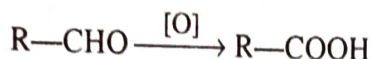


Oxidation

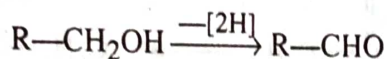
2.0 INTRODUCTION

Oxidation of an organic compound is defined as addition of oxygen, removal of hydrogen or removal of electron/s from that compound.

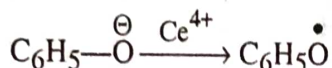
Addition of oxygen



Removal of hydrogen



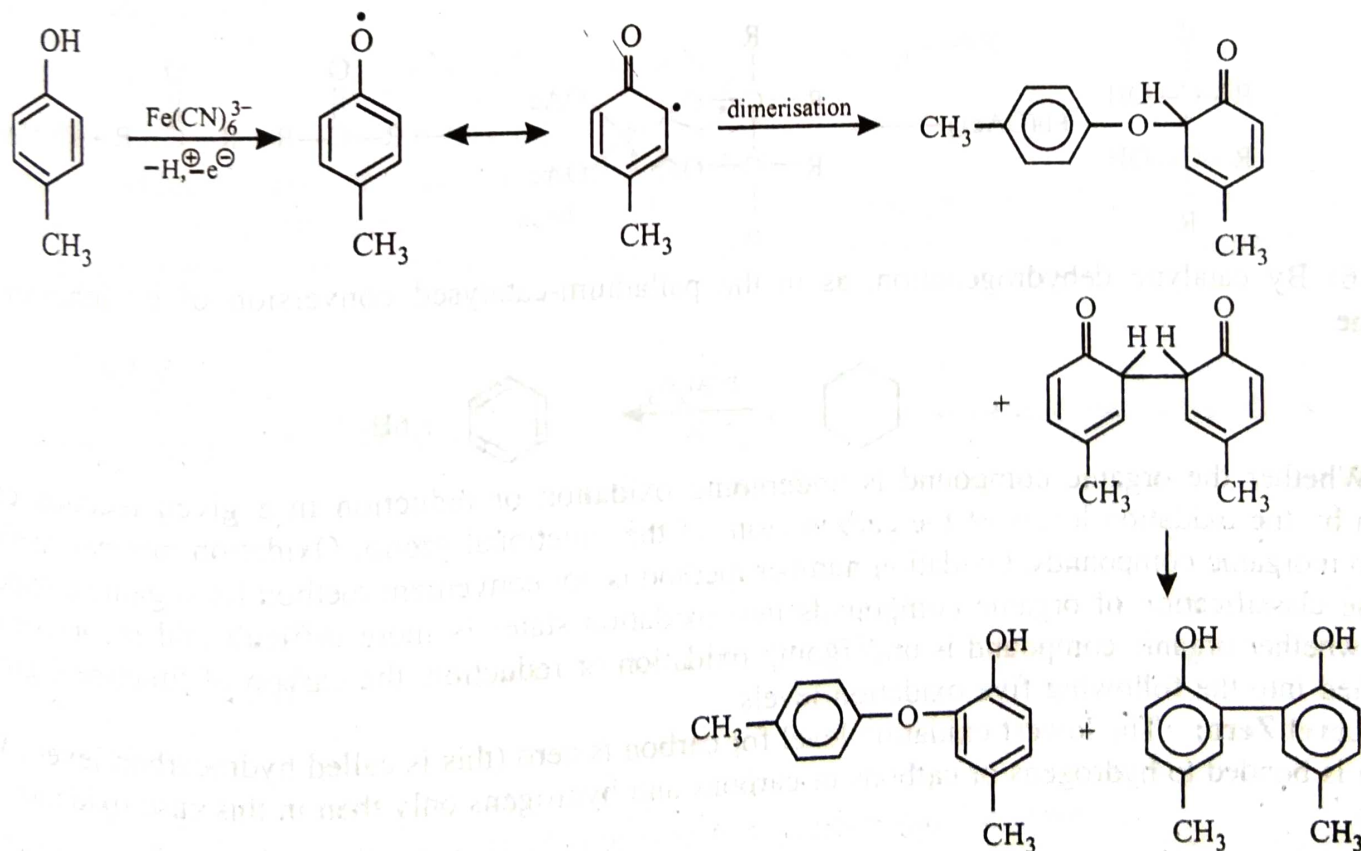
Removal of electron



Reduction is used to describe the converse reactions. Oxidation and reduction are complementary in that in any system in which one species is oxidised, another is reduced. The term used is customarily that which is appropriate to the reaction undergone by the organic compound concerned, e.g., the reaction of an aldehyde with dichromate is described as oxidation, although of course the dichromate ion is reduced.

Oxidation is normally brought about in one of the following ways:

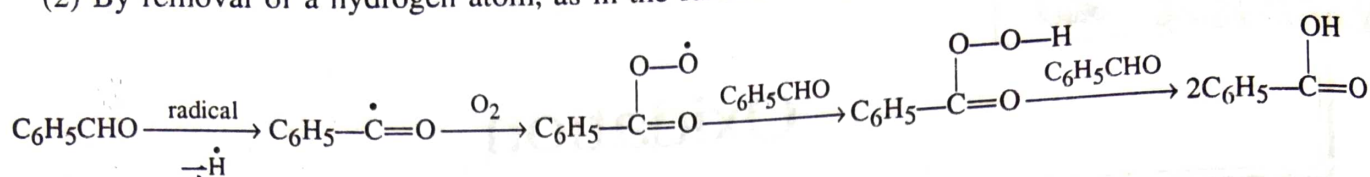
(1) By removal of an electron, as in the oxidation of phenols by ferricyanide, e.g.



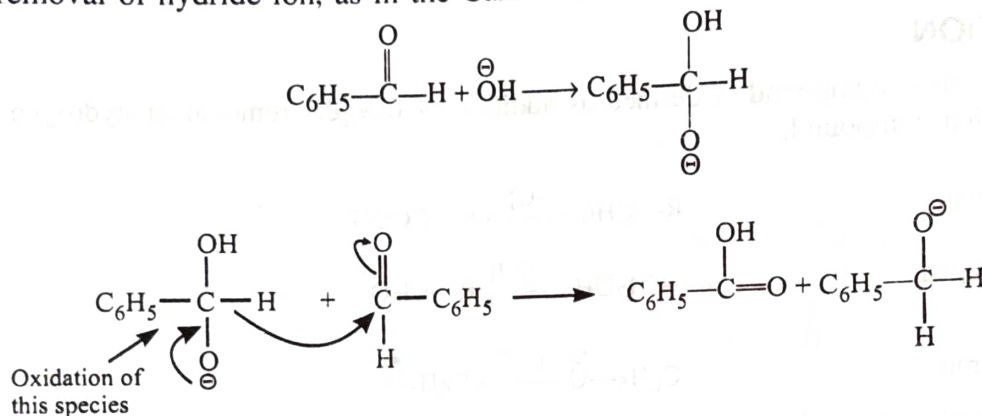
The requirement for the oxidising agent is that it should be capable of one electron reduction

(here, $e^- + \text{Fe(III)} \longrightarrow \text{Fe}^{++}$) characterised by suitable redox potential. The requirement of organic compound is that it should give a relatively stable radical on oxidation.

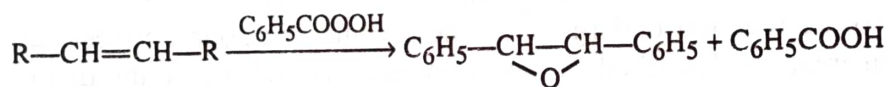
(2) By removal of a hydrogen atom, as in the radical catalysed autooxidation of aldehydes,



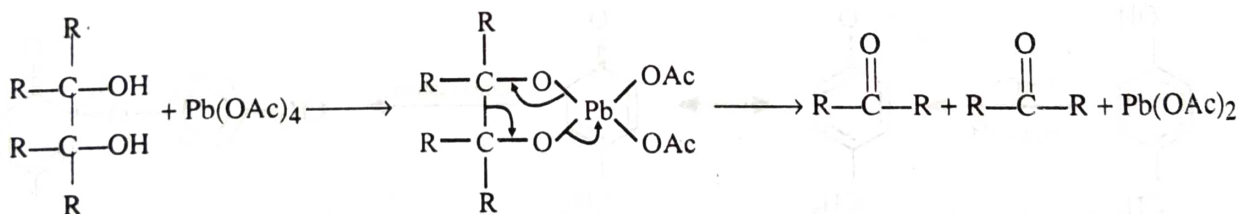
(3) By removal of hydride ion, as in the Cannizzaro reaction, e.g.



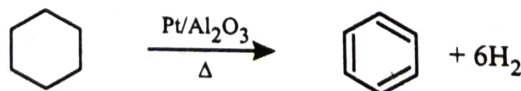
(4) By the insertion of oxygen, as in the epoxidation of an alkene by a per acid:



(5) By a concerted reaction in which the oxidising agent undergoes a two electron reduction, as in the oxidation of glycols by lead tetra-acetate.

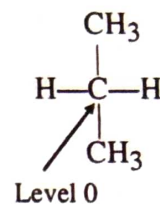
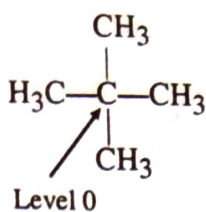
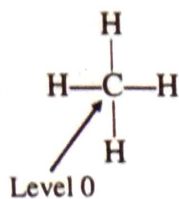


(6) By catalytic dehydrogenation, as in the palladium-catalysed conversion of cyclohexane into benzene.

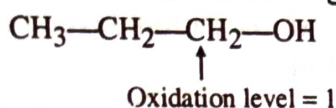


Whether the organic compound is undergoing oxidation or reduction in a given reaction can be known by the oxidation levels of the carbon atom of the functional group. Oxidation number method is used in inorganic compounds. Oxidation number method is not convenient method for organic compounds because classification of organic compounds into oxidation states is more difficult and inconsistent. To know whether organic compound is undergoing oxidation or reduction, the carbon of functional group is classified into the following five oxidation levels

Level Zero: The lowest oxidation level for carbon is zero (this is called hydrocarbon level). When carbon is bonded to hydrogens or carbons or carbons and hydrogens only then in this case oxidation level is zero.



Level 1: The next oxidation level is one (level one is also called alcohol oxidation level). In this category are carbon atoms which have one bond to an electronegative atom, such as O, N, S, X etc.

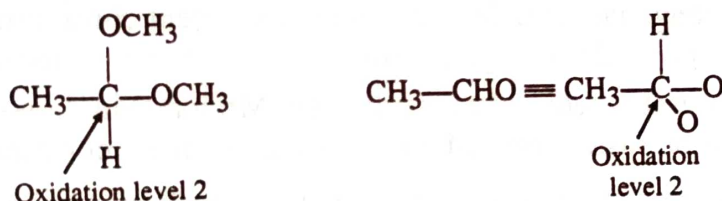


Some other examples are:

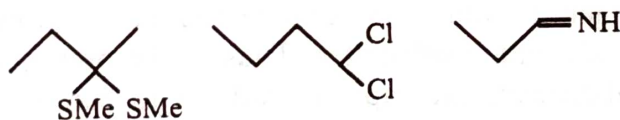


Note: Carbon-carbon double bonded group is also included in this category. Thus oxidation level of carbon in ethylene and benzene is one.

Level 2: The third oxidation level two (level two is also called ketone oxidation level) contains carbon with two bonds to electronegative atom (double bonded electronegative atom is treated equivalent to two electronegative atoms bonded to carbon). Examples are

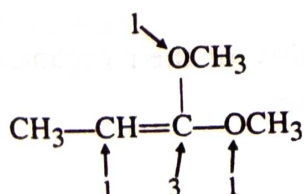
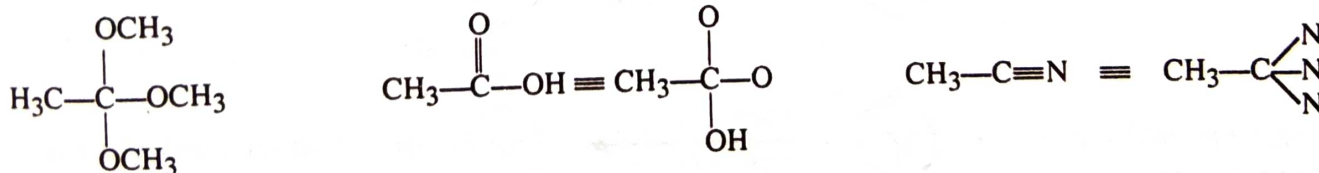


Other examples are:



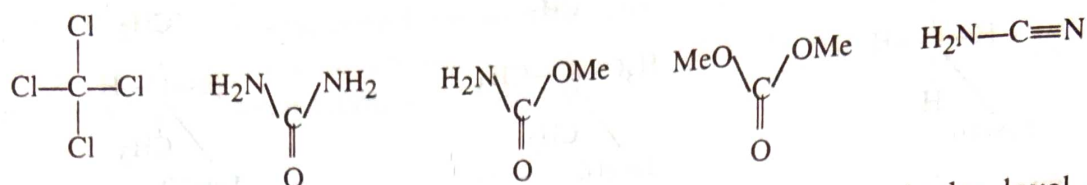
Note: Oxidation level of acetylenic carbon is also 2.

Level 3: Level 3 (the carboxylic acid level) contains carbon with three bonds to electronegative atoms (triple bonded electronegative atom is treated equivalent to three electronegative atoms bonded to carbon).

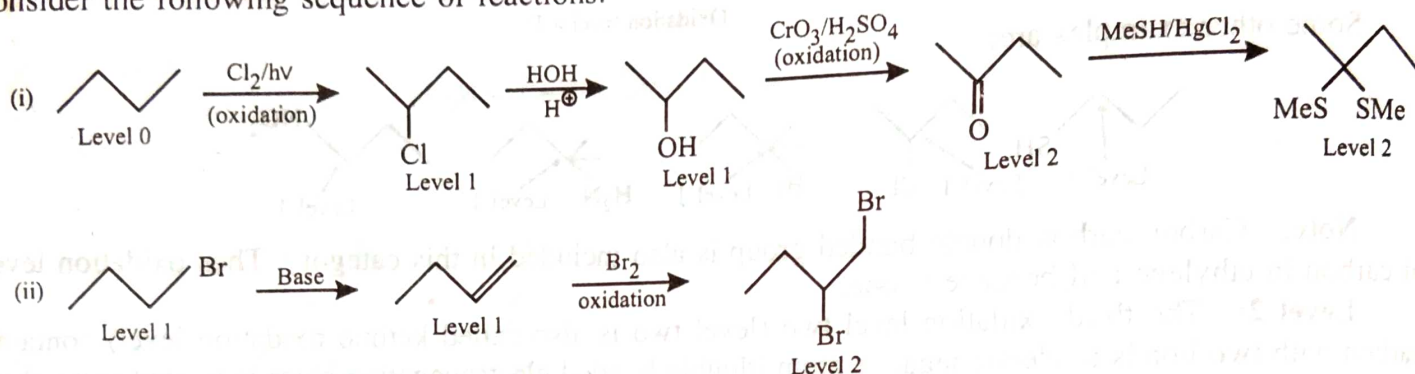


Thus level is three

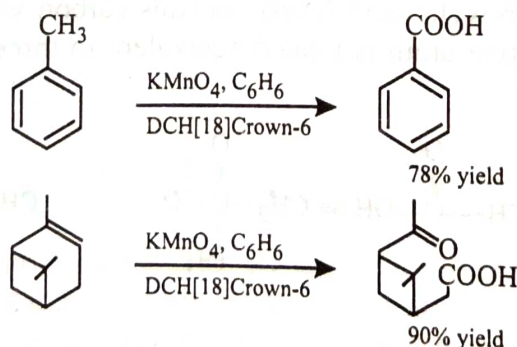
Level 4: The most oxidised level of carbon is four (carbon dioxide level).



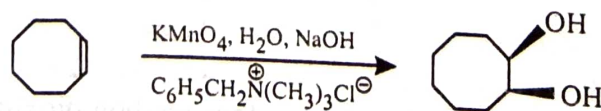
The important point to remember is that one can move within a particular level by performing chemistry that is classified as neither an oxidation nor a reduction. However, if oxidation level moves down, the process is reduction whereas if oxidation level moves up, the process is oxidation. Let us consider the following sequence of reactions:



Of the wide variety of agents available for the oxidation of organic compounds, probably the most widely used are potassium permanganate and derivatives of hexavalent chromium. Permanganate is a very powerful oxidant. Its reactivity depends to a great extent on whether it is used under acidic, neutral or basic conditions. In acidic solution it is reduced to the divalent Mn ion ($\text{Mn}^{7+} \longrightarrow \text{Mn}^{2+}$) with net transfer of five electrons while in neutral or basic media MnO_2 is usually formed, corresponding to a three electron change ($\text{Mn}^{7+} \longrightarrow \text{Mn}^{4+}$). Permanganate is used in aqueous as well as in non-aqueous medium. When it is used in non-aqueous medium, the reaction is carried out in the presence of phase transfer catalyst. In the presence of PTC the reagent is soluble in benzene and the resulting solutions are excellent reagents for the oxidation of a variety of organic substrates. Thus in the presence of DCH[18] crown-6, alkenes, alcohols, aldehydes and alkylbenzenes are rapidly oxidised to carboxylic acids in high yield at room temperature



The catalytic action of quaternary salts is believed to be due to the ability of their organic-soluble cations to transfer anion (e.g., MnO_4^-) from the aqueous into the organic phase.



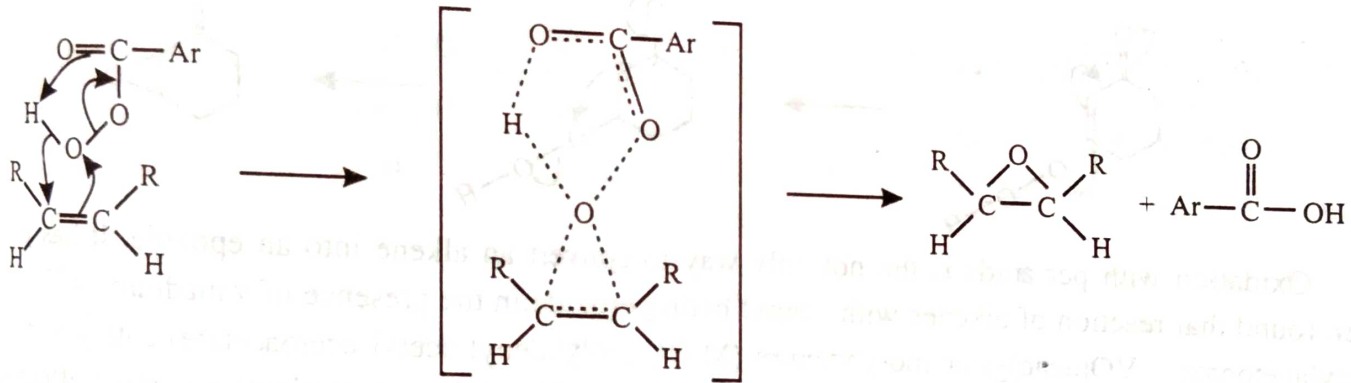
Chromic acid is one of the most versatile of the available oxidising agents, and reacts with almost all types of oxidisable groups. The reactions can often be controlled to yield largely one product, and for this reason chromic acid oxidation is a useful process in synthesis. In oxidation chromium is reduced from

the Cr^{6+} to Cr^{3+} . The commonest reagents are chromium (VI) oxide and $K_2Cr_2O_7$. The oxidation is carried out in the presence of H_2SO_4 . Chromium (VI) oxide may also be used in solution in acetic anhydride, *tert*-butanol or in pyridine. In these solutions the reactive species present are chromyl acetate, *tert* butyl chromate (VI) and the pyridine-chromium (VI) oxide complex.

2.1 OXIDATION OF HYDROCARBONS

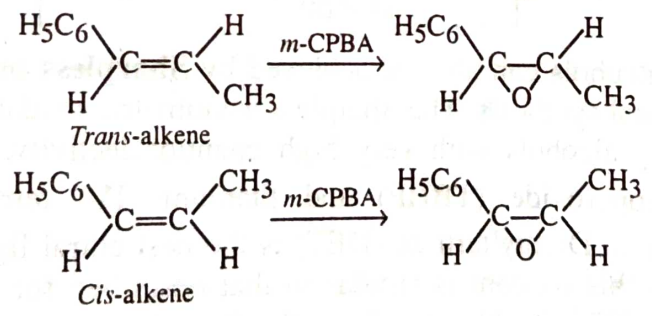
2.1.1 Oxidation of Alkenes

(1) **Epoxidation:** Olefinic double bonds react with per acids to give epoxides. The most useful reagent for effecting the alkene-epoxidation oxidation is *meta*-chloroperbenzoic acid (*m*-CPBA). *m*-CPBA is an electrophilic reagent and accordingly, reacts well with nucleophilic alkenes. Consequently electron-releasing groups in the alkene and electron-attracting groups in the per acid facilitate the reaction. Thus more alkyl substituted alkenes are more reactive than the less alkyl substituted alkenes. The reaction proceeds via a single (concerted) step which involves nucleophilic attack of the alkene π -electrons on to the per acid (Scheme-1).

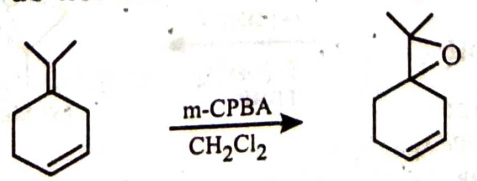


Scheme-1

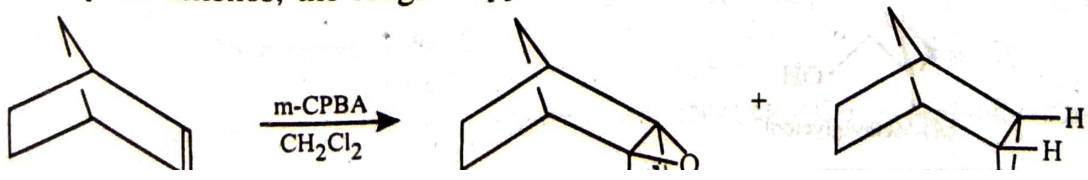
The epoxidation with per acids is stereospecific and takes place by *syn*-addition to the double bond. As the *cis* alkene gives only *cis* oxirane and *trans* alkene gives *trans* oxirane as expected from the mechanism.



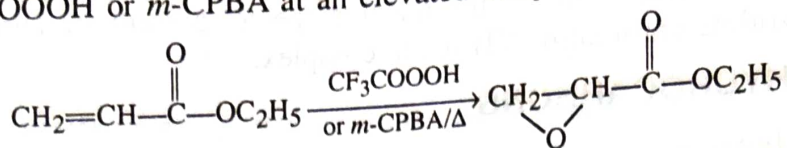
It has already been mentioned that more alkyl substituted alkenes react faster than the less alkyl substituted alkenes. Thus, it is possible to oxidise more substituted alkenes in the presence of less-substituted ones, so long as we do not use more than one equivalent of oxidant.



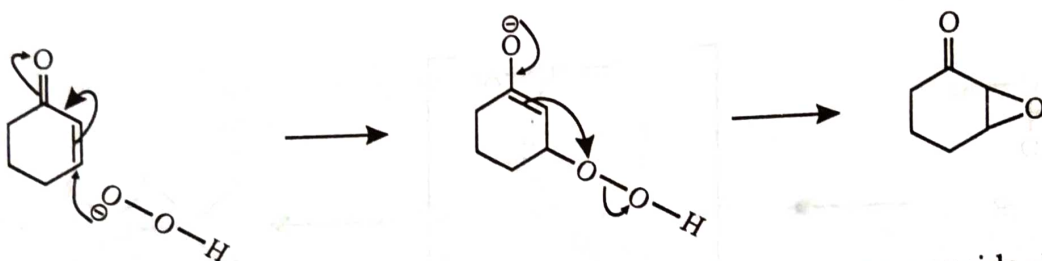
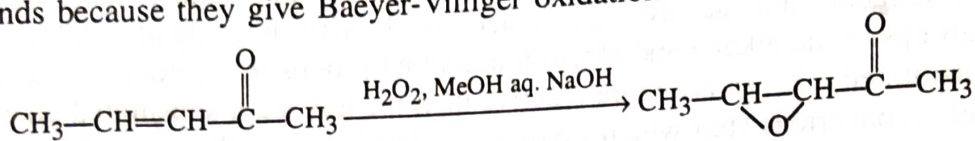
In case of cyclic alkenes, the reagent approaches from the less hindered side of the double bond.



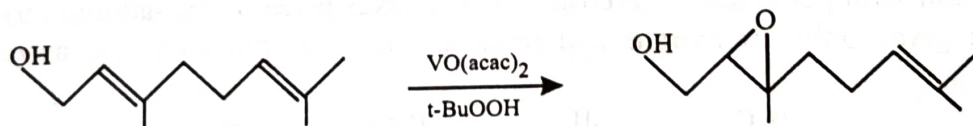
Conjugation of the alkene double bond with other unsaturated groups reduces the rate of epoxidation because of the delocalisation of the π electrons. α,β -unsaturated acids and esters, due to this reason, require stronger reagent, CF_3COOOH or *m*-CPBA at an elevated temperature for successful oxidation.



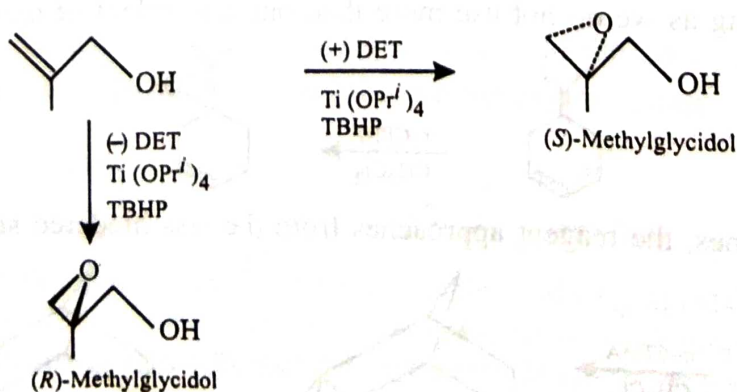
Epoxidation of α,β -unsaturated aldehydes and ketones is best performed by the action of nucleophilic reagents such as H_2O_2 or *t*-butyl hydroperoxide in alkaline solution. Per acids cannot be used in these compounds because they give Baeyer-Villiger oxidation.



Oxidation with per acids is the not only way to convert an alkene into an epoxide. It has recently been found that reaction of alkenes with *t*-butyl hydroperoxide in the presence of vanadium (V^{5+} ; vanadyl acetylacetonate: $\text{VO}(\text{acac})_2$) or molybdenum (Mo^{6+} , molybdenyl acetyl acetoacetate) catalysts provides another excellent method for the preparation of epoxides. Molybdenum catalysts are most effective for the epoxidation of isolated double bonds and vanadium catalysts for allylic alcohols.



Epoxidation of allylic alcohols can also be achieved by **Sharpless method**. This method is one of the most valuable tools for chiral synthesis. The Sharpless asymmetric oxidation is a method for converting allyl alcohols to chiral epoxy alcohols with very high enantioselectivity. It involves treating the allyl alcohol with *tert* butylhydroperoxide (TBHP) and titanium (IV) tetraisopropoxide $[\text{Ti}(\text{OPr}^i)_4]$ in conjugation with a chiral ligand. Diethyltartrate (DET) is the best chiral ligand. The reaction that ensues between an allyl alcohol and this oxidant is similar to that described for vanadium-with one important difference. The chiral ligand (DET) is able to enforce the formation of essentially a single enantiomer of epoxide product.

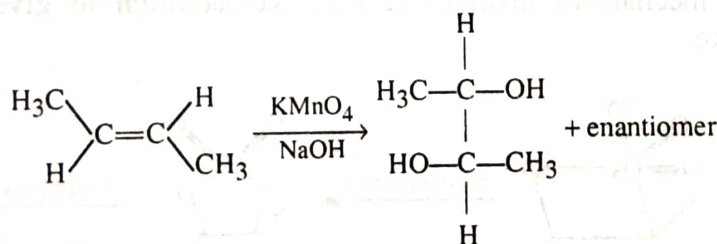
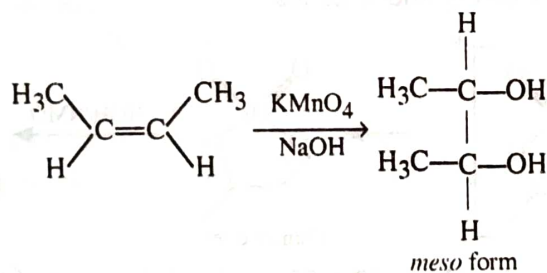
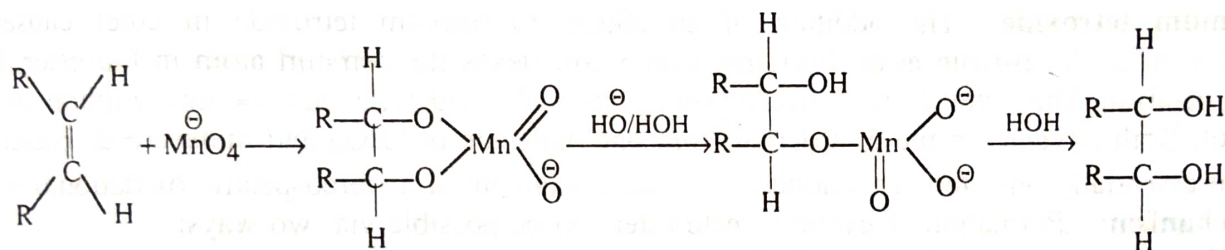


(2) **Perhydroxylation:** Perhydroxylation of carbon-carbon double bonds is useful in organic synthesis and can be effected with a number of different reagents. The most important reagents for this purpose are potassium permanganate, osmium tetroxide and iodine and silver acetate.

Potassium Permanganate

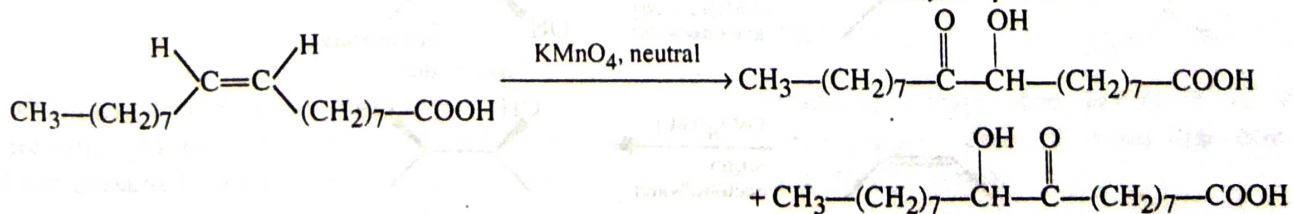
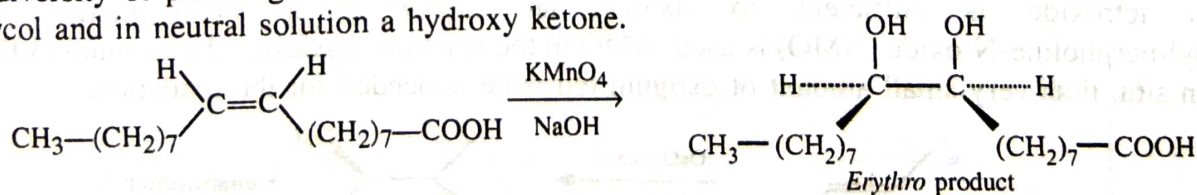
Oxidation with KMnO_4 is a widely used method for *cis* hydroxylation of alkenes, but it needs careful control to avoid over-oxidation. Best results are obtained in alkaline solution, using water or aqueous organic solvents. Poor yield of the diols is obtained because of the insolubility of the substrate in aqueous solvent. Greatly improved yields in such cases can be obtained by effecting the oxidation in the presence of a phase transfer catalyst, such as quaternary ammonium halide, or a crown ether.

The oxidation with KMnO_4 proceeds through the formation of cyclic manganese esters and it is this product which controls the *syn* addition of two hydroxyl groups. This reaction is stereospecific reaction. *Cis*-2-butene on hydroxylation gives *meso* form whereas *trans*-2-butene gives (*dl*) mixture.

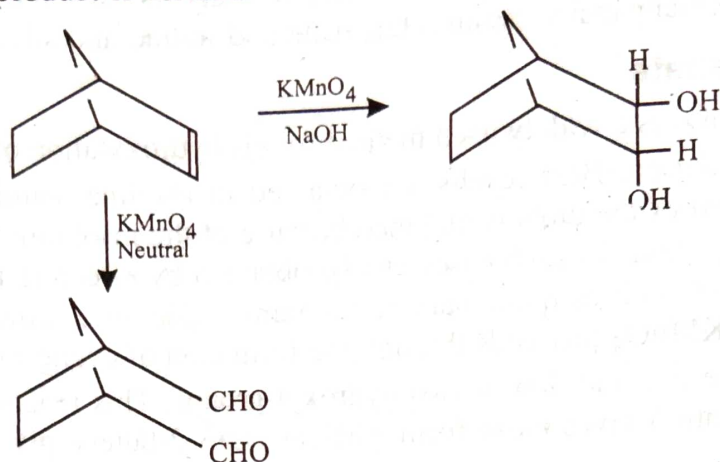


Although basic KMnO_4 forms *vic cis* diol but the reaction does not give good yield since it is difficult to stop the oxidation at the diol stage. Other products—ketones and hydroxy ketones, aldehydes, acids are also formed from 1,2-disubstituted alkenes.

The diversity of permanganate oxidation can be illustrated for oleic acid, which in basic solution gives a glycol and in neutral solution a hydroxy ketone.



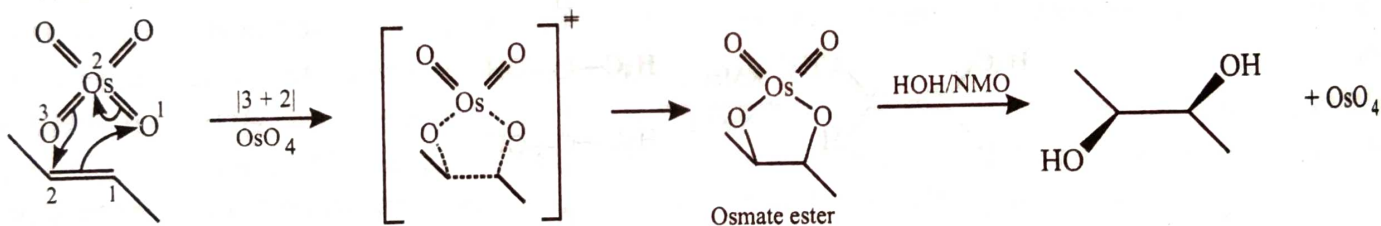
Similarly in basic solution norbornene gives glycol with basic permanganate whereas in neutral solution, a higher oxidation product is formed.



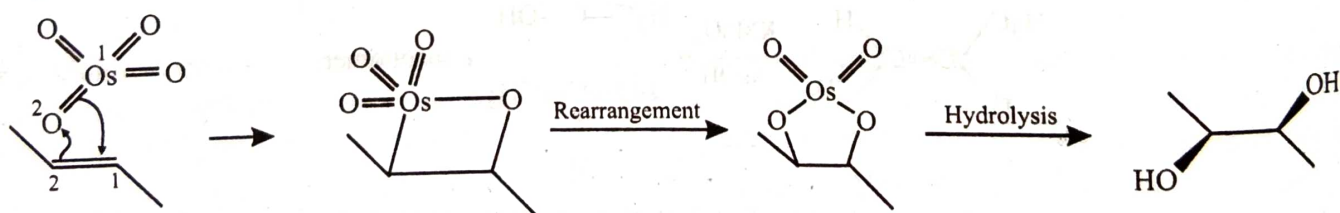
Osmium tetroxide: The addition of an alkene to osmium tetroxide in ether causes rapid precipitation of cyclic osmate ester. Pyridine, which complexes the osmium atom in the ester, is often added as catalyst. The ester is then hydrolysed, commonly with aqueous sodium sulphite to give a *cis-vic* diol. Both oxygens in the diol derive from one molecule of OsO_4 and these are delivered to the alkaline in essentially one step. This addition is classic example of a stereospecific oxidation.

Mechanism: Formation of cyclic osmate ester can be possible via two ways:

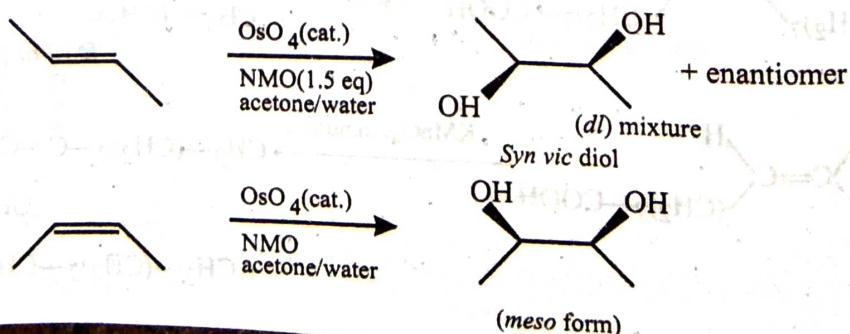
(i) [3 + 2] cycloaddition between OsO_4 and alkenes

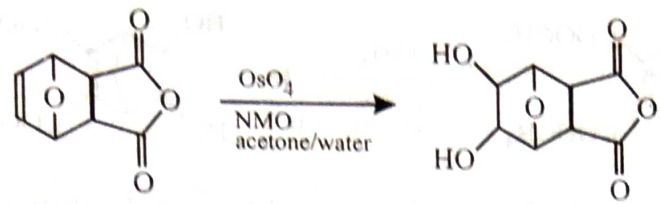


(ii) Second possible mechanism involves [2 + 2] cycloaddition to give osmaoxetane which on rearrangement gives oximate.

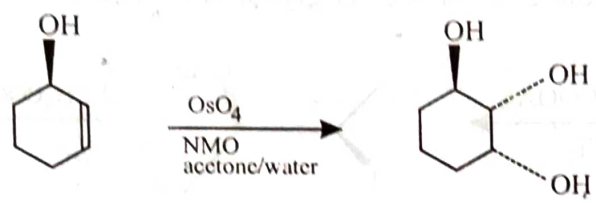


Osmium tetroxide is both highly toxic and expensive, but is really reliable and valuable reagent because of its specificity with double bonds and the ease of its application. Since osmium tetroxide is expensive, so conditions were developed that enable it to be used as a catalyst. It is found that 5 mole % osmium tetroxide is sufficient to oxidise an alkene if a stoichiometric amount of N-methylmorpholine-N-oxide (NMO) is used. NMO in the reaction reoxidises the osmium (VI) to osmium (VIII) in situ, thus very small amount of osmium tetroxide is needed for the oxidation.

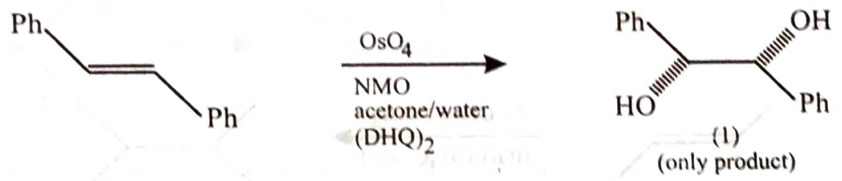




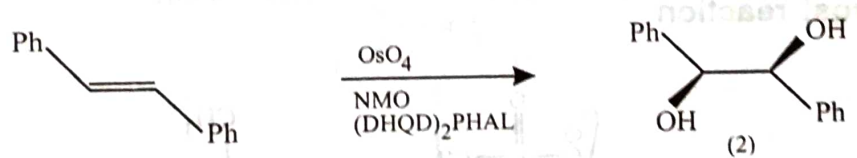
Oxidation of allylic alcohols with osmium tetroxide provides a route to 1,2,3-triols, a structural feature found in some natural products. The reaction of allyl alcohols and allyl ethers with osmium tetroxide is highly stereospecific giving preferentially the isomer in which the original hydroxyl group or alkoxy group and the adjacent newly introduced hydroxyl groups are in anti (*erythro*) relationship.



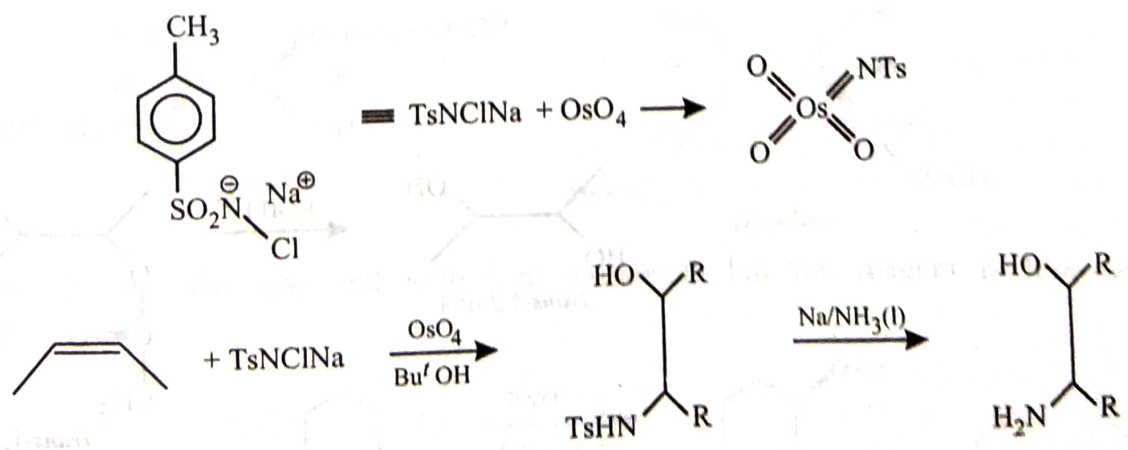
Sharpless has recently developed conditions which lead to control the enantioselectivity of the dihydroxylation reaction. The oxidation of *trans*-stilbene to the corresponding diol can be accomplished with OsO_4 , NMO and catalyst [mixture of dihydroquinine dimer: $(\text{DHQ})_2$ and phthalazine (PHAL)] to give the diol shown in $\geq 99\%$ ee.



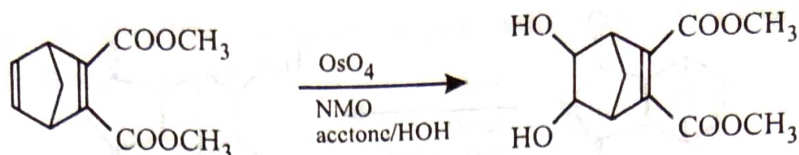
On the otherhand, when the reaction is carried out in the presence of dihydroquinidine (DHQD)] dimer and DHAL enantiomer of the product (1) is obtained as the only product.



