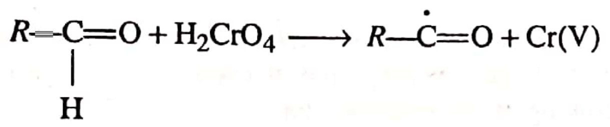
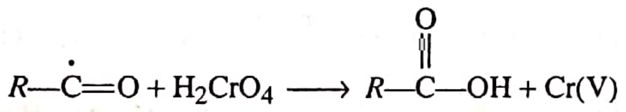
M. Sc. II Semester
Sub - Chemistry
Paper-II (Organic Chemistry)

8.5 OXIDATION OF ALDEHYDES TO CARBOXYLIC ACIDS

Oxidation of aldehydes to carboxylic acids has been carried out with many oxidising agents, the most popular of which is acidic, basic, or neutral solution of permanganate, chromic acid, silver oxide, bromine, Benedict's solution and Fehling's solution. The mechanism of aldehyde oxidation may be free radical or ionic. Both the mechanisms may take place together. In the free radical mechanism, the aldehydic hydrogen is abstracted to give an acyl radical, which obtains OH from the oxidising agent, for example : .



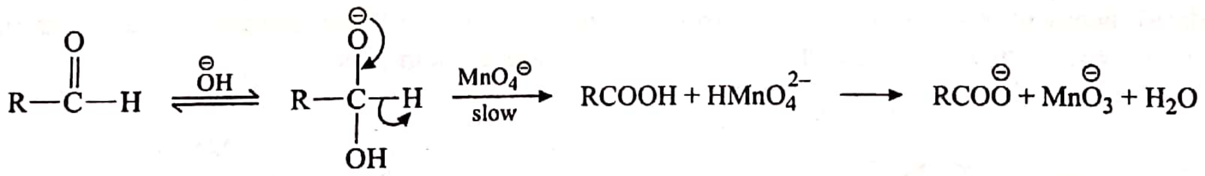
$$R-\underset{\displaystyle H}{\underset{|}{C}}=O + H_2CrO_4 \longrightarrow R-\dot{C}=O + Cr(V)$$



$$R-\dot{C}=O + H_2CrO_4 \longrightarrow R-\overset{\displaystyle O}{\overset{\|}{C}}-OH + Cr(V)$$

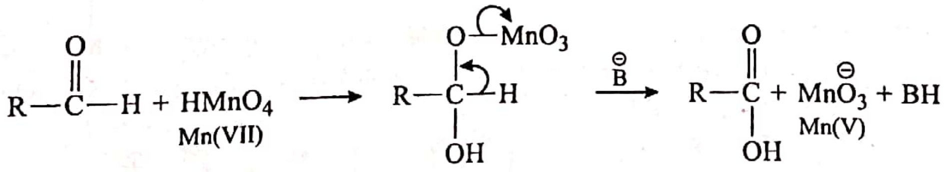
The mechanism is similar with $KMnO_4$ also.

For alkaline permangnate, the ionic mechanism is as follows :



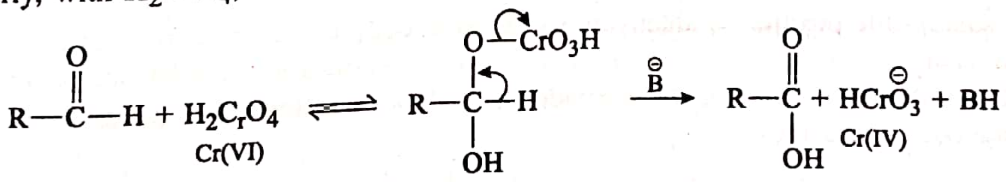
$$R-\overset{O}{\overset{\|}{C}}-H \xrightleftharpoons{\overset{\ominus}{O}H} R-\underset{OH}{\underset{|}{\overset{\overset{\ominus}{O}}{\overset{|}{C}}}}-H \xrightarrow[\text{slow}]{MnO_4^{\ominus}} RCOOH + HMnO_4^{2-} \longrightarrow RCO\overset{\ominus}{O} + Mn\overset{\ominus}{O}_3 + H_2O$$

