

Catalysis through Induced Intramolecularity using Reversible Covalent Bondings

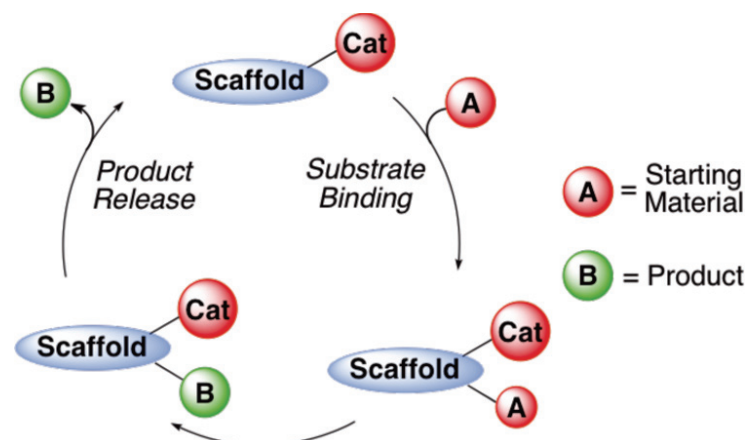
Literature Seminar
April 22, 2013
Taisuke Itoh (M1)

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1. Introduction

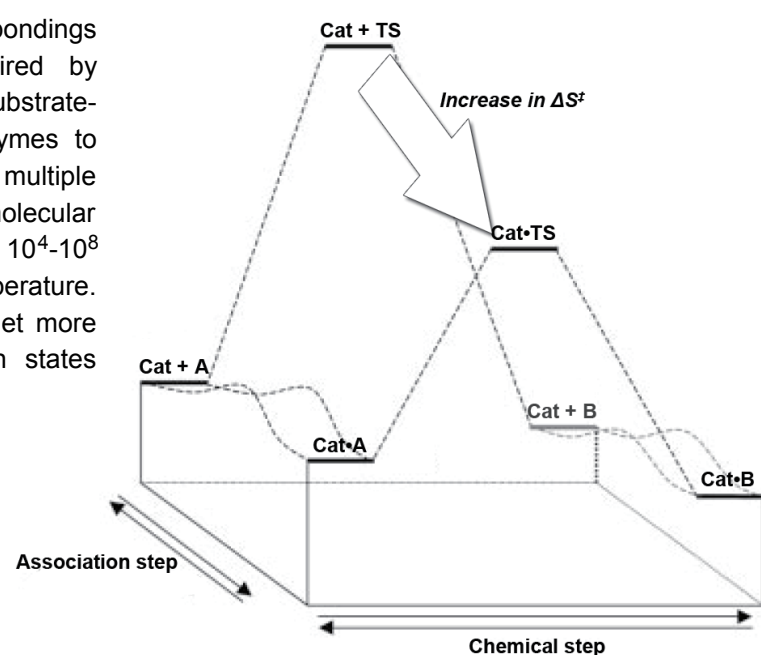
"The use of reversibly formed covalent bonds to induce intramolecular reactions is a powerful way of controlling regio- and stereoselectivity, as well as accelerating reactions. Although this mode of activation was demonstrated in catalytic systems over 60 years ago, it is infrequently used in catalyst design. 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. Furthermore, this design element can be used in concert with more traditional forms of catalyst activation."



Tan, K. L. *ACS Catal.* **2011**, *1*, 877.

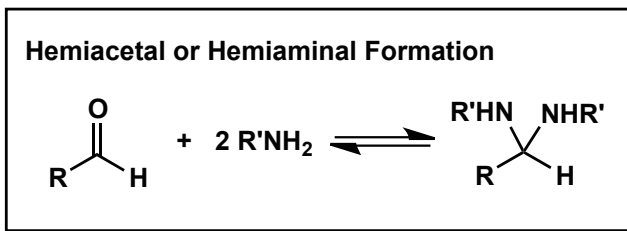
2. Non-Metal Catalysis through Induced Intramolecularity

The application of reversible covalent bondings to organic catalysis is often inspired by enzymes. The incorporation of a substrate-binding step allows catalysts or enzymes to prepay the entropic penalty for bringing multiple molecules together. By inducing intramolecular reactions, it gains rate accelerations of 10^4 - 10^8 for 1 M reactants at room temperature. Furthermore, non-covalent bondings get more effective for stabilization of transition states through induced intramolecularity.

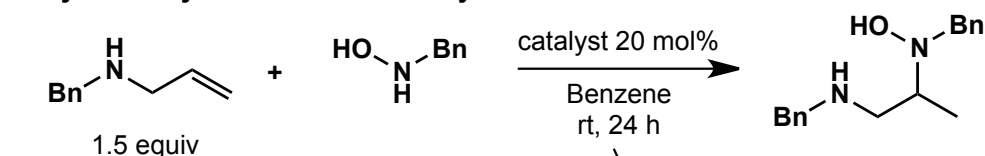


Pascal, R. *Eur. J. Org. Chem.* **2003**, *10*, 1813.

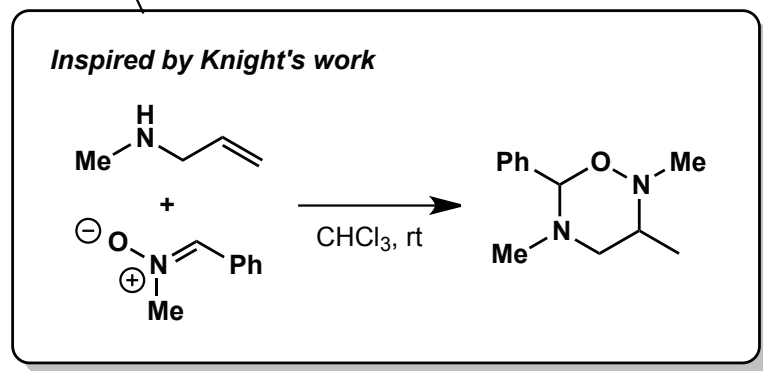




Aldehyde-Catalyzed Intermolecular Hydroamination of Alkenes

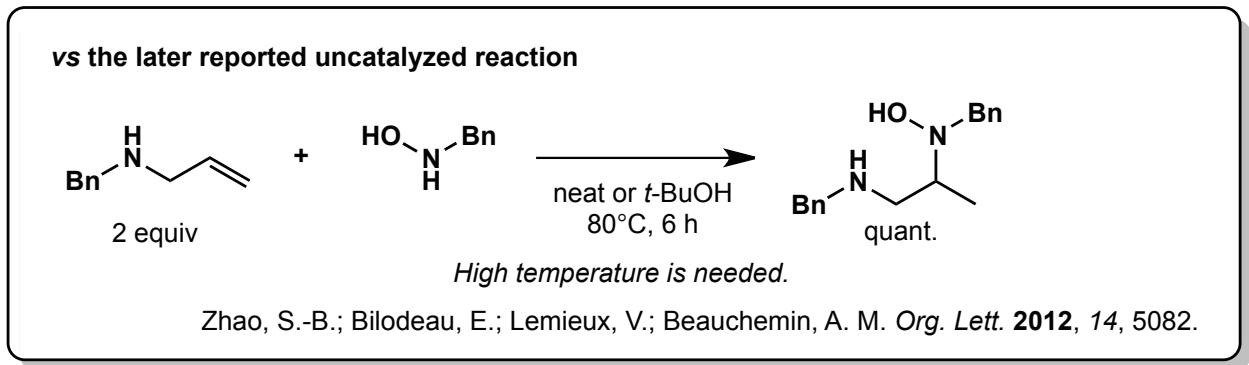


catalyst	yield (%)
none	0
	12
	77

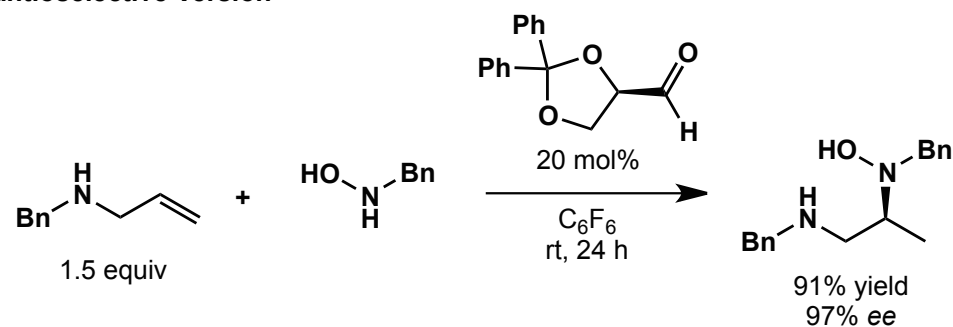


MacDonald, M. J.; Schipper, D. J.; Ng, P. J.; Moran, J.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2011**, *133*, 20100.

