Oxidation is an important process and has played an important role in organic synthesis\(^1\). Oxidation of various compounds such as alkanes, alkenes, alkynes, arenes, ethers, alcohols, aldehydes, ketones amines etc. are oxidized by several oxidizing agents such as KMnO\(_4\), Osmium tetroxide, Ruthenium tetroxide, Cr(VI) compounds, Palladium (II) and Platinum (II) compounds, Lead (IV), Hg(II), Thallium (II) compounds, copper (II), Vanadium pentoxide, Manganese dioxide, Cobalt (III), selenium dioxide, glycol-cleavage agents in the oxidative scission of carbon-carbon double bonds, peracid, peroxide.

Majority of the oxidation processes employed industrially involve catalysis by metal and their compounds.

A brief discussion on different reactions related to oxidation of alcohols with different oxidizing agents has been given below.

**II. 1. Oxidation of Alcohols with Different Oxidizing Agents**

**II. 1. A. Oxidation of alcohols with Potassium permanganate:**

Primary and secondary alcohols are readily oxidized by permanganate ion both in acidic and basic medium.\(^2\^-\)\(^5\) Permanganate ion is a strong oxidizing agent and the product obtained from the oxidation of alcohol is mainly corresponding carboxylic acid\(^3\). (Scheme-1)

![Scheme-1](image-url)
Under neutral or mild acidic conditions the rate of reaction is very slow; e.g. the relative rates of oxidation of 2-butanol under alkaline, acid and neutral conditions are 21:25:1; however, addition of peroxide is known to accelerate the rate of oxidation in dilute acid.\(^6\)

Stewart & Co-Workers \(^7\)-\(^11\) reported that the rate acceleration in basic solution is caused by ionization of the alcohols to give alkoxide ion which readily transfers electrons to the oxidants. (Scheme-2)

\[
\begin{align*}
R_2\text{CHOH} & \overset{\text{OH}^-}{\rightleftharpoons} R_2\text{CHO}^- \\
R_2\text{CHO}^- & \overset{\text{MnO}_4^-}{\rightarrow} R_2\text{CO}
\end{align*}
\]

In general good yields are obtained from alkaline permanganate oxidation except when the initial product is an enolizable aldehyde or ketone. In such cases oxidation of the enolic C-C double bond may become a serious side reaction.

Alkaline permanganate has been successfully used in the oxidation of carbohydrates to monocarboxylic acid derivatives.\(^12\), \(^13\) In this procedure all the hydroxyl except the one undergoing oxidation are first protected by acetoneation or similar means. For example Link and Sell\(^12\) have been describing the
conversion of diacetone D-galactose (8) to diacetone D-galacturonic acid (9).

(Scheme-3)

\[ \text{MnO}_4^- + H^+ \rightleftharpoons \text{HMnO}_4 \]

Since permanganate is a fairly vigorous and non-selective oxidant, it does not readily lend itself to use in organic solvents. However, acid permanganate oxidation can be conducted in glacial acetic acid; e.g., Neidig and co-workers \(^ {15}\) obtained good yields of alkyl phenyl ketones (71-96\%) by the oxidation of alkylphenylcarbinol. A solution of potassium permanganate dissolved in 175ml water and 400ml of glacial acetic acid was added dropwise to a stirred solution of
the alcohol over a period of 3 hr during which time the temperature was maintained between 25-30°C. The products then isolated by steam distillation and purified by conventional methods. Yields were greatly decreased with t-alkylphenylcarbinols because these compounds readily undergo cleavage to give benzaldehyde. (Scheme-4)

![Scheme-4]

Under neutral aqueous conditions 1, 4-diols undergo an oxidative cyclization to give γ-lactones when treated with permanganate ion. (Scheme-5)

![Scheme-5]

II. 1.B. Oxidation of alcohols with Manganese Dioxide:

Manganese dioxide occupies an important place as oxidants because of its considerable selectivity. MnO₂ exhibits considerable selectivity and under mild conditions it is a specific oxidant for α, β-unsaturated alcohols. However in the
absence of unsaturation. It will also slowly attack primary and secondary alcohols to give aldehydes and ketones in good yields. It can be used as a suspension in a variety of solvents (water, acetic acid, carbon tetrachloride, chloroform, methylene chloride, hexane, benzene, tetrahydrofuran, isopropyl alcohol, acetonitrile, ether ethyl acetate, pyridine, DMSO etc.) to selectively convert α, β-unsaturated alcohols to α, β-unsaturated carbonyl compounds but other easily oxidizable functional groups such as carbon-carbon double bonds, saturated alcohols and vicinal glycols are much less readily attacked by this reagent at room temperature. These may be understood from following reactions. 17-19 (Scheme-6)

Scheme-6
It is apparent that it makes little difference if the unsaturation is part of an olefinic, acetylenic, aromatic, and allylic or carbonyl system. \( \alpha \)-hydroxy ethers are also oxidized by \( \text{MnO}_2 \), suggesting that the reaction may be initiated with any structure that provides an electron-rich source in the position adjacent to the hydroxyl\(^{20} \). Much evidence has accumulated suggesting that the activity of this reagent depends on the procedure used in its preparation.\(^{17,21-23} \)

**II.1.C. Oxidation of alcohols with Lead Tetraacetate:**

Lead Tetraacetate can be used as an alcohol oxidant in a variety of solvents including acetic acid, benzene, heptane, pyridine, chloroform and mixtures of these. Isolation of the crystalline ester from a wet methanol solution of lead tetraacetate indicates that the reaction probably proceeds by way of an esterification mechanism reminiscent of the one previously discussed for chromic acid oxidations\(^{24} \). In nonpolar solvents these esters can then undergo decomposition to give carbonyl compounds, cyclic ethers or olefins. All these products can be formally accounted for by assuming a cyclic transfer of electrons with concomitant hydrogen abstraction from either the \( \alpha \)-, \( \beta \)-, \( \delta \)- or \( \varepsilon \)-carbons.

If hydrogen is abstraction from \( \alpha \)-position, the products are carbonyl compounds.(**Scheme-7**)
With short chain primary aliphatic alcohols almost equal quantities of ether and aldehyde are formed, but with longer chain primary and secondary alcohols the yield of carbonyl product decreases.\(^{(26, 27)}\) (Scheme-8)

Mihailovic and co-workers\(^{(28)}\) investigated optimum conditions for the formation of cyclic ethers from aliphatic alcohols and found it best to dissolve both the alcohol and the oxidant in benzene before starting the reaction by applications of heat.

The products obtained from oxidations of $\delta$,$\varepsilon$- and $\gamma$, $\delta$-unsaturated alcohols can be satisfactorily accounted for by similar cyclic electron transfers.\(^{(29, 30)}\)

In such cyclic mechanism it is difficult to assign the direction of electron flow and thus determine if the hydrogen is being transferred as a proton, as a hydride ion, or as an unchanged atom. Hence the arrows used in the above
formulation are illustrative of only one of three possibilities. Current evidence, in fact, indicates that an ionic mechanism predominate in acetic acid and pyridine solutions, with single-electron shifts being more likely in nonpolar solvents such as benzene and heptanes. (Scheme-9)

(Scheme-9)

For example:

\[
\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{OH} \quad \text{Pb(OAc)}_2/\text{C}_6\text{H}_6 \quad \text{reflux} \quad \text{CH}_2=\text{CHCH}_2\text{OAc} + \text{CH}_2=\text{CHCH}_2\text{CH}_2\text{OCH}_2\text{CH=CH}_2
\]

\[(30\%) + \text{CH}_2=\text{CHCH}_2\text{CH}_2\text{OAc} + \text{CH}_2=\text{CHCH}_2\text{CH}=\text{CH}_2 \quad (13\%)
\]

Nonpolar solvents would favor the hemolytic process, while polar and basic solvents such as pyridine would promote carbonyl formation. Thus when primary and secondary alcohols are oxidized in pyridine, the yield of carbonyl
product is generally increased (50-90%) and no cyclic ether is formed. Hence use of lead tetraacetate in this solvent provides an easy route from primary alcohols to aldehydes. (Scheme-10)

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} & \xrightarrow{\text{Pb(OAc)}_4/\text{Pyridine}} \text{reflux, 18 hr} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CHO} \\
32 & \rightarrow 33 \ (75\%)
\end{align*}
\]

Scheme-10

**II.1.D. Oxidation of alcohols with Copper and Cupric ion:**

Primary and secondary alcohols may be dehydrogenated to aldehydes and ketones, respectively, by passing the vapors at an elevated temperature over activated copper, copper-chromium or copper-nickel catalysts in the presence of oxygen.\(^{33}\) Fair yields (46-72%) of aldehydes are obtained by passing primary alcohol vapors over copper gauze at 500\(^0\) C and 80-150 mm of Hg pressure\(^{33}\). Copper catalysts have also been employed in the commercial preparation of \(\alpha, \beta\)-unsaturated carbonyl compounds from the corresponding alcohols. Thus methacrolein can be prepared in good yield (95%) from methallyl alcohol by passing the vapor along with air 1 atm and about 350\(^0\) C over copper gauze.\(^{34}\) (Scheme-11)

\[
\begin{align*}
\text{CH}_3 \quad \text{CH=CH-C(CH}_2\text{OH}} & \xrightarrow{\text{Cu, O}_2} \text{CH}_2=\text{CH-CHO} \\
34 & \rightarrow 35 \ (95\%)
\end{align*}
\]

Scheme-11
Cupric ion can also be used in aqueous acetic acid or pyridine solution to convert $\alpha$-ketols into the corresponding $\alpha$-diketones.$^{35-36}$ The typical application of this reactions are found in the conversion of benzoin ($36$) to benzil$^{35,36}$; the oxidation of sebacoin ($38$) to sebacil.$^{35}$ (Scheme-12)

![Scheme-12](image)

Wendler and Coworkers have reported the conversion of $\alpha$-ketols ($40$) and ($42$) to the corresponding disophenol$^{37}$ ($43$) or the glyoxal ($41$).$^{38}$ (Scheme-13)
In addition, both liquid and vapor phase dehydrogenation of 1,4-, 1,5- and 1,6-diols to the corresponding lactones is accomplished by use of a copper chromite catalyst.39-41 (Scheme-14)

**II.1.E. Oxidation of alcohols with Platinum and Oxygen:**

Primary and secondary alcohols are readily oxidized by oxygen in the presence of platinum.42 The reaction is of particular importance because of its unique selectivity. Primary alcohols are usually oxidized more than secondary alcohols and with polyhydroxy compounds such as carbohydrates, oxidation of only the primary hydroxyl can be achieved.43-46 Under alkaline conditions (water or aqueous acetone) primary alcohols are converted, often in quantitative yields, to the corresponding carboxylic acids. However when the reactions is carried out under neutral conditions in an organic solvent (heptane, dioxane, ethyl acetate,
glacial acetic acid, chloroform, butanone or benzene), the products are aldehydes.\textsuperscript{47}

Steroids containing two or more hydroxyls, with one being in the 3-position, undergo selective oxidation at that position.\textsuperscript{48-52} (Scheme-15)

\begin{equation}
\text{OH} \quad \text{CO}_2\text{H}_3 \\
\text{Pt, O}_2/\text{EtOAc} \\
25^\circ\text{C}, 16\text{ hr} \\
\text{OH} \quad \text{CO}_2\text{H}_3
\end{equation}

