Organocatalytic Enantioselective Intramolecular $S_N2'$ Reaction

Significance: Takasu, Yamada, and co-workers report an enantioselective intramolecular $S_N2'$ reaction using a trichloroacetimidate as leaving group. The reaction is catalyzed by a chiral Brønsted acid to give optically active pyrrolidines in excellent yields and enantioselectivities. The reaction tolerates halo groups, which are rarely compatible in the usual transition-metal-catalyzed reaction. The possibility of an $S_N1$ pathway via an allylic carbocation is ruled out by control experiments using the ($Z$)-olefin as a substrate. A mechanism involving nucleophilic catalysis is also excluded by the use of phosphate as a leaving group. The proposed dual-activation mechanism is further supported by the calculated geometries for a transition-state model.

Comment: Although there are many reports on asymmetric allylic aminations catalyzed by transition metals, organocatalytic enantioselective $S_N2'$ reactions have rarely been reported. The presented methodology offers a facile and efficient access to enantioenriched 2-vinylpyrrolidines. Attempts to synthesize piperidine rings by this method resulted in poor reactivities and selectivities. The acidity of the nucleophile is crucial for both reactivity and selectivity, and the authors explain this by suggesting a stronger interaction between the substrate and catalyst. Although the substrate scope is limited, this study provides new insights into organocatalytic substitution reactions.