

II.M.Sc.,CHEMISTRY
ORGANIC CHEMISTRY -III
SEMESTER-III

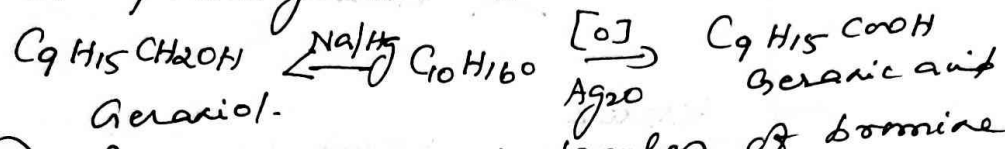
UNITS – 4
TERPENES

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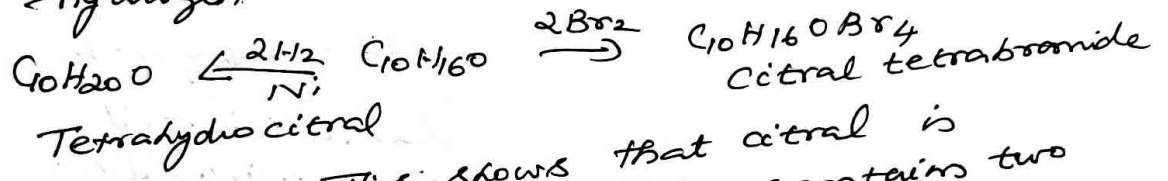
TERPENES

STRUCTURAL DETERMINATION OF CITRAL:-

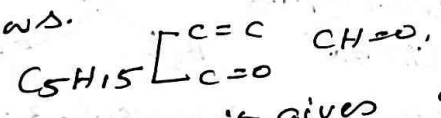
- 1. Molecular formula of citral is $C_{10}H_{16}O$
- 2. It contains an aldehyde group since it
 - (i) forms bisulphite adduct
 - (ii) Semicarbazone & osime
 - (iii) reduces Fehling's reagent
 - (iv) oxidised by moist Ag_2O to geranic acid containing same number of carbon atoms.
 - (v) reduced by sodium amalgam to geraniol, a primary alcohol.



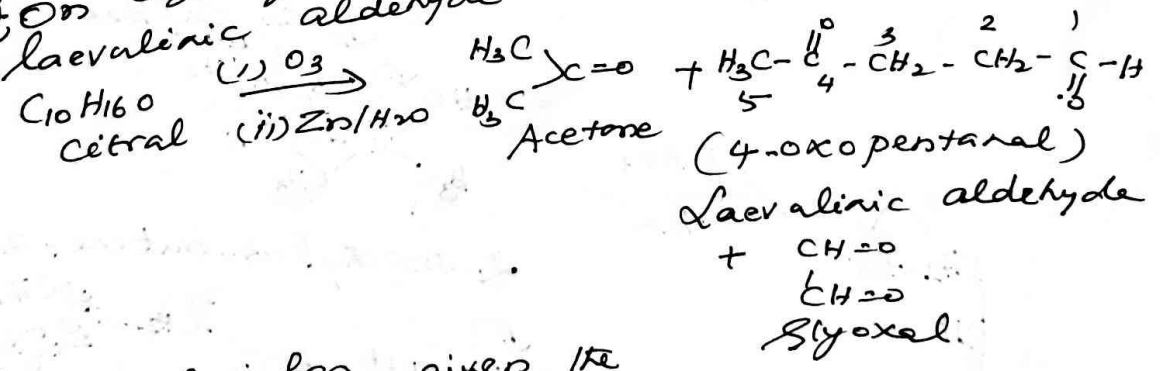
- 3. It adds two molecules of bromine and hydrogen.



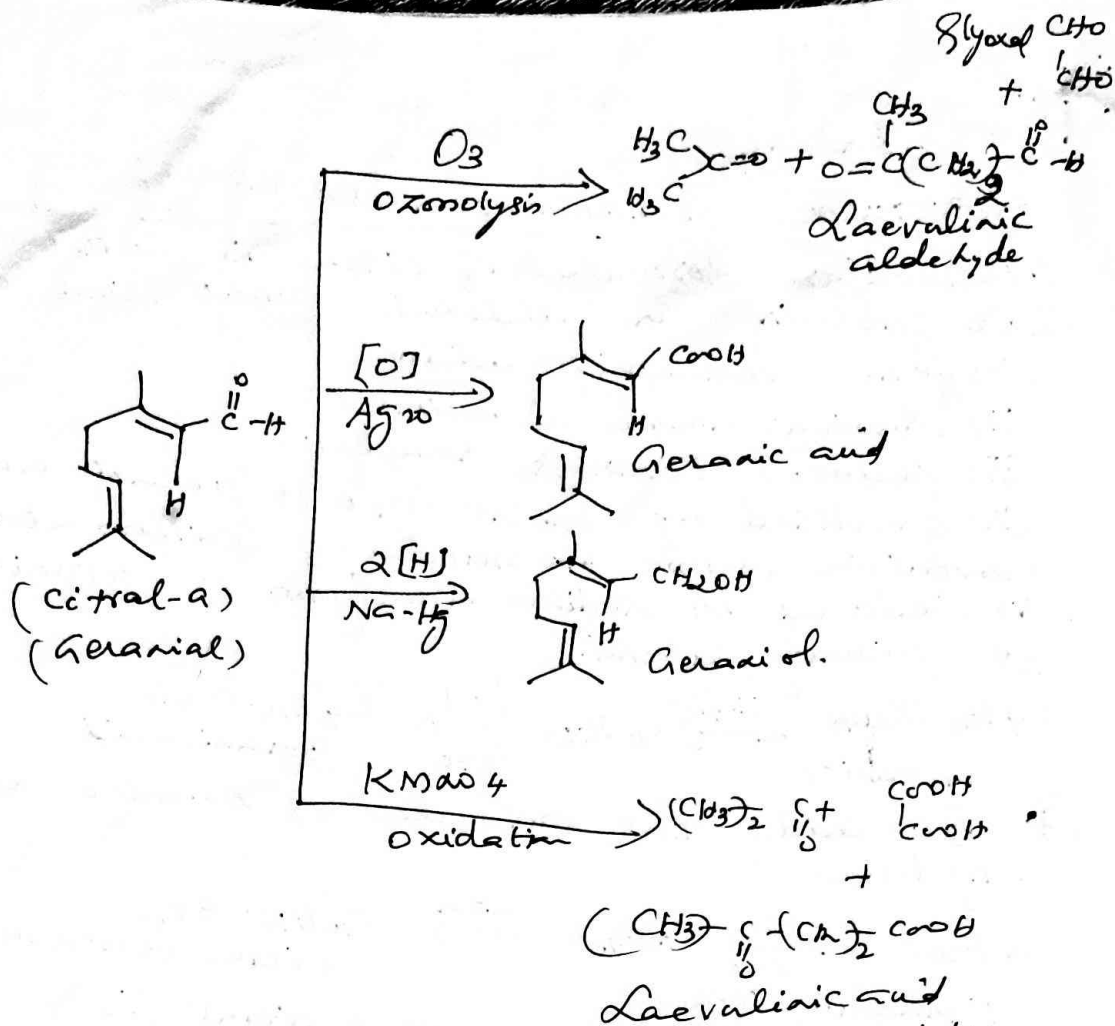
This shows that citral is a di-unsaturated aldehyde (contains two double bonds) and it can be split up as follows.



