

Direct Asymmetric Functionalization of α -Amino C–H Bonds

Category

Organo- and Biocatalysis

Key words

organocatalysis

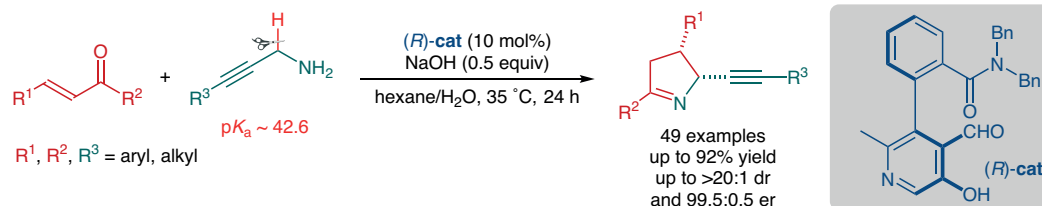
conjugate addition

propargylamines

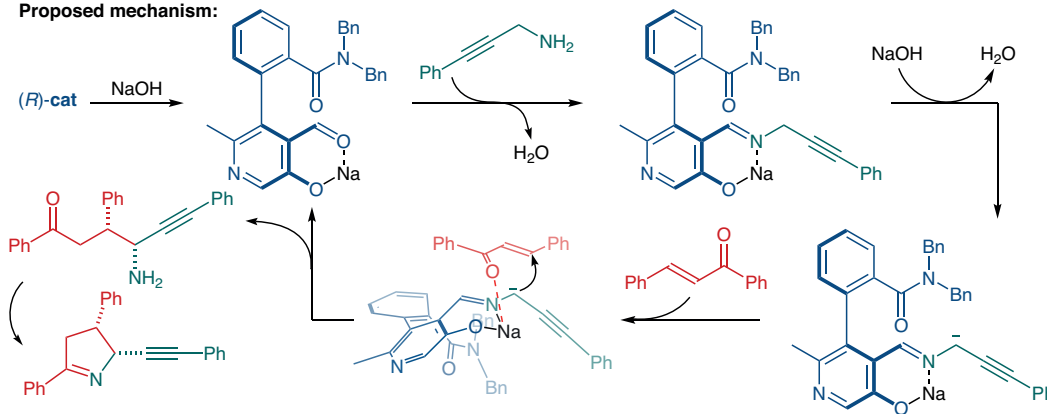
cyclization

1-pyrrolines

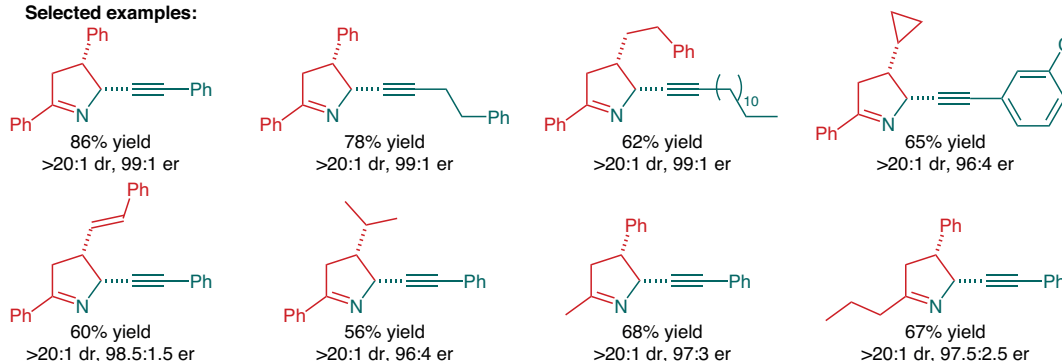
biomimetic catalysis



Proposed mechanism:



Selected examples:



Significance: The Zhao group presents a direct asymmetric α -C–H conjugate addition of NH_2 -unprotected propargylamines to α,β -unsaturated ketones by using a chiral pyridoxal catalyst. The reaction provides a wide range of chiral alkynyl 1-pyrrolines bearing two contiguous stereocenters in good yields, with excellent diastereo- and enantioselectivities. This work furnishes a streamlined approach for accessing pyrroline-containing pharmaceuticals.

Comment: Direct asymmetric functionalization of the poorly reactive α -C–H bonds of NH_2 -unprotected propargylic amines poses a significant challenge in chemical synthesis. First, the low acidity ($\text{p}K_a \sim 42.6$) of the α -C–H bond makes it difficult to deprotonate (*Angew. Chem. Int. Ed.* **2022**, *61*, e202206111). Second, classical N-addition may interfere with the overall reaction. Third, the highly reactive alkynyl group also has the potential to disrupt the transformation.