

Unit - V

Natural Products

TERPENES (C_5H_8)

Plants have many fragrant steam volatile Components in them. These are called essential oils. These are used in perfumery, food flavouring and medicines. They are mixtures hydrocarbons containing 10, 15, 20, 30 or 40 carbon atoms or their oxygenated derivatives. The individual compounds of essential oils are called terpenes or terpenoids.

Isolation of Terpenes

Terpenes are isolated from the essential oils. The essential oil is extracted from the plant tissues by

1. Steam distillation
2. Digestion with solvents or
3. Adsorption in purified fats steam distillation is widely used.

The plant tissues are ground and the steam distilled. Solvent extraction method is used in cases of terpenes which decompose during steam distillation. This is done with light petrol at 50°C .

The essential oils obtained by the above methods is subjected to fractional distillation or chromatography. We get individual terpenes.

Classification of Terpenes

Terpenes are classified according to the number of isoprene units present in them. The following table gives the various classes of terpenes found in nature.

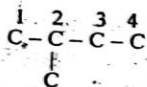
<i>Class</i>	<i>Number of isoprene units</i>
Mono terpenes	2
Sesqui terpenes	3
Diterpenes	4
Triterpenes	6
Tetra terpenes	8
Poly terpenes	n

Isoprene Rule :

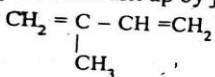
Rule : The skeleton structures of all naturally occurring terpenoids are built up of isoprene units.

Explanation :

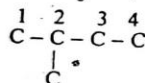
The building block of the structure of terpenes is an isoprene skeleton namely,



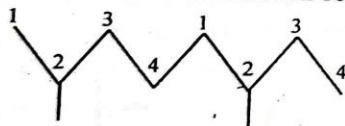
Such isoprene units are joined together through carbon atoms 1 and 1 or 4 and 4 or 1 and 4. The carbon atom marked 1 is called the head and 4 is called the tail. Many of the terpenes are built up by joining the head and the tail. We know isoprene



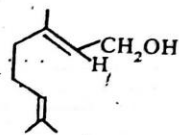
So, the isoprene unit will be



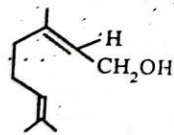
When two such units are joined by carbon 4 of the first unit and the carbon 1 of the second unit the structure will be as follows :



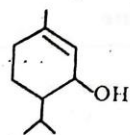
Examples of some common terpenes are given below. Dotted lines divide the molecules into isoprene units.



Geraniol



Nerol



Menthol

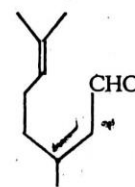
Properties of Terpenes**Physical :**

Most of them are sweet smelling colourless liquids. They are lighter than water. They are readily volatile in steam. They are optically active.

Chemical :

Most of them are unsaturated. So they add HBr, Br₂, H₂ and ozone. They form characteristic addition compounds with NO₂ and NaOBr. These addition compounds are used for the identification of the terpenes. Terpenes are easily oxidised. On exposure to air they become resins.

CITRAL : (C₁₀H₁₆O)



Citral

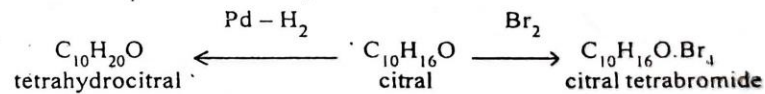
Citral is the most important member of the acyclic monoterpenoids since the structures of most of the other compounds in this group are based on that of citral. It finds much industrial applications, the most important being the synthesis of β-ionone, is frequently used in perfumery.

Isolation :

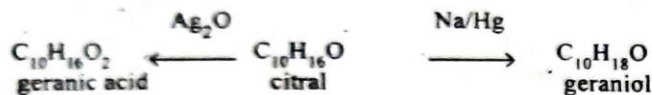
It is optically inactive oil with lemon like smell. It occurs widely distributed in nature, the principle source being the lemon grass oil which has 60 – 80% of citral. Citral is isolated as its crystalline bisulphite product which on hydrolysis gives back citral.

Structure :

- Its molecular formula is C₁₀H₁₆O.
- By the usual reactions, citral is found to have two double bonds.

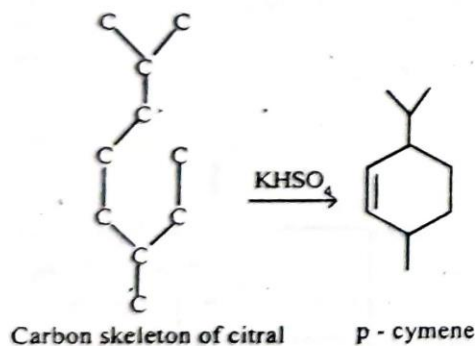


3. As citral forms an oxime and reduces Fehling solution, oxygen must be present as an aldehydic group. It is confirmed by its reduction to geraniol (a primary alcohol) $C_{10}H_{18}O$, and oxidation by silver oxide to geranic acid $C_{10}H_{16}O_2$, without loss of any carbon atom.



