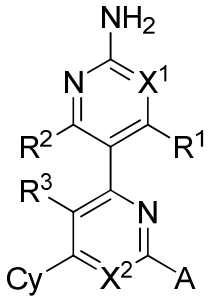
WHAT IS CLAIMED IS:

1. A process for preparing a compound of Formula I



I

wherein

R^1, R^2 and R^3 are each independently selected from the group consisting of H, F, Cl, Br, I, C_{1-6} alkyl and C_{1-6} haloalkyl;

X^1 is C-R^4, wherein R^4 is selected from the group consisting of -F, -Cl, -Br, -I, -$(L^1)_{0-1}$-C_{1-6} alkyl, -$(L^1)_{0-1}$-C_{1-6} haloalkyl, -$(L^1)_{0-1}$-C_{1-6} heteroalkyl, -$(L^2)_{0-1}$-C_{3-8} cycloalkyl, -$(L^2)_{0-1}$-3-7-membered heterocycloalkyl, -$(L^2)_{0-1}$-6-10-membered aryl, and -$(L^2)_{0-1}$-5-10-membered heteroaryl, wherein

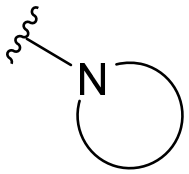
L^1 is selected from the group consisting of -O-, -N(H)-, -S-, -N(C_{1-6} alkyl)- and =O, and

L^2 is selected from the group consisting of -O-, -N(H)-, -N(C_{1-6} alkyl)-, -S-, =O, C_{1-4} alkylene, C_{1-4} alkenylene, C_{1-4} alkynylene, C_{1-4} alkoxylene, C_{1-4} aminoalkylene, C_{1-4} thioalkylene and C_{1-4} heteroalkylene, and

wherein R^4 is optionally substituted on carbon atoms and heteroatoms with R^{R4} substituents selected from the group consisting of F, Cl, Br, I, C_{1-6} alkyl, C_{1-6} haloalkyl, 3-5-membered cycloalkyl, 3-5-membered heterocycloalkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{1-6} dialkylamino, C_{1-6} alkylthio, =O, -NH_2, -CN, -NO_2 and -SF_5;

wherein R^5 and R^6 are independently selected from straight or branched C_{1-6} alkyl, or R^5 and R^6 together with the oxygen atoms to which they are attached and the boron atom form 5- to 7-membered heterocyclic ring, wherein the each ring carbon atom may be substituted with 1 or 2 C_{1-4} straight chain alkyl groups;

X^2 is N;



A is a 3- to 12-membered N-containing heterocycloalkyl,

wherein A is optionally substituted with 1-5 R^A substituents selected from the group consisting of F, Cl, Br, I, -OH, -CN, $-NO_2$, $-SF_5$, C_{1-8} alkyl, C_{1-8} haloalkyl, C_{1-8} heteroalkyl, $-(L^A)_{0-1}$-3-8-membered cycloalkyl, $-(L^A)_{0-1}$-3-8-membered heterocycloalkyl, $-(L^A)_{0-1}$-5-6-membered heteroaryl, $-(L^A)_{0-1}$-C_6 aryl, $-(L^A)_{0-1}$-$NR^{R1a}R^{R1b}$, $-(L^A)_{0-1}$-OR^{R1a}, $-(L^A)_{0-1}$-SR^{R1a}, $-(L^A)_{0-1}$-$N(R^{R1a})C(=Y^1)OR^{R1c}$, $-(L^A)_{0-1}$-$OC(=O)N(R^{R1a})(R^{R1b})$, $-(L^A)_{0-1}$-$N(R^{R1a})C(=O)N(R^{R1a})(R^{R1b})$,

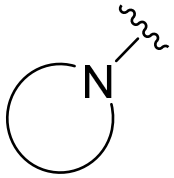
$-(L^A)_{0-1}$-$C(=O)N(R^{R1a})(R^{R1b})$, $-(L^A)_{0-1}$-$N(R^{R1a})C(=O)R^{R1b}$, $-(L^A)_{0-1}$-$C(=O)OR^{R1a}$, $-(L^A)_{0-1}$-$OC(=O)R^{R1a}$, $-(L^A)_{0-1}$-$P(=O)(OR^{R1a})(OR^{R1b})$, $-(L^A)_{0-1}$-$S(O)_{1-2}R^{R1c}$, $-(L^A)_{0-1}$-$S(O)_{1-2}N(R^{R1a})(R^{R1b})$, $-(L^A)_{0-1}$-$N(R^{R1a})S(O)_{1-2}N(R^{R1a})(R^{R1b})$ and $-(L^A)_{0-1}$-$N(R^{R1a})S(O)_{1-2}(R^{R1c})$, wherein

Y^1 is O or S;

L^A is selected from the group consisting of C_{1-4} alkylene, C_{1-4} heteroalkylene, C_{1-4} alkoxylene, C_{1-4} aminoalkylene, C_{1-4} thioalkylene, C_{2-4} alkenylene, and C_{2-4} alkynylene;

R^{R1a} and R^{R1b} are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} haloalkyl, 3-8-membered cycloalkyl, phenyl, benzyl, 5-6-membered heteroaryl and 3-8-membered heterocycloalkyl;

R^{R1c} is selected from the group consisting of C_{1-8} alkyl, C_{1-8} haloalkyl, 3-8- membered cycloalkyl, phenyl, benzyl, 5-6-membered heteroaryl and 3-7-membered heterocycloalkyl, and wherein R^A is optionally substituted on carbon atoms and heteroatoms with R^{RA} substituents selected from, F, Cl, Br, I, $-NH_2$, -OH, -CN, $-NO_2$, =O, $-SF_5$, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} (halo)alkyl-C(=O)-, C_{1-4} (halo)alkyl-$S(O)_{0-2}$-, C_{1-4} (halo)alkyl-$N(H)S(O)_{0-2}$-, C_{1-4} (halo)alkyl-$S(O)_{0-2}N(H)$-, (halo)alkyl-N(H)-$S(O)_{0-2}N(H)$-, C_{1-4} (halo)alkyl-C(=O)N(H)-, C_{1-4} (halo)alkyl-N(H)-C(=O)-, $((halo)alkyl)_2N$-C(=O)-, C_{1-4} (halo)alkyl-OC(=O)N(H)-, C_{1-4} (halo)alkyl-OC(=O)N(H)-, (halo)alkyl-N(H)-C(=O)O-, $((halo)alkyl)_2N$-C(=O)O-, C_{1-4} alkylthio, C_{1-4} alkylamino and C_{1-4} dialkylamino; and

