Literature Report

Changbin Yu 2012-12-04 检查: 蔡先锋

Rhodium Catalyzed Hydroacylation

Vy M. Dong*

Education

Ph.D. California Institute of Technology, 2004
M.S. University of California at Berkeley, 2000
B.S. University of California at Irvine, 1998

Professional Appointments

Full Professor
University of California at Irvine, Oct 2012 to present.
Associate Professor
University of Toronto, July 2010 to Sep 2012.
Assistant Professor
University of Toronto, July 2006 to June 2010.

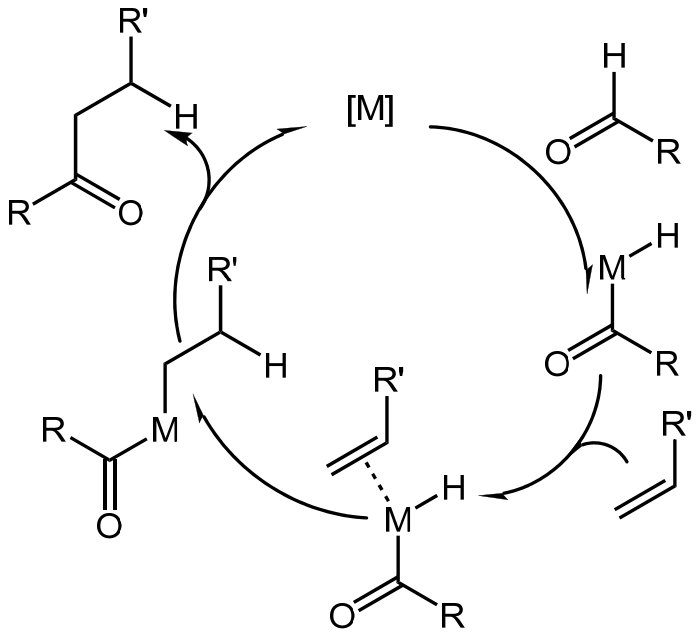
Research Interests

Our research mission is to invent better tools for organic synthesis, including new reagents, catalysts, and strategies. More specific goals include finding ways to directly convert carbon-hydrogen bonds into other functional groups, use carbon dioxide as a raw material, and make biologically active heterocycles.

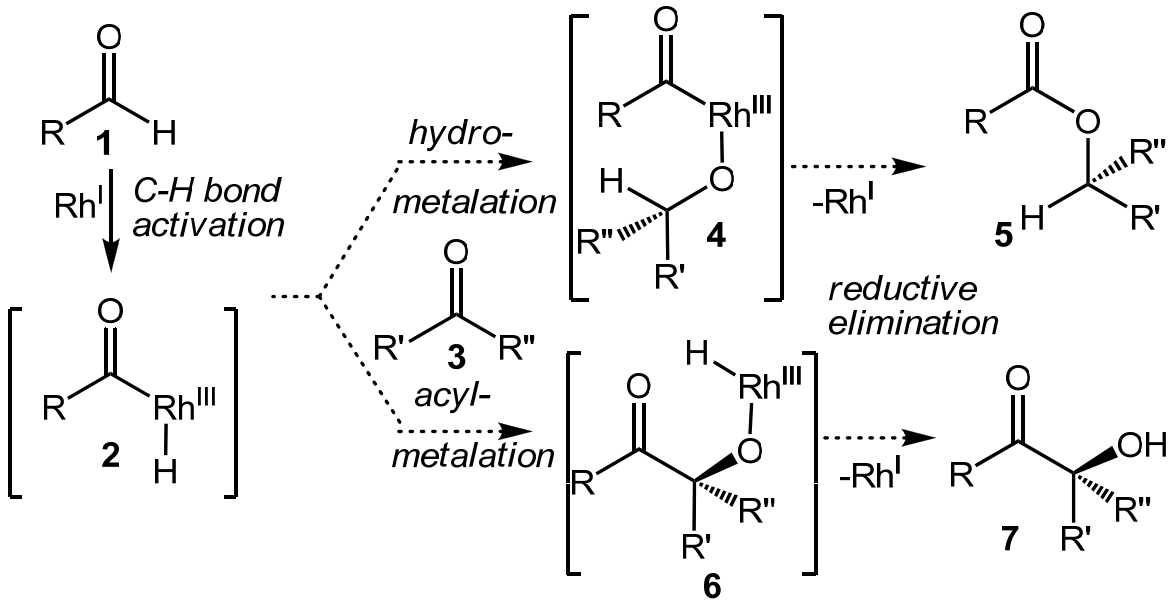
Hydroacylation：

Hydroacylation is a type of organic reaction in which an aldehyde is added over an alkene or alkyne bond. The reaction product is a ketone .