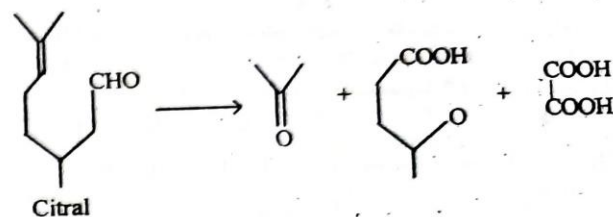
4. The presence of two double bonds and an aldehydic group in citral ($C_{10}H_{16}O$) led to $C_{10}H_{22}$ as the molecular formula of its fully saturated hydrocarbon. Now as $C_{10}H_{22}$ corresponds to the general formula for acyclic compounds (C_nH_{2n+2}) citral must be acyclic compounds.

5. Citral, on heating with potassium hydrogen sulphate, gives a well known aromatic compound *p*-cymene and thus the carbon skeleton and hence the position of the alkyl groups, viz., methyl and isopropyl, are established.

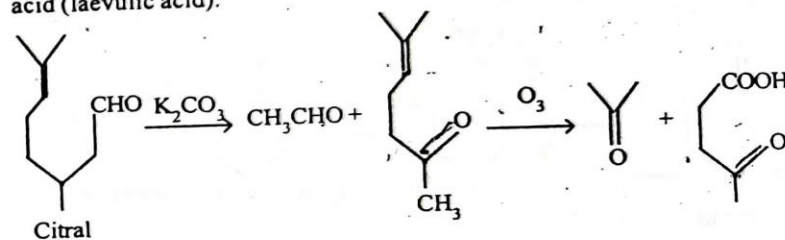


6. On treatment with sodium bisulphite citral forms mono as well as di-bisulphite addition products, indicating the presence of α, β -unsaturated aldehydic group. The α, β -unsaturated aldehydic group in citral is confirmed by its ultraviolet absorption spectrum (λ_{max} 2.38 nm).

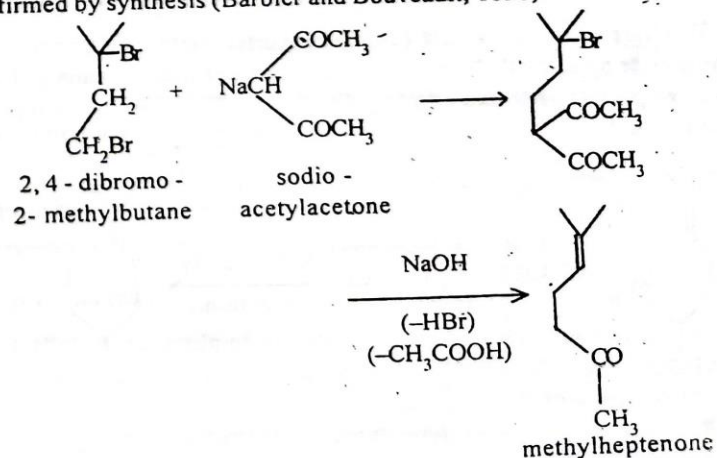
7. The position of the other double bond and the complete structure of citral is established by its oxidation with alkaline permanganate followed by chromic acid to give acetone, oxalic acid and laevulinic acid (Tiemann and Semmler, 1895).



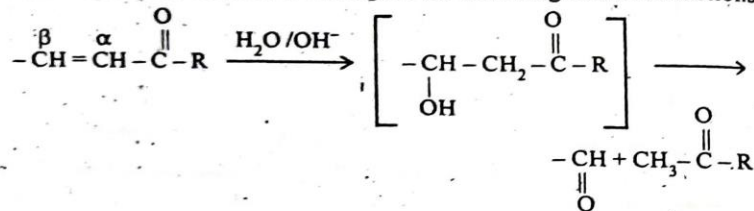
8. The above structure for citral is proved by Verley's work (1897) who found that citral when treated with aqueous K_2CO_3 solution is converted into acetaldehyde and an unsaturated ketone which was identified as 6-methylhept-5-en-2-one by its ozonolysis to acetone and laevulinic acid (laevulinic acid).



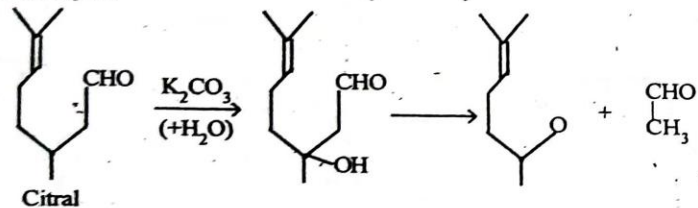
Moreover, the structure of methylheptenone has already been confirmed by synthesis (Barbier and Bouveault, 1896).



The conversion of citral to methylheptenone and CH_3CHO is actually owing to the presence of an α, β -unsaturated carbonyl group which whenever treated with alkali undergoes the following series of reactions.