For neutral and acidic permanganate, the following ionic mechanism has been proposed :



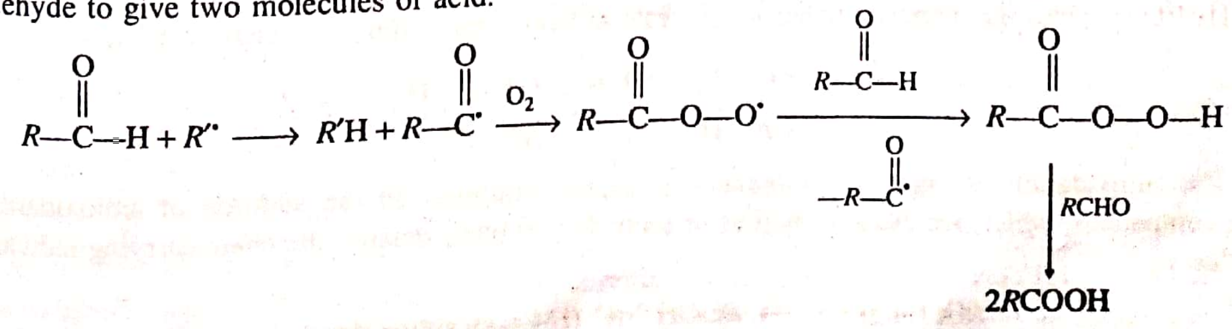
$$R-\overset{O}{\overset{\|}{C}}-H + \underset{Mn(VII)}{HMnO_4} \longrightarrow R-\underset{OH}{\underset{|}{\overset{O-MnO_3}{\overset{|}{C}}}}-H \xrightarrow{\overset{\ominus}{B}} R-\underset{OH}{\underset{|}{\overset{O}{\overset{\|}{C}}}} + \underset{Mn(V)}{Mn\overset{\ominus}{O}_3} + BH$$

Similarly, with H_2CrO_4, the ionic mechanism is as follows :



$$R-\overset{O}{\overset{\|}{C}}-H + \underset{Cr(VI)}{H_2C_rO_4} \rightleftharpoons R-\underset{OH}{\underset{|}{\overset{O-CrO_3H}{\overset{|}{C}}}}-H \xrightarrow{\overset{\ominus}{B}} R-\underset{OH}{\underset{|}{\overset{O}{\overset{\|}{C}}}} + \underset{Cr(IV)}{HCr\overset{\ominus}{O}_3} + BH$$

Aldehydes are also oxidised to carboxylic acids by atmospheric oxygen. The direct oxidation product in this case is the peroxyacid RCO_3H, which disproportionates with another molecule of aldehyde to give two molecules of acid.



$$R-\overset{O}{\overset{\|}{C}}-H + R'^{\bullet} \longrightarrow R'H + R-\overset{O}{\overset{\|}{C}}{}^{\bullet} \xrightarrow{O_2} R-\overset{O}{\overset{\|}{C}}-O-O^{\bullet} \xrightarrow[-R-\overset{O}{\overset{\|}{C}}{}^{\bullet}]{R-\overset{O}{\overset{\|}{C}}-H} R-\overset{O}{\overset{\|}{C}}-O-O-H \xrightarrow{RCHO} 2RCOOH$$

8.6 AUTOXIDATION—HYDROPEROXIDE AND PEROXIDE FORMATION

The slow oxidation (without combustion) of organic substances by atmospheric oxygen is called *autoxidation*. The reaction occurs when compounds are allowed to stand in air. It is catalysed by light and initiators and inhibited by antioxidants such as hydroquinone. These observations suggest that a free radical mechanism is involved.

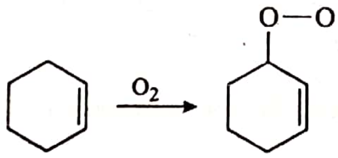
It is because of autoxidation that foods, rubber, paint, lubricating oils, etc. deteriorate on exposure to the atmosphere for a long time. A useful application of autoxidation is the atmospheric drying of paints and varnishes.