Cy is a 3- to 12-membered N-containing heterocycloalkyl, 

wherein Cy optionally comprises one or two additional heteroatoms selected from the group consisting of O, S, and N,

wherein Cy is optionally substituted on carbon or heteroatoms with R^{Cy} substituents selected from the group consisting of F, Cl, Br, I, -OH, -CN, -NO_2, -SF_5, C_{1-8} alkyl, C_{1-8} haloalkyl, C_{1-8} heteroalkyl, -$(L^{Cy})_{0-1}$-3-8-membered cycloalkyl, -$(L^{Cy})_{0-1}$-3-8-membered heterocycloalkyl, -$(L^{Cy})_{0-1}$-5-6-membered heteroaryl, -$(L^{Cy})_{0-1}$-phenyl, -$(L^{Cy})_{0-1}$-$NR^{RCa}R^{RCb}$, -$(L^{Cy})_{0-1}$-OR^{RCa}, -$(L^{Cy})_{0-1}$-SR^{RCa}, -$(L^{Cy})_{0-1}$-$N(R^{RCa})C(=Y^1)OR^{RCc}$, -$(L^{Cy})_{0-1}$-$OC(=O)N(R^{RCa})(R^{RCb})$, -$(L^{Cy})_{0-1}$-$N(R^{RCa})C(=O)N(R^{RCa})(R^{RCb})$, -$(L^{Cy})_{0-1}$-$C(=O)N(R^{RCa})(R^{RCb})$, -$(L^{Cy})_{0-1}$-$N(R^{RCa})C(=O)R^{RCb}$, -$(L^{Cy})_{0-1}$-$C(=O)OR^{RCa}$, -$(L^{Cy})_{0-1}$-$OC(=O)R^{RCa}$, -$(L^{Cy})_{0-1}$-$P(=O)(OR^{RCa})(OR^{RCb})$, -$(L^{Cy})_{0-1}$-$S(O)_{1-2}R^{RCc}$, -$(L^{Cy})_{0-1}$-$S(O)_{1-2}N(R^{RCa})(R^{RCb})$, -$(L^{Cy})_{0-1}$-$N(R^{RCa})S(O)_{1-2}N(R^{RCa})(R^{RCb})$ and -$(L^{Cy})_{0-1}$-$N(R^{RCa})S(O)_{1-2}(R^{RCc})$, wherein

L^{Cy} is selected from the group consisting of C_{1-4} alkylene, C_{1-4} heteroalkylene, C_{1-4} alkoxylene, C_{1-4} aminoalkylene, C_{1-4} thioalkylene, C_{2-4} alkenylene, and C_{2-4} alkynylene;

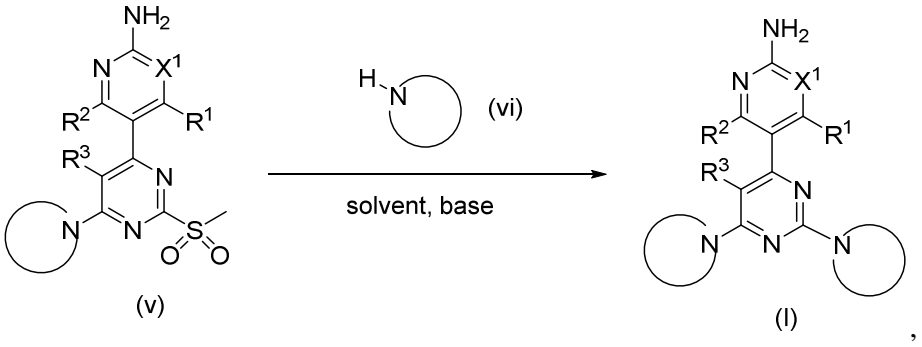
R^{RCa} and R^{RCb} are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} haloalkyl, 3-8-membered cycloalkyl, phenyl, benzyl, 5-6-membered heteroaryl and 3-8-membered heterocycloalkyl;

R^{RCc} is selected from the group consisting of C_{1-8} alkyl, C_{1-8} haloalkyl, 3-8-membered cycloalkyl, phenyl, benzyl, 5-6-membered heteroaryl and 3-7-membered heterocycloalkyl, and

wherein R^{Cy} is optionally substituted on carbon atoms and heteroatoms with from 1 to 5 R^{RCy} substituents selected from the group consisting of F, Cl, Br, I, -NH_2, -OH, -CN, -NO_2, =O, -SF_5, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} (halo)alkyl-C(=O)-, C_{1-4} (halo)alkyl-$S(O)_{0-2}$-, C_{1-4} (halo)alkyl-N(H)$S(O)_{0-2}$-, C_{1-4} (halo)alkyl-$S(O)_{0-2}$N(H)-, (halo)alkyl-N(H)-$S(O)_{0-2}$N(H)-, C_{1-4} (halo)alkyl-C(=O)N(H)-, C_{1-4} (halo)alkyl-N(H)-C(=O)-, ((halo)alkyl)$_2$N-C(=O)-, C_{1-4} (halo)alkyl-OC(=O)N(H)-, C_{1-4} (halo)alkyl-OC(=O)N(H)-, (halo)alkyl-N(H)-C(=O)O-, ((halo)alkyl)$_2$N-C(=O)O-, C_{1-4} alkylthio, C_{1-4} alkylamino and C_{1-4} dialkylamino;

said process comprising:

displacing the methoxysulfonyl group of compound (v) under basic conditions in a solvent with a 3 to -12-membered amine-containing heterocycloalkyl compound (vi) to provide the compound of Formula (I)



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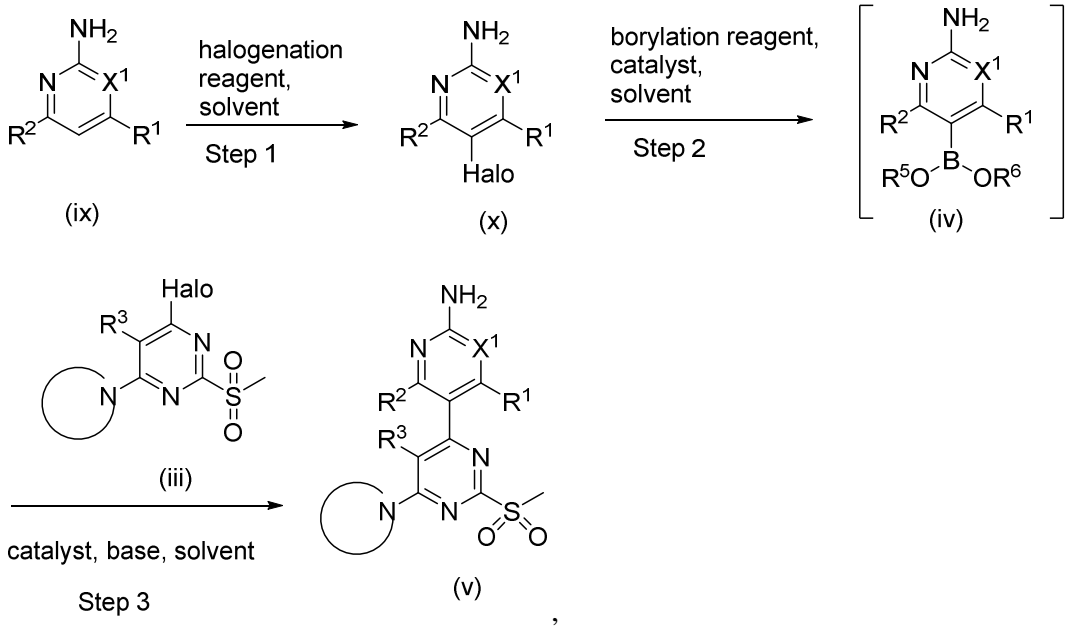
wherein said process further comprises preparing compound (v) according to one of schemes (A) to (C):

scheme (A) wherein sulfone compound (v) is prepared according to the following reaction scheme



