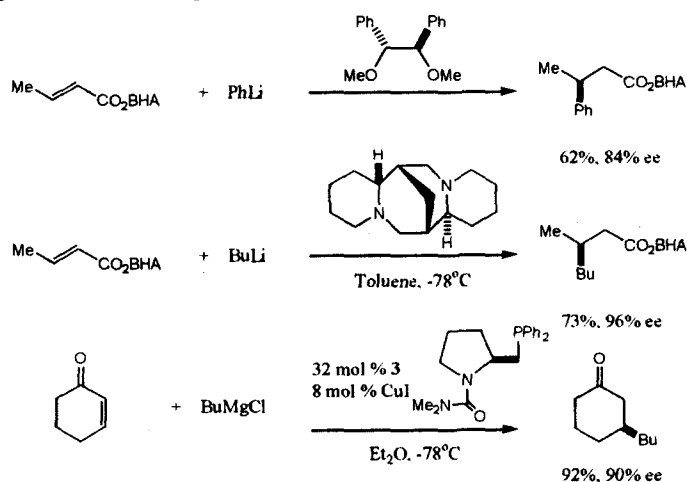


A Catalytic Asymmetric Way in Carbon-Carbon Bond Formation

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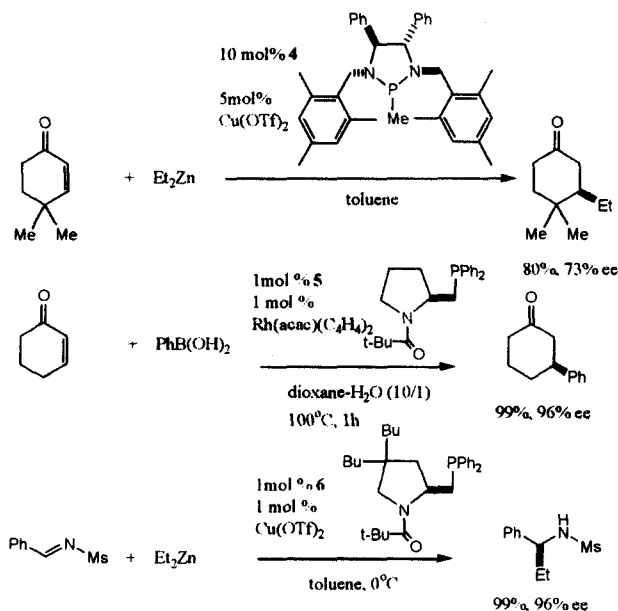
Catalytic asymmetric control of the absolute and relative stereochemistry in carbon-carbon bond forming process has been a challenging target for synthetic organic chemists.^{1,2} We have been attacking this target through two kinds of different approaches starting from designing a chiral ligand. One approach is based on the use of highly reactive organolithium reagents as carbon nucleophiles. Another uses bimetallic reagents generated by complexation of transition metals with relatively mild organometallics such as Grignard reagents, organozincs, and so on. In either approach, the concept for design of chiral ligands is based on activation of organometallic reagents by chelate formation. For example, we have developed a chiral dimethyl ether of stilbenediol **1** as a suitable ligand for organolithium reagents, which forms a five-membered chelate and increases a reactivity of organolithium reagents.³



Asymmetric conjugate addition reaction of organolithium reagents with enoates was realized using **1** and **2** as chiral ligands. Each ligand **1** or **2** is complementary to afford aryl and alkyl addition products in high enantioselectivity. Ligand **1** mediates an addition of aryllithiums and **2** does that

of alkyllithium reagents, giving each product in high selectivity up to 99%.⁴ Catalytic reaction using substoichiometric amount of **1** and **2** is possible to afford the addition products in reasonably high ees.⁵

The most reliable conjugate 1,4- addition reaction relies on organocopper species, which are usually generated by treating copper salt with organolithium or Grignard reagents. Since these hetero-bimetallic reagents involves two different kind of metals, it is necessarily to design a ligand in a different way to those for monometallic reagents. We introduced the novel concept metal differentiating coordination for this purpose.⁶ For example, an amidophosphine **3**⁷ was a successful ligand for lithium or magnesium organocuprates. The carbonyl oxygen and phosphorous atoms of **3** coordinate metal-selectively to lithium or magnesium and copper atoms, respectively. The metal selective coordination of **3** creates a efficient chiral environment around organocuprate. Thus, a really catalytic asymmetric conjugate addition reaction of Grignard reagent with cycloalkenones was realized using **3** as a catalytic ligand to afford the corresponding adducts in up to 98% ee.^{8,9}



Organozinc also becomes a good conjugate addition reagent when organocuprate species are generated from copper salt and complexed with chiral phosphines such as **4**.^{10,11} The powerful conjugate addition of arylboronic acids to cycloalkenones has been realized using rhodium(I)-**5** catalyst. For example, the reaction of phenyl-boronic acid with cyclohexenone provided 3-phenylcyclohexanone in 96% ee and 99% yield in the presence of 1 mol % of the catalyst.

The catalytic asymmetric addition reaction of organometallic reagents with

C=N of imines has been also focus of recent synthetic chemistry. Organolithium reagents behave well as good carbo-nucleophiles under the control of a chiral amino ether ligand.¹² Much more promising is a copper-6-catalyzed addition of organozinc reagents to C=N of imines, giving the corresponding adducts in up to 94% ee and quantitative yield in the presence of 1 mol % of the catalyst in toluene.

In the lecture, catalytic behavior of chiral phosphines will be focused.

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