Enantioselective CuH-Catalyzed Anti-Markovnikov Hydroamination of 1,1-Disubstituted Alkenes


CuH-Catalyzed Enantioselective Anti-Markovnikov Hydroamination

**Significance:** β-Chiral amines are ubiquitous motifs in a range of biologically active molecules, including pharmaceuticals and natural products. The catalytic enantioselective hydroamination of alkenes provides an efficient route to such molecules using simple, and often commercially available, starting materials. Herein, Buchwald and co-workers present an enantioselective CuH-catalyzed anti-Markovnikov hydroamination of 1,1-disubstituted alkenes.

**Comment:** The report expands upon the authors’ previous work on the Cu-catalyzed enantioselective hydroamination of styrene derivatives (J. Am. Chem. Soc. 2013, 135, 15746). The proposed mechanism involves hydrocupration of the 1,1-disubstituted olefin in an anti-Markovnikov manner, which is intercepted by the hydroxylamine ester to give the final product and a Cu(II) alkoxide complex. The active CuH catalyst is regenerated by the addition of stoichiometric amounts of hydro-silane.

**Selected examples:**

- 88% yield, 95% ee (CyNBn2)
- 91% yield, 99% ee (t-BuNBn2)
- 96% yield, 90% ee (PhMe2SiOBz)
- 90% yield, 96% ee (TBSO)
- 88% yield, 95% ee (PhOBn)
- 91% yield, 99% ee (t-BuNBn2)
- 90% yield, 96% ee (PhMe2Si)

**Proposed mechanism:**

The reaction takes place in THF at 40 °C for 36 h, with Cu(OAc)₂ (2 mol%), (R)-DTBM-SEGPHOS (2.2 mol%), (EtO)₂MeSiH (2.0 equiv). 32 examples up to 96% yield and up to 99% ee are reported. The active CuH catalyst is regenerated by the addition of stoichiometric amounts of hydro-silane.