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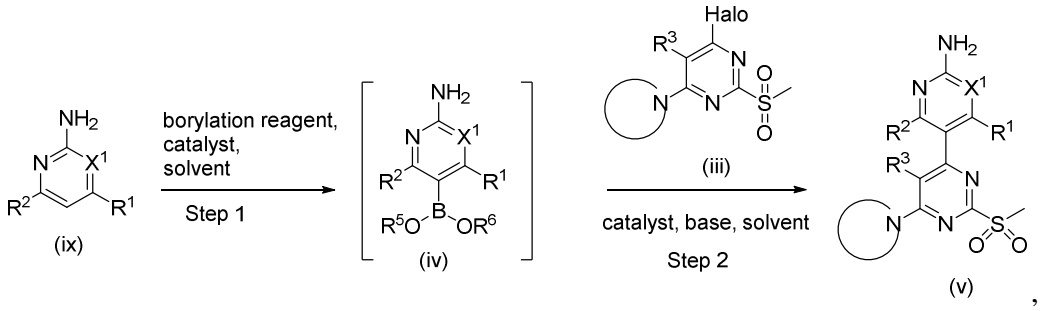
scheme (A) comprising

step 1 wherein compound (ix) is combined with a halogenation reagent in a solvent and reacted to form compound (x),

step 2 wherein compound (x) is borylated with a borylation reagent to form a solution of compound (iv), and

step 3 wherein a solution of compound (iv), compound (iii), a catalyst, a base and a solvent is formed and reacted to form compound (v);

scheme (B) wherein sulfone compound (v) is prepared according to the following reaction scheme



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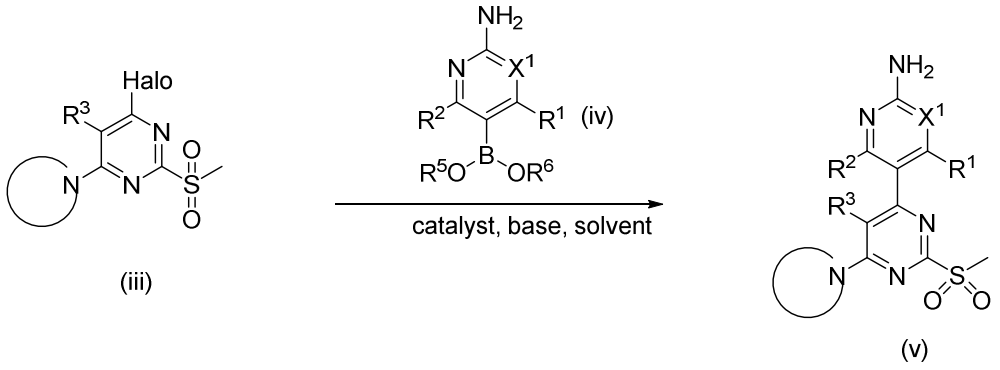
scheme (B) comprising

step 1 wherein compound (ix) is directly borylated with a borylation reagent to form a reaction product mixture comprising compound (iv) predominantly in solution, and

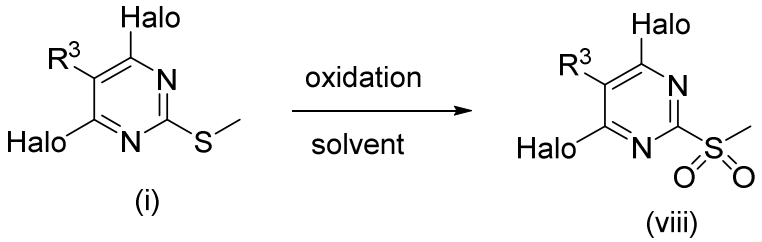
step 2 wherein the reaction product mixture from step 1 is combined with compound (iii), a catalyst, a base and a solvent, and reacted to form compound (v); and

scheme (C) wherein sulfone compound (v) is prepared according to the following reaction scheme by performing a coupling reaction between a sulfone compound (iii) and a boronate reagent (iv) with a catalyst in the presence of a base and a solvent to provide compound (v)



wherein scheme (C) further comprises scheme (1), scheme (2), or a combination of scheme (1) and scheme (2),

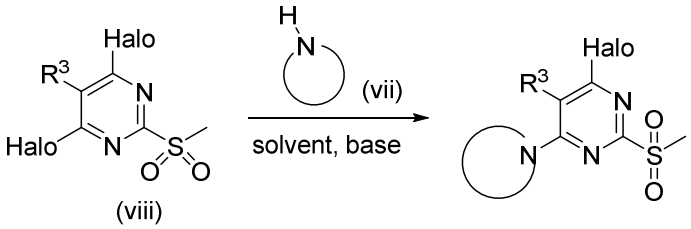
wherein scheme (1) comprises preparing sulfone compound (iii) according to the following reaction scheme comprising treating an alkylthio compound (i) with at least one oxidizing agent in a solvent to provide a mixture of oxidized sulfone compound (viii)



(i) (viii)

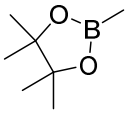
, and

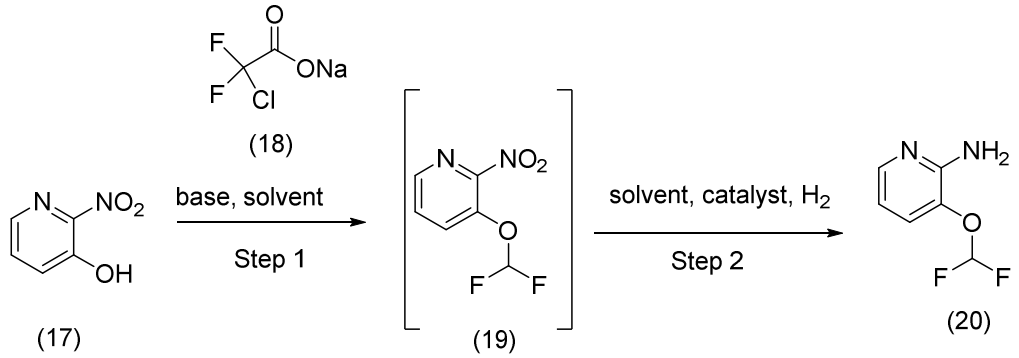
displacing a halogen atom from sulfone compound (viii) with an optionally substituted 3- to 12-membered amine-containing heterocycloalkyl compound (vii) under basic conditions in a solvent to form a reaction product mixture comprising sulfone compound (iii)

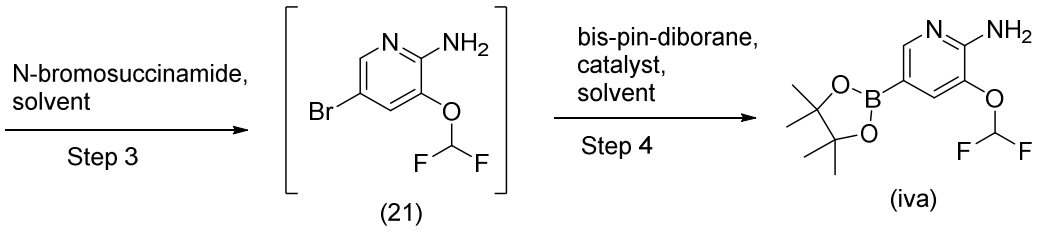


(viii) (iii)

, and

scheme (2) wherein the sulfone compound (iv) is the species compouind (iva) wherein X^1 is C-O-CHF_2, R^1 and R^2 are each H, and the moiety -$B(OR^5)(OR^6)$ is , and wherein compound (iva) is prepared according to the following reaction scheme,





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scheme (2) comprising

step 1 wherein a reaction mixture comprising compound (17), compound (18), a solvent and base is formed and reacted to form a reaction product mixture comprising compound (19) predominantly in solution,

step 2 wherein a reaction mixture comprising the solution of compound (19) is hydrogenated in the presence of catalyst to form a reaction product mixture comprising compound (20),

step 3 wherein a reaction mixture comprising compound (20), N-bromosuccinamide and a polar aprotic solvent is reacted to form a reaction product mixture comprising compound (21) predominantly in solution, and

step 4 wherein a reaction mixture comprising compound (21) in solution, bis-pin-diborane, and a precious metal catalyst is formed and reacted to form a reaction product mixture comprising compound (iva).

