TERPENOIDS

There are many different classes of_naturally occurring compounds . Terpenoids also form a group of naturally occurring compounds majority of which occur in plants, a few of them have also been obtained from other sources. Terpenoids are volatile substances which give plants and flowers their fragrance. They occur widely in the leaves and fruits of higher plants, conifers, citrus and eucalyptus.

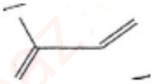
The term terpene' was given to the compounds isolated from terpentine, a volatile liquid isolated from pine trees. The simpler mono and sesqui terpenes are chief constituent of the essential oils obtained from sap and tissues of certain plants and trees. The di and tri terpenoids are not steam volatile. They are obtained from plant and tree gums and resins. Tetraterpenoids form a separate group of compounds called Carotenoids.

The term 'terpene was originally employed to describe a mixture of isomeric hydrocarbons of the molecular formula $C_{10}H_{16}$ occurring in the essential oils obtained from sap and tissue of plants, and-trees. But there is a tendency to use more general term terpenoids which include hydrocarbons and their Oxygenated derivatives. However the term terpene is being used these days by some authors to represent terpenoids.

By the modern definition: "Terperioids are the hydrocarbons of plant origin of the general formula $(C_5H_8)_n$ as well as their oxygenated, hydrogenated and dehydrogenated derivatives".

Isoprene rule: Thermal decomposition of terpenoids give isoprene as one of the product. Otto Wallach pointed out that terpenoids can be built up of isoprene unit.

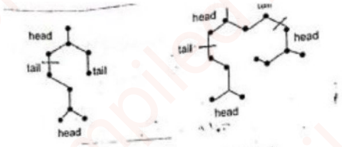
Isoprene rule stats that the terpenoid molecules are constructed from two or more isoprene unit.



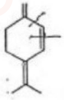
Further Ingold suggested that isoprene units are joined in the terpenoid via 'head to tail' fashion. Special isoprene rule states that the terpenoid_molecule are constructed of two or more isoprene units joined in a 'head to tail' fashion.

But this rule can only be used as guiding principle and not as a fixed rule. For example carotenoids are joined.tail to tail at their central and there are also some terpenoids whose carbon content is not a multiple of five.

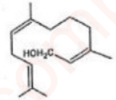
In applying isoprene rule we look only for the skeletal unit of carbon. The carbon skeletons of open chain mono terpenoids an sesqui terpenoids are,



Examples.

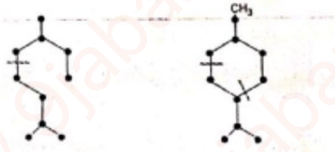


Myrcene
(monoterpene)



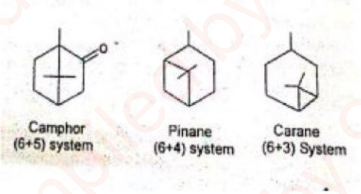
Farnesol (Sesquiterpene)

Ingold (1921) pointed that a gem alkyl group affects the stability of terpenoids. He summarized these results in the form of a rule called `gem dialkyl rule' which may be stated as "Gem dialkyl group tends to render the cyclohexane ring unstable where as it stabilizes the three, four and five member rings."
This rule limits the number of possible structure in closing the open chain to ring structure. Thus the monoterpenoid open chain give rise to only one possibility for a monocyclic monoterpenoid i.e the p-cymene structure.



P-cymene structure

Bicyclic monoterpenodis contain a six member and a three member ring. Thus closure of the ten carbon open chain monoterpenoid gives three possible bicyclic structures.



Classification of Terpinoids

Most natural terpenoids hydrocarbon have the general formula $(C_5H_8)_n$. They can be classified on the basis of value of n or number of carbon atoms present in the structure.

Table-1: Classification of Terpenoids

S.No.	Number of carbon atoms	Value of n	Class
1.	10	2	Monoterpenoids($C_{10}H_{16}$)
2.	15	3	Sesquiterpenoinds($C_{15}H_{24}$)
3.	20	4	Diterpenoids($C_{20}H_{32}$)
4.	25	5	Sesterpenoids($C_{25}H_{40}$)
5.	30	6	Troterpenoids($C_{30}H_{48}$)
6.	40	8	Tetraterpenoids($C_{40}H_{64}$)
7.	>40	>8	Polyterpenoids(C_5H_8)n

Each class can be further subdivided into subclass according to the number of rings present in the structure.

i)**Acyclic Terpenoids**: They contain open structure.

ii)**Monocyclic Terpenoids**: They contain one ring in the structure

iii)**Bicyclic Terpenoids**: They contain two rings in the structure.

iv)**Tricyclic Terpenoids**: They contain three rings in the structure.

v)**Tetracyclic Terpenoids:** They contain four rings in the structure.

Some examples of mono, sesqui and di Terpenoids:

A) Mono terpenoids

Atwole nt Verah

4th April, 2024

Classification of Tapenoids

Most natural tapenoids hydrocarbon have the general formula $(C_5H_8)_n$.

They can be classified on the basis on the value of n or the number of carbon atoms, present in the structure.

Isoprene unit	No. of carbon atoms	Class of terpenoid	Remark.
1	~~C_5H_8~~ 5	Isoprene (C_5H_8)	—
2	~~$C_{10}H$~~ 10	monoterpenes $(C_{10}H_{16})$	They are usually volatile oils and they are used in perfumery
3.	15	Sesquiterpenes $(C_{15}H_{24})$	
4	20	Diterpenes $(C_{20}H_{32})$	Non volatile solids obtained from plants gums and resins
5	25	Sestertepenes $(C_{25}H_{40})$	
6	30	Triterpenes $(C_{30}H_{48})$	
8	40	tetraterpenes $(C_{40}H_{64})$	Carotenoids

Terpene unit	n		
[illegible]	>40	polyterpenoids $(C_5H_8)_n$	rubber

Classes of oils

Food oils	Vegetable

Each class can be further subdivided into sub classes according to the number of rings present in the structure.

no ring

(i) Acyclic Terpenoids: These are terpenoids that contain open structure. An example is monoterpenes

(ii) Monocyclic Terpenoids: These are terpenoids that contains one ring in the structure

(iii) Bicyclic Terpenoids: They are terpenoids that contain two rings in the structure

(iv) Tricyclic Terpenoids: Contains three rings in the structure

(v) Tetracyclic Terpenoids: Contains four rings in the structure

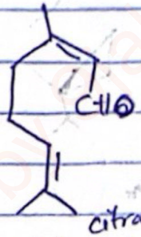
Ⓐ Monoterpenoids: we have;

(i) Acyclicmonoterpenoids: e.g

(i)

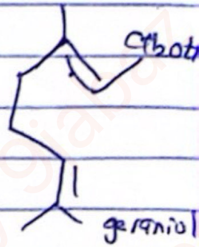
myrcene

(ii)



citral

(iii)



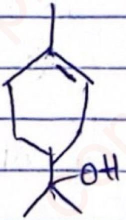
geraniol

(2) Monocyclic monoterpenoids: Examples are;

(i)

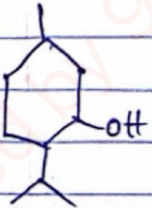
limonene

(ii)



α- terponeol

(iii)



menthol

(3) Bicyclic monoterpenoids: These are further divided into three classes

ⓐ Contains (6 +3 membered rings)

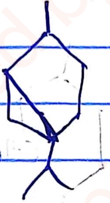
ⓑ Contans (6+4 membered rings)

ⓒ Contans (6+5 membered rings)

08-04-2025

Examples of Bicyclic monoterpenoids

(a) (i)



Thujane

(ii) (6+3 membered ring)

Carane

(b) (i)

Pinane

(6+4 membered ring)

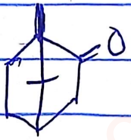
(ii)

Pinene

(c) (i)

Bornane

(ii)



Camphor

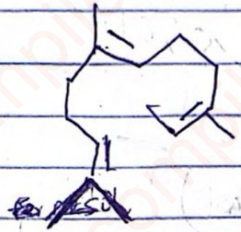
~~(iii)~~

(B) ~~Sesquiterpenoids~~

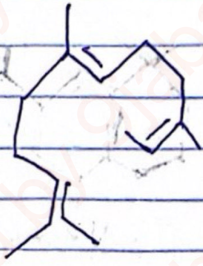
(I) ~~Acyclic Sesquiterpenoids~~

~~B~~ Sesquiterpenoids

(i) Acyclic Sesquiterpenoids



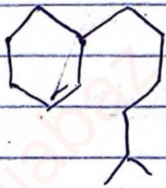
fernesol



farnesene

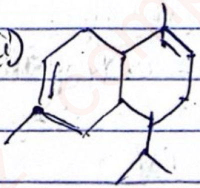
(ii) Monocyclic Sesquiterpenoids

(i)



zinziberene

(ii)



cardinene

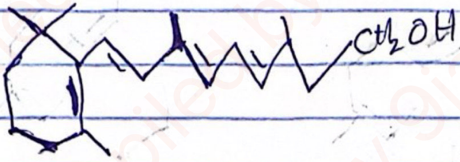
(B) Diterpenoids

(A) Acyclic diterpenoid

(i)

Phytol

(2.) Monocyclic diterpenoids



Vitamin A (retinol)

15-04-2025

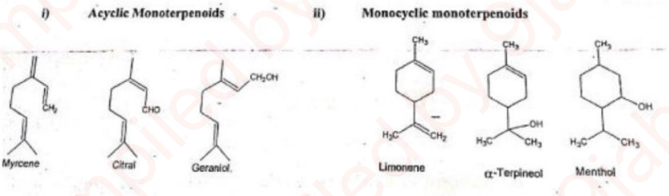
(i) Isolation of essential oil: comes out as mixture of different essential oils.

Methods of extractions of oils

(a) Expression method: eg peel of orange
(b) Steam distillation
(c) extration by means of volatile solvent
(d) adsorption in purified fats

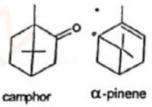
(ii) Separation of Terpenoids from essential oils: Terpenes comes up first (more volatile)

* Isoprene 2-methyl butan-1-3-diene



iii) **Bicyclic monoterpenoids**: These are further divided into three classes.
a)Containing -6+3-membered rings
b)Containing -6+4- membered rings.
c)Contining -6+5-membered rings

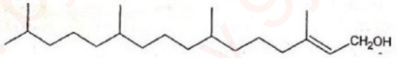
Some bicyclic monoterpenes are:



B) Sesquiterpenoids:

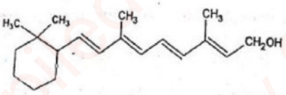
C) **Diterpenoids:**

i) **Acyclic diterpenoids**



Phytol

ii) **Mono cyclic diterpenoids:**



Vitamin A

Isolation of mono and sesquiterpenoids

Both mono and sesquiterpenoids have common source i.e essential oils. Their isolation is carried out in two steps:

i)Isolation of essential oils from plant parts
ii)Separation of Terpenoids from essential oils

i) **Isolation of essential oils from plant parts**: The plants having essential oils generally have the highest concentration at some particular time. Therefore better yield of essential oil plant material have to be collected at this particular time. e.g. From jasmine at sunset.there are four methods of extractions of oils.

a) Expression method
b) Steam distillation method
c) Extraction by means of volatile solvents
d) Adsorption in purified fats

Steam distillation is most widely used method. In this method macerated plant material is steam distilled to get essential oils into the distillate form these are extracted by using pure organic volatile solvents. If compound decomposes during steam distillation, it may be extracted with petrol at 50°C. After extraction solvent is removed under reduced pressure.

ii) **Separation of Terpenoids from essential oil**: A number of terpenoids are present in essential oil obtained from the extraction. Definite physical and chemical methods can be used for the separation of terpenoids. They are separated by fractional distillation. The terpenoid hydrocarbons distill over first followed by the oxygenated derivatives.

More recently different chromatographic techniques have been used both for isolation and separation of terpenoids.

General properties of Terpenoids

1.Most of the terpenoids are colourless, fragrant liquids which are lighter than water and volatile with steam. A few of them are solids e.g. camphor. All are soluble in organic solvent and usually insoluble in water. Most of them are optically active.

2.They are open chain or cyclic unsaturated compounds having one or more double bonds. Consequently they undergo addition reaction with hydrogen, halogen, acids, etc. A number of *addition* products *have* antiseptic properties.

3. They undergo polymerization and dehydrogenation.

4.They are easily oxidized nearly by all the oxidizing agents. On thermal decomposition, most of the terpenoids yields isoprene as one of the product.

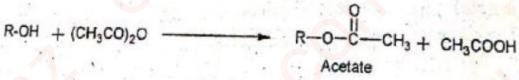
General Methods of structure elucidation

Terpenoids

1) Molecular formula: molecular formula is determined by usual quantitative analysis and mol.wt determination methods and by means of mass spectrometry. If terpenoid is optically active, its specific rotation can be measured.

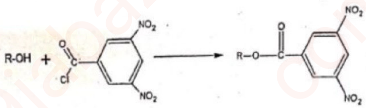
2)Nature of oxygen atom present: If oxygen is present in terpenoids its functional nature is generally as alcohol aldehyde, ketone or carboxylic groups.

a) **Presence of oxygen atom present:** presence of —OH group can be determined by the formation of acetates with acetic anhydride and benzoyate with 3.5-dinitirobenzoyl chloride.



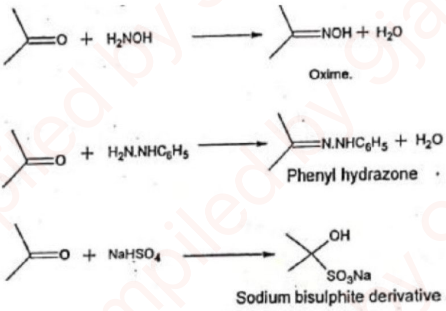
$$R\text{-}OH + (CH_3CO)_2O \longrightarrow R{-}O{-}\overset{\overset{O}{\|}}{C}{-}CH_3 + CH_3COOH$$

Acetate



Primary alcoholic group undergo esterification more readily than secondary and tertiary alcohols.

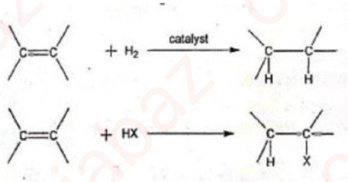
b) **Presence of >C=0 group**: Terpenoids containing carbonyl function form crystalline addition products like oxime, phenyl hydrazone and bisulphite etc.



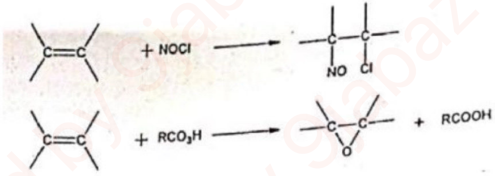
if carbonyl function is in the form of aldehyde it gives carboxylic acid on oxidation without loss of any carbon atom whereas the ketone on oxidation yields a mixture of lesser number of carbon atoms.

iii)**Unsaturation**: The presence of olefinic double bond is confirmed by means of bromine, and number of double bond determination by analysis of the bromide or by quantitative hydrogenation or by titration with monoperpthalic acid.

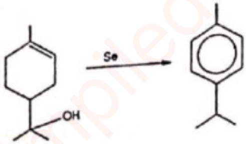
Presence of double bond also confirmed by means of catalytic hydrogenation or addition of halogen acids. Number of moles of HX absorbed by one molecule is equal to number of double bonds present.



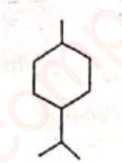
Addition of nitrosyl chloride(NOC1) **(Tilden's reagent)** and epoxide formation with peracid also gives idea about double bonds present in terpenoid molecule.



iv)Dehydrogenation: On dehydrogenation with sulphur, selenium, polonium or palladium terponoids converted to aromatic compounds. Examination of these products the skelton structure and position of side chain in the original terpenoids can be determined.
For example α-terpenol on Se-dehydrogenation_yields *p*-cymene.



Thus the carbon Skelton of terpenol is as follows.

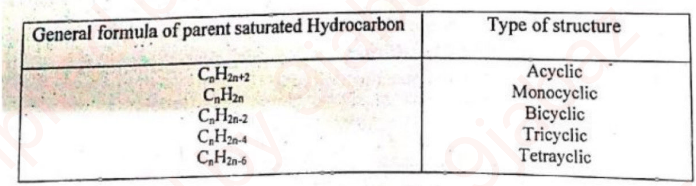


v)Oxidative degradation: Oxidative degradation has been the parallel tool for elucidating the structure of terpenoids. Reagents for degradative oxidation are ozone, acid, neutral or alkaline potassium permanganate, chromic acid, sodium hypobromide, osmium tetroxide, nitric acid, lead tetra acetate and peroxy acids. Since oxidizing agents are selective, depending on a particular group to be oxidized, the oxidizing agent is chosen with the help of stfucture of degradation product.

vi)Number of the rings present: With the help of general formula of corresponding parent saturated hydrocarbon, number of rings present in that molecule can be determined.

vii)Relation between general formula of compound and type of compounds: Table 2

Table-2: Relation between general formula of compound and type of compounds



General formula of parent saturated Hydrocarbon	Type of structure
C_nH_{2n+2}	Acyclic
C_nH_{2n}	Monocyclic
C_nH_{2n-2}	Bicyclic
C_nH_{2n-4}	Tricyclic
C_nH_{2n-6}	Tetrayclic

For example limonene (mol. formula. $C_{10}H_{16}$)absorbs 2 moles of hydrogen to give tetrahydro limonene (mol. Formula $C_{10}H_{20}$) corresponding to the general formula. C_nH_{2n}. It means limonoene has monocyclic structure.

viii) **Spectroscopic studies:** All the spectroscopic methods are very helpful for the confirmation of structure of natural terpenoids and also structure of degradation products. The various methods for elucidating the structure of terpenoids are:

a)**UV Spectroscopy**: In terpenes containing conjugated dienes or α,β–unsaturated ketones, UV spectroscopy is very useful tool. The values of λ_{max} for various types of terpenoids have been calculated by applying Woodward's empirical rules. There is generally good agreement between calculation and observed values. Isolated double bonds, α,β-unsaturated esters , acids, lactones also have characteristic maxima.

b)**IR Spectroscopy**: IR spectroscopy is useful in detecting group such as hydroxyl group (-3400cm^{-1}) or an oxo group (saturated 1750-1700cm^{-1}). Isopropyl group, cis and trans also have characteristic absorption peaks in IR region.

c)**NMR Spectroscopy**: This technique is useful to detect and identify double bonds, to determine the nature of end group and also the number of rings present, and also to reveal the orientation of methyl group in the relative position of double bonds.

d)**Mass Spectroscopy**: It is now being widely used as a means of elucidating structure of terpenoids. Used for determining mol. Wt., Mol. Formula, nature of functional groups present and relative positions of double bonds.

ix**) X-ray analysis**: This is very helpful technique for elucidating structure and stereochemistry of terpenoids.

x)**Synthesis**: Proposed structure is finally confirmed by synthesis. In terpenoid chemistry,many of the synthesis are ambiguous and in such cases analytical evidences are used in conjunction with the synthesis.

MYRCENE

Myrcene has molecular formula $C_{10}H_{16}$. It occurs in verbena and bay oils. It is a liquid with b. pts of 166 – 168˚C.

- Catalytic hydrogenation of myrcene in the presence of Pt converts it to decane, $C_{10}H_{22}$.

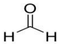
$$C_{10}H_{16} \xrightarrow[\text{[H]}]{\text{Pt}} C_{10}H_{22}$$

Thus, myrcene contains 3 double bonds (dbs) and it is an open chain (structure) compound. Since myrcene forms an adduct with maleic anhydride, therefore, 2 of the dbs are conjugated. This conjugation is supported by the fact that myrcene shows optical exaltation (i.e. increase in the refractive index).

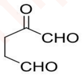
- Ozonolysis of myrcene produce acetone, formaldehyde and ketodialdehyde;

(i)

(ii)

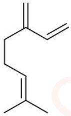


(iii)

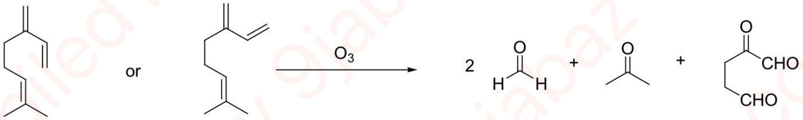


The suggested structure based on the above chemical analysis is;

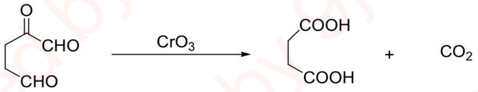
or



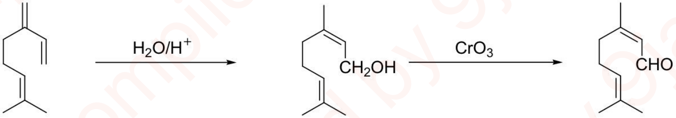
Which implies that;



- The ketodialdehyde on oxidation with chromic acid gave succinic acid and CO_2



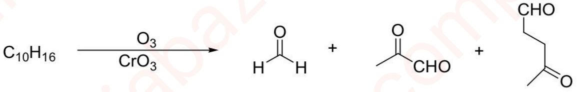
- Hydration of myrcene in acidic medium gave an alcohol known as geraniol, $C_{10}H_{18}O$, which on further oxidation gave citral



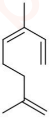
OCIMENE

Ocimene has molecular formula $C_{10}H_{16}$. It occurs in the leaves of a plant called *Ocimium basilicum.* It has a boiling point of 81˚C/30 mm Hg.

