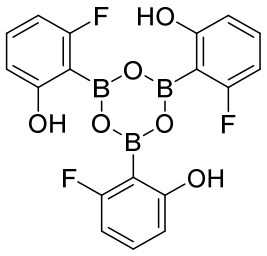
CLAIMS

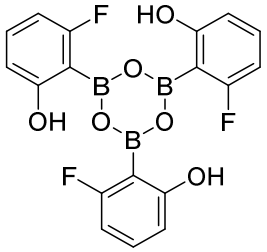
What is claimed is:

1. A compound of Formula 6A



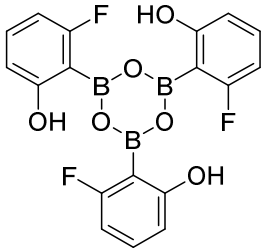
(6A).

2. A composition, the composition comprising a compound of Formula 6A



(6A).

3. A process of preparing a compound of formula 6A



(6A),

comprising admixing (2-fluoro-6-methoxyphenyl) boronic acid with an acid in a solvent to form the compound of Formula 6A.

4. The process of claim 3, wherein 1.0 molar equivalents of the (2-fluoro-6-methoxyphenyl) boronic acid are admixed with 1.2 molar equivalents of the acid.

5. The process of claim 3 or claim 4, comprising preparing a first mixture of the acid in the solvent before admixing the (2-fluoro-6-methoxyphenyl) boronic acid and the acid.

6. The process of claim 5, wherein the first mixture is cooled to -20°C.

7. The process of any one of claims 3-6, comprising preparing a second mixture of the (2-fluoro-6-methoxyphenyl) boronic acid in the solvent before admixing the (2-fluoro-6-methoxyphenyl) boronic acid and the acid.

8. The process of claim 7, comprising adding the second mixture to the first mixture while maintaining the solvent temperature between -15°C and -25°C.

9. The process of claim 8, wherein the (2-fluoro-6-methoxyphenyl) boronic acid and the acid are maintainted in the combined first and second mixture for approximately 2 hours.

10. The process of any one of claims 3-9, wherein the acid is boron tribromide.

11. The process of any one of claims 3-10, wherein the solvent comprises dichloromethane.

12. The process of any one of claims 3-11, wherein the process further comprises a process of making (2-fluoro-6-methoxyphenyl) boronic acid, comprising:

a) a first step of admixing a first base, a secondary amine base and a catalyst in a solvent to prepare a first mixture;

b) a second step of admixing 3-fluoroanisole to the first mixture to prepare a second mixture; and

c) a third step of admixing a reagent to the second mixture to form the (2-fluoro-6-methoxyphenyl) boronic acid.

13. The process of claim 12, wherein the first base is n-butyl lithium.

14. The process of claim 12 or claim 13, wherein 1.5 molar equivalents of the first base are admixed.

15. The process of any one of claims 8-14, wherein the secondary amine base is diisopropylamine.

16. The process of claim 15, wherein 1.4 molar equivalents of the secondary amine base are admixed.

17. The process of any one of claims 12-16, wherein the catalyst is triethylamine hydrochloride.

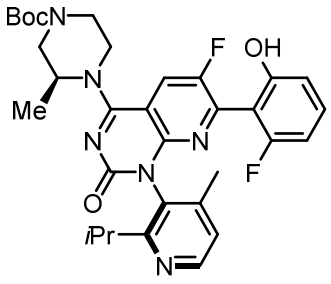
18. The process of claim 17, wherein 0.01 molar equivalents of the catalyst are admixed.

19. The process of any one of claims 12-18, wherein the reagent is triethyl borate.

20. The process of claim 19, wherein 2.0 molar equivalents of the reagent are admixed.

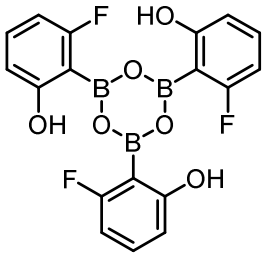
21. The process of any one of claims 12-20, wherein the first, second and third steps are conducted at -70°C.

22. A process of preparing a compound of Formula 7



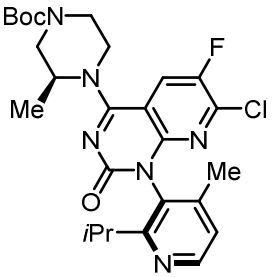
(7),

comprising admixing a compound of Formula 6A



(6A),

with a compound of Formula 6



(6), in the presence of dichlorobis(diphenylphosphinophenyl)ether palladium (II) ($Pd(dpePhos)Cl_2$), and potassium acetate to form the compound of Formula 7.

