

## TERPENOIDS

⇒ Originally, the term terpene was applied to a mixture of isomeric hydrocarbons of the molecular formula  $C_{10}H_{16}$  occurring in turpentine and many other essential oils. The oxygenated derivatives, like alcohols, aldehydes, ketones etc., at that time were called camphors. But as the discovery of the related compounds increased with time, the definition changed and empirical formula is given  $C_5H_8$  which will cover all the compounds under the name of terpenoids; i.e. the terpenes and camphors of the earlier time are thus now called as the terpenoids.

⇒ The term terpene represents only hydrocarbons  $(C_5H_8)_n$  while the term terpenoids represent the hydrocarbon as well as the oxygenated derivatives, i.e. all the compounds having  $(C_5)_n$ , so all the terpenes are terpenoids but not vice-versa.

Occurrence:- In our daily practice we see that the fruits, flowers, leaves, stems, barks and roots of nearly all the plants have some pleasant smell. It has been observed that this pleasant smell of the fruits is actually due to the presence of certain steam volatile oils known as essential oils. The essential oils are complex mixtures of hydrocarbons and their oxygenated derivatives, though some, such as oil of bitter almond and oil of wintergreen consists mainly of one constituent, viz.  $C_6H_5CHO$  and methyl salicylate, respectively.

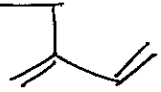
Among the chief constituents of the essential oils are the terpenoids having carbon atoms upto  $C_{15}$  (i.e. mono and sesqui-terpenoids) and their oxygenated derivatives such as alcohols, aldehydes and ketones, as well as some closely related open chain alcohols, aldehydes and ketones.

Due to their pleasant smelling nature the mono and sesqui-terpenoids are of considerable commercial importance particularly in perfumery industry. Moreover various terpenoids show biological activity, viz. insecticidal, anthelmintic, or antiseptic action and thus also useful in pharmacy. As far as the occurrence of higher terpenoids is concerned the di- and tri-terpenoids are thus found in plant<sup>l</sup> gums and resins.

Classification:- As we shall see, a common feature of terpenes is that the carbon skeletons of their molecules are built of isoprene ( $C_5$ )

units. They are, therefore, classified into different categories - depending on the number of isoprene units present in them. The various categories are:

(i) Hemiterpenes: are the compounds having one isoprene unit, the simplest compound is isoprene itself ( $C_5H_8$ ).

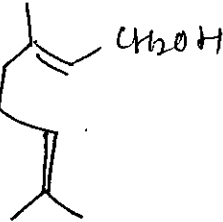


(ii) Monoterpenes: - are the compounds having two isoprene units (10 carbons) depending upon the nature of carbon skeleton, they are further subdivided into acyclic, monocyclic, and bicyclic monoterpenes.

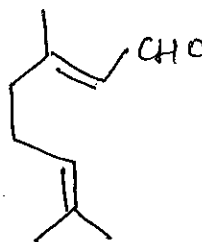
① Acyclic monoterpenes



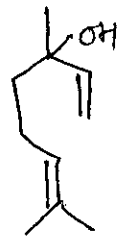
$\beta$ -myrcene



Geraniol



citral

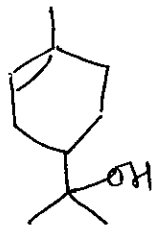


Linalool

② monocyclic monoterpenes:



Limonene



$\alpha$ -terpineol



$\alpha$ -pinene



$\beta$ -pinene

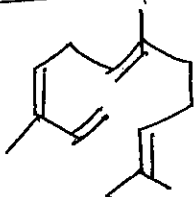


Camphor

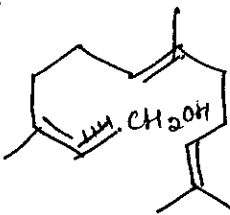
③ bicyclic monoterpenes:

(iii) Sesquiterpenes: - are the compounds having three isoprene units ( $C_{15}$ ). They form higher boiling fractions of essential oils and like monoterpenes, they are also divided into various subgroups.

① Acyclic sesquiterpenes:

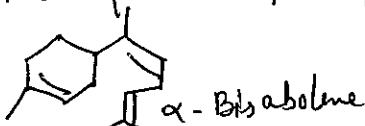


$\alpha$ -farnesene



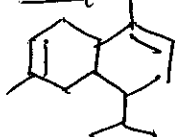
Farnesol

② monocyclic sesquiterpenes:



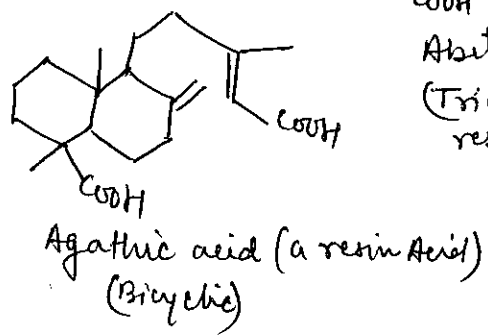
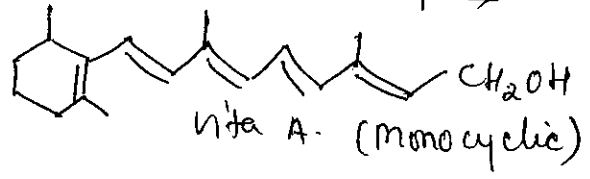
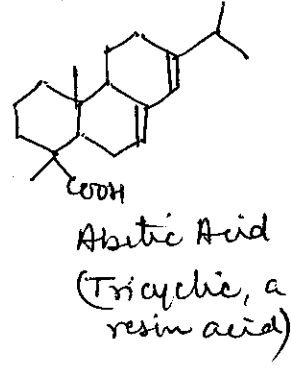
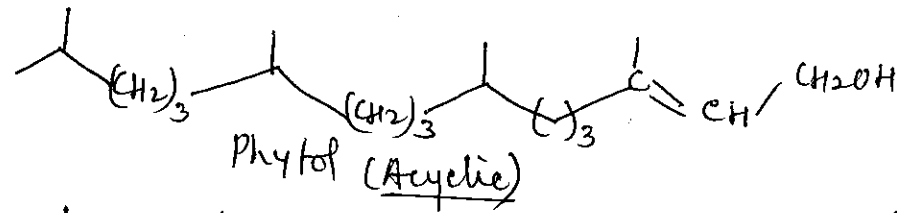
$\alpha$ -Bisabolene

③ bicyclic sesquiterpenes:

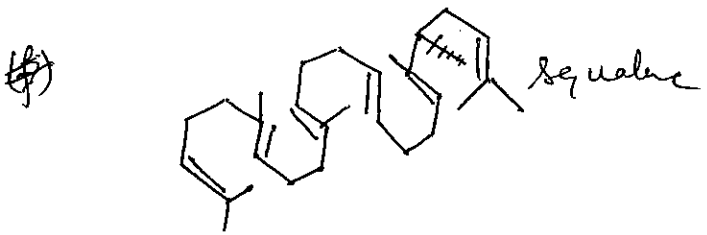


$\alpha$ -cadinene

(iv) Diterpenes:- are the compounds having four isoprene units (20 carbons)



(v) Triterpenoids:- are the compounds having six isoprene units (30). ~~Carotenoids, the colouring principles of <sup>carrots</sup> belong to this class.~~ Squalene, an important constituent of shark liver oil.



(vi) Tetraterpenes:- May be regarded as composed of eight isoprene unit (C<sub>40</sub>) Carotenoids, the colouring principles of carrots, belong to this class.

(vii) Polyterpenes:- have more than 40 carbon atoms. Rubber, (C<sub>5</sub>H<sub>8</sub>)<sub>n</sub> is an example of this class.

Isolation:- Essential oils are extracted from plants by several methods,

(i) Steam distillation:- The powdered plant material is steam distilled when the constituents of the essential oil go into the distillate from which they are extracted by low-boiling solvents such as ether or light petroleum. This method has a disadvantage that some of the constituents of essential oils, such as esters, are hydrolysed to non or less-fragrant products during the course of steam distillation.

(ii) Solvent Extraction:- The essential oil which are sensitive to heat are extracted from the plant material with low boiling solvents such as light petroleum or ether at room temperature. Distillation of the solvent from the filtered extract under reduced pressure leaves the essential oil.

