Development of synthetic strategies toward vinylboronates

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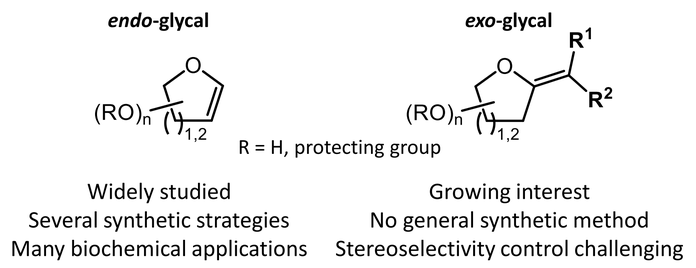
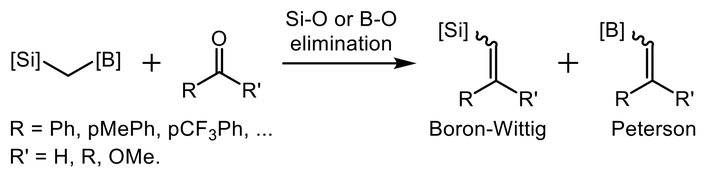
Background

Glycals are unsaturated sugar derivatives. In contrast to the *endo*-glycals, the chemistry and biology of *exo*-glycals remained unexplored until recently; they are becoming the subject of increasing research interest. However, their double bond formation remains challenging in terms of substitution and stereoselectivity control.[1] Furthermore, even if boron chemistry has witnessed major novel achievements and has stimulated the pharmaceutical industry's interest, no synthesis of borylated *exo*-glycal has been reported so far.



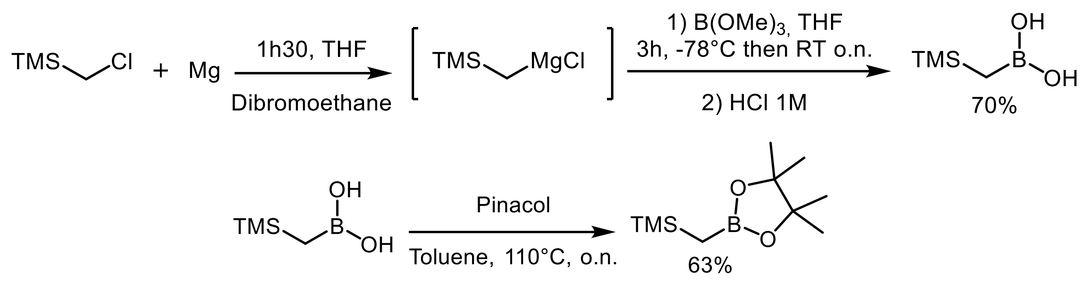
Strategy

Our work aims at the development of methodologies toward vinylboronates which could be applied to the synthesis of borylated *exo*-glycals. After our first unsuccessful work on the boron-Wittig reaction using *gem*-diborylalkanes,[2] we turned our attention to *gem*-borylsilylalkanes. We plan to use the silica-based Peterson olefination for the formation of vinylboronates, what necessitates to control the chemoselectivity with the competitive Boron-Wittig reaction.

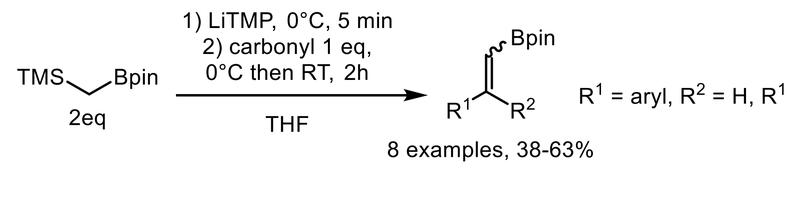


Experimental work

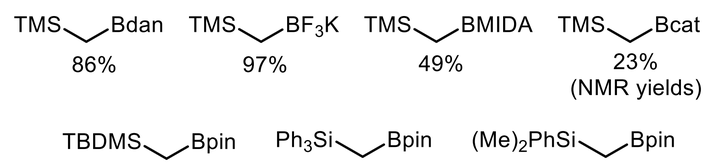
The *gem*-borylsilylalkane of reference was synthesized by adapting the work of Matteson.[3] Variation of the starting methylchloride silane will allow us to change the silyl moety, while the esterification in the second step could be modified to access other boryl groups.