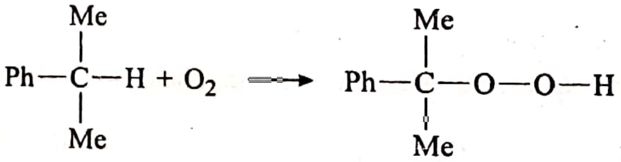
Oxygen itself (a diradical) is not reactive enough to abstract the hydrogen. But if a trace of free radical (say $R'^{\bullet}$) is produced by some initiating step, it reacts with oxygen to give R'—O—$O^{\bullet}$ which abstracts hydrogen. The following is the reaction chain :

$$R'^{\bullet} + O_2 \longrightarrow R'\text{—O—O}^{\bullet} \xrightarrow{R\text{—H}} R^{\bullet} + R'\text{—O—O—H}$$

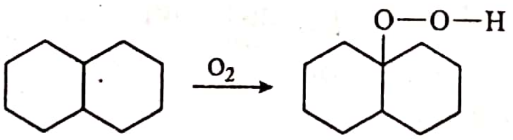
$$R^{\bullet} + O_2 \longrightarrow R\text{—O—O}^{\bullet} \xrightarrow{R\text{—H}} \underset{\text{Hydroperoxide}}{R\text{—O—O—H}} + R^{\bullet}\text{, etc.}$$

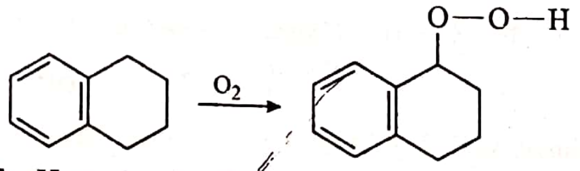
As with other free radical reactions, resonance stabilisation of tertiary (to a lesser extent secondary), benzylic, and allylic (allylic rearrangements are common) free radicals, the abstraction of these hydrogens is greatly facilitated. The following are actual examples :



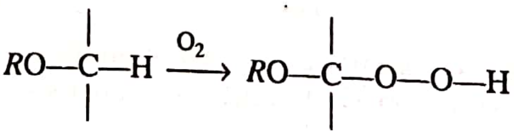


$$\text{Ph—}\overset{\text{Me}}{\underset{\text{Me}}{\text{C}}}\text{—H} + O_2 \longrightarrow \text{Ph—}\overset{\text{Me}}{\underset{\text{Me}}{\text{C}}}\text{—O—O—H}$$





Another susceptible position is aldehydic C—H as already discussed above. The α positions of ethers are also easily attacked by oxygen. This reaction is responsible for a hazard in the storage of ethers because solutions of these hydroperoxides and their rearrangement products in ethers are potential spontaneous explosives.



$$RO\text{—}\overset{|}{\underset{|}{\text{C}}}\text{—H} \xrightarrow{O_2} RO\text{—}\overset{|}{\underset{|}{\text{C}}}\text{—O—O—H}$$

Hydroperoxides decompose further to generate radicals which start new chain reactions :

$$R\text{—O—O—H} \longrightarrow R\text{—O}^{\bullet} + \text{O}^{\bullet}\text{—H}$$

$$R\text{—O}^{\bullet} + R\text{—H} \longrightarrow R\text{—OH} + R^{\bullet}$$

The autoxidation of organic compounds is usually inhibited by the addition of antioxidants. These compounds, which are usually phenols or secondary amines, destroy the chain carrying radicals as follows :

$$ROO^{\bullet} + HA \longrightarrow ROOH + A^{\bullet} \text{ (HA = an antioxidant)}$$