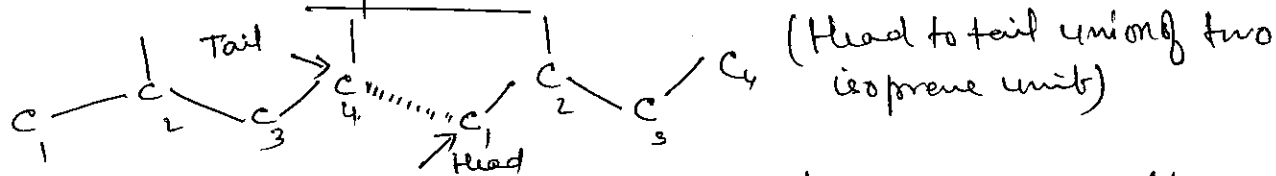
(iii) Adsorption method:- The petals of the flowers are left in contact with a fat preparation (a mixture of lard and tallow) for several days at about 30°C until the fat is saturated with the essential oil. The saturated fat is then

extracted with ethanol and the solvent (ethanol) removed under reduced pressure at 0°C. Recently activated charcoal has been used instead of fat. After isolation of essential oils, which are mixtures of a number of compounds the constituents are separated by a variety of methods depending upon their physical ~~or~~ chemical properties.

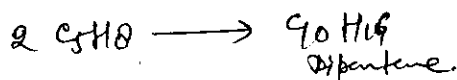
- ① Physical Methods: The most commonly used physical methods are fractional distillation and chromatography. Of these two methods, chromatography is now more in use. The essential oil is adsorbed on a column of a suitable adsorbent such as alumina or silica gel and subsequently eluted using solvents of increasing polarity. Each elute representing a class of terpenes is then further chromatographed to separate its constituents.
- ② Chemical Methods: - The actual method to be adopted depends upon the chemical nature of the constituents. For instance, an unsaturated terpene hydrocarbon such as myrcene may be separated through its crystalline adducts with hydrogen halides or nitrosyl chlorides. An alcohol, for instance, geraniol may be separated through its ester with phthalic anhydride or through phenylurethane obtained by treatment with phenylisocyanate. The aldehyde or ketonic terpenes may be separated by reaction with carbonyl reagents such as sed. bisulphite, semicarbazide or dimethylphenyl hydrazine, etc. The terpene is then regenerated by hydrolysis of the products.

### Isoprene Rules: - OR Structural features!

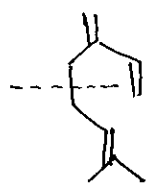
The observation that almost all terpene hydrocarbons on pyrolysis give isoprene (2-methyl-1,3-butadiene;  $C_5H_8$ ) as one of the products led to the generalization that the carbon skeletons of terpenes are divisible into isoprene units which are generally joined in a head to tail fashion, i.e. the C<sub>1</sub> position of one unit is linked to the C<sub>4</sub> position of another. This is known as special isoprene rule and that is why terpenoids are also called or known as isoprenoids:



⇒ The isoprene rule has received support from the observation that isoprene can be dimerized in the laboratory to give a widely occurring terpene, i.e. dipentene ((+)-limonene).



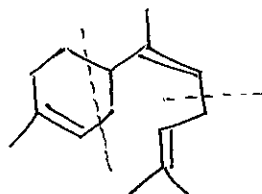
Structures of some terpenes given below showing (by broken lines) the head to tail union of two or more isoprene units,  $C_5H_8$  with or without concomitant cyclisation.



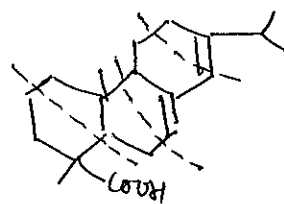
Myrcene

2 x  $C_5H_8$ 

Limonene

2 x  $C_5H_8$ 

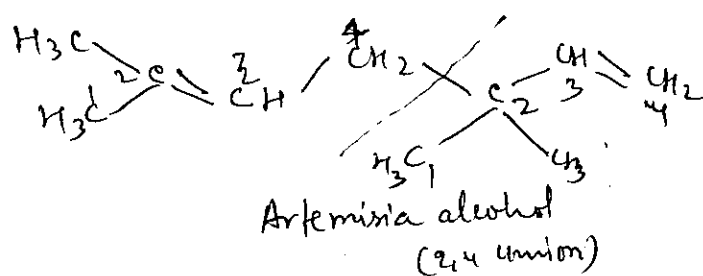
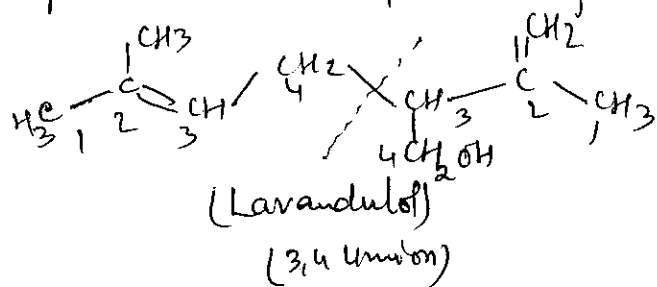
Bisabolene

3 x  $C_5H_8$ 

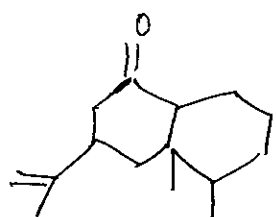
Abietic Acid

(4 x  $C_5H_8$ )

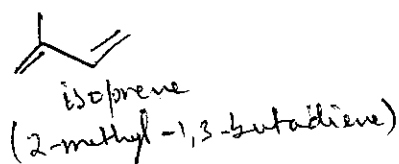
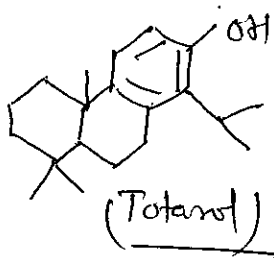
⇒ on the other hand, there are some examples of terpenoids whose carbon skeletons are divisible into isoprene units but they are not linked head to tail. Lavandulol and artemisia alcohol provide good examples. The relationship of such compounds with isoprene forms the basis of the General Isoprene rule which embraces all structures that are divisible into isoprene units irrespective of the positions of their linkage.

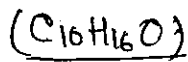


But isoprene rule is valid in most of the cases, but there are a few exceptions which violate the rule. For instance, eremophilone and totalol structures cannot be divided into isoprene units.



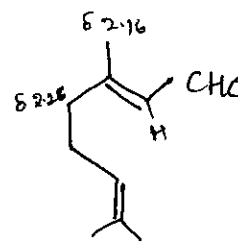
Eremophilone





CITRAL

135



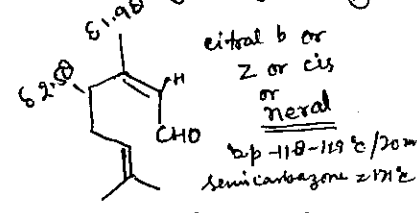
citral a or E or trans geranial  
 semicarbazone = 184°C  
 b.p = 117-119°C / 20 mm

⇒ A cyclic monoterpenoids

⇒ citral an optically inactive monoterpene aldehyde, occurs widely in lemon grass oil.

⇒ It is isolated as its crystalline mono bisulphite which on hydrolysis regenerates citral.

⇒ b.p. = 224-228°C.

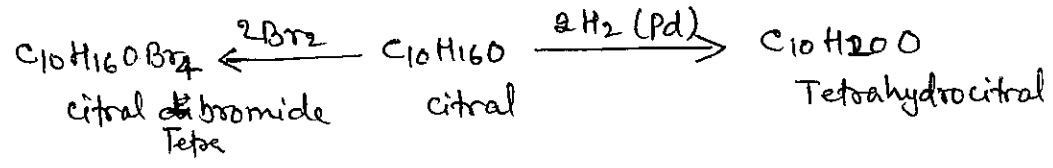


citral b or Z or cis or neral  
 b.p = 118-119°C / 20 mm  
 semicarbazone = 171°C

CONSTITUTION:-

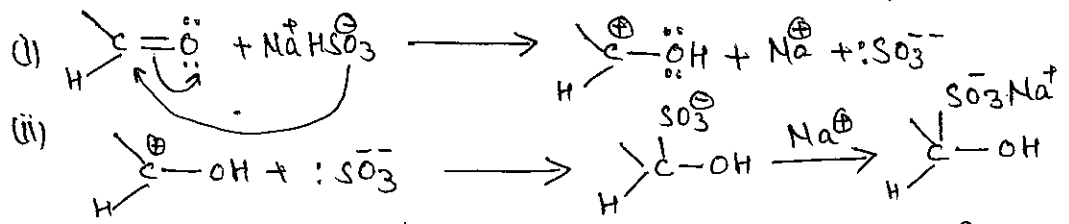
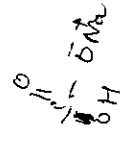
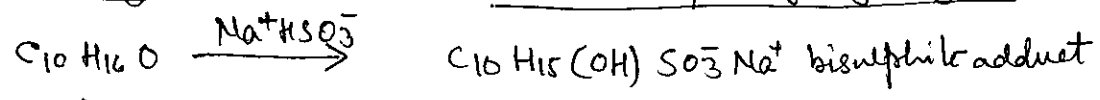
⇒ Its molecular formula is  $C_{10}H_{16}O$ , has been obtained by usual procedure.

