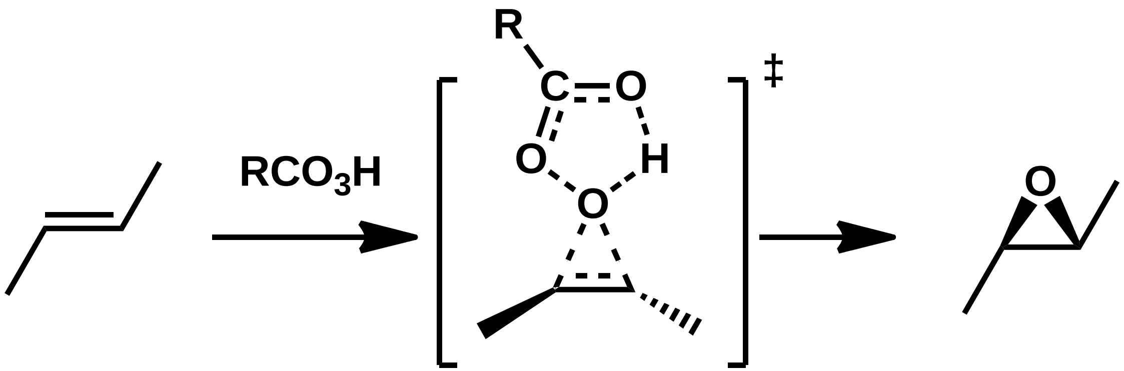
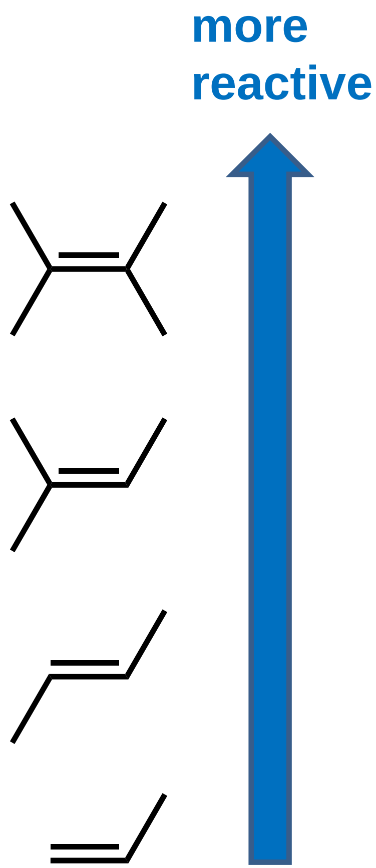
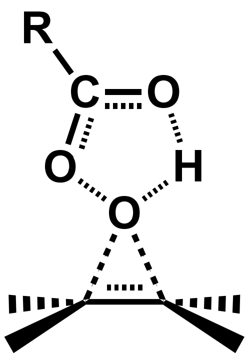
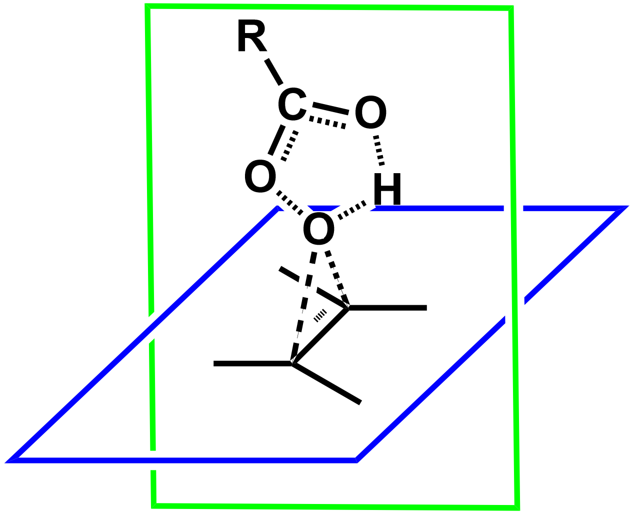
Epoxidation with Peroxy Acids







butterfly TS

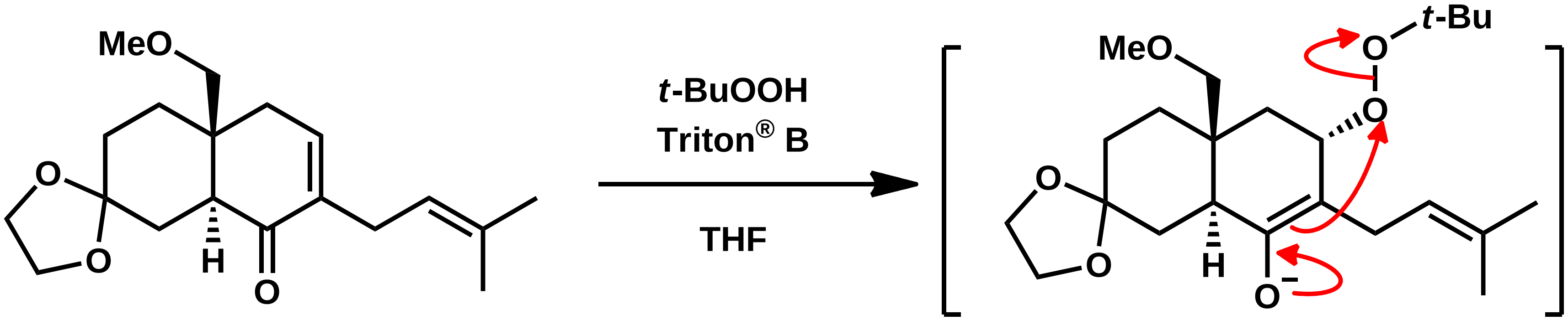


spiro-butterfly TS

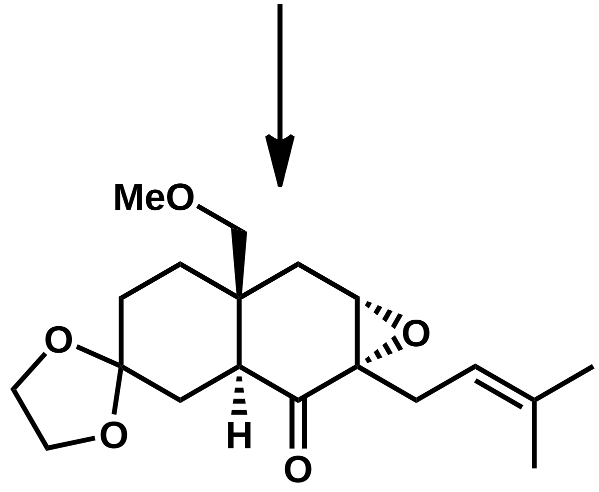
more likely

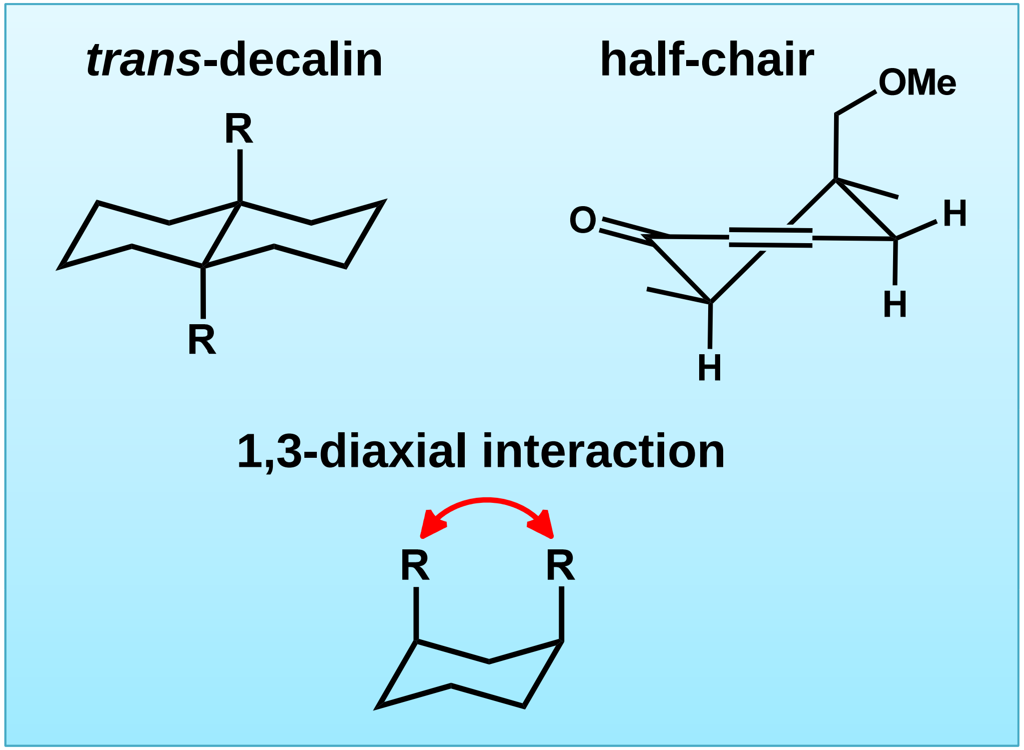
Freccero, M.; Gandolfi, R.; Sarzi-Amadè, M.; Rastelli, A. *J. Org. Chem.* **2000,** *65,* 2030.
Singleton, D. A.; Merrigan, S. R.; Liu, J.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 3385.

