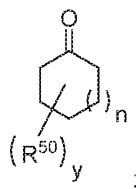


CLAIMS

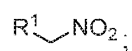
We claim:

1. A process to prepare a spirocyclic compound comprising:
 - a. reacting a cyclic ketone with a nitroalkane to afford a cycloalkyl group substituted with nitroalkylene;
 - b. reacting the compound of step (a) with a glycinate to afford a compound of Formula III;
 - c. reducing the compound of Formula III with a reducing agent;
 - d. cyclizing the compound of step (c);

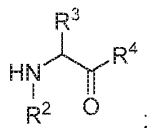
wherein the cyclic ketone is of Formula:



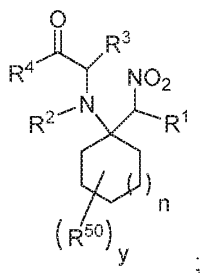
wherein the nitroalkane is of Formula:



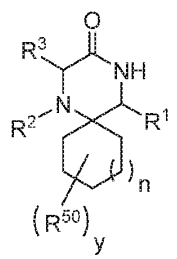
wherein the glycinate is of Formula:



wherein Formula III is:



wherein the spirocyclic compound is of Formula:



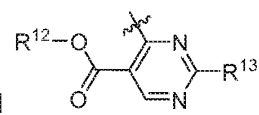
wherein

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

n is 0 or 1;

R¹ is selected from hydrogen, alkyl, and aryl;

R² is selected from hydrogen, substituted heteroaryl, and



R³ is selected from hydrogen, NR⁵R⁶, OR⁷, SR⁷, and halogen;

R⁴ is selected from NR⁸R⁹ and OR¹⁰;

R⁵ and R⁶ are independently selected from hydrogen, alkyl, aryl, -alkyl-aryl, and -C(O)R¹¹;

R⁷ is selected from alkyl, aryl, and -alkyl-aryl;

R⁸ and R⁹ are independently selected from hydrogen, alkyl, aryl, and -alkyl-aryl;

R¹⁰ is selected from alkyl, aryl, and -alkyl-aryl;

R¹¹ is selected from alkyl and aryl;

R¹² is selected from alkyl, aryl, and -alkyl-aryl;

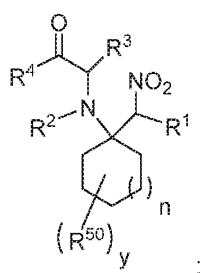
R¹³ is selected from -S-alkyl and Cl; and

each instance of R⁵⁰ is independently selected from hydrogen, halogen, and alkyl.

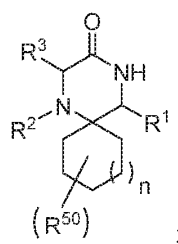
2. The process of claim 1, wherein the nitroalkane is also a solvent.
3. The process of claim 1, wherein a base is used in step (a).
4. The process of claim 3, wherein the base is an organic base.
5. The process of claim 3, wherein the base is an inorganic base.

6. The process of claim 3, wherein the base is a carbonate.
7. The process of claim 3, wherein the base is potassium carbonate.
8. The process of any one of claims 1-7, wherein oxalic acid is added after step (b) to precipitate and remove undesired byproducts.
9. The process of any one of claims 1-8, wherein an acid is added after step (b) to isolate the compound of Formula I as a salt.
10. The process of claim 9, wherein the acid is hydrobromic acid.
11. A process to prepare a spirocyclic compound comprising:
 - a. reducing a compound of Formula III with a reducing agent;
 - b. cyclizing the compound of step (a);

wherein Formula III is:



wherein the spirocyclic compound is of Formula:

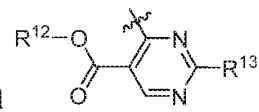


wherein

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

n is 0 or 1;

R¹ is selected from hydrogen, alkyl, and aryl;



R² is selected from hydrogen, substituted heteroaryl, and

R³ is selected from hydrogen, NR⁵R⁶, OR⁷, SR⁷, and halogen;

R⁴ is selected from NR⁸R⁹ and OR¹⁰;

R⁵ and R⁶ are independently selected from hydrogen, alkyl, aryl, -alkyl-aryl, and -C(O)R¹¹;

R⁷ is selected from alkyl, aryl, and -alkyl-aryl;

R⁸ and R⁹ are independently selected from hydrogen, alkyl, aryl, and -alkyl-aryl;

R¹⁰ is selected from alkyl, aryl, and -alkyl-aryl;

R¹¹ is selected from alkyl and aryl;

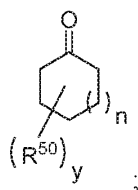
R¹² is selected from alkyl, aryl, and -alkyl-aryl;

R¹³ is selected from -S-alkyl and Cl; and

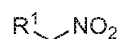
each instance of R⁵⁰ is independently selected from hydrogen, halogen, and alkyl.