The radical $A^\bullet$ is resonance stabilised and relatively unreactive, thus, it is not capable of initiating a fresh chain. It is destroyed either by combination with a peroxy radical or with a similar radical :

$$ROO^\bullet + A^\bullet \longrightarrow ROOA$$

$$A^\bullet + A^\bullet \longrightarrow A{-}A$$

Formation of peroxides

$$RH + R'OOH \xrightarrow{\text{CuCl}} ROOR'$$

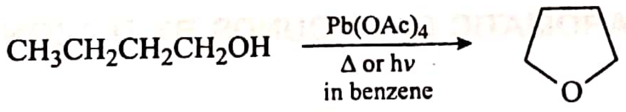
Peroxy groups (ROO) can be introduced into organic compounds by treatment with hydroperoxide in the presence of cuprous chloride or other catalysts, *e.g.*, cobalt and manganese salts. Very high yields can be obtained. The type of hydrogen replaced is mainly benzylic, allylic, and tertiary. The mechanism involved is :

$$R'OOH \xrightarrow{\text{CuCl}} R'OO^\bullet$$

$$R{-}H + R'OO^\bullet \longrightarrow R^\bullet + R'OOH$$

$$R^\bullet + R'OO^\bullet \longrightarrow ROOR'$$

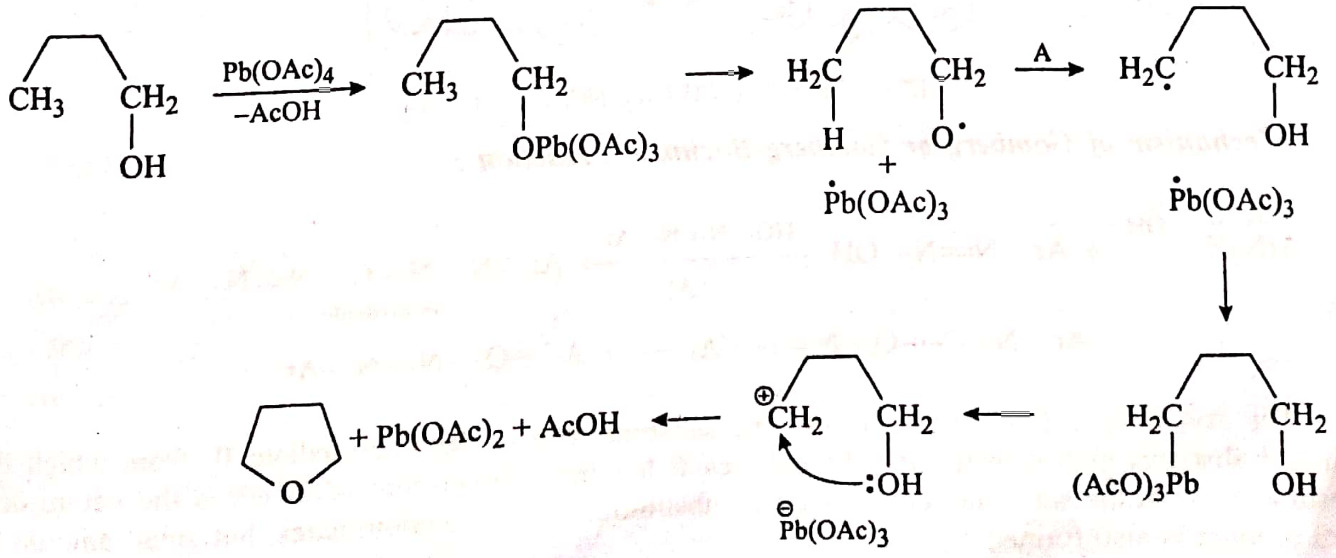
8.7 FORMATION OF CYCLIC ETHERS



Tetrahydrofuran (THF)

Alcohols having a δ hydrogen undergo cyclisation with lead tetraacetate to give tetrahydrofurans in high yields. Little or no four and six-membered cyclic ethers (oxetanes and tetrahydropyrans, respectively) are obtained in the case of alcohols having a γ or ε hydrogen. The reaction has also been carried out with a mixture of halogen (Br_2 or I_2) and a salt or oxide of silver or mercury (especially HgO or AgOAc).

The following mechanism has been proposed for the cyclisation with lead tetraacetate. The step marked A is a 1,5 internal hydrogen abstraction which is greatly favoured over 1,4 or 1,6 abstractions.