2. The process of claim 1, wherein

R^1, R^2 and R^3 are each H;

X^1 is C-R^4, wherein R^4 is -$(L^1)_{0\text{-}1}$-$C_{1\text{-}6}$ haloalkyl, wherein L^1 is -O-;

A is 3 to 12 membered N-containing heterocycloalkyl optionally substituted with 1 to 5 R^A substituents wherein each R^A is F; and

Cy is 3 to 12 membered N-containing heterocycloalkyl.

3. The process of claim 2, wherein

R^4 is selected from: monofluoromethoxy, difluoromethoxy, and trifluoromethoxy;

A is a 4 to 7 membered N-containing heterocycloalkyl substituted with from 1 to 3 F atoms; and

Cy is a 5 to 9 membered N-containing heterocycloalkyl further comprising an oxygen heteroatom.

4. The process of any one of claims 1 to 3, wherein the coupling reaction catalyst is a palladium catalyst.

5. The process of claim 4, wherein the catalyst is a Pd(0) catalyst.

6. The process of claim 4, wherein the catalyst is selected from the group consisting of: $[PdCl(X)]_2$ where X is allyl, cinnamyl or crotyl; $[Pd(X)PR^{R7}]$ where R^7 is alkyl or aryl; [Pd(X)(Y)] where X is allyl, cinnamyl or crotyl, Y is cyclopentandienyl or p-cymyl; $Pd(dba)_2$; $Pd_2(dba)_3$; $Pd(OAc)_2$; PdZ_2 where Z is Cl, Br or I; $Pd_2Z_2(PR^8)_2$ where Z is Cl, Br or I, and R^8 is alkyl or aryl; and PdPd(TFA)2, each catalyst in combination with a phosphine ligand, a base, or a combination thereof.

7. The process of claim 4, wherein the catalyst is selected from the group consisting of: $Pd(dppf)Cl_2$, $Pd(dppe)Cl_2$, $Pd(PCy_3)_2Cl_2$, $Pd(PPh_3)_2Cl_2$, $Pd(OAc)_2(PPh_3)_2$., $Pd(PPh_3)_4$, $Pd(PPh_3)_4Cl_2$, $Pd(PCy_3)_2$, $Pd(PCy_3)_2Cl_2$, and $Pd(t\text{-}Bu_3P)_2$.

8. The process of claim 7, wherein the catalyst is $Pd(dppf)Cl_2$.

9. The process of any one of claims 1 to 8, wherein the coupling reaction solvent for the preparation of compound (v) is selected from the group consisting of: cyclic ethers, toluene, acetonitrile, ethyl acetate, isopropyl acetate, *n*-propyl acetate, dimethylformamide, dimethyl sulfoxide, and combinations thereof

10. The process of claim 9, wherein the organic solvent is combined with water.

11. The process of claim 9, wherein the solvent is a cyclic ether.

12. The process of claim 9, wherein the solvent is tetrahydrofuran or methyl-tetrahydrofuran.

13. The process of claim 10, wherein the solvent is tetrahydrofuran and water.

14. The process of claim 13, wherein the base is selected from the group consisting of a carbonate, a phosphate, a tertiary amine, a cyclic amidine, and a guanidine.

15. The process of claim 14, wherein the base is a carbonate.

16. The process of claim 15, wherein the base is sodium carbonate or potassium carbonate.

17. The process of any one of claims 1 to 16, wherein the coupling reaction further comprises scavenging the catalyst with at least one added catalyst scavenger.

18. The process of claim 17, wherein at least one of the catalyst scavengers is selected from the group consisting of: a thiol, a thiourea, a thiocarbamate, and a xanthate or a salt thereof.

19. The process of claim 18, wherein the catalyst scavenger is a thiol.

20. The process of claim 19, wherein the catalyst scavenger is N-acetylcysteine.

21. The process of any one of claims 1 to 20, the process further comprising precipitation of compound (v) from solution by addition of at least one anti-solvent thereto.

22. The process of claim 21, wherein the anti-solvent is a nonpolar solvent.

23. The process of claim 22, wherein the anti-solvent is *n*-heptane.

24. The process of any one of claims 21 to 23, further comprising isolating and drying compound (v).

25. The process of any one of claims 1 to 24, wherein the mole ratio of sulfone compound (iii) to boronate reagent compound (iv) is from 1:1.01 to 1:1.49, from 1:1.05 to 1:1.4, from 1:1.1 to 1:1.3, or about 1:1.15.

26. The process of any one of claims 1 to 25, wherein the step for preparing compound (v) is done in the absence of a chromatographic purification step, solvent exchange step, or a combination thereof.

27. The process of any one of claims 1 to 26, wherein the yield of compound (v), based on compound (iii), is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, or at least 90%.

28. The process of any one of claims 1 to 27, wherein the purity of compound (v) by high pressure liquid chromatography is at least 98 area%, at least 98.5 area%, at least 99 area%, or at least 99.5 area%.

29. The process of any one of claims 1 to 28, wherein the solvent for the reaction of compound (v) with compound (vi) comprises at least one polar or apolar solvent.

30. The process of any one of claims 1 to 28, wherein the solvent for the reaction of compound (v) with compound (vi) is selected from the group consisting of: alkylaromatic, haloaromatic, secondary amine, tertiary amine, and combinations thereof.

31. The process of claim 30, wherein the solvent is selected from the group consisting of: di-*n*-butylamine, tri-*n*-butylamine, dimethylsulfoxide, dimethylformamide, dimethylacetamide, N-methyl-2-pyrrolidone, acetonitrile, toluene, mesitylene and combinations thereof.

32. The process of claim 31, wherein the solvent is a secondary amine or a tertiary amine.

33. The process of claim 32, wherein the solvent is di-*n*-butylamine or tri-*n*-butylamine.

34. The process of claim 33, wherein the base is selected from the group consisting of a carbonate, a phosphate, a tertiary amine, a cyclic amidine, and a guanidine.

35. The process of claim 34, wherein the base is a cyclic amidine.

36. The process of claim 35, wherein the base is 1,8-diazabicyclo[5.4.0]undec-7-ene.

37. The process of any one of claims 1 to 36, wherein compound (I) is in solution after formation thereof by reaction of compounds (v) and (vi), and wherein the process further comprises precipitation of compound (I) from solution by addition of at least one anti-solvent thereto.

38. The process of claim 37, wherein the anti-solvent is selected from the group consisting of: water, alcohols, and combinations thereof.

39. The process of claim 38, wherein the anti-solvent is an alcohol.

40. The process of claim 39, wherein the anti-solvent is 1-propanol.

41. The process of any one of claims 37 to 40, further comprising isolating and drying compound (I).

42. The process of any one of claims 1 to 41, wherein the mole ratio of compound (v) to compound (vi) is from 1:1.01 to 1:2.4, from 1:1.1 to 1:2, from 1:1.2 to 1:1.8, or about 1:1.5.

43. The process of any one of claims 1 to 42, wherein the step for preparing compound (I) is done in the absence of a chromatographic purification step, a solvent exchange step, or a combination thereof.

44. The process of any one of claims 1 to 43 wherein the yield of compound (I), based on compound (v), is at least 65%, at least 70%, at least 75%, at least 80%, or at least 85%.

45. The process of any one of claims 1 to 44, wherein the purity of compound (I) by high pressure liquid chromatography is at least 98 area%, at least 98.5 area%, at least 99 area%, or at least 99.5 area%.

