Nickel-Catalyzed Borylation of Halides and Pseudohalides with Tetrahydroxydiboron [$B_2(OH)_4$][1]

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INTRODUCTION

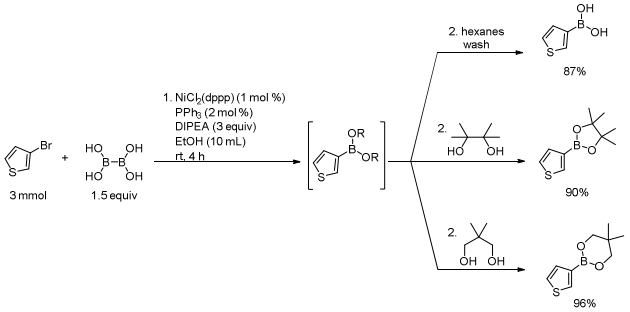
Arylboronic acids are important structures in organic synthesis and have also find application as biological and medicinal target.[2] Traditional methods to synthesize these molecules utilizes wasteful boron sources, such as bis(pinacolato) diboron (B_2Pin_2). Recently, our group developed the palladium-catalyzed synthesis of arylboronic acids employing the atom-economical tetrahydroxydiboron [$B_2(OH)_4$] reagent. The limitations associated with the method along with the high cost of palladium prompted us to develop a nickel-catalyzed borylation of aryl and heteroaryl halides utilizing BBA.

RESULTS AND DISCUSSION

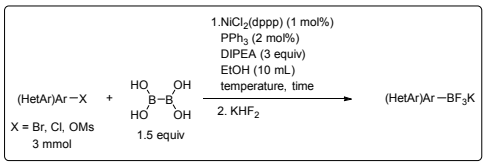
After extensive screening using microscale high-throughput experimentation (HTE), it was determined that the combination of BBA (1.5 equiv), 1 mol % of $NiCl_2$(dppp), 2 mol % of PPh_3, and 3 equiv of DIPEA in EtOH was the best set of condition. With optimal conditions in hand, the substrate scope for aryl halides and pseudo-halides was investigated (Scheme 1). Because boronic acids are relatively unstable species, the crude reaction mixture was treated with aqueous KHF_2 to afford the more robust potassium trifluoroborate salts. The reaction proved to be efficient for a variety of aryl and heteroaryl bromides, chlorides and mesylates electrophiles. The reaction of 2-Bromonaphthalene was performed on a 48 mmol scale (10 g), providing the product in 81% yield.

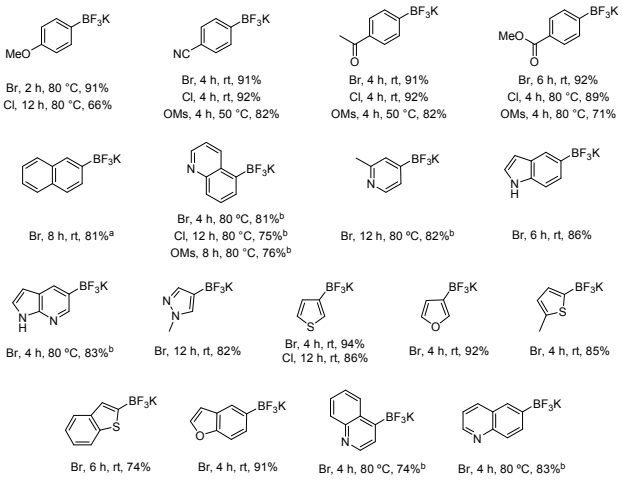
The use of BBA provides direct access to different boron derivatives upon different workups of the crude mixture (Scheme 2).

Scheme 2. Synthesis of different boron derivatives



Scheme 1. Ni-Catalyzed Borylation of Aryl and Heteroaryl bromides, chlorides and mesylates with BBA.





[a] 48 mmol scale using 0.1 mol % of $NiCl_2$(dppp) and 0.2 mol % of PPh_3 in EtOH (90 mL)
[a] 5 mol % of $NiCl_2$(dppp) and 10 mol % of PPh_3

CONCLUSION

A nickel-catalyzed borylation using BBA has been developed. The same set of conditions was efficient to borylate a wide array of aryl and heteroaryl bromides, chlorides and mesylates containing diverse functional groups. All reagents utilized in this method are stable and can be stored on the benchtop.

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