Oxidation

- Oxidation state of carbon and Oxidizing agents

- Oxidation of alcohol to carbonyl compounds :
(TEMPO, Swern, Moffatt , Corey-Kim TPAP, Dess-Martin and IBX oxidation)

- Oxidation of aldehyde (or equivalent) to carboxylic acid derivative
(Pinnick oxidation, Oxidation by N-heterocyclic carbene)

- C-H oxidation
(Radical halogenation, dehydrogenation, allylic C-H oxidation, Benzylic C-H oxidation)

- Alkene oxidation
(Epoxidation , Dihydroxylation, Wacker oxidation, Ozonolysis, Baeyer-Villiger)

- Heteroatom oxidation
(Borane and Fleming-Tamao oxidation)

- Other functional groups and their oxidation state

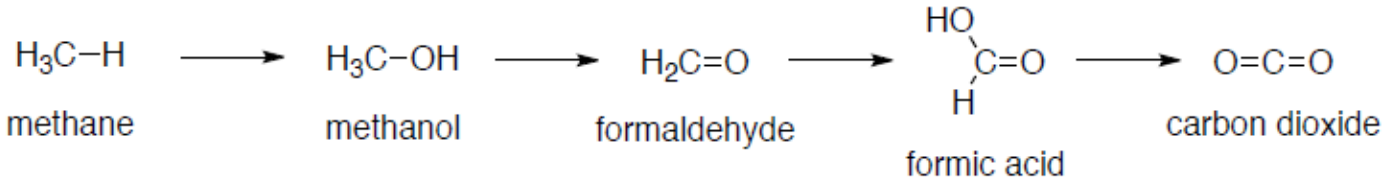
- Oxidation used in industrial setting

- Biological oxidation

Oxidation state of carbon

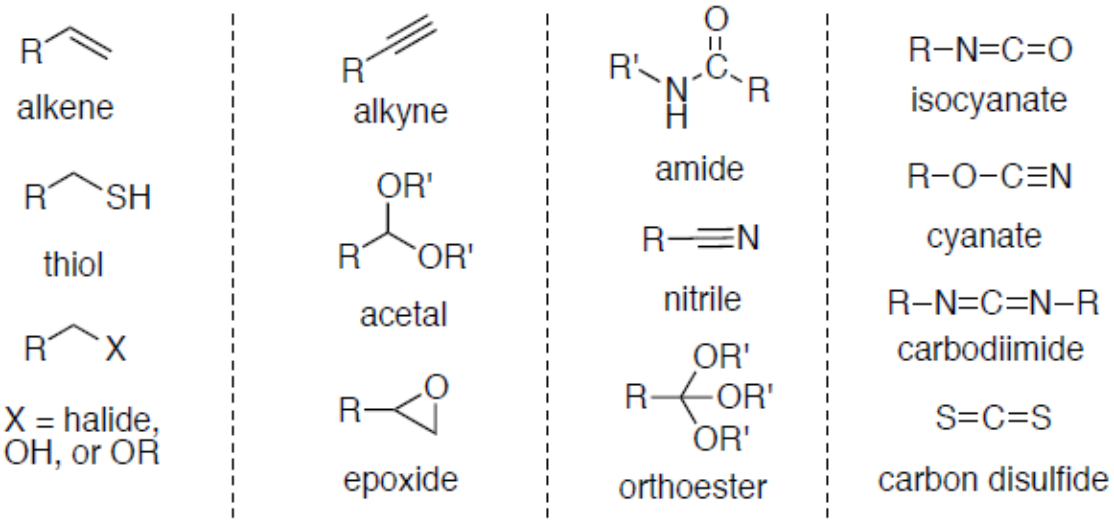
Oxidation is a process in which a chemical species loses electron.

Reduction is a process in which a chemical species gains electron.



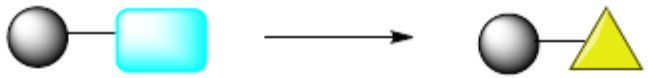
most reduced **most oxidized**

Other functional groups with equivalent oxidation state

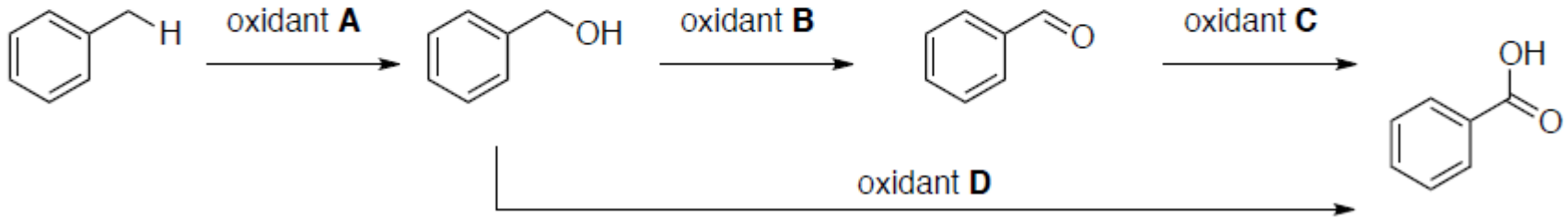


Functional group interconversion

Key to organic synthesis is the interconversion of functional groups. Oxidation and reduction allow for the change up and down the oxidantion ladder. Part of organic chemistry is learning how to master the manipulation of oxidation state and knowing the appropriate reagent for the desired transformation.



For example:



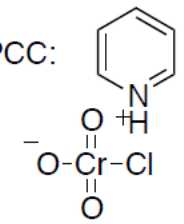
Oxidizing agents

Oxidizing agents increases the oxidation state of the substrate but itself undergoes a reduction. The net process is called a redox reaction. There are many oxidants available in the "tool box." Here we are categorizing them based on their mode of action (mechanism).

Some class of oxidizing agents:

[Metal]=O

PCC:



MnO_2

RuO_4^-

$KMnO_4$

CrO_3

"X-Y"

$Me_2\overset{+}{S}-Cl$

$NaClO_2$

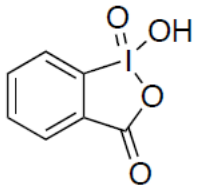
$HO-OH$

Br_2

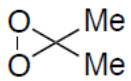
I_2

Cl_2

IBX:

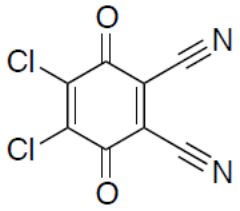


DMDO:

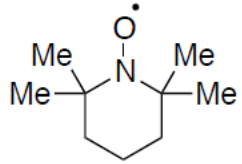


organic oxidant

DDQ:

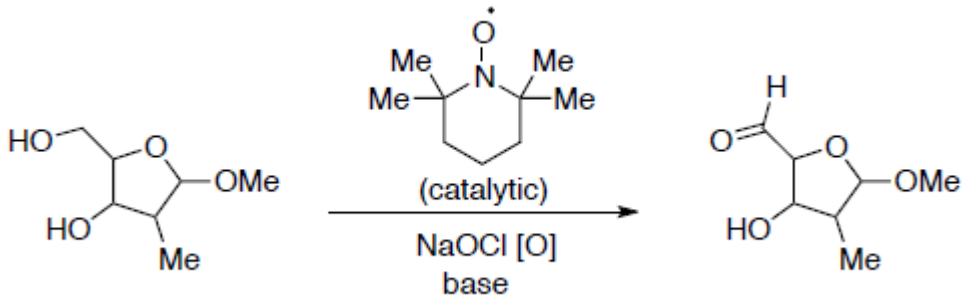


TEMPO:

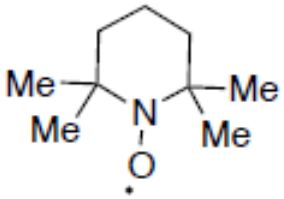


Oxidation of alcohol to carbonyl compounds

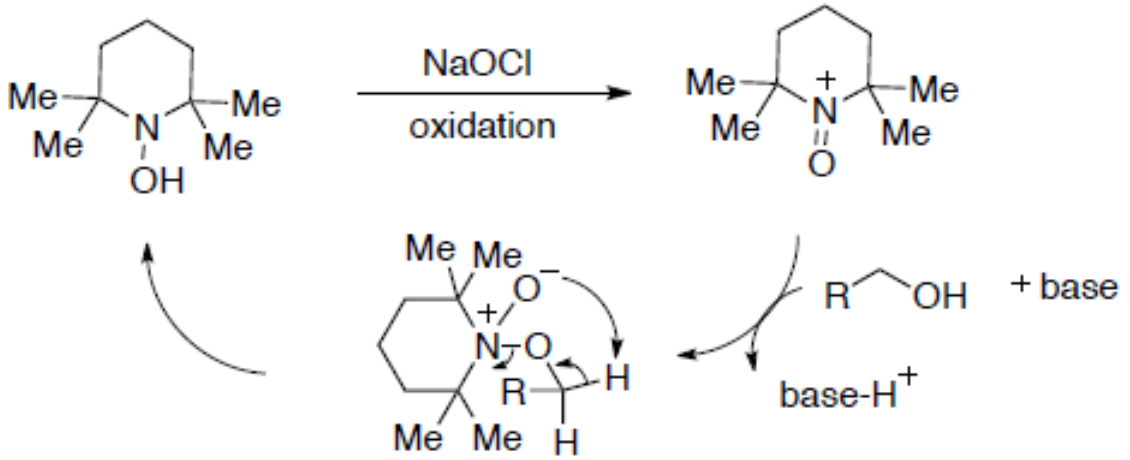
TEMPO oxidation



Mechanism

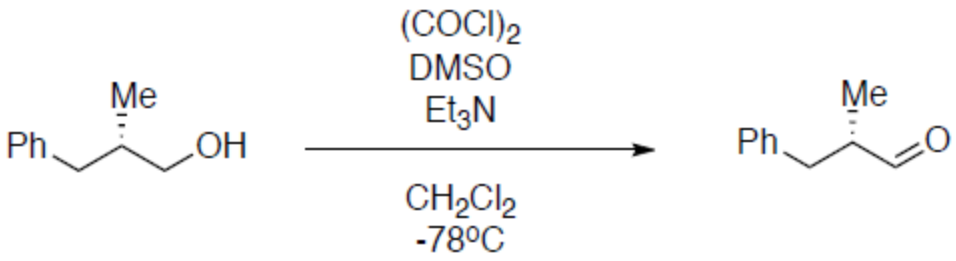


oxidation

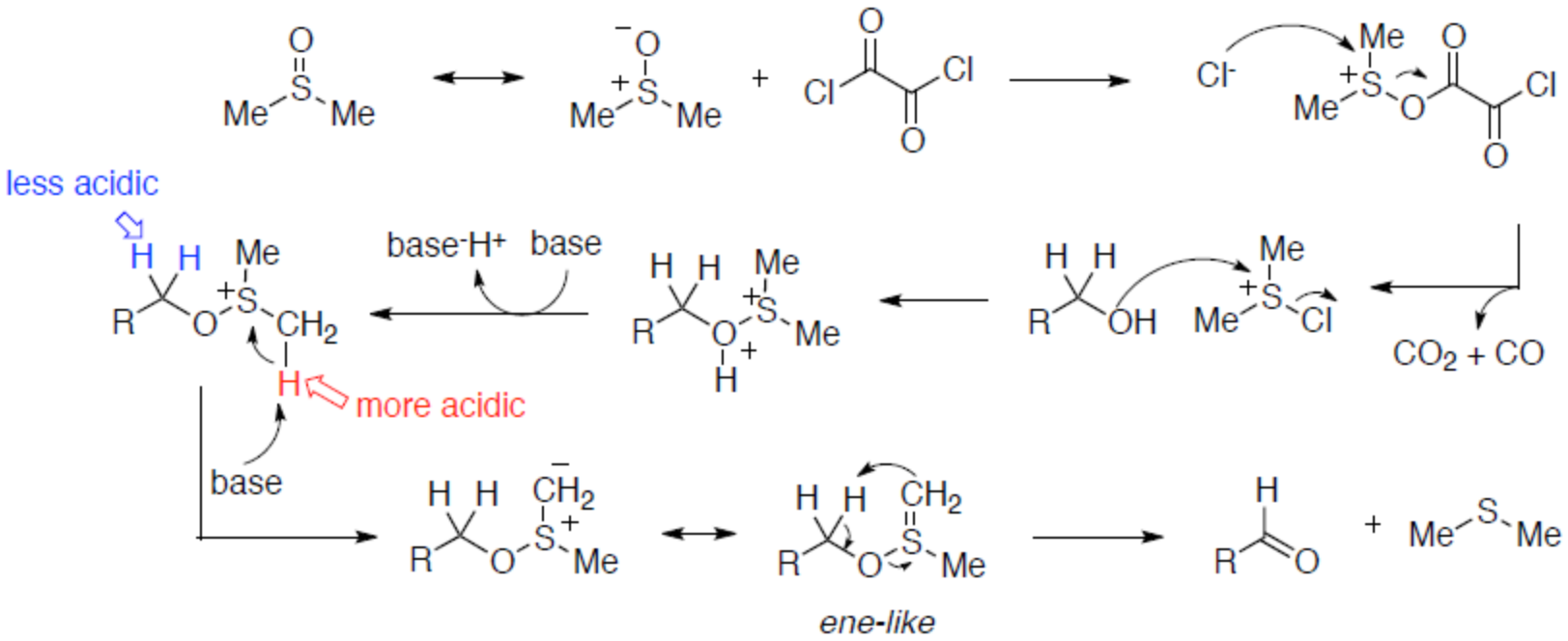


Swern oxidation and other variants

Swern oxidation:

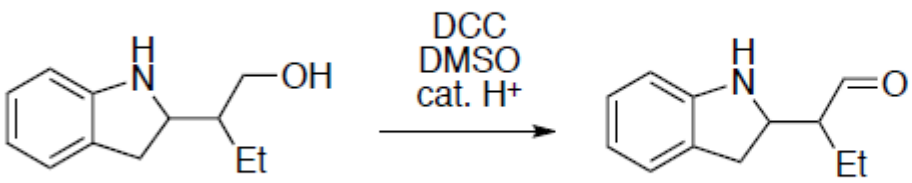


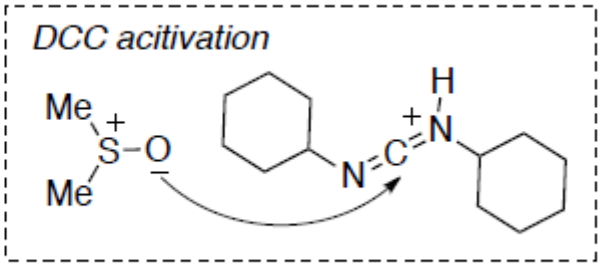
Mechanism:



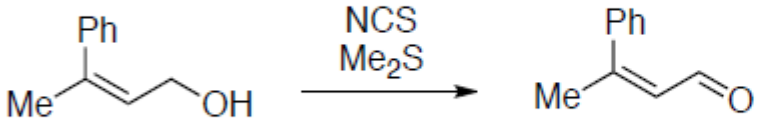
Other varients

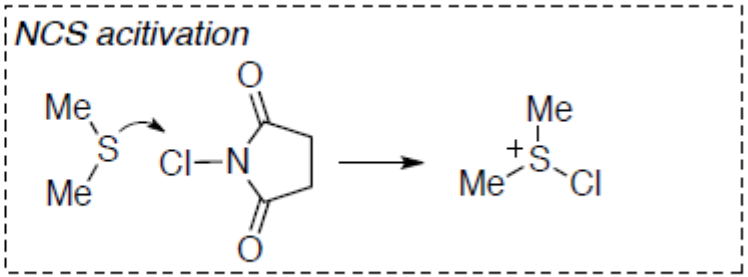
Moffatt oxidation:



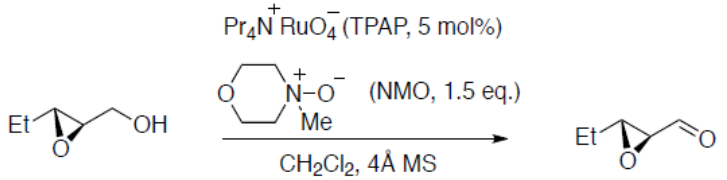


Corey-Kim oxidation:

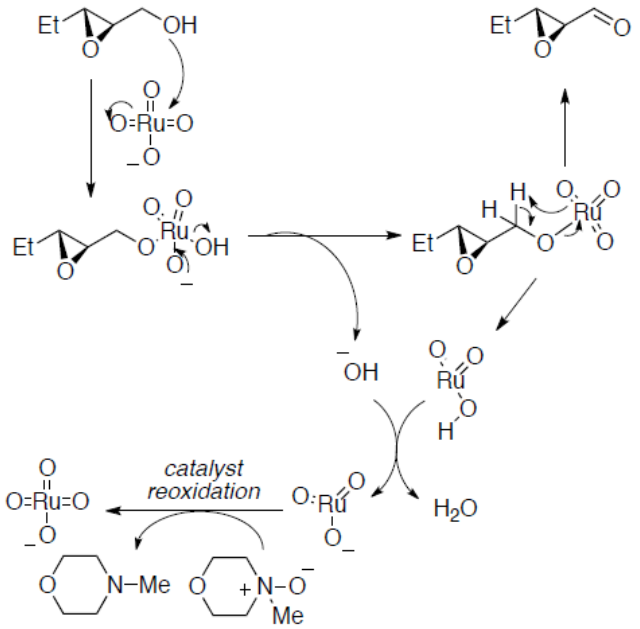




TPAP oxidation

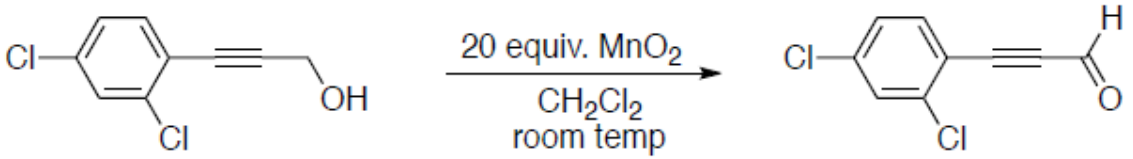


Mechanism

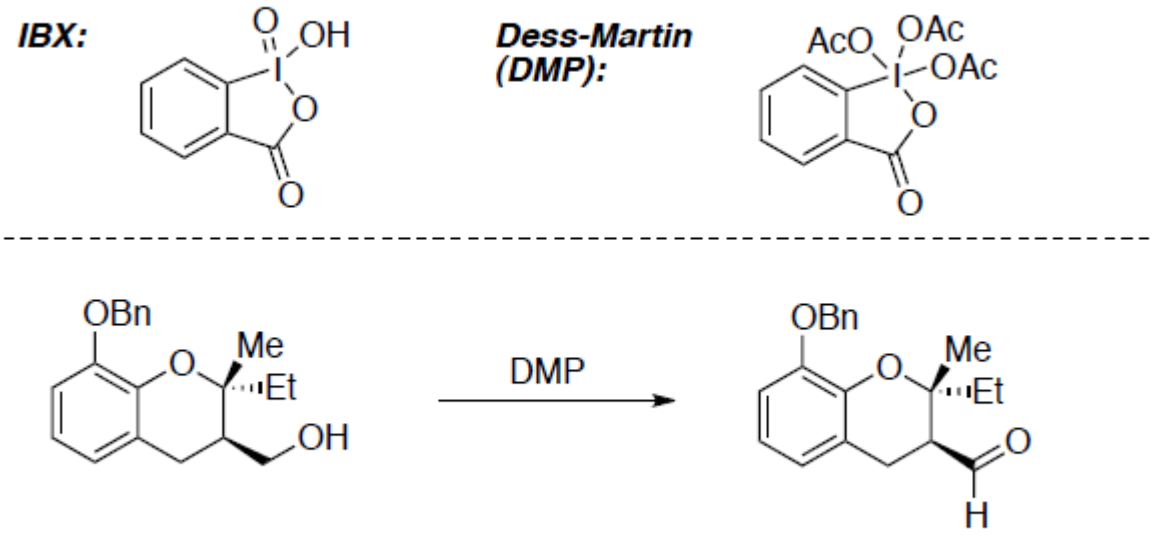


Other metal oxides oxidation (i.e. Cr or Mn) have similar mechanism.

A special feature of MnO_2 oxidation is a mild and selective oxidation of unsaturated system.