⇒ Citral has two carbon-carbon double bond as shown by following reaction.

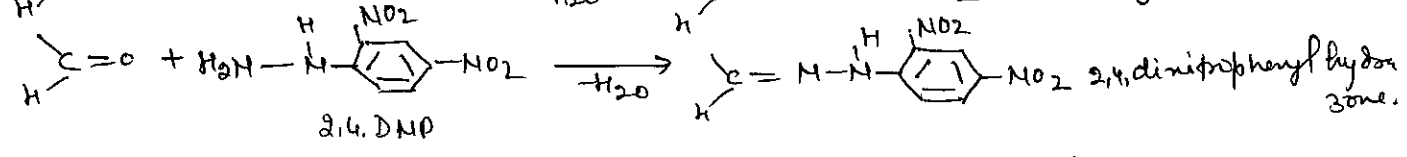
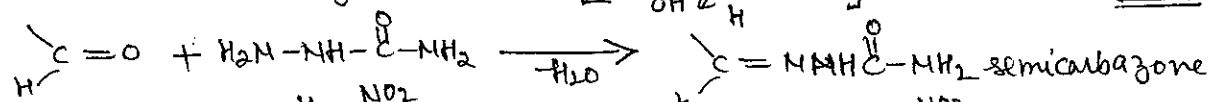
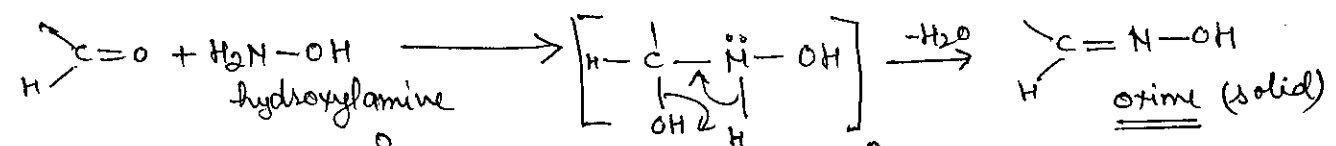


thus  $\begin{matrix} C=C \\ | \\ C=C \end{matrix}$  may be present in aldehyde

⇒ Nature of oxygen:- The oxygen present in citral is in the form of a carbonyl group since it forms a bisulphite derivative, an oxime, a semicarbazone and a red 2,4 dinitrophenylhydrazone.



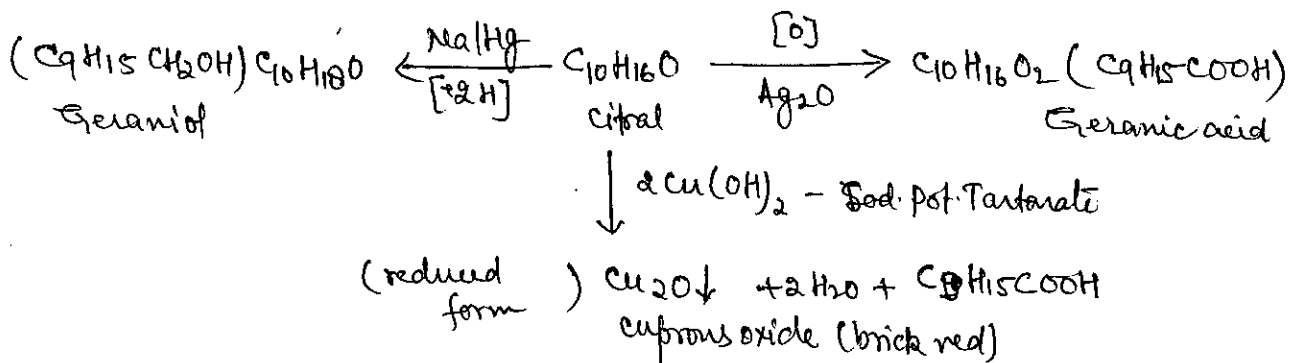
(C is more nucleophilic than O, a C-S bond is formed in the adduct)



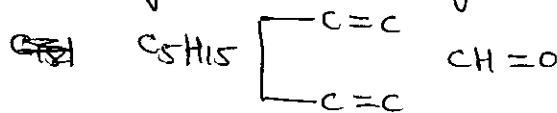
Thus these reactions suggests that oxygen is as in carbonyl group

## Nature of Carbonyl group (Aldehydic or Ketonic)

⇒ It was found that carbonyl group is in the form of aldehyde because it reduces Fehling solution, and is oxidised into geranic acid by  $\text{Ag}_2\text{O}$  and reduced to geraniol, a primary alcohol with a sodium amalgam. Both geranic acid and geraniol have the same no. of carbon atom as citral have. Thus carbonyl group is in the form of ~~aldehyde~~ aldehyde.



⇒ Thus on the basis of two carbon-carbon double bond and a aldehydic group is present in the ~~ring~~ citral, it may be written as:

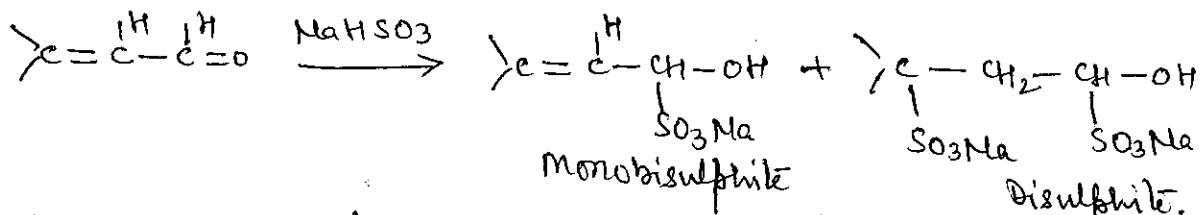


⇒ Complete reduction in the presence of catalyst it gives  $\text{C}_{10}\text{H}_{22}$  which corresponds to an alicyclic structure. Thus citral is alicyclic.

### POSITION OF DOUBLE BOND:

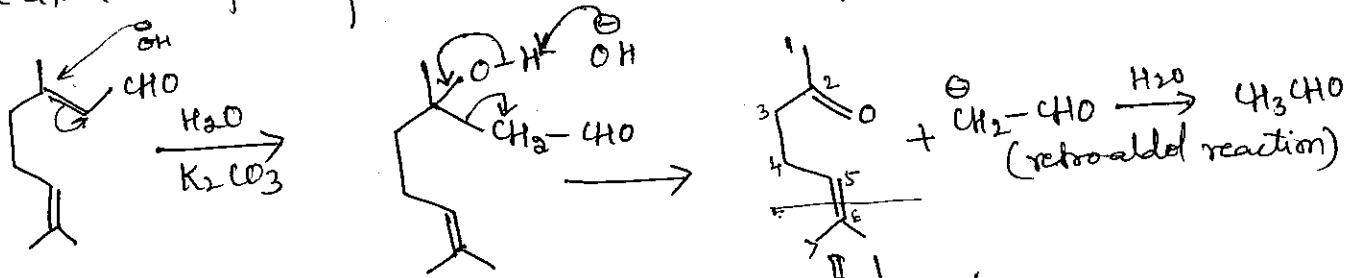
⇒ One of the two double bonds is present as an isopropylidene moiety as is evident by the appearance of an absorption band in IR at  $\sim 800\text{cm}^{-1}$ .

⇒ Citral gives both mono and di bisulphite addition compounds which indicates that one of the double bonds is conjugated with the carbonyl group, and this is confirmed by its UV spectrum ( $\lambda_{\text{max}} 238\text{nm}$ ).



# Further the  $\alpha, \beta$  nature of one of the double bonds is proved by prolonged heating with aq.  $\text{K}_2\text{CO}_3$  with citral undergoes hydration and retroaldol reaction (a reaction characteristic of  $\alpha, \beta$  unsaturated carbonyl system) to give 6-methyl-hept-5-ene-2-one (II) which on ozonolysis yields acetone and acrylic acid.

