# 2.4. Activation of electrophiles other than carbonyl/imines

**2.4.1 Epoxidation**

**2.4.2 Aziridination**

**2.4.3 Cyclopropanation**

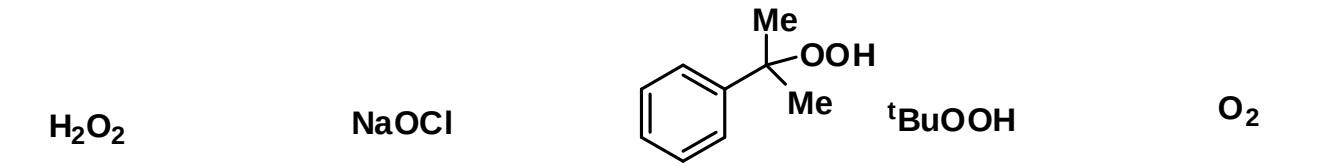
**2.4.4 Dihydroxylation**

**2.4.5 C-H/X-H Functionalization**

**2.4.6 Other Reactions**

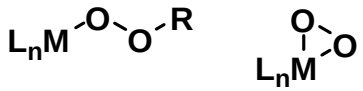
# 2.4.1 Epoxidation: Introduction

**Often Used (Ep)Oxidation Reagents**

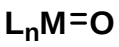



Hydrogen Peroxide | Bleach | Hydroperoxides | Oxygen

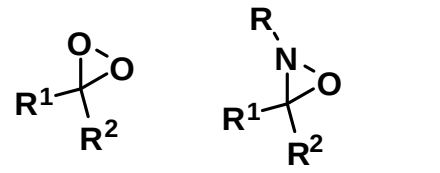
**Principles for Catalytic Activation via Lowering of the LUMO of the Reagent**




Metal Peroxo Complexes




Metal Oxo Complexes

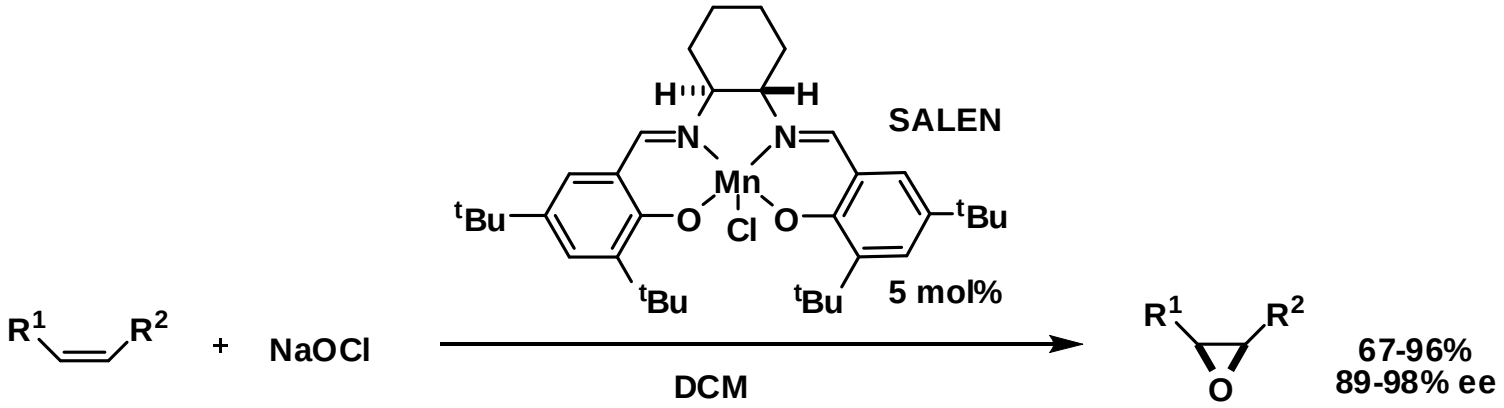



Dioxiranes | Oxaziridines

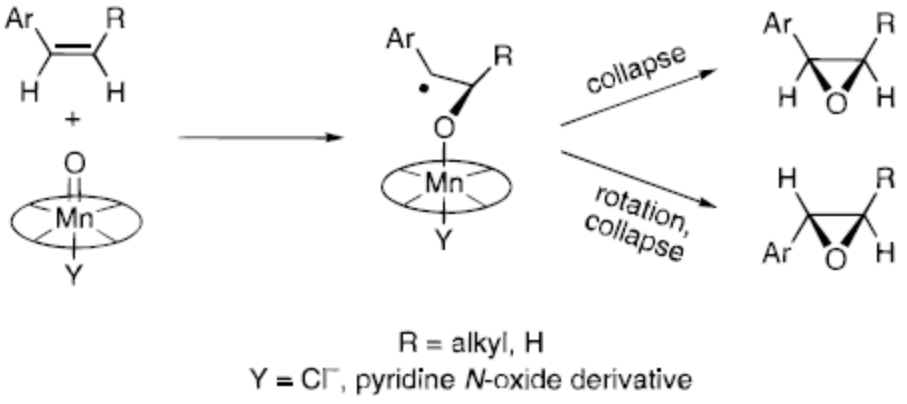
Strained Organic Molecules

# 2.4.1 Epoxidation: Jacobsen

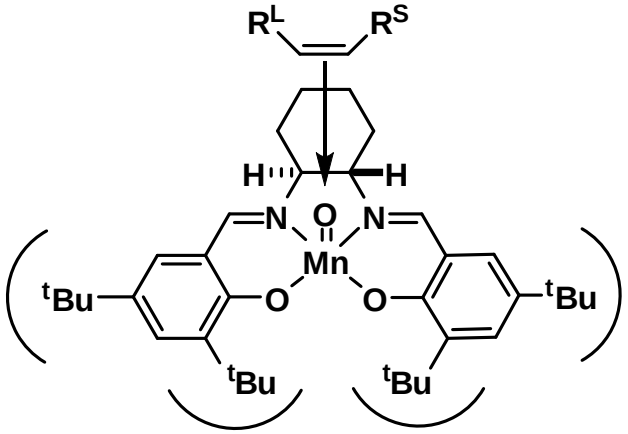
**The Classical Jacobsen Epoxidation for Cis Olefins**




**Mechanism**



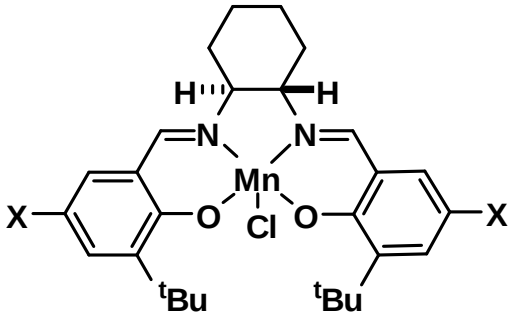

**Model for Selectivity**



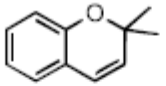
(1) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991,** *113,* 7063-7064. (2) Palucki, M.; Finney, N. S.; Pospisil, P. J.; Guler, M. L.; Ishida, T.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998,** *120,* 948-954.

# 2.4.1 Epoxidation: Jacobsen

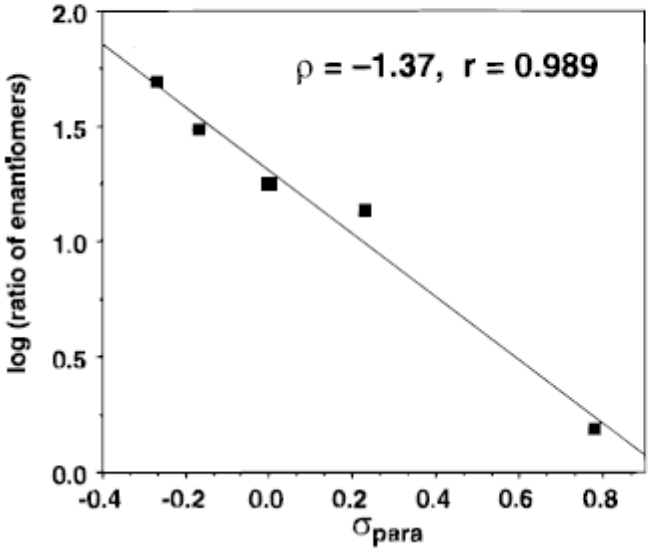
**Electronic Influence on Selectivity**

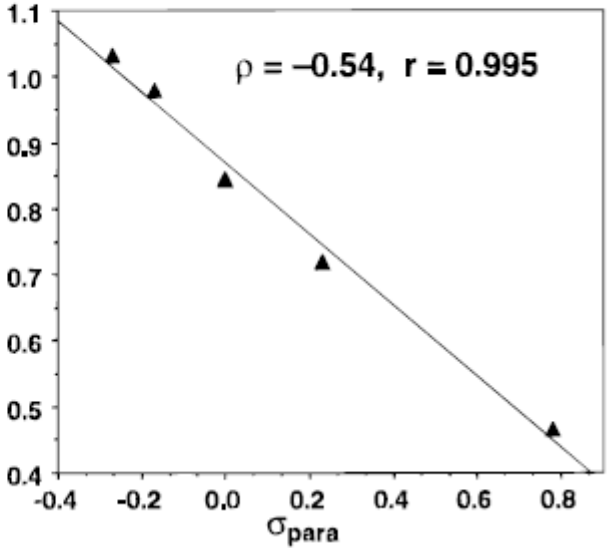



**X = OMe, Me, H, Cl, $NO_2$**

a) Epoxidation of  (4)

b) Epoxidation of  (5)



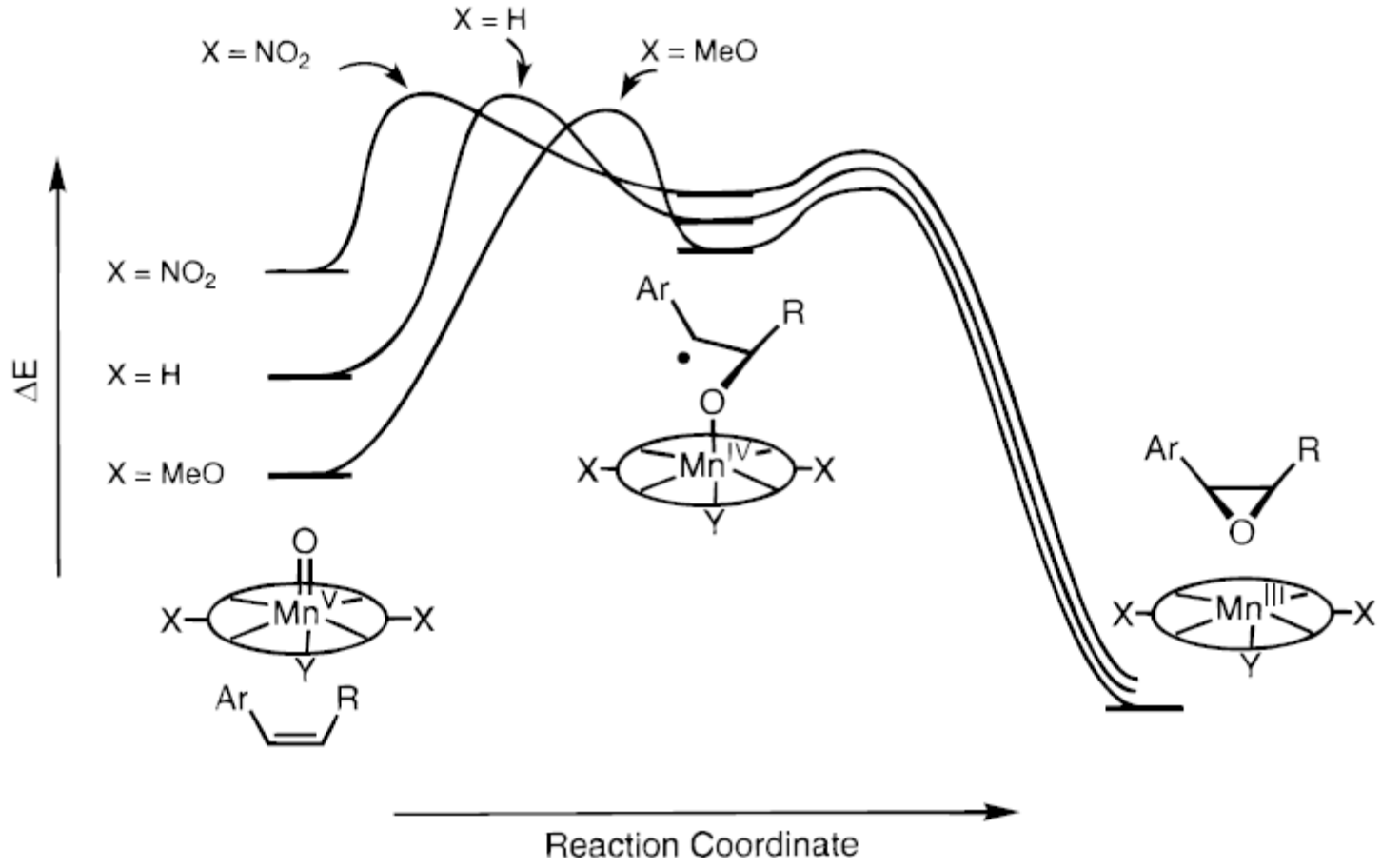




**$\sigma_{para}$ = Hammet parameter = strenght of electron-withdrawing effect**

(1) Palucki, M.; Finney, N. S.; Pospisil, P. J.; Guler, M. L.; Ishida, T.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998,** *120,* 948-954.

# 2.4.1 Epoxidation: Jacobsen

**Electronic Influence on Selectivity**

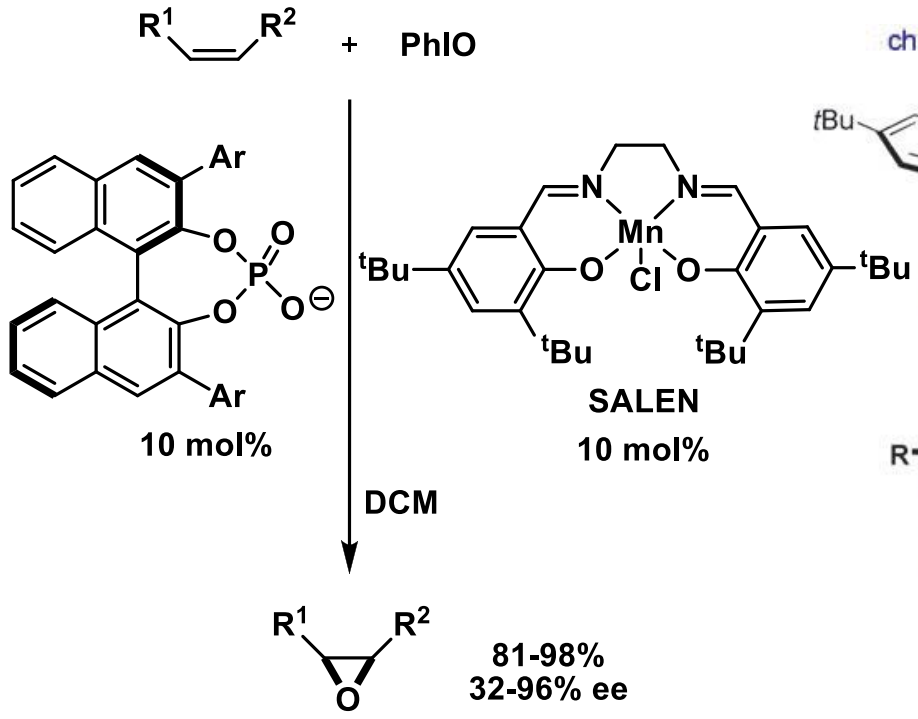


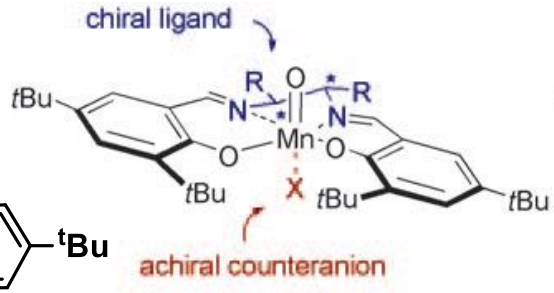

**Hammond Postulate: structure of transition state similar to reactive intermediate**

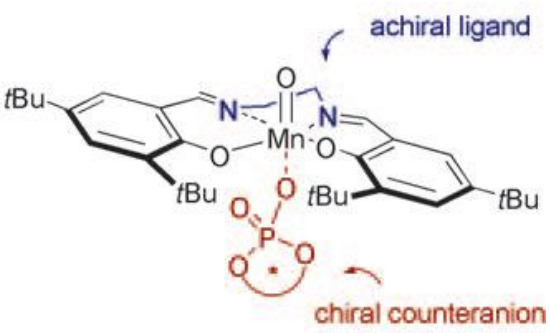
(1) Palucki, M.; Finney, N. S.; Pospisil, P. J.; Guler, M. L.; Ishida, T.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998,** *120,* 948-954.

# 2.4.1 Epoxidation: Counter Anion directed

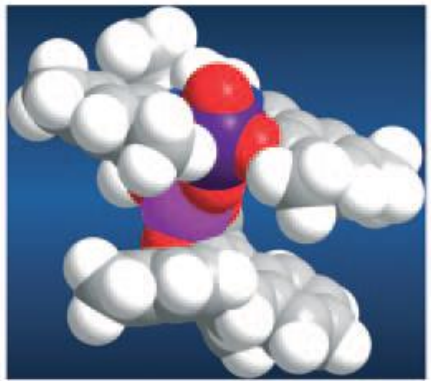
**List: achiral salen complex with chiral countera anion[1]**



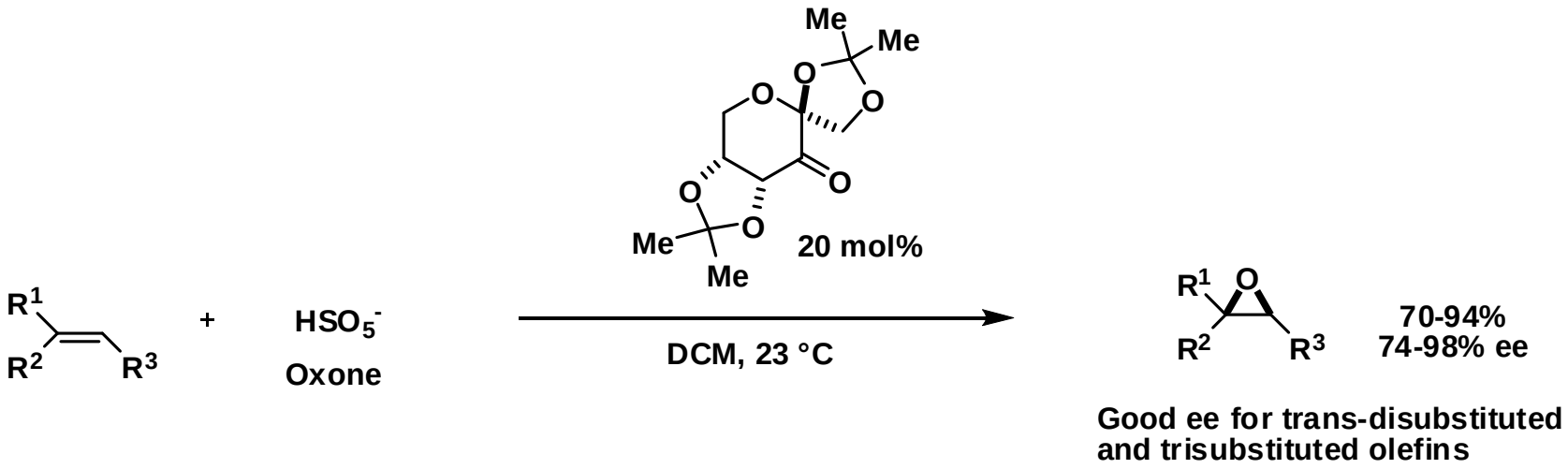




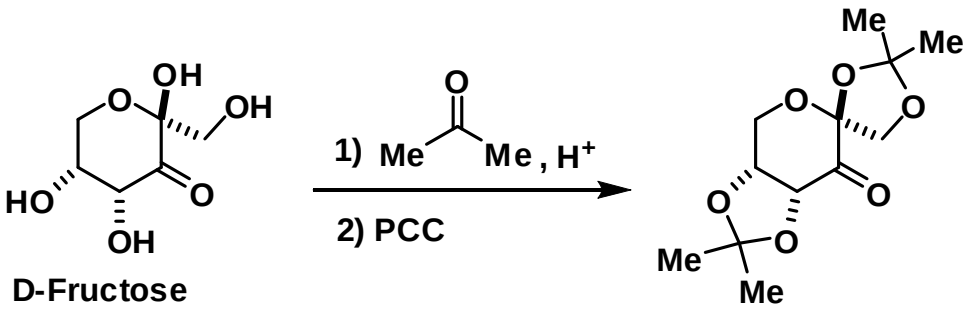
(1) Liao, S. H.; List, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 628-631.

# 2.4.1 Epoxidation: Ketones as Catalysts

**Shi: Use of Chiral Ketones as Catalysts**



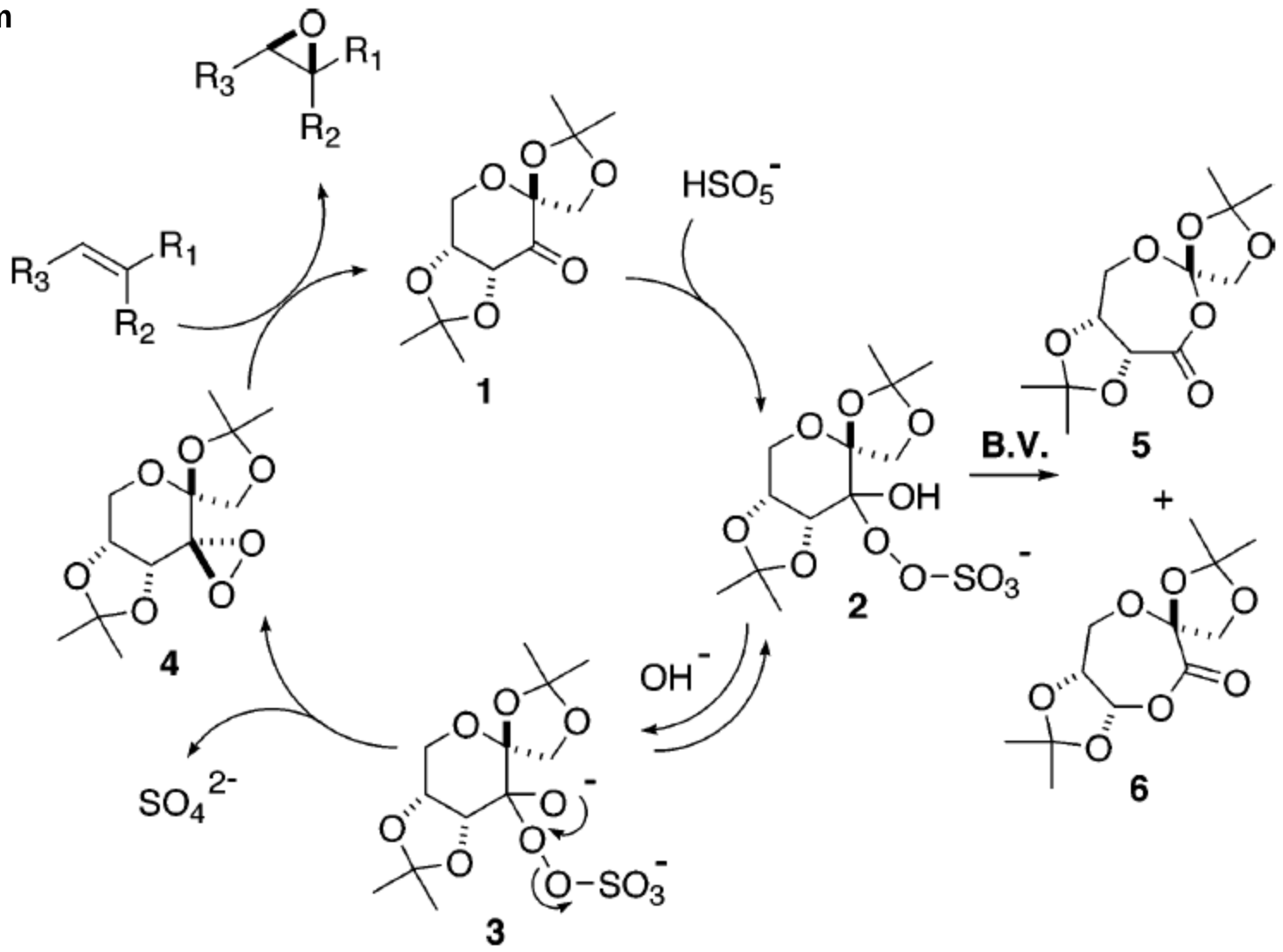

**Synthesis of Catalyst**




(1) Wang, Z. X.; Tu, Y.; Frohn, M.; Zhang, J. R.; Shi, Y. *J. Am. Chem. Soc.* **1997,** *119,* 11224-11235. (2) Shi, Y. *Acc. Chem. Res.* **2004,** *37,* 488-496.

# 2.4.1 Epoxidation: Ketones as Catalysts

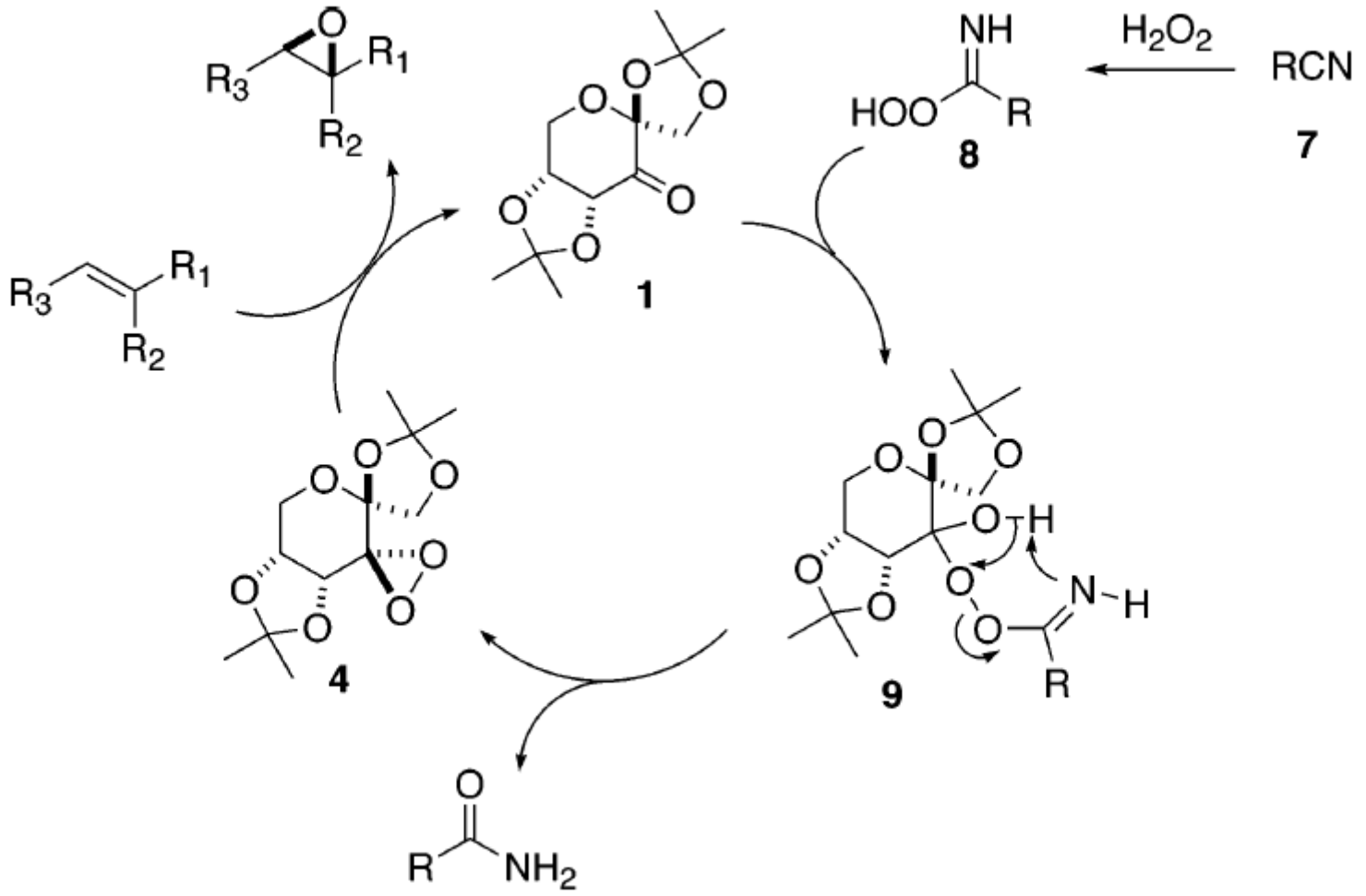
**Mechanism**




(1) Wang, Z. X.; Tu, Y.; Frohn, M.; Zhang, J. R.; Shi, Y. *J. Am. Chem. Soc.* **1997,** *119,* 11224-11235. (2) Shi, Y. *Acc. Chem. Res.* **2004,** *37,* 488-496.

