Scaffolding Catalysis: An Effective Strategy for Controlling Selectivity

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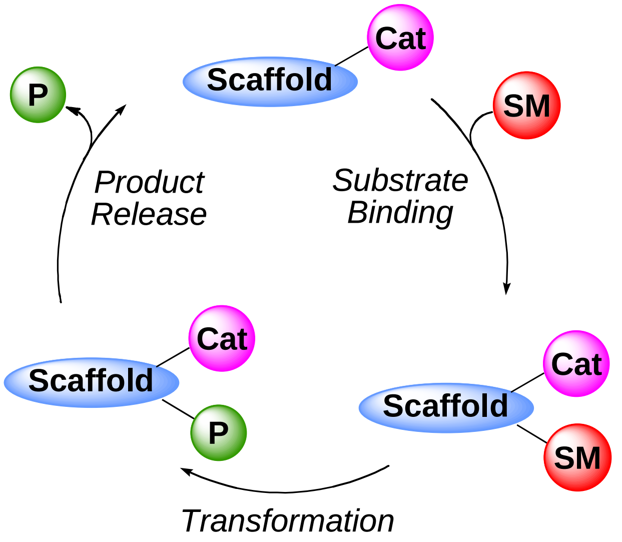
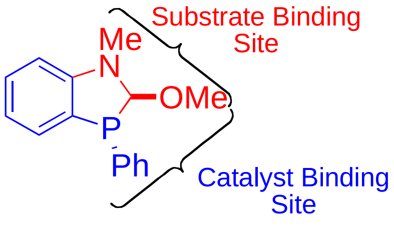
The control of site-, regio-, and stereoselectivity is a paramount goal for any synthetic chemist. We have launched a program aimed at developing general approaches for controlling selectivity in organic reactions. The use of reversibly formed covalent bonds to induce intramolecular reactions is a powerful means of controlling regio- and stereoselectivity, as well as accelerating reactions. We have engineered a series of compounds that capitalize on this concept, which we have termed scaffolding catalysis (Scheme 1). Using this simple design principle we have developed catalysts that afford highly enantioselective reactions for both hydroformylation and silyl transfer reactions. A key aspect of this type of catalysis is that it is an entropically driven process, so it has the potential to be applied to a broad variety of reactions.

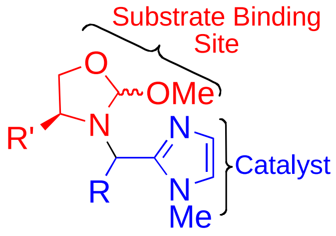


Scheme 1. Scaffolding Catalytic Cycle



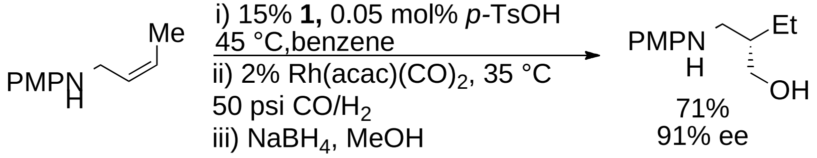
1

Hydroformylation Catalyst



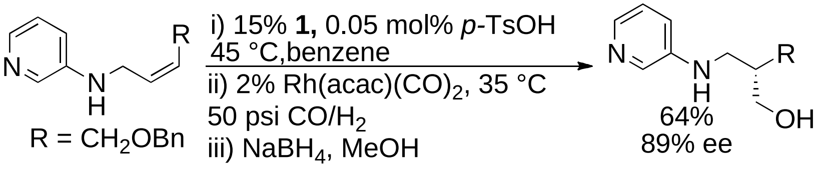
2

Silylation Catalyst



i) 15% **1,** 0.05 mol% *p*-TsOH
45 °C,benzene
ii) 2% $Rh(acac)(CO)_2$, 35 °C
50 psi CO/H_2
iii) $NaBH_4$, MeOH

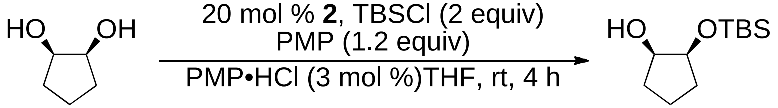
71%
91% ee



R = CH_2OBn

i) 15% **1,** 0.05 mol% *p*-TsOH
45 °C,benzene
ii) 2% $Rh(acac)(CO)_2$, 35 °C
50 psi CO/H_2
iii) $NaBH_4$, MeOH

64%
89% ee



20 mol % **2**, TBSCl (2 equiv)
PMP (1.2 equiv)
PMP•HCl (3 mol %)THF, rt, 4 h

PMP = pentamethylpiperidine

92%
94% ee