

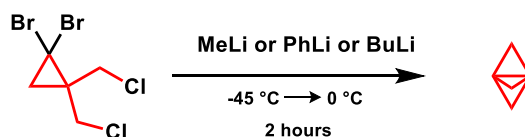
Summary for EKA Grant

2022/045-P144-1

Elte Novel Scaffolds Research Group, Gergely Tolnai

With the aid of ELTE EKA grant, our small group was able to research several aspects of molecules with new scaffolds. These new type of molecules can have an impact on several fields of science. These can be rigid building blocks for material science and can be especially useful for medicinal chemistry, where they can serve as unprecedented functions or bioisosters of proven groups.¹

An interesting aspect of these types of molecules, that their simplest synthesis might involve even more strained molecules. One of these species is [1.1.1]propellane (*Scheme 1*). The synthesis of this substance is relatively simple, but only stable for a few weeks in the freezer if not disturbed.



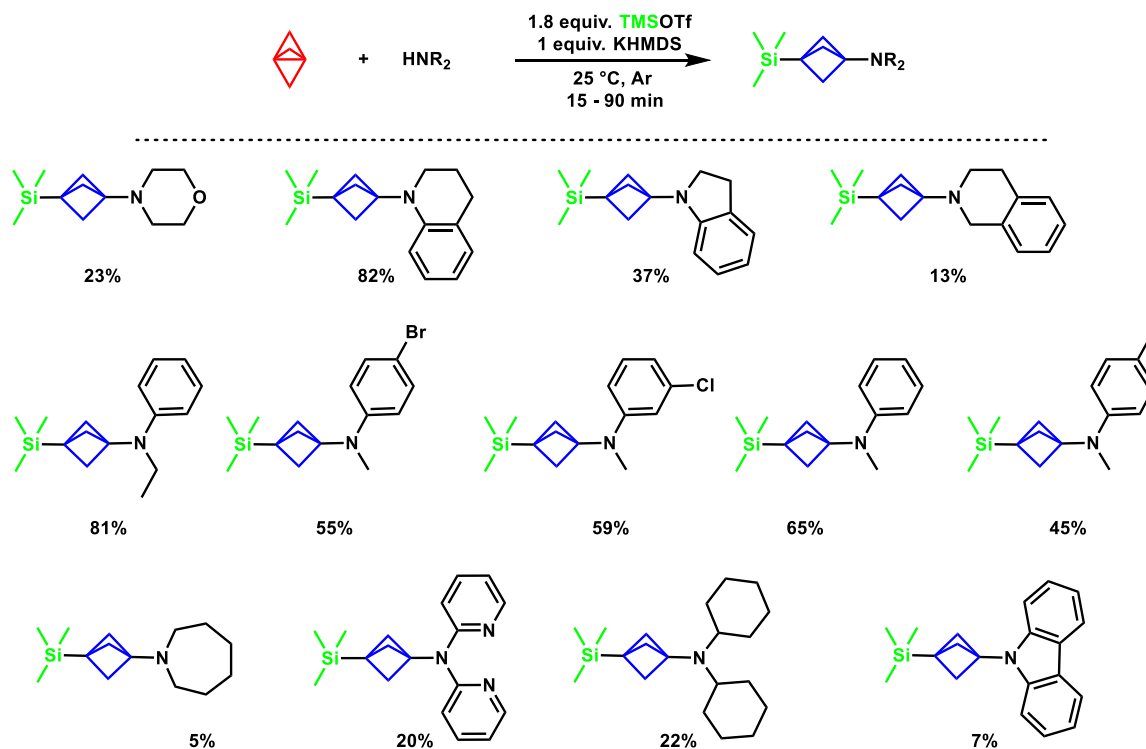
Scheme 1. Synthesis of [1.1.1]propellane

One of our main goals is to produce stable building blocks, that can be stored and readily used.

I. Synthesis of silylated BCPs

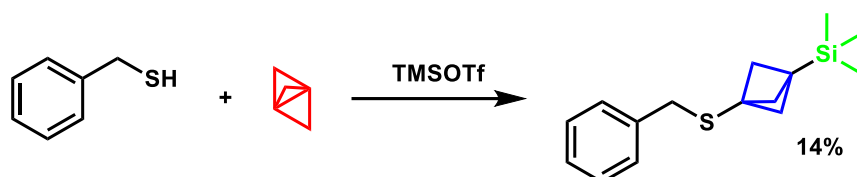
Silylated BCPs are rarely found in the literature. Scarce examples include silaboryl and TMS-BCP examples.² Their synthesis may lead to novel types of molecules with a 3D scaffold, and possibly create a new platform for further functionalization.

Our main focus on this field was the aminosilylated BCP-s, as amines are an essential part of pharmaceuticals. Silylation made possible by the Lewis-acid TMSOTf, and after several rounds of optimization, we have settled on free amines, instead of silylamines, as they gave more reproducible results and easier handling. Timing of addition of reagents and the choice of base were proven to be an important factor during optimization. We could utilize this method for creating several new molecules(*Scheme 2*). Many noticeably congested tertiary amines could be created. The best substrates seem to be aryl-alkylamines.



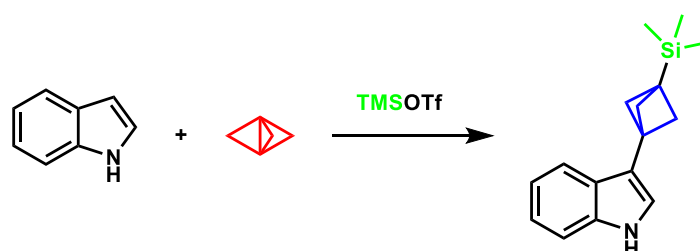
2. Scheme Synthesis of BCP silylamines

We also currently working on other nucleophiles: thiols and indoles. Thiols are generally very reactive towards [1.1.1]propellane, this create a challenge to include the silyl part in the molecule. Currently we are able to synthesize silylbicyclopentylated thiol, albeit with a low yield.



3. Scheme Reaction with a thiol

Indoles are a very important building blocks in pharmaceuticals. The inherent nucleophilicity of C3 site make a hopeful target for this reaction, but the Lewis base can create unwanted dimers. We were able to verify that the product formation by NMR, but the yields are low.



4. Scheme silylbicyclopentylaton of indole

II. Teaching and Science/ELTE popularization aspects

In the last period of the grant, two MSc student (Dorina Jobbágy, Máté Kernya) and one BSc student (Kristóf Gergely) had finished their degree. Dániel Lasányi has defended his PhD with summa cum laude.

Science popularization has never been more important, we gave presentations in Secondary schools and organized the “chemist’s playground” event at Scientist’s night.

III. References

¹ Dilmaç, A. M.; Spuling, E.; de Meijere, A.; Bräse, S. *Angew. Chem. Int. Ed.* **2017**, *56*, 5684.

² M. Kondo, J. Kanazawa, T. Ichikawa, T. Shimokawa, Y. Nagashima, K. Miyamoto, M. Uchiyama, *Angew. Chem. Int. Ed.* **2020**, *59*, 1970-1974.