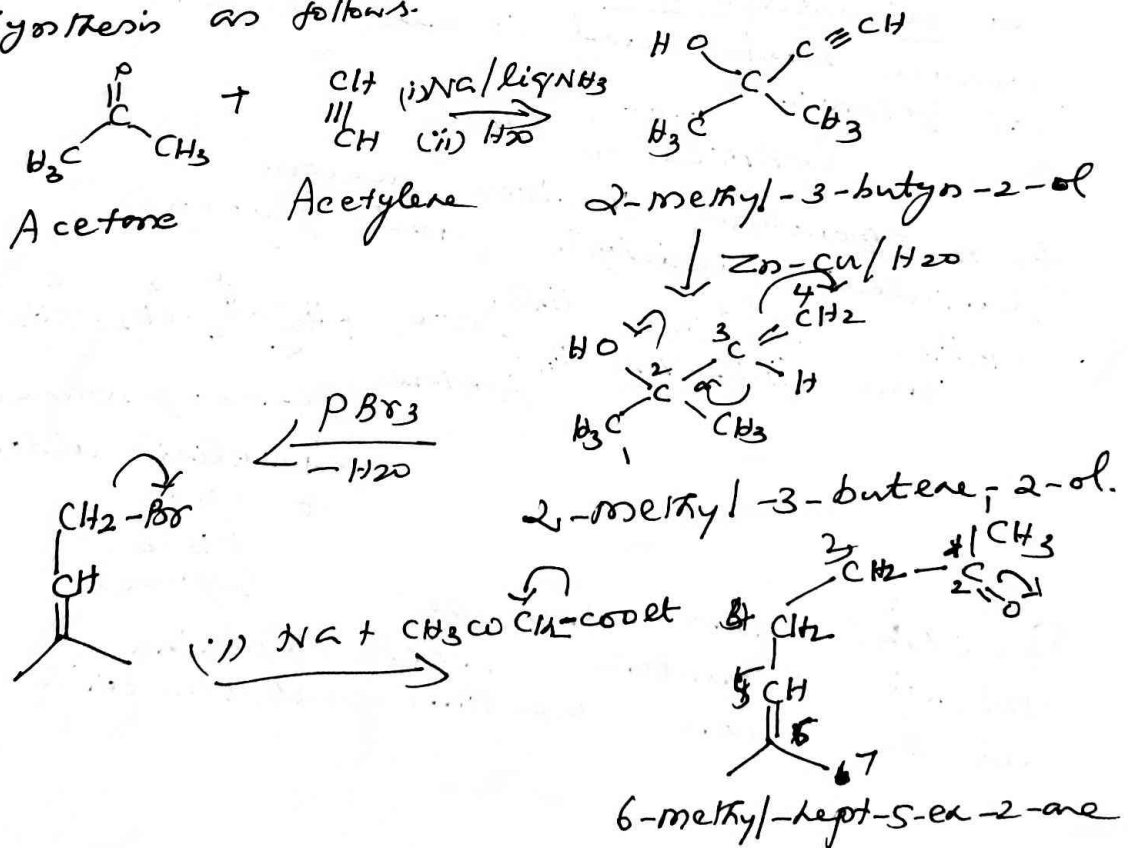
- 4. On ozonolysis, it gives acetone, laevulinic aldehyde and glyoxal.

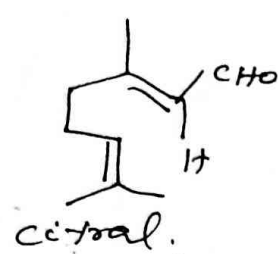
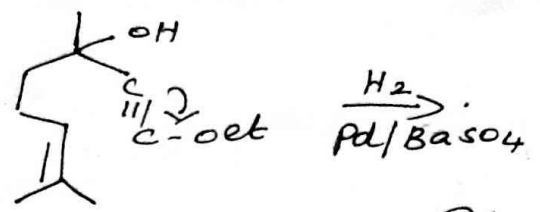
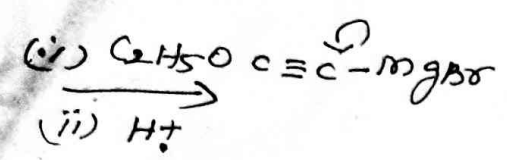


- 5. Citral has given the following structure which explains all the above reactions satisfactorily.

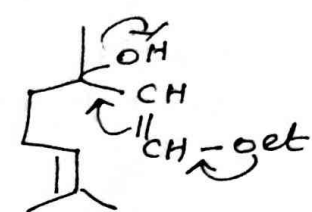


The above structure is confirmed by synthesis as follows.



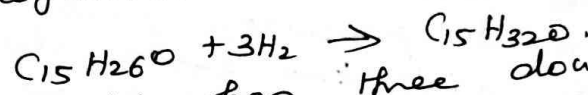


H^+
-H₂O
Allylic
Rearrangement



FARNESOL:-

- (i) Its molecular formula is $C_{15}H_{26}O$
- (ii) On hydrogenation, it takes up 3 moles of hydrogen to form fully saturated compound hexahydrofarnesol.

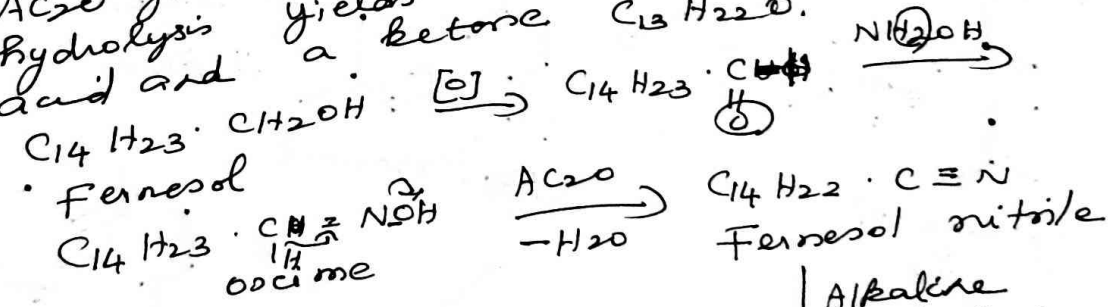


So it has three double bonds.

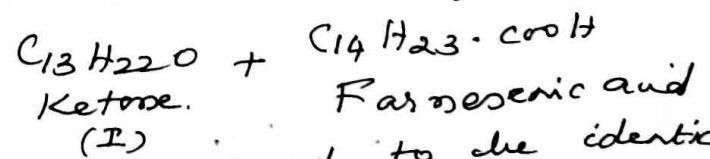
- (iii) Farnesol on oxidation gives an aldehyde known as farnesal and so primary alcoholic group is present.

So it is a saturated hydrocarbon and hence it is acyclic.

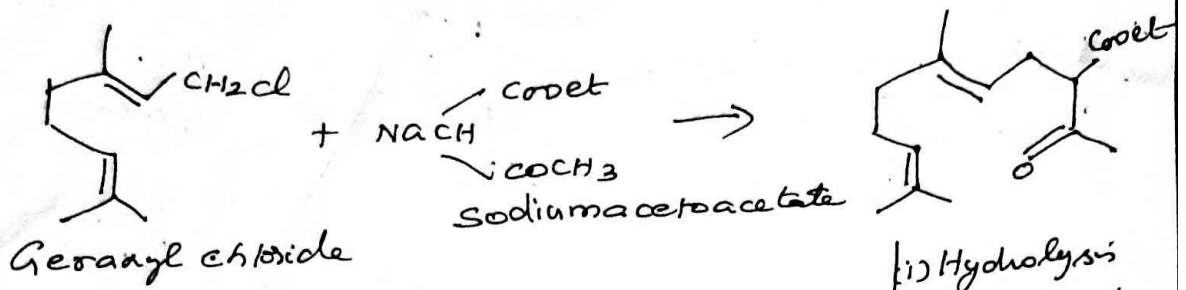
- (iv) Complete structure is arrived by the fact that farnesol on dehydration with Ac_2O gives nitrile which on alkaline hydrolysis yields a mixture of farnesenic acid and a ketone $C_{13}H_{22}O$.



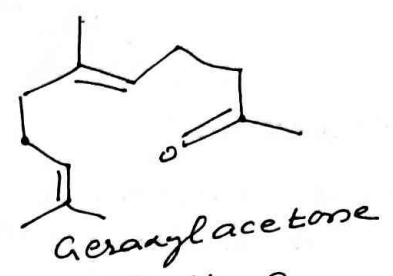
Alkaline Hydrolysis



(v) The ketone (I) was found to be identical with α, β -dihydropseudoionone (geranylacetone) obtained from geranyl chloride and sodium acetoacetate.

