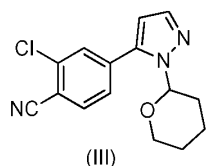


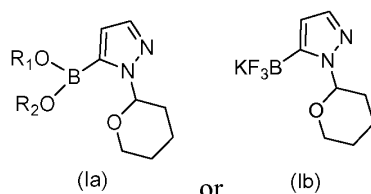
Claims

1. A method for the preparation of 2-chloro-4-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl)benzonitrile of formula (III)

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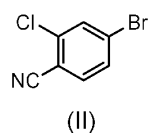


comprising reacting a compound of formula (Ia) or (Ib)



10 wherein R₁ and R₂ are hydrogen, or R₁ and R₂ together form a straight or a branched C₂₋₆ alkyl chain or a -C(O)-CH₂-N(CH₃)-CH₂-C(O)- chain,

with 4-bromo-2-chlorobenzonitrile of formula (II)



15

at an elevated temperature in the presence of heterogeneous palladium catalyst, a solvent and a base.

20 2. A method according to claim 1, wherein the heterogeneous palladium catalyst is palladium on carbon, palladium on barium sulfate, palladium on metal oxides, palladium on silicon dioxide or palladium on zeolites.

3. A method according to claim 2, wherein palladium on metal oxides is palladium on alumina.

25

4. A method according to any of preceding claims, wherein the solvent comprises dimethyl sulfoxide (DMSO).

5. A method according to claim 4, wherein the solvent comprises a mixture of dimethyl sulfoxide (DMSO) and water.

5 6. A method according to claim 5, wherein the ratio of water to DMSO is from about 0:100 to about 50:50, preferably from about 1:99 to about 35:65, more preferably from about 5:95 to about 20:80, for example 10:90, by volume.

7. A method according to any of the preceding claims, wherein the
10 base is diisopropylethylamine (DIPEA).

8. A method according to any of the preceding claims, wherein the reaction is carried out in the presence of phase transfer catalyst.

15 9. A method according to claim 8, wherein phase transfer catalyst is a quaternary ammonium salt.

10. A method according to claim 9, wherein the quaternary ammonium salt is tetrabutylammonium bromide or tetrabutylammonium chloride.

20 11. A method according to claim 1, wherein the reaction is conducted in DMSO-water solvent in the presence of a base which is diisopropylethylamine (DIPEA) and a phase transfer catalyst which is tetrabutylammonium bromide or tetrabutylammonium chloride.

25 12. A method according to any of the preceding claims, wherein the reaction temperature is from about 60 °C to about 100 °C, preferably from about 70 °C to about 80 °C, for example 72 – 78 °C.

30 13. A method according to any of the preceding claims, wherein the amount of palladium catalyst used per amount of compound of formula (II) is from about 0.2 to about 1 mol-%, preferably from about 0.4 to about 0.8, mol-%.

14. A method according to any of the preceding claims, wherein the reaction
35 is carried out under nitrogen atmosphere.

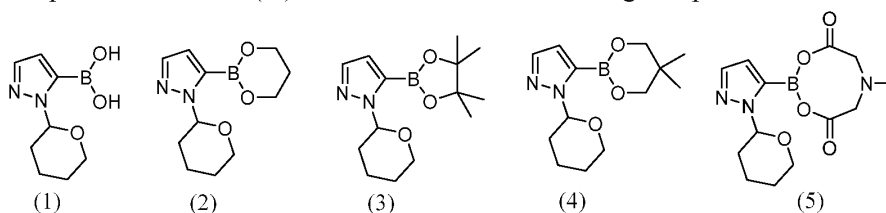
15. A method according to any of the preceding claims, wherein the reaction time is 1 – 5 h, preferably 2 – 4 h.

16. A method according to any of the preceding claims, further comprising
 5 the steps of
 (b) removing the catalyst from the reaction mixture;
 (c) adding water to the cooled reaction mixture; and
 d) isolating the precipitated compound of formula (III).

17. A method according to claim 16, further comprising adding ethanol to the reaction mixture before removing the catalyst from the reaction mixture.