23. The process of claim 22, wherein 1.0 molar equivalents of the compound of Formula 6 are admixed with 0.5 molar equivalents of the compound of Formula 6A.

24. The process of claim 22 or claim 23, wherein 1.0 molar equivalents of the compound of Formula 7 are admixed with 0.003 molar equivalents of $Pd(dpePhos)Cl_2$.

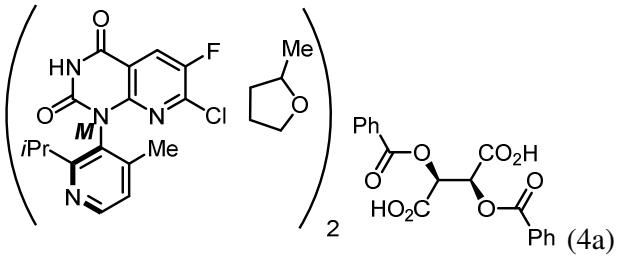
25. The process of any one of claims 22-24, wherein 1.0 molar equivalents of the compound of Formula 7 are admixed with 2.0 molar equivalents of potassium acetate.

26. The process of any one of claims 22-25, wherein the compound of Formula 7, the compound of Formula 6A, the Pd(dpePhos)Cl2, and the potassium acetate are admixed in a solvent, wherein the solvent comprises 2-methyl tetrahydrofuran.

27. The process of claim 26, wherein the solvent further comprises water.

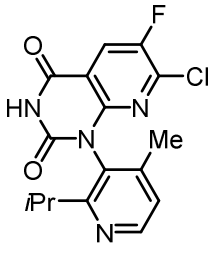
28. The process of claim 26 or claim 27, wherein the solvent is maintained at 75±5°C.

29. A process of preparing a compound of Formula 4a



(4a)

comprising admixing 1.0 molar equivalent of a compound of Formula 4



(4)

with 3.0 molar equivalents of (+)-2,3-dibenzoyl-D-tartaric acid in the presence of 2-methyltetrahydrofuran to form the compound of Formula 4a.

30. The process of claim 29, wherein the compound of Formula 4 and the (+)-2,3-dibenzoyl-D-tartaric acid are admixed in a solvent, wherein the solvent comprises 2-methyltetrahydrofuran and heptane.

31. A process of preparing 4,7-dichloro-6-fluoro-1-(2-isopropyl-4-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one, comprising

(a) a first step of preparing a first mixture of 7-chloro-6-fluoro-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione and a solvent;

(b) a second step of preparing a second mixture of POCl3, N,N-diisopropylamine, and a solvent; and

(c) a third step of admixing the first mixture to the second mixture to form 4,7-dichloro-6-fluoro-1-(2-isopropyl-4-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one.

32. The process of claim 31, wherein one molar equivalent of the 7-chloro-6-fluoro-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione is admixed with 1.5 molar equivalents of the $POCl_3$.

33. The process of claim 31 or claim 32, wherein one molar equivalent of the 7-chloro-6-fluoro-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione is admixed with 2.0 molar equivalents of the N,N-diisopropylamine.

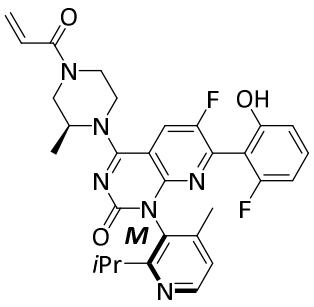
34. The process of any one of claims 31-33, wherein the solvent comprises toluene.

35. The process of any one of claims 31-34, wherein the admixing of the third step is conducted at 30±5°C.

36. The process of any one of claims 31-35, wherein the 7-chloro-6-fluoro-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione is stereoisomerically enriched with 7-chloro-6-fluoro-(1M)-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione.

37. The process of claim 31-35, wherein the 7-chloro-6-fluoro-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione is substantially stereoisomerically pure 7-chloro-6-fluoro-(1M)-1-[4-methyl-2-(propan-2-yl)pyridin-3-yl]pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione.

38. A process of preparing a compound of Formula 9



(9)

or a pharmaceutically acceptable salt thereof, comprising a process of any one of claims 3-37.