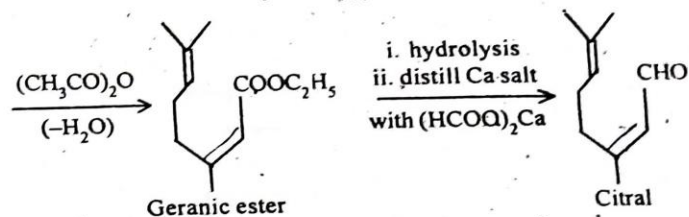
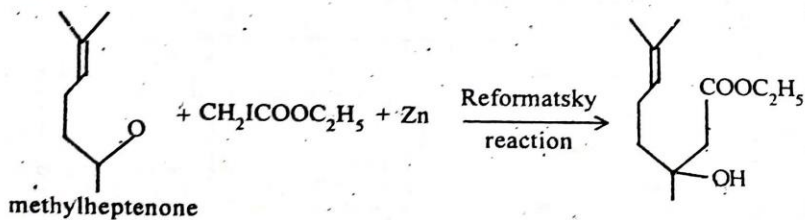
Let us apply this reaction to citral which yield methylheptenone and acetaldehyde.



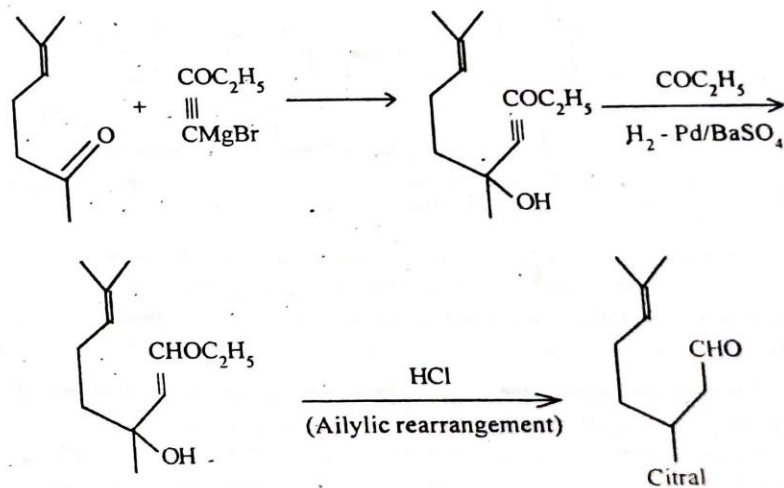
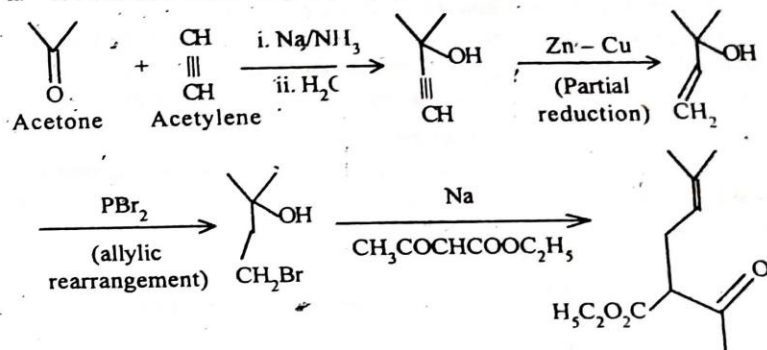
Synthesis :

Finally the structure of citral has been confirmed by various synthesis.

i. **Barbier and Bouveault (1896)** converted methylheptenone into geranic ester by using Reformatsky reaction. After this **Tiemann (1898)** converted geranic ester into citral by distilling a mixture of calcium salts of geranic and formic acids.

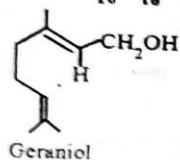


ii. **Arens and Van Drop (1948)** synthesis



GERANIOL (C₁₀H₁₈O)

148.

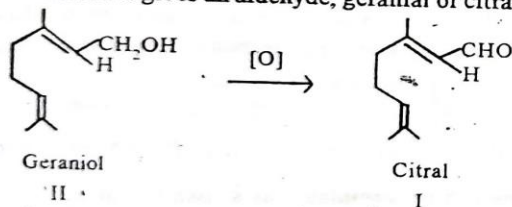


Isolation

It occurs in rose, lemon - grass, geranium, lavender and citronella oils. It is isolated from the oil of palmrosa. Palmrosa is treated with anhydrous calcium chloride. We get a crystalline complex. It is filtered and decomposed with water. We get geraniol.

Structure

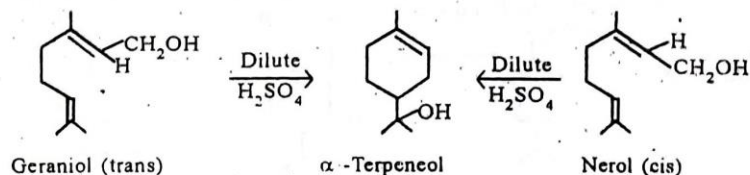
- The molecular formula of geraniol is C₁₀H₁₈O.
- On oxidation it gives an aldehyde, geranial or citral.



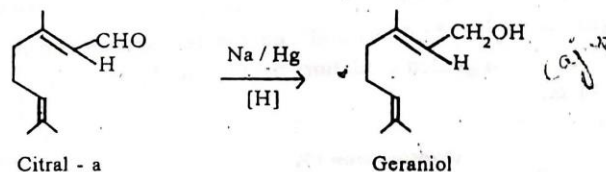
Citral on further oxidation gives an acid, geranic acid. Both the citral and geranic acid have the same number of carbon atoms. Therefore geraniol is a primary alcohol.

