group consisting of pulmonary fibrosis, bone marrow fibrosis, intestine fibrosis, pancreatic fibrosis, joint fibrosis, liver fibrosis, retroperitoneum, myelofibrosis, and dermal fibrosis.

64. The method of claim 60, wherein the viral infection is a chronic viral infection.

65. The method of claim 64, wherein the chronic viral infection is AIDS, HIV infection, Hepatitis B virus infection, Hepatitis C virus infection, or Epstein-Barr virus infection.

66. The method of claim 60, wherein the disorder is asthma, psoriasis, inflammatory bowel disease, uveitis, scleritis, multiple sclerosis, graft-versus-host diseases, pancreatitis, pulmonary lymphangioleiomyomatosis, age-related macular degeneration, or amyloidosis.

67. The method of claim 60, wherein the anaphylaxis comprises anaphylactic shock.

68. The method of claim 60, wherein the disorder is selected from the group consisting of muscle wasting, muscle weakness, cachexia, and a combination thereof; and the human has or is at risk of having muscle wasting, cachexia, renal failure, cancer, AIDS, HIV infection, chronic obstructive lung disease (including emphysema), multiple sclerosis, congestive heart failure, tuberculosis, familial amyloid polyneuropathy, acrodynia, hormonal deficiency, metabolic acidosis, infectious disease, chronic pancreatitis, autoimmune disorder, celiac disease, Crohn's disease, electrolyte imbalance, Addison's disease, sepsis, burns,

trauma, fever, long bone fracture, hyperthyroidism, prolonged steroid therapy, surgery, bone marrow transplant, atypical pneumonia, brucellosis, endocarditis, Hepatitis B, lung abscess, mastocytosis, paraneoplastic syndrome, polyarteritis nodosa, sarcoidosis, systemic lupus erythematosus, visceral leishmaniasis, prolonged bed rest, or drug addiction.

69. The method of claim 68, wherein the chronic obstructive lung disease is emphysema.

70. The method of claim 60, wherein the neurodegenerative disease is chemotherapy-induced peripheral neuropathy, diabetic neuropathy or chemobrain.

71. A method of treating or preventing a disorder in a mammalian species in need thereof, comprising administering to the mammalian species a therapeutically effective amount of at least one compound according to any one of claims 1-52 or a pharmaceutically acceptable salt thereof, wherein the disorder is selected from the group consisting of a neurodegenerative disease, anaphylaxis, muscle wasting, muscle weakness, cachexia, asthma, ulcerative colitis, non-alcoholic fatty liver disease, fibrosis, steatohepatitis, chagasic cardiomyopathy, scleroderma, a hyperproliferative disease, a viral infection, myelodysplastic syndrome, asthma, psoriasis, inflammatory bowel disease, uveitis, scleritis, multiple sclerosis, graft-versus-host diseases, pancreatitis, pulmonary lymphangiomyomatosis, age-related macular degeneration, amyloidosis, astrogliosis in Alzheimer's or other neurodegenerative disease, and a combination thereof.

72. The method of claim 71, wherein the mammalian species is a human, a dog, a cat, a horse, a cow, a pig, a sheep, or a goat.

73. The method of claim 72, wherein the mammalian species is a human.

74. The method of claim 72, wherein the human is suffering from, at risk of having, or susceptible to have the disorder.

75. The method of claim 71, wherein the hyperproliferative disease is selected from the group consisting of head and neck cancer, lung cancer, liver cancer, breast cancer, skin cancer, kidney cancer, testicular cancer, colon cancer, rectal cancer, gastric cancer, metastatic melanoma, prostate cancer, ovarian cancer, cervical cancer, bone cancer, spleen cancer, gall bladder cancer, brain cancer, pancreatic cancer, stomach cancer, anal cancer,

prostate cancer, multiple myeloma, post-transplant lymphoproliferative disease, restenosis, myelodysplastic syndrome, and leukemia.

