From 2-cyanoazetidines to multi-click reactions: an eventful journey

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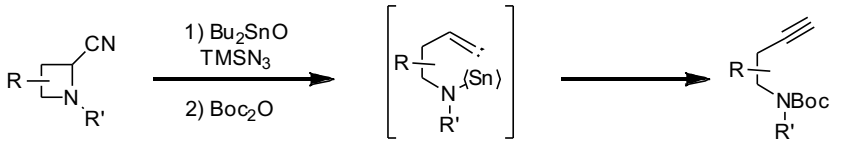
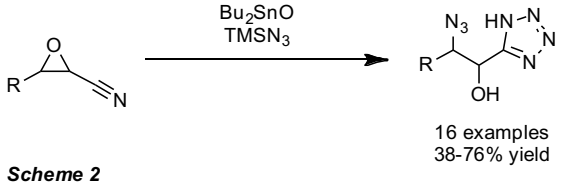
Substituted homopropargylamines are valuable and hardly accessible building blocks, especially in an enantiopure form. We describe here the unexpected formation of such compounds starting from 2-cyanoazetidines by reaction with dibutyltin oxide and trimethylsilylazide.[1] This reaction involves a cycloaddition on the nitrile moiety followed by a ring opening and the formation of a vinylidene carbene (scheme 1).

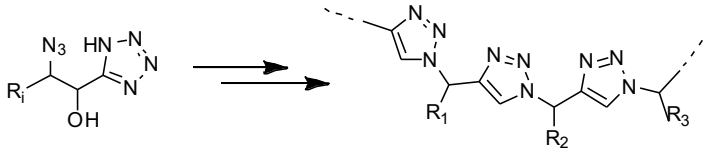


Scheme 1

Reports of such carbene generations from a nitrile with a leaving group at the alpha position are extremely rare in the literature.[2] We thus wanted to transpose this underexplored method to epoxynitriles, another class of cyclic nitriles. In the same conditions, those substrates lead unexpectedly to α-hydroxy-β-azidotetrazoles[3] (scheme 2) that appeared to have promising applications in click chemistry. They are indeed accurate compounds to achieve multiple sequential click reactions (scheme 3).[4]



Scheme 2



Scheme 3

[1] Quinodoz, P.; Drouillat, B.; Wright, K.; David, O.; Couty F. *Chem. Comm.,* **2016**, *52*, 10072-10075

[2] A. Nguyen Van Nhien, R. Leon, D. Postel, M. C. Carreiras, A. G. Garcia, J. Marco-Contelles, *Journ. J. Carbohy. Chem*. **2005**, *24*, 369-377.

[3] P. Quinodoz, C. Lo, M. Kletskii, O. Burov, J. Marrot, F. Couty, *Org. Chem. Front*. **2015**, *2*, 492-496.

[4] Wright K., Couty F., Quinodoz P., Drouillat B., *EP16159846.1*, **2016**