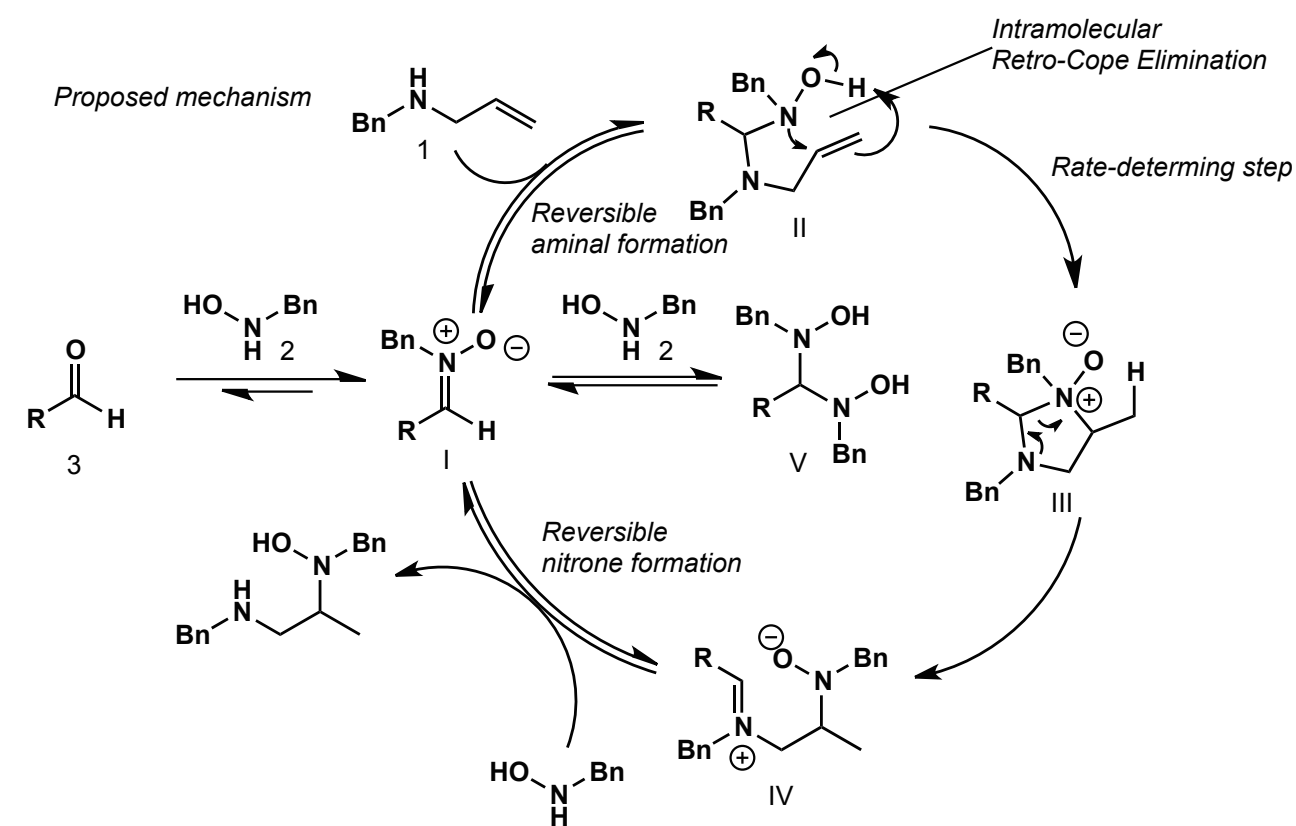
This is the first aldehyde catalysis which preassociates two substrates using covalent bonding.



Enantioselective Version



MacDonald, M. J.; Hesp, C. R.; Schipper, D. J.; Pesant, M.; Beauchemin, A. M.; *Chem. Eur. J.* **2013**, *19*, 2597.



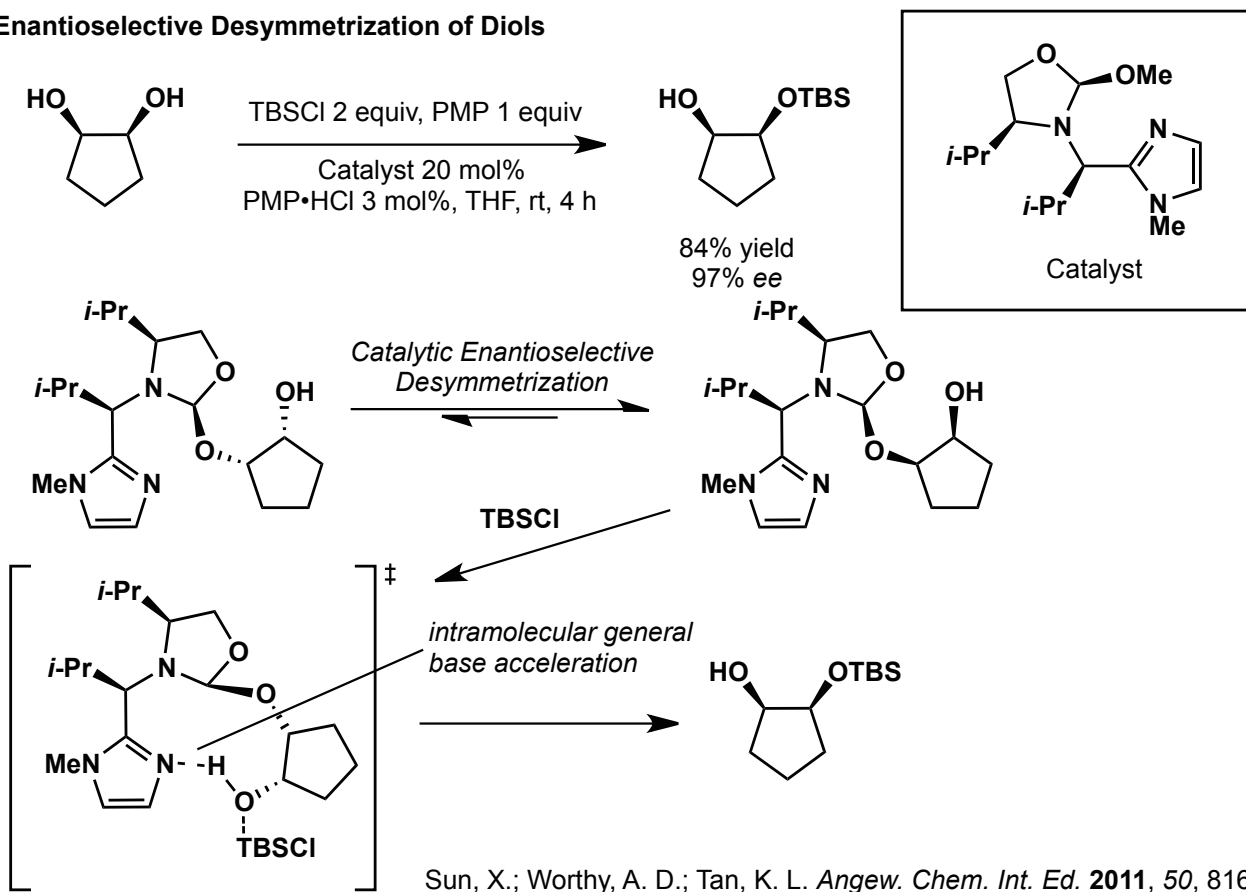
Given that the rate-determining step of the catalytic cycle is proposed to be hydroamination, the rate law can be expressed as follows:

$$\text{rate} = k_{HA}K_B[1][3]/(1 + K_B[1] + K_A[2])$$

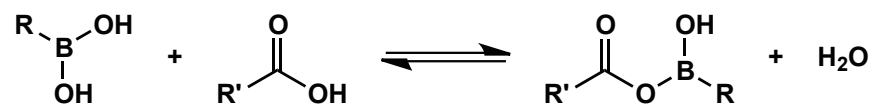
This is consistent with the rate dependence on the concentration of the reaction.

Guimond, N.; MacDonald, M. J.; Lemieux, V.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2012**, *124*, 16571.

Enantioselective Desymmetrization of Diols

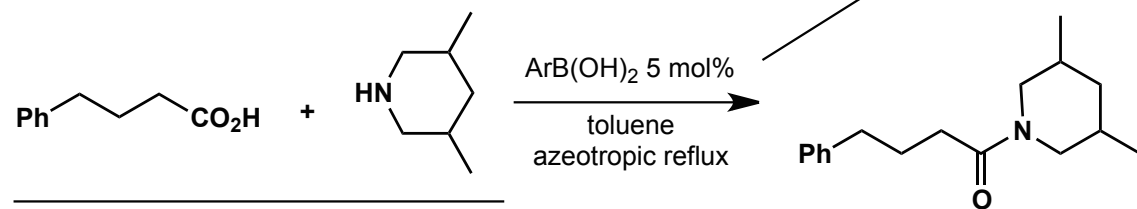


Equilibrium between Boronic Acids and Carboxylic Acids



Inspired by stoichiometric boron chemistry

Boronic Acid-Catalyzed Direct Amidation of Carboxylic Acids

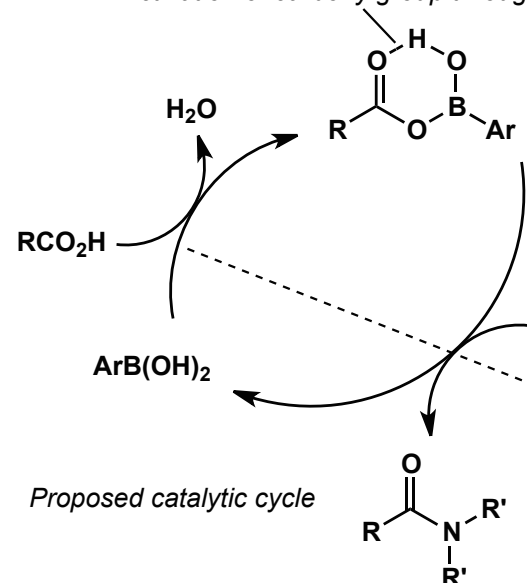


entry	Ar	yield (%)
1	3,4,5-F ₃ C ₆ H ₂	74
2	C ₆ H ₅	23
3	no catalyst	<2

Boronic acids which had electron-withdrawing group excellently catalyzed direct amidation of carboxylic acids. α -Hydroxy carboxylic acids were also stable for this method.