46. The process of any one of claims 1-45, wherein the solvent for the reaction for scheme A for forming compound (viii) and for the reaction for forming compound (iii) are each independently selected from the group consisting of: dimethylsulfoxide, dimethylformamide, N,N-dimethylacetylamide, N-methyl-2-pyrrolidone, acetonitrile, methanol, ethanol, *n*-propanol, *i*-propanol, *n*-butanol, tetrahydrofuran, 2-Me-tetrahydrofuran, ethyl acetate, *n*-propyl acetate, and *i*-propyl acetate.

47. The process of claim 46, wherein the solvent is an alcohol.

48. The process of claim 47, wherein the alcohol is methanol or ethanol.

49. The process of any one of claims 46 to 48, wherein the at least one oxidizing agent is selected from the group consisting of: peracid or its salt, peroxide, peroxysulfuric acid or its salt, a hypochloride, a tungstate, a molybdate, and combinations thereof.

50. The process of claim 49, wherein the oxidizing agent is a tungstate.

51. The process of claim 50, wherein the oxidizing agent is sodium tungstate dihydrate.

52. The process of claim 49, wherein the oxidizing agent is a peroxide.

53. The process of claim 52, wherein the oxidizing agent is hydrogen peroxide.

54. The process of claim 49, wherein the oxidizing agent is the combination of a tungstate and a peroxide.

55. The process of claim 54, wherein the oxidizing agent is sodium tungstate dihydrate and hydrogen peroxide.

56. The process of any one of claims 46 to 55, wherein the oxidation of the alkylthio compound (i) further comprises quenching the oxidizing agent with an oxidizing agent quencher.

57. The process of claim 56, wherein the oxidizing agent quencher is selected from the group consisting of: sulfite, hydrogenosulfite, and thiosulfate.

58. The process of claim 57, wherein the oxidizing agent quencher is sodium bisulfite.

59. The process of any one of claims 46 to 58, wherein compound (i) and sulfone compound (viii) are each in suspension in the solvent in the oxidation step.

60. The process of any one of claims 46 to 59, further comprising isolating and drying sulfone compound (viii).

61. The process of any one of claims 46 to 60, wherein the step for preparing sulfone compound (viii) is done in the absence of a chromatographic purification step, a solvent exchange step, or a combination thereof.

62. The process of any one of claims 46 to 61 wherein the yield of sulfone compound (viii) is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, or at least 75%.

63. The process of any one of claims 46 to 62, wherein the purity of sulfone compound (viii) by high pressure liquid chromatography is at least 98 area%, at least 98.5 area%, or at least 99 area%.

64. The process of any one of claims 46 to 63, wherein the base for the reaction for forming compound (iii) is selected from the group consisting of: a carbonate, a hydrogenocarbonate, a phosphate, an amine, and a cyclic amidine.

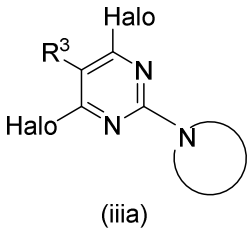
65. The process of claim 64, wherein the base is an amine base.

66. The process of claim 65, wherein the base is a tertiary amine.

67. The process of claim 66, wherein the base is triethylamine.

68. The process of any one of claims 46 to 67, wherein the mole ratio of compound (viii) to compound (vii) is from 1:1.01 to 1:1.5, from 1:05 to 1:2, or about 1:1. 2 to 1:1.8.

69. The process of any one of claims 1 to 68, wherein the reaction product mixture of scheme (A) of claim 1 comprising sulfone compound (iii) further comprises compound (iiia)



(iiia) , wherein:

(a) compounds (iii) and (iiia) are each substantially in solution after completion of the addition of the base; and

(b) the molar ratio of compound (iii) to compound (iiia) is from about 3:1 to about 20:1, from about 5:1 to about 15:1, or about 10:1.

70. The process of claim 69 further comprising:

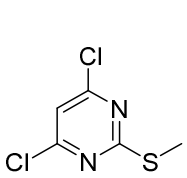
(c) adding water to the cooled solution of compounds (iii) and (iiia) and aging to form a slurry, wherein the molar ratio of solid compound (iii) to solid compound (iiia) in the slurry is at least 50:1 at least 75:1, at least 90:1 or at least 95:1; and

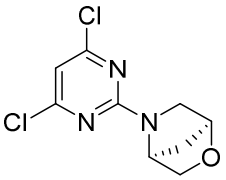
(d) isolating and drying the solids from the slurry.

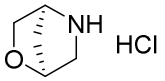
71. The process of any one of claims 46 to 70 wherein the yield of compound (iii), based on compound (viii), is at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, or at least 85%.

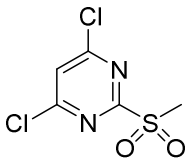
72. The process of any one of claims 46 to 71, wherein the purity of compound (iii) by high pressure liquid chromatography is at least 97 area%, at least 97.5 area%, at least 98 area%, at least 98.5 area%, or at least 99 area%.

73. The process of any one of claims 46 to 72, wherein compounds (i), (iiia), (vii), and (viii) are the following species:


(ia) ;


(iiia) ;


(viia) ; and


(viiia) .

74. The process of any one of claims 1 to 73, wherein the step for preparing compound (iii) is done in the absence of a chromatographic purification step, a solvent exchange step, or a combination thereof.

75. The process of any one of claims 1 to 74 wherein the compound of Formula (I) is a crude crystalline solid, the process further comprising crystallizing a crude form of compound (I) to form a crystalline form of said compound (I), the crystallization process comprising:

dissolving the crude form of compound (I) in a solvent at a temperature below the solvent boiling point to form a solution of compound (I) having a saturation temperature that is less than the dissolution temperature;

filtering the solution of compound (I) through a polish filter at a temperature above the saturation temperature;

seeding the filtered solution of compound (I) with crystalline form of compound (I) and cooling the solution to form crystallized compound (I); and

isolating crystalline compound (I).

76. The process of claim 75, wherein the solvent is a ketone.

77. The process of claim 75 or claim 76, wherein: the solvent is methyl isobutyl ketone; the dissolution temperature is about 90°C; the concentration of compound (I) in solution is from about 7 wt.% to about 7.5 wt.%; compound (I) is crystallized at a final temperature of less than 20°C; and compound (I) is dried to form the purified crystalline compound (I).

78. The process of any one of claims 75 to 77, wherein the yield of crystalline compound (I) in the crystallization step is at least 80%.

79. The process of any one of claims 75 to 78, wherein the purity of crystalline compound (I) is at least 99.5 area%.

80. The process of any one of claims 1 to 79, wherein X^1 is C-R^4.

81. The process of any one of claims 1 to 80, wherein X^2 is N.

82. The process of any one of claims 1 to 81, wherein L^1 is -O-.

83. The process of any one of claims 1 to 82, wherein R^4 is -$(L^1)_{0-1}$-C_{1-6} haloalkyl.

84. The process of any one of claims 1 to 83, wherein R^4 is selected from the group consisting of: methoxy, monofluoromethoxy, difluoromethoxy, trifluoromethoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, tert-butoxy, methyl, monofluoromethyl difluoromethyl, and trifluoromethyl.

85. The process of claim 84, wherein R^4 is selected from the group consisting of: monofluoromethoxy, difluoromethoxy, and trifluoromethoxy.

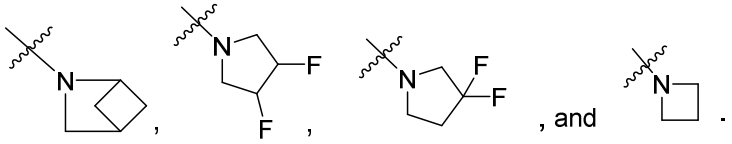
86. The process of claim 85, wherein R^4 is difluoromethoxy.

