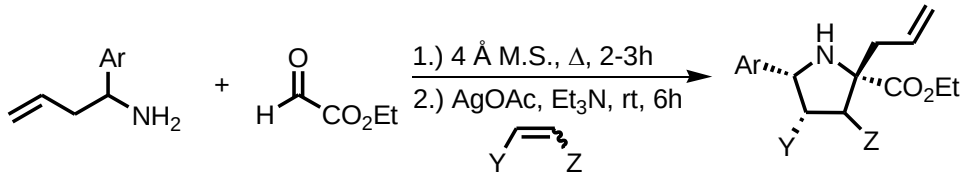
One-Pot Domino 2-Aza-Cope-[3+2] Dipolar Cycloaddition (AC/DC)



Abstract: Highly functionalized pyrrolidine rings are ubiquitous scaffolds in natural products and pharmaceuticals that exhibit a wide range of biological activity. Some examples of natural products with desirable medicinal properties include pancracrine, iscocculinine, and lycorine. New reactions that rapidly assemble such complex targets in a stereocontrolled fashion are highly desirable. In order to meet these goals, new multicomponent reactions that minimize synthetic steps, amplify stereocomplexity, and afford a diverse array of functionality must be pursued. Toward these goals, a novel one-pot, multicomponent protocol for the assembly of highly functionalized pyrrolidine rings via a domino 2-aza-Cope-[3+2] dipolar cycloaddition has been developed. This two-step sequence was found to be both high yielding and highly stereoselective for the *endo*-cycloadduct. A series of five homoallylamines were examined across three different dipolarophiles. This route offers a new quaternary stereogenic center with allyl, ester, and secondary amine functionalities within close proximity of one another. The dense functionality inherent in these scaffolds may be further elaborated to afford additional ring systems. Currently, work is being done to catalyze the dipolar cycloaddition asymmetrically by coordinating chiral ligands to the metal catalyst and in the near future this sequence will be applied to some natural products containing pyrrolidine rings.