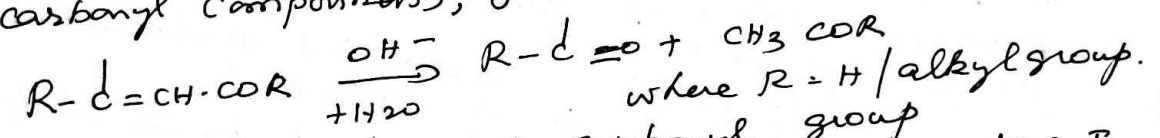


(i) Hydrolysis
(ii) Decarboxylation

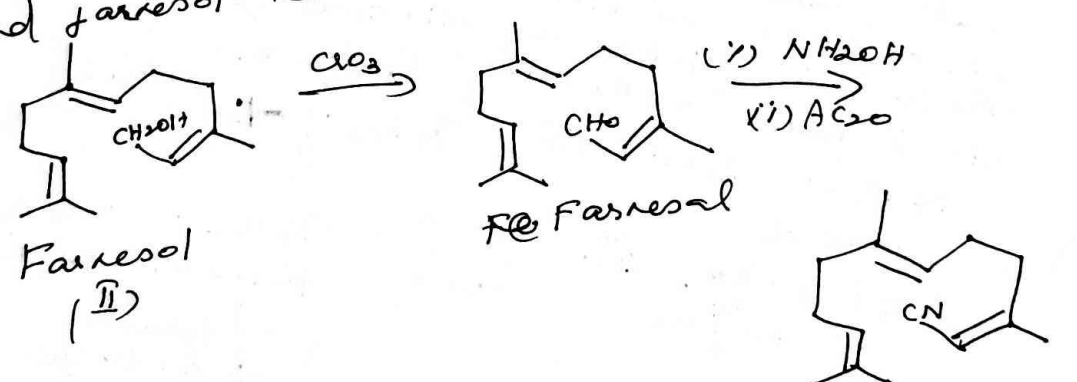


$C_{13}H_{22}O$

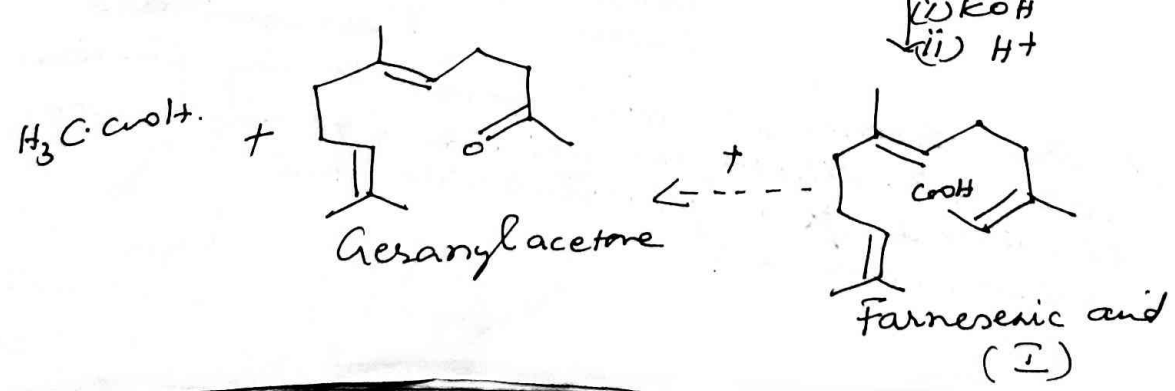
(vi) Formation of Ketone
 $C_{13}H_{22}O$ from its precursor farnesone nitrile or farnesic acid, two carbon atoms are lost (a reaction characteristic of α, β -unsaturated carbonyl compounds), farnesic acid must have



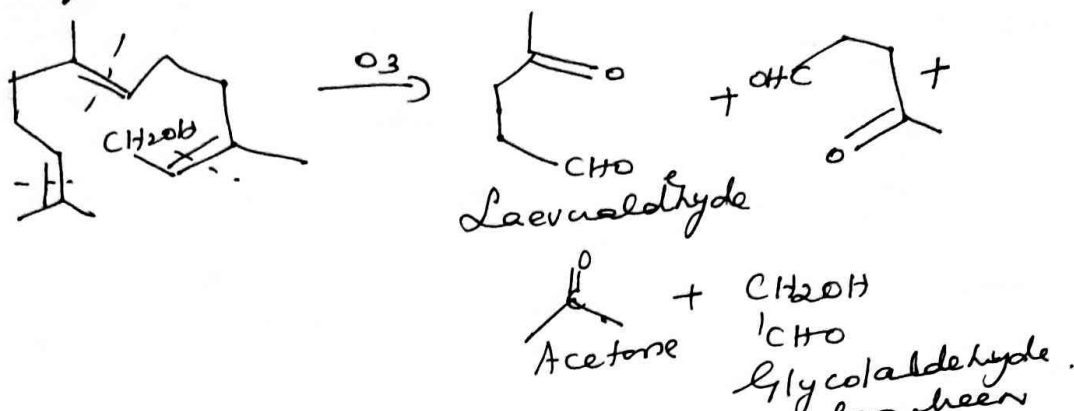
an α, β -unsaturated carbonyl group
 (i.e) farnesic acid should have structure I and farnesol should have structure II.



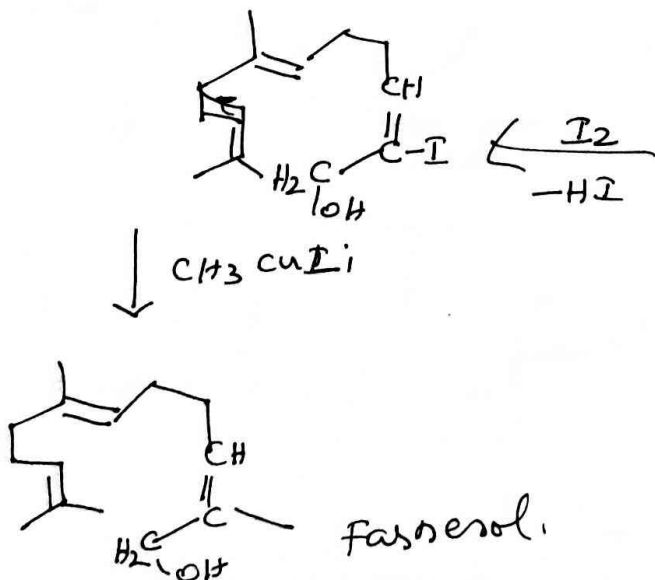
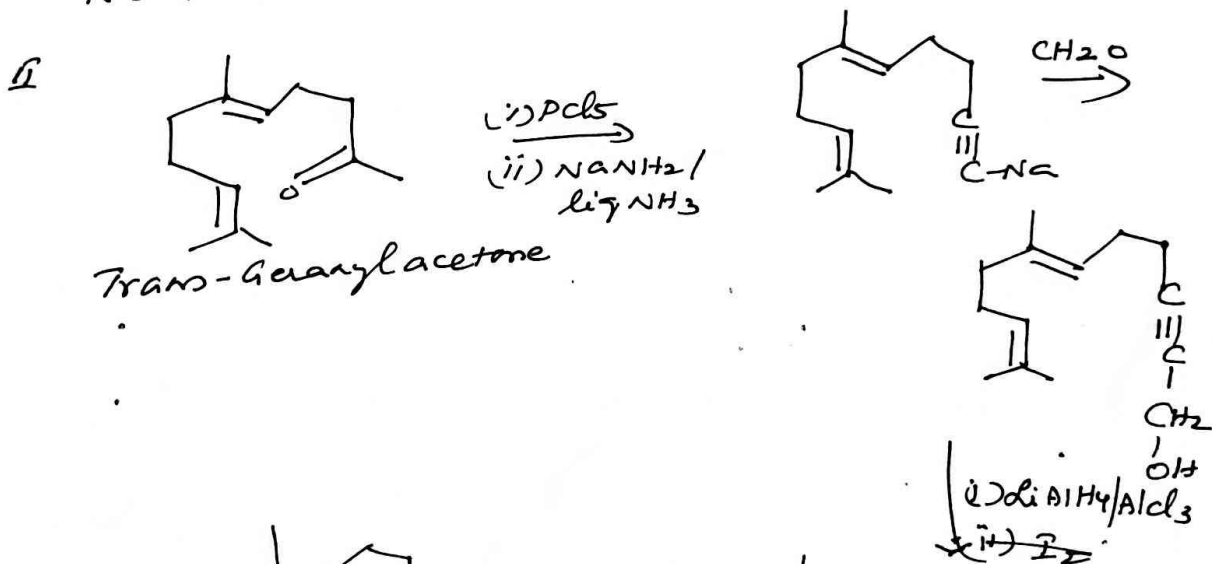
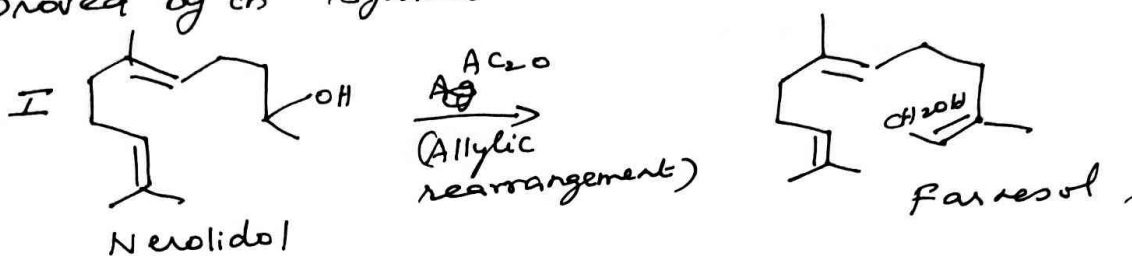
(i) KOH
(ii) H+



(vii) The structure of farnesol is confirmed by its ozonolysis to acetone, laevualdehyde and glycolaldehyde. (3)



(viii) Finally the structure of farnesol has been proved by its synthesis.



NATURAL PRODUCTS:

TERPENES:

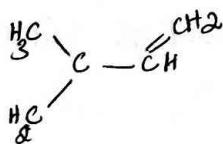
Terpenes are a class of compounds that give plants their odour, flavour and in some cases colour. They occur widely in the leaves and fruits of higher plants as conifers, citrus and eucalyptus.

When the plant source is distilled with steam, the oily materials so obtained are called essential oils (essential parts of oils). The essential oils are generally composed of mixture of either oils are generally composed of mixture of either the hydrocarbons (polyenes) having general formula $(C_5H_8)_n$, or their oxygenated derivatives (alcohols, aldehyde, ketones), known as Terpenes or Terpenoids.

