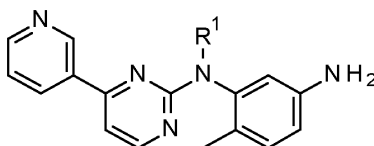
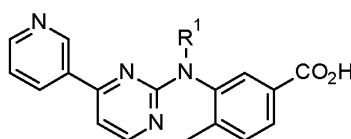


Claims:

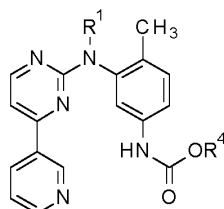
1. A method for the synthesis of a compound of Formula IIIa:

**Formula IIIa**

- wherein R¹ is H or a nitrogen protecting group, the method comprising treating a compound of Formula Ia
5 with reagents to form an acyl azide:

**Formula Ia**

- wherein R¹ is H or a nitrogen protecting group;
followed by decomposition of the acyl azide to provide an isocyanate; which isocyanate undergoes
nucleophilic attack with an alcohol or water.
10
2. The method of claim 1, wherein the isocyanate undergoes nucleophilic attack with an alcohol
R⁴OH to provide a compound of Formula XIII:

**Formula XIII**

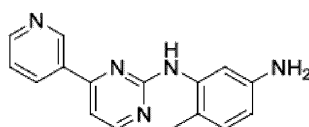
- wherein R⁴ is an optionally substituted C₁-7 alkyl.
15
3. The method of claim 2, wherein R⁴ is selected from *t*-butyl and an optionally substituted benzyl
group.
20
4. The method of claim 3, wherein R⁴ is selected from *t*-butyl, benzyl and 2,4-dimethoxybenzyl.
5. The method of claim 4, wherein R⁴ is *t*-butyl.
6. The method of any preceding claim, wherein the reagents for acyl azide formation comprise
diphenylphosphoryl azide (DPPA).
25

7. The method of any preceding claim, wherein R¹ is *t*-butyloxycarbonyl.

8. The method of any preceding claim, wherein R¹ is not H and the method further comprises a deprotection step to remove the R¹ nitrogen protecting group.

5

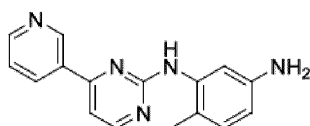
9. The method of claim 8, wherein the deprotection step uses trifluoroacetic acid and the deprotection affords a compound of Formula III as the free base:



Formula III

10. The method of claim 8, wherein the deprotection step uses hydrochloric acid and the deprotection affords a compound of Formula III as the hydrochloride salt:

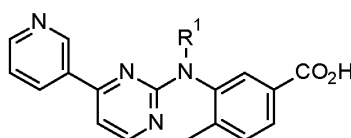
10



Formula III

.HCl.

11. A compound of Formula Ia:

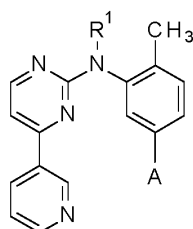


Formula Ia

15

wherein R¹ is a nitrogen protecting group.

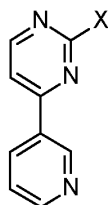
12. A compound of Formula VIIIa:



Formula VIIIa

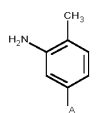
20 wherein R¹ is H or a nitrogen protecting group; and A is CN.

13. The compound of either claim 11 or claim 12, wherein R¹ is selected from *tert*-butyloxycarbonyl (Boc), fluorenylmethyloxycarbonyl (Fmoc), α,α -dimethyl-3,5-dimethoxybenzyloxycarbonyl (Ddz), 2-(4-biphenyl)isopropoxycarbonyl (Bpoc), *p*-methoxybenzyl (PMB) and 2,4-dimethoxybenzyl.
- 5 14. A method for the synthesis of a compound of Formula Ia, the method comprising effecting a coupling reaction between a compound of Formula XI:



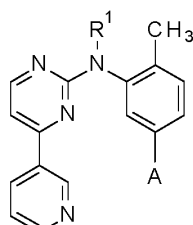
Formula XI

and a compound of Formula XIIa:



Formula XIIa

- 10 to provide a compound of Formula VIIIa:



Formula VIIIa

wherein R¹ is H;

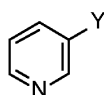
X is a halogen, OTf or OTs, optionally Cl;

and A is COOR² or CN;

- 15 wherein R² is an optionally substituted C₁₋₄ alkyl.

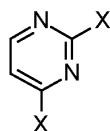
15. The method of claim 14, wherein A is COOR².

16. The method of either claim 14 or claim 15, the method comprising providing a compound of
- 20 Formula XI by coupling of a compound of Formula IX:



Formula IX

with a compound of Formula X:

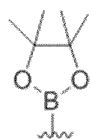


Formula X

wherein each substituent X in Formula X is independently a halogen or OTf, optionally Cl;

5 and Y is a halogen, OTf, OTs, or other group suitable for cross coupling.

17. The method of claim 16, wherein Y is selected from a halogen, OTf, OTs, $-\text{SnR}^{\text{A}}_3$, $-\text{B}(\text{OH})_2$ and



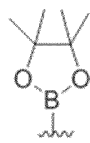
; wherein R^{A} is C_{1-4} alkyl.

10 18. The method of claim 17, wherein Y is a halogen, OTf or $-\text{B}(\text{OH})_2$.

19. The method of any one of claims 16 to 18, the method comprising treating the compound of Formula IX with magnesium to form a Grignard reagent.

15 20. The method of any one of claims 16 to 18, the method comprising treating the compound of Formula IX with zinc to form an organozinc Negishi reagent.

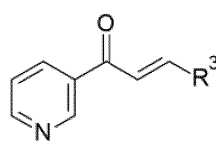
21. The method of either claim 16 or claim 17, the method comprising providing a compound of Formula XI by Suzuki coupling of a compound of Formula IX with a compound of Formula X; wherein Y is



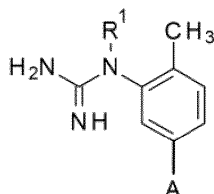
20 $-\text{B}(\text{OH})_2$ or

22. A method for the synthesis of a compound of Formula Ia, the method comprising reacting a compound of Formula VII:

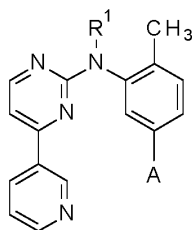
46

**Formula VII**

with a compound of Formula VIa:

**Formula VIa**

5 to provide a compound of Formula VIIIa:

**Formula VIIIa**

wherein Formula VIa is the free base or a chloride, bromide, iodide, mesylate, sulfate, phosphate, nitrate, acetate, oxalate, citrate, or tartrate salt; A is CN; R¹ is H or a nitrogen protecting group; and R³ is a suitable leaving group, optionally dialkyl-substituted nitrogen.

10

23. The method of claim 22, wherein R¹ is H.

24. The method of either claim 22 or claim 23, wherein R³ is NMe₂.