- On bromination it gives a tetrabromide. On reduction four hydrogen atoms are added. This shows the presence of two double bonds.
- Since it gives citral on oxidation the arrangement of carbon atoms in its molecule is the same as in citral. The structure of citral is shown to be I. Therefore the structure of geraniol is II.
- Geraniol and nerol have been shown to be geometrical isomers. Both nerol and geraniol on treatment with dilute sulphuric acid undergo cyclisation and give α -terpineol. This reaction is nine times as fast with nerol as with geraniol. Therefore the trans configuration has been given to geraniol and cis configuration to nerol.

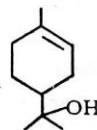
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Synthesis



α -TERPINEOL (C₁₀H₁₈O)



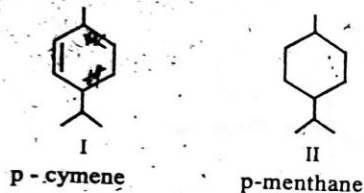
Isolation

It occurs in oils of petitgrain and neroli. α -terpineol, is isolated from camphor and dl- α -terpinol from cajuput oils by extraction with light petrol at 50°C.

Structure

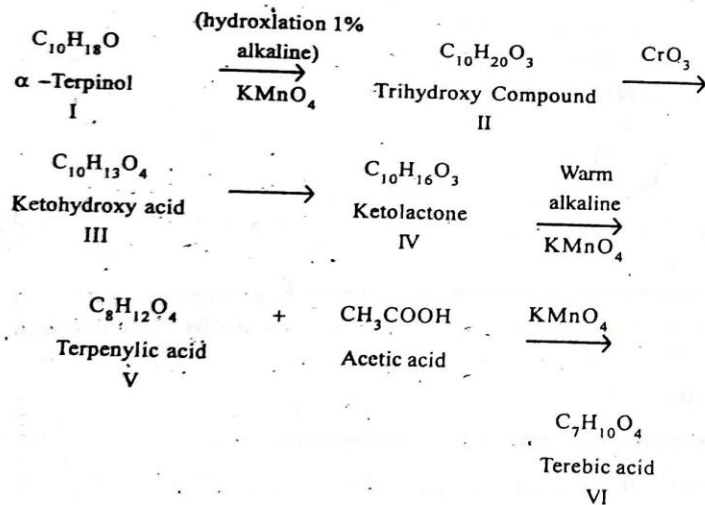
- The molecular formula of α -terpineol is C₁₀H₁₈O.
- It shows the reactions of a tertiary alcohol.
- It adds a molecule of bromine. Therefore it contains one double bond. Therefore the parent (saturated) hydrocarbon of terpinol has the molecular formula C₁₀H₂₀. This corresponds to C_nH_{2n}. Therefore α -terpineol is a monocyclic compound.

4. On heating with sulphuric acid it gives p-cymene I. Therefore α -terpinol contains the p-cymene skeleton.



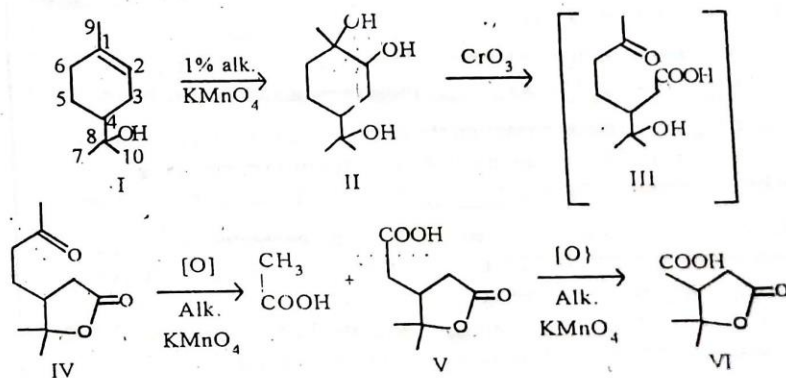
Thus α -terpineol is p-menthane (II) with one double bond and a tertiary alcoholic group.

v. Positions of the double bond and the tertiary alcoholic group (Wallach): On graded oxidation, α -terpineol gives the following products.



- vi. The compound IV was shown to contain a keto group. But when it was refluxed with excess standard sodium hydroxide solution and then back titrated, it was found that alkali had been consumed. The amount of alkali consumed corresponds to the presence of one carboxylic group. Thus IV is a lactone of a mono carboxylic acid.
- vii. Since it is the lactone that is isolated and not the hydroxy acid III, suggests that the lactonisation of III is spontaneous. That is III is a γ - or δ -hydroxy acid and that IV is a γ - or δ -lactone.
- viii. Since IV is formed from II by scission of the glycol bond and since there is no loss of carbon atoms. The double bond must be in a ring. Thus I is a cyclic compound.
- ix. IV gave terpenylic acid, V and acetic acid. The formation of acetic acid suggests that IV is a methyl ketone. That is IV contains a CH_3CO -group. Thus IV is a methyl ketone and, a lactone.
- x. Terpenylic acid V has been shown to be a lactone of a monohydroxy dicarboxylic acid. Terpenylic acid has been found to be identical with synthetic γ -keto lactone. So, terpenylic acid must be a γ -keto lactone.
- xi. Terpenylic acid, V on further oxidation gives terebic acid VI.
- xii. Terebic acid is also the lactone of a monohydroxy dicarboxylic acid.

