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Homogeneous Asymmetric Catalysis

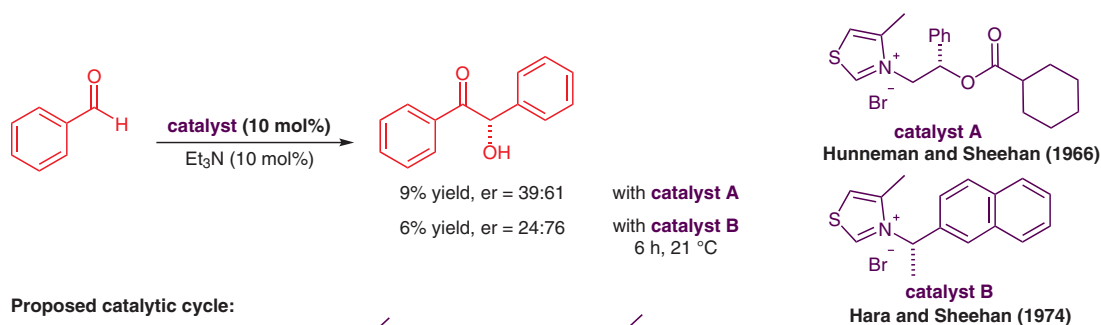
J. Am. Chem. Soc. **1966**, 88, 3666–3667.

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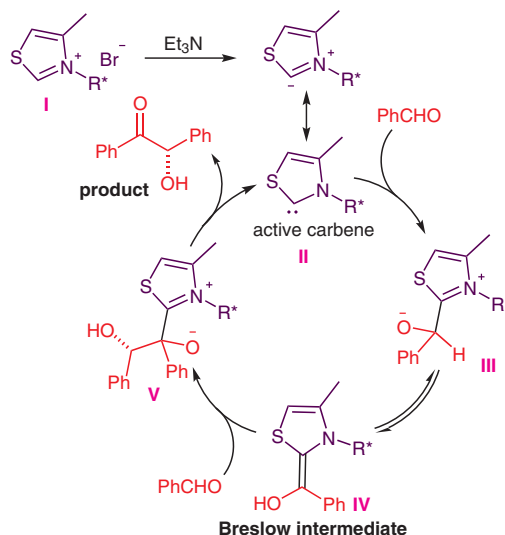
Asymmetric Thiazolium Salt Catalysis of the Benzoin Condensation

J. Org. Chem. **1974**, 39, 1196–1199.

Thiazolium Salt Catalyzed Asymmetric Benzoin Reaction



Proposed catalytic cycle:



Significance: In 1966, Hunneman and Sheehan reported the first asymmetric benzoin reaction mediated by a chiral thiazolium salt to form the corresponding product with low yield and enantioselectivity. Based on the catalytic cycle proposed by Breslow (*J. Am. Chem. Soc.* **1958**, 80, 3719), Hara and Sheehan later studied the stereochemical effect of various enantiopure thiazolium salts on the reaction. Although the authors could not improve the yield, they did observe slight improvements in enantioinduction. Following this seminal work, several other groups have reported the use of related N-heterocyclic carbene precursors to catalyze reactions with excellent enantioselectivities and have further applied such motifs in metal catalysis as chiral ligands.

Comment: Reactions such as pyruvate decarboxylation and benzoin addition can also be catalyzed by enzymes using similar thiazolium ions (vitamin B1, thiamine) as a cofactor, where the electrophilic carbonyl carbon is converted into an acyl anion equivalent (*Umpolung*). In analogy to biocatalysis, the simple thiazolium salt **I** can also generate catalytically active carbene **II** upon deprotonation. Nucleophilic attack of **II** on an aldehyde gives intermediate **III**, which, after tautomerization, furnishes the crucial Breslow intermediate **IV** (A. Berkessel, V. R. Yatham, S. Elfert, J.-M. Neudörfl *Angew. Chem. Int. Ed.* **2013**, 52, 11158). Subsequently, **IV** reacts with a second aldehyde molecule to give addition product **V**, which then furnishes the benzoin product with regeneration of the active catalyst.

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