76. The method of claim 75, wherein the leukemia is acute myelogenous leukemia.

77. The method of claim 71, wherein the fibrosis is selected from the group consisting of pulmonary fibrosis, bone marrow fibrosis, intestine fibrosis, pancreatic fibrosis, joint fibrosis, liver fibrosis, retroperitoneum, myelofibrosis, and dermal fibrosis.

78. The method of claim 71, wherein the viral infection is a chronic viral infection.

79. The method of claim 78, wherein the chronic viral infection is AIDS, HIV infection, Hepatitis B virus infection, Hepatitis C virus infection, or Epstein-Barr virus infection.

80. The method of claim 71, wherein the disorder is asthma, psoriasis, inflammatory bowel disease, uveitis, scleritis, multiple sclerosis, graft-versus-host diseases, pancreatitis, pulmonary lymphangioleiomyomatosis, age-related macular degeneration, or amyloidosis.

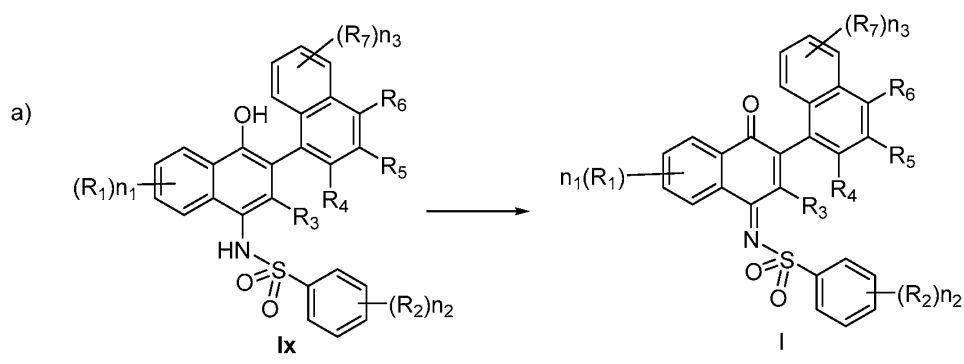
81. The method of claim 71, wherein the anaphylaxis comprises anaphylactic shock.

82. The method of claim 71, wherein the disorder is selected from the group consisting of muscle wasting, muscle weakness, cachexia, and a combination thereof; and the human has or is at risk of having muscle wasting, cachexia, renal failure, cancer, AIDS, HIV infection, chronic obstructive lung disease (including emphysema), multiple sclerosis, congestive heart failure, tuberculosis, familial amyloid polyneuropathy, acrodynia, hormonal deficiency, metabolic acidosis, infectious disease, chronic pancreatitis, autoimmune disorder, celiac disease, Crohn's disease, electrolyte imbalance, Addison's disease, sepsis, burns, trauma, fever, long bone fracture, hyperthyroidism, prolonged steroid therapy, surgery, bone marrow transplant, atypical pneumonia, brucellosis, endocarditis, Hepatitis B, lung abscess, mastocytosis, paraneoplastic syndrome, polyarteritis nodosa, sarcoidosis, systemic lupus erythematosus, visceral leishmaniasis, prolonged bed rest, or drug addiction.

83. The method of claim 82, wherein the chronic obstructive lung disease is emphysema.

84. The method of claim 71, wherein the neurodegenerative disease is chemotherapy-induced peripheral neuropathy, diabetic neuropathy, or chemobrain.

85. A method of making a compound of Formula I, comprising the step of oxidizing a compound of Formula IX to form the compound of Formula I using an oxidation reagent in step a):



wherein each occurrence of R_1 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $C(=O)R_a$, $OC(=O)R_a$, $C(=O)OR_a$, NR_bR_c , $NR_bC(=O)R_c$, $C(=O)NR_bR_c$, $NR_bC(=O)OR_c$, $OC(=O)NR_bR_c$, $NR_aC(=O)NR_bR_c$, alkyl, alkenyl, cycloalkyl, optionally substituted aryl, or optionally substituted heterocycle;