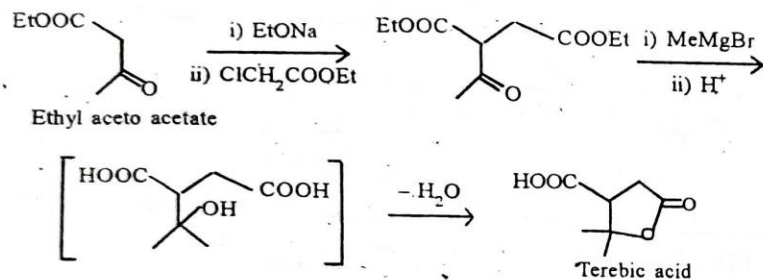
The above reactions can be formulated as shown below assuming the structure of α -terpineol as I. (P-Menth-1-en-8-ol)



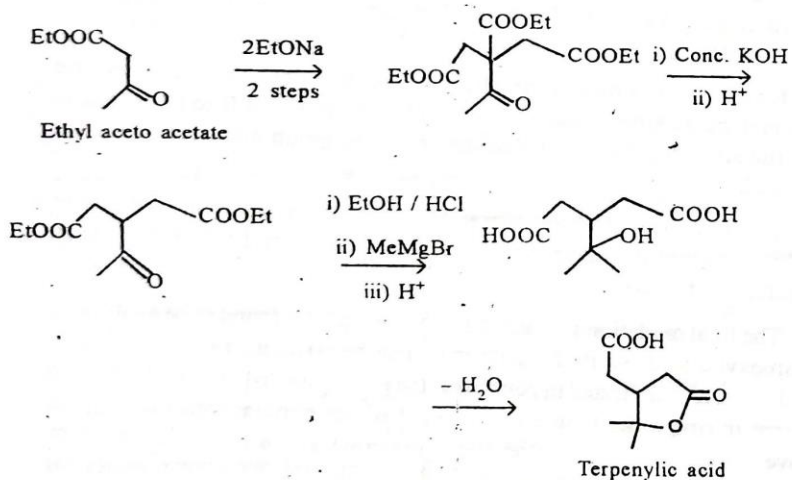
xiii. Structures of terpenylic acid (V), terebic acid (VI) and α -terpineol (4) were confirmed by their synthesis.

Synthesis

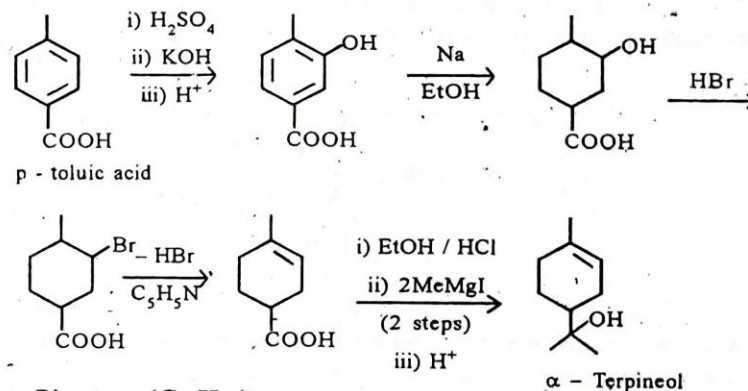
a. Terebic acid



b. Terpenylic acid



c. α -Terpineol



α - Pinene : ($C_{10}H_{16}$)



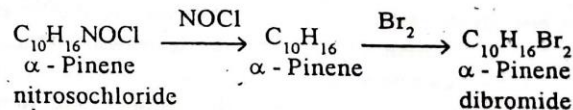
α - Pinene (b, p 156°) is the most widely distributed among all the terpenoids. It forms the principal constituent of turpentine oil. α - Pinene exists in optically active forms. α - Pinene constitutes the starting material for the synthesis of α - terpineol, borneol, camphor, etc.

Isolation :

It is isolated by the steam distillation of turpentine oil or light petrol at 320K

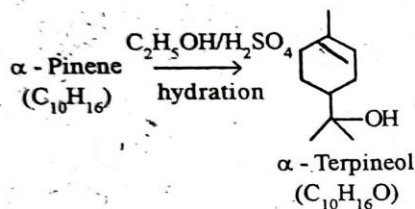
Structure :

1. Its molecular formula is $C_{10}H_{16}$.
2. On treatment with Br_2 and nitrosyl chloride separately, α - pinene forms dibromide and nitroso - chloride, respectively suggesting the presence of a double bond.



Now as the molecular formula of its saturated hydrocarbon $C_{10}H_{18}$ corresponds for bicyclic compounds (C_nH_{2n-2}), α - pinene must be bicyclic compound.

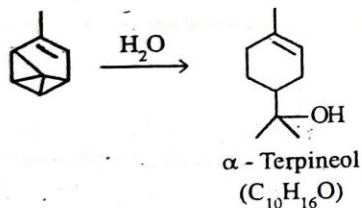
3. α - Pinene on treatment with alcoholic sulphuric acid gives α - terpineol a compound, of well - known structure.