Mechanism：

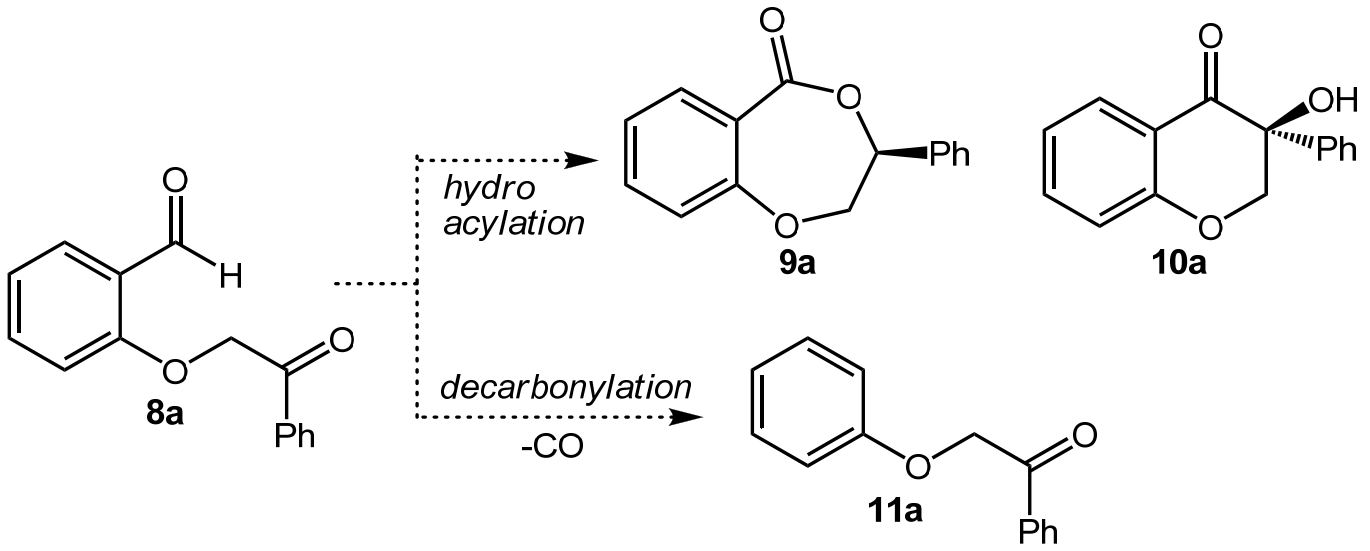


Proposal for Hydroacylation

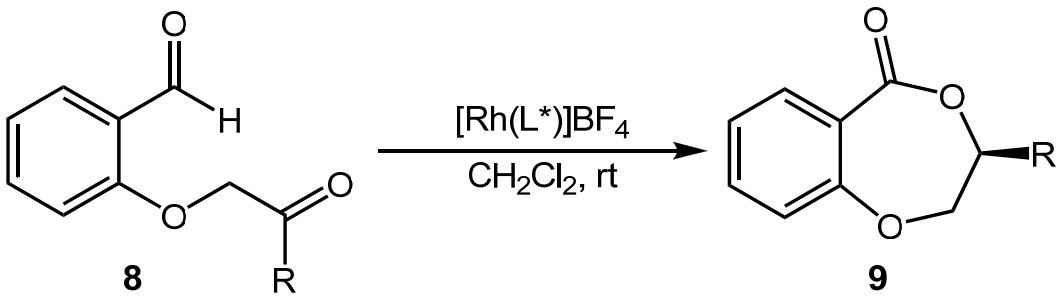


Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2008**, *130*, 2916−2917.

Competing Transformations for Model Substrate

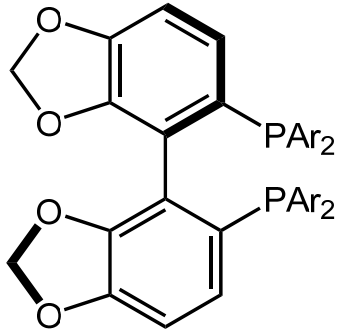


Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2008**, *130*, 2916−2917.



8 **9**

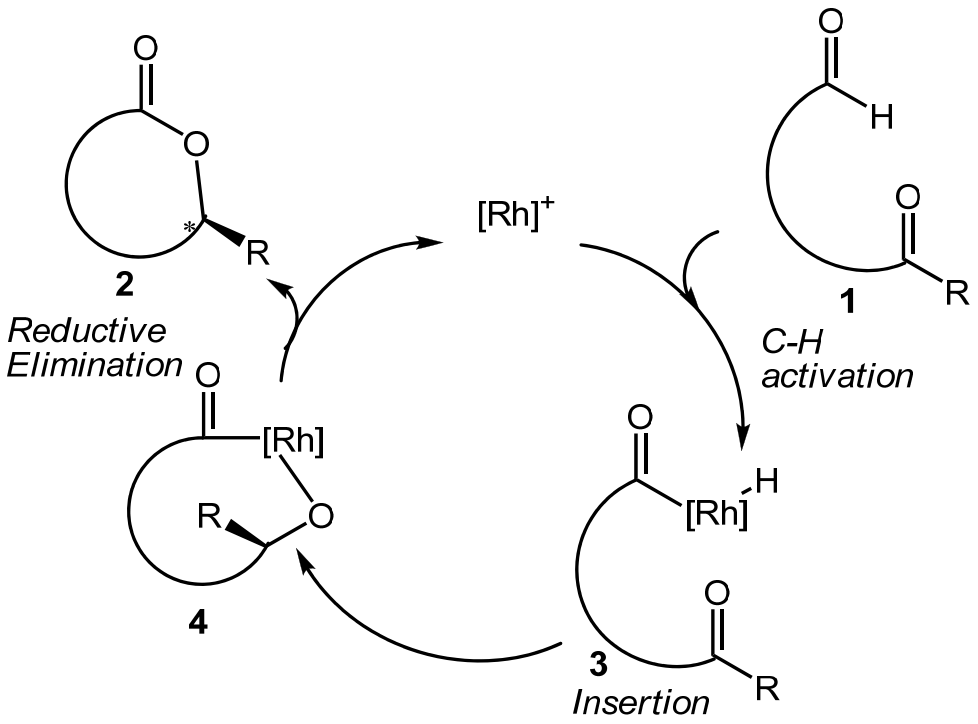
8 examples, Yield: 89-99%, Ee: 99->99%



L: Ar = 3,5-*t*-Bu-4-MeOC_6H_2

Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2008**, *130*, 2916−2917.

Mechanistic Research:

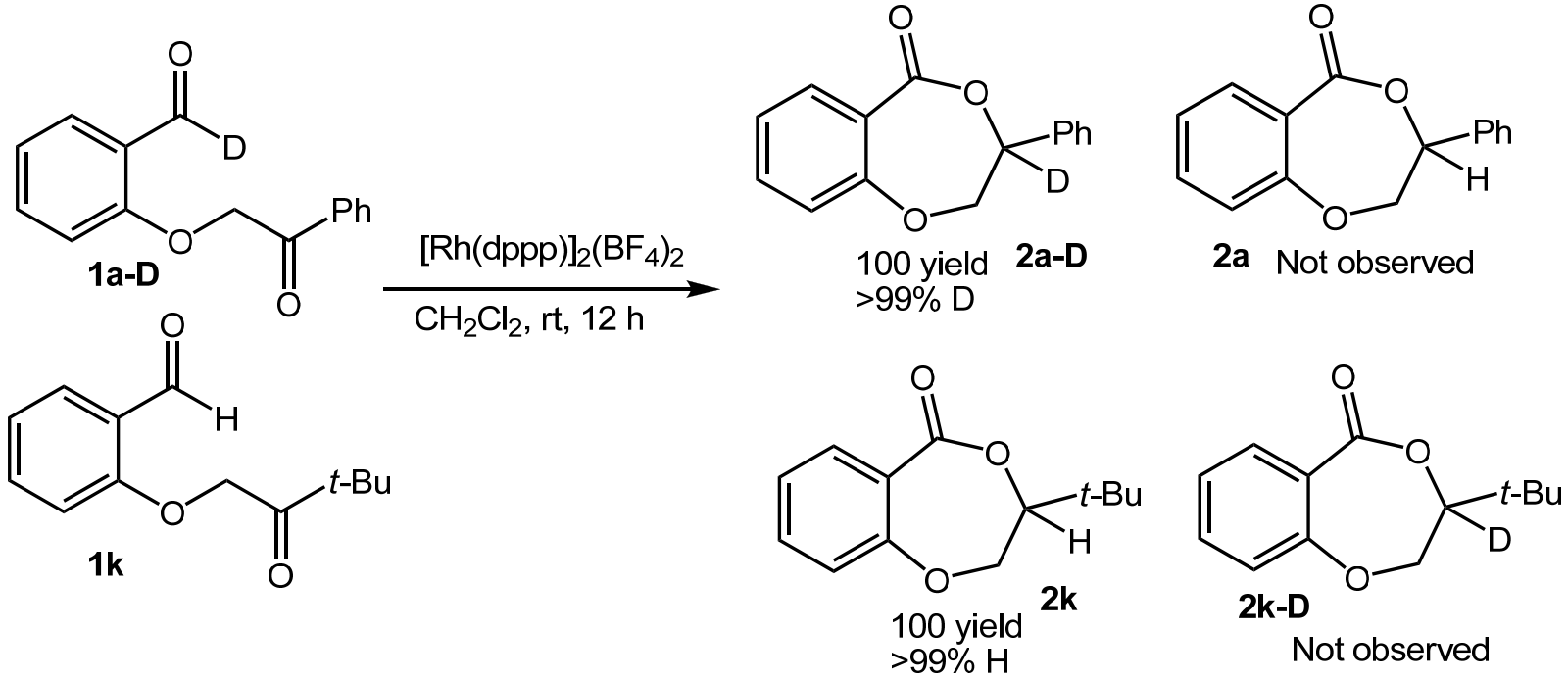


(1) rhodium(I) oxidative addition into the aldehyde C-H bond.

(2) insertion of the ketone C=O double bond into the rhodium hydride.

(3) C-O bond-forming reductive elimination.

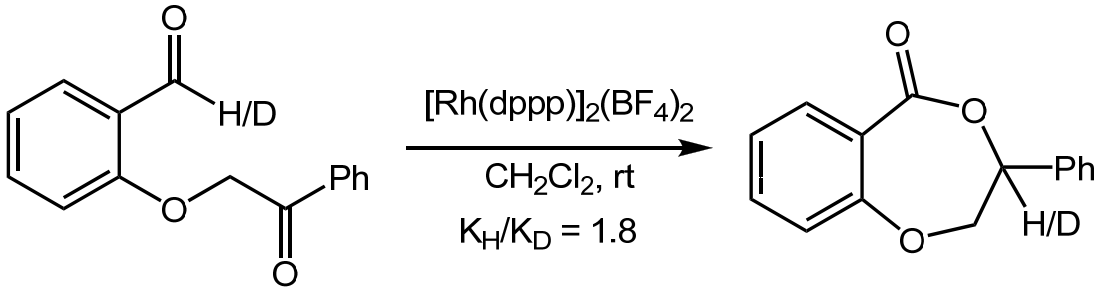
Crossover Experiment to Confirm Intramolecular Hydride Transfer



Conclusion: The results supports a mechanism where hydride transfer occurs intramolecularly.

Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 1077−1091.

