

GENERATION AND UTILIZATION OF UNSTABLE CARBENOID INTERMEDIATES USING CONTINUOUS FLOW TECHNOLOGY

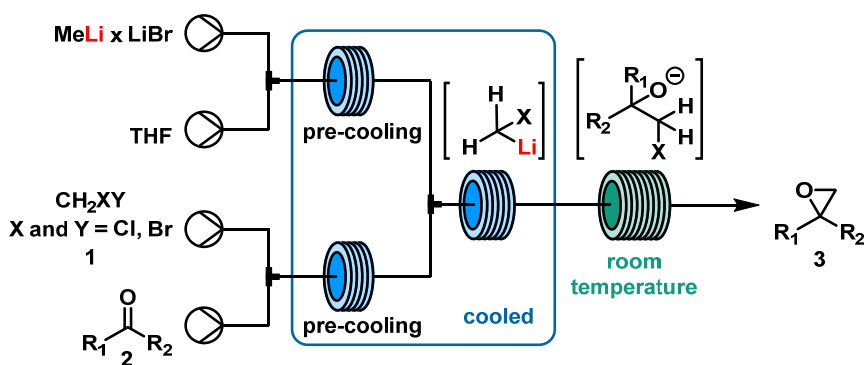
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Organolithium compounds are widely used in organic synthesis since they serve as carbanion equivalents for C-C bond formation reactions. α -Haloorganolithiums, in particular, are very attractive from the synthetic viewpoint due to their carbenoid character, which enables simple generation of oxiranes and other valuable building blocks.^[1] Transformations involving organolithium species are often rapid and highly exothermic, and therefore difficult to control using conventional batch reactors. Large scale synthesis of organic compounds involving carbenoids and organolithium compounds in general is often restricted due to high amounts of heat generated. Flow chemistry has been shown as an excellent tool to tackle highly exothermic reactions. In addition, unstable intermediates such as carbenoids can be generated and utilized *in situ* in a sequential flow process, thus avoiding the accumulation of hazardous compounds in the reaction mixture.^[2,3]

Herein, we present a robust and readily scalable continuous flow procedure for the *in situ* generation of α -halomethylolithiums (LiCH₂X) and their utilization for the synthesis of oxiranes. The process is based on a rapid lithium-halogen exchange reaction of a dihalomethane (**1**) and methyl lithium. Subsequently, the carbenoid is mixed with the ketone, yielding the corresponding oxirane. The procedure has been tested for a diverse set of ketones as substrates, producing the target oxiranes in good to excellent yields.



[1] L. Degennaro, F. Fanelli, A. Giovine, R. Luisi, *Adv. Synth. Catal.* 2015, 357, 21–27.

[2] M. B. Plutschack, B. Pieber, K. Gilmore, P. H. Seeberger, *Chem. Rev.* 2017, 117, 11796–11893.

[3] B. Gutmann, D. Cantillo, C. O. Kappe, *Angew. Chemie Int. Ed.* 2015, 54, 6688–6728.