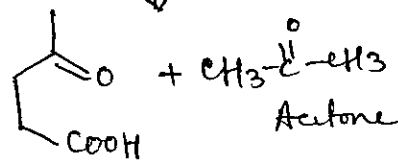
If the citral has following structure then these products can be rationalised



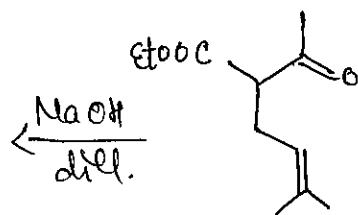
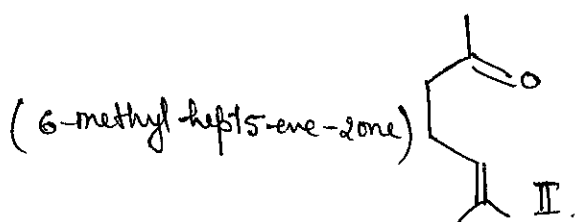
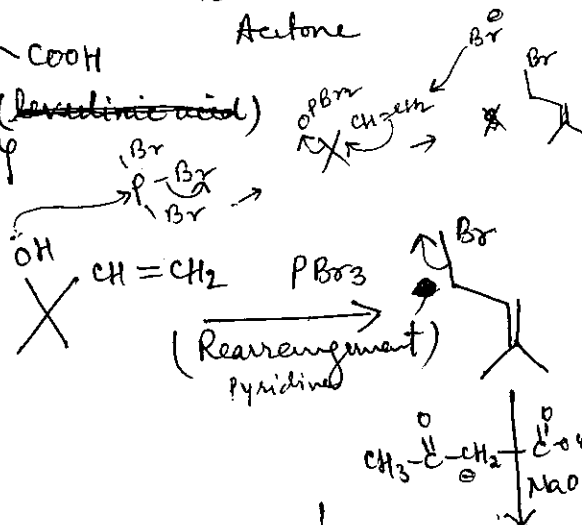
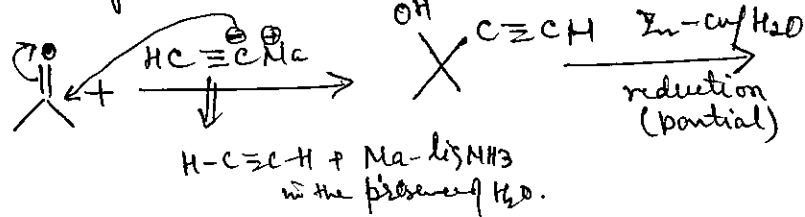
Formation of these product suggests that it contains a  $\alpha, \beta$  unsaturated double bond.

(acrylic acid)

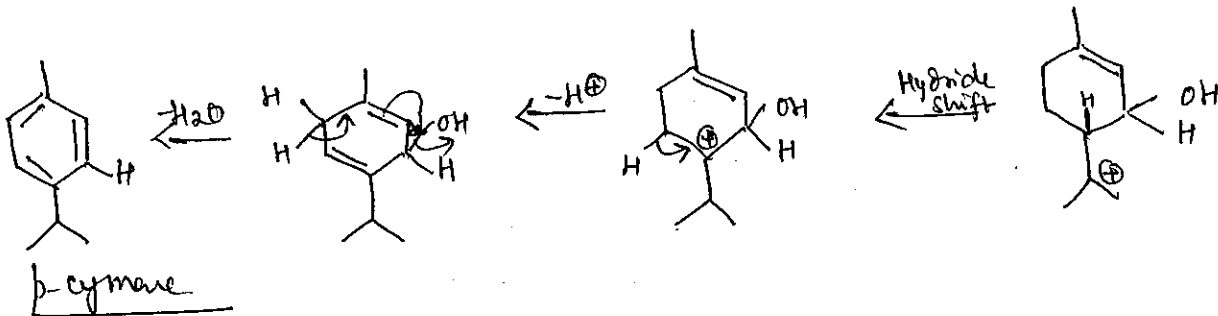
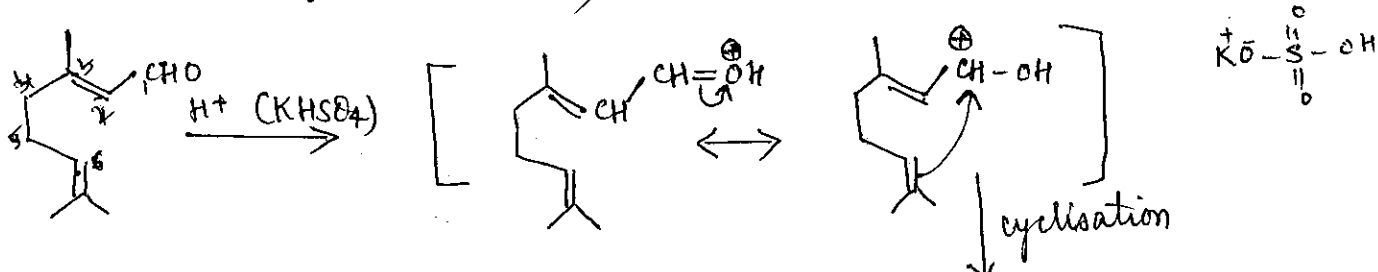
$\text{O}_3$  (ozone)



$\Rightarrow$  structure of compound II can be proved by its synthesis

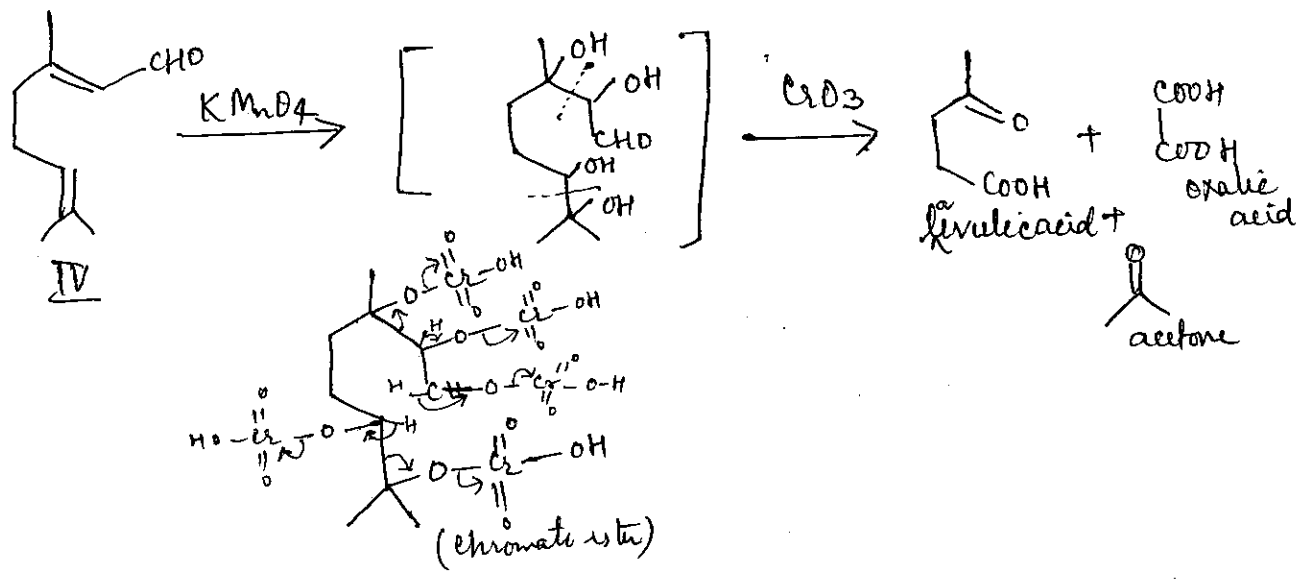


$\Rightarrow$  on heating with  $\text{KHSD}_4$  citral forms  $\beta$ -cymene, a compound of known structure. Thus the relative position of the methyl group and the isopropylidene moiety are fixed in citral (at the 3rd)





