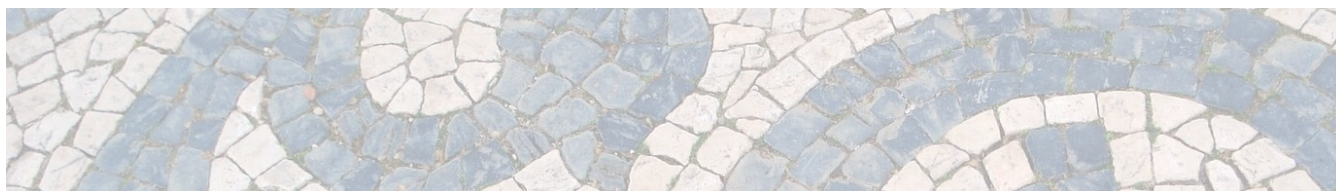


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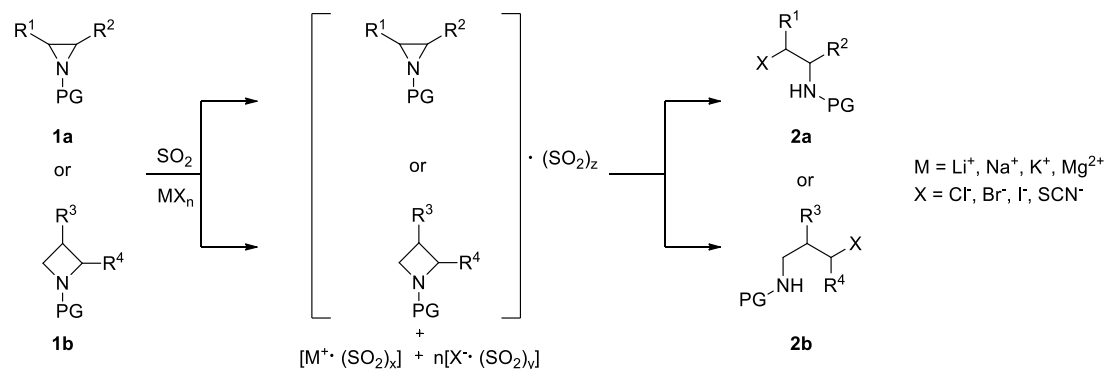
NUCLEOPHILIC RING OPENING OF SMALL SIZE N-HETEROCYCLES IN LIQUID SULFUR DIOXIDE

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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 a building blocks.^[1] Modifications of these aza-heterocycles can lead to the formation of various classes of compounds, such as heterocycles,^[2] alkaloids^[3] and non-natural amino acids.^[4] The reactivity of aziridines and azetidines strongly depends on variation of 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). NRORs have been exhaustively described in excellent reviews.^[5]

Halogen nucleophiles can be introduced under acidic conditions (e.g.: with HCl).^[6] Another source of halogen nucleophiles are metal halides. However, there are only a few precedents of ring opening using halides MX_n.^[7]



Here we present a new synthetic process of aziridine and azetidine NRORs with metal halides and other nucleophiles in liquid sulfur dioxide. The use of sulfur dioxide in organic synthesis has recently seen a renaissance [8]. Reactions were carried out in three temperature modes. The efficiency of each aziridine or azetidine ring opening reaction was monitored in several solvents in parallel experiments: SO₂(liq.), DMSO, MeCN, TFE. We have used I and II group metal halides as a nucleophile source.

The obtained results showed that the aza-heterocycles NRORs in liquid sulfur dioxide occurs noticeably faster and cleaner than in other solvents.

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