Epoxidation under Basic Conditions



Triton® B = benzyltrimethylammonium hydroxide in H_2O





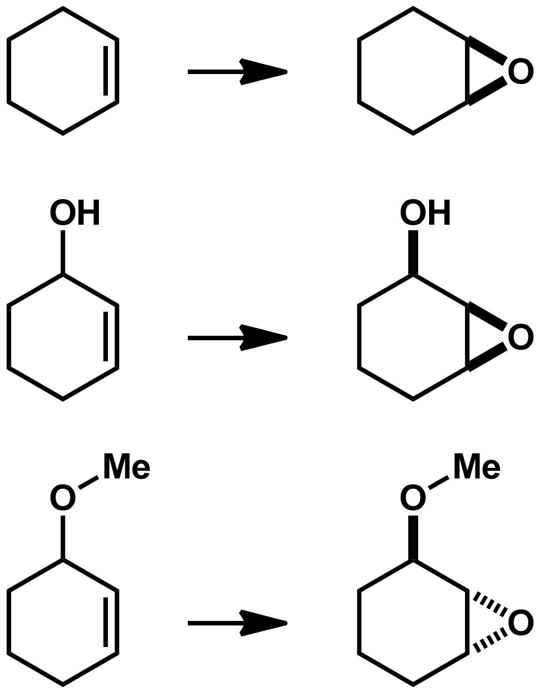
Grieco, P. A. et al. *J. Am. Chem. Soc.* **1977,** *99,* 5773.

Epoxidation of Allyl Alcohols

Henbest epoxidation

relative rate

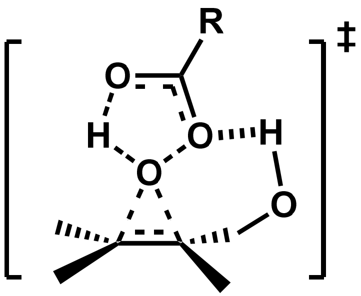
$PhCO_3H$



1.00

0.55

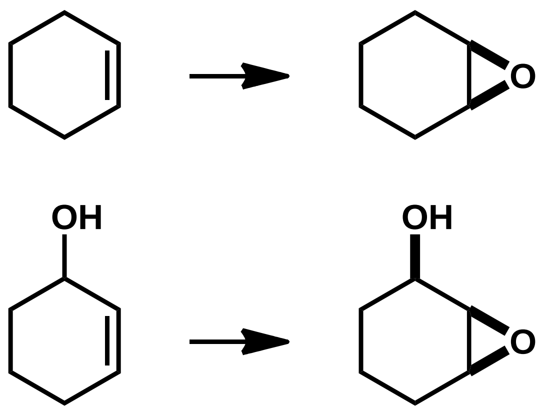
0.067



transition metal-catalyzed epoxidation

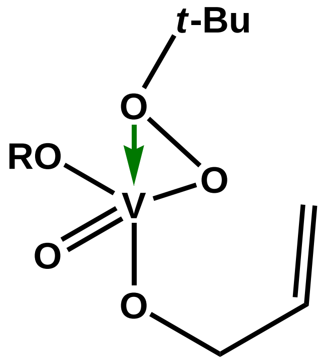
relative rate

$VO(acac)_2$
t-BuOOH

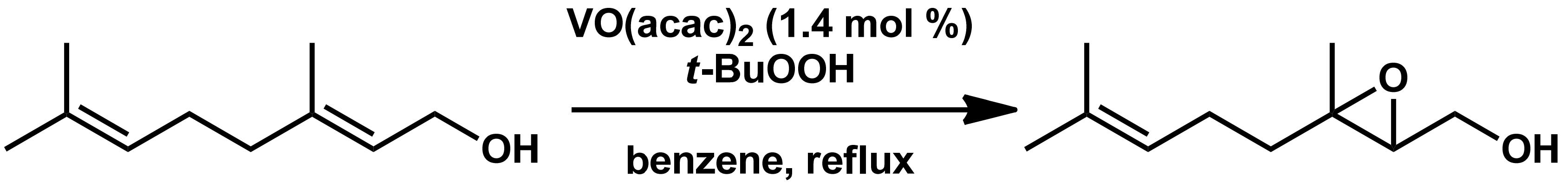


1.00

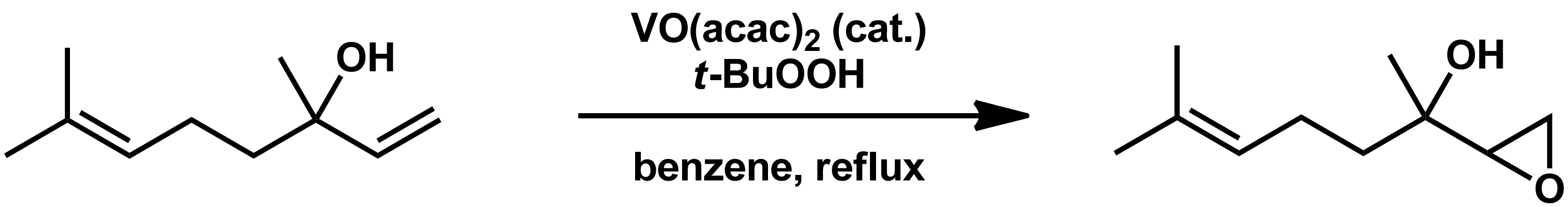
>200



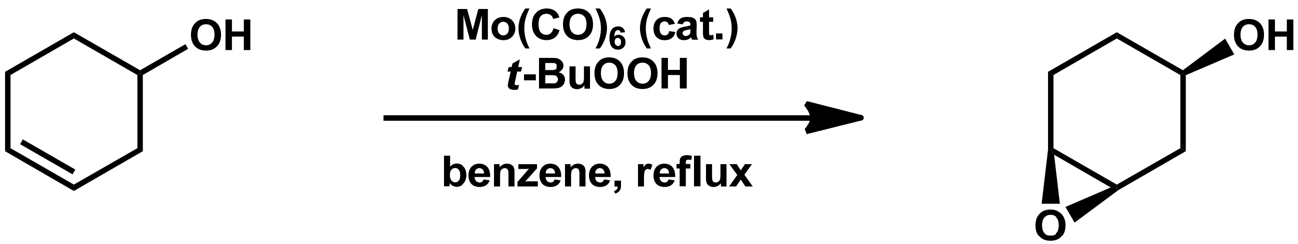
Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.Henbest, H. B.; Wilson, R. A. I. *J. Chem. Soc.* **1957**, 1958.
Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136.



93% yield after acetylation
98% isomeric purity (= 98:2)