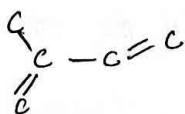
ISOPRENE RULE:

OTTO WALLACH gave the so-called isoprene rule from a study of the molecular structure of a large number of the known terpenes. It states that: the molecules of all terpenes are constructed of two or more isoprene ($iso-C_5$) units, usually joined in a head to tail fashion.

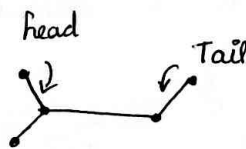
Isoprene is 2-methyl-1,3-butadiene may be represented as,



Isoprene



condensed formula



Isoprene skeleton

CLASSIFICATION OF TERPENES:

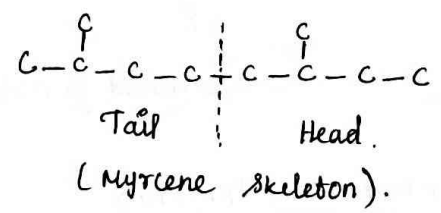
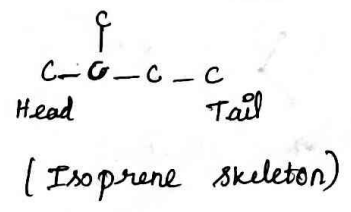
Terpenes are classified according to the value of n in the molecular formula of the most of the terpenoids.

	<u>Value of n</u>	<u>Formula</u>	<u>class.</u>
i)	2	$C_{10}H_{16}$	Monoterpenoids
ii)	3	$C_{15}H_{24}$	Sesquiterpenoids
iii)	4	$C_{20}H_{32}$	Diterpenoids
iv)	5	$C_{25}H_{40}$	Triterpenoids
v)	6	$C_{30}H_{48}$	Tetra terpenoids
vi)	8	$C_{40}H_{64}$	Tetra terpenoids
vii)	>8	$(C_5H_8)_n$	polyterpenoids.

Monoterpenoids are classified into three types

- i) Open-chain or Acyclic monoterpenoids containing three double bonds
- ii) Monocyclic monoterpenoids containing one carbon ring and two double bonds
- iii) Bicyclic monoterpenoids containing two carbon rings and one double bond.

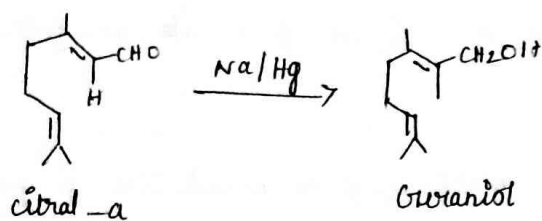
According to Ingold, molecules of terpenoids are built up of Isoprene units joined head to tail. The branched end of the Isoprene molecule is termed the head and the other end is called the tail.



This divisibility of terpenoids into Isoprene units and their head to tail union is referred to as Ingold's special Isoprene rule.

(* represent the carbon atoms involved in ring closure). The cis structure of geraniol is confirmed by NMR studies.

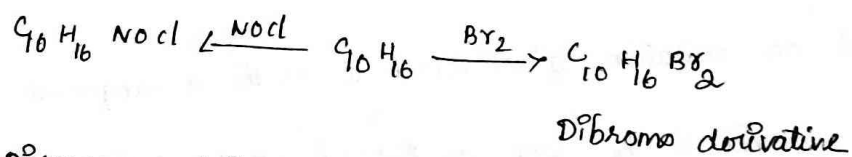
(b) The structure of geraniol is confirmed by the following synthesis



STRUCTURAL ELUCIDATION OF α -PINENE, $C_{10}H_{16}$

α -pinene is present in all turpentine oils in (+) and (-) forms. On steam distillation, this oil gives α -pinene. or with light petroleum at 320 K, it is separated.

- (1) From elemental analysis and molecular weight determination, the molecular formula is got as $C_{10}H_{16}$.
- (2) With one mole Br_2 it gives dibromoderivative and with one mole $NOCl$, it gives addition product as follows.

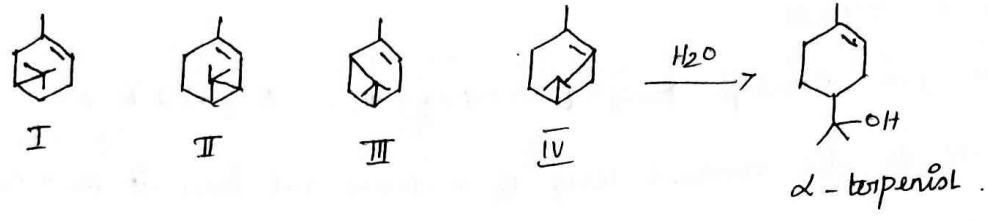


So, α -pinene contains one double bond.

(3) Its parent hydrocarbon has molecular formula $C_{10}H_{18}$. This matches with the general formula C_nH_{2n-2} and so this compound is bicyclic in nature.

(4) With alcoholic sulphuric acid, α -pinene gives α -terpenol. So compound has one six membered ring and in this reaction H_2O is added.

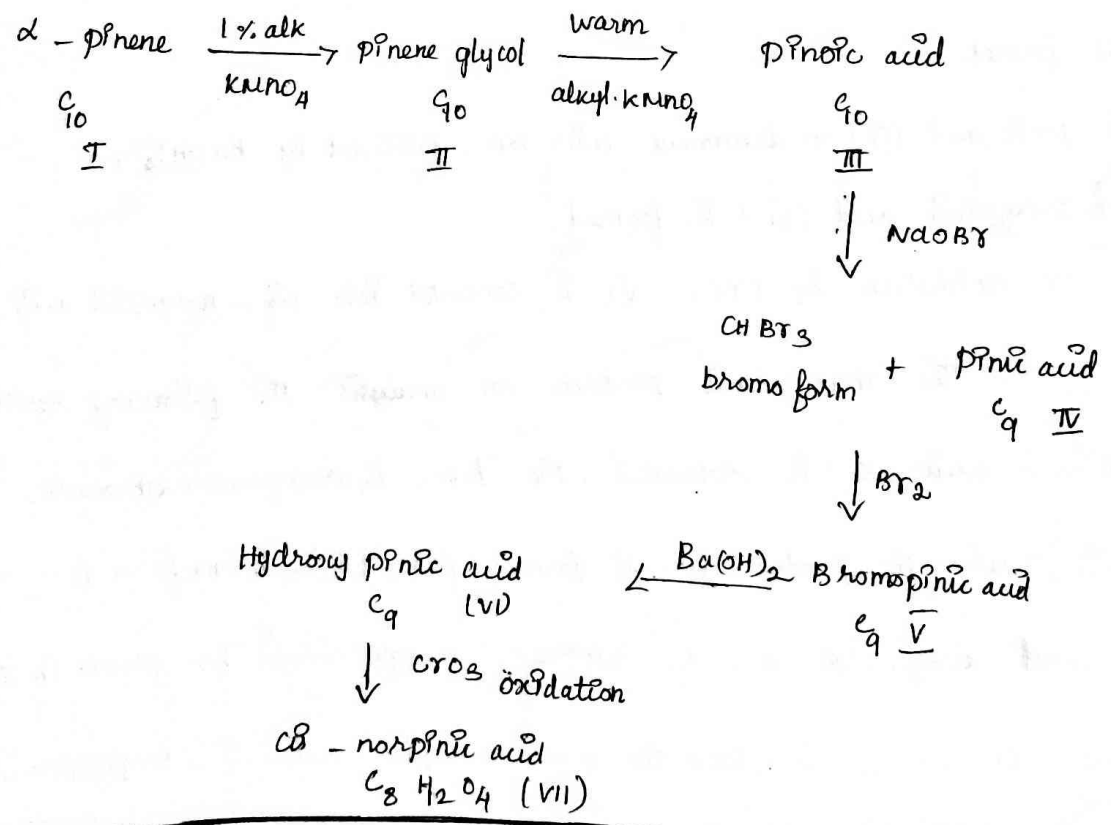
⑤ In α -terpenol, OH group is attached at 8th position, so in α -pinene with the help of C_3 another ring may be formed. α -pinene should be any one of the following structures.



⑥ Structures I & II are ruled out since the second ring should contain 4 'C' atoms according to Bayer who proved it by the following degradation reaction.

⑦ Structure IV is ruled out since the carbon which joins two rings should not be attached to double bond according to Bred.

⑧ So assuming the structure of α -pinene as III, Bayer proceed the degradation reaction



6

① Since the structure of α -terpinol is known, its formation by hydration of α -pinene leads to the following points.

a) α -pinene possesses one six-membered ring having the double bond of α -terpinol.

b) The gem-dimethyl group [$-\text{C}(\text{Me})_2$] of α -terpinol is not present in the six-membered ring of α -pinene and hence it must be present in the other ring.

