

Oxidations (cont)

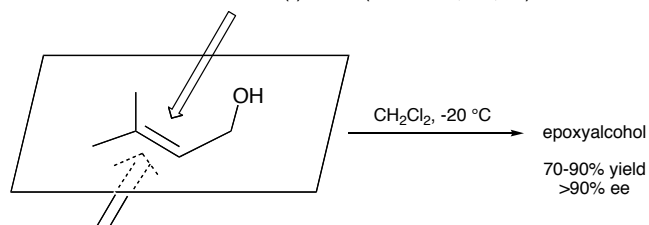
- Jones Oxidation; PCC
- Swern Oxidation
- Dess-Martin Periodinane
- TPAP
- Sharpless Epoxidation
- Dihydroxylations
- Peracids
- Baeyer-Villiger Oxidation
- Ozonolysis

Sharpless Asymmetric Epoxidations

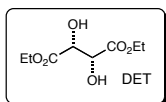
1980: Katsuki & Sharpless; Ti(IV)alkoxide, tartrate, *t*-BuOOH.
References: *Comprehensive Organic Synthesis* **1991**, vol. 7, chapter 3.2; pp 389; *Chem. Rev.* **1991**, 91, 437. *Org. React.* **1996**, 48, 1-300.



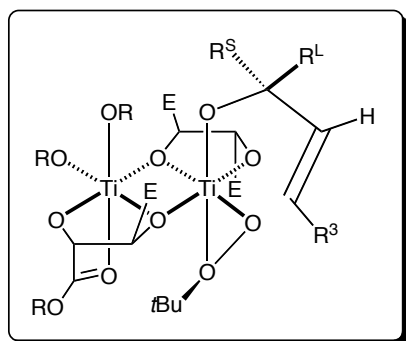
"O" with D-(-)-DIPT (unnatural; 2S,3S)



"O" with L-(+)-DIPT (natural; 2R,3R)

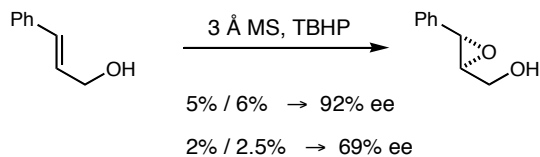
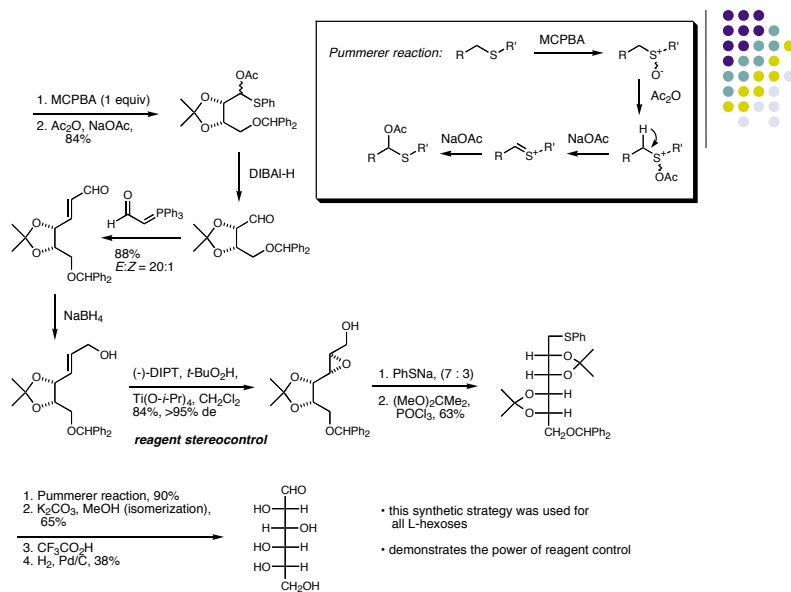
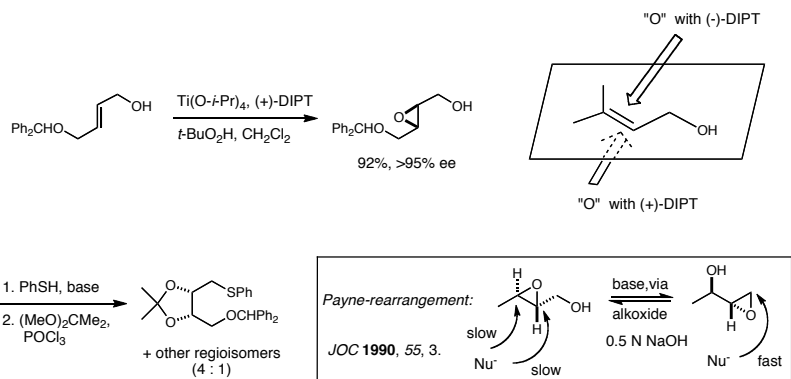


mechanism: dimer is active species (Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, 113, 112).



- incompatible functional groups: amines, -CO₂H, -SH, phenols, phosphines.

Stoichiometry: 5% Ti / 6% tartrate to 10% Ti / 12% tartrate:

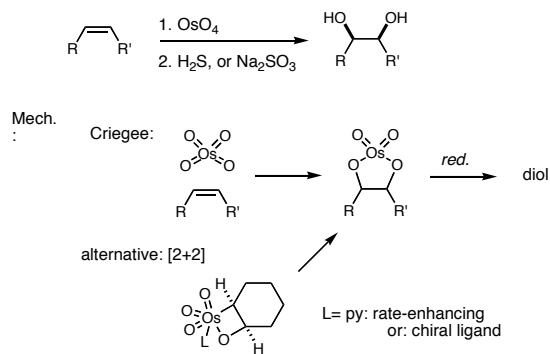
Masamune, S.; Sharpless, K. B. *Tetrahedron* **1990**, *46*, 245. Total synthesis of L-hexoses.