\textbf{Scheme-15}

In an investigation of the oxidation of several cyclitols it was observed that axial hydroxyl were attacked in preference to equatorial hydroxyl groups; i.e., myo-inositol (48) underwent oxidation only at the lone axial hydroxyl to give the corresponding ketone (49) as the product, while scylo-inositol (50) lacking axial hydroxyls, was resistant to oxidation\textsuperscript{42} When two or more axial hydroxyls are present, only one is oxidized, no diketones have been found in the products. (Scheme-16)

\begin{equation}
\text{OH} \quad \text{OH} \\
\text{Pt, O}_2 \\
\text{OH} \quad \text{OH}
\end{equation}

\textbf{Scheme-16}
The reagent can also be used in the oxidation of unsaturated alcohols since it does not readily attack carbon-carbon double bonds.\textsuperscript{53}

\textbf{II.1.F. Oxidation of alcohols with Ruthenium Tetroxide:}

Ruthenium tetroxide is a vigorous oxidant that can be used for the oxidation of secondary alcohols to ketones. Following reactions indicate the successful use of RuO\textsubscript{4} as an oxidant for different types of alcohols.\textsuperscript{54-56} (\textbf{Scheme-17})
Although benzyl alcohol has been reported to give benzaldehyde in good yield (90%) when oxidized by RuO₄, the yield from other primary alcohols is much lower.⁵⁶

**II.1.G. Oxidation of alcohols with Bismuth Trioxide:**

Bismuth trioxide has been used in the oxidation of acyloins and it appears to be a specific reagent for this type of compound. Acyloins are easily oxidized to α-diketones by heating in acetic acid.⁵⁷ For example, octane-4, 5-dione is obtained in good yield (84%) from the oxidation of butyroin with bismuth trioxide in acetic acid for 15 min at 100°C. **(Scheme-18)**

![Scheme-18](image)

Application of this reaction to steroids has been made in the conversion of α-ketols into diosphenols.⁵⁸ **(Scheme-19)**

![Scheme-19](image)
**II.1.H.Oxidation of alcohols with Ceric ammonium Nitrate (Ceric ion):**

Ceric ion is a strong oxidant which readily attacks alcohols. However carbonyl compounds bearing α-hydrogen are also very rapidly degraded by this reagent thus unless a large excess of alcohol is used its synthetic usefulness is limited to the preparation of aldehydes and ketones which do not bear α-hydrogen.⁶⁰-⁶¹

For example, benzaldehyde and several substituted benzaldehyde were prepared in over 90% yield by oxidation of the corresponding benzyl alcohols with 0.5 M ceric ammonium nitrate in 50% aqueous acetic acid.⁶² *(Scheme-20)*  

![Scheme-20](image)

This is most useful and widespread oxidation, as it encompasses the alcohols to aldehydes to carboxylic acids sequence that is used so often in synthesis.
II.2. Oxidation with Cr(VI) Compounds:

A great variety of compounds containing Cr (VI) have been proved to be versatile reagents capable of oxidizing almost every oxidizable organic functional group. In spite of this wide spectrum of action the reagents may be controlled to give largely just one single product. Chromic acid is the most popular reagent of this type used in organic chemistry for well over a century. In the last two decades, however, a number of new chromium (VI) containing reagents together with special reaction conditions have been developed to improve the selectivity of oxidation and to deal with complex, highly sensitive compounds.

II.2. Oxidation of Different Substrates with Cr(VI) Compounds:

II.2. A. Oxidation of alkanes:

Chromium (VI) oxidation of saturated hydrocarbons does not represent a useful synthetic procedure since the reaction lacks selectivity and owing to the vigorous reaction conditions and considerable second stage oxidation occur. As a result complex mixtures of products are obtained, e.g. it is difficult to oxidize a methylene group to secondary alcohols without further oxidation of the alcohol to ketone and in some cases it is necessary to use condition sufficiently vigorous to cause carbon-carbon bond cleavage as well. Usually it is possible to convert tertiary C-H bonds to tertiary alcohols and isolated methylene to ketones. However, many tertiary alcohols undergo a facile dehydration, making these compounds difficult to obtain in good yield with reagents such as chromic acid which require acidic conditions.
In principle it might seem that compound containing Cr(VI) (chromic acid, chromyl acetate, chromyl chloride, t-butyl-chromate, or dichromate ion) should be excellent oxidants for alkanes since they are soluble in a number of non-aqueous solvents such as acetic acid, acetone and pyridine. However it has been found difficult to avoid further oxidation of the initial products when chromium (VI) oxidants are used due to the presence of tertiary C-H bonds, it is usually possible to oxidize tertiary hydrogens preferentially in the presence of secondary hydrogens. For example cis-decalin gives as the major products cis 9-decalol when oxidized by dichromate ions in aqueous acetic acid.\textsuperscript{65} However, the tertiary alcohols so produced often dehydrate readily and undergo a facile second stage oxidation.

The Sager and Bradley\textsuperscript{66} reported that triethylmethane was easily oxidized to triethylcarbinol, but unfortunately the product underwent dehydration and further oxidation to diethyl ketone. The alcohol was obtained in 41% yield only if the reaction was quenched after an appropriate time interval. Clearly maximum possible yield for particular compounds will be determined by the relative oxidation rate for the hydrocarbon and the corresponding alcohols reaction shown below (Scheme-21):

![Scheme-21](image-url)

\textsuperscript{63}  \textsuperscript{64}(41\%)  \textsuperscript{65} (36\%)

Scheme-21
Wiberg and Foster studied the oxidation of tertiary C-H bonds with chromic acid predominantly to retention of configuration about the carbon atoms. Oxidation of (+)-3- methylheptane by dichromate ion in 91% acetic acid gives (+)-3- methyl-3-heptanol in only about 10% yield, but 70-85% retention of configuration.67 (Scheme-22)

![Scheme-22](image)

II.2.B. Oxidation of alkenes:

Chromium (VI) oxidation of C-C double bonds can lead to formation of a variety of compounds, including epoxides, α-ketol and cleavage products. Since mixtures of products are usually obtained, the synthetic value of this reaction is minimized. However, it is possible to obtain respectable yields of some products if experimental conditions are carefully controlled and if structure of the oxidant is such possible number of oxidation path is limited.68

II.2.B. (i) oxidation of allylic C-H bonds

Good yields of α, β unsaturated ketones have been obtained from certain compounds (usually steroidal alkenes) when they are subjected to oxidation by Cr (VI) in acetic acid solution.
Marshall et. al.\textsuperscript{69} has reported the introduction of a carbonyl at the C-7 position of pregnenolone acetate by use of sodium chromate in an acetic acid – acetic anhydride solution. (Scheme\textsuperscript{23})

\begin{center}
\textbf{Scheme-23}
\end{center}

With $\Delta^8$-pregnene derivatives, oxidation of allylic C-H bond is complicated by the possibility of carbonyl formation at both the C-7 and C-11 position. For example 3\textbeta{}, 21- diacetoxy- 4,4,14 \textalpha{}-trimethyl $\Delta^8$-5\textalpha{}-pregnene-20-one (70) gives the triketone (71) when oxidized by chromium trioxide in acetic acid.\textsuperscript{70} (Scheme\textsuperscript{24})

\begin{center}
\textbf{Scheme24}
\end{center}
From other compounds which have two unsubstituted allylic position, mixture of products has been obtained. Thus both carvotanacetone (73) and piperitone (74) obtained from carvomenthene (72).\(^{71, 72}\) (Scheme-25)

![Scheme-25]

The products of these reactions are sometimes contaminated by side products arising from epoxide formation or double bond migration. For example Wintersteiner and Moore\(^{73}\) obtained fine products (76-80) in varying yields when they oxidized \(\Delta^8-14\) –cholesteryl acetate (75) with chromium trioxide in acetic acid. (Scheme-26)

![Scheme-26]
II.2.B. (ii) Formation of epoxide and cleavage products:

Phenyl substituted C-C double bonds often yield epoxides and/or cleavage products when oxidized by chromium (VI). These reactions are considerable interest from a mechanistic point of view but because of the variety of products usually obtained and because the epoxides and Cleavage products can be more easily produced using other above reagents, they have little synthetic value. For example A synthetically useful cleavage of a double bond by means of chromium trioxide in acetic acid has been devised by Barbier which has first applied for degradation of bile acid side chains by Wieland. The degradation involves oxidation of trisubstituted olefins obtained by reaction of a carboxylic ester with Grignard reagent (usually phenyl magnesium bromide or, less frequently methyl magnesium iodide). Followed by dehydration of the resulting tertiary alcohol.

(Scheme-27)
II.2.C. Oxidation of arenes:

Chromium (VI) is the most versatile reagents for the oxidation of arenes used in its various forms \([\text{HCrO}_4^-], \text{Cr}_2\text{O}_7^{2-}, \text{CrO}_2\text{Cl}_2, \text{CrO}_2\text{(OAC)}_2\) . Under proper condition it will selectively convert side chain to carboxylic acids, aldehydes, ketones, and diacetates. Under other conditions it attacks polynuclear arenes and leaves the side chains intact.

Chromic acid oxidizes the side chain of phenylalkanes to give benzoic acid derivatives\(^77, 78\) but benzene ring is itself attacked only under very vigorous condition\(^79\). Polynuclear aromatic hydrocarbons, however readily undergo ring oxidation to yield the corresponding quinine\(^80\). This chemoselectivity is shown in the Cr (VI) oxide in anhydrous acetic acid (Fieser reagent).

A dichromate ion in neutral aqueous solution does not attack aromatic systems but instead oxidizes aryl alkanes to the corresponding carboxylic acids or ketones\(^81-82\). Chromyl chloride converts toluene derivatives to substituted benzaldehydes and other aryl alkanes primarily to \(\beta\)-phenyl carbonyl products\(^83\).

Chromyl acetate reacts with toluene derivatives to give fair yields of the corresponding benzal diacetates\(^84\).

The selectivity that can be achieved with these reagents is indicated by the reactions on the following pages\(^78, 82-84\) (Scheme-28).
Chromic acid probably attacks arylalkanes at the C-H bond adjacent to the ring. Four piece of evidence support this view. (Scheme-29)

1. Chromic acid will not oxidize side chain such as t-butyl which lack α-hydrogens.

2. The oxidation of secondary alkyl chain gives phenyl ketones and a carboxylic acid from CrO₃.
(3) oxidation of n-alkyl benzene gives benzoic acid and an aliphatic carboxylic acid with one carbon atom less than the original side chain.  

(Scheme-30)

(Scheme-30)

(4) The products obtained from the oxidation of equilenin acetate (94) and similar compounds obviously result from α attack.  

(Scheme-31)
**II.2.D. Oxidation of ethers:**

Inorganic oxidants have seldom been used to convert ether to more highly oxidized compounds. However several reagents are capable of reacting with methylene groups activated by adjacent oxygen.

Chromic acid converts ethers into esters or lactones by oxidation of $\alpha$-methylene groups to carbonyl functions.