12. The process of any one of claims 1-11, wherein the reducing agent is zinc.
13. The process of claim 12, wherein an acidic additive is used in with the reducing agent.
14. The process of claim 13, wherein the acidic additive is ammonium chloride.
15. The process of any one of claims 1-11, wherein the reducing agent is platinum(IV) oxide in the presence of hydrogen gas.
16. The process of any one of claims 1-11, wherein the reducing agent is Raney nickel in the presence of hydrogen gas.
17. The process of any one of claims 1-11, wherein the reducing agent is iron.
18. The process of any one of claims 1-11, wherein the reducing agent is samarium diiodide.
19. The process of any of claims 1-18, wherein the reduction and cyclization occur in the same reaction vessel.

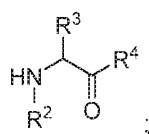
20. The process of any of claims 1-19, wherein water is a solvent used in the reduction step.
21. The process of any of claims 1-19, wherein a mixture of water and acetone is used as the solvent in the reduction step.
22. The process of any of claims 1-21, wherein the reduction and cyclization is conducted at about 25 °C.
23. The process of any of claims 1-21, wherein the reduction and cyclization is conducted at about 15 °C.
24. The process of any of claims 1-21, wherein the reduction and cyclization is conducted at about 35 °C.
25. The process of any of claims 1-24, wherein the cyclization is acid catalyzed.
26. The process of any of claims 1-24, wherein the cyclization is base catalyzed.
27. A process to prepare a compound of Formula III comprising:
- reacting a cyclic ketone with a nitroalkane to afford a cycloalkyl group substituted with nitroalkylene;
 - reacting the compound of step (a) with a glycinate;
- wherein the cyclic ketone is of Formula:



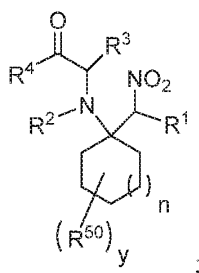
wherein the nitroalkane is of Formula:



wherein the glycinate is of Formula:



wherein Formula III is:



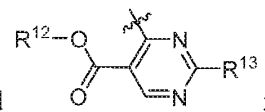
wherein

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

n is 0 or 1;

R¹ is selected from hydrogen, alkyl, and aryl;

R² is selected from hydrogen, substituted heteroaryl, and



R³ is selected from hydrogen, NR⁵R⁶, OR⁷, SR⁷, and halogen;

R⁴ is selected from NR⁸R⁹ and OR¹⁰;

R⁵ and R⁶ are independently selected from hydrogen, alkyl, aryl, -alkyl-aryl, and -C(O)R¹¹;

R⁷ is selected from alkyl, aryl, and -alkyl-aryl;

R⁸ and R⁹ are independently selected from hydrogen, alkyl, aryl, and -alkyl-aryl;

R¹⁰ is selected from alkyl, aryl, and -alkyl-aryl;

R¹¹ is selected from alkyl and aryl;

R¹² is selected from alkyl, aryl, and -alkyl-aryl;

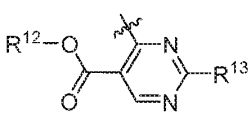
R¹³ is selected from -S-alkyl and Cl; and

each instance of R⁵⁰ is independently selected from hydrogen, halogen, and alkyl.