# 2.4.1 Epoxidation: Ketones as Catalysts

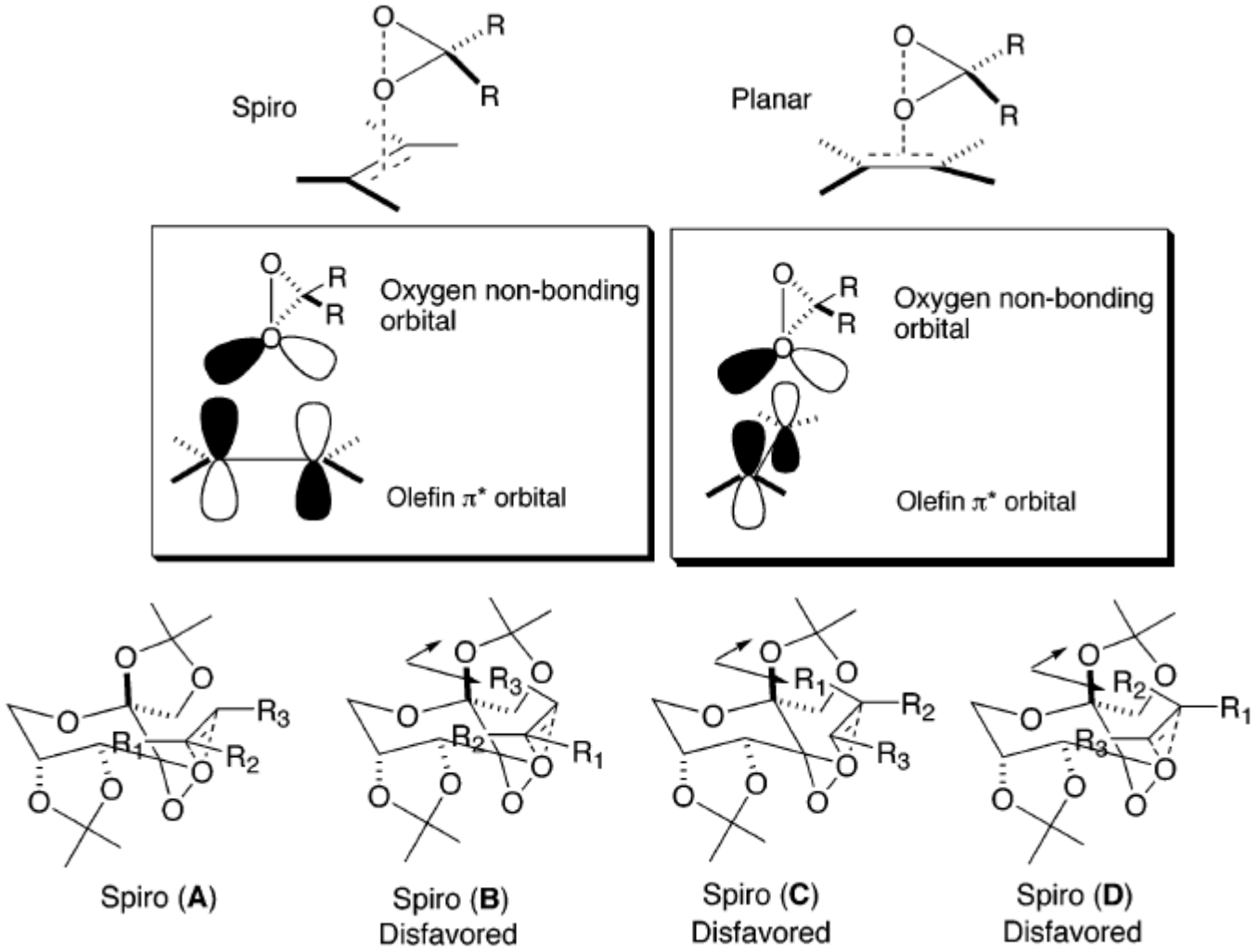
**Use of Acetonitrile/Hydrogen Peroxide as Oxidant**




(1) Wang, Z. X.; Tu, Y.; Frohn, M.; Zhang, J. R.; Shi, Y. *J. Am. Chem. Soc.* **1997,** *119,* 11224-11235. (2) Shi, Y. *Acc. Chem. Res.* **2004,** *37,* 488-496.

# 2.4.1 Epoxidation: Ketones as Catalysts

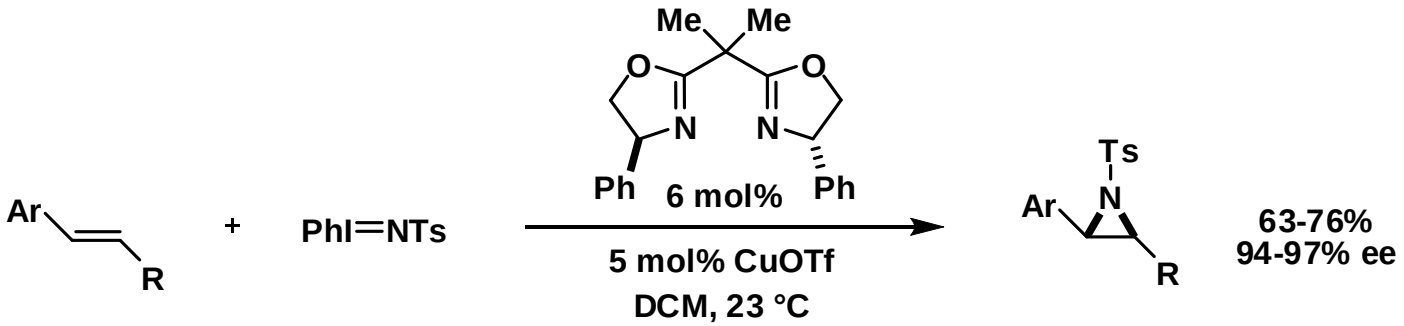
**Model for Selectivity**



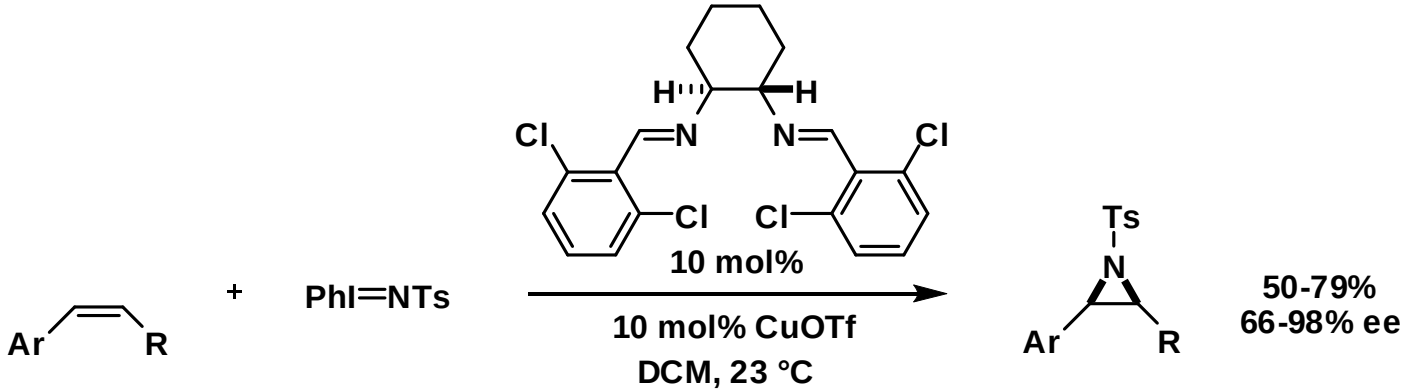

(1) Wang, Z. X.; Tu, Y.; Frohn, M.; Zhang, J. R.; Shi, Y. *J. Am. Chem. Soc.* **1997,** *119,* 11224-11235. (2) Shi, Y. *Acc. Chem. Res.* **2004,** *37,* 488-496.

# 2.4.2 Aziridination

**Evans Copper Catalyst with BOX Ligands[1]**



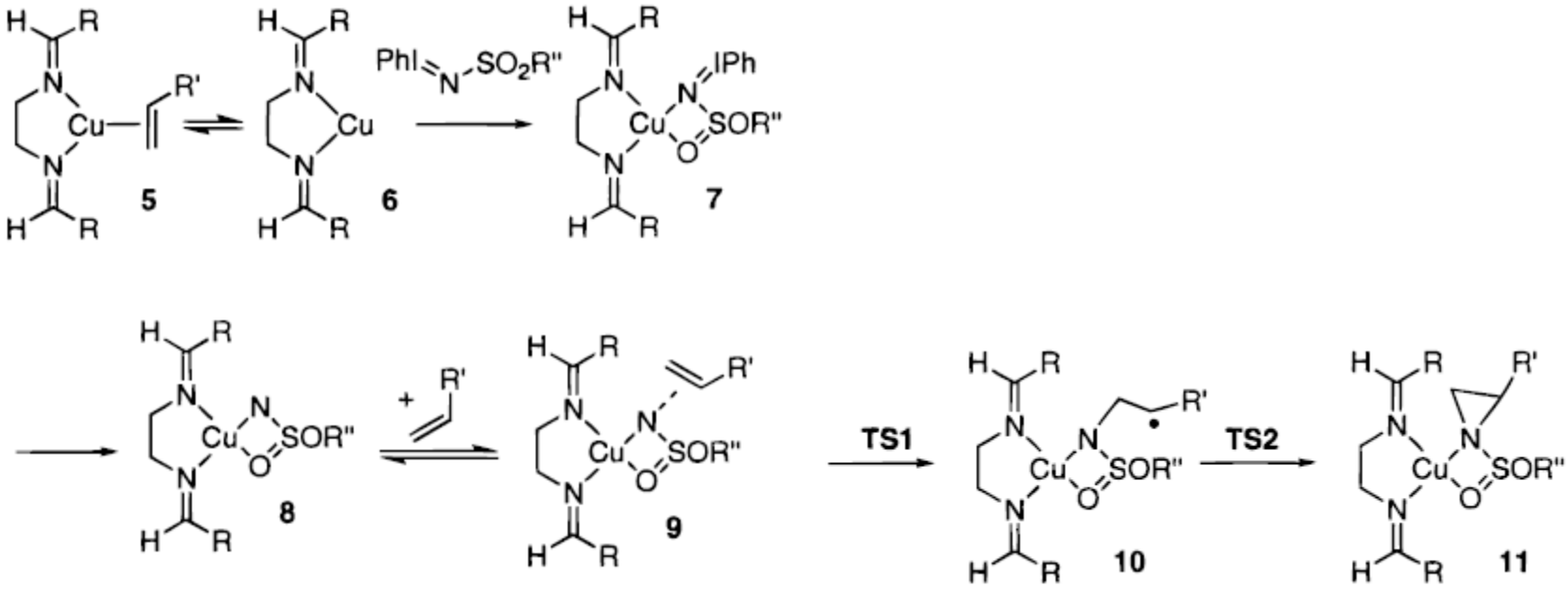

**Jacobsen Copper Catalyst with Diimine Ligands[2]**

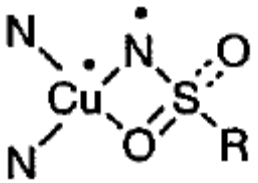



(1) Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993,** *115,* 5328-5329.
(2) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993,** *115,* 5326-5327.

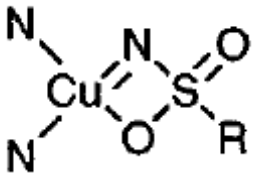
# 2.4.2 Aziridination

**Possible Mechanism**



**Triplet Intermediate**



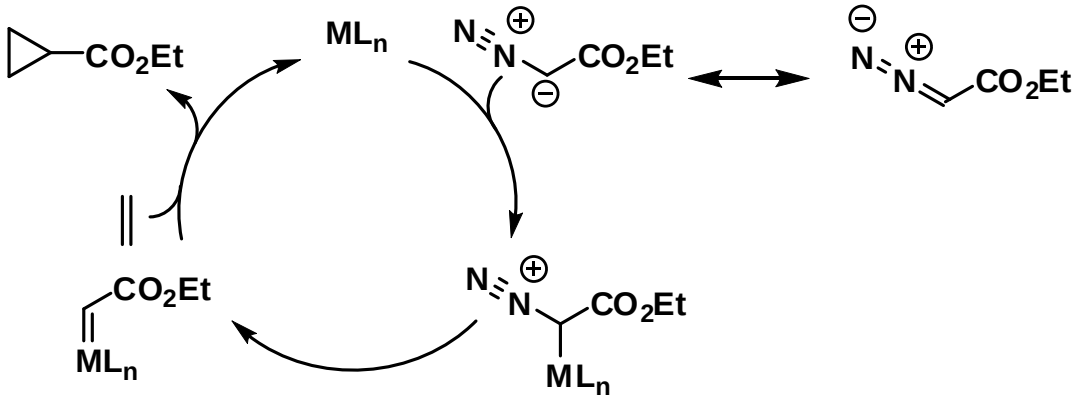
**Singlet Intermediate**

**Singlet and Triplet are very close in energy**

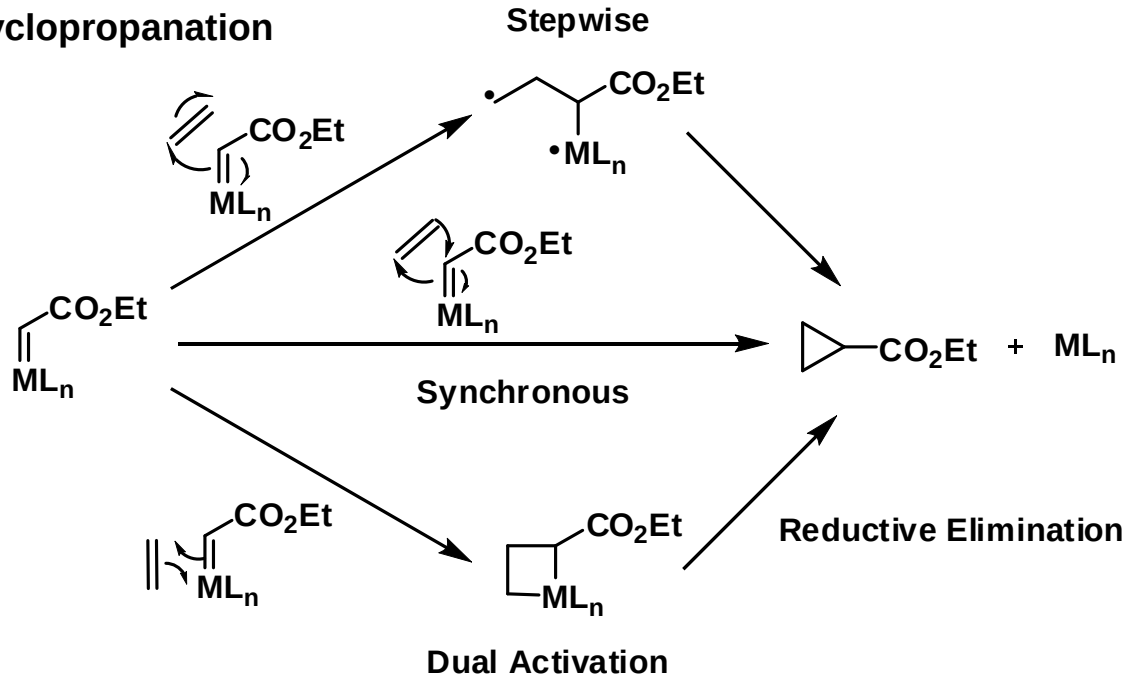
(1) Brandt, P.; Sodergren, M. J.; Andersson, P. G.; Norrby, P. O. *J. Am. Chem. Soc.* **2000,** *122,* 8013-8020.

# 2.4.3 Cyclopropanation: Introduction

**Cyclopropanation with Diazo Compounds**

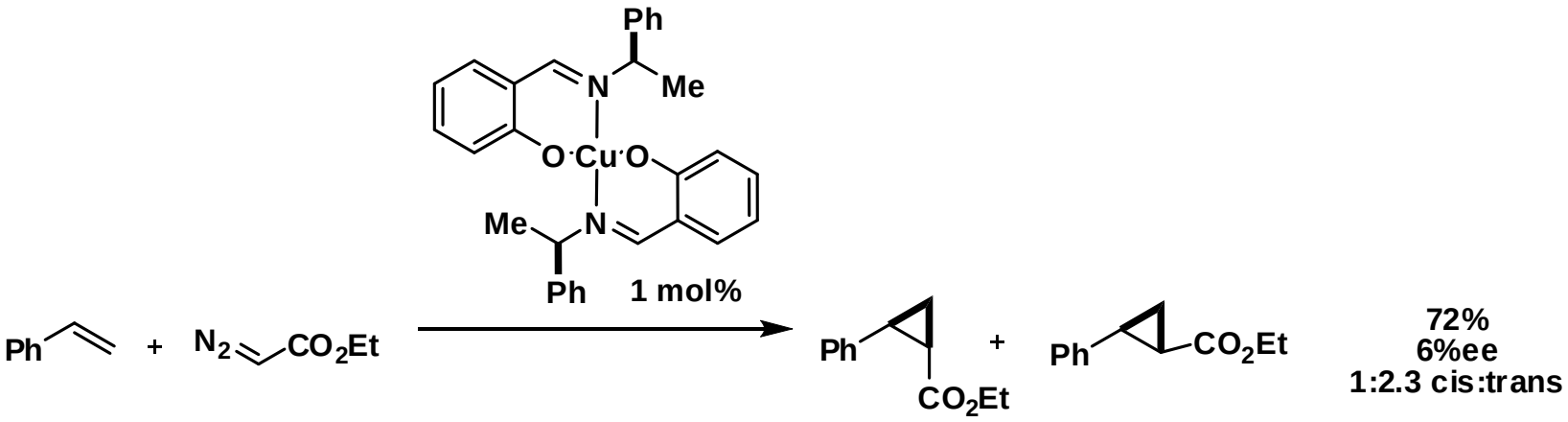



**Several Pathways for Cyclopropanation**

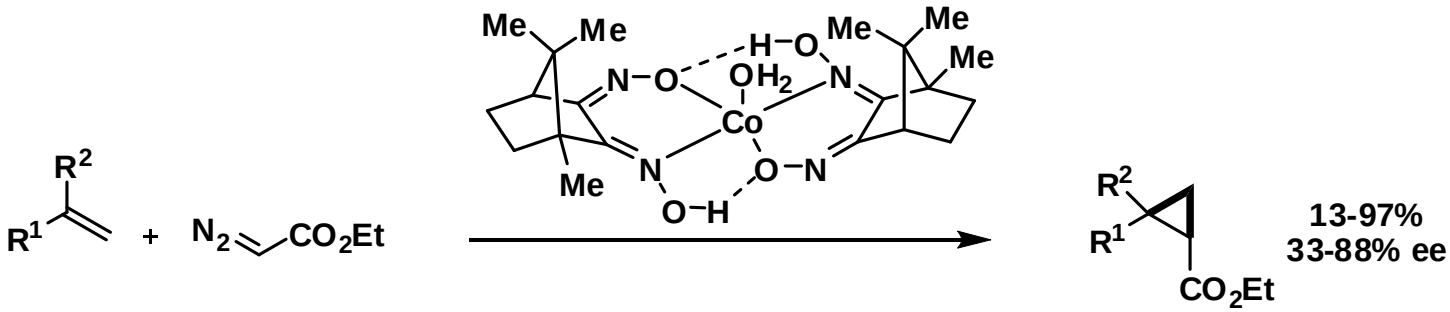


# 2.4.3 Cyclopropanation: Early Examples

**Cyclopropanation of Styrene: One of the First Catalytic Asymmetric Reaction[1]**



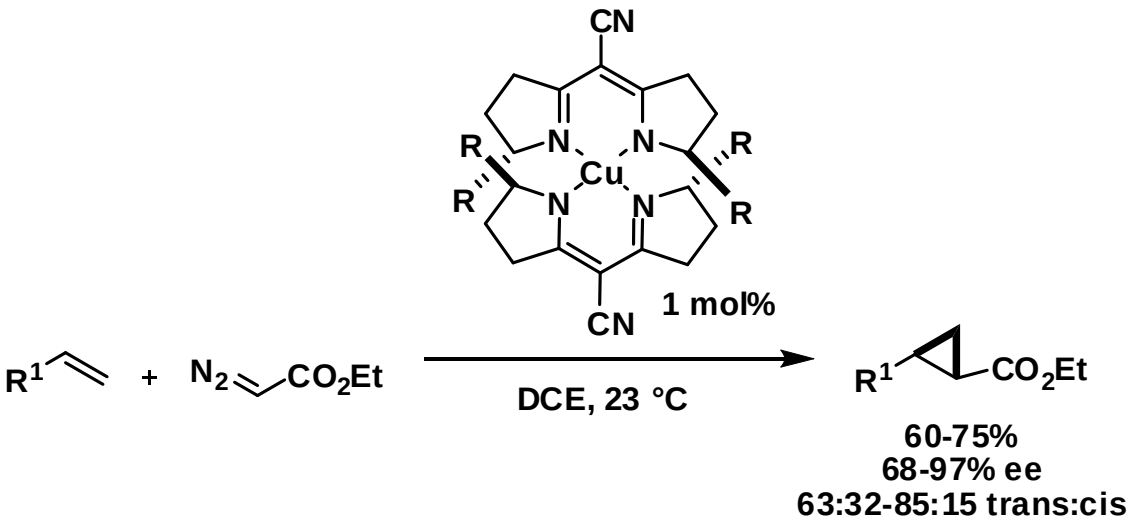

**Nakamura: Towards Useful Enantioselectivity[2,3]**



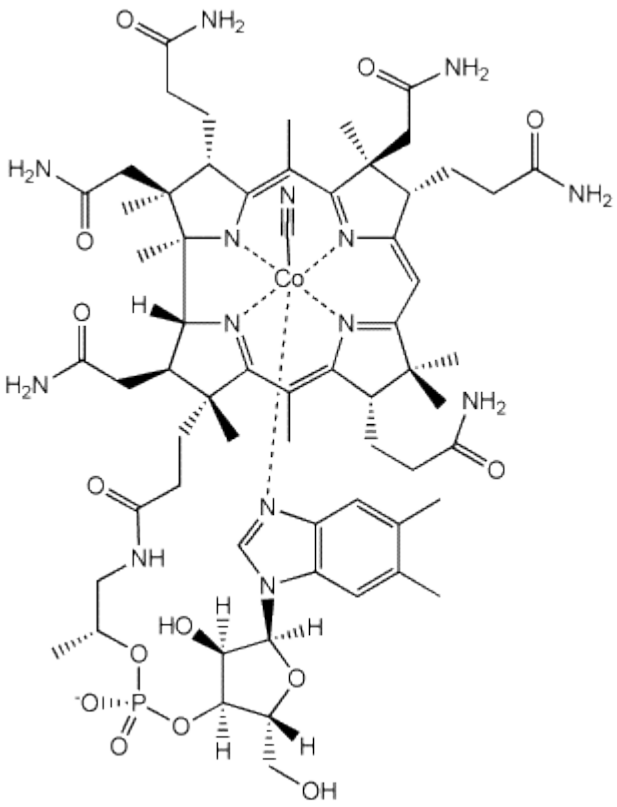

(1) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968,** *24,* 3655. (2) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978,** *100,* 3443-3448. (3) Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M.; Otsuka, S. *J. Am. Chem. Soc.* **1978,** *100,* 3449-3461.

# 2.4.3 Cyclopropanation: Early Examples

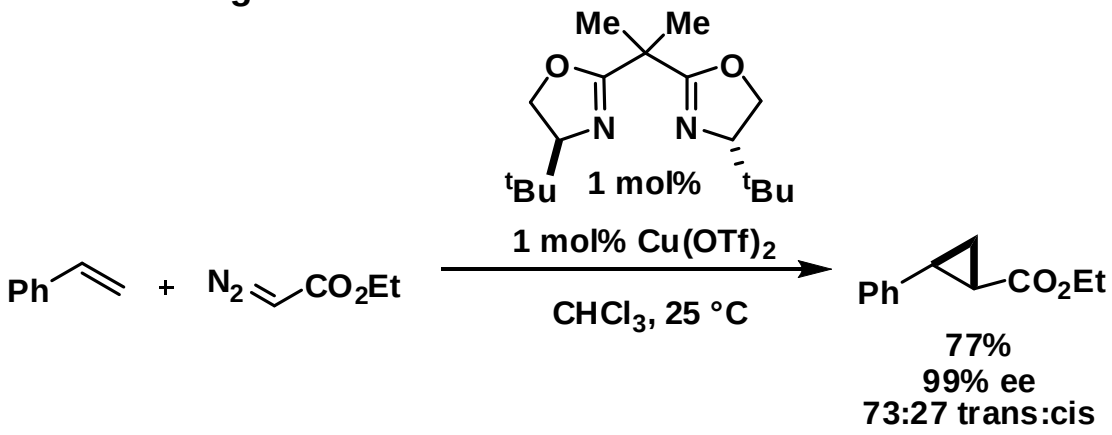
**Pfaltz: Vitamin $B_{12}$ Inspired Semicorrin Ligands[1]**




**Vitamin $B_{12}$**



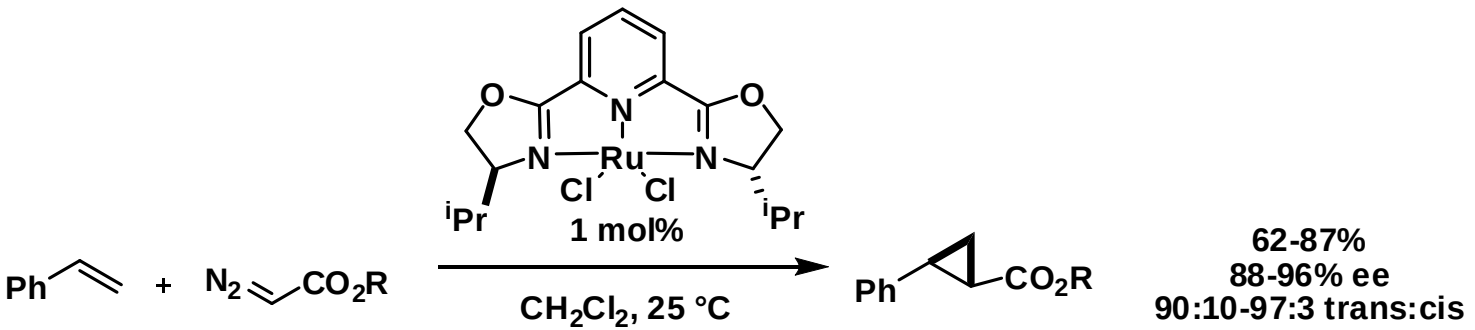

**Evans: BOX Ligands[2]**



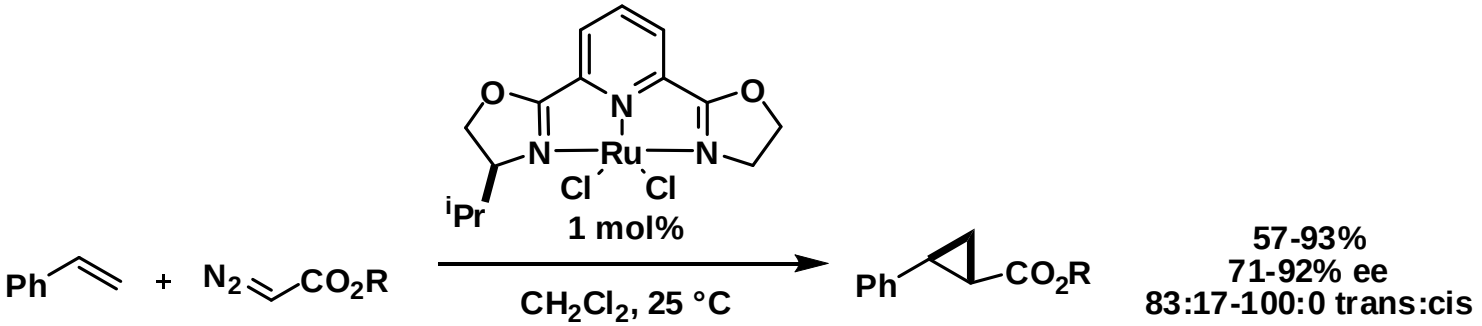

(1) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1986,** *25,* 1005-1006. (2) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991,** *113,* 726-728.