② Oxidative degradation of α -pinene:-

① α -pinene (I) on oxidation with 1% alk KMnO₄ gives pinene-glycol in which double bond is broken and two hydroxyl groups are added.

② pinene glycol (II) on oxidation with KMnO_4 , pinonic acid (III) is formed. one hydroxyl group of II is oxidised to $>\text{C}=\text{O}$ and another hydroxyl group is oxidised into $-\text{COOH}$ group.

③ pinonic acid (III) on oxidation with NaOBr bromoform and pinic acid (IV) are formed.

④ pinic acid (IV) on treatment with Br_2 , followed by $\text{Ba}(\text{OH})_2$, hydroxypinic acid (V) is formed.

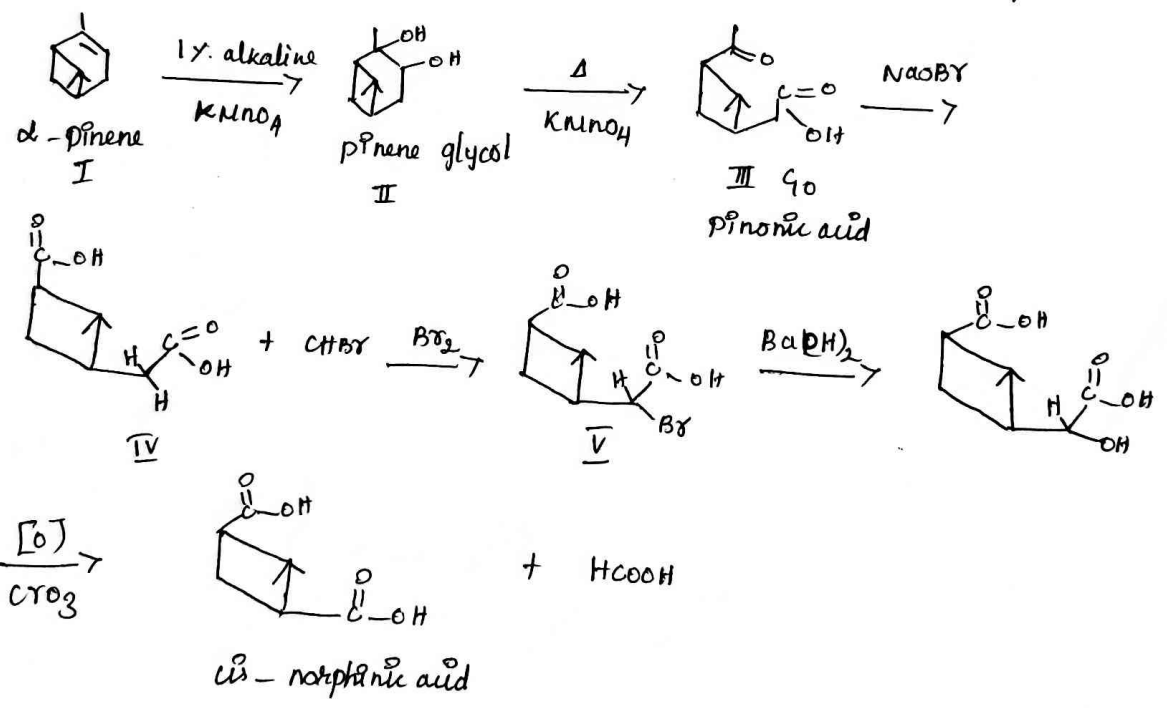
⑤ on oxidation by CrO_3 , V is converted into α -norpinic acid.

The above said products on analysis, the following results, pinonic acid (III) is saturated, the keto, hydroxymonocarboxylic acid. when the product IV is formed from (III), bromoform is formed along with it. So $\text{CH}_3-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-$ group should be present in III. The product V is saturated monocarboxylic acid. α -norpinic acid

has the molecular formula $C_8H_{12}O_4$. This product is proved to be dicarboxylic acid. So the molecular formula is re-written as $C_8H_{16}(COOH)_2$. Since gem-dimethyl group is not present in six-membered ring it should be reacted in six-membered ring it should be reacted in oxidation reaction. Hence gem-dimethyl group is present in is-norpinic acid and its molecular formula is re-written as $Me_2C_2H_4(COOH)_2$. So norpinic acid is the derivative of cyclobutane and it is

1,1-dimethyl-cyclobutane-2,4-dicarboxylic acid.

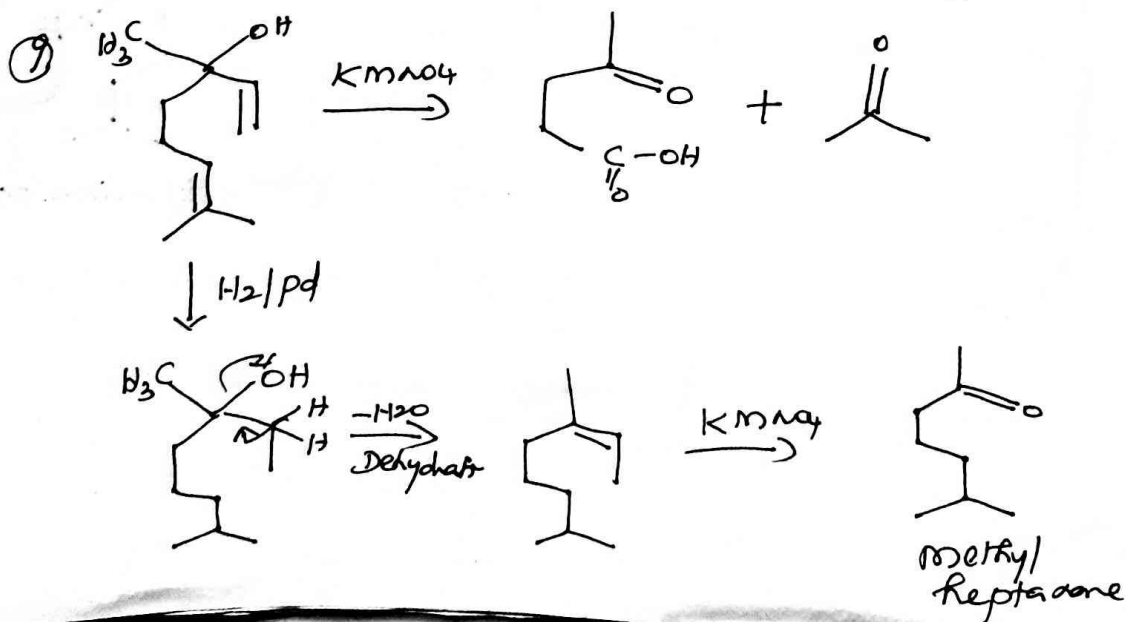
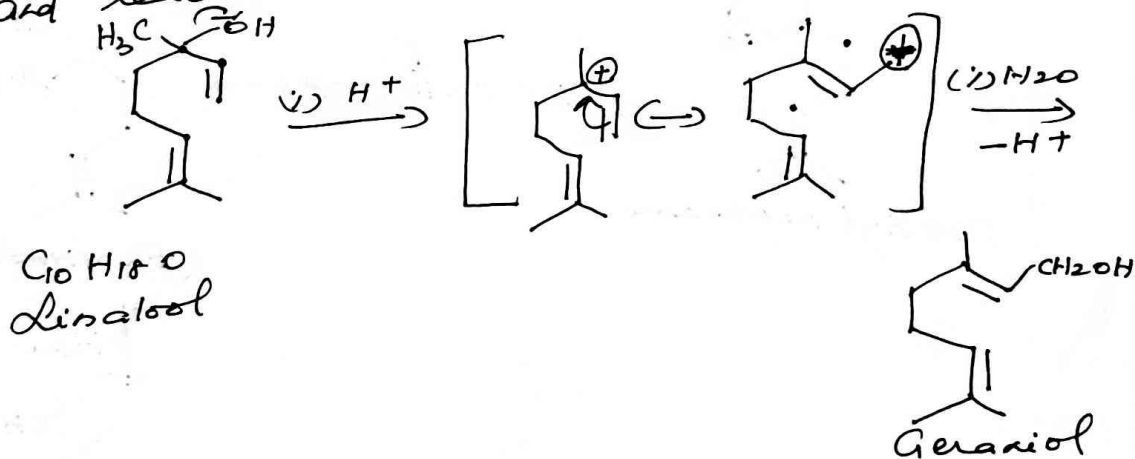
(11) From the above analysis, it is concluded that α -pinene has the following structure and its oxidation reactions are explained.



