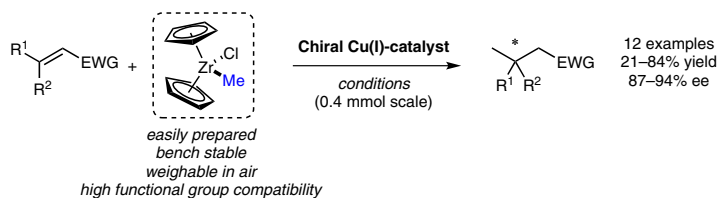
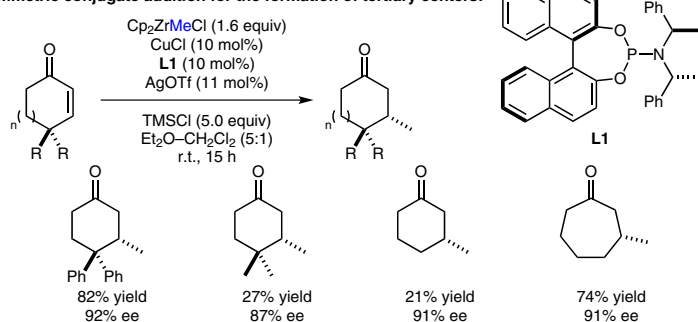


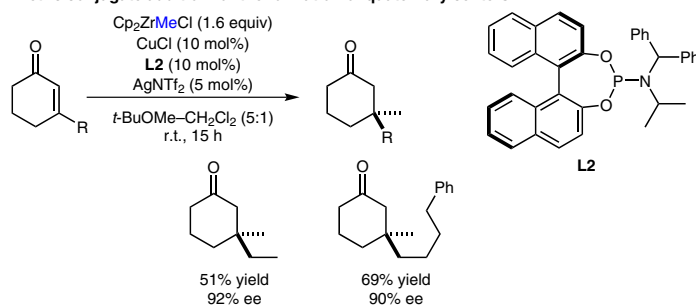
# Convenient Reagent for the Copper-Catalyzed Asymmetric Methyl 1,4-Addition Reaction



## Asymmetric conjugate addition for the formation of tertiary centers:



## Asymmetric conjugate addition for the formation of quaternary centers:



**Significance:** Tertiary and quaternary stereocenters bearing a methyl group are common structural units in a wide array of natural products and pharmaceuticals. The synthesis of such compounds is usually performed by the asymmetric conjugate methyl addition to  $\alpha,\beta$ -unsaturated carbonyl compounds. Unfortunately, this approach usually relies on the use of impractical reagents (e.g. pyrophoric reagents, low functional group compatibility). In this work, the authors disclosed the use of Cp<sub>2</sub>ZrMeCl as an efficient and operationally friendly reagent in copper-catalyzed methyl 1,4-addition reactions.

**Comment:** The use of Cp<sub>2</sub>ZrMeCl as a methyl source in combination with a chiral copper catalyst allowed the formation of  $\beta$ - and  $\delta$ -tertiary and quaternary centers in generally good yields and excellent enantioselectivities. The reaction was applied to a variety of cyclic and acyclic carbonyl compounds, allyl chlorides and in the synthesis of (*R*)-(-)-muscone. The zirconium reagent was prepared on a 10 g scale reaction from Cp<sub>2</sub>ZrCl<sub>2</sub> and was demonstrated to be stable for up to six months when stored under inert gas at room temperature.

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