Since the structure of α - terpineol is known, its formation by hydration of α - pinene leads to the following points.

i. α - Pinene possesses one six - membered ring having the double bond of α - terpineol.

ii. The presence of hydroxyl group at C_8 in α - terpineol, which is not present in α - pinene, indicates that this carbon atom must be involved in the formation of other ring of α - pinene. (There are three possibilities (as represented by dotted lines in the following structure) for the C_8 to form other ring of α - pinene and hence its complete structure which can be easily cleaved on hydration to form α - terpineol can be drawn as below.

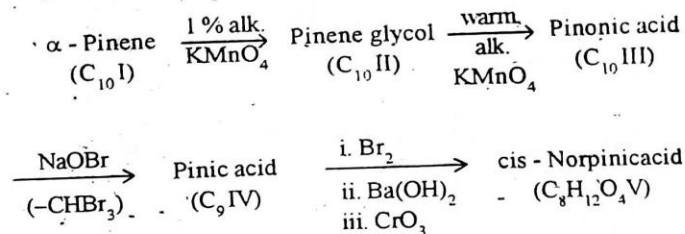


Although theoretically there are four possibilities yet one of them is discarded on the grounds of Bredt's rule according to which a double bond can not be formed by a carbon atom occupying the bridge - head of bicyclic system. Out of the rest three possibilities, one gives four membered ring and the two give three membered ring. The exact structure of the other ring i.e., whether 4 - or - 3 - membered is established by the oxidative degradation of α - pinene.

iii. The gem dimethyl group ($-\text{CHMe}_2$) of α - terpineol is not present in the six - membered ring of α - pinene and hence it must be present in the other ring.

iv. *Oxidative degradation of α - pinene :*

Baeyer degraded α - pinene according to the following scheme.



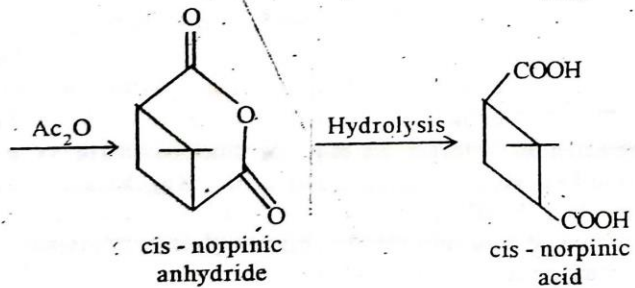
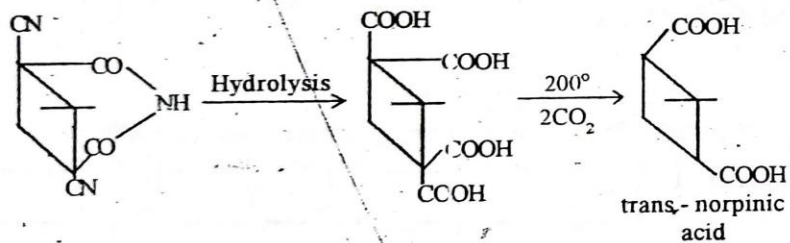
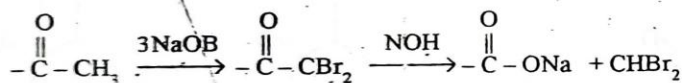
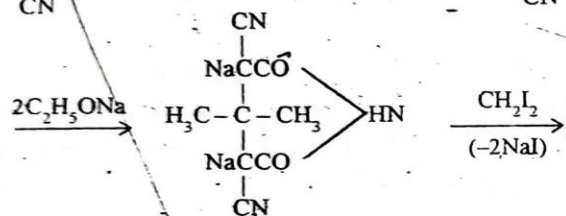
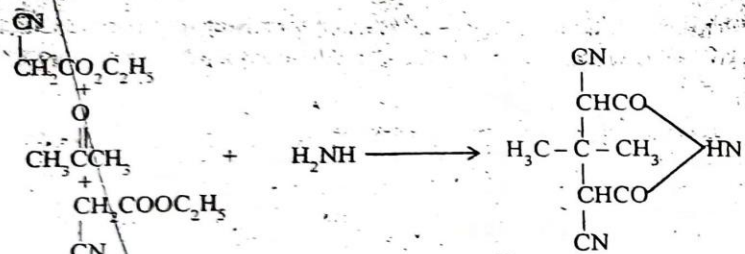
The above set of oxidative degradation led in the following conclusion.

i. In the conversion of I to II, the double bond of the former is hydroxylated.

