

Selective Di-Nucleophile Suzuki Cross-Coupling enable by Copper-Catalysed Chemoselective Chlorination

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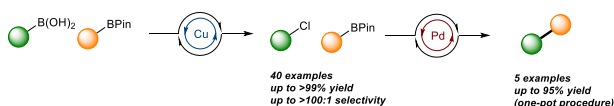
Abstract

We have succeeded in developing a one-pot organoboron di-nucleophile cross-coupling *via* chemoselective chlorination.

Introduction

Boronic acids and esters can be applied in a substantial range of reactions, being good building blocks to enable access to a broad variety of functionalized compounds.¹

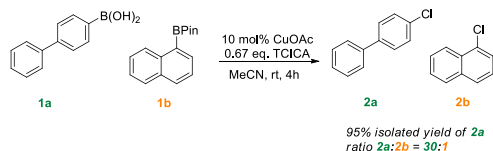
Lately, our group enabled chemoselective procedures in the presence of more than one organoboron species.² In this work, we successfully developed the first one-pot di-nucleophile Suzuki-Miyaura cross-coupling, starting from two boron species, *via* a chemoselective chlorination (Scheme 1).



Scheme 1. Chemoselective di-nucleophile project.

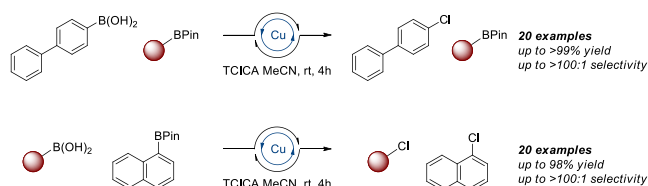
Results and Discussion

Taking into consideration the aim of the project and examples published in the literature around the subject, the chlorination of un-protected boron species was optimized, accessing a monochlorination in both excellent yields and selectivity (Scheme 2).^{3,4}



Scheme 2. Scheme of the selective di-nucleophile project.

After obtaining the optimum conditions, the methodology was applied to a range of different substrates, with good to excellent yields and, in some cases, complete selectivity (Scheme 3).



Scheme 3. Copper-catalysed chemoselective chlorination.

Based on this, a chemoselective di-nucleophile Suzuki-Miyaura cross-coupling has been developed.⁵ For future work, further studies will be carried out in order to investigate the mechanistic pathway of this reaction.



Scheme 4. Chemoselective di-nucleophile Suzuki-Miyaura cross-coupling.

Conclusion

In summary, we successfully showed, using a vast variety of substrates, the chemoselective chlorination of boronic acids over pinacol esters. Also, the methodology was applied using different protected boron species. Furthermore, investigations will be carried out to address a more precise mechanism as well as demonstrate the applicability of the developed methodology.

Aknowledgements

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¹ Hall, D. G. *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials 2nd Ed*; Wiley & Sons: New York, **2011**, 1-133.

² J. W. B. Fyfe, E. Valverde, C. P. Seath, A. R. Kennedy, J. M. Redmond, N. A. Anderson, and A. J. B. Watson, *Chem.-Eur. J.*, **2015**, *24*, 8951–8964.

³ (a) G. A. Molander,* L. N. Cavalcanti. *J. Org. Chem.* **2011**, 7195-7203. (b) Hong Wu and John Hynes, Jr.*. *Org. Lett.* **2010**, 1192-1195.

⁴ (a) Molander, G. A.; Trice, S. L. J.; Kennedy, S. M. *J. Org. Chem.*, **2012**, *77*, 8678. (b) Molander, G. A.; Trice, S. L. J.; B. Tschäen, *Tetrahedron*, **2015**, *71*, 5758-5764.

⁵ G. K. S. Prakash, C. Panja, T. Mathew, V. Surampudi, N. A. Petasis, G. A. Olah, *Org. Lett.* **2004**, *6*, 2205-2208.