# 2.4.3 Cyclopropanation: Early Examples

**Nishiyama: Ru-Pybox Catalyst[1]**



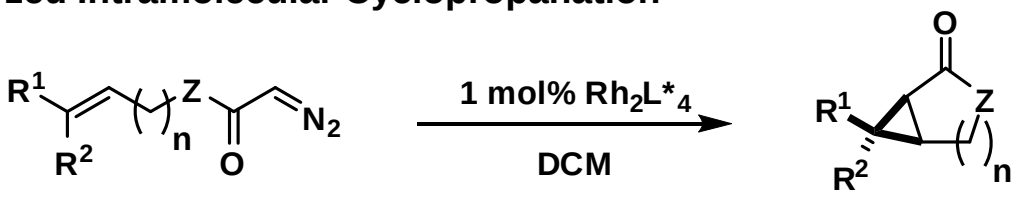

**Also ligands with C1 symmetry can be successful[2]**

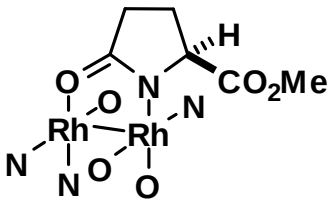



(1) Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S. B.; Itoh, K. *J. Am. Chem. Soc.* **1994,** *116,* 2223-2224. (2) Nishiyama, H.; Soeda, N.; Naito, T.; Motoyama, Y. *Tetrahedron: Asymmetry* **1998,** *9,* 2865-2869.

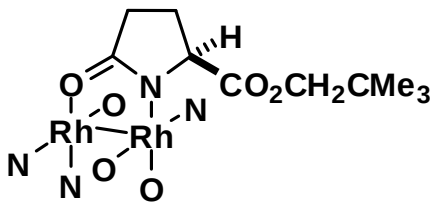
# 2.4.3 Cyclopropanation: Rh Catalysis

**Doyle: Rh-Catalyzed Intramolecular Cyclopropanation**

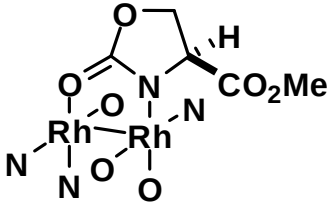


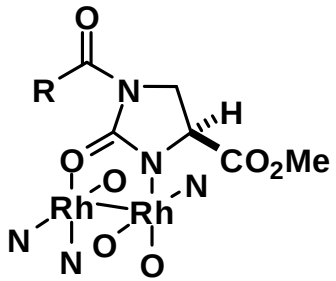

$Rh_2(5S\text{-MEPY})_4$




$Rh_2(5S\text{-NEPY})_4$

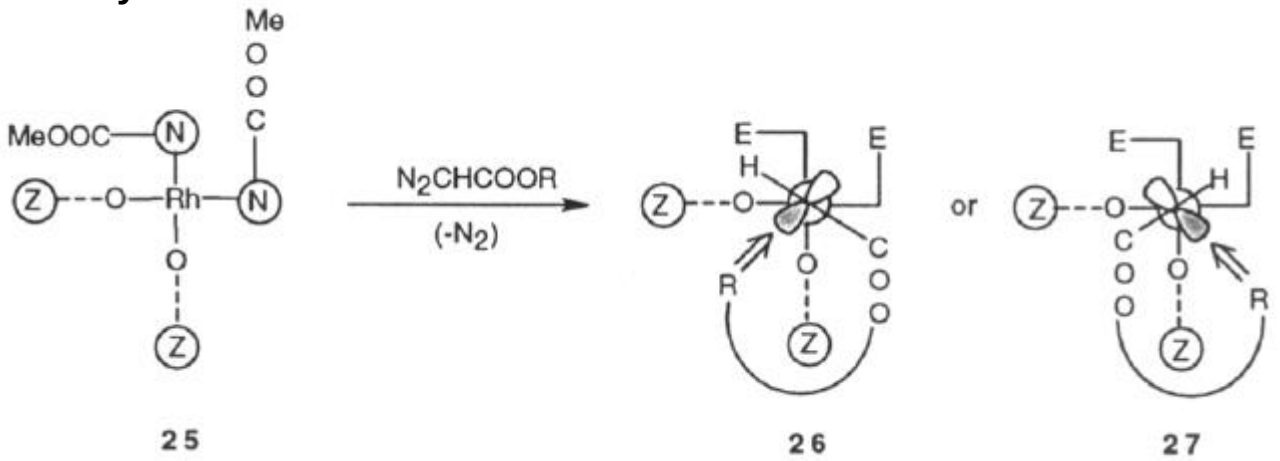



$Rh_2(4S\text{-MEOX})_4$




$Rh_2(4S\text{-MPAIM})_4$

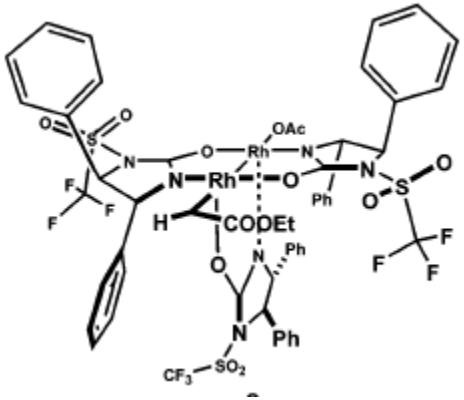
**Model for Selectivity**

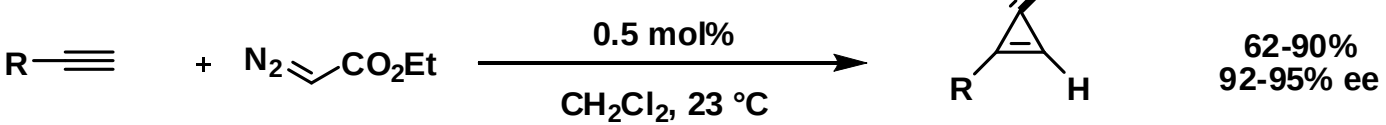



(1) Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q. L.; Martin, S. F. *J. Am. Chem. Soc.* **1995,** *117,* 5763-5775.

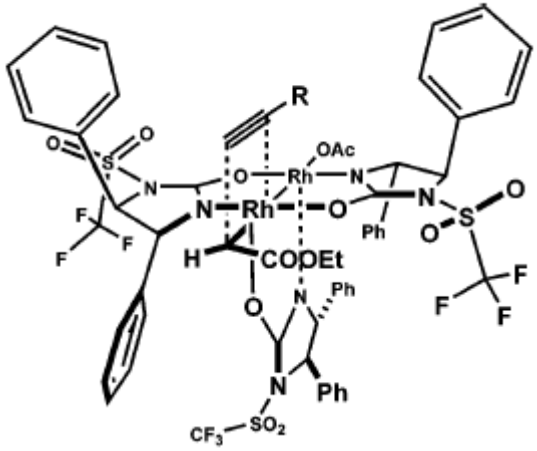
# 2.4.3 Cyclopropanation: Rh Catalysis

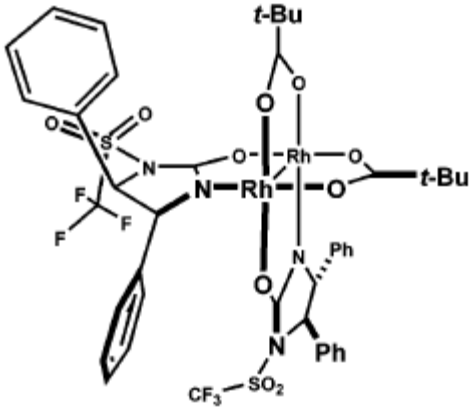
**Corey: Rh-Catalyzed Cyclopropanation of Alkynes**

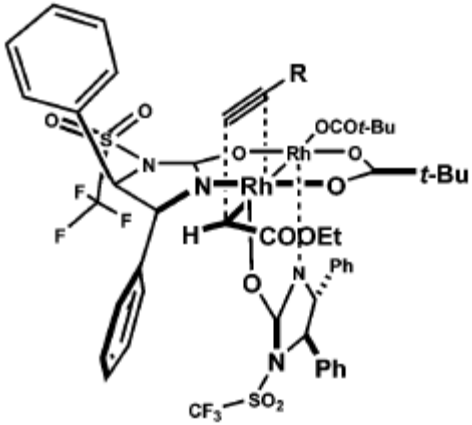





**Model for Selectivity**



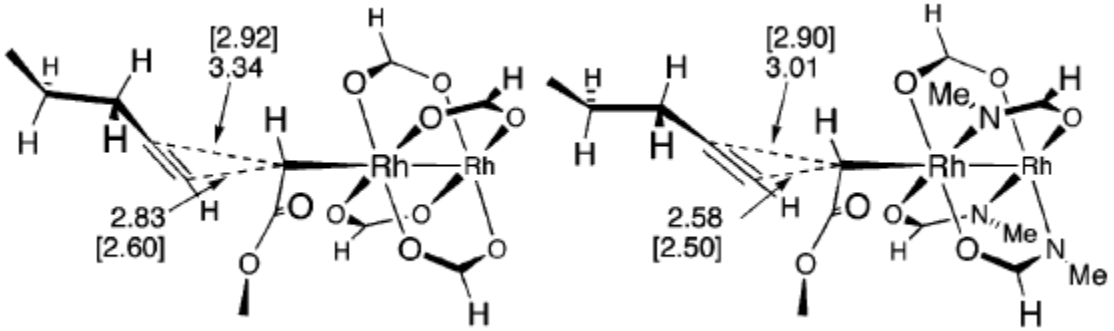




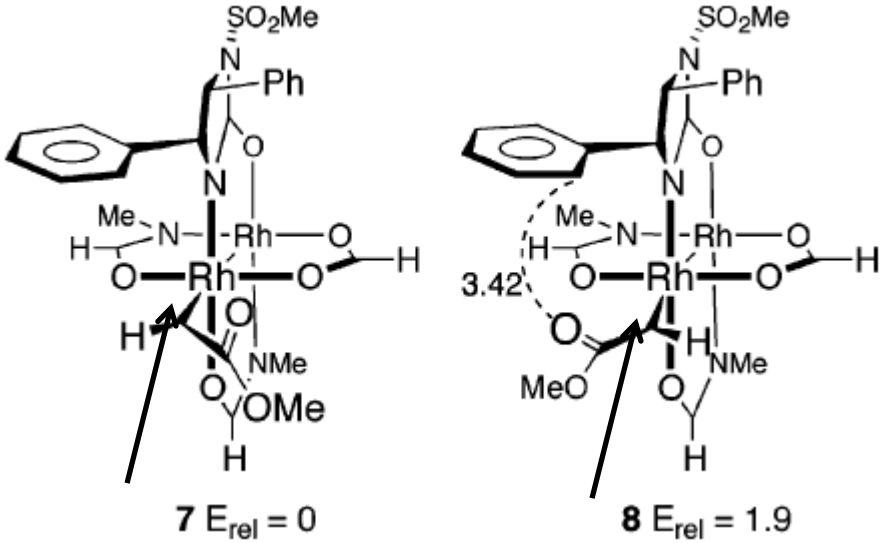
(1) Lou, Y.; Horikawa, M.; Kloster, R. A.; Hawryluk, N. A.; Corey, E. J. *J. Am. Chem. Soc.* **2004,** *126,* 8916-8918. (2) Lou, Y.; Remarchuk, T. P.; Corey, E. J. *J. Am. Chem. Soc.* **2005,** *127,* 14223-14230.

# 2.4.3 Cyclopropanation: Rh Catalysis

**Calculation: Tetrabridged Structures and Direct Cyclopropanation are Favored**




**Model for Selectivity**

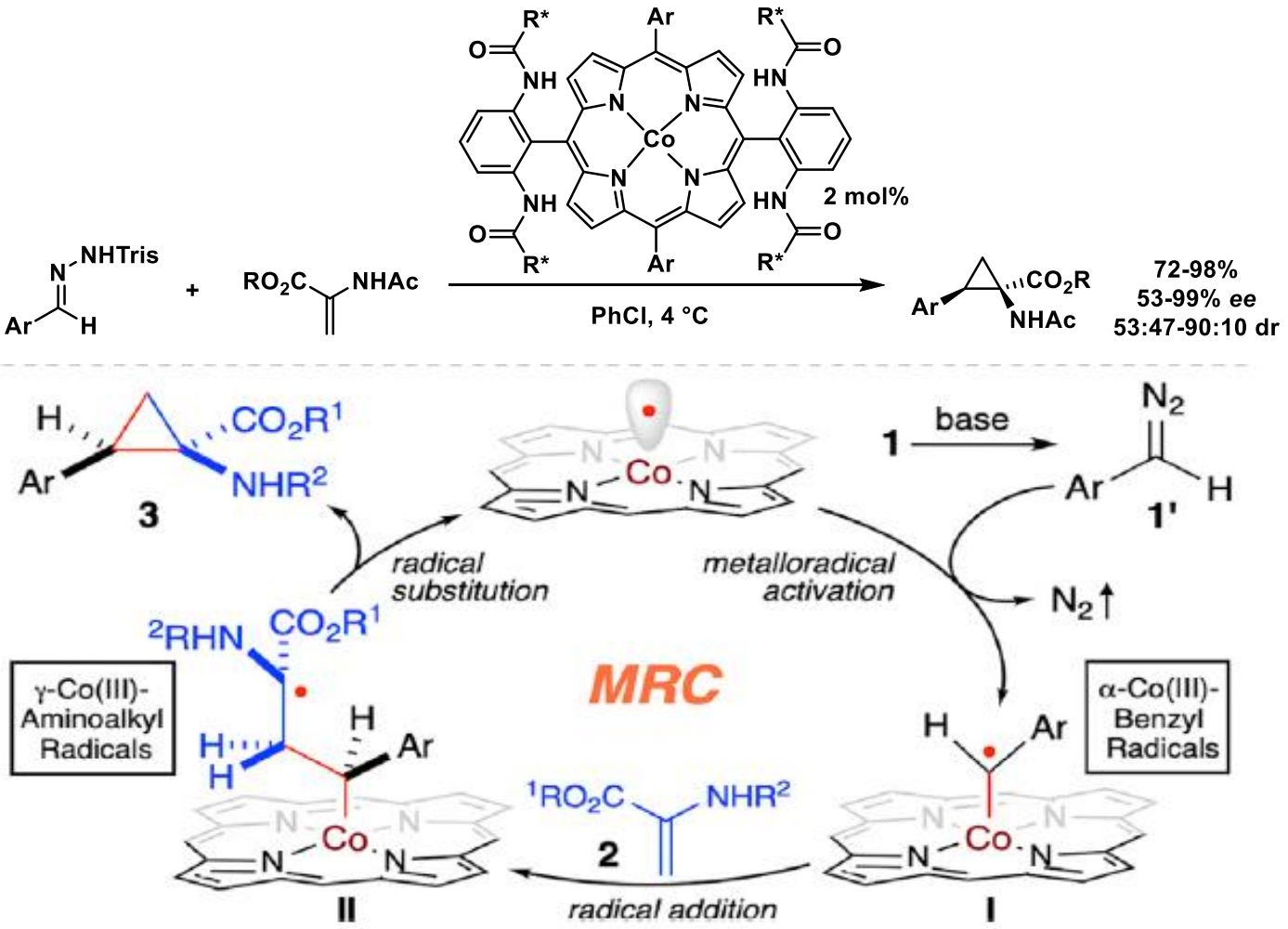



**7** $E_{rel} = 0$ **8** $E_{rel} = 1.9$

(1) Nowlan, D. T.; Singleton, D. A. *J. Am. Chem. Soc.* **2005,** *127,* 6190-6191.

# 2.4.3 Cyclopropanation: Alternative Radical Mechanism

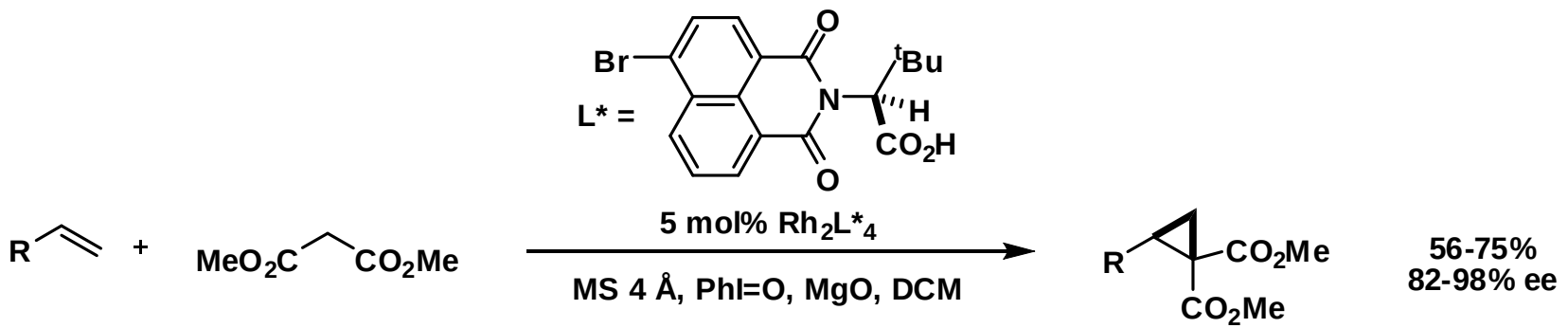
**Zhang: Cobalt porphyrin catalysts favoring a radical rebound mechanism**



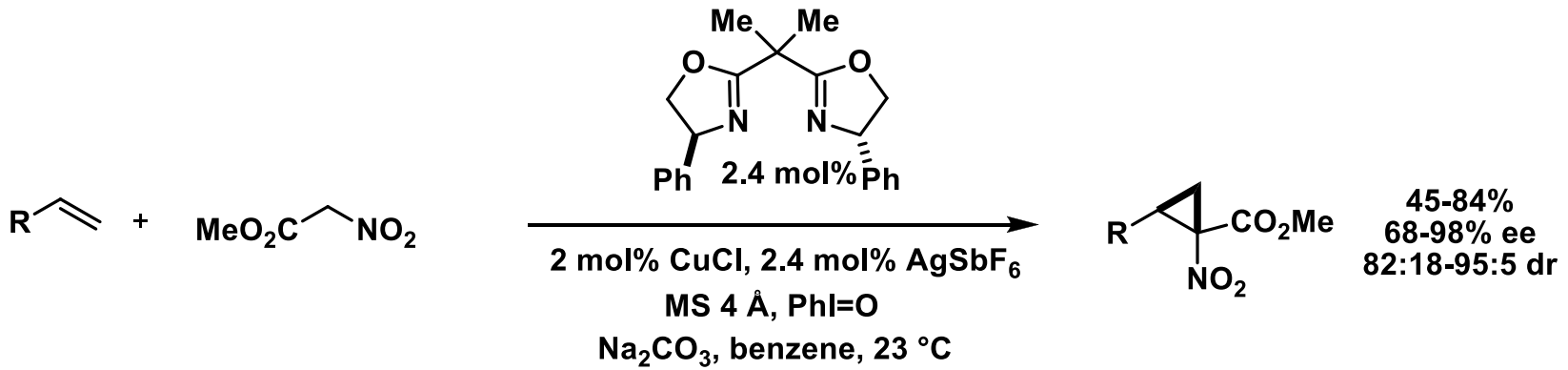

Lee, W.-C. C.; Wang, D.-S.; Zhang, C.; Xie, J.; Li, B.; Zhang, X. P. *Chem* **2021**, 1588-1601.

# 2.4.3 Cyclopropanation: Alternative to Diazo Compounds

**Hypervalent Iodine as Carbene Precursor: Rh Catalyst[1]**



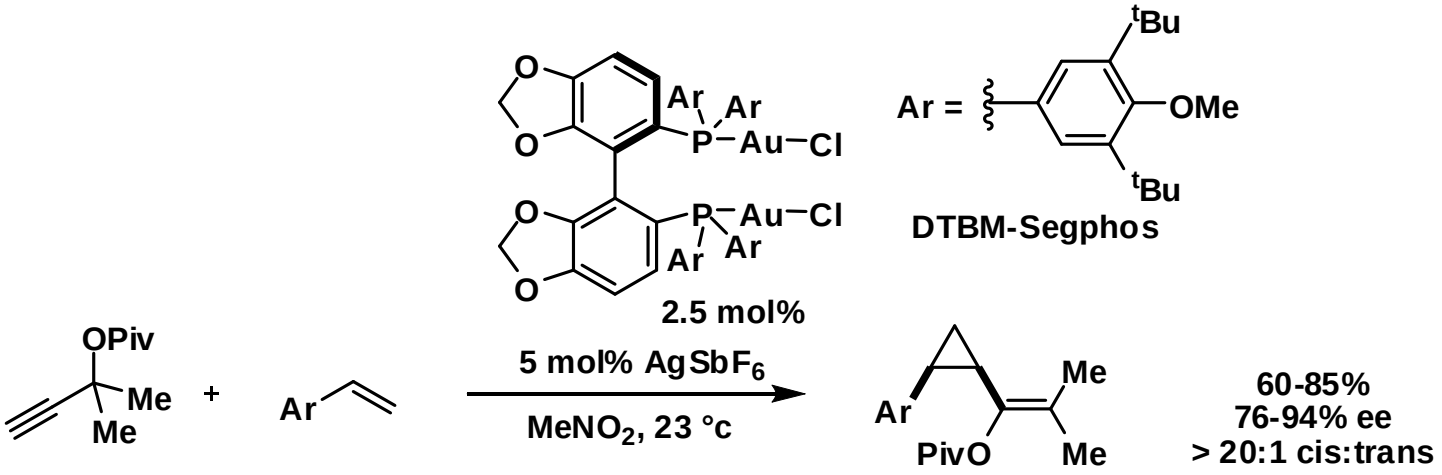

**Hypervalent Iodine as Carbene Precursor: Cu Catalyst[2]**



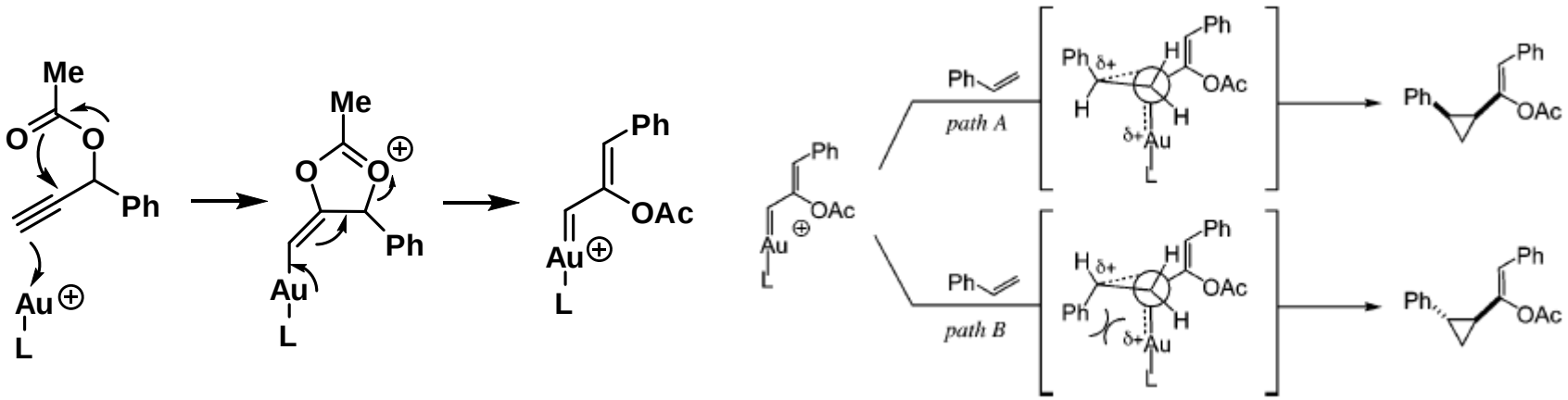

(1) Muller, P.; Ghanem, A. *Org. Lett.* **2004,** *6,* 4347-4350. (2) Moreau, B.; Charette, A. B. *J. Am. Chem. Soc.* **2005,** *127,* 18014-18015.

# 2.4.3 Cyclopropanation: Alternative to Diazo Compounds

**Toste: Propargylic Ester as Au-Carbenes Precursors**



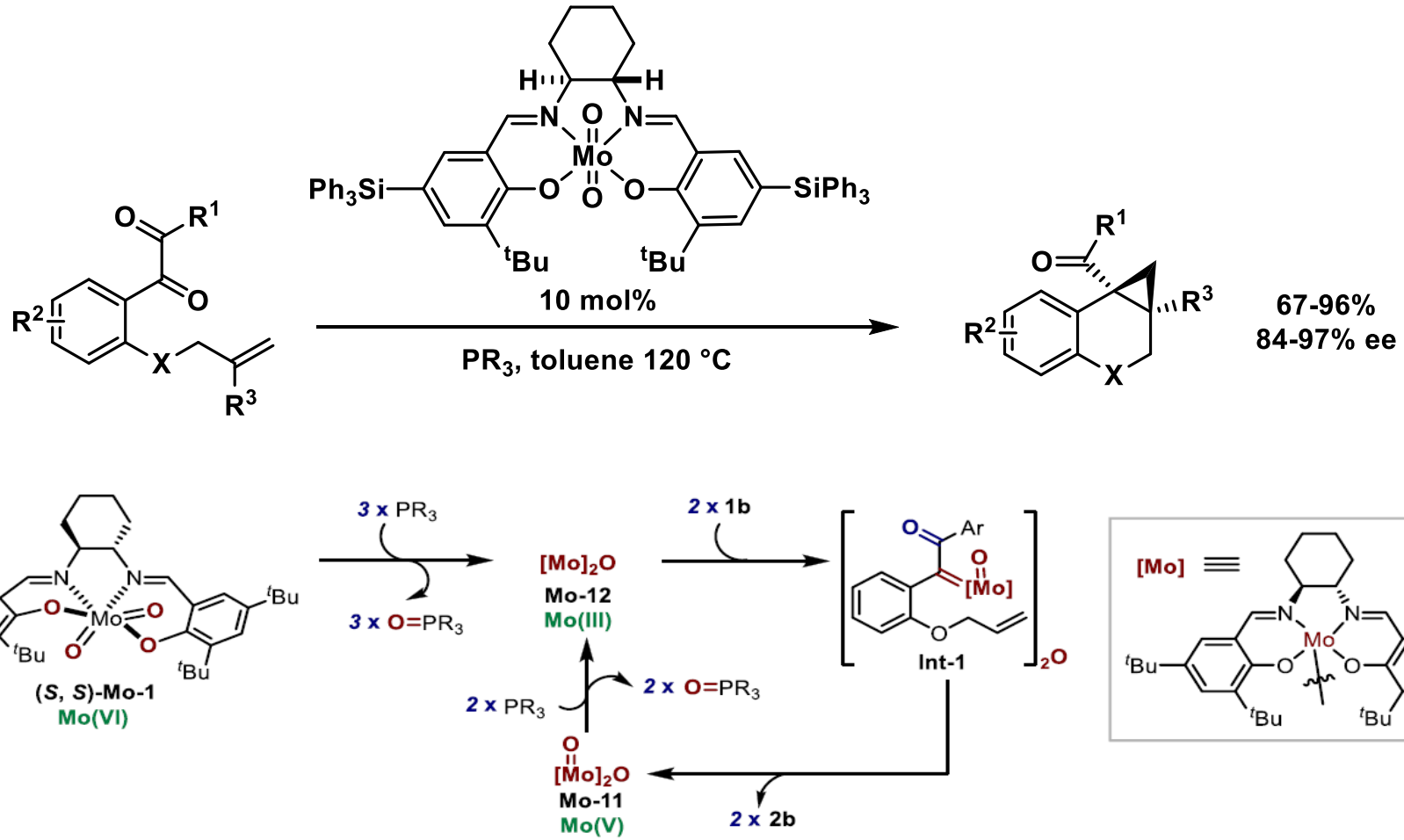

**Mechanism**




(1) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005,** *127,* 18002-18003.