8.8 COUPLING OF ALKYNES

$$2R\text{—C}\equiv\text{C—H} \xrightarrow[\text{Pyridine}]{\text{Cu}X_2} R\text{—C}\equiv\text{C—C}\equiv\text{C—}R$$

Terminal alkynes can be coupled by heating with stoichiometric amounts of cupric salts in pyridine or similar base. This reaction produces symmetrical diynes in high yields and is called *Eglinton reaction.* Another common procedure is the use of catalytic amount of cuprous salts in the presence of ammonia or ammonium chloride. Atmospheric oxygen or some other oxidising agent, *e.g.*, permanganate or H_2O_2 is required in this method, which is called *Glaser reaction.* Unsymmetrical diynes can be prepared by *Cadiot-Chodkiewicz* coupling (mechanism is not fully understood) :

$$R\text{—C}\equiv\text{C—H} + R'\text{—C}\equiv\text{C—Br} \xrightarrow{\overset{\oplus}{\text{Cu}}} R\text{—C}\equiv\text{C—C}\equiv\text{C—}R' + \text{HBr}$$

The mechanism of Eglinton and Glaser reactions is outlined below :

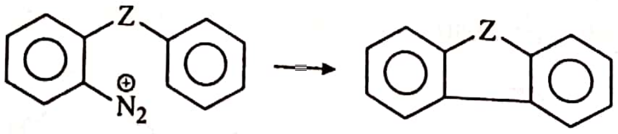
$$R\text{—C}\equiv\text{C—H} \xrightarrow{\text{Base}} R\text{—C}\equiv\overset{\ominus}{\text{C}} \xrightarrow[\text{or oxidising agent}]{\text{Cu}^{2+}} R\text{—C}\equiv\text{C}^{\bullet}$$

$$2R\text{—C}\equiv\text{C}^{\bullet} \longrightarrow R\text{—C}\equiv\text{C—C}\equiv\text{C—}R$$

8.9 ARYLATION OF AROMATIC COMPOUNDS BY DIAZONIUM SALTS

$$\text{Ar}'\text{H} + \text{Ar}\overset{\oplus}{\text{N}}_2\overset{\ominus}{\text{X}} \xrightarrow{\overset{\ominus}{\text{OH}}} \text{Ar—Ar}'$$

When diazonium salt solution is made alkaline, the aryl portion of the diazonium salts can couple with another aromatic ring. This reaction is known as the *Gomberg* or *Gomberg-Bachmann reaction,* and has been performed on several types of aromatic rings and on quinones. When the Gomberg-Bachmann reaction is performed intramolecularly, either by the alkaline solution or by the copper ion procedure, it is called *Pschorr ring closure.*



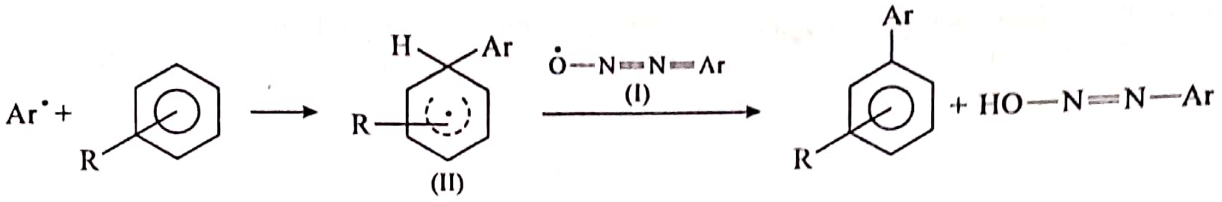
[Z = CH=CH, CH_2CH_2, NH, C=O, CH_2]

Mechanism of Gomberg or Gomberg-Bachmann reaction :

$$\text{Ar}\overset{\oplus}{\text{N}}_2\overset{\ominus}{\text{X}} \xrightarrow{\overset{\ominus}{\text{OH}}} \text{Ar—N=N—OH} \xrightarrow[-\text{H}_2\text{O}]{\text{HO—}\ddot{\text{N}}\text{=N—Ar}} \underset{\text{Anhydride}}{\text{Ar—N=N—O—N=N—Ar}}$$

$$\text{Ar—N=N—O—N=N—Ar} \longrightarrow \text{Ar}^{\bullet} + \underset{\text{(I)}}{\text{O}^{\bullet}\text{—N=N—Ar}}$$

The aryl radical thus formed attacks the substrate to give the intermediate II, from which the radical I abstracts hydrogen to give the product. It has been shown that whatever is the nature of a substituent (R) in the substrate, *ortho* or *para* substitution always predominates, but small amount of *meta* product is also formed.



