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.

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

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

CH₂Cl₂, -20 °C  →  epoxyalcohol

70-90% yield  >90% ee

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:

Dihydroxylation Reactions

Francois, 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):

\[
\begin{align*}
R & \quad R' \\
1. OsO_4 \\ 2. H_2S, \text{ or } Na_2SO_3 \quad \text{HO} & \quad \text{OH}
\end{align*}
\]

Mech.: Criegee:

alternative: [2+2]

\[
\begin{align*}
L=\text{py} & \quad \text{rate-enhancing} \\
& \quad \text{or: chiral ligand}
\end{align*}
\]

cat. OsO_4; co-oxidant: TBHP, NMO (Upjohn process), K_2Fe(CN)_6 - K_2CO_3.

chiral ligands:

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{OsO}_4 & \quad \text{L}^* & \quad \text{Ph} & \quad \text{Ph} \\
& \quad + \quad \text{OH} & \quad \text{OH}
\end{align*}
\]

83% ee

\[
\begin{align*}
\text{N} & \quad \text{O} & \quad \text{N} & \quad \text{OAc}
\end{align*}
\]

82% ee

\[
\begin{align*}
\text{N} & \quad \text{O}
\end{align*}
\]

dihydroquinine

dihydroquinidine

dihydroquinine

dihydroquinidine

Peracid/Peroxide Epoxidations

Standard peracids are: MCPBA, CH_3CO_3H, MMP, CF_3CO_2H, 3,5-dinitrobenzoic acid.

\[
\begin{align*}
\text{mechanism:} & \quad \text{RCOOH} \\
\text{related:} & \quad \text{dimethyldioxirane}
\end{align*}
\]

epoxidation under neutral conditions!
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.