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](https://doi.org/10.1021/jacs.6b06835)), 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:**

- Ph$_2$P(O)NH$_2$OH$_2$, H$_2$I, H$_2$O, H+, I$^-$
- 77% yield
- dr > 20:1
- er = 99:1

- Ph$_2$P(O)NH$_2$OH$_2$, H$_2$I, H$_2$O, H+, I$^-$
- 67% yield
- dr > 20:1
- er = 99:1

**Proposed reaction mechanism:**

- **Catalyst:** Ph$_2$P(O)NH$_2$OH$_2$, H$_2$I, H$_2$O, H+, I$^-$
- **Product:** Ph$_2$P(O)NH$_2$OH$_2$, H$_2$I, H$_2$O, H+, I$^-$

**32 examples**

- 47–94% yield
- dr from 17:1 to >20:1
- er from 97:3 to 99.5:0.5

**Key words**

- carbonyl catalysis
- Mannich reaction
- pyridoxal
- α,β-diamino acid esters