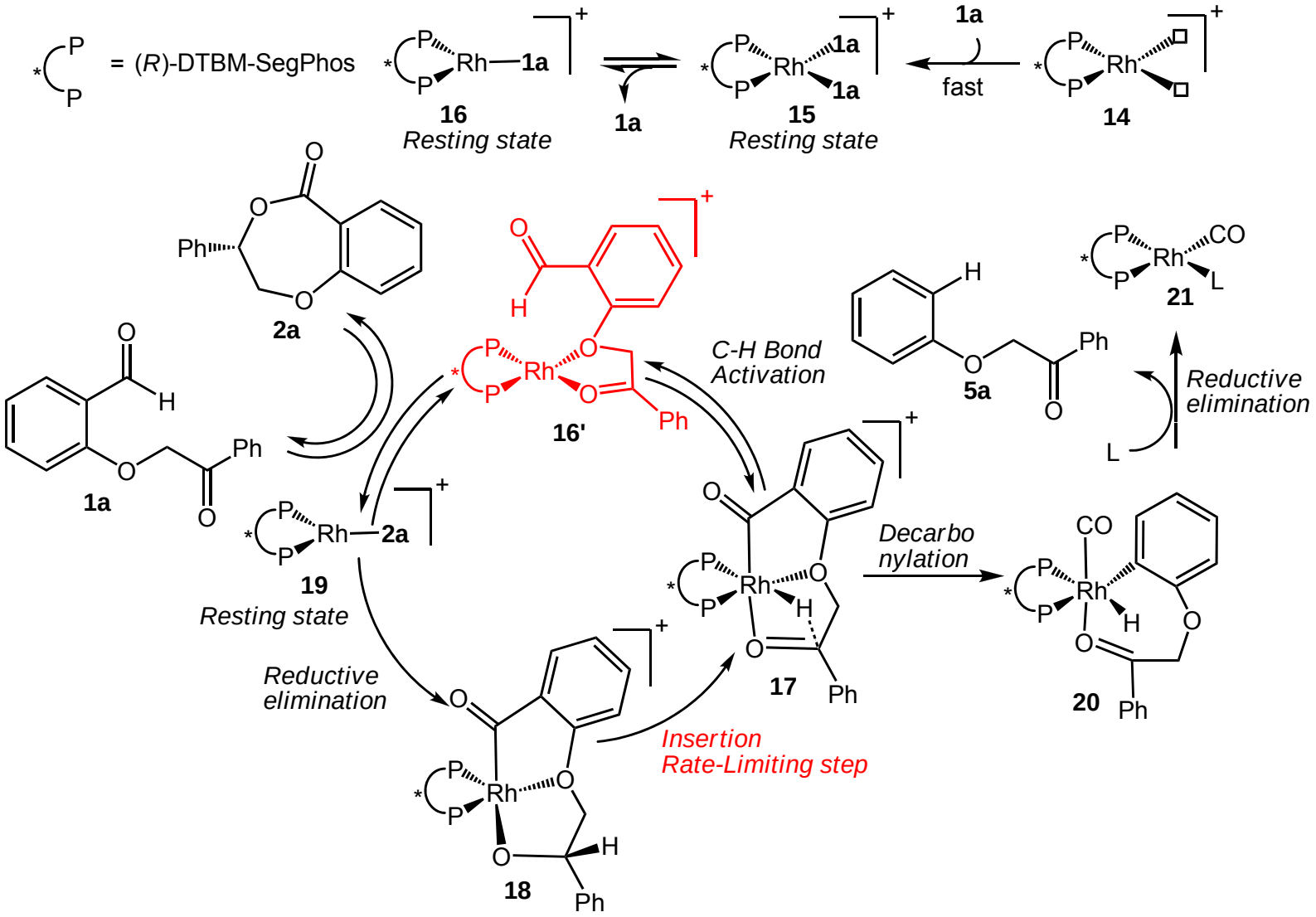
The H/D Kinetic Isotope Effect(KIE**)**



Conclusion: The results supports that reductive elimination is not the turnover-limiting step.

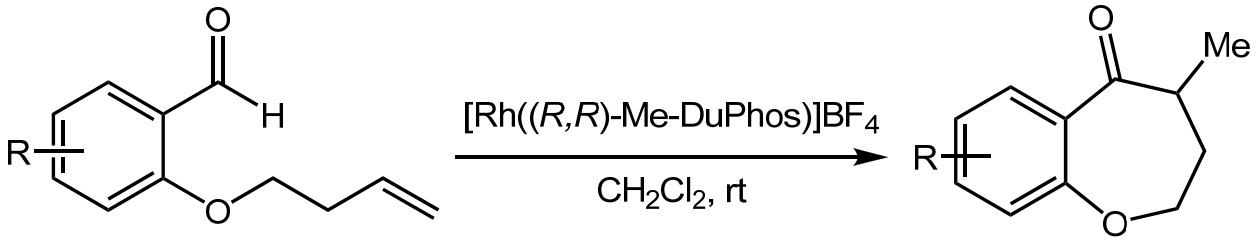
Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 1077−1091.

Proposed Mechanism for Rh Catalyzed hydroacylation of **1a**

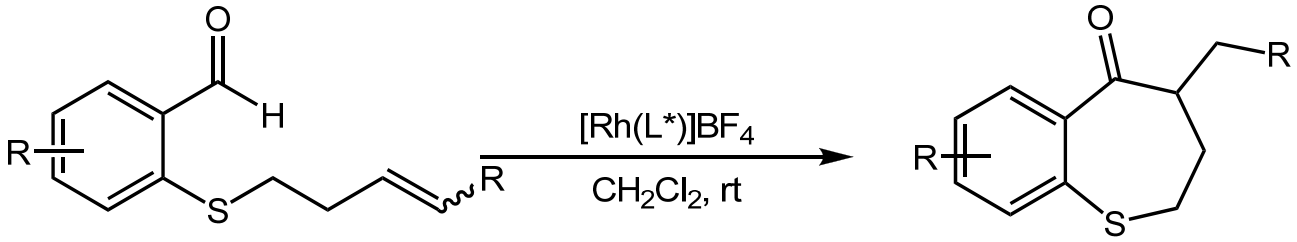


Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 1077−1091.

Rh-Catalyzed Intramolecular Olefin Hydroacylation: Enantioselective Synthesis of Seven- and Eight-Membered Heterocycles