Ishihara, K.; Ohara, S.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4196.

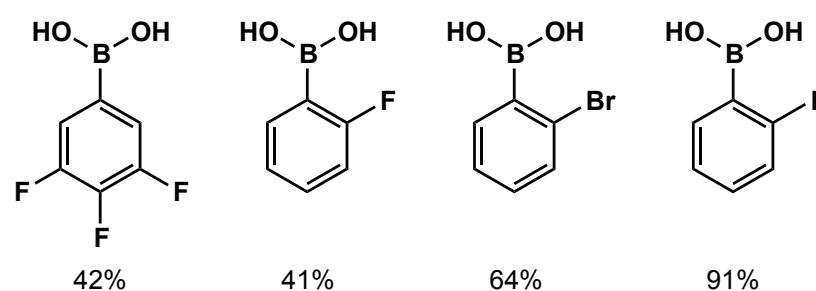
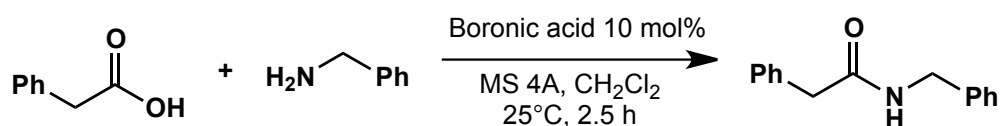
Activation of carbony group through induced intramolecularity?



When they prepared the monoacyloxyboronic acid and to a solution of this substrate in toluene was added 1 equiv of benzylamine at room temperature without removal of the water, the amidation proceeded even at room temperature, but with 50% conversion. So Ishihara thought that the rate-determining step was the generation of the monoacyloxyboronic acid and electron-withdrawing group was effective for this transformation.

Is this step really the rate-determining step?

Acceleration Effect by *ortho*-Halophenylboronic Acids

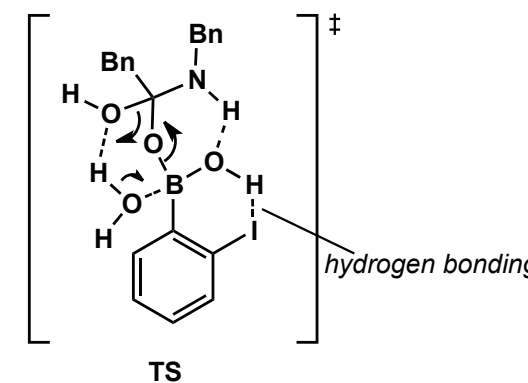
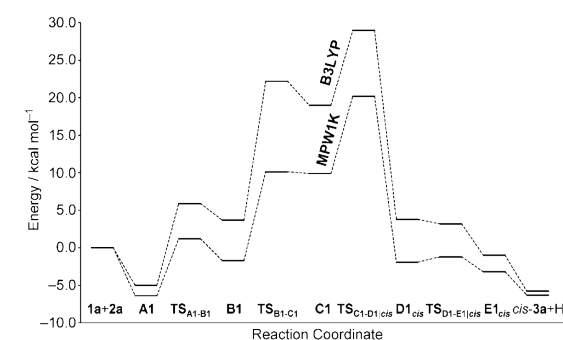
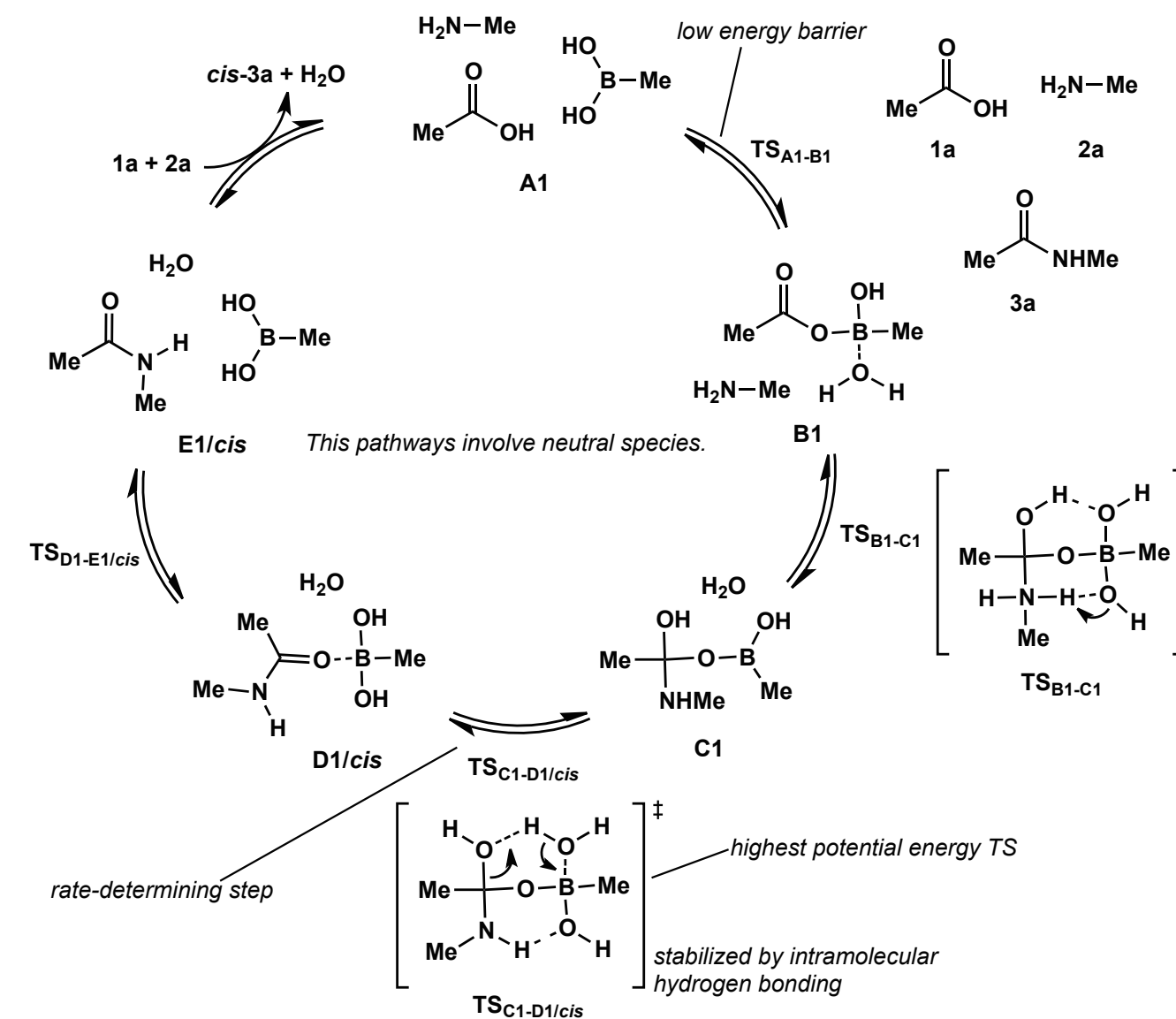


ortho-Halophenylboronic acids catalyzed direct amidation of carboxylic acid at room temperature.

How is the effect of *ortho*-halogen substituents?

Al-Zoubi, R. M.; Marion, O.; Hall, D. G. *Angew. Chem. Int. Ed.* **2008**, *47*, 2876.

Lowest-energy Calculated Catalytic Cycle



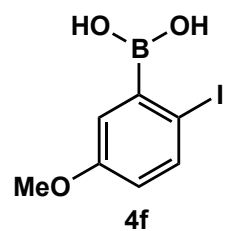
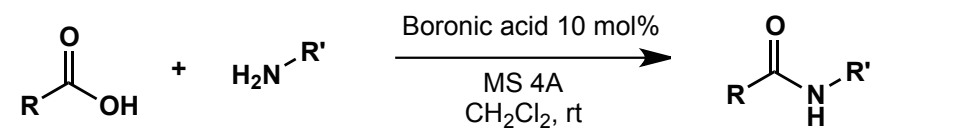
Pathways involving ionized reactants were found to be more energetically demanding than those involving neutral species. In fact, while aliphatic amines and carboxylic acids readily form salts in water and highly polar solvents, their pK_a order switches in aprotic organic solvents of lower polarity.^[40]

The calculated potential energy profile for the reaction of compound 1a and 2a catalyzed by methylboronic acid indicated that formation of the boron-bound amide from the corresponding hemiaminal is the rate determining step, in contradiction with previous hypothesis^[22] that formation of monoacyloxyboronic acid was the rate determining step.

Following this theory, the factor that stabilize TS_{C1-D1/cis} is important for the acceleration of this reaction. *ortho*-Halogen substituents are thought to be engage in an O-H...X hydrogen bonding stabilizing the rate-determining transition state, which is greater for iodine than for chlorine due to the geometrical constraints determining the intramolecular hydrogen bonding.^[41]

Marcelli, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 6840.

