Carbonyl-Catalyzed Biomimetic Asymmetric Mannich Reaction

Significance: The Zhao group reports the activation of primary amines by carbonyls. Using an N-quaternized pyridoxal catalyst for the direct asymmetric Mannich reaction of glycinate with aryl N-diphenylphosphinyl imines, α,β-diamino acid esters were obtained in good yields and excellent stereoselectivities.

Comment: Based on their recently developed chiral pyridoxal and pyridoxamine catalysts for transamination reactions (J. Am. Chem. Soc. 2016, 138, 10730), the authors developed a catalyst that activates primary amines through carbonyl catalysis. In contrast to other α-functionalizations of primary amines, this fascinating catalysis strategy does not require protecting-group manipulation.

Selected examples:

- 90% yield, dr > 20:1, er = 99:1
- 82% yield, dr > 20:1, er = 97:3
- 77% yield, dr > 20:1, er = 99:1
- 67% yield, dr > 20:1, er = 99:1

Proposed reaction mechanism:

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