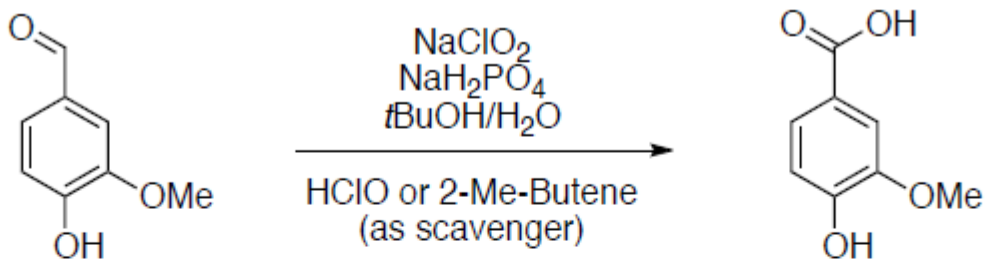


Dess-Martin and IBX oxidation

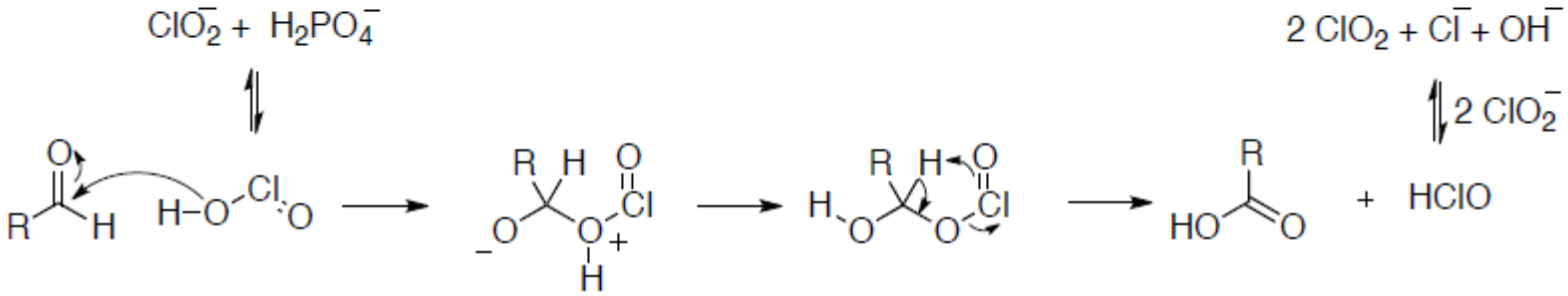


Oxidation of aldehyde (or equivalent) to carboxylic acid derivative

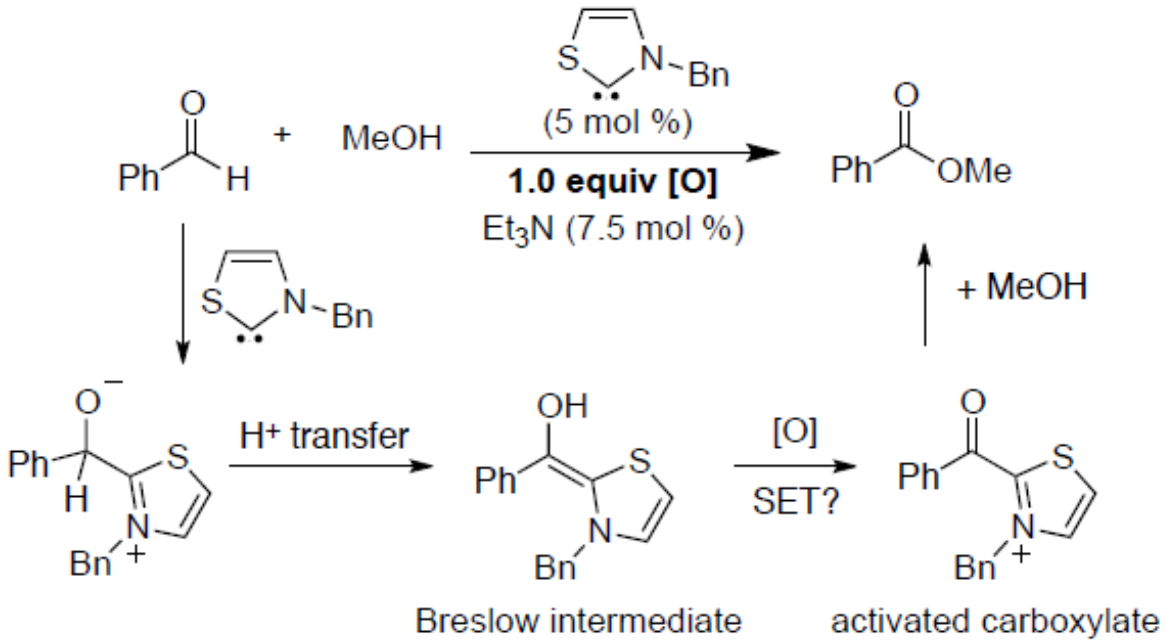
Pinnick oxidation also sometime known as Lindgren oxidation



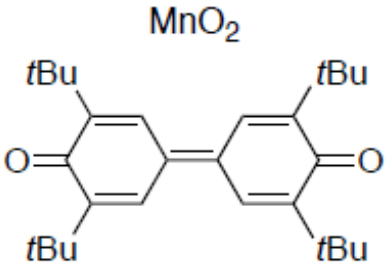
Mechanism



Oxidation by N-heterocyclic carbene (NHC)

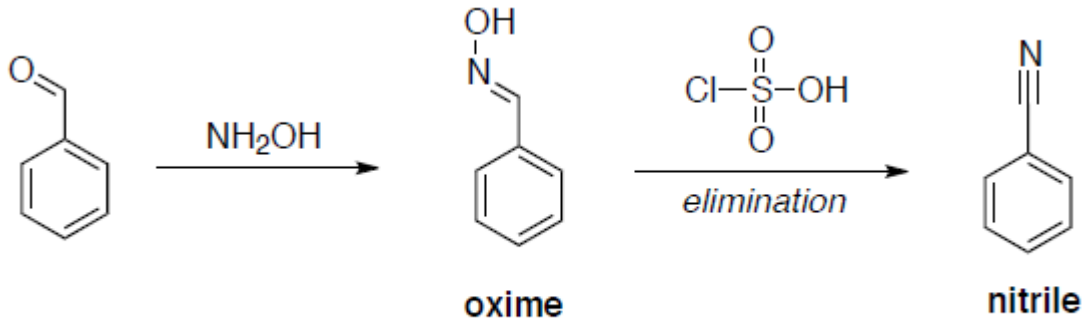


Common oxidant:



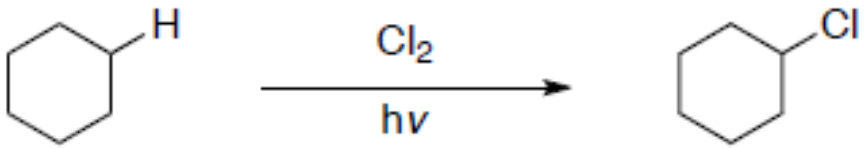
Formal oxidation of aldehyde to nitrile

This is technically an elimination reaction with the net outcome of oxidation of C=O to C≡N bond

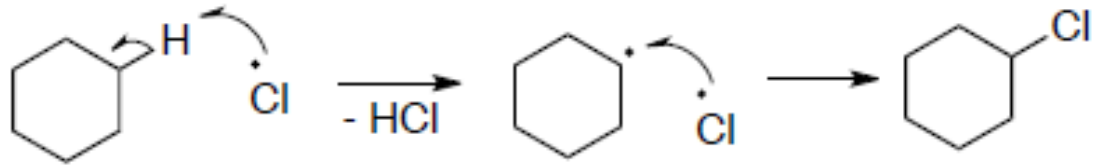


C-H oxidation

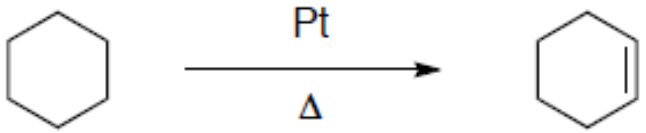
Radical halogenation



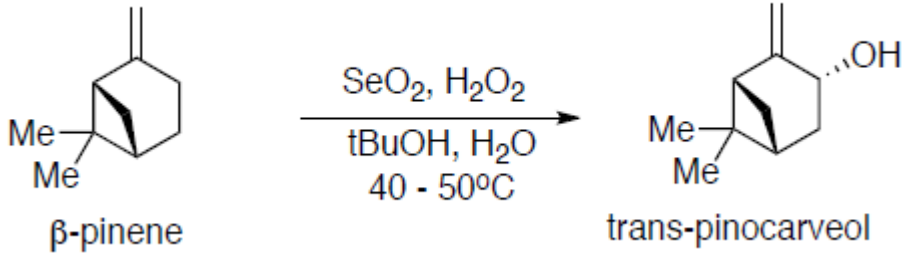
mechanism:



Dehydrogenation: alkane to alkene

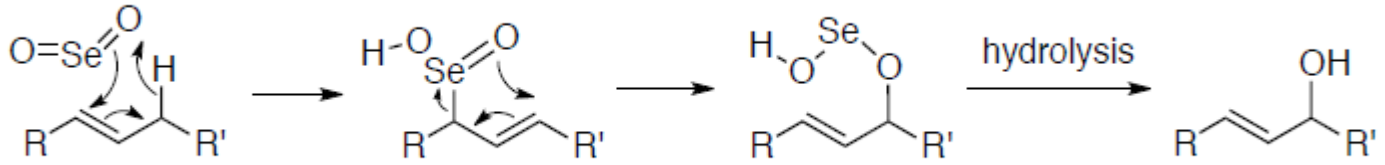


Allylic C-H oxidation



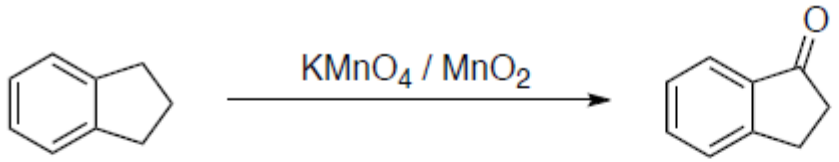
Hartshorn and Masamune *Org. Synth.*, ***1988, 6 , 946.***