- Catalytic hydrogenation resulted in addition of 3 moles of H_2 to form decane, this implies that ocimene is an acyclic compound with 3 dbs.
- It also forms an adduct with maleic anhydride, therefore, 2 of the dbs are conjugated.
- Ozonolysis of Ocimene produce formaldehyde, methylglyoxal, laevulaldehyde, acetic & malonic acids & acetone.

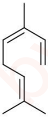


Proposed Structures:



I

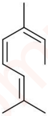
or



II

From relative amount of aldehyde z& ketone, it is believed that structure (II) is the major constituent of the mixture.

Ocimene is unstable and is yet to be obtained in the pure form. When heated, it readily isomerizes to Allo-ocimene in which all the 3 dbs are conjugated.



Allo-ocimene

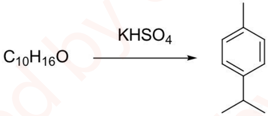
CITRAL

Citral is the most important of the acyclic monoterpenoids because the structures of most other compounds in this group are based on that of citral. It has a molecular formula $C_{10}H_{16}O$. It has a boiling point of -77˚C. It is widely distributed. About 60-80% is obtained in lemon grass oil. It is liquid with lemon odour.

- It contains an oxo-group (carbonyl functional group), hence, it forms an oxime (This reaction was used to determine the structure of citral).

oxime

- On heating with $KHSO_4$, it forms p-cymene



- It can be reduced by Na/Hg to form an alcohol, called geraniol.

$$C_{10}H_{16}O \xrightarrow[NaHg]{2[H]} C_{10}H_{18}O$$

- It can be oxidized by Ag_2O to geranic acid $C_{10}H_{16}O_2$

$$C_{10}H_{16}O \xrightarrow[Ag_2O]{[O]} C_{10}H_{16}O_2$$

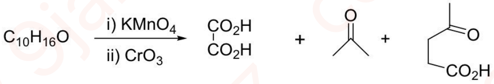
Both the above 2 last reactions show that oxo group in citral is therefore an aldehydic group. Citral also reduces Fehling's solution, further confirming the presence of aldehydic group.

Also, since there is no loss of C on oxidation to the acid, the oxo group in citral is, therefore an RCHO group.

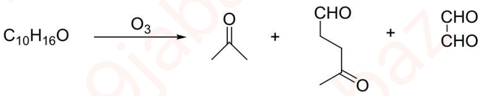
- It adds on 2 molecules of Br_2, shows the presence of 2 dbs.

$$C_{10}H_{16}O \xrightarrow{4[Br]} C_{10}H_{16}Br_4O$$

- Oxidation of citral with alkaline $KMnO_4$ followed by CrO_3 gives acetone, oxalic acid and laevulic acid.



- Ozonolysis of citral also yields acetone, laevulaldehyde and glyoxal



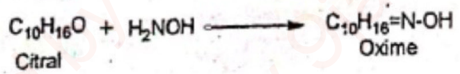
Citral

Citral is an acyclic monoterpenoid. It is a.major constituent of lemon grass oil in which it occurs to an extent of 60-80%. It is pale yellow liquid having strong lemon like odour and can be obtained by fractional distillation under reduced pressure from Lemongrass oil.

Constitution:

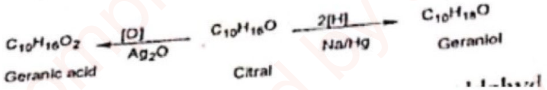
i) Mol. formula $C_{10}H_{16}O$, b.p-77°C

ii)Nature of Oxygen atom: Formation of oxime of citral indicates the presence of an oxo group in citral molecule.



$$C_{10}H_{16}O + H_2NOH \longrightarrow C_{10}H_{16}{=}N\text{-}OH$$

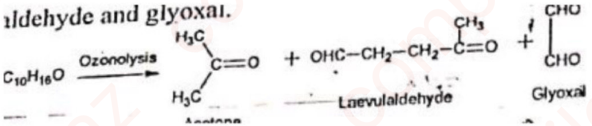
On reduction with Na/Hg it gives an alcohol called geraniol and on oxidation with silver oxide it give a monocarboxylic acid called Geranic acid without loss of any carbon atom.



$$C_{10}H_{16}O_2 \xleftarrow[Ag_2O]{[O]} C_{10}H_{16}O \xrightarrow[Na/Hg]{2[H]} C_{10}H_{18}O$$

Both these reaction reveal that oxo group in citral is therefore an aldehyde group. Citral reduces Fehling's solution. further confirming the presence of aldehydic group.

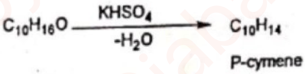
iii)It adds on two molecule of Br_2 shows the presence of two double bonds. On ozonlysis, it gives acetone, laevulaldehyde and glyoxal.



$$C_{10}H_{16}O \xrightarrow{\text{Ozonolysis}} (H_3C)_2C{=}O + OHC{-}CH_2{-}CH_2{-}\overset{CH_3}{C}{=}O + \underset{CHO}{CHO}$$

Formation of above products shows that citral is an acyclic compound containing two double bonds. Corresponding saturated hydrocarbon of citral (mol. Formula $C_{10}H_{22}$) corresponds to the general formula C_nH_{2n+2} for acyclic compounds, indicating that citral must be an acyclic compound.

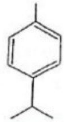
iv) Formation of *p*-cymcne and product obtained from the ozonolysis reveals that citral is formed by the joining of two isoprene units in the head to tail fashion



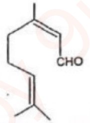
$$C_{10}H_{16}O \xrightarrow[-H_2O]{KHSO_4} C_{10}H_{14}$$

v) On the basis of above facts following structure was proposed for citral.

Carbon skelton of citral

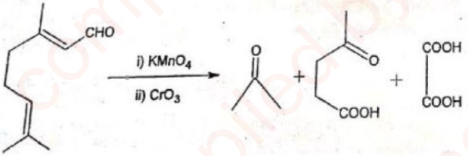


p-cymene

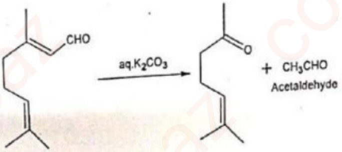


Citral

vi) Above structure was further supported by the degradation of citral on treatment with alkaline $KMnO_4$ followed by chromic acid.



Verley found that citral on boiling with aqueous potassium carbonate yielded 6-methyl hept-5- ene-2-one and acetaldehyde. The formation of these can only be explained on the basis of proposed structure.

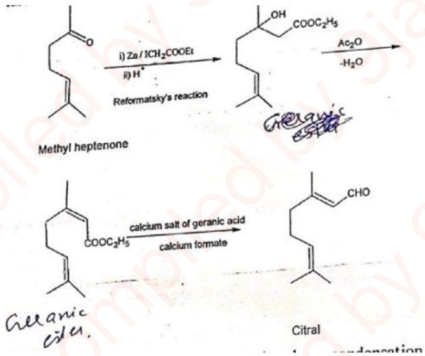


Methyl heptenone

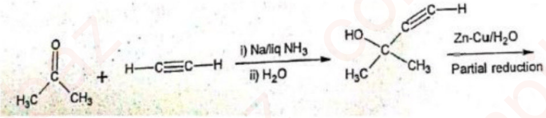
It Appears that citral is product of aldol condensation of these two.

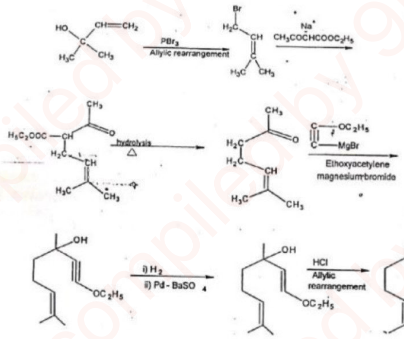
Synthesis: Finally the structure of citral was confirmed by its synthesis.

a) **Barbier-Bouveault-Tiemann's synthesis**: In this synthesis methyl heptenone is converted to geranic ester by using Reformatsky's reaction. Geranic ester is then converted to citral by distilling a mixture of calcium salts of geranic and formic acids.

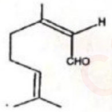


b)**Arens-Van Drop's Synthesis**: This synthesis involves condensation of acetone with acetylene in the presence of liquid ammonia. Condensation product is then reduced and treated with PBr_3, allylic rearrangement takes place. The rearranged product so obtained is treated with sodium salt of acetoacetic ester and then hydrolysed to yield methyl heptenone. The latter compound on condensation with ethoxy acetylene magnesium bromide, followed by the partial reduction and acidification yields citral by allylic rearrangement.

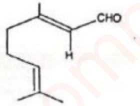




Isomerism of citral: two geometrical isomers occur in nature.



Cis-citral; citral-b: neral; Z-form

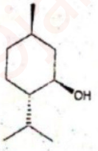


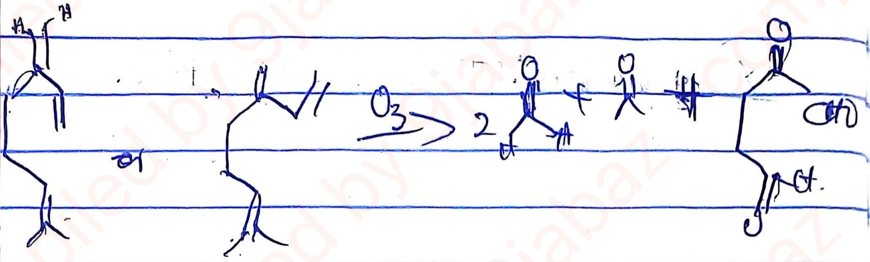
Trans-citral; Citral-a; geranial; E-form

The existence of the two isomeric Citrals in natural citral has been confirmed chemically by the formation of two different semicarbazones and formation of geraniol and nerol on reduction.

Menthol

Menthol is the major constituent of Mentha Piperi. It is used as an antiseptic and anesthetic. Menthol (also called peppermint camphor or mint camphor) is the major constituent of peppermint oil and is responsible for its odour and taste and the cooling sensation when applied to the skin. It is ingredient in cold balms. Menthol is optically active compound with mol. formula $C_{10}H_{20}O$.





A Myrcene hydrolysed in water will produce myrcenol

CITRAL

Formula: $C_{10}H_{16}O$, boiling point = 77°C, it is found in large quantity in Lemon grass. it has the largest concentration of citral.

$C_{10}H_{16}O \xrightarrow[\Delta]{KHSO_4}$

p-Cymene

Reduction of citral (Na(Hg)) → Geraniol
Oxidation of citral (Ag_2O) → Geranic acid

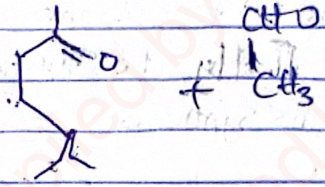
$C_{10}H_{16}O \xrightarrow[Na/Hg]{2[H]} C_{10}H_{18}O$
Geraniol

$C_{10}H_{16}O \xrightarrow[Ag_2O]{[O]} C_{10}H_{16}O_2$
Geranic acid

$K_2CO_{3(aq)}$ +

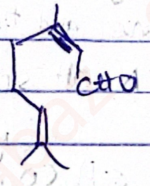
Aqueous K_2CO_3 converted citral into ~~6-methyl~~ 6-methyl hept-5-en-2-one

$C_{10}H_{16}O \xrightarrow{aq\ K_2CO_3}$

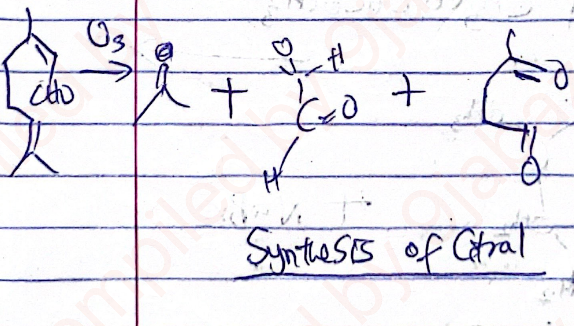


This last reaction implies that citral undergoes cleavages at the α-β unsaturation

On the basis of the above chemical analysis, citral is therefore



or



Synthesis of Citral

Synthesis of Citral

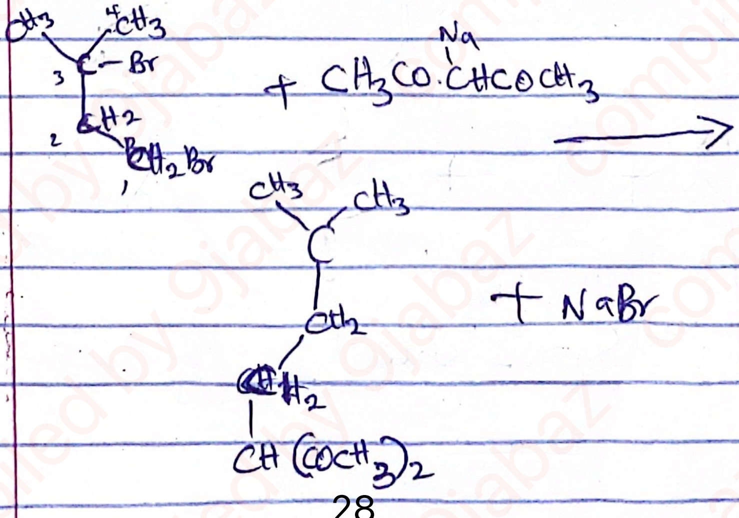
Synthesis of 6-methylhept-5-en-2-one

This cleavage by alkali reagent is a general reaction by α-β unsaturated carbonyl compounds. The methyl heptenone itself is oxidized to acetone and laevulic acid

Finally, the structure of citral was confirmed by its synthesis

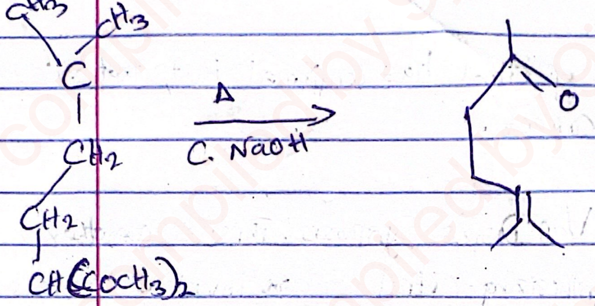
Synthesis of 6-methylhept-5-en-2-one

1,3 dibromo-3-methylbutane is condensed with sodium acetylacetone and the resulting compound is heated with conc. NaOH solution



Reformatsky rxn   Condenses aldehyde and ketones to halo ester

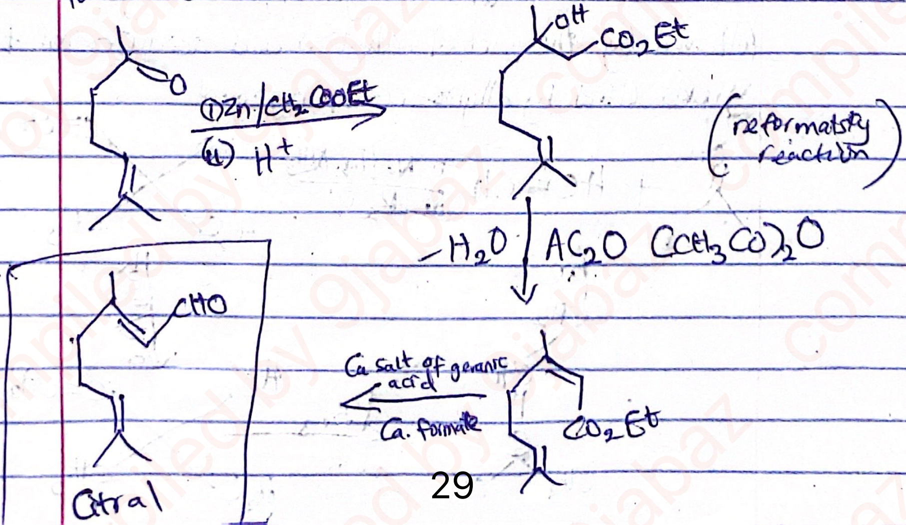
AC (CH_3CO)



Conversion of 6-methyl hept-5-en-2-one to Citral

① Using Barbier - Boureault - Tiemann's synthesis:

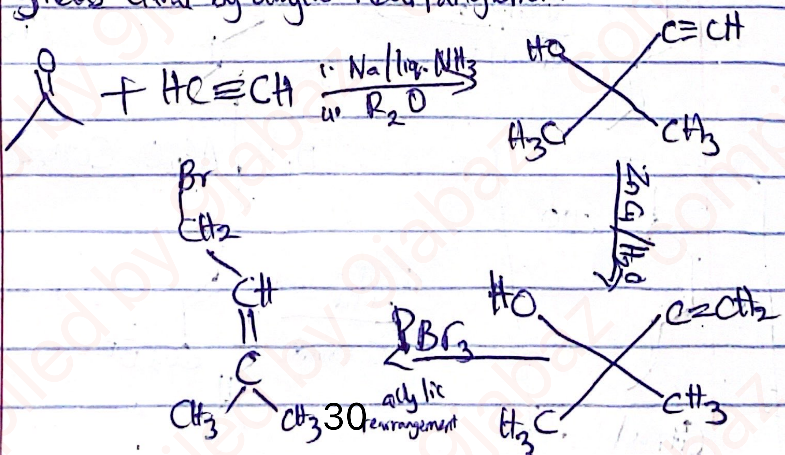
This reaction convert 6-methyl hept-5-en~~e~~-2-one to ~~conver~~ geranic ester by using Reformatsky reaction. Geranic ester is then converted to citral by distilling a mixture of calcium salts of geranic acid and formic acid.

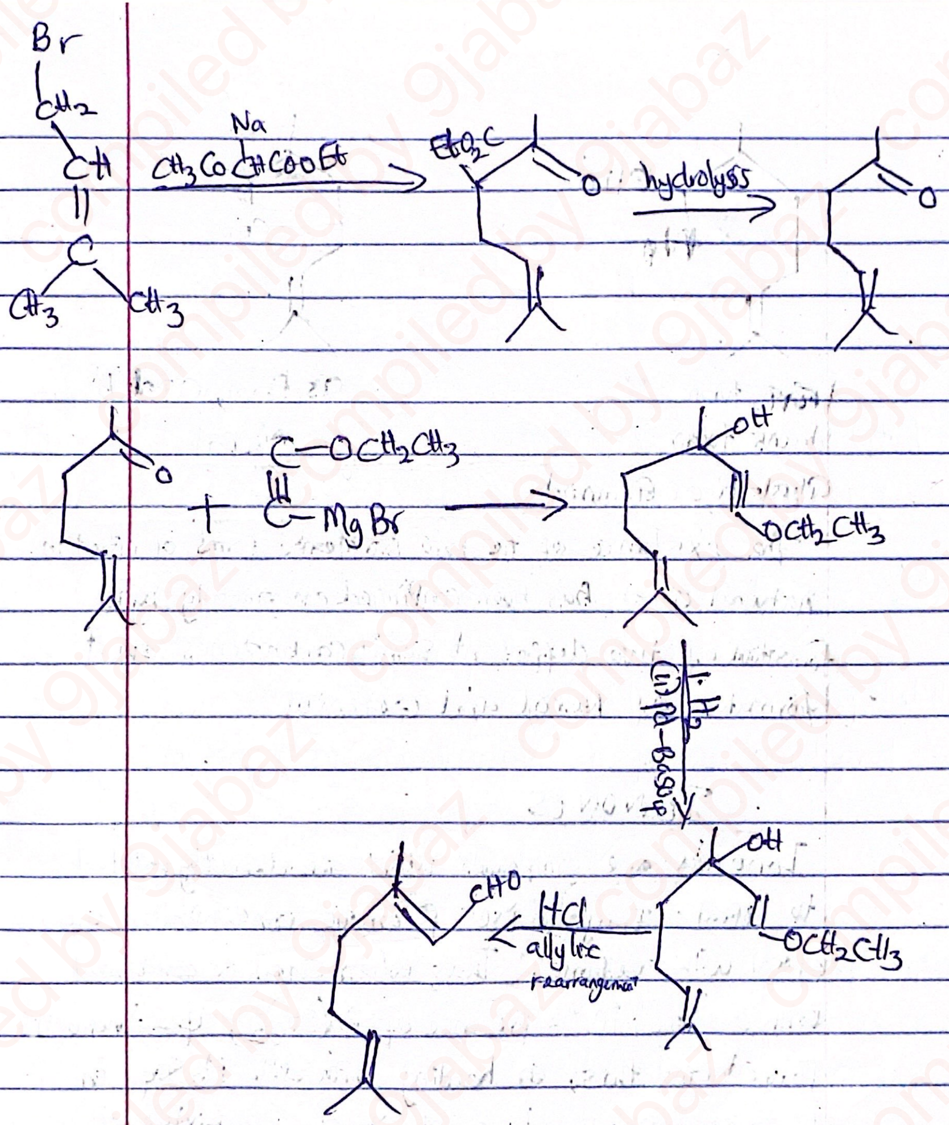


The synthesis of citral has confirmed that, that structure of citral is correct.

