Cu-Catalyzed Asymmetric 1,6-Conjugate Addition of Dialkylzinc

Selected examples:

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\begin{align*}
R^1 & = n-C_7H_{15}, R^2 = Ph: 80\% \text{ yield} \\
R^1 & = n-C_7H_{15}, R^2 = n-C_7H_{15}: 70\% \text{ yield} \\
n-C_7H_{15} & + R^3Zn (3.0 \text{ equiv}) \xrightarrow{\text{Cu(OTf)}_2 (5 \text{ mol\%}) \ L_1 (10 \text{ mol\%}) \ \text{MeTHF–cyclohexane}} \ R^3 \ O \\
n-C_7H_{15} & + R^3Zn (3.0 \text{ equiv}) \xrightarrow{\text{Cu(OTf)}_2 (5 \text{ mol\%}) \ L_1 (10 \text{ mol\%}) \ \text{MeTHF–cyclohexane}} \ R^3 \ O
\end{align*}
\]

Isomerization and 1,4-conjugate addition of 1,6-adducts:

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\begin{align*}
R^1 & = n-C_7H_{15}, R^2 = Ph: 41\% \text{ yield} \\
R^1 & = n-C_7H_{15}, R^2 = n-C_7H_{15}: 57\% \text{ yield} \\
n-C_7H_{15} & + R^3Zn (3.0 \text{ equiv}) \xrightarrow{\text{DBU (1 equiv)} \ \text{CH}_2\text{Cl}_2, r.t., 24 \text{ h}} \ R^3 \ O \\
n-C_7H_{15} & + R^3Zn (3.0 \text{ equiv}) \xrightarrow{\text{DBU (1 equiv)} \ \text{CH}_2\text{Cl}_2, r.t., 24 \text{ h}} \ R^3 \ O
\end{align*}
\]

Plausible reaction mechanism:

Significance: The authors reported the asymmetric 1,6-conjugate addition of dialkylzinc to acyclic dienones catalyzed by copper/phosphinoazomethinylate salt (DiPPAM). After the isomerization of the conjugate adducts, stereoselective sequential 1,4-conjugate addition of diethylzinc was also demonstrated.

Comment: The control of regioselectivity of the 1,6-conjugate addition is difficult due to many parameters. Using copper and the DiPPAM ligand, a highly enantio- and regioselective 1,6-conjugate addition was achieved. With the BINAP ligand, unprecedented highly stereoselective induction is noteworthy.