# 2.4.3 Cyclopropanation: Alternative to Diazo Compounds

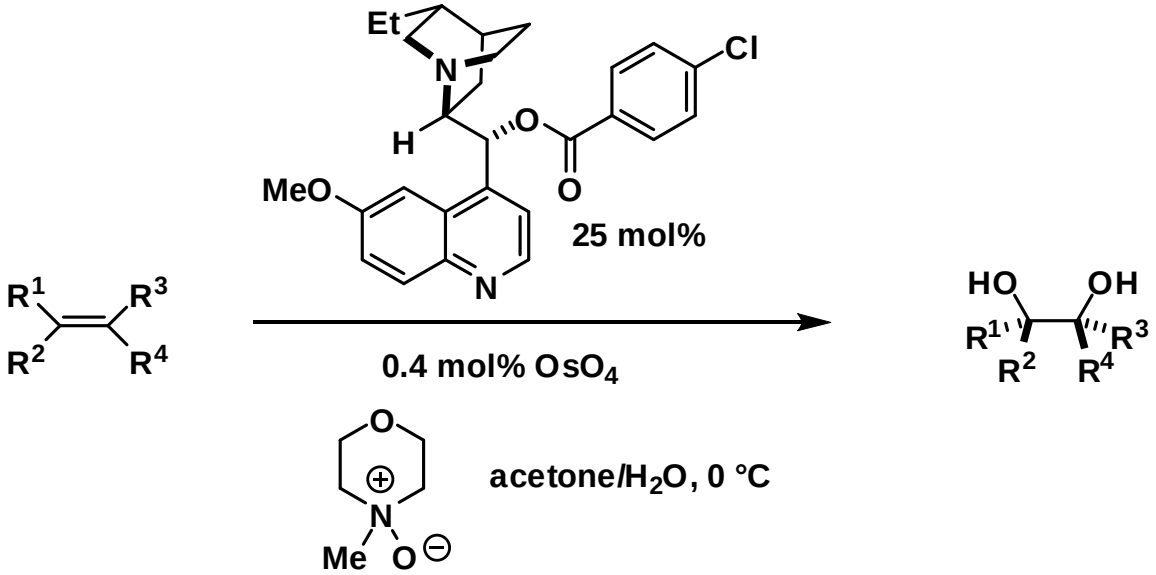
**Zhuo: From carbonyl groups using a Mo catalyst and phosphine as reductant**



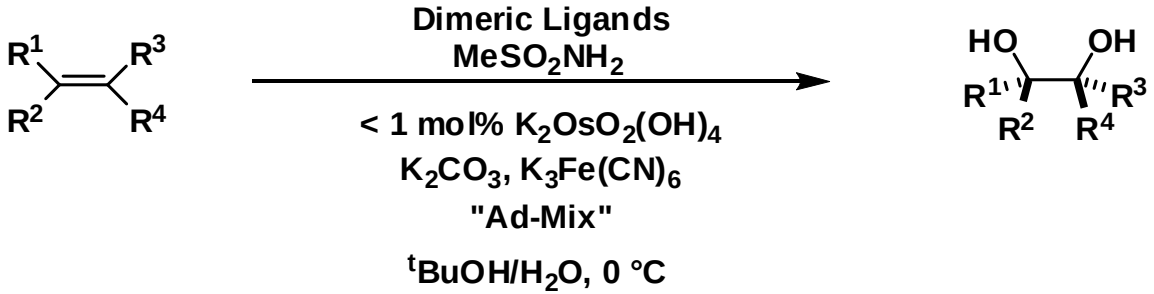

(1) Cao, L.-Y.; Wang, J.-L.; Wang, K.; Wu, J.-B.; Wang, D.-K.; Peng, J.-M.; Bai, J.; Zhuo, C.-X. *J. Am. Chem. Soc.* **2023**, *145*, 2765-2772.

# 2.4.4 Dihydroxylation: Sharpless

**1. Generation Sharpless Dihydroxylation[1]**



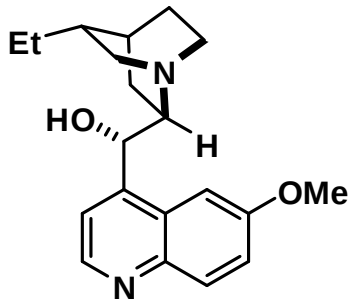

**2. Generation Sharpless Dihydroxylation: Dimeric Ligands and Ad-Mix[2,3]**



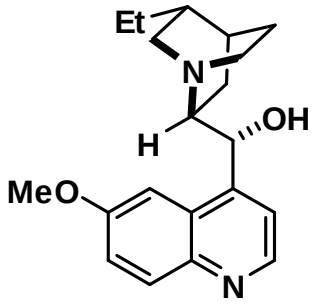

(1) Wai, J. S. M.; Marko, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989,** *111,* 1123-1125. (2) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M.; Xu, D. Q.; Zhang, X. L. *J. Org. Chem.* **1992,** *57,* 2768-2771. (3) Kolb, H. C.; Vannieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994,** *94,* 2483-2547.

# 2.4.4 Dihydroxylation: Sharpless

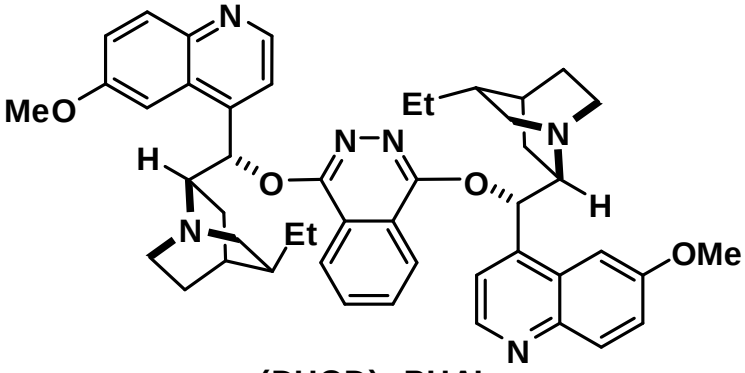
**Ligands for Asymmetric Dihydroxylation**



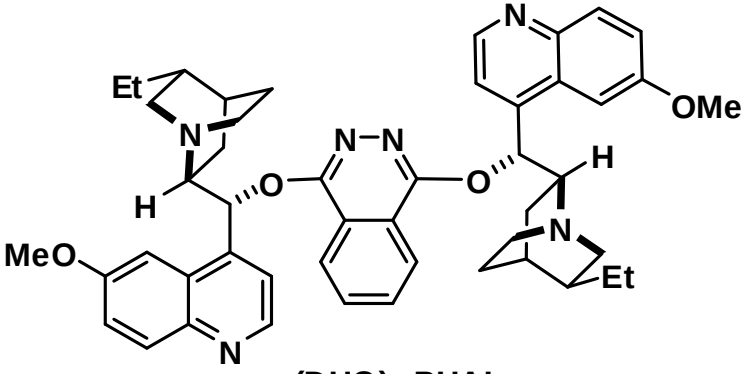

**Dihydroquinidine**
**DHQD**




**Dihydroquinine**
**DHQ**

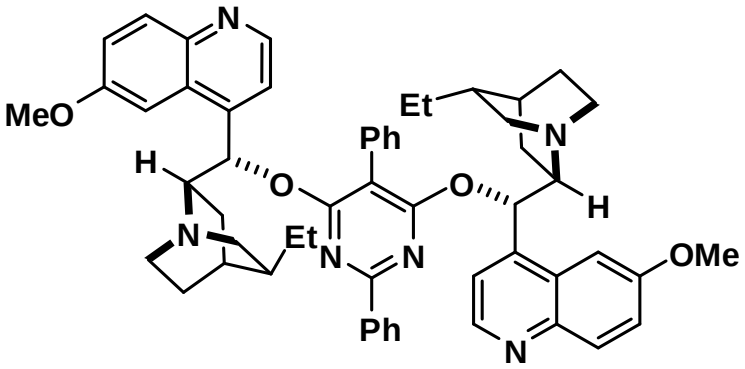



**$(DHQD)_2$-PHAL**

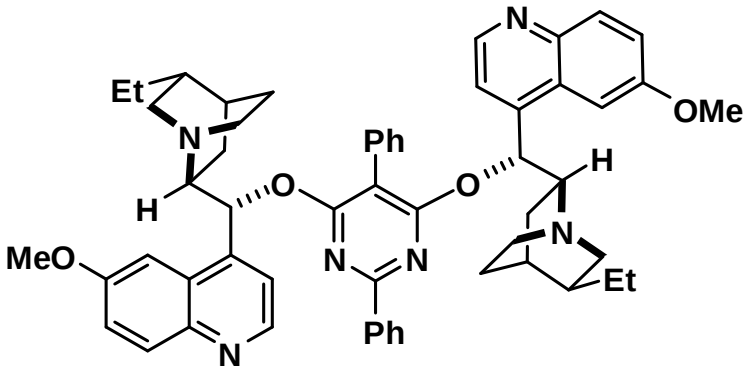



**$(DHQ)_2$-PHAL**

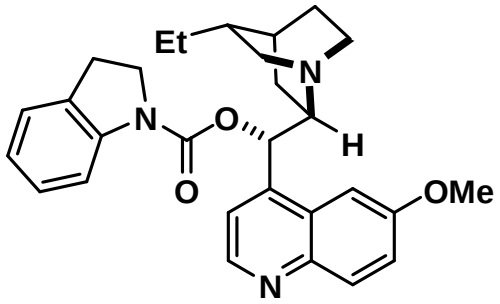
# 2.4.4 Dihydroxylation: Sharpless



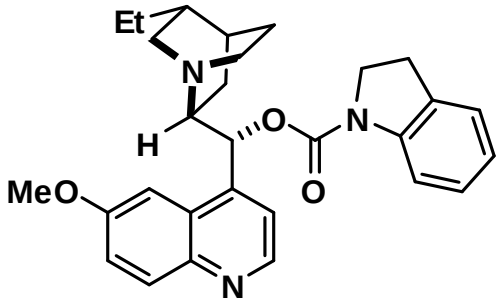

$(DHQD)_2$-PYR




$(DHQ)_2$-PYR




DHQD-IND

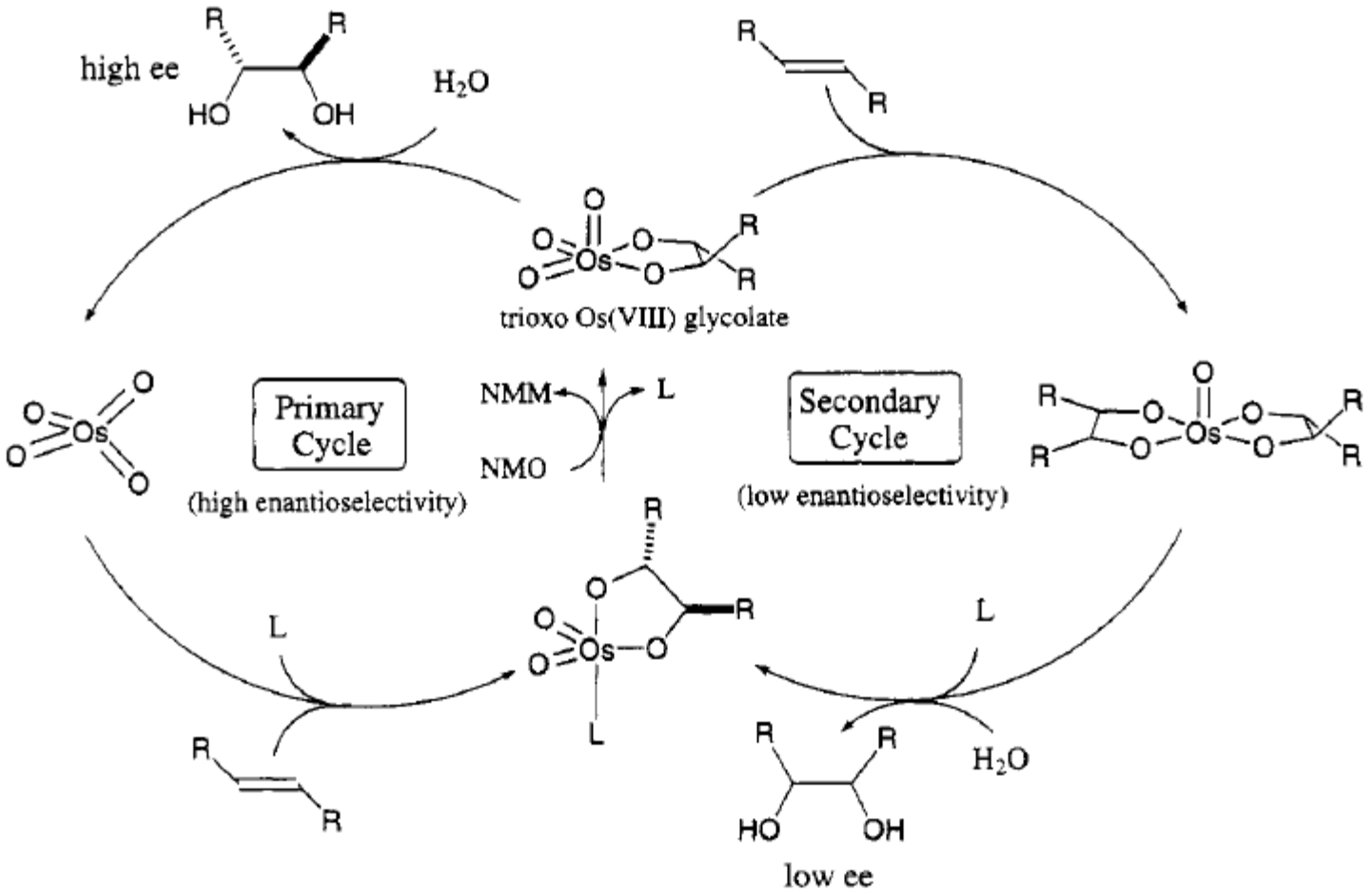



DHQ-IND

| *Olefin class* | | | | | | |
|---|---|---|---|---|---|---|
| *Preferred ligand* | PYR PHAL | PHAL | IND | PHAL | PHAL | PYR PHAL |
| *ee range* | 30-97 % | 70-97 % | 20-80 % | 90-99.8 % | 90-99 % | 20-97 % |

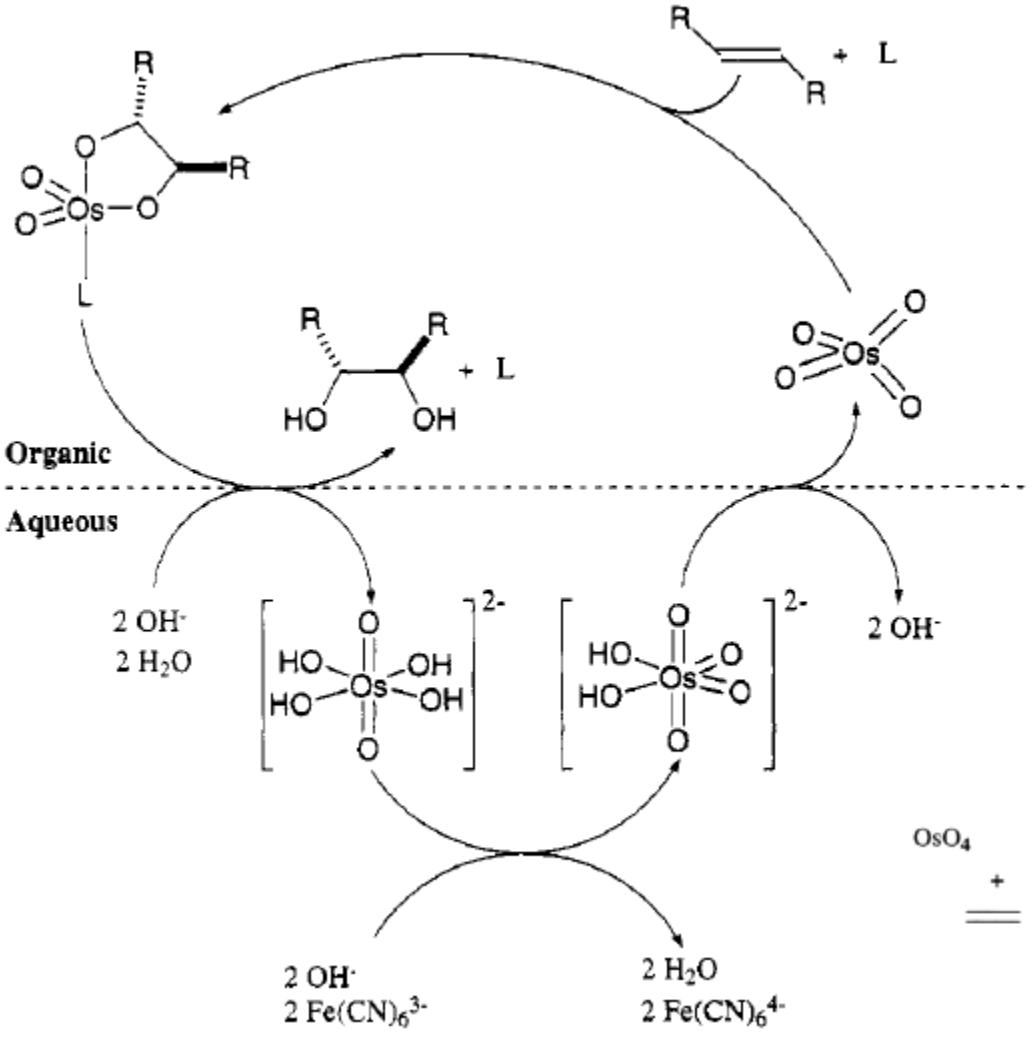
# 2.4.4 Dihydroxylation: Sharpless

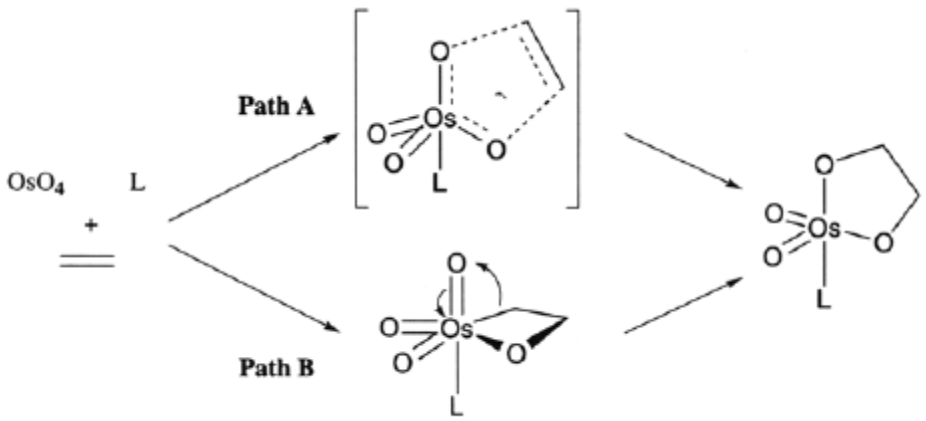
**Mechanism for Dihydroxylation Using NMO**



# 2.4.4 Dihydroxylation: Sharpless

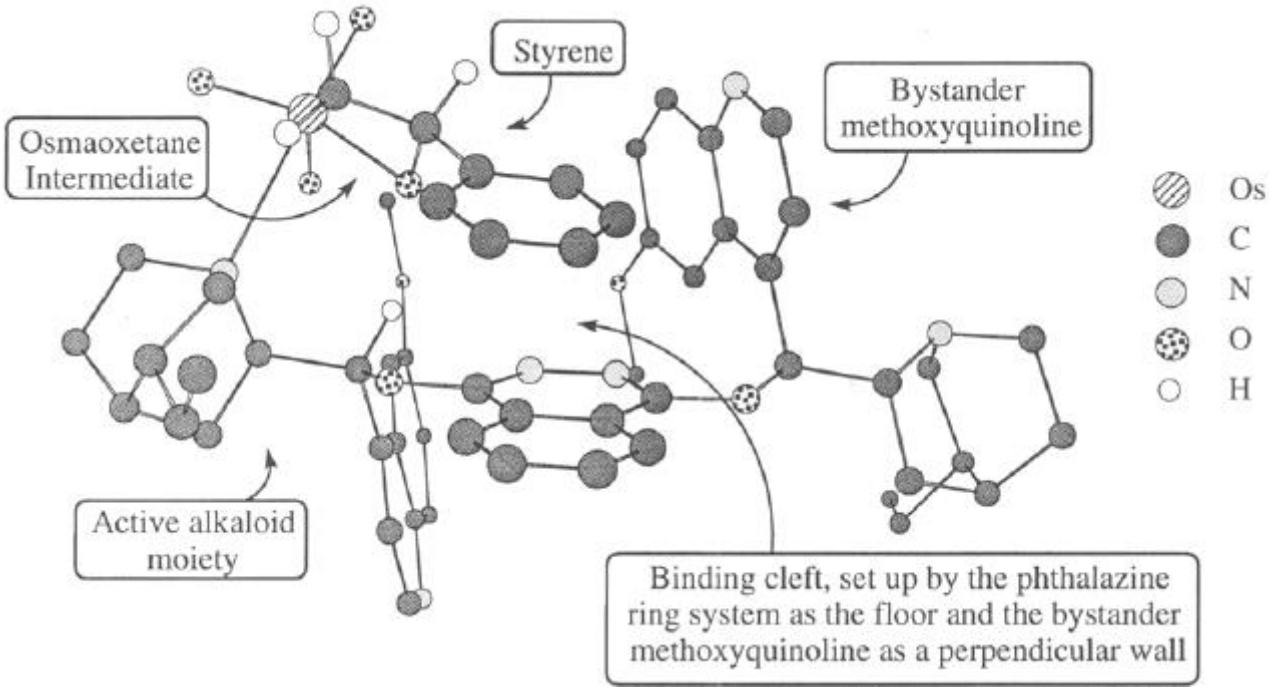
**Mechanism for Dihydroxylation Using Add Mix**



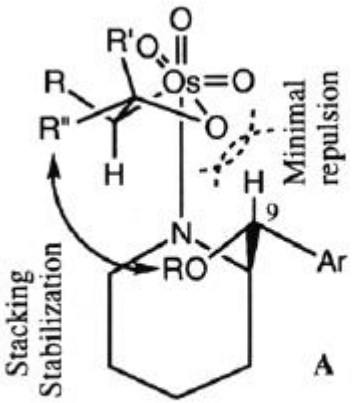



# 2.4.4 Dihydroxylation: Sharpless

**Origin of Enantioselectivity**

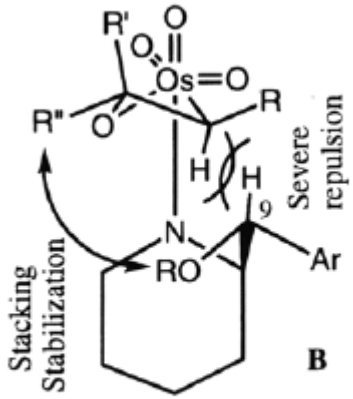



**Major pathway**




Best isomer (**A**), leads to (*R*)-diol, good attractive stabilization and minimal repulsion

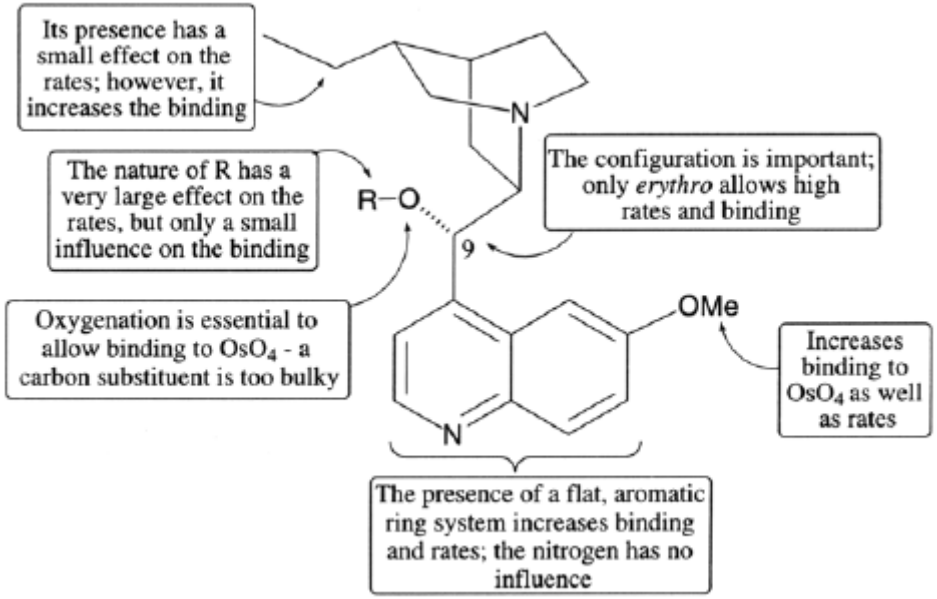
**Minor pathway**

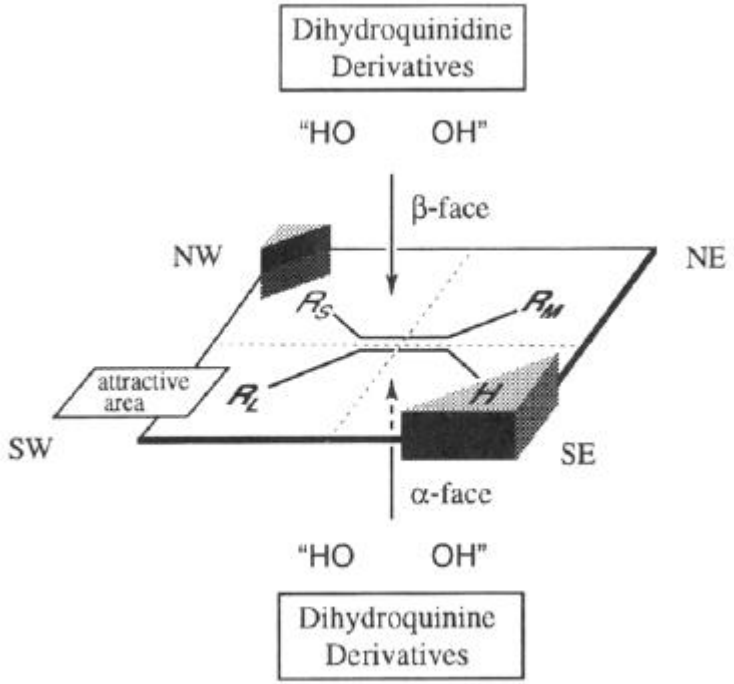



Steric repulsion destabilizes this isomer (**B**), an (*S*)-diol precursor

# 2.4.4 Dihydroxylation: Sharpless

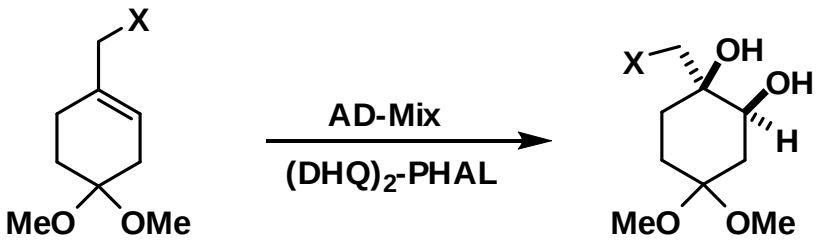
**Importance of Structure and Mnemotechnic Model**



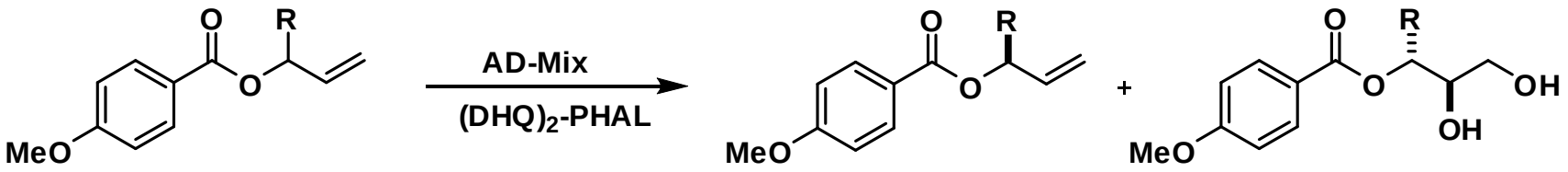
# 2.4.4 Dihydroxylation: Sharpless

**Corey: The Importance of π–π Interactions for Selectivity**




**X = OH: 18% ee**
**X = OTIPS: 13% ee**
**X = OBn: 90% ee**
**X = *p*-MeO-BzO: > 99% ee**

**Kinetic Resolution Using Sharpless Dihydroxylation**

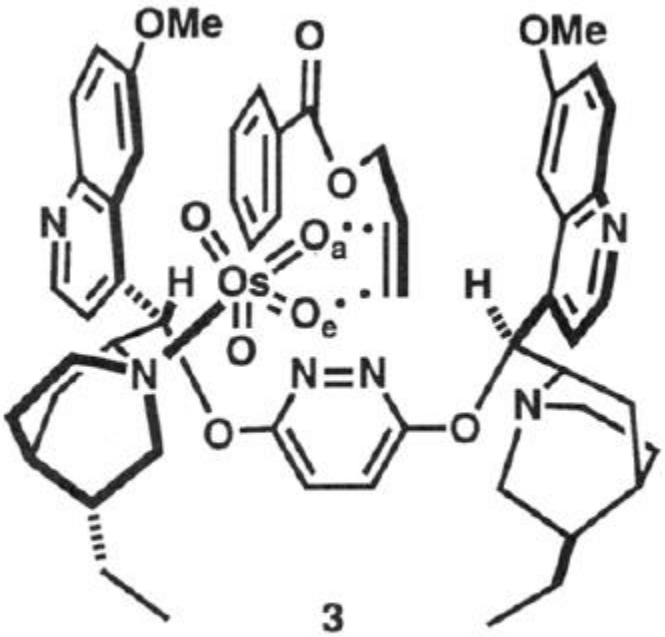



**S Factor: 20-79**

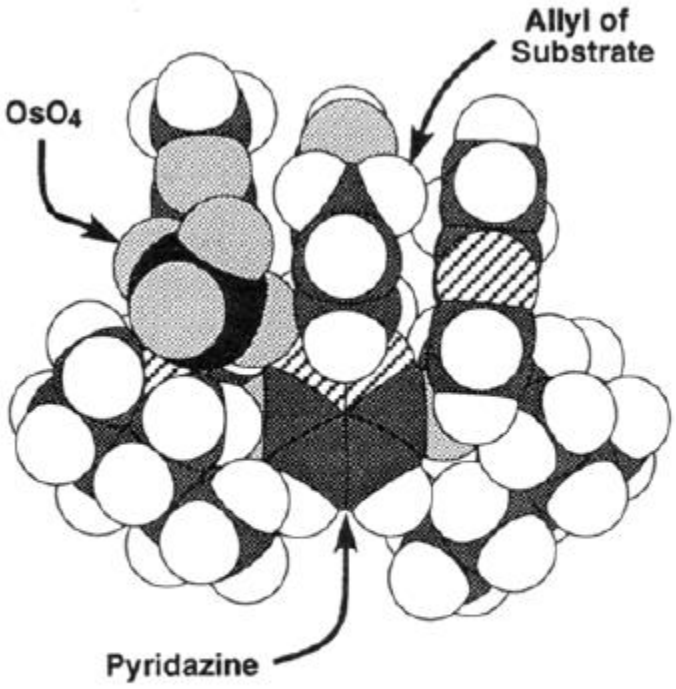
(1) Corey, E. J.; Guzmanperez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1995,** *117,* 10805-10816. (2) Corey, E. J.; Noe, M. C.; Guzmanperez, A. *J. Am. Chem. Soc.* **1995,** *117,* 10817-10824.