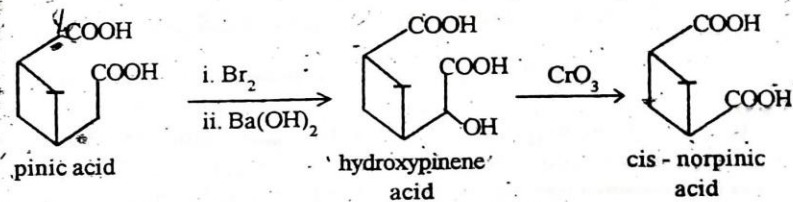
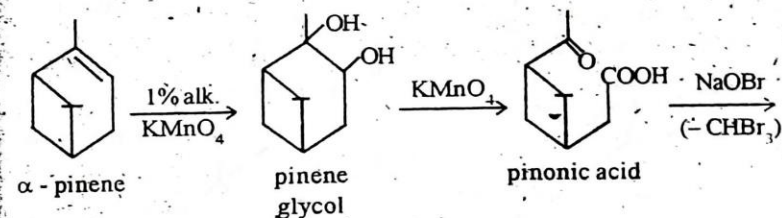
ii. Now as we know that the double bond is present in the six - membered ring, oxidation of the glycolic group of II to III indicates that the six - membered ring having glycolic group and double bond is oxidised.

iii. The formation of bromoform as one of the oxidation products of III suggests that the compound III is having an acetyl ($-\text{COCH}_3$) group (haloform reaction).

iv. The final oxidation product, cis - norpinic acid is found to be a saturated dicarboxylic acid, so its formula may also be written as $\text{C}_6\text{H}_{10}(\text{COOH})_2$. Furthermore, as indicated in point 3(i) the gem - dimethyl group ($-\text{CHMe}_2$) is present in ring other than 6 - membered which remains intact during the above oxidation reactions, the gem - dimethyl group ($-\text{CHMe}_2$) must be present in the cis - norpinic acid. Thus now the detailed formula for cis - norpinic acid may be written as $\text{Me}_2\text{C}_4\text{H}_2(\text{COOH})_2$ which indicates that the saturated parent hydrocarbon of this acid is C_4H_8 and hence the acid must be cyclobutane derivative. The acid was identified as 1, 1 - dimethyl cyclobutane, 2, 4 - dicarboxylic acid by synthesis (Kerr, 1929).

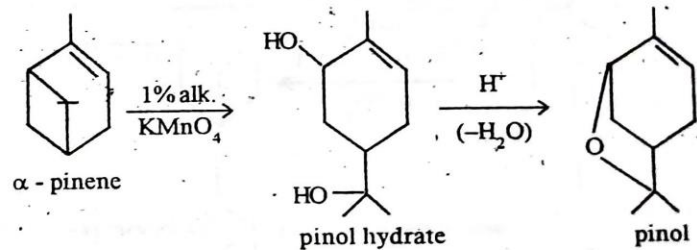


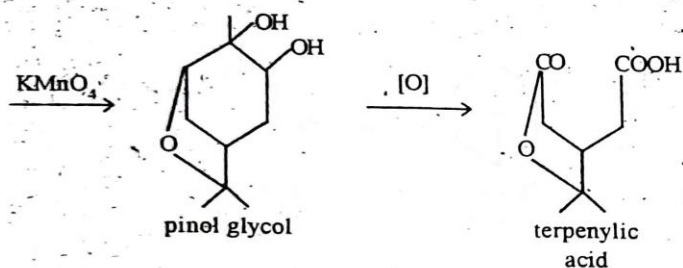
5. On the basis of the above points, α -pinene may be given structure I which explains all the reactions.



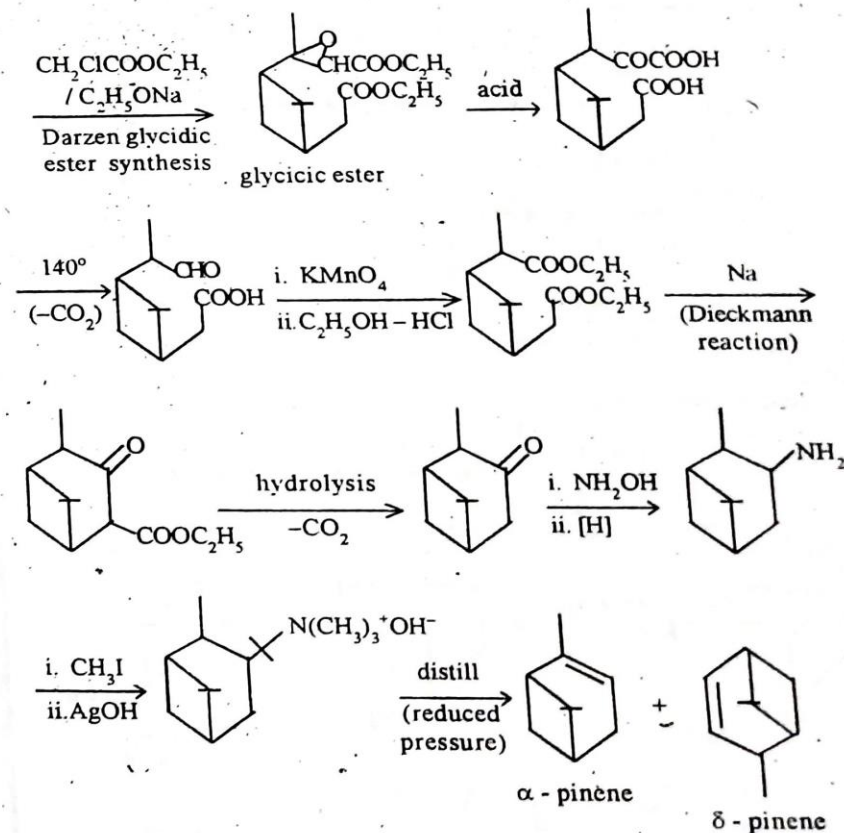
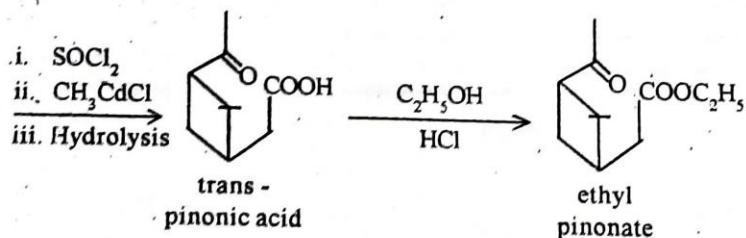
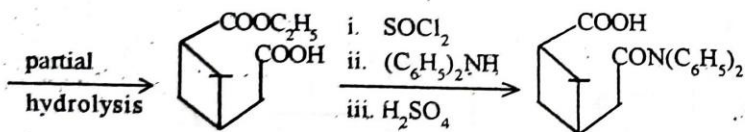
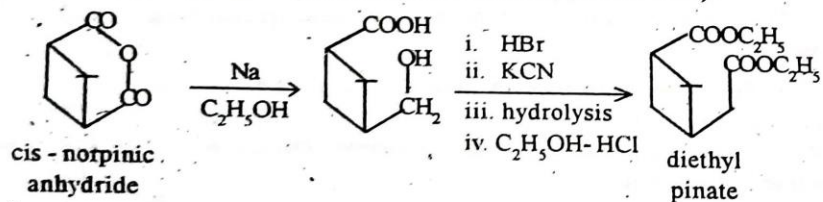
6. The above structure of α -pinene also explain the following Wallach observation.