Henbest and Nicholls\(^8\) obtained a high yield of the (97) from the corresponding cyclic ether (96). Use of acetic acid as the solvent in a similar reaction gave a lower yield (54%) of lactone.\(^8\) (Scheme-32)

![Scheme-32](image)

**Scheme-32**

Anhydrous chromium trioxide in acetic acid can also be used to convert methyl ethers (98) into the corresponding (99).\(^8\) (Scheme-33)

![Scheme-33](image)

**Scheme-33**
II.2.E. Oxidation of aldehydes:

Dichromate ions readily oxidize aldehydes to the corresponding carboxylic acids in aqueous solutions. With both reagents however, and particularly under strongly acidic or basic conditions, enolizable aldehydes suffer C-C bond cleavage. Hence because of its greater reactivity under neutral conditions, permanganate ion is probably the more useful oxidant for these compounds.

Furoic (101) for example, has been prepared in good yield from furfural by use of potassium dichromate in an aqueous sulphuric acid solution.\(^{90}\) (Scheme-34)

\[
\begin{align*}
\text{K}_2\text{Cr}_2\text{O}_7 \cdot 9\text{H}_2\text{SO}_4 & \quad \text{100} \quad \text{101 (75%)} \\
\end{align*}
\]

Scheme-34

Aldehydes hydrates form chromate esters which undergo an acid catalyzed decomposition with cleavage of the \(\alpha\) C-H bond in the rate determining step. (Scheme-35)

\[
\begin{align*}
\text{RCHO} & \quad + \quad \text{H}_2\text{O} \quad \leftrightarrow \quad \text{RCH(OH)}_2 \\
\text{RCH(OH)}_2 & \quad + \quad \text{HCrO}_4^- \quad \leftrightarrow \quad \text{RCH(OH)OCrO}_3^- \quad + \quad \text{H}_2\text{O} \\
\text{RCH(OH)OCrO}_3^- & \quad + \quad \text{H}^+ \quad \rightarrow \quad \text{RCOOH} \quad + \quad \text{H}_2\text{O} \quad + \quad \text{Cr(IV)}
\end{align*}
\]

Scheme-35
In contrast to alcohols oxidation however the rate of reaction is not greatly increased by replacing water with acetic acid as solvent.\(^9\) Such a change suppresses the hydration equilibrium and this reagent is a C-C bond cleavage initiated by attack at the \(\alpha\) position of enolizable aldehydes. Thus oxidation of normal and isobutylaldehyde results in formation of approximately 30\% CO\(_2\) by the following reactions.\(^9\) (Scheme-36)

\[
\begin{align*}
\text{(CH}_3\text{)}_2\text{CHCHO} & \rightarrow \quad \text{(CH}_3\text{)}_2\text{C}=\text{CHOH} \xrightarrow{\text{Cr(VI)}} \text{CH}_3\text{COCH}_3 + \text{CO}_2 \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO} & \rightarrow \quad \text{CH}_3\text{CH}_2\text{CH}=\text{CHOH} \xrightarrow{\text{Cr(VI)}} \text{CH}_3\text{CH}_2\text{CO}_2\text{H} + \text{CO}_2
\end{align*}
\]

Scheme-36

**II.2.E. (i) Oxidation of aldehydes with heterocyclic halochromate:**

Pyridinium Chlorochromate (PCC) is a mild acidic oxidizing agent which can promote oxidative cationic cyclization of certain unsaturated aldehydes.\(^9\)

This 2 isobutenylcyclohexan carboxaldehyde is converted to 3-methyl \(\Delta^2\)-1-octalone in 78\% yield in methylene chloride with 3 equivalent of PCC at room temperature, followed by acidic treatment of the crude cyclization product with p-toluenesulphonic acid. Formations of intermediate bicyclic alcohols which further oxidize to the corresponding ketones have also been observed. (Scheme-37)
Jameel have investigated the oxidation of disubstituted benzaldehyde by PCC in binary solvent mixture of 50 % (v/v) aqua-acetic acid. The reaction is first order with respect to [aldehyde], [PCC] and [H+].

Pyridinium dichromate (PDC) is found as an useful oxidant of aldehydes in aprotic media. Unconjugated aldehydes are readily oxidized to the corresponding carboxylic acids by PDC in dimethylformamide at 25°C. Cyclohexene-4-carboxyaldehyde and 4-methyl cyclohexene-4-carboxaldehyde have been converted under these conditions into the corresponding carboxylic acid in 90% yield. (Scheme-38)
Oxidation of both aliphatic and aromatic aldehydes by PFC has been reported.\textsuperscript{96, 97} The kinetics is similar to those observed in the oxidation of alcohols. Oxidation of deuteriated acetaldehyde and benzaldehyde indicated the presence of substantial primary kinetic isotope effects. The following mechanism has been proposed to account for the observed data (Scheme-39).

\[
\begin{align*}
R\quad & + \quad \begin{array}{c}
\text{CrO}_2\text{PyH}^+ \\
\text{H}
\end{array} \\
\rightarrow \\
R\quad & + \quad \begin{array}{c}
\text{O}_2\text{CrO}_2\text{PyH}^+ \\
\text{H}
\end{array} \\
\rightarrow \\
R\quad & + \quad (\text{HO}_2\text{CrO}_2\text{PyH})^- \\
\rightarrow \\
\text{RCOOH} & + \quad \text{CrOFOPyH}
\end{align*}
\]

Scheme-39

The oxidation of aliphatic aldehyde by BPCC in DMSO has been reported by Banerji \textit{et.al.}\textsuperscript{98}. The reaction was found first order with respect to aldehyde and BPCC. The reaction is catalyzed by hydrogen ion, the hydrogen ion dependence taking the form \(k_{obs} = a + b \ [H^+]\). The oxidation of deuterated acetaldehyde indicated the presence of primary isotope effect. A mechanism involving transfer via a chromate ester has been proposed.
Pandurangan et al.\textsuperscript{99} observed that the oxidation of substituted benzaldehydes by QFC is first order with respect to each of the reductant, QFC and hydrogen ions. They obtained a reaction constant of 1.16 for the oxidation of \textit{m-} and \textit{p-}substituted benzaldehydes. The authors have suggested a mechanism involving formation of a chromate ester in a rapid pre-equilibrium step. The decomposition of the chromate ester, in the rate-determining step, is base-catalyzed.

Jameel\textsuperscript{100} studied the kinetics of oxidation of benzaldehyde and several \underline{\underline{p}}ara and \underline{meta} substituted benzaldehydes to corresponding carboxylic acid. The reaction proceeds with the formation of QCC-ester as the intermediate.

\textbf{II.2.F. Oxidation of ketones:}

Oxidation of ketones with dichromate ion usually results in formation of a carboxylic acid by cleavage of an adjacent C-C bond.

\underline{2-acetylfluorene (110)} is converted to fluorenone -2-carboxylic acid (111) in fair yield by treatment with sodium dichromate in acetic acid\textsuperscript{101}. Oxidation of cyclic ketone gives a dicarboxylic acid as principle product containing the same number of carbons as the parent compound\textsuperscript{102} (\textbf{Scheme-40})

\begin{center}
\textbf{Scheme-40}
\end{center}
Sometimes when glacial acetic acid is used as the solvent, it is found helpful to add acetic anhydride in the midway of the reaction to remove water which is produced during the oxidation. At the completion of the reaction excess chromium (VI) is reduced by addition of a few milliliters of ethanol.

Rocek & Riehl\textsuperscript{102,103} have shown from a kinetic study of the oxidation of isobutyrophenone and 2-chlorocyclohexanone that the reaction proceeds via an end intermediate. At high oxidant concentrations the rate of reaction becomes approximately equal to rate of enolization and independent of the hexavalent chromium concentration. Oxidation of the enol produce a diketone which can in some cases be isolated\textsuperscript{104,105} but which usually undergo a facile cleavage to give final products. For example the oxidation of cyclohexanone has been studied in some details. It has been shown that the first step of the reaction in aqueous perchloric acid is an $\alpha$-oxidation leading to 2-hydroxycyclohexanone. Less than 3\% of the reaction proceeds by dehydrogenation 2-cyclohexen-1-one, 2-hydroxycyclohexanone is then oxidized further to 1, 2- cyclohexandione and cleaved to adipic acid.\textsuperscript{102} (Scheme-41)

\begin{center}
\begin{align*}
\text{O} & \xrightarrow{\text{aq. perchloric acid}} \text{OH} & \text{O} & \xrightarrow{} \text{COOH} & \text{COOH} \\
112 & \xrightarrow{} 113 & 114 & + 115
\end{align*}
\end{center}

\textbf{Scheme-41}
**II.2.G. Oxidation of amines:**

Cr(VI) compounds react with amines by abstraction of a hydrogen atom from the α-position to give either a compound with an oxygen function in that position or one containing a carbon nitrogen double bond. In the latter case the double bond is often cleaved to give carbonyl compounds. An example is provided by reaction of an indole derivative, deoxygajmaline O-acetate, with chromium trioxide.\(^{106}\) (Scheme-42)

![Scheme-42](image)

\[
\text{NCH}_3 \xrightarrow{\text{CrO}_3/\text{Pyridine}} \text{NCH}_3\text{OH} + \text{NCH}_2\text{OH} \quad 116 \quad 117 (19\%) \quad 118 (15\%)
\]

Scheme-42

The oxidation is affected simply by adding the amine in pyridine to an ice-cold solution of CrO\(_3\) in 30 ml of pyridine and stirring at room temperature for several hours.

Bottini and Olsen\(^{107}\) have developed a procedure whereby primary and secondary amines can readily be converted to the corresponding carbonyl compounds. In this procedure the amine is first reacted with 2, 4-dinitroaniline (119) which can then be oxidized with hexavalent chromium. (Scheme-43)

![Scheme-43](image)

\[
\text{RRCNH}_2 \xrightarrow{\text{CrO}_3/\text{H}_2\text{SO}_4} \text{RCON}^+ \quad 119 \quad 120 (25-95\%)
\]

Scheme-43
The greater difficulty with this reaction is the fact that although 2,4-dinitroaniline is relatively resistant to further oxidation under these conditions, the carbonyl compounds are not, and lowest yields were observed for those aldehydes and ketones that are most susceptible to further reaction with chromic acid.

**II.2.H. Oxidation of Alkyl Halides:**

The direct conversion of alkyl halide into the corresponding carbonyl compounds, despite its potential interest for organic synthesis, is seldom referred to in the literature. Only few examples of the oxidation of benzylic halides with aqueous acidic chromic acid or with aqueous sodium dichromate and alkali hydroxides under rather drastic conditions have been reported.\(^\text{108}\) A preparatively useful example is the oxidation of \(\alpha\)-chlorohydrindene to \(\alpha\)-chlorohydrindanone in 50-60% yield by means of chromic acid in aqueous acetic acid at 40\(^\circ\) C.\(^\text{109}\) (Scheme-44)

Oxidation of steroidal vicinal dibromide to the \(\alpha\)-bromoketone by means of chromic acid in aqueous acetone in the presence of silver chromate at room temperature forms a key step in an early procedure for the synthesis of corticoids from bile acids.\(^\text{110}\) (Scheme-45)
The reaction is performed in hexamethylphosphoramidine using a slight excess of potassium chromate in the presence of one equivalent of dicyclohexyl-18-crown-6 at 100°C. The yields are in the range of 80%.