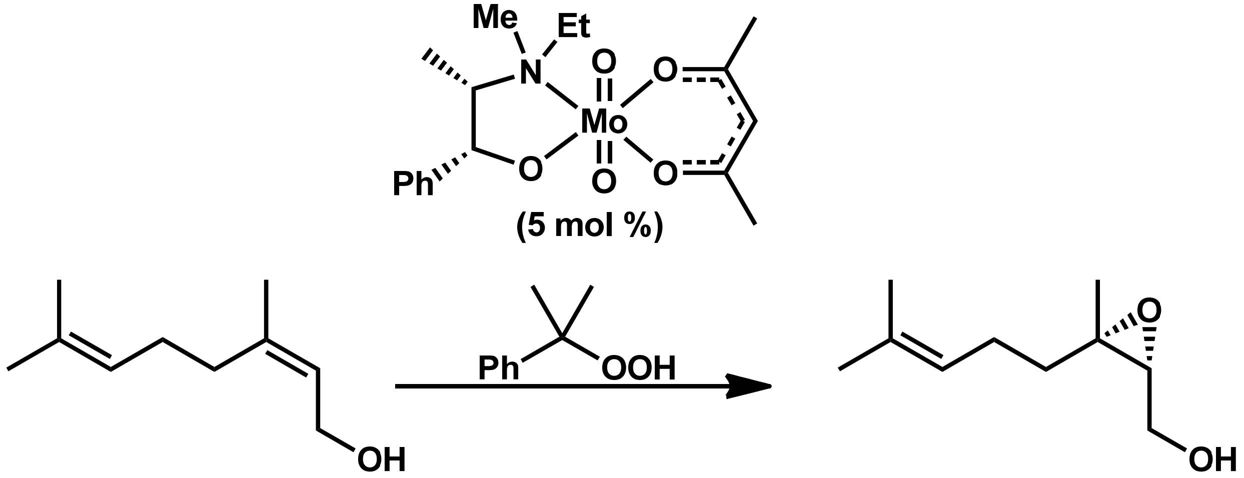
84% yield
95% isomeric purity



90% yield after acetylation
98% isomeric purity

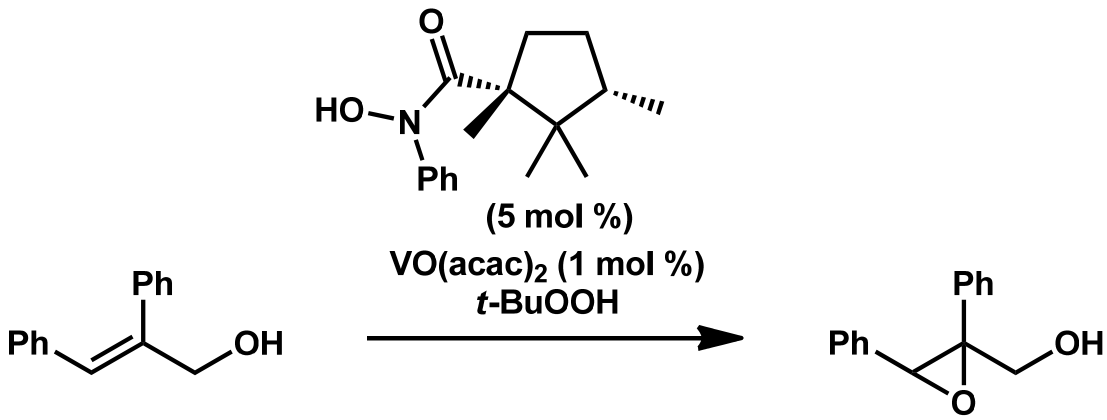
Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136.

Early Examples of Asymmetric Epoxidation of Allyl Alcohols



48% yield
33% opt. yield

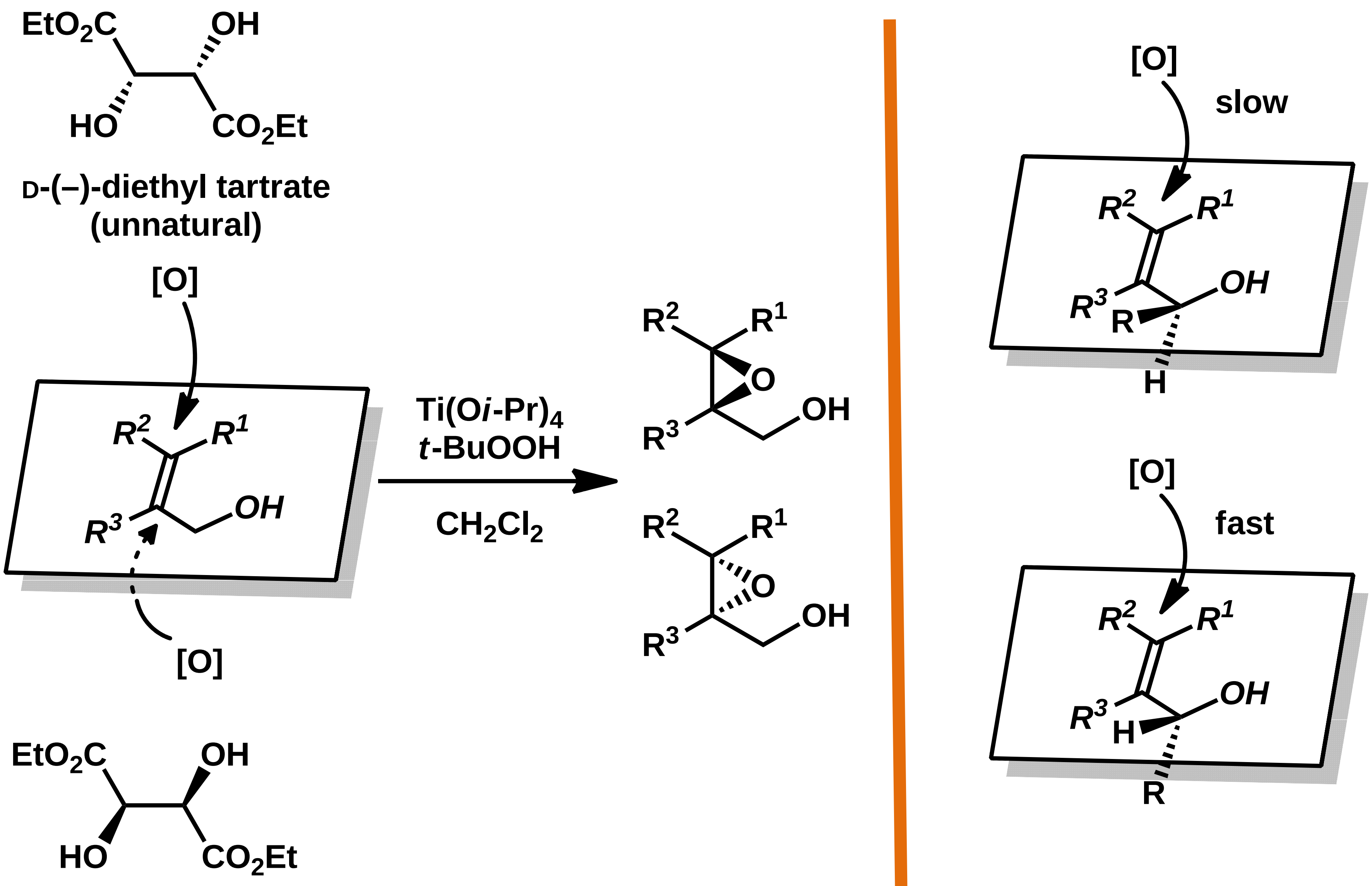
Yamada, S. et al. *J. Am. Chem. Soc.* **1977**, *99*, 1988.



>30% yield
50% ee

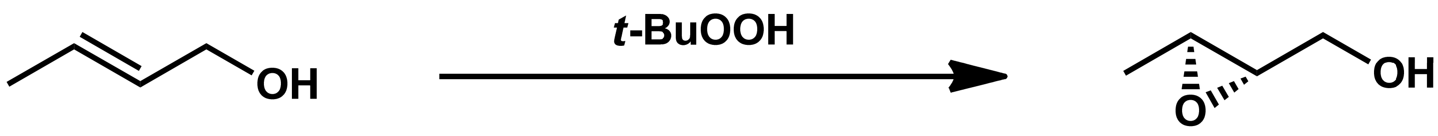
Sharpless, K. B. et al. *J. Am. Chem. Soc.* **1977**, *99*, 1990.

Essence of Sharpless Asymmetric Epoxidation



L-(+)-diethyl tartrate
(natural)

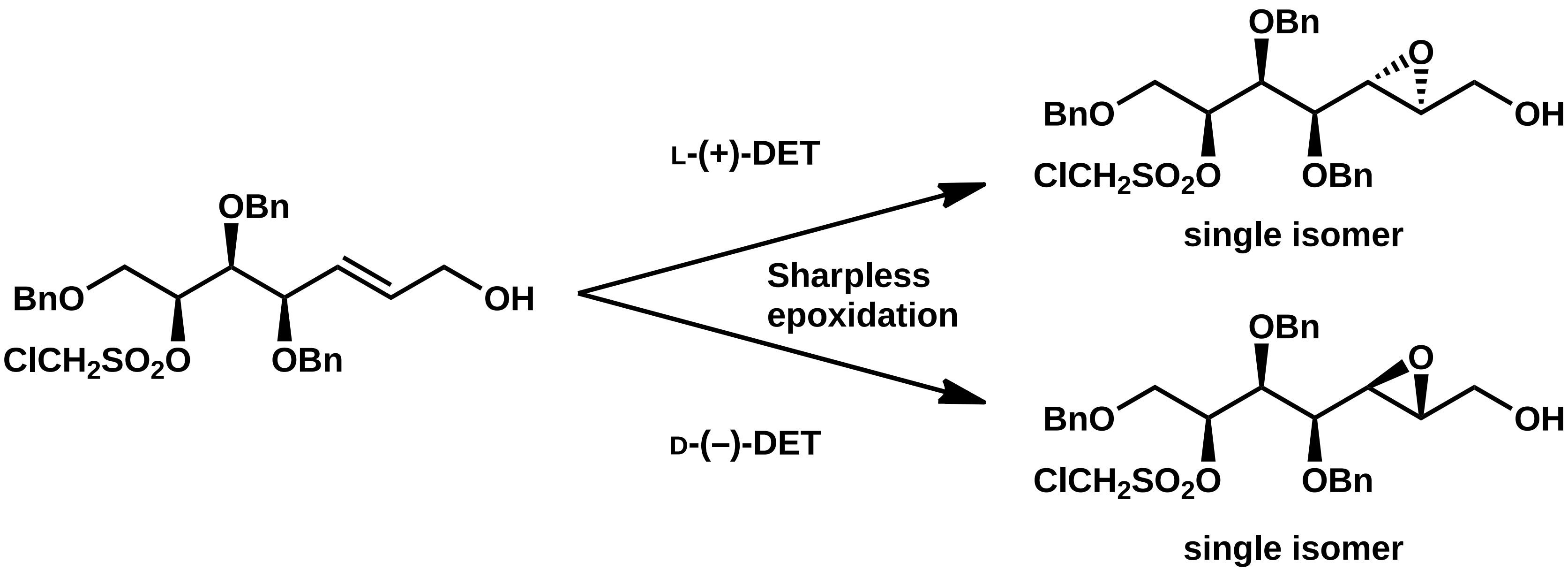
Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis, 2nd ed.*; Ojima, I. Ed.; Wiley-VCH: New York; 2000.