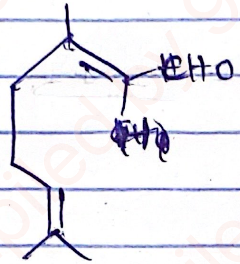
② Using Arens-Van Drop's Synthesis: This is another method of synthesizing citral and involves condensation of acetone with acetylene in the presence of liquid ammonia. The condensation product is then reduced and treated with phosphorus tri bromide (PBr_3) in which there is an allylic rearrangement.

The rearranged product so obtained is treated with sodium salt of acetoacetic ester and then hydrolyzed to yield methyl heptenone and the compounds obtained on condensation with ethoxyacetylene magnesium bromide followed by the partial reduction and acidification that yields citral by allylic rearrangement

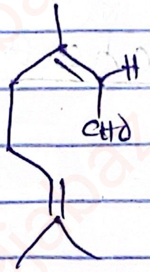




Citral exists in two isomeric forms, i.e. cis and trans forms;



~~trans form~~
trans form
Citral-'a' or Geranial

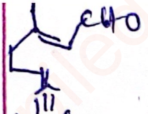


cis form, citral 'b'
or Neral

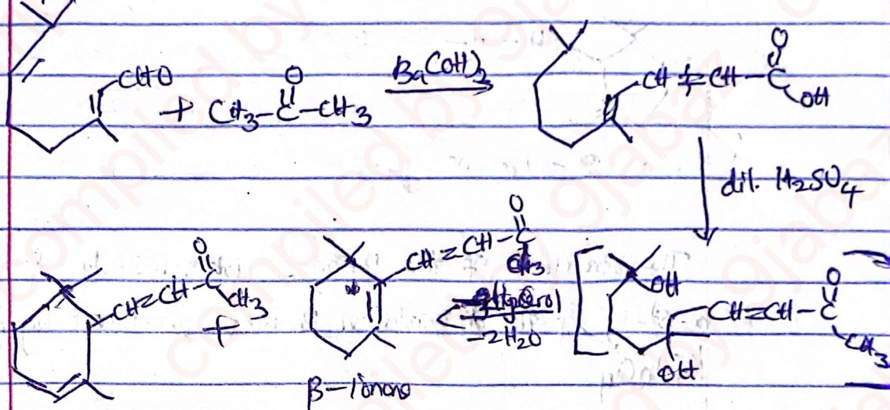
The existence of the two isomeric forms of citral in natural citral has been confirmed chemically by the formation of two different semi-carbazones and formation of Nerol and Geraniol

IONONES

Ionones are compounds which are directly related to citral. They arise from the condensation of citral with acetone. Thus, when citral is condensed with acetone, in the presence of $Ba(OH)_2$, ψ-ionone is formed and this, on heating with dil. H_2SO_4 in the presence of glycerol, it forms a mixture of α-ionone and β-ionone



24th April, 2024



β-ionone

α-ionone Main product

- Glycerol is acting as cyclising agent.

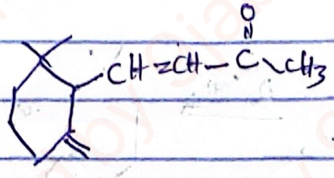
The proportion of α & β ionone varies with the nature of the cyclizing agent used

H_3PO_4 (o-phosphoric acid)

With H_2SO_4, β-ionone is the main product, but with H_3PO_4 α-ionone is the main product.

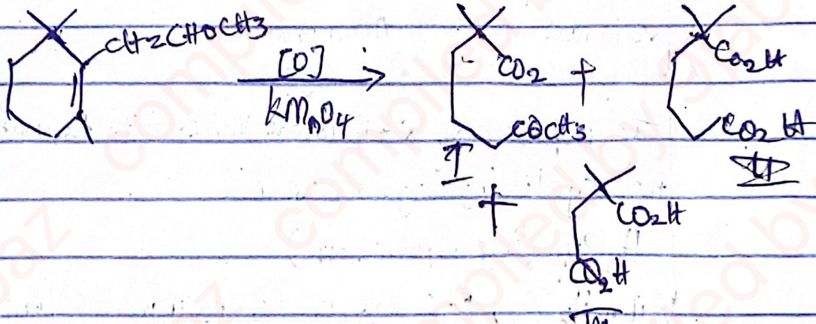
Both ionones can be obtained from natural sources, the β-ionone / β-isomer is optically inactive. i.e, (does not have chiral carbon), while α-ionone is optically active (contains chiral carbon). It can exist in optically active forms since it contains 1 assymetric carbon

We also have the γ-ionone which is synthetic.



γ- Ionone.

The structure of the Ionones were established by a study of the ~~the~~ oxidation product produced by ~~KMnO4~~ $KMnO_4$



I

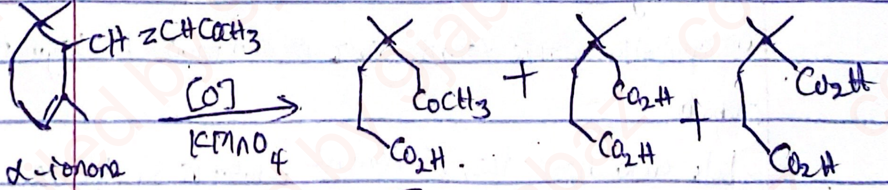
II

III

(II) β-ionone gives Geronic acid from geronic acid,

(II) α,α-dimethyl adipic acid

(III) α,α-dimethyl succinic acid



IV

V

VI

On the other hand, α-ionone gives a mixture of

(IV) Iso geronic acid

(V) β, β-dimethyl adipic acid

(VI) α, α-dimethyl glutaric acid

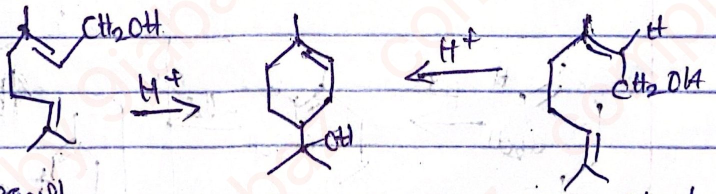
Geraniol, $C_{10}H_{18}O$

Boiling point range (229-230°C) / 757 mmHg

It is found in many essential oils, especially rose oil

It is a primary alcohol, on oxidation form RCHO. It forms a tetrabromide with two molecule of bromide. It has 2-double bonds

Reduction of citral produces geraniol + Nerol (cis form)

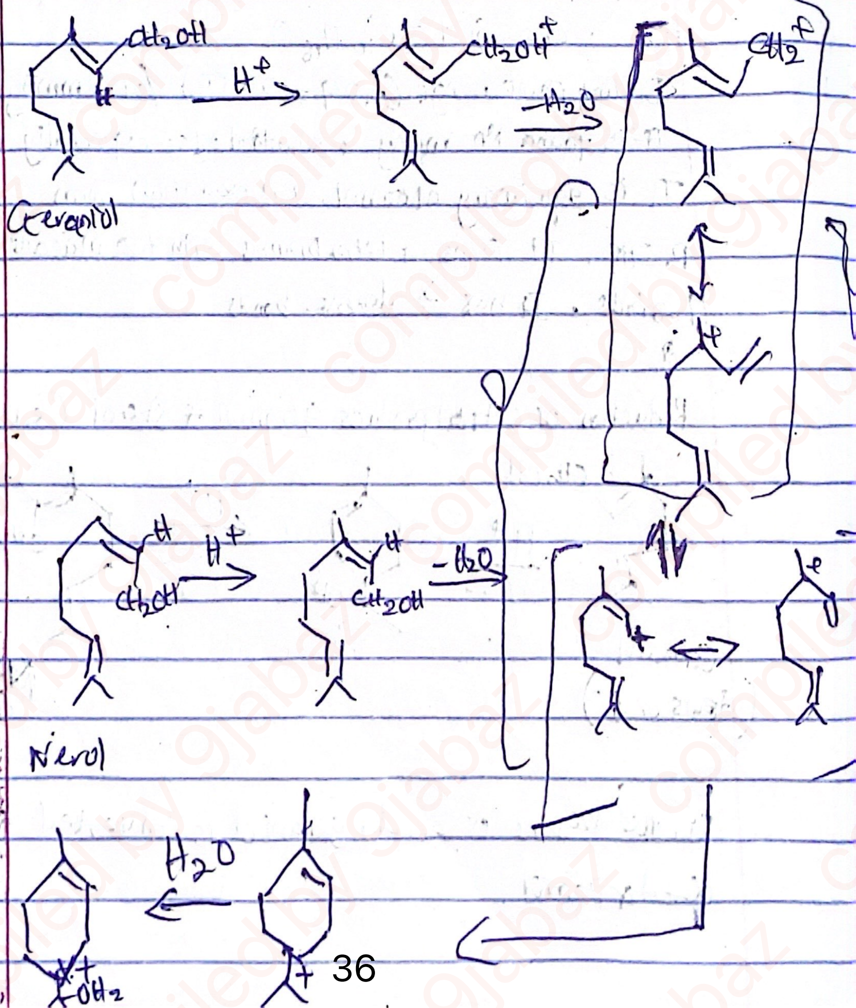


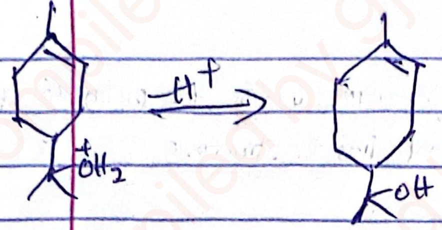
Geraniol
(trans or E-)

Nerol
(cis or Z-)

In the presence of acid, geraniol is converted to α-terpeniol most acyclic monoterpenoid under cyclization to form 6-membered rings, usually in paramethane derivative (4-isopropyl ~~1-me~~methyl cyclohexane).

Cyclization of Geraniol and Nerol





α - terpineol

Nerol occurs naturally in various essential oils e.g oil of Neroli, oil of bergamots etc.

The boiling point of Nerol is 225°C - 226°C

LINALOOL ($C_{10}H_{18}O$)

Boiling point range is 198-199°C

It is an optically active (+) compound, the (−) negative form occurs in rose and the positive form in orange oil. It is a tertiary ROH

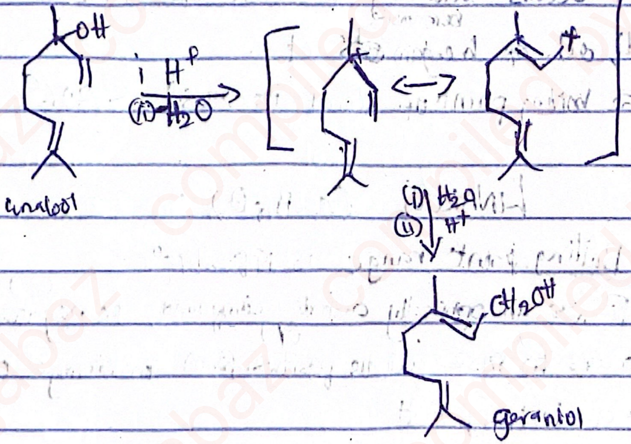
* It is tertiary ROH

* It has two moles of hydrogen on catalytic hydrogenation Therefore, Linalool must contain two double bonds.

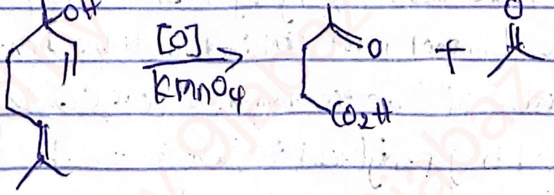
* When heated with acetic anhydride ($(CH_3CO)_2O$), linalool is converted to geranylacetate, which can be converted back to linalool by heating with steam at 200°C under pressu

$C_{10}H_8O \xrightarrow[\Delta]{(CH_3CO)_2O}$ Geranylacetate

* Linalool isomerises to geraniol under the influence of acids. Therefore, linalool has the structure

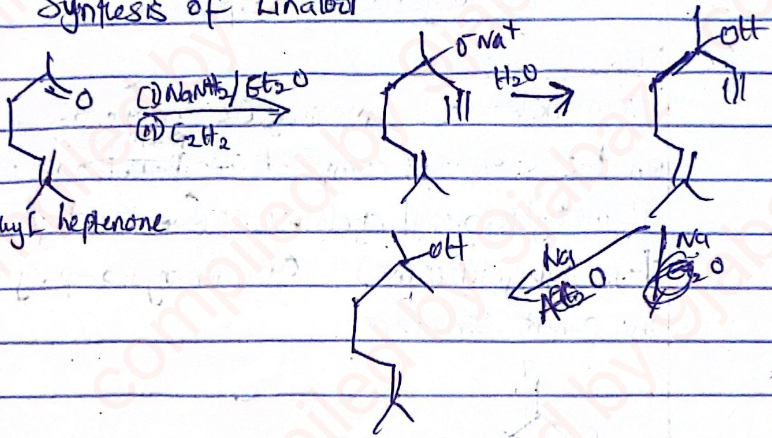


Oxidation of linalool gives laevulic acid and acetone



Synthesis of Linalool

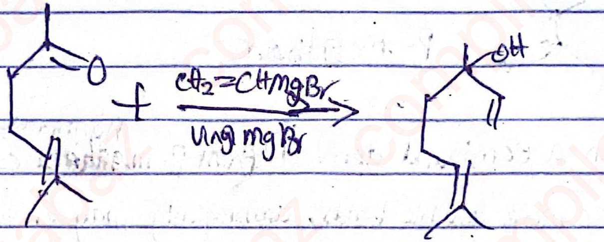
(i)



methyl heptenone

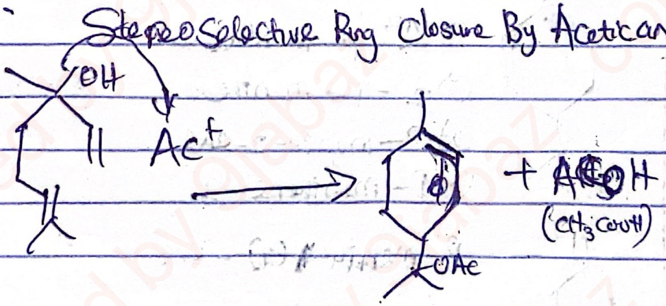
Linalool

(ii)



(+)-linalool

Stereoselective Ring Closure By Acetic anhydride



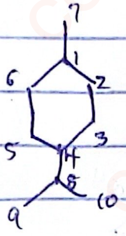
α-terpineol acetate
or
α-terpinyl acetate

p-methane →

Monocyclic Monoterpenoid

Nomenclature

Nomenclature of monocyclic monoterpenoid is based on the saturated compound of ~~p-methane~~ p-menthane or ~~p~~ p-methylisopropyl cyclohexane ~~(or 4-methyl~~ (or 4-isopropy 1-methylcyclohexane) or hexahydro-p-cymane as the parent structure.



P- menthane

When a compound derived from p-menthane contains one or more double bonds, ambuguity may arise as to the position off the double bond.

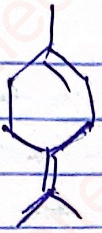
①

(i) Δ^2-p-menthene
(ii) 2-p-menthane
(iii) p-menth-2-ene
(iv) p-menthene-2

②

P- mentha-~~[illegible]~~(7) -ene

(3)



p-menth-1(2), 4(8)-diene

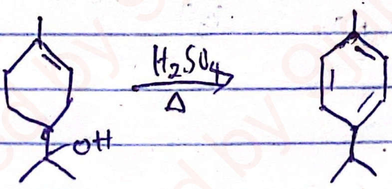
29/04/2025

α- Terpeneol $C_{10}H_{18}O$, mp 35°c (solid)

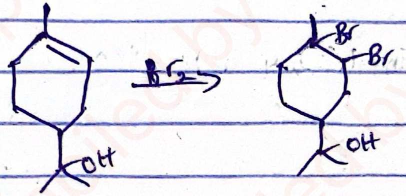
It is a solid, liquid or vapour especially for the racemic medication

* It is optically active and occur naturally in the (+) and (−) forms and also (±) - forms can also be found in nature.
* The oxygen atom is present as a tertiary -ROH group
* It adds on 2 Br atoms, therefore it contains one double bond
* The saturated α- terpeneol will therefore have $C_{10}H_{20}O$, indicating 1 DBE that it is a monocyclic.

When heated with H_2SO_4, it forms para-cymene, implies that it contains p-cymane skeleton/structure. Thus the structure of α - terpeneol



α- terpeneol p- cymene

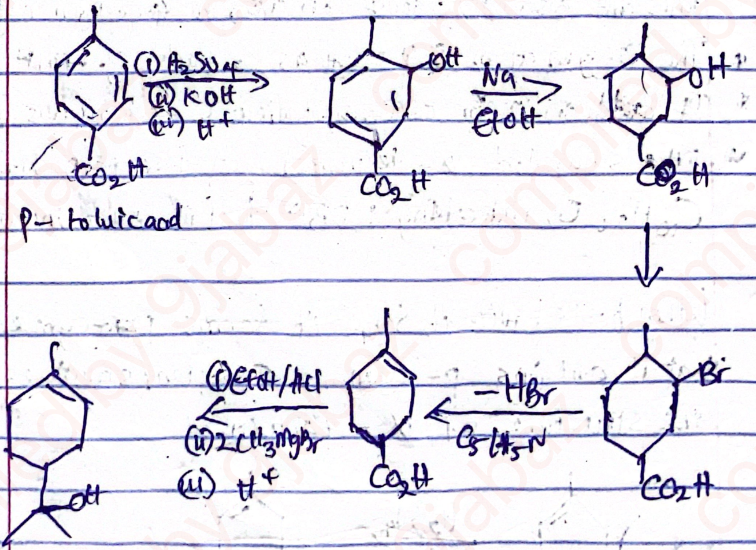


Possible Synthetic Routes of α- Terpineol

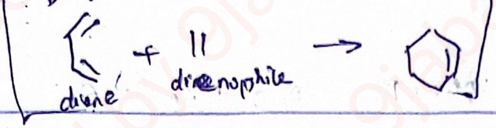
~~How can we sy~~

α- terpeneol can be synthesized in the lab through;

(i) Starting with p- toluene acid

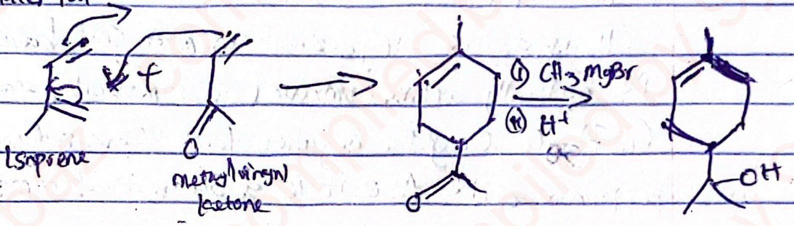


cf Dield — alder's reaction

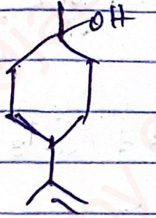


* read diels-alder's reaction

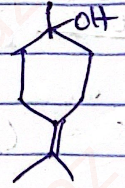
㉗ A much simpler method of synthesizing α-terpeneol was carried out ~~As by Carrying out~~ by Alder and Vogt, in 1949 through the use of Diels-Alder's reaction, using isoprene and methyl vinyl ketone as the starting material



Other Terpeneols



β-terpeneol
Mp. 32–33°C



γ-terpeneol
Mp 68–70

MENTHOL AND MENTHONE

Mentol is the major constituent of Mentha piperita. It is known as (peppermint camphor or mint camphor) is the major constituent of peppermint oil, and it is responsible for its odour and taste and the cooling sensation when it is applied on the skin.

It is active ingredient in most cold balms. Mentol is optically active compound with molecular formular $C_{10}H_{20}O$, Only the negative form occurs naturally in peppermint oil. Also, it is a saturated compound, and the oxygen is an alcoholic group.