A remarkable improvement of this reaction which avoids the use of hexamethylphosphramidine and the crown ether has been obtained by using polymer supported chromic acid as oxidant.¹¹¹ (Scheme-46)

**II.2.I. Oxidation of Acetals:**

Cyclic methylene or benzylidene acetics of alditols cleaved by chromium trioxide in glacial acetic acid to give derivatives of ketoses, provided that the hydroxyl groups are suitably protected, e.g. by acylation. For example, 1, 3, 5-tri-O-benzylidene-DL-xylitol (127) is oxidized smoothly by the reagent in 1 hr at
room temperature to 1, 3, 5-tri-O-acetyl-4-O-benzoyl-keto-DL-thero-pentulose (128) in 84% yield.\textsuperscript{112} (Scheme-47)

Unsymmetrical acetals, however, can open at either position of attachment to yield two products. Thus, 1,3,5,6-tetra-O-acetyl-2,4-O-benzylidene-D-glucitol (129) is oxidized to yield 1,3,5,6-tetra-O-acetyl-2,4-O-benzoyl-keto-D-fructose (130), as the main product, together with small amounts of 5-O-benzoyl-oxyhex-3-ulose (131).\textsuperscript{112} (Scheme-48)

Methylene acetals behave similarly. For example, 3, 4, 6-tetra-O-acetyl-2,5-O-methylene-D-mannitol (132) under similar conditions affords 1,3,4,6-tetra-O-acetyl-5-O-formyl-keto-D-fructose (133) in 87% yield.\textsuperscript{112} (Scheme-49)
The oxidation of aromatic acetals by acidic Pyridinium chlorochromate (PCC) has been studied by P.S. Ramakrishnan \(^{113}\). The reaction is first order each in [PCC] and [Acetal]. The reaction does not induce polymerization of acrylonitrile. The presence of electron withdrawing substituents in the benzene ring enhances the rate of oxidation. The rate of oxidation depends on the nature of alkyl group.

**II.2. J. Oxidation of sulphides:**

Oxidation of Sulphides is oxidized to sulphones by chromic acid under acidic conditions although the conversion is under acidic medium affected more efficiently using other oxidants such as potassium permanganate. For example, 2, 2, 4, 4', 6, 6'-hexanitro-3-methyldiphenyl sulphone (134) is converted to the corresponding sulphone (135) in 95% yield on treatment with chromium trioxide in concentrate nitric acid at room temperature.\(^ {114}\)(Scheme-50)
Meenakshisundaram et al.\textsuperscript{115} studied the oxidation of organic sulphides by PDC in acetonitrile medium. They observed a first order dependence on PDC and sulphide but second order in TsOH. In case of aryl methyl sulphides, the order with respect to TsOH is >1 and < 2, while Michaelis–Menten type kinetics were observed with respect to the sulphide. A nonlinear Hammett plot was obtained with both electron donating and electron withdrawing groups slowing down the rate of reaction. The reaction was retarded by acrylonitrile, thereby indicating a one electron oxidation giving rise to free radicals.

The oxidation of a number of organic sulphides\textsuperscript{116} showed by PFC that the reaction is second order, first in each reactant. The substituent effect was analyzed using techniques of correlation analysis. Solvent effect showed that the transition state is more polar than the reactants.

Meenakshisundaram et al.\textsuperscript{117} studied the oxidation of sulfides by QFC in non-aqueous medium. The oxidation kinetics of sulfides was studied under pseudo first order condition with QFC and second order in catalyst, MeCN α-MeC\textsubscript{6}H\textsubscript{4}SO\textsubscript{3}H. Sulfide concentration has no effect on the reaction rate. CH\textsubscript{2} =CHCN retard the oxidation rate significantly in di-Ph sulfides, indicating the involvement of free radical cation intermediate in rate determining step. The Michaelis - Menten dependence each on [sulfide] [α-MeC\textsubscript{6}H\textsubscript{4}SO\textsubscript{3}H] was well explained by two-pathway mechanism in sulfide oxidation.

The rate of oxidation of dialkyl and alkyl phenyl sulphides by QCC has been studied in aqueous acetic acid.\textsuperscript{118} The proposed mechanism envisages oxygen transfer from QCC, which is in agreement with the earlier observations.
II.2.K. **Oxidation of Oximes:**

Chromic acid in 50% aqueous acetic acid, Jones’ reagent and chromium trioxide-(pyridine)$_2$ in methylene chloride have been shown to bring about oxidative deoximation of ketoximes to the corresponding carbonyl compounds with varying degrees of success.$^{119}$ (Scheme-51)

![Scheme-51](image)

Palaniappan *et al.*$^{120}$ studied the oxidation of oxime by PDC in 60 % acetic acid-water (v/v) medium. The order of reaction is first with respect to [oxidant], second with respect to the [substrate] and zero with respect to [H$^+$].

The use of 2 equivalent of pyridinium chlorochromate was in methylene chloride at room temperature for 12 hrs. It is also effective in converting ketoximes to the corresponding ketones in yields of 50-85% while benzaldoxime affords benzaldehyde without further oxidation & oxime ethers are resistant to the reagent.$^{121}$ (Scheme-52)

![Scheme-52](image)
The oxidative deoximation of several aldo and ketoximes by Quinolinium fluorochromate [QFC] in DMSO exhibited a first order dependence on both the oxime & QFC.\textsuperscript{122} The oxidation of ketoximes is slower than that of aldoximes. The oxidation of aldoximes correlated well in term of PAVELICH-TAFT dual substituent–parameter equation. The low positive value of polar reaction constant indicated a nucleophillic attack by a chromate-oxygen on the carbon. The reaction is subject to steric hindrance by alkyl groups. A mechanism involving the formation of a cyclic intermediate in the rate determining step has been proposed.

\textit{II.3. Oxidation of Alcohols with Cr(VI) Compounds:}

The first review pertaining to the use of novel chromium (VI) reagents for the oxidation of primary and secondary alcohols was published in 1982, which summarized the salient features of several hexavalent chromium compounds\textsuperscript{123}.

The oxidation of alcohols constitutes the synthetically most important application of Cr (VI) compounds. It has been largely divided into four sections.

1. Acid catalyzed oxidation with chromium trioxide and chromic acid in acetone (Jones’s reagent), DMSO and dimethylforamide (DMF)

2. Oxidation promoted by a family of Cr (VI) reagents obtained from chromium trioxide, chromic acid and halochromic acids heterocyclic bases.

3. Oxidation carried out under neutral or almost neutral conditions

4. Chromium (VI) reagents supported on various insoluble organic and inorganic matrices.
II.3.A. Oxidation of alcohols by Cr(VI) under acid conditions:

Much important chromium (VI) oxidation of alcohols are carried out under acid condition. Aqueous acidic solution of chromium trioxide as well as chromate and dichromate salts in the presence of co-solvents like acetic acid or acetone have been widely used as oxidizing reagents. Oxidations have also been performed in a two phase system consisting of an aqueous acidic solution of chromic acid and an organic immiscible solvent like benzene, DCM, or ether or without a phase transfer catalyst.

In 1859 G.Stadler\textsuperscript{124} reported that the first description of oxidation of primary alcohols with potassium dichromate in aqueous sulfuric acid.

\[
3 \text{R-CH}_2\text{OH} + 2 \text{Cr}_2\text{O}_7^{2-} + 3 \text{H}_2\text{SO}_4 \rightarrow 3 \text{R-CHO} + 2 \text{Cr}_2(\text{SO}_4)_3 + 6 \text{H}_2\text{O}
\]

Beckmann\textsuperscript{125} and Kilani\textsuperscript{126} introduced two standard chromic acid solutions in aqueous sulfuric acid. The first is made with Na\textsubscript{2}Cr\textsubscript{2}O\textsubscript{7}/K\textsubscript{2}Cr\textsubscript{2}O\textsubscript{7}, and the second with chromium trioxide. This method seems to be particularly useful for the preparation of aromatic aldehydes\textsuperscript{127} even if they are sterically hindered.\textsuperscript{128} (Scheme-53)

![Scheme-53](image-url)
Oxidations with aqueous chromic acid in a heterogeneous system have proved to be useful the direct conversion of low molecular weight primary alcohols to the corresponding acid. The absence of a co-solvent in this case greatly facilities the isolation of oxidation products. In respect to reaction conditions best results were obtained by adding the alcohol to an excess of the oxidizing mixture.\textsuperscript{129,130} (Scheme-54)

\[
\begin{align*}
&\text{CH}_2\text{FCH}_2\text{OH} & \xrightarrow{\text{K}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{SO}_4, \text{H}_2\text{O}} & \text{CH}_2\text{FCH}_2\text{COOH} \\
&\text{142} & \text{143 (80%)}
\end{align*}
\]

Scheme-54

Unlike primary alcohols; the secondary ones which are sufficiently in water are generally oxidized in good yield when other oxidation sensitive groups absent.\textsuperscript{131} (Scheme-55)

\[
\begin{align*}
&\text{144} & \xrightarrow{\text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{SO}_4, \text{H}_2\text{O}} & \text{145 (90%)}
\end{align*}
\]

Scheme-55

A common co-solvent with water in chromic acid oxidation of alcohols is acetic acid. The use of acetic acid not only improves the solubility of the organic substrates in the oxidizing mixture but also increase the rate of the reaction. The oxidation rate can be further increased by adding sulfuric acid.
Primary alcohols have been oxidized to aldehydes under these conditions in moderate yield.\textsuperscript{132} (Scheme-56)

![Chemical reaction](image1)

\begin{center}
146 \quad 147 (33-35\%)
\end{center}

**Scheme-56**

Less hindered primary alcohols may be converted to the corresponding carboxylic acid under milder conditions. Thus, for example, a variety of halogenated primary alcohols were oxidized to carboxylic acids in moderate yields upon overnight-treatment with chromium trioxide in acetic acid at room temperature.\textsuperscript{133} (Scheme-57)

![Chemical reaction](image2)

\begin{center}
148 \quad 149 (93\%)
\end{center}

**Scheme-57**

Chromic acid oxidation of secondary alcohols in aqueous acetic acid yields cleavage products (route A) in addition to the expected ketones (route B). (Scheme-58)

![Chemical reaction](image3)

**Scheme-58**
The cleavage products may then be further oxidized to corresponding acids and carbonyl compounds or may combine, via the formation and oxidation of the hemiacetal to the ester. The cleavage reaction becomes more pronounced for secondary alcohols bearing one or more alkyl group in α position. For example, the oxidation of n-propyl-t-butylcarbinol with chromium trioxide in aqueous acetic acid yields 41% of the corresponding ketone, 4% tert-butylcarboxaldehyde and a corresponding amount of tert-butyl cabinol.

Detailed investigations 134 (a) revealed that Cr (VI) oxidized cyclobutanol to the “normal” product of cyclobutanone in a C-H bond cleavage reaction, whereas the intermediate chromium (IV) reacts by carbon-carbon cleavage to give a free radical CH₂CH₂CH₃CHO which, upon further oxidation, gives rise to the hydroxyaldehyde. (Scheme-59)

![Scheme 59](image)

Tertiary alcohols are generally inert toward oxidation by chromic acid. Expectations have, however been reported.

Several tertiary cyclopropanols 134(a,b) 124,125 bicyclic tertiary alcohols react quickly135 with chromic acid yielding ketones arising by cleavage products may be considered to arise from breakage of the C₁-C₇ or C₁-C₂ bond. The relative yields depend on the substituents at C₂-C₇. (Scheme-60)
A notable improvement in the oxidation of alcohols was achieved by using a solution of chromic acid/sulphuric acid in water for which oxygen 8 N (the so called Jones reagent) using acetone as co-solvent. The procedure involves titration of alcohol in acetone with the standard chromium trioxide-sulphuric acid solution. The reaction mixture separates into a green layer of chromium salts with an upper layer of an acetone solution of the oxidation product.