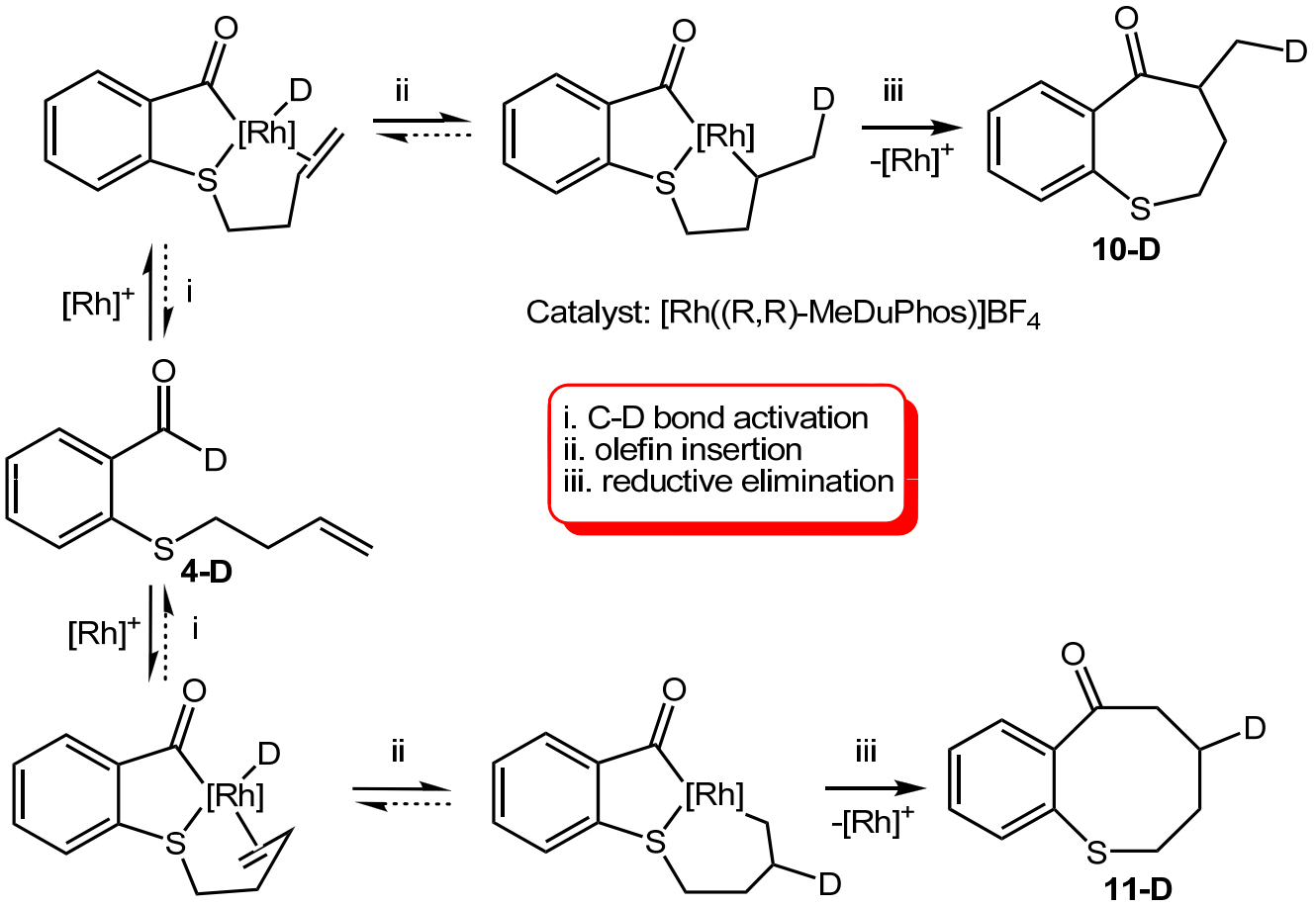
8 examples, Yield: 80-95%, Ee: 94-98%



5 examples, Yield: 85-97%, Ee: 93-99%

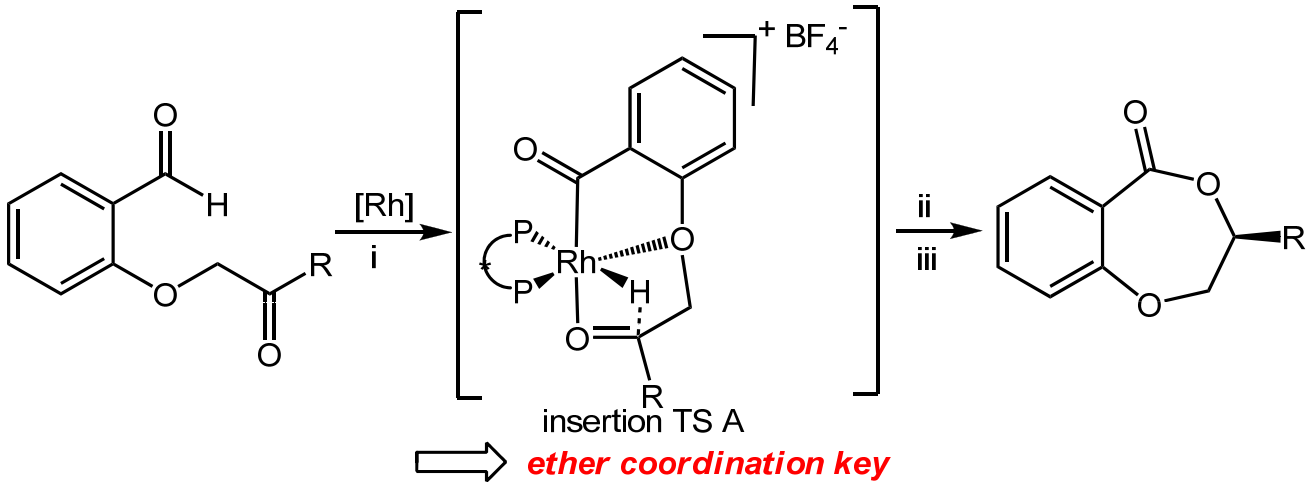
Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 6932−6933.

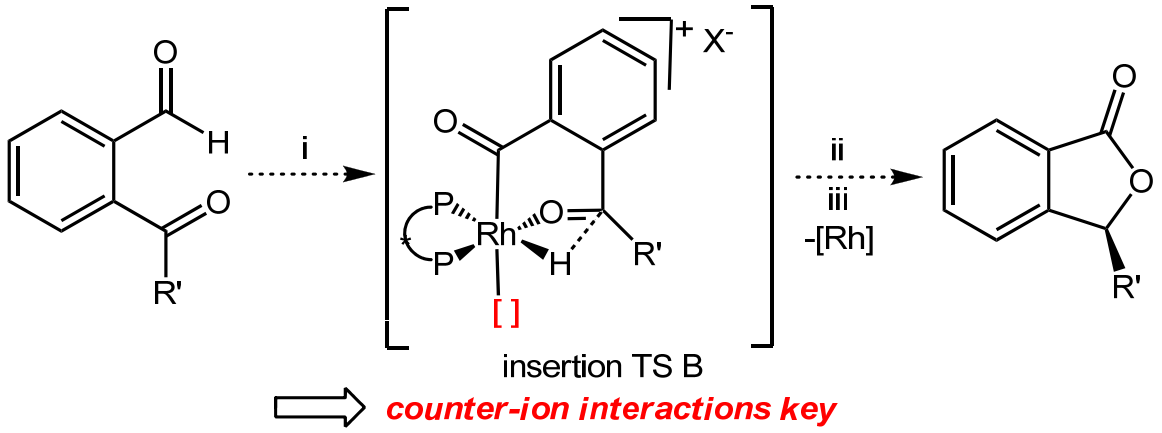
Rh-Catalyzed Intramolecular Olefin Hydroacylation: Enantioselective Synthesis of Seven- and Eight-Membered Heterocycles



Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 6932−6933.

