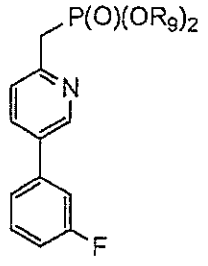
Claims

1. A process for preparing Compound 16:



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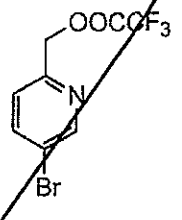
said process comprising the steps of:

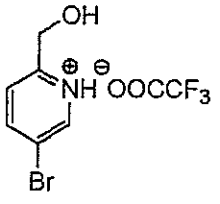
(a) treating 5-bromo-2-methylpyridine N-oxide with the anhydride of trifluoroacetic acid to produce intermediate Compound 35:

35



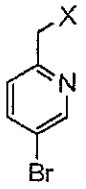
(b) treating the non-isolated intermediate Compound 35 with an alcohol at an elevated temperature to produce Compound 36:

36



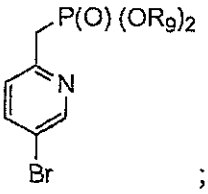
(c) treating Compound 36 with a leaving group reagent to produce Compound 37:

37



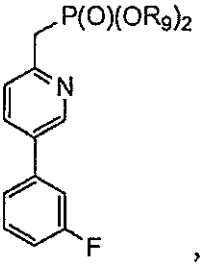
(d) treating Compound 37 with a phosphate reagent to produce Compound 38 or a salt thereof:

38



; and,

(e) treating Compound 38 with 3-$FC_6H_4B(OR_{11})_2$, to produce Compound 16 using PdL_n or Pd/C to form compound 16



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wherein:

R_{11} is H, C_1 to C_{10} alkyl, aryl, or heteroaryl;

L is PR'_3 or $NR"_3$, wherein R'_3 is selected from alkyl, aryl and alkylaryl, and R" is selected from the group consisting of alkyl, aryl, and alkylaryl; and

n is between 0 and 8.

2. The process of claim 1, wherein said anhydride is selected from the group consisting of aromatic acid anhydride, acetic anhydride, and trihalogenated acetic anhydride.

3. The process of claim 1 or claim 2, wherein R_{12} is CF_3

4. The process of claim 1, wherein said alcohol is selected from the group consisting of methanol, ethanol, propanol, isopropanol, butanol, sec-butanol, t-butanol, pentanol, and octanol, and mixtures of 2 or more thereof.

5. The process of any one of claims 1 to 4, wherein said elevated temperature is about 20 to about 80°C, preferably about 30 to 70°C, more preferably about 45 to about 55°C

6. The process of claim 1, wherein said temperature is between about 45 and about 55°C.

7. The process of claim 1, wherein said leaving group reagent is selected from the group of consisting $SOCl_2$, $SOBr_2$, PCl_3, PBr_3, PCl_5, PBr_5, R_8COCl, and R_8SO_2Cl, and wherein R_8 is selected from the group consisting of C_1 to C_{10} alkyl, aryl, and arylalkyl.

8. The process of claim 1, wherein said phosphate reagent is prepared from a strong base and $(R_9O)_2P(O)H$, wherein R_9 is selected from the group consisting of C_1-C_{10} alkyls, aryls, heteroaryls, and arylalkyls.

9. The process of claim 6, wherein said strong base is selected from the group consisting of metal hydrides, $R_{10}Li$, and $((R_{10})_3Si)_2Li$, wherein R_{10} is selected from C_1 to C_{10} alkyl and aryl groups.

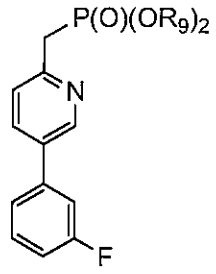
10. The process of claim 1, wherein R_{11} is H.

11. The process of claim 1, wherein L is PPh_3.

12. The process of claim 1, wherein n is between 0 and 4.

Claims

1. A process for preparing Compound 16:



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said process comprising the steps of:

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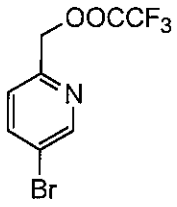
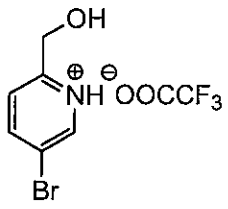


(b) treating the non-isolated intermediate Compound 35 with an alcohol at an elevated temperature to produce Compound 36:

36



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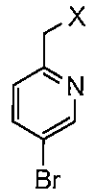
37



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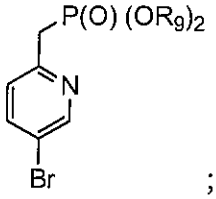
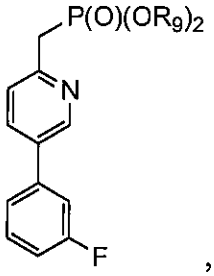


; and,

(e) treating Compound 38 with 3-$FC_6H_4B(OR_{11})_2$, to produce Compound 16 using PdL_n or Pd/C to form compound 16



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wherein:

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L is PR'_3 or $NR"_3$, wherein R'_3 is selected from alkyl, aryl and alkylaryl, and R" is selected from the group consisting of alkyl, aryl, and alkylaryl; and

n is between 0 and 8.

2. The process of claim 1, wherein said anhydride is selected from the group consisting of aromatic acid anhydride, acetic anhydride, and trihalogenated acetic anhydride.

3. The process of claim 1, wherein said alcohol is selected from the group consisting of methanol, ethanol, propanol, isopropanol, butanol, sec-butanol, t-butanol, pentanol, and octanol, and mixtures of 2 or more thereof.

4. The process of any one of claims 1 to 3, wherein said elevated temperature is about 20 to about 80°C, preferably about 30 to 70°C, more preferably about 45 to about 55°C

5. The process of claim 1, wherein said temperature is between about 45 and about 55°C.

6. The process of claim 1, wherein said leaving group reagent is selected from the group of consisting $SOCl_2$, $SOBr_2$, PCl_3, PBr_3, PCl_5, PBr_5,

R_8COCl, and R_8SO_2Cl, and wherein R_8 is selected from the group consisting of C_1 to C_{10} alkyl, aryl, and arylalkyl.

7. The process of claim 1, wherein said phosphate reagent is prepared from a strong base and $(R_9O)_2P(O)H$, wherein R_9 is selected from the group consisting of C_1-C_{10} alkyls, aryls, heteroaryls, and arylalkyls.

8. The process of claim 5, wherein said strong base is selected from the group consisting of metal hydrides, $R_{10}Li$, and $((R_{10})_3Si)_2Li$, wherein R_{10} is selected from C_1 to C_{10} alkyl and aryl groups.

9. The process of claim 1, wherein R_{11} is H.

10. The process of claim 1, wherein L is PPh_3.

11. The process of claim 1, wherein n is between 0 and 4.