# 2.4.4 Dihydroxylation: Sharpless

**Model for Selectivity**




3

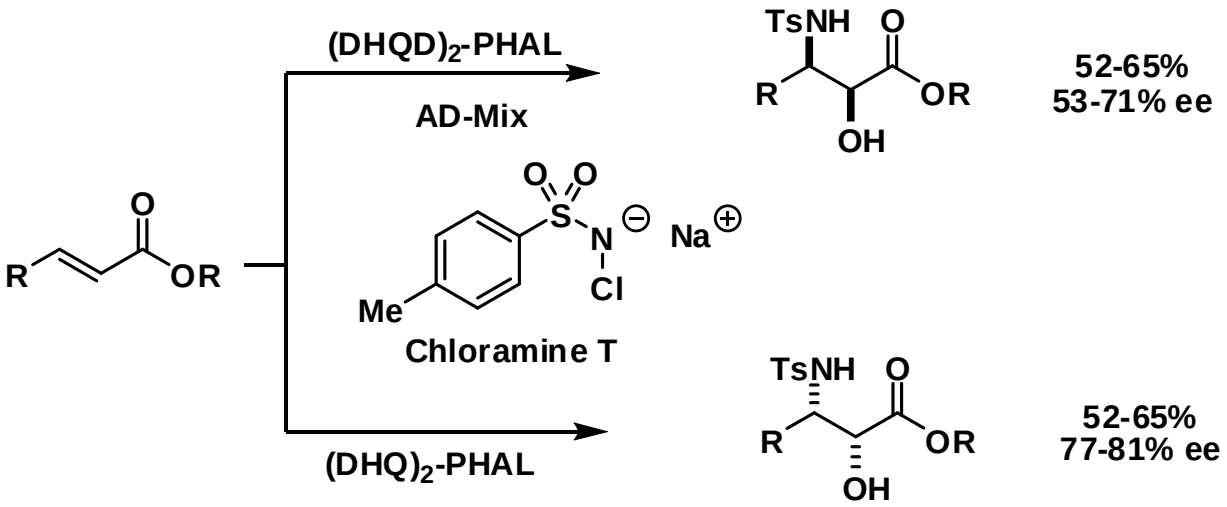



= Carbon = Nitrogen = Oxygen = Osmium

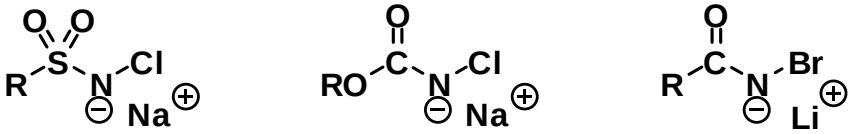
(1) Corey, E. J.; Guzmanperez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1995,** *117,* 10805-10816. (2) Corey, E. J.; Noe, M. C.; Guzmanperez, A. *J. Am. Chem. Soc.* **1995,** *117,* 10817-10824.

# 2.4.4 Aminohydroxylation: Sharpless

**Sharpless: Asymmetric Aminhydroxylation**

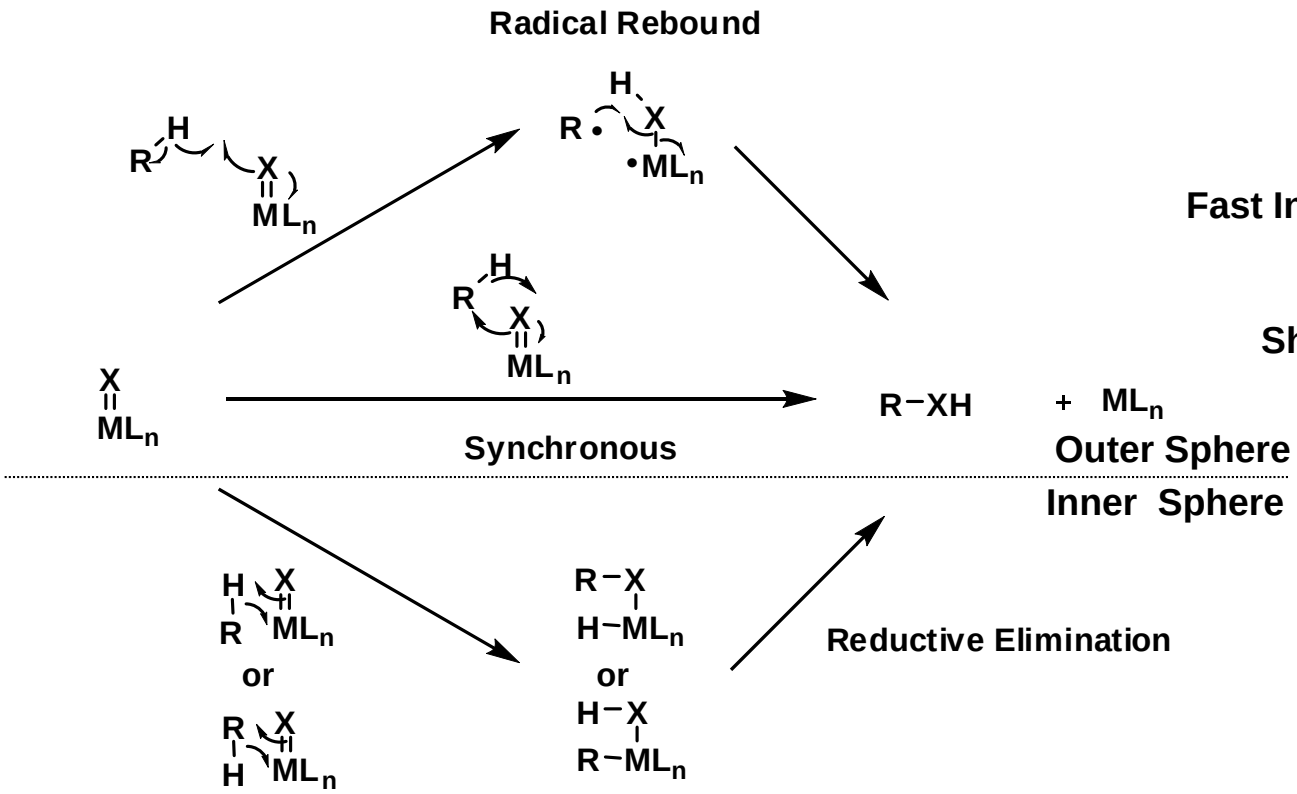



**Best Nitrogen Sources**




(1) Li, G. G.; Chang, H. T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996,** *35,* 451-454. (2) Bodkin, J. A.; McLeod, M. D. *J. Chem. Soc. Perkin Trans. 1* **2002,** 2733-2746.

# 2.4.5 C-H/X-H Functionalization: Introduction




CH Functionalization

Fast Introduction of Functional Groups

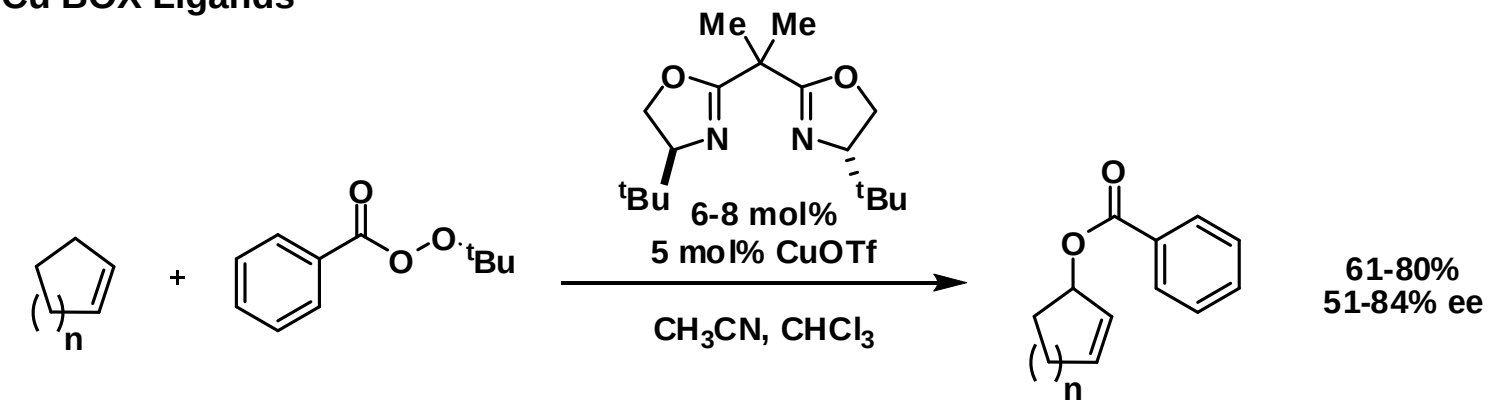
Short and Efficient Synthesis

Less Waste

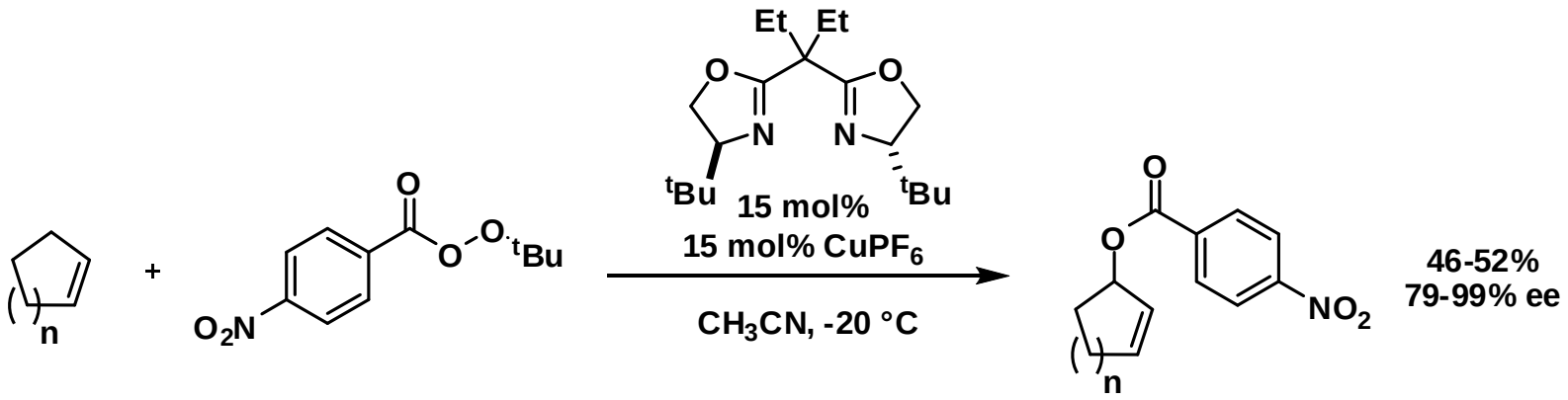
# 2.4.4 C-H Functionalization: Oxygen Transfer

**Karasch-Sosnovsky Allylic Oxidation**

**Pfaltz: Cu BOX Ligands[1]**



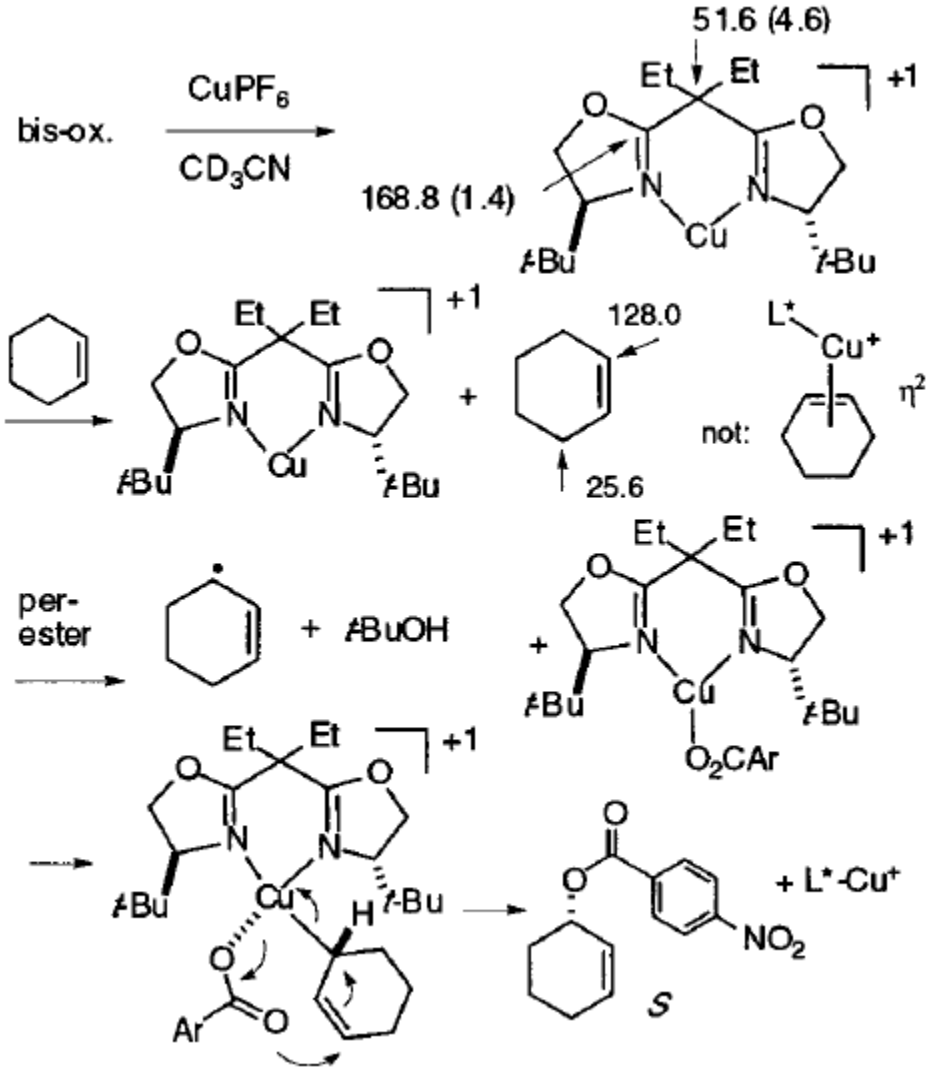

**Andrus: Minor Improvements[2]**




(1) Gokhale, A. S.; Minidis, A. B. E.; Pfaltz, A. *Tetrahedron Lett.* **1995,** *36,* 1831-1834. (2) Andrus, M. B.; Zhou, Z. N. *J. Am. Chem. Soc.* **2002,** *124,* 8806-8807.

# 2.4.4 C-H Functionalization: Oxygen Transfer

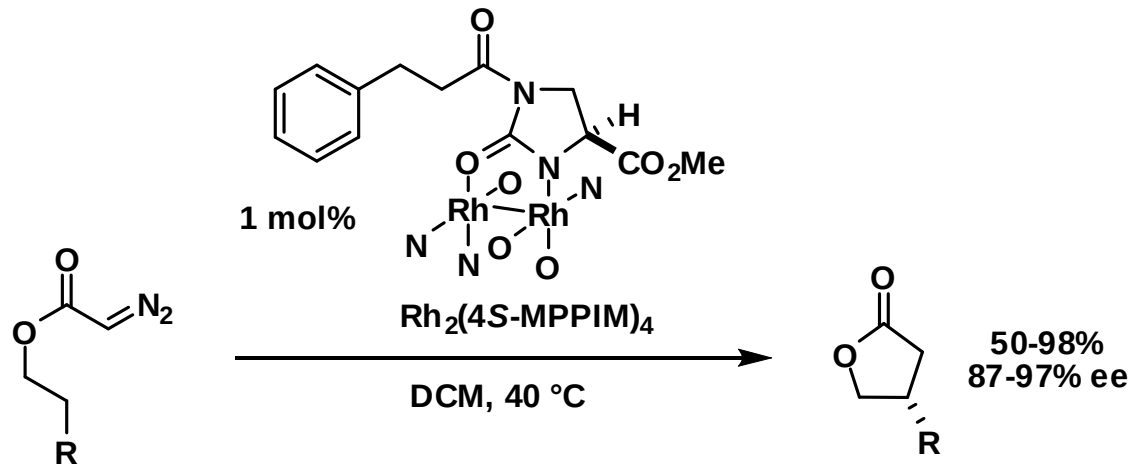
**Proposed Mechanism**



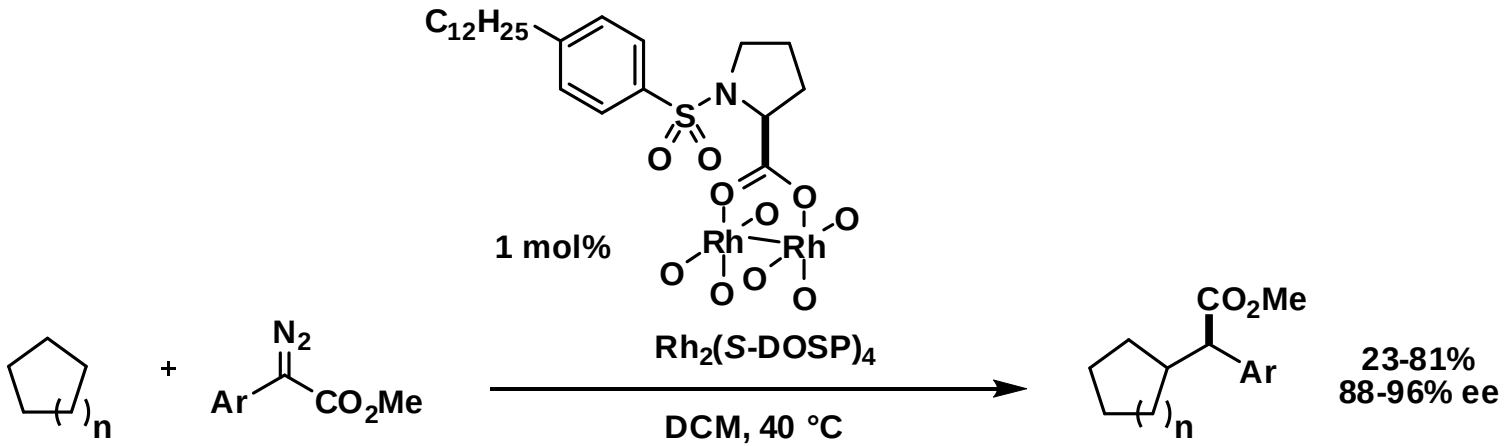

(1) Gokhale, A. S.; Minidis, A. B. E.; Pfaltz, A. *Tetrahedron Lett.* **1995,** *36,* 1831-1834. (2) Andrus, M. B.; Zhou, Z. N. *J. Am. Chem. Soc.* **2002,** *124,* 8806-8807.

# 2.4.4 C-H Functionalization: Carbenes

**Doyle: Intramolecular C-H Insertion[1]**



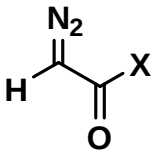

**Davies: Intermolecular C-H Insertion[2]**



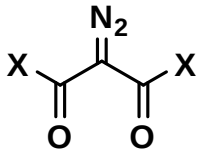

(1) Doyle, M. P.; Vanoeveren, A.; Westrum, L. J.; Protopopova, M. N.; Clayton, T. W. *J. Am. Chem. Soc.* **1991,** *113,* 8982-8984. (2) Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev.* **2003,** *103,* 2861-2903. (3) Davies, H. M. L.; Manning, J. R. *Nature* **2008,** *451,* 417-424.

# 2.4.4 C-H Functionalization: Carbenes

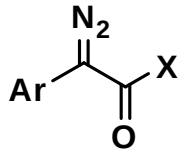
**Different Kinds of Carbenoids**




**Acceptor Carbenoid**
**Fast Dimerization**
**Tendence Towards Cyclopropanation**

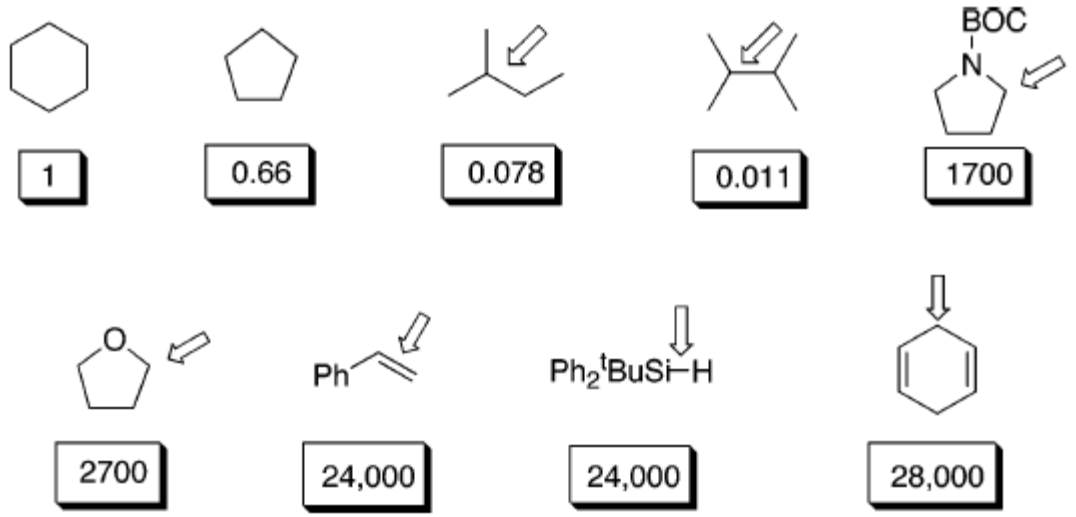



**Acceptor-Acceptor Carbenoid**
**Dimerization**
**Tendence Towards Cyclopropanation**




**Donor-Acceptor Carbenoid**
**Slow Dimerization**
**Tendence Towards Insertion**

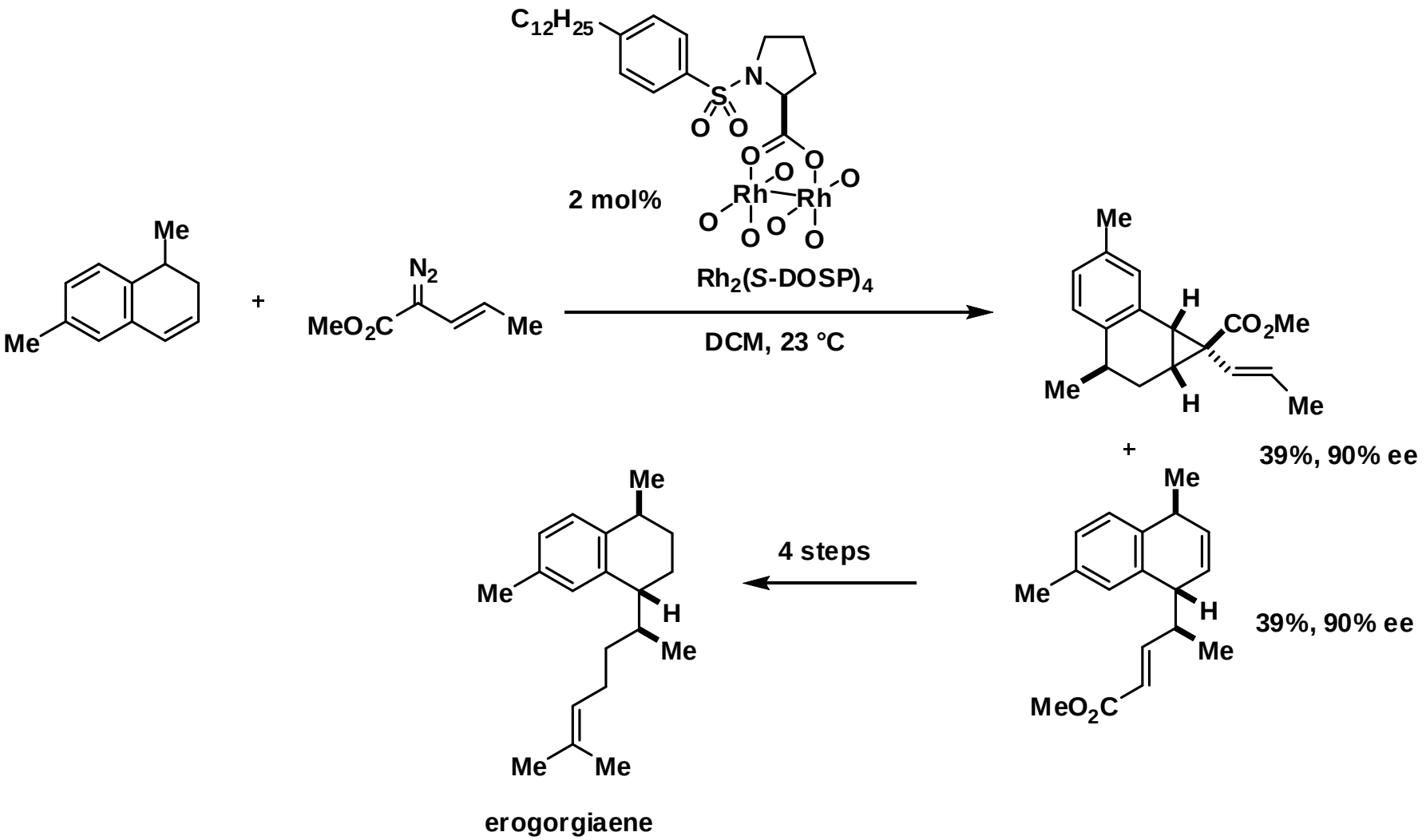
**Compared Reactivity of Substrates with $Rh_2$(*S*-DOSP)$_4$ and Donor-Acceptor Carbenoids**




(1) Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev.* **2003,** *103,* 2861-2903.