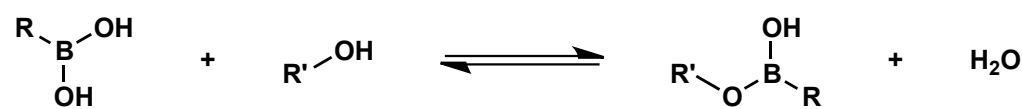
Acceleration Effect by *ortho*-Halophenylboronic Acids



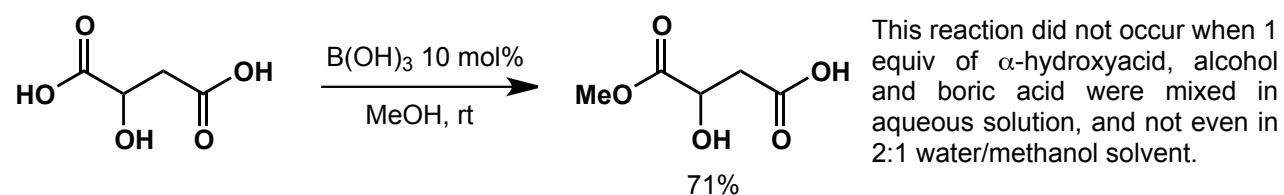
Following Marcelli's theory, *meta*-methoxy substituent is thought to increase the electron density of *ortho*-iodide substituent and reinforce the hydrogen bonding network.

Gernigon, N.; Al-Zoubi, R. M.; Hall, D. G. *J. Org. Chem.* **2012**, *77*, 8386.

Equilibrium between Boronic Acids and Alcohols

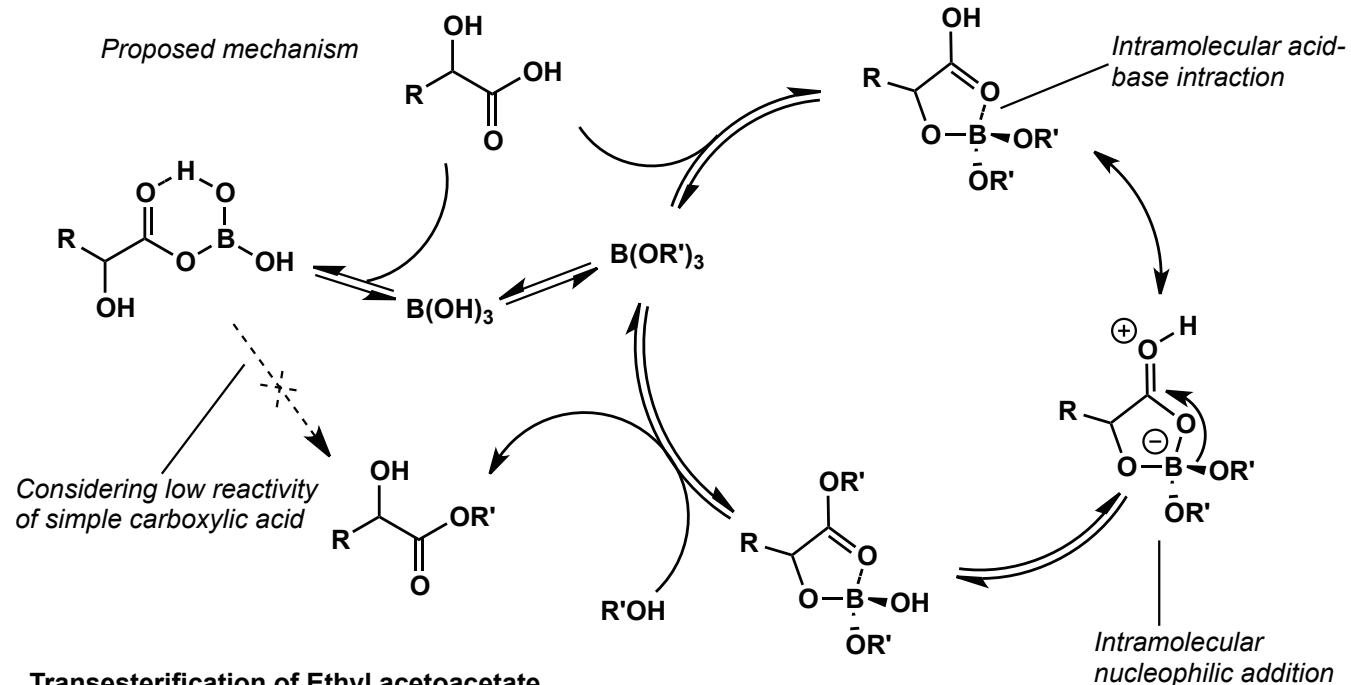


Chemoselective Esterification of α -Hydroxycarboxylic Acids



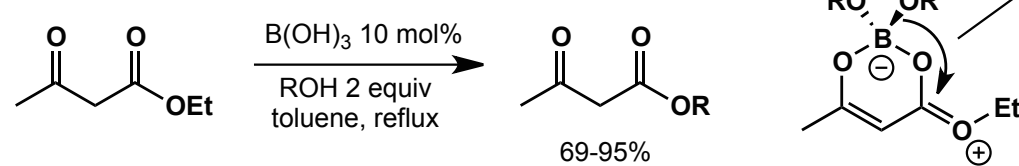
This reaction did not occur when 1 equiv of α -hydroxyacid, alcohol and boric acid were mixed in aqueous solution, and not even in 2:1 water/methanol solvent.

Proposed mechanism



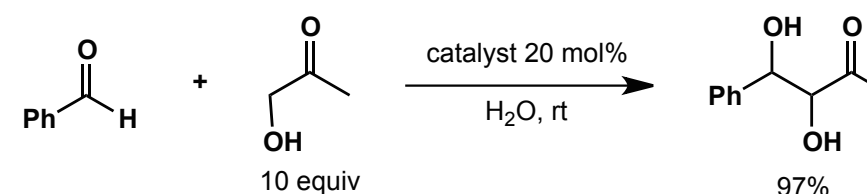
Considering low reactivity of simple carboxylic acid

Transesterification of Ethyl acetoacetate

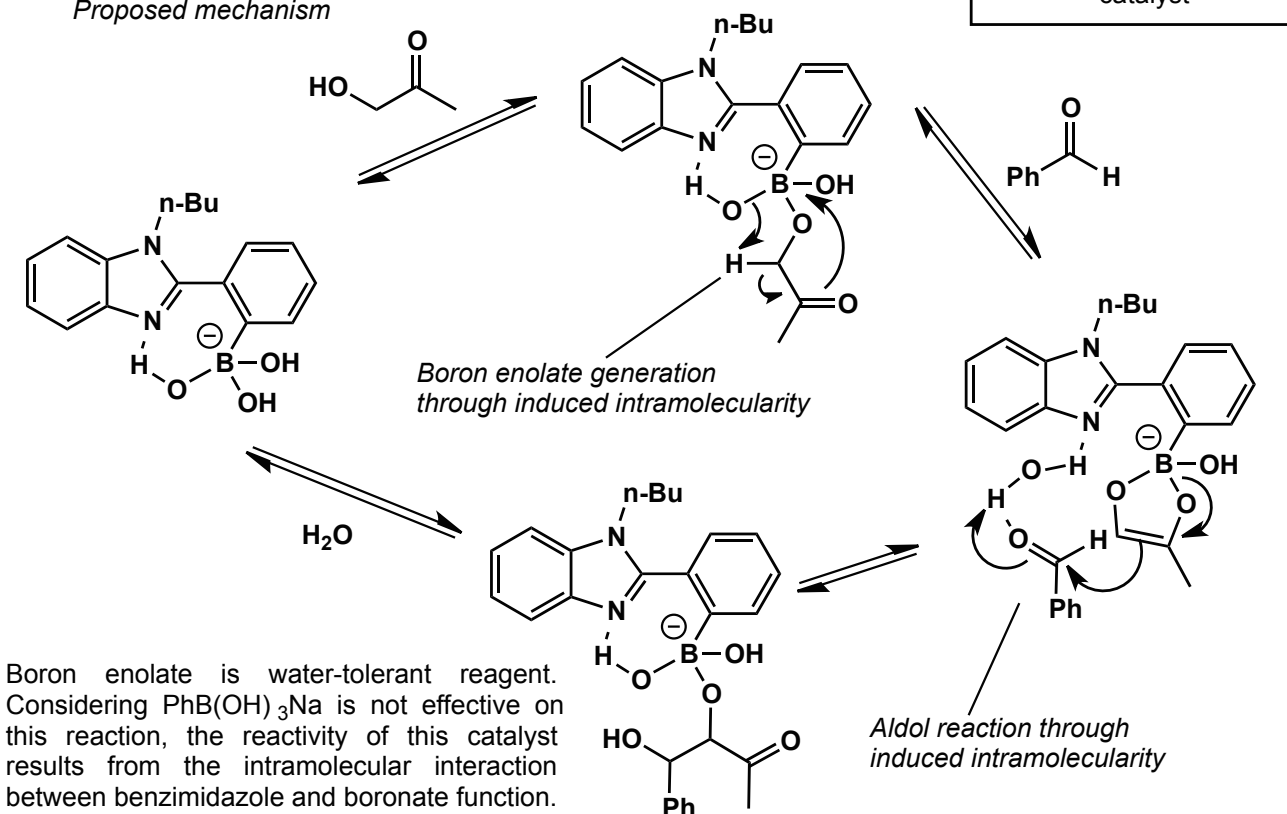


Kondaiah, G. C. M.; Reddy, L. A.; Babu, K. S.; Gurav, V. M.; Huges, K. G.; Bandichhor, R.; Reddy, P. P.; Bhattacharya, A.; Anand, R. V. *Tetrahedron Lett.* **2008**, *49*, 106.

