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Nucleophilic ring opening of small N-heterocycles in liquid SO_2

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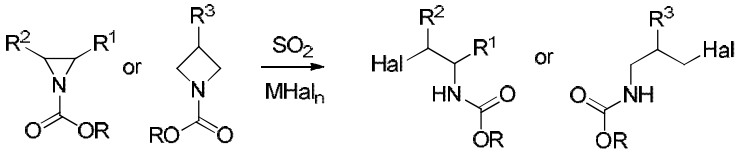
Aziridine and azetidine moieties are important small ring *N*-heterocycles in organic synthesis due to their biological and pharmacological properties and synthetic potential as the building blocks [1]. Modifications of these aza-heterocycles can lead to the formation of various useful compounds, such as heterocycles [2], alkaloids [3] and non-natural amino acids [4]. The reactivity of aziridines and azetidines strongly depends on ring substituents, activation of nitrogen atom and ring strain. Due to the latter, the most common transformations of these heterocycles are the nucleophilic ring-opening reactions (NRORs) [5]. However, there are only a few precedents of ring opening using halides MX_n [6].



Here we present a new synthetic process of aziridine and azetidine NRORs with metal halides in liquid sulfur dioxide. The use of sulfur dioxide in organic synthesis has recently seen a renaissance [7]. The reactions were carried out in three temperature modes: 1) low temp. (-70…-10 °C); 2) ambient temp. (20 °C) and 3) elevated temp. (60 °C). The efficiency of each aziridine or azetidine ring opening reaction was monitored in several solvents in parallel experiments: $SO_{2(liq.)}$, DMSO, MeCN, TFE. We have used I and II group metal halides as the source of nucleophile. The obtained results showed that the NRORs of carbamate-protected aza-heterocycles in liquid sulfur dioxide occur noticeably faster and cleaner than in other solvents.

These are the rare examples of NRORs of carbamate-protected aziridines and azetidines that proceed in the absence of common Lewis acid additives. Additionally, we have found that the reaction products are more stable in liquid sulfur dioxide than in DMSO or MeCN. Although opening of the azetidine requires a higher reaction temperature, to the best of our knowledge these are the first examples of ring opening reactions of *N*-carbamate protected 3-substituted azetidines.

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