Asymmetric Remote C–H Borylation of Aliphatic Amides and Esters with a Modular Iridium Catalyst
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Asymmetric ϒ-Borylation of Aliphatic Amides and Esters

Significance: The authors report on an asymmetric borylation of aliphatic amides and esters in ϒ-position. The efficient catalytic system delivers chiral pinacolboronates in high yield and enantiomeric excess.

Comment: The complex catalytic system is comprised of an iridium precatalyst, a chiral ligand and a receptor ligand. The receptor ligand has a pyridine moiety intended for binding to the catalyst and a urea moiety for substrate binding. The absence of either of these components results in no reaction. 2,6-Lutidine has a positive impact on both yield and enantiomeric excess. Preliminary quantum chemical calculations show that the amide substrate is bound to the catalytic cavity not only through hydrogen bonding with receptor ligand but also through other noncovalent interactions.

Selected examples:

- Et₂BPin NHt-Bu (89% yield, 93% ee)
- Et₂BPin NHPh (91% yield [83% at gram scale], 98% ee)
- Et₂BPin OH (73% yield, 92% ee)
- Et₂BPin NBn₂ (99% yield, >99% ee)
- Et₂BPin OEt (80% yield, 90% ee)
- Et₂BPin OBn (83% yield, 95% ee)
- Et₂BPin NHPh (81% yield, 94% ee)
- Et₂BPin NBn₂ (81% yield, 96% ee)

Derivatizations:

- MeOBr (4.0 equiv) NBS (4.0 equiv) THF, −78 °C to r.t.
- n-BuLi (4.0 equiv) THF–H₂O (1:1), 25 °C, 3 h
- NaBO₃ ⋅ 4H₂O (3.0 equiv) THF–H₂O (1:1), 25 °C, 3 h
- H₂N-DABCO (1.0 equiv) KOt- Bu (2.4 equiv) THF, 80 °C, 1 h
- then Ac₂O, 80 °C, 1 h
- 95% yield, 98% ee
- 64% yield, 97% ee

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