Mechanistic Rationale for Ketone Hydroacylation

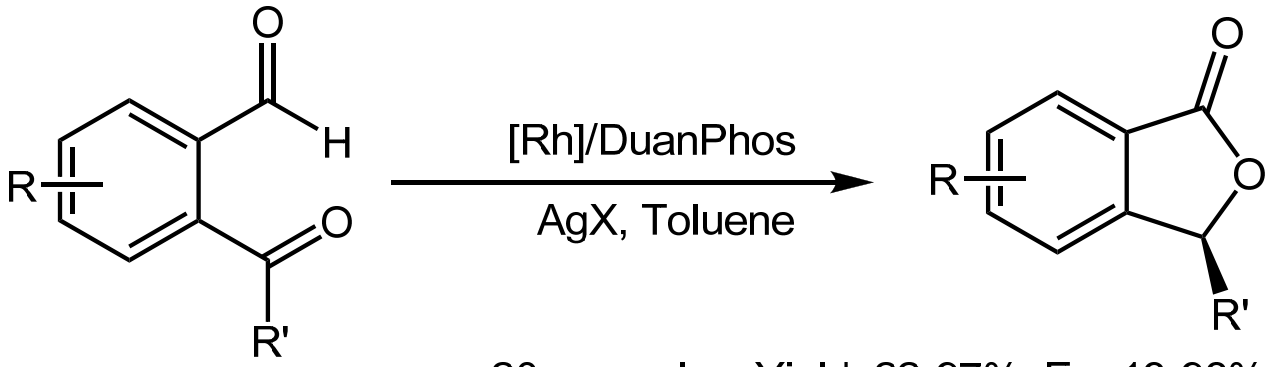




mechanism: i) C-H activation ii) insertion iii) reductive elimination

Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 15608−15609.

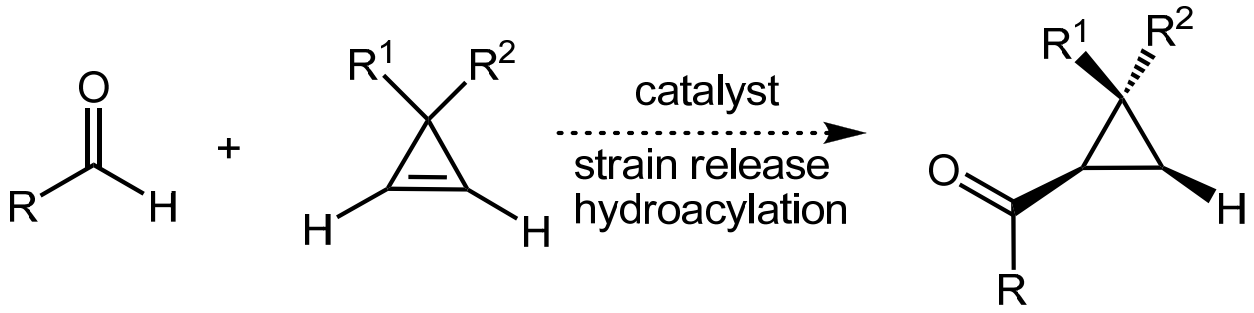
Phthalides by Rhodium-Catalyzed Ketone Hydroacylation



20 examples, Yield: 22-97%, Ee: 13-98%

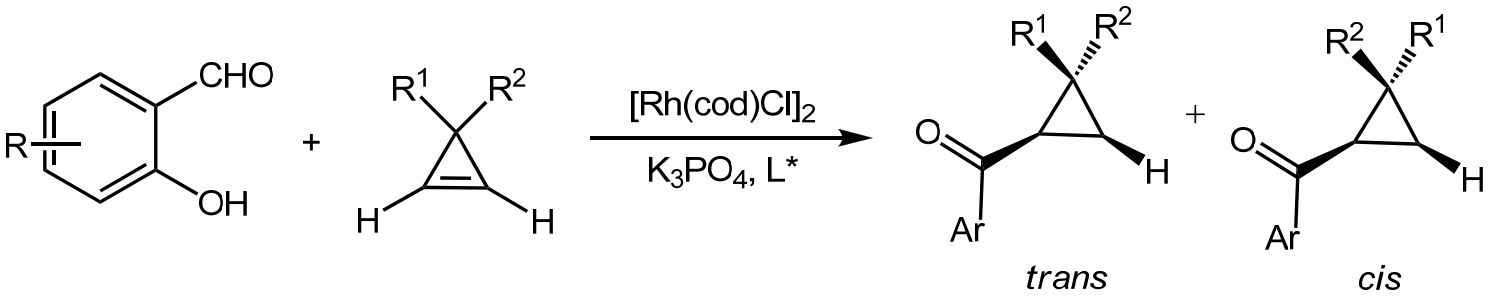
Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2009**, *131*, 15608−15609.

Enantioselective Desymmetrization of Cyclopropenes by Hydroacylation

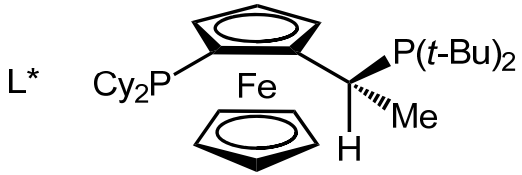


Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2010**, *132*, 16354−16355.

Enantioselective Desymmetrization of Cyclopropenes by Hydroacylation

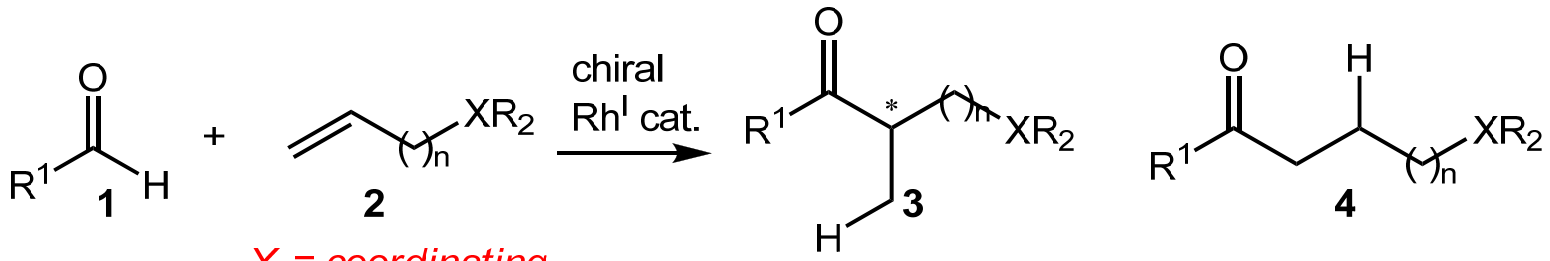


18 examples, *Trans* yield: 76-92%, Ee: 95-99%



Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2010**, *132*, 16354−16355.