87. The process of any one of claims 1 to 86, wherein R^1, R^2 and R^3 are each hydrogen.

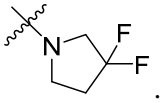
88. The process of any one of claims 1 to 87, wherein A is optionally substituted with from 1 to 5 R^A substituents selected from the group consisting of F, Cl, Br, I, CN, CH_3O-, CH_3, cyclopropylmethyl, CF_3, and butyl.

89. The process of claim 88 wherein A is substituted with F.

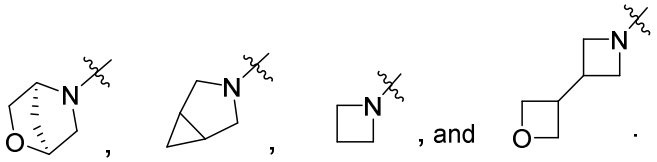
90. The process of any one of claims 1 to 89, wherein A is selected from the group consisting of:



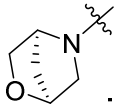
91. The process of claim 90, wherein A is



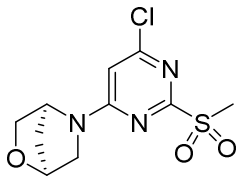
92. The process of any one of claims 1 to 91, wherein Cy is selected from the group consisting of:



93. The process of claim 92, wherein Cy is

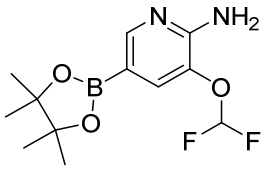


94. The process of any one of claims 1 to 93, wherein compound (iii) is the following species



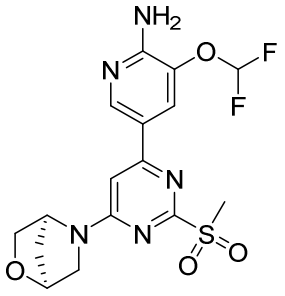
(iiib)

95. The process of any one of claims 1 to 94, wherein compound (iv) is the following species



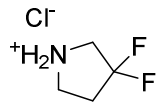
(iva) .

96. The process of any one of claims 1 to 95, wherein compound (v) is the following species



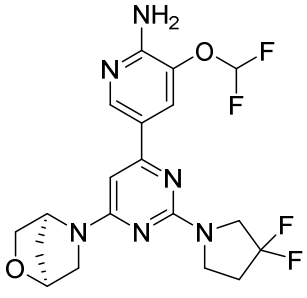
(va) .

97. The process of any one of claims 1 to 96, wherein compound (vi) is the following species



(via) .

98. The process of any one of claims 1 to 97, wherein the compound of formula (I) is the following compound 1 species



1 .

99. The process of claim 98, wherein compound 1 is crystalline free base Form A having a powder X-ray diffraction pattern in accordance with FIG. 1.

100. The compound of formula (I) as defined herein when obtained by the process according to any one of claims 1 to 99.

101. The process of any one of claims 1 to 100 wherein for scheme (C) of claim 1:

R^1, R^2 and R^3 are each H;

X^1 is $–O\text{-}CHF_2$;

halo is Br or Cl and the halogenation reagent is N-bromosuccinamide;

the borylation reagent is bis-pin-diborane; and

R^5 and R^6 together form $\text{-}C(CH_3)_2\text{-}C(CH_3)_2\text{-}$.

102. The process of any one of claims 1 to 101 wherein step 2 and step 3 of scheme (C) are done sequentially in a single vessel.

103. The process of any one of claims 1 to 102 wherein for scheme (D):

R^1 and R^2 are each H;

X^1 is $–O\text{-}CHF_2$;

halo is Br or Cl;

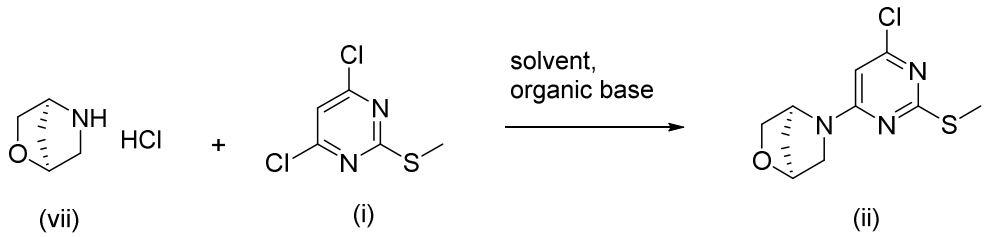
the borylation reagent is bis-pin-diborane; and

R^5 and R^6 together form $\text{-}C(CH_3)_2\text{-}C(CH_3)_2\text{-}$.

104. The process of any one of claims 1 to 103 wherein scheme (D) step 1 and step 2 are done sequentially in a single vessel.

105. A process for preparing compound 1, the process comprising the following steps:

(1) reacting compound (vii) with compound (i) in the presence of a solvent and an organic base to form a reaction mixture comprising compound (ii) according to the following scheme



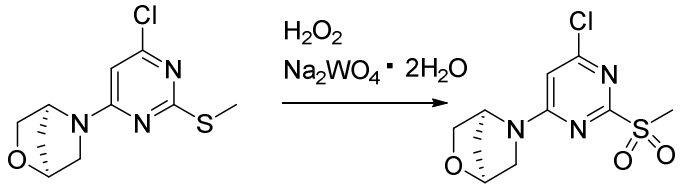
(vii) (i) (ii)

wherein

the solvent is selected from the group consisting of dimethylsulfoxide, acetonitrile, and ethanol, and

the equivalents of the organic base to compound (vii) is from about 2.2:1 to about 2.6:1;

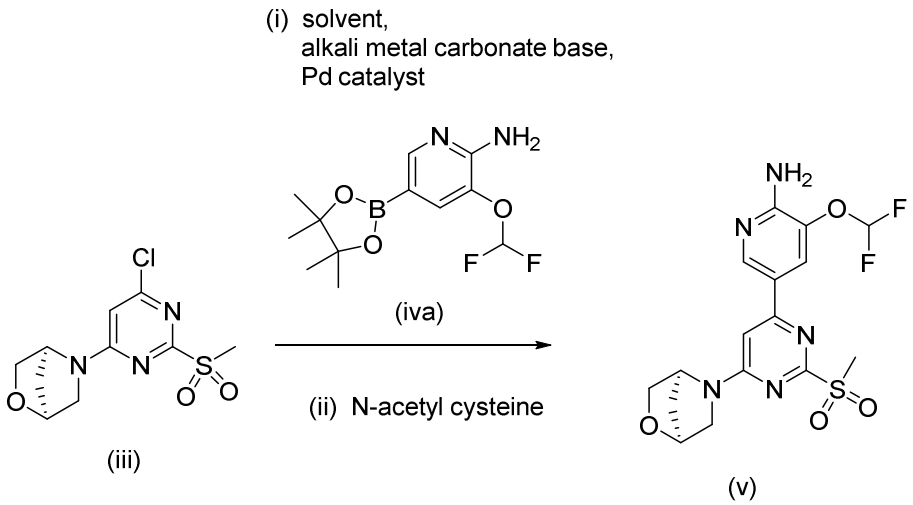
(2) oxidizing compound (ii) with hydrogen peroxide in the presence of sodium tungstate dihydrate ($Na_2WO_4 \cdot 2H_2O$) to form a reaction product mixture comprising compound (iii) according to the following reaction scheme



(ii) (iii)

