BORON-WITTIG AND PETERSON OLEFINATION: A COMPARATIVE STUDY FOR VINYL BORONATE SYNTHESIS

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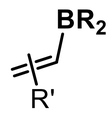
Background

Vinylboronates are versatile intermediates enabling a variety of synthetic transformations, such as carbon-carbon bond formations, in particular in the Suzuki-Miyaura coupling reaction.[1-2] This makes them crucial in the fields of pharmaceuticals, agrochemicals, and advanced materials. Therefore, the exploration of alternative synthetic strategies to form vinylboronates remains a compelling research area.

Our work aims at the development of new methodologies toward vinylboronates. We plan to use the Peterson olefination to access vinylboronates, what requires control of the chemoselectivity with the competing boron-Wittig reaction.



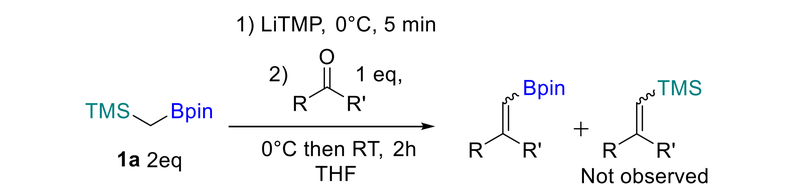
Vinylboronate

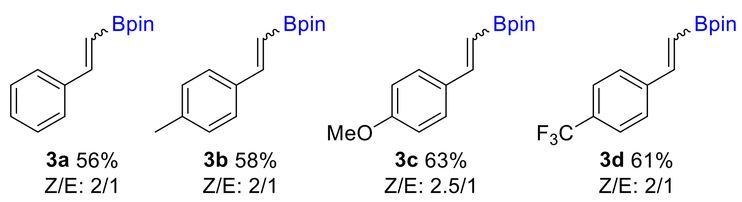
Valuable building block

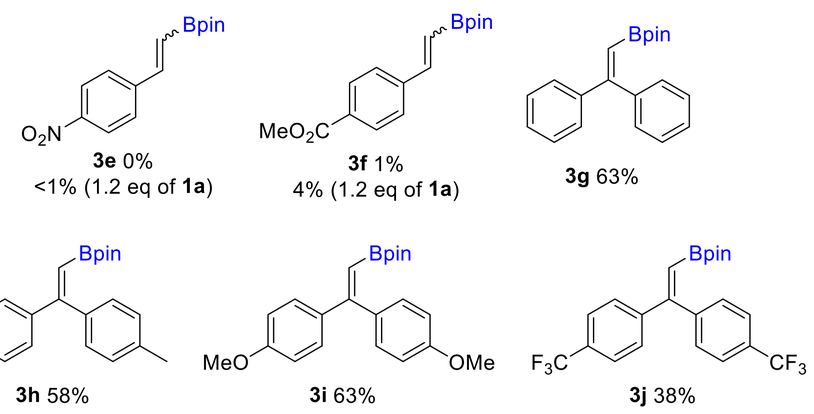
Increasing need for synthetic methods

Optimisation and Scope

The *gem*-borylsilylalkane of reference **1a** was synthesized by adapting the work of Matteson.[3] Its reaction with model ketones and aldehydes was explored. Only the vinylboronate resulting from a Peterson olefination was observed, in a 2:1 Z/E ratio. The electropoor aldehydes (products **3e-f**) showed a decreased reactivity, most likely due to the side reactivity of the substituent group. The impact of the carbonylated substrate's nature is minimal on the yield, and non-existent on the chemoselectivity.

