Chiral γ-Lactams by Enantioselective Cyclopropane Functionalization

**Significance:** Cyclopropanes are important components of many biologically active molecules and they can be found fused to a pyrrolidine ring in certain medicines. The authors present a new approach to this ring system using an enantioselective C–H functionalization of a cyclopropane, enabled by a Pd/TADDOL catalyst. This work constitutes a notable advance in the field of C(sp^3)–C(sp^3) bond formation by C–H activation.

**Comment:** The reaction shows good functional group tolerance and allows the synthesis of a library of diverse cyclopropane-fused pyrrolidines in high yield and with high enantioselectivity. The substrates can be accessed in a sequence by using a variant of the Kulinkovich reaction. The authors also demonstrate that the catalyst can efficiently activate methyl C–H groups in other substrates.

**Selected examples:**

- **PMB N**
  - 89% yield
  - er = 95:5:4.5
- **PhMe, 70 °C**
  - 17 examples up to 99% yield
  - er up to 98:2

**Additional examples:**

- **Pd(dba)₂ (10 mol%)**
  - ligand (20 mol%)
  - AdCO₂H (10 mol%)
  - Cs₂CO₃ (1.5 equiv)
  - PhMe, 110 °C
  - 99% yield
  - er = 85:15

**Mes = 2,4,6-Me₃C₆H₂**

**Ar = 3,5-t-BuC₆H₃**

**Category**
- Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

**Key words**
- cyclopropanes
- C–H bond activation
- lactams