

12.7: Oxidizing Agents

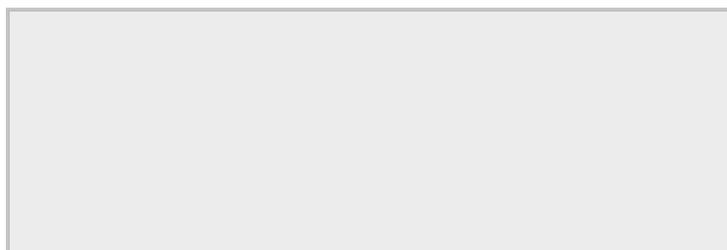
The laboratory oxidation of an alcohol to form an aldehyde or ketone is mechanistically different from the biochemical oxidations with NAD(P)^+ that we saw earlier in this chapter. The general picture of laboratory oxidations is illustrated below. Essentially what happens is that the hydroxide hydrogen of the alcohol is replaced by a leaving group (X in the figure below).



Then, a base can abstract the proton bound to the alcohol carbon, which results in elimination of the X leaving group and formation of a new carbon-oxygen double bond. As you can see by looking closely at this general mechanism, *tertiary alcohols cannot be oxidized in this way* – there is no hydrogen to abstract in the final step!

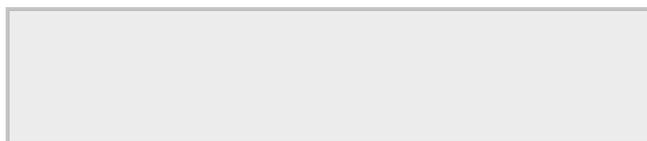
A common method for oxidizing secondary alcohols to ketones uses **chromic acid** (H_2CrO_4) as the oxidizing agent. Chromic acid, also known as **Jones reagent**, is prepared by adding chromium trioxide (CrO_3) to aqueous sulfuric acid.

A mechanism for the chromic acid oxidation of a ketone is shown below.



Note that the chromium reagent has lost two bonds to oxygen in this reaction, and thus has been reduced (it *must* have been reduced - it is the oxidizing agent!).

Ketones are not oxidized by chromic acid, so the reaction stops at the ketone stage. In contrast, primary alcohols are oxidized by chromic acid first to aldehydes, then straight on to carboxylic acids.



It is actually the hydride form of the aldehyde that is oxidized (recall from section 11.3 that aldehydes in aqueous solution exist in rapid equilibrium with their hydrate forms).



One of the hydroxyl groups of the hydrate attacks chromic acid, and the reaction proceeds essentially as shown for the oxidation of a secondary alcohol.

Under some conditions, chromic acid will even oxidize a carbon in the benzylic position to a carboxylic acid (notice that a carbon-carbon bond is broken in this transformation).



A number of other common oxidizing agents are discussed below.

The **pyridinium chlorochromate (PCC)** and **Swern oxidation** reactions are useful for oxidizing primary alcohols to aldehydes. Further oxidation of the aldehyde to the carboxylic acid stage does not occur with these reagents, because the reactions are carried out in anhydrous (water-free) organic solvents such as dichloromethane, and therefore the hydrate form of the aldehyde is not able to form.

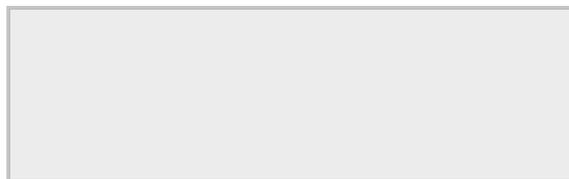
The Swern oxidation uses dimethylsulfoxide and oxalyl chloride, followed by addition of a base such as triethylamine. The actual oxidizing species in this reaction is the dimethylchlorosulfonium ion, which forms from dimethylsulfoxide and oxalyl chloride.



You will be asked to propose a mechanism for these reactions in the end of chapter problems.

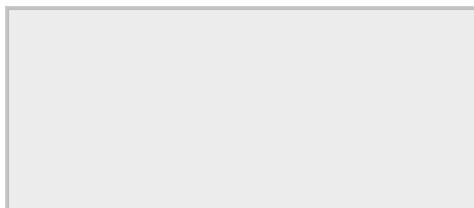


Pyridinium chlorochromate is generated by combining chromium trioxide, hydrochloric acid, and pyridine.



The PCC and Swern oxidation conditions can both also be used to oxidize secondary alcohols to ketones.

Silver ion, Ag(I), is often used to oxidize aldehydes to carboxylic acid. Two common reaction conditions are:



The set of reagents in the latter reaction conditions are commonly known as '**Tollens' reagent**'.

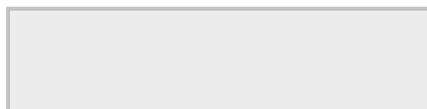
Alkenes are oxidized to *cis*-1,2-diols by **osmium tetroxide (OsO₄)**. The stereospecificity is due to the formation of a cyclic osmate ester intermediate. Osmium tetroxide is used in catalytic amounts, and is regenerated by *N*-methylmorpholine-*N*-oxide.



cis-1,2-diol compounds can be oxidized to dialdehydes (or diketones, depending on the substitution of the starting diol) using **periodic acid**:



Alkenes can also be oxidized by treatment with ozone, O₃. In **ozonolysis**, the carbon-carbon double bond is cleaved, and the alkene carbons are converted to aldehydes:

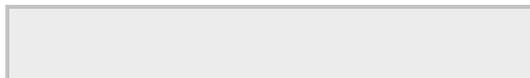


Dimethyl sulfide or zinc is added in the work-up stage of the reaction in order to reduce hydrogen peroxide, which is formed in the reaction, to water.

Alternatively, hydrogen peroxide and aqueous base can be added in the workup to obtain carboxylic acids:



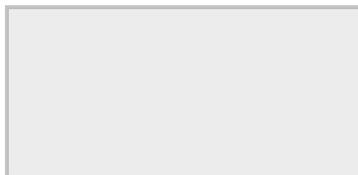
Potassium permanganate (KMnO₄) is another very powerful oxidizing agent that will oxidize primary alcohols and aldehydes to carboxylic acids. KMnO₄ is also useful for oxidative cleavage of alkenes to ketones and carboxylic acids:



Finally, alkenes can be oxidized to epoxides using a '**peroxyacid**' such as *m*-chloroperoxybenzoic acid. Notice the presence of a third oxygen in the peroxyacid functional group.



The mechanism is similar to that of the biological epoxidation catalyzed by squalene epoxidase (section 16.10A), with the π electrons in the alkene double bond attacking the 'outer' oxygen of the peroxyacid and cleaving the reactive O-O peroxide bond.



Uncatalyzed epoxidation of an asymmetric alkene generally results in two diastereomeric epoxide products, with the epoxide adding either from above or below the plane of the alkene.



Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

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