Ti(O*i*-Pr)$_4$ (1 equiv), (+)-DIPT (1 equiv) — **40% yield, 95% ee**

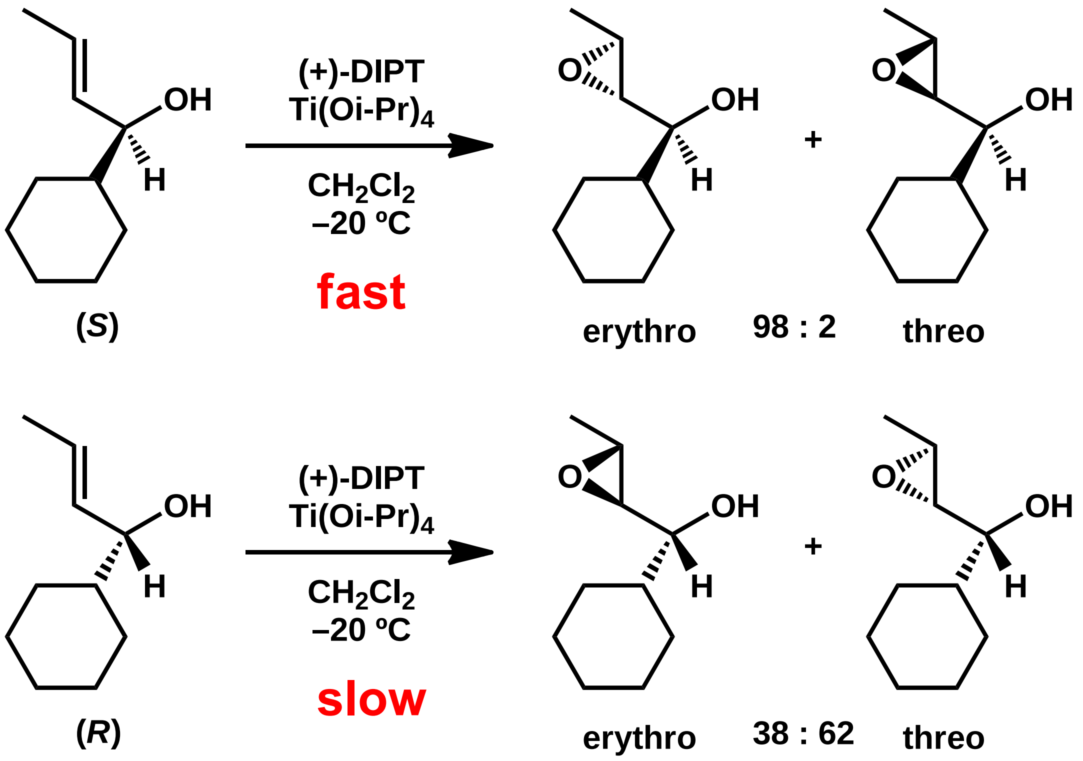
Ti(O*i*-Pr)$_4$ (0.05 equiv), (+)-DIPT (0.06 equiv), MS3A — **70% yield, 91% ee**

Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
Sharpless, K. B., et al. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
Katsuki, T. In *Comprehensive Asymmetric Synthesis, Vol II*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer:Berlin; 1999.

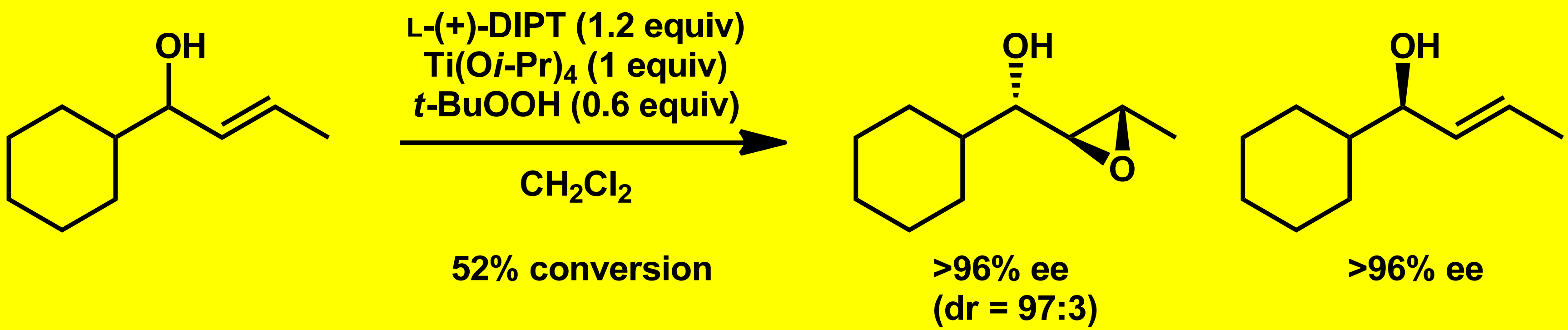


Kajimoto, T.; Wong, C.-H. *Tetrahedron Lett.* **1995**, *36*, 8247.

Kinetic Resolution of Racemic Allylic Alcohols

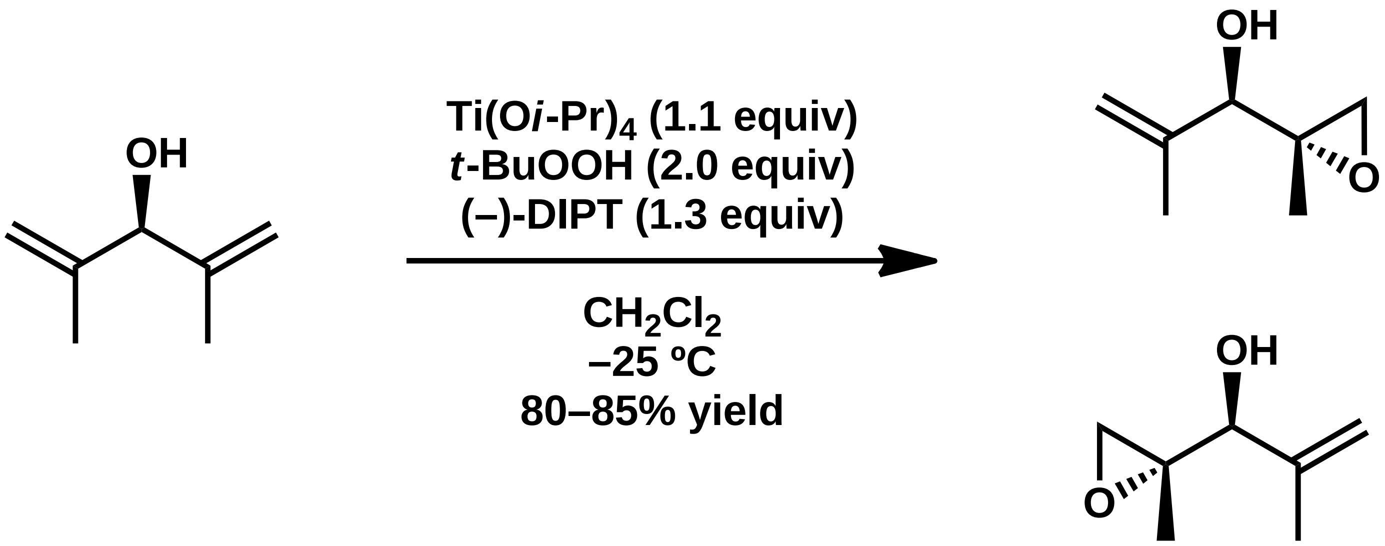


$k_{fast}/k_{slow} = 104$



Sharpless, K. B., et al. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

Combination of asymmetric synthesis and kinetic resolution can deliver products with very high ee.



