

CHEMISTRY OF NATURAL PRODUCTS

Terpenoids

Sameena Bano
Department of Chemistry
Faculty of Science
Jamia Hamdard
New Delhi-110062

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Keywords

Terpenes, isoprene, citral, menthol, camphor and eugenol

Introduction

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.

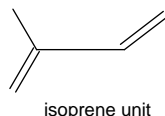
The term 'terpene' was given to the compounds isolated from turpentine, a volatile liquid isolated from pine trees. The simpler mono and sesqui terpenes are chief constituent of the essential oils obtained from sap and tissues of certain plant and trees. The di and tri terpenoids are not steam volatile. 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: "Terpenoids are the hydrocarbons of plant origin of the general formula $(C_5H_8)_n$ as well as their oxygenated, hydrogenated and dehydrogenated derivatives."

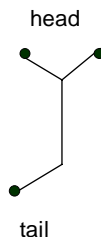
Isoprene rule: Thermal decomposition of terpenoids give isoprene as one of the product. Otto Wallach pointed out that terpenoids can be built up of isoprene unit.

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



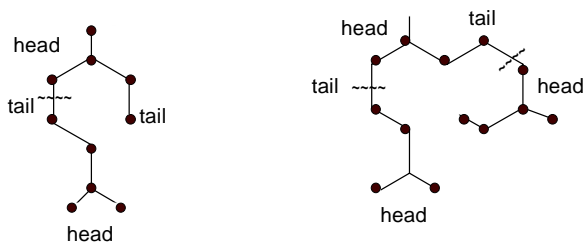
Further Ingold suggested that isoprene units are joined in the terpenoid via 'head to tail' fashion.

Special isoprene rule states that the terpenoid molecule are constructed of two or more isoprene units joined in a 'head to tail' fashion.

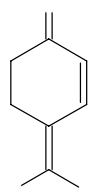


But this rule can only be used as guiding principle and not as a fixed rule. For example carotenoids are joined tail to tail at their central and there are also some terpenoids whose carbon content is not a multiple of five.

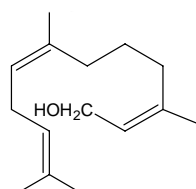
In applying isoprene rule we look only for the skeletal unit of carbon. The carbon skeletons of open chain monoterpenoids and sesqui terpenoids are,



Examples.



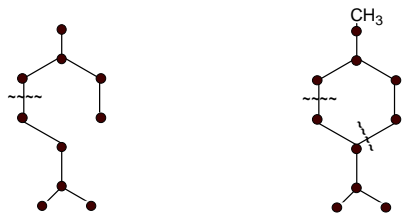
Myrcene
(monoterpene)



Farnesol (Sesquiterpene)

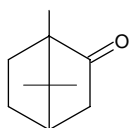
Ingold (1921) pointed that a gem alkyl group affects the stability of terpenoids. He summarized these results in the form of a rule called 'gem dialkyl rule' which may be stated as "Gem dialkyl group tends to render the cyclohexane ring unstable whereas it stabilizes the three, four and five member rings."

This rule limits the number of possible structure in closing the open chain to ring structure. Thus the monoterpene open chain give rise to only one possibility for a monocyclic monoterpene i.e the p-cymene structure.

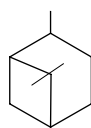


P-cymene structure

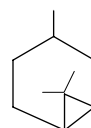
Bicyclic monoterpenoids contain a six member and a three member ring. Thus closure of the ten carbon open chain monoterpene gives three possible bicyclic structures.



Camphor
(6+5) system



Pinane
(6+4) system



Carane
(6+3) System

Classification of Terpenoids

Most natural terpenoid 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 | Sesquiterpenoids($C_{15}H_{24}$) |
| 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) $_n$ |

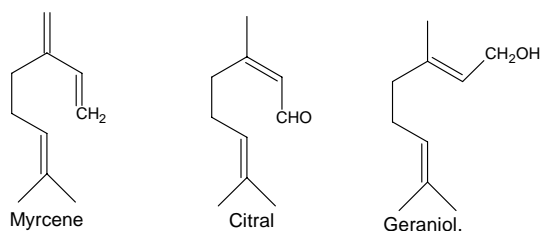
Each class can be further subdivided into subclasses according to the number of rings present in the structure.

- Acyclic Terpenoids:** They contain open structure.
- Monocyclic Terpenoids:** They contain one ring in the structure.
- Bicyclic Terpenoids:** They contain two rings in the structure.
- Tricyclic Terpenoids:** They contain three rings in the structure.
- Tetracyclic Terpenoids:** They contain four rings in the structure.

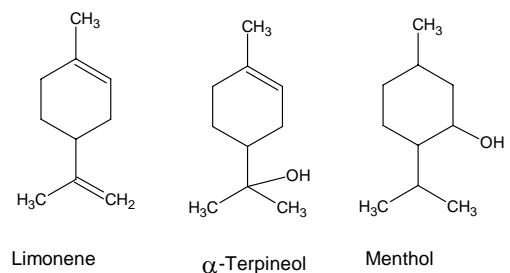
Some examples of mono, sesqui and di Terpenoids:

A) Mono Terpenoids:

i) Acyclic Monoterpenoids

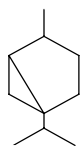


ii) Monocyclic monoterpenoids

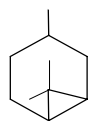


iii) Bicyclic monoterpenoids: These are further divided into three classes.

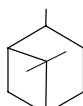
- Containing -6+3-membered rings
- Containing -6+4-membered rings.
- Containing -6+5-membered rings.