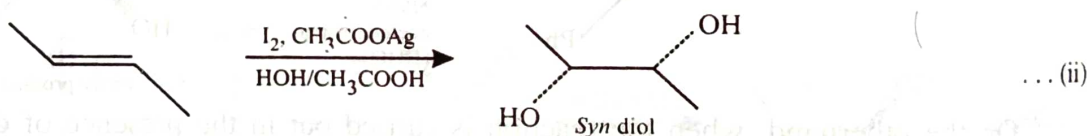
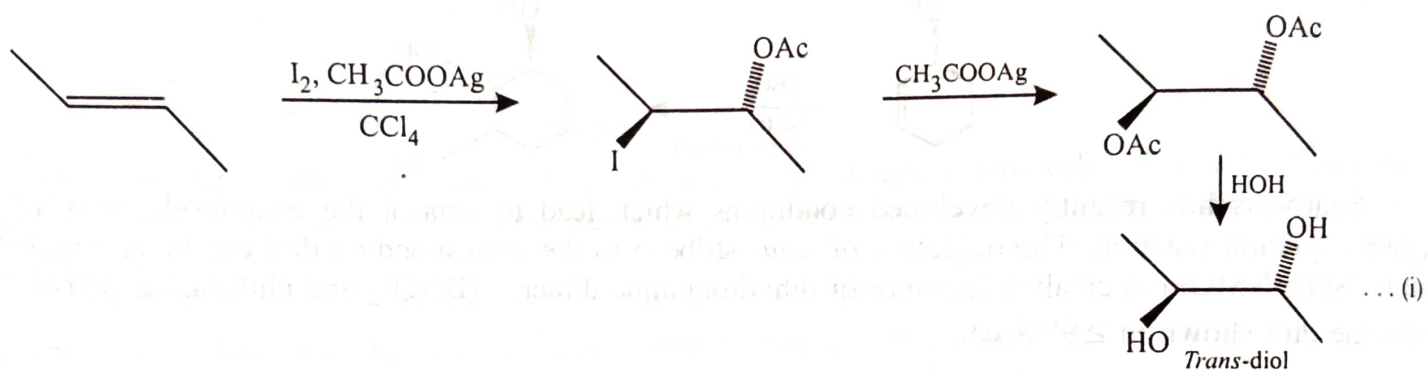
Osmium tetroxide can also be used for the preparation of *vicinal* hydroxylamines. Reaction of the alkene with chloramine T in the presence of catalytic amount of OsO_4 affords the corresponding *vicinal* hydroxyl toluene-*p*-sulphonamide. The sulphonamides are readily converted into the *cis* α -hydroxylamines by cleavage with sodium in liquid ammonia.



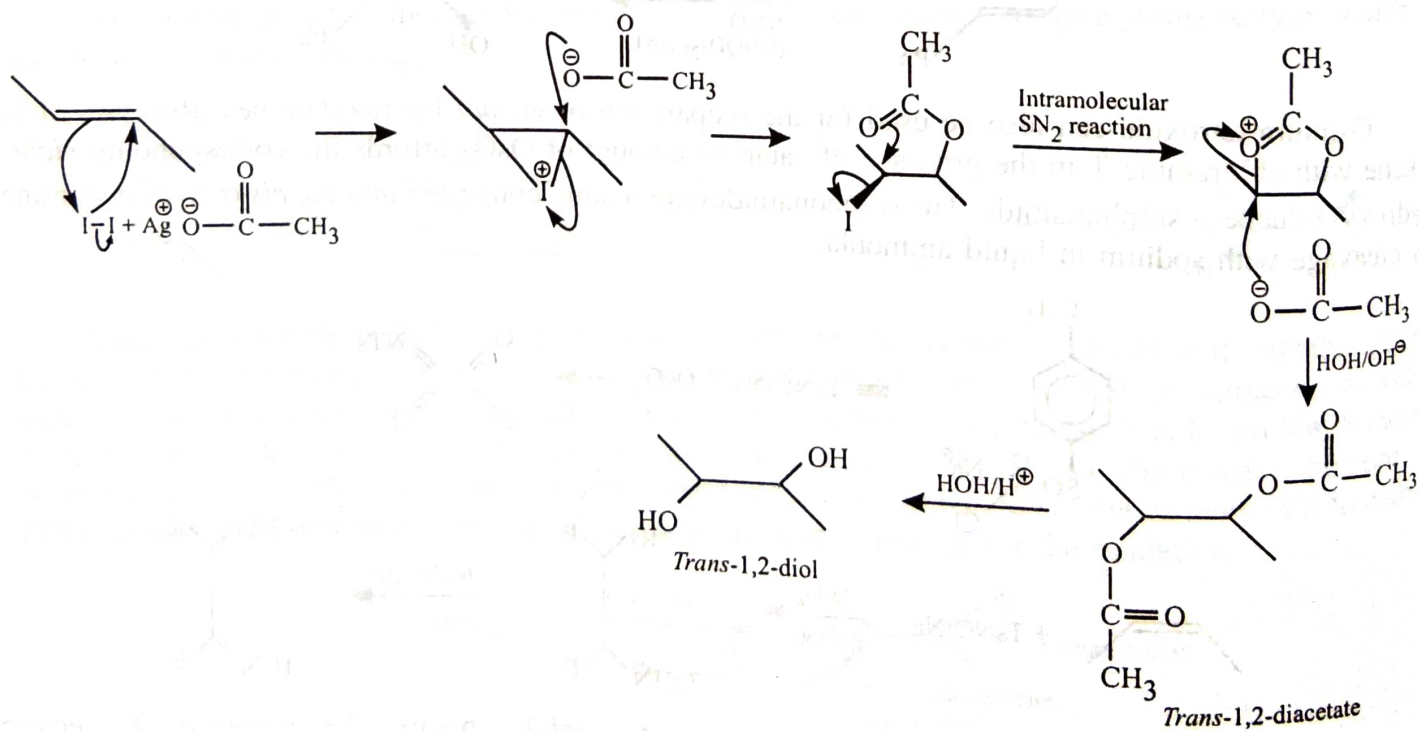
Osmium tetroxide is electrophile. Due to its electrophilic nature, the presence of electron withdrawing groups to the alkene double bond retards the hydroxylation. Thus, if more than one double bond are present hydroxylation occurs at the most electron-rich double bond.



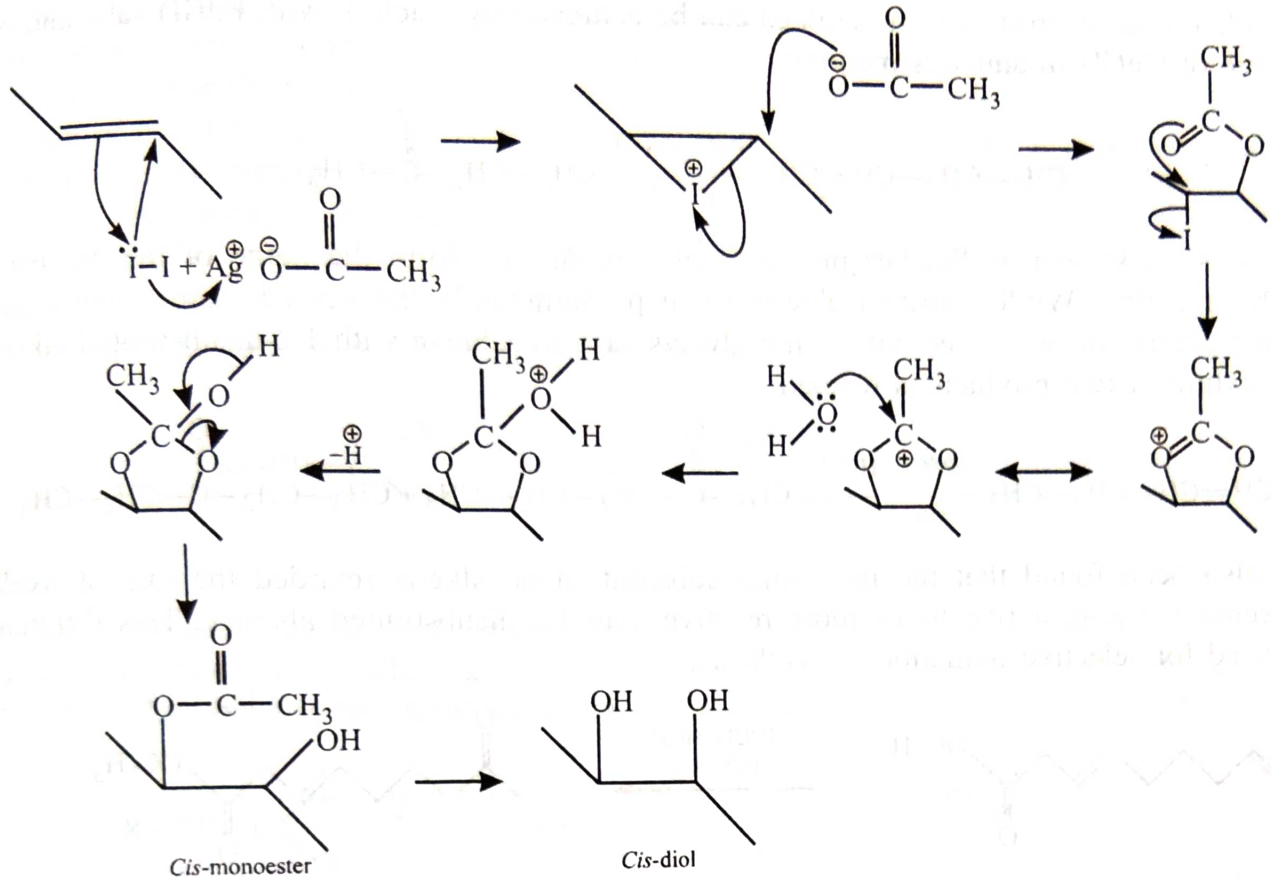
(3) **Oxidation with iodine and silver carbonate:** Many of the difficulties attending the oxidation of alkenes to *vic* diols with other reagents can be avoided by using Prevost reagent—a solution of iodine in carbon tetrachloride together with an equivalent of silver acetate or silver benzoate. Under anhydrous conditions this oxidant directly yields the diacetyl derivative of the *trans*-glycol (Prevost conditions), while in the presence of water the monoester of the *cis* glycol is obtained (Woodward conditions).



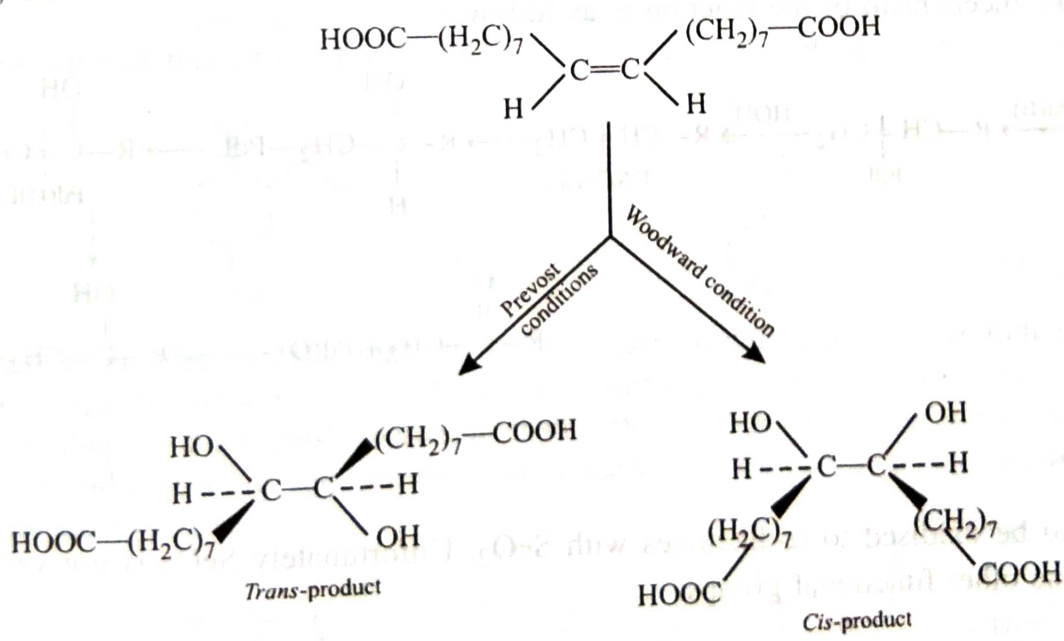
Mechanism: Prevost reaction



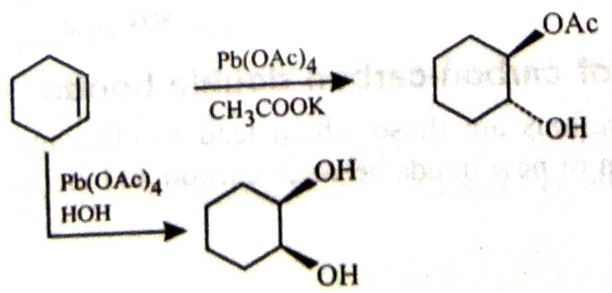
Woodward reaction



The value of these reagents is due to their specificity and to the mildness of the reaction conditions, free iodine, under the conditions used, hardly affects other sensitive groups in the molecule.

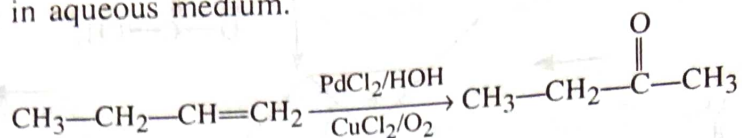


Similar results are also obtained with lead tetracetate but the reagent is less selective than I_2/CH_3COOAg

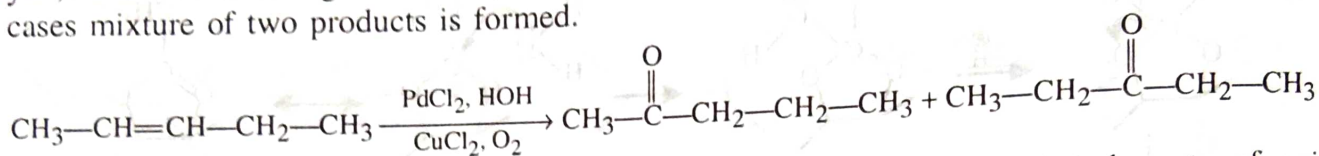


(4) Formation of ketones from alkenes: The Wacker process.

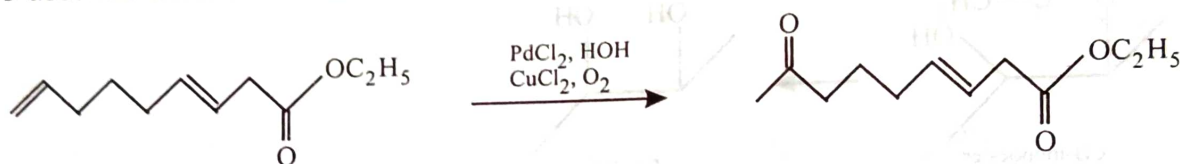
The oxidation of alkenes to form ketones can be achieved by reaction with Pd(II) salts and oxygen in the presence of CuCl₂ in aqueous medium.



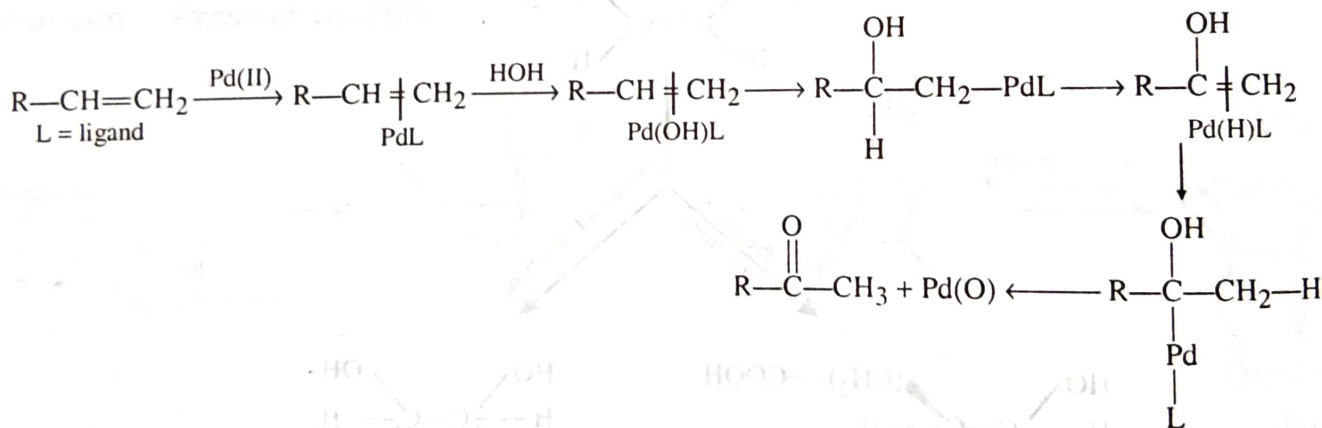
The process is known as Wacker process which is derived from the name of the company that developed this reaction. While terminal alkenes give predominantly the ketone isomer rather than the aldehyde, such control of regioselectivity is not always easy to achieve with 1,2-disubstituted alkenes. In such cases mixture of two products is formed.



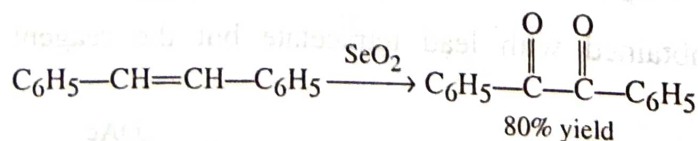
It has also been found that the increasing substitution on alkene retarded the rate of oxidation. Terminal alkenes are almost five times more reactive than 1,2-disubstituted alkenes. This difference in rate can be used for selective oxidation in synthesis.



During the course of oxidation Pd(II) is reduced to Pd(O). As Pd(II) is quite expensive, the reaction is carried out in the presence of Cu(II) which converts Pd(O) to Pd(II) *in situ* so that catalytic amount of Pd(II) is required. The mechanism of the reaction is as follows:



Alkenes can also be oxidised to α -diketones with SeO₂. Unfortunately SeO₂ is not very selective reagent and can oxidise other functional groups.



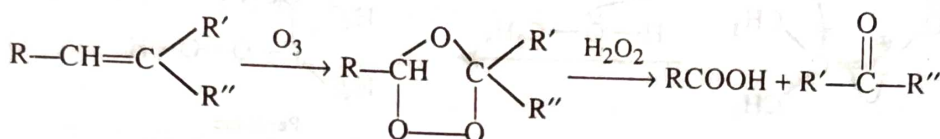
(5) Oxidative cleavage of carbon-carbon double bonds

Oxidative cleavage reactions are those which lead to cleavage of carbon-carbon bond (single or multiple) and the introduction of new bonds between carbon and electronegative element, such as oxygen.

(A) Oxidative cleavage of alkenes by ozone

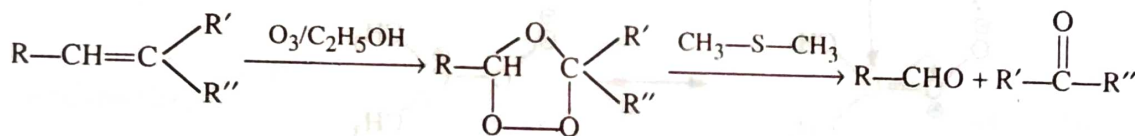
Ozonolysis, that is reaction of an alkene with ozone followed by splitting of the resulting ozonide, is a very convenient method for oxidative cleavage of carbon-carbon double bonds.

Ozonides, which can be cleaved oxidatively or reductively to carboxylic acids, ketones or aldehydes, the nature of the products formed depends on the method used and on the structure of the alkene. The reaction is usually carried out by passing a stream of oxygen containing 2-9 per cent of ozone into a solution or suspension of the compound in a suitable solvent, such as CH_2Cl_2 or CH_3OH at or below room temperature. This leads to the formation of ozonide. Oxidation of the crude ozonide, without isolation, by hydrogen peroxide or other reagent leads normally to carboxylic acids or ketones or both, depending upon the degree of substitution of the alkene. The whole process is known as oxidative workup.



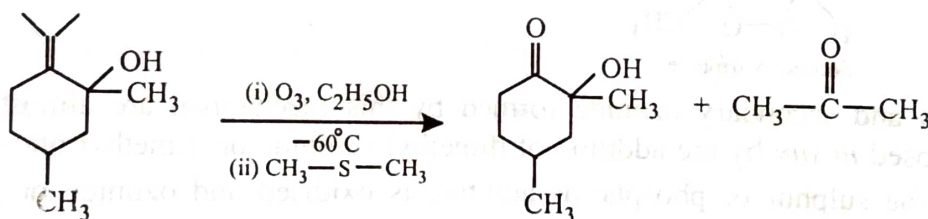
Oxidative work up

Reductive decomposition of the crude ozonide leads to aldehydes and ketones. Various methods of reduction have been used including catalytic hydrogenation and reduction with zinc and acids or with triethyl phosphite but the best result is obtained with dimethyl sulphide.

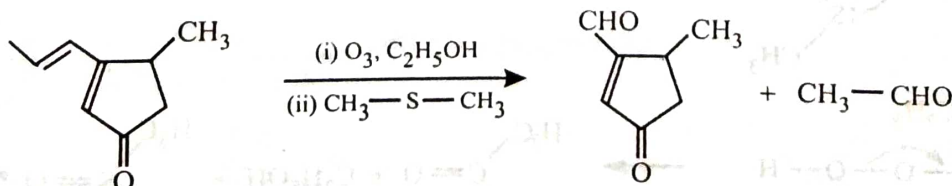


Reductive work up

This reagent is extremely specific for alkenes and so ozonolysis can be performed on multi-functional compounds without fear of oxidising alcohols, esters, carbonyl groups, ester or aromatic rings.



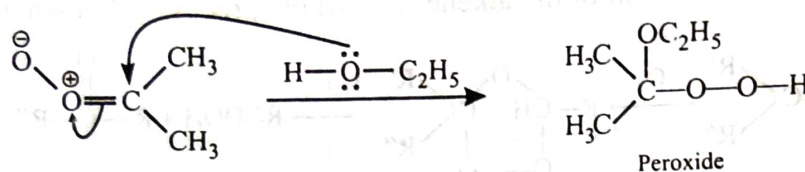
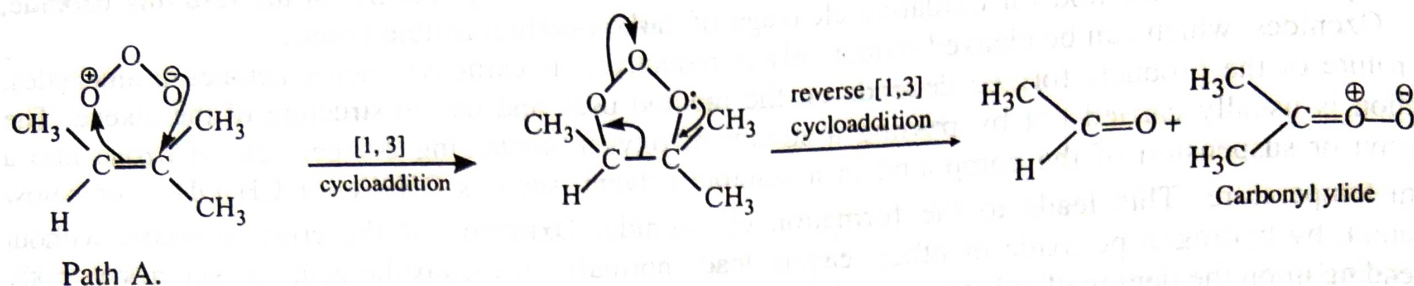
Ozone is an electrophilic reagent and so reacts faster with electron-rich alkenes. However, the difference in rate for ozonolysis of alkenes with varying numbers of alkyl groups is small and it is not usually possible to distinguish between them. What is possible, however, is the oxidation of an alkyl-substituted alkene in the presence of a carbonyl, nitro, cyano substituted (and therefore very electron-deficient) alkene.



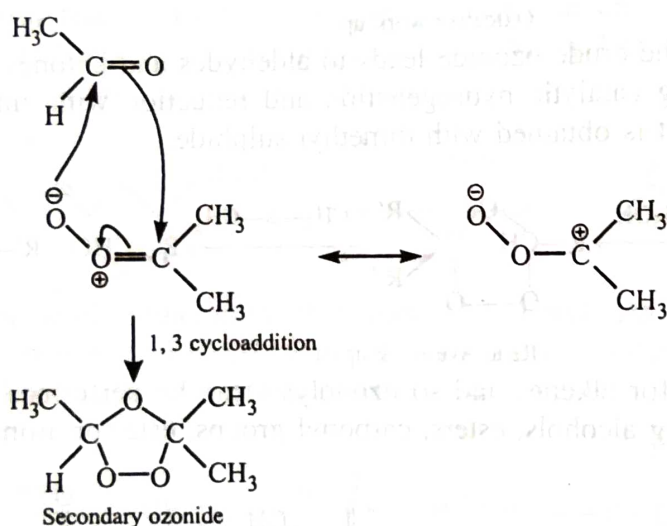
The mechanism of the reaction is as follows:

In the first step, ozone participates in a cycloaddition reaction with alkene. This cycloaddition reaction is pericyclic [4 + 2] cycloaddition. Since ozone is 1,3-dipolar species, therefore reaction is also an example of 1,3-dipolar cycloaddition reaction. This leads to the formation of primary ozonide (also known as molozonide). Primary ozonide is unstable and collapses *via* another pericyclic reaction, this

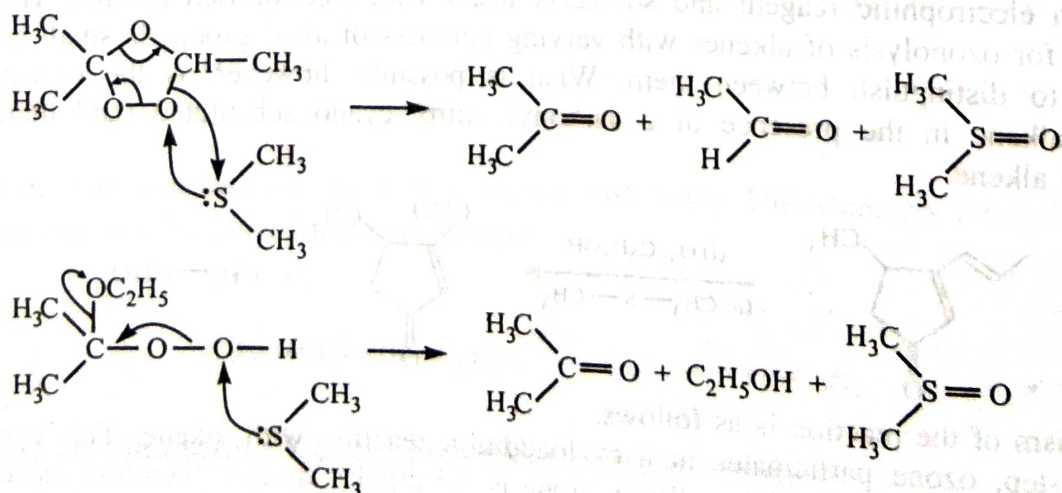
time it is reverse [1, 3] cycloaddition. A carbonyl compound and a carbonyl ylide are formed by this path and these may combine either with solvent (path-A) or with each other (path-B).



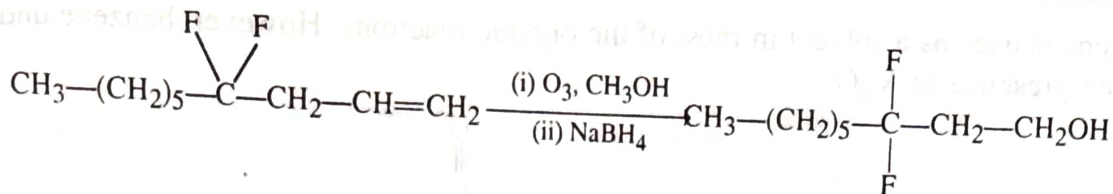
Path B.



The peroxides and secondary ozonide formed by this mechanism are almost never isolated but instead are decomposed *in situ* by the addition of dimethyl sulphide or trimethyl phosphite $[(\text{MeO})_3\text{P}]$. In this process either the sulphur or phosphorus additive is oxidised and ozonide or peroxide reduces to carbonyl compounds.

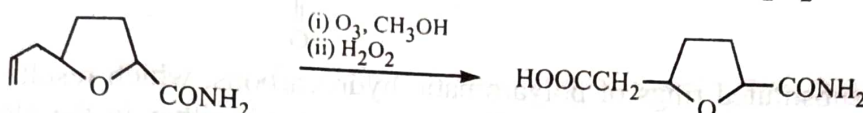


It is possible to decompose secondary ozonides in a variety of ways. For example, reaction with NaBH_4 , instead of dimethyl sulphide, reduces the ozonide to give alcohols.



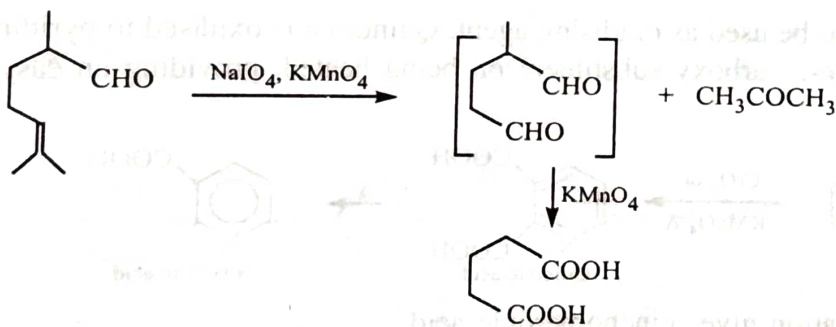
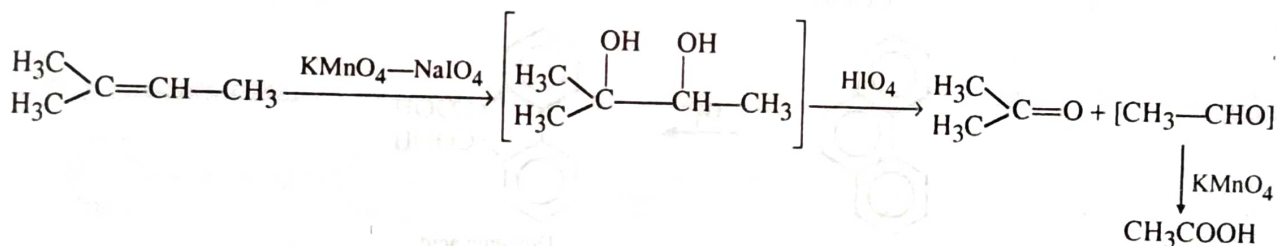
reductive work-up

Ozonide can also be oxidised by the use of oxidising agents like H_2O_2 .

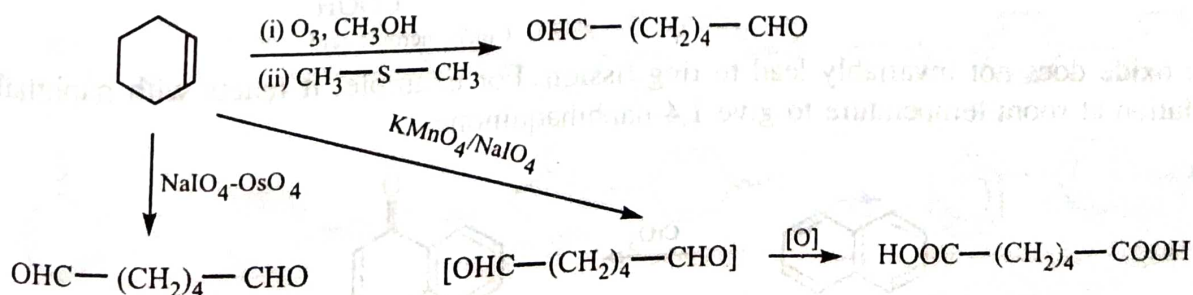


(B) Oxidative Cleavage of alkenes by Lemieux reagents

Ozone is unpleasant and is not selective for tertiary C—H group. Ozone has, therefore, largely been displaced by the Lemieux reagents, which consist of dilute aqueous solution of NaIO_4 with a catalytic quantity of potassium permanganate and of osmium tetroxide respectively. In each case, the alkene is first oxidised to the *cis*-diol which is then cleaved by periodate to give aldehyde and/or ketone. The permanganate reagent then oxidises aldehydic products to carboxylic acids. The low valent manganese and osmium generated during the reaction are reoxidised by the periodate to their original state *in situ*, so that only catalytic amounts are required. The reactions are rapid at room temperature, and are selective for alkenes, as for example:



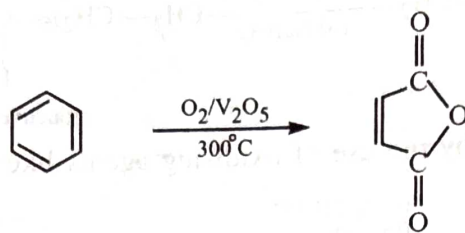
Oxidation by $\text{NaIO}_4-\text{OsO}_4$ has the advantage (over $\text{NaIO}_4-\text{KMnO}_4$) that it does not proceed beyond the aldehyde stage. It produces the same result as ozonolysis followed by reductive cleavage of the ozonide.



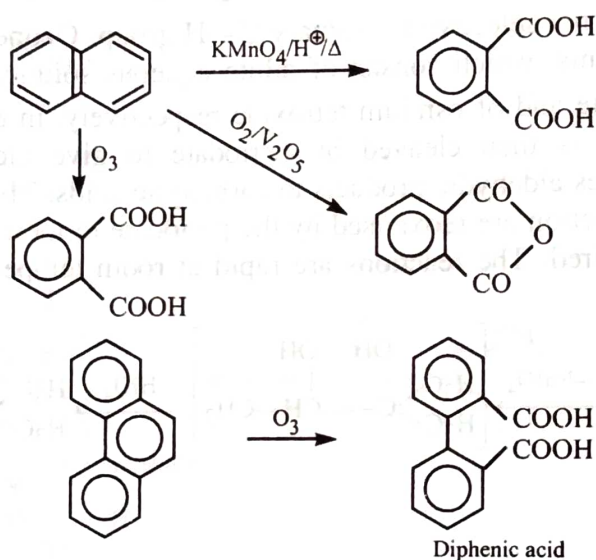
2.1.2 Oxidation of Aromatic rings

Benzene is an exceptionally stable compound and is not effected by usual oxidising agents. It is for

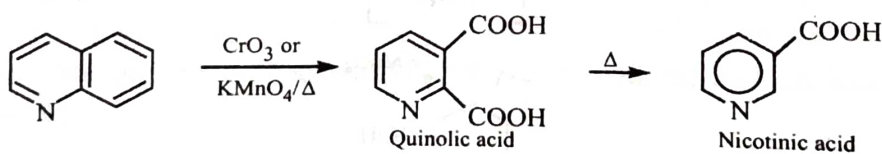
this reason that benzene is used as a solvent in most of the organic reactions. However, benzene undergoes aerial oxidation in the presence of V_2O_5 .



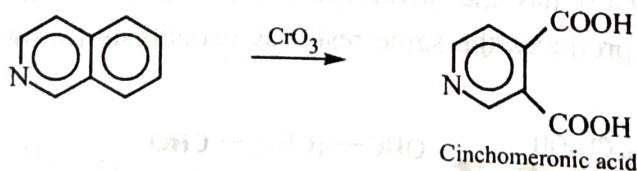
The oxidation of unsubstituted rings of polyaromatic hydrocarbons, which results in the loss of the stabilisation energy requires vigorous conditions. Reaction can result either in the cleavage of the ring or in the formation of quinones.



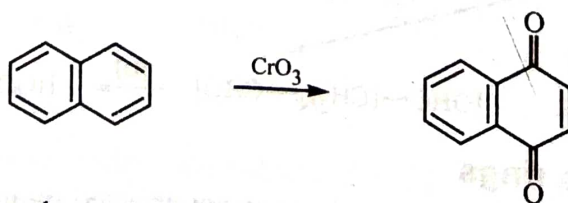
Chromic acid can also be used as oxidising agent. Quinoline is oxidised to pyridine-2,3-dicarboxylic acid which easily loses the-2-carboxy substituent on being heated, providing an easy route to nicotinic acid:



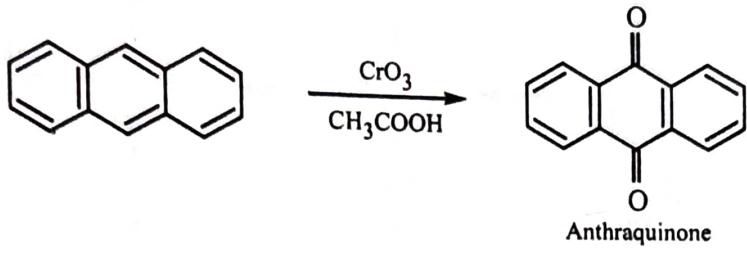
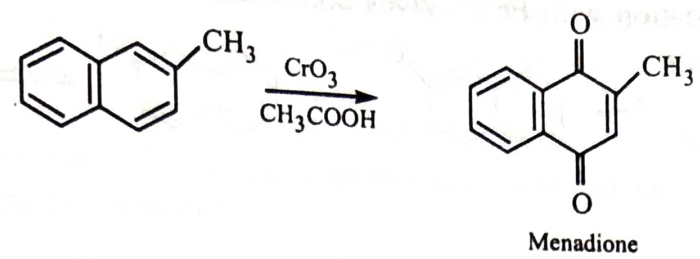
Isoquinoline on oxidation gives cinchomeronic acid



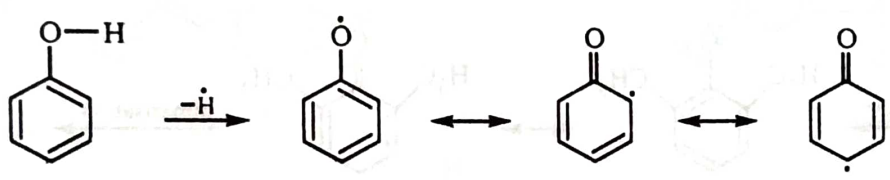
Chromic oxide does not invariably lead to ring-fission. For example, it reacts with naphthalene in acetic acid solution at room temperature to give 1,4-naphthaquinone.



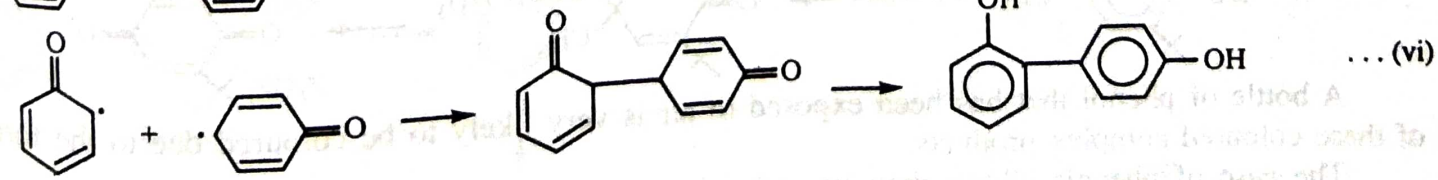
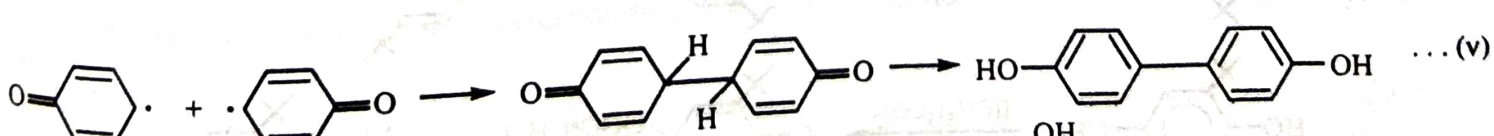
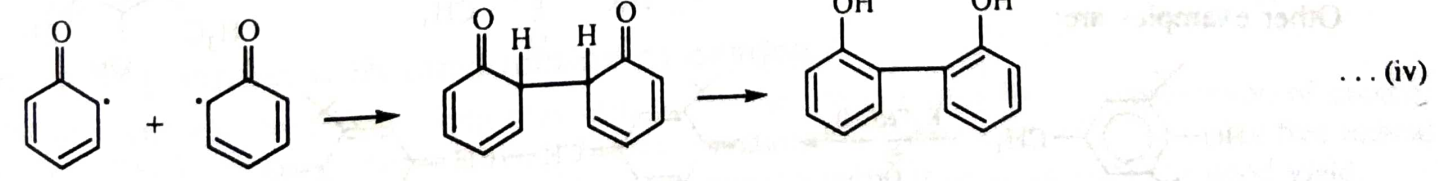
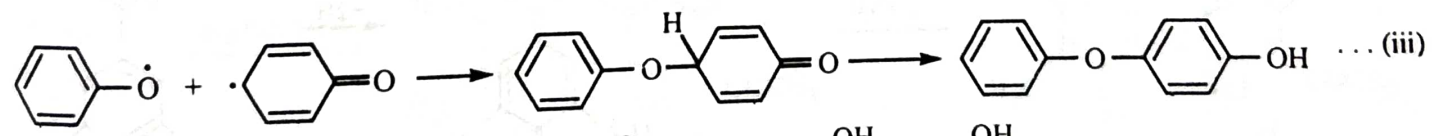
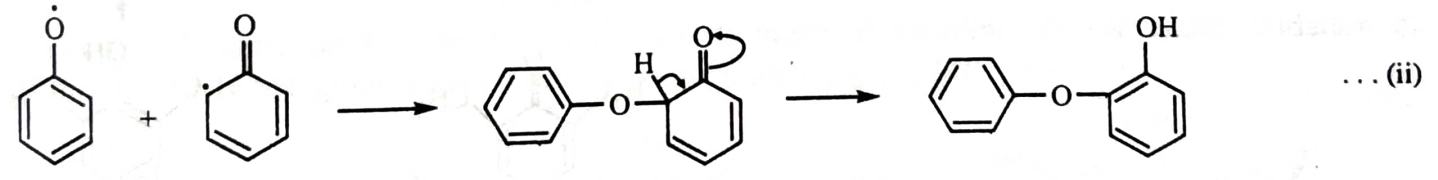
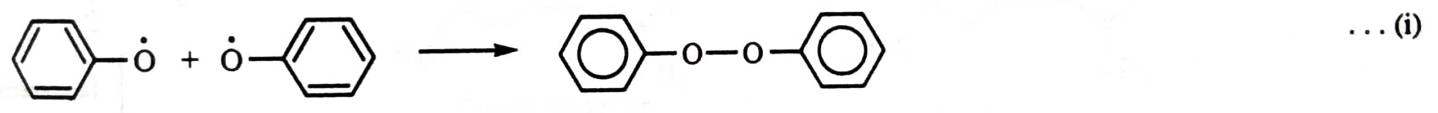
Chromic acid also oxidises other polynuclear aromatic hydrocarbons into quinones.



