SUPPLEMENTARY MATERIAL

Palladium catalyzed Suzuki cross-coupling of 2-halo-deazapurines with potassium organotrifluoroborate salts in the regioselective synthesis of imidazo[4,5-b]pyridine analogues

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1) Procedure for the coupling of 2-halo imidazo[4,5-b]pyridine with different potassium organotrifluoroborates

**Method A**

To a degassed solution of 3-substituted-2-halo imidazo[4,5-b]pyridine derivative, 3 (1 equiv.) in acetonitrile/water (1:2), was added Palladium catalyst (4 mol %), and phosphine ligand (8 mol %). The solution was again purged with nitrogen and stirred at room temperature for 15 min, at this time the potassium organotrifluoroborate salts (1.3 equiv.), cesium acetate (3 equiv.) and tetrabutylammonium acetate (1 equiv.) were added. The reaction solution was purged again with nitrogen and then placed in the microwave and heated for 20 to 50 min at 150 °C. When TLC and LC-MS showed full consumption of starting materials, the reaction mixture was diluted with ethyl acetate, separated the ethyl acetate layer, washed with water, followed by brine wash and was dried over anhydrous sodium sulfate and concentrated to get the crude material. The crude product was directly purified by column chromatography (0–20% hexane/EtOAc) to isolate the 3-substituted-2-aryl/heteroaryl imidazo[4,5-b]pyridine derivatives.

**Method B**

To a degassed solution of 3-substituted-2-halo imidazo[4,5-b]pyridine derivative (1 equiv.) in acetonitrile/water (1:2) in a sealed vial, was added palladium catalyst (4 mol%), and phosphine ligand (8 mol%). The solution was again purged with nitrogen, stirred at room temperature for 15 min. and potassium organotrifluoroborate salts (1.3 equiv.) and cesium acetate (3 equiv.) were added. The reaction contents were then heated to 90 °C for 15 h. When TLC and LC-MS showed complete consumption of the starting materials, the reaction mixture was diluted with ethyl acetate, separated the ethyl acetate layer, washed with water, followed by brine wash and dried over anhydrous sodium sulfate and concentrated to get the crude material. The crude product was directly purified by column chromatography (0–20% hexane/EtOAc) to isolate the 3-substituted-2-aryl/heteroaryl imidazo[4,5-b]pyridine derivatives.

**Method C**

To a degassed solution of 3-substituted-2-halo imidazo[4,5-b]pyridine derivative (1 equiv.) in acetonitrile/ water (1:2) in a sealed vial, was added palladium catalyst (4 mol%), and phosphine ligand (8 mol%). The solution was again purged with nitrogen, stirred at room temperature for 15 min. and potassium organotrifluoroborate salts (1.3 equiv.) and cesium
acetate (3 equiv.) were added. The reaction contents were then heated to 90 °C for 3 h. When TLC and LC-MS showed full consumption of starting materials, the reaction mixture was diluted with ethyl acetate, separated the ethyl acetate layer, washed with water, followed by brine wash and dried over anhydrous sodium sulfate and concentrated to get the crude material. The crude product was directly purified by column chromatography (0–20% hexane/EtOAc) to isolate the 3-substituted-2-aryl/heteroaryl imidazo[4,5-b]pyridine derivatives.

The synthesis of the halo intermediates 3 (3a, 3b, and 3c) was done according to the procedures mentioned in reference 21. The intermediates were found to be very labile and was found to degrade over a period of time (stored at −20 °C and used immediately for the coupling step)
Method Info:
Solvent A: 0.1% TFA
Solvent B: Acetonitrile
Flow Rate: 4.0 mL/Min
Temp: 45°C
Column: Xbridge C18 (4.6x50)mm, 5um
Time (min.): 0-4.0
Flow: 5-95

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![Molecule Image]
Method info:
A: 10mM NH4OAC in Water
B: Methanol
Flow: 4 ml/min
Temp: 45°C
Column: Xbridge C18 (50x4.6), 5µm
Time (min): 0---4
5---95
1-(2,4-dimethoxybenzyl)-1H-imidazo[4,5-b]pyridine