Nickel-Catalyzed Borylation of Halides and Pseudo-Halides with Tetrahydroxydiboron \([\text{B}_2(\text{OH})_4]\)\(^1\)

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INTRODUCTION

Arylboration 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 \((\text{B}_2\text{Pin}_2)\). Recently, our group developed the palladium-catalyzed synthesis of arylboron acids employing the atom-economical tetrahydroxydiboron \([\text{B}_2(\text{OH})_4]\) 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 \(\text{NiCl}_2(\text{dpdp})\), 2 mol % of \(\text{PPh}_3\), 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 1. Ni-Catalyzed Borylation of Aryl and Heteroaryl bromides, chlorides and mesylates with BBA.

Scheme 2. Synthesis of different boron derivatives

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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REFERENCES