The First Enantioselective Rhodium-Catalyzed 1,4-Addition

Significance: Although Miyaura was the first to report rhodium-catalyzed conjugate addition of boronic acid reagents (M. Sakai, H. Hayashi, N. Miyaura *Organometallics* 1997, 16, 4229), it was the combined effort of Hayashi and Miyaura that, in the present work, demonstrated that this process can be done with a high level of enantioselectivity. This reaction, now often referred to as the Hayashi–Miyaura reaction, has become highly popular because: 1) it proceeds under neutral reaction conditions, 2) no background uncatalyzed 1,4-addition occurs, 3) no 1,2-addition in the presence or absence of catalyst takes place, and 4) it has a high functional group tolerance.

Comment: The authors noted that the reaction works best with \([\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2]\) as opposed to the racemic version, which proceeded with \([\text{Rh}(\text{acac})(\text{CO})_2]\). The ethylene complex enables facile formation of the active \([\text{Rh}(\text{acac})(\text{BINAP})]\) species. Another modification from the original work is the higher reaction temperature. This work represented the first time that high yields and enantioselectivities could be achieved in an aryl group 1,4-addition using a chiral BINAP ligand. Since this seminal report, other ligand classes have been elucidated, and this venerable methodology has been expanded to include domino reaction systems.

**Selected examples:**

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\begin{align*}
\text{Ph} & \quad 93\% \text{ yield, } 97\% \text{ ee} \\
\text{Ph} & \quad 99\% \text{ yield, } 97\% \text{ ee} \\
\text{Ph} & \quad 51\% \text{ yield, } 93\% \text{ ee} \\
\text{Ph} & \quad 82\% \text{ yield, } 97\% \text{ ee} \\
\text{Ph} & \quad 88\% \text{ yield, } 92\% \text{ ee} \\
\text{MeO} & \quad 99\% \text{ yield, } 97\% \text{ ee} \\
\text{F} & \quad 70\% \text{ yield, } 99\% \text{ ee} \\
\text{Cl} & \quad 94\% \text{ yield, } 96\% \text{ ee} \\
\text{t-Bu} & \quad 76\% \text{ yield, } 91\% \text{ ee}
\end{align*}
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