Aldol Reaction in Water



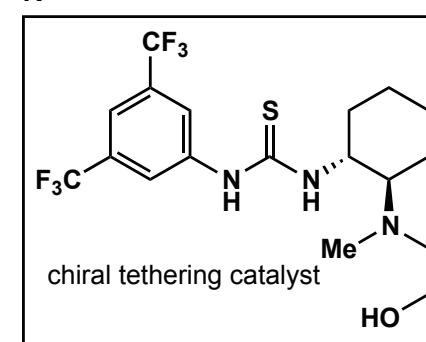
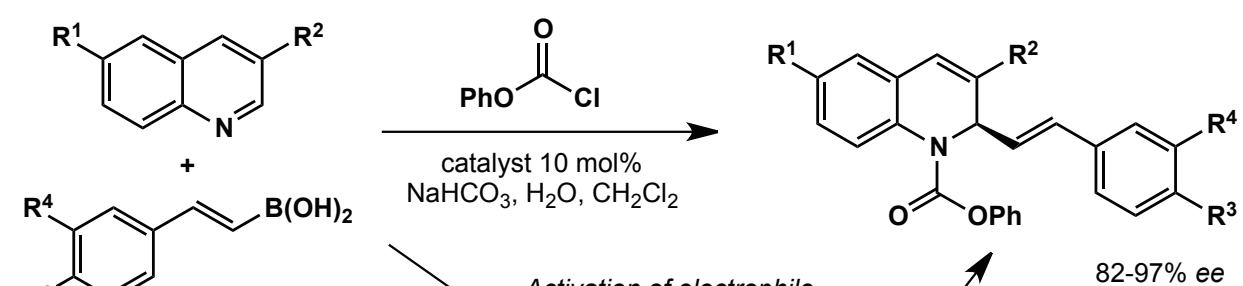
Proposed mechanism



Boron enolate is water-tolerant reagent. Considering $PhB(OH)_3Na$ is not effective on this reaction, the reactivity of this catalyst results from the intramolecular interaction between benzimidazole and boronate function.

Aelvoet, K.; Batsanov, A. S.; Blatch, A. J.; Grosjean, C. Patrick, L. G. F.; Smethurst, C. A.; Whiting, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 768.

Asymmetric Petasis-Type Reaction



Activation of electrophile

Activation of nucleophile

Induced intramolecularity

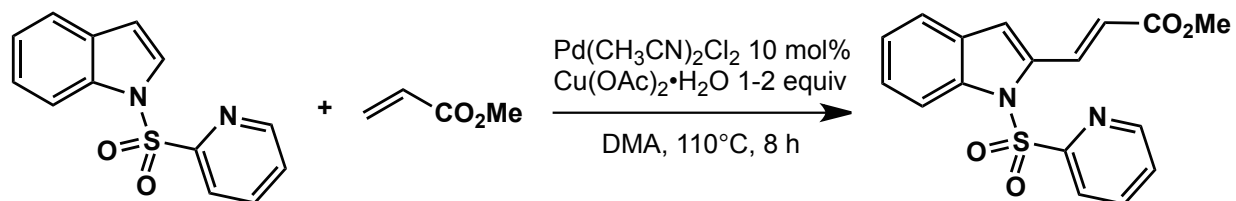
Yamaoka, Y.; Miyabe, H.; Takemoto, Y. *J. Am. Chem. Soc.* **2007**, *129*, 6686.

3. Catalytic Directing Groups

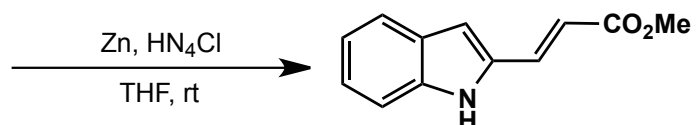
Irremovable Directing Groups

Irremovable directing group cannot be used synthetically.

Removable Directing Groups

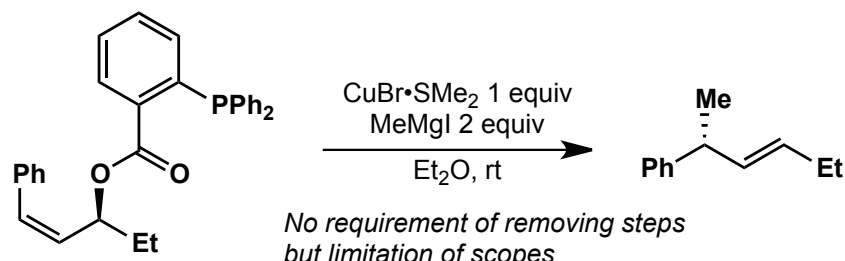


Requirement of installing and removing steps
(two additional nonproductive steps)



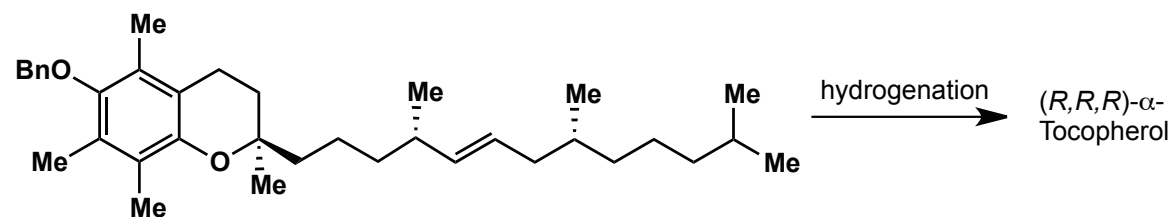
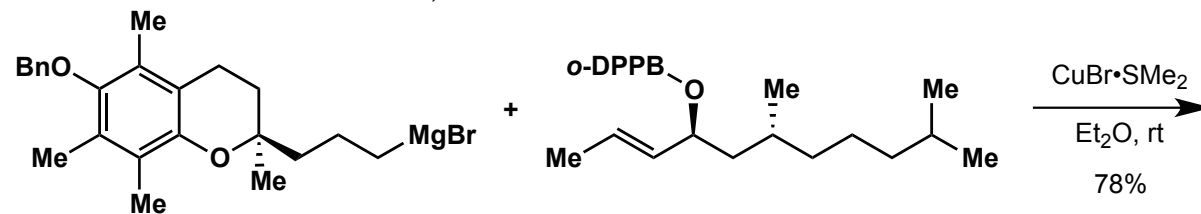
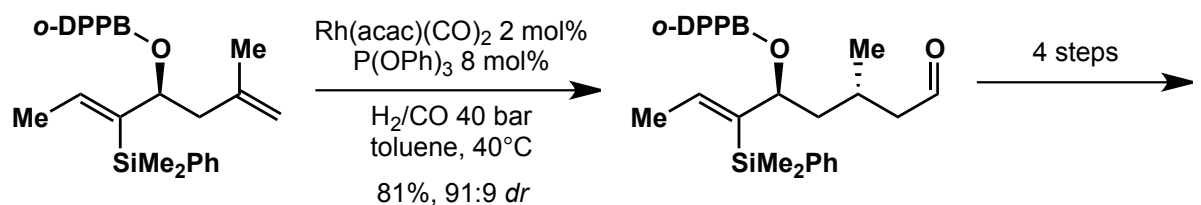
García-Rubia, A.; Gómez Arrayás, R.; Carretero, J. C. *Angew. Chem. Int. Ed.* **2009**, *48*, 6511.

Leaving Directing Groups



Breit, B.; Demel, P. *Adv. Synth. Catal.* **2001**, *343*, 429.

Sequential Use of Removable Directing Groups



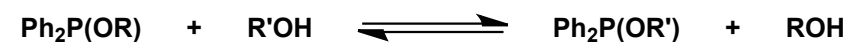
Minimization of installing and removing steps

Rein, C.; Demel, P.; Outten, R. A.; Netscher, T.; Breit, B. *Angew. Chem. Int. Ed.* **2007**, *46*, 8670.