major

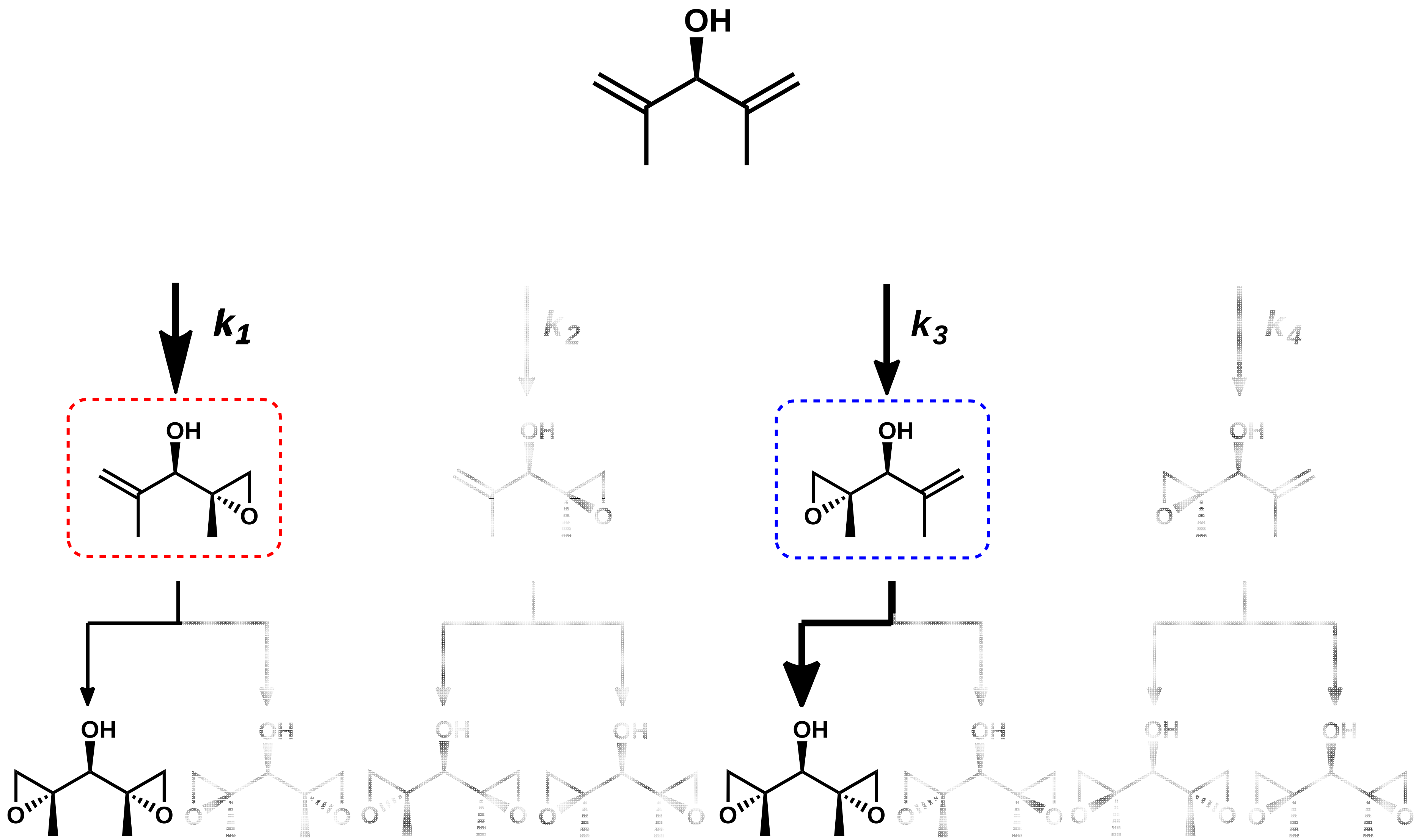
minor

0.5 h: 88% ee

1 h : 94% ee

1.5 h: >99.3% ee

Schreiber, S. L., et al. *J. Am. Chem. Soc.* **1987**, *109*, 1525.


OH
k_1
k_2
k_3
k_4
OH
O
OH
O
OH
O
OH
O
OH
O
O
OH
O
O
OH
O
O
OH
O
O
OH
O
O
OH
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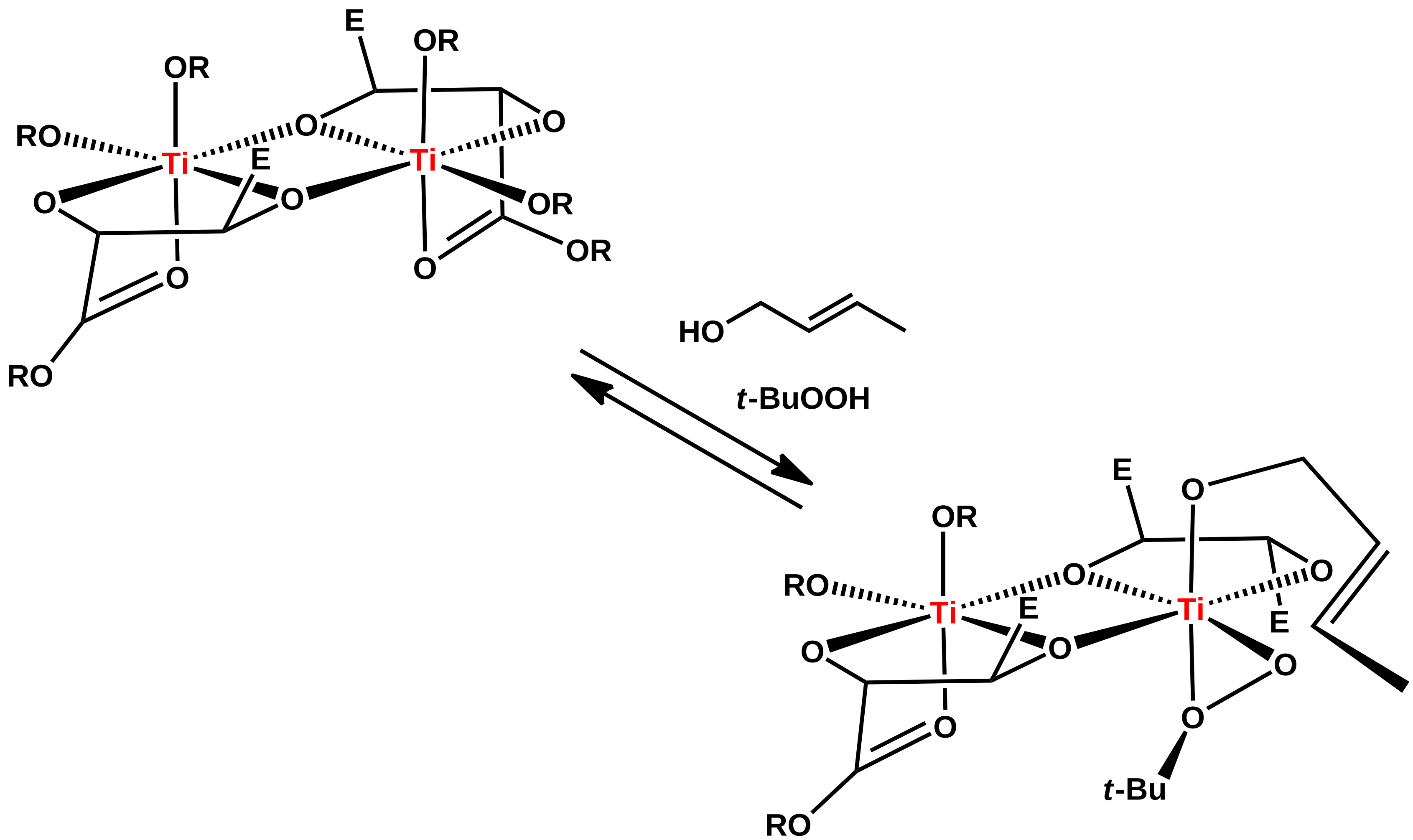
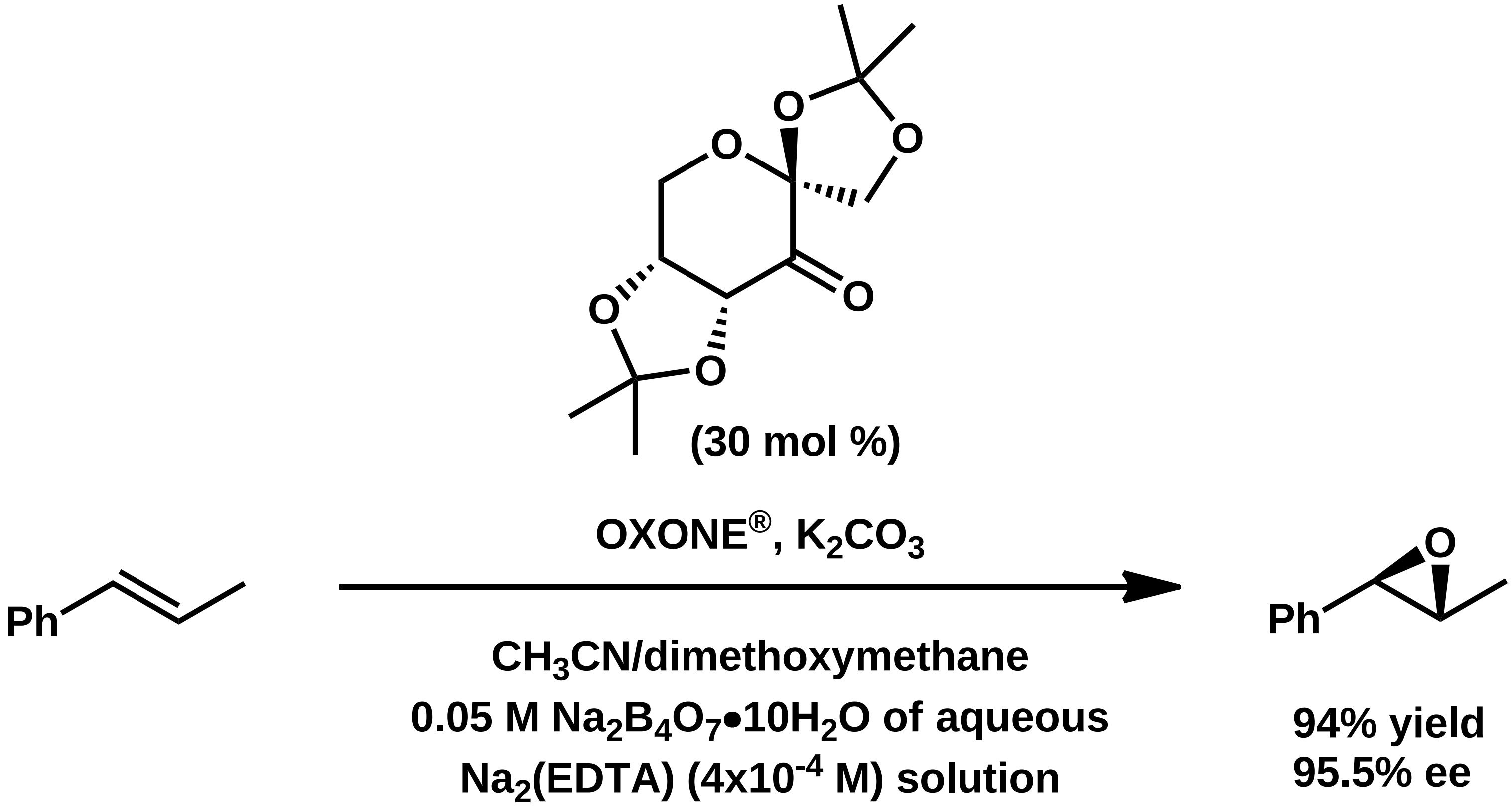
O
OH
O
O
OH
O
O