A limitation of the method is the low solubility power of acetone and strong acidic conditions of the reaction. Primary alcohols are rapidly oxidized by this reagent to yield good amounts of carboxylic acids, even in the presence of double or triple carbon-carbon bonds.

Primary α, β unsaturated alcohols may be converted into high yields of the corresponding aldehydes under nitrogen at 0°C. As a matter of fact α, β unsaturated and aromatic aldehydes seems to be relatively inert towards the normal conditions of the Jones’s oxidation. However, a small amount of isomerization of the double bond occurs in certain cases. (Scheme-61)
Chromium trioxide dissolves in DMF to give solution with very little oxidation power toward alcohols. Thus cholesterol is recovered unchanged after three weeks of exposure to the solution and only a 50 % conversion of 5 α-cholestan-3-ones is observed after heating 5α-cholestan-3 β-ol for 45 hours at 50°C. However, the oxidation is strongly catalyzed by adding a few drops of con.H₂SO₄ acid. Under these conditions a number of steroidal alcohols have been converted to ketones at room temperature with 80% yield.¹³⁹

DMSO acts as an excellent solvent for sodium dichromate dehydrate. The solution at 70°C cause only slight oxidation of benzyl alcohol to benzaldehyde, but the addition of small amount of H₂SO₄ strongly accelerates the reaction. Primary and secondary saturated, allylic and benzylic alcohols are oxidized by this procedure to aldehydes and ketones in 80-90% yield.¹⁴⁰

Many modified procedures have been developed to simplify the isolation process, to achieve certain selectively, and to improve the yield as well as the purity of products. A simple useful procedure consists in stirring a solution of the compound to be oxidized in an immiscible solvent stable to chromic acid (benzene, DCM, ether) with an acidic aqueous solution of the oxidant. The organic phase protects the carbonyl compound from undesirable side reactions,
such as further oxidation or epimerization. In this way sensitive ketones may be isolated in high yield without appreciable epimerization of adjacent chiral centers.

Benzene and DCM have been widely used as an organic phase. As an example, 2, 5, 5, - trimethylcyclohex-2-en-1-one has been obtained in a 91% yield from the corresponding alcohol in a benzene- water two phase system.\textsuperscript{141} (Scheme-62)

\[ \text{HO} \xrightleftharpoons{\text{Na}_2\text{Cr}_2\text{O}_7/\text{H}_2\text{SO}_4} \text{C}_6\text{H}_6\text{O} \]

\[ \begin{array}{c}
157 \\
\text{158 (90%)}
\end{array} \]

\textbf{Scheme-62}

An advantage of the use of water immiscible solvents like hydrocarbon and chlorinated hydrocarbon lies in the fact that they easily from emulsion which hamper the isolation of the product. Ethyl ether has proved\textsuperscript{142(a, b)} to be superior, oxidation proceeds smoothly as no emulsions are formed. Under these conditions oxidation of (-) menthol give to (-) menthone in 97% yield along with mere traces of (+)–isomenthone.

The two phase procedure has recently been modified by adding a phase transfer catalyst \textsuperscript{143,144} Under these conditions primary alcohols which were insoluble in the aqueous phase were oxidized to aldehydes at a higher than 90% yield. The temperature and concentration of acid in the aqueous phase and that of the substrate are crucial factors for the reaction.
II.4. Oxidation of Alcohols with Compounds of Cr(VI) and Heterocyclic Bases

Chromium trioxide is capable of reacting as Lewis acid with many heterocyclic bases leading to a number of addition compounds. Pyridine, dipyridine, quinolone, 3, 5, dimethyl pyrazole etc. are among the bases which gives complexes by simple additions of the compounds at room temperature.\textsuperscript{145}

Moreover, chromic acid and chlorochromic acid was found to give a variety of heterocyclic bases.

Such useful reagents are dipyridine-chromium (VI) oxide complex \textsuperscript{146}, 1, 8-naphthpyridinium chlorochromate and pyrazinium chlorochromate \textsuperscript{147}, tetrakis(pyridine) silver dichromate \textsuperscript{148}, nicotinium dichromate and isonicotinium dichromate\textsuperscript{149}, quinolinium dichromate\textsuperscript{150}, imidazolinium Fluorochromate\textsuperscript{151}, imidazolinium dichromate\textsuperscript{152}, tetraalkylammonium chlorochromate\textsuperscript{153}, 2,4-bipyridinium chlorochromate\textsuperscript{154}, pyridinium dichromate\textsuperscript{95}, trimethylysilyl chlorochromate\textsuperscript{155}, 2,2'-bipyridinium chlorochromate\textsuperscript{156}, pyridinium Fluorochromate\textsuperscript{157}, pyridinium bromo-chromate\textsuperscript{158}, quinolinium chlorochromate\textsuperscript{159}, quinolinium Fluorochromate\textsuperscript{160}, quinolinium bromochromate\textsuperscript{161}, 4-(Dimethylamino) pyridinium chlorochromate\textsuperscript{162}, bis[benzyltrimethyl ammonium]dichromate\textsuperscript{163}, 3,5-dimethylpyrazole chromium(VI) complexes\textsuperscript{164}, benzotriazole trioxide complexes\textsuperscript{165}, halosilanes chromium trioxide\textsuperscript{166}, butylammonium chlorochromate & teramethyl-ammonium fluorochromium trioxide\textsuperscript{167}, chromium peroxide etheratem (CPE) and pyridine chromium peroxide (PCP) and 2,2’–bipyridyl chromium peroxide (BPCP)\textsuperscript{168}, biphosphonium
Some heterocyclic base and halochromate Cr(VI) reagents were described in this section.

**II.4. A. Oxidation of alcohols with Chromium Trioxide-(Pyridine)$_2$ Complex.**

Chromium trioxide in pyridine was introduced as a unique, nonacidic reagent for alcohol oxidations and has been used extensively to prepare ketones,

but has been applied with only limited success to the preparation of aldehydes.

2-Methoxybenzaldehyde was obtained in 89% yield, 4-nitrobenzaldehyde and heptanal were obtained in 28% and 10% yields, respectively.

Using the performed dipyridine chromium (VI) oxide in DCM, the rate of chromium ester formation and decay to the aldehyde is enhanced at least twentyfold over the rate observed in pyridine solution. Isolation of products is facile, and aldehydes appear to be relatively stable to excess reagent. The reagent has been used extensively to prepare acid-sensitive aldehydes, particularly intermediates in the total synthesis of prostaglandins and steroids. An 85% yield was reported for the conversion of 2-vinylcyclopropylcarbinol to the aldehydes. Although excess reagent is required for the oxidations (usually
sixfold), the reaction conditions are so mild and isolation of products so easy that the complex will undoubtedly find broad use as a specialty reagent. Isolation of complex can be avoided by in situ preparation of the chromium oxide/pyridine complex.\textsuperscript{181}

**II.4.B. Pyridinium Dichromate (PDC)**

PDC reagent was prepared from pyridine, CrO\textsubscript{3} in water. It is bright orange solid. It is very soluble in water, DMF, DMSO, dimethylacetamide (DMA) and it is soluble in DCM, ethanol-free chloroform or acetone and not soluble in hexane, toluene, ether or ethyl acetate. Although PDC dissolve in acetonitrile, the solutions are not stable.

This reagent was first used for oxidation of alcohols by J.W.Conforth\textsuperscript{182} for the oxidation of 2, 4'-dimethyl-4-(3-hyroxy-4-methyl pentyl)-1, 3-dioxane to the corresponding ketone with a yield of 88%.

The wide applicability of PDC for oxidation of alcohols to aldehydes, ketones and carboxylic acid has been shown by E.J. Corey.\textsuperscript{95} The reagent was used in most cases in the form of DMF solution or a DCM suspension. In DMF primary and secondary allylic alcohols and secondary saturated ones are rapidly oxidized to the corresponding carbonyl compounds. Thus, 2-cyclohexen-1-ol, cinnamyl alcohol and geraniol are converted to high yields to α, β- unsaturated carbonyl derivatives at 0\textdegree C in 4-5 hours using only 1.25 equivalent of the reagent. Oxidation occurs without overoxidation in the case of aldehydes and no E to Z isomerization for geraniol.\textsuperscript{95} Saturated primary alcohols are readily converted to
carboxylic acids in good yield with 3.5 equivalents of PDC in DMF at 25°C in 7-9 hours via the corresponding aldehydes which have been isolated.  

B. L. Hiran and J. Choudhary developed a new reagent 4-Methyl pyridinium dichromate (m. p. 109°C), and they studied oxidation of some substituted benzhydrols (4-methyl, 2-methyl, 4-chloro, 4, 4-dichlorobenzhydrol etc.) in acetic acid–water medium and observed first order with respect to [substrate], [oxidant] and [H+] each. The rate of reaction increases with increase in hydrogen ion concentration and percentage of acetic acid. Thermodynamic activation parameters have been computed. A plausible mechanism consistent with the observed experimental results and suitable rate law has been deduced. In rate determining step water acts as proton abstracting agent and C-H bond breaking takes place.

Hiran & Kailash Chand studied oxidation of aliphatic alcohols by PDC in aquo-dioxane medium and observed first order with respect to [substrate], [oxidant] and [H+] each. The rate of reaction increases with increase in hydrogen ion concentration. Thermodynamic activation parameters have been computed. A plausible mechanism consistent with the observed experimental results and suitable rate law has been deduced. In rate determining step water acts as proton abstracting agent and C-H bond breaking takes place.

**II.4.C. Pyridinium Chlorochromate (PCC)**

Corey and Suggs introduced PCC for the oxidation of both primary and secondary alcohols to carbonyl compounds. PCC was prepared from pyridine
and CrO$_3$ in HCl. This reagent which appears particularly suitable for moderate to large scale oxidations is normally used in a 1:1.5 molar ratio as a suspension in DCM at room temperature. More polar solvents, like acetone and acetonitrile in which the reagent was soluble greatly reduce the reaction times.

The stochiometry of the oxidation of 1-octanol with PCC in DCM has been studied by H.C. Brown$^{187}$ by using varying amounts of reagents. The use of both 16.5 and 22.5 mmole of reagent for 15 mmole of alcohol affords a quantitative yield of octanol. It, therefore, seems likely that a substrate: reagent molar ratio of 1:1.1 should be to perform quantitative oxidation.

The oxidation of secondary hydroxyl groups in sugars has been found to be very slow with PCC in DCM, even in the presence of a large excess of oxidant under reflux conditions. Instead, benzene was found to be a good alternative solvent. Oxidation of sugars, which failed with DMSO- dicyclohexylcarbodimide and other reagent related to DMSO, was readily accomplished in good yield, also on a molar scale, simply by heating a benzene solution of the sugar under reflux in the presence of 1.7 equivalent of PCC.