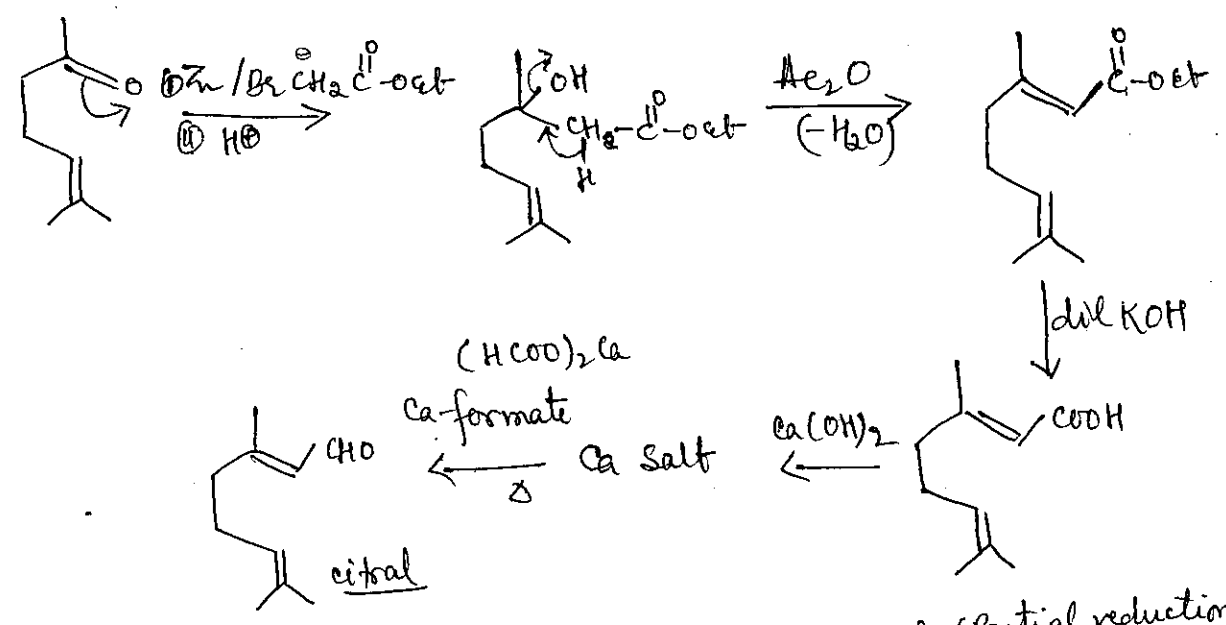
⇒ The structure arrived from the above experiments is corroborated by oxidation of citral with alkaline KMnO<sub>4</sub> followed by chromic acid, when it gives acetone, oxalic acid and levulic acid.



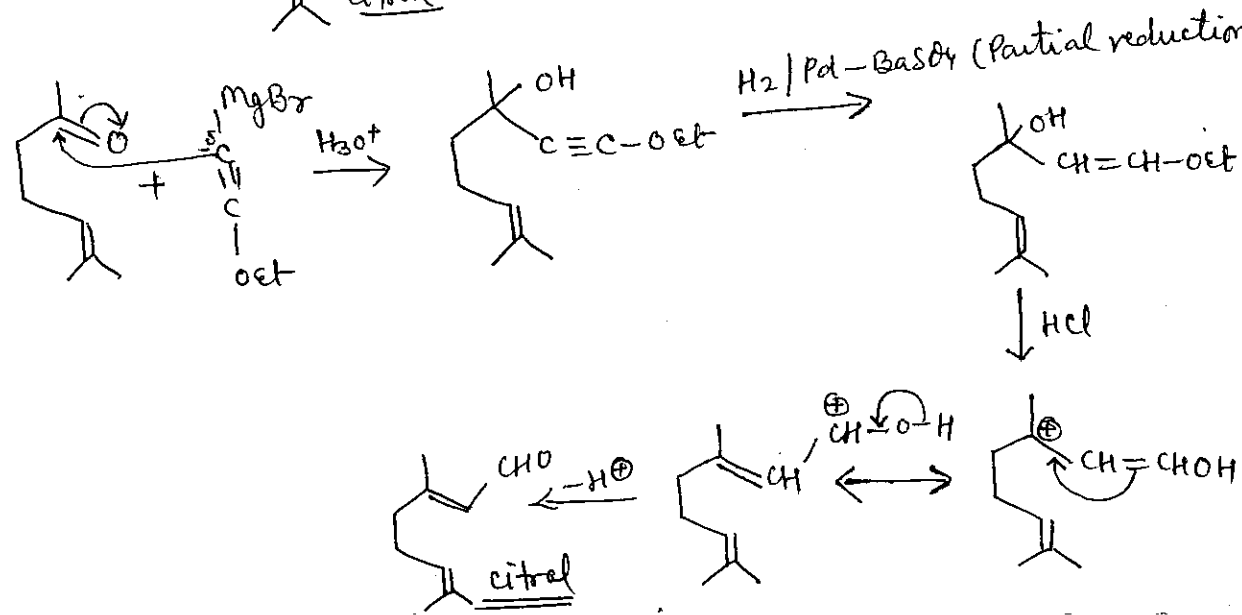
The above structure can also be explained by synthesis of citral

Synthesis:-

Method 1:-

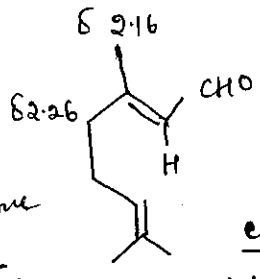


Method 2 :-



cis-trans isomerism in citral! Since citral has the double bonds and one double bond has different substituent at each end, citral shows cis-trans isomerism. citral a and citral b (opposite side) occur in nature.

