Massachusetts Institute of Technology

Organic Chemistry 5.512

May 4, 2007
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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

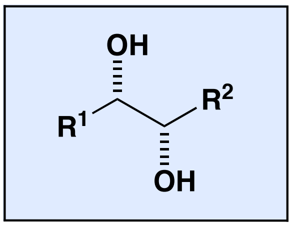
Review on Sharpless ADH

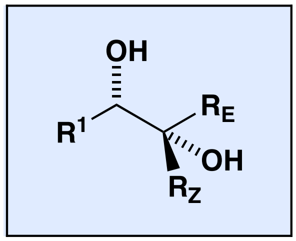
"Catalytic Asymmetric Dihydroxylation" Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483

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

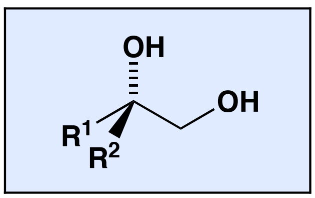
"Asymmetric Aminohydroxylation" Schlingloff, G.; Sharpless, K. B. In *Asymmetric Oxidation Reactions*; Katsuki, T., Ed.; Oxford, 2001, pp 104-114.

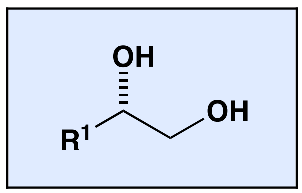
Retrons





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





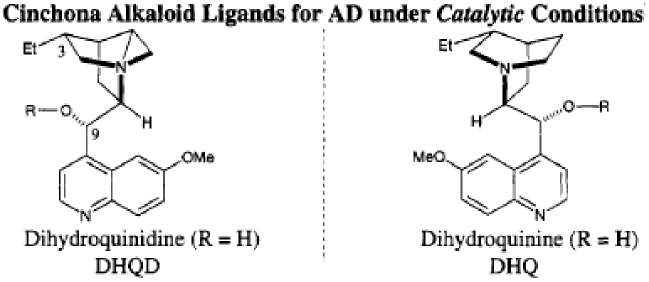
Borderline to good selectivity for terminal alkenes and 1,1-disubstituted alkenes (use AQN ligand for aliphatic derivatives)

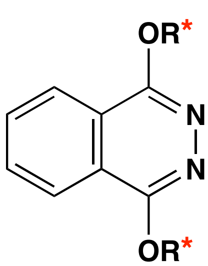
AD-mix α $(DHQ)_2PHAL + K_2OsO_2(OH)_4 + K_3Fe(CN)_6$

AD-mix β $(DHQD)_2PHAL + K_2OsO_2(OH)_4 + K_3Fe(CN)_6$

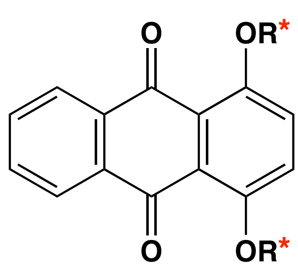
$81.70/50 g

Cinchona Alkaloid Ligands for AD under *Catalytic* Conditions

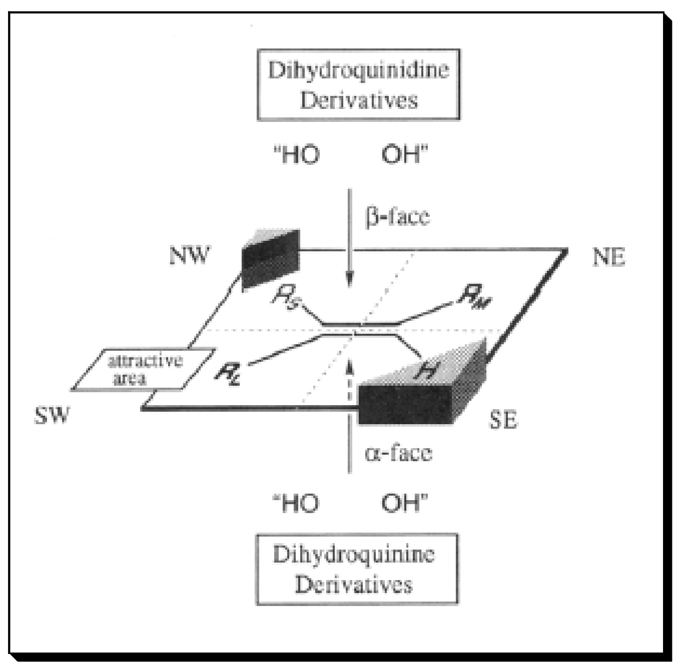




$(DHQD)_2$PHAL
(phthalazine)