The aromatic rings of phenols are very susceptible to oxidation by one-electron oxidants (such as potassium ferricyanide) for the removal of a hydrogen atom gives a delocalised aryloxy radical,

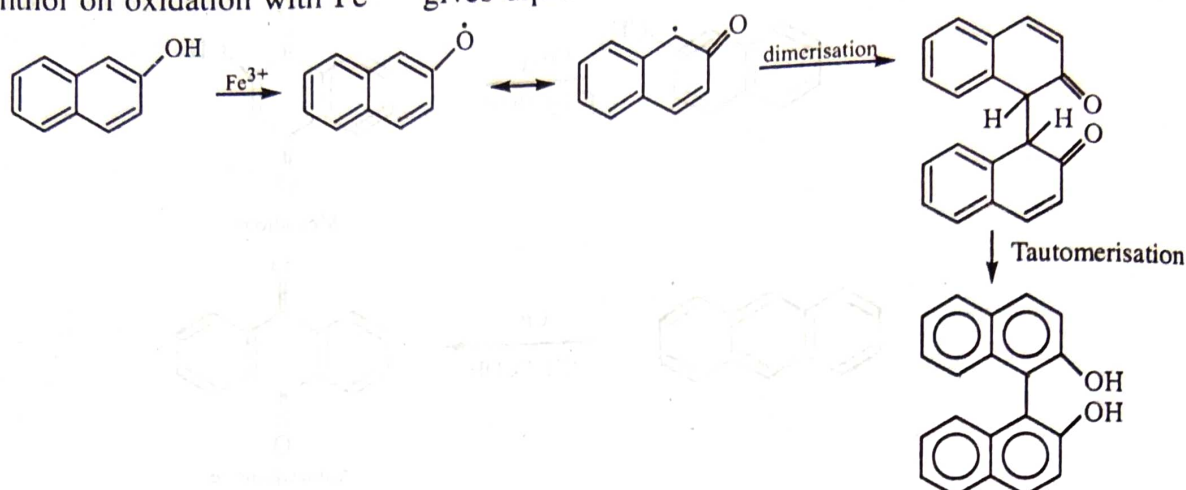


The radicals obtained undergo coupling reaction and the process is known as oxidative coupling.

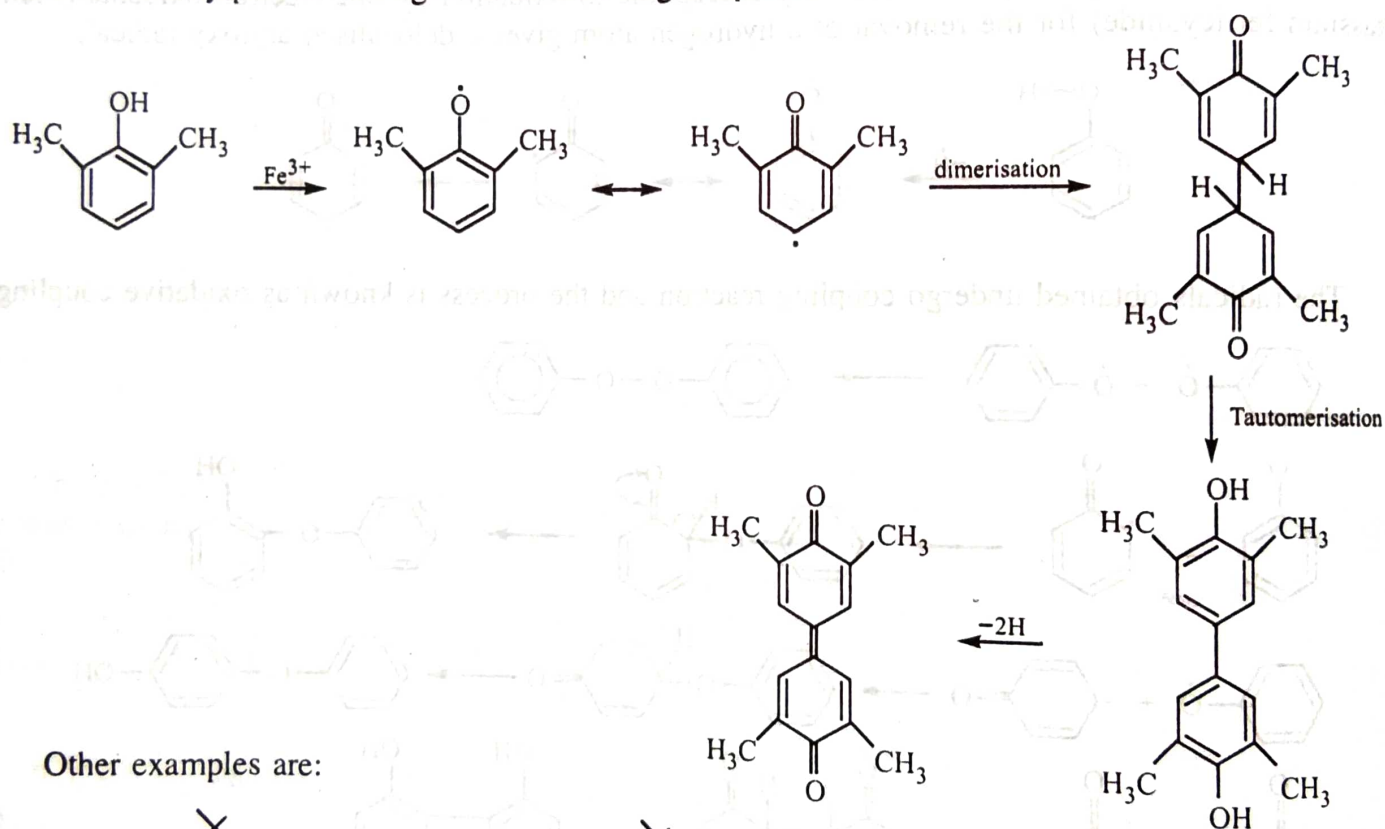


These coupling reactions are most common in biosynthesis.

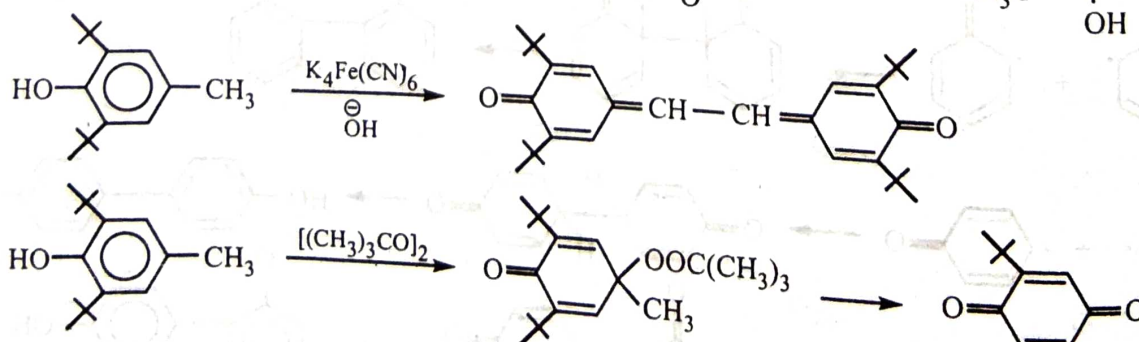
2-Naphthol on oxidation with Fe^{+++} gives diphenols.



2,6-Dimethylphenol undergoes oxidation to give quinones:



Other examples are:

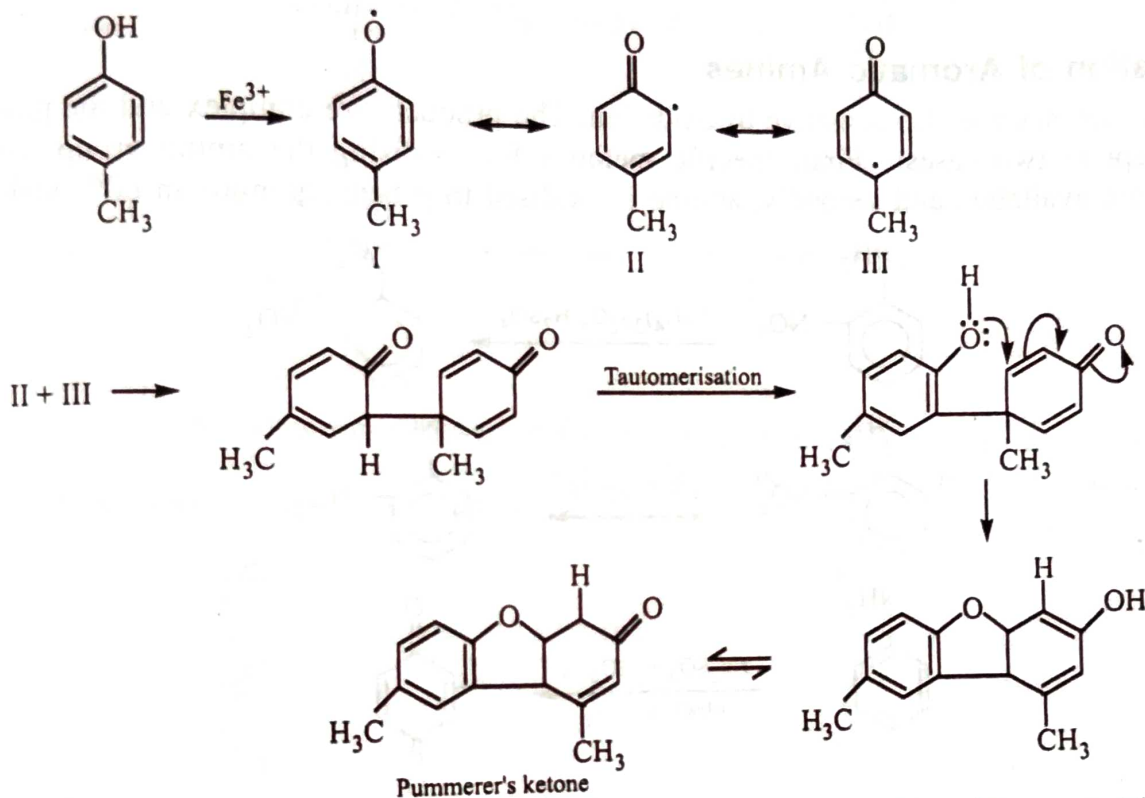


A bottle of phenol that has been exposed to air is very likely to be coloured due to the formation of these coloured complex products.

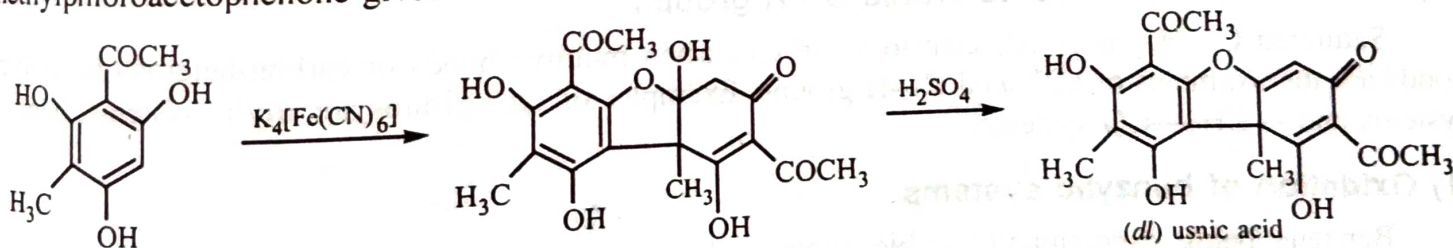
The ease of phenols allows their use where antioxidants are needed as scavengers of radicals to prevent chain reactions. Particularly effective in this respect is 2,6-di-*t*-butyl-4-methylphenol, which is a commercial antioxidant used to prevent polymerisation of alkenes as well as oxidation of highly

susceptible compounds. This phenol with neither free *ortho* nor free *para* positions, cannot couple like the phenols already noted and is relatively stable. When it does react, it often does so by loss of alkyl groups.

Oxidation of *p*-cresol by ferricyanide or by ceric ammonium nitrate [CAN is a good one electron oxidant, during oxidation process the Ce^{4+} ion gains an electron to be reduced to Ce^{3+}] gives in addition to carbon-carbon dimers, Pummerer's ketone:

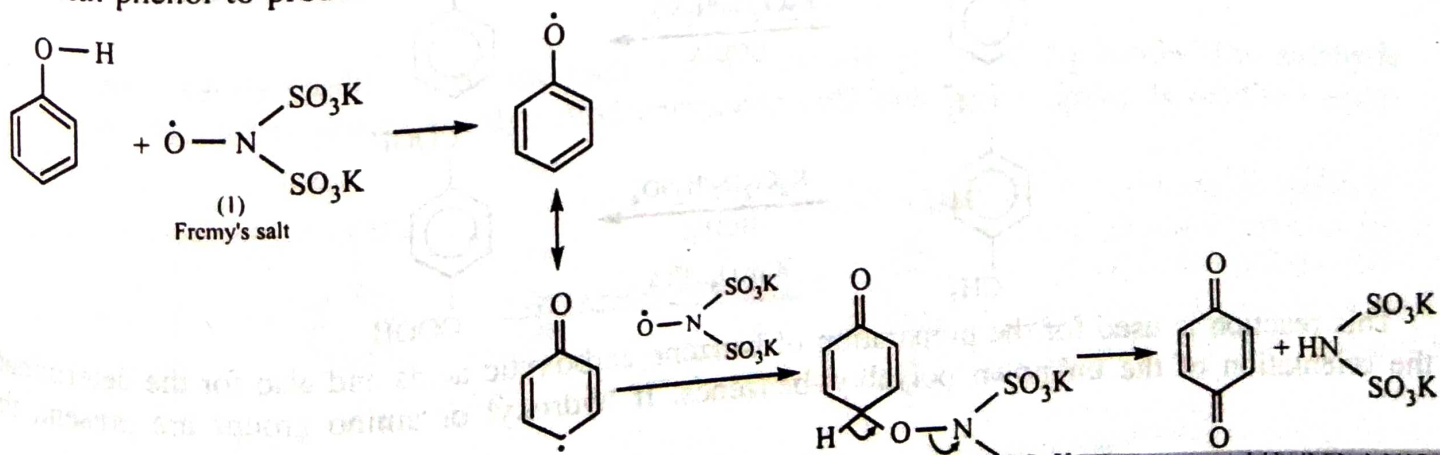


A synthesis of usnic acid is based on the above mode of coupling. Ferrocyanide oxidation of methylphloroacetophenone gives a dimer which on dehydration gives (*dl*) usnic acid.

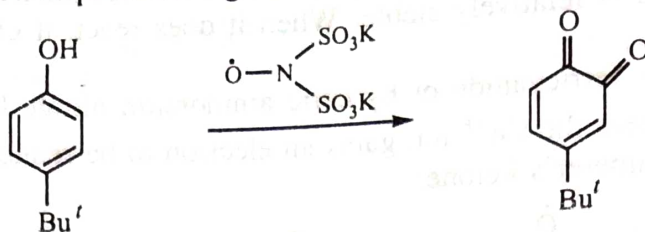


Oxidation of phenols with introduction of oxygen

Phenols with one hydroxyl group may also be oxidised to quinones by the introduction of another oxygen atom. The best reagent for achieving this transformation is Fremy's salt (1). This stable free radical reacts with phenol to produce the corresponding 1,4-quinone rather than 1,2-quinone in good yield.

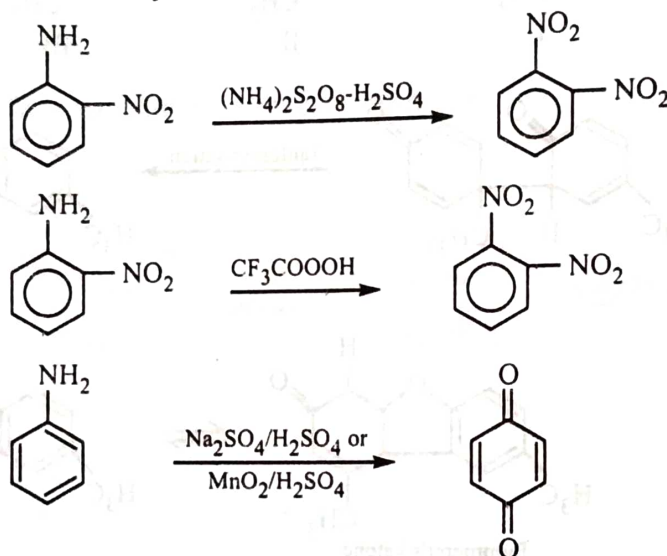


Phenols that are blocked at position-4 give 1,2-quinones with Fremy's salt.



2.1.3 Oxidation of Aromatic Amines

Aromatic amines are also sensitive to oxidation. The products are complex and the processes are of little use except in two cases: First, specific methods for oxidising the amino group rather than the benzene ring are available, and secondly, aniline is oxidised to *p*-benzoquinone in 60% yield.



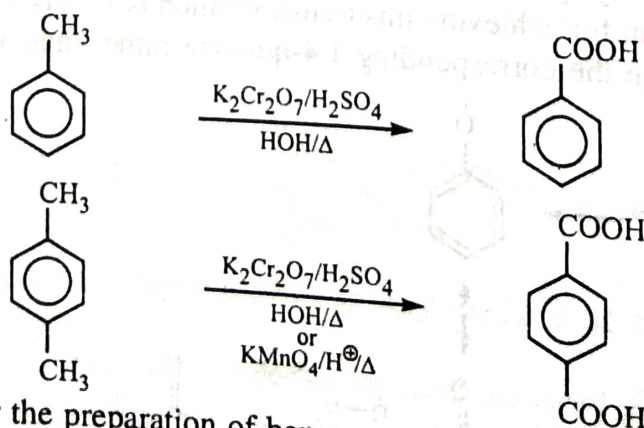
2.1.4 Oxidation of Saturated C—H groups (activated and unactivated)

(A) Oxidation of activated saturated C—H groups

Saturated C—H groups adjacent to a carbon-carbon multiple bonds or carbon-heteroatom multiple bonds are the examples of activated C—H groups. Examples of such groups are allylic systems, benzylic systems and $-\text{CH}_2-\text{CO}$ systems.

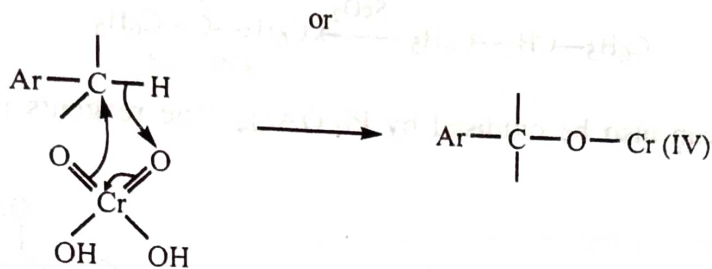
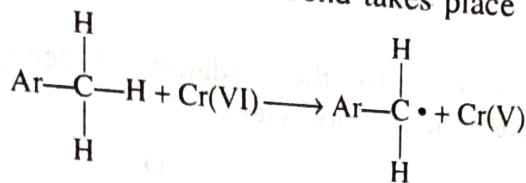
(1) Oxidation of benzylic systems

Benzene being exceptionally stable compound is not affected by most of the oxidising agents. However, if an alkyl group is present in the benzene ring the side chain can be oxidised to corresponding carboxylic acid.

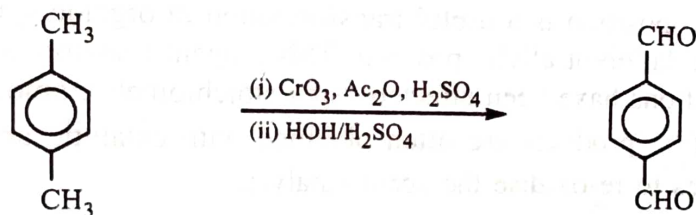


This reaction is used for the preparation of benzene carboxylic acids and also for the determination of the orientation of the unknown polyalkyl-benzenes. If hydroxyl or amino groups are present, these

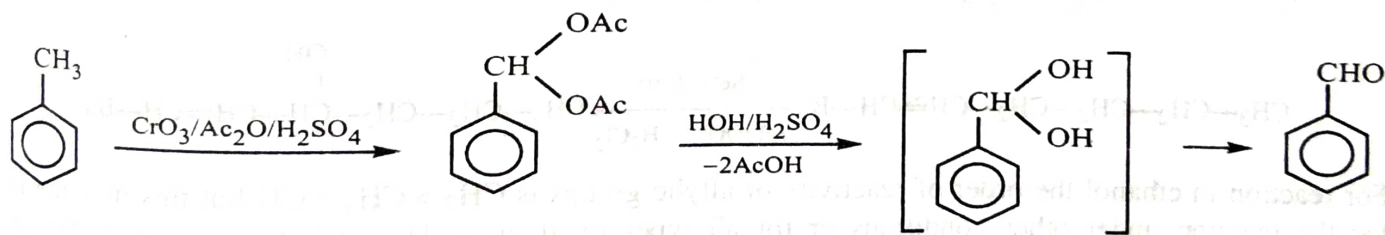
should be protected before carrying out the oxidation. With side chains longer than methyl, initial attack is to take place at the benzylic carbon atom. This is suggested by the fact that *t*-butylbenzene is very resistant to oxidation. The rate-determining step in the chromic acid oxidation is known to be cleavage of the benzylic C—H bond. The cleavage of C—H bond takes place as follows:



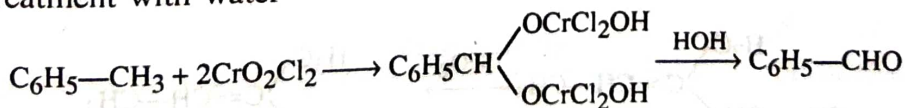
The conversion of a methyl group attached to benzene ring into the formyl group can be achieved by oxidation with chromium (VI) oxide in acetic anhydride in the presence of strong acid or with a solution of chromyl chloride in CCl₄ or CS₂ (**Etard reaction**).



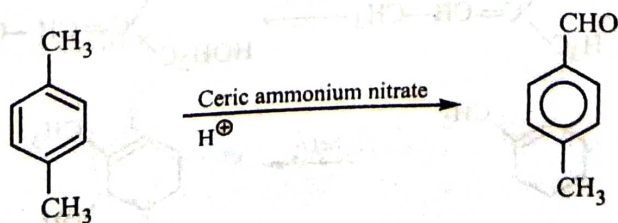
The success of CrO₃/acetic anhydride/H₂SO₄ is due to the initial formation of the diacetate which protects the aldehyde group against further oxidation.



In the Etard reaction chromyl chloride forms a complex with the hydrocarbon which is decomposed into aldehyde by treatment with water

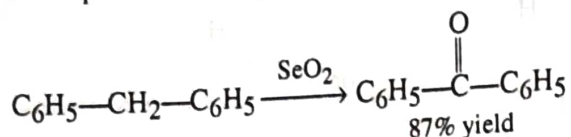


Ceric ion also readily oxidises aromatic methyl group to aldehyde in acidic media. The aldehyde group is not oxidised further and in a polymethyl compound only one methyl group is oxidised under normal conditions.

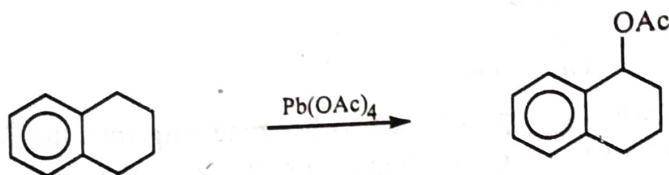




Selenium dioxide can also be used for the oxidation of benzylic carbon. Diphenylmethane on oxidation with SeO_2 gives benzophenone in good yield.

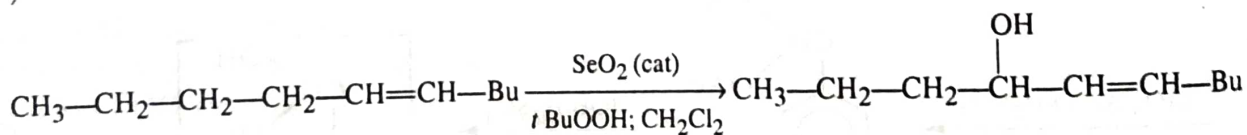
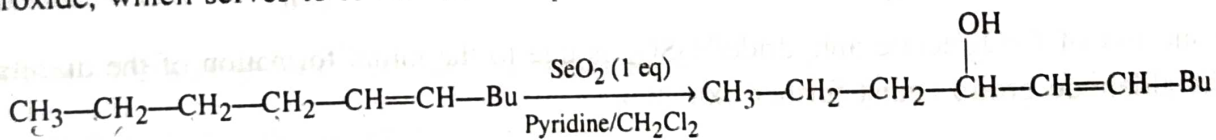


Benzylic carbon can also be oxidised by $\text{Pb}(\text{OAc})_4$. The reagents introduce acetoxy group in the benzylic carbon.

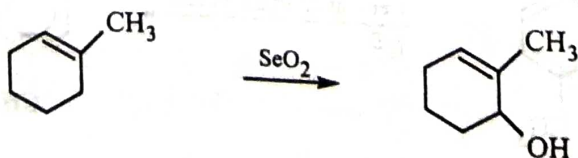
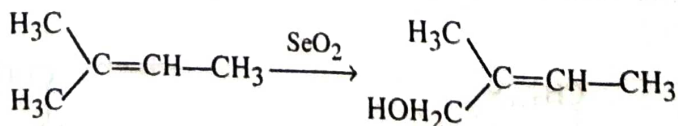
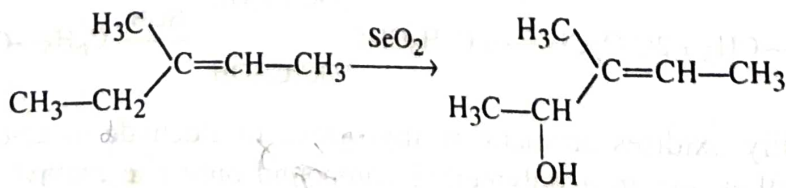


(2) Oxidation at allylic positions

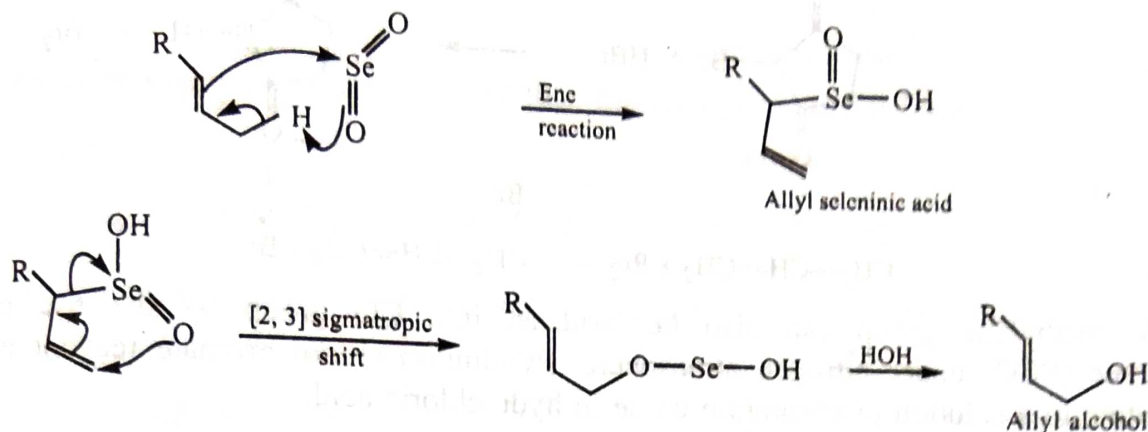
Oxidation at an allylic position is a useful transformation in organic synthesis. Selenium dioxide is a unique reagent for the oxidation at allylic position. This reagent transforms alkenes into allylic alcohol in one step. Generally, reactions have been effected using stoichiometric amounts of SeO_2 , but very good yields of most easily purified products are often obtained with catalytic amounts of SeO_2 and *t*-butyl hydroperoxide, which serves to re-oxidise the spent catalyst.



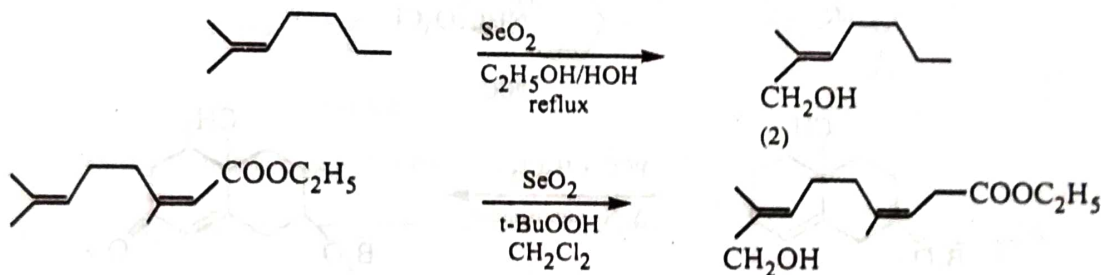
For reaction in ethanol the order of reactivity of allylic groups is $\text{CH}_2 > \text{CH}_3 > \text{CH}$ but this may not hold for the reaction under other conditions or for all types of alkenes. The oxidation occurs at the more substituted end of the double bond.



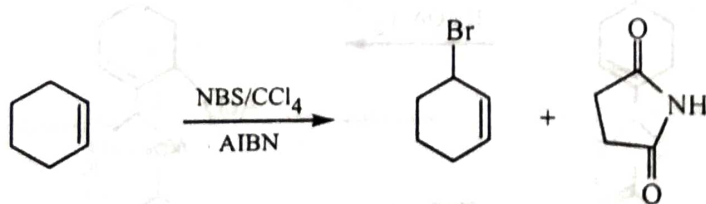
The reaction proceeds via an initial *ene* reaction of allylic compounds with SeO_2 to give allyl seleninic acid which undergoes a [2, 3] sigmatropic shift to yield compound (1). Hydrolysis of (1) affords the allylic alcohol.



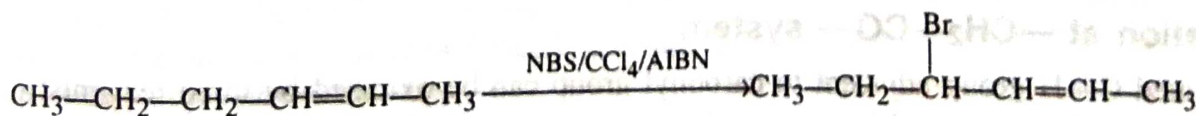
A useful application of this reaction is in the oxidation of 1,1-dimethyl-alkenes to the corresponding *E*-allyl alcohols or aldehydes by selective attack on the *E*-methyl group. Thus 2-methyl-2-heptene is converted almost exclusively into the (*E*) allyl alcohol (2) and the corresponding aldehyde. (*E*) Selectivity is due to the concerted [2, 3] sigmatropic rearrangement.



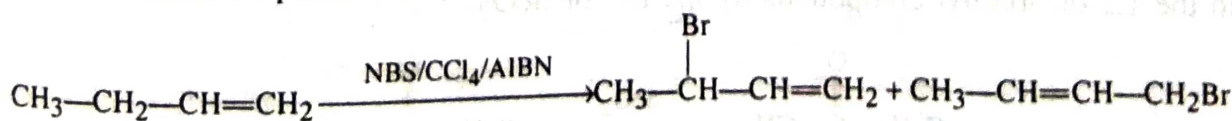
N-Bromosuccinimide (NBS) is another reagent that is effective at oxidising allylic positions. The reaction takes place by free radical mechanism. NBS-promoted bromination works best in a non-polar solvent, such as CCl_4 , and with a small amount of radical initiator, such as AIBN.



If there are two allylic positions, then monobromo-derivatives may be obtained. Allylic methylene groups are attacked much more rapidly than allylic methyl groups.



Whenever a structure permits, allylic bromination leads to allylic rearrangement.

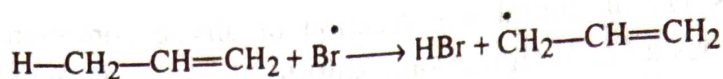


The reaction takes place as follows:

Step 1



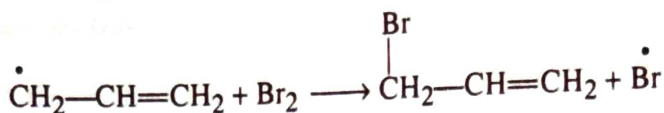
Step 2.



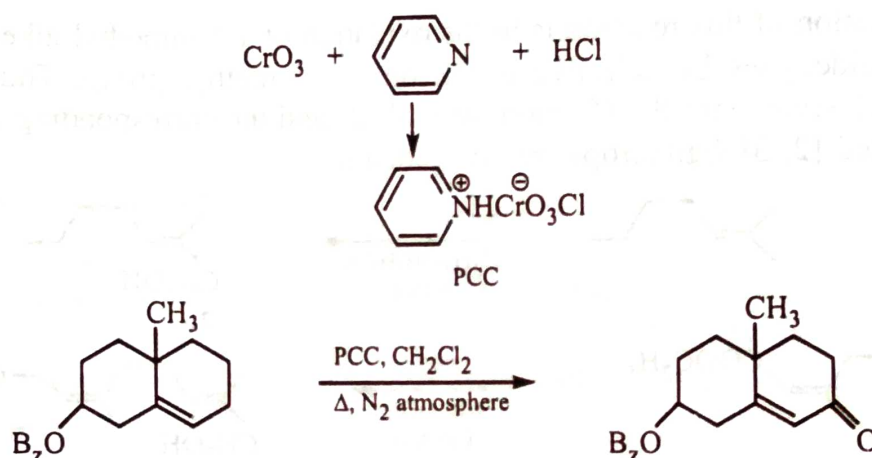
Step 3



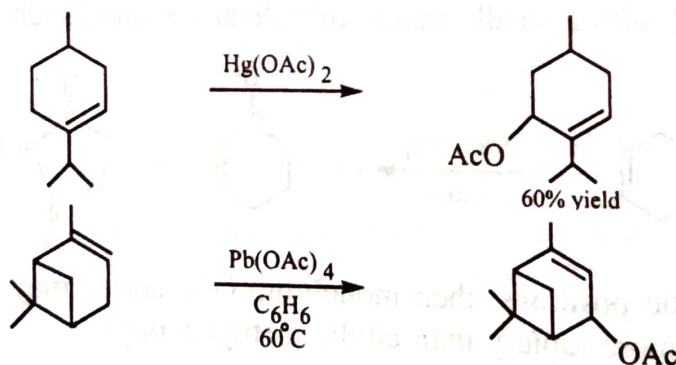
Step 4.



Allylic methylene group can also be oxidised into CO group by the use of pyridinium chlorochromate (PCC) under nitrogen atmosphere. Pyridinium chlorochromate reagent is obtained by adding pyridine to a solution of chromium oxide in hydrochloric acid.



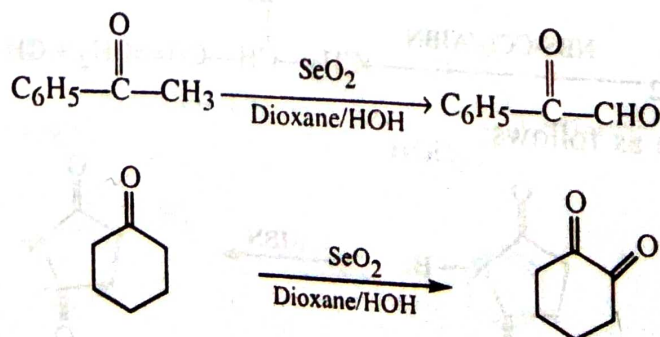
$\text{Hg}(\text{OAc})_2$ and $\text{Pb}(\text{OAc})_4$ can also be used for the oxidation at allylic positions. These two reagents usually introduce acetoxy groups at allylic position.

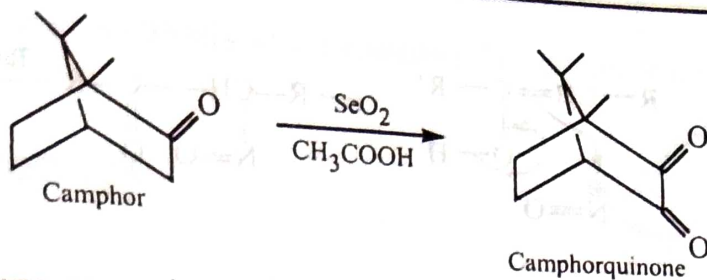


(B) Oxidation at $-\text{CH}_2-\text{CO}-$ system

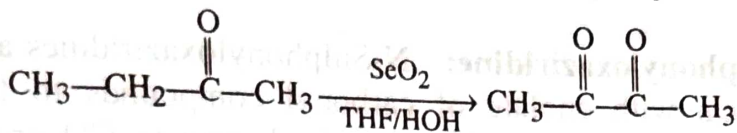
Activated C—H group adjacent to carbonyl group can be oxidised by three reagents:

(i) SeO_2 : Aldehydes and ketones with a methyl or methylene group α -to the carbonyl group are oxidised to the 1,2-dicarbonyl compounds by the use of SeO_2 .

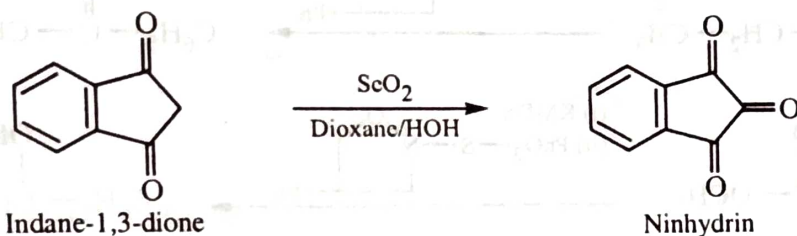
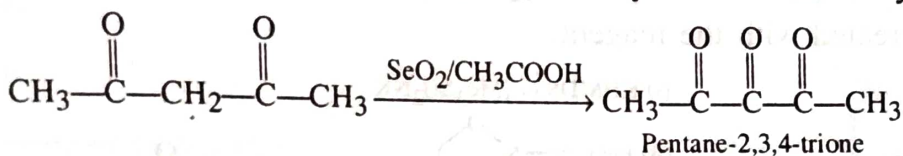




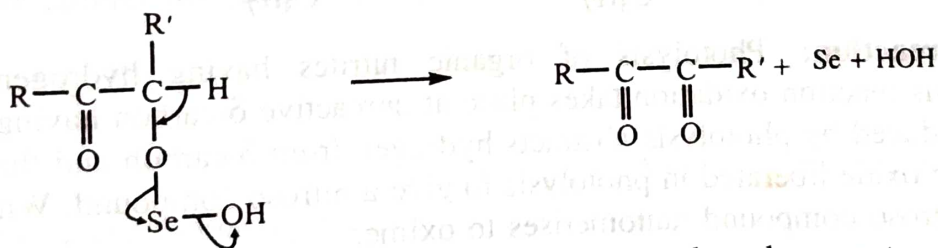
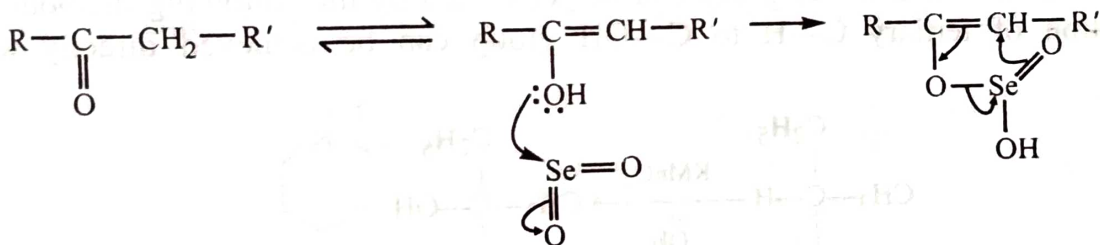
The reactivity of methylene group is more than the methyl group for SeO_2 .



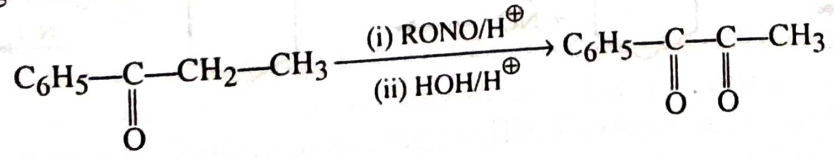
The oxidation of methylene group to carbonyl group is easy if it is flanked by two carbonyl groups.



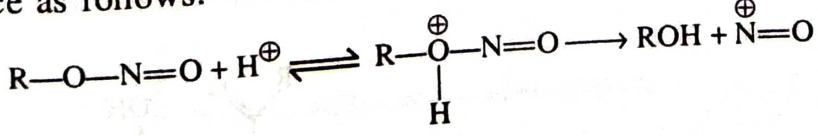
Oxidation at α -carbon by SeO_2 takes place as follows:



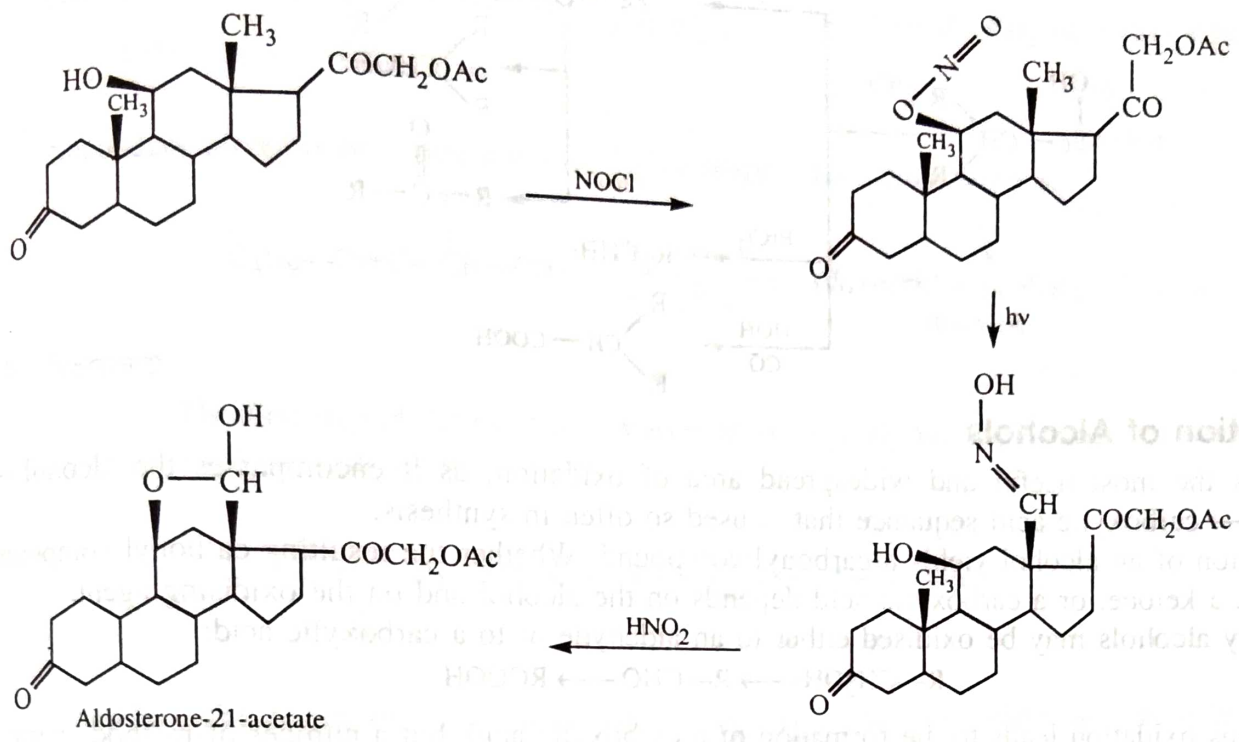
(ii) **Alkyl nitrite:** The methylene group is activated by the carbonyl group towards reaction with organic nitrites in the presence of acid or base. The resulting nitroso compound tautomerises to the oxime which, on hydrolysis, gives α -dicarbonyl compound.



