Cobalt-Catalyzed Enantioselective Hydrogenation of Enamides

Category

Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words

cobalt catalysis
asymmetric hydrogenation
enamides
single-electron reduction

Synfact
of the month

Previous work on cobalt catalysts relied on activation by alkyl lithium reagents:

Cobalt-catalyzed asymmetric hydrogenation with zinc:

Mechanism:

dehydro-levetiracetam

Zn-free hydrogenation:

Significance: On the basis of a discovery from high-throughput reaction studies, the authors have developed a low-catalyst-loading enantioselective hydrogenation of functionalized alkenes through activation by zinc instead of the more-usual alkyl reagents. The optimized catalytic system $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}/(R,R)\text{-Ph-BPE}$ or $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}/(R,R)\text{-i-Pr-DuPhos}$ realized a high reactivity and enantioselective hydrogenation in MeOH.

Comment: A series of mechanistic studies revealed that Co(II) metal dissociates from the Co(II)/phosphine complex in MeOH, and that Zn reduces Co(II) to Co(I) through one-electron reduction to form a more stable Co–phosphine bond, which is key to the efficient enantioselective reduction of alkenes. The hydrogenation can be applied to a large-scale reaction requiring only 0.08 mol% of the cobalt catalyst.

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Synfacts 2018, 14(08), 0819 Published online: 18.07.2018
DOI: 10.1055/s-0037-1610460; **Reg-No.:** H07818SF