The reactivity of PCC towards slow reacting alcohols like nucleosides or sugars may be increased by adding 3A molecular sieve powder to a suspension of PCC in DCM.$^{188}$ The attempts to catalyze the reaction by celite, alumina and silica gel were unsuccessful. Thus, for instance, the oxidation of benzhydrol to benzophenone with two equivalent of PCC and 0.5 g of molecular sieve powder leads to a quick and complete in 15 min. The acidic character of PCC (pH of a
0.01 M solution=1.75)\textsuperscript{170} may be convenient to bring about a one-step conversion (70%) of citronellol essentially to pulegone.\textsuperscript{189}

Efficient cyclization with PCC is only observed with substrates which produce tertiary cations as initial cyclic intermediate which then lead to six membered enones. This process represents a milder and more efficient alternative in organic synthesis to the two-step cationic cyclization of preparing \( \alpha, \beta \)-unsaturated enones\textsuperscript{190}. The oxidation of cyclic tertiary allylic alcohols to \( \alpha, \beta \)-unsaturated cyclic ketones with 2 equivalent of PCC in DCM affords transposed 3-alkyl - \( \alpha, \beta \)-unsaturated in good yields.\textsuperscript{191} Various tertiary vinylic alcohols of natural origin have also been transformed into the corresponding unsaturated aldehydes following the same procedure. A cyclic allylic tertiary alcohols\textsuperscript{192} also afford transposed \( \alpha, \beta \)-unsaturated ketones albeit in lower yield. However, byproducts are frequently observed. For exp. Oxidation of 2-phenyl-3-buten-2-ol gives a 35 % yield of acetophenone in addition to the transposed aldehyde.

The first report about the kinetics and mechanism of the oxidation of alcohol was published in 1978. Banerjee\textsuperscript{193,194} and Venkatusubramaian et.al\textsuperscript{195} reported the oxidation of alcohols by PCC in 1:1 (v/v) DCM and nitrobenzene solution. The reaction was first order with respect to PCC and the alcohol. Banerjee\textsuperscript{193, 194} reported the reactions catalyzed by toluene-p-sulphonic acid (TsOH). The reactions exhibited negative reaction constants. The oxidation of deuteriated benzyl alcohol\textsuperscript{193} and ethanol\textsuperscript{194} showed the presence of substantial kinetic isotope effects. This confirmed the cleavage of an \( \alpha \)-C-H bond in the rate determining step. The oxidation of cycloalkanols by PCC\textsuperscript{196} in chlorobenzene-
nitobenzene solvent presented similar kinetics. The author suggested, on the basis of the reactivity of the cycloalkanol and effect of solvent, that probably a chromate ester mechanism is operative. Banerjee studied the temperature dependence of kinetic isotope effect in the oxidation of substituted benzhydrol by PCC in DMSO. An analysis of the temperature-dependence of the kinetic isotope effect by the method of Kwart and Nickle, in the oxidation of benzhydrol, showed that the hydride-transfer take place via a chromate ester through a symmetrical cyclic transition state. Agarwal et.al studied the oxidation of 2-pentanol by PCC in chloroform solution. They observed that kinetically the oxidation is comprised of two reactions. The first one consisted of the formation of a chromate ester and the second one a decomposition of ester. They obtained a kinetic isotope effect, $k_{O-H}/k_{O-D} = 1.30$, for the first reaction. In essence, their data support a hydride-ion transfer via a chromate ester.

**II.4.D. Pyridinium Fluorochromate (PFC)**

Development of PFC was essential to overcome the practical difficulties associated with PCC, which was found unfortunately quite unstable. Mihir Kanti et.al. reported a noble and environmentally cleans process for the preparation of Pyridinium salt of fluorotrioxychromate (VI) having a chemical formula $C_5H_5NH[CrO_3]$\(^{200}\). The compound was prepared by direct reaction of HF acid, chromium trioxide and pyridine. This complex is soluble in benzene, $CCl_4$, chloroform and hexane. Unlike PDC, the reagent does not react with acetonitrile which also may be used as a solvent. The acidity of PFC is less pronounced than that of PCC which may have advantage of preventing side reactions.
The first preliminary report on the oxidation of alcohols by PFC was published by Bhattacharjee et al. In this reaction the molar stoichiometry of the oxidation of n-butanol, isopropanol, benzyl alcohol and cyclohexanol involving PFC in DCM has been found to be 1:1.5. They obtained Michaelis-Menten type kinetics with respect to the alcohols and observed that the reactions were catalyzed by TsOH but could not determine the order with respect to the acid, as the reactions were very fast. A systematic study of the oxidation of substituted benzyl alcohol and of aliphatic alcohols by PFC in DMSO was reported by Banerjee. He also observed Michaelis-Menten type kinetics with respect to alcohols, suggesting the formation of an intermediate in a pre-equilibrium and its subsequent disproportionation in the rate-determining step. The oxidation of deuteriated ethanol and benzyl alcohol exhibited a substantial primary kinetics isotope effect. This confirmed the α-C-H bond in the rate-determining step. The oxidation of aliphatic alcohols is susceptible to both the polar and steric effects of the alkyl group. The polar reaction constants have negative values. The oxidation of benzyl alcohol was studied in nineteen organic solvents. An analysis of the solvent effect, in term of swains equation, indicated the greater importance of the cation-solvating power of solvents. In both the cases, the in analysis of the temperature-dependence of the kinetic isotope effect indicated the presence of a symmetrical cyclic transition state in the rate –determining step of the oxidation. The oxidation of vicinal and non-vicinal diols by various halochromates viz. PFC in DMSO has been studied. The oxidation of vicinal diols correlated well with the polar and steric substituent constant of the alkyl group. Kinetics and mechanism of the oxidation of p-chlorophenol, p-
nirophenol and p-cresol in glacial acetic acid as a solvent at 25-45°C using PFC as have been studied and reported by Patil and Coworkers.\textsuperscript{209} The oxidation of D-glucose and some other monosaccharaiides by PFC\textsuperscript{210} in aqueous perchloric acid solution has been reported. The reactions are first order with respect to each of the oxidant, the sugar and hydrogen ions. The oxidation by PFC\textsuperscript{210} on the other hand, yields only formic acid and D-arabinose. In the PFC oxidation, a solvent isotope effect, \( k (\text{D}_2\text{O})/ k (\text{H}_2\text{O}) = 3.1 \) has been obtained. The author interpreted this in term of two acid-catalyzed reactions

(i) The acid-catalyzed anomerization of \( \alpha\)-D-glucose to \( \beta\)-D-glucose

(ii) A pre-equilibrium protonation of PFC

The author suggested a bimolecular hydride ion transfer in the rate determining step.

**II.4.E. Bopyridinium Chlorochromate (BPCC)**

Frank S. Guziec reported the successful use of 2,2'-Bopyridinium Chlorochromate (BPCC) for the oxidation of 2-isopropyl cyclohexanol in DCM at room temperature\textsuperscript{211} 2-isopropylcyclohexanone was the main oxidized product. Percentage yield was as high as 86 %. Kabilan et.al reported the kinetics and mechanism of the oxidation of cyclopentanol, cyclohexanol, cycloheptanol and cyclooctanol by BPCC in the presence of H\(^+\) ions.\textsuperscript{212} The oxidation of benzyl alcohol \textsuperscript{213} by BPCC was examined in various solvents and greater yield of benzaldehyde was observed in the solvent with higher dielectric constant such as chloroform, dichloromethane etc. The oxidation of benzyl alcohol derives by
BPCC in DMF was examined and similar product was observed regardless of substituent. The oxidation rate was dependent linearly on the concentration of acid and Arrhenius equation indicated that there was a charge transition state.

Kinetics of the oxidation of substituted benzyl alcohol with 4, 4’ BPCC has also been reported in the literature. Treatment of primary and secondary alcohol in DCM or acetone with 2:1 to 4:1 excess of bipy H+ CrO3Cl- affords aldehydes or ketone in high yields. The chromium containing byproducts from these reactions are water soluble crystalline materials which are easily removed by filtration through a 1 cm celite pad. The bipy H+ CrO3Cl- complex may prove to be especially useful in oxidation of compounds with acid-sensitive protecting groups, due to the internal buffering of the 2, 2’- bipyridyl system.

II.4.F. Quinolinium Chlorochromate (QCC)

Quinolinium chlorochromate was first reported in 1986 by Kalsi et al. as effective and mild oxidant for organic substrates under mild condition.

R. Srinivasan, and Coworkers have reported the selective oxidation of 1° alcohols in presence of 2° alcohols by mild, stable and efficient QCC. QCC is prepared by treating a solution of CrO3 in 6M HCl with quinoline at 0°C. The orange red solid compound is stable to ordinary exposure to air, moisture and light. It efficiently oxidizes 1° and 2° alcohols to the corresponding carbonyl compounds. QCC is soluble in water, DMF and DMSO, sparingly soluble in DCM and chloroform and insoluble in ether, ethyl acetate, toluene, and heptane.
QCC (1 molar equivalent) oxidizes $1^0$ alcohols to the corresponding aldehydes in refluxing DCM and reasonably oxidizes $2^0$ alcohols to ketones. Solution of QCC in DMF oxidizes benzoin and benzhydrol to the corresponding ketones in excellent yields. Mechanism and comparative study with IQCC has also been reported.$^{214\text{ a}}$

The oxidation of aliphatic primary alcohol$^{215}$ by QCC has been studied in aqueous acetic acid medium. The rate shows first order dependence each in [QCC] and [alcohol]. The linear increase in the oxidation rate of alcohol with acidity suggest the involvement of protonated Cr(VI) species in the rate determining step which is confirmed by decrease in the rate of reaction with an increase in dielectric constant with the change in ionic strength. The reaction does not induce the polymerization of acrylonitrile. As a result, hydrogen abstraction mechanism is unlikely. The oxidation of [1, 1-$\text{D}_2$]- ethanol shows the presence of primary kinetic isotope effect. The observed results suggest a hydride transfer in the rate determining step. In a concerted sigmatropic reaction a cyclic hydride transfer takes place.

The oxidation of substituted benzyl alcohols by QCC involves the decomposition of an initially formed chromate ester via a concerted symmetrical transition state.$^{214\text{ b}}$ It has been found as a more efficient reagent for the oxidation of aromatic alcohols as compared to the oxidation of aliphatic alcohols.
II.4.G. Quinolinium Fluorochromate (QFC)

Chaudhary and coworkers reported the synthesis of quinolinium fluorochromate (QFC) in 1991 though the details were published in 1994\textsuperscript{216} in the meanwhile, Murugesan and Pandurangan also reported the synthesis of QFC.\textsuperscript{160} The preparations, reported by the two groups of workers are similar. Chaudhury et al.\textsuperscript{216} observed that QFC was univalent electrolyte and corresponds to the formula C\textsubscript{9}H\textsubscript{7}NH\textsuperscript{+}[CrO\textsubscript{3}]. They characterized the compound by IR and EPR spectroscopy and SEM techniques. QFC is less acidic as compared to PCC and PFC.

QFC was prepared from quinoline, 40% HF acid and chromium trioxide in molar ratio of 1:1.5:1. QFC is soluble in water, DMF, DMSO and acetone. It is sparingly soluble in DCM and chloform and insoluble in benzene, 1, 4 dioxane, heptane, ethyl acetate, toluene, ether.

Further QFC does not react with acetonitrile and nitrobenzene which is a suitable medium for showing oxidation kinetics and mechanism.\textsuperscript{1}O\textsuperscript{0} alcohols are oxidized to aldehydes by QFC in DCM at room temperature. The diverse types of organic substrates that have been oxidized by it have highlighted the versatile nature of QFC. Recently Chandrasekhar et al.\textsuperscript{217} reported that QFC in DCM was able to deprotect and oxidize the \textsuperscript{1}O\textsuperscript{0} alcoholic group, while leaving the protect secondary \textsuperscript{1}O\textsuperscript{0} alcoholic group intact.