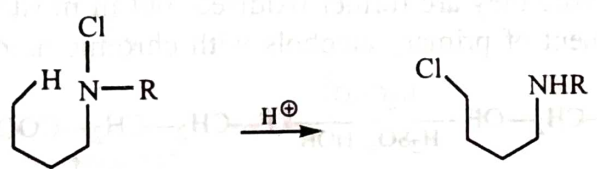
Reaction takes place as follows:



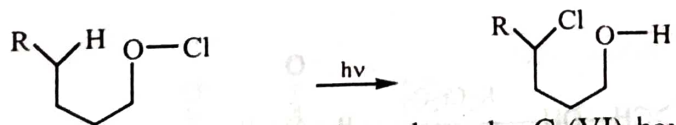
This method has been used in synthesis of aldosterone 21-acetate from corticosterone acetate.



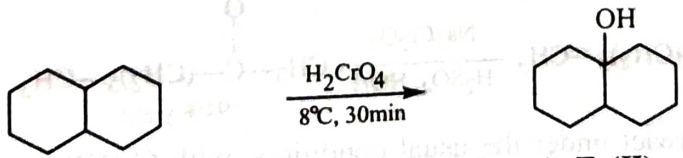
(iii) **The Hofmann-Loeffler-Freytag Reaction:** This reaction is given by N-haloamines having hydrogen on δ -carbon. The reaction is effected by warming a solution of the halogenated amine in strong acid or by irradiation of the acid solution with UV light. The product of the reaction is the δ -halogenated amine. In this way oxidation takes place at unactivated δ -carbon having hydrogen.



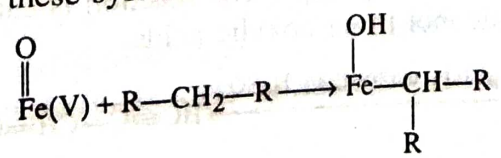
Hypohalites also give similar reactions.

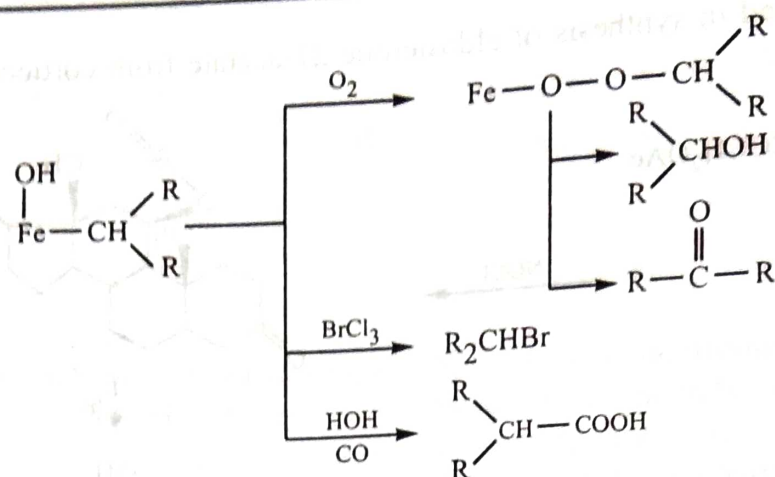


Other successful selective oxidations of hydrocarbons by Cr(VI) have been reported, for example, the oxidation of *cis*-decalin to corresponding alcohol.



Interesting hydrocarbon oxidations have been observed with Fe(II) catalysts with oxygen as the oxidant. These catalytic systems have become known as "Gif chemistry" after the location of their discovery in France. An improved system involving Fe(III), Picolinic acid and H₂O₂, has been developed. The reactive species generated in these systems is believed to be at the Fe(V) = O oxidation level.



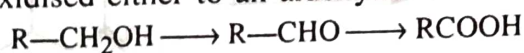


2.2 Oxidation of Alcohols

This is the most useful and widespread area of oxidation, as it encompasses the alcohol \rightarrow aldehyde \rightarrow carboxylic acid sequence that is used so often in synthesis.

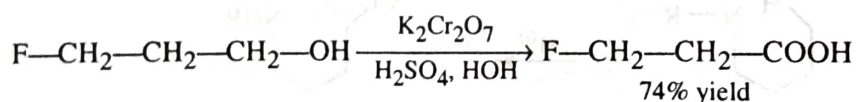
Oxidation of an alcohol yields a carbonyl compound. Whether the resulting carbonyl compound is an aldehyde, a ketone, or a carboxylic acid depends on the alcohol and on the oxidising agent.

Primary alcohols may be oxidised either to an aldehyde or to a carboxylic acid:

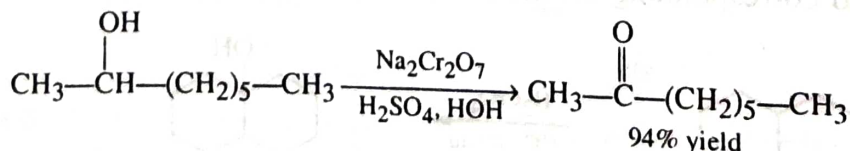
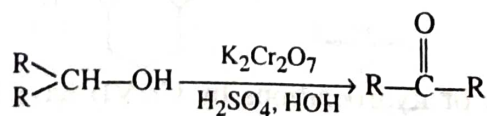


Vigorous oxidation leads to the formation of a carboxylic acid, but a number of methods permit to stop the oxidation at the intermediate aldehyde stage. The reagents most commonly used for oxidising alcohols are based on high-oxidation-state transition metals, particularly chromium(VI).

2.2.1 Oxidation by chromic acid: It is a good oxidising agent and is formed when solutions containing chromate (CrO_4^{2-}) or dichromate ($\text{Cr}_2\text{O}_7^{2-}$) are acidified. Sometimes it is possible to obtain aldehydes in satisfactory yield before they are further oxidised, but in most cases carboxylic acids are the major products isolated on treatment of primary alcohols with chromic acid.

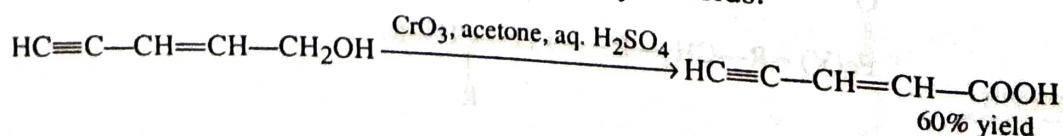


Secondary alcohols on the other hand give ketones in high yield. Ketones usually do not undergo further oxidation.

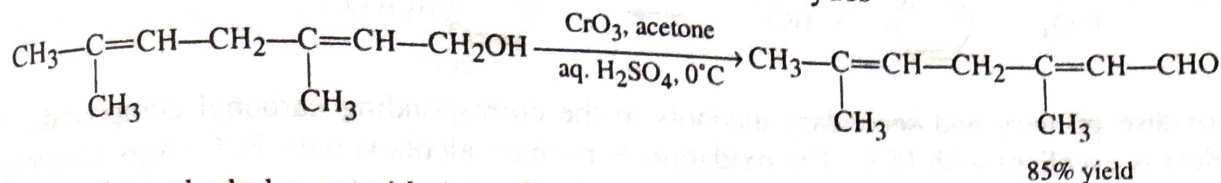


Tertiary alcohols do not react under the usual conditions with Cr(VI).

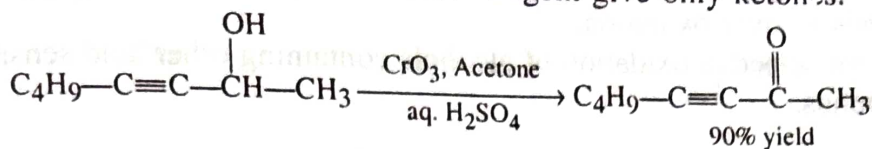
A relatively mild oxidising agent for alcohol is the Jones reagent (combination of CrO_3 , H_2SO_4 and acetone solvent). Oxidation of alcohol by this reagent is known as Jones oxidation. This reagent is very sensitive as it is useful for oxidation of alcohols which contain C—C double or triple bonds, allylic or benzylic C—H bonds and other acid sensitive groups. The reaction is carried out at 0–20°C. Jones reagent oxidises primary alcohol to carboxylic acids.



However, at 0°C primary alcohols are oxidised to aldehydes

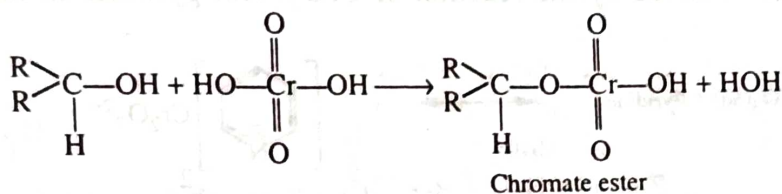


Secondary alcohols on oxidation with Jones reagent give only ketones.

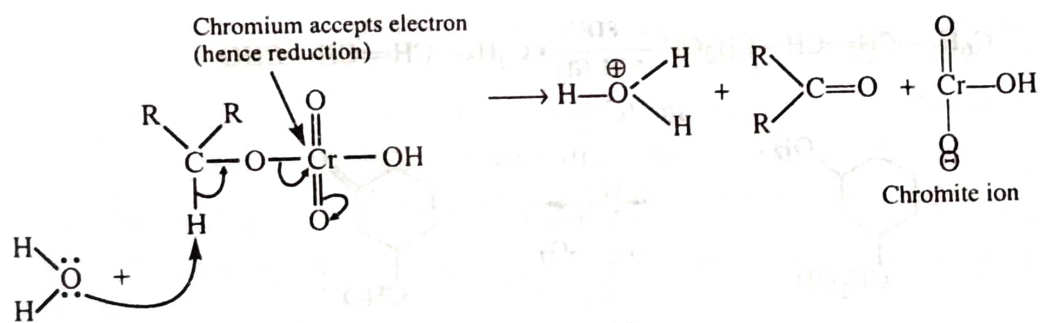


Mechanism

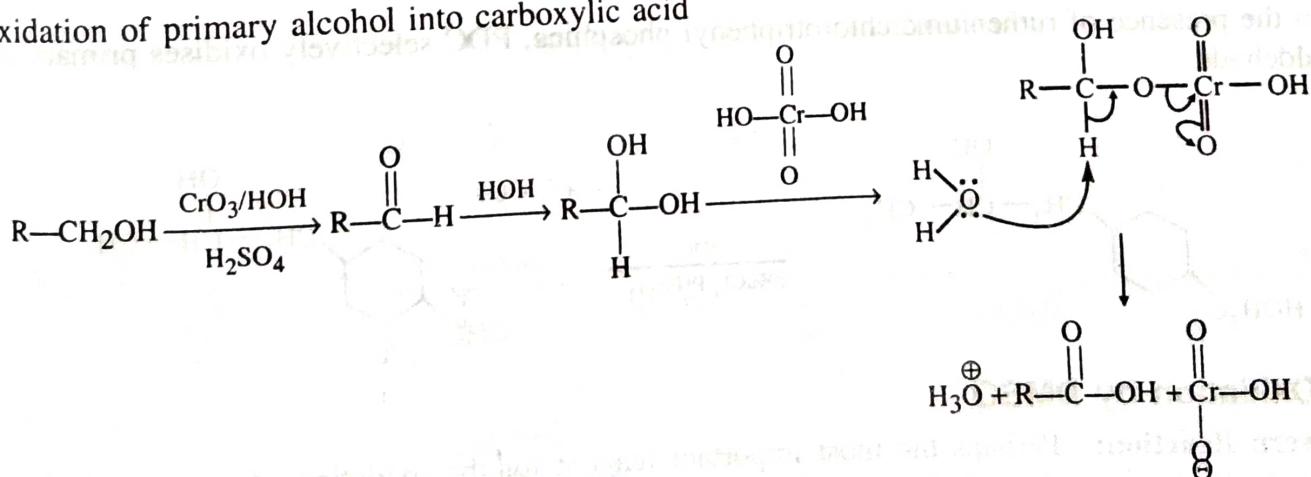
Step-I. The first step of the reaction involves an acid-catalysed displacement of water from chromic acid by the alcohol to form chromate ester.



Step-II. The oxidation step can be viewed as a β -elimination. Water acts as a base to remove a proton from carbon while the Cr—O bonds break

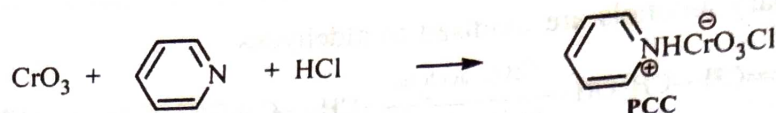


Oxidation of primary alcohol into carboxylic acid



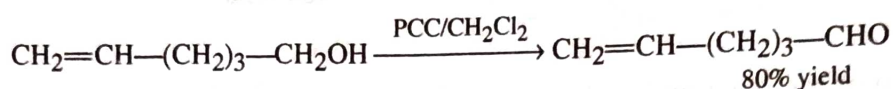
Conditions that do permit the easy isolation of aldehydes in good yield by oxidation of primary alcohols employ various Cr(VI) species as oxidant in *anhydrous* media. Two such reagents are **pyridinium chlorochromate** (PCC) and **pyridinium dichromate** (PDC), both are used in CH_2Cl_2 .

Pyridinium chlorochromate is obtained by adding pyridine to a solution of chromium(VI) oxide in hydrochloric acid.



PCC can oxidise primary and secondary alcohols to the corresponding carbonyl compounds. The yield of the product is excellent with PCC. The oxidation of primary alcohols with PCC stops at aldehyde stage because reaction is carried out in anhydrous conditions where no water is present to hydrate the aldehyde product and so leads to over oxidation.

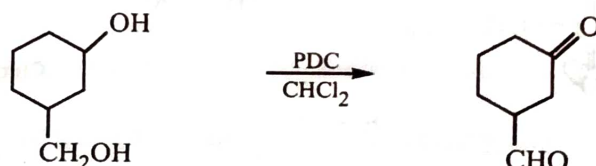
PCC can also be used for selective oxidation of alcohols containing other acid sensitive groups such as carbon-carbon multiple bonds.



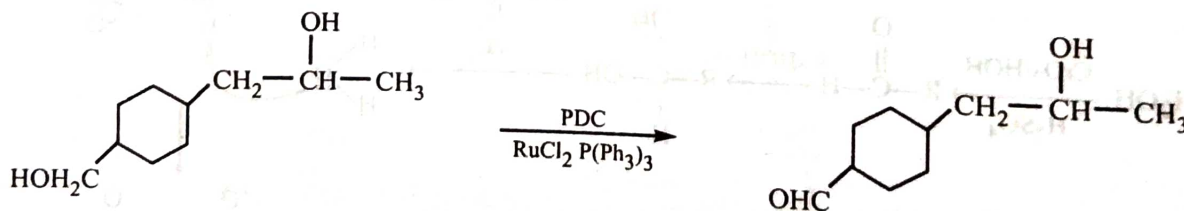
Pyridinium dichromate is obtained by the reaction of CrO_3 with pyridine in the presence of water.



It oxidises primary alcohols to aldehydes in excellent yield.

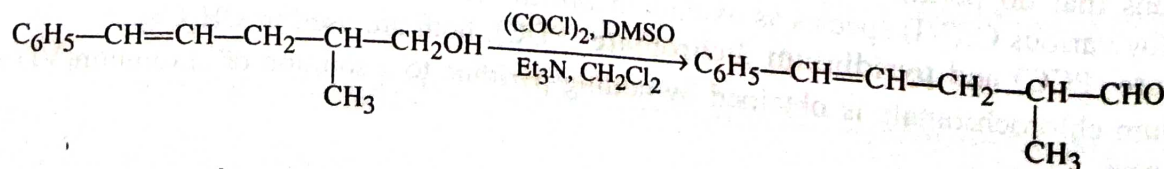


In the presence of rutheniumdichlorotriphenyl phosphine, PDC selectively oxidises primary alcohol to an aldehyde.

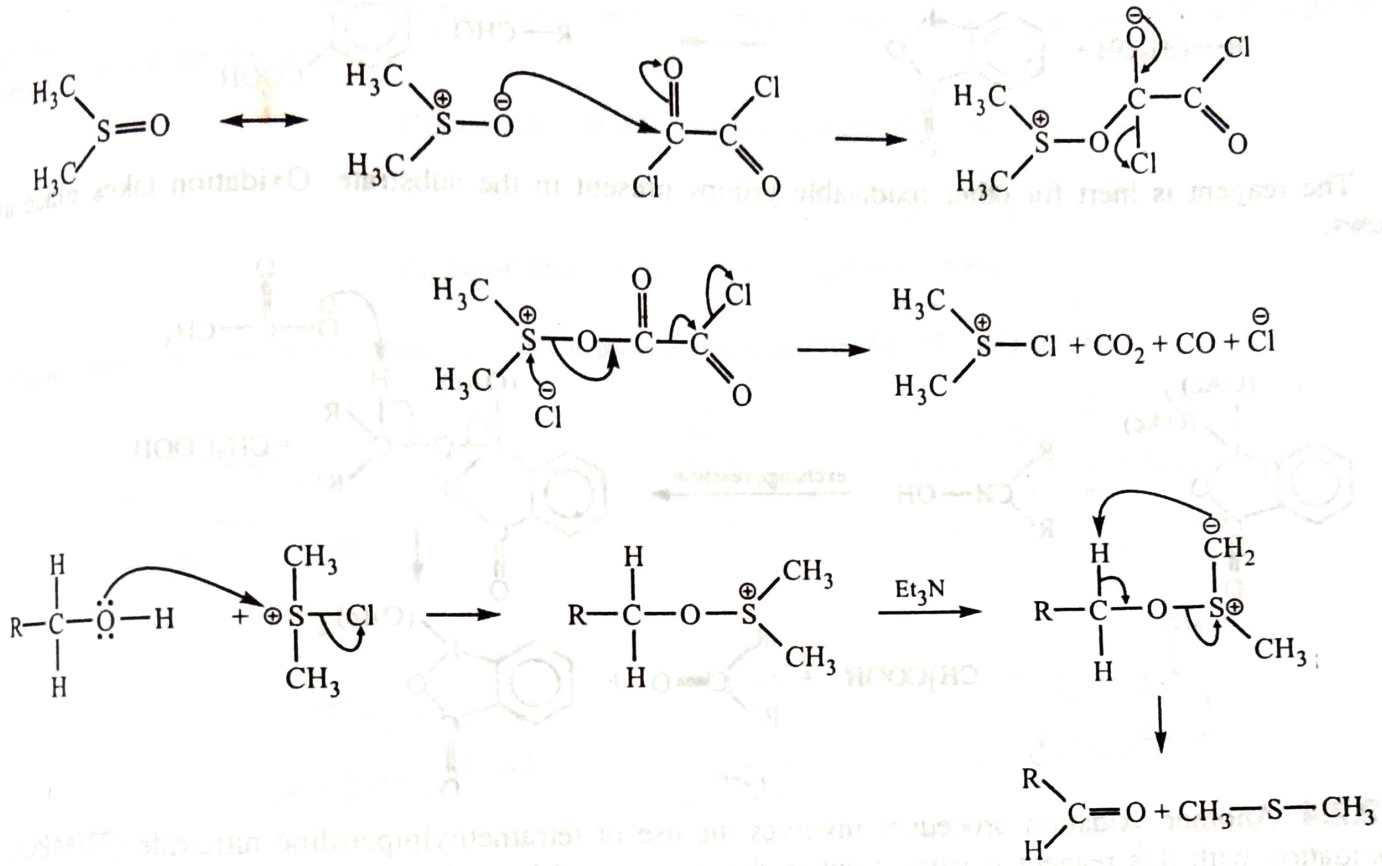


2.2.2 Oxidation by DMSO

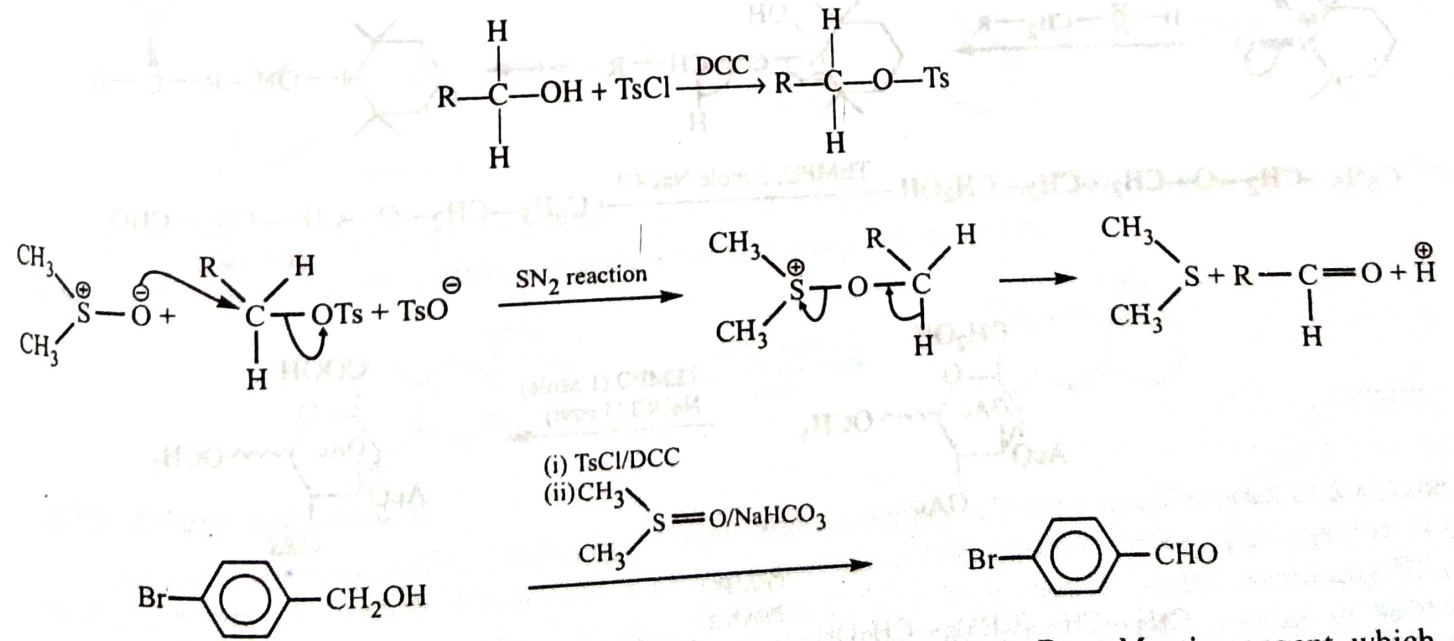
Swern Reaction: Perhaps the most important reagent for the oxidation of primary alcohols into aldehydes is the mixture of triethylamine, dimethyl sulphoxide and oxalyl chloride. There are many good reasons for the popularity of this reaction and these include the use of mild conditions, volatile by-products and lack of over-oxidation of aldehydes to carboxylic acids.



The reaction takes place as follows:



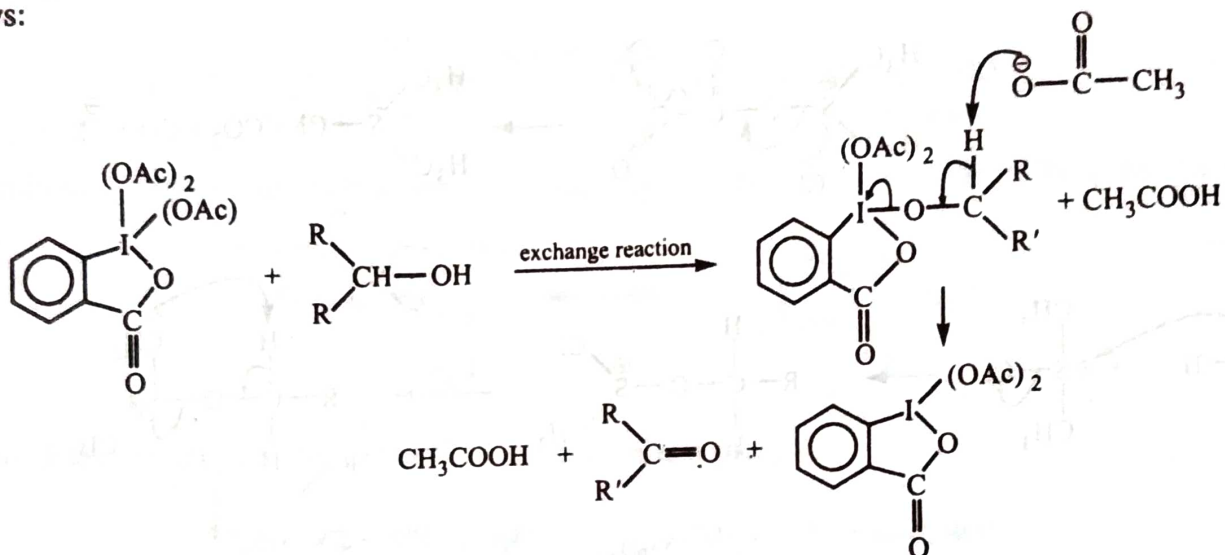
Alcohol can also be oxidised by DMSO by converting it into tosylate ester. The formation of tosylate is achieved *in situ* by the reaction of primary alcohol with TsCl in the presence of DCC followed by treatment with DMSO.



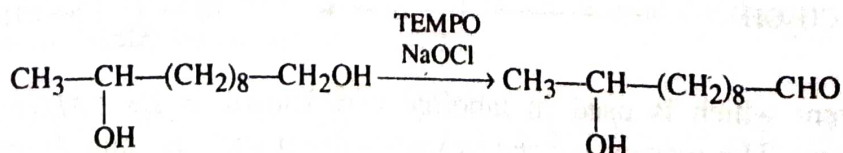
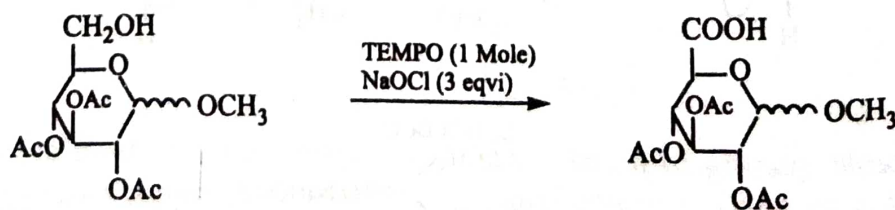
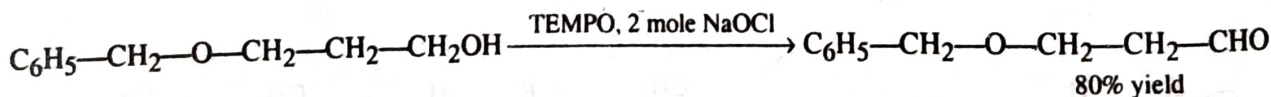
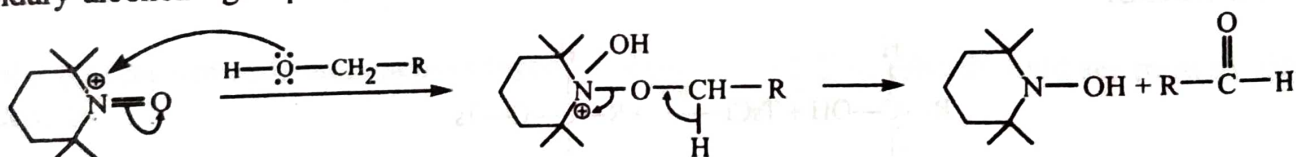
2.2.3 Another reagent which is used in laboratory is known as *Ders-Martin* reagent which is heptavalent iodine compound. The reagent is used in inert solvent such as chloroform or methyl cyanide and gives rapid oxidation of primary and secondary alcohols. The by-product *o*-iodobenzoic acid, can be extracted with base and recycled.



The reagent is inert for other oxidisable groups present in the substrate. Oxidation takes place as follows:



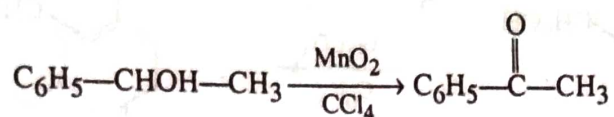
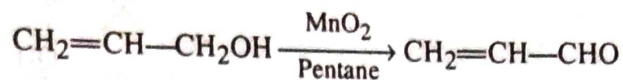
2.2.4 Another oxidation procedure involves the use of tetramethylpiperidine nitroxide (TEMPO). The oxidation with this reagent is carried out in the presence of hypochlorite ion which regenerates the reagent *in situ*. This reagent oxidises primary alcohol in the presence of secondary hydroxyl group. In the presence of excess hypochlorite ion, primary alcohol oxidises to carboxylic acid without affecting the secondary alcoholic group.



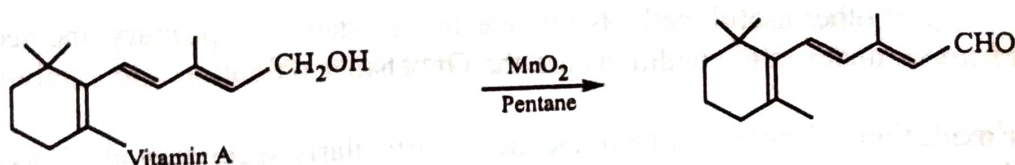
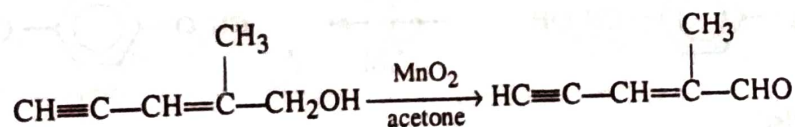
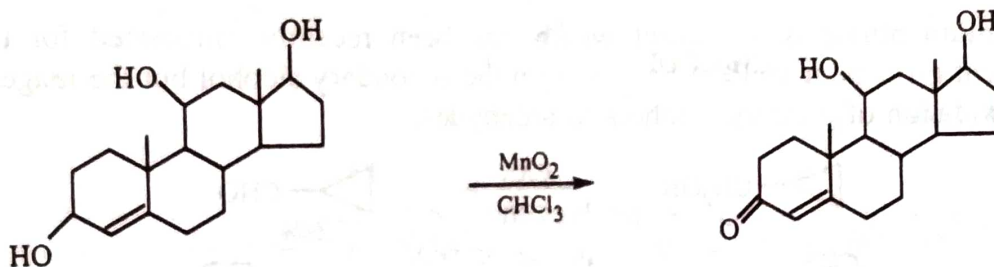
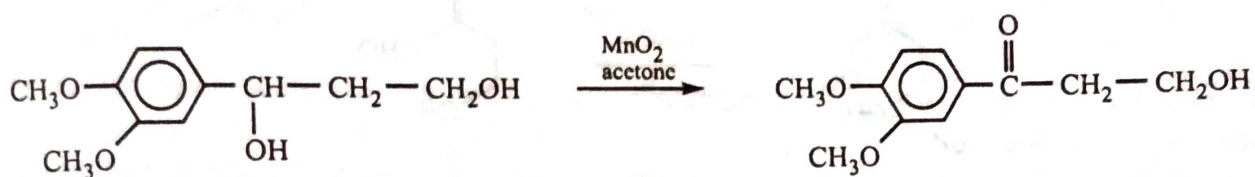
2.2.5 Manganese dioxide (MnO₂)

Another useful mild reagent for the oxidation of primary and secondary alcohols to carbonyl

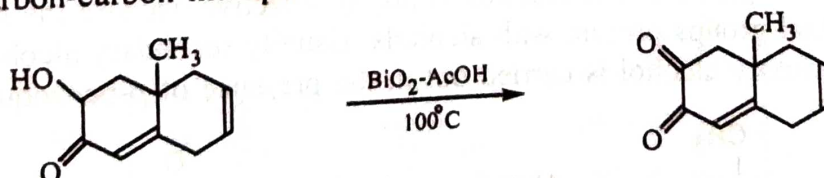
compounds is manganese(IV) oxide. The advantage of this reagent is that it is specific for allylic and benzylic hydroxyl groups, and the reaction takes place under mild conditions (room temperature) in a neutral solvent (water, benzene, chloroform, petroleum). The general technique is simply to stir a solution of the alcohol in the solvent with the manganese(IV) oxide for some hours. Carbon-carbon multiple bonds are unaffected by the reagent.



Under ordinary conditions saturated alcohols are not oxidised by Mn(IV) oxide.

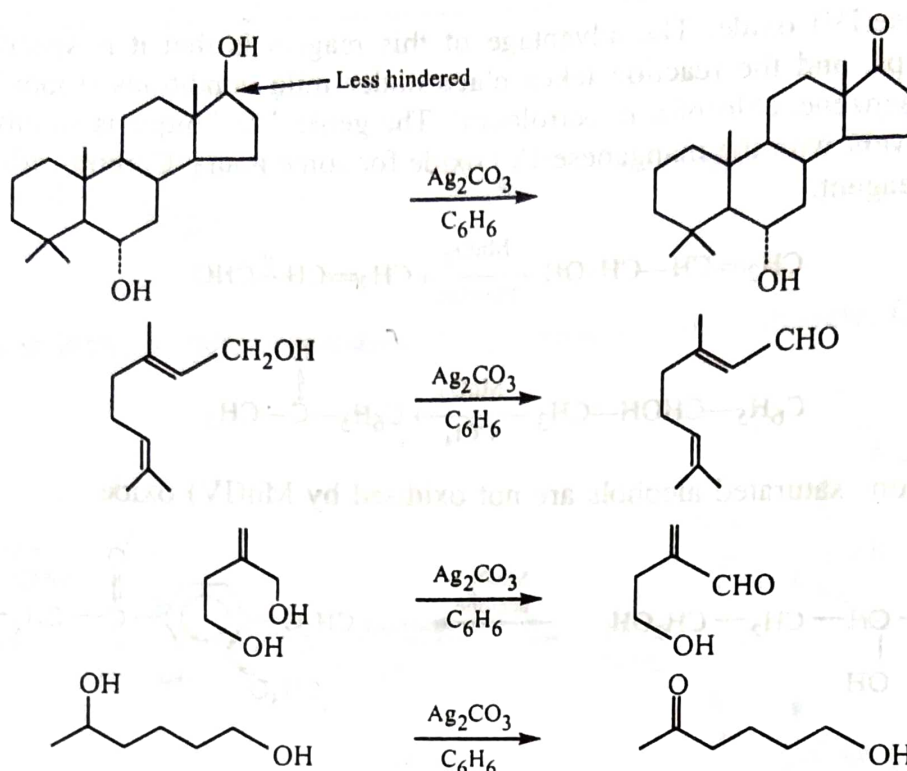


Bismuth oxide also oxidises hydroxy group of α -hydroxy ketones. The reagent is selective because it does not oxidise carbon-carbon multiple bonds, conjugated or isolated.

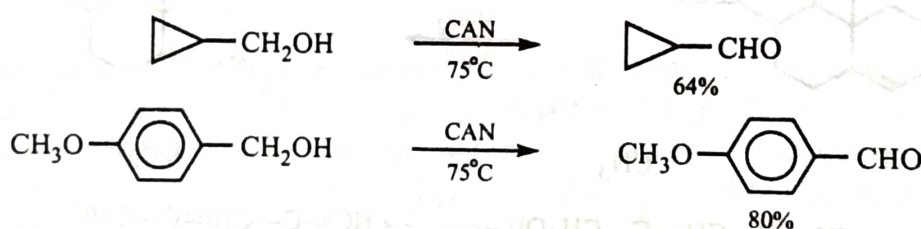


2.2.6 Silver carbonate

An excellent reagent for oxidising primary and secondary alcohols to aldehydes and ketones under mild and essentially neutral conditions is silver carbonate precipitated on celite. The reaction is effected in boiling benzene and the product is recovered, usually in a high state of purity, by simply filtering off the spent reagent and evaporating off the solvent. Other functional groups present in substrate are unaffected. Highly hindered groups are not attacked, allowing selective oxidation in appropriate cases. Primary alcohols are oxidised more slowly than secondary which are themselves much less reactive than benzylic and allylic alcohols.



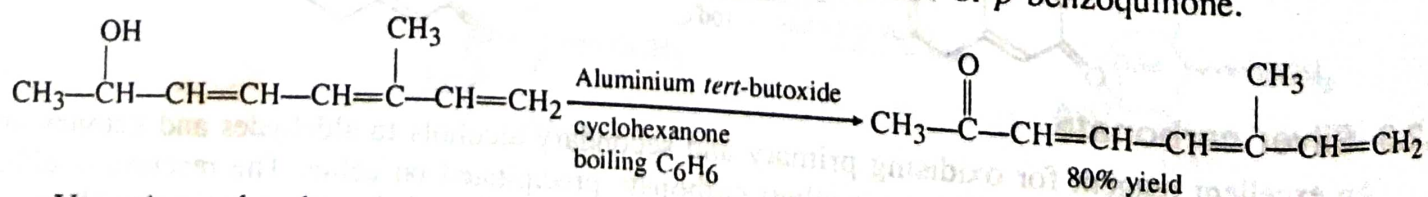
Ceric ammonium nitrate is a reagent which has been recently introduced for the oxidation of alcohols. The reagent gives poor yield of ketone from the secondary alcohol but the reagent is very useful for the selective oxidation of primary alcohols to aldehydes.



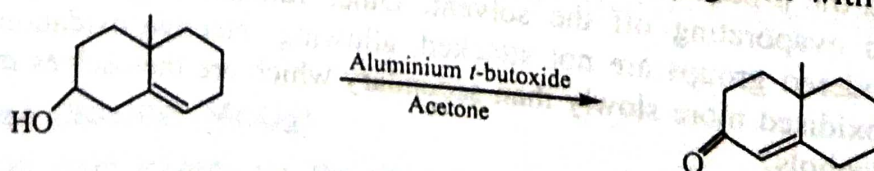
2.2.7 Other methods

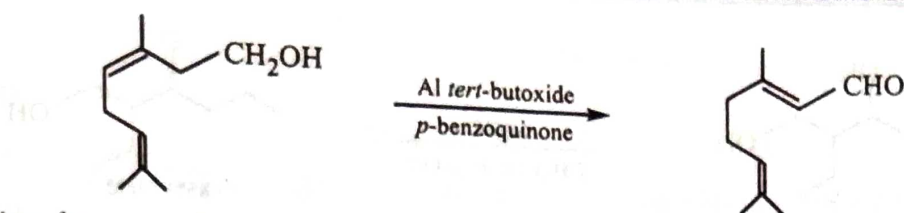
Among a number of other useful methods for selective oxidation of primary and secondary alcohols to aldehydes and ketones under mild conditions are the Oppenauer oxidation and catalytic oxidation with oxygen and Pt.

Oppenauer oxidation: The oxidation of alcohols (particularly secondary alcohols) with aluminium *tert*-butoxide in the presence of hydrogen acceptor (generally ketones) is known as Oppenauer oxidation. Since reaction is reversible, the oxidant, *i.e.*, ketone, is usually added in excess amount so that equilibrium mixture favours the desired product. The reaction is highly selective because the reagent has no effect on other oxidisable functional groups present with alcohols. Usually secondary alcohols are oxidised by this method. Oxidation of primary alcohol is carried out in the presence of *p*-benzoquinone.

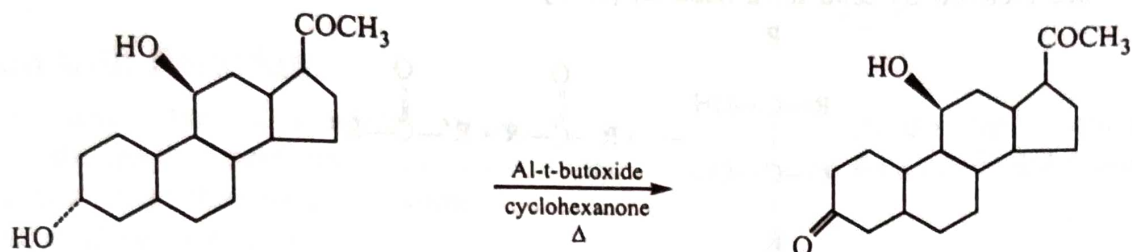


Unconjugated carbon-carbon double bonds isomerise into conjugation with the ketone formed.

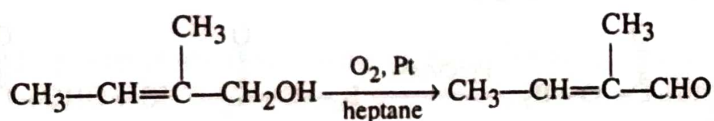
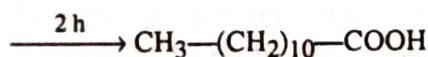
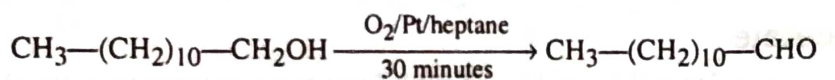




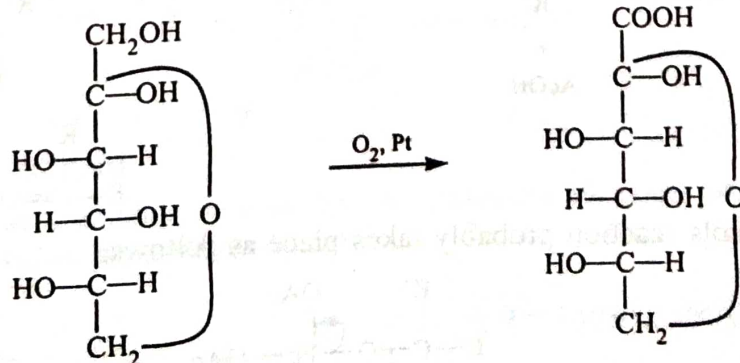
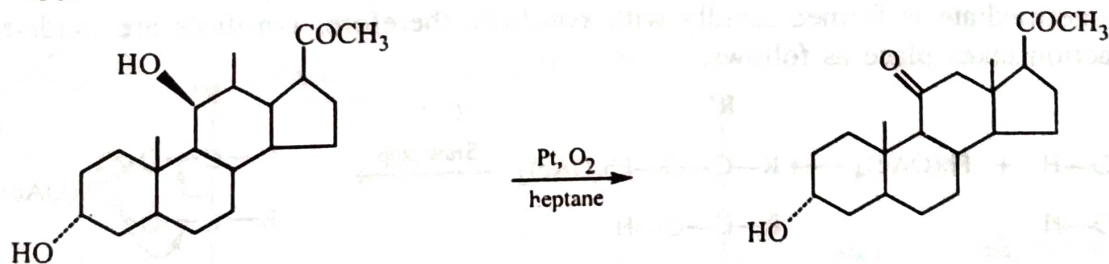
This oxidation has mostly been used in steroids. Equatorial hydroxyl groups tend to be oxidised preferentially over axial hydroxyl groups.



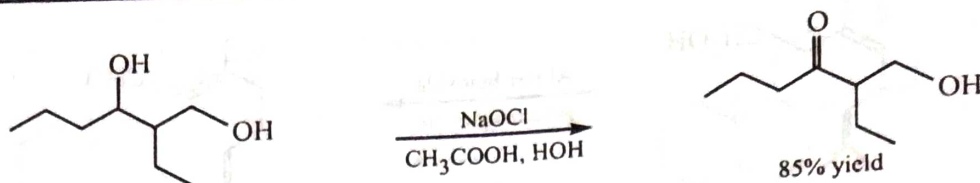
Catalytic oxygenation with a platinum catalyst and molecular oxygen is another valuable method for oxidation of primary and secondary hydroxyl groups under mild conditions. With primary alcohols the reaction can be regulated to give aldehydes or acids. Double bonds, in general, are not affected.



