Electrophile Induced 1,2-Silyl Shift In Terminally Functionalized Propargyl Silanes For The Synthesis Of Small Heterocycles

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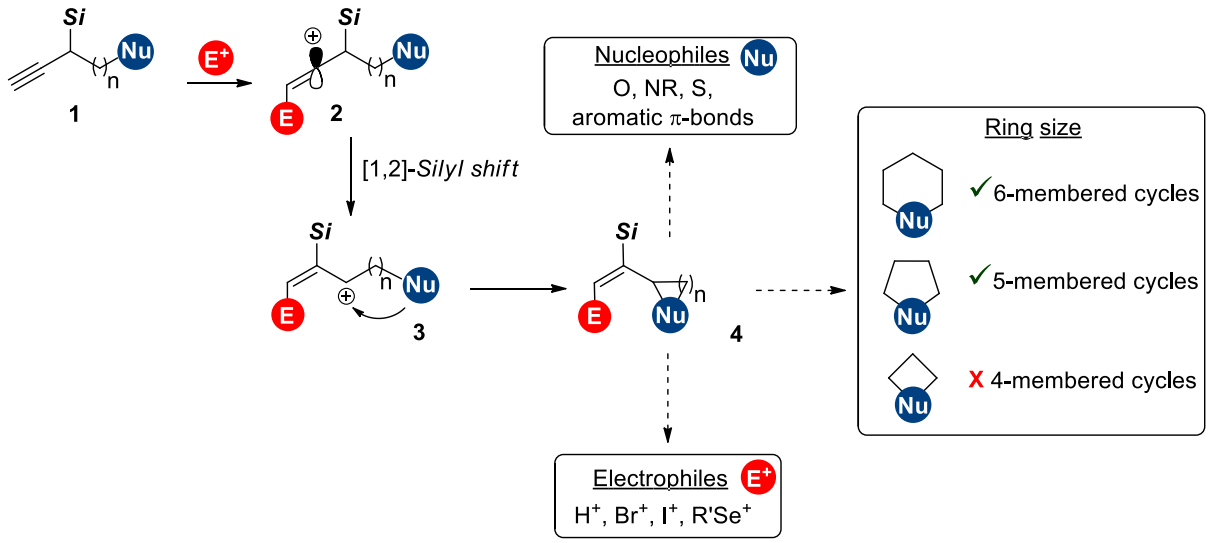
About 80% of all FDA approved drugs consist of small molecules, among which 59% are nitrogen heterocycles,[1] 27% are oxygen heterocycles, but 26% are sulfur-containing drugs.[2] Their extensive use in medicinal chemistry offers perspective to the development of new synthetic pathways towards heterocyclic structures, especially those containing at least one *N*-, *O*- or *S*-atom.

Previously our group studied electrophilic activation of propargylsilanes for the synthesis of 3-silylated 3-sulfolenes[3] and indenes.[4] These transformations were made possible by the stabilizing properties of the *β*-silicon effect and 1,2-silyl migration, which is observed in activated propargylic systems.[5] To further expand the concept of propargyl silanes as precursors for heterocycles, we designed a series of terminal-nucleophile-containing substrates **3**, which upon electrophilic activation underwent intramolecular cyclization, yielding *N*-, *O*- and *S*-containing heterocycles **4** (**Scheme 1**). Various electrophiles have been shown to induce the discussed transformation, such as H^+, Br^+, I^+ and $PhSe^+$, providing diverse substitution patterns for the resulting alkene side chain. To demonstrate the reaction scope, substrates containing alcohol, carboxylic acid, aldehyde, oxime, acyl amide, carbamate, sulfonamide and thioacetate functionalities have been cyclized. In case of aryl-moiety containing substrates, an intramolecular Friedel-Crafts reaction was observed, yielding bicyclic structures. The provided methodology allows the synthesis of 2-vinylsubstituted heterocycles with double or triple functionalized C=C bond with a distinct preference for *E*-geometry.



Scheme 1: Heterocyclization of propargyl silanes.

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