Activating Ketones with Low Catalyst Loadings of a Potent Chiral Lewis Acid

**Significance:** List and co-workers report the use of chiral organic Lewis acids at ppm- and sub-ppm levels as catalysts for the challenging asymmetric Mukaiyama aldol reaction of ketones with silyl ketene acetics. The corresponding products were obtained in excellent yields and enantioselectivities, even on a decagram scale. The extremely low catalyst loading is unprecedented in catalytic asymmetric C–C bond-forming reactions.

**Comment:** Aldehydes are commonly used as electrophiles in the catalytic asymmetric Mukaiyama aldol reaction, whereas ketones have remained a challenge as substrates for this transformation. The presented work shows the excellent performance of silylated chiral imidodiphosphorimidates (Angew. Chem. Int. Ed. 2016, 55, 13200) as powerful Lewis acid catalysts in the aforementioned reaction of both aryl- and alkyl-substituted ketones.

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**Selected examples:**

- **Gram scale (20 °C):** 1.92 g product, 99% yield, er = 95:5
- **Decagram scale (5 °C):** 59.2 g product, 86% yield, er = 95:5
- **Sub-ppm-level catalysis:** 91% yield, er = 95:5