Most of the workers have explained the hydrogen ion dependence by assuming the formation of a protonated chromium (VI) species in a pre-
equilibrium, either both the unprotonated and protonated or only the protonated form being the reactive species. In the oxidation by QFC\textsuperscript{218} the rates were obtained in different organic solvents and the analysis of the solvent effect indicated the greater importance of the cation-solvating power of the solvents. The temperature-dependence of reactions indicated a symmetrical transition state in the rate-determining step of this oxidation. The oxidation of vicinal and non-vicinal diols by various halochromates, viz QFC in DMSO has been studied.

Kinetics and mechanism of the oxidation of substituted benzyl alcohols by QFC have been reported. Itishri Dave et.al. \textsuperscript{219} reported the correlation analysis of reactivity in the oxidation of substituted benzyl alcohols by QFC. Oxidation of benzyl alcohol and some ortho, meta, and para-monosubstituted ones by Quinolinium Fluorochromate in DMSO leads to the formation of corresponding benzaldehydes. The reaction is first order each in both QFC and alcohol. The effect of hydrogen ions was studied in the oxidation by QFC. In the oxidation by QFC, the hydrogen-ion dependence has the form

\[ k_{\text{obs}} = a + b[H^+] \]

Oxidation of α, α- dideuteriobenzyl alcohol has exhibited a sustainable primary kinetic isotope effect. The reaction has been studied in nineteen organic solvents and the effect of solvent analyzed using Taft’s and Swain’s multiparametric equations. The rates of oxidation of para and meta substituted benzyl alcohols have been correlated in terms of Charton’s triparametric LDR equation. Whereas the oxidation of ortho-substituted benzyl alcohols with tetraparametric LDRS equation. The oxidation of para-substituted benzyl alcohols is more
susceptible to the delocalization effect than that of ortho- and meta substituted compounds, which display a greater dependence on the field effect. The positive value of $\eta$ suggests the presence of an electron-deficient reaction center in the rate determining step. The reaction is subjected to steric acceleration by the ortho-substituents.

II.5. Oxidation of Alcohols with Cr(VI) Under Neutral Conditions

The oxidations of particularly sensitive alcohols may require complete neutral conditions to attain good yields. For this purpose some neutral Cr (VI) containing reagent and special reactions conditions have been developed.

Chromium trioxide dissolves in tert-butyl alcohol by depolymerization to give di-tert-butyl chromate which acts an oxidation in a variety of apolar solvents. di-tert-butyl chromate (DTBC) has been especially used for oxidation of allylic oxidation of double bonds, it may also be used for oxidation of alcohols. The reaction is performed in non-polar media such as pet.ether, benzene, or carbon tetrachloride. The oxidation of primary alcohols in pet.ether or benzene at room temperature with 1 equivalent of TBC does not appear to be particularly promising; however, a mixture of the aldehyde, acid and the ester of the acid is invariably obtained.\[\text{Scheme-63}\]

\[\text{Scheme-63}\]
In each case a small percentage of starting material was recovered. On the other hand, oxidation of benzylic primary alcohols gave the aldehyde in good yields together with small amounts of the corresponding acid, but not the ester.\textsuperscript{221} (Scheme-64)

![Scheme-64](image)

Better results were obtained by using TBC in situ from chromyl chloride. This procedure avoids the formation of water which may cause side reaction.\textsuperscript{222} When chromyl chloride is added to a solution of pyridine/ tert-butyl alcohol in DCM in a dry ice/ acetone bath and the reaction mixture allowed warming at room temperature, the solution becomes orange-red and a white precipitate of pyridine hydrochloride appears. (Scheme-65)

![Scheme-65](image)

This solution is capable of oxidizing aliphatic, allylic and benzylic alcohols to aldehydes and ketones in high yield when treated at room temperature for 2 hours with a ratio of chromyl chloride to substrate of 1.1:1.
Solutions of chromium trioxide in hexamethylphosphoramide (HMPA) are also capable of converting alcohols to carbonyl compounds under mild conditions. Chromium trioxide readily dissolves in HMPA at room temperature to give stable, deep red solutions which have been used on steroids under neutral conditions for the selective oxidation of certain allylic and benzylic hydroxyl group in the presence of other unprotected saturated groups.\(^{223}\) (Scheme-66)

![Diagram of Scheme-66](image)

Scheme-66

Saturated alcohols are oxidized more slowly while aldehydes may, nevertheless, be obtained in good yields from saturated primary alcohols under appropriate conditions. The reagent was found useful for performing selective oxidations of primary alcohols in the presence of unprotected secondary ones for example; strophantidol is slowly converted to strophantidine in about 35 % yield without ketonic products being formed.\(^{224}\)

Chromate salt of tetraalkylammonium ions is soluble in aprotic solvents, as e.g. benzene (orange benzene), resulting in solutions which show interesting oxidizing properties. The use tetraalkylammonium salts to facilitate the solubility of inorganic ions in organic solvents of low solvating ability has recently called increasing attention.\(^{225}\) It was eventually found that a liquid commercial mixture of methyl trialkyl ammonium chlorides, facilitates the solubilization of potassium...
dichromate in several apolar organic solvents as DCM, CHCl₃, tetrachloromethane, and benzene; a 2:1 adogen to dichromate molar ratio is used. The organic solution of the dichromate can be formed without priorly dissolving the salt in water, simply by vigorously stirring the crushed salt in the desired solvent containing two equivalents of adogen. The resulting orange solutions are fairly stable at room temperature but slowly darken after several days. Dichromate anions in orange benzene reveal to be a very mild oxidizing reagent which discriminately oxidizes alcohols to the corresponding carbonyl compounds. In fact, α, β unsaturated alcohols are oxidized to corresponding carbonyl compounds at 55°C in good yield while saturated alcohols only give poor yields under acidic conditions. This procedure may, therefore be useful for neutral oxidations of activated alcohols where acidic or basic conditions must be avoided.

**II.6. Oxidation of Alcohols with Oxochromium(VI) Supported on Polymers.**

Literature survey reveals that through a good number of oxochromium (VI) reagents have been developed for the oxidation of alcohols but their commercial uses are still restrict mainly due to long reaction time, low selectivity, non-catalyzed nature and above all the difficulty in product isolation.

The concept of supporting Cr (VI) reagents onto inert inorganic and organic polymeric matrices may be circumvented some of the problems associated with the soluble Cr (VI) reagents. It has been found that Cr (VI) derivatives supported on an insoluble organic or inorganic matrix are particularly convenient in organic synthesis. The insoluble support provides a particular environment
The use of polymeric reagents facilitates the purification of final product. In order to increase the industrial applicability of soluble Cr (VI) compound, significant attempts have been made to anchor the soluble reagent to both organic and inorganic polymers. The polymer supported reagent often exhibits higher thermal stability and better selectivity.

Reported polymer supported Cr (VI) reagents may be broadly classified as follow:

(i) Polymeric analogue of heterocyclic halochromate. \(^{230, 231, 236(a, b)}\)

(ii) Chromium trioxide supported on inert inorganic supports. \(^{237(a-i)}\)

(iii) Heterocyclic halochromate supported on inert inorganic supports. \(^{238 (a-d)}\)

Poly (vinylpyridine) was used as an organic polymer support for PCC \(^{230}\) and PDC\(^{231}\). Both the reagents were found moderately effective towards the oxidation of different types of allylic, benzylic primary and secondary alcohols. (Scheme-67)

![Scheme-67](image-url)
The main disadvantage associated with these organic polymers were their very low accessibility requiring a two to five fold excess of the reagent.

Literature survey reveals that in many occasions chromium trioxide were supported on inert inorganic polymers such as silica gel, α-alumina, γ-alumina, ZSM-5 etc\textsuperscript{233-235, 239}.

Chromium acid adsorbed on silica gel was found suitable for the oxidation of alcohols to the corresponding carbonyl compounds\textsuperscript{237(b)} This reagent prepared by addition of silica gel to an aqueous solution of chromic anhydride subsequently evaporated to dryness. The yellow resultant solid was then kept overnight at 100\textdegree C and stored under vacuum in the dark.

Pyridinium chromate on silica gel was obtained by treating chromic acid adsorbed on silica gel with pyridine and was used for the oxidation of alcohols containing acid-labile functions\textsuperscript{237(c)} Chromyl chloride was supported onto silica – alumina\textsuperscript{240} and the reagent was used for the oxidation of primary and secondary alcohols to respective aldehydes and ketones. (\textbf{Scheme-68})
B. Khadikar and coworkers\cite{237} prepared silica gel supported chromium trioxide by co-grinding anhydrous CrO$_3$ with silica gel. This reagent was used in equimolar quantity to oxide alcohols to carbonyl compounds with good yields. γ-Alumina, which is frequently used as a solid support consists of very high area. Dispersion of CrO$_3$ and wet alumina in hexane afforded the alumina-supported chromium reagents may be used for the chemoselective oxidation of a wide range of alcohols. Thus 2-cyclohexen-1-ol in hexane afforded 94\% 2-cyclohexenone on treatment with alumina-supported chromium (VI) reagents\cite{237}. Masao Hirano et.al.\cite{241} reported the oxidation of alcohols with chromium trioxide in the presence of wet alumina oxide in aprotic solvents.

In some cases the bulk of a high surface area material serves as catalyst. Such material is called a uniform catalyst. One such example of uniform catalyst is ZSM-5. It has three dimensional, network built from AlO$_4$ and SiO$_4$ tetrahedral.\cite{242} Zeolites are used as catalyst in various synthetic organic transformations much more effectively and selectively than the Lewis acid catalysts. Thus the use of heterogeneous catalysis in different areas of organic synthesis has now reached to significant level not only because it enables environmentally begin synthesis, but also due to the good yields, accompanied by excellent selectivities. These properties of ZSM-5 may allow it to act as a highly effective solid support for oxochromium (VI) reagents and may lead the hybrid reagents highly effective and catalytic towards the oxidation of primary and secondary alcohols.
A variety of alcohols were oxidized to the corresponding carbonyl compounds in excellent yields by chromium trioxide / ZSM-5 in DCM at room temperature. The oxidation of alcohols to the corresponding carbonyl compounds using zeolites has been reported by a number of researchers.

Attempts were also made to have solution of some the problems associated with the soluble heterocyclic halochromate by immobilizing the same with inert inorganic supports.

Frederick A. Luzzio et.al. reported a facile oxidation of cis, trans-4 – tert-butyl cyclohexanol to 4- tert-butyl cyclohexanone and dl menthol to dl menthone using PCC on silica gel. It was used in conjunction with silica gel to facilitate removal of reduced chromium byproduct and to provide anhydrous conditions that would otherwise lead to unwanted side reaction with decreased yields.

M. M. Heravi and coworkers were reported a simple and efficient method for oxidation of alcohols to carbonyl compounds under non-aqueous conditions employing 3-carboxypyridinium Chlorochromate (CPCC) adsorbed on alumina. CPCC adsorbed on alumina was prepared by adding alumina to a solution of CPCC in DCM and evaporating to dryness. The yellow orange solid was then kept in vacuum at room temperature and stored in the dark before use.

