

Oxidation Reactions

Based on the discussion at the beginning of reductions, it's apparent what is meant in organic terms by oxidation - the removal of H atoms or the addition of O atoms.

The most common oxidation is the oxidation of an alcohol.



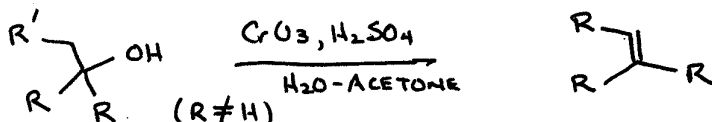
Usually, the most well known oxidation reagents are inorganic reagents containing metal atoms in very high oxidation states.



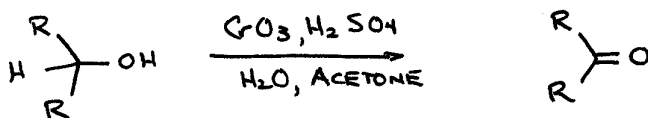
-these oxidations are usually performed in an acidic medium, such as the Jones reagent $\text{CrO}_3 + \text{H}_2\text{SO}_4 + \text{H}_2\text{O}$ /acetone

The result of addition of these oxidants to alcohols depends of the alcohol used.

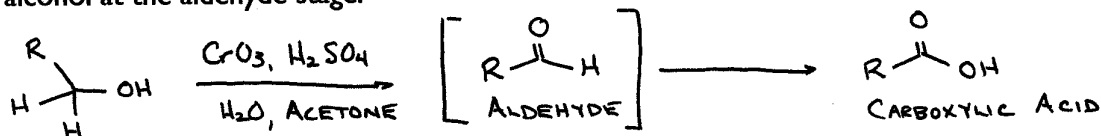
Tertiary alcohols (3°) don't have an α -H, so they don't oxidize, although they may eliminate to alkenes (E1) under the strongly acidic conditions.



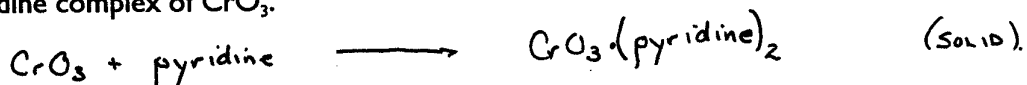
Secondary alcohols oxidize cleanly to ketones



Primary alcohols oxidize to aldehydes, but aldehydes themselves are very easily oxidized in turn up to carboxylic acids. It is usually impossible, with Jones type conditions, to stop the oxidation of a 1° alcohol at the aldehyde stage.



So how do you stop the oxidation of a 1° alcohol at the aldehyde. Much like in the reduction of alkynes problem, by tempering the reactivity of the oxidant. This was originally done by making a pyridine complex of CrO_3 .

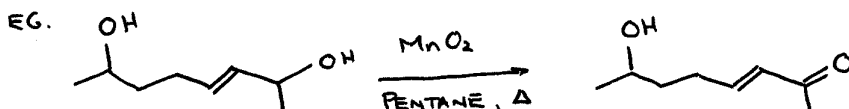
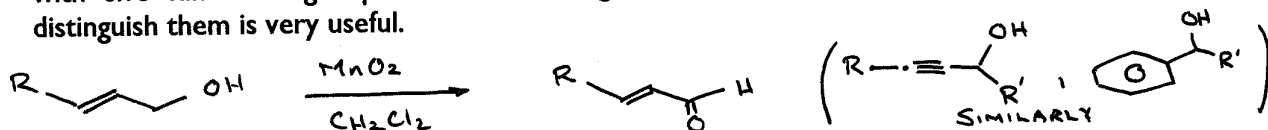


If this complex is used in an inert solvent, such as CH_2Cl_2 or pyridine itself, the 1° alcohol oxidation will stop at the aldehyde.

To reemphasize, this is very mild. Any HCl liberated is consumed by the NEt_3 , so that acid sensitive groups (i.e., protecting groups) are not affected. Furthermore, the side products are gases or low boiling liquids (CO , CO_2 , Me_2S), so that the product is easily separable. The *only* drawbacks are that the actual reagent is only stable at low temperature ($< -50^\circ\text{C}$) and the dimethyl sulphide stinks.

Allylic Oxidations - Manganese Dioxide

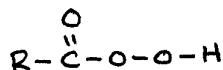
One more conventional oxidation reagent is useful for its specificity. MnO_2 is not an especially active oxidant, so it will oxidize only the most reactive alcohol. These are normally restricted to allylic alcohols (or propargylic alcohols, or benzylic alcohols); alcohols not immediately next to a π -system simply don't oxidize. As a result, one can do a selective oxidation on a system with two functional groups which at first glance look pretty much the same. This ability to distinguish them is very useful.



