

Massachusetts Institute of Technology
Organic Chemistry 5.512

May 10, 2006
Prof. Rick L. Danheiser

Unit 9
Stereocontrolled Hydroboration
and Dihydroxylation of Alkenes

- ★ Substrate Control: 1,2-Asymmetric Induction in Hydroboration
- ★ Reagent Controlled Hydroboration
- ★ Substrate Control: 1,2-Asymmetric Induction in Dihydroxylation
- ★ Reagent Controlled Dihydroxylation: Sharpless ADH Reaction

Background Reading

Carey and Sundberg (Part B) 4th Ed. (2001) Chapter 4 pp 226-241 (Hydroboration), Chapter 12 pp 757-762 (Dihydroxylation), and Chapter 12 pp 762-782 (Epoxidation - the next unit)

Review on Hydroboration

"Catalytic Asymmetric Hydroboration: Recent Advances and Applications in Carbon-Carbon Bond-Forming Reactions" Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695

Reviews on Asymmetric Dihydroxylation and Aminohydroxylation

"Catalytic Asymmetric Dihydroxylation: Discovery and Development" Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH, 2000, pp 357-398

"Recent Advances in Asymmetric Dihydroxylation and Aminohydroxylation" Bolm, C.; Hildebrand, J. P.; Muniz, K. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH, 2000, pp 398-428.



H. C. Brown



K. Barry Sharpless

Sharpless Asymmetric Dihydroxylation

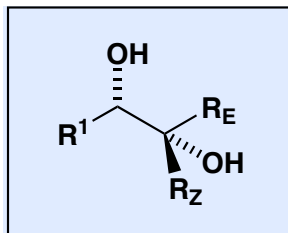
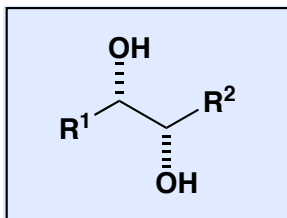
Review on Sharpless ADH

"Catalytic Asymmetric Dihydroxylation" Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, 94, 2483

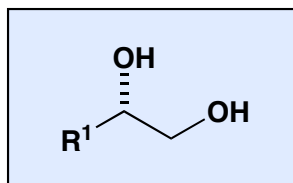
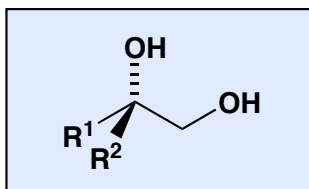
"Asymmetric Dihydroxylation" Becker, H.; Sharpless, K. B. In *Asymmetric Oxidation Reactions*; Katsuki, T., Ed.; Oxford, 2001, pp 81-104.

"Asymmetric Aminohydroxylation" Schlingloff, G.; Sharpless, K. B. In *Asymmetric Oxidation Reactions*; Katsuki, T., Ed.; Oxford, 2001, pp 104-114.

Retrons



Generally very good selectivity for E-disubstituted and trisubstituted alkenes (for either enantiomer)



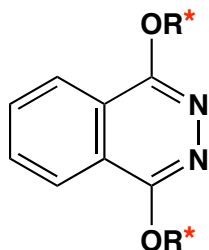
Borderline to good selectivity for terminal alkenes and 1,1-disubstituted alkenes (use AQN ligand for aliphatic derivatives)