# 2.4.4 C-H Functionalization: Carbenes

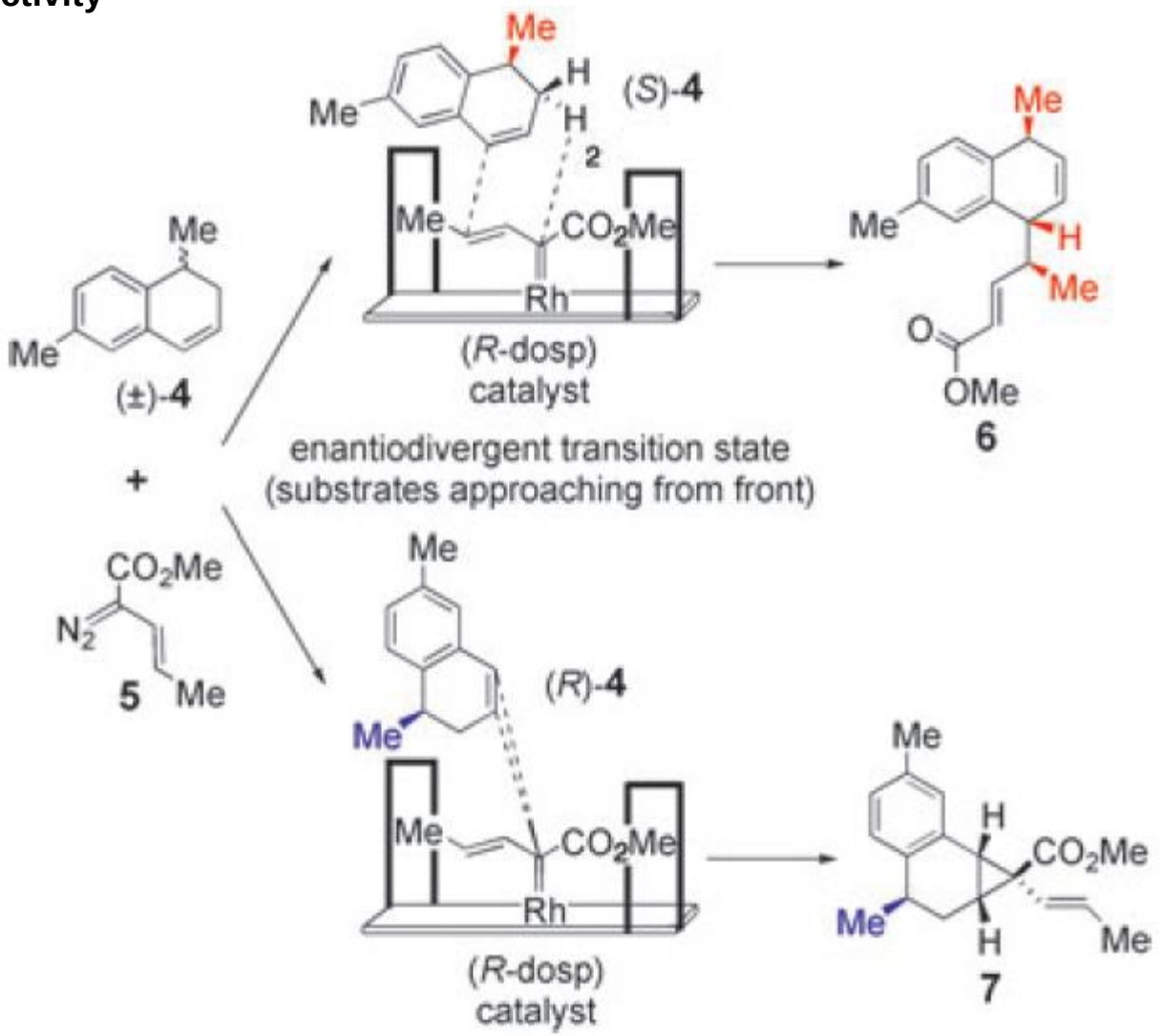
**Davies: Asymmetric Synthesis of Erogorgiaene**




(1) Davies, H. M. L.; Walji, A. M. *Angew. Chem., Int. Ed.* **2005,** *44,* 1733-1735.

# 2.4.4 C-H Functionalization: Carbenes

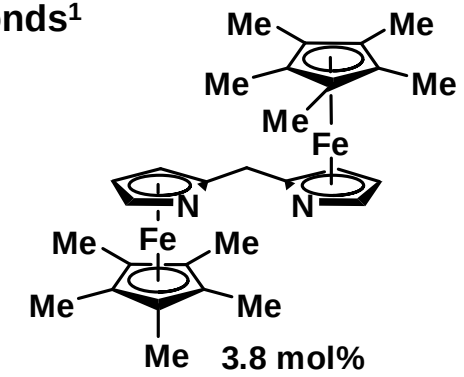
**Model for Selectivity**



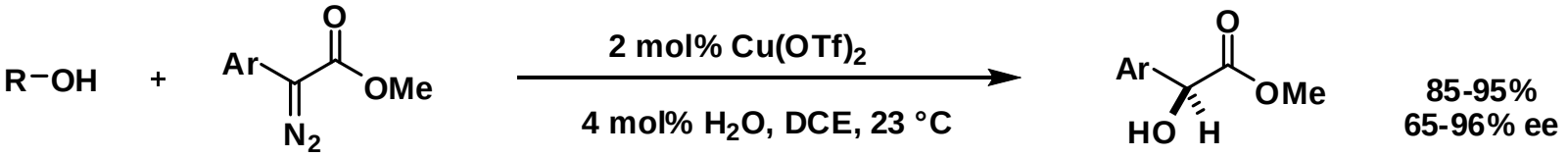

(1) Davies, H. M. L.; Walji, A. M. *Angew. Chem., Int. Ed.* **2005,** *44,* 1733-1735.

# 2.4.4 X-H Functionalization: Carbenes

**Fu: Cu-Catalyzed Insertion into OH Bonds[1]**

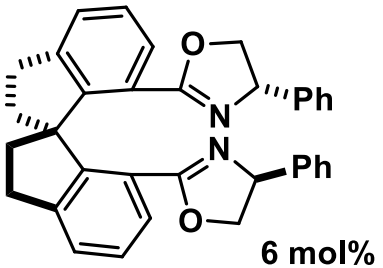



3.8 mol%

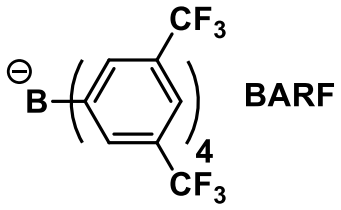


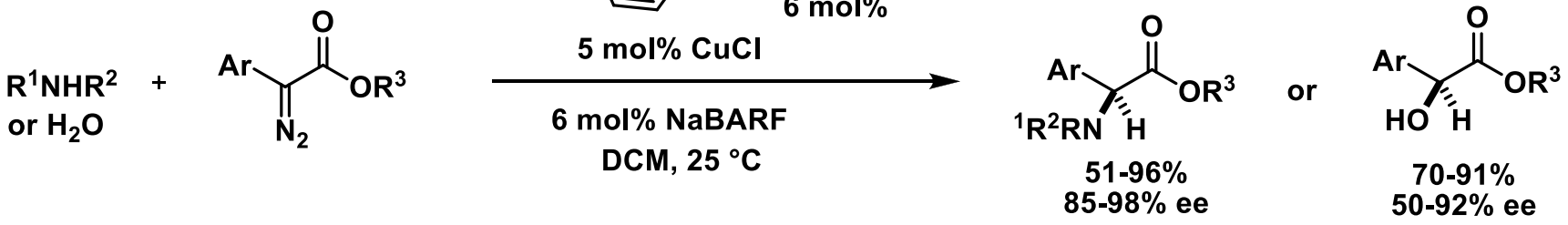

85-95%
65-96% ee

**Zhou: Cu-Catalyzed Insertion into NH Bonds[2] or water[3]**




6 mol%



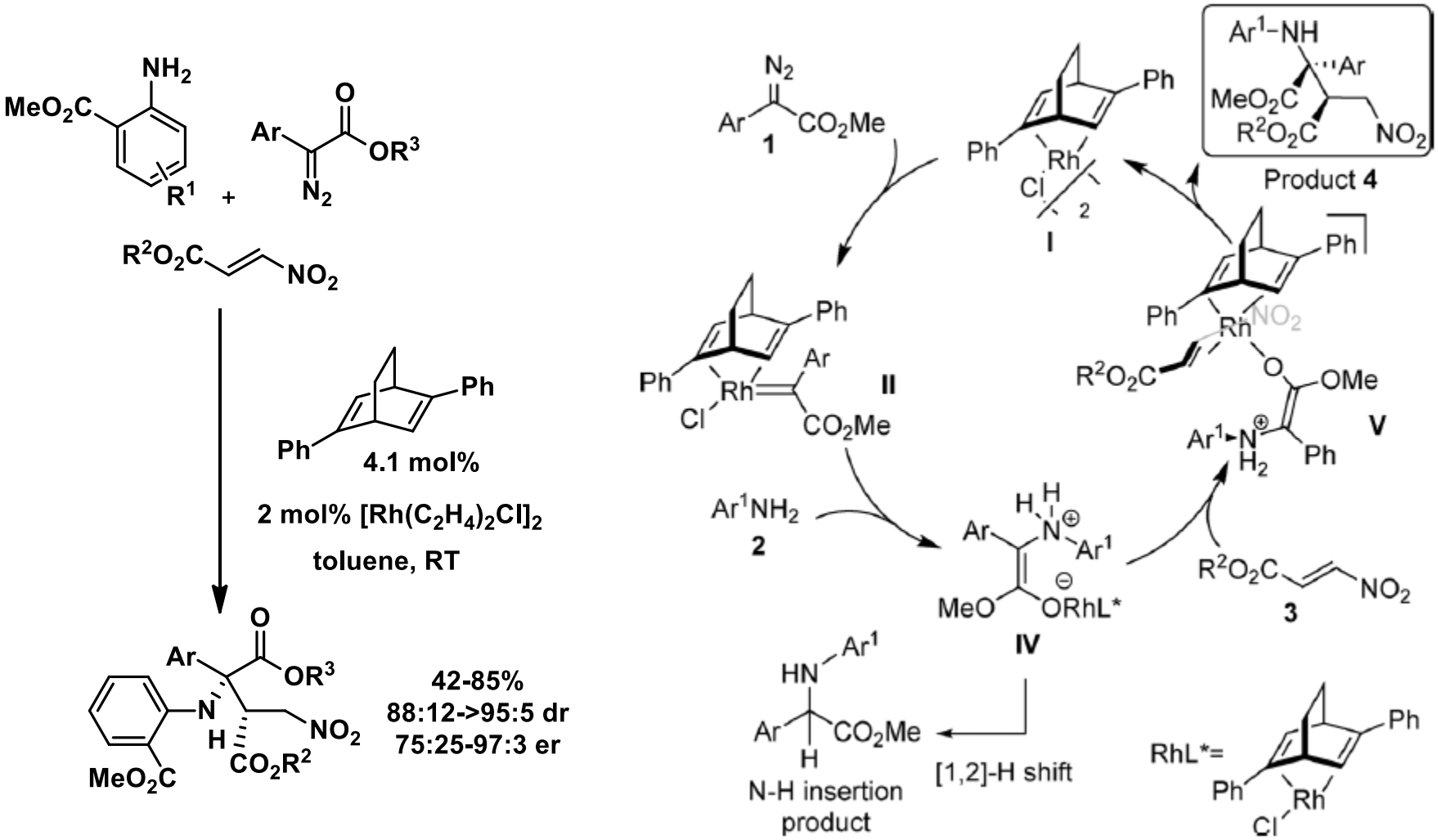

51-96%
85-98% ee

70-91%
50-92% ee

(1) Maier, T. C.; Fu, G. C. *J. Am. Chem. Soc.* **2006,** *128,* 4594. (2) Liu, B.; Zhu, S. F.; Zhang, W.; Chen, C.; Zhou, Q. L. *J. Am. Chem. Soc.* **2007,** *129,* 5834. (3) Zhu, S. T.; Chen, C.; Cai, Y.; Zhou, Q. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 932.

# 2.4.4 Carbene multi-functionalization

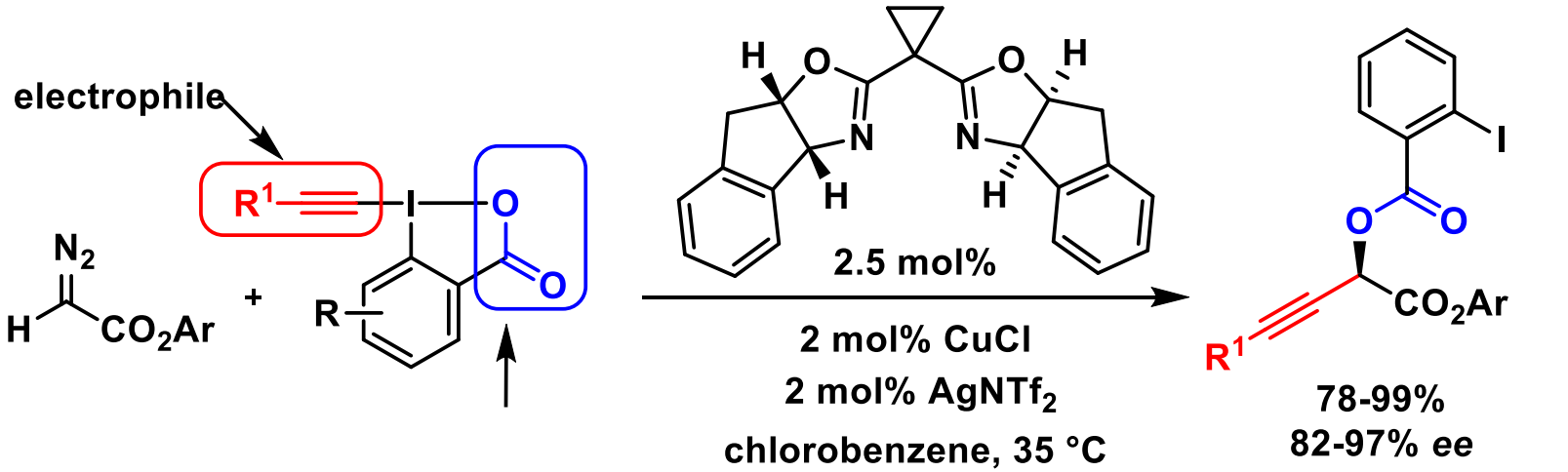
**Hu: Rh-Catalyzed multi-functionalization cascade**

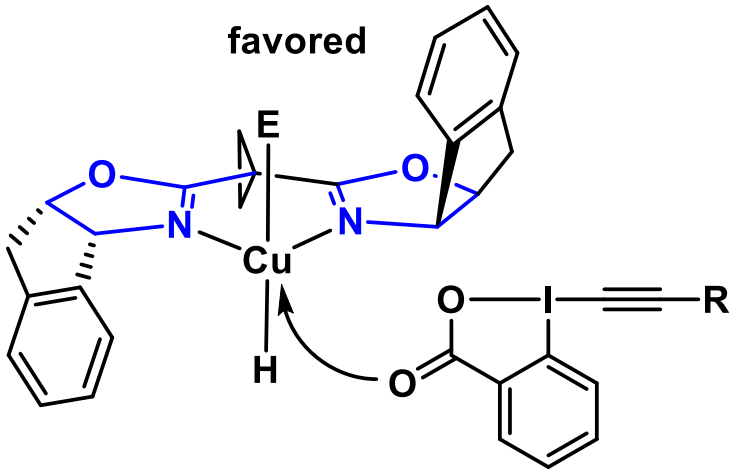


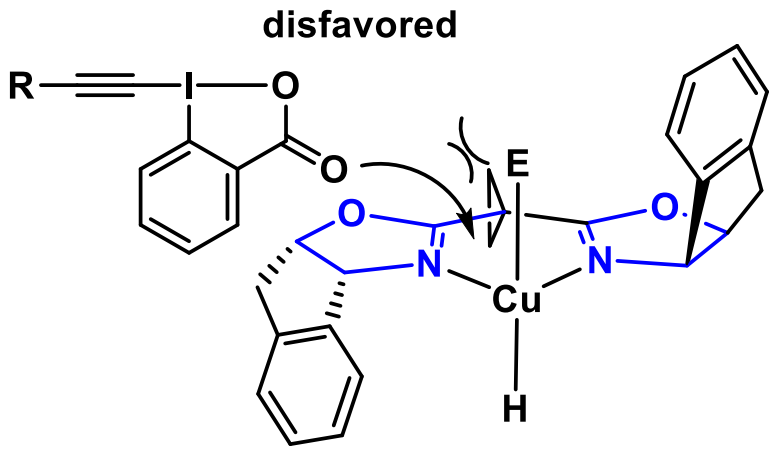

Ma, X.; Jiang, J.; Lv, S.; Yao, W.; Yang, Y.; Liu, S.; Xia, F.; Hu, W. *Angew. Chem. Int. Ed.* **2014**, *53*, 13136.

# 2.4.4 Carbene multi-functionalization

**Waser: Multi-functionalization with EBX (Ethynylbenziodoxolone) hypervalent iodine reagents**



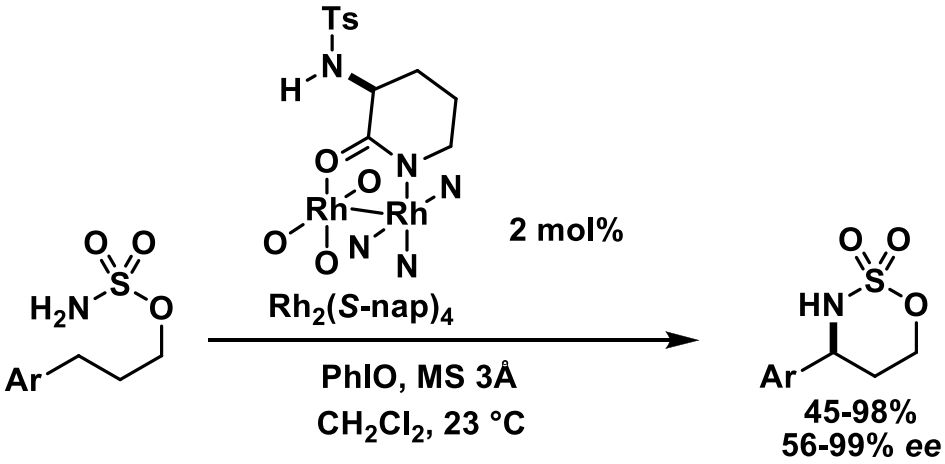



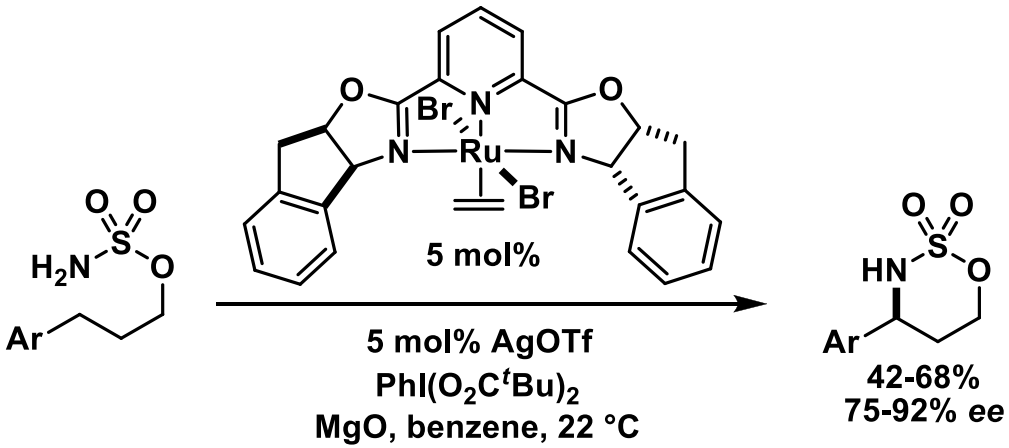

Hari, D. P.; Waser, J. *J. Am. Chem. Soc.* **2017**, *139*, 8420-8423.

# 2.4.4 C-H Functionalization: Nitrenes

**Du Bois: Rh-catalyzed nitrene insertion with hypervalent iodine[1]**



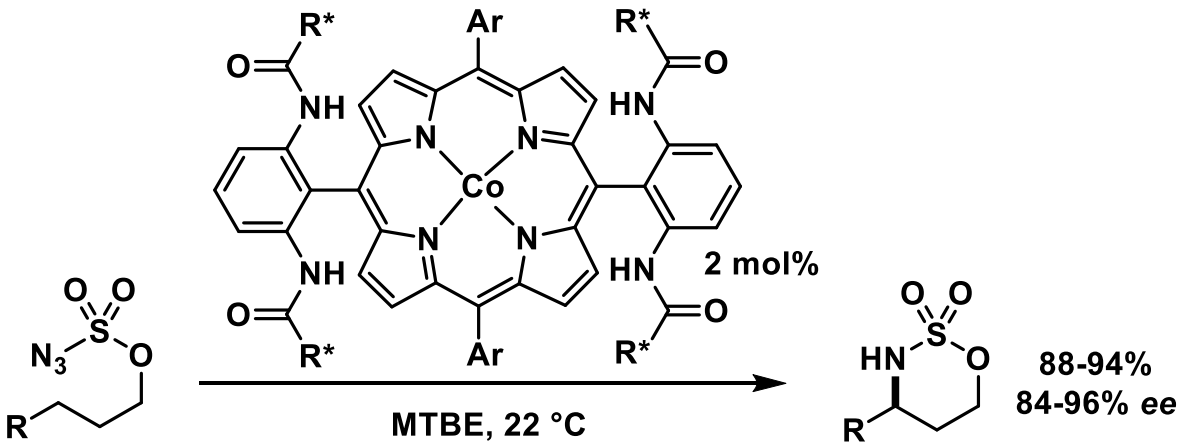

**Blakey: Ru-catalyzed nitrene insertion with hypervalent iodine[2]**

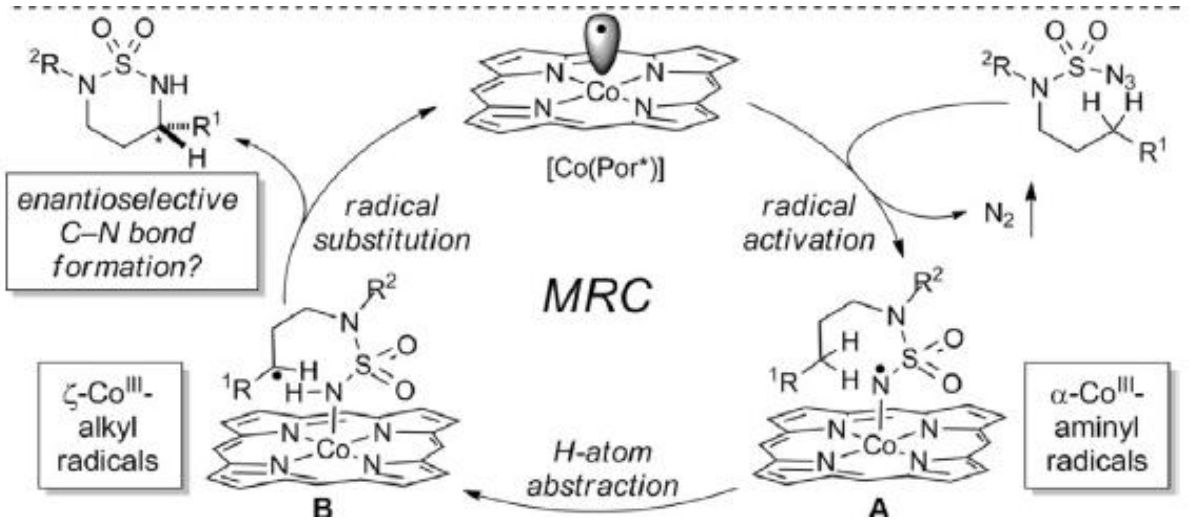



(1) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2008**, *130*, 9220. (2) Milczek, E.; Boudet, N.; Blakey, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 6825.

# 2.4.4 C-H Functionalization: Nitrenes

**Zhang: Co-catalyzed nitrene insertion via radicals[1]**

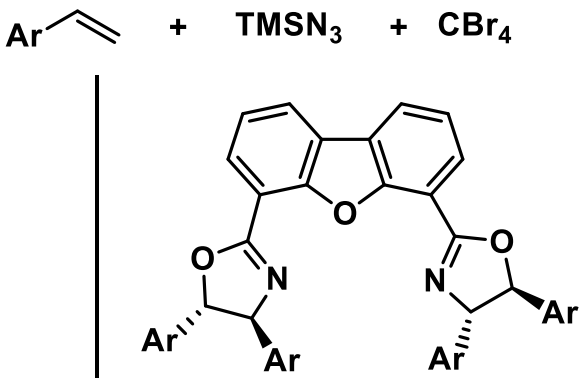


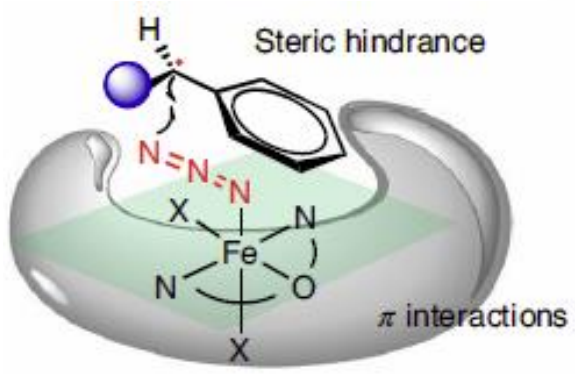



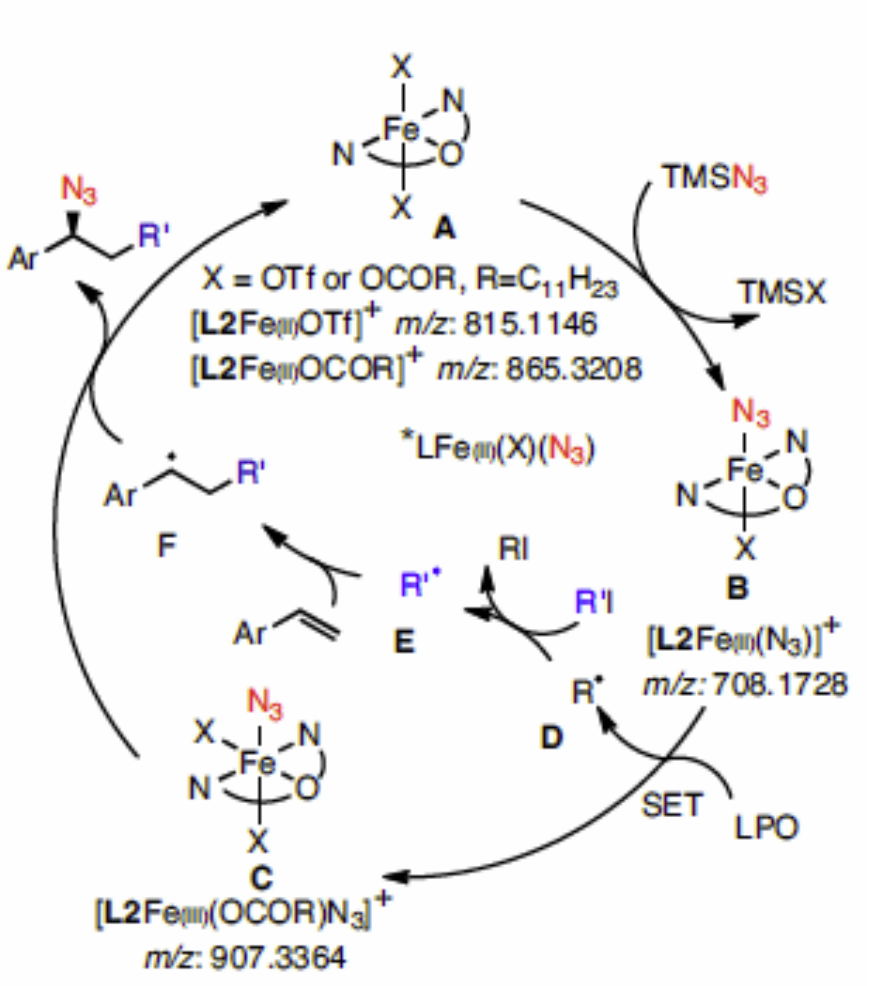

(1) Li, C. Q.; Lang, K.; Lu, H. J.; Hu, Y.; Cui, X.; Wojtas, L.; Zhang, X. P., Angew. Chem., Int. Ed. **2018**, *57*, 16837-16841.