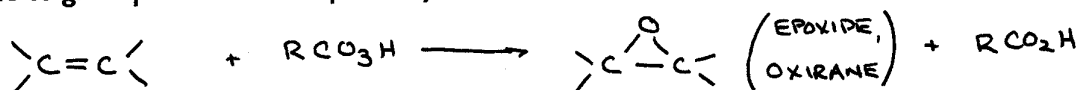
Oxidation of C=X Compounds

1) Epoxidation - Peracids (March 5-36)

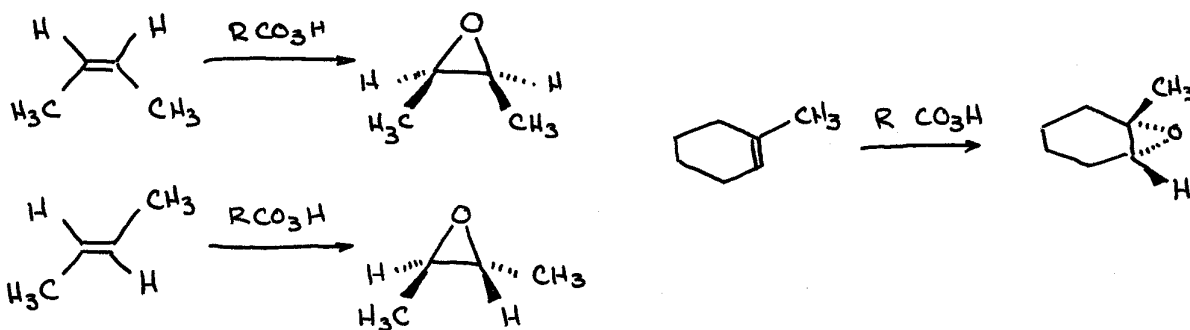
Peracids have the structure
i.e., an ester of HOOH



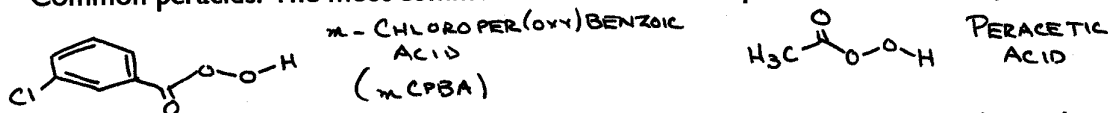
They are normally prepared by oxidation of an aldehyde. The O-O bond of these is relatively weak, and they can be used for oxidation purposes. Their most common reaction is with the $\text{C}=\text{C}$ of an alkene to give epoxides. This is probably the most common way of preparing an epoxide.



Comments: The peracid induced epoxidation of alkene is stereospecific; one gets *cis* addition across the $\text{C}=\text{C}$. (Aside: You should look up the term *stereospecific*, as it is distinguished from the term *stereoselective*)

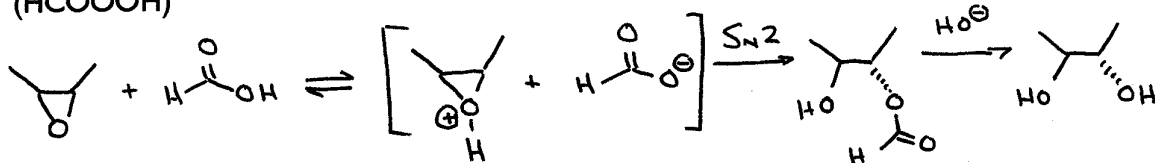


Common peracids: The most common ones are *m*-chloroperbenzoic acid and peracetic acid.



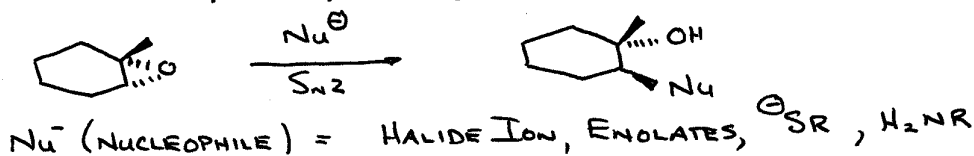
This reaction is very useful because of the subsequent reactivity of the epoxide products:

- 1) Certain peracids lead to further reaction of the epoxide, particularly performic acid (HCOOOH)

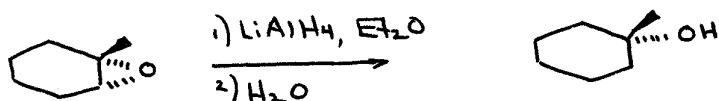


This occurs due to the fact that formic acid is a relatively strong acid - it is an excellent way to make *trans* 1,2-diols (starting from *cis* alkenes).

- 2) Ring opening by nucleophiles
-Epoxides are susceptible to nucleophilic attack due to the ring strain in the three membered ring. Therefore, many nucleophiles which participate in S_N2 type reactions will open the epoxide ring.



- 3) Ring opening by reduction
This is really just a variation on 2), but $LiAlH_4$ (but not normally $NaBH_4$ will also open epoxides (by an S_N2 mechanism), to the alcohol.



Note: There are other reagents which will epoxidize alkenes. The most common of these are alkyl peroxides (usually *t*BuOOH), catalyzed by a transition metal complex { $Ti(O^iPr)_4$, $V(O)(OR)_3$ }. These are especially useful, because they are amenable to chiral epoxidations. This will be left for future courses, though.

Mechanism: The peracid induced epoxidation of alkenes appears to be a concerted, one step mechanism. The alkene is clearly the electron rich partner, and the peracid the electron deficient one. As a result, more electron rich alkenes are normally epoxidized more rapidly, and peracids with more electron withdrawing groups (i.e., CF_3CO_3H) are especially reactive peracids for this purpose.