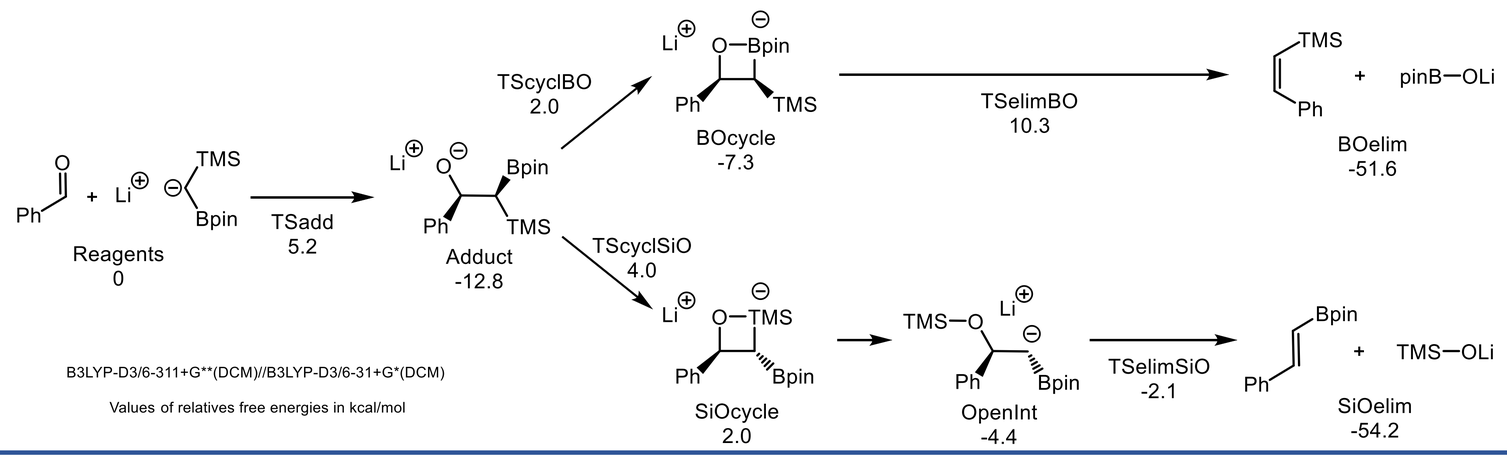
This compound and its reactions with model ketones and aldehydes were explored. This experimental work is completed by a computational investigation of the olefination mechanism.



Only the vinylboronate resulting from a Peterson olefination was observed, in a 2:1 Z/E ratio. In order to deepen our understanding of the process, we are currently synthesizing a library of new *gem*-borylsilylalkanes to engage them in reaction with carbonyl compounds.



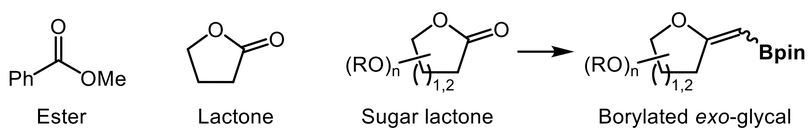
Computational studies



The barrier for the boron-Wittig path (23.3 kcal/mol) is computed to be higher than the one for the Peterson path (16.8 kcal/mol). This difference can be explain by a fast elimination in this latter case, releasing of the vinylboronate.
The predicted total chemoselectivity toward the Peterson olefination is in very good agreement with our experimental observations.

Project pespectives

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) and the biological activity (Prof. Vincent) of this new family of borylated sugar derivatives.



[1] Taillefumier, C.; Chapleur, Y. *Chem. Rev.* **2004**, *104*, 263.
[2] Grygorenko, O. O. *Eur. J. Org. Chem*. **2019**, *33*, 5624-5635.
[3] Matteson, D. S.; Majumdar, D. *J. Chem. Soc., Chem. Commun.* **1980**, *1*, 39-40.