Chiral Lewis Base Catalyzed Aldol Reaction of Unprotected Carboxylic Acids

**Significance:** Nakajima and co-workers report the first example of a chiral Lewis base-catalyzed SiCl₄-mediated enantioselective aldol reaction of unprotected carboxylic acids. The method is highly enantio- and diastereoselective, and it shows a broad substrate scope.

**Comment:** Previous works on asymmetric aldol reactions of unprotected carboxylic acids by various groups (see, for example: K. Yu et al. *J. Am. Chem. Soc.* 2017, 139, 527) required stoichiometric chiral reagents to achieve enantioselectivity, but in the presented method, the authors use SiCl₄ to activate the carboxylic acid, permitting the use of only a catalytic amount of a chiral Lewis base to achieve high enantioselectivity.

**Selected examples:**

- **R¹ = Ar, alk, R² = Ar, alk**
  - **77% yield**
  - **dr = 81:19**
  - **er = 86:14**

- **78% yield**
  - **dr = 91:9**
  - **er = 90:10**

- **84% yield**
  - **dr = 91:9**
  - **er = 90.5:9.5**

- **79% yield**
  - **dr = 91:9**
  - **er = 95.5:4.5**

- **72% yield**
  - **dr = 71:29**
  - **er = 91:9**

Plausible stereochemical pathway:

- The rate-determining step involves the formation of the phosphorus-carbon bond.