Nickel-Catalyzed Enantioselective Hydroalkylation of 1,3-Dienes

**Significance:** Transition-metal-catalyzed asymmetric addition of enols or enolates to unsaturated hydrocarbons remains an unanswered challenge. The authors have developed a regio- and stereoselective hydroalkylation of 1,3-dienes by nickel catalysis.

**Comment:** This catalytic reaction provides a wide range of γ,δ-unsaturated ketones or esters in good yields and with high enantioselectivities. One product was easily converted into the nonsteroidal anti-inflammatory drug (R)-flobufen, which also exhibits immunomodulatory properties.

**Selected examples:**

- **Ph**
  - ![Chemical Structure](image)
  - 78% yield, er = 96:4
  - 91% yield, er = 96:4

- **Ph**
  - ![Chemical Structure](image)
  - 91% yield, dr = 1.1:1, er = 90.5:9.5
  - 70% yield, dr = 1.4:1, er = 90.5:9.5

- **Ph**
  - ![Chemical Structure](image)
  - 40% yield, er = 86:14

**Derivatization:**

- **Ph**
  - ![Chemical Structure](image)
  - er = 96:4
  - 75% yield, er = 98:2

* (S)-DTBM-HO-BIPHEP was employed. **Performed with (S)-DTBM-MeO-BIPHEP and reacted at 90 °C.