α -Pinene on treatment with dilute KMnO_4 gives pinol hydrate which on dehydration by means of acid gives pinol. The latter on oxidation with potassium permanganate gives pinol glycol which on further oxidation gives terpenylic acid.

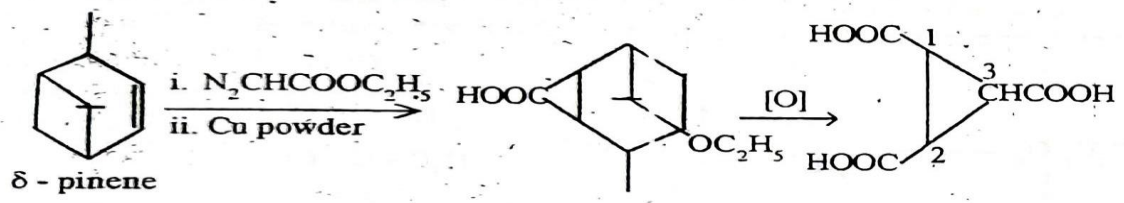
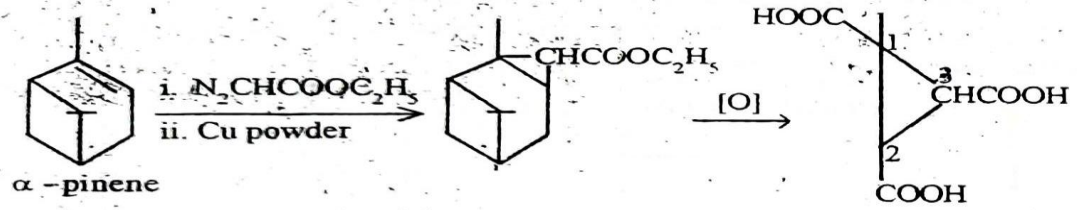


**Synthesis :**

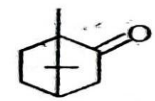
Lastly, the above structure for α - pinene is proved by its synthesis from *cis* - norpinic acid which has already been synthesised. In the total synthesis of α - pinene, norpinic acid was synthesised by Simonsen et al 1929; norpinic acid was converted into pinic acid by Guha et al (1937), pinic acid was converted into pinonic acid by Rao (1943), and lastly pinonic acid was converted into α - pinene by Ruzicka et al, (1920 - 1924).



The presence of α - pinene in the above mixture of α - and δ - isomers is detected by its formation of nitrosochloride and thus the mixture of α - and δ - pinenes is separated and identified by the action of diazoacetic ester when the α - pinene gives 1 - methyl cyclopropane - 1, 2, 3 - tricarboxylic acid and the δ - pinene gives cyclopropane - 1, 2, 3 - tricarboxylic acid.



Camphor : (C₁₀H₁₆O)



Camphor is the most important constituent of the oil of camphor. The camphor, although very important, is not very widely distributed in nature and the main source is *Cinnamomum camphora* (camphor tree) which is extensively found in Formosa. In this tree, although camphor is present in all the parts, the highest proportion is in the trunk.

Manufacture :

Camphor was exclusively used to be obtained from the camphor tree, but as the supplies of natural camphor proved to be inadequate, now - a - days it is prepared industrially from α - pinene which in turn is obtained from turpentine oil by the following series of reaction.

α - Pinene \longrightarrow Bornyl chlorids \longrightarrow Camphene
 Isobornyl acetate \longrightarrow Isoborneol \longrightarrow Camphor

Thank YOU