# 2.4.5 Other Reactions: Azidation of Radicals

**Bao: Iron-catalyzed carboazidation[1]**



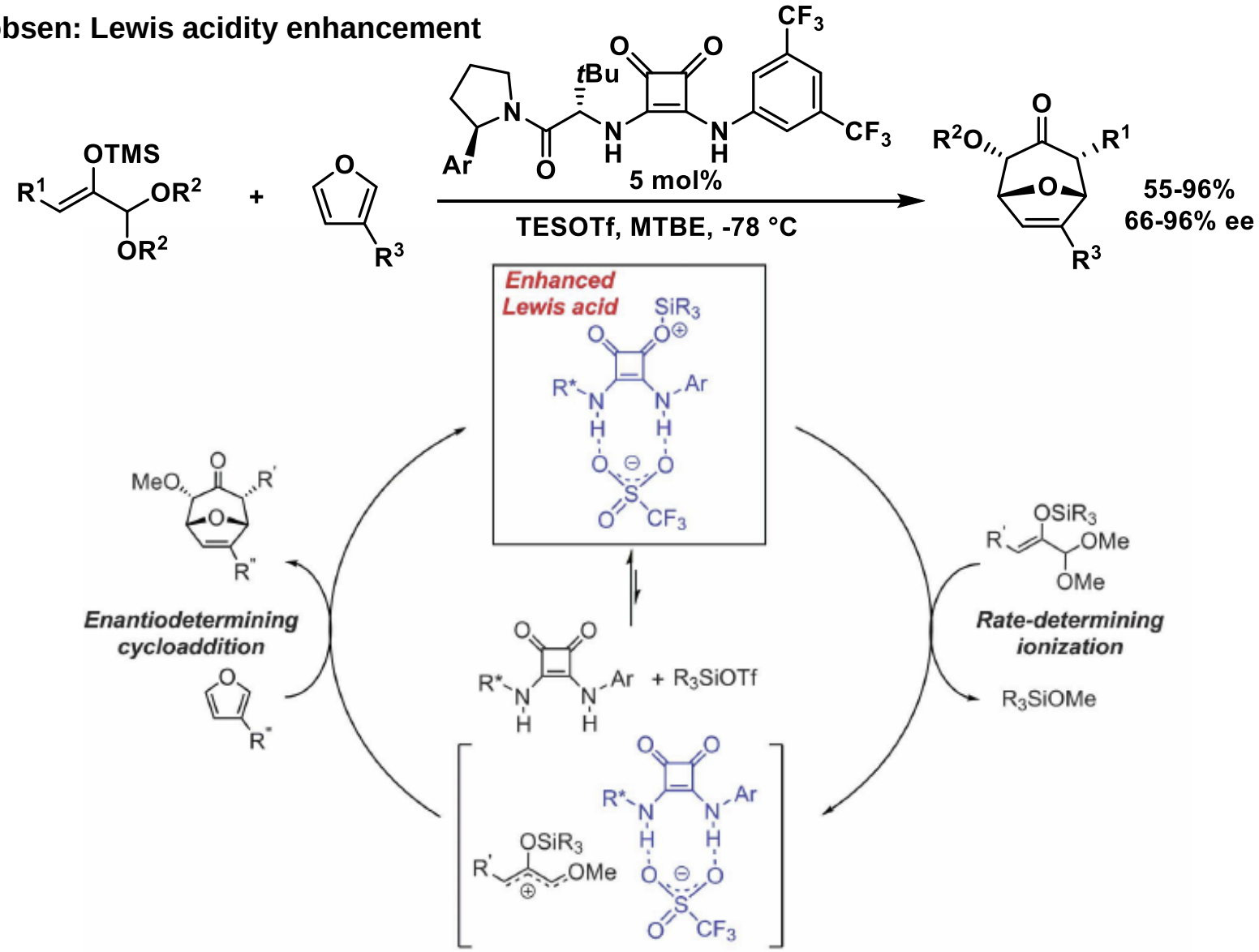




**Also possible starting from benzylic C-H bonds[2]**


(1) Ge, L.; Zhou, H.; Chiou, M.-F.; Jiang, H.; Jian, W.; Ye, C.; Li, X.; Zhu, X.; Xiong, H.; Li, Y.; Song, L.; Zhang, X.; Bao, H. *Nat. Catal.* **2021**, *4*, 28. (2) Cao, M.; Wang, H.; Ma, Y.; Tung, C.-H.; Liu, L. *J. Am. Chem. Soc.* **2022,** *144*, 15383-15390.

# 2.4.5 Other Reactions: Reaction of Oxy-Allyl Cation

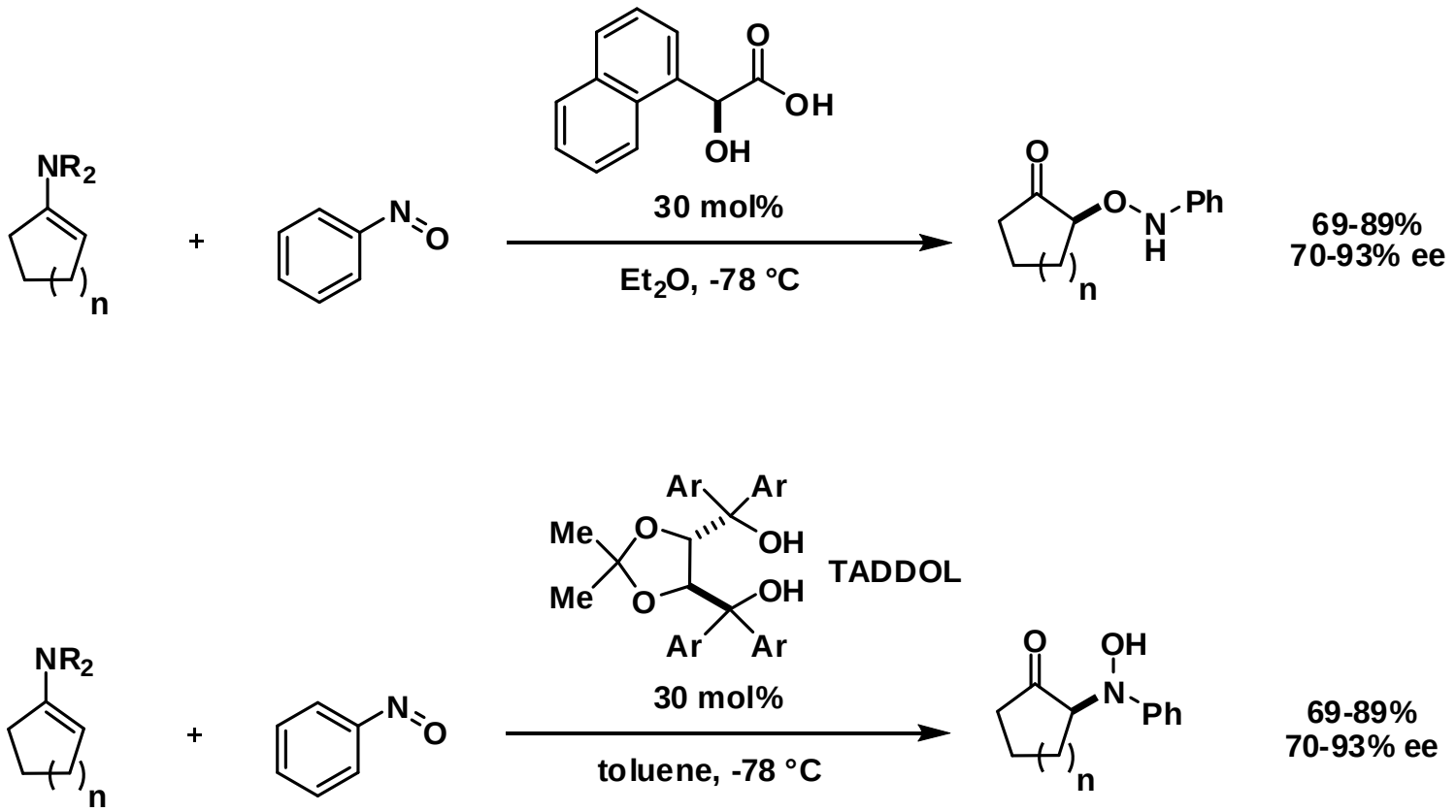
**Jacobsen: Lewis acidity enhancement**




Banik, S. M.; Levina, A.; Hyde, A. M.; Jacobsen, E. N. *Science* **2017,** *358*, 761-764.

# 2.4.5 Other Reactions: Amination of Enolates

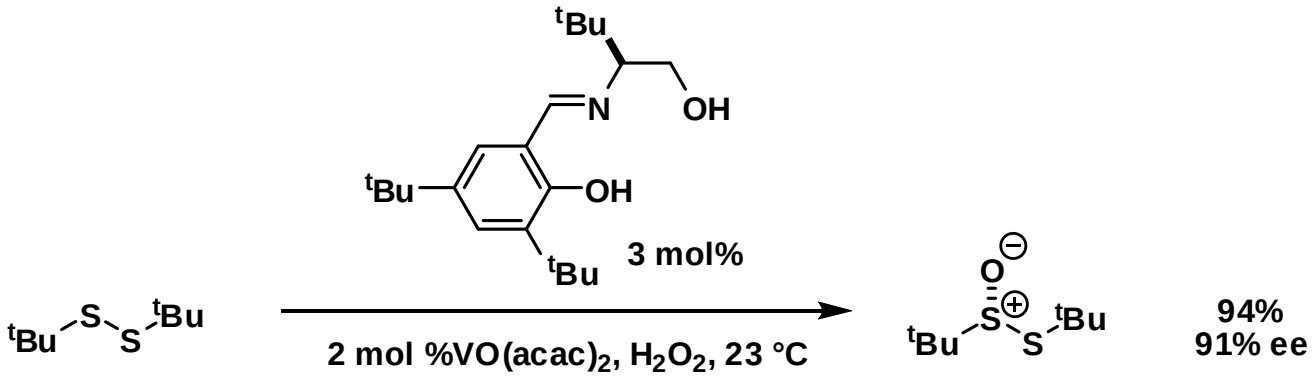
**Yamamoto: Acid-Catalyzed Nitroso-Aldol Reaction with Enamines: Amination or Hydroxylation Depending on Catalyst**



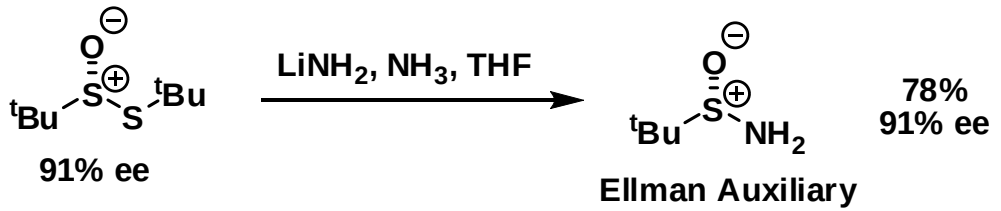

(1) Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2005,** *127,* 1080-1081.

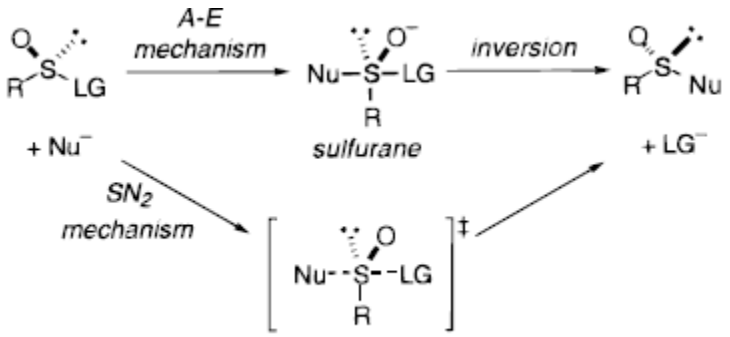
# 2.4.5 Other Reactions: Sulfide Oxidation

**Ellman: Asymmetric Oxidation of Disulfide**




**Synthesis of Ellman's Auxiliary**

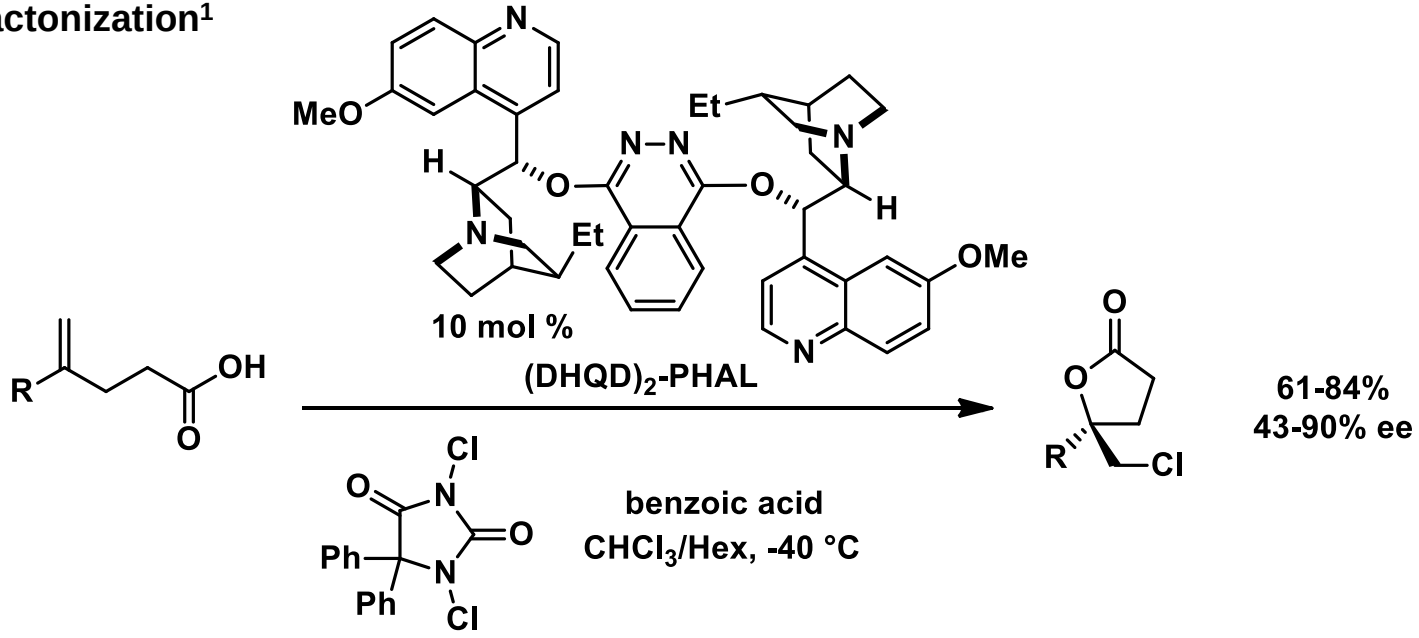


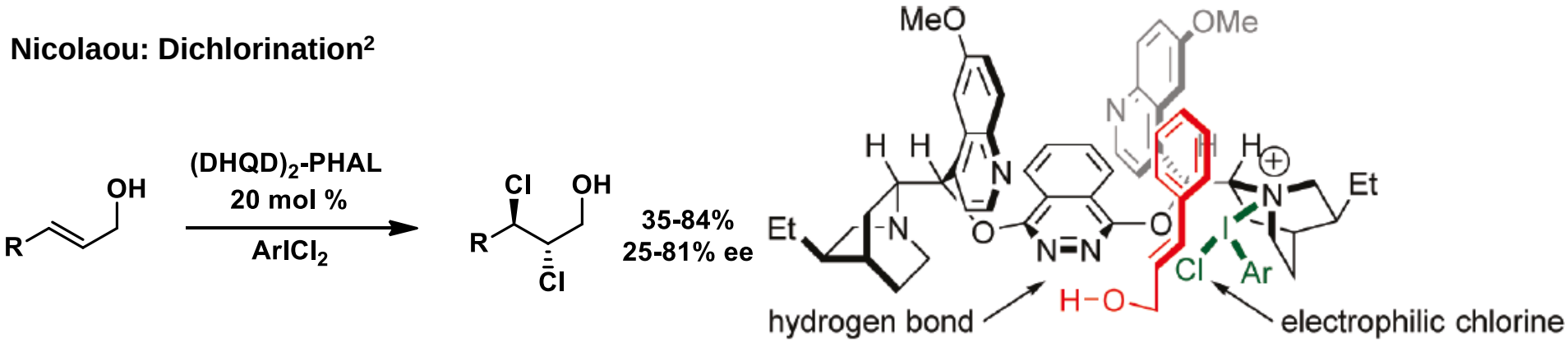

(1) Blum, S. A.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2003,** *68*, 150-155.

# 2.4.5 Other Reactions: Asymmetric Chlorination

**Bohran: Chlorolactonization[1]**



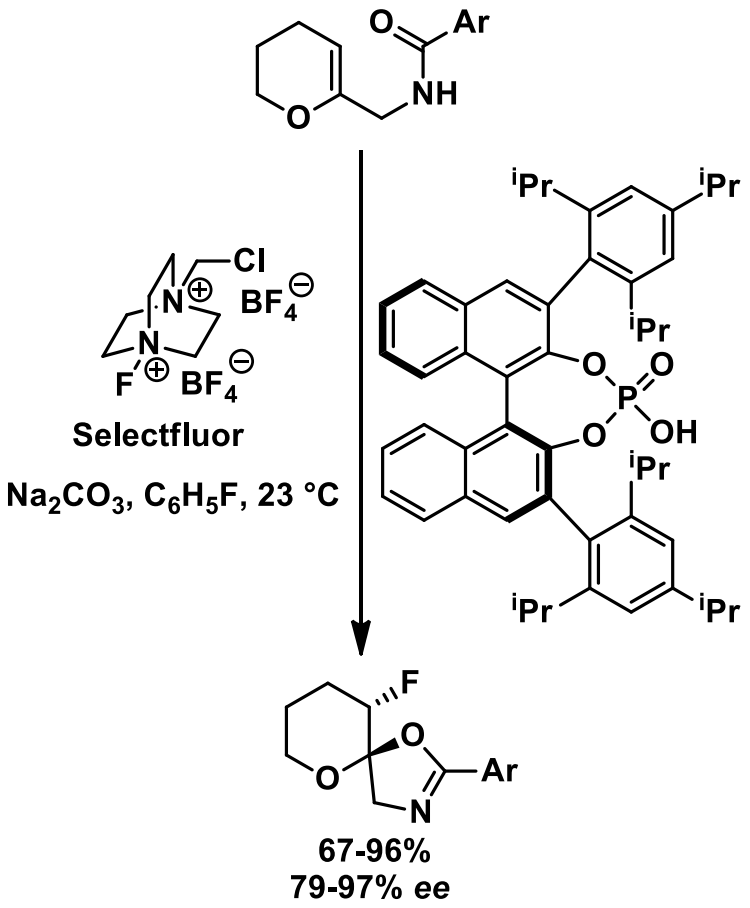

**Nicolaou: Dichlorination[2]**

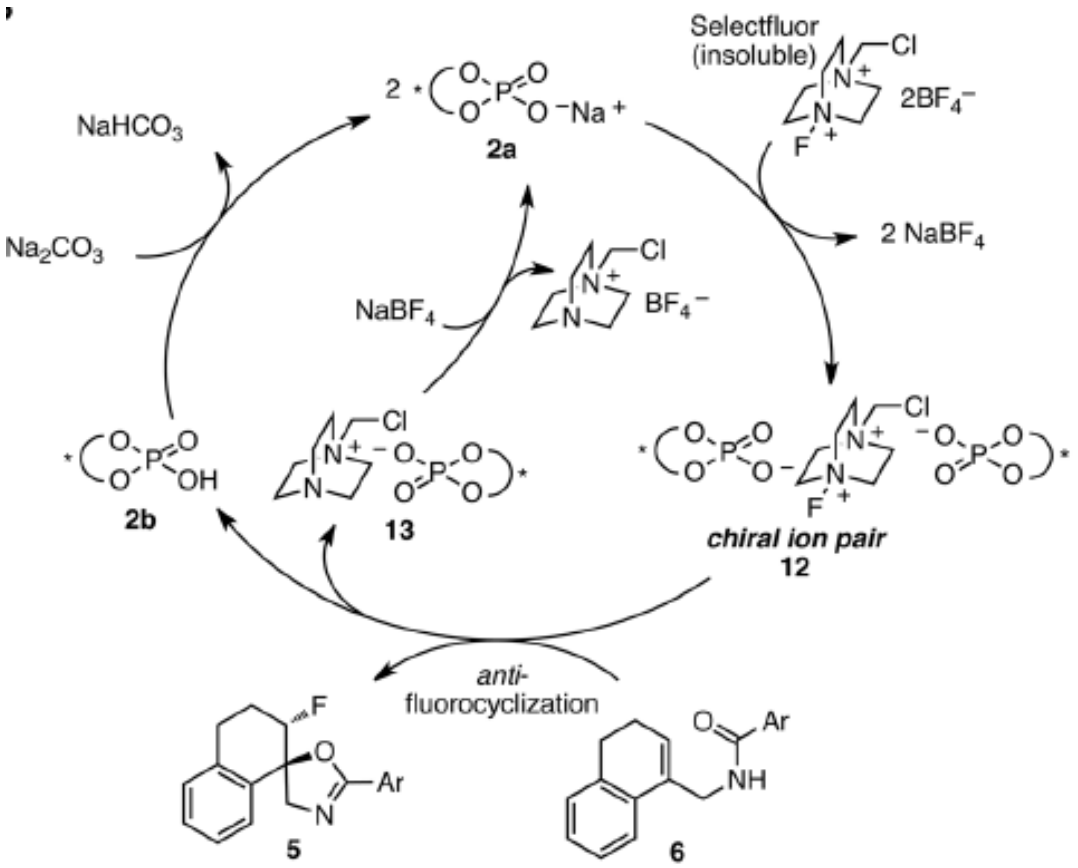



(1) Whitehead, D. C.; Yousefi, R.; Jaganathan, A.; Borhan, B., *J. Am. Chem. Soc.* **2010**, *132*, 3298. (2) Nicolaou, K. C.; Simmons, N. L.; Ying, Y. C.; Heretsch, P. M.; Chen, J. S., *J. Am. Chem. Soc.* **2011**, *133*, 8134.

# 2.4.5 Other Reactions: Asymmetric Fluorination

**Toste: Enantioselective oxyfluorination based on phase-transfer of the cation!**

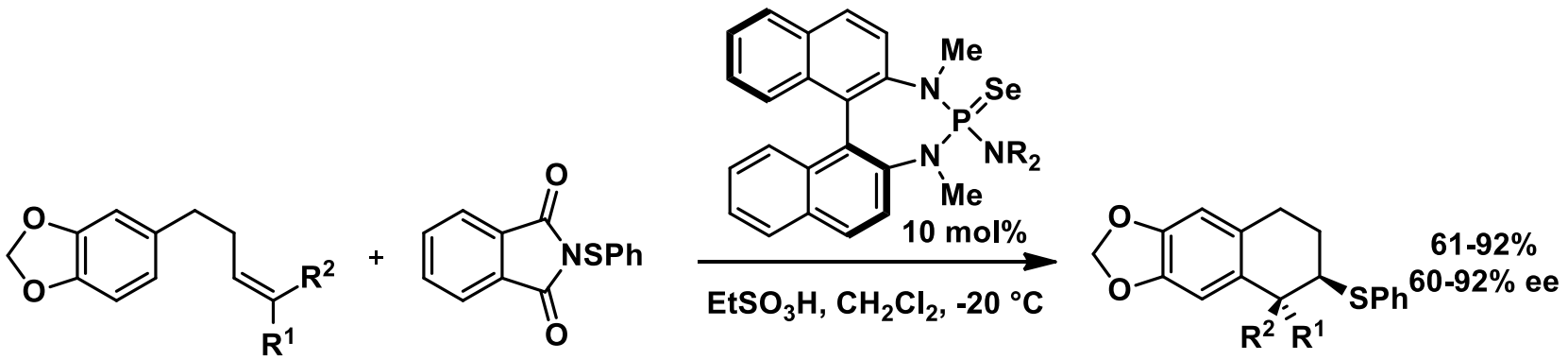


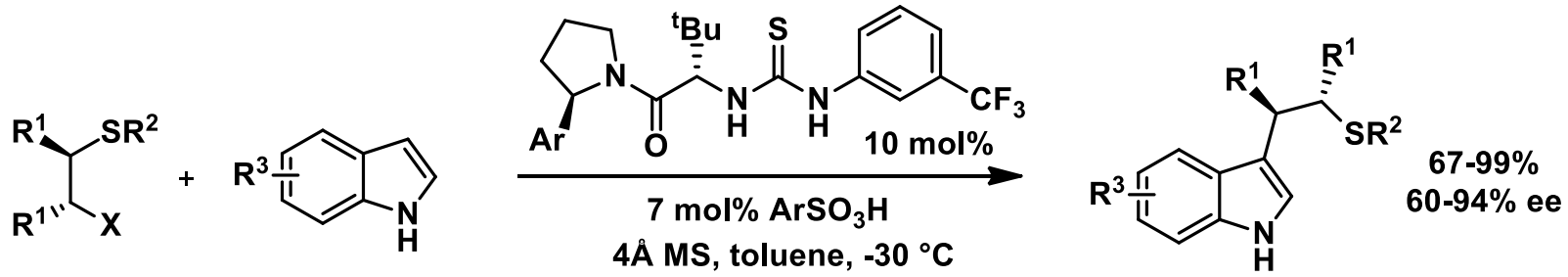

Rauniyar, V.; Lackner, A. D.; Hamilton, G. L.; Toste, F. D. *Science* **2011,** *334*, 1681-1684.