Noe, M. C.; Letavic, M. A.; Snow, S. L. "Asymmetric dihydroxylation of alkenes." *Org. React.* **2005**, *66*, 109-625.

Drudis-Sol, G.; Ujaque, G.; Maseras, F.; Lled, A. "Enantioselectivity in the dihydroxylation of alkenes by osmium complexes." *Top. Organomet. Chem.* **2005**, *12*, 79-107.

Francais, A.; Bedel, O.; Haudrechy, A., "Is osmylation always preferring the richest double bond?" *Tetrahedron* **2008**, *64*, 2495-2524.

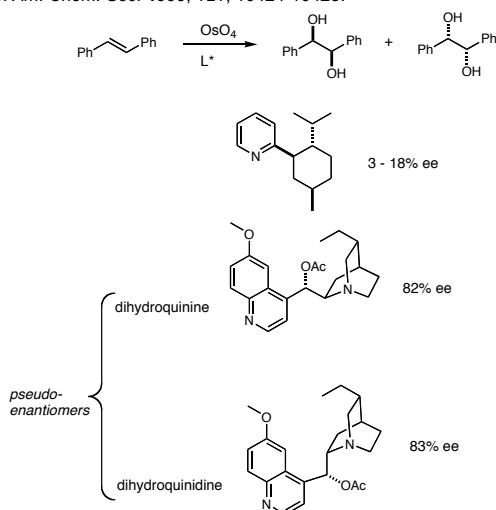
cis-Dihydroxylation of alkenes (rep. in 1908):



cat. OsO_4 ; co-oxidant: TBHP, NMO (Upjohn process), $\text{K}_3\text{Fe}(\text{CN})_6 - \text{K}_2\text{CO}_3$.

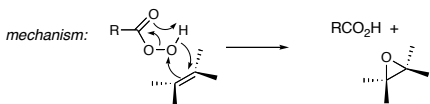
For the use of a flavin analogue with $\text{NMM}/\text{H}_2\text{O}_2$ in the Upjohn process, see: Bergstad, K.; Jonsson, S. Y.; Bäckvall, J.-E., "A new coupled catalytic system for dihydroxylation of olefins by H_2O_2 ." *J. Am. Chem. Soc.* **1999**, *121*, 10424-10425.

chiral ligands:

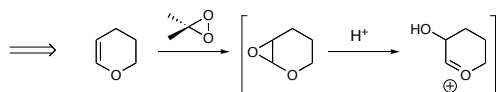
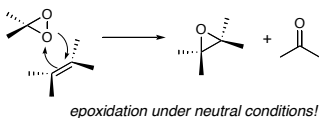
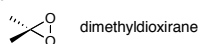


Peracid/Peroxide Epoxidations

Standard peracids are: MCPBA, $\text{CH}_3\text{CO}_3\text{H}$, MMP, $\text{CF}_3\text{CO}_3\text{H}$, 3,5-dinitroperbenzoic acid.

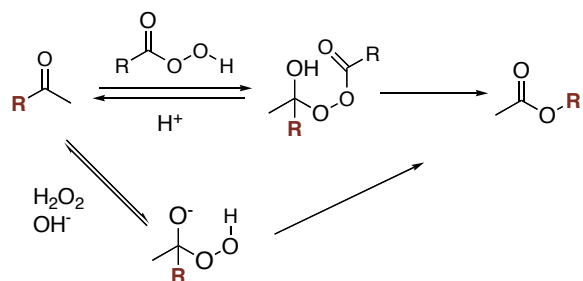


related:



Bayer-Villiger Oxidations

Ketones react with peroxyacids or hydrogen peroxides to give esters via a C→O rearrangement. Both acid- and base-catalyzed mechanisms have been proposed.



The migratory aptitudes are *t*-alkyl > cyclohexyl = 2°alkyl = benzyl = phenyl > vinylic > 1°alkyl > cyclopropyl > methyl.

Ozonolysis

According to the Criegee mechanism, 1,3-dipolar cycloaddition gives a 1,2,3-trioxolane product that rearranges to a 1,2,4 trioxolane (the *ozonide*) by fragmentation into a ketone and a carbonyl oxide followed by a second dipolar addition. In addition to catalytic hydrogenation, LAH, NaBH₄, Zn/AcOH, and Me₂S/MeOH can be used to decompose the ozonide.

1,3-Dipolarophiles, such as ketones, methyl formate, phenanthrene quinone and methyl pyruvate have been employed to trap the carbonyl oxides to give tri- and tetra-substituted ozonides. The goal of these trapping experiments is simply to prepare the ozonides which are difficult to obtain by normal procedures (*Tetrahedron* **1997**, *53*, 5217-5232).

Alkenes can usually be ozonized in the presence of alkynes (since ozone is an electrophilic reagent, it actually prefers alkenes). Non-compatible functional groups are:

- anilines and other electron-rich aromatic rings.
- thioethers and phosphines
- hydrazones, oximes, enamines

-Marshall, J. A.; Garofalo, A. W. *J. Org. Chem.* **1993**, *58*, 3675. The ozonolysis of alkenes in methanolic NaOH or NaOMe with CH₂Cl₂ as a cosolvent leads directly to methyl esters.

-Pyridine serves to attenuate the reactivity of ozone toward electron-rich functional groups such as a PMB-ether:

-Schreiber, S. L. et al. *J. Am. Chem. Soc.* **1990**, *112*, 5583.