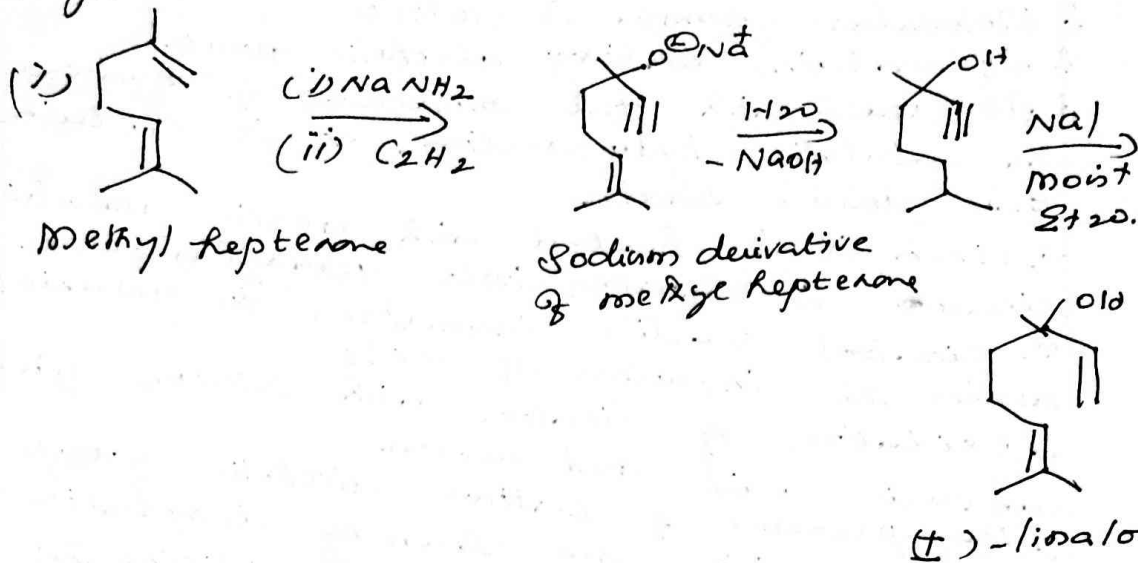
LINALOOL

STRUCTURAL DETERMINATION:-

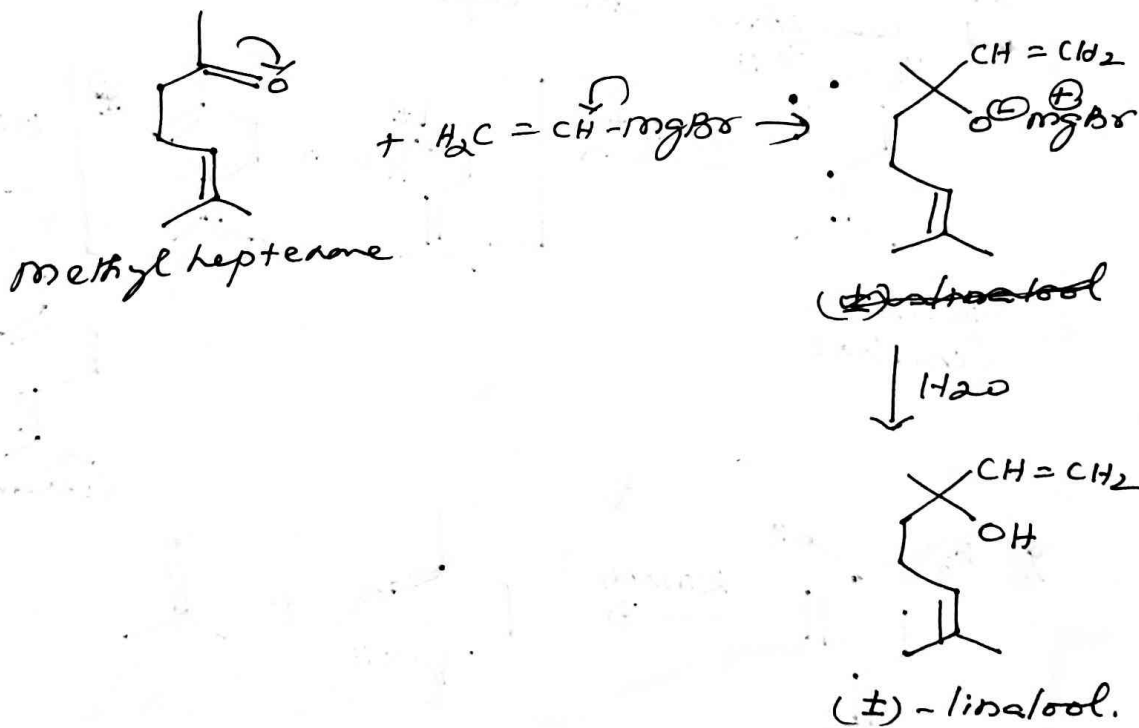
1. Molecular formula is $C_{10}H_{18}O$
2. It contains tertiary alcoholic group.
3. It reacts with two molecules of hydrogen on catalytic hydrogenation. So it contains two double bonds.
4. When it is heated with acetic anhydride, linalool is converted into geranyl acetate.
5. Linalool readily isomerises to geraniol under the influence of acids.
6. Oxidation of linalool with $KMnO_4$ gives laevulinic acid and acetone.
7. The presence of tertiary alcoholic group and its position are shown by dehydrating tetrahydro linalool and then acidifying the alkene produced.
8. Considering all the above facts, the structure of linalool is given as follows and reactions are explained.



(10) Structure of linalool is confirmed by synthesis as follows.

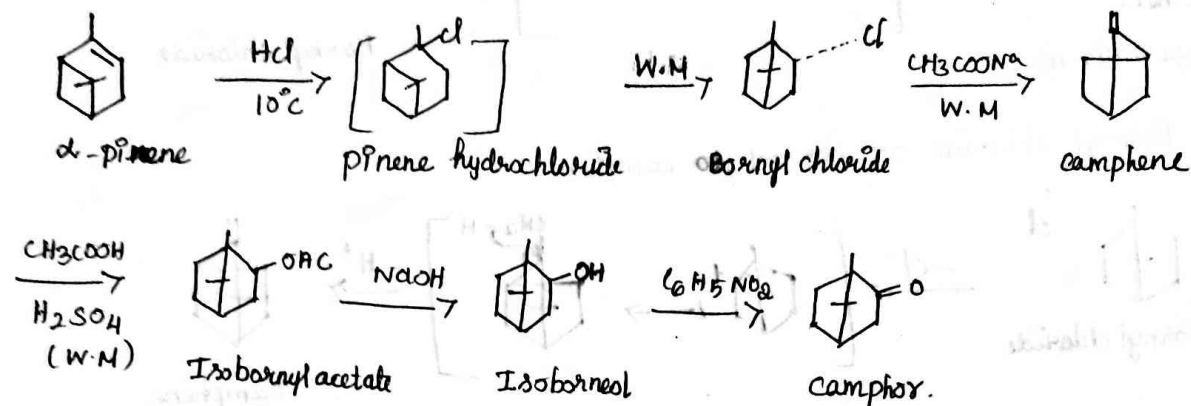


(ii) Nozomant synthesised linalool in one step by the action of vinylmagnesium bromide on methyl heptenone

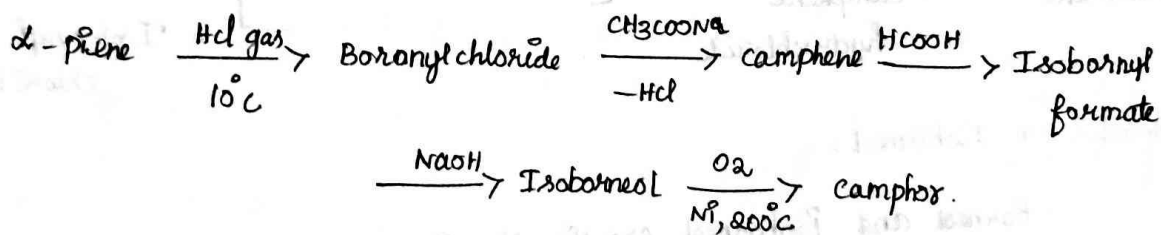


COMMERCIAL SYNTHESIS OF CAMPHOR:

As described already the commercial camphor of today mainly comes from synthesis because the natural source could not meet the demand of camphor. As outlined in the introductory portion camphor is synthesised from α -pinene which in turn is isolated turpentine oil. Synthetic camphor is usually obtained as the racemic modification.



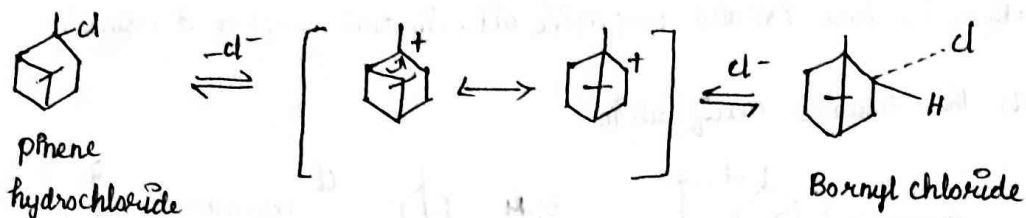
The method is now a days modified by replacing acetic acid by formic acid when isobornyl formate is formed. Moreover, the isoborneol is oxidised by atmospheric oxygen to camphor.