In general, primary hydroxyl groups are attacked before secondary and in cyclic secondary alcohol axial groups appear to react before equatorial.

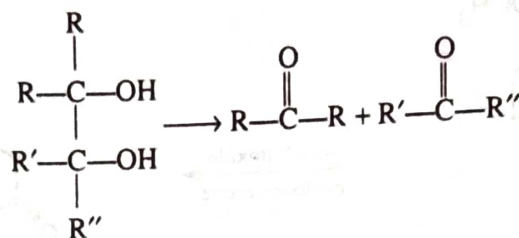


Selective oxidation of a primary or a secondary hydroxyl group in the presence of the other is a useful conversion in organic synthesis. Few methods are available for such selective oxidation of primary hydroxyl groups but secondary alcohols can be selectively oxidised in the presence of primary ones in several ways using silver carbonate, sodium bromate in the presence of catalytic amount of CAN or sodium hydrochlorite in aqueous acetic acid.



2.3 Oxidation of 1,2-Diols

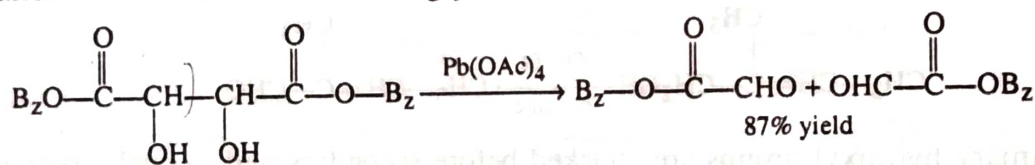
1,2-Diols are cleaved by lead tetra-acetate, phenyliodosoacetate and periodic acid.



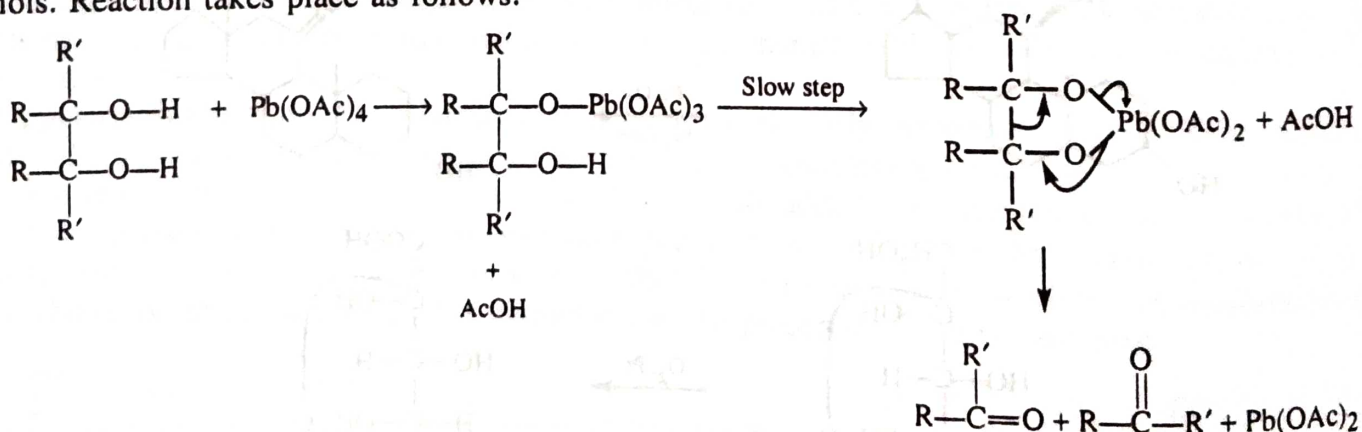
The first two reagents are used in an organic medium, commonly glacial acetic acid, whereas periodate is used in aqueous solution. In this oxidation aldehydes formed are not oxidised further. Yields are usually excellent.

2.3.1 Lead tetra-acetate

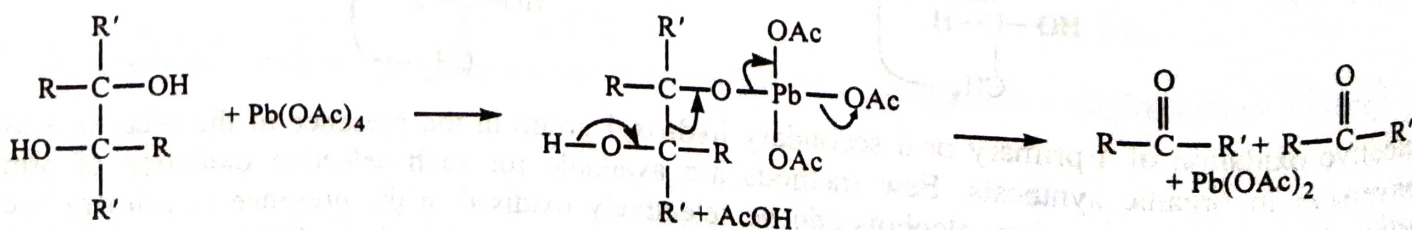
1,2-Diols are cleaved under mild conditions with lead tetra-acetate to give aldehydes and/or ketones. Nature of product(s) depends upon the structure of the 1,2-diols. The reaction is quantitative and rapid enough to allow titrimetric estimation of glycols.



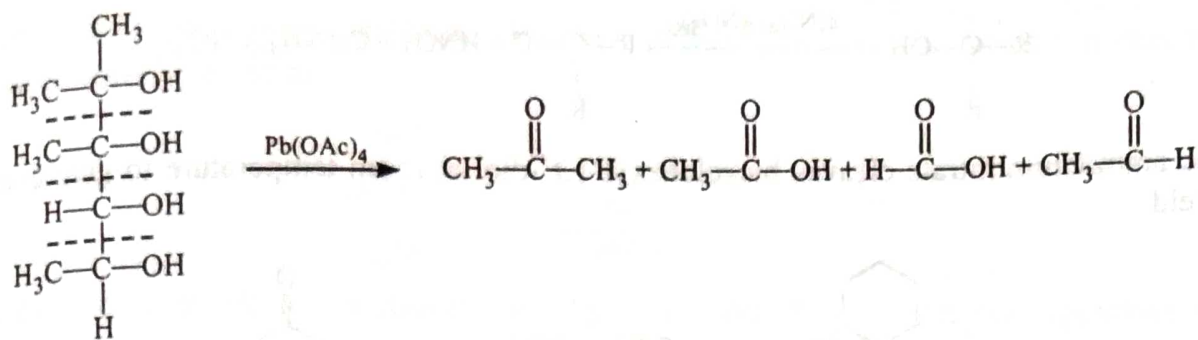
Oxidation normally occurs by two-electron oxidation [Pb(IV) \rightarrow Pb(II)] with a cyclic intermediate. Since, cyclic intermediate is formed rapidly with *syn*-diols, therefore, *syn*-diols are oxidised faster than *anti* diols. Reaction takes place as follows:



In the case of *trans* diols reaction probably takes place as follows:



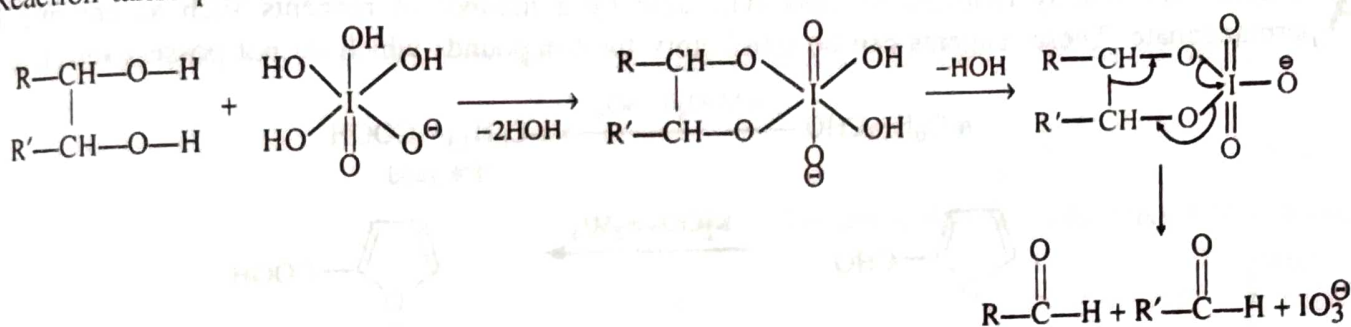
When compound has more than one diol group, the terminal carbons convert into carbonyl groups and middle carbons are oxidised into carboxylic groups.



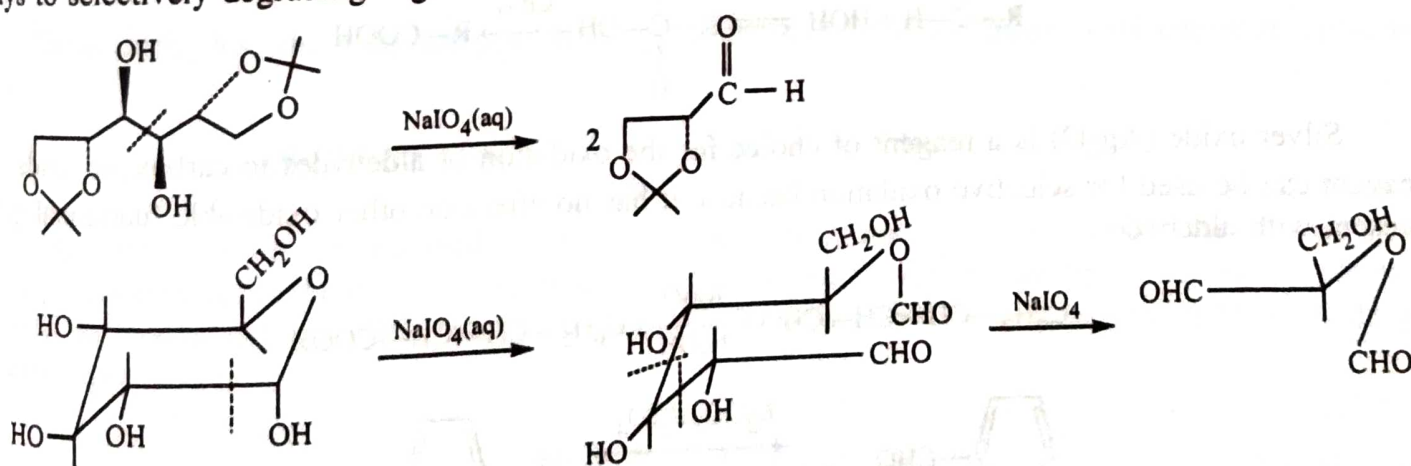
2.3.2 Oxidation with Periodate

This reagent also gives 2 electron oxidation [I(VII) \rightarrow I(V)] with the formation of cyclic intermediate. Thus the reagent oxidises *cis* diols faster than the *trans* diols, e.g., *cis* cyclohexane-1,2-diol reacts about 25 times faster than its *trans* isomer.

Reaction takes place as follows:

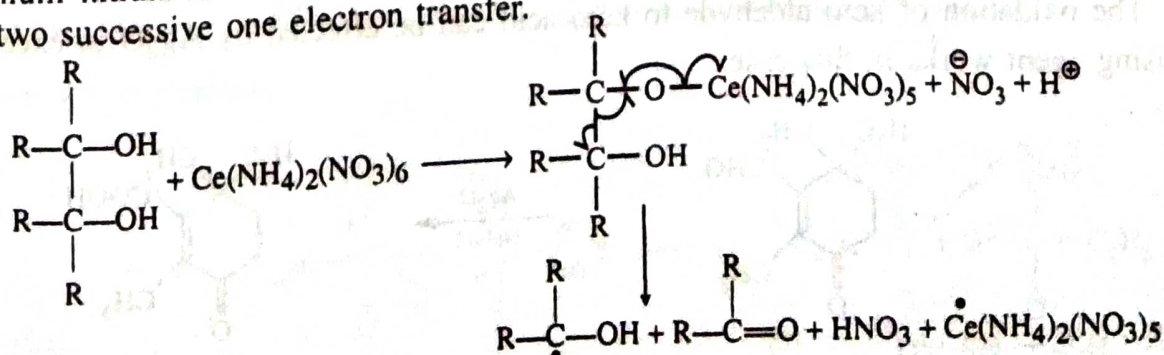


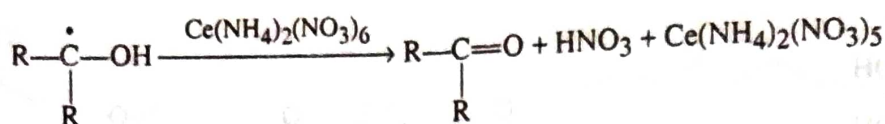
It does not matter if the diol unit is part of a ring or not: cleavage occurs just the same. Imagine cleaving a polyhydroxylated substrate such as glucose with excess periodate. Each 1,2-diol will be cleaved and then each α -hydroxy carbonyl group will be cleaved again. This method is, therefore, one of the best ways to selectively degrading sugars.



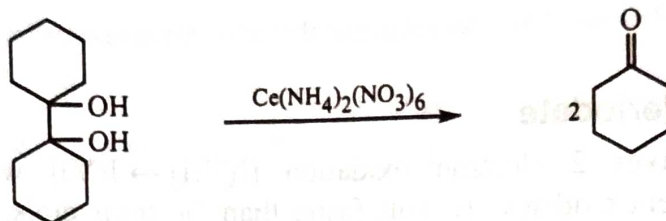
2.3.3 Ceric ammonium nitrate

Ceric ammonium nitrate can also be used for the oxidative cleavage of an 1,2-diols. Oxidative cleavage involves two successive one electron transfer.



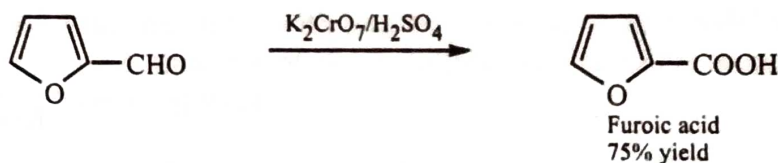
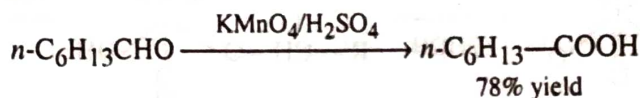


Ceric ammonium nitrate cleaves bicyclohexyl-1,1'-diol at room temperature to give cyclohexanone in 97% yield.

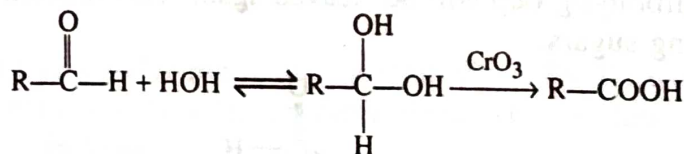


2.4 OXIDATION OF ALDEHYDES

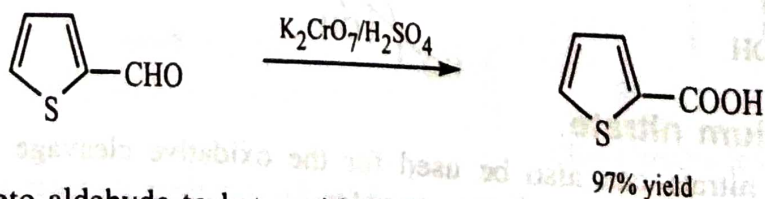
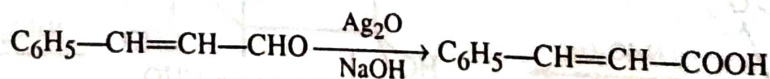
Aldehydes are readily oxidised to carboxylic acid by a number of reagents such as chromic acid and permanganate. These reagents can be satisfactory for compounds which do not possess sensitive groups.



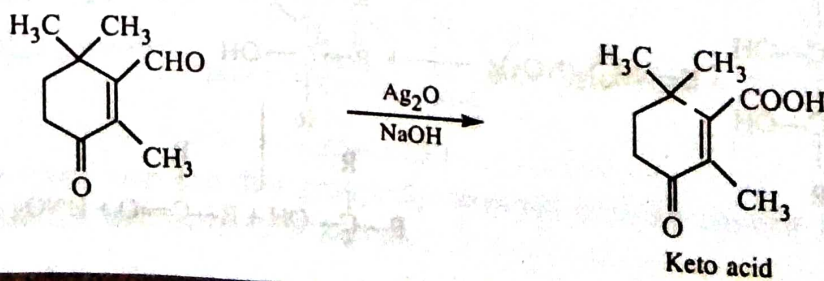
These reactions probably proceed through the hydrate of the aldehyde and follow a course similar to that of alcohol oxidation.



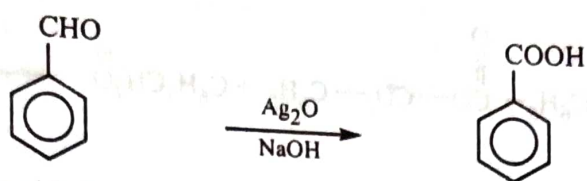
Silver oxide (Ag_2O) is a reagent of choice for the oxidation of aldehydes to carboxylic acids. This reagent can be used for selective oxidation because it has no effect on other oxidisable functional groups present with aldehydes.



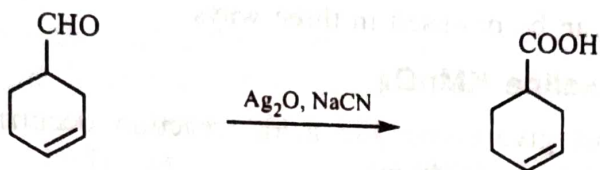
The oxidation of keto aldehyde to keto acid can be effected by Ag_2O in excellent yield. No other oxidising agent works in this case.



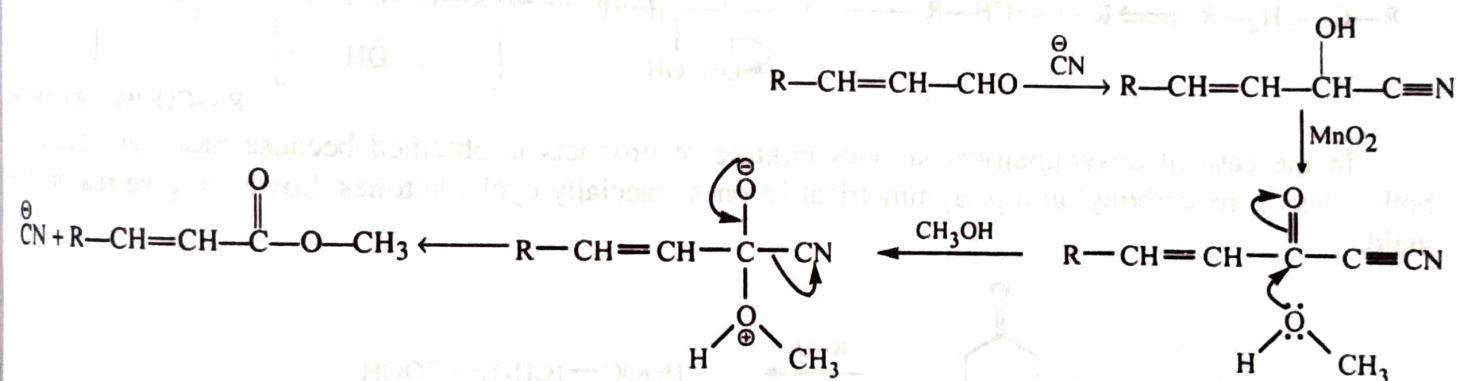
Silver(II) oxide is also a powerful oxidising agent. This reagent is prepared by the oxidation of silver nitrate with $K_2S_2O_8$ in alcoholic medium. Oxidation of aldehydes with the reagent in neutral or alkaline medium gives carboxylic acids.



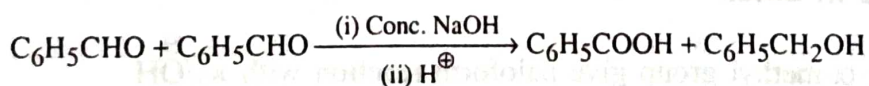
Unsaturated aldehyde on oxidation with Ag_2O and NaCN gives the corresponding acid without isomerisation of double bond into conjugation.



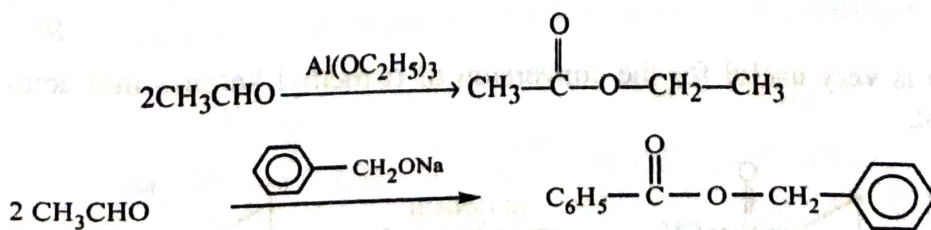
Conjugated aldehydes can be oxidised to conjugated esters with MnO_2 in the presence of CN^- in alcoholic medium.



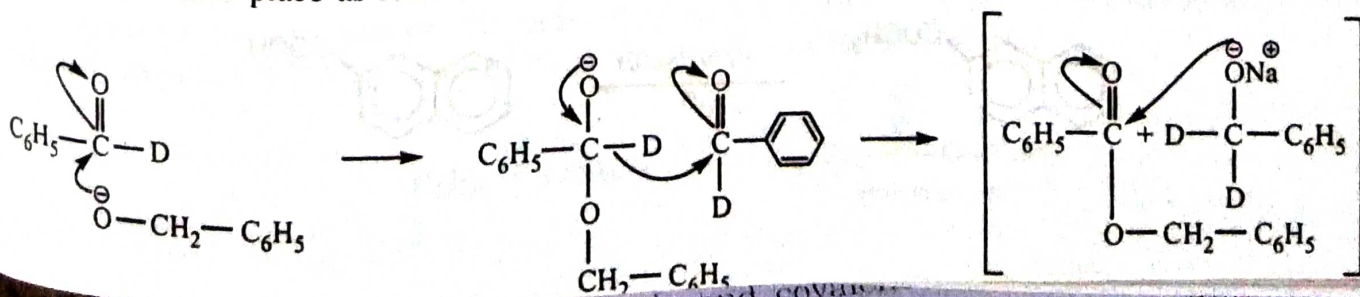
Those aldehydes which do not possess α -hydrogen atoms undergo disproportionation reaction with base.

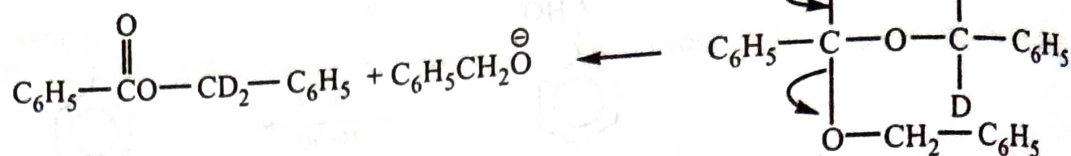


Aldehydes can also be oxidised by the use of Tischenko reaction. The reaction takes place in the presence of aluminium ethoxide. Instead of aluminium ethoxide sodium alkoxide of alcohol of aldehyde can also be used as catalyst. This reaction is used for the preparation of ethyl acetate from acetaldehyde on large scale.



Reaction takes place as follows:



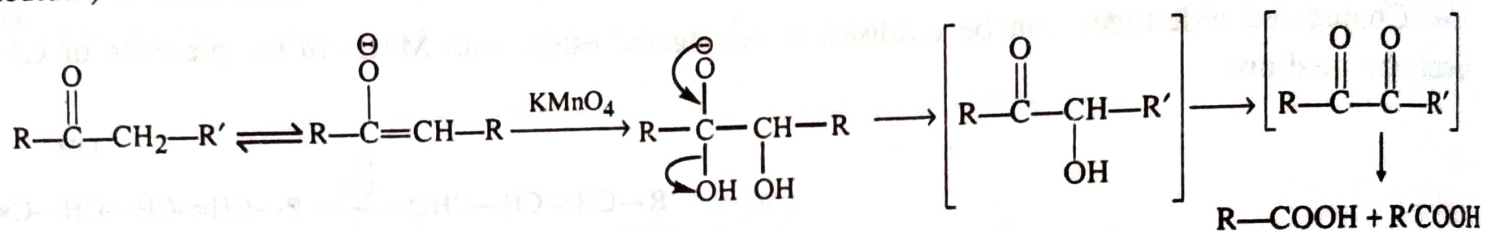


2.5 OXIDATION OF KETONES

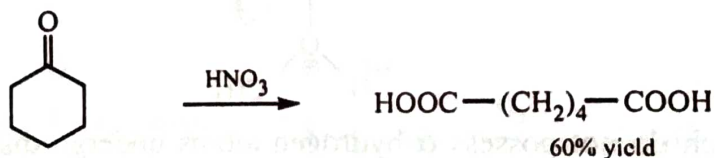
The C—CO bond in ketone can be oxidised in three ways.

2.5.1 By nitric acid or alkaline KMnO_4

These powerful reagents give carboxylic acids, reaction occurring through the enol (in acidic medium) or the enolate anion (basic medium).

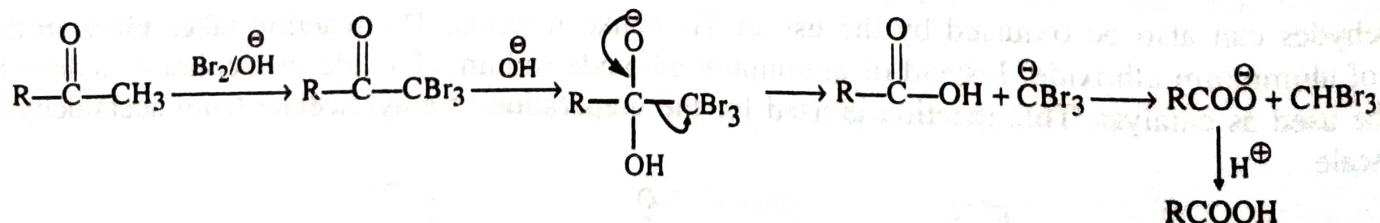


In the case of unsymmetrical ketones mixture of products is obtained because base can attack on both sides of the carbonyl group. Symmetrical ketones, specially cyclic ketones, however, give reasonable yield.

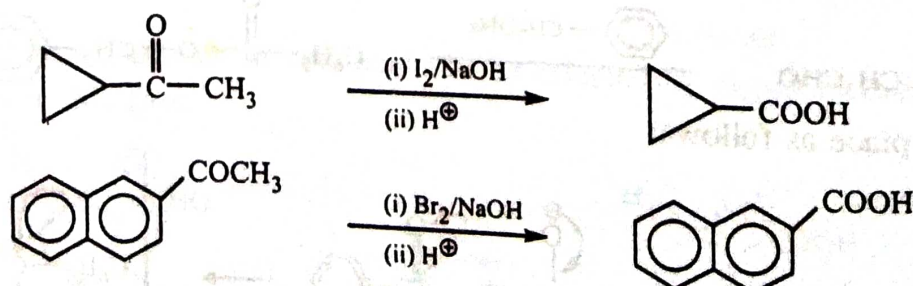


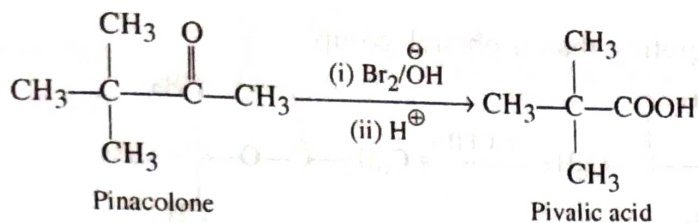
2.5.2 By halogens in alkali

Ketones having α -methyl group give haloform reaction with x_2/OH^- .



This reaction is very useful for the conversion of α -methyl ketones into acids and the yield of the product is excellent.



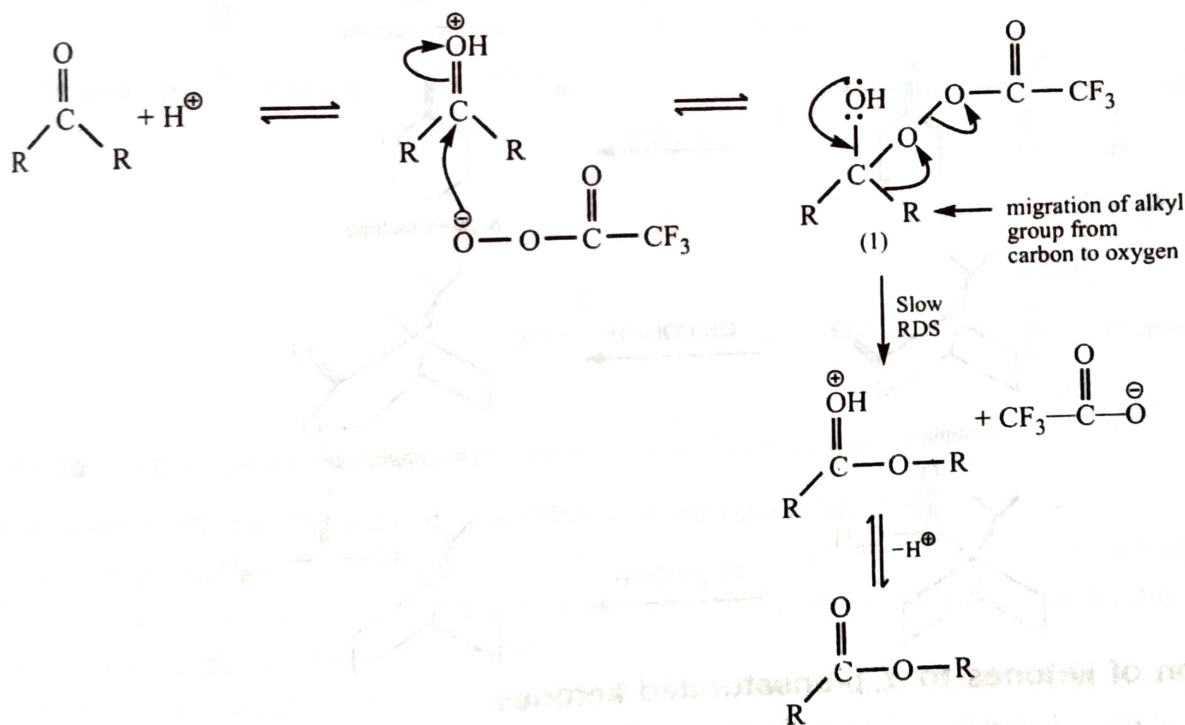


2.5.3 By per acids

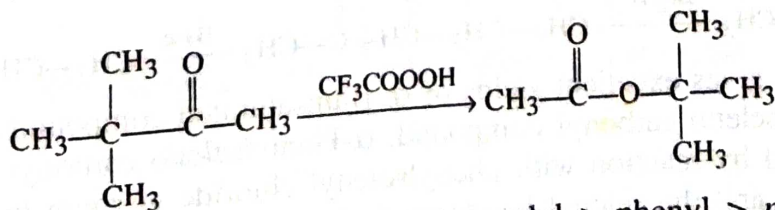
Reaction of a ketone with a per acid results in an oxidative cleavage of one of the substituents attached to the carbonyl group; this is known as the **Baeyer-Villiger** reaction. In this reaction ketones are converted into esters and cyclic ketones into lactones by treatment with a per acid.

A number of per acids, including peracetic, monoperothalic, monopersulphuric trifluoroacetic, and *m*-chloroperbenzoic acid, have been successfully employed in the reaction. Trifluoroacetic acid is the most reactive of the per acids, probably because of the trifluoroacetate ion which is very good leaving group. It is necessary to buffer the solution for otherwise transesterification occurs to give the trifluoroacetate ester.

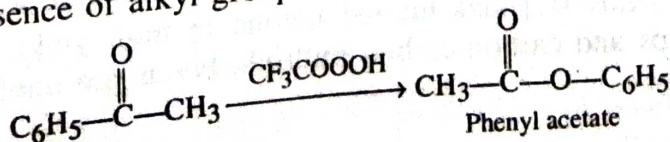
Oxidation takes place as follows:



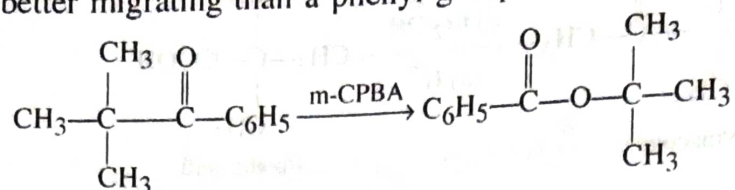
As an unsymmetrical ketone, that group migrates which is better able to supply electrons. Thus amongst the alkyl groups, the ease of migration is, tertiary > secondary > primary, that is pinacolone gives *t*-butyl acetate.



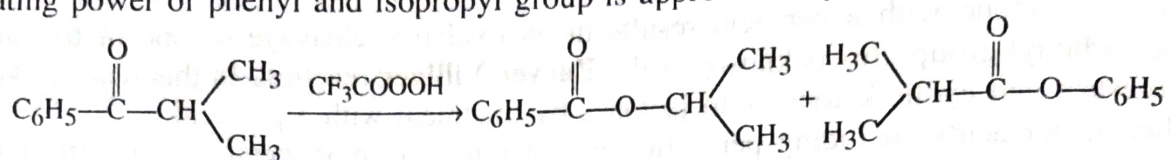
Amongst the aryl groups, the order is, *p*-anisyl, *p*-tolyl > phenyl > *p*-chlorophenyl. Aryl group normally migrates in the presence of alkyl groups, (Ph > CH₃, Ph > C₂H₅)



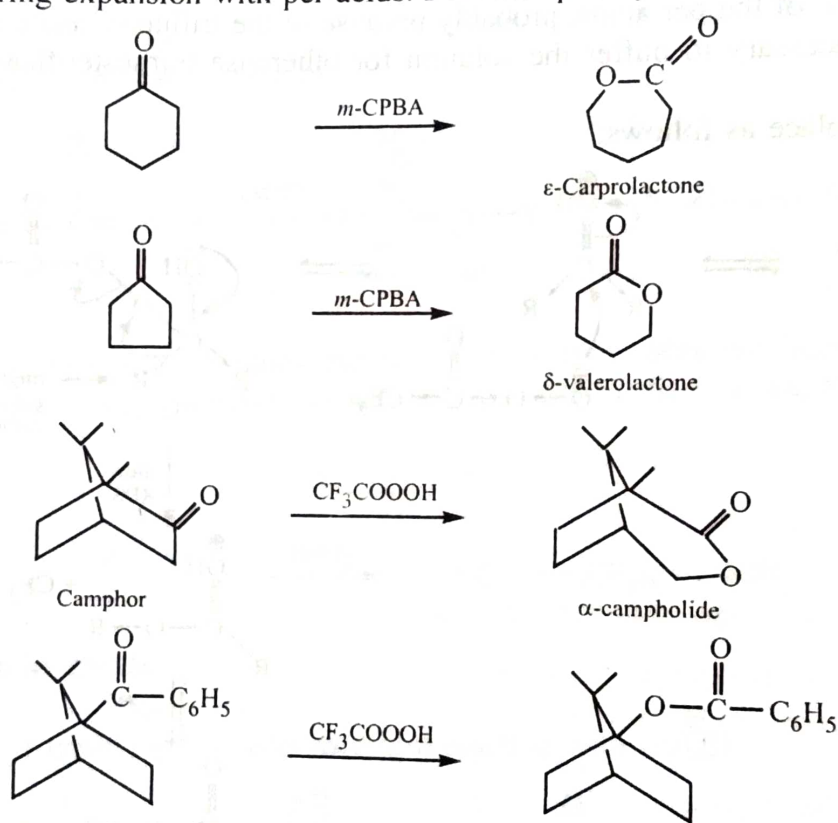
Tert-butyl group is better migrating than a phenyl group.



Migrating power of phenyl and isopropyl group is approximately equal thus mixture is formed.

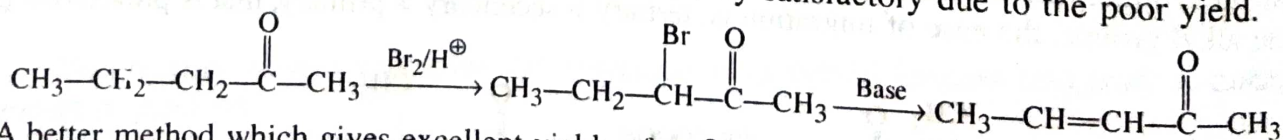


Cyclic ketones undergo ring-expansion with per acids. For example, cyclohexanone gives ϵ -caprolactone.

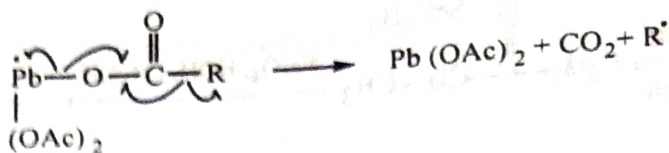


2.5.4 Oxidation of ketones to α, β -unsaturated ketones

Oxidation of ketones into α, β -unsaturated ketones has been effected by bromination-dehydrobromination but the method is not very satisfactory due to the poor yield.

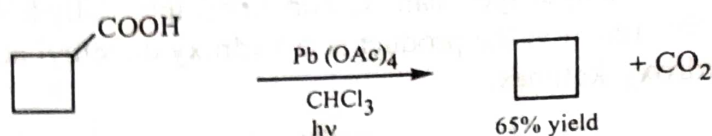


A better method which gives excellent yields of α, β -unsaturated compounds under mild conditions proceeds from the α -phenylseleno carbonyl compound. α -Phenylseleno carbonyl compound is prepared from the carbonyl compound by reaction with phenylselenenyl chloride at room temperature, or from the H_2O_2 or NaIO_4 the selenide is converted into the corresponding selenoxide which immediately undergoes *syn* β -elimination to form the *trans* α, β -unsaturated ketone in high yield. Functional groups such as alcoholic hydroxyls, ester groups and carbon-carbon multiple bonds are unaffected during the course of the reaction.

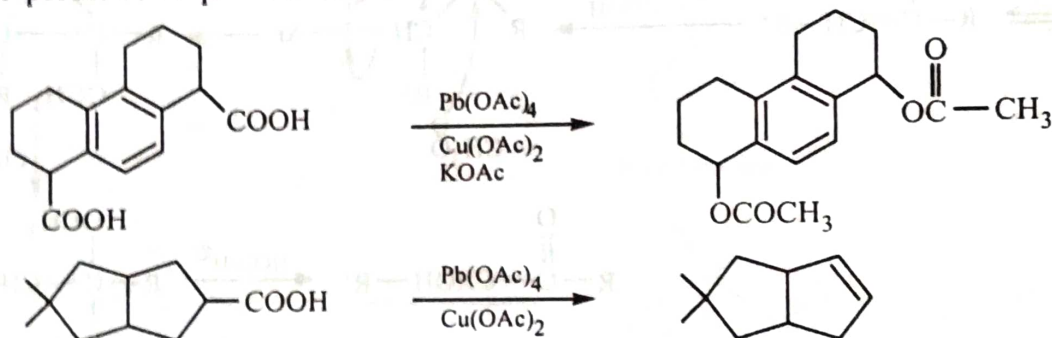


Products can be formed either from free radical or carbocation. Primary free radical abstracts H from solvent molecules to give RH. R^\oplus can lose H^\oplus from β -carbon to give alkene, react with acetic acid to give the carboxylic ester, R^\bullet can also dimerise to give $\text{R}-\text{R}$. The effect of Cu^{++} is to oxidise the radicals to alkene, thus producing good yields of alkenes from the primary and secondary substrate. Cu^{++} has no effect on tertiary free radicals.

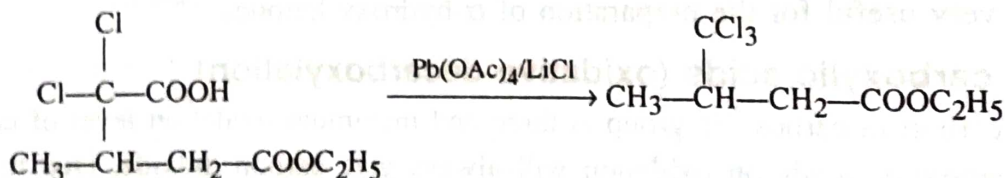
The most favourable conditions for alkane formation involve photochemical decomposition of the carboxylic acids in chloroform, which is relatively good hydrogen atom donor.



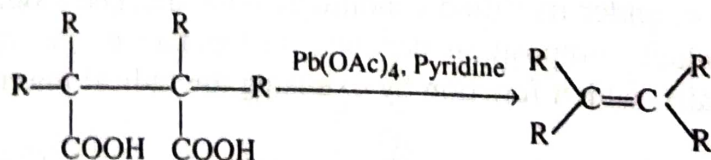
Normally, the dominant products are alkene and acetate ester, which arise from the carbocation intermediate. The presence of potassium acetate increases the alkene : ester ratio.



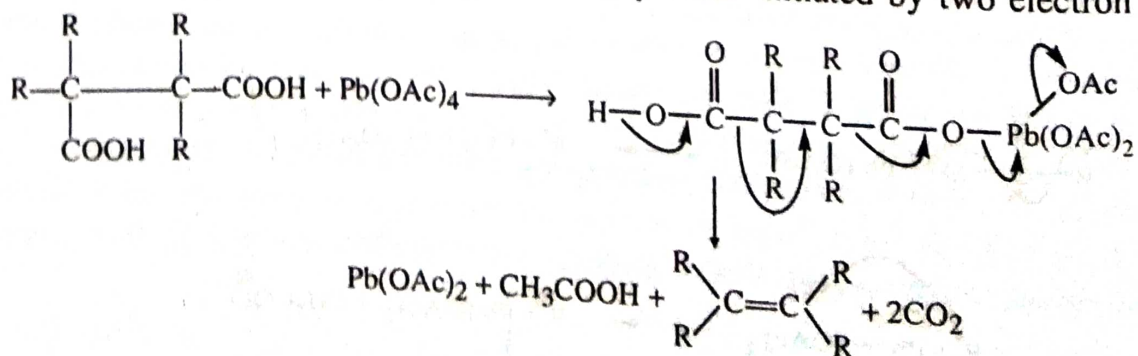
In the presence of LiCl, the product is the corresponding chloride



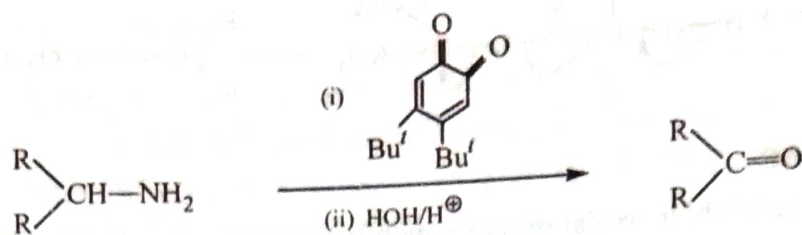
1,2-Dicarboxylic acids undergo *bis*-decarboxylation on treatment with lead tetraacetate to give alkenes.



The reaction occurs by concerted fragmentation process initiated by two electron oxidation.