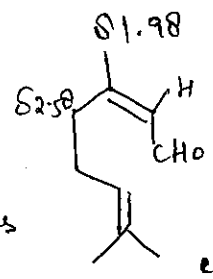
Semicarbazone derivative  
164°C



geraniol  
or

citral a or E or trans  
b-p 117-119°C / 20mm

semicarbazone derivative  
171°C

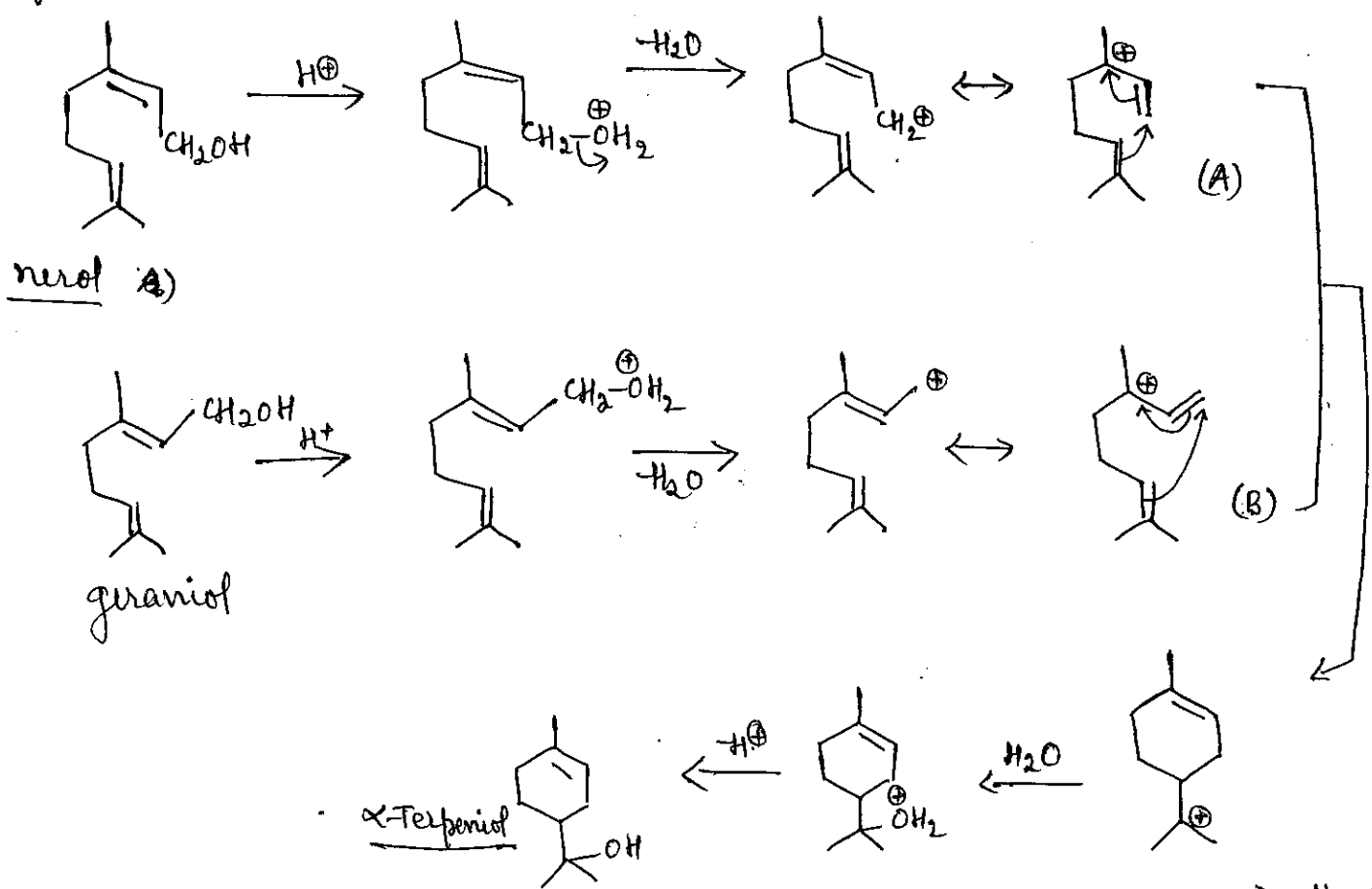


b-p = 118-119°C / 20mm

citral b. or Z or cis or neral

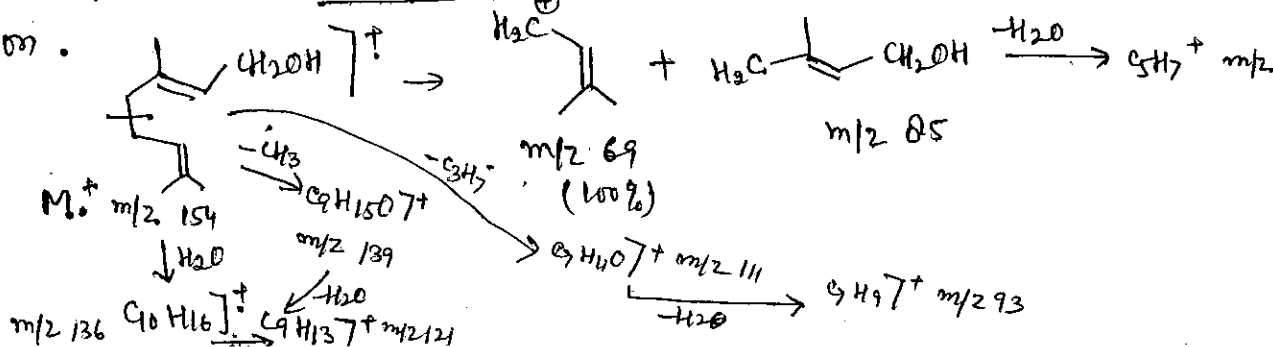
They can not be separated easily by physical methods, but their semicarbazone derivatives can be separated.

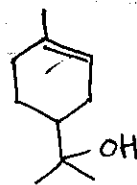
configuration of geraniol relative to nerol has been further proved by the fact that nerol undergoes acid-catalysed cyclisation to a  $\alpha$ -terpineol nine times faster than geraniol. The large difference in the rates is explained by proximity effect. In the intermediate carbocation (A), the carbon atom bearing the positive charge and carbon-carbon double bond involved in the cyclisation are sufficiently close. On the other hand, in the case of geraniol there is a loop before the intermediate carbocation B can assume the configuration B. Thus nerol must have the  $\text{CH}_2\text{OH}$  group cis to the main chain of the molecule.



Synthesis and other structural features can be proved as given in the citrus

Mass spectrum :- The mass spectrum of geraniol (and nerol) shows the molecular ion peak at  $m/z$  154. The base peak at  $m/z$  69 ( $\text{C}_7\text{H}_9^+$ ) is attributed to ready allylic fission.





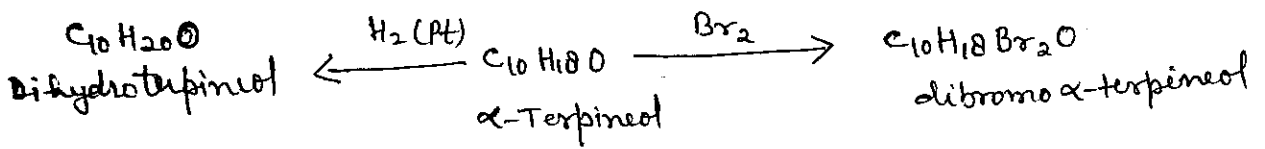
⇒ α-Terpineol (m.p 35°C), an optically-active monoterpenic alcohol, occurs naturally both as (+) forms in oils of petit grain and neroli and as (-) form in camphor and cajuput oils.

⇒ It is a solid

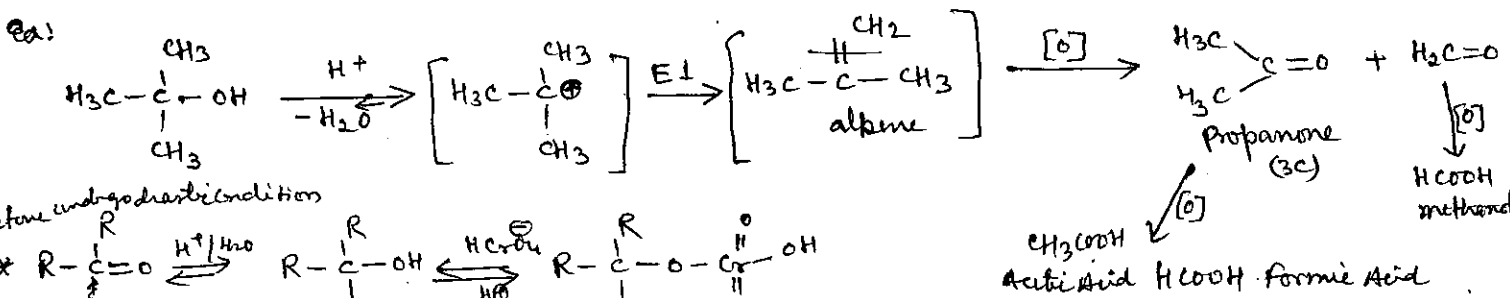
Constitution and Structure:-

⇒ The molecular formula, determined by the usual methods, is C<sub>10</sub>H<sub>18</sub>O.

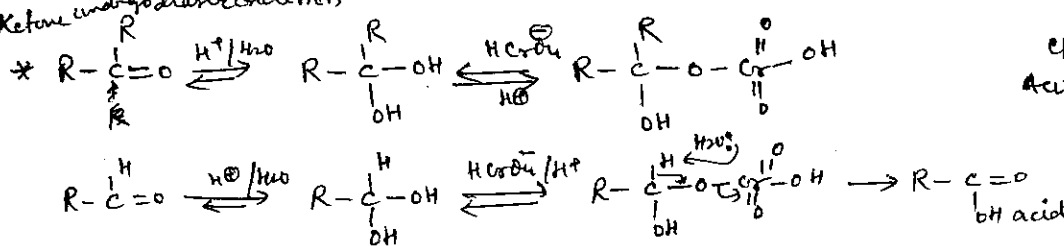
⇒ It has only one double bond because only one mole<sup>cul</sup> of bromine and hydrogen are adsorbed during bromination and hydrogenation for each α-terpineol.



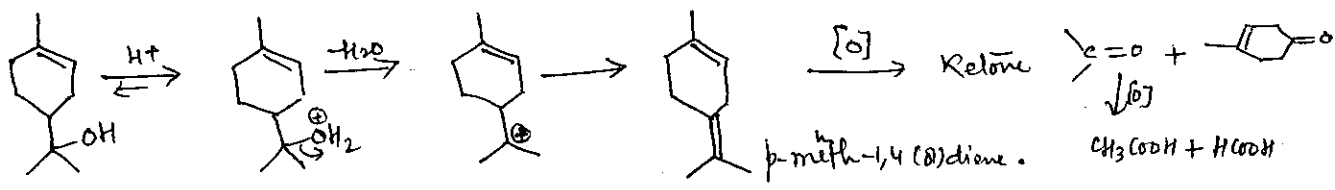
⇒ The Nature of oxygen: was found as a tertiary alcoholic group because it does not give aldehyde or ketone on mild oxidation. Because if primary alcoholic group, then, on oxidation it gives aldehydes with the same no. of carbon which on further oxidation give will give a carboxylic acid with the same no. of carbon, but it is <sup>not</sup> actually found with α-Terpineol. If secondary it would give a ketone with the same no. of carbon atom as a original alcohol. But it is also not true with the α-Terpineol. Thus, when α-Terpineol was oxidised under acidic condition (drastic) formation of alkene will take place with same no. of carbon ~~which~~ The alkene will go further oxidation and produces a ketone and other derivatives with a lesser no. of carbon atom than parent alcohol.