- Oxidation of mentol gives mentone i.e a ketone. This implies that the OH group in menthol is 3° -ROH

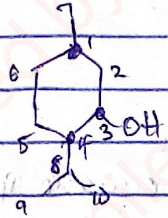
$$C_{10}H_{20}O \xrightarrow{[O]} \underset{\text{mentone}}{C_{10}H_{18}O}$$

- $C_{10}H_{20}O \xrightarrow{PCl_5} C_{10}H_{19}Cl + POCl_3 + HCl$

- On dehydration followed by dehydrogenation, it gives P-cymene

$$C_{10}H_{20}O \xrightarrow[\text{(ii) Dehydrogenation}]{\text{(i) Dehydration}}$$

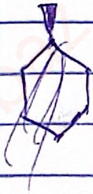
Therefore, the structure of mentol is

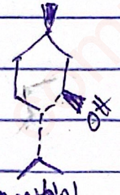


It has three chiral carbon on Position 1, 3, 4

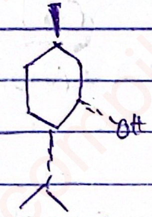
Optically active = $2^3 = 8$

Racemic mixture = 4

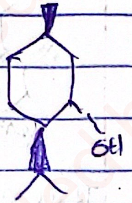




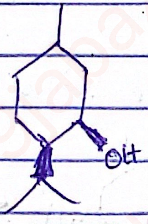
menthol



neomenthol



Isomenthol



Neo isomenthol

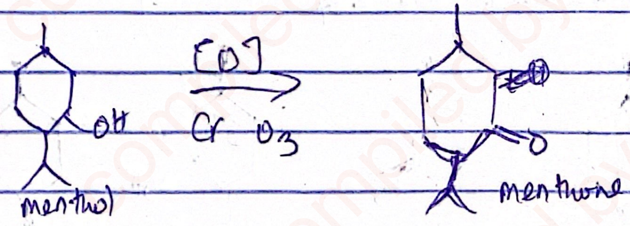
MENTHONE

molecular formular $C_{10}H_{18}O$

bp: 204°C / 750mmHg

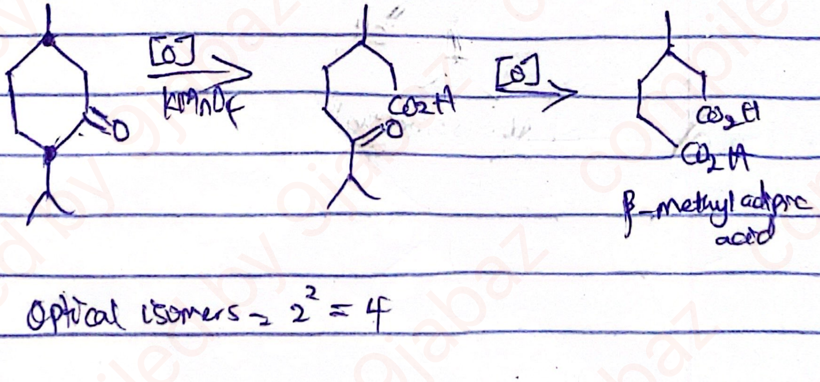
[illegible] ~~form~~

(-)- form of menthone occurs in peppermint oil and can also be prepared from (-)- form methone by using chromic acid for oxidation.



It is also a saturated compound with characteristic properties of ketone

* Oxidation of menthone leads to a ketoacid



Optical isomers = $2^2 = 4$

CARVONE

Carvone is $C_{10}H_{14}O$ and has a bp 230°C/750mmHg.
It occurs in various essential oils, e.g in spearmint and caraway oils in optically active forms.

* And as racemic modifications, it behaves as a ketone and adds on four atoms of bromine, i.e it has two double bonds

$$C_{10}H_{14}O \xrightarrow{4[Br]} C_{10}H_{14}OBr_2.$$

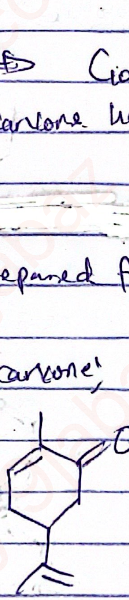
* It is converted to carvacrol when heated with Phosphoric acid

$$C_{10}H_{14} \xrightarrow[\Delta]{H_3PO_4} C_{10}H_{14}O$$

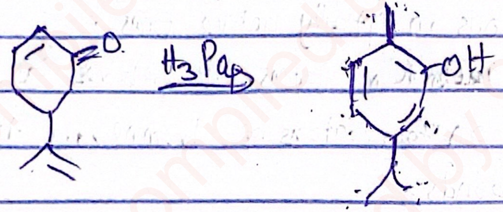
This implies that carvone has the p-cymene skeleton

* Carvone can be prepared from α-terpeneol

Structure of carvone;



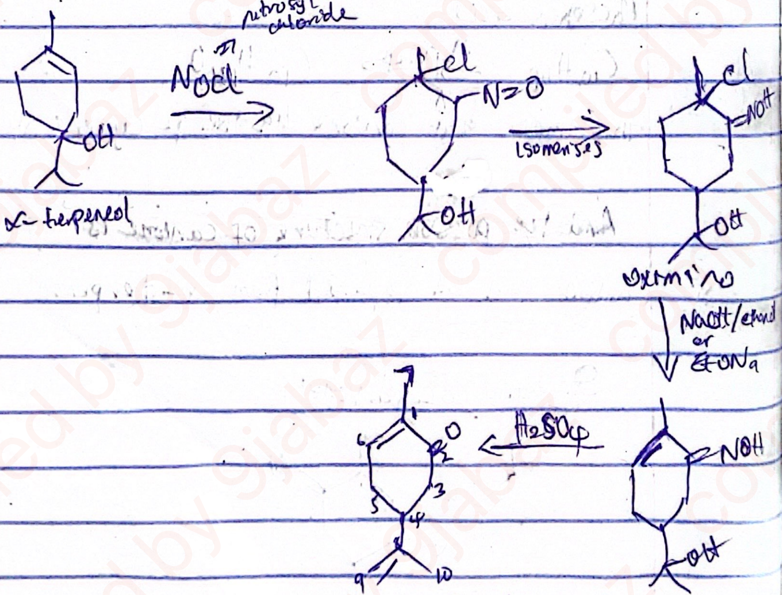
* When Carvone is heated H_3PO_4, we are left with Carvacrol



Carvacrol

$C_{10}H_{14}O$

Preparation from α-Terpeneol

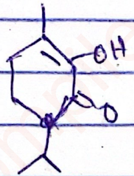


p-ment-6,8-dien-2-one

DIOSPHENOL

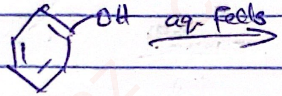
molecular formular $C_{10}H_{16}O_2$, mp is 83°C

It is found is leaves of buchu plants



λmax = 274nm

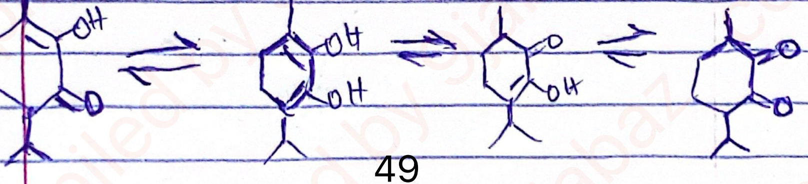
The enolic structure accounts for its acidic properties (soluble in alkaline solution) and gives intense green colour with ferric chloride



intense blue black colouration

It is optically active ~~but~~ only as racemate because of the number of negative and positive forms ((−)- and (+)- forms)

The molecule contains a chiral center, but diosphenol has been obtained only as a racemate, this could also be due to either or both of the following mechanism.



* Linalool
* Limolene

Bicyclic Monoterpenoids

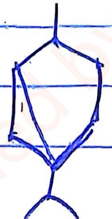
These are classified into three classes depending on the ring sizes of the molecule.
Generally, they consist of two rings;

(i) Six membered ring and the other ring is varied on
(ii) size

Class 1: (6 + 3 membered ring) e.g Thujane
Class 2: (6 + 4 membered ring) e.g Pinane
Class 3: (6 + 5 membered ring) e.g Bornane

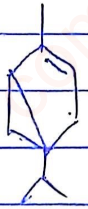
Class 1: (6 + 3 membered ring)

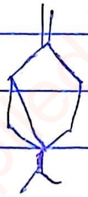
It consists of a six membered ring plus a three membered ring. This class is known as Thujane



The Thujane group are characterized by the ease at which the three membered ring opens under acidic condition.

The unsaturated derivative is therefore known as Thujene

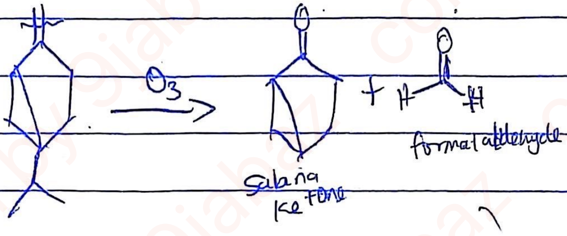


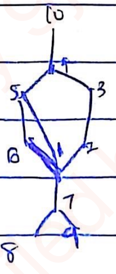


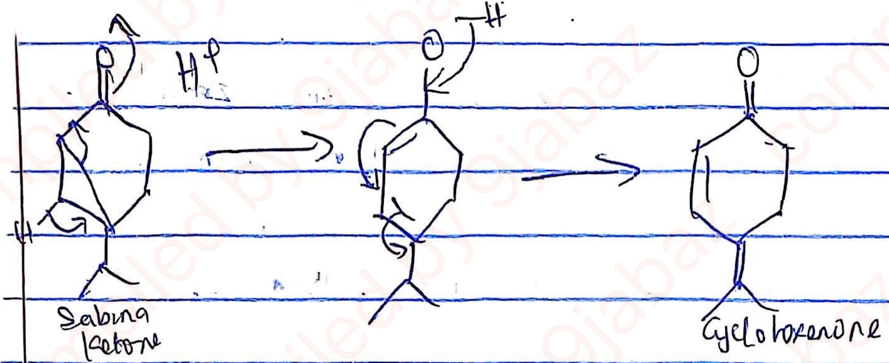
Sabinene

This unsaturated derivative occurs naturally in oil of Turpentine

Ozonolysis of sabinene gives sabinaketone which isomerises cyclohexenone, which in the presence of acid







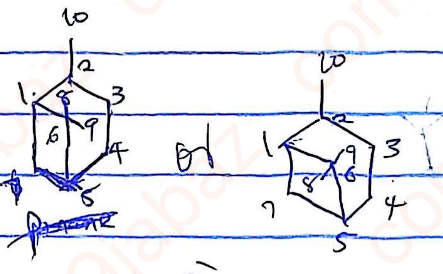
In this case, the cyclopropane ring opens contrary to markovnikov's rule, this may be explained by the nucleophilic oxygen being involved as shown

Class II: The pinane Group

This is the most important member of bicyclic monoterpenoid and α-Pinane with boiling point of 156°C is a major member of the pinane group

It is found in the oil of turpentine

α-Pinene
$C_{10}H_{16}$



α-Pinane

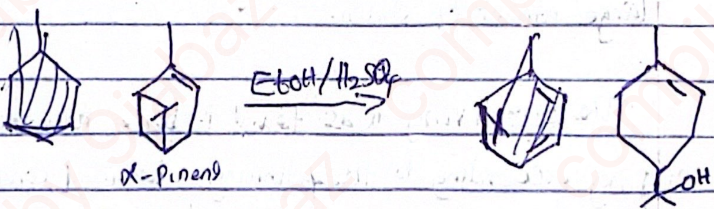
DBE = 3

Catalytic hydrogenation gives the parent hydrocompound pinane

α-pinene add two atoms of hydrogen to form a saturated compound which implies there is one double bond in α-pinene. Therefore the parent hydrocarbon is $C_{10}H_{18}$ corresponding to C_nH_{2n-2} which means two rings, therefore α-pinene is bicyclic

13-05-2025

When α-pinene is treated with ethanolic H_2SO_4, it is converted into α-terpineol



α-Pinene

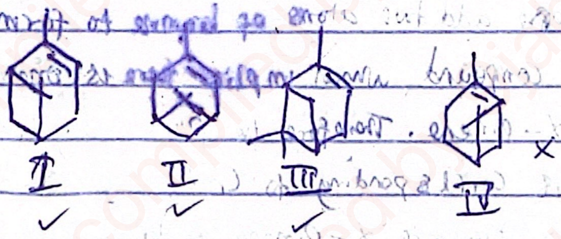
which implies that α-pinene contains a 6-membered ring and another ring since it is bicyclic

In the formation of terpineol, one molecule of water is taken up and the -OH group is attached to carbon 6

This suggests that the C6 is involved in ~~the~~ forming

Second-4-membered ring in α-pinene

There are three possible attachment for the C-6

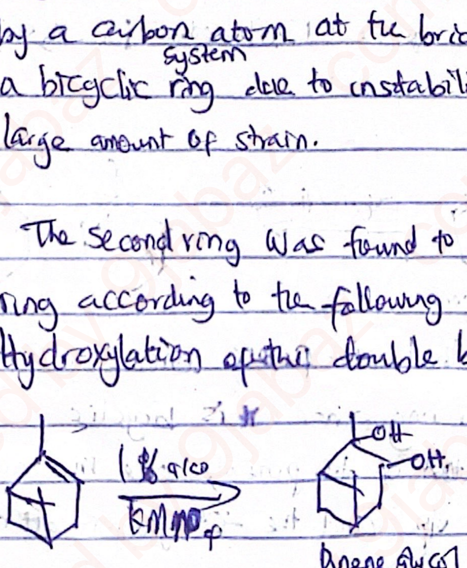


The possibility for the fourth point of attachment is rejected according to Bredt's rule

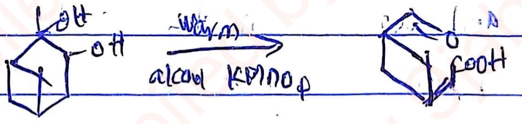
Bredt's rule states a double bond cannot be formed by a carbon atom at the bridge head of a bicyclic ring system due to instability as a result of large amount of strain.

The second ring was found to be a four membered ring according to the following chemical analysis

① Hydroxylation of the double bond gave pinene glycol

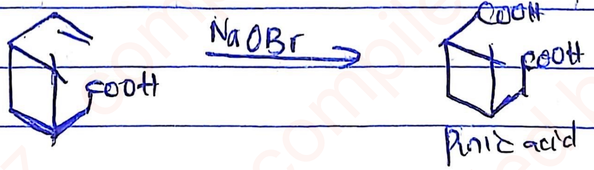


2. Pinonic acid is saturated mono-carboxylic acid with the formula $C_{10}H_{16}O_3$ is formed by scission of the glycol bond



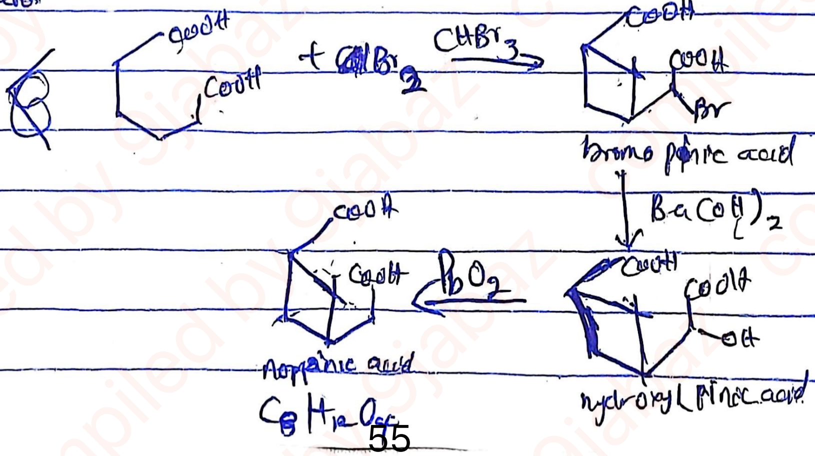
Pinonic acid
($C_{10}H_{16}O$)

(3) Action of hypo bromide (HOBr) on pinonic acid gives Pinic acid



Pinic acid

On treatment with bromine, barium hydroxide and then oxidation of the product using PbO_2 gives norpinic acid



This above analysis gave cis-norpinic acid ($C_8H_{12}O_4$) in saturated dicarboxylic acid.

This analysis above confirms the structure of α-pinene and also confirm the fact that the second ring is a 4-membered ring as shown in the last product.

Also that α-pinene contains 2 methyl groups attached to alpha carbon in the second ring.

~~This~~ Norpinic acid hasn't been second ring intact contains these two methyl groups. Therefore, its structure may more accurately becomes.

$$C_8H_{12}O_4 \longrightarrow (CH_3)_2C_4H_4\cdot(CO_2H)_2$$

(gem-geminal)

There are ~~also~~ other isomeric forms of α-pinene and they are β and δ-Pinene

β-Pinene

δ-pinene

α-Pinene

The NMR Spectral of α and β pinene shows that the two gem dimethyl groups have different chemical

Shift. ~~have different Value~~s

For example

α-pinene: 1.27 & 0.85

β-pinene: 1.23 & 0.72

The methyl groups with lower δ value is the one closer to the double bond and therefore shielded by the π-electron cloud. The two isomers are distinguished by the fact that NMR of α-pinene shows three methyl groups.

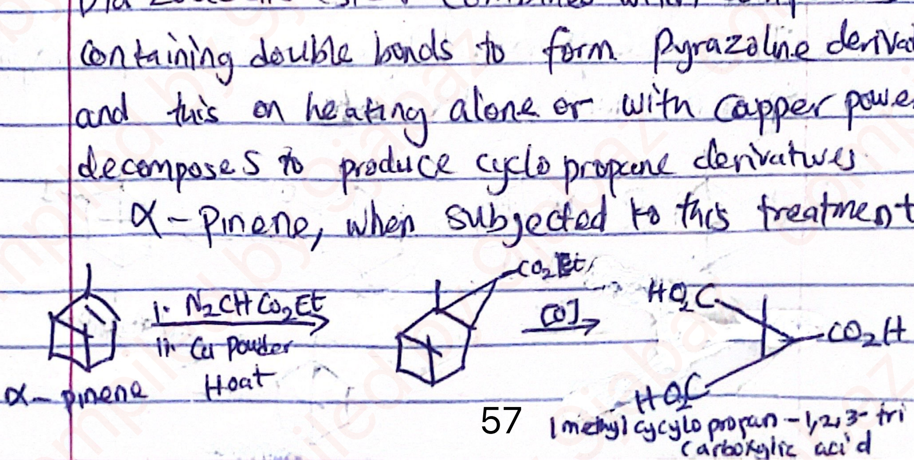
The third (α-pinene) has d-value of 1.63. While β-pinene only shows two methyl groups.

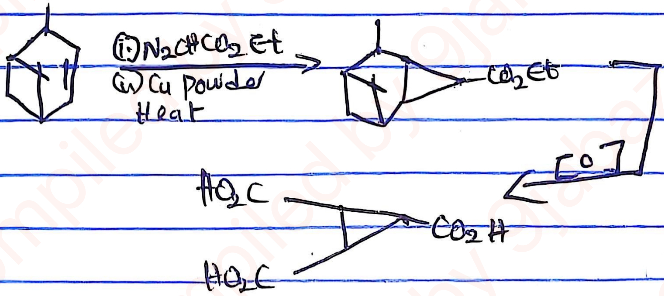
Chemical way of distinguishing α & β pinene

The α and δ pinene are distinguished thus

Diazoacetic ester combines with compounds containing double bonds to form Pyrazoline derivative and this on heating alone or with copper power decomposes to produce cyclopropane derivatives

α-pinene, when subjected to this treatment,





cyclopropan-1,2,3-tricarboxylic acid.

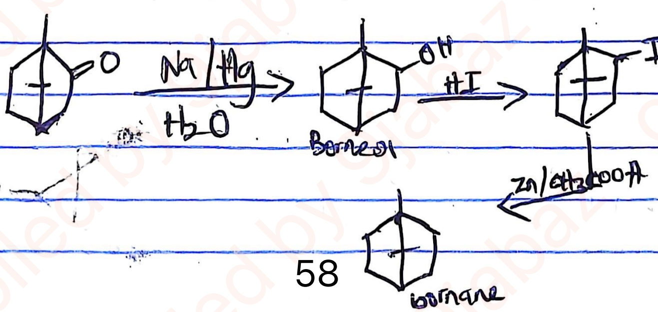
α pinene when subjected to the treatment gave 1-methylcyclopropan-1,2,3-tricarboxylic acid, while δ-pinene gave cyclopropan-1,2,3-tricarboxylic acid.

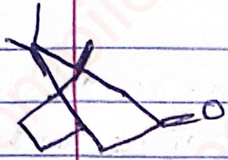
6+5 membered group

Bornane ~~& Norbornane~~ Group.