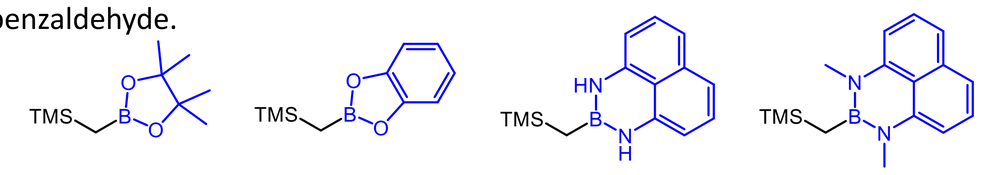


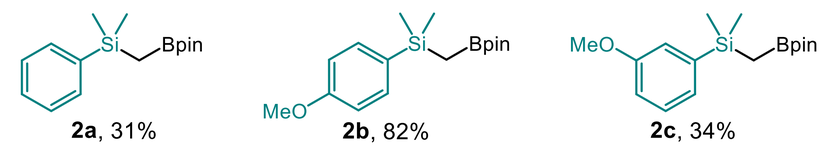




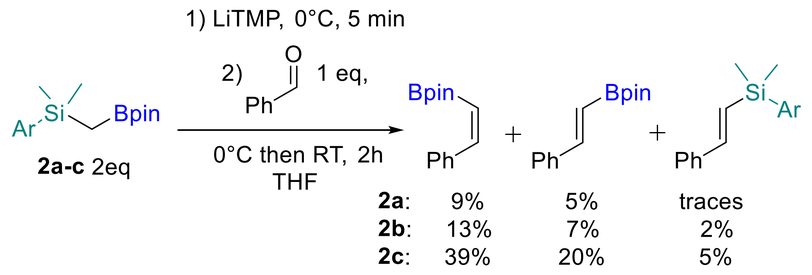
Boron and Silicon variations

In order to deepen our understanding of the process, we synthesized a library of new *gem*-borylsilylalkanes and engaged them in reaction with benzaldehyde.



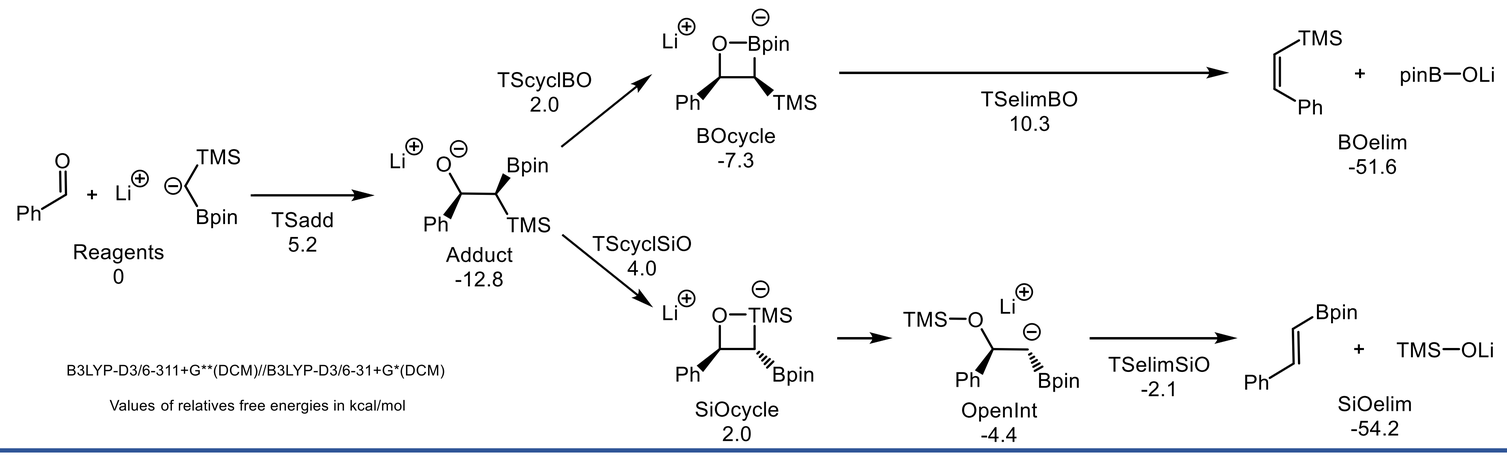


While none of the boron group variation (**1b-h**) reacted succesfully in our olefination protocole, the modification of the silicon group (**2a-c**) yielded both the vinylboronates (*cis* and *trans*) and the silylated olefin.



The bulkiness of an aromatic group on the silicon disfavors the Peterson olefination, allowing for the Boron-Wittig to be competitive. The electrodensity on the silicon arises as a key parameter to tune the chemoselectivity.

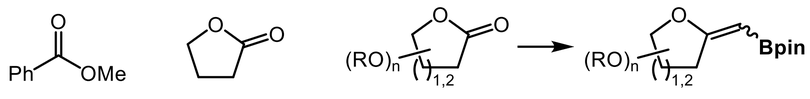
Computational studies



The free energy barrier for the boron-Wittig pathway (23.3 kcal/mol) is computed to be higher than the one for the Peterson pathway (16.8 kcal/mol), in good agreement with experiment. This predicted total chemoselectivity can be explain by a fast elimination in this latter case, releasing of the vinylboronate.

Project perspectives

After the exploration of the olefination process with various *gem*-borylsilylalkanes, the most promising substrates will be used in reaction with esters, lactones, and eventually sugar lactones. This will lead to the unprecedented synthesis of borylated *exo-glycals*. A collaboration with UNamur will enable to assess the reactivity (Prof. Berionni & Sophie Rodrigues, poster 212) and the biological activity (Prof. Vincent & Jenny Ha, poster 100) of this new family of borylated sugar derivatives.



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[2] Miyaura, N.; Suzuki, N. *Chem. Rev.* **1995**, *95*, 2457-2483,

[3] Matteson, D. S.; Majumdar, D. *J. Chem. Soc., Chem. Commun.* **1980**, *1*, 39-40.