Ketone undergo drastic condition



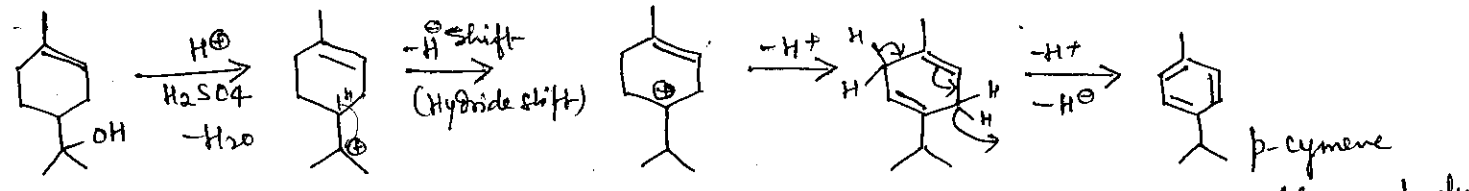
Mechanism of oxidation on t-OH



which corresponds to

⇒ If it is fully saturated hydrocarbon, then ~~it follows~~ the  $C_{10}H_{20}$ , which corresponds to monocyclic monoterpene alcohol (C<sub>10</sub>H<sub>18</sub>O)

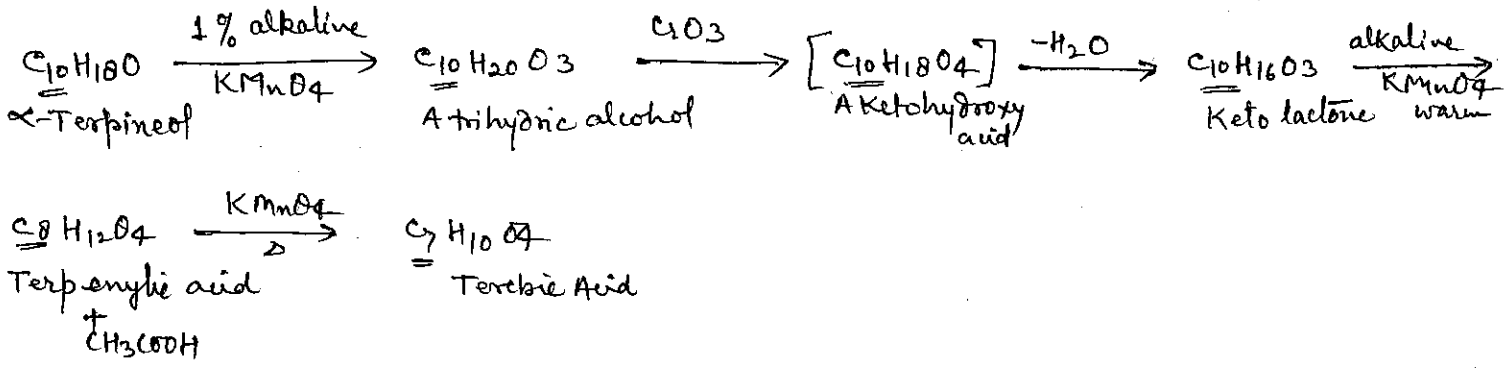
⇒ when treated with concentrated sulfuric acid, α-terpineol gives some p-cymene which indicates that it belongs to p-menthane group.



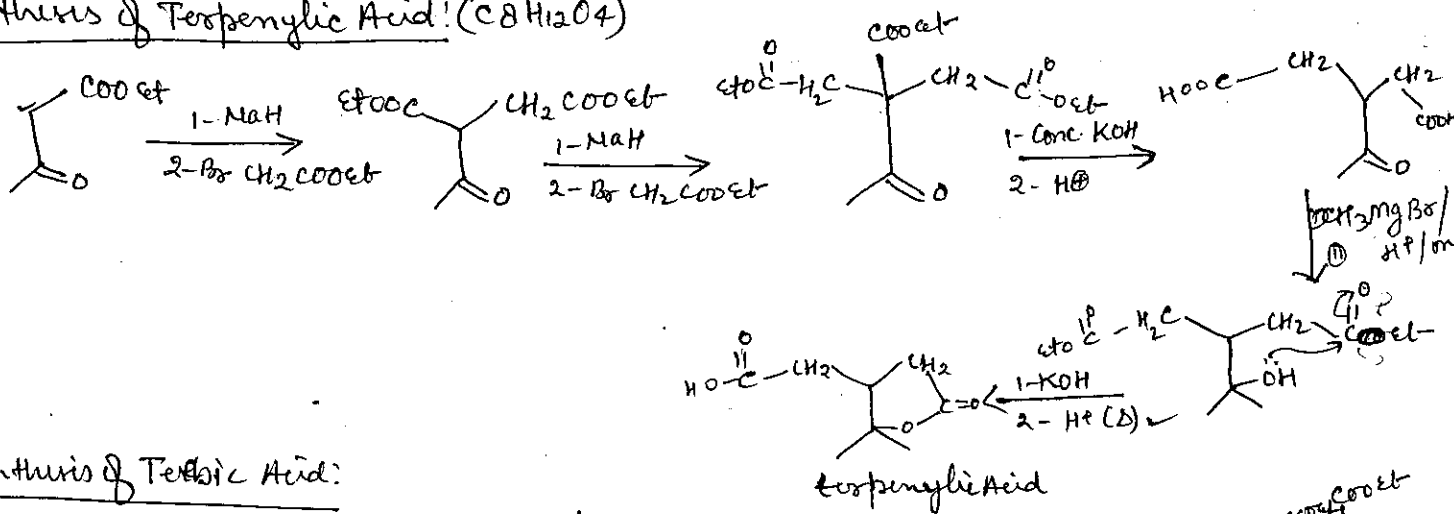
Thus we can say that α-Terpineol is probably p-menthane with one double bond and a tertiary alcoholic group.

(few molecules) traces.

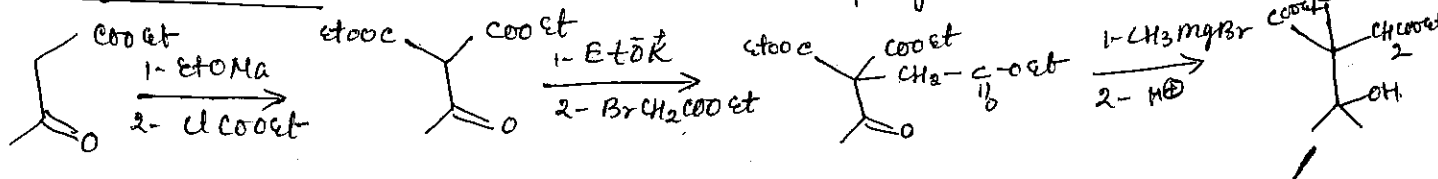
The following sequence of oxidation experiments proves the structure of α-Terpineol.



Synthesis of Terpenylic Acid! (C<sub>8</sub>H<sub>12</sub>O<sub>4</sub>)



Synthesis of Terebic Acid:



DBE Rule: (A)  $DBE = x + 1 - \frac{y}{2}$  if  $C_xH_y$

$C_6H_6 = 6 + 1 - \frac{6}{2} = 4$   
 $\Delta_3 = 1, 1, 2$

② divalent atom, then (S, O, etc) ignore it,  $C_3H_8O_2 = 3 + 1 - \frac{8}{2} = 0$

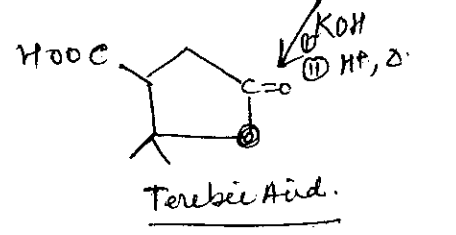
③ If halogens are there, then  $C_xH_yH_z = x + 1 - \frac{y+z}{2}$ , like  $C_9H_7Br$

$10 + 1 - \frac{7+1}{2} = 11 - 4 = 7$

④ trivalent atom like N, P, then it must be subtracted.