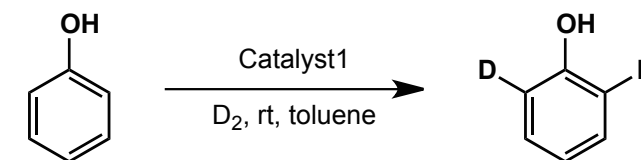
Catalytic Directing Groups

No requirement of installing and removing steps

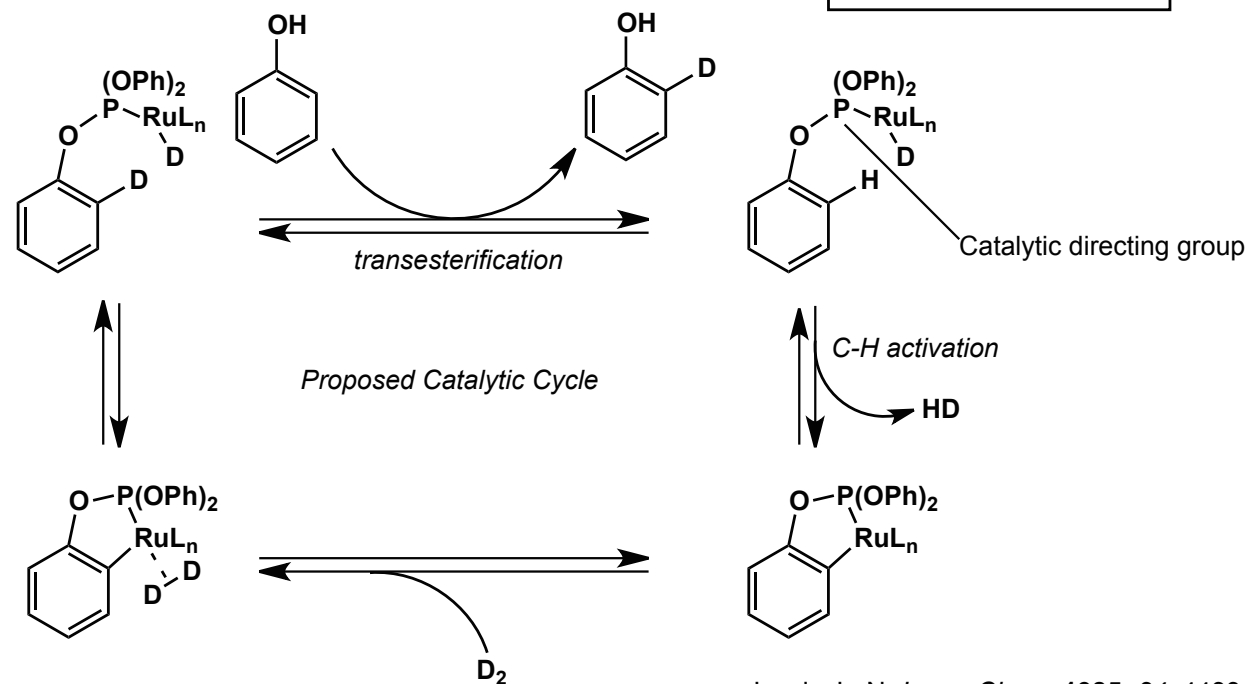
Transesterification of Phosphinite or Phosphite



Ortho Deuteration of Phenol

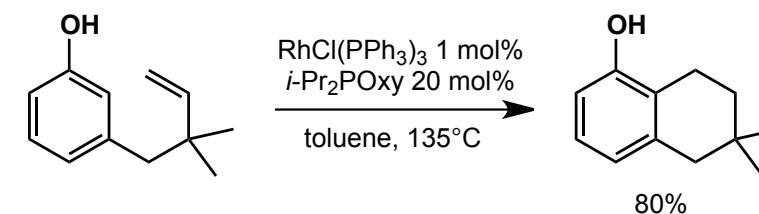


Inspired by Parshall's stoichiometric reaction in 1969.^[42]

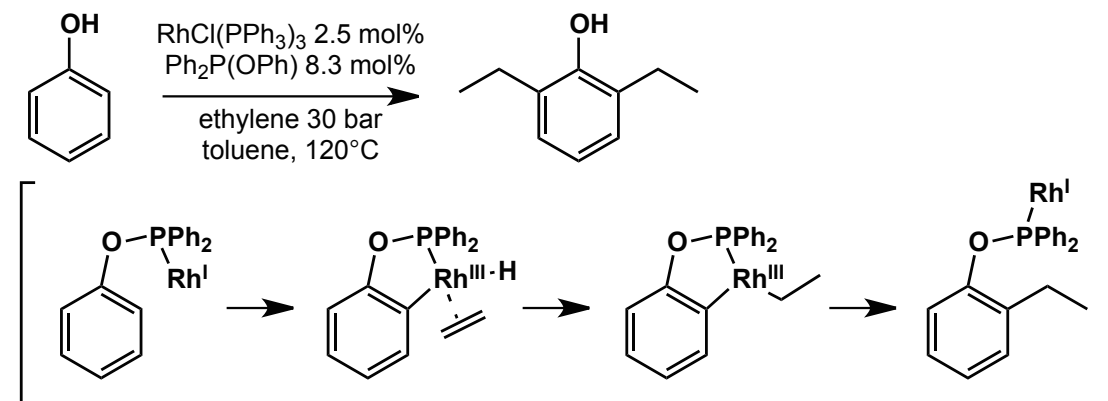


Lewis, L. N. *Inorg. Chem.* **1985**, *24*, 4433.

Application to ortho alkylation of phenol

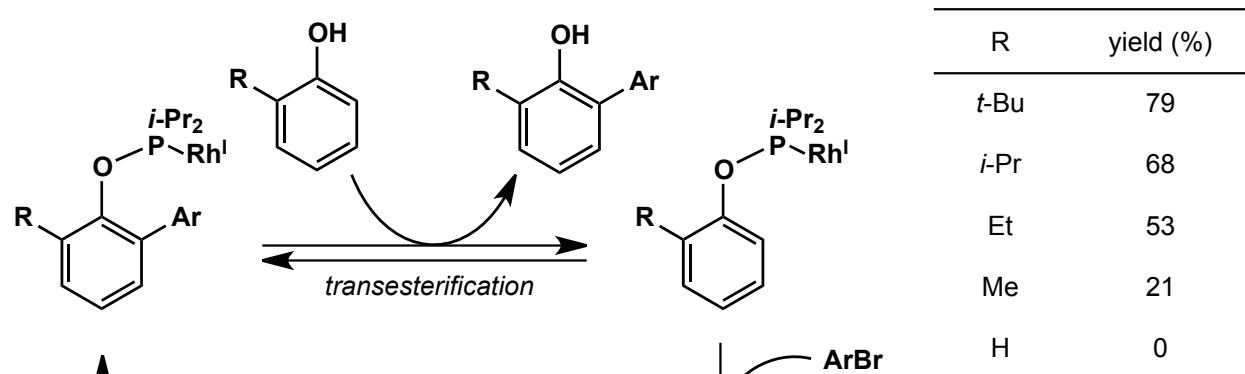
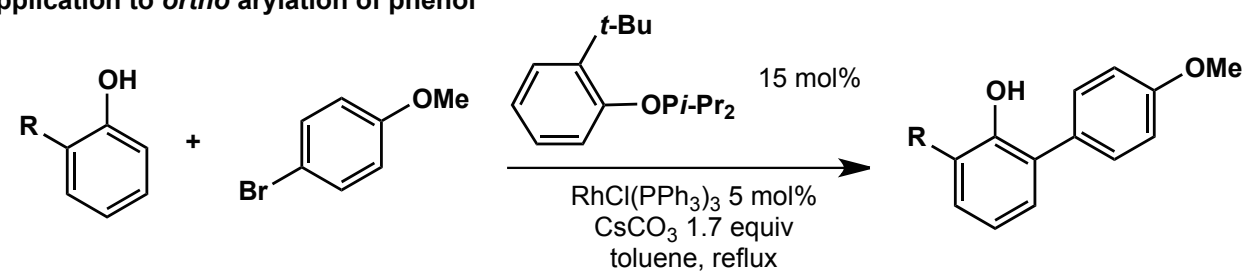


Lewis, J. C.; Wu, J.; Bergman, R. G.; Ellman, J. A. *Organometallics* **2005**, *24*, 5737.

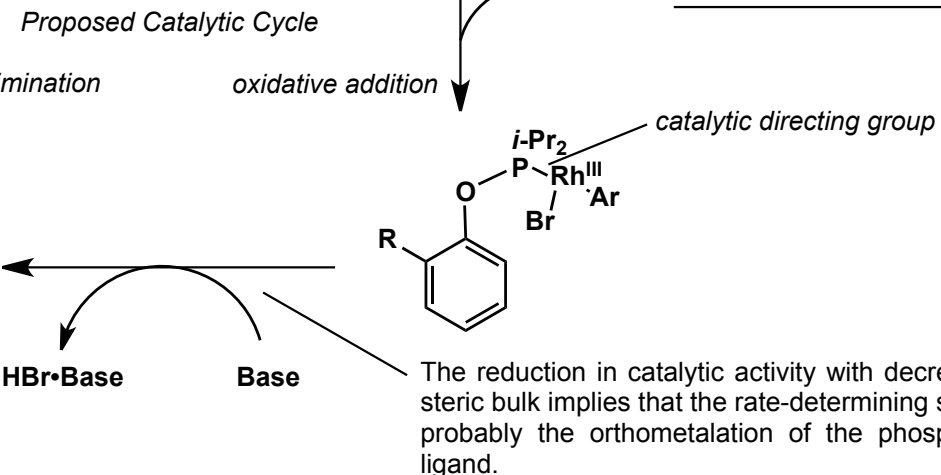


Carrión, M. C.; Cole-Hamilton, D. J. *Chem. Commun.* **2006**, 4527.

Application to *ortho* arylation of phenol

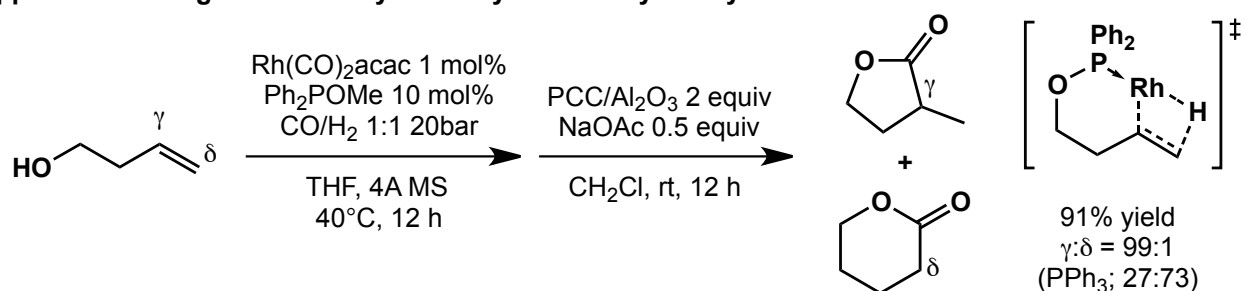


R	yield (%)
<i>t</i> -Bu	79
<i>i</i> -Pr	68
Et	53
Me	21
H	0

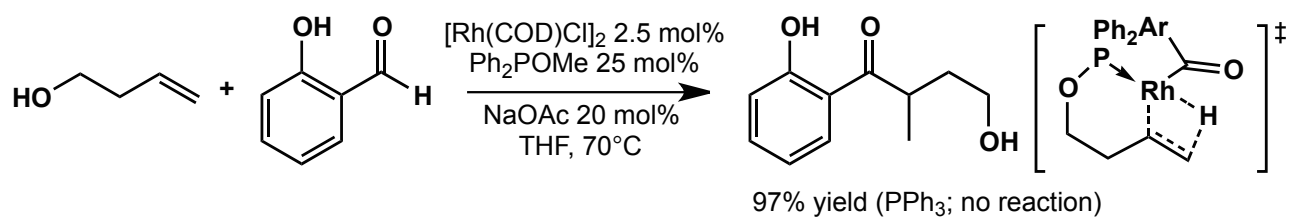


Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. *Angew. Chem. Int. Ed.* **2003**, 42, 112.
 Bedford, R. B.; Betham, M.; Caffyn, A. J. M.; Charmant, J. P. H.; Lewis-Alleyne, L. C.; Long, P. D.; Polo-Cerón, D.; Prashar, S. *Chem. Commun.* **2008**, 990.