Bornane or Camphane has the structural formular $C_{10}H_{18}$. It can be prepared from Camphour and in other ways

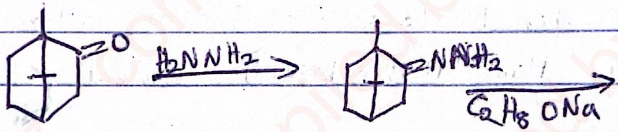
① It can be prepared by a reduction of camphour to a mixture of borneols



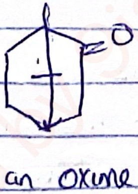


camphor

② Reduction of camphor by wolf-kishner



melting point bornane is 156°c
It is optically inactive.
Camphor occurs as Solid in nature with melting point of 180°c. It is optically active, the (+) ~~a~~ α (–)- forms occur naturally and the racemic form is obtained in synthetic camphor.
It is has a molecular formular of $C_{10}H_{16}O$



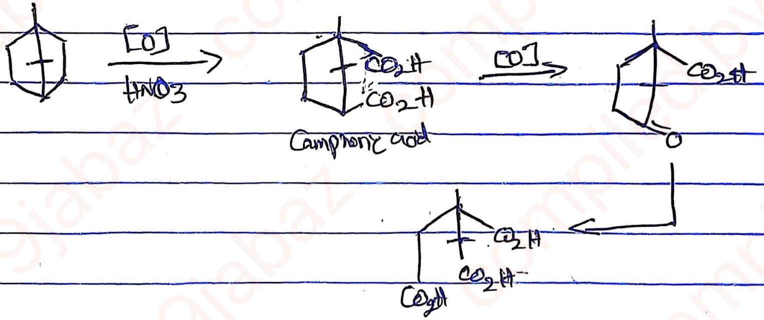
It form an oxime, therefore, the functional nature of the oxygen is oxo

Chemical analysis

1. Oxidation of Camphor gives a dicarboxylic acid with ten carbon atoms. Therefore, this confirms that the oxo group is keto. If it were CHO, it would have resulted to a monocarboxylic acid.

It proves to be a saturated compound, thus the parent hydrocarbon has the molecular formular $C_{10}H_{18}$ with DBE of 2. Hence, it is a bicyclic compound

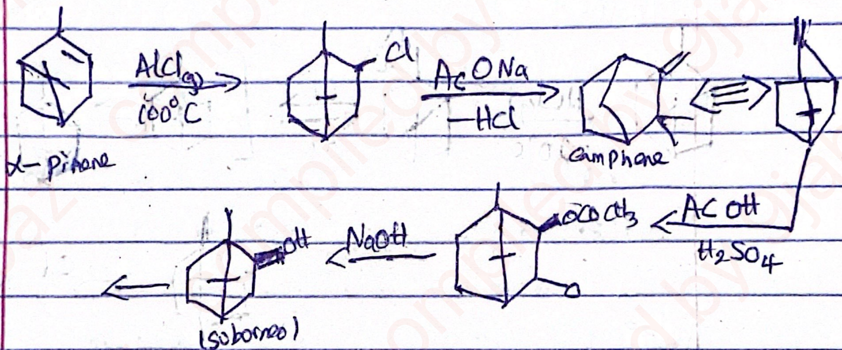
Reactions



camphoronic acid

Camphour has two chiral centers, i.e two pairs of enantiomers are possible, but due to its stereochemistry only one pair of enantiomers exists. Only the cis form is possible; the trans fusion of the gem-dimethyl bridge to the cyclohexane ring is impossible. Therefore, only the enatiomers of the 6 form are known

Commercial preparation of complex.



Wagner-Meerwein Rearrangement

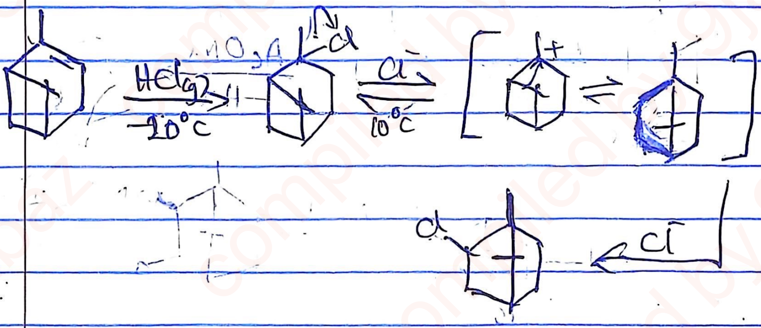
Wagner proposed a molecular rearrangement for ~~the~~ interconversion of camphene to borneol and bornylchloride. And also, conversion of α-pinene to bornyl chloride.

Meerwein investigated this rearrangement in the terpenoid compound or groups.

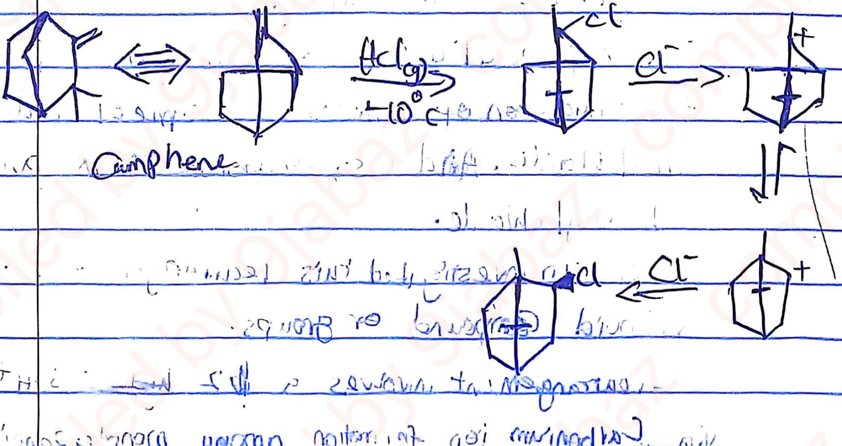
The rearrangement involves a 1,2 ~~hydride~~ shift via Carbonium ion formation among monoterpenoids.

and this is widely refers to as Wagner Meerwin rearrangement.

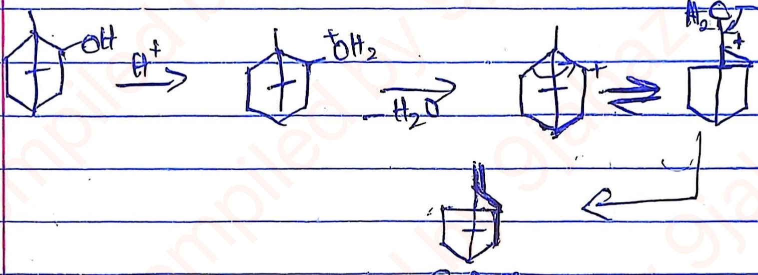
* Conversion of α-pinene hydrochloride to bornyl chloride



* Conversion of camphene hydrochloride to isobornane chloride



Dehydration of Borneol to Camphene



Camphene

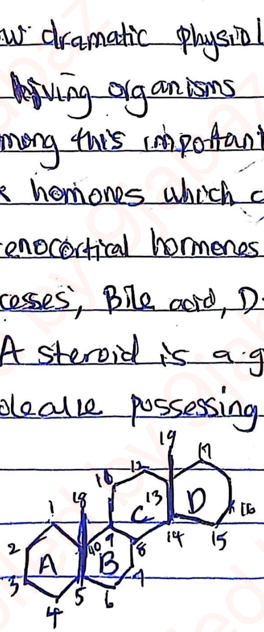
30th May, 2025

In addition to fats, phospholipids and terpenes, the lipid extracts of ~~[illegible]~~ plants and animals also contain steroid. Steroids are important biological regulatory that nearly show dramatic physiological effect where they are administered to living organisms

Among this important steroid compound are male and female sex hormones which controls maturation and reproduction; adrenocortical hormones which regulate a varieties; metabolic processes; Bile acid, D-vitamins and certain cardiac poison.

Most hormones are steroids.

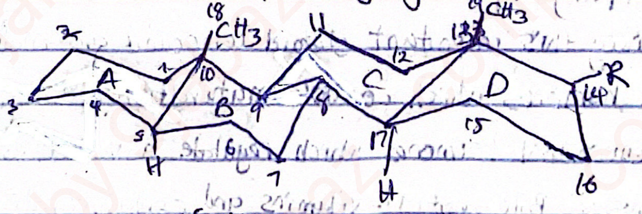
A steroid is a general term used to describe organic molecule possessing perhydrocyclopentanophenanthrene nucleus



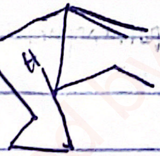
The four rings in this nucleus are designated by the alphabet A, B, C, D, begining from the lower left to the upper right and the carbon atoms are numbered begining from the A ring.

In most steroids, the BC and CD rings junction are trans. The AB junction however, may be either cis or trans. The C_{18} and C_{19} methyl groups are called angular methyl groups can serve as a reference point for sterochemical disintegration. Groups that lie on the same side are the angular methyl groups, which are designated as ~~methyl~~ β group. while those on the other side are called α-group.

When the AB ring is trans, the H-atom at position 5 is α and when it is cis, the hydrogen is β



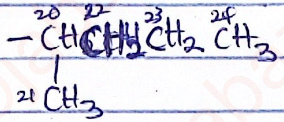
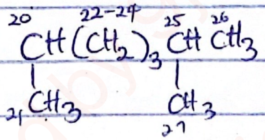
5α- Series of steroids



Unlike like simple cyclohexane ring, steroids are confrained to a rigid conformation and cannot undergo ring flip.

A systematic numenclature, the R group at position 17 primarily determined the base name of individual steroids

(i) If R is $-H$: The name of the steriod will be Androstane.

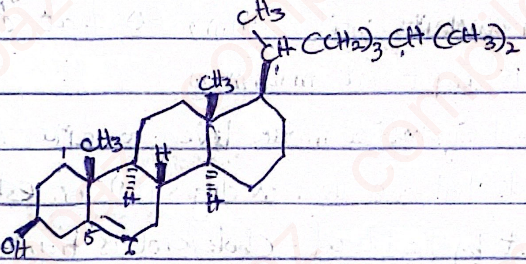
	R	Name
(i)	$-H$	Androstane
ii	$-H$ (with H replacing CH_3 in position 19)	Enstrane
(iii)	$-CH_2CH_3$	Pregnane
IV	 $-\underset{{}^{21}CH_3}{\overset{20}{C}H}\overset{22}{C}H_2\overset{23}{C}H_2\overset{24}{C}H_3$	Cholane
(V)	 $\underset{{}_{21}CH_3}{\overset{20}{C}H}\overset{22-24}{(CH_2)_3}\underset{CH_3\,{}_{27}}{\overset{25}{C}H}\overset{26}{C}H_3$	Cholestane

Steroids

These are group of crystalline steroidal alcohol containing between 27 - 30 C- atom usually.

They all possess a 3-β-hydroxyl group, and an endocyclic double usually at position 5 and 6.

ⓐ Cholesterol: It is the principal steroid, but by no means, the only one found in the mammalian tissue. It occurs in high concentration in the brain, spinal cord and adrenal gland



5-cholesten-3β-ol

Cholest-5-en-3β-ol

Cholesterol occurs widely in human body, but not all of its biological function are known. However, it is known to serve as a intermediate or precursor in the biosynthesis of all steroids in the body and therefore, essential to life.

However, there is no need for extra cholesterol in the human diet because the body can synthesize all the

Cholesterol its need

High level of blood cholesterol has been indicated in the development of arteriosclerosis (hardening of the arteries) and in heart attack that occurs when cholesterol containing plaques block the arteries of the heart.

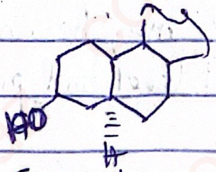
For an organism to remain healthy, there has to be an intricate balance between the biosynthesis of cholesterol and its utilization, so that arterial deposition is kept at minimum

Cholesterol synthesized in the liver is either converted to bile acids that are used in digestion or esterified for transport by the blood. Cholesterol is transported by the blood and taken up in cells in form of lypo protein complexes named on the basis of their densities

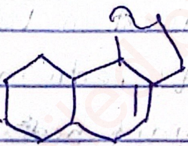
Low Density Lypoprotein (LDL) transports cholesterol from the liver to the peripheral tissues while High Density Lypoprotein (HDL) transports cholesterol back to the liver where surplus cholesterol is disposed off as bile acid.

HDL are called good cholesterol because high level of HDL may reduce LDL deposit in arteries, because high level of LDL are associated with the arterial deposition of cholesterol that causes cardiovascular diseases (heart disease) and that why LDL is called the bad cholesterol.

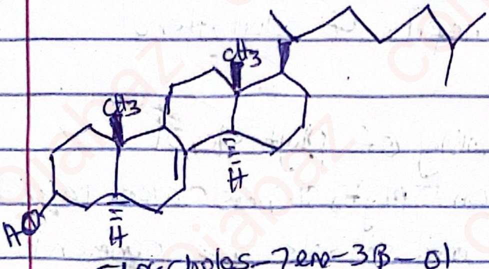
In most tissues, cholesterol is accomplished by small amounts of other steroids, e.g 5α-cholestanol,



5-α-Cholestanol



7α-dehydrocholesterol



5α Cholest-7en-3β-ol

Phytosterols

Phytosterols are family of compounds similar to Cholesterol which is been shown/found to lower the cholesterol level when supplemented in the diet. 2~3g of Phytosterols have been shown to reduce LDL cholesterol by 5 - 15. It kan be consumed in the form of ~~exact~~ phytosterol enriched function food or neutraceticeal. Increasing the amount of Phytosterols consumed in Variety of foods may be an important way of reducing cholesterol level and prevent coronary heart diseases

Assignment

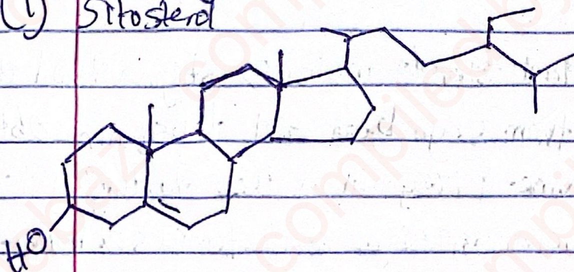
The health benefits of Phytosterol

The chemistry of phytosterol

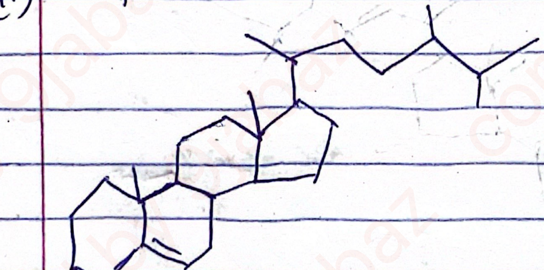
Phytosterols and phytostanols also refer to as plant sterols and stanols are common plant and vegetable constituents and are therefore normal constituents of human diet. They are structurally related to cholesterol, but differ~~ent~~ from Cholesterol in the structure of the side chain, but sterols and stanols have high melting points and can be esterified with fatty ~~carboxylic~~ acids of vegetable origin. The resulting esters are liquid or semi-liquid material, having comparable chemical and physical properties to edible fats and oils enabling supplementation of various processed foods with phytosterols and phytostanol esters

The phytosterols include the following

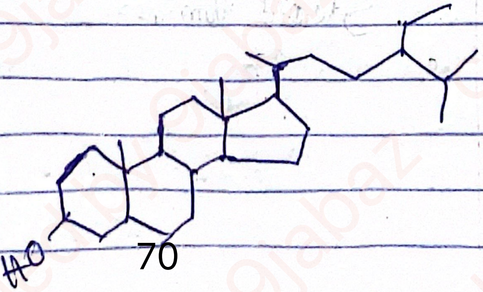
(i) Sitosterol



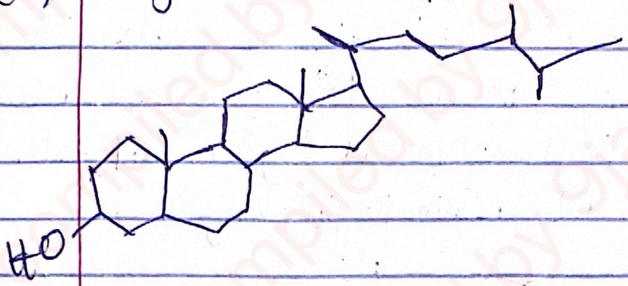
(ii) Campesterol



(iii) Sitostanol;

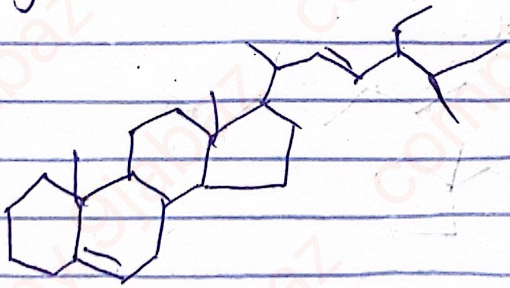


(iii) ~~Stigmasterol~~ Campestanol



Other important sterols include, Stigmasterol obtained commercially from soya bean and diosgenin obtained from mexican vine. Diosgenin is the starting material for the commercial synthesis of cortisone and sex homones

(iv) Stigmasterol



Steroid Homones

13th June, 2025

Steroids that have a phenolic ring A (i.e those in which ring A is aromatic and bears the hydroxyl group) are ubiquitous Product of the ovary of vertebrate animals.

The two important classes of steroidal hormones found in nature are the sex hormones produced in the sexual organ also (Known as gonads) and the adrenocortical hormones produced by the adrenal cortex

Sex Hormone

Sex hormone can be classified into three major groups

(i) Estrogens (female sex hormone)
(ii) Progestins (pregnancy hormone)
(iii) Androgens (male sex hormone)

(i) Estrogen possesses an aromatic ring A and consquently they have no angular methyl group ~~at~~ carbon 10, ~~the~~

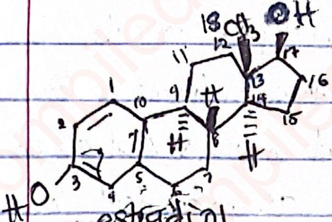
The Androgens, of which estradiol is the most potent, estradiol is the primary estrogen while estrone is a metabolized form of estradiol that is excreted.

Estrogen are excreted by the mammalian ovum and they promote the development of secondary sexual characteristics that appear at the onset of puberty.

Estogen also stimulates the ~~deve~~ development of mammary gland

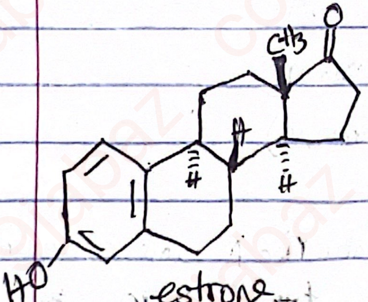
✱ functions and importances of hormones

(milk producing gland): during pregnancy and the induced estrus (heat) in animals



estradiol

1, 3, 5 (10) - estratrian-3,17β-diol



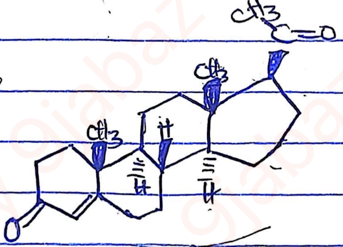
estrone

3-hydroxyl-1,3, 5(10) estratrien-17-one

11. Progestene ; The most important progestine is progesterone. Progesterone prepares the lining uterus for the implantation of fertilized ovien during pregnancy.

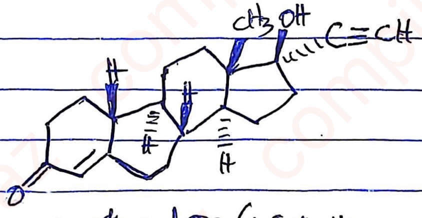
Continued progesterone secretion is necessary for the completion of pregnancy and lactation. It suppresses ovulation and keeps pregnant women from conceiving again while pregnant.

This is the reason why synthetic progestien are now taken as oral contraceptive



(progesterone)

4-Pregnene-3,20-dione



Norethindron (A synthetic progesten)

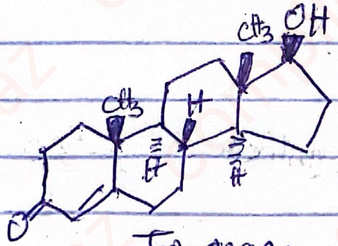
17α-ethynyl-17β-hydroxyl-4-

4 esteren-3-one

3. Testo sterone and Androsterone: This are the two main important main sex hormone (androgen) and both are synthesized in the testiles from cholesterol

1. Testoterone: It is the primary sex hormone which controls the development of male genitals and secondary male sexual characteristics

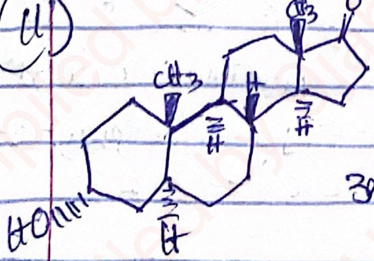
(I)



Testosterone

17β-hydroxy-4-androsten-3-one

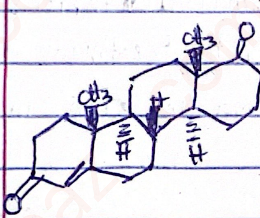
(II)



Androsterone

3α-hydroxy-5α-androstan-17-one

(ii) Androstenedione: This are important minor hormone that have particular recieved attention because of its use by prominent athletics. They are usually synthetically prepared/made.



Androstenedione

4-androstene-3,17-dione

Adrenal Cortical Hormone

Over 28 different hormones have been isolated from the adrenal cortex (which is part of the adrenal gland that sits on the kidney).

