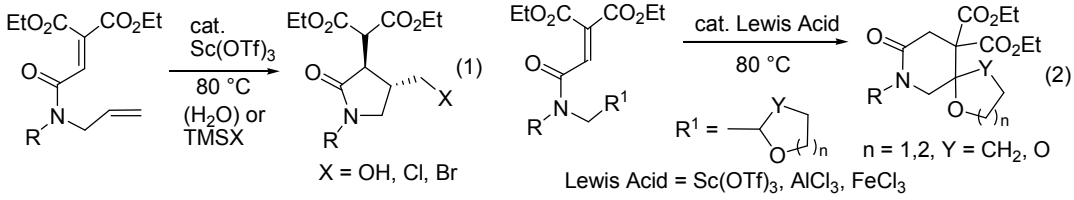
Lewis acid-catalyzed cyclization reactions of amides of ethenetricarboxylates

Shoko Yamazaki, Mamiko Niina

Nara University of Education, Nara, Japan

Nitrogen-containing heterocyclic systems are versatile core structures in organic chemistry because of their presence in many biologically active compounds. The development of new efficient synthetic strategies for the construction of nitrogen-containing heterocycles is of considerable interest. We have developed Lewis acid-promoted stereoselective five-membred ring formation of alkenyl ethenetricarboxylates.[1] To promote the cyclization/halogenation, 1-2 equivalents of Lewis acids such as $AlCl_3$, $AlBr_3$, $TiCl_4$, $TiBr_4$ and ZnI_2 are required. In this study, catalytic cyclization of allyl amides of ethenetricarboxylate leading to pyrrolidines has been examined. Reaction of allyl amides of ethenetricarboxylate with $Sc(OTf)_3$ (0.2 equiv.) gave 4-hydroxymethyl-2-oxopyrrolidine derivatives stereoselectively (eq 1). The formation of the hydroxymethylpyrrolidines may arise from participation of water in situ. $Sc(OTf)_3$-catalyzed cyclization reactions of the allyl amides with TMSX (X= Cl, Br) also proceeded efficiently to give halogenated 2-oxopyrrolidine derivatives. Catalytic cyclization of amides of ethenetricarboxylate bearing acetal and ether groups has also been examined. The reaction of the amides bearing cyclic acetal in the presence of $Sc(OTf)_3$ gave piperidine derivatives as major products (eq 2). The cyclized products may be formed via internal redox process.[2] Similarly, Lewis acid-catalyzed reaction of cyclic ethers gave spiro cyclic piperidine products selectively. The scope and the factors to control selectivities in the catalytic reactions of amides of ethenetricarboxylates are under investigation.



[1] Yamazaki, S.; Fujinami, K.; Maitoko, Y.; Ueda, K.; Kakiuchi, K. *J. Org. Chem.* **2013**, *78*, 8405. [2] Haibach, M. C.; Seidel, D. *Angew. Chem. Int. Ed.* **2014**, *53*, 5010.