Mechanism

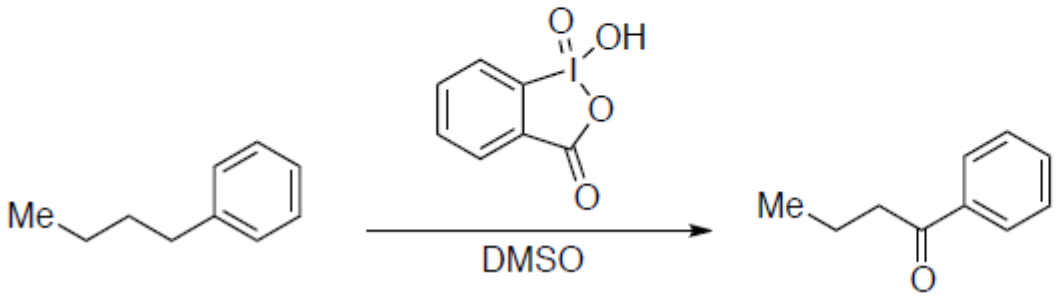


Benzylic C-H oxidation

Many strong oxidants such as KMnO4, IBX or H2O2 may be used for benzylic oxidation



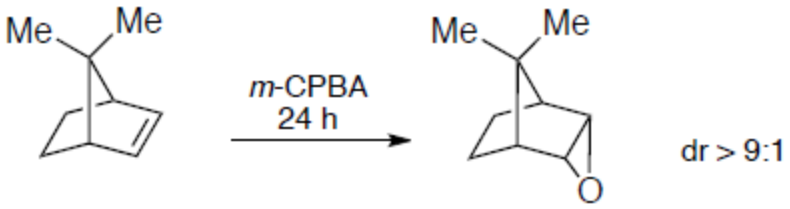
Shaabania *Tetrahedron*, **2004**, *60*, 11415



Nicolaou *JACS* **2002**, *124*, 2245

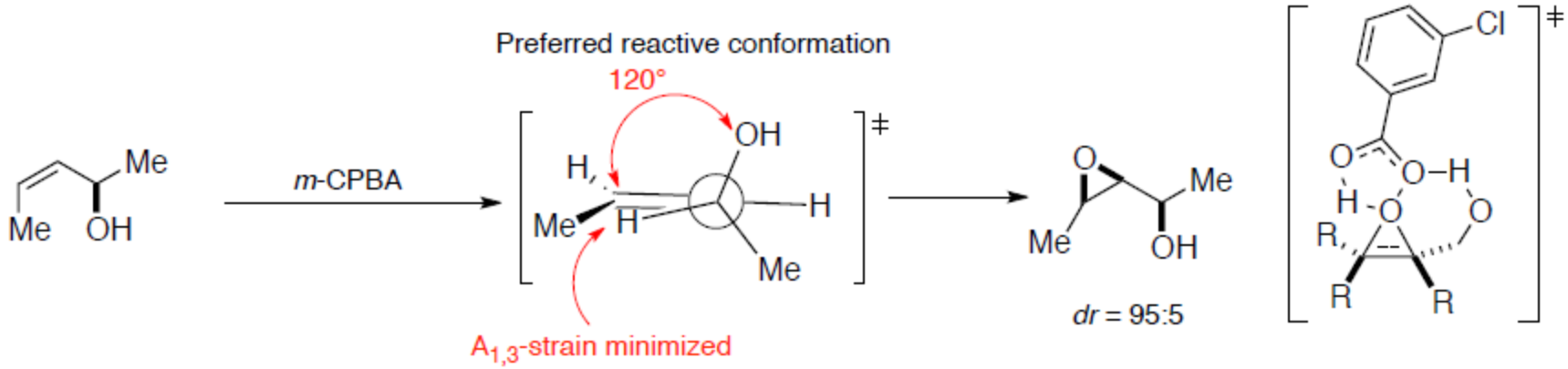
Alkene oxidation

Epoxidation by mCPBA
- This reaction is stereospecific



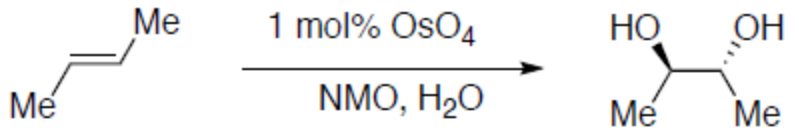
dr > 9:1

Stereochemistry:

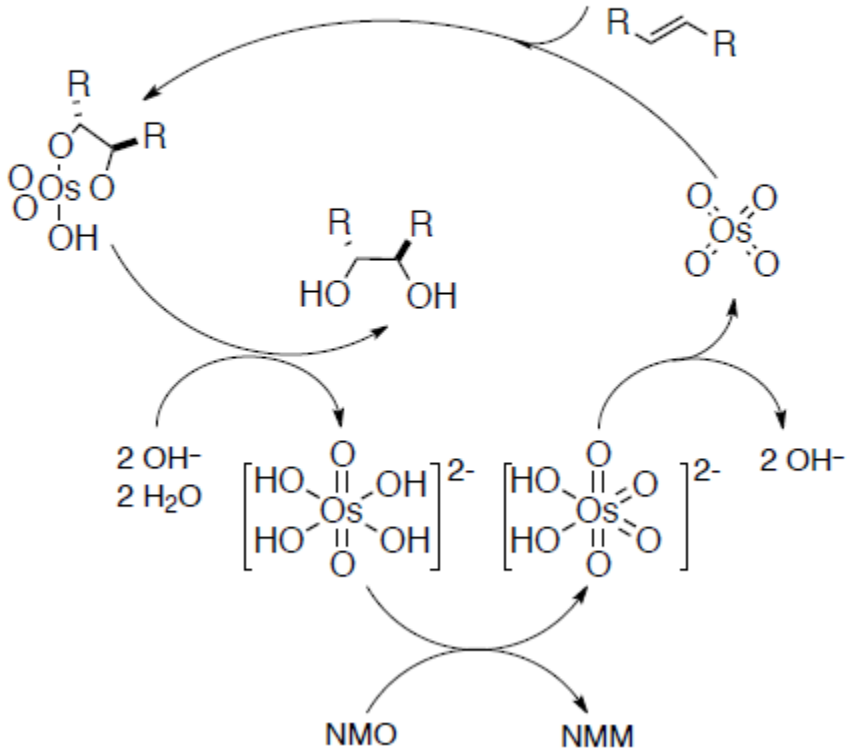


Dihydroxylation

- This reaction is also stereospecific

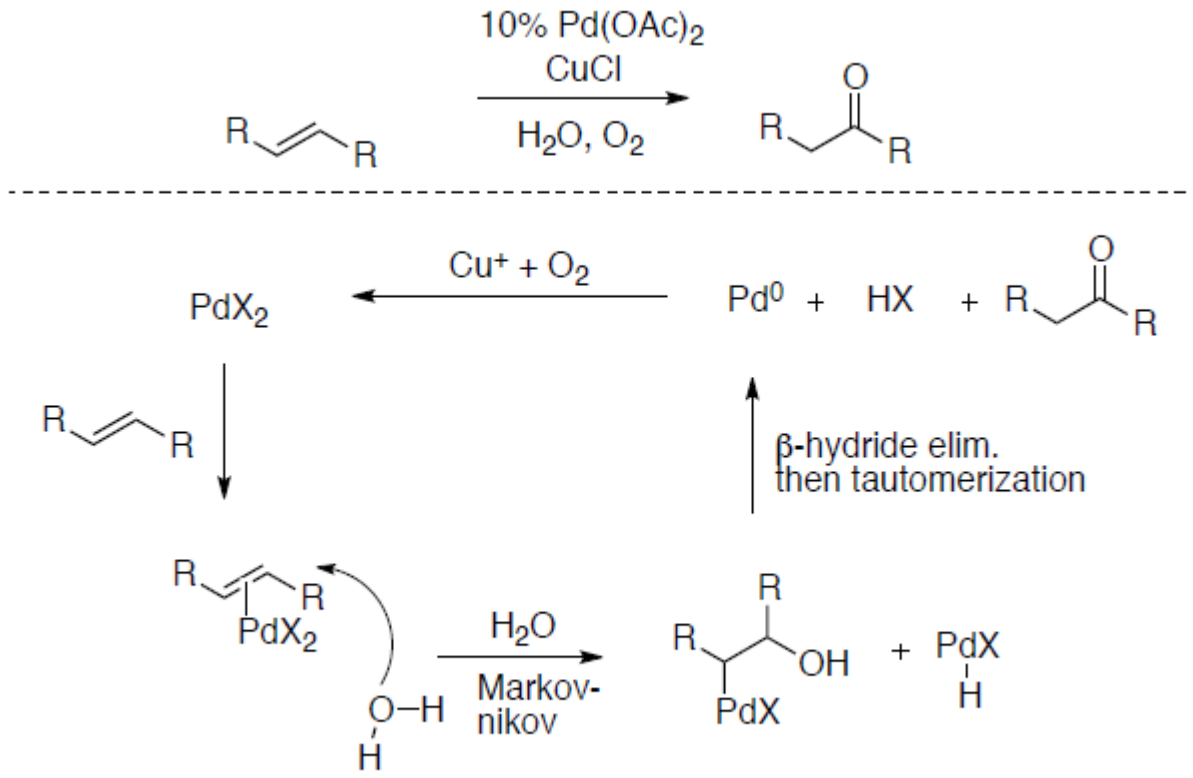


mechanism

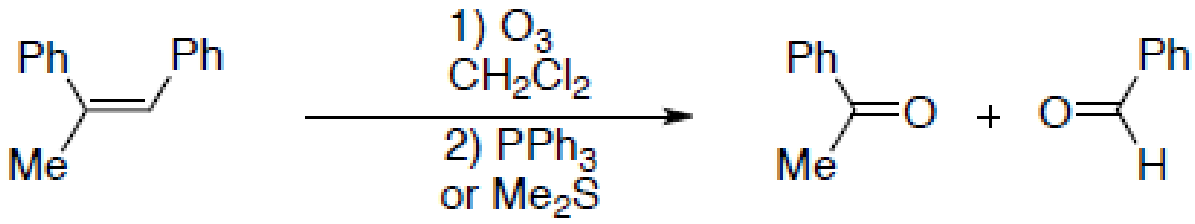


Wacker oxidation

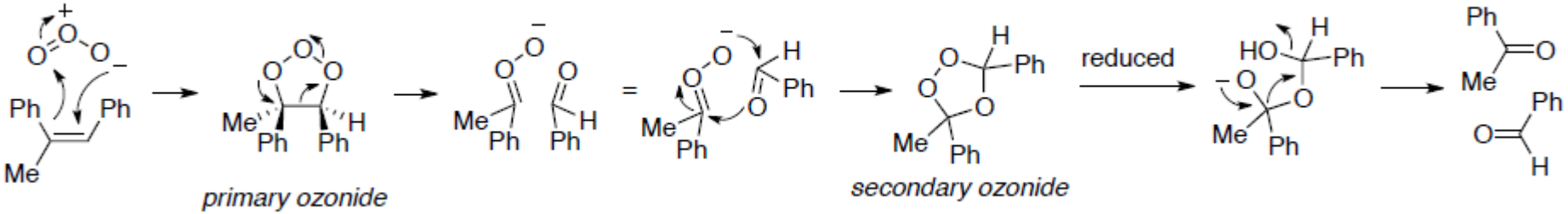
- This reaction generally follows Markovnikov selectivity