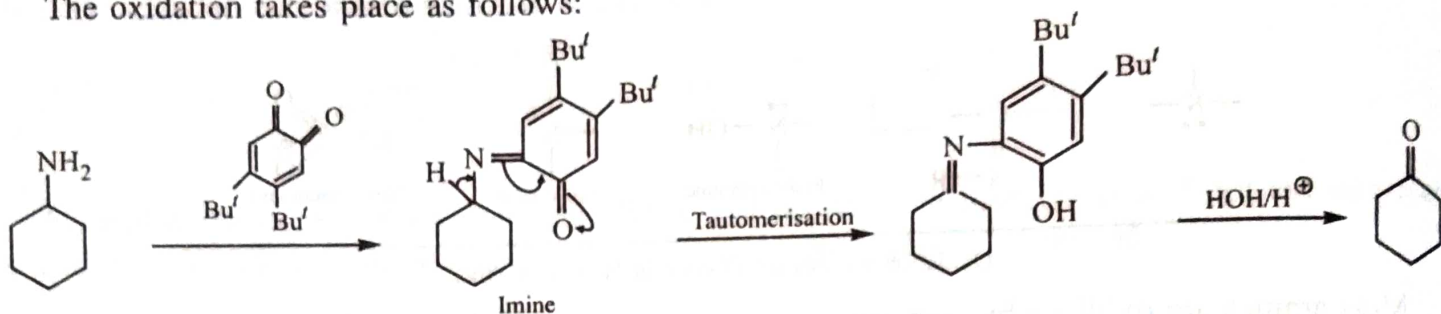


effective in transforming primary amines into imines which are then hydrolysed *in situ* to the corresponding ketones.



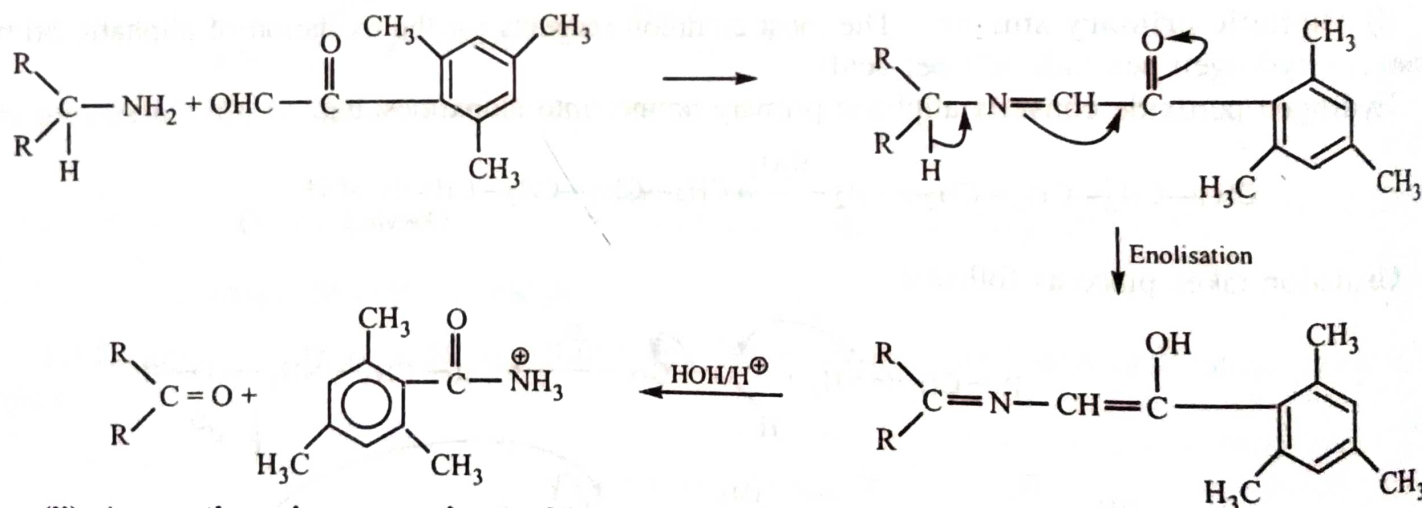
The reagent oxidises only those aliphatic primary amines whose α -carbon is only secondary. Unfortunately one cannot transform $\text{R}-\text{CH}_2-\text{NH}_2$ into an aldehyde by this method.

The oxidation takes place as follows:

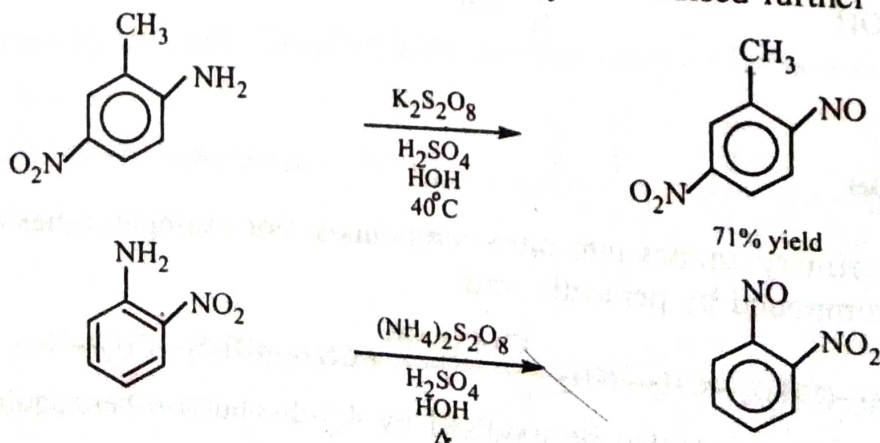


Mesityl glyoxal is also used for the oxidation of primary amines having only one hydrogen on α -carbon. Product of the reaction is ketone. In this oxidation $>\text{C}-\text{NH}_2$ group converts into $>\text{C}=\text{O}$ group.

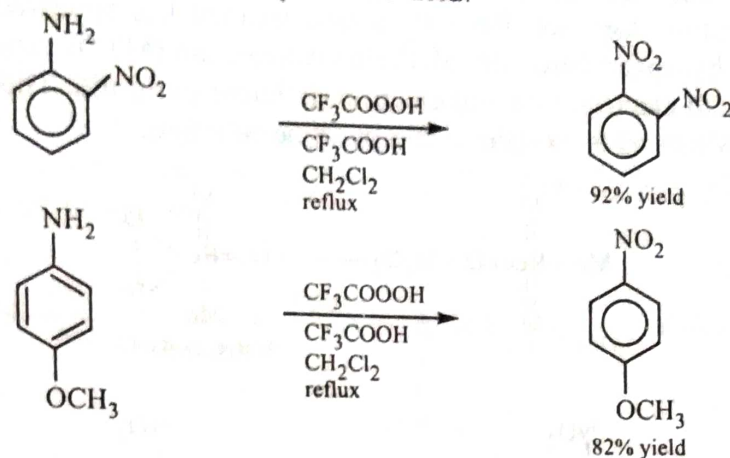
Oxidation takes place as follows:



(ii) Aromatic primary amines: Nitroso compounds are formed by the oxidation of aromatic primary amines with per acids. The nitroso compounds may be oxidised further to nitro compounds.

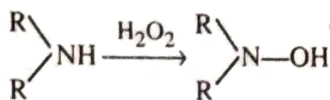


Trifluoroperacetic acid has been found a useful reagent for the direct oxidation of aromatic primary amines to nitro compounds. Although trifluoroperacetic acid has proved to be unsuitable for the oxidation of aromatic primary amines which contain electron donating groups. Amines of this type have been oxidised to nitro compounds with anhydrous peracetic acid.

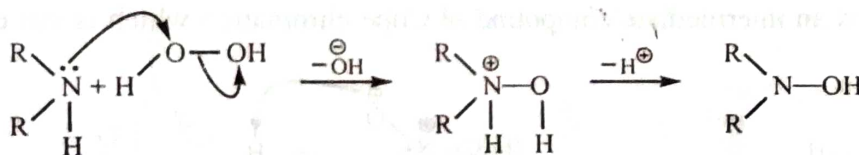


2.7.2 Secondary amines

Secondary amines are oxidised by hydrogen peroxide and the product of the reaction is hydroxyl amine.

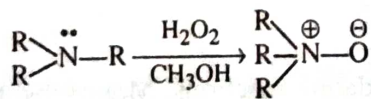


Reaction takes place as follows:

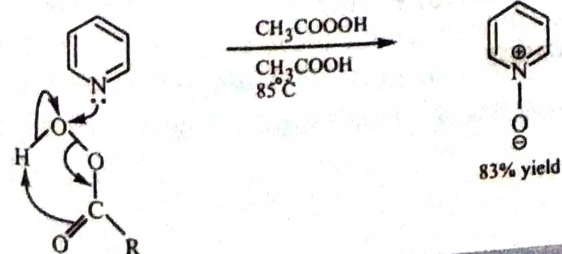
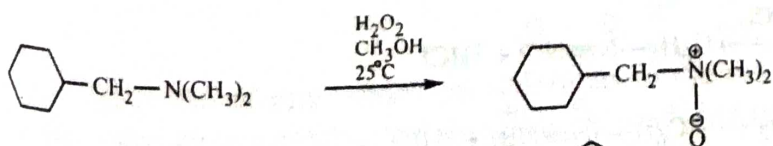
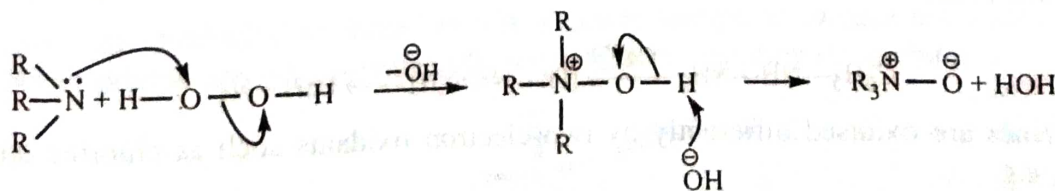


2.7.3 Tertiary amines

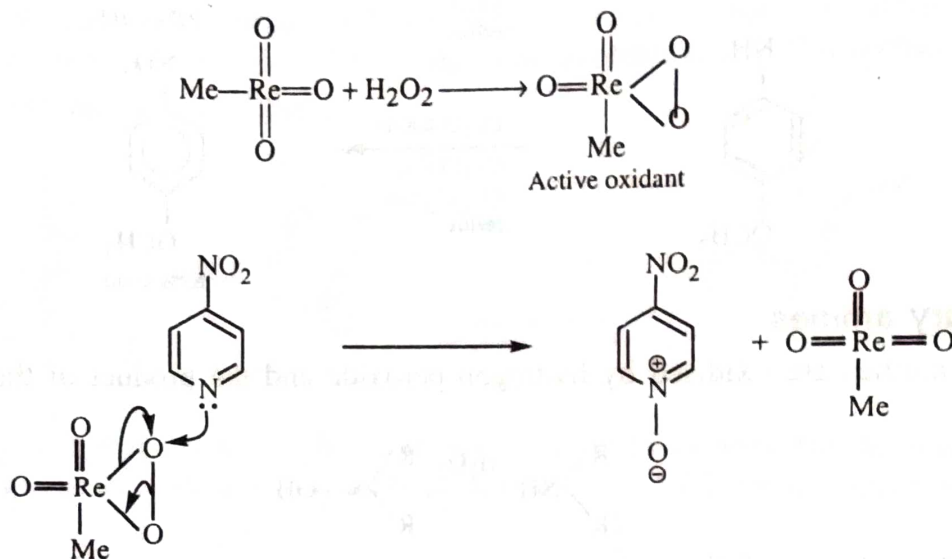
Tertiary amines are oxidised by either hydrogen peroxide or per acids to produce amine oxides that serve as useful synthetic intermediates.



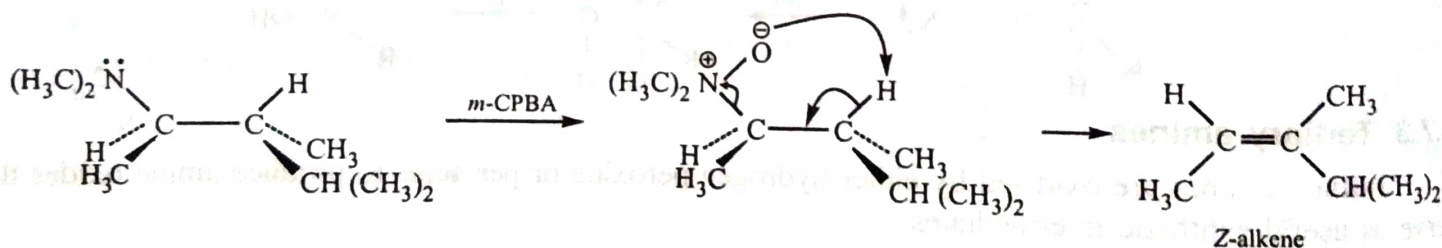
Formation of product takes place as follows:



In comparison with aliphatic amines, the oxidation of heterocyclic aromatic amines is less easy to accomplish with hydrogen peroxide—probably as a consequence of the trigonal nitrogen (which is more electronegative and less basic) reduced nucleophilicity (See mechanism). Hydrogen peroxide oxidises only electron-rich pyridines. It does not oxidise electron-deficient pyridines. Pyridine undergoes oxidation with *m*-CPBA but 4-cyanopyridine does not. Recently a new oxidant has appeared which catalyses the slow reaction of pyridine with hydrogen peroxide. Methyltrioxorhenium (MTO) very successfully promotes the oxidation of a range of both electron rich and electron deficient pyridines. The active oxidant may be the peroxy complex shown which adds oxygen to the pyridine nitrogen.

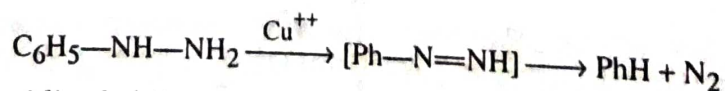


Amine oxide is an intermediate compound of Cope elimination which is *syn* elimination of N-oxide.

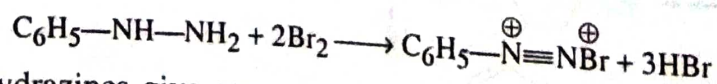
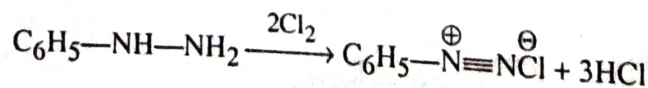


2.8 Oxidation of hydrazines

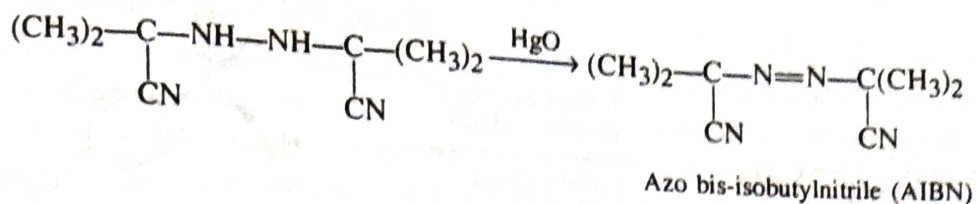
Hydrazines are very susceptible for oxidation reactions. Monosubstituted hydrazines react with one electron oxidants such as cupric and ferric ion to give unstable azo compounds which decompose with loss of nitrogen to hydrocarbons.



Arylhydrazines are oxidised differently by two electron oxidants such as chlorine and bromine to diazonium salts, e.g.

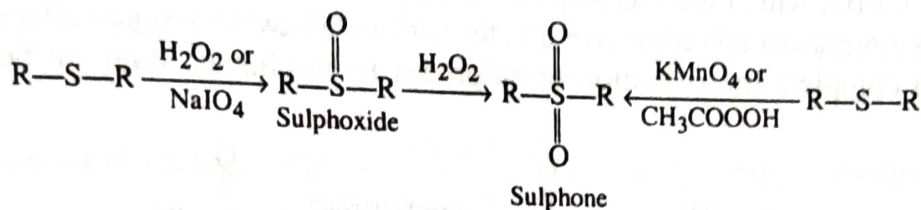


N,N'-Disubstituted hydrazines give azo compounds readily.

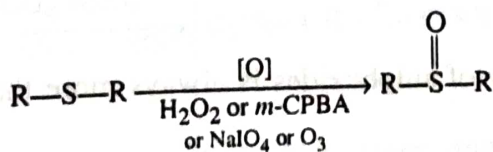
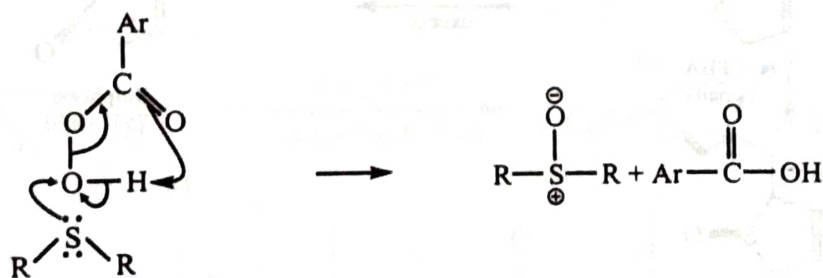


2.9 Oxidation of Sulphides

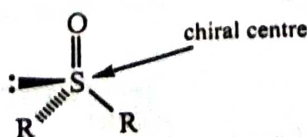
Sulphides can be oxidised to both sulphoxides and sulphones. Most reagents which will oxidise a sulphide will also oxidise a sulphoxide to a sulphone. Useful reagents include hydrogen peroxide (one equivalent in acetone), *m*-CPBA, sodium periodate, and ozone.



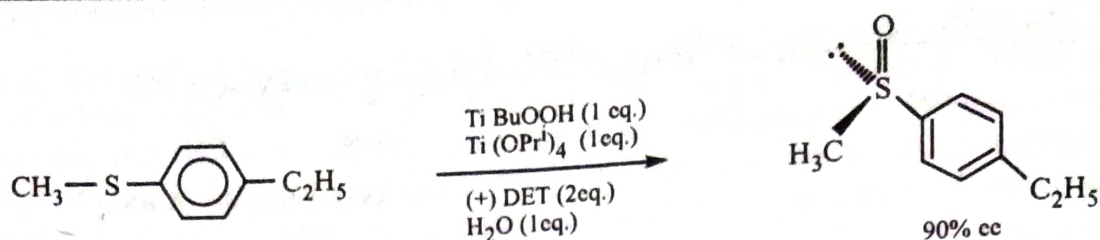
Although oxidation of sulphide to sulphoxides with hydrogen peroxide can be accomplished in the presence of other oxidisable groups such as tertiary amino and carbon-carbon double bonds, care must always be taken to ensure that excess oxidant is not present, otherwise overoxidation of the sulphoxide to the sulphone can occur. The mechanism of oxidation with *m*-CPBA involves nucleophilic attack of sulphide on to the per acids: if this is to be believed then there should be a correlation between the nucleophilicity of a sulphide and its rate of oxidation. This is indeed the case and, for example, dialkyl sulphides are oxidised more rapidly than their more hindered and electronically deactivated diaryl counterparts.



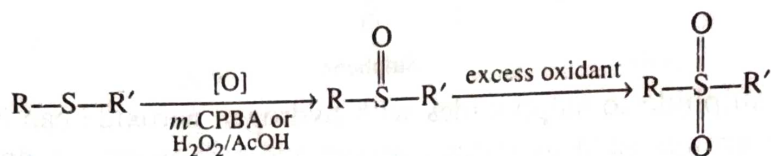
Sulphoxides are tetrahedral in shape, with two carbon groups, an oxygen and a lone pair of electrons. When two carbon groups are nonequivalent ($\text{R} \neq \text{R}'$) then the sulphoxide is chiral.



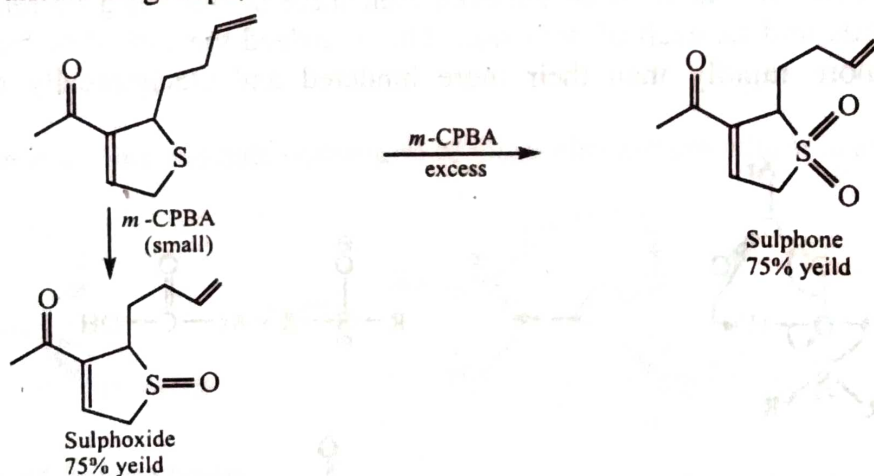
Oxidation of unsymmetrical sulphides to the corresponding sulphoxides involves the formation of a new stereogenic centre at sulphur. All the oxidising reagents (H_2O_2 , *m*-CPBA, NaIO_4 or O_3) are achiral and therefore give a racemic mixture of the products. However, oxidation using a chiral oxidant can give a single enantiomer of product. One such reagent for such type of high selectivity for the formation of a single enantiomer of product is titanium tertiaryisopropoxide and (+) (*R,R*)-diethyl tartrate.



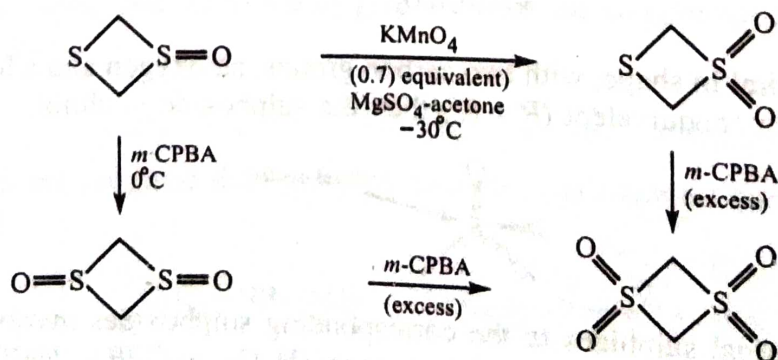
It is fortunate that the oxidation of sulphides to sulfoxides can be controlled so as to stop at the sulphoxide stage. This is because the oxidation of sulfoxides to sulphones is generally slower than the oxidation of sulphides to sulfoxides (by a factor of $10^2 - 10^3$). This reactivity difference is to be expected with oxidants such as *m*-CPBA which are electrophile-sulfoxides are bound to be less nucleophilic than sulphides as they are more hindered and also have an electron-withdrawing oxygen attached to the sulphur atom. So, if we want to complete the oxidation of sulphides to sulphones, then we need to add excess oxidant.



Despite their reduced reactivity towards *m*-CPBA, sulfoxides can still be oxidised in the presence of other sensitive functional groups, such as carbon-carbon double bonds and carbonyls.



In the case of KMnO_4 reactivity of sulfoxides is always more than the sulphides.



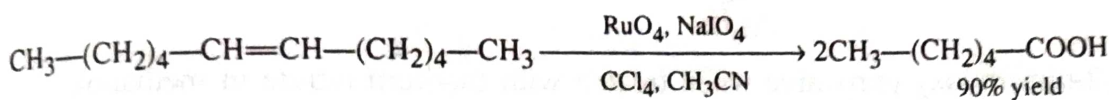
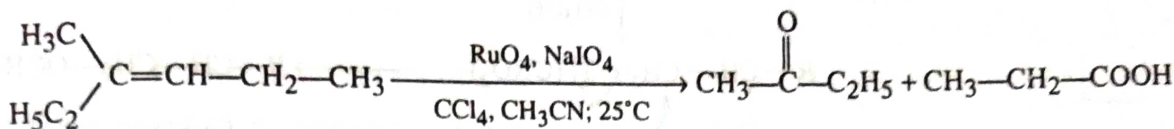
Scheme-1

The reverse reactivity is due to the nucleophilic character of the oxidant, MnO_4^- . This oxidant prefers to react first with an electrophilic sulfoxide rather than a nucleophilic sulphide. Using KMnO_4 it is possible to oxidise sulfoxides to sulphone in the presence of sulphide (Scheme-1).

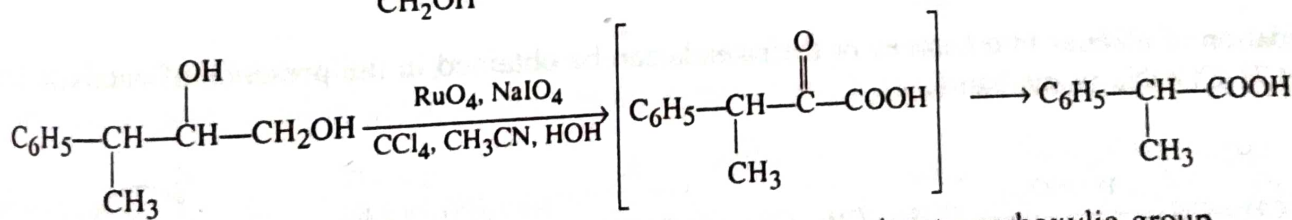
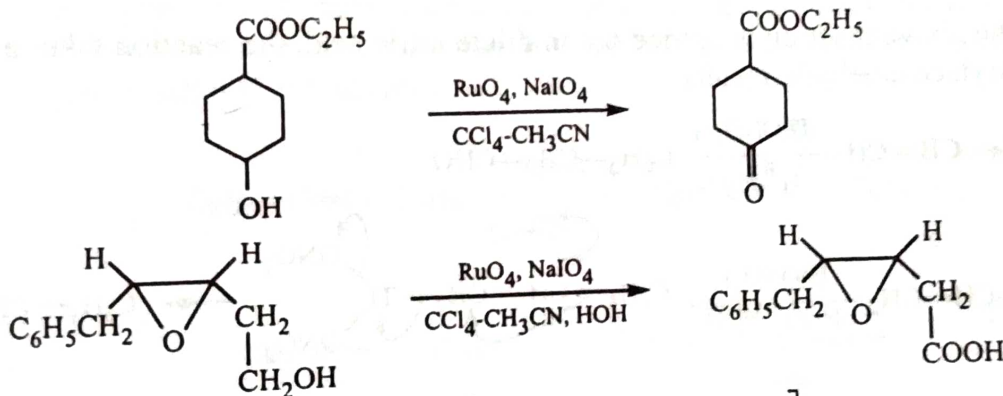
2.10 Oxidation with ruthenium tetroxide

Ruthenium tetroxide is a powerful oxidising agent which oxidises a variety of functional groups at room temperature. Oxidation with ruthenium tetroxide is generally carried out in carbon tetrachloride-methyl cyanide solution. Since ruthenium tetroxide is costly, it is convenient to use catalytic amount of ruthenium tetroxide in the presence of sodium periodate, which oxidises the reduced ruthenium back to the active tetroxide *in situ*.

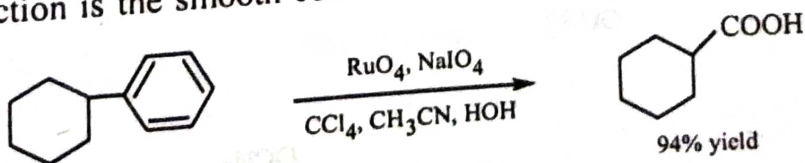
Ruthenium tetroxide cleaves the carbon-carbon double bonds, ketones or carboxylic acids. Nature of the products depends on the degree of substitution of the double bonds. Thus ruthenium tetroxide sodium periodate is good alternative to oxidative ozonolysis.



Alcohols can also be oxidised by this reagent. Primary alcohols give carboxylic acids and secondary alcohols are oxidised to ketones in excellent yield at room temperature. The reagent has no effect on ester and epoxide groups.

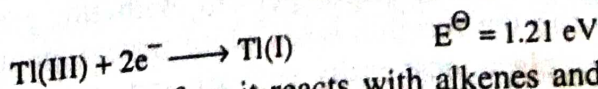


A remarkable reaction is the smooth conversion of benzene ring to carboxylic group.

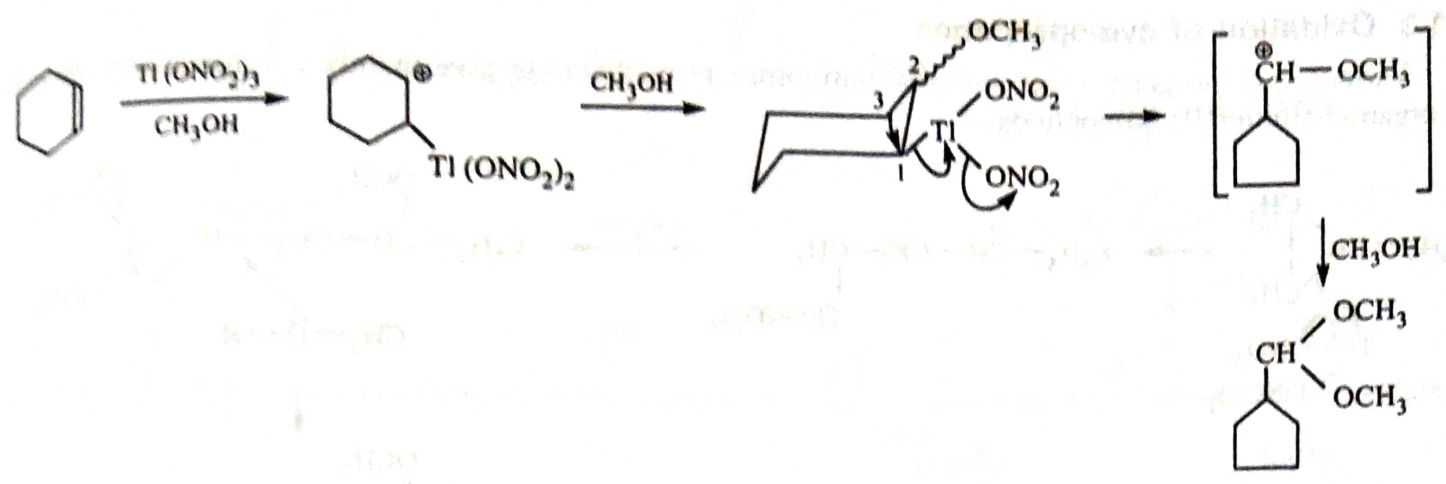


2.11 Oxidation with Thallium nitrate [Tl(NO₃)₃]

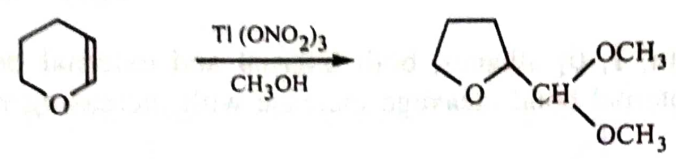
Thallium nitrate is a selective and versatile oxidising agent, generally accompanied by reduction of Tl(III) to Tl(I). The conversion of Tl(III) to Tl(I) is energetically favourable because reduction potential of this half cell reaction is positive and high.



Thallium nitrate is electrophilic in character, therefore it reacts with alkenes and alkynes to give addition products. This reaction is used for oxidations of alkenes and alkynes. The effectiveness of this reagent in oxidation is due to the high reduction potential and to the weakness of the carbon-metal bond (105-125

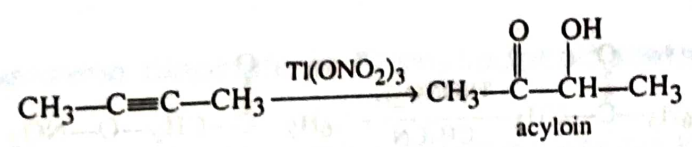
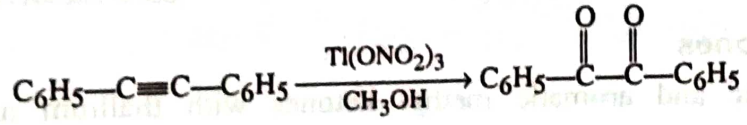


This reaction can also be applied to heterocyclic compounds.

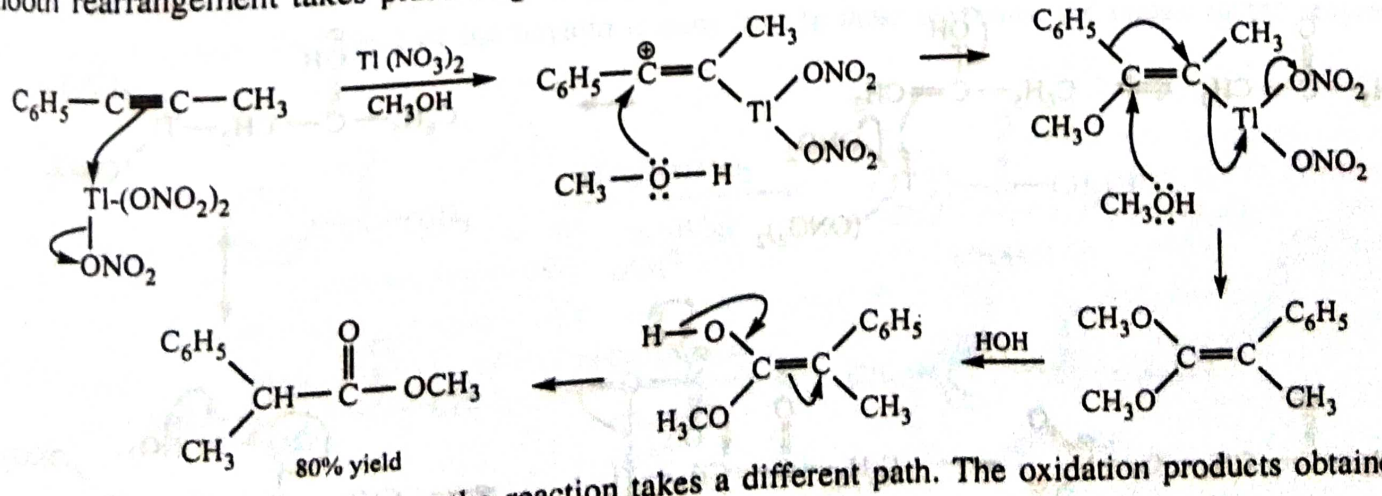


2.11.2 Oxidation of alkynes

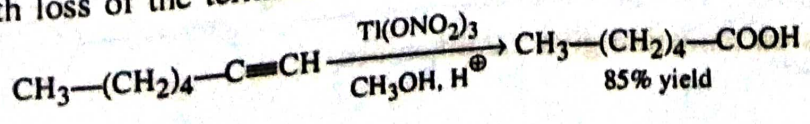
With alkynes the product obtained depends on the structure of the alkyne. Diaryl alkynes react with two equivalents of thallium nitrate in acid solution or in methanol to give benzils in high yield, but with dialkylalkynes reaction stops at the acyloin.



On the other hand, alkyl aryl alkynes in acid solution give mixture of products, but in methanol a smooth rearrangement takes place to give methylesters of α -alkylaryl acetic acid.

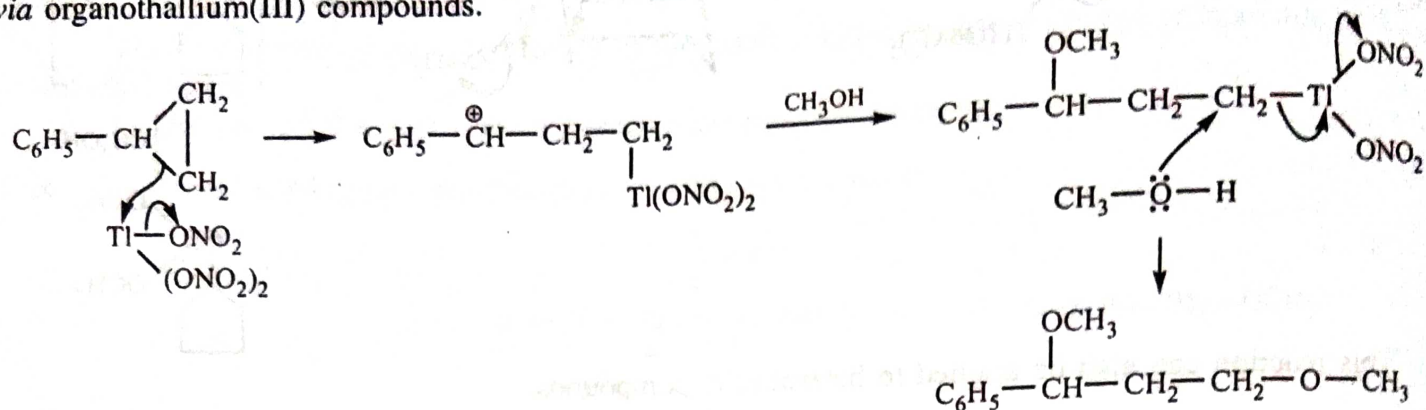


With monoalkylacetylenes, the reaction takes a different path. The oxidation products obtained are carboxylic acids with loss of the terminal carbons.

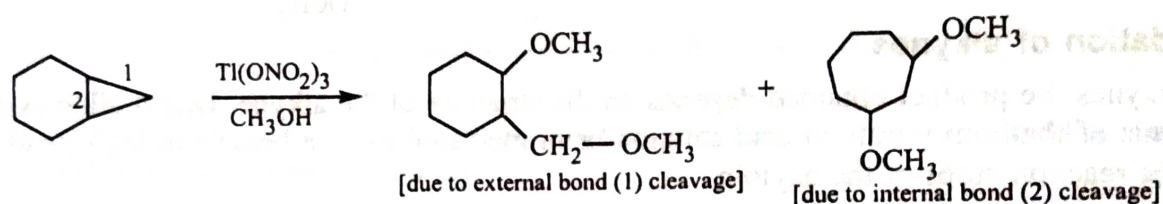


2.11.3 Oxidation of cyclopropanes

Various cyclopropanes react with thallium nitrate in methanol to give mainly 1,3-dimethoxy alkanes via organothallium(III) compounds.

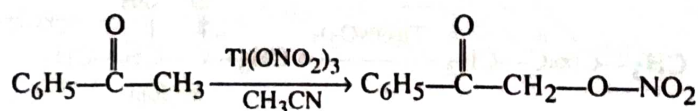


In the case of bicyclo [n, 1, 0] alkanes, both internal and external bond cleavage occur and the products resulting from the internal bond cleavage increase with increasing ring size.

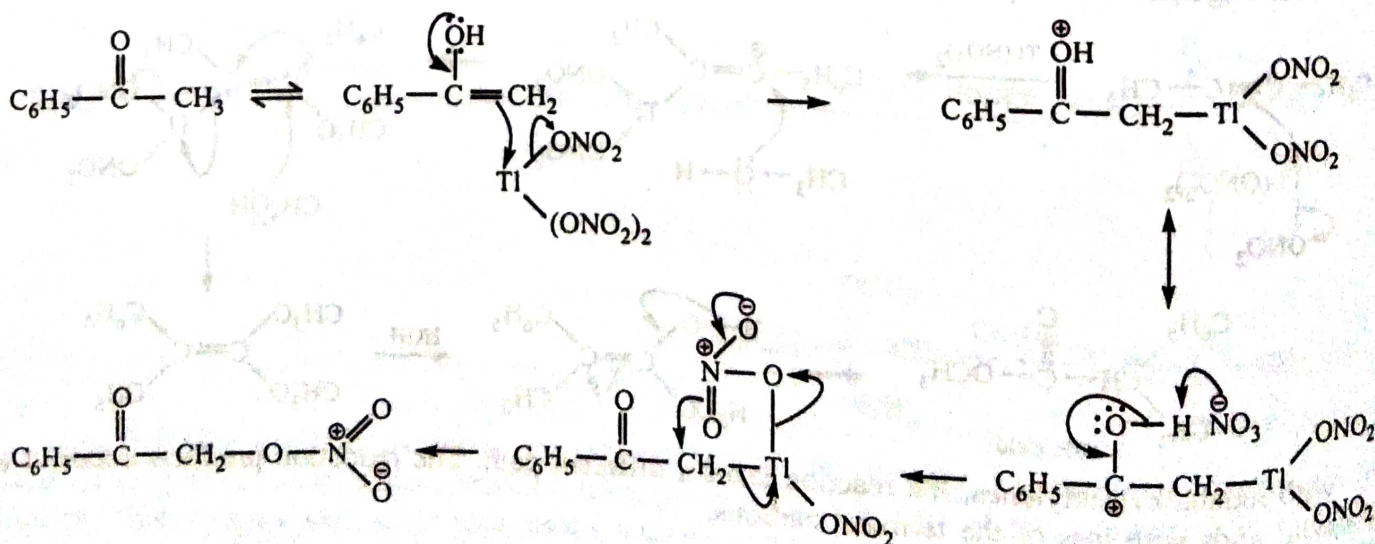


2.11.4 Oxidation of ketones

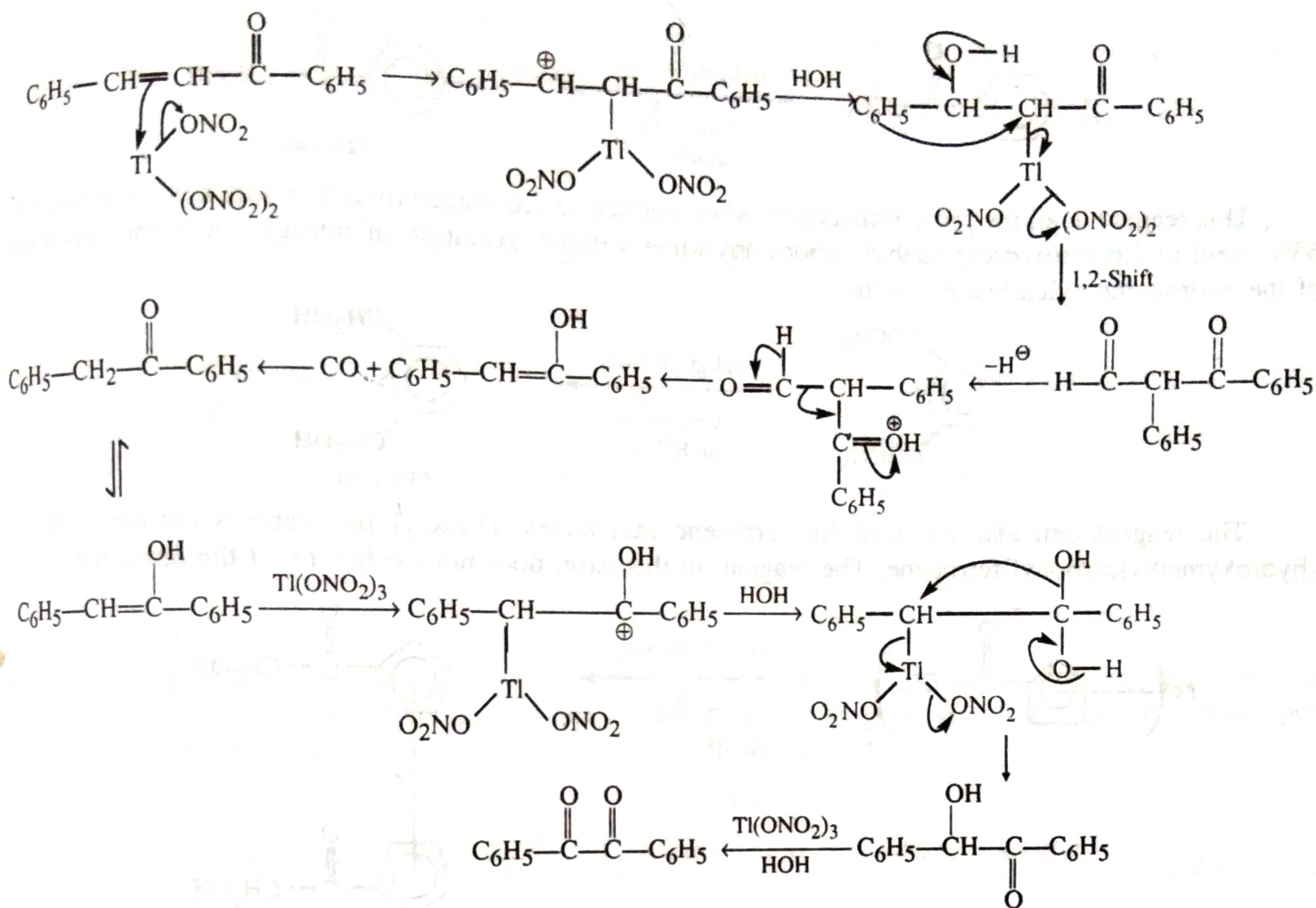
Treatment of aliphatic and aromatic methyl ketones with thallium nitrate in CH_3CN gives α -nitratoketones.