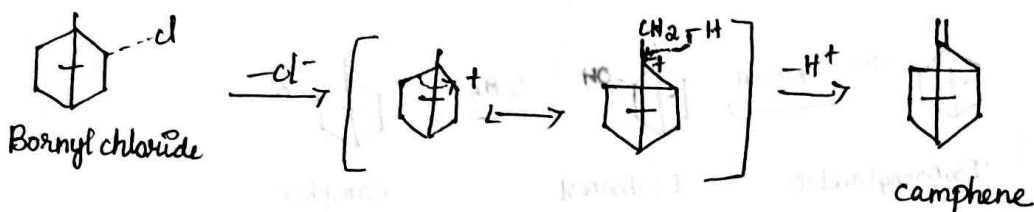
In the above steps we see that the α -pinene although first gives α -pinene hydrochloride the latter rearranges very readily even at room temperature to the stable product bornyl chloride. There are several examples of this type of transformation which were first observed by Wagner and Meerwein, who also gave the mechanism for this rearrangement and thus called such type of rearrangement as Wagner-Meerwein.

rearrangements (W.M). For details, the readers are referred to Author's reactions and reagents in organic chemistry and here only some example which come across in bicyclic terpenoids are mentioned.

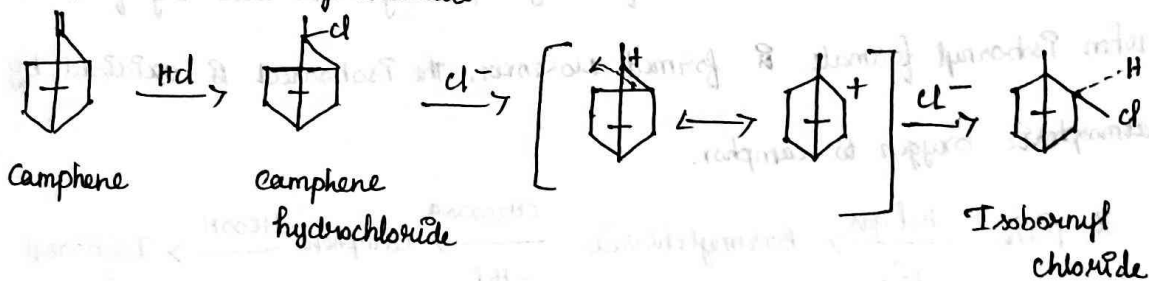
(a) α -pinene hydrochloride into bornyl chloride.



(b) Bornyl chloride or bornol to camphene.



(c) Camphene to isobornyl chloride

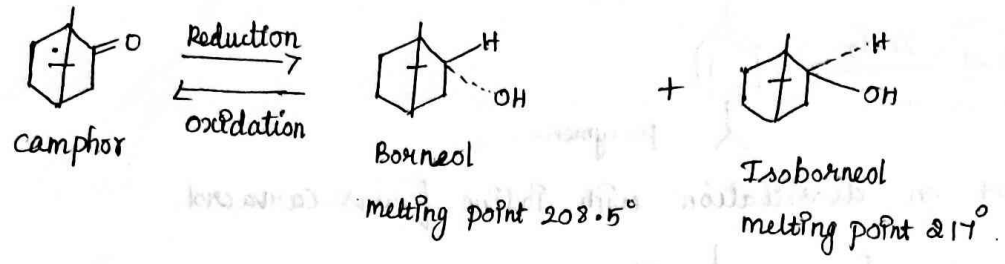


Bornol or Isobornol:

Bornol and Isobornol are the stereoisomeric secondary alcohols obtained by the reduction of camphor. out of the two isomers, the former is widely distributed in nature in the (+), (-) and γ -isomers; the (+) bornol occurs in the tree *Dryobalanops camphora* (growing in Sumatra and Bornol), in rosemary and spike oils; the (-) and γ -isomers occur in Valerian oil. Bornol resembles camphor in smell and burning taste. Isobornol has been isolated from only one essential oil.

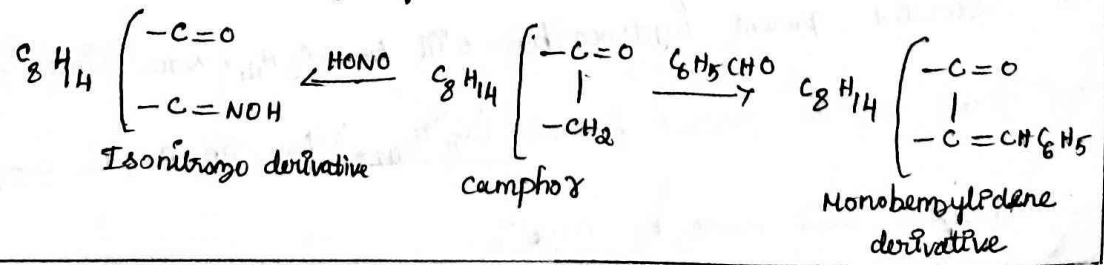
Their constitutions are established by the fact that on oxidation both of them give camphor which on reduction gives back a mixture of borneol and isoborneol and hence the two borneols are the stereoisomeric

secondary alcohols corresponding to the ketone, camphor.



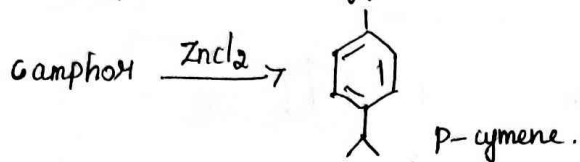
STRUCTURAL ELUCIDATION OF CAMPHOR:

1. Its molecular formula is $C_{10}H_{16}O$. The general reactions and molecular refraction of camphor show that it is saturated.
2. The nature of oxygen atom is found to be cyclic ketone by the fact that the camphor forms an oxime with NH_2OH , semicarbazone with semicarbazide and a dicarboxylic acid having the same number of carbon atoms on oxidation.
3. The presence of ketonic group in camphor ($C_{10}H_{16}O$) led $C_{10}H_{18}$ as the molecular formula of its saturated hydrocarbon. Since $C_{10}H_{18}$ corresponds to C_nH_{2n-2} , camphor must be bicyclic.
4. Camphor on condensation with C_6H_5CHO forms monobenzylidene derivative suggesting the presence of $-CO-CH_2-$ group which is confirmed by the formation of isonitroso derivative with nitrous acid (isoamyl nitrite and hydrogen chloride).

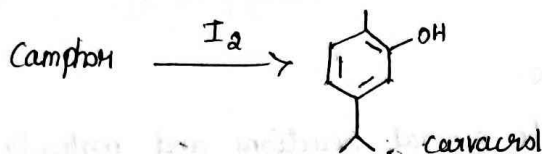


The presence of $-CO-CH_2-$ grouping is further confirmed by its oxidation to a dibasic acid, camphoric acid, with the same number of carbon atoms.

5. Camphor on distillation with zinc chloride or phosphorous pentoxide gives p-cymene. This suggests that in camphor, one ring is six-membered.

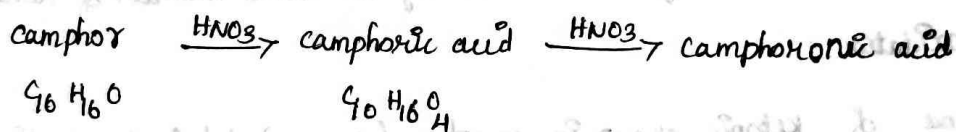


6. Camphor on distillation with iodine forms carvacrol.



The presence of phenolic group in carvacrol suggests the presence of ketonic group in camphor.

7. Oxidation of camphor with HNO_3 produces camphoric acid then camphoronic acid.



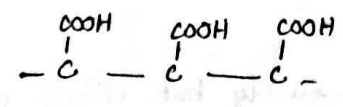
Thus for elucidating the structure of camphor, we must first know the structures of its oxidative degraded products i.e. camphoric acid and camphoronic acid.

8. Constitution of camphoronic acid, $C_9H_{14}O_6$:

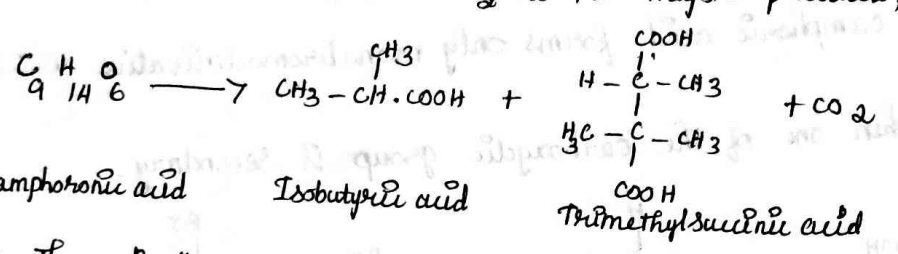
i) Since the camphoronic acid is found to be a saturated tricarboxylic acid, its formula $C_9H_{14}O_6$ may be written as $C_6H_{11}(COOH)_3$ and hence

its saturated parent hydrocarbon will be C_6H_{14} . Now since C_6H_{14} corresponds to the general formula (C_nH_{2n+2}) for an acyclic compound, camphoronic acid must be acyclic.

