From Lithium to Silicon: a handy way to access Heterocycles through Intramolecular Processes

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Developing new accesses to heterocyclic compounds is a constant challenge in synthetic chemistry. While heterocyclic motifs are abundant in natural products, new methodologies have recently been developed in our laboratory, enabling the heterocyclization of variously functionalized acetylenic compounds.

In recent decades, carbometallation methodologies using organolithium reagents have been widely developed. In our case, we described a method leading to highly functionalized heterocycles by intramolecular carbolithiation of acetylenic triple bonds bearing an acetal appendage.[1] Moreover, it was the first time that direct *anti*-addition was observed, induced by chelation of the acetal and confirmed by DFT calculations. We then extended this reaction to other heterosubstituted alkyne, including germanium, or selenium and a variety of substrates with a chlorine substituent in the acetylenic position.[2]

At the same time, our group has engaged in a research program dedicated to accessing silylated or germylated heterocycles *via* cyclization reactions, the presence of silicon/germanium atoms being known to increase the lipophilicity of the corresponding molecules. We first developed a convenient access to silylated and germylated heterocycles based on anionic rearrangement,[3] and devised a cyclization process, involving a C–H activation step on a Csp^3 by palladium catalysis.[4] Later, we developed regio- and stereoselective intramolecular silapalladation reactions of alkynes, starting from disilanes.[5] The oxidative addition of Pd(0) into the Si–Si bond provides, after cyclization and reductive elimination, heterocyclic derivatives in good yields, as single (*Z*) isomers, *via* a *syn* addition process. We recently discovered a simple access to germoles by treating *o*-alkynyl aryldiphenylgermanes in the presence of diethylzinc and AIBN as radical initiator.[6] Interestingly, the application of this process to more challenging alkynes led to a polar germylzincation process, without the need for a radical initiator.[7]

This presentation will focus on our recent contributions to the access to functionalized heterocycles by intramolecular carbolithiation and to silylated and germylated heterocycles.

References :
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