AD-mix α (DHQ)₂PHAL + K₂OsO₂(OH)₄ + K₃Fe(CN)₆

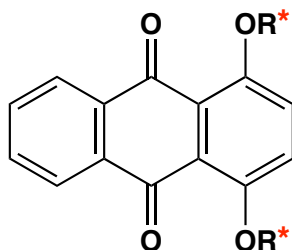
\$81.70/50 g

AD-mix β (DHQD)₂PHAL + K₂OsO₂(OH)₄ + K₃Fe(CN)₆

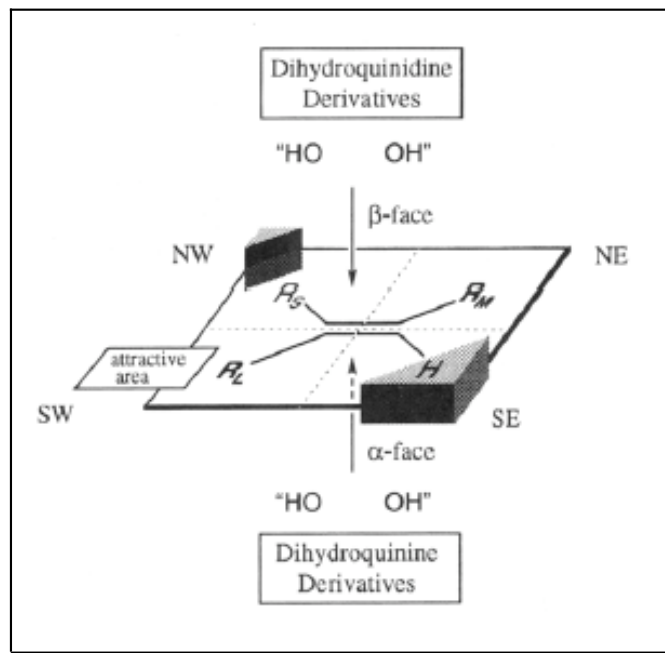
Cinchona Alkaloid Ligands for AD under *Catalytic* Conditions



(DHQD)₂PHAL
(phthalazine)

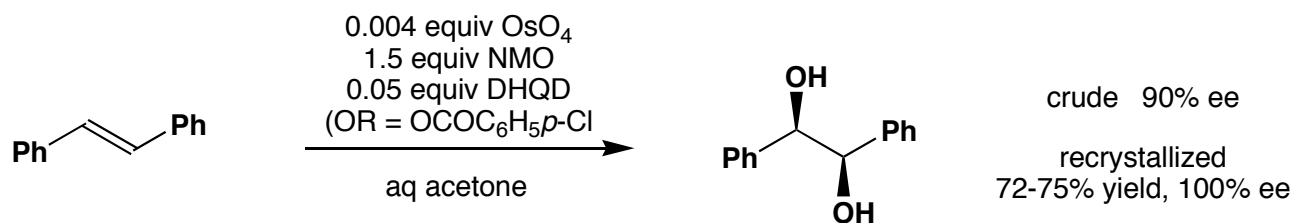


(DHQD)₂AQN
(anthraquinone) 500 mg \$65.50

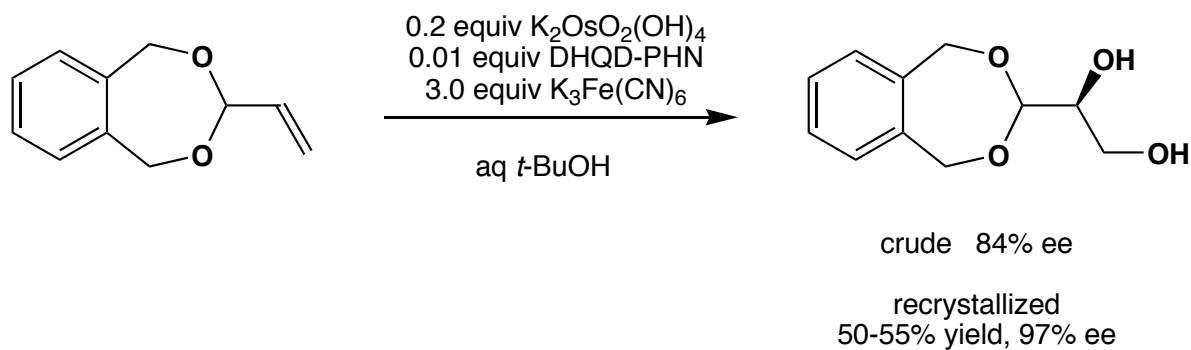


Organic Syntheses Procedures

McKee, B. H.; Gilheany, D. G.; Sharpless, K. B. *Org. Synth.* **1992**, 70, 47



Oi, R.; Sharpless, K. B. *Org. Synth.* **1996**, 73, 1



Case Study

Synthesis of C₆-C₁₃ Fragment of Miyakolide

S. Masamune et al.
J. Org. Chem. **1997**, 62, 8978

