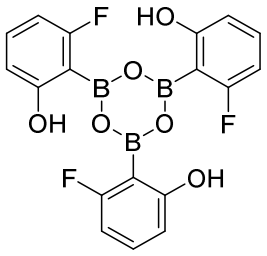
CLAIMS

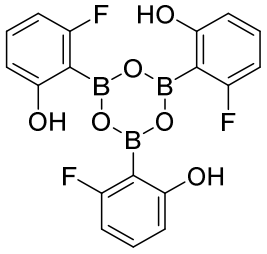
What is claimed is:

1. A compound of Formula 6A~~:~~



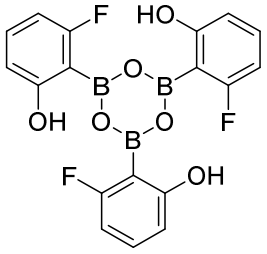
(6A).

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



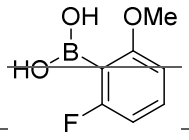
(6A).

3. A ~~method of making~~process of preparing a compound of formula 6A~~:~~



(6A),

~~the method~~ comprising admixing (2-fluoro-6-methoxyphenyl) boronic acid ~~reacting a mixture comprising a compound having the structure:~~



with an acid ~~with at least one~~ 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.

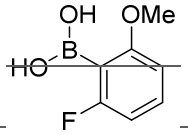
9. The process of claim 8, wherein the (2-fluoro-6-methoxyphenyl) boronic acid and the acid are maintainted in the combined first and second mixture for approximately 2 hours.

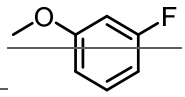
~~4.~~10. The~~n method~~ process of any one of claims 3-9, wherein the acid is boron tribromide~~BBr_3~~.

~~5.~~11. The ~~method~~ process of any one of claims 3-10, wherein the ~~at least one~~ solvent ~~is~~ comprises dichloromethane.

~~6. The method of claim 3, wherein the at least one solvent is heptane.~~

~~7. The method of claim 3, wherein the mixture is cooled to approximately -20 °C.~~

~~8. The method of claim 3, wherein the method of making a compound of the structure:~~ 

~~comprises mixing a compound having the structure:~~ 

~~with a reagent, a first base, a secondary amine base, a catalyst, and an acid.~~

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.

~~9.~~13. The ~~method~~ process of claim ~~8~~12, wherein the first base ~~in~~is n-~~B~~butyl lithium.

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

~~10.~~15. The ~~method~~ 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.

~~11.~~17. The ~~method~~ process of any one of claims ~~8~~12-16, wherein the catalyst is triethylamine hydrochloride.

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

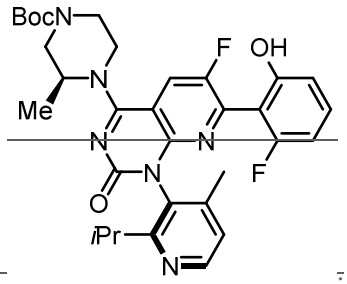
~~12.~~19. The ~~method~~ process of any one of claims ~~8~~12-18, wherein the reagent is triethyl borate.

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

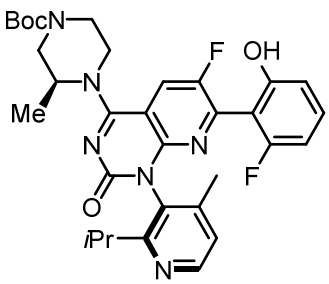
21. The process of any one of claims 12-20, wherein the first, second and third steps are conducted at -70°C.

~~13. The method of claim 8, wherein the acid is HCl.~~

~~14. The method of claim 3, wherein the compound of formula 6A is used to generate a compound having the Formula 7:~~

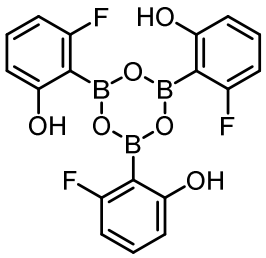


~~15.~~22. ~~The method of making~~ A process of preparing a compound of Formula 7~~,~~



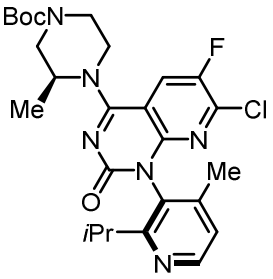
(7),

comprising admixingthe steps of reacting 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 7KOAc.

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.

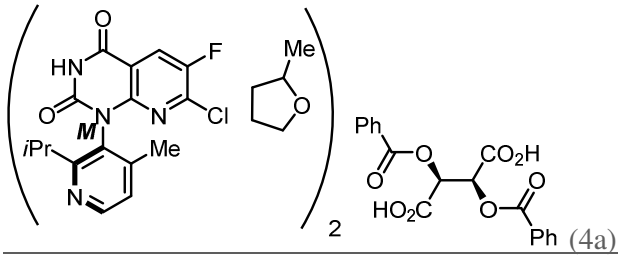
25. The process of any one of claims 22-24, wherein 1.0 molar equivalents of the compound of Formula 7 are admixed with 2.0 molar equivalents of potassium acetate.

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.

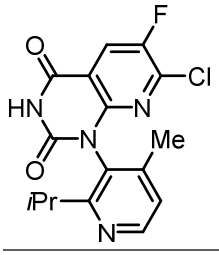
28. The process of claim 26 or claim 27, wherein the solvent is maintained at 75±5°C.

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.

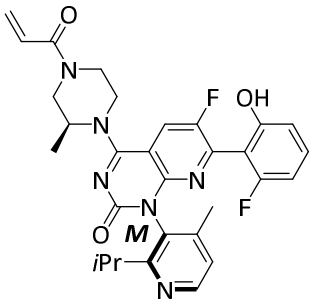
34. The process of any one of claims 31-33, wherein the solvent comprises toluene.

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.

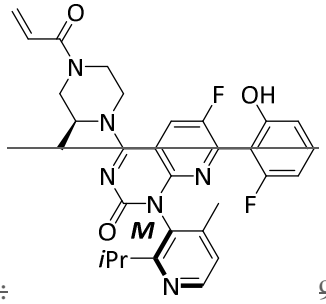
38. A process of preparing a compound of Formula 9



(9)

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

~~16. The method of claim 3, wherein the compound of formula 6A is used to generate a compound having the Formula 9:~~



~~9.~~

~~17. The method of claim 16, wherein the method further comprises mixing the compound of Formula 9 with at least one pharmaceutically acceptable excipient to form a pharmaceutical composition.~~