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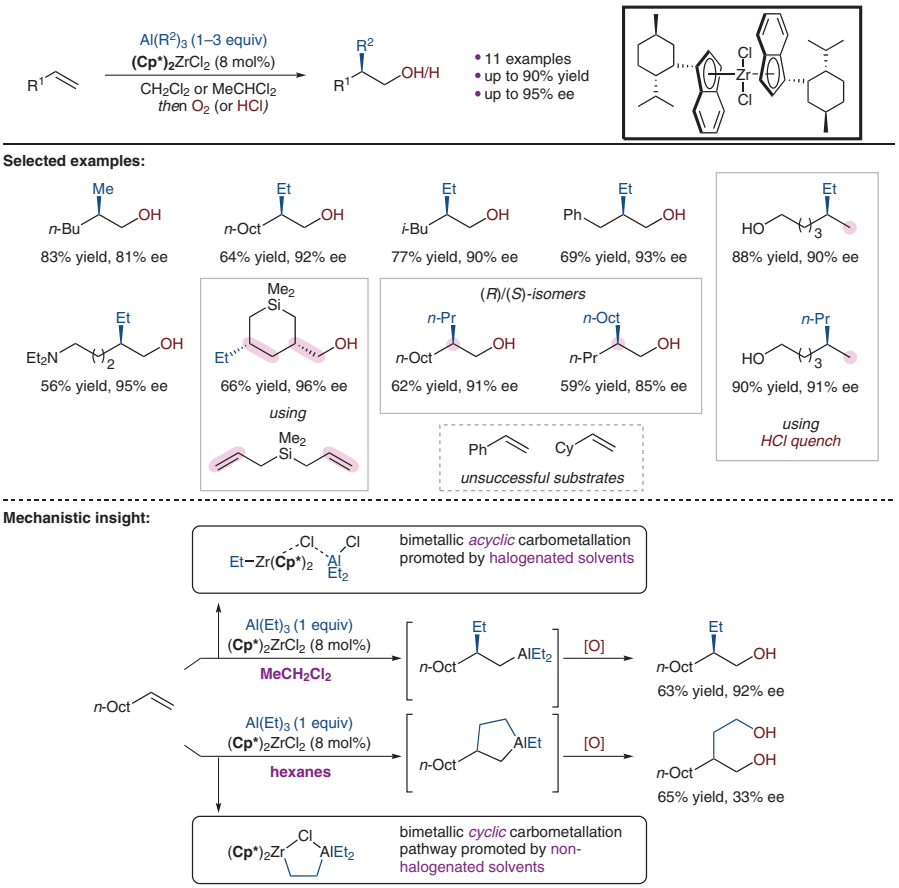
Zirconium-Catalyzed Enantioselective Alkylalumination of Monosubstituted Alkenes Proceeding via Noncyclic Mechanism
J. Am. Chem. Soc. **1996**, *118*, 1577–1578, DOI: 10.1021/ja953655m.

Asymmetric Zirconium-Catalyzed Alkylalumination of Alkenes



Significance: Negishi and Kondakov reported the **z**irconium-catalyzed **a**symmetric **c**arboalumination of monosubstituted **a**lkenes (the **ZACA** reaction) using (–)-$(NMI)_2ZrCl_2$. While previously the ZACA reaction was limited to *methyl*alumination, this report disclosed the use of Al(**Et**)$_3$ and Al(***n*-Pr**)$_3$ as reagents in a highly enantioselective transformation. Notably, the use of polar halogenated solvents was shown to be crucial. Terminal alkenes with alkyl chains, including alcohols and amines, engaged in the reaction with high selectivity and synthetically useful yields. The ZACA reaction has since evolved as a powerful strategy for the synthesis of versatile chiral building blocks.

Review: S. Xu, E. Negishi *Acc. Chem. Res.* **2016**, *49*, 2158–2168.

Comment: Notably, the solvent effect gave insight into the mechanism of this transformation. In hexanes, *ethyl*alumination was unsuccessful, where, following oxidation, the diol derivative was exclusively synthesized with low selectivity. This outcome has been proposed to occur through the in-situ generation of a bimetallic Zr–Al intermediate which undergoes a cyclic carbometallation pathway. In contrast, the choice of polar chlorinated solvent can dislocate the cyclic bimetallic species and allow for an acyclic carbometallation sequence to occur, which leads to the desired product in high enantioenrichment, as reported.

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