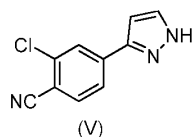
18. A method according to 16 or 17, wherein the isolation of the compound of formula (III) is carried out at 10 – 30 °C, preferably at 15 – 25 °C.

19. A method according to any of the preceding claims, wherein the compound of formula (Ia) is selected from the following compounds:



20. A method according to claim 19, wherein the compound of formula (Ia) is 1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (3).

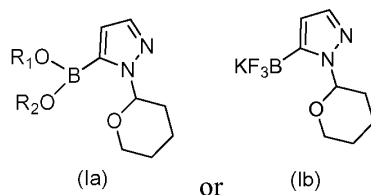
21. A method for the preparation of 2-chloro-4-(1H-pyrazol-3-yl)benzonitrile
 25 of formula (V)



comprising the steps of

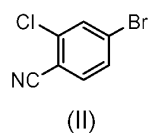
(a) reacting a compound of formula (Ia) or (Ib)

18



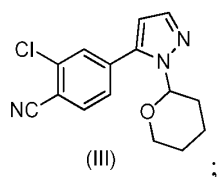
wherein R_1 and R_2 are hydrogen, or R_1 and R_2 together form a straight or a branched C_{2-6} alkyl chain or a $-C(O)-CH_2-N(CH_3)-CH_2-C(O)-$ chain,

5 with 4-bromo-2-chlorobenzonitrile of formula (II)



at an elevated temperature in the presence of heterogeneous palladium catalyst, a solvent and a base to obtain a compound of formula (III)

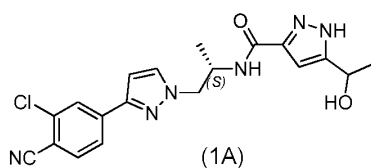
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(b) treating the compound of formula (III) with HCl;
(c) adding a base to obtain the compound of formula (V).

15

22. A method for the preparation of the compound of formula (1A)

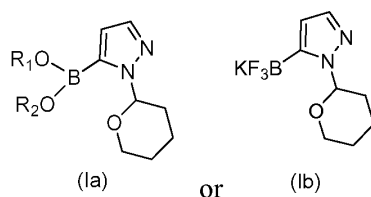


comprising the steps of

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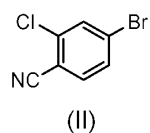
(a) reacting a compound of formula (Ia) or (Ib)

19



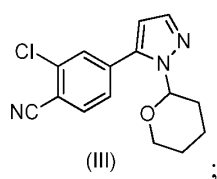
wherein R_1 and R_2 are hydrogen, or R_1 and R_2 together form a straight or a branched C_{2-6} alkyl chain or a $-C(O)-CH_2-N(CH_3)-CH_2-C(O)-$ chain,

5 with 4-bromo-2-chlorobenzonitrile of formula (II)



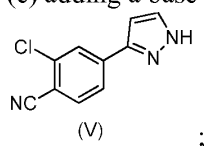
at an elevated temperature in the presence of heterogeneous palladium catalyst, a solvent and a base to obtain a compound of formula (III)

10



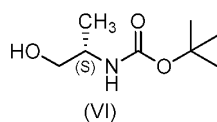
(b) treating the compound of formula (III) with HCl;

(c) adding a base to obtain the compound of formula (V)

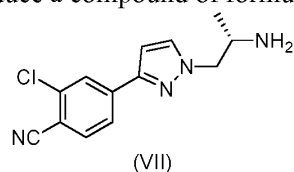


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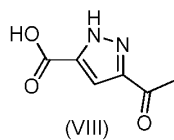
(d) reacting a compound of formula (V) with a compound of formula (VI)



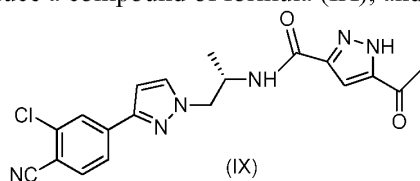
to produce a compound of formula (VII);



(e) reacting the compound of formula (VII) with a compound of formula (VIII)



to produce a compound of formula (IX); and



5

(f) reducing the compound of formula (IX) to produce the compound of formula (1A).