OXIDATION

FUNCTIONAL GROUP TRANSFORMATIONS

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Oxidation of Alcohols to Aldehydes and Ketones

1. Jones Reagent (\(\text{CrO}_3+\text{H}_2\text{SO}_4\) or \(\text{Na}_2\text{Cr}_2\text{O}_7+\text{H}_2\text{SO}_4\))

The Jones reagent is an excellent reagent for the oxidation of secondary alcohols that do not contain acid-sensitive groups such as acetal. Jones reagent consists of chromium trioxide and sulfuric acid dissolved in a mixture of acetone and water. As an alternative, potassium dichromate can be used in place of chromium trioxide. The oxidation is very rapid, quite exothermic, and the yields are typically high. The reagent rarely oxidizes unsaturated bonds.

Oxidation of primary alcohols with Jones reagent may result in the conversion of the aldehydes initially formed to the corresponding carboxylic acids.

**Work up**- The reagent is added to the alcohol contained in acetone at 0-25 °C, and the excess Cr(VI) is destroyed in the reaction workup by adding some isopropyl alcohol (colour change from orange to blue green).

**Reaction Mechanism**-
Jones oxidation is very easy to carry out as it does not need anhydrous or inert conditions. It is the oxidation of choice for robust substrates on a big scale. It is not suitable for acid sensitive substrates and also for the preparation of many aldehydes.

2. Pyridinium Chlorochromate (PCC)-

Pyridinium chlorochromate (PCC) is an oxidizing agent which can oxidized alcohols to aldehydes and ketones. PCC is formed from the reaction between pyridine, chromium trioxide and hydrochloric acid. Chlorochromatic acid can be prepared by the dissolution of chromium trioxide in aqueous hydrochloric acid. Addition of pyridine gives pyridinium chlorochromate as orange crystals.

3. Swern Oxidation-

The Swern oxidation, named after Daniel Swern, is a chemical reaction whereby a primary or secondary alcohol is oxidized to an aldehyde or ketone using oxalyl chloride, dimethyl sulfoxide (DMSO) and an organic base, such as triethylamine.

Activation of dimethylsulfoxide (DMSO) by oxalyl chloride produces intermediate A (below) that decomposes rapidly at -78 °C to furnish chlorodimethylsulfonium chloride (B) along with CO and CO$_2$. Reaction of B with RCH$_2$OH (or R$_2$CHOH) leads to intermediate C, which upon addition of Et$_3$N and warming affords the corresponding carbonyl compound, Me$_2$S and Et$_3$NH$^+$Cl$^-$.

**Reaction Mechanism**

![Reaction Mechanism Diagram]

**Examples**-

![Examples Diagram]
4. Dess-Martin Periodinane (DME oxidation)

The Dess-Martin oxidation of alcohols has proven to be an efficient method for the conversion of primary and secondary alcohol to aldehydes and ketones respectively.

![Reaction mechanism diagram]

The oxidation proceeds under mild reaction conditions and is especially suitable for multifunctional substrates containing acid-sensitive groups.

The DMP reagent has several advantages over Cr(VI) and DMSO-based oxidizing reagents. These include use of DMP in a near 1 to 1 stoichiometry, relative ease of preparation, shorter reaction times, simplified workups, and lower toxicity.

Example-

![Example reaction diagram]

5. Activated Manganese Dioxide (MnO₂)

MnO₂ is a highly chemoselective oxidant. Allylic, benzylic and propargylic alcohols are oxidized faster than saturated alcohols. The oxidation takes place under mild conditions in H₂O, acetone, or CHCl₃.
The reaction is selective because allylic and benzylic alcohols react much more rapidly than “ordinary” alcohols. An understanding of this selectivity comes from the mechanism. In the first step of the mechanism, the $\text{O}—\text{H}$ group of the alcohol rapidly adds to $\text{MnO}_2$ to give an ester.

\[
\text{ROH} + \text{MnO}_2 \rightleftharpoons \text{RO\text{MnO}} \text{H}
\]

(The solid-state structures of the Mn-containing species are simplified in these equations.) In the next step, which is rate-limiting, Mn(IV) accepts an electron to become Mn(III), and, at the same time, a hydrogen atom is transferred from the allylic or benzylic carbon to an oxygen of the oxidant. The product has an unpaired electron on the allylic or benzylic carbon and is therefore a resonance-stabilized radical.

The stability of the radical intermediate, by Hammond’s postulate, increases the rate of this step. The allylic/benzylic selectivity occurs because the analogous radical intermediate in the oxidation of an alcohol that is not allylic or benzylic is less stable and is formed more slowly. In the rapid final step, Mn(III) is reduced to the more stable Mn(II), and a strong CAO double bond is formed to give the aldehyde product, which is washed away from the oxidant surface by the solvent.
6. The Babler Oxidation

A carbonyl transposition can be effected via the addition of a vinyl or an alkyl Grignard reagent to an α β -unsaturated ketone. Acid-catalysed rearrangement of the resultant allylic alcohol during oxidation with PCC affords the transposed α β unsaturated carbonyl substrate. This reaction represents a useful alternative when Wittig olefination of the ketone is problematic.
7. Corey-Kim Oxidation

The Corey-Kim Oxidation allows the synthesis of aldehydes and ketones from primary alcohols and secondary alcohols, respectively.
Mechanism-

Dimethylchlorosulphonium ion is generated *in situ* from NCS and DMS

8. Parikh–Doering oxidation –

The Parikh–Doering oxidation is an oxidation reaction that transforms primary and secondary alcohols into aldehydes and ketones, respectively. The
procedure uses dimethyl sulfoxide (DMSO) as the oxidant, activated by the sulphur trioxide pyridine complex in the presence of triethylamine base.