Catalyst Structure and Proposed "Loaded" Catalyst



Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113.
Katsuki, T. In *Comprehensive Asymmetric Synthesis, Vol II*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer:Berlin; 1999.

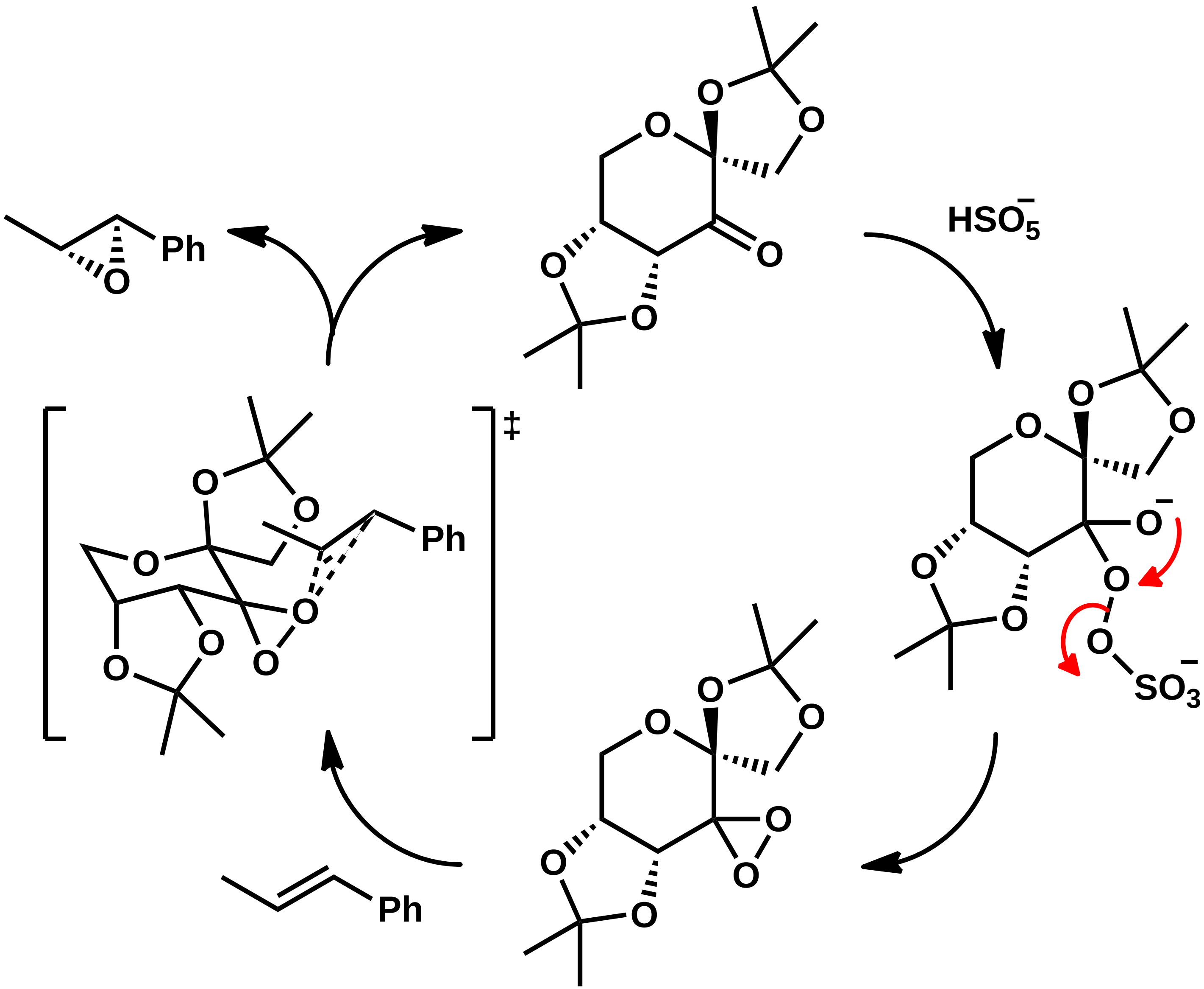
Asymmetric Epoxidation of Unfunctionalized Olefins



OXONE® = $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$

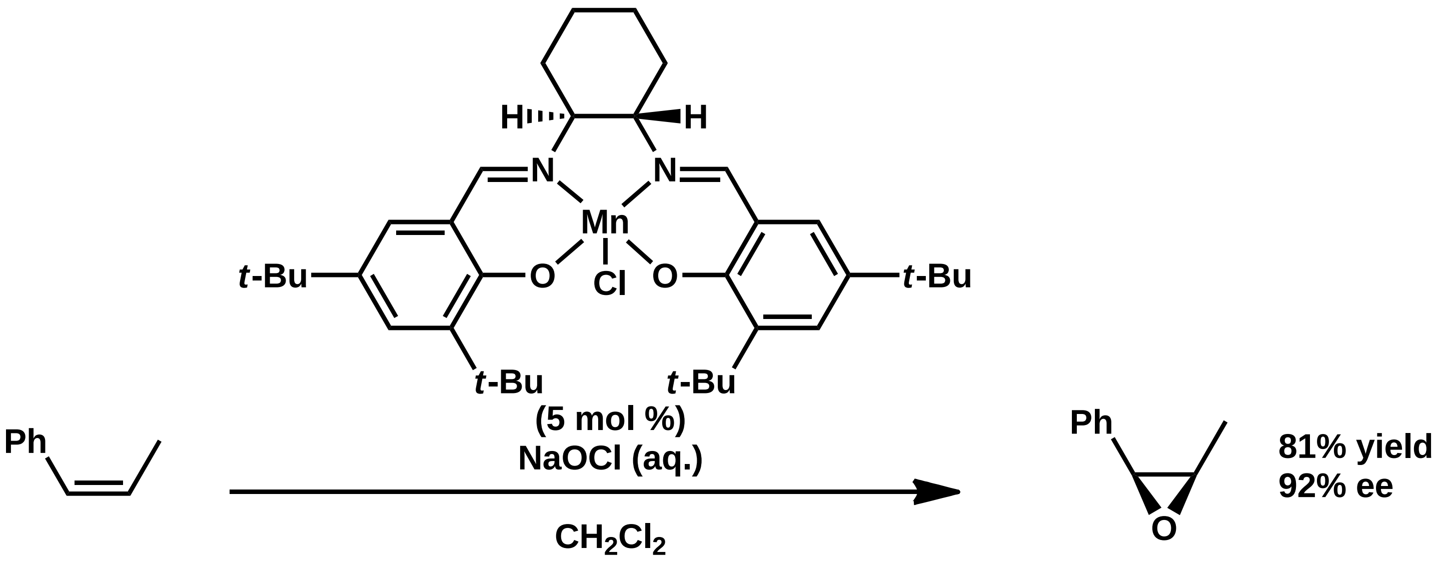
Shi, Y. et al. *J. Am. Chem. Soc.* **1997**, *119*, 11224.