n_1 is 0, 1, 2, 3, or 4;

each occurrence of R_2 is independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $C(=O)R_a$, $OC(=O)R_a$, $C(=O)OR_a$, NR_bR_c , $NR_bC(=O)R_c$, $C(=O)NR_bR_c$, $NR_bC(=O)OR_c$, $OC(=O)NR_bR_c$, $NR_aC(=O)NR_bR_c$, alkyl, alkenyl, cycloalkyl, cycloalkenyl, optionally substituted aryl, optionally substituted aryloxy, or optionally substituted heterocycle;

n_2 is 0, 1, 2, 3, 4, or 5;

R_3 is hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , $OC(=O)R_a$, alkyl, alkenyl, cycloalkyl, or optionally substituted aryl, or heteroaryl;

R_4 is hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , OR_a , SR_a , NR_bR_c , $OC(=O)R_a$, alkyl, alkenyl, or cycloalkyl;

each occurrence of R₅, R₆, and R₇ is independently hydrogen, halogen, cyano, nitro, CF₃, OCF₃, OR_a, SR_a, C(=O)R_a, OC(=O)R_a, C(=O)OR_a, NR_bR_c, NR_bC(=O)R_c, C(=O)NR_bR_c, NR_bC(=O)OR_c, OC(=O)NR_bR_c, NR_aC(=O)NR_bR_c, alkyl, alkenyl, cycloalkyl, optionally substituted aryl, or optionally substituted heterocycle;

n₃ is 0, 1, 2, 3, or 4; and

each occurrence of R_a, R_b, and R_c is independently hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, heterocycle, or aryl; or said R_b and R_c together with the nitrogen atom to which they are bonded optionally form a heterocycle comprising 1-4 heteroatoms.

86. The method of claim 85, wherein the oxidation reagent is selected from the group consisting of NaIO₄, H₂O₂, MCPBA, and a combination thereof.

87. The method of claim 86, wherein the oxidation reagent is NaIO₄.

88. The method of claim 87, wherein NaIO₄ is prepared *in situ*.

89. The method of claim 85, wherein the oxidation reagent is used in the amount of 1.5-4.0 equivalence to the compound of Formula Ix.

90. The method of claim 89 wherein the oxidation reagent is used in the amount of 2.0-3.5 equivalence to the compound of Formula Ix.

91. The method of claim 85, wherein step a) is conducted for 12 hours to 2 days.

92. The method of claim 91, wherein step a) is conducted for 1 day.

93. The method of claim 85, wherein each occurrence of R₁ is independently hydrogen, halogen, cyano, nitro, CF₃, OCF₃, OR_a, or SR_a.

94. The method of claim 93, wherein each occurrence of R₁ is H.

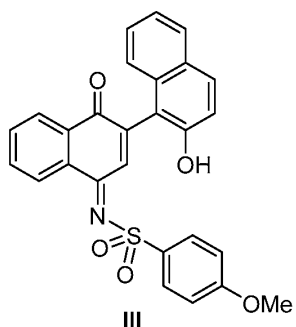
95. The method of claim 85, wherein each occurrence of R₂ is independently halogen, cyano, nitro, CF₃, OCF₃, OR_a, or SR_a.

96. The method of claim 95, wherein R₂ is OMe and n₂ is 1.

97. The method of claim 85, wherein R₃ is OCF₃, OR_a, SR_a, OC(=O)R_a, alkyl, alkenyl, or cycloalkyl.

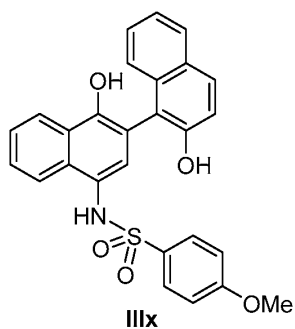
98. The method of claim 97, wherein R₃ is H.

99. The method of claim 85, wherein the compound of Formula I has the structure



of Formula III,

; and the compound of Formula Ix has the



structure of Formula IIIx,