Mechanism-

Dimethyl sulfoxide (DMSO), which exists as a hybrid of the resonance structures with sulphur trioxide giving intermediate A. Nucleophilic attack by alcohol and deprotonation by pyridine gives intermediate B. The addition of two equivalents of base deprotonates the alkoxysulfonium ion to give sulphur ylide and removes the pyridinium sulphate counterion. In the last step, the ylide goes through a five-membered ring transition state to give the desired ketone or aldehyde as well as an equivalent of dimethyl sulphide.

Not surprisingly, acid sensitive functionalities and protecting groups are not deprotected under Parikh–Doering conditions. Such groups include: acetals, glycosides, amines protected with Boc and alcohols protected with TMS, TBS, MOM and t-Bu. The Parikh–Doering oxidation provides a very high regioselectivity for the oxidation of alcohols. Oxidation-sensitive functionalities, like indoles, sulphide, and selenides, as well as oxidation-sensitive protecting groups, like dithiaoacetals, PMB, and dimethoxybenzyl ethers do not react.
9. Fetizon’s Reagent-

The mild oxidation of alcohols into carbonyl compounds in refluxing benzene using silver carbonate absorbed on celite as the oxidant is generally referred to as Fétizon oxidation, and the silver carbonate on celite is often called Fetizon’s reagent. This reaction is found to be useful in the preparation of aldehydes, ketones, lactones, quinones, and quinoxalines.

It is a mild reagent, suitable for both acid and base sensitive compounds. Its great reactivity with lactols makes the Fétizon oxidation a useful method to obtain lactones from a diol. The reaction is inhibited significantly by polar groups within the reaction system as well as steric hindrance of the α-hydrogen of the alcohol.

Mechanism

The oxidation proceeds via a highly symmetric transition state whereby the oxygen from the alcohol complexes with a silver cation, while another silver cation interacts with the hydrogen at the α-position of the alcohol.
Thus, Fetizon’s oxidation must be performed in very apolar solvents because even solvents with very weak basicity, such as ethyl acetate or methyl ethyl ketone, severely inhibit the oxidation. That is why, Fetizon’s oxidation is routinely performed in boiling benzene, which is a very apolar solvent with the added advantage of allowing the elimination of water produced during the oxidation by azeotropic distillation.

**Examples**

An alcohol is oxidized with Fetizon’s reagent in the presence of oxidation-sensitive dialkoxy alkene that, for instance, suffers selective cleavage with no reaction on the alcohol moiety on contact with PCC.
A Fetizon’s oxidation allows the attention of the desired a hydroxyketone with a 90% yield, while Collins reagent, PCC and PDC produce an oxidative breakage of a C-C bond, Jones and Moffatt oxidations yield complex mixtures and a Corey-Kim oxidation returns unreacted material.

As Fetizon’s oxidation is carried out under neutral conditions, acid and base-sensitive protecting groups resist its action. The oxidation-sensitive p-methoxybenzyl (PMB) protecting group resists the action of Fetizon’s reagent.

10. Oppenauer Oxidation-

Oppenauer oxidation, named after Rupert Viktor Oppenauer is a gentle method for selectively oxidizing secondary alcohols to ketones. The reaction is the opposite of Meerwein–Ponndorf–Verley reduction. The alcohol is oxidized with aluminium isopropoxide in excess acetone. This shifts the equilibrium toward the product side.

Normally, Oppenauer oxidations are performed employing $\text{Al}^{3+}$ cations as catalyst because aluminium alkoxides possess a good balance of a desired high hydride transfer capability versus a low propensity to promote undesired base-induced reactions, like aldol condensations and Tischtschenko reactions. In the reaction, as originally described by Oppenauer, aluminium t-butoxide is used as catalyst because its high basicity allows a very favourable equilibrium towards the formation of the aluminium alkoxide of the alcohol whose oxidation is desired.

Mechanism-
Mechanism for the Oppenauer oxidation, involving an initial complexation of a carbonyl group with the aluminium from an aluminium alkoxide, followed by a rate-determining hydride transfer via a six-membered transition state.

Oxidation of Aldehydes Carboxylic Acids

Oxidation of Aldehydes Carboxylic Acids to many of the oxidants employed to prepare aldehydes from primary alcohols may be used to further oxidize the aldehyde initially formed to the corresponding carboxylic acid. The most common oxidants for this purpose include KMnO$_4$, chromic acid, sodium chlorite, silver oxide and PDC in DMF.

\[
\text{RCHO} \xrightarrow{\text{KMnO}_4, \text{t-BuOH}} \text{RCOOH} \\
\text{RCH}_2\text{OH} \xrightarrow{\text{Jones Reagent}} \text{RCOOH} \\
\text{RCHO} \xrightarrow{\text{Ag}_2\text{O}, \text{H}^+} \text{RCOOH}
\]

Allylic oxidation of alkenes

1. Selenium Dioxide (SeO$_2$)

Alkenes possessing allylic C-H bonds are oxidized by SeO$_2$ either to allylic alcohols or esters or to $\alpha$ $\beta$-unsaturated aldehydes or ketones, depending on the experimental condition. The reaction involves an ene-type reaction (A)
followed by a sigmatropic [2,3]-shift (B) to give the selenium ester (C), which is converted to the corresponding allylic alcohol (D) on solvolysis.

Examples-

2. Chromic Anhydrides
Reaction of chromic anhydride (CrO₃) with t-butanol yields t-butyl hydrogen chromate, a powerful oxidant suitable for allylic oxidation of electron-deficient alkenes. Oxidations using tBuOCrO₃ in CCl₄, are highly exothermic and should be performed with caution.
Thank You!