28. The process of claim 27, wherein the nitroalkane is also a solvent.

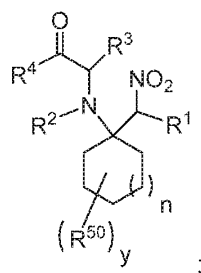
29. The process of claim 27, wherein a base is used in step (a).
30. The process of claim 29, wherein the base is an organic base.
31. The process of claim 29, wherein the base is an inorganic base.
32. The process of claim 29, wherein the base is a carbonate.
33. The process of claim 29, wherein the base is potassium carbonate.
34. The process of any one of claims 27-33, wherein oxalic acid is added after step (b) to precipitate and remove undesired byproducts.
35. The process of any one of claims 27-34, wherein an acid is added after step (b) to isolate the compound of Formula III as a salt.
36. The process of claim 35, wherein the acid is hydrobromic acid.
37. The process of any one of claims 1-36, wherein the cyclic ketone is cyclohexanone.
38. The process of any one of claims 1-37, wherein the glycinate is methyl glycinate.
39. The process of any one of claims 1-37, wherein the glycinate is ethyl glycinate.
40. The process of any one of claims 1-39, wherein the nitroalkane is nitromethane.
41. The process of any one of claims 1-36, wherein R^1 is hydrogen.
42. The process of any one of claims 1-41, wherein n is 0.
43. The process of any one of claims 1-41, wherein n is 1.
44. The process of any one of claims 1-43 wherein y is 1.

45. The process of any one of claims 1-43, wherein y is 2.
46. The process of any one of claims 1-43, wherein y is 0.
47. The process of any one of claims 1-45, wherein R⁵⁰ is alkyl.
48. The process of any one of claims 1-45, wherein R⁵⁰ is halogen.
49. The process of any one of claims 1-45, wherein R⁵⁰ is methyl.
50. The process of any one of claims 1-45, wherein R⁵⁰ is ethyl.
51. The process of any one of claims 1-45, wherein R⁵⁰ is cyclopropyl.
52. The process of any one of claims 1-51, wherein all the steps are conducted at about 25 °C.
53. The process of any one of claims 1-52, wherein R⁴ is -O-alkyl.
54. The process of claim 53, wherein alkyl is methyl or ethyl.
55. The process of any one of claims 1-54, wherein R² is hydrogen.
56. The process of any one of claims 1-54, wherein R² is substituted heteroaryl.

57. The process of any one of claims 1-54, wherein R² is .

58. The process of any one of claims 1-57, wherein R³ is hydrogen.

59. A compound of Formula



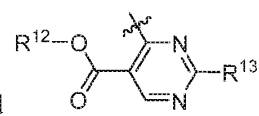
or an acceptable salt, *N*-oxide, or isotopic derivative thereof;
wherein

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

n is 0 or 1;

R¹ is selected from hydrogen, alkyl, and aryl;

R² is selected from hydrogen, substituted heteroaryl, and



R³ is selected from hydrogen, NR⁵R⁶, OR⁷, SR⁷, and halogen;

R⁴ is selected from NR⁸R⁹ and OR¹⁰;

R⁵ and R⁶ are independently selected from hydrogen, alkyl, aryl, -alkyl-aryl, and -C(O)R¹¹;

R⁷ is selected from alkyl, aryl, and -alkyl-aryl;

R⁸ and R⁹ are independently selected from hydrogen, alkyl, aryl, and -alkyl-aryl;

R¹⁰ is selected from alkyl, aryl, and -alkyl-aryl;

R¹¹ is selected from alkyl and aryl;

R¹² is selected from alkyl, aryl, and -alkyl-aryl;

R¹³ is selected from -S-alkyl and Cl; and

each instance of R⁵⁰ is independently selected from hydrogen, halogen, and alkyl.

60. The compound of claim 59, wherein R¹ is hydrogen.

61. The compound of claim 59 or claim 60, wherein n is 0.

62. The compound of claim 59 or claim 60, wherein n is 1.

63. The compound of any one of claims 59-62, wherein y is 1.
64. The compound of any one of claims 59-62, wherein y is 2.
65. The compound of any one of claims 59-62, wherein y is 0.
66. The compound of any one of claims 59-64, wherein R⁵⁰ is halogen.
67. The compound of any one of claims 59-64, wherein R⁵⁰ is alkyl.
68. The compound of any one of claims 59-64, wherein R⁵⁰ is methyl.
69. The compound of any one of claims 59-68, wherein R² is hydrogen.
70. The compound of any one of claims 59-69, wherein R³ is hydrogen.
71. The compound of any one of claims 59-70, wherein R⁴ is -OMe.
72. The compound of any one of claims 59-70, wherein R⁴ is -OEt.