A BROADLY APPLICABLE AND STRAIGHTFORWARD ENTRY TO SELECTIVELY DEUTERATED AMINES

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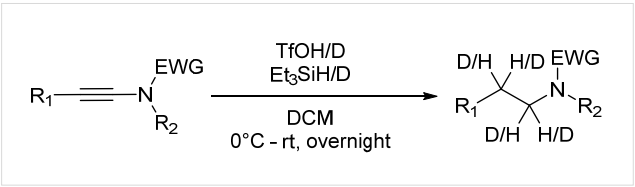
Deuterated molecules are commonly used not only as powerful probes for mechanistic investigations of organic/organometallic reactions but also for the elucidation of biosynthetic pathways, to alter the selectivity of a given reaction or even to enhance the metabolic stability of a drug and study its toxicity.[1] Among all deuterated functional groups, amines selectively substituted with deuterium atom(s) α and/or β to the nitrogen atom are especially relevant in various areas, notably in medicinal chemistry.

Despite the apparent simplicity of such deuterium-labeled amines, their synthesis is far from being trivial and classical strategies for their preparation usually require several steps and still suffer from major limitations such as harsh reaction conditions, expensive catalytic systems and lack of selectivity when different alkyl chains are attached to the nitrogen atom.[2] The selective synthesis of amines possessing deuterium atoms at the α and/or β position(s) of the nitrogen atom is therefore still an open challenge with potential applications in many areas of science.

In this context, and in continuation of our studies on the chemistry of ynamides[3] and keteniminium ions,[4] we have recently developed a new process for the preparation of selectively deuterated amines starting from readily available ynamides. The development of this reaction, its scope and limitations as well as its use for the synthesis of biologically relevant amines will be discussed.



[1] Y. Jaemon Deuterium, Discovery and Applications in Organic Chemistry; Elsevier: Cambridge, **2016**.

[2] For representative examples, see: (a) M. Takahashi, K. Oshima, S. Matsubara *Chem. Lett*. **2005**, *34*, 192. (b) L. Neubert, D. Michalik, S. Bähn, S. Imm, H. Neumann, J. Atzrodt, V. Derdau, W. Holla, M. Beller *J. Am. Chem. Soc*. **2012**, *134*, 12239.

[3] G. Evano, C. Theunissen, M. Lecomte *Aldrichimica Acta* **2015**, *48*, 59.

[4] G. Evano, M. Lecomte, P. Thilmany, C. Theunissen *Synthesis* **2017**, *49*, 3183.