Sandmeyer reaction :

$$\mathrm{Ar}\overset{\oplus}{\mathrm{N}}_2\overset{\ominus}{X} \xrightarrow{\mathrm{Cu}X} \mathrm{Ar}X + \mathrm{N}_2$$

$$[X = \mathrm{Cl} \text{ or } \mathrm{Br}]$$

Treatment of diazonium salts with cuprous chloride or bromide gives aryl chlorides or bromides, respectively. This reaction is called the *Sandmeyer reaction*. The reaction can also be carried out with copper and HBr or HCl, in this case it called the *Gattermann reaction*. The *Sandmeyer reaction* is not useful for the preparation of fluorides and iodides, but it is prabably the best way of introducing bromine or chlorine into an aromatic ring.

Mechanism : The reaction involves two steps. The first step is the reduction of diazonium ion by cuprous ion to give an aryl radical :

$$\mathrm{Ar}\overset{\oplus}{\mathrm{N}}_2\overset{\ominus}{X} + \mathrm{Cu}X \longrightarrow \mathrm{Ar}^{\bullet} + \mathrm{N}_2 + \mathrm{Cu}X_2$$

In the second step, the aryl radical abstracts halogen from cupric chloride, reducing it. CuX is regenerated and is thus, a true catalyst.

$$\mathrm{Ar}^{\bullet} + \mathrm{Cu}X_2 \longrightarrow \mathrm{Ar—}X + \mathrm{Cu}X$$

8.10 HUNSDIECKER REACTION

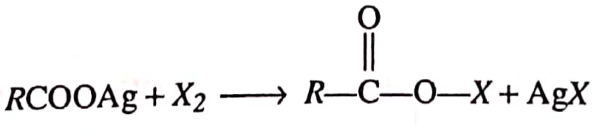
$$R\mathrm{COOAg} + \mathrm{Br}_2 \longrightarrow R\mathrm{—Br} + \mathrm{CO}_2 + \mathrm{AgBr}$$

Reaction of a silver salt of a carboxylic acid with bromine leading to an alkyl or aryl halide is called the *Hunsdiecker reaction*. It is a way of degrading a carbon chain by one unit. Although bromine is the most often used halogen, chlorine and iodine have also been used.

When iodine is used, the ratio between the reactants is very important because it determines the product. A 1 : 1 ratio of salt to iodine gives the alkyl or aryl halide as above. A 2 : 1 ratio gives the ester $R\mathrm{COO}R$, and this is called the *Simonini reaction*.

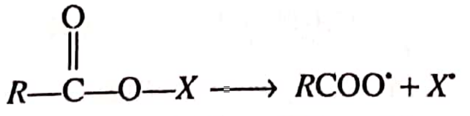
The following is the mechanism of the *Hunsdiecker reaction* :

Step 1.



$$R\mathrm{COOAg} + X_2 \longrightarrow R\text{—}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\text{—O—}X + \mathrm{Ag}X$$

Step 2.



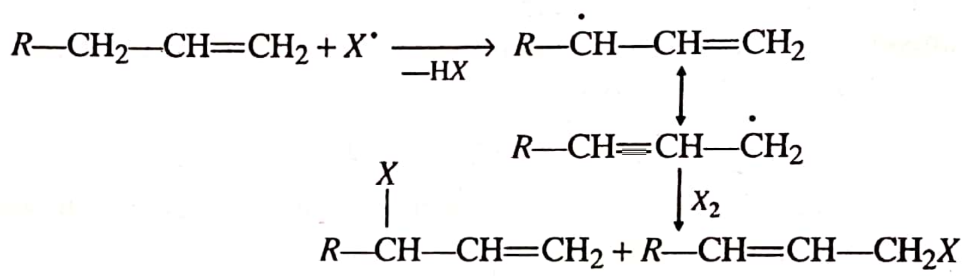
$$R\text{—}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\text{—O—}X \longrightarrow R\mathrm{COO}^{\bullet} + X^{\bullet} \qquad \text{(initiation step)}$$