Oxidation takes place as follows:

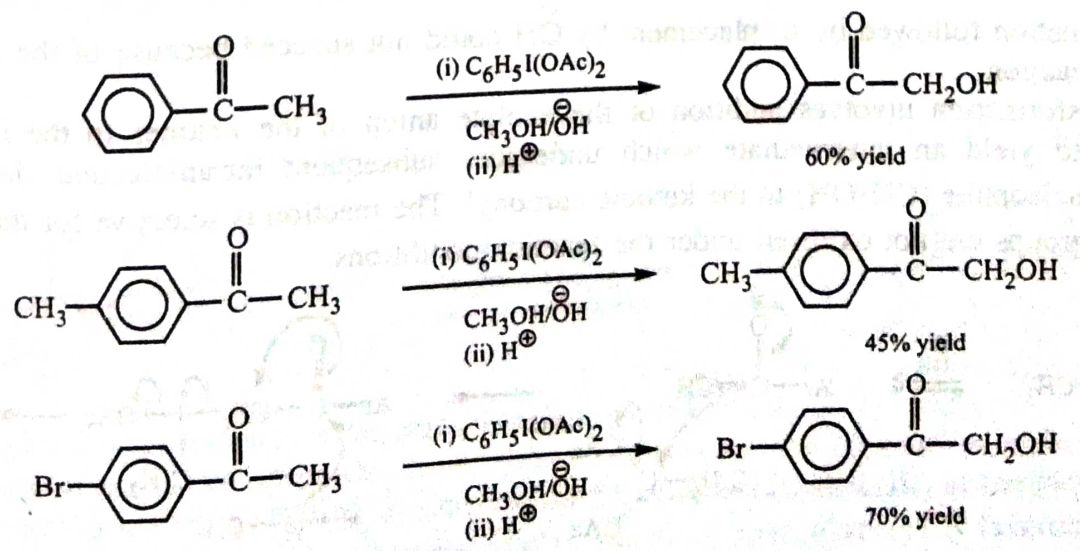


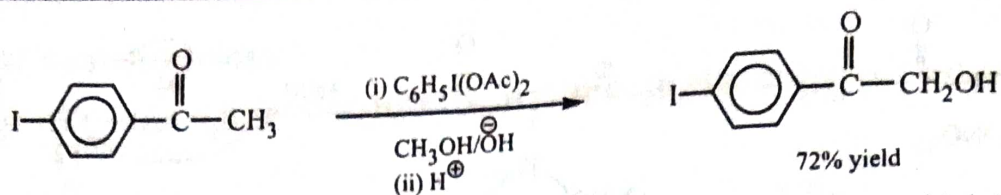
α , β -unsaturated ketones on oxidation give 1,2-diketones.



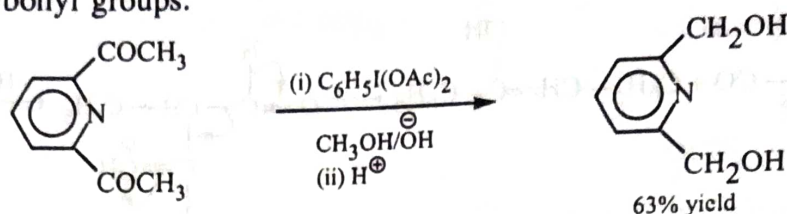
2.12 Oxidation with Iodobenzene diacetate or Phenylidosodiaceate $C_6H_5-I(OAc)_2$

Phenylidosodiaceate is specific reagent for the oxidation of ketones. Ketones are converted smoothly into the corresponding acyloin with a high degree of selectivity upon treatment with phenylidosodiaceate in methanolic sodium hydroxide. The reagent is mainly used for the oxidation of aryl methyl ketones into the corresponding acyloins. The yield of the acyloin is excellent. In these reactions, the nature of the reagent is electrophilic.

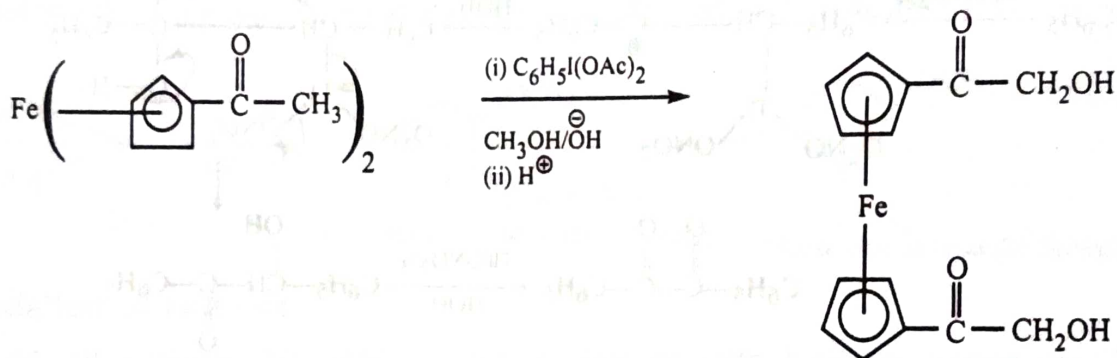




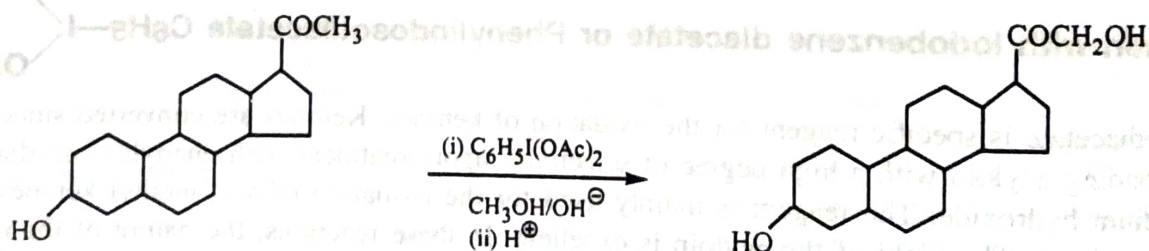
This reagent is all the more remarkable when applied to 2,6-diacetylpyridine which is converted into 2,6-bis(hydroxymethylcarbonyl)pyridine without oxidation of nitrogen or further oxidation of the hydroxymethylcarbonyl groups.



The reagent can also be used for ferrocene derivatives. Diacetyl ferrocene is converted to bis(hydroxymethylcarbonyl)ferrocene. The reagent, in this case, does not oxidise Fe of the ferrocene.

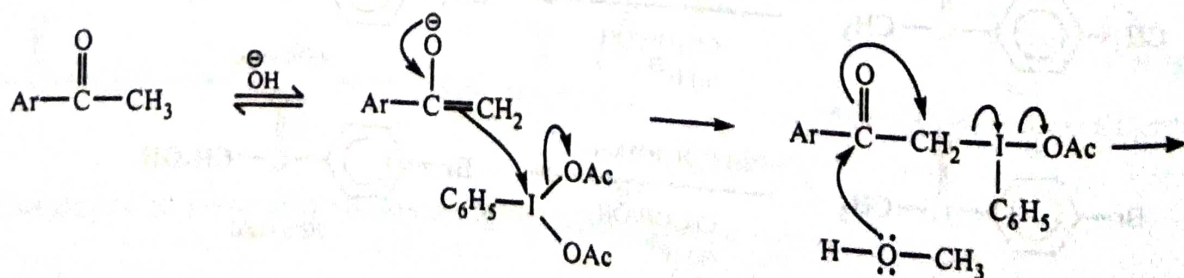


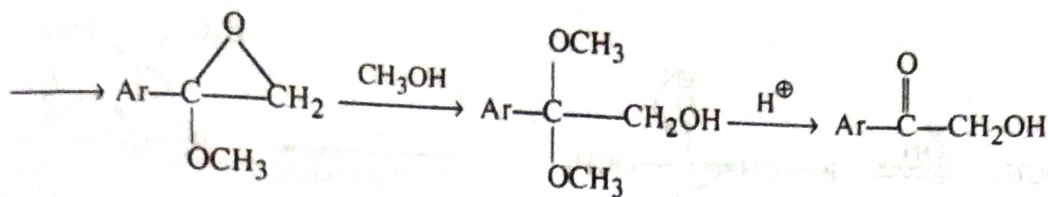
The reagent is selective because free hydroxyl group is not oxidised by the reagent.



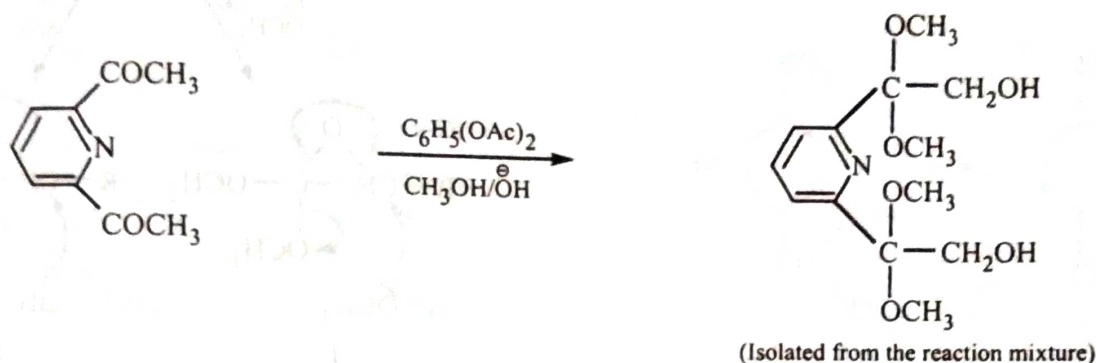
Clearly, alternative routes to these reactions would present serious difficulties. For example, in these cases α -halogenation followed by displacement by OH^{\ominus} could not succeed because of the intervention of the haloform reaction.

This transformation involves addition of the enolate anion of the ketones to the iodine atom of $\text{C}_6\text{H}_5\text{I(OAc)}_2$ to yield an intermediate which undergoes subsequent intramolecular displacement by addition of a nucleophile (CH_3OH) to the ketonic carbonyl. The reaction is selective for the enolate since free hydroxyl groups are not oxidised under the reaction conditions.

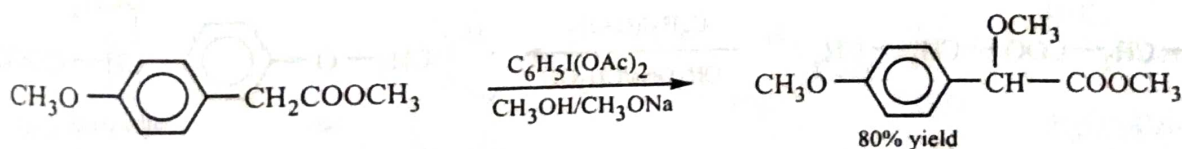
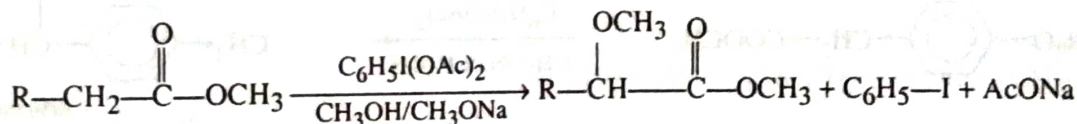
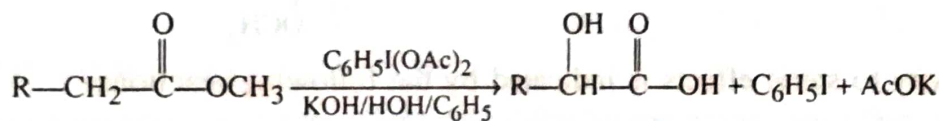




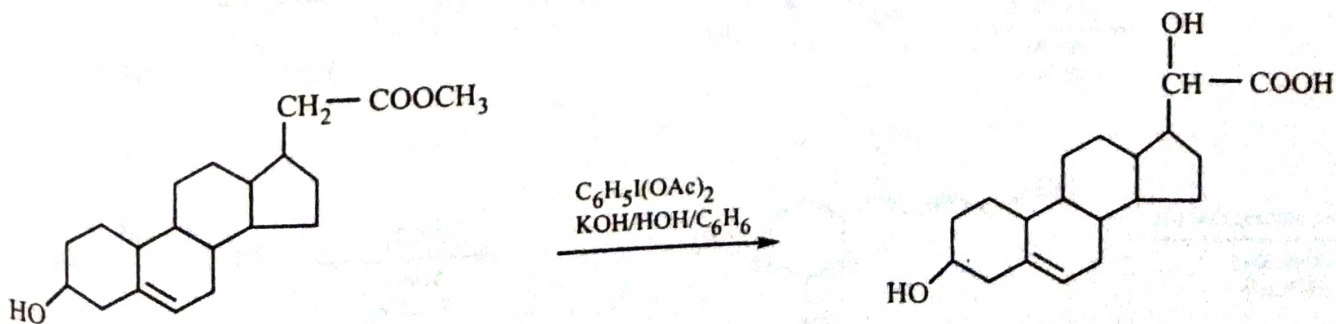
When reaction is carried out in the absence of acid, the product is dimethyl ketal of the acyloin. The proposed mechanism was confirmed by isolation of dimethyl ketal of acyloin.



The reagent can also be used for α -hydroxylation of aryl and alkyl carboxylate. Aryl and alkylcarboxylate esters are converted into the corresponding α -hydroxy acids or α -alkoxy esters upon treatment with $\text{C}_6\text{H}_5\text{I}(\text{OAc})_2$ and base in the appropriate solvent.

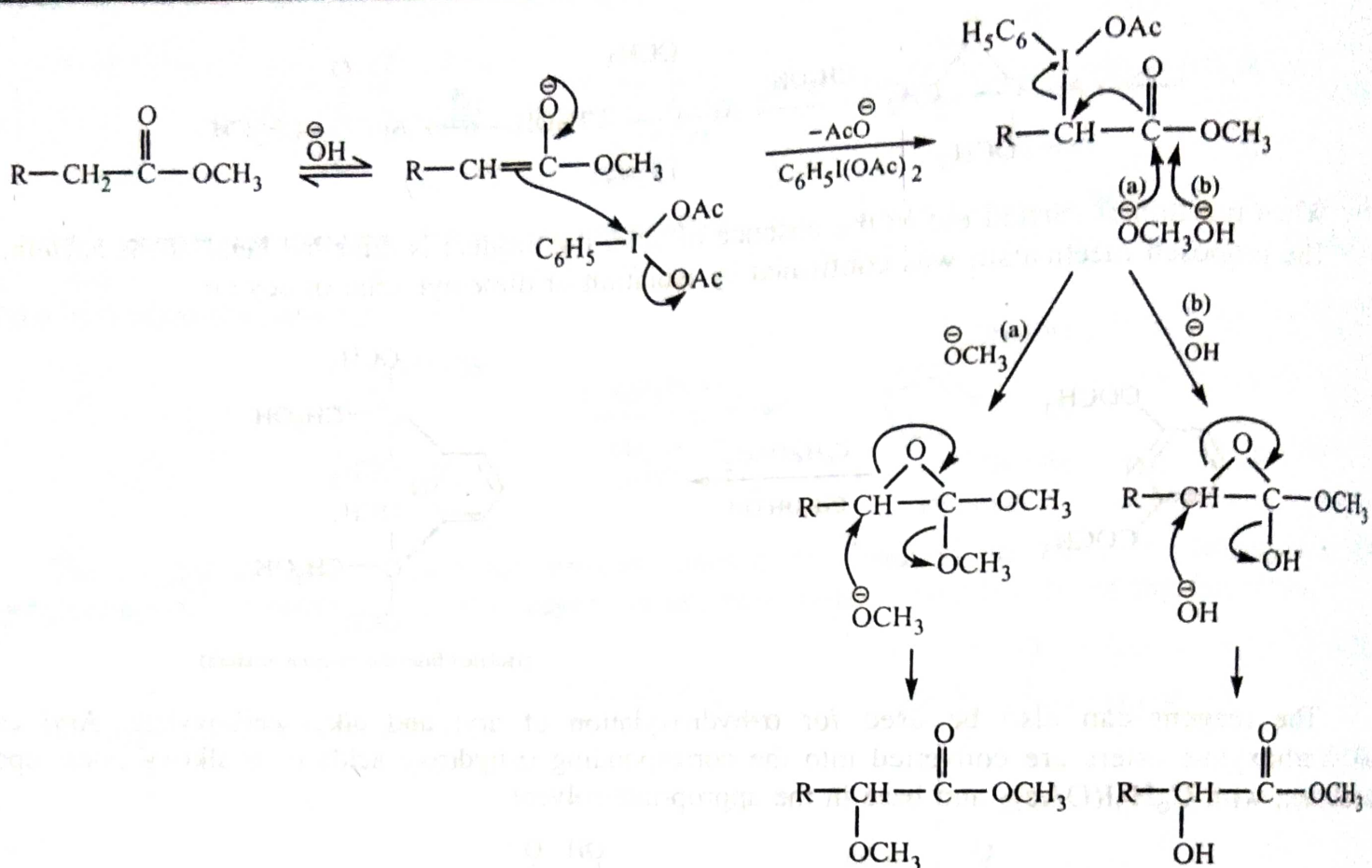


The reagent is selective for the enolate since free hydroxyl groups are not oxidised under the reaction conditions.

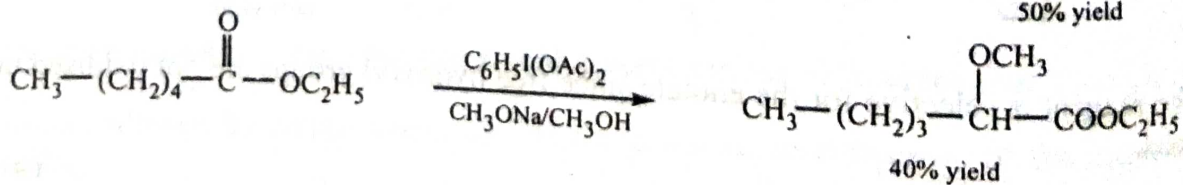
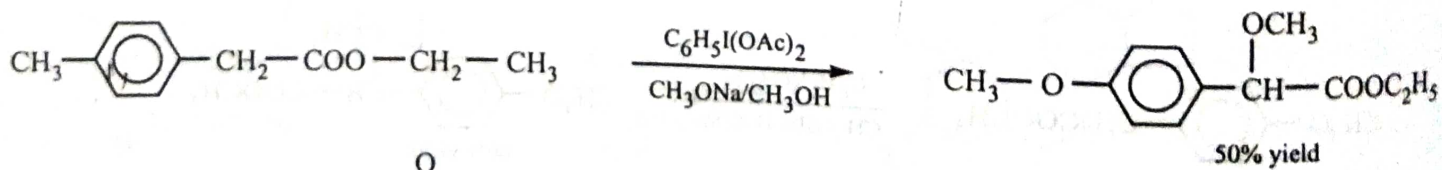
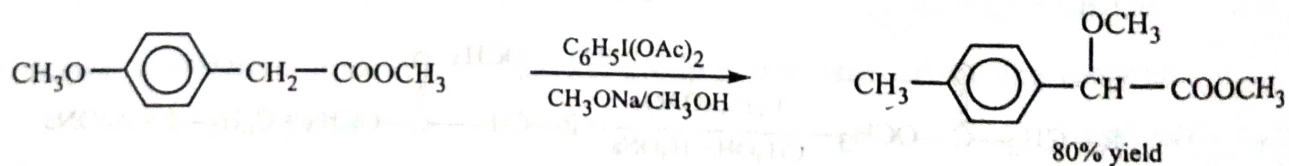


The reagent is also unreactive for carbon-carbon multiple bonds.

In the case of esters the initial step in the reaction is enolate anion formation, as in case of ketones, followed by attack upon the $\text{C}_6\text{H}_5\text{I}(\text{OAc})_2$ to yield intermediate (I). Iodine(III) at the hypervalent state is known to be a good leaving group and in the case of (I), C—I bond cleavage is favourable.



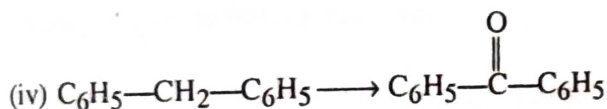
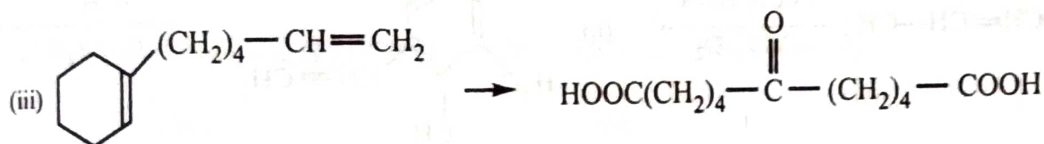
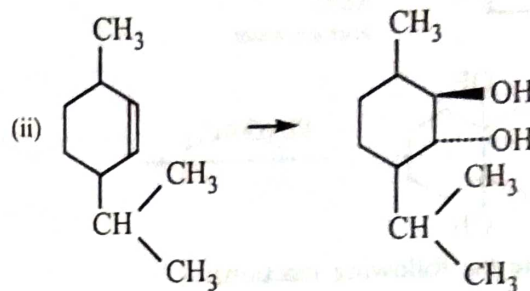
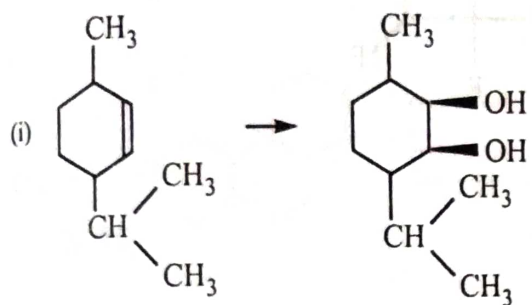
A mild selectivity to steric effects is indicated by the following reactions:



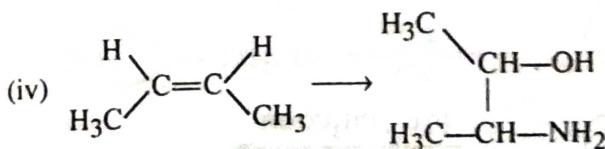
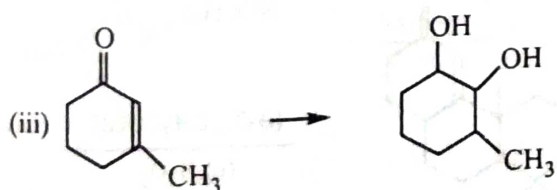
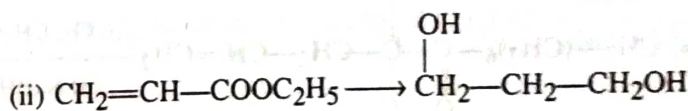
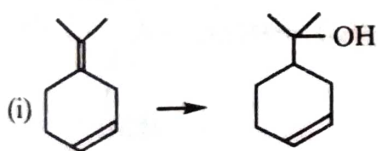


Problems

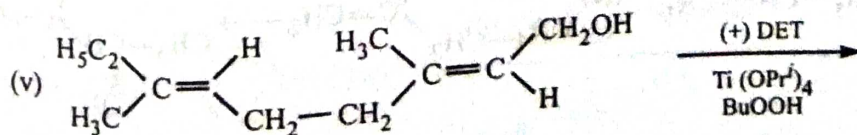
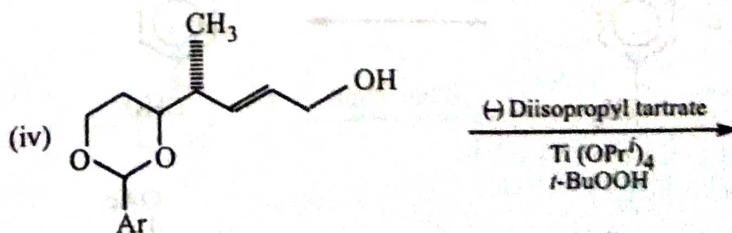
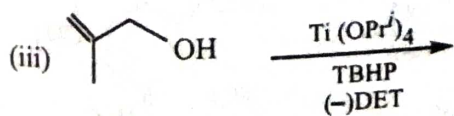
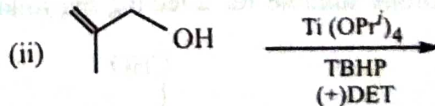
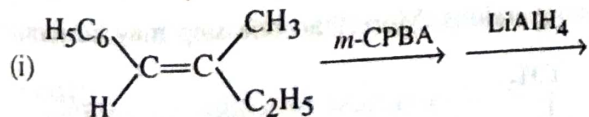
1. Suggest reaction conditions (reagents, catalysts, etc.) suitable for affecting the following conversions. More than one step may be required.



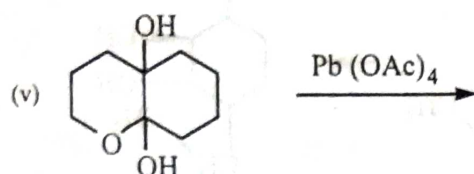
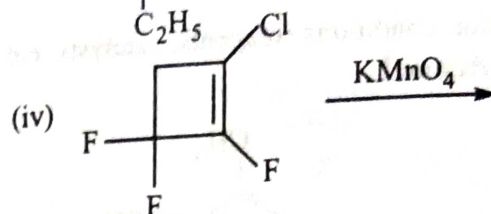
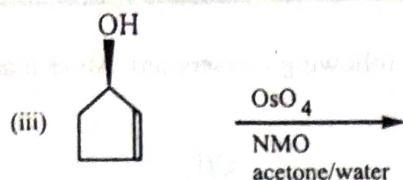
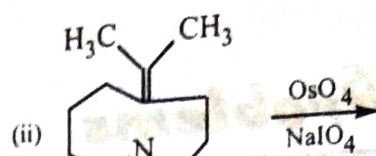
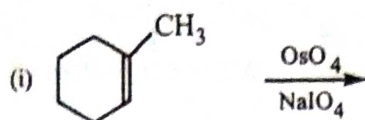
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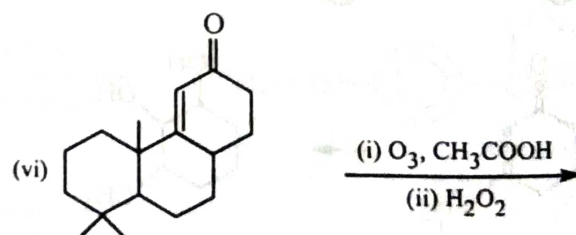
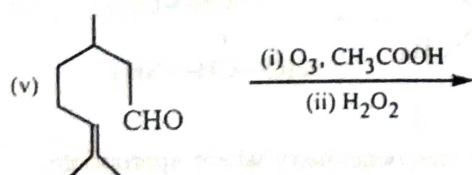
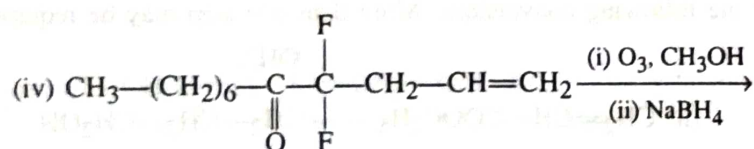
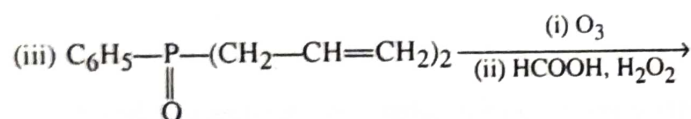
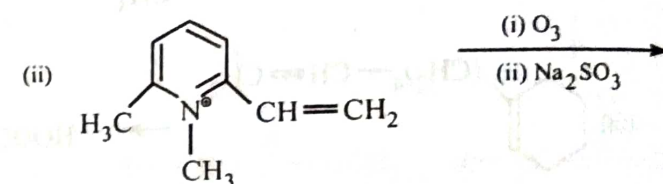
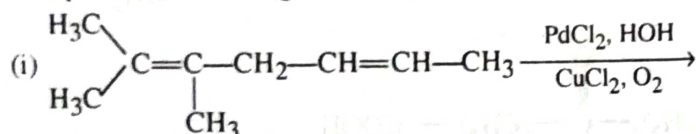
3. Indicate the expected product/products of the following reactions. Show stereochemistry where appropriate.



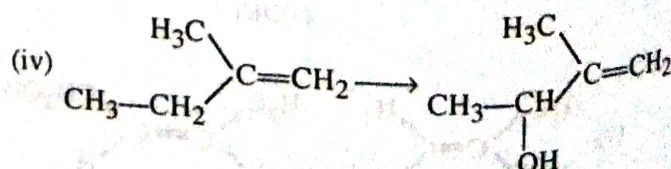
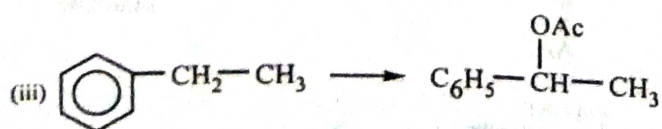
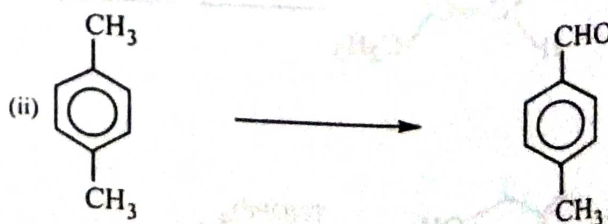
4. Complete the following reactions:



5. Complete the following reactions:

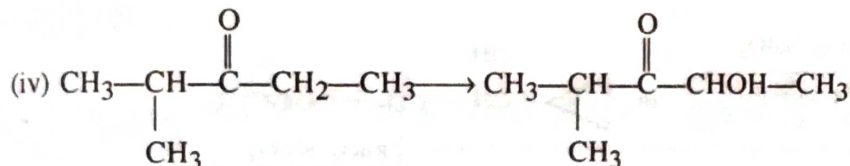
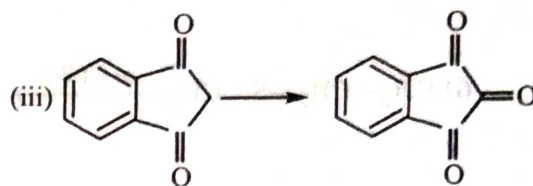
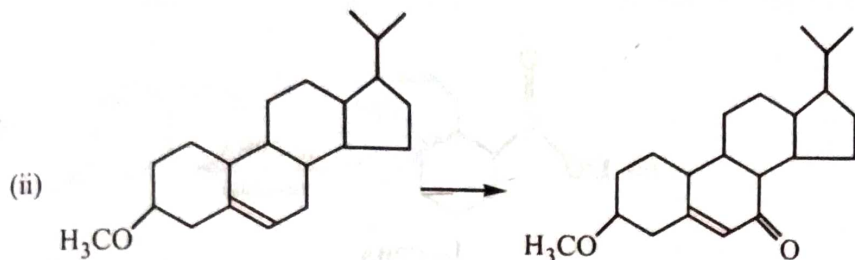


6. Suggest reaction conditions suitable for affecting the following conversions. More than one step may be required.

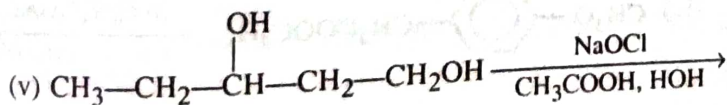
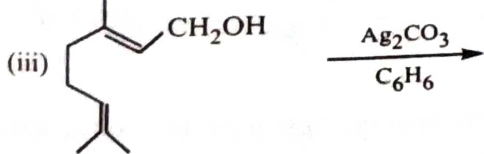
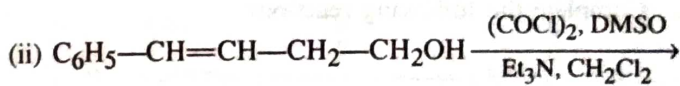
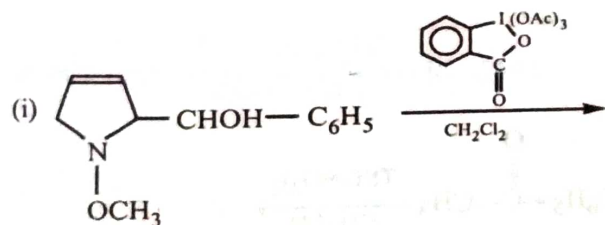




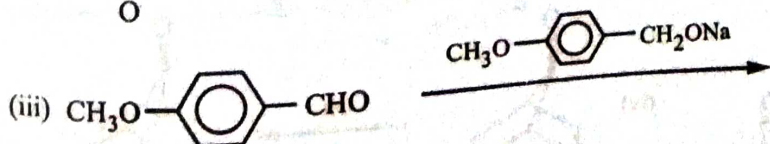
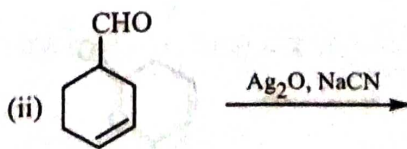
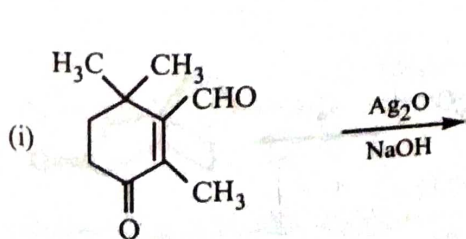
7. Indicate the expected product/products of the following reactions. Show stereochemistry where appropriate.



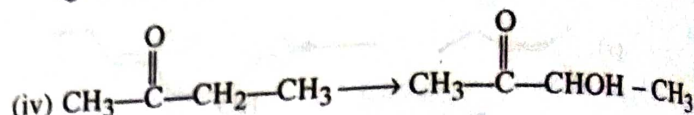
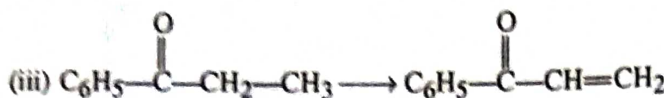
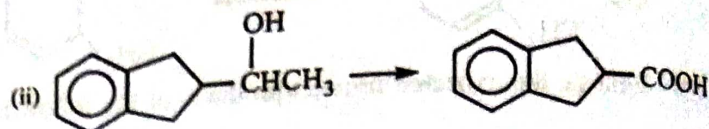
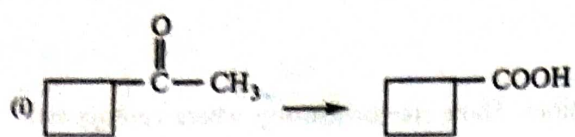
8. Complete the following reactions:



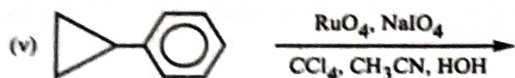
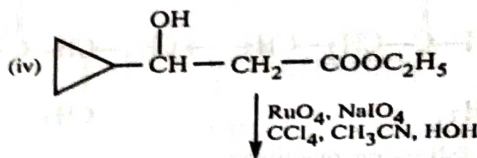
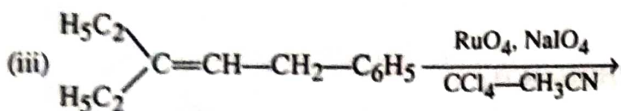
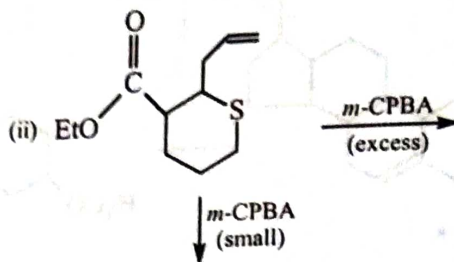
9. Complete the following reactions:



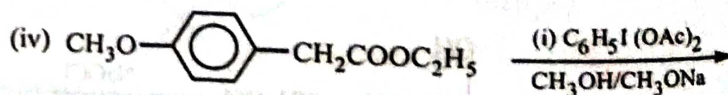
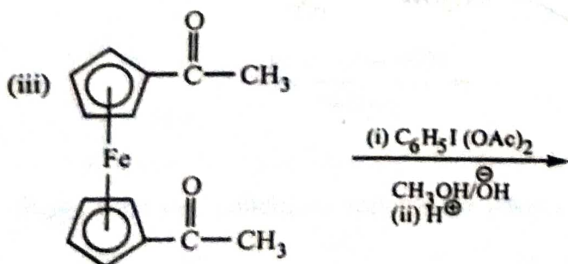
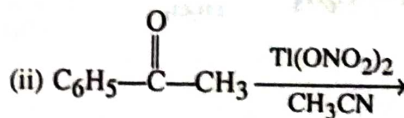
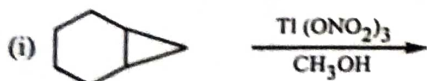
10. Suggest reaction conditions suitable for affecting the following conversions:



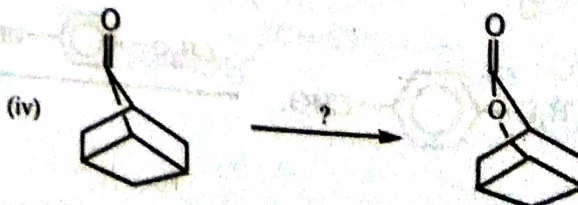
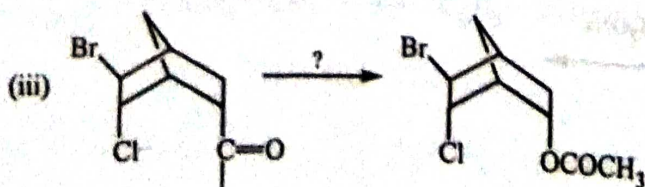
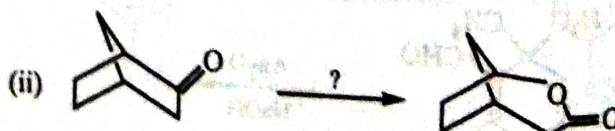
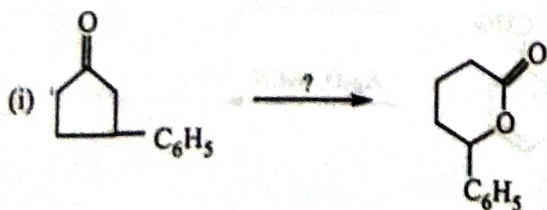
11. Complete the following reactions:

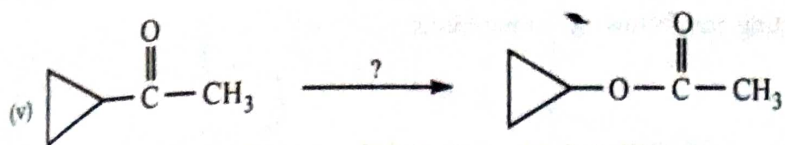


12. Complete the following reactions:

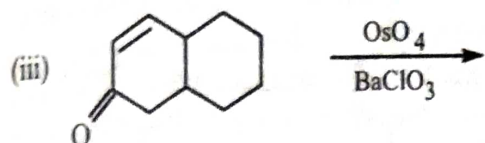
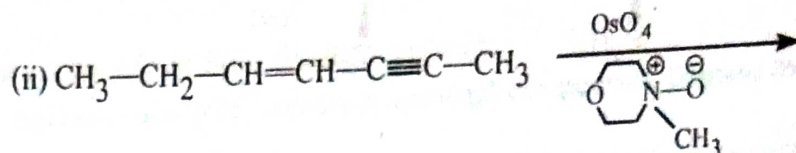
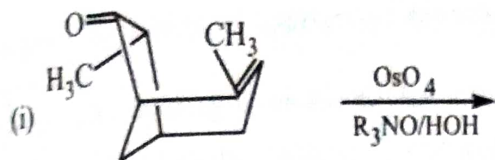


13. Indicate the reagents required to bring about the following conversions:



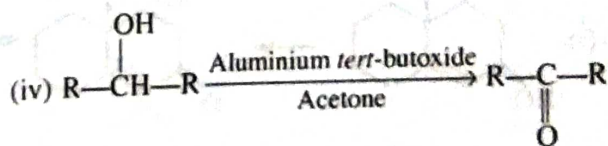
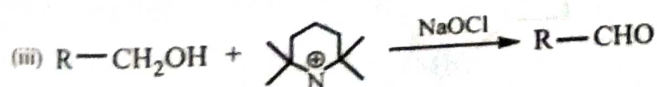
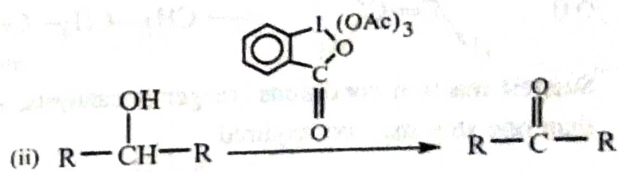
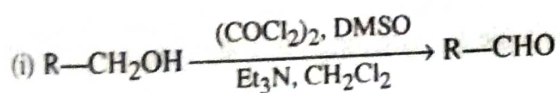


14. Indicate the expected product/products in the following:

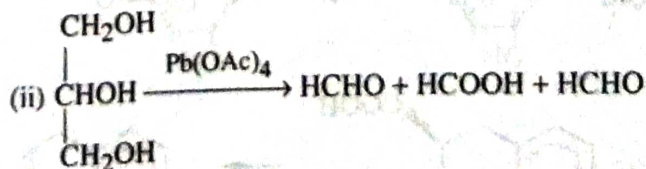
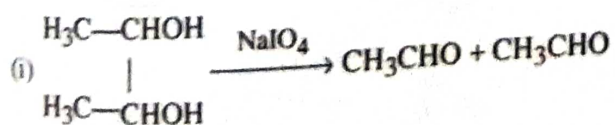


Problems for Self Assessment

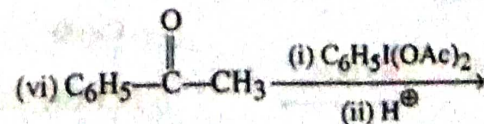
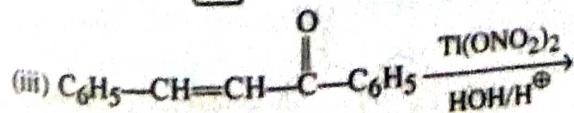
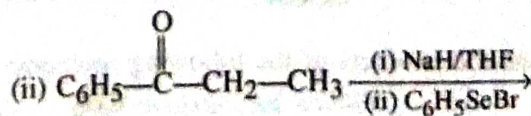
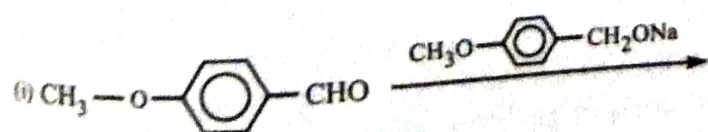
1. Give mechanism of the following reactions:



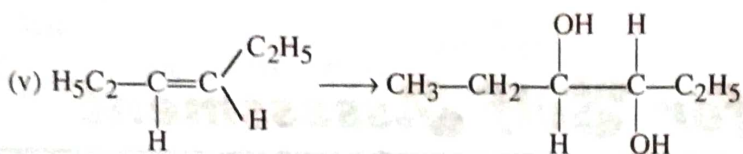
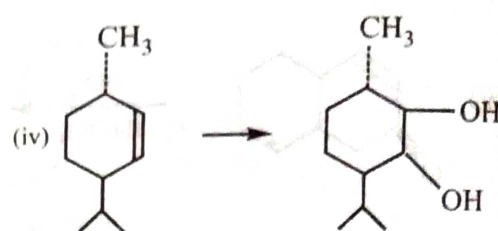
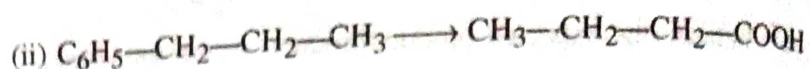
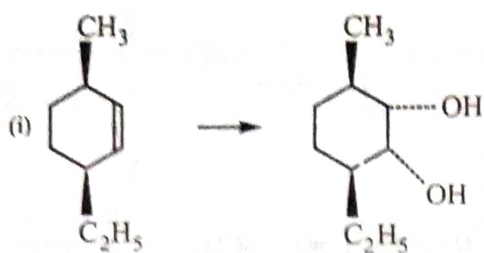
2. Complete the following reactions and give their mechanism:



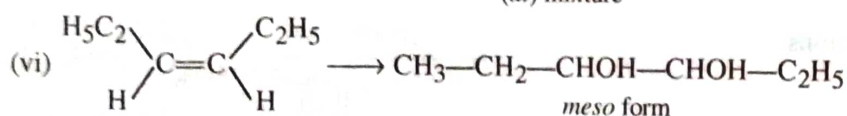
3. Complete the following reactions and give their mechanism:



4. Suggest reaction conditions suitable for affecting the following conversions:

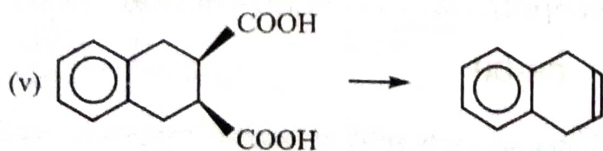
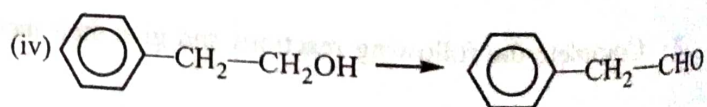
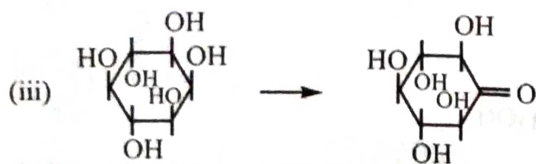
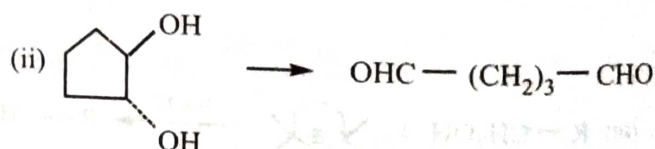
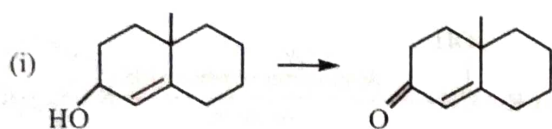


(dl) mixture

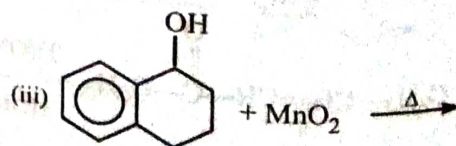
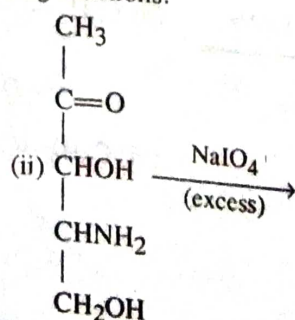
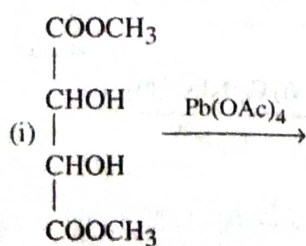


meso form

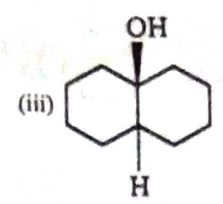
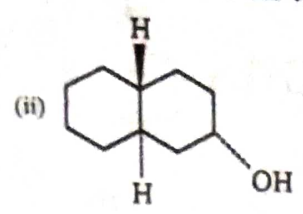
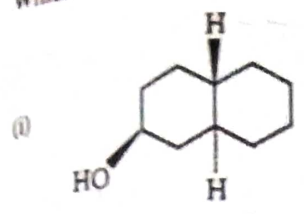
5. Suggest reaction conditions (reagents, catalysts, solvents, etc.) suitable for affecting the following conversions. More than one step may be required.