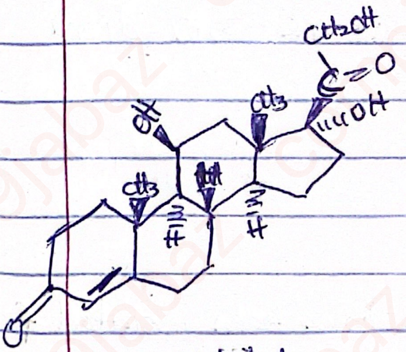
Most of the adrenal cortical steroid have an oxygen function at position 11.

(i) Cortisol: This is the major hormone synthesized by the human adrenal cortex.

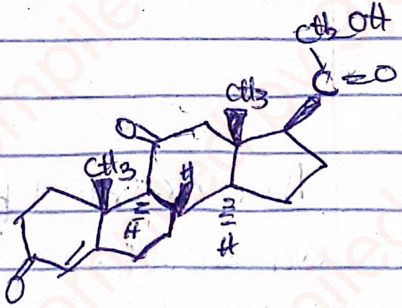
Adrenocortical hormons have many biological hormons which includes carbohydrate, protein and lipid metabolism. They are also involved in the regulation of water and electrolyte balance and in reaction to allergic and inflammatory conditions

~~It also helps in reg~~

② Cortisone for example, is an antiinflamatory Compound used in the treatment of rheumatoid arthritis. Other similar compounds are now used in the treatment of variety of disorders such as ~~asthma~~ asthma and skin inflammation



11β, 17α, 21-trihydroxy-4-Pregnen-3,20-dione (Cortisol)



17α,21-dihydroxy-4-pregnene-3,11,20-trione (Cortisone)

Dr. Taiwo's Part

Alicyclic Compounds

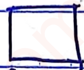
The "Ali" part comes from aliphatic and the "cyclic" comes from carbocyclic compounds in which the atoms of the rings are made of only carbon.

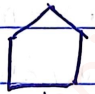
Therefore alicyclic compounds are compounds which includes saturated and unsaturated.

The behaviour of alicyclic compounds are similar to aliphatic hydrocarbon e.g properties of Δ is similar to C_3H_8

Example of alicyclic Compounds


Cyclopropane


Cyclobutane

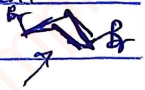

Cyclopentane


Cyclohexane

Stereo Chemistry and Conformation in Alicyclic Compounds

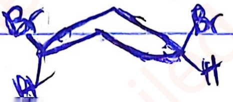
~~(i) Cyc~~

(1) Cyclopropanes, cyclo butanes and Cyclopentanes: All these three classes of compounds are planar molecules, i.e their conformation and stereochemistry is dependent on the substituent attached to the molecule.



If we have a cyclobutane that is non planar the conformation will reduce the torsional strain.

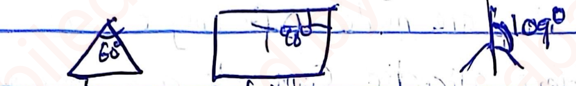
e.g in 1,3 dibromobutane



Equatorial are stable

Types of Strains

① Bayer's strains (Angular): For 3- or 4- membered ring. e.g (cyclopropane & cyclobutane) we have bound to have strain in the molecule.



cyclopropane cyclobutane

In an acyclic molecule, the ~~bond~~ tetrahedral angle of 109° about the sp^3 hybridized C is preferred to reduce C—C and C—H repulsion

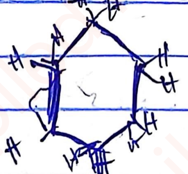
But, in a 3- or 4- membered ring, this cannot be achieved.
This situation raises the energy of the system/molecule relative to an acyclic one.

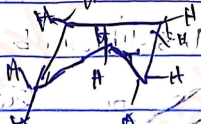
This excess energy that is as a result of the constraint on the ring is called Bayer (Angular) strain.

② Pizer or Torsional Strain: ~~It~~ occurs along rotation about Carbon-Carbon (C—C)

Any molecule that is forced to adopt an eclipsed conformation is said to suffer from torsional strain, because the molecule cannot rotate to avoid repulsion-

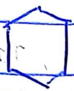
torsional strain is reduced can.





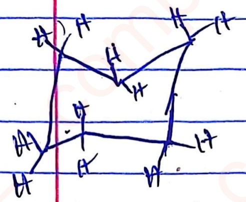
envelop conformation of cyclopentane

For cyclohexane (has: chain, boat & twisted boat conformation)



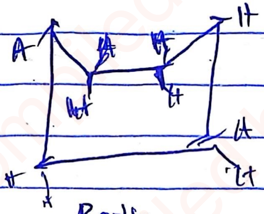
lowest energy (least torsional strain)
↑
Chair < boat < twisted boat
↘ least stable with highest energy

(3) Bolz



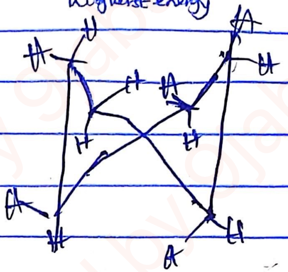
chair Conformation

most stable in least energy



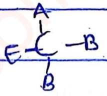
Boat

more stable
Higher Energy



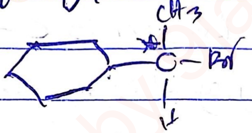
twisted boat
least stable
higher Energy

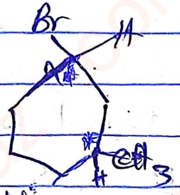
Cyclic molecules can be chiral



$E-\overset{A}{\underset{B}{C}}-B$, (A ≠ B ≠ D ≠ E)

Identify the chiral molecule





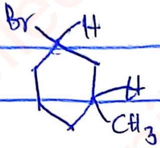
3 chiral centers

1-bromo-3-methylcyclohexane

To draw a stereoisomer;
For a cyclic system, the chiral centre must first be identified

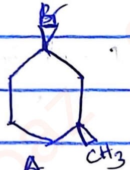
no of conformation = 2^n, where n is the number of chiral centers

So for,



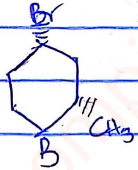
$2^2 = 4$ stereoisomers/conformation is expected.

2 cis & 2 trans conformation



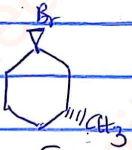
A

cis



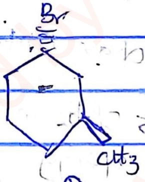
B

cis



C

trans



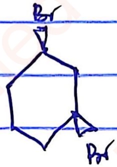
D

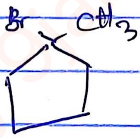
trans

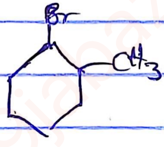
Since cis bromomethylcyclohexane is a pair of enantiomer A&B while trans bromo 3-methylcyclohexane is a pair of enantiomers C & D

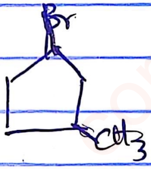
Since A or B are each diastereomer to C or D, then cis and trans 1 bromo 3 methylcyclohexane are diastereomer of each other.

* Read up R and S configuration *









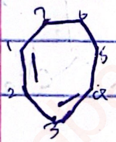
Give R & S configuration of the above

Numenclature of Alicyclic ~~Aliphatic~~ Compound

① The prefix "Cyclo" is used in naming alicyclic compounds when the structure contains more than one close ring, the prefix bicyclo, tricyclo, tetracyclo etc are used.

② The size of the ring is indicated by the use of standard IUPAC name for n-alkanes, alkenes, or alkyne chains of different length
In case, of cycloalkenes containing several double bonds, the location of the bonds are located.

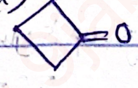
Example



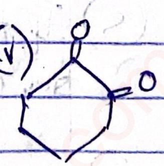
③ Functional groups such as hydroxyl, Carbonyl, ~~which could be~~ carboxylic acids are indicated as in corresponding acyclic compounds.

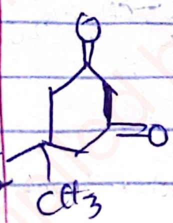
e.g

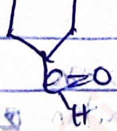
(i)


(ii)


(iii)


(iv)


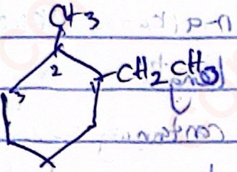
(v)


(vi)


④ If two or more substituents are present, the numbering is done from the substituent which ~~forms~~ comes first in the alphabetical order provided it satisfies the lowest sum rule

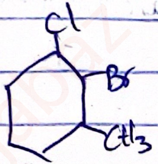
Example

(i)

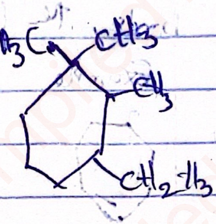


~~1~~-ethyl-2 methy cyclo hexane

(ii)



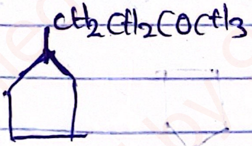
(iii)



(iv)

⑤ If there is a presence of the functional group in a side chain, the functional group is given the priority

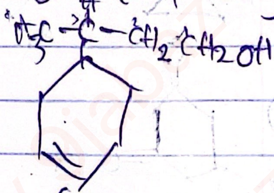
(i)



~~4-cyclopentane 2-one~~

4-cyclopent butan-2-one

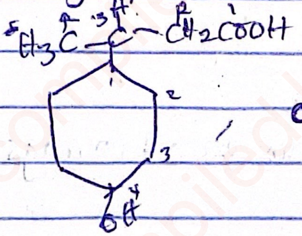
(ii)



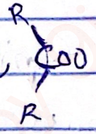
3-(cyclohex-3-ene-1-yl) butanol

2A

⑥ If the alicyclic ring as well as the side chain contains the functional group - The compound is named as a derivative of the one which contains the principal functional group

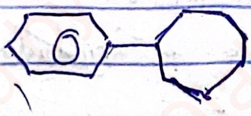


OH, NH_2, COOH,



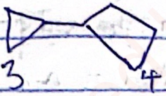
3-(4-hydroxycyclohexanol-yl) butanoic acid

⑦ If a compound contains an alicyclic ring and a benzene ring, then the compound is named as a derivative of alicyclic ring. If it contains more atom than the benzene, Hence the compound is named as derivative of benzene



phenylcycloheptane

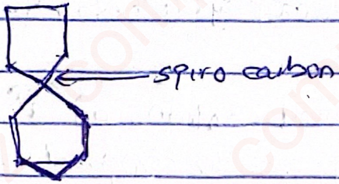
⑧ If two allicyclic rings are attached, then the Compound is made as a derivative of the one that contains greater number of carbons.



cyclopropylcyclobutane

Spiro carbon

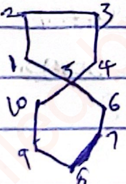
Spirocompounds occurs when two rings shares one carbon atom.



① The prefix "Spiro" is used for the compounds in which one carbon is present between the two rings

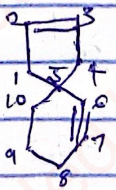
② The number of carbon atom linked to the Spiro atom in each ring is indicated in decending order.

③ The smaller ring is numbered first, then through the Spir, then around the second ring.

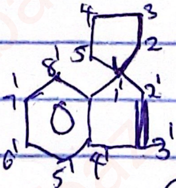


numbering pattern

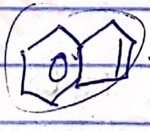
(4) When unsaturation is present the same enumeration pattern is used, but in such a direction around the rings that gives the double bond/triple bond the lowest number possible.

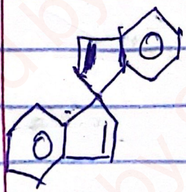


(5) If one or both of the spiro compound are fused polycyclic system, spiro is placed before the name of the component arranged in alphabetical order. The lowest number possible is given to the spiro atom and the number of the second component are marked with prime



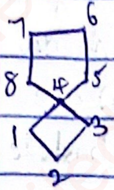
spiro (cyclo pentane-1, 1'-indene)



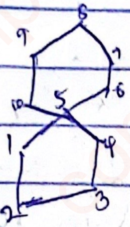


1, 1'-spirobiindene

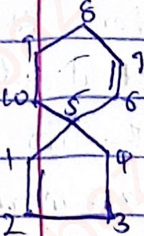
Examples

①


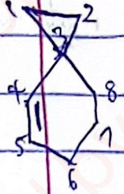
Spiro(4,3) octane

②


Spiro(5,4) decane

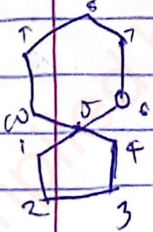
③


Spiro[5,4]
dec-1-6-diene

④


Spiro[5,2]
octan-4-ene

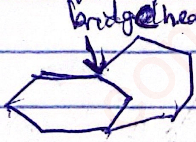
Questions

①


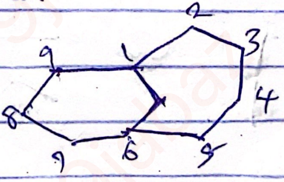
6-oxaspiro
(5,4) decane

Bicyclo compounds

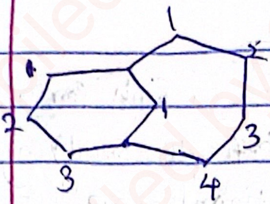
① The prefix "bicyclo" is used for such compound
② Number the larger ring first before the small ring
③ Find the highest priority functional group, this will be the suffix, then count the total number of carbon in the molecule which gives the root name
④ Identify the two rings of the bicyclic molecule (they should share a perimeter). The bridge head carbon are where those ring met



⑤ The numbering begins at bridge head and follows the longest path to the second bridge head. Continue numbering along the next longest until all carbons are numbered.

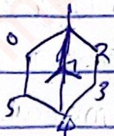


⑥ Find all unique pathway between the bridge head carbons and count the number of carbons along the bridge pathway, then arrange in descending order.

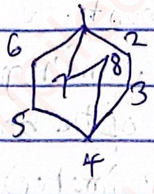


4-Carbon
3-carbon
1-carbon

Bicyclo(4,3,1)decane



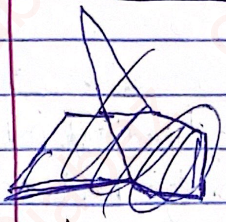
bicyclo(2,2,1)heptane



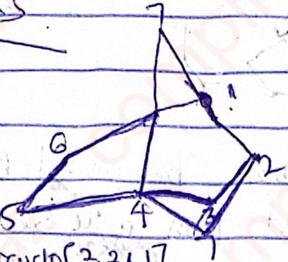
2-carbons
2-carbons
2-carbon

bicyclo(2,2,2) octane

Questions

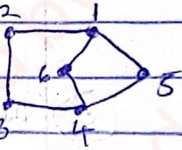


①



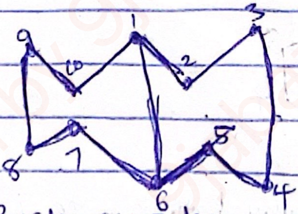
bicyclo[2,2,1]
heptane

③



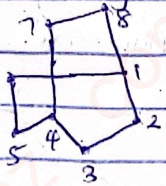
b~~icyclo[2,1,]~~
bicyclo[2,1,1]hexane

②



Byclo (4,4] decane

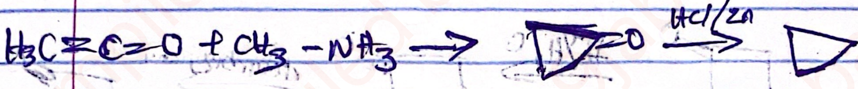
④

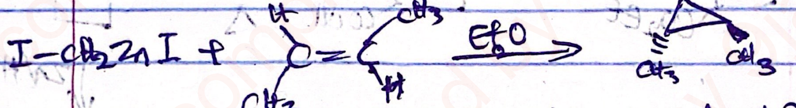


bicyclo[2,2,2]octane

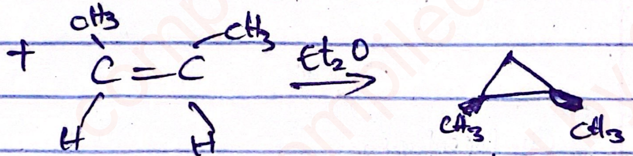
Synthesis of Cyclopropane

Cyclopropanes are prepared by Simmons-Smith reaction, then Clemmensasson reaction.





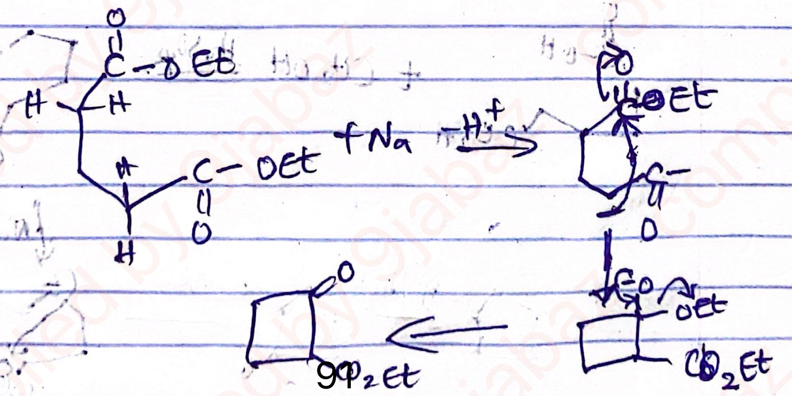
trans-1,2-dimethyl cyclopropane



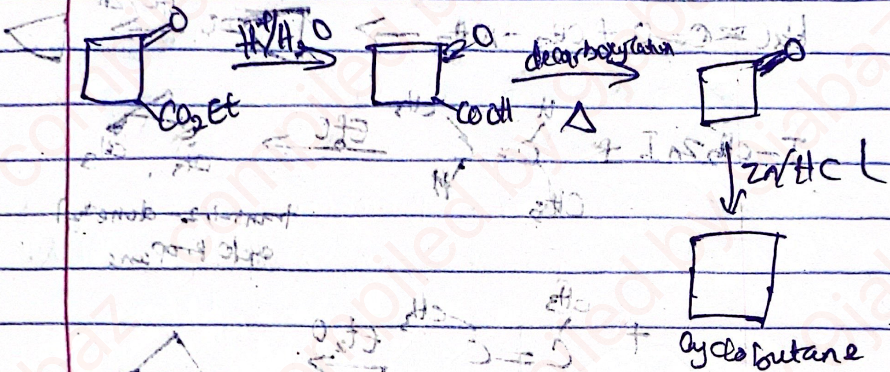
cis-1,2-dimethyl cyclopropane

Cyclobutanes

Cyclobutanes are prepared by Dieckmann Condensation reaction (intramolecular claisen condensation): We must have active methylene protons (acidic protons)

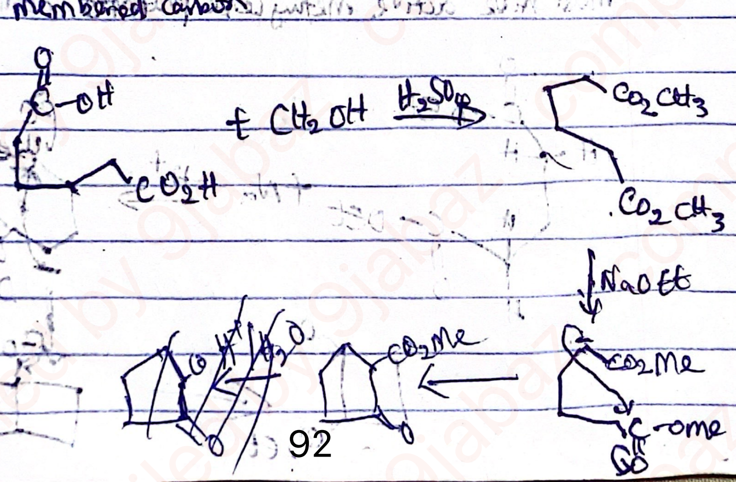


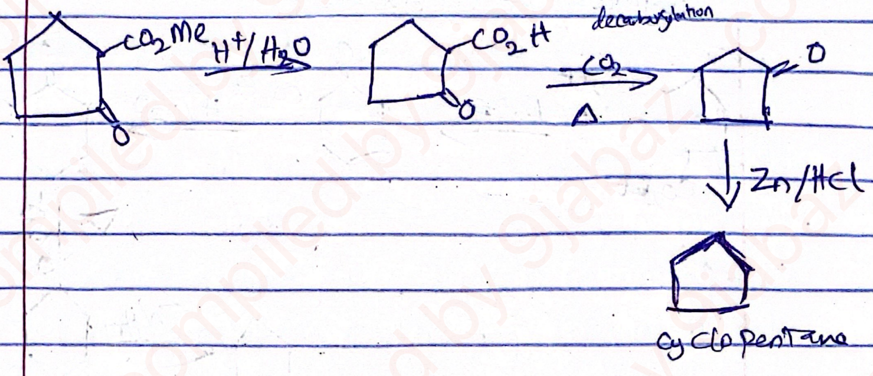
In the presence of a base such as Na or NaOEt, the protons can be extracted to form a carbanion



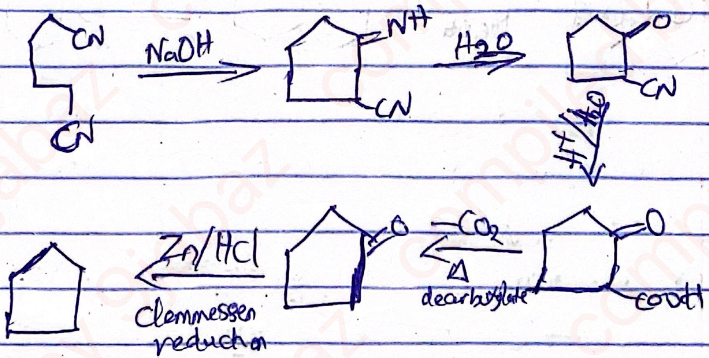
Cyclopentanes

Cyclopentanes are prepared by the same method, Dieckmann condensation (intramolecular claisen condensation), but we are starting with a six membered carbon

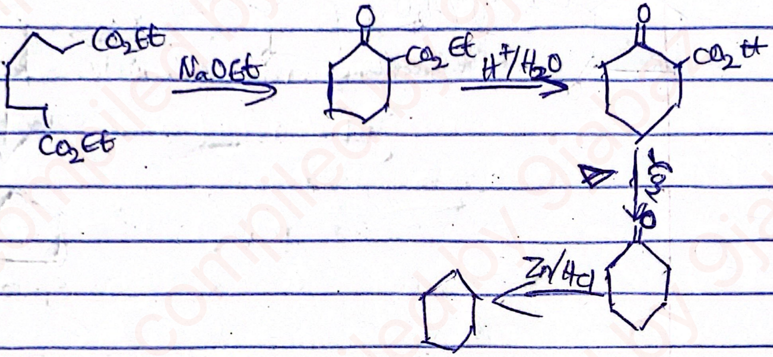




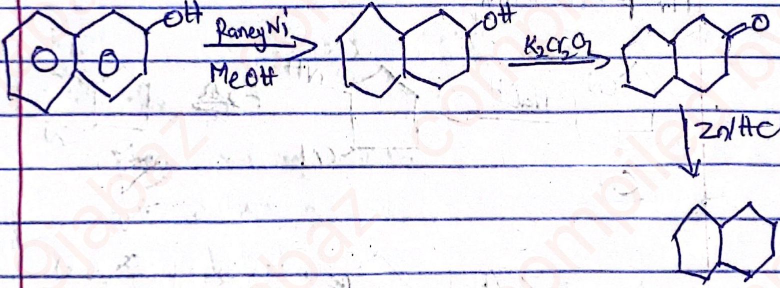
Another way to make cyclopentanes is through Thorpe reaction



Synthesis of Cyclohexanes



Other synthesis



⇒ means we have two functional groups on the compound.