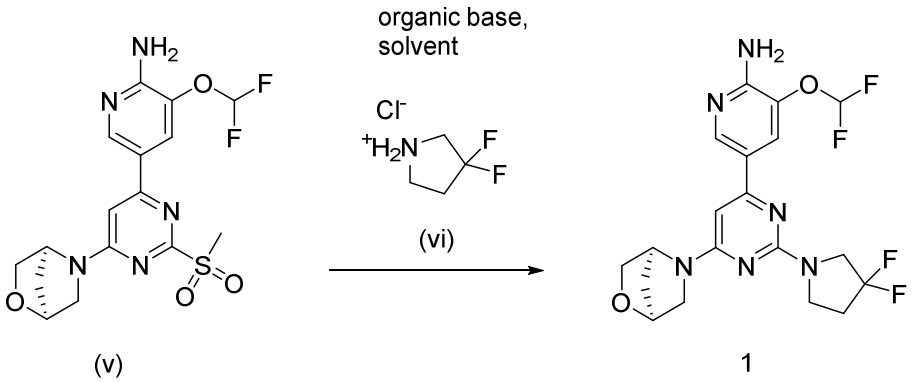
wherein the hydrogen peroxide is added to the reaction product mixture from step (1) and the equivalent ratio of hydrogen peroxide to compound (ii) is from about 2:1 to about 3.5:1;

(3) (i) performing a Suzuki coupling of compound (iii) with compound (iva) in the presence of an alkali metal carbonate base, a palladium catalyst, and a solvent to form a reaction product mixture compound (v), and (ii) adding a catalyst scavenger to the reaction product mixture to scavenge palladium, according to the following scheme



wherein the solvent is tetrahydrofuran and water, and the palladium catalyst is $PdCl_2$(dppf); and

(4) reacting compound (v) with compound (vi) in the presence of at least one organic base, and a solvent to form a reaction product mixture comprising compound 1 according to the following reaction scheme



wherein

the at least one organic base is selected from the group consisting of 1,1,3,3-tetramethylguanidine and 1,8-diazabicyclo[5.4.0]undec-7-ene, and the solvent is selected from the group consisting of toluene, anisole, mesitylene, diethylamine, di-*n*-propylamine, di-isopropylamine, di-*n*-butylamine, and combinations thereof.

106. The process of claim 105, wherein for step (1), the solvent is ethanol, the organic base is triethylamine, and the reaction temperature is from about 30°C to about 40°C.

107. The process of claim 105 or claim 106, wherein for step (2):

the hydrogen peroxide is added over a period of from about 4 hours to about 6 hours;

the reaction temperature is from about 55°C to about 65°C; and

the Na_2WO_4 is $Na_2WO_4 \cdot 2H_2O$ in methanol and water.

108. The process of any one of claims 105 to 107 wherein about two equivalents of hydrogen peroxide are added during a first portion of the reaction, and the remaining hydrogen peroxide is added during a second portion of the reaction.

109. The process of any one of claims 105 to 108, wherein for step (3):

the equivalents of alkali metal carbonate base to compound (iii) is about 3:1, and the alkali metal carbonate base is K_2CO_3 or Na_2CO_3;

the palladium catalyst content is about 0.5 mol% based on compound (iii);

the catalyst scavenger is N-acetyl cysteine; and

the reaction temperature is from about 55°C to about 65°C.

110. The process of any one of claims 105 to 109, wherein for step (3), compound (v) is isolated from the reaction product mixture by the following order of steps: adding seed crystals to the reaction product mixture; adding n-heptane; cooling to form a slurry comprising solid compound (v); and isolating solid compound (v).

111. The process of any one of claims 105 to 110, wherein for step (4):

the solvent is di-n-butylamine;

the at least one organic base further comprises a second base selected from the group consisting of 2,6-lutidine, di-isopropyl ethylamine, and 1,4-diazabicyclo[2.2.2]octane; and

the reaction temperature is from about 115°C to about 125°C.

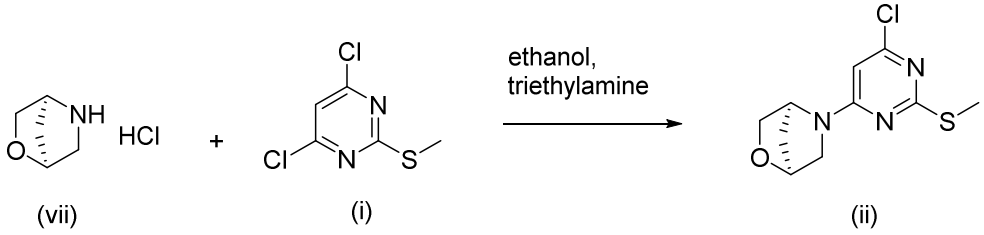
112. The process of any one of claims 105 to 111 further comprising isolating compound 1 from the reaction product mixture by the following order of steps: adding an anti-solvent to the reaction product mixture; cooling to form a slurry comprising solid compound 1; and isolating solid compound 1.

113. The process of claim 112, wherein the anti-solvent is selected from the group consisting of isopropanol and n-propanol.

114. The process of any one of claims 105 to 113, further comprising: forming a supersaturated solution of compound 1 and methyl isobutyl ketone; seeding the supersaturated solution with crystalline compound 1 Form A; cooling the solution to form a slurry comprising crystalline compound 1 Form A; and isolating crystalline compound 1 Form A from the slurry.

115. A process for preparing compound 1 Form A, the process comprising:

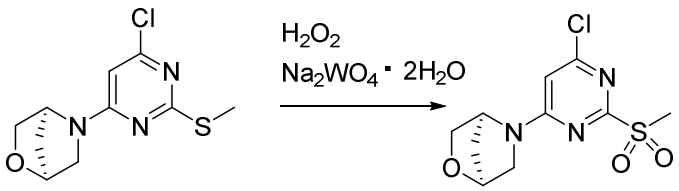
(1) reacting compound (vii) with compound (i) in the presence of ethanol and triethylamine to form compound (ii) according to the following reaction scheme



(vii) (i) (ii)

wherein the equivalents of trimethylamine to compound (vii) is about 2.4:1;

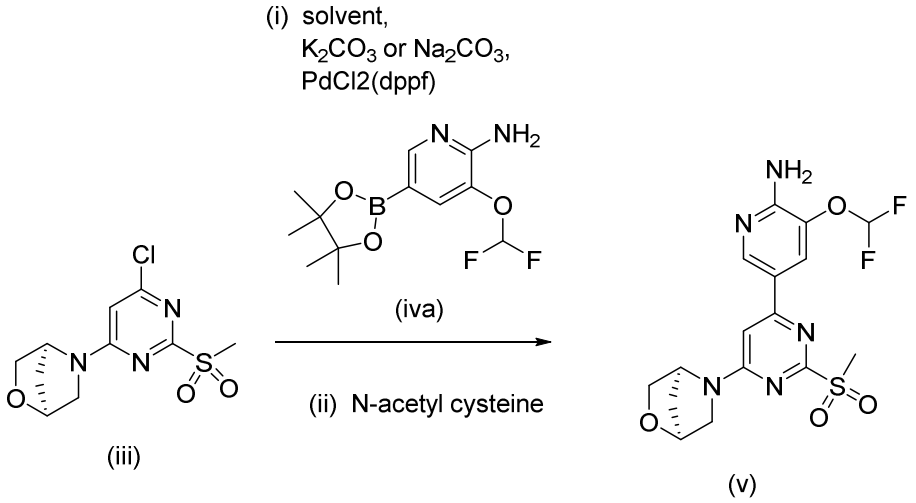
(2) oxidizing compound (ii) with hydrogen peroxide in the presence of sodium tungstate dihydrate ($Na_2WO_4 \cdot 2H_2O$) to form a reaction product mixture comprising compound (iii) according to the following reaction scheme