Mohammed M. Hasmi and coworkers were introduced silica gel supported 4-aminopyridinium Chlorochromate. It was prepared from reaction of 4-aminopyridine with activated silica gel which was then reacted with a solution of chromium trioxide in hydrochloric acid. The oxidation of alcohols is performed in DCM as solvent and work up was simply by separation of the heterogeneous
supported oxidant by filtration and purification by column chromatography led to aldehydes and ketones in high yields. Mild reaction conditions, easy work up, high yield and reusability of the supported reagent are the most significant aspect of this method. Quinolinium fluochrome (QFC) supported on alumina prepared by a new method oxidizes selectively aliphatic 1° and 2° alcohols, substituted benzylic alcohols and allylic alcohols to their corresponding carbonyl compounds in good yields. The effect of solvent in the oxidation reaction was evaluated by carrying out the oxidation in a series of solvents with varying polarity. The period for maximum conversion was found to be minimum in hexane. Although the oxidation reactions proceed smoothly in DCM, hexane was chosen as the solvent for the entire oxidation process keeping in view of the environmental hazards associated with chlorinated hydrocarbon. A comparative study of the oxidation by this reagent and the one already reported (prepared by a different method) was carried out with a series of aliphatic 1° alcohols, benzyl alcohol, furfurol, cyclohexanol and benzoil. Studies revealed that the present reagent is a better one in terms of reaction period and percentage yield.

A new selective method of QFC-supported silica gel for the oxidation of a wide variety of alcohols to the corresponding carbonyl compounds in good yield has been reported. The maximum conversion of benzyl alcohol to benzaldehyde occurred in a shorter reaction period in hexane and DCM. The oxidation of a series of aliphatic 1° alcohols with QFC-silica gel revealed that the lower homologues up to 1-octanol are readily converted to the corresponding aldehydes at room temperature while the higher homologues such as 1-nonanol and 1-decanol require reflux conditions. It was interesting to note that the
oxidation of $1^0$ alcohols with alkyl group at C-2 position such as 2-ethyl 1-hexanol and neopentyl alcohols proceeds smoothly at a faster rate than 1-hexanol and 1-pentanol. It was observed that the oxidation of $2^0$ alcohols with QFC-silica gel proceeds smoothly only under reflux conditions resulting in high conversion of alcohols to the corresponding ketones. The reagent selectively oxidizes $1^0$ hydroxyl group in the presence of secondary hydroxyl group. The selectivity is also exhibited in the oxidation of axial hydroxy group of the cis-t-butyl cyclohexanol in preference to equatorial hydroxyl group. Oxidation of steroidal homoallylic alcohols is a crucial step in the synthesis of most of the steroidal hormones; oxidation of 3-β-chloestanol with QFC-silica gel gave chloestanone with 60% yield. These reactions clearly indicate the potential utility of QFC-silica gel in biosynthesis. QFC-silica gel is quite effective for the oxidation of heterocyclic alcohols also. On the other hand the oxidation 3-pyridyl methanol afforded 3-pyridyl carboxaldehyde with 65 % along with 20 % quinoline. ESR spectral analysis of the reduced product of the QFC-silica gel showed a single band with a g value of 1.982 and this value shows the presence of $d^2$ Cr (IV) species.

Synthesis organic chemist has wide variety of technique and method in this repertoire to tailor an elegant synthesis but today any new development in synthesis has to take into consideration of ecological aspect, toxic waste generation, and formation of unwanted byproducts and cost of manufacture, no matter how innovative chemistry is employed in the process. Therefore, the demand today is for a synthesis which (a) is environmentally begin (b) minimizes or eliminates waste generation (c) uses chemicals which do not need for special
methods of preparation (d) avoids the use of environmentally unfriendly solvents (e) is stereoselective or regioselective for the desired enantiomers or isomers and (f) a number of steps into a single operation. Microwave assisted organic synthesis is the outcome of these progressive thoughts.

II.7. Microwave Technology

Since the appearance of the first article on the uses of microwave for chemical reactions, the approach has blossomed into a useful technique for a variety of applications in organic synthesis and functional group transformations. Microwave technique has a great potential and can be utilized as a highly innovative synthetic tool for the generation of highly functionalized products.

The practical utility of MW assisted green protocol has been realized in several synthetic operations such as protection/deprotection, condensation, oxidation, reduction, rearrangement reaction and in the synthesis of various heterocyclic systems. The reviews on this subject illustrate clearly the ingenuity and imaginative breath in this area by presenting a showcase of research over the past ten years.

With easy availability of ultrasound and microwaves, their use in chemistry has gained momentum recently. Microwave heating emerged as a powerful technique to promote a variety of chemical reactions.

Microwave was first reported by the group of Gedye and Giguere Majetich in 1986, but the use of microwave in organic synthesis was initially
hampered by a lack of understanding of basic principles of MW dielectric microwave ovens. Today over 2000 articles have been published in the area of MW assisted organic synthesis, including several reviews.259-265

II.7.A. Application of Microwave for the oxidation of alcohols

Balogh and Coworkers266 have introduced a facile method for the oxidation of alcohols to carbonyl compounds with yields wherein clayfen [Iron (III) nitrate] was used under microwave irradiation in solvent free condition (Scheme-69)

\[
\begin{align*}
\text{Clayfen} & \quad \text{MW, 15-60 Sec.} \\
\text{R}_2\text{CH-OH} & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
& \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
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\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\text{R}_1 & \quad \text{Clayfen} \\
\text{R}_2 & \quad \text{Clayfen} \\
\end{align*}
\]

\[\begin{align*}
\text{176} & \quad \text{177 (87-96%)} \\
\text{R}_1 & \quad \text{Ph, p-MeC}_6\text{H}_4, p\text{-MeOC}_6\text{H}_4; R_2=H \\
\text{R}_1 & \quad \text{Ph; R}_2=\text{Et, PhCO} \\
\text{R}_1 & \quad p\text{-MeOC}_6\text{H}_4 R_2=p\text{-MeOC}_6\text{H}_4\text{CO} \\
\end{align*}\]

Scheme-69

R.S.Varma and Coworkers267 have developed a new reagent manganese dioxide-silica for the oxidation of alcohols to carbonyl compounds under microwave irradiation. Benzyl alcohol were selectively oxidized to carbonyl compounds using 35% MnO\textsubscript{2} ‘doped’ silica under MW irradiations (Scheme-70)
R.S. Varma and coworkers\textsuperscript{268} have studied the facile oxidation of alcohols to carbonyl compounds with alumina supported iodobenzene diacetate (IBD) under solvent free condition in microwave irradiation with quantitative yields. The advantage of using alumina as a support was apparent in marked improvement in yields obtained with the alumina-IBD system as compared to neat IBD. (Scheme-71)

\begin{equation}
\begin{array}{c}
\begin{array}{c}
\text{R}_1\text{CH-OH} \\
\text{R}_1
\end{array}
\xrightarrow{\text{MnO}_2 \cdot \text{Silica} \ \text{MW, 20-60 Sec.}} \\
\begin{array}{c}
\text{R}_1\text{C=O} \\
\text{R}_1
\end{array}
\end{array}
\end{equation}

\text{178} \quad 179(67-96\%)

R_1 = \text{Ph, } p\text{-MeC}_6\text{H}_4, p\text{-MeOC}_6\text{H}_4, \text{PhCH}=\text{CH} \ ; \ R_2 = \text{H}

R_1 = \text{Ph} ; \ R_2 = \text{Et, PhCO}

R_1 = p\text{-MeOC}_6\text{H}_4 ; R_2 = p\text{-MeOC}_6\text{H}_4\text{CO}

\text{Scheme-70}

R.S. Varma and coworkers\textsuperscript{269} were used chromium trioxide impregnated pre-moistened alumina for the oxidation of benzyl alcohol at room temperature. The reactions were observed clean with no tar formation. No over oxidation to carboxylic acid was observed (Scheme-72).
R.S. Varma and coworkers\(^{270}\) have studied the oxidation of symmetrical and unsymmetrical benzoin to benzil by copper (II) sulfate-alumina or oxone-wet alumina under microwave heating (Scheme-73).

\[
\begin{align*}
\text{Scheme-72}
\end{align*}
\]

M. M. Heravi and coworkers\(^{271}\) reported a facile and selective oxidation of alcohols to carbonyl compounds using ammonium chlorochromate on
montmorillonite k-10 under solvent free conditions that was accelerated in most cases by exposure to microwaves. Primary alcohols were oxidized to the corresponding aldehydes and the oxidation of aldehydes to the corresponding acid derivative was not observed even after prolonged irradiation and with excess of supported chromium reagent.

M. M. Heravi and coworkers\textsuperscript{272} reported oxidation of various alcohols to the corresponding carbonyl compounds in excellent yields by chromium trioxide – HZSM-5 zeolite under microwave irradiation in a solventless system. Two equivalent of CrO\textsubscript{3} and a weight equivalent of HZSM-5 zeolite per mol of benzyl alcohol was used and exposed to microwave irradiation for 30 sec. which led to the formation of benzaldehyde almost quantitatively, no trace of benzoic acid was observed showing that no overoxidation occurs. Cinnamyl alcohol (186) was converted to cinnamylaldehyde (187) in 90 % yield. (Scheme-74).

\begin{center}
\begin{tikzpicture}
\node at (0,0) (a) {\text{\textbf{186}}};
\node at (2,0) (b) {\text{\textbf{187}}};
\draw[->] (a) -- node[above] {$\text{HZSM-5 Zeolite, CrO}_3$ \text{MW}$} (b);
\end{tikzpicture}
\end{center}

\textbf{Scheme-74}

M. M. Heravi and coworkers\textsuperscript{273} reported the selective oxidation of alcohols by silica-gel supported ammonium Chlorochromate in solvent less system. The oxidation reaction is conducted by mixing finely ground reagent with alcohols. This procedure was found a rapid, economic, manipulatively, simple, selective and environmentally benign protocol when compared to the conventional solution phase reaction.
M.M. Heravi and coworkers used CrO$_3$/wet silica gel for oxidation of alcohols to corresponding carbonyl compounds under microwave irradiation in solvent free conditions. The oxidation of cinnamyl alcohol (188) with this method gave a moderate yield of cinnamaldehyde (189) (70%) and benzaldehyde (190) (30%) showing the carbon-carbon bonds are prone to cleavage by this procedure. (Scheme-75).

![Scheme-75](image)

N. Noroozi –Pesyan and Coworkers have used the alumina or silica gel as catalysts for a solvent-free oxidation of benzoins to the corresponding benzils. These catalysts were easily recovered after completion of the reactions. Comparison of the results obtained with both catalysts indicates that all the reactants were oxidized faster on alumina than on silica under these conditions. (Scheme-76)

![Scheme-76](image)
Jitender M. Khurana and Coworkers\textsuperscript{276} have reported the simple and efficient protocol for microwave-assisted solvent-free oxidation of hydrobenzoins to benzoins or benzils, benzoins to benzils, and alcohols to the corresponding aldehydes or ketones, using \textit{N}-bromosuccinimide – neutral alumina.

Amit Sahu and coworkers\textsuperscript{277} have been studied chromium based oxidants like PCC, BIFC, PFC ACC etc. supported on alumina for oxidation of benzoin under MW irradiation. Alumina was acted both as a catalyst as well as a solid support in the reaction and increases the yield of product (Scheme-77).

\begin{center}
\textbf{Scheme-77}
\end{center}
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