DIVERGENT 1,3-DIFUNCTIONALIZATION OF AMINOCYCLOPROPANES

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Aminocyclopropanes are important building blocks in synthetic chemistry. Their reactivity was explored mainly by utilizing transition-metal catalysis to form a metallocyclobutane intermediates, or by photoredox chemistry to oxidize the amino group to a radical cation species.[1] Our group has focused in the past on the ability of donor-acceptor substituted aminocyclopropanes (D-A aminocyclopropanes) to react as zwitterionic synthons(Figure 1A),[2] we herein report a different strategy for the activation of mono-substituted aminocyclopropanes giving access to biscationic synthons(Figure 1B).

We developed a mild ring-opening strategy to transform acyl, sulfonyl or carbamate protected aminocyclopropanes into 1,3-dielectrophiles bearing halide atoms (Br, I) and hemi-aminals. Substitution of the halides by a series of nucleophiles can be done under basic conditions via S_N2 pathway while replacing the alkoxy group of the hemi-aminal can be done under acidic conditions via an elimination-addition pathway, thus generating a wide range of 1,3-difunctionalized propylamines in one pot or in two steps.

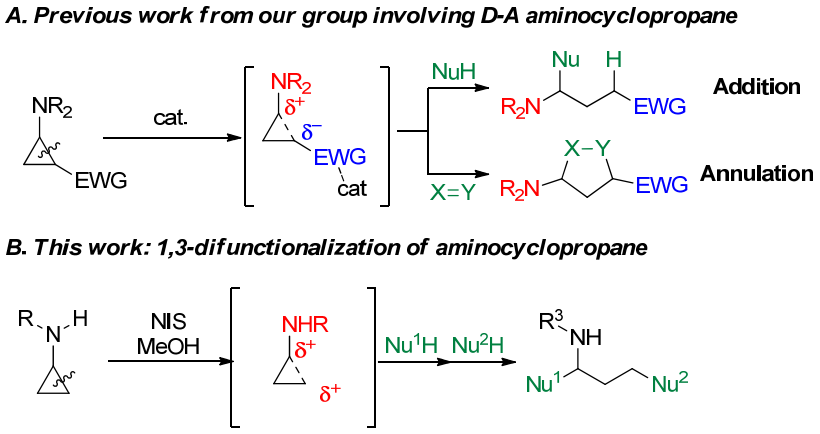

Figure 1. Our previoius work of D-A aminocyclopropanes (A). This work: radical-initiated ring opening strategy towards α, γ-difunctionalized amines (B).

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[1] Rassadin, V. A.; Six, Y. *Tetrahedron* **2016**, *72*, 4701.

[2] a) F. de Nanteuil, F. De Simone, R. Frei, F. Benfatti, E. Serrano, J. Waser, *Chem. Commun.* **2014**, *50*, 10912; b) S. Racine, B, Hegedus, R. Scopelliti, J. Waser, *Chem. Eur. J.* **2016**, *55*, 12881; c) J. Preindl, S, Chakrabarty, J. Waser, *Chem. Sci.* **2017**, *8*, 7112; d) D. Perrotta, M.-M. Wang, J. Waser, *Angew. Chem. Int. Ed.* **2018**, *57*, 5120.