Palladium-Catalyzed Asymmetric C–H Functionalizations of Isobutanamides

**Significance:** Desymmetrization of isopropyl moieties has remained an unanswered challenge. The authors have developed new ligands for the formation of a chiral center at the α-position of isobutyric acid derivatives through β-C(sp³)–H functionalization.

**Comment:** This palladium-catalyzed protocol promotes an asymmetric β-C(sp³)–H arylation, alkenylation, or alkyynylation to form a chiral center at the α-position of a range of isobutyric acid derivatives with moderate yields and excellent enantioselectivities.

**Selected examples:**

- **First set of reactions:**
  - O
    - NHArF + Ar-I
    - Pd(MeCN)_2Cl_2 (10 mol%), Ag_2CO_3 (2 equiv), NaTFA (2 equiv), PhMe, 60 °C, 72 h
  - ArF = 4-F_3CC_6F_4
  - 68% yield, er = 98:2
  - 70% yield, er = 98:2
  - 70% yield, er = 96:4
  - 73% yield, er = 97:3
  - 62% yield, er = 95:5
  - 50% yield, er = 98:2
  - 52% yield, er = 97:3
  - 60% yield, er = 98:2

- **Second set of reactions:**
  - O
    - NHArF + R^1I + R^2I
    - Pd(OAc)_2 (10 mol%), Ag_2CO_3 (2 equiv), PhMe, 50 °C, 48 h
  - ArF = 4-F_3CC_6F_4
  - 60% yield, er = 94:6
  - 42% yield, er = 95:5
  - 61% yield, er = 94:6
  - 57% yield, er = 94:6
  - 60% yield, er = 95:5
  - 43% yield, er = 94:6