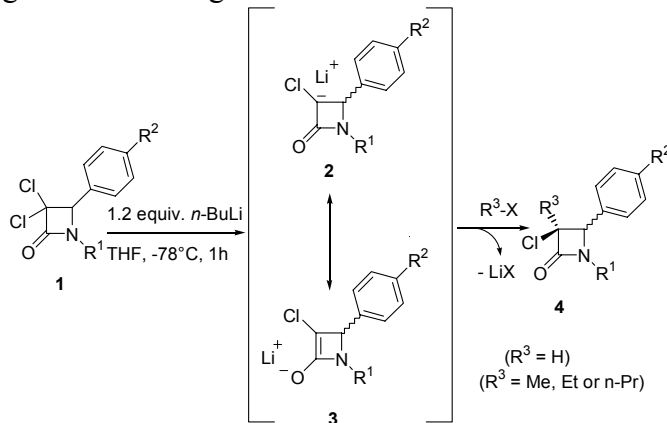


## Lithium-Halogen Exchange Reactions of 3,3-Dichloro-2-azetidiones

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Previously, the synthesis of 2-aryl-3,3-dichloroazetidines and their ring transformation towards functionalized aziridines via intermediate 2-azetines has been described.<sup>1</sup> The scope of their reactivity was further investigated and it was found that reaction of 2-aryl-3,3-dichloroazetidines with lithium aluminum hydride in diethyl ether led to a mixture of *trans*-2-aryl-3-chloroazetidines and *cis*-2-aryl-3-chloroazetidines. In order to characterize unequivocally the new compounds, their synthesis was performed independently. While this was straightforward for the *trans* derivatives, the synthesis of *cis*-2-aryl-3-chloroazetidines proved to be more difficult. The straightforward synthesis of 4-aryl-3-chloro-2-azetidiones by [2+2]-cycloaddition between chloroketene and the appropriate imine is known to give exclusively *trans*-stereoselectivity, or mainly *trans*-stereoselectivity when different substituents are present on the aromatic group. Although some methods are known that give mainly *cis*-stereoselectivity by *in situ* generation of the ketene from the corresponding acid and an activating compound, these methods were not elaborated towards application to  $\alpha$ -halogenated acids. Therefore, the use of metal-halogen exchange reactions on 3,3-dichloroazetid-2-ones **1** to accomplish the aforementioned goal was investigated.



4-Aryl-3,3-dichloroazetidiones **1** were easily obtained by [2+2]-cycloaddition between dichloroketene and the appropriate imine. The compounds were used as substrates in the subsequent lithium-halogen exchange strategy. The use of proton sources allowed to synthesize 4-aryl-3-chloro-2-azetidiones, although the stereochemical outcome of each reaction was somewhat different. To avoid steric interactions, the incoming electrophile preferentially approaches the intermediate **3** from the opposite face of the space in which the aryl-substituent resides. This reasoning satisfactorily explains the formation of *cis*-4-aryl-3-chloro-2-azetidiones. This stereochemistry was also observed when alkyl halides were used as electrophiles. In these cases, only the formation of the *cis*-3-alkyl-3-chloro-4-phenylazetid-2-ones **4** was detected.

(1) Dejaegher, Y.; Mangelinckx, S.; De Kimpe, N. *J. Org. Chem.* **2002**, *67*, 2075.