Regio- and Enantioselective Intermolecular Hydroacylation: Substrate-Directed Addition of Salicylaldehydes to Homoallylic Sulfides

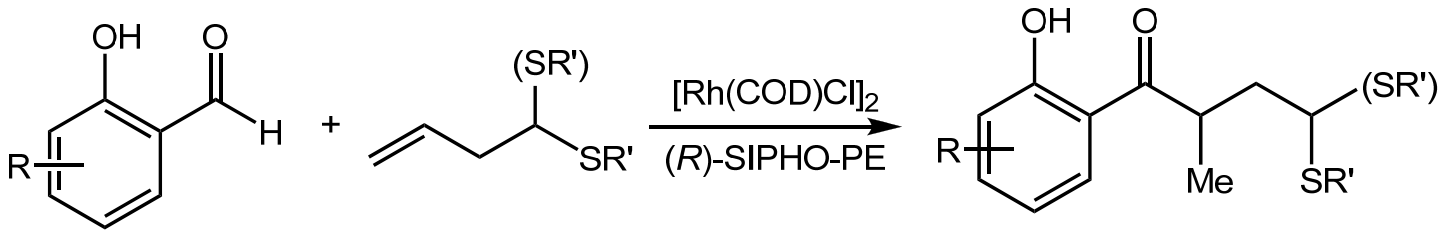


X = coordinating heteroatom

heteroatom-directed, branch-selective asymmetric hydroacylation

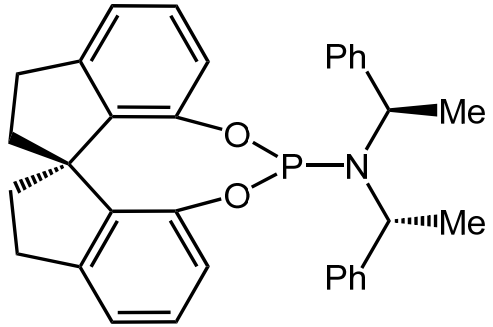
Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2010**, *132*, 16330−16333.

Regio- and Enantioselective Intermolecular Hydroacylation: Substrate-Directed Addition of Salicylaldehydes to Homoallylic Sulfides



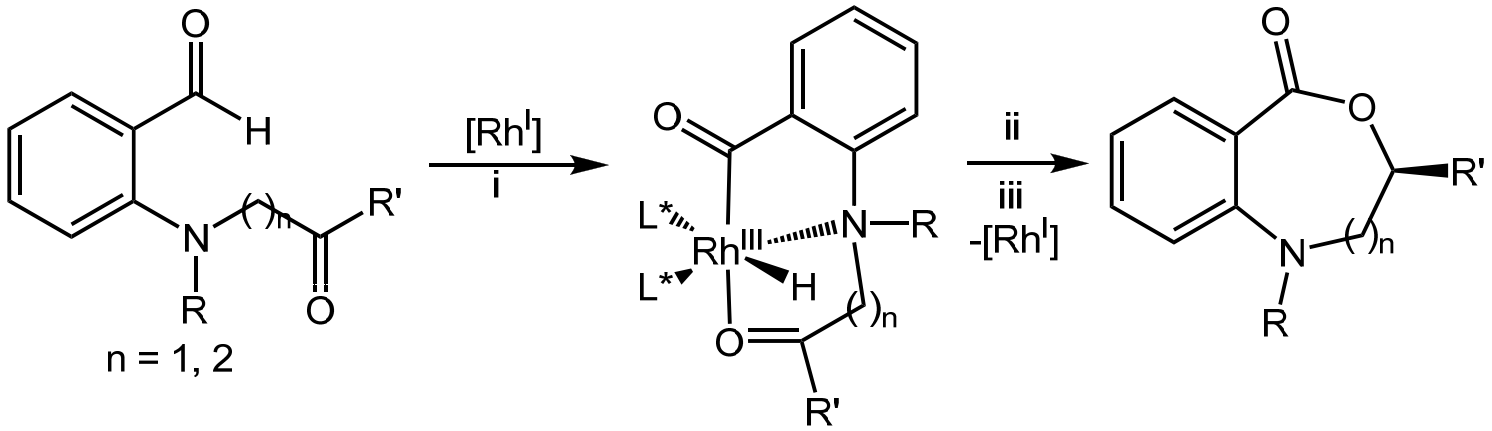
18 examples, Yield: 74-97%, Ee: 36-97%

(*R*)-SIPHO-PE



Vy M. Dong* *et al*. *J. Am. Chem. Soc.* **2010**, *132*, 16330−16333.

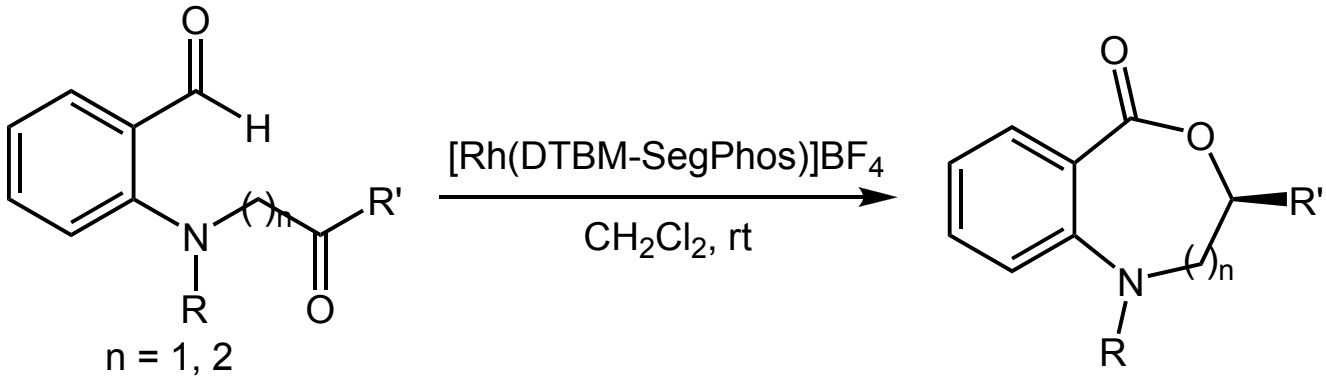
Nitrogen-directed ketone hydroacylation: Enantioselective synthesis of benzoxazecinones



i. C-H activation ii. insertion iii. reductive elimiation

Vy M. Dong* *et al*. *Chem. Sci.* **2011**, *2*, 407−410.