Step 3. $$R\mathrm{COO}^{\bullet} \longrightarrow R^{\bullet} + \mathrm{CO}_2 \qquad \text{(3 and 4 propagation steps)}$$

Step 4. $$R^{\bullet} + R\mathrm{COO}X \longrightarrow R\text{—}X + R\mathrm{COO}^{\bullet}, \text{ etc.}$$

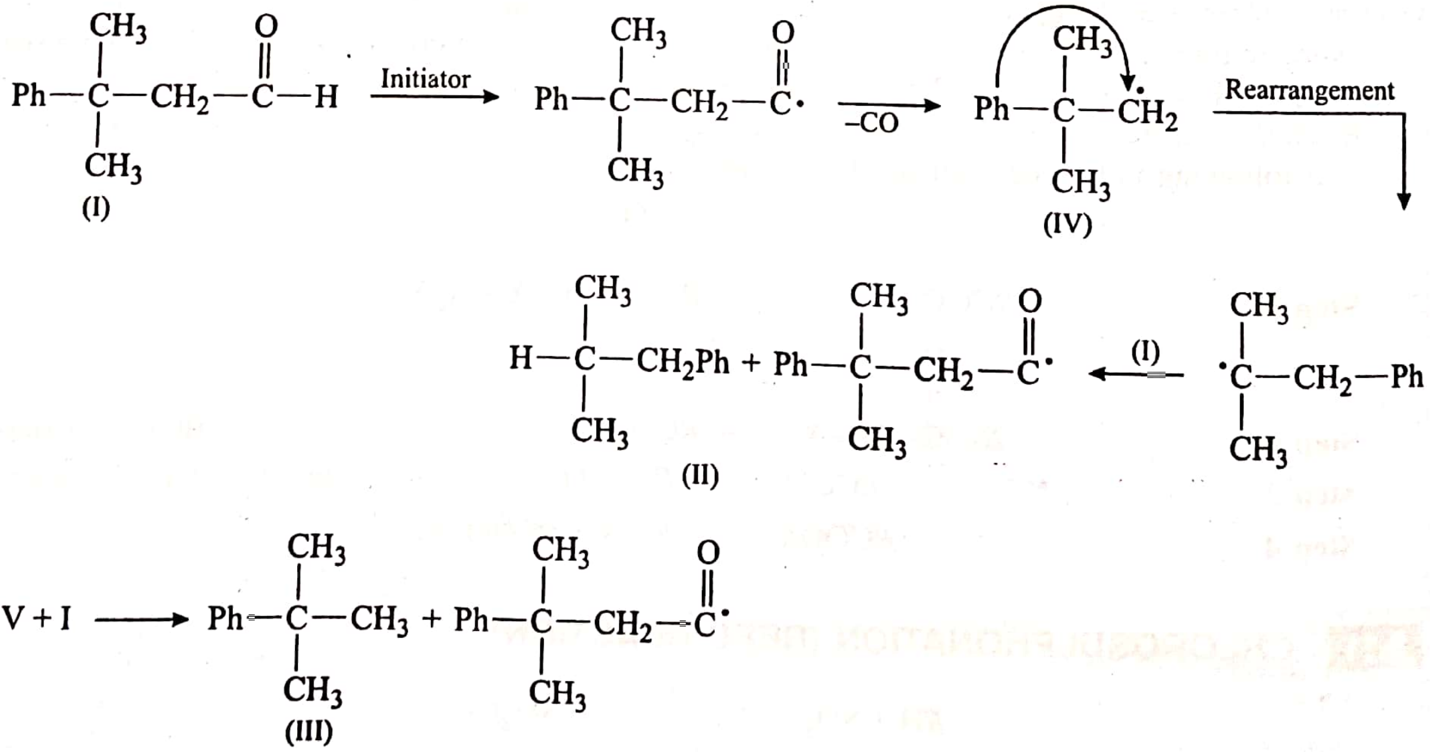
8.12 FREE RADICAL REARRANGEMENT

Allylic rearrangements are very common in free radical reactions on allylic substrates, for examples :



