K. GARREC, S. P. FLETCHER* (UNIVERSITY OF OXFORD, UK)
$Cp_2ZrMeCl$: A Reagent for Asymmetric Methyl Addition
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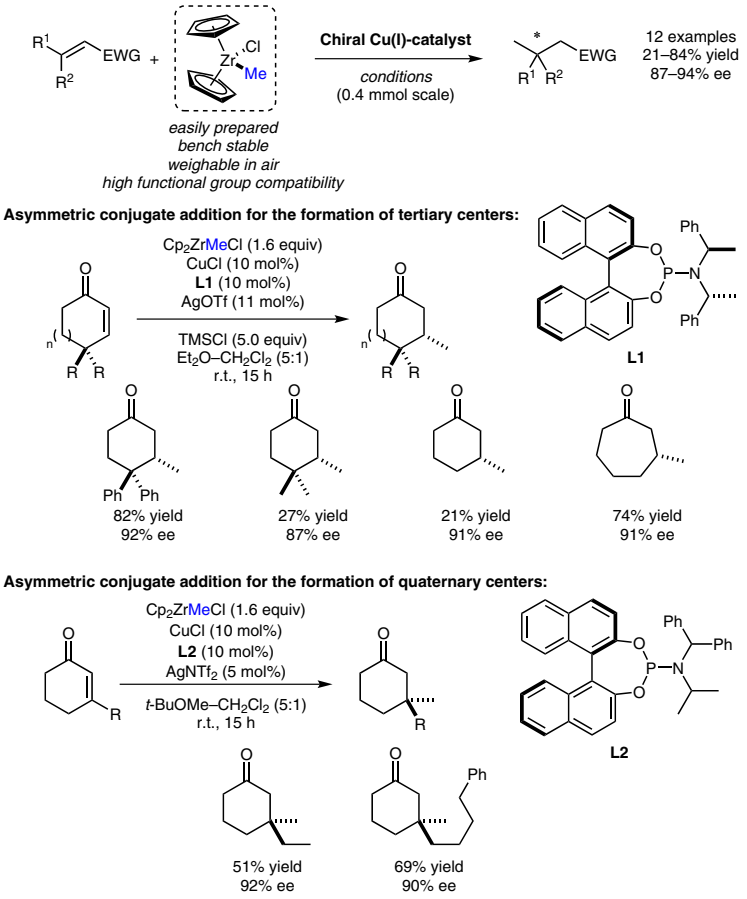
# Convenient Reagent for the Copper-Catalyzed Asymmetric Methyl 1,4-Addition Reaction




**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 α,β-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 $Cp_2ZrMeCl$ as an efficient and operationally friendly reagent in copper-catalyzed methyl 1,4-addition reactions.

**Comment:** The use of $Cp_2ZrMeCl$ as a methyl source in combination with a chiral copper catalyst allowed the formation of β- and δ-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 $Cp_2ZrCl_2$ and was demonstrated to be stable for up to six months when stored under inert gas at room temperature.

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**Category**

**Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions**

**Key words**

**copper catalysis**

**asymmetric reaction**

**1,4-conjugate addition**

**stable zirconium reagent**