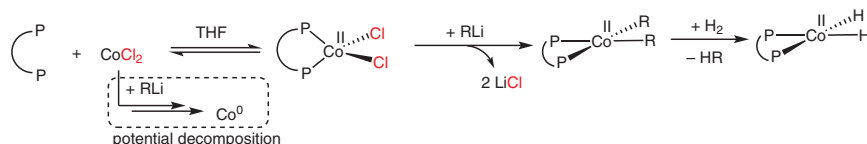
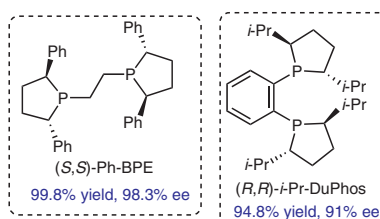
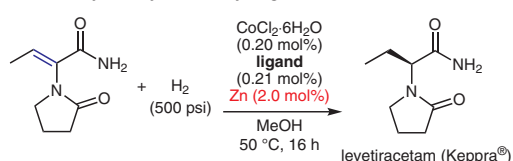


# Cobalt-Catalyzed Enantioselective Hydrogenation of Enamides

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

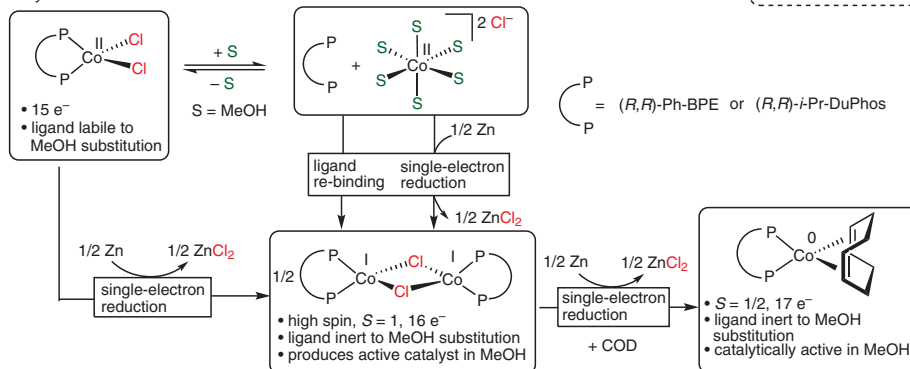


Cobalt-catalyzed asymmetric hydrogenation with zinc:

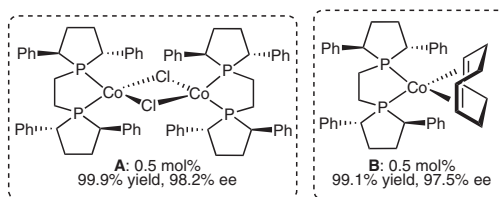
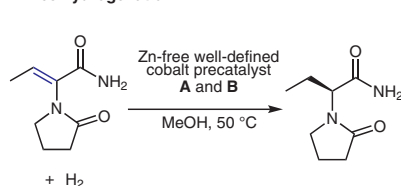


Mechanism:

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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