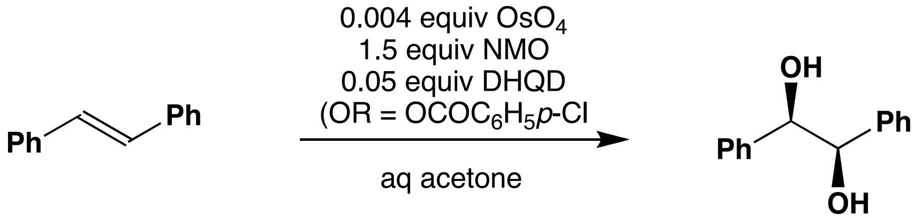


$(DHQD)_2$AQN
(anthraquinone) 500 mg $65.50



Organic Syntheses Procedures

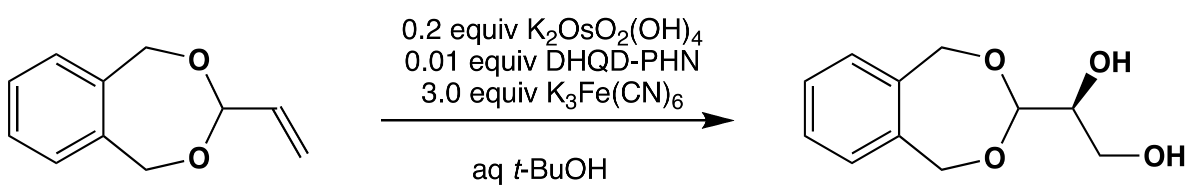
McKee, B. H.; Gilheany, D. G.; Sharpless, K. B. *Org. Synth.* **1992**, *70*, 47



crude 90% ee

recrystallized
72-75% yield, 100% ee

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

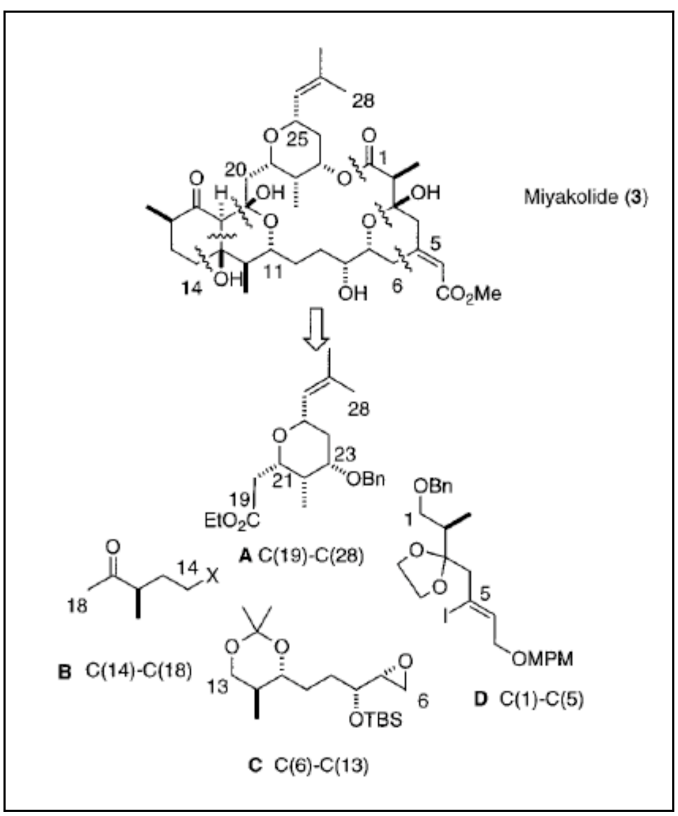


crude 84% ee

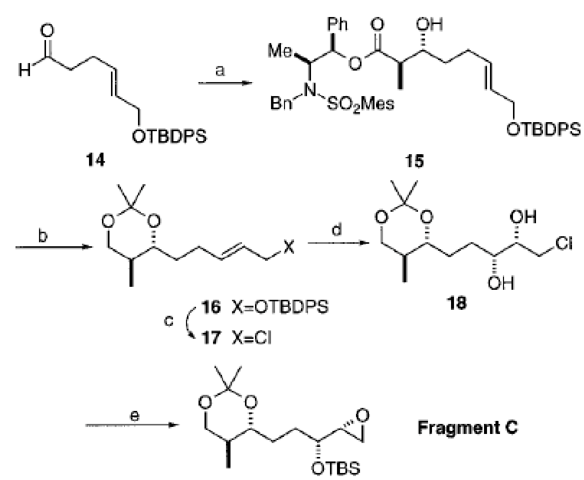
recrystallized
50-55% yield, 97% ee

Case Study — Synthesis of C_6-C_{13} Fragment of Miyakolide

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



Scheme 4



[a] Key: (a) *ent*-**2** (1*R*, 2*S*), (*c*-Hex)$_2$BOTf, Et_3N, CH_2Cl_2, −78 °C, then **14** −78 to 0 °C (85%); (b) (1) LAH, THF, 0 °C (85%); (2) 2,2-dimethoxypropane, PPTS, CH_2Cl_2, 25 °C (91%); (c) (1) TBAF, THF, 25 °C (95%); (2) PPh_3, CCl_4, THF, reflux (87%); (d) AD-mix-β, $CH_3SO_2NH_2$, *t*-BuOH, H_2O, 25 °C (65%); (e) (1) NaOH, THF, 0 °C (60%); (2) TBSCl, imidazole, CH_2Cl_2, 25 °C (95%).