BIFUNCTIONAL COMPOUNDS

DIOLS

Diols are compounds containing two –OH group in the molecule. The common name is dihydric alcohols

Nomenclatures:

The common names are assigned to individual diols after the name of the corresponding alkanes or the ~~dimeth~~ polymethylene from which they could be obtained directly by hydroxylation

	Formular	Common name	IUPAC
1.	$HOCH_2CH_2OH$	Ethylene glycol	1,2-ethanediol / ethane-1,2-diol
2.	$HOCH_2CH_2CH_2OH$	Trimethylene glycol	1-3-propanediol
3.	$HOCH_2\underset{\substack{\vert\\OH}}{C}HCH_3$	Propylene glycol	1,2-propanediol

Diols are designed as α, β, or γ according to relative positions of the two –OH groups.

1,2-diols are α-glycol
1,3-diols — β-glycol
1,4-diols — γ-glycol

Properties

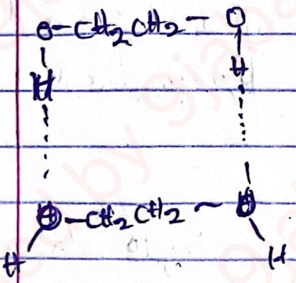
① The lower diols are colourless, viscous liquids which are soluble in water. ~~Diol~~

② Diols have higher boiling points than the corresponding monohydric alcohol of similar molecular weights.

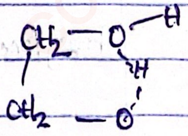
Eg $OHCH_2CH_2OH$	$CH_3CH_2CH_2OH$	
$C_2H_6O_2$	$C_3H_7O_7$	
62 g/mol	60 g/mol	why?
BP : 197°C	97°C	

The difference in boiling point is due to extensive hydrogen bonding in the molecules as a result of the two -OH groups.

Hydrogen bond is the interaction between hydrogen and a small highly electronegative atom (F, O, N)



Inter Hydrogen bond



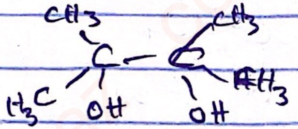
intramolecular hydrogen bonding

1,2-diol	Propanol
high boiling poing	low boiling point
high viscosity	low viscosity

(3) The solubility of the diol is larger than the corresponding alcohol

Pinacol – Pinacolone Rearrangement

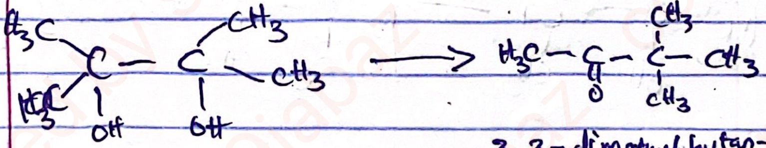
Completely substituted 1,2-diols, such as;



2,3-dimethyl butan-1,2-diol :

are known as pinacols

They undergo dehydration and rearrangement in acid to form ketones



3,3-dimethyl butan-2-one

2,3-dimethyl butan-1,2-diol

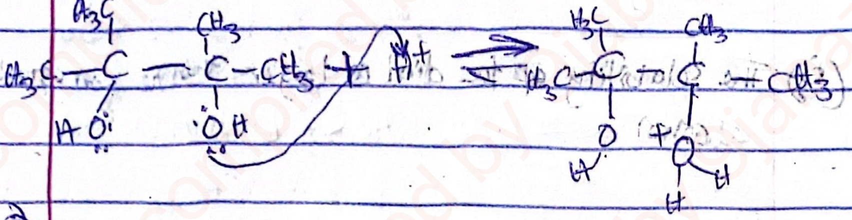
Pinacolone

Pinacol

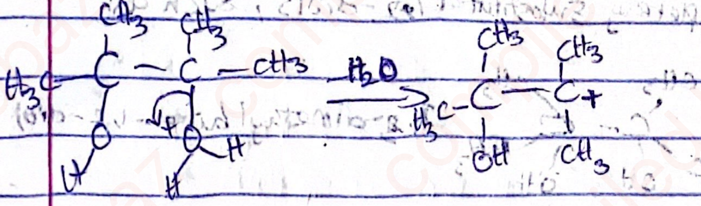
05-05-2025

The mechanism of the reaction involves ~~three to~~ four major Steps.

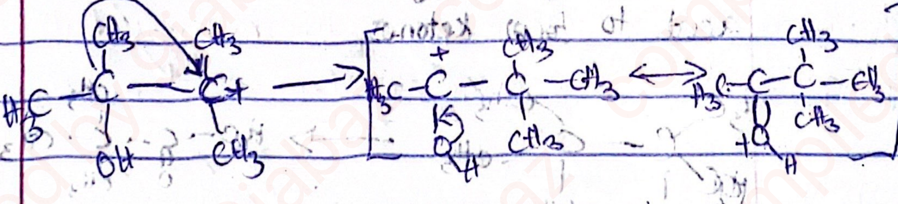
(i) protonation



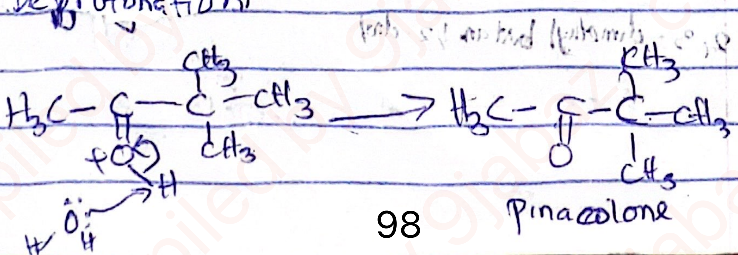
(ii) Loss of water



(iii) 1,2 - alkyl shift

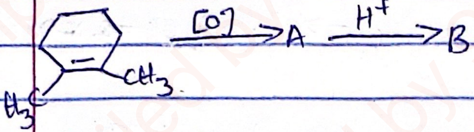


(iv) Deprotonation

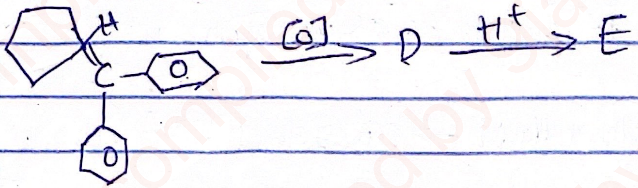


Assignment

(i)



(ii)



Write the possible structure for lettered A-E.

Ethylene glycol

Ethylene glycol is the simplest of dihydrate alcohol and is referied to as glycols CH_2OHCH_2OH

Preparation

(i) By hydroxylation of ethene: ethyleneglycol can be prepared by casting ethene into cold dilute $KMnO_4$ in the presence of Na_2CO_3

$$CH_2CH_2 + H_2O + [O] \xrightarrow[Na_2CO_3]{KMnO_4} OHCH_2CH_2OH$$

~~② By~~

② By hydrolysis of 1-2, dibromoethane with aqueous Na_2CO_3

$$CH_2BrCH_2Br + Na_2CO_{3(aq)} \rightarrow OHCH_2CH_2OH + 2NaBr + CO_2$$

③ From hydrolysis of ethylene chloro hydrin: ~~Eth~~ Ethylene chloro hydrin is prepared from the reaction of ethene with HOCl

$$CH_2CH_2 + HOCl \rightarrow \underset{\substack{\downarrow \\ \text{ethylenchloro hydrin}}}{OHCH_2CH_2Cl} \xrightarrow{NaHCO_3} CH_2OHCH_2OH + NaCl + CO_2$$

Physical properties

① Ethylene glycol is a colourless viscous liquid liquid with ~~B~~ bp 147°C and mp 11.5°C, specific gravity of 1.11g/cm³

② It has a sweet taste and it is miscible with water and ethanol in all proportion, but insoluble in ether

③ It is toxic, just like methanol when taken orally

Reactions

⑴ Ethylene glycol reacts with sodium at 50°c to form the mono alkoxide, and dialkoxide, when the temperature is raised to 160°C, ~~it forms dialkoxide~~

$$\begin{array}{l} CH_2-OH \\ | \\ CH_2OH \end{array} \xrightarrow[80^\circ C]{Na} \begin{array}{l} CH_2O^-Na^+ \\ | \\ CH_2OH \end{array}$$

$$\downarrow 160^\circ C$$

$$\begin{array}{l} CH_2O^-Na^+ \\ | \\ CH_2O^-Na^+ \end{array}$$

② It reacts with HCl in two steps to form chlorohydrin at 160°C and ethylene dichloride at 200°C

$$\begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + HCl \xrightarrow{160^\circ C} \begin{array}{l} CH_2Cl \\ | \\ CH_2OH \end{array}$$

$$\downarrow 200^\circ C$$

$$\xrightarrow[2HCl]{200^\circ C} \begin{array}{l} CH_2Cl \\ | \\ CH_2Cl \end{array}$$

2

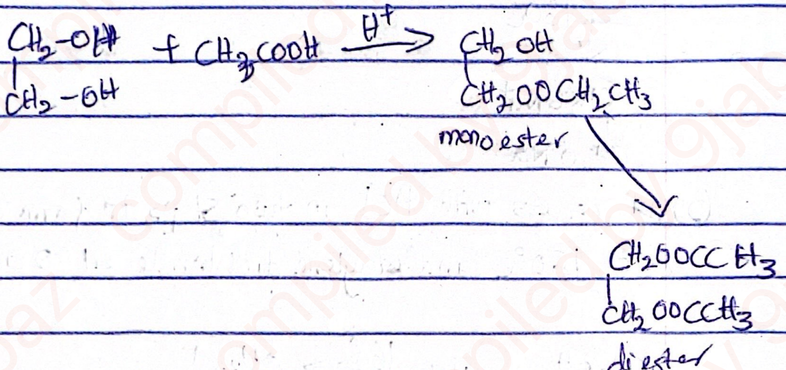
③ It reacts with phosphorus halide, such as phosphorus tribromide to form 1,2-dibromoethane

$$2\begin{pmatrix} CH_2OH \\ | \\ CH_2OH \end{pmatrix} \xrightarrow{PBr_3} CH_2BrCH_2Br + 2H_3PO_4$$

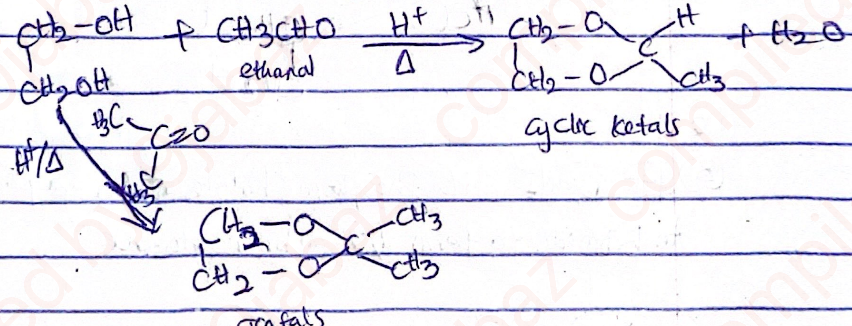
$$\xrightarrow{PI_3} CH_2ICH_2I + CH_2CH_2 + I_2$$

→ e.g ethanoic acid

④ It reacts with carboxylic acid to form monoesters and diesters



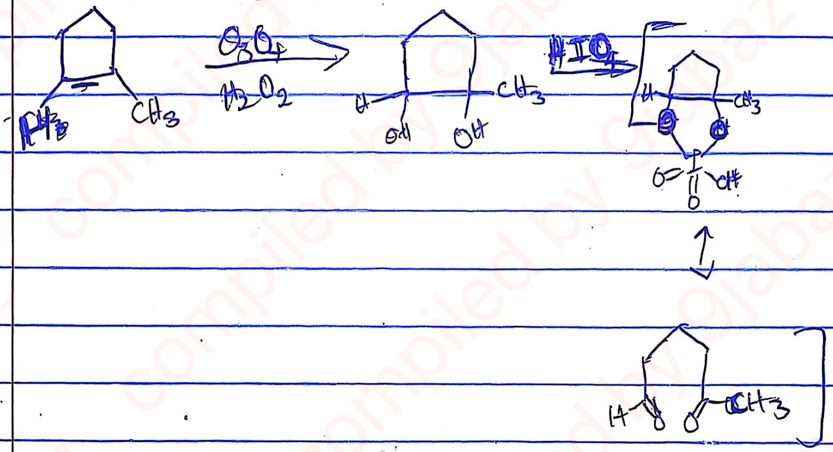
5. It reacts with aldehydes and ketones to form ~~ethers~~ ketals and acetals respectively



The formation of cyclic ketals and acetals can be used to protect carbonyl group when the reaction is carried out in alkaline

The carbonyl can be regenerated by action of periodic acid.

⑥ Periodic cleavage of diols

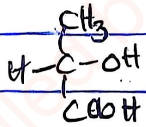


19th May, 2025

Lactic Acid

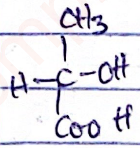
α-hydroxyl propanoic acid ($CH_3CH(OH)COOH$)

Lactic acid is the main constituent of sour milk. It is found in the blood and muscle tissue where it is found by decomposition of glycogen. ($C_6H_{10}O_5$). This reaction produce the energy needed for muscular work. The lactic acid molecule is assymetric;



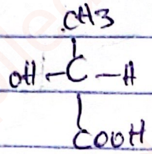
$$\begin{array}{c} CH_3 \\ | \\ H-C-OH \\ | \\ COOH \end{array}$$

Therefore, exhibit optical isomerism. It is prepared as a racemic mixture of: D- lactose acid and L- lactic acid



L- lactic acid

2(R)- hydroxyl propanoic acid



D - lactic acid

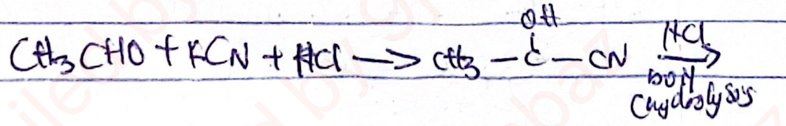
2(S)- hydroxyl propanoic acid.

Preparation of Lactic Acid → or propanoic acid

① By bromination of propronic acid followed by hydrolysis when heated with dilute NaOH solution

$$CH_3CH_2COOH + Br_2 \xrightarrow[\Delta]{NaOH} CH_3CH(OH)COOH$$

② In the industry, it is prepared by hydrolysis of acetalaldehyde cyanohydrin which is obtained from a reaction of acetalaldehyde.



$$CH_3CHO + KCN + HCl \longrightarrow CH_3-\overset{OH}{C}-CN \xrightarrow[\substack{boil \\ (hydrolysis)}]{HCl} CH_3CH(OH)COOH$$

3- By oxidation of propyleneglycol with dilute HNO_3 (nitric acid) - a mild oxidizing agent

$$CH_3CH(OH)CH_2OH \xrightarrow{HNO_3} CH_3CH(OH)COOH$$

4. By fermentation of sucrose. Sucrose can be hydrolysed to glucose and fructose

$$C_{12}H_{12}O_{11} + H_2O \longrightarrow \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{fructose}}{C_6H_{12}O_6}$$

$$C_6H_{12}O_6 \xrightarrow[\text{acidification}]{\text{Bacillus}} CH_3CH(OH)COOH$$

(BAC)

Properties

① It is colourless, crystalline solid. The two enantiomeric form form (D & L) melt at at 53°C while the racemate melts at 18°C at ordinary temperature and pressure. The commercially available lactic acid is a syrupic liquid having a sour taste. It is hygroscopic and miscible with water, ethanol and ether. Optically pure lactic acid has a specific rotation of +3.82 of D-lactic acid and

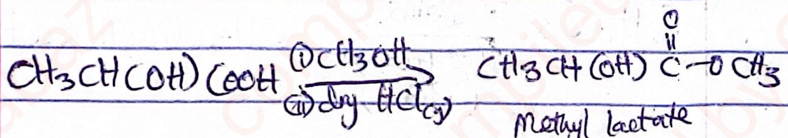
−3.82 for L-lactic acid

Reactions

① Reaction with NaOH: It reacts with excess NaOH to form a salt.

$CH_3CH(OH)COOH \xrightarrow{NaOH} CH_3CH(OH)COO^-Na^+$

② It reacts with alcohol to form esters



$$CH_3CH(OH)COOH \xrightarrow[\text{(ii) dry } HCl_{(g)}]{\text{(i) } CH_3OH} CH_3CH(OH)\overset{O}{\overset{\|}{C}}-OCH_3$$

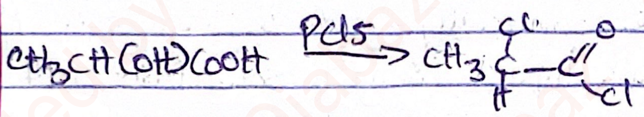
Methyl lactate

③ Reaction with H_2SO_4

$CH_3CH(OH)COOH + H_2SO_4 \xrightarrow{130°C} CH_3CHO + CH_2O_2$

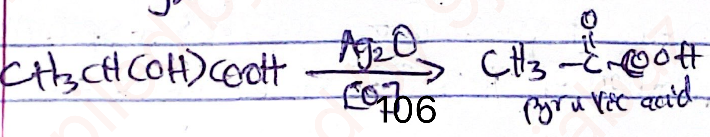
ethanal formic acid

④ Reaction with PCl_5



$$CH_3CH(OH)COOH \xrightarrow{PCl_5} CH_3\underset{H}{\overset{Cl}{C}}-\overset{O}{\overset{\|}{C}}-Cl$$

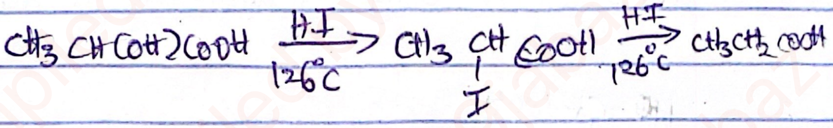
⑤ With Ag_2O (oxidation reaction)



$$CH_3CH(OH)COOH \xrightarrow[[O]]{Ag_2O} CH_3-\overset{O}{\overset{\|}{C}}-COOH$$

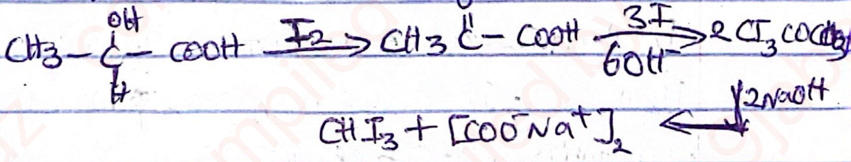
Pyruvic acid

⑥ It is reduced by H.I



$CH_3CH(OH)COOH \xrightarrow[126^\circ C]{H.I} CH_3\underset{I}{CH}COOH \xrightarrow[126^\circ C]{H.I} CH_3CH_2COOH$

⑦ Iodoform reaction



$CH_3-\overset{OH}{\underset{H}{C}}-COOH \xrightarrow{I_2} CH_3\overset{O}{\overset{\|}{C}}-COOH \xrightarrow[6OH^-]{3I} 2CI_3COC$

$\downarrow 2NaOH$

$CHI_3 + [COO^-Na^+]_2 \leftarrow$

Uses

① As Mordant for drying woods.