# 2.4.5 Other Reactions: Via Sulfonium

**Denmark: intermolecular sulfonium formation[1]**

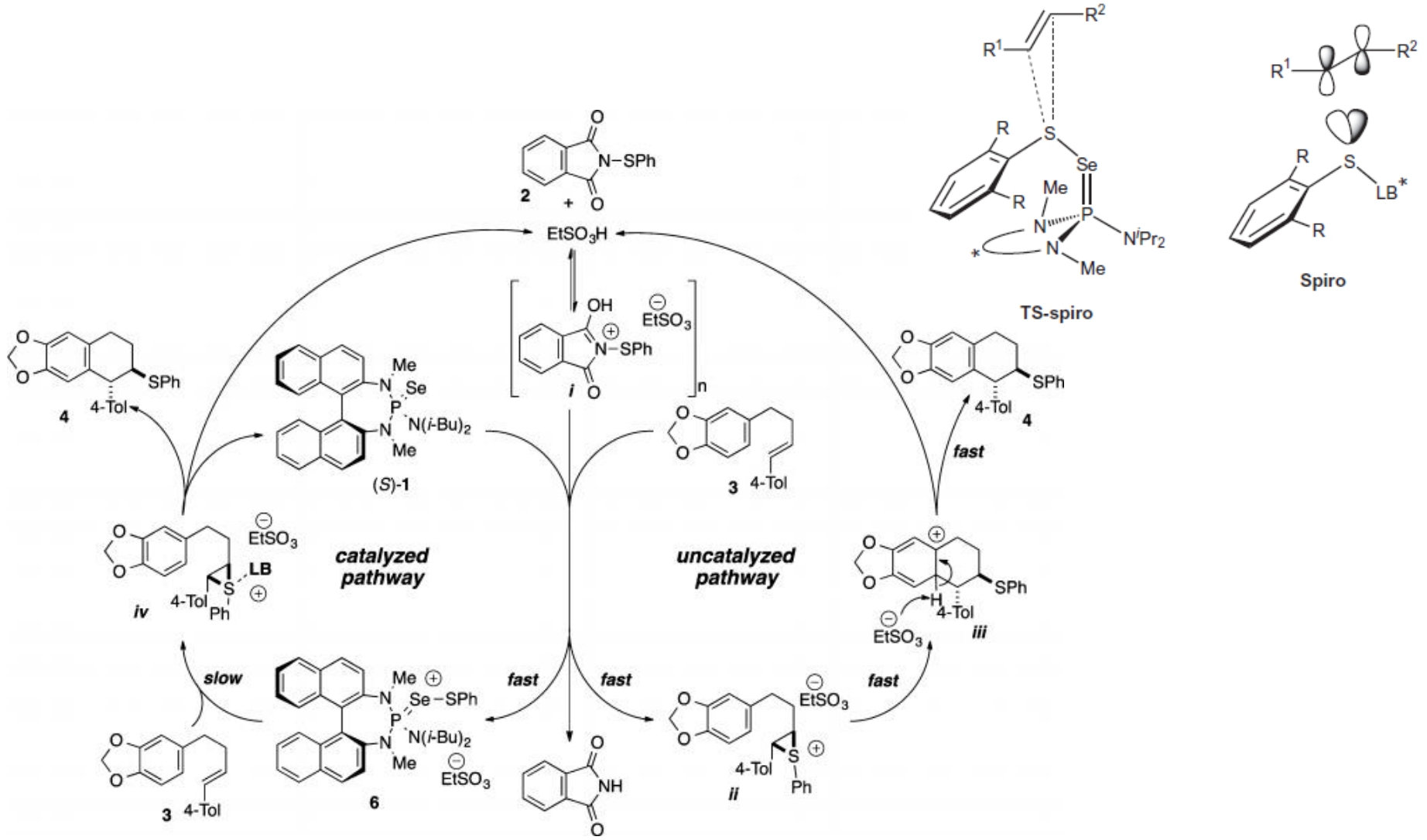



**Jacobsen: intramolecular sulfonium formation[2]**



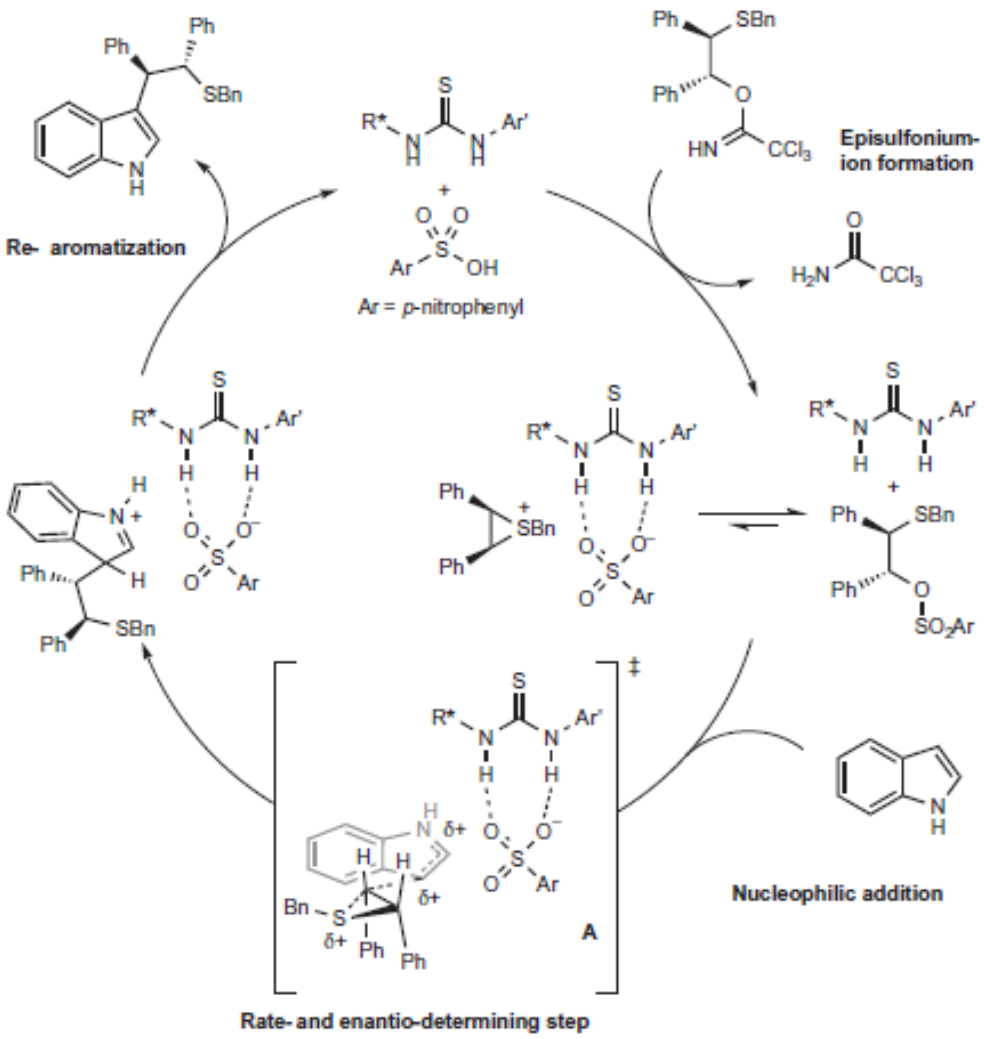

(1) Denmark, S. E.; Jaunet, A. *J. Am. Chem. Soc.* **2013**, *135*, 6419. (2) Lin, S.; Jacobsen, E. N. *Nat. Chem.* **2012**, *4*, 817.

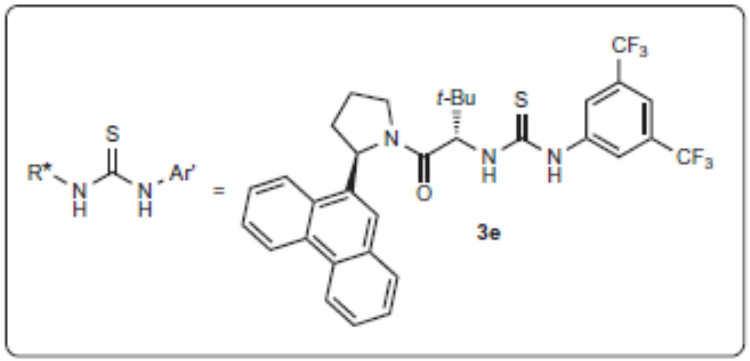
# 2.4.5 Other Reactions: Via Sulfonium




(1) Denmark, S. E.; Chi, H. M. *J. Am. Chem. Soc.* **2014**, *136*, 3655. (2) Denmark, S. E.; Hartmann, E.; Kornfilt, D. J. P.; Wang, H. *Nat. Chem.* **2014**, *6*, 1056.

# 2.4.5 Other Reactions: Via Sulfonium

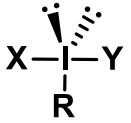



Lin, S.; Jacobsen, E. N. *Nat. Chem.* **2012**, *4*, 817.

# 2.2.4 Other Reactions: Hypervalent Iodine

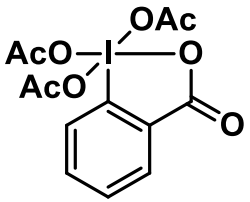
Iodane
Iodine(I)
8 electrons



$\lambda^3$-iodane
Iodine(III)
10 electrons

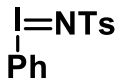
$\lambda^5$-iodane
Iodine(V)
12 electrons

- Hypervalent with involvement of 5p orbitals
- Only partial bond character (4 electrons-3 centres bond)
- Exceptional reactivity



Oxidant

Dess-Martin

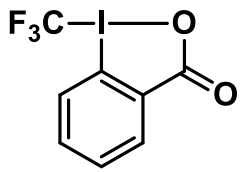


:NTs

Evans

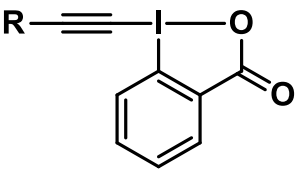
Ph

Gaunt, Sanford



$CF_3$

Togni

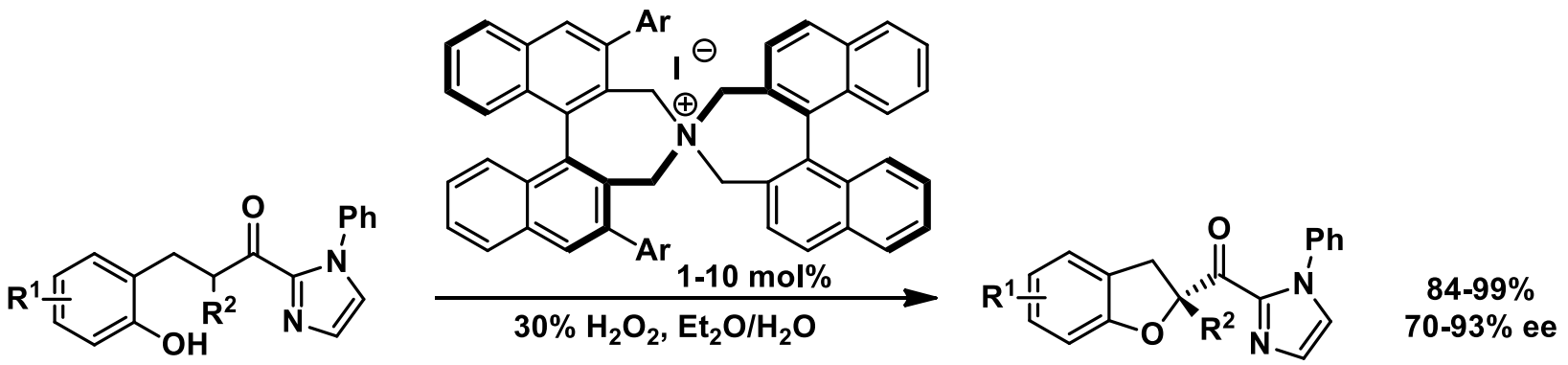


R

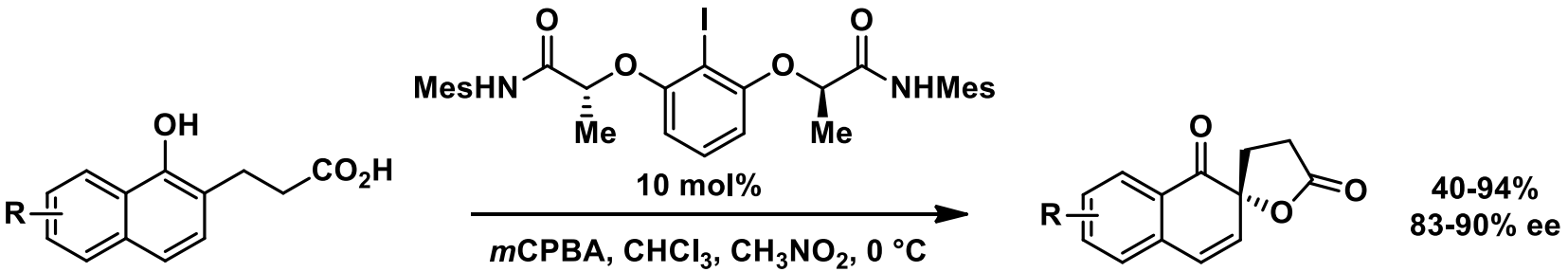
Zhdankin, Waser

# 2.4.5 Other Reactions: Hypervalent Iodine

**Ishihara: Oxidative cyclization with inorganic hypervalent iodine[1-2]**



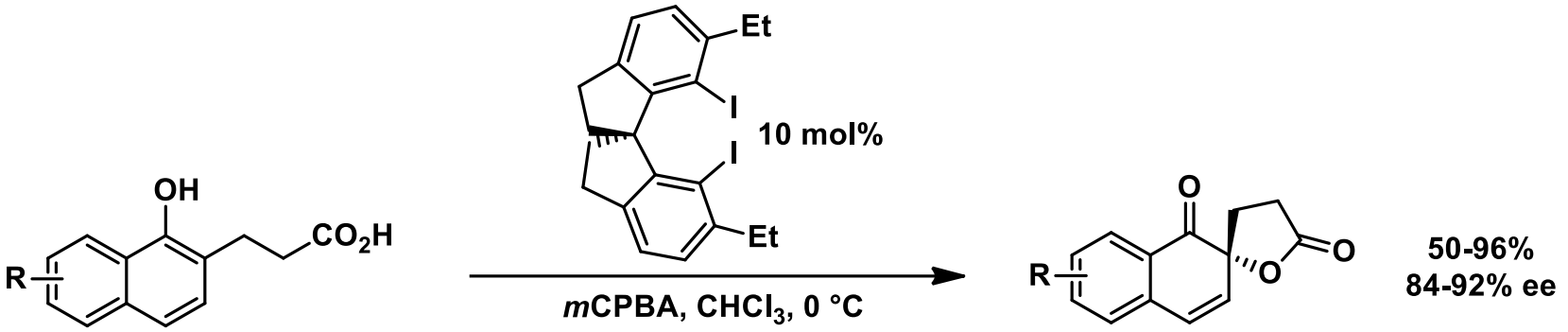

**Ishihara: Oxidative Spirolactonization[3]**

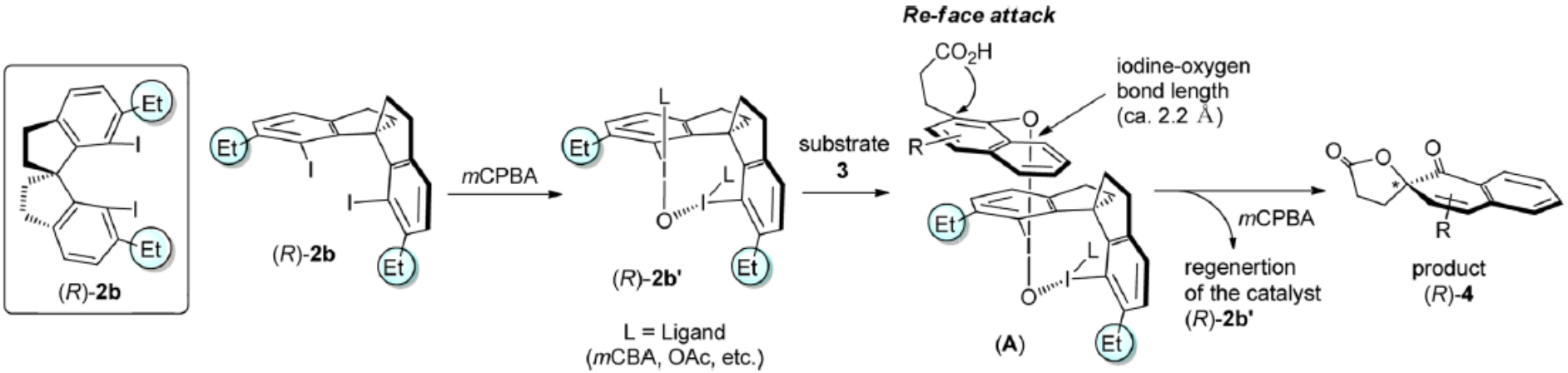



(1) Uyanik, M.; Okamoto, H.; Yasui, T.; Ishihara, K. *Science* **2010**, *328*, 1376. (2) Uyanik, M.; Hayashi, H.; Ishihara, K. *Science* **2014**, *345*, 291. (3) Uyanik, M.; Yasui, T.; Ishihara, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 2175.

# 2.4.5 Other Reactions: Hypervalent Iodine

**Kita: Oxidative Spirolactonization[1]**

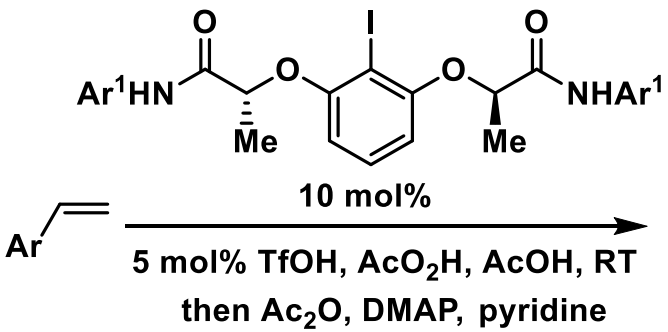


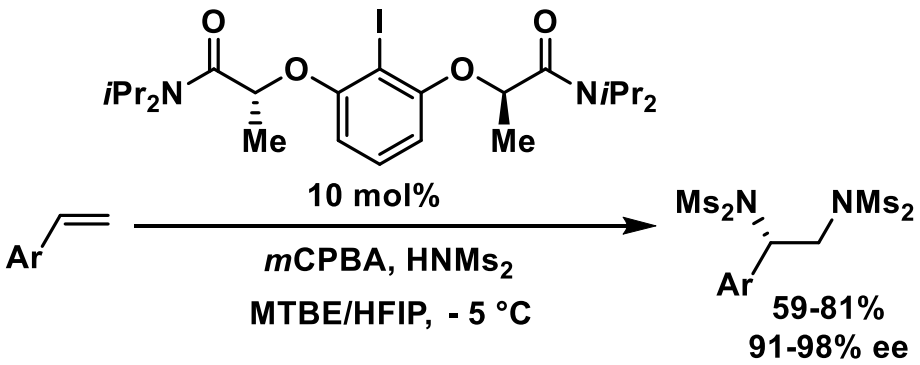

(1) Dohi, T.; Takenaga, N.; Nakae, T.; Toyoda, Y.; Yamasaki, M.; Shiro, M.; Fujioka, H.; Maruyama, A.; Kita, Y. *J. Am. Chem. Soc.* **2013**, *135*, 4558.

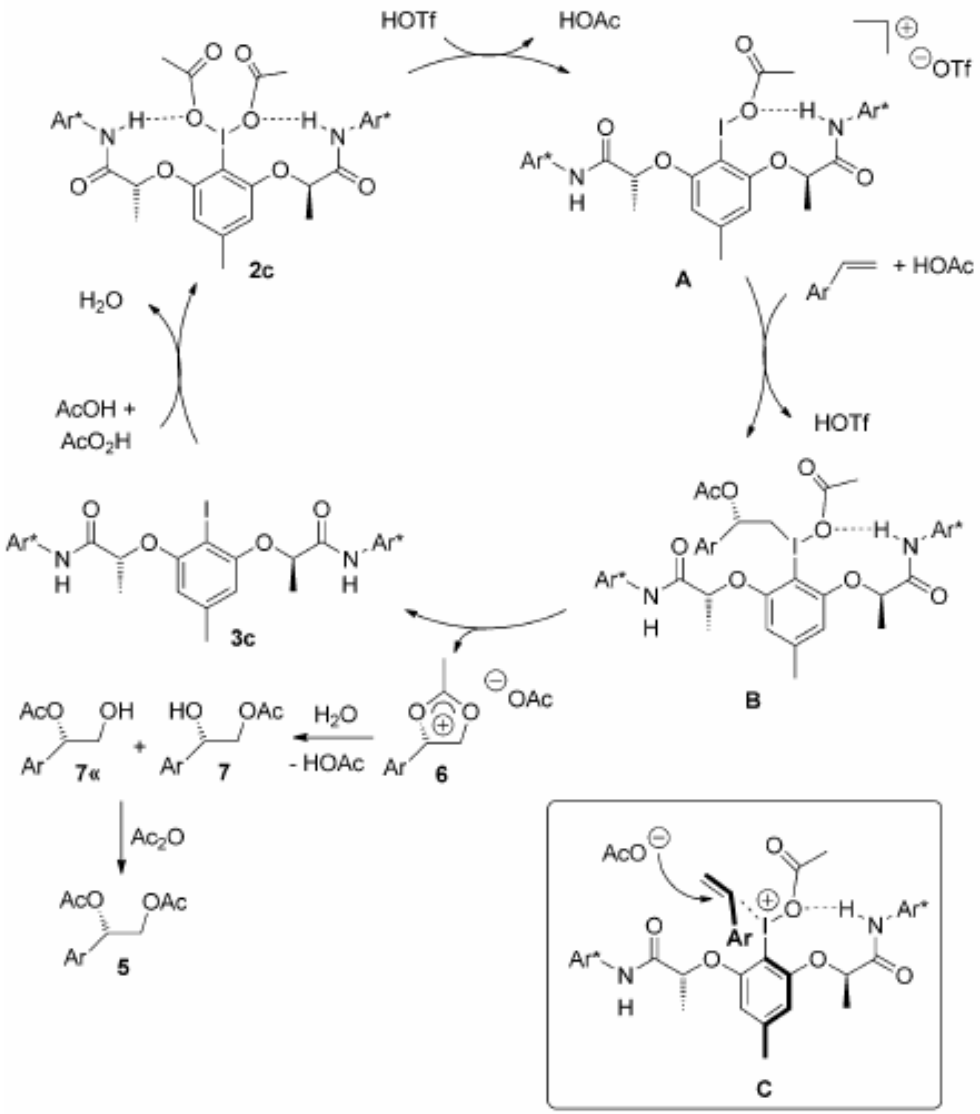
# 2.4.5 Other Reactions: Hypervalent Iodine

**Muniz/Ishihara: Diacetoxylation of olefins[1]**




**Muniz: Diamination[2]**

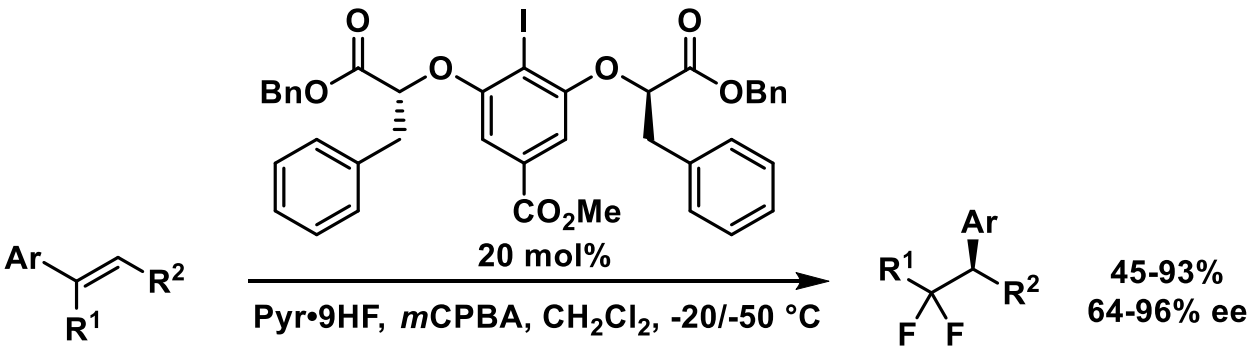


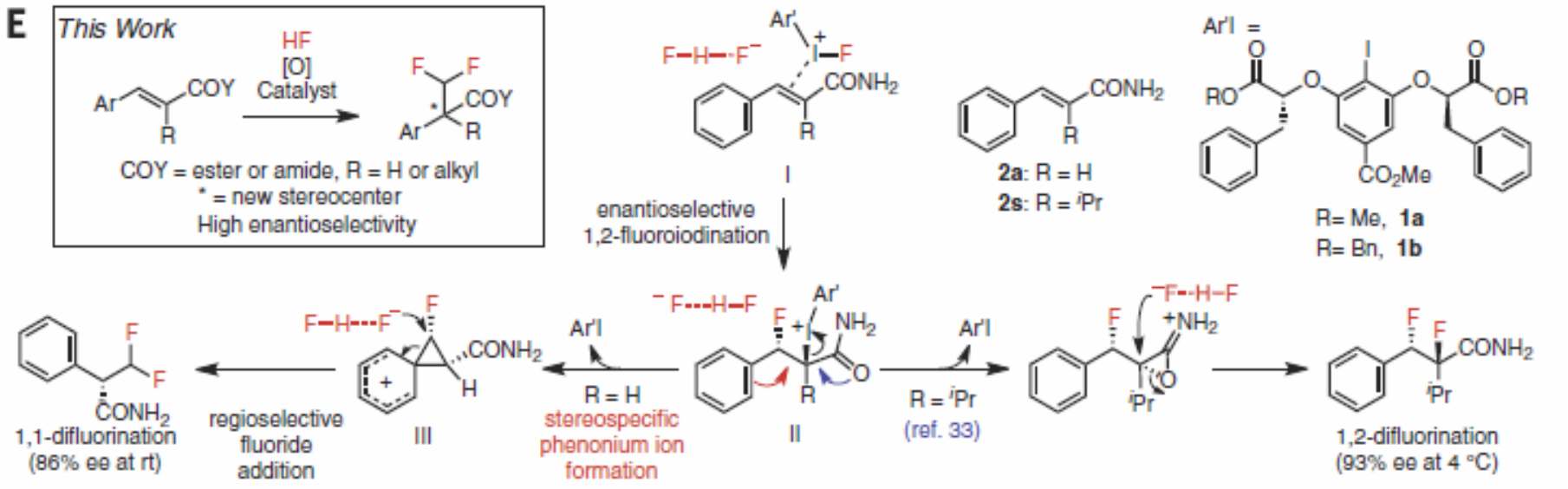




(1) Haubenreisser, S.; Woste, T. H.; Martinez, C.; Ishihara, K.; Muniz, K. *Angew. Chem., Int. Ed.* **2016**, *55*, 413-417. (2) Muniz, K.; Barreiro, L.; Romero, R. M.; Martinez, C. *J. Am. Chem. Soc.* **2017**, *139*, 4354-4357.

# 2.4.5 Other Reactions: Hypervalent Iodine

**Jacobsen/[1,2] Gilmour:[3] enantioselective difluorination.**



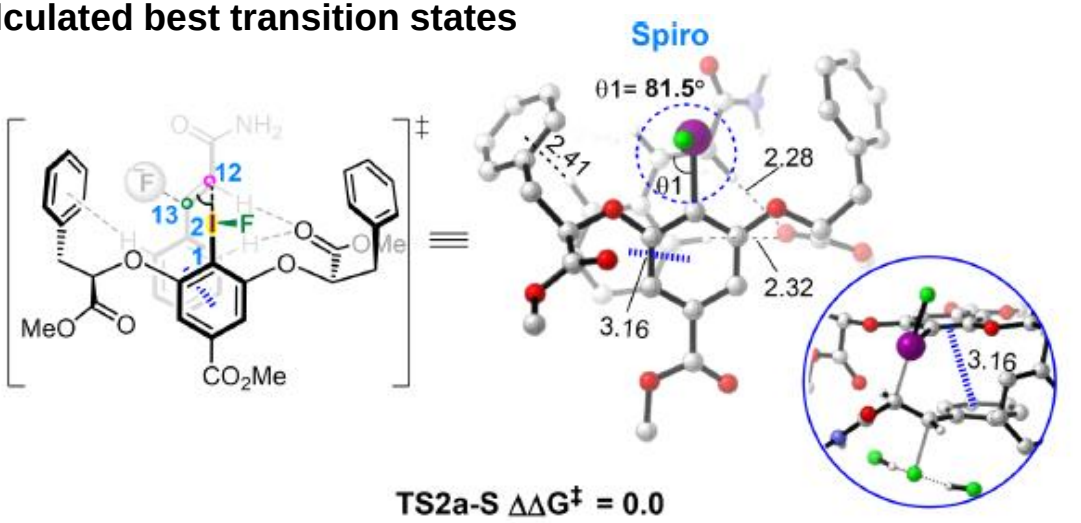





Banik, S. M.; Medley, J. W.; Jacobsen, E. N. *Science* **2016**, *353*, 51-54. (2) Banik, S. M.; Medley, J. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2016**, *138*, 5000-5003. (3) Scheidt, F.; Schafer, M.; Sarie, J. C.; Daniliuc, C. G.; Molloy, J. J.; Gilmour, R. *Angew. Chem.-Int. Edit.* **2018,** *57*, 16431-16435.

# 2.4.5 Other Reactions: Hypervalent Iodine

**Jacobsen/Houk: Calculated best transition states**




Jacobsen, E. N.; Houk, K. N.; Xue, X. S., *J. Am. Chem. Soc.* **2018**, *140*, 15206-15218.