$$R{-}CH_2{-}CH{=}CH_2 + X^{\bullet} \xrightarrow[-HX]{} R{-}\dot{C}H{-}CH{=}CH_2 \longleftrightarrow R{-}CH{=}CH{-}\dot{C}H_2 \xrightarrow{X_2} R{-}\underset{}{\overset{X}{CH}}{-}CH{=}CH_2 + R{-}CH{=}CH{-}CH_2X$$

A primary radical may sometimes produce a tertiary radical by the migration of a substituent from the neighbouring carbon. However, such radical rearrangements are less common than carbocation rearrangements because the stability difference between a primary and a tertiary radical is not as much as that between a primary and a tertiary carbocation. Most of the reported rearrangements involve the shift of an aryl group from one atom to the adjacent atom. For example, the rearrangement of β-phenylisovaleraldehyde I accompanying decarbonylation. The reaction is initiated by *t*-butyl peroxide and yeilds a mixture of almost equal amounts of isobutylbenzene II and *t*-butylbenzene III.

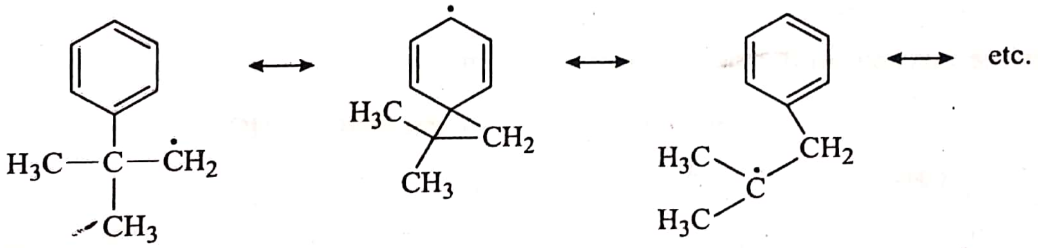


$$\underset{(I)}{Ph{-}C(CH_3)_2{-}CH_2{-}CHO} \xrightarrow{\text{Initiator}} Ph{-}C(CH_3)_2{-}CH_2{-}\dot{C}{=}O \xrightarrow[-CO]{} \underset{(IV)}{Ph{-}C(CH_3)_2{-}\dot{C}H_2} \xrightarrow{\text{Rearrangement}} {}^{\bullet}C(CH_3)_2{-}CH_2{-}Ph$$

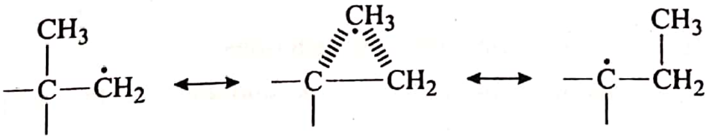
$${}^{\bullet}C(CH_3)_2{-}CH_2{-}Ph \xrightarrow{(I)} \underset{(II)}{H{-}C(CH_3)_2{-}CH_2Ph} + Ph{-}C(CH_3)_2{-}CH_2{-}\dot{C}{=}O$$

$$IV + I \longrightarrow \underset{(III)}{Ph{-}C(CH_3)_2{-}CH_3} + Ph{-}C(CH_3)_2{-}CH_2{-}\dot{C}{=}O$$

The yield of the rearranged product II increases with the dilution of the reaction mixture. This supports the above mechanism because a decrease in the concentration of a hydrogen donor I would increase rearrangement at the expense of the hydrogen abstraction by the radical IV. Further, the rate of the rearrangement is inhibited by the addition of an effective hydrogen donor such as thiophenol. The above rearrangement proceeds through the intermediate bridged radical.



The intermediacy of a bridged radical also explains why a methyl migration does not take place as readily as in carbocation rearrangements. For a methyl migration via a bridged radical there will be three electrons spread over three carbons.



Molecular orbital calculations have shown that such a bridged system is very unstable as compared to a two electron bridged system of a carbocation.