Application to Regioselective Hydroformylation or Hydroacylation

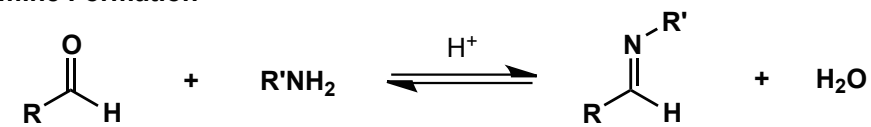


Grünanger, C. U.; Breit, B. *Angew. Chem. Int. Ed.* **2008**, 47, 7346.

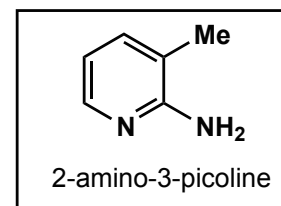
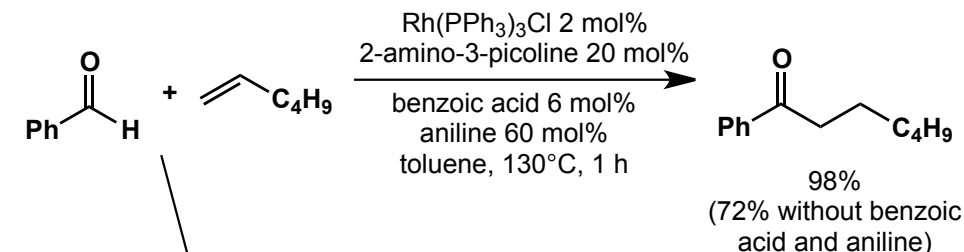


Murphy, S. K.; Petrone, D. A.; Coulter, M. M.; Dong, V. M. *Org. Lett.* **2011**, 13, 6216.
 Murphy, S. K.; Coulter, M. M.; Dong, V. M. *Chem. Sci.* **2012**, 3, 355.

Imine Formation

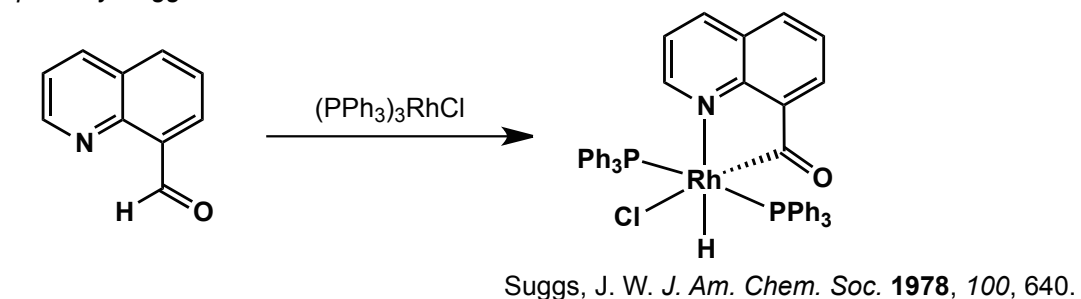


Hydroacylation of Olefin with Simple Aldehyde

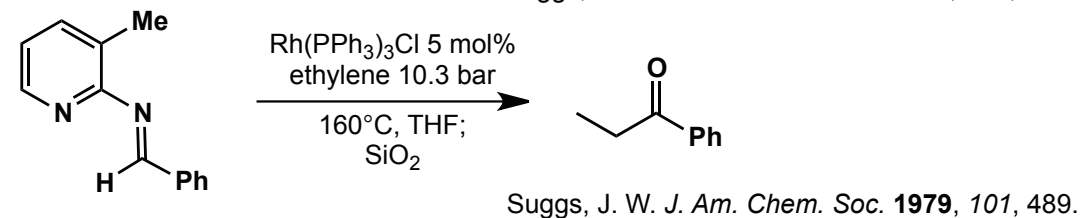


Aliphatic aldehydes underwent hydroacylation to give ketones in moderate yield, accompanied with the byproducts, the aldol condensation products.

Inspired by Suggs's work



Suggs, J. W. *J. Am. Chem. Soc.* **1978**, 100, 640.



Suggs, J. W. *J. Am. Chem. Soc.* **1979**, 101, 489.

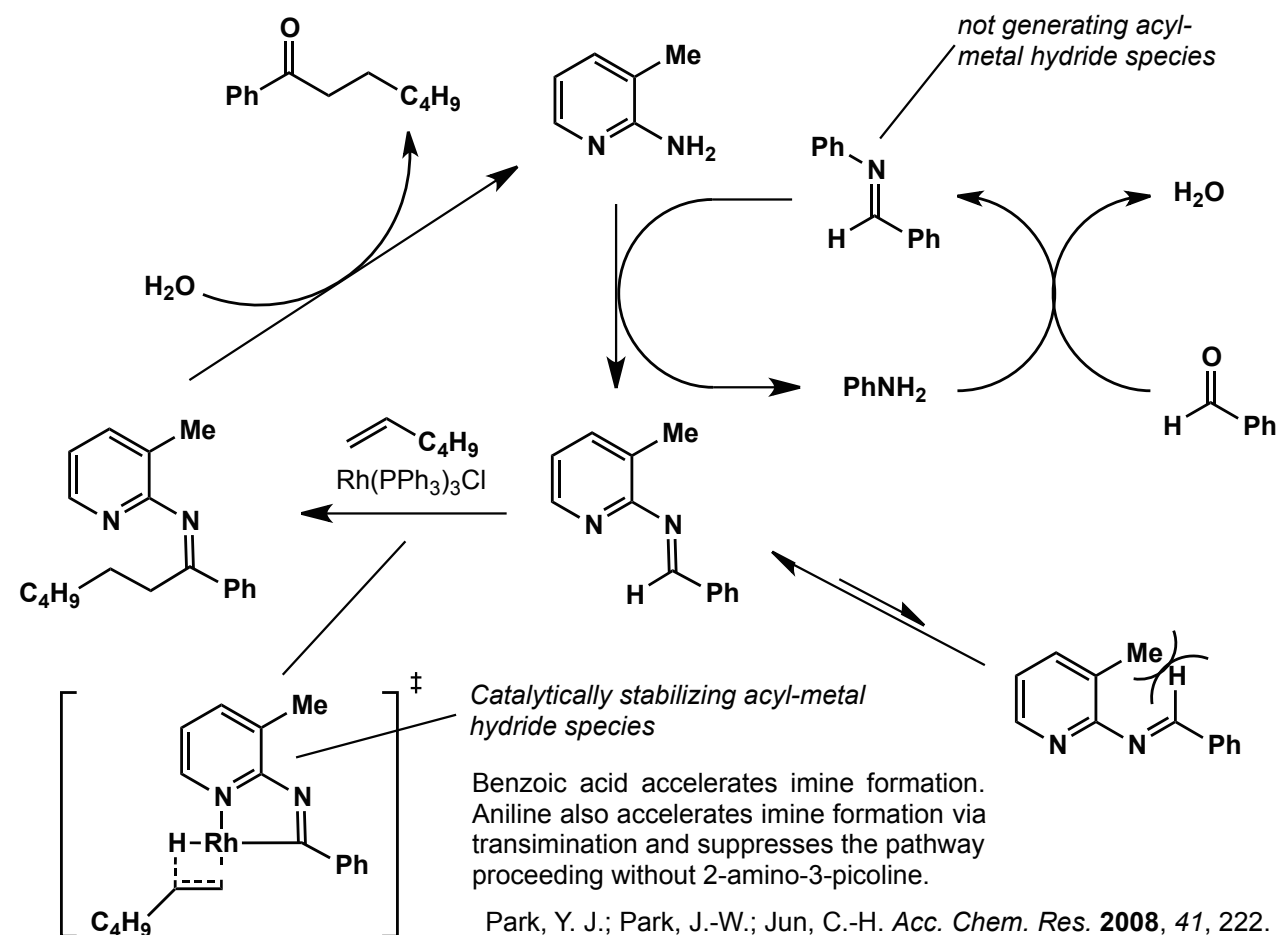
A significant challenge associated with C-H bond cleavage of an aldehyde has been the suppression of decarbonylation. One solution to this problem was that the reaction was conducted under a high pressure of carbon monoxide. However, this system are not general and efficient due to the harshness of the reaction condition. An alternative solution was incorporation of chelating functional groups onto the aldehyde to stabilize the acyl-metal hydride species.