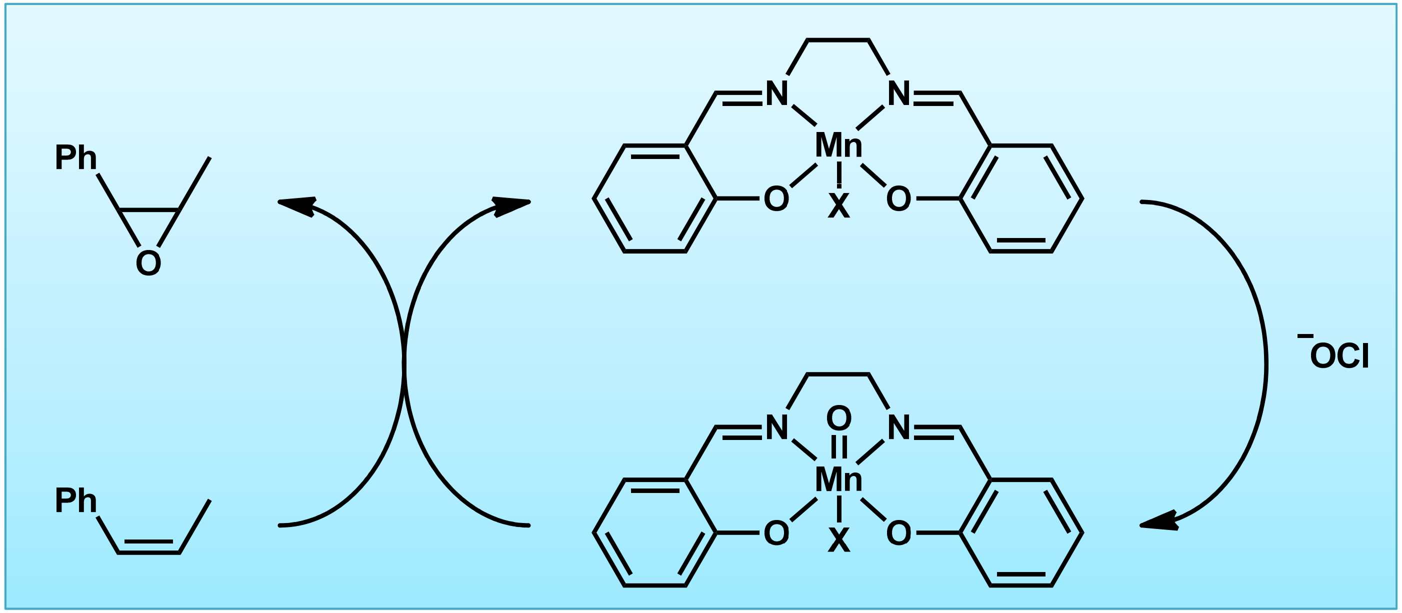
Na_2(EDTA) is used to prevent trace-metal-catalyzed peroxide decomposition.



dioxirane

Mn–Salen-Catalyzed Asymmetric Epoxidation

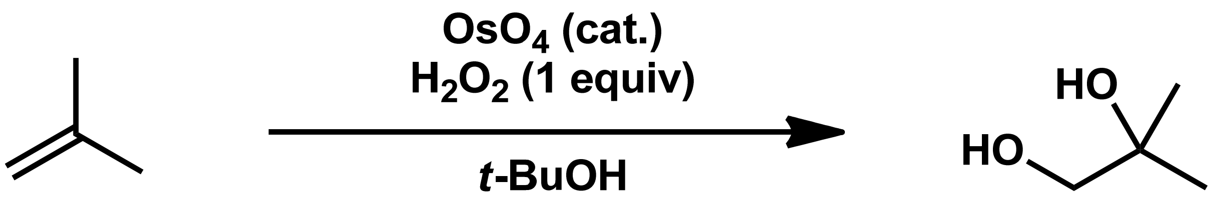




Jacobsen, E. N. et al. *J. Am. Chem. Soc.* **1991**, *113*, 7063. Jacobsen, E. N. et al. *J. Am. Chem. Soc.* **1990**, *112*, 2081.
Katsuki, T. et al. *Tetrahedron Lett.* **1990**, *31*, 7345.

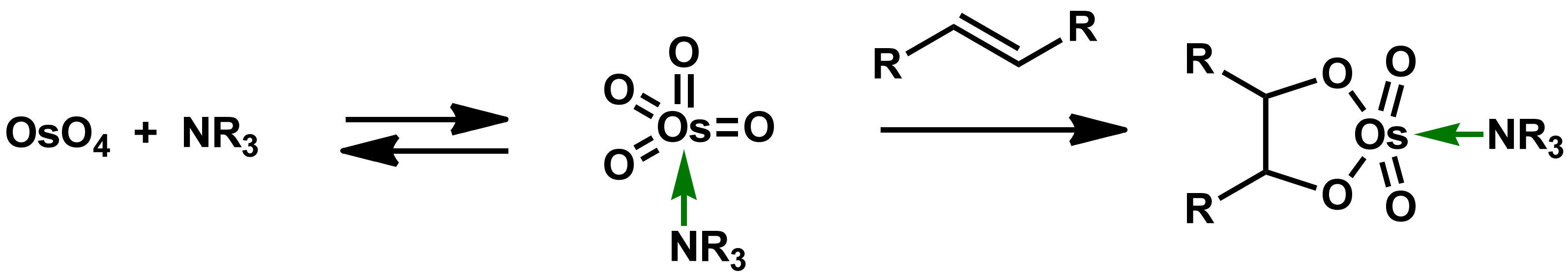
Dihydroxylation with Osmium Tetroxide

catalytic reaction



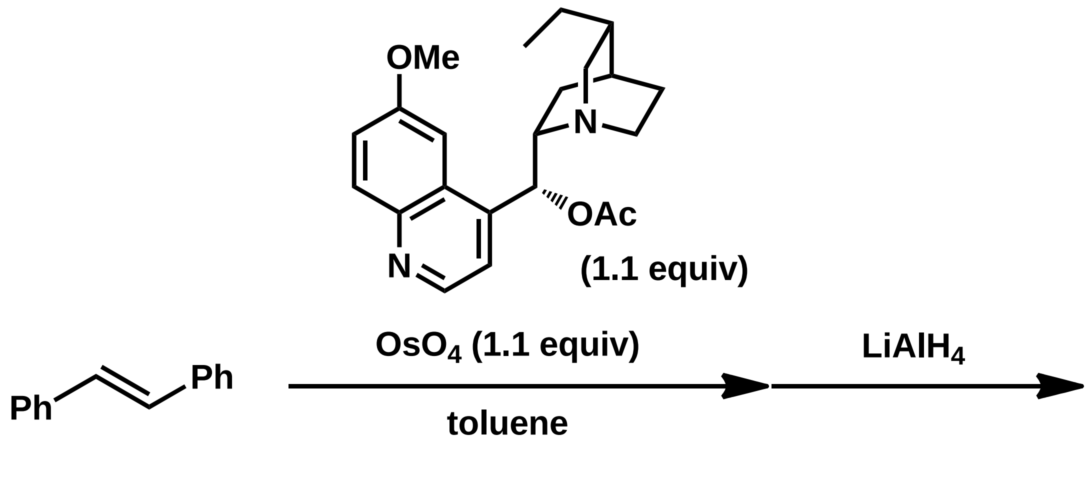
Milas, N. A.; Sussman, S. *J. Am. Chem. Soc.* **1936**, *58*, 1302.

acceleration by tertiary amines



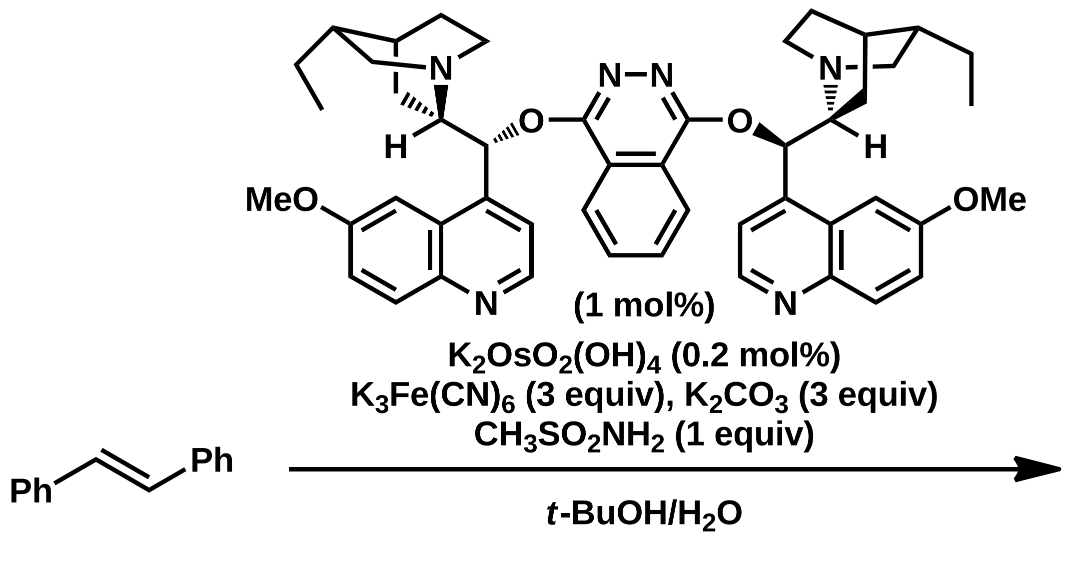
Criegee, R.; Marchand, B.; Wannowius, H. *Liebigs Ann. Chem.* **1942**, *550*, 99.