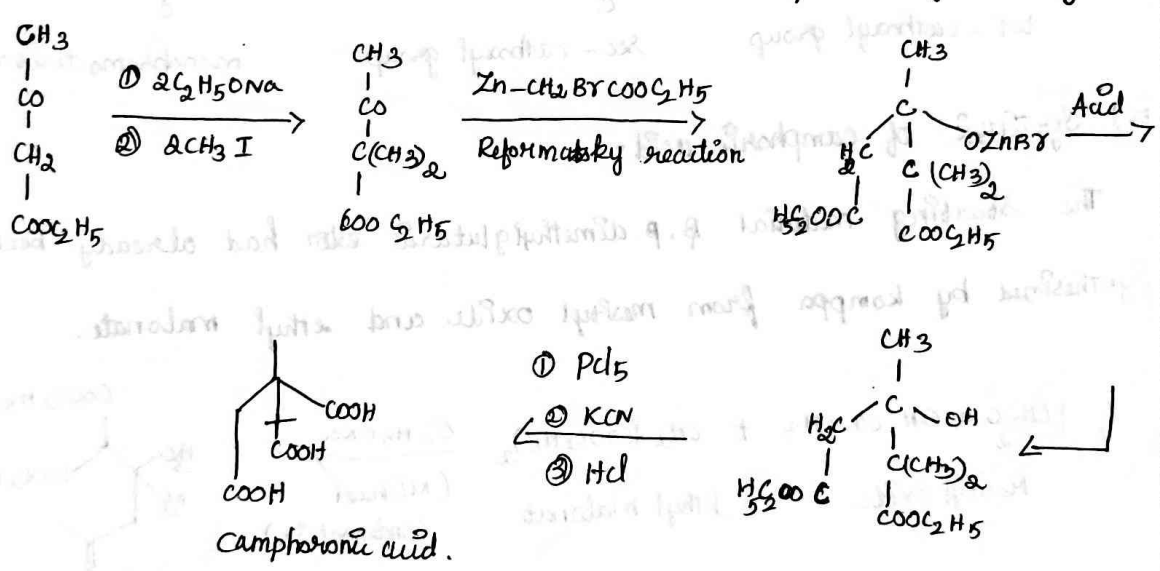
ii) Since camphoric acid is not easily decarboxylated under ordinary conditions its three carboxylic groups are attached to three different carbon atoms.



iii) The exact structure of camphoric acid is established by its distillation at atmospheric pressure when it gives isobutyric acid, trimethyl succinic acid and CO₂ as the major products,



iv) The Bredt structure for camphoric acid is proved by its synthesis



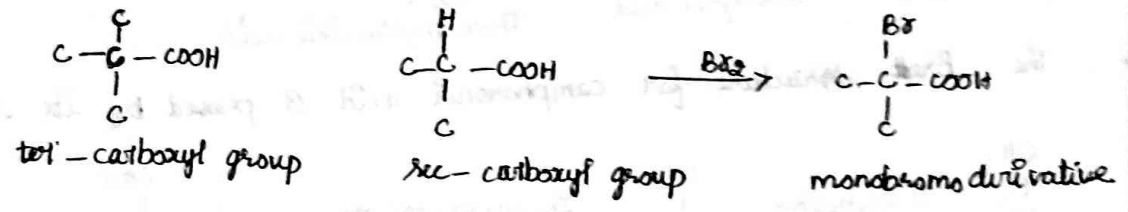
9. Constitution of camphoric acid :

i) The camphoric acid C₉H₁₆O₄ is found to be a saturated dicarboxylic acid.

ii) Now since its oxidised product camphoric acid has a gem dimethyl group and a separate methyl group, camphoric acid and camphor also must have three methyl groups. Thus now the formula for camphoric acid may be written as (CH₃)₃C₂H₅(COOH)₂ which leads C₉H₁₆O₄ as its

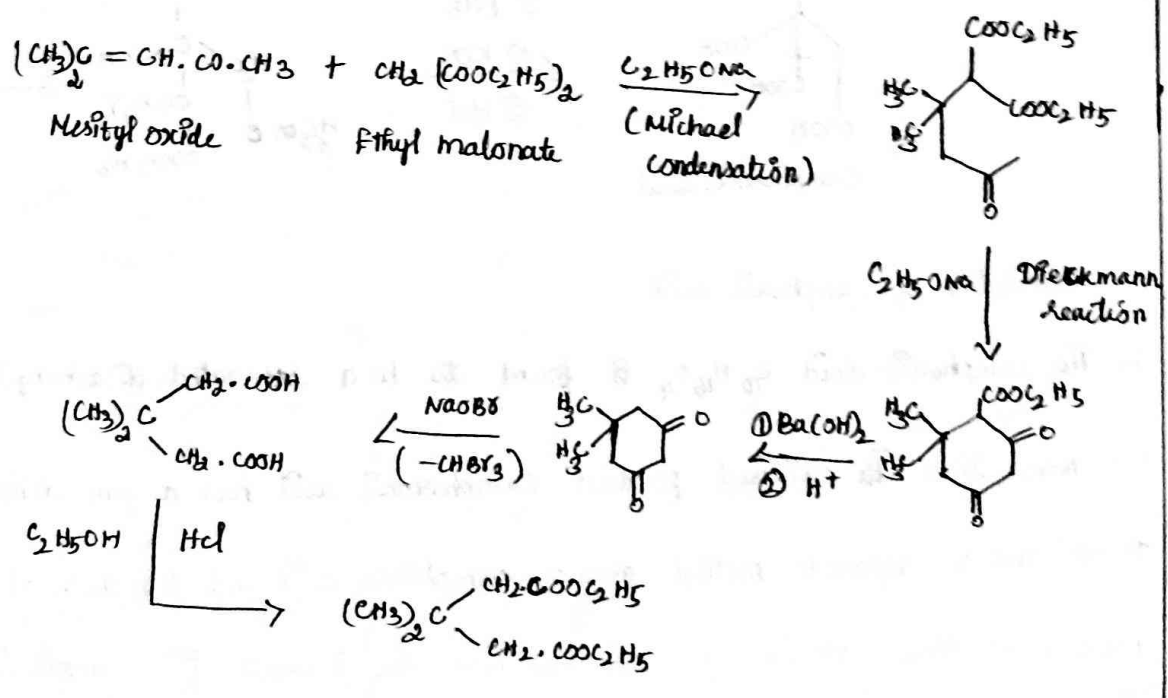
Saturated parent hydrocarbon. The molecular formula C_5H_{10} i.e. (C_nH_{2n}) of its saturated parent hydrocarbon suggests that camphoric acid is a cyclopentane dicarboxylic acid.

iii) Camphoric acid forms monoester very easily but diester with some difficulty indicating that the two carboxyl groups are not similar i.e. one is primary or secondary, and the other is tertiary. This is confirmed by the fact that camphoric acid forms only monobromoderivative which is possible only when one of the carboxylic group is secondary.

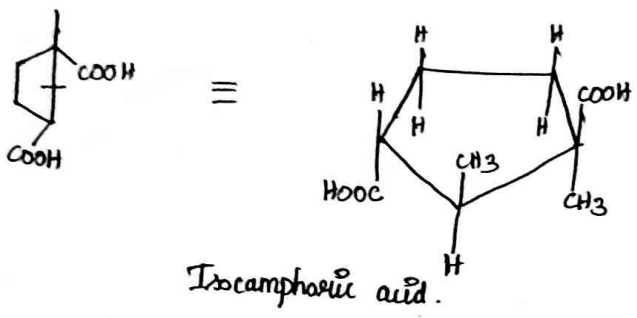
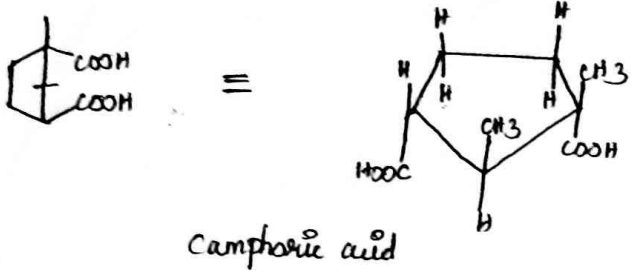


iv) Synthesis of camphoric acid:

The starting material β, β -dimethylglutaric ester had already been synthesized by Komppa from mesityl oxide and ethyl malonate.



Camphoric acid can exist two geometrical forms, cis and trans; commonly known as camphoric acid and Isocamphoric acid. Since camphoric forms an anhydride while Isocamphoric acid does not form anhydride, the former is the cis-Isomer and that latter the trans.



Synthesis of camphor: The above structure for camphor is also proved by its synthesis (Haller, 1896) starting from camphoric acid which has already been synthesized.