Jun, C.-H.; Lee, H.; Hong, J.-B. *J. Org. Chem.* **1997**, 62, 1200.

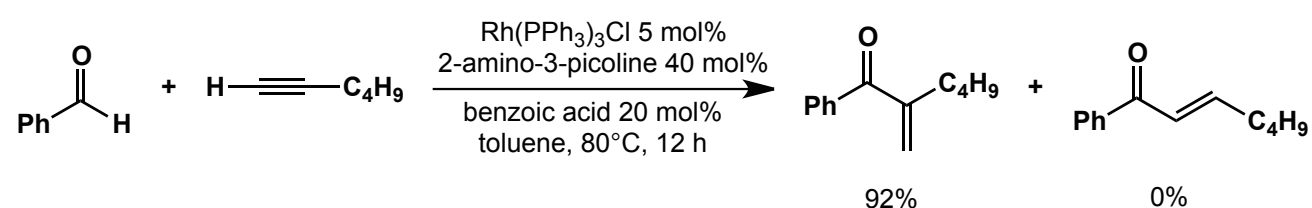
Jun, C.-H.; Hong, J.-B. *Org. Lett.* **1999**, 1, 887.

Jun, C.-H.; Lee, D.-Y.; Lee, H.; Hong, J.-B. *Angew. Chem. Int. Ed.* **2000**, 39, 3070.

Proposed Catalytic Cycle



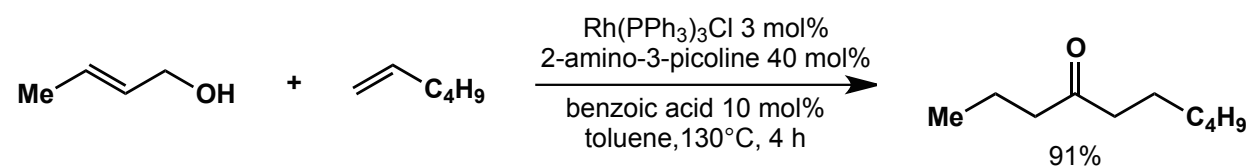
Application to Hydroacylation of 1-Alkynes



Most aromatic aldehydes underwent hydroacylation with 1-alkynes smoothly to produce branched α,β -enones exclusively in good yield. With aliphatic aldehydes, good branched selectivity was observed. When the reaction was performed with an alkyne substituted with a sterically demanding group, *t*-butylacetylene, *E*- α,β -enone was produced exclusively. These selectivity suggests that other mechanistic scenarios, such as a carbometalation pathway, may be involved in this reaction.

Jun, C.-H.; Lee, H.; Hong, J.-B.; Kwon, B.-I. *Angew. Chem. Int. Ed.* **2002**, *41*, 2146.
Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222.

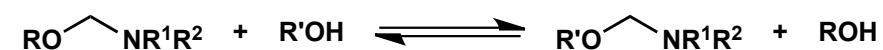
Application to Isomerization of Allylic Alcohols Followed by Hydroacylation



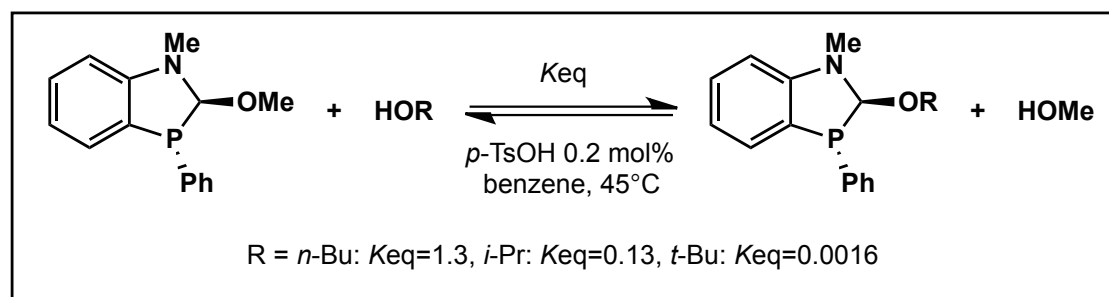
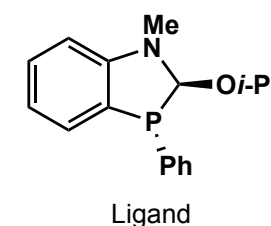
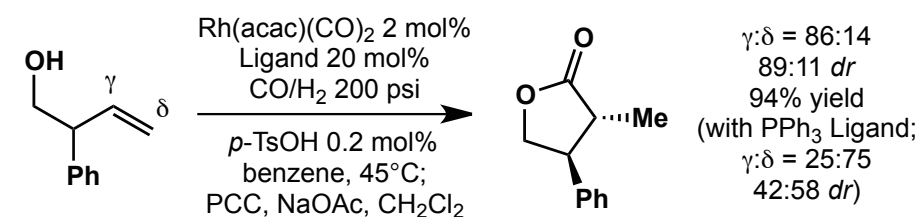
No byproduct such as aldol condensation product was obtained, which was the side reaction when aliphatic aldehydes were used as substrates.

Lee, D.-Y.; Moon, C. W.; Jun, C.-H. *J. Org. Chem.* **2002**, *67*, 3945.

Equilibrium between Hemiaminal Ethers and Alcohols

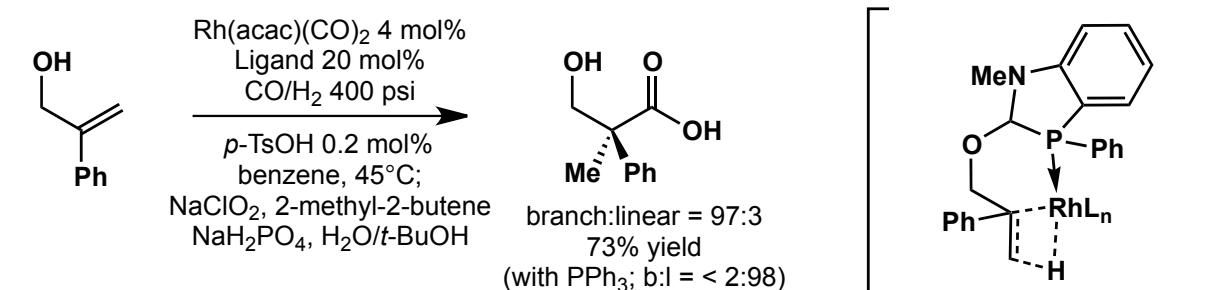


Regio- and Diastereoselective Hydroformylation of Homoallylic Alcohols



Lightburn, T. E.; Dombrowski, M. T.; Tan, K. L. *J. Am. Chem. Soc.* **2008**, *130*, 9210.

Application to Hydroformylation of Allylic Alcohols to Synthesize Quaternary Carbon Centers

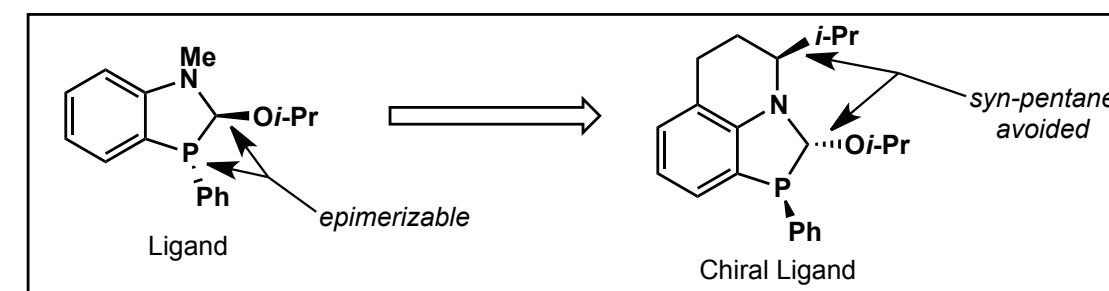
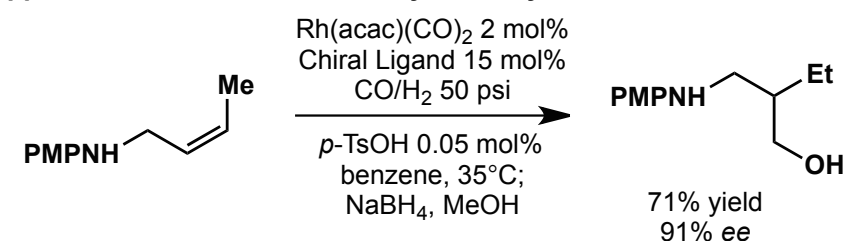


Efficient generation of quaternary carbon center! (Strong Entropy Effect)

6-membered cyclic TS

Sun, X.; Frimpong, K.; Tan, K. L. *J. Am. Chem. Soc.* **2010**, *132*, 11841.

Application to Enantioselective Hydroformylation



Worthy, A. D.; Joe, C. L.; Lightburn, T. E.; Tan, K. L. *J. Am. Chem. Soc.* **2010**, *132*, 14757.

4. Summary

Advantages

Through induced intramolecularity using reversible covalent bondings, significant rate enhancements can be obtained, such that challenging reactions can be performed under mild conditions.

Furthermore, the conformational restrictions required by covalent bondings generally allow for high regio- and stereoselectivity.

Disadvantage

It can require additional catalysts such as acids and bases.

X. References

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