

Silver-Catalyzed Transformation of Propargylamine N-Oxides to Enones and Acyloxy Ketones via Isoxazolinium Intermediates

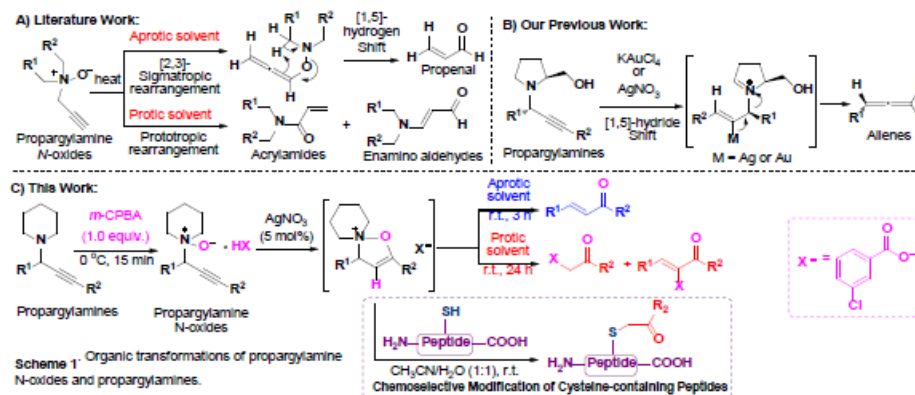
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Abstract

Propargylamine *N*-oxides, easily accessed from their corresponding propargylamines through oxidation, have been reported to undergo thermal Meisenheimer-type [2,3]-sigmatropic rearrangement and [1,5]-hydrogen shift to give propenal in aprotic medium or go through prototropic rearrangement to afford acrylamides and enamino aldehydes in protic medium (Scheme 1A). However, only limited examples were reported and elevated temperature was required for the reactions. Transformation studies of the propargylamine *N*-oxides using transition metal catalysis remain unexplored.

Silver catalysis is able to activate alkynes towards nucleophilic attack through π coordination to the carbon-carbon multiple bonds. In our previous work, we found that translation of propargylamines to allenes was easily achieved by gold(III) or silver(I) catalysis (Scheme 1B). Recently, we found that a novel silver-catalyzed transformation of propargyl-amine *N*-oxides with switchable product profiles has been developed. A diversity of enones with excellent *E/Z* ratio (up to >20:1) were obtained when the reactions were conducted in aprotic solvents. In contrast, 3-chloro-benzoxymethyl ketones and α -(3-chloro)-benzoxy enones were obtained by using protic solvents. Mechanistic studies suggested that *in situ* generated isoxazolinium ions are the key intermediates involved in these novel silver-catalyzed reaction pathways. Application on chemo-selective modification of cysteine-containing peptides in aqueous medium has also been achieved (Scheme 1C).



Reference

Cui, J.-F.; Kung, K. K.-Y.; Ko, H.-M.; Hui, T.-Z.; Wong, M.-K. *Adv. Synth. Catal.* 2014, 356, 2965.