Asymmetric Dihydroxylation (AD)



Sharpless, K. B., et al. *J. Am. Chem. Soc.* **1980**, *102*, 4263.

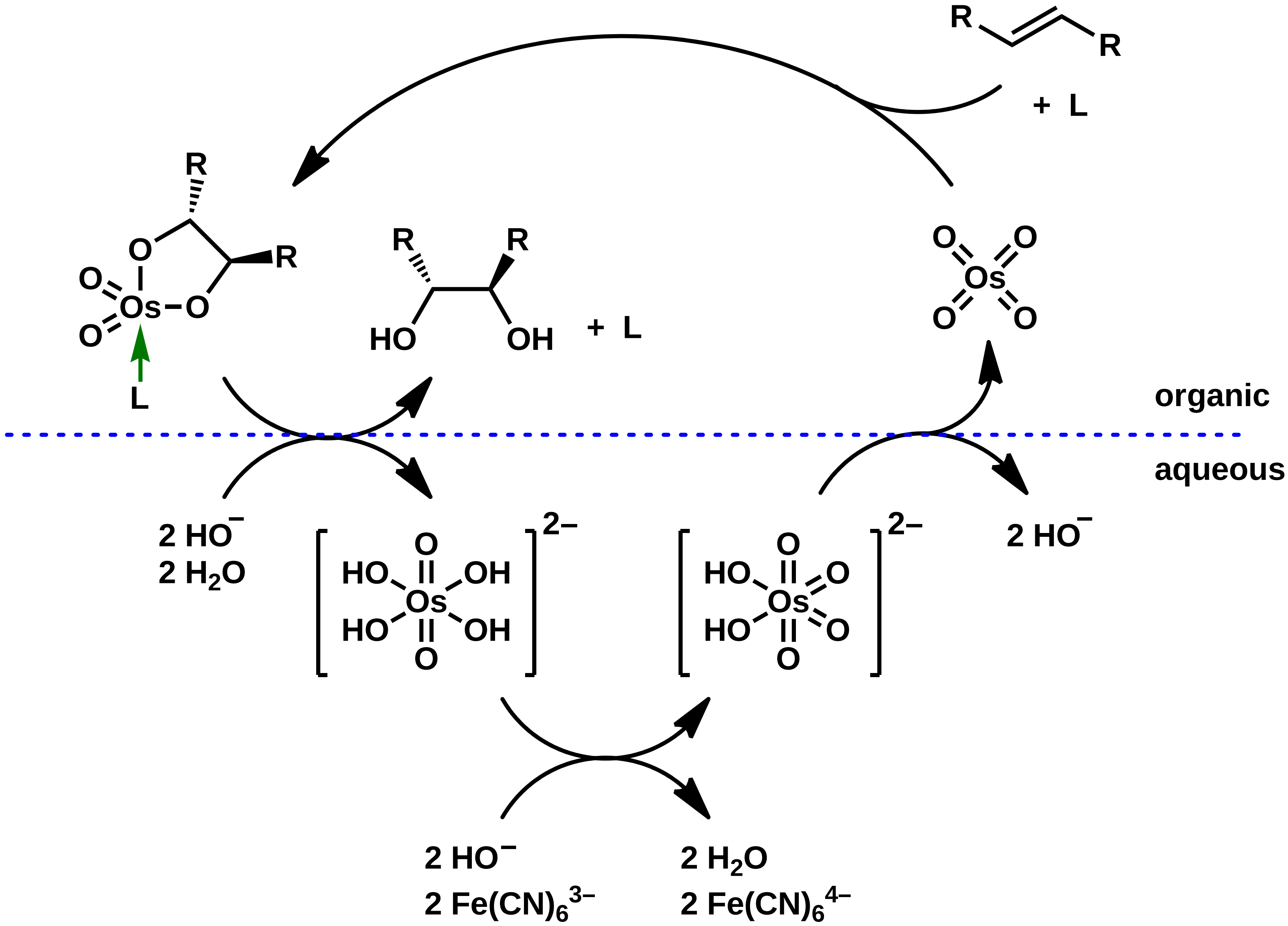
90% yield
83.2% ee



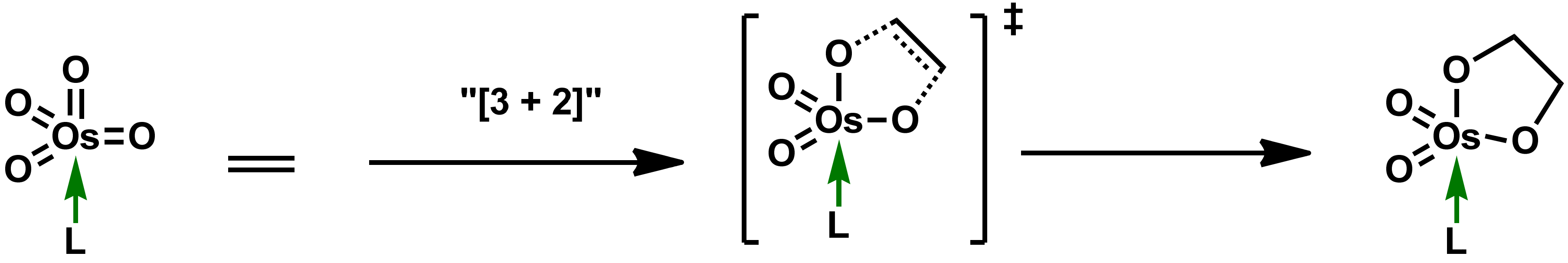
Sharpless, K. B., et al. *J. Org. Chem.* **1992**, *57*, 2768.
.

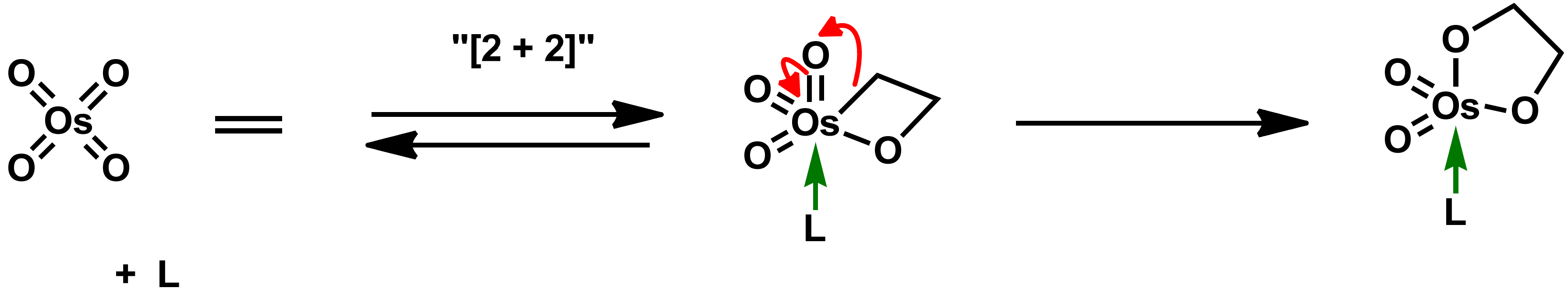
>80% yield
>99.5% ee

Catalytic Cycle



Two Proposed Mechanisms





Hoffmann, R., et al. *J. Am. Chem. Soc.* **1986**, *108*, 1867.
Corey, E. J., et al. *J. Am. Chem. Soc.* **1996**, *118*, 11038.
Sharpless, K. B., et al. *J. Am. Chem. Soc.* **1997**, *119*, 1840.
Houk, K. N.; Sharpless, K. B.; Singleton, D. A., et al. *J. Am. Chem. Soc.* **1997**, *119*, 9907.

Click Chemistry: Diverse Chemical Function from a Few Good Reactions

Hartmuth C. Kolb, M. G. Finn, and K. Barry Sharpless*

Angew. Chem. Int. Ed. **2001**, *40*, 2004.

“Nature is a matchless creator of C-C linkages and we propose leaving the tough job of C-C bond synthesis as much as possible to her.”