6. Indicate the products of the following reactions:



7. Which of the following compounds will be oxidised more rapidly by chromic oxide and why?



8. Explain by means of appropriate reactions why 2,6-di-*t*-butyl-4-methylphenol is sometimes added as an oxidant to gasoline.

9. What is the driving force for allylic oxidation? Discuss the role of SeO₂ for such oxidation.

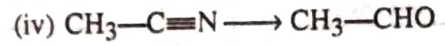
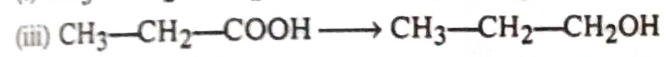
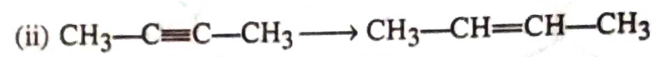
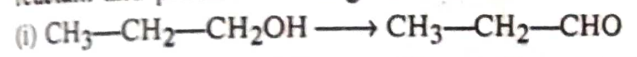
10. What are the reagents commonly employed for the oxidation of allylic alcohols to carbonyl compounds. Discuss the mechanism involved in the process.

11. What are (is) the reagent/s commonly employed for the oxidation of aliphatic primary amines to carbonyl compounds? Discuss the mechanism involved in any one of these.

12. What type of products arise by the oxidation of olefinic double bonds with different oxidising agents.

13. With suitable examples, illustrate the role of various reagents used for the oxidation of hydroxy groups into carbonyl groups. Give mechanism of any one of these.

14. Define oxidation and oxidation levels. On the basis of calculation of oxidation level find the oxidation level of the reactant and product of the given reactions.



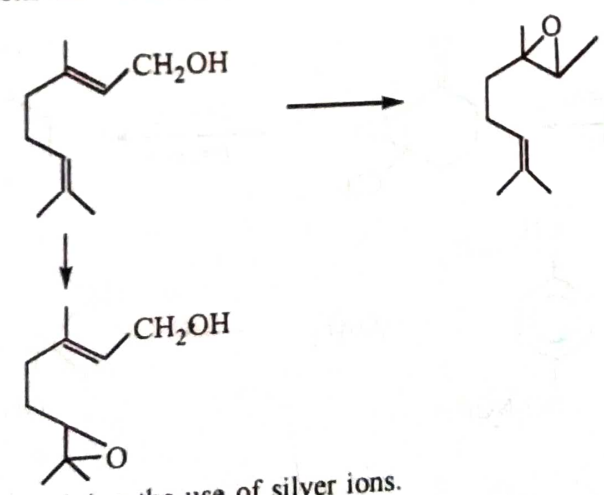
15. Give a suitable mechanism for the oxidation of primary alcohol to aldehyde with chromic acid.

16. Give the uses of the following reagents as oxidising agents in organic synthesis.

- (i) PCC
- (ii) Jones reagent
- (iii) DMSO

17. Give the use of *m*-CPBA in oxidations.

18. How the following conversions can be achieved?



19. Give examples of oxidation involving the use of silver ions.

20. Starting with oleic acid how will you obtain *threo* and *erythro*-9,10-dihydroxystearic acid with the use of different oxidising agents.

21. Write notes on each of the following:

- (i) Ruthenium tetroxide
- (ii) Oxidation of sulphides
- (iii) Oxidation of amines

22. Give synthetic applications of the following reagents.

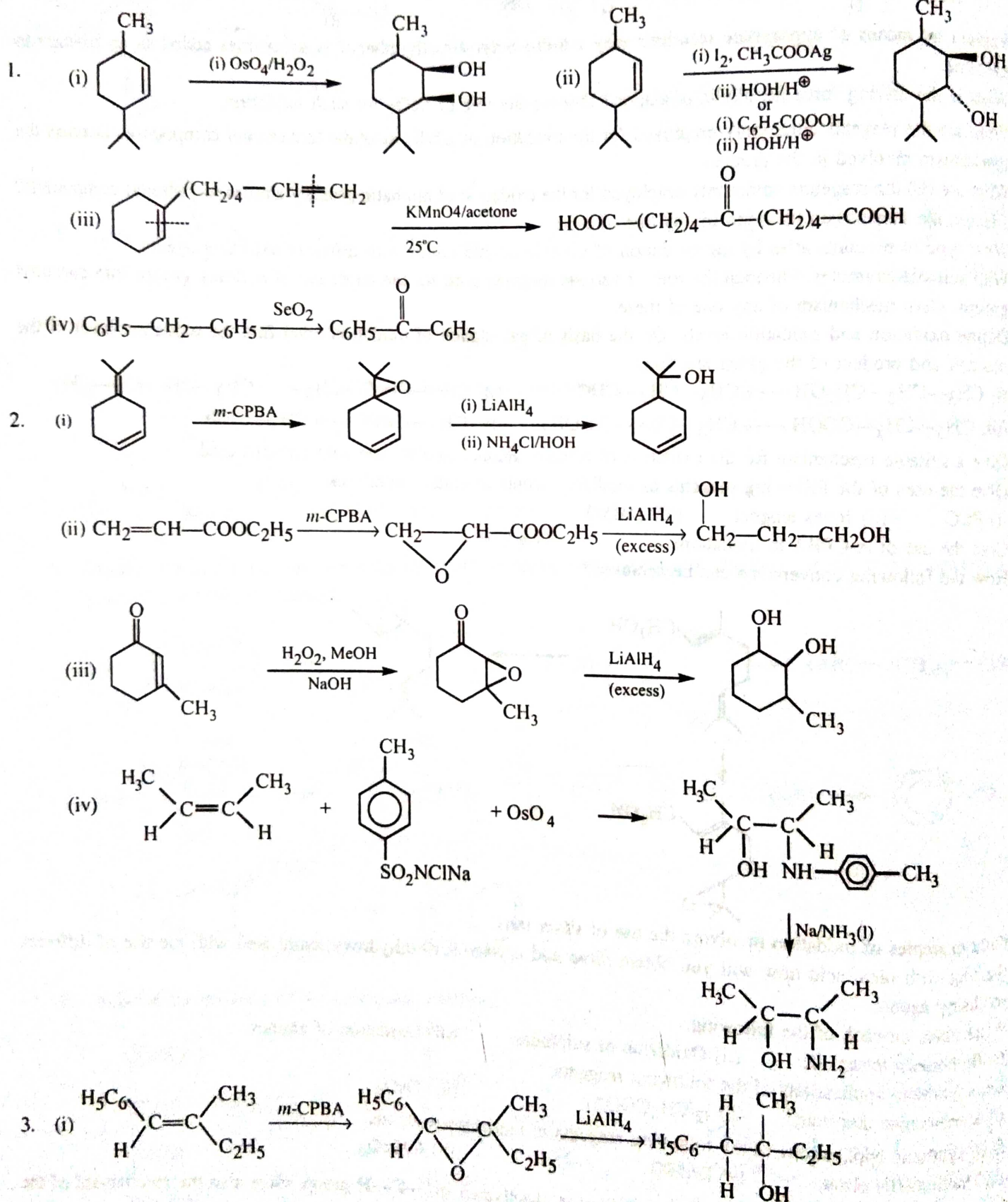
- (i) Iodobenzene diacetate
- (ii) I₂/CH₃COOAg
- (iii) OsO₄

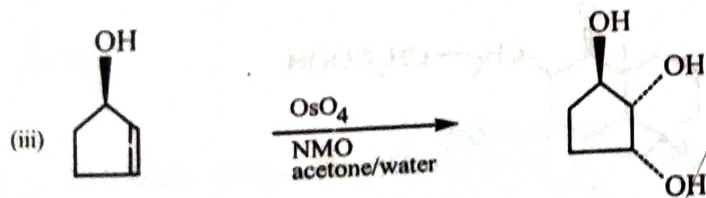
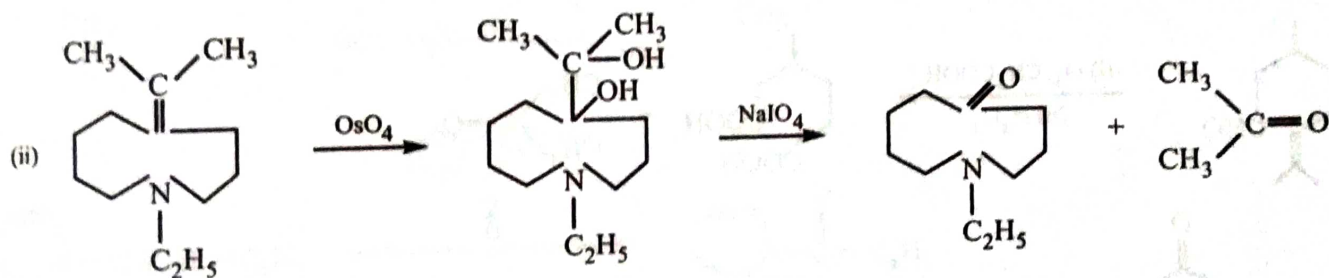
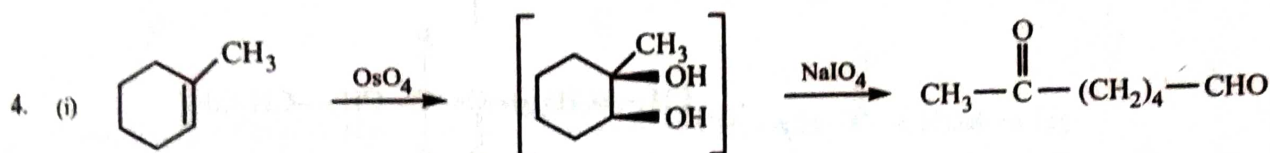
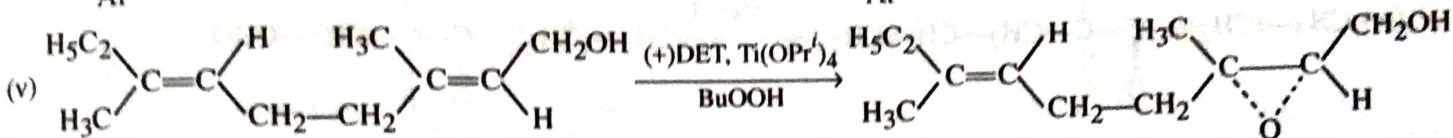
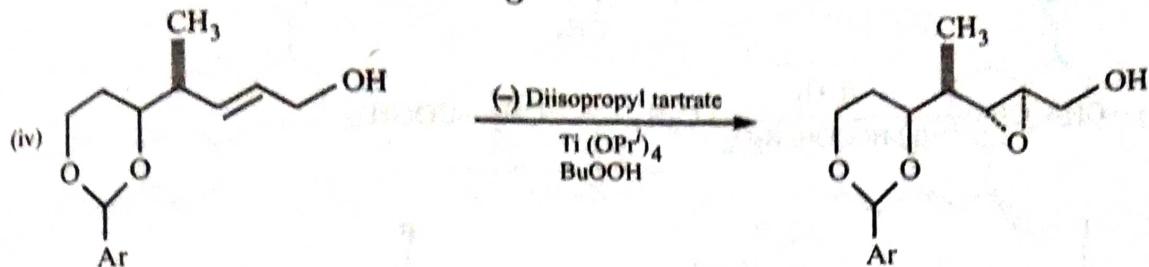
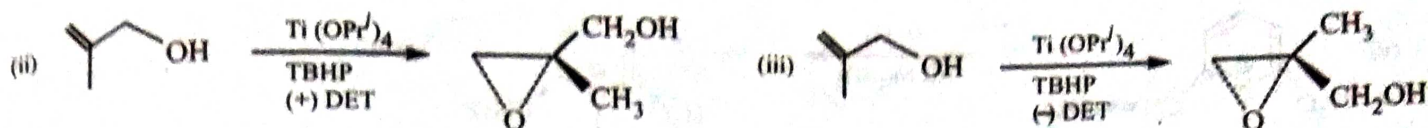
23. Give synthetic applications of the following reagents in oxidation reactions:

- (i) Thallium(III) nitrate
- (ii) DMSO
- (iii) KMnO₄

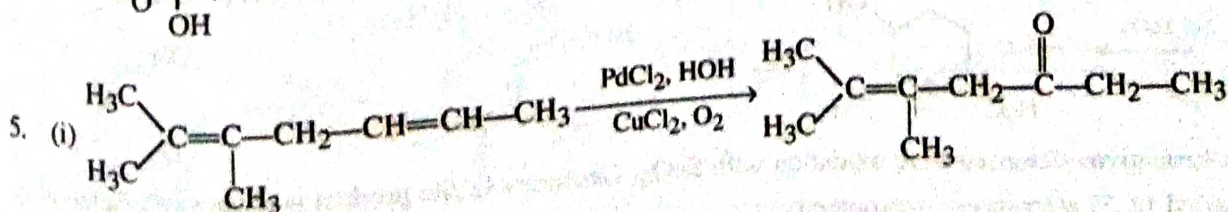
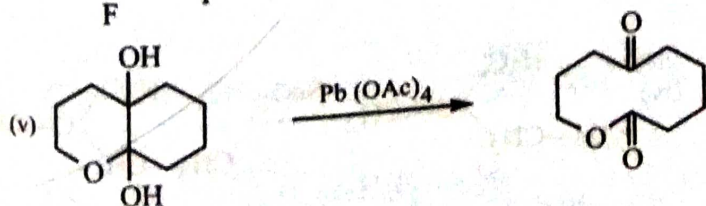
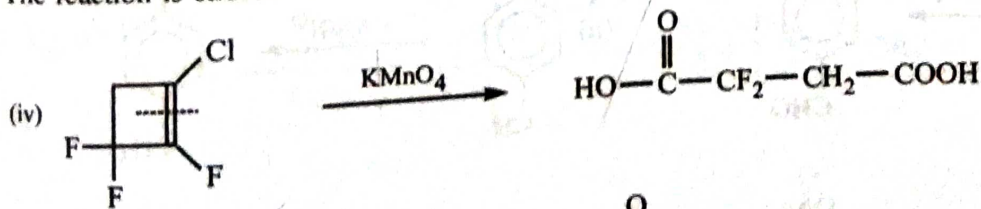
24. What are the oxidation methods for the oxidation of unactivated sp³-C-H group. Give also the mechanism of the reaction.

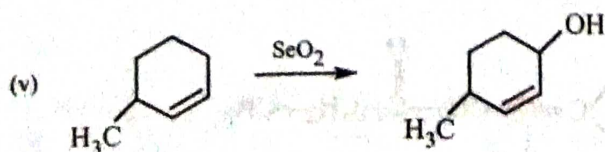
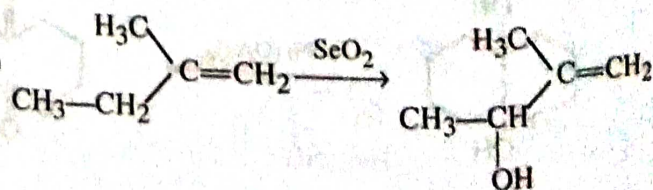
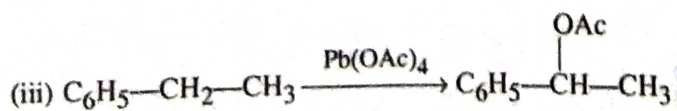
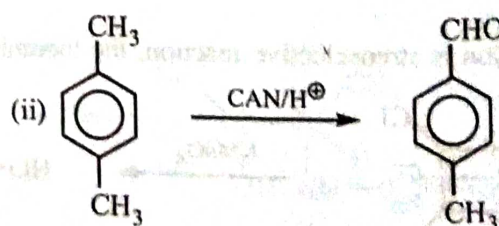
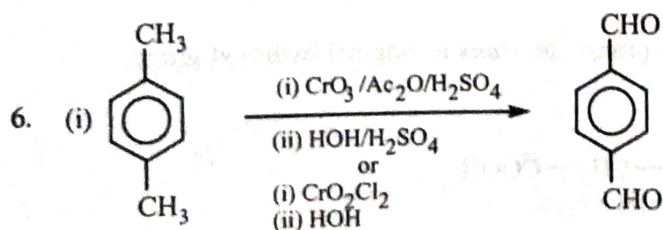
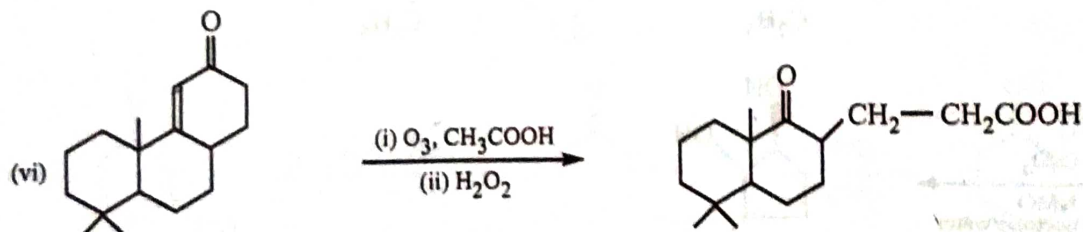
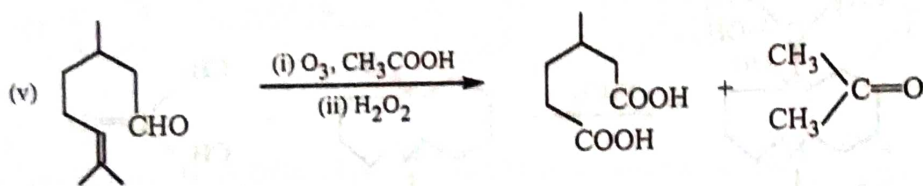
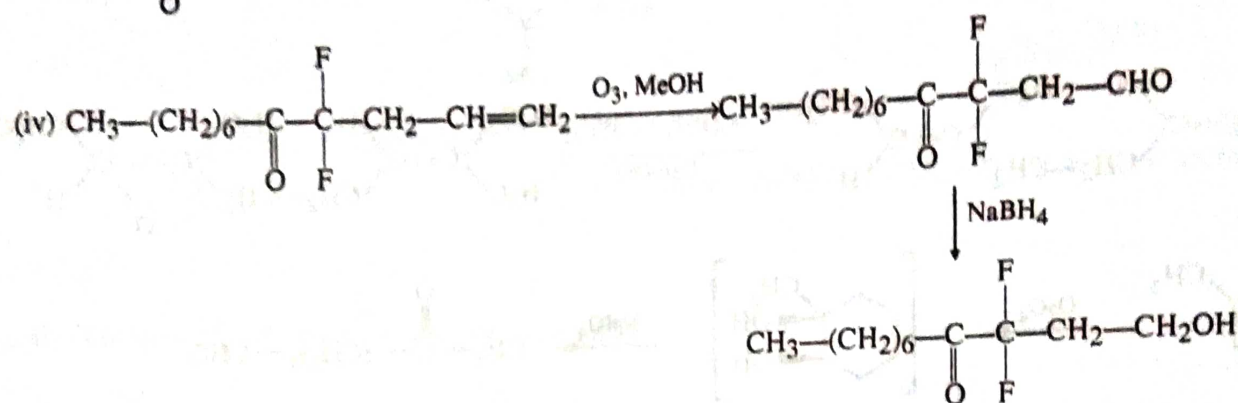
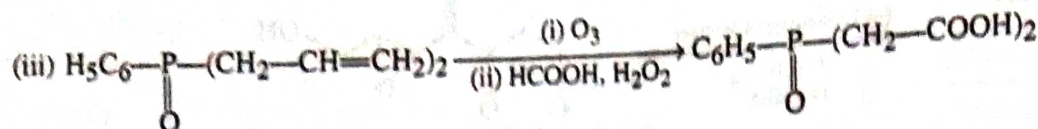
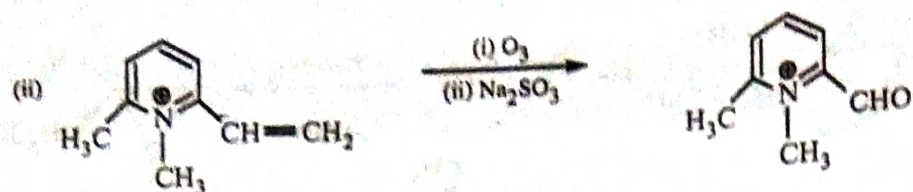
Solutions



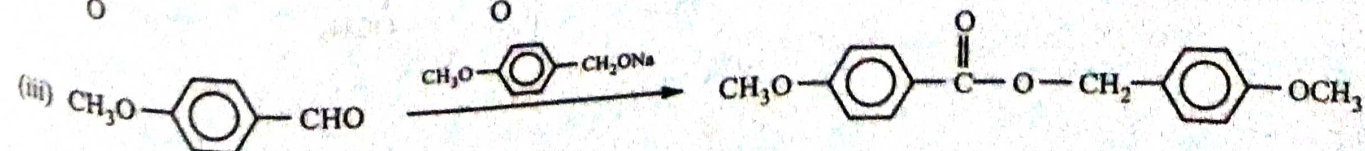
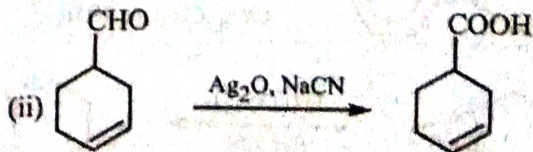
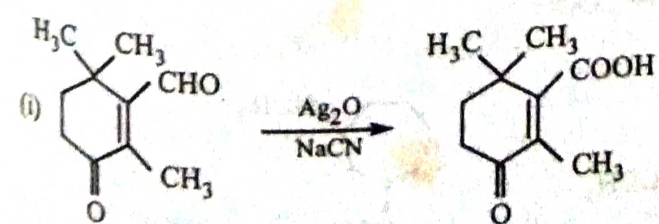
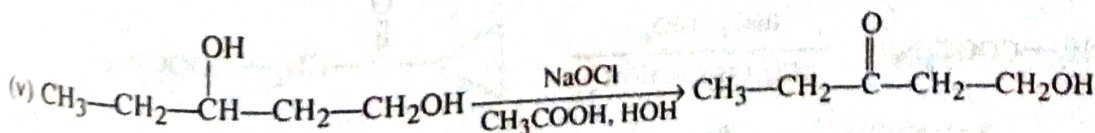
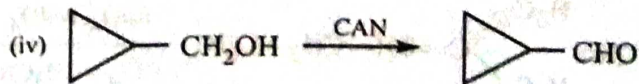
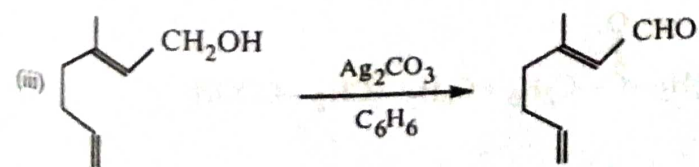
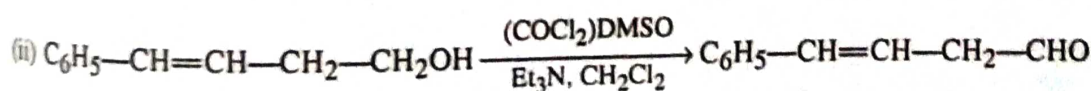
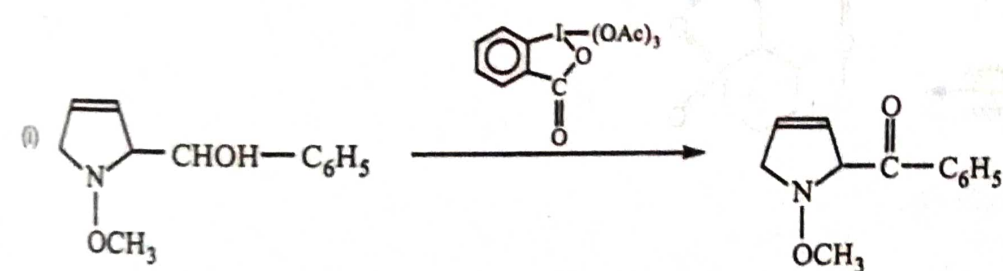
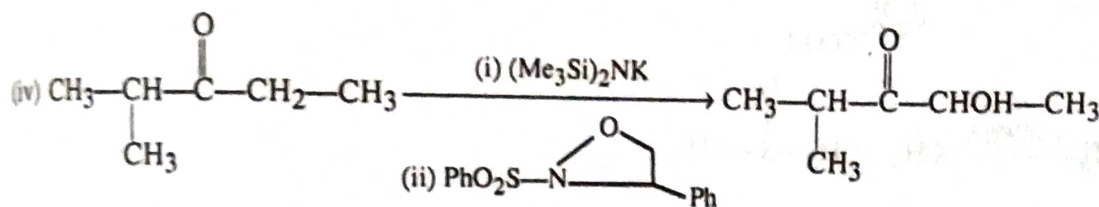
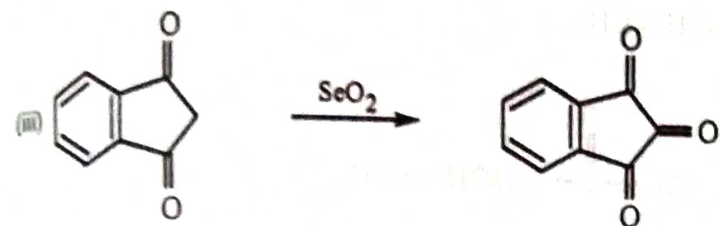
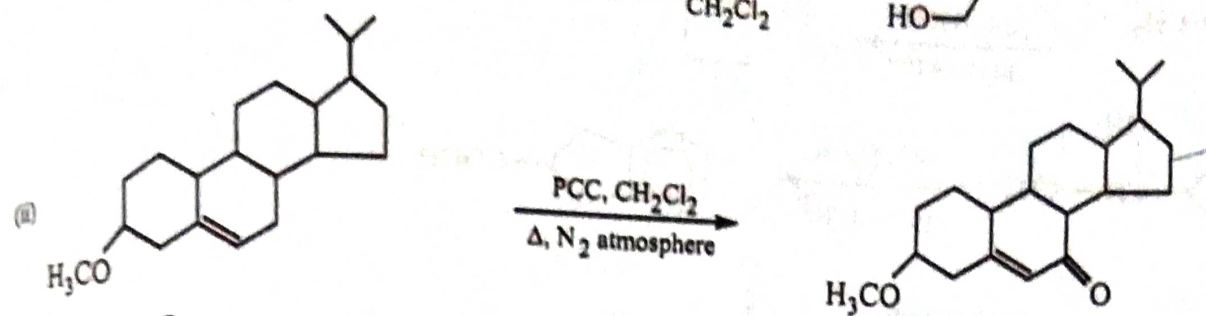


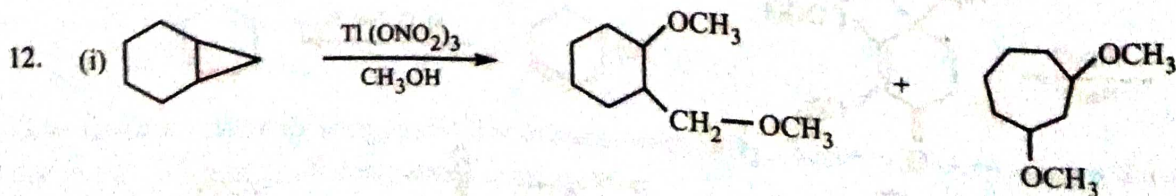
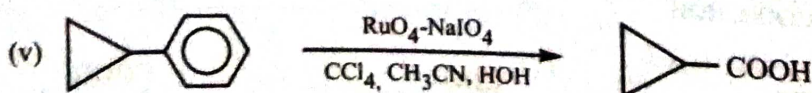
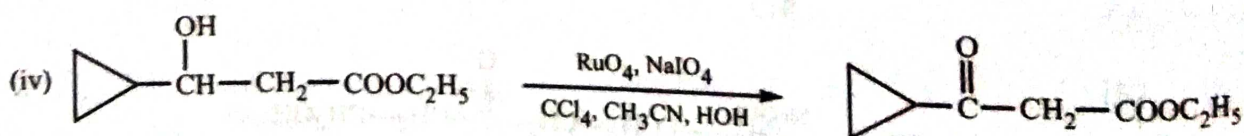
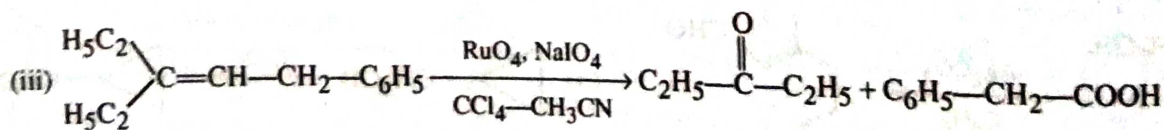
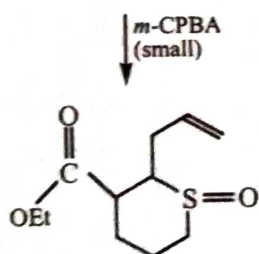
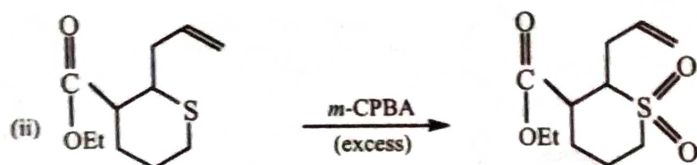
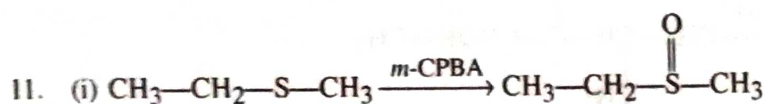
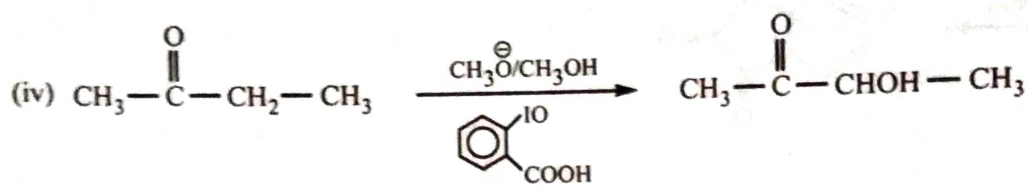
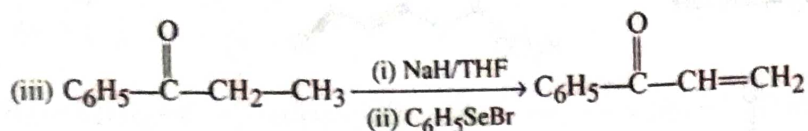
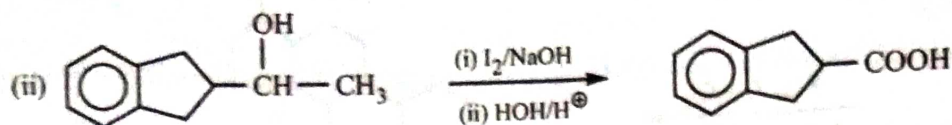
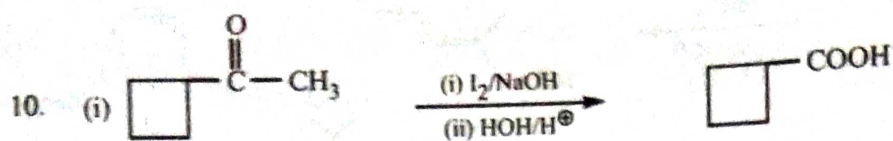
The reaction is stereoselective reaction, the incoming hydroxyl groups are *trans* to original hydroxyl group.

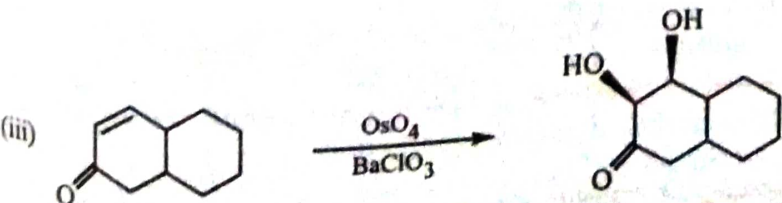
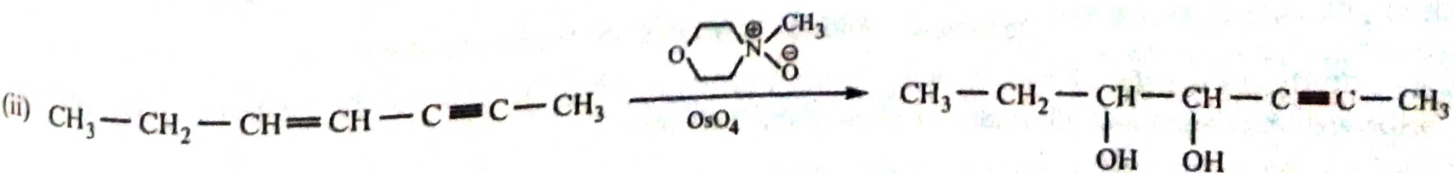
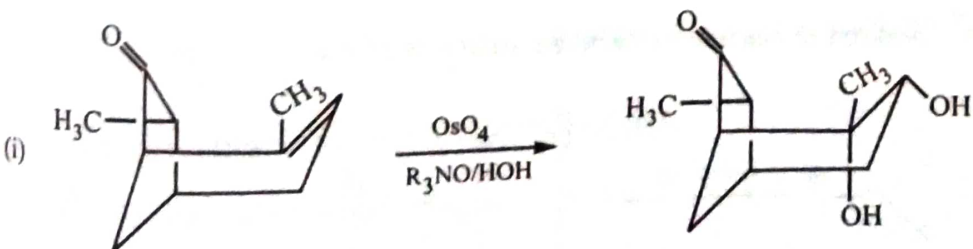
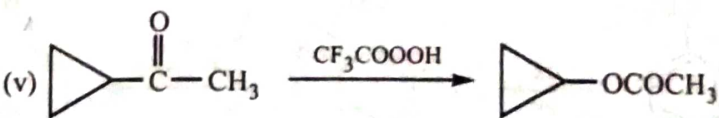
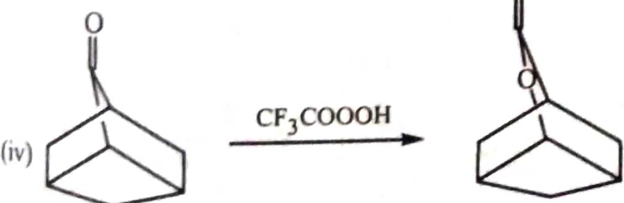
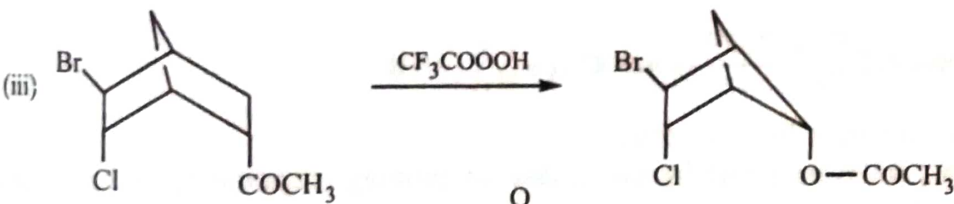
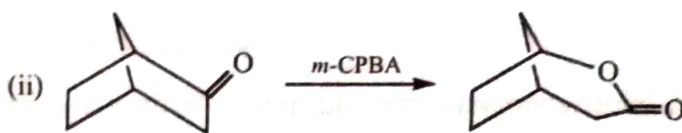
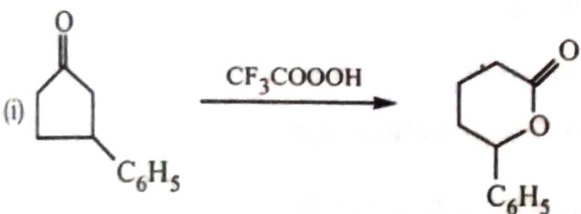
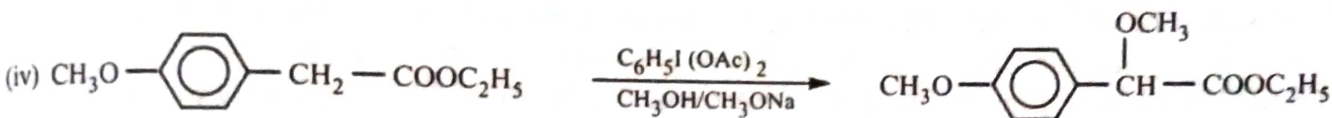
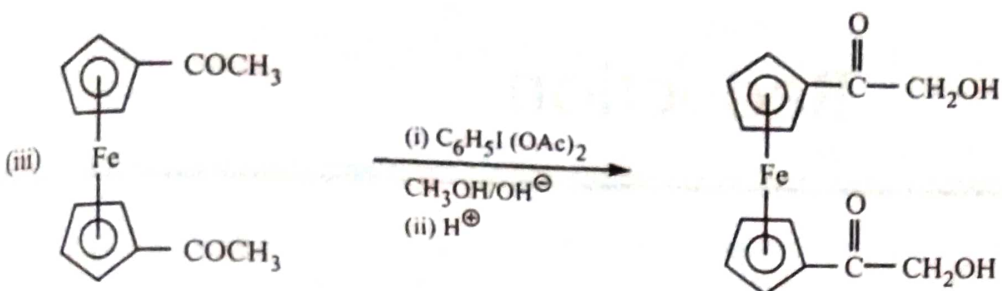
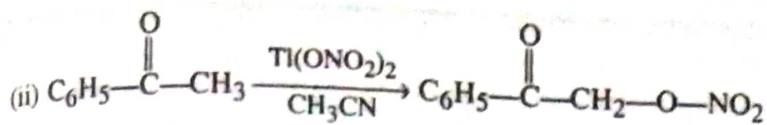




7. (i) Gem dimethyl alkene gives stereoselective oxidation with SeO_2 . Geometry of the product is always (*E*). Selectivity is due to the concerted [2, 3] sigmatropic rearrangement.







OXIDATION

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