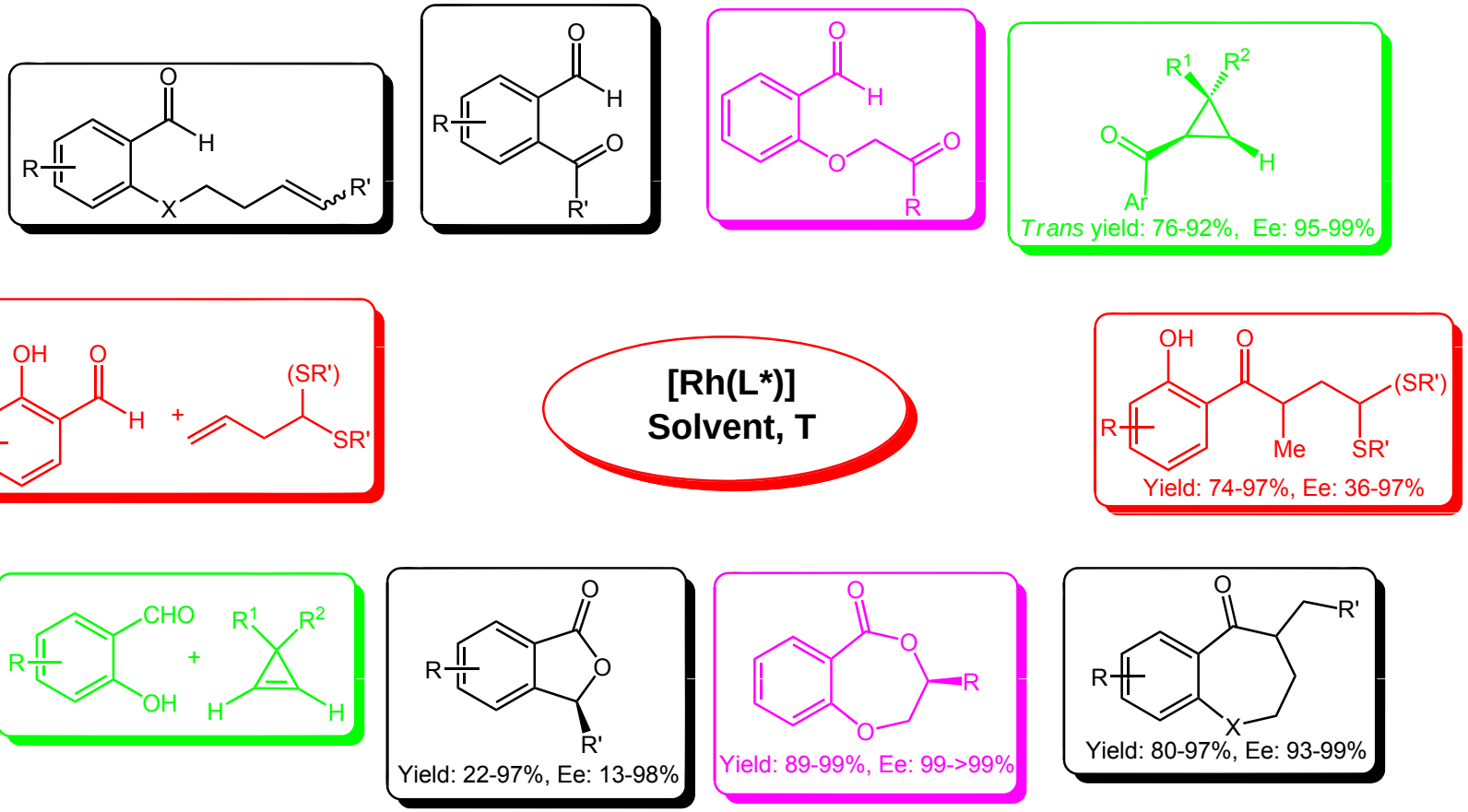
Nitrogen-directed ketone hydroacylation: Enantioselective synthesis of benzoxazecinones



9 examples, Yield: 91-99%, Ee: 88-99%

Vy M. Dong* *et al*. *Chem. Sci.* **2011**, *2*, 407−410.

总结:


[Rh(L*)]
Solvent, T
Trans yield: 76-92%, Ee: 95-99%
Yield: 74-97%, Ee: 36-97%
Yield: 22-97%, Ee: 13-98%
Yield: 89-99%, Ee: 99->99%
Yield: 80-97%, Ee: 93-99%

The ester is a prevalent motif found in diverse synthetic and biological architectures, from fatty acid triesters to macrolide antibiotics. Nature uses enzymes (e.g., polyketide synthase) to form ester bonds by coupling alcohols to activated thioesters. The majority of synthetic approaches to constructing esters involve this same *natural carbon-oxygen bond formation. For example, many* stoichiometric reagents, including Corey-Nicolaou's PySSPy and Yamaguchi's acid chloride, have been developed to activate carboxylic acids and achieve macrolactonizations. We envisioned a fundamentally different approach to lactonization based on the ability of Rh(I) complexes to activate the C-H bond of aldehydes (Scheme 1). Herein, we report a novel and atom economical strategy for making chiral lactones starting from keto-aldehydes. In contrast to conventional strategies, this ester synthesis features an unprecedented regio- and enantioselective carbonyl hydroacylation.

In summary, we have designed and executed a new approach to forming chiral lactones. This C-H bond functionalization strategy involves an unprecedented Rh-catalyzed hydroacylation of ketones. The basicity of the phosphine ligand plays a critical role in promoting hydroacylation over competitive decarbonylation. Intramolecular hydroacylation of keto-aldehydes **8** occurs with complete regiocontrol to yield formal Tishchenko lactones in large enantiomeric excess. Further scope and mechanistic studies are underway to determine the origin of regio- and enantioselectivity in this transformation.