② As acidulant ~~to~~ candles

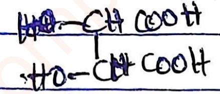
③ As Calcium and iron lactate in medicine to make up for calcium ~~ion~~ (Ca^{2+}) and iron deficiency in the body

④ As ethyl and butyl lactate which are used in Plastic industry

Tartaric Acid

α, α' - dihydroxyl succinic Acid a

Iupac: 2,3-dihydroxyl butan-1,4-dioic acid



$$\begin{array}{l} HO-CH\,COOH \\ \quad\;\; | \\ HO-CH\,COOH \end{array}$$

tartaric acid

D-tartaric acid is the most widely distributed plant acid. It occurs in grapes, tamarind and in other fruits, either free or as a potassium acid tatarate (ester)

During the later stage of fermentation of grape juice to wine, the pottasium acid tartarate is thrown out as a reddish brown crust called algol

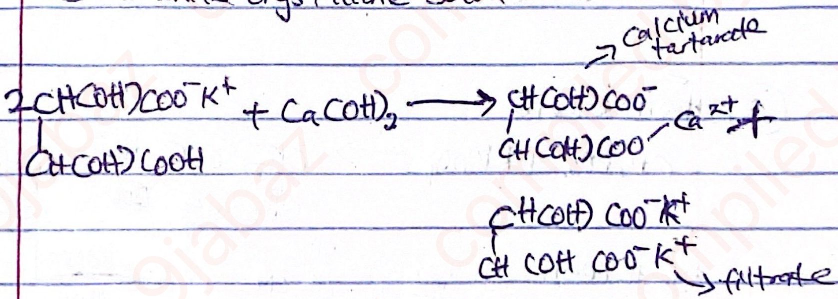
Isolation of Tartaric Acid from Algol

Tartaric acid was first isolated from algol. Algol is first recrystallise to give a purer form which is called cream of tartar.

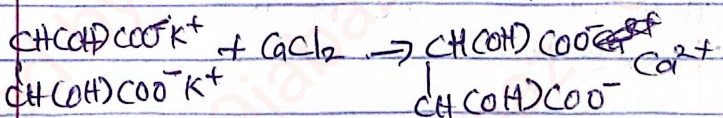
The cream of tar tar is dissolved in boiling water and the solution is nearly neutralized with milk of brine ($Ca(OH)_2$). The potassium acid tartarate react with lime to give normal pottasium tartarate and an insoluble calcium tartarate. The precipitated calcium tartarate is filtered off and $CaCl_2$ is added to the filtrate to obtain a fresh crop of calcium tartarate.

The calcium tartarate from the two lot is combined and decomposed to calculated quantities of dil. H_2SO_4

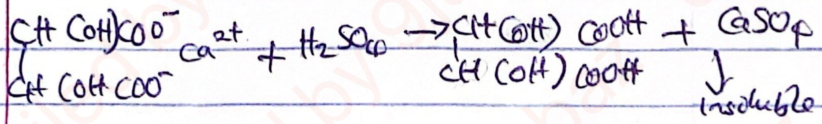
The precipitated calcium sulphate is removed by filtration. The tataric acid is obtained as a white crystalline solid.



$$2\begin{array}{l}CH(OH)COO^-K^+\\ |\\ CH(OH)COOH\end{array} + Ca(OH)_2 \longrightarrow \begin{array}{l}CH(OH)COO^-\\ |\\ CH(OH)COO^-\end{array}Ca^{2+} + \begin{array}{l}CH(OH)COO^-K^+\\ |\\ CH\ COH\ COO^-K^+\end{array}$$



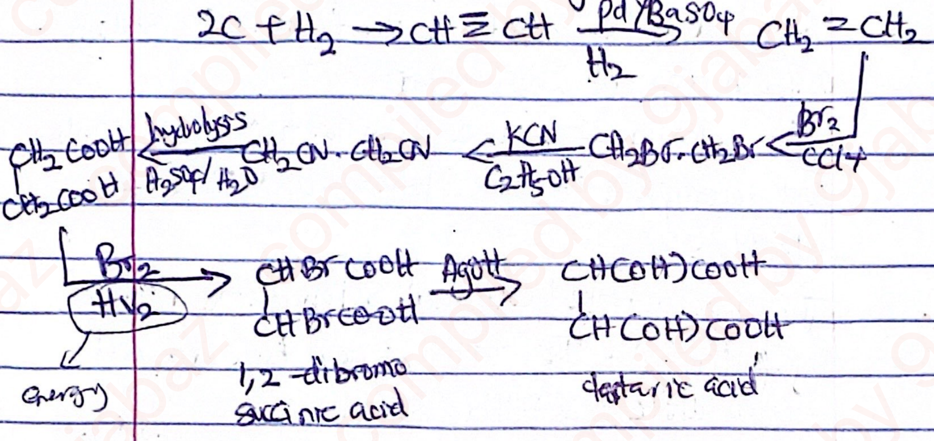
$$\begin{array}{l}CH(OH)COO^-K^+\\ |\\ CH(OH)COO^-K^+\end{array} + CaCl_2 \rightarrow \begin{array}{l}CH(OH)COO^-\\ |\\ CH(OH)COO^-\end{array}Ca^{2+}$$



$$\begin{array}{l}CH(OH)COO^-\\ |\\ CH(OH)COO^-\end{array}Ca^{2+} + H_2SO_4 \rightarrow \begin{array}{l}CH(OH)COOH\\ |\\ CH(OH)COOH\end{array} + CaSO_4$$

Laboratory Preparation

① from ethyne: It can be prepared from the reaction of carbon and hydrogen



$$2C + H_2 \rightarrow CH \equiv CH \xrightarrow[H_2]{Pd/BaSO_4} CH_2 = CH_2$$

$$CH_2 = CH_2 \xrightarrow[CCl_4]{Br_2} CH_2Br\text{-}CH_2Br \xrightarrow[C_2H_5OH]{KCN} CH_2CN\text{-}CH_2CN \xrightarrow[H_2SO_4/H_2O]{hydrolysis} \begin{matrix} CH_2COOH \\ | \\ CH_2COOH \end{matrix}$$

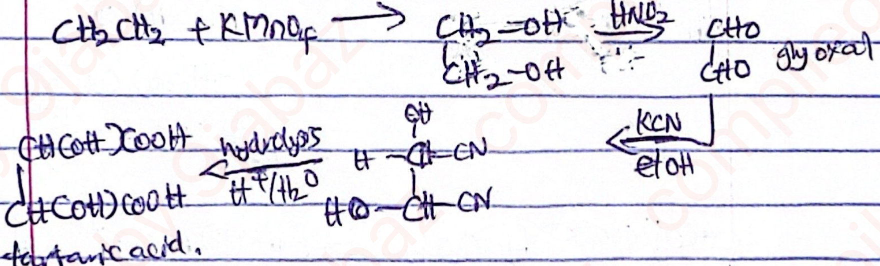
$$\xrightarrow[HV_2]{Br_2} \begin{matrix} CHBrCOOH \\ | \\ CHBrCOOH \end{matrix} \xrightarrow{AgOH} \begin{matrix} CH(OH)COOH \\ | \\ CH(OH)COOH \end{matrix}$$

energy

1,2-dibromo succinic acid

tartaric acid

② from ethene

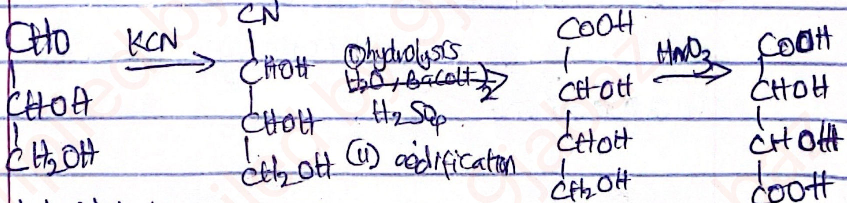


$$CH_2CH_2 + KMnO_4 \rightarrow \begin{matrix} CH_2-OH \\ | \\ CH_2-OH \end{matrix} \xrightarrow{HNO_3} \begin{matrix} CHO \\ | \\ CHO \end{matrix} \text{ glyoxal}$$

$$\begin{matrix} CHO \\ | \\ CHO \end{matrix} \xrightarrow[etOH]{KCN} \begin{matrix} OH \\ | \\ H-CH-CN \\ | \\ HO-CH-CN \end{matrix} \xrightarrow[H^+/H_2O]{hydrolysis} \begin{matrix} CH(OH)COOH \\ | \\ CH(OH)COOH \end{matrix}$$

tartaric acid.

Killiani-Fisher Synthesis

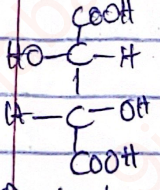


Glyacetalaldehyde

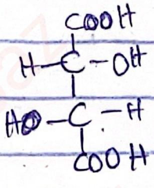
Physical properties

① Tataric acid is a classical example of compound containing two assymetric C-atom.

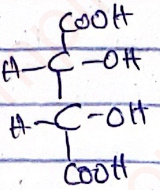
② ~~It~~ exibibit optimer isomerism and exists in four forms, D-tartapic acid, L-tatargic acid, meso-tataric acid and racemic mixture



(S,S)-tartaric acid
L-tartaric acid



(R,R)-tartaric acid
D-tartaric acid



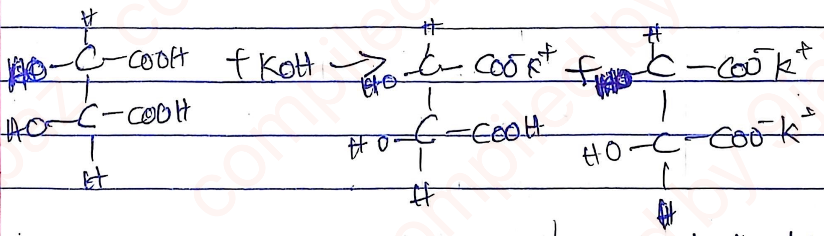
meso tartaric acid
(R, S)-tartaric acid

Natural Tartaric Acid

D-tartaric acid form colourless mono-clinic prism without any water of crystallization. It melt at 170°c and it is soluble in water and ethanol, but insoluble in ether. An aqueous solution of D-tartaric acid upon heating is rendered optically inactive due to racemization.

Reactions

1. With KOH

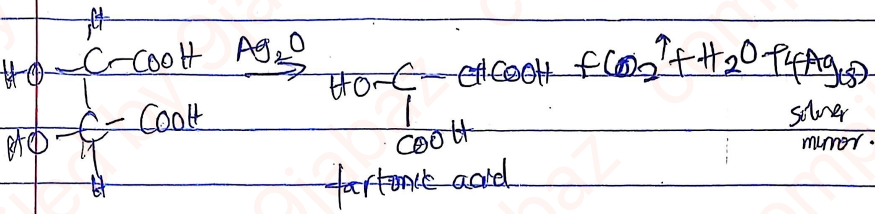


Potassium tartarate

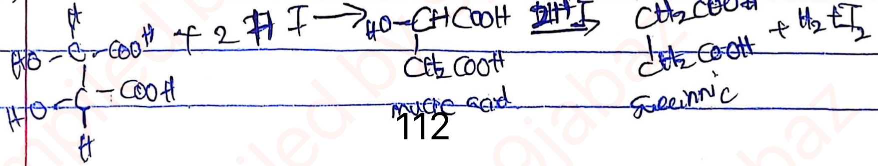
2. With Ag_2O

$4AgNO_3 + 4NH_4OH \rightarrow 4AgOH + 4NH_4NO_3$

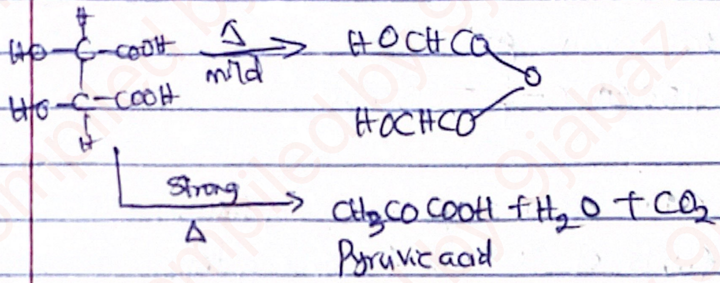
$2AgOH \rightarrow 2Ag_2O + 2H_2O$



③ Reduction



A Heat



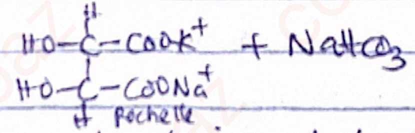
$$\mathrm{HO{-}CH(COOH){-}CH(COOH){-}OH} \xrightarrow[\text{mild}]{\Delta} \mathrm{HOCHCO{-}O{-}COCHOH}$$

$$\xrightarrow[\Delta]{\text{Strong}} \underset{\text{Pyruvic acid}}{CH_3COCOOH} + H_2O + CO_2$$

Uses

(1) It is used as acidulant in making ~~[illegible]~~ drinks

(2) It is used as laxative, e.g a mixture of rochel Salt
Which is ~~the~~ ~~mixture of~~ double salt of K and Na rochel salt and ~~[illegible]~~ bicarbonate
~~Sodium bicarbonate~~



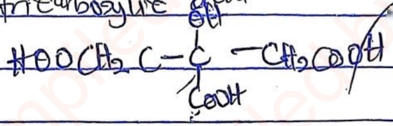
$$\mathrm{HO{-}CH(COO^-K^+){-}CH(COO^-Na^+){-}OH} + NaHCO_3$$

(3) It is used as baking powder / used for baking purposes
potassium acid tartarate is used to generate CO_2
to make the dough swell

(4) It is used as microphone crystals and in making mirrors
(5) ~~[illegible]~~ Fehling solution contains Rochelle salt
6. It is used as mordant in dyeing

Citric Acid.

β-hydroxyl carboxylic acid. or 2-hydroxyl propane-1,2,3-tricarboxylic acid.



$HOOCH_2C-C(OH)(COOH)-CH_2COOH$

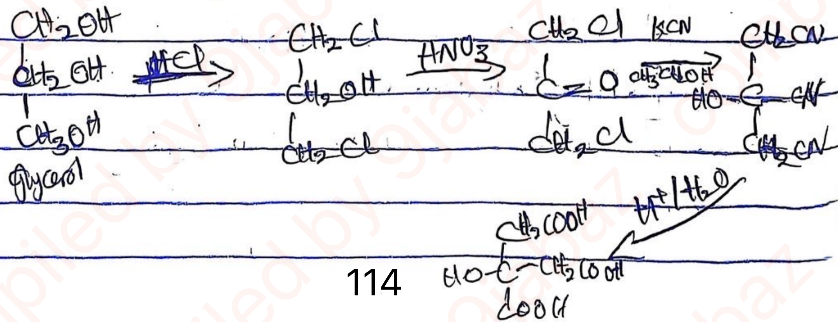
Citric acid occurs in many fruits, especially unripe fruits of the citrus family, e.g lemon, oranges and galgal

Preparations

From lemon juice: The juice is extracted and boiled to coagulate the proteinous matter. The coagulated matter or material is filtered off and the filtrate neutralize with lime while solution is boiling. The precipitated calcium filtrate is collected by filtration and it is decomposed with calculated amount of dil. H_2SO_4

The $CaSO_4$ is filtered off and citric acid evaporate to crystallize

Synthesis



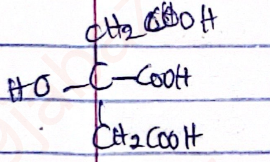
Physical properties

① It forms large prismatic crystrals containing one molecule of water of Crystallization

② The hydrated citric acid looses its water of crystalliation when heated at 130°C and melts at 153°C.

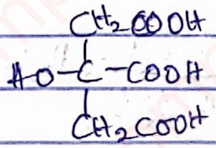
③ It is readily soluble in water and ethanol but sparingly soluble in eter

④ It is not optically active



$$\begin{array}{l} \quad CH_2COOH \\ HO-C-COOH \\ \quad CH_2COOH \end{array}$$

α-hydroxyl citric acid

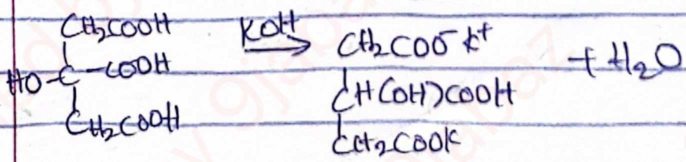


$$\begin{array}{l} \quad CH_2COOH \\ HO-C-COOH \\ \quad CH_2COOH \end{array}$$

β-citric acid

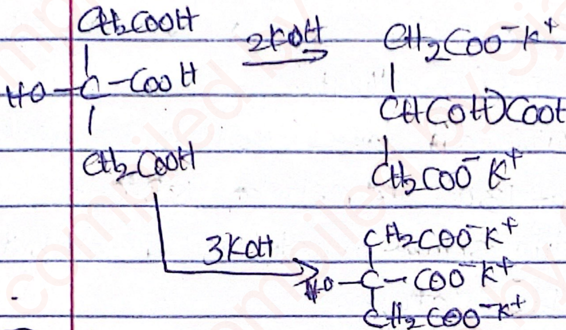
Reactions

(i) Formation of salt: It forms three series of salt mono-di-tri salts.



$$\begin{array}{l} \quad CH_2COOH \\ HO-C-COOH \\ \quad CH_2COOH \end{array} \xrightarrow{KOH} \begin{array}{l} CH_2COO^-K^+ \\ CH(OH)COOH \\ CH_2COOK \end{array} + H_2O$$

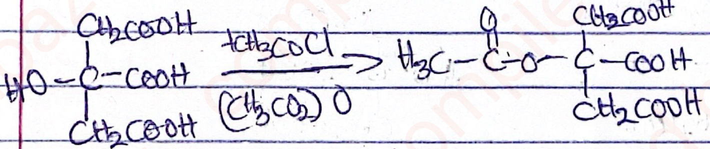
mono potassium citrate



$$\begin{array}{c}CH_2COOH\\ |\\ HO-C-COOH\\ |\\ CH_2COOH\end{array}\xrightarrow{2KOH}\begin{array}{c}CH_2COO^-K^+\\ |\\ CH(OH)COOH\\ |\\ CH_2COO^-K^+\end{array}$$

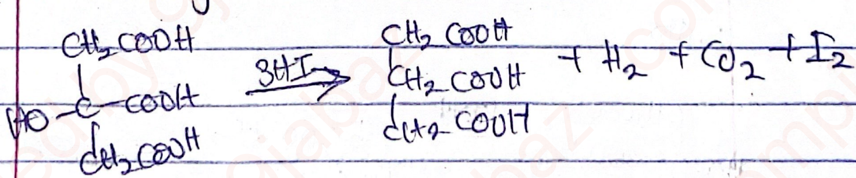
$$\xrightarrow{3KOH}\begin{array}{c}CH_2COO^-K^+\\ |\\ HO-C-COO^-K^+\\ |\\ CH_2COO^-K^+\end{array}$$

② Acetylation: It reacts with acetyl anhydride to form mono acetyl citrate



$$\begin{array}{c}CH_2COOH\\ |\\ HO-C-COOH\\ |\\ CH_2COOH\end{array}\xrightarrow[(CH_3CO_2)O]{+CH_3COCl}H_3C-\overset{O}{\overset{\|}{C}}-O-\begin{array}{c}CH_2COOH\\ |\\ C-COOH\\ |\\ CH_2COOH\end{array}$$

③ Reduction: The alcoholic hydroxyl group can be reduced by the action of hydrogen iodide/hydroiodic acid to yield tricarboxylic acid



$$\begin{array}{c}CH_2COOH\\ |\\ HO-C-COOH\\ |\\ CH_2COOH\end{array}\xrightarrow{3HI}\begin{array}{c}CH_2COOH\\ |\\ CH_2COOH\\ |\\ CH_2COOH\end{array}+H_2+CO_2+I_2$$