Ozonolysis

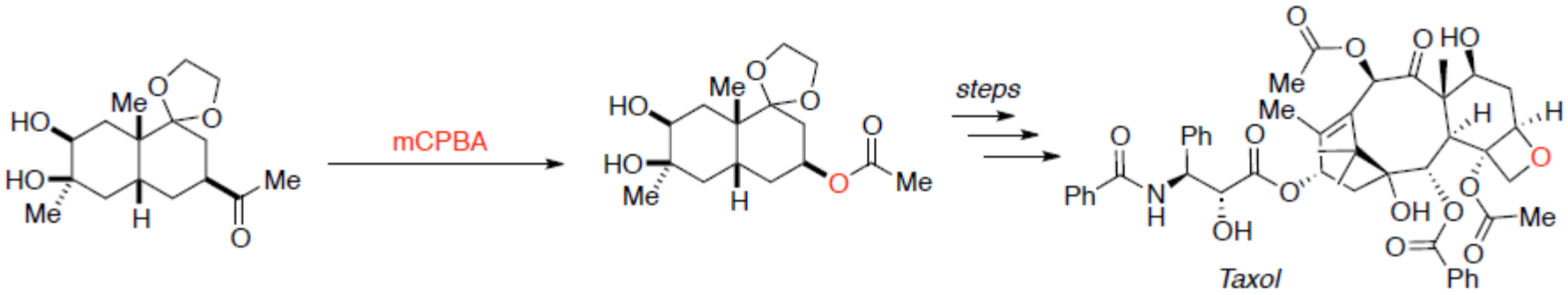


mechanism

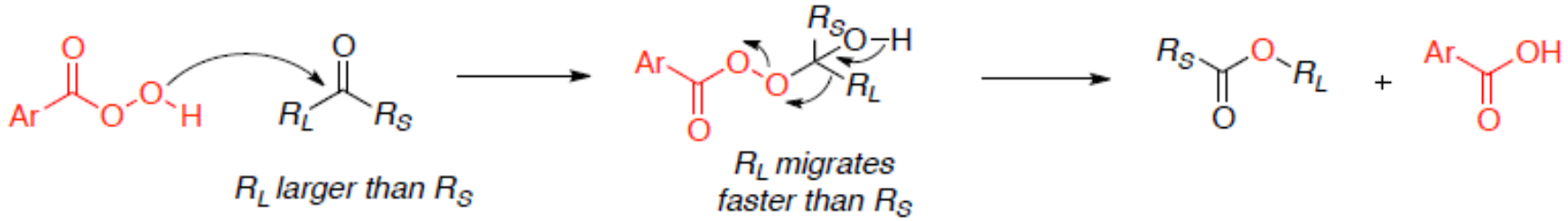


Baeyer-Villiger oxidation

- This reaction is stereoretentive

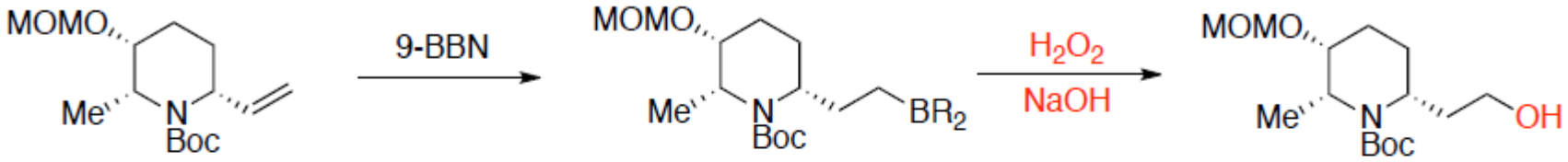


mechanism

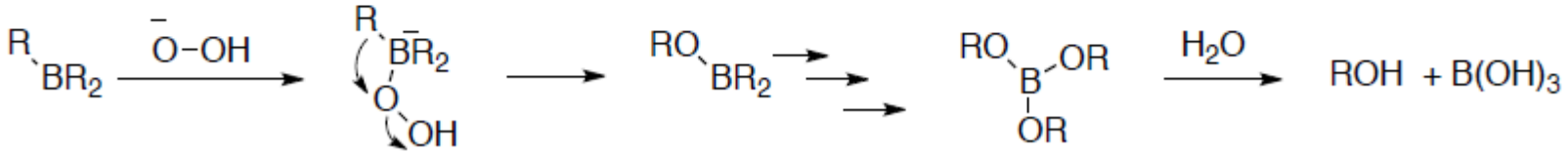


Heteroatom oxidation

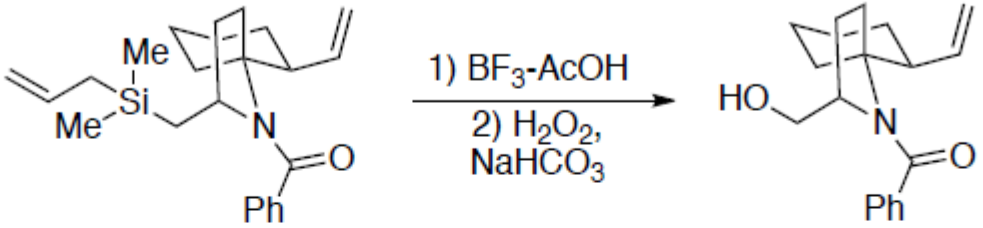
Borane oxidation (in hydroboration sequence)



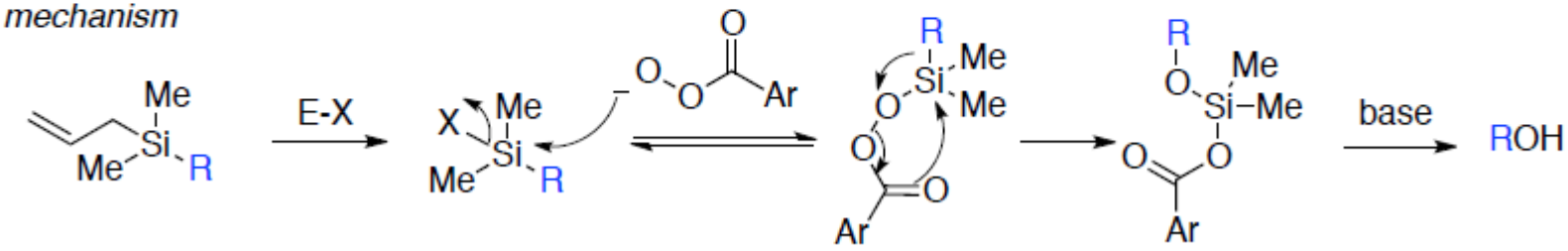
mechanism



Fleming-Tamao oxidation

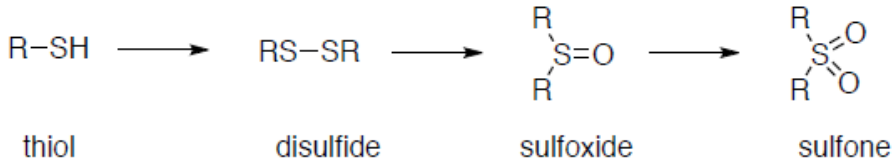


mechanism



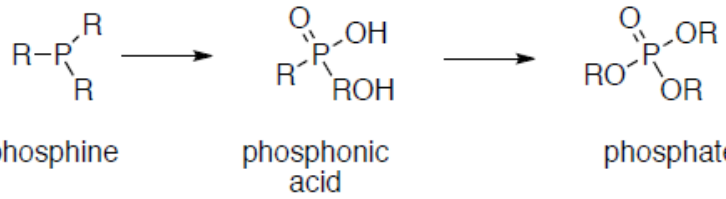
Other functional groups and their oxidation state

Organosulfur reagent



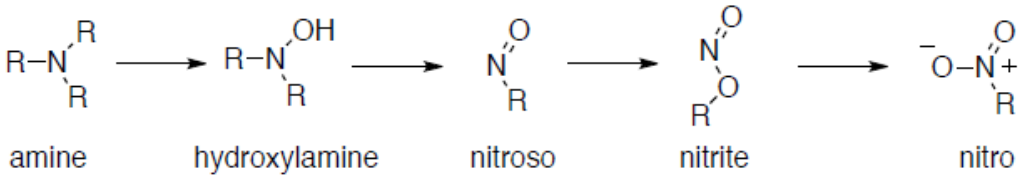
most reduced **most oxidized**

Organophosphorus reagent



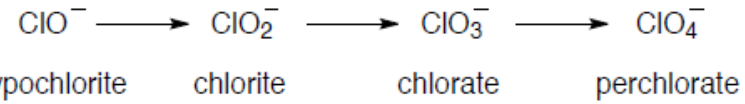
most reduced **most oxidized**

Nitro compound



most reduced **most oxidized**

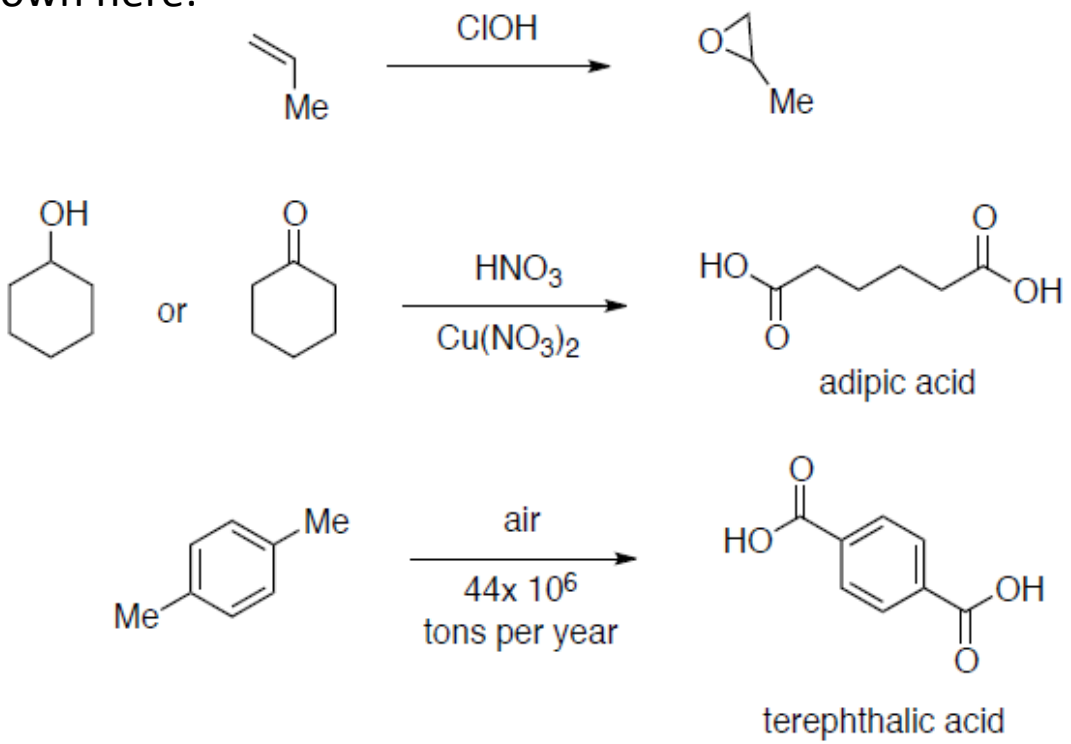
Halogen



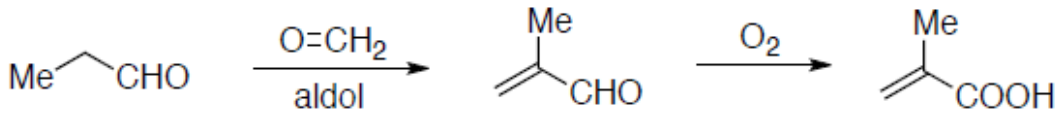
most reduced **most oxidized**

Oxidation used in industrial setting

Oxidation is commonly done in and industrial setting. Many of these processes have been performed in large scale. Examples include oxidation of p-xylene to terephthalic acid (44x 106 tons per year), oxidation of cyclohexane to cyclohexanol and cyclohexanone (6 x 106 tons per year), and the synthesis of ethylbenzene hydroperoxide (6 x 106 tons per year). A few examples are shown here:



BASF's methacrylic acid process:



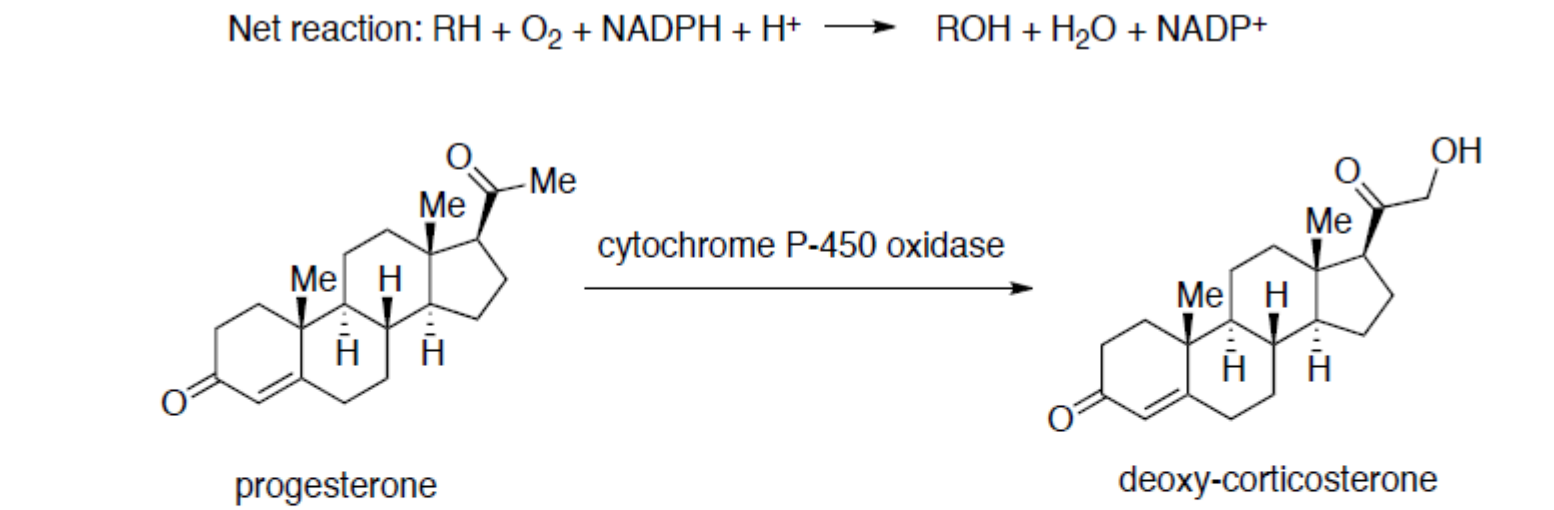
Cavani *ChemSusChem* **2009,** *2*, 508

Biological oxidation

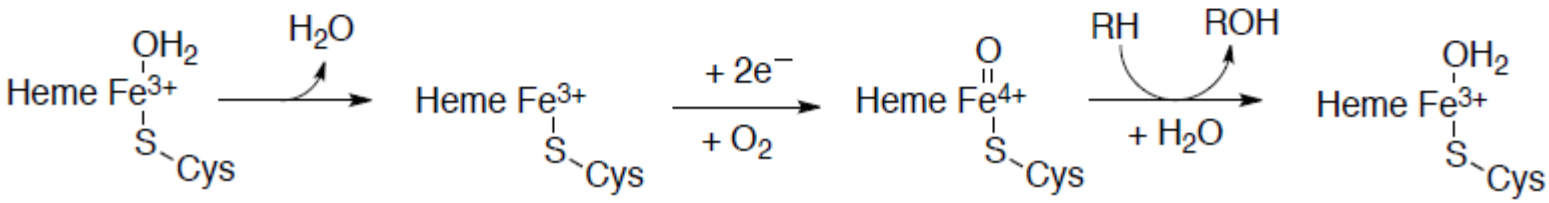
Similar to organic chemists, biology utilizes many oxidation strategies (radical peroxide, metal oxide, etc) for synthesis of important metabolites and for regulation processes.

Cytochrome P-450

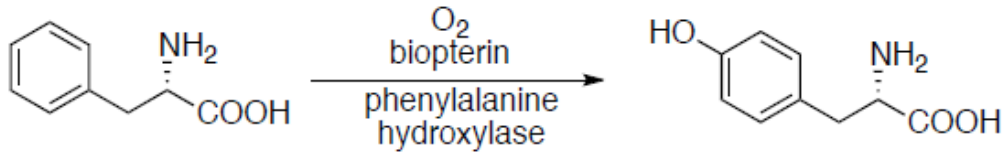
Cytochrome P-450 is a family of enzymes that catalyzes the oxidation of many metabolic intermediates:



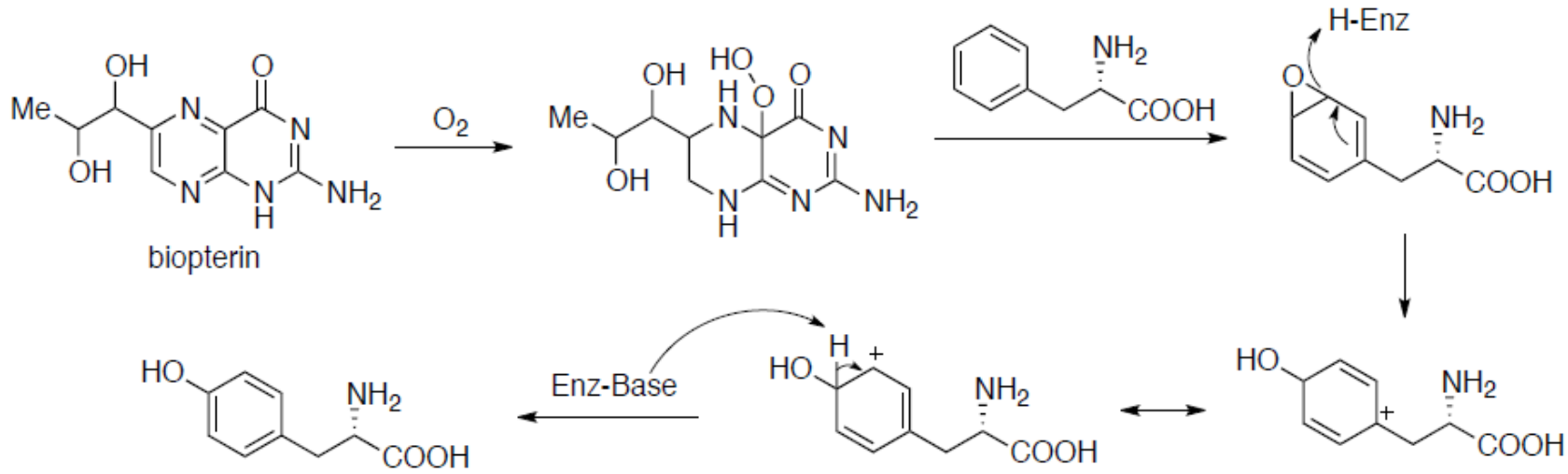
Mechanism



Oxidation of phenylalanine to tyrosine



Mechanism



How does biology stores energy?
Trapping energy released from oxidation in the form of ATP