(ii) (iii)

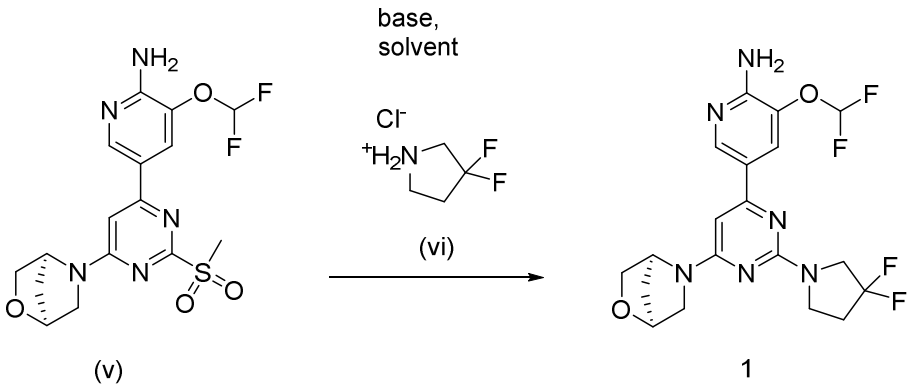
wherein the hydrogen peroxide is added to the reaction product mixture from step (1) and the equivalent ratio of hydrogen peroxide to compound (ii) is about 3:1;

(3) (i) performing a Suzuki coupling of compound (iii) with compound (iva) in the presence of K_2CO_3 or Na_2CO_3, PdCl2(dppf) catalyst, and a tetrahydrofuran and water solvent to form a reaction product mixture compound (v), and (ii) adding a N-acetyl cysteine to the reaction product mixture to scavenge palladium, according to the following scheme



wherein the equivalent ratio of K_2CO_3 or Na_2CO_3 to compound (iii) is about 3:1, and the PdCl2(dppf) content is about 0.5 mol% based on compound (iii);

(4) reacting compound (v) with compound (vi) in the presence of at least one base, and a solvent to form a reaction product mixture comprising compound 1 according to the following reaction scheme



wherein

the at least one base is selected from the group consisting of 1,1,3,3-tetramethylguanidine and 1,8-diazabicyclo[5.4.0]undec-7-ene, and

the solvent is selected from the group consisting of toluene, anisole, mesitylene, diethylamine, di-*n*-propylamine, di-isopropylamine, di-*n*-butylamine, and combinations thereof; and

(5) isolating compound 1 from the step (4) reaction product mixture by the following order of steps: adding an anti-solvent selected from isopropanol and

n-propanol to the reaction product mixture; cooling the reaction product mixture to form a slurry comprising solid compound 1; and isolating solid compound 1 from the reaction product mixture; and

(6) forming a supersaturated solution of compound 1 and methyl isobutyl ketone; seeding the supersaturated solution with crystalline compound 1 Form A; cooling the solution to form a slurry comprising crystalline compound 1 Form A; and isolating crystalline compound 1 Form A from the slurry.

116. The process of claim 115, wherein for step (2), the hydrogen peroxide is added over a period of from about 4 hours to about 6 hours.

117. The process of clam 115 or claim 116, wherein for step (2), about two equivalents of H_2O_2 are added during a first portion of the reaction, and the remaining H_2O_2 is added during a second portion of the reaction.

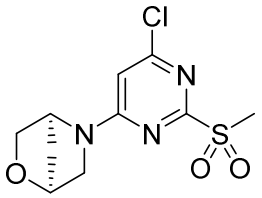
118. The process of any one of claims 115 to 117, wherein for step (3), the reaction temperature is from about 55°C to about 65°C; and the Na_2WO_4 is $Na_2WO_4 \cdot H_2O$ in methanol and water.

119. The process of any one of claims 115 to 118, wherein for step (3), compound (v) is isolated from the reaction product mixture by the following order of steps: adding seed crystals to the reaction product mixture; adding n-heptane to the reaction product mixture; cooling the reaction product mixture to form a slurry comprising solid compound (v); and isolating solid compound (v).

120. The process of any one of claims 115 to 119, wherein for step (4): the solvent is di-n-butylamine; the at least one base further comprises a second base selected from the group consisting of 2,6-lutidine, di-isopropyl ethylamine, and 1,4-diazabicyclo[2.2.2]octane; and the reaction temperature is from about 115°C to about 125°C.

121. The process of any one of claims 115 to 120, wherein compound 1 Form A has an X-ray powder diffraction pattern having at least two peaks at positions selected from the group consisting of 7.7 ± 0.3 (º2θ), 12.1 ± 0.3 (º2θ), 16.2 ± 0.3 (º2θ), 16.4 ± 0.3 (º2θ), 16.6 ± 0.3 (º2θ), 17.1 ± 0.3 (º2θ), 18.8 ± 0.3 (º2θ), 19.4 ± 0.3 (º2θ), 19.8 ± 0.3 (º2θ), 20.3 ± 0.3 (º2θ), 20.5 ± 0.3 (º2θ), 23.3 ± 0.3 (º2θ), 24.7 ± 0.3 (º2θ), 25.3 ± 0.3 (º2θ), and 26.5 ± 0.3 (º2θ).

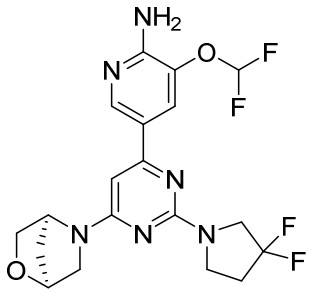
122. A compound of formula (iii)



(iii)

.

123. A crystalline form of compound I



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wherein the crystalline form has an X-ray powder diffraction pattern having at least two peaks at positions selected from the group consisting of 7.7 ± 0.3 (º2θ), 12.1 ± 0.3 (º2θ), 16.2 ± 0.3 (º2θ), 16.4 ± 0.3 (º2θ), 16.6 ± 0.3 (º2θ), 17.1 ± 0.3 (º2θ), 18.8 ± 0.3 (º2θ), 19.4 ± 0.3 (º2θ), 19.8 ± 0.3 (º2θ), 20.3 ± 0.3 (º2θ), 20.5 ± 0.3 (º2θ), 23.3 ± 0.3 (º2θ), 24.7 ± 0.3 (º2θ), 25.3 ± 0.3 (º2θ), and 26.5 ± 0.3 (º2θ).

124. The crystalline form of claim 123, wherein the crystalline form has an X-ray powder diffraction pattern having at least two peaks at positions selected from the group consisting of 7.7 ± 0.3 (º2θ), 18.8 ± 0.3 (º2θ), 19.8 ± 0.3 (º2θ), 24.7 ± 0.3, (º2θ) and 26.5 ± 0.3 (º2θ).

125. The crystalline form of claim 123, wherein said crystalline form has the X-ray powder diffraction pattern of FIG. 1.

126. A pharmaceutical composition comprising the crystalline form of claim 123 and at least one excipient.

127. A process of preparing the crystalline form of compound I of claim 123, the method comprising dissolving compound I in a solvent to form a solution, forming a slurry of crystals of compound I therefrom, and isolating crystallilzed compound I.

128. The process of 127, wherein the solution of compound I is filtered prior to crystal formation thereof, and the filtered solution is seeded with crystalline compound I and cooled to form crystallized compound I.

129. Use of the crystalline form of claim 123 in the manufacture of a medicament for ~~A method of~~ treating a neurodegenerative condition ~~comprising administering an effective amount of the crystalline form of claim 123~~.