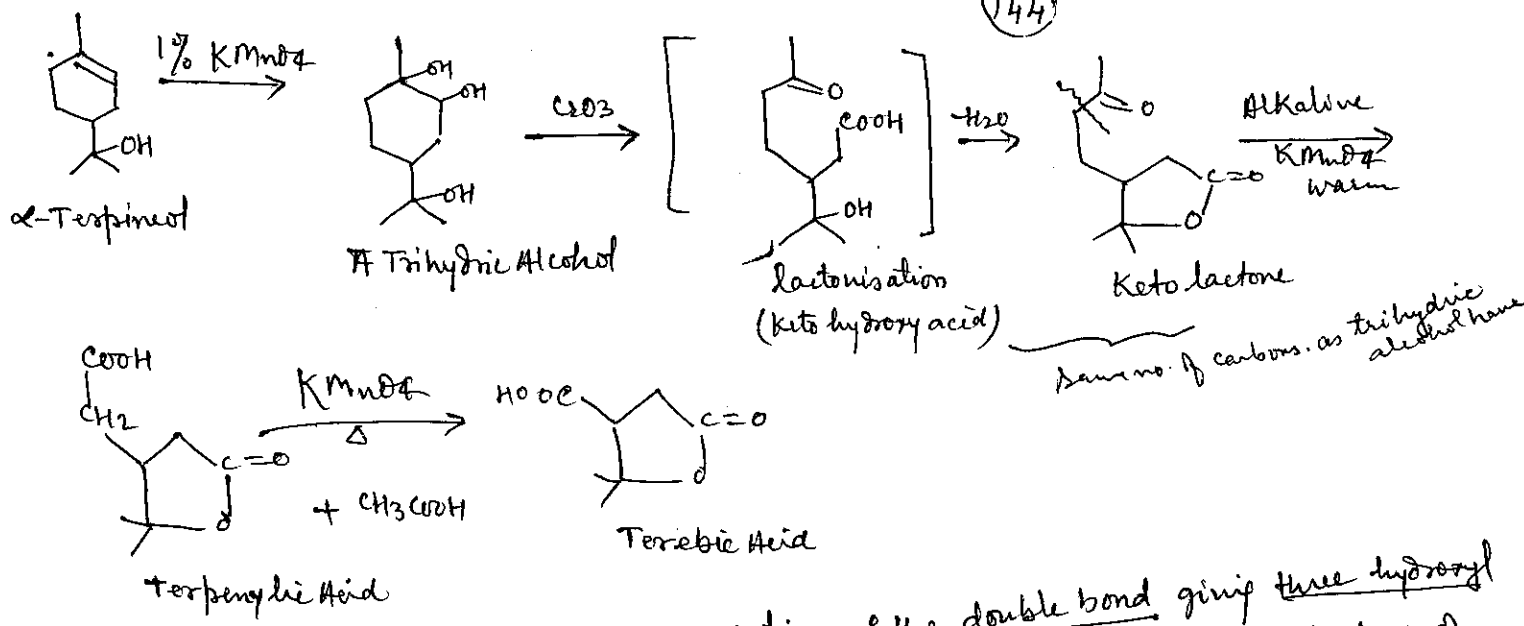
$x + 1 - \frac{y-z}{2}$ ,  $C_{12}H_{12}H_2 = 12 + 1 - \frac{12-2}{2} = 13 - 5 = 8$

No S, N atom present odd, molecular weight  $\frac{m}{2}$  always will odd.



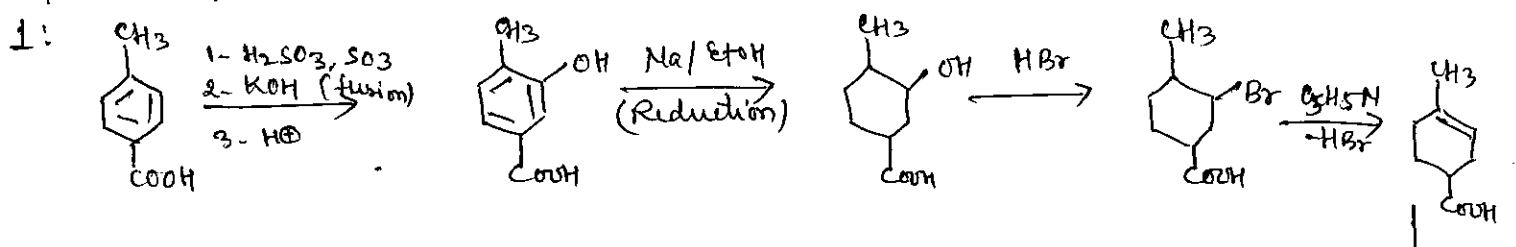
Thus all the transformation can be explained on the basis of following structure of  $\alpha$ -Terpineol.

(144)

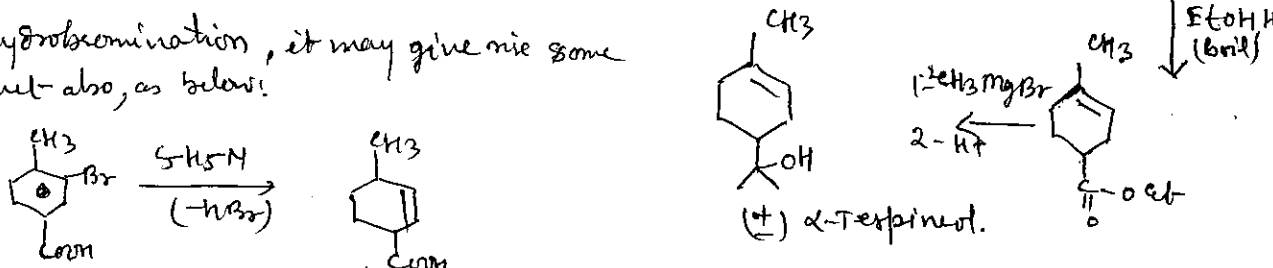


A Trihydroxy alcohol is a product of hydroxylation of the double bond giving three hydroxyl groups including the original one. This on further oxidation with  $CrO_3$  gives a lactone of monocarboxylic acid and since it is readily formed from keto hydroxy acid, it is most probably a  $\gamma$ -lactone. Since keto hydroxy acid and keto lactone have the same no. of carbon atoms as trihydroxy alcohol have. Thus fissioned double bond must belong to the ring. The formation of acetic acid on oxidation of keto lactone with warm alkaline  $KMnO_4$  indicates that the keto lactone is a methyl ketone and terpenylic acid is the lactone of monohydroxy dicarboxylic acid. Further, oxidation of terpenylic acid gives its lower homologue terebic acid which is also a lactone of monohydroxy dicarboxylic acid.

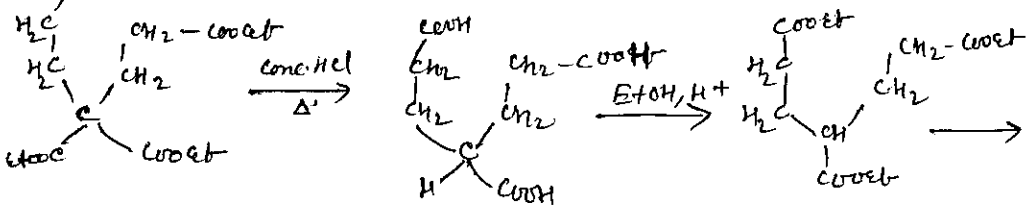
Synthesis of  $\alpha$ -Terpineol will prove its structure:

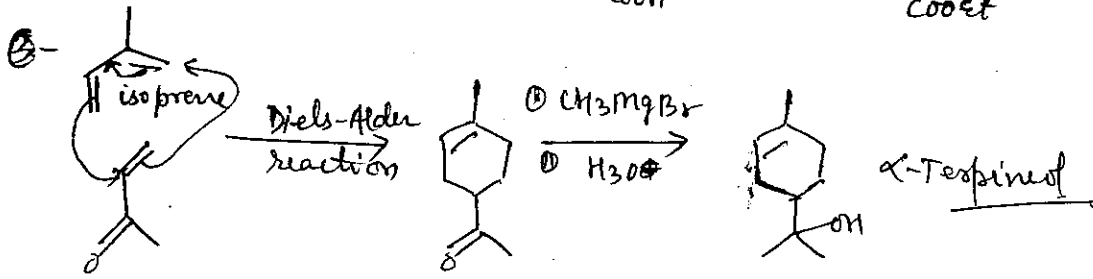
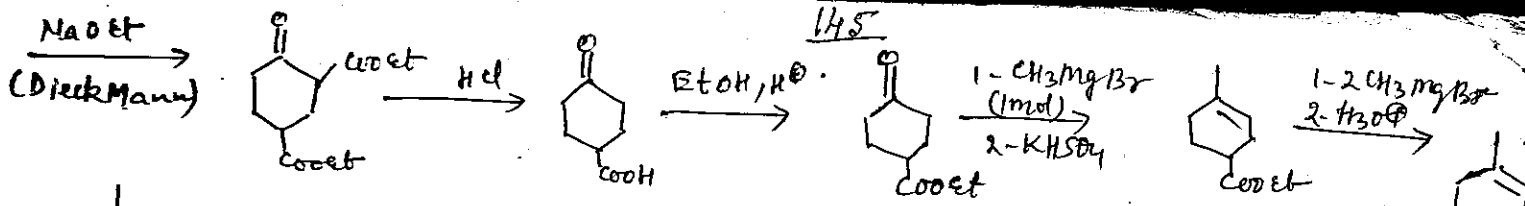


Since on dehydrobromination, it may give rise some other product also, as below:



2. from Alicyclic compd.  
1.  $KOEt$   
2.  $CH_2CH_2COOEt$   
in two steps





methyl vinyl ketone  
 In this method also a ~~another~~ possibility of another product.

