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USE OF TERMINALLY FUNCTIONALIZED PROPARGYL SILANES FOR THE SYNTHESIS OF VARIOUS 5-MEMBERED HETEROCYCLES VIA 1,2-SILYL MIGRATION

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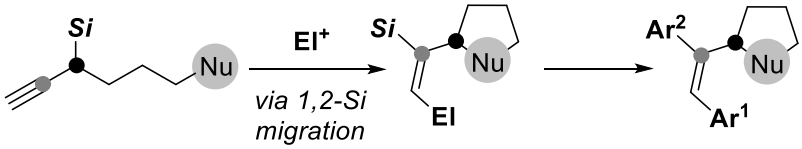
Small heterocycles, particularly those containing a 5-membered cycle, are popular motifs in pharmaceuticals, displaying a broad range of biological properties [1]. A well-established strategy for the synthesis of 5-membered saturated/partially saturated heterocycles involves intramolecular cyclization, made possible by internal nucleophile attack on carbocations.

In this work we investigate the use of electrophile induced 1,2-silyl migration in terminally functionalized propargyl silanes to generate stabilized carbocations, capable of reacting with various internal nucleophiles, forming heterocyclic units (scheme 1). Various nucleophilic species could be utilized, namely alcohols, carboxylic acids, oximes, acyl and sulfonyl amides, carbamates and thioacetates.

The synthetic utility of the cyclization products was demonstrated by difunctionalization of the alkene moiety in cross-coupling reactions to selectively obtain trisubstituted alkenes. The resulting heterocycle derivatives were obtained with a high degree of stereoselectivity and yields up to 82%.



•Multiple electrophilic species:
H^+, Br^+, I^+, $PhSe^+$
•Multiple internal nucleophiles:
-OH, -COOH, -NOH, -NHCOR, -$NHSO_2R$, -SAc
•Site selective alkene functionalization

Scheme 1. Heterocyclization of propargyl silanes.

References:

[1] Vitaku, E.; Smith, D. T.; Njardarson, J. T. *J. Med. Chem.* **2014**, *57*, 10257–10274.