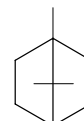
Thujane



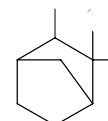
Carane



Pinane



Bornane
(Camphane)



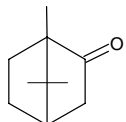
non bornane
(iso camphane)

Containing -6+3-membered rings

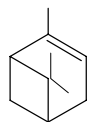
-6+4-membered rings

-6+5-membered rings

Some bicyclic monoterpenes are:



camphor



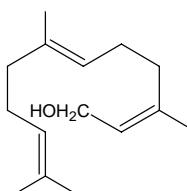
α -pinene

B) Sesquiterpenoids:

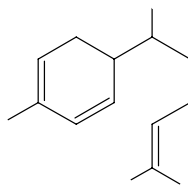
i) Acyclic sesquiterpenoids

ii) Monocyclic sesquiterpenoids

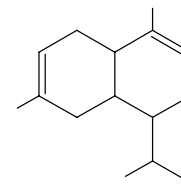
iii) Bicyclic sesquiterpenoids.



Farnesol



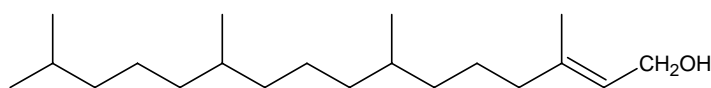
Zinziperene



Cadinene

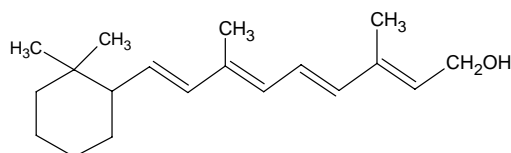
C) Diterpenoids:

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.

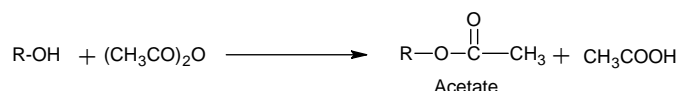
General properties of Terpenoids

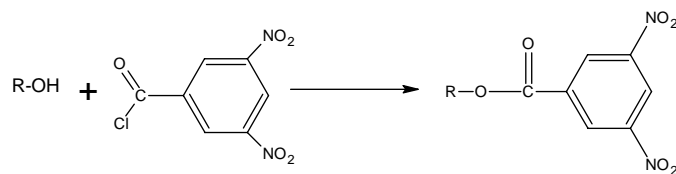
1. Most of the terpenoids are colourless, fragrant liquids which are lighter than water and volatile with steam. A few of them are solids e.g. camphor. All are soluble in organic solvent and usually insoluble in water. Most of them are optically active.
2. They are open chain or cyclic unsaturated compounds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

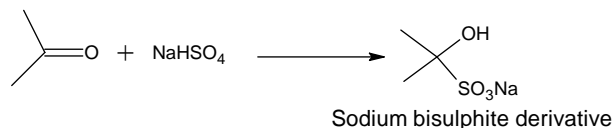
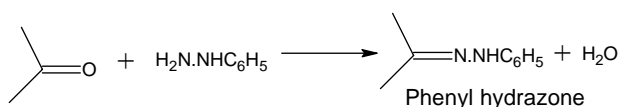
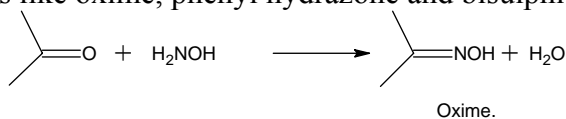
- i) **Molecular formula:** molecular formula is determined by usual quantitative analysis and mol.wt determination methods and by means of mass spectrometry. If terpenoid is optically active, its specific rotation can be measured.
- ii) **Nature of oxygen atom present:** If oxygen is present in terpenoids 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-dinitrobenzoyl chloride.





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

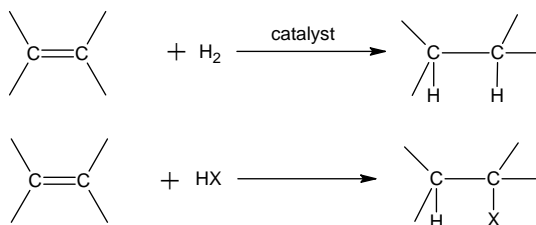
b) **Presence of >C=O group:** Terpenoids containing carbonyl function form crystalline addition products like oxime, phenyl hydrazone and bisulphite etc.



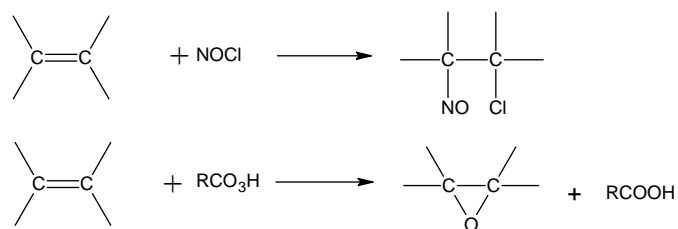
If carbonyl function is in the form of aldehyde it gives carboxylic acid on oxidation without loss of any carbon atom whereas the ketone on oxidation yields a mixture of lesser number of carbon atoms.

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 monoperothalic acid.

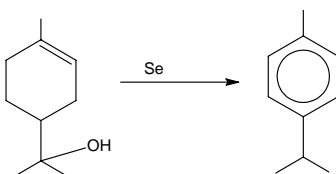
Presence of double bond also confirmed by means of catalytic hydrogenation or addition of halogen acids. Number of moles of HX absorbed by one molecule is equal to number of double bonds present.



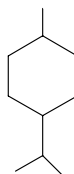
Addition of nitrosyl chloride (NOCl) (**Tilden's reagent**) and epoxide formation with peracid also gives idea about double bonds present in terpenoid molecule.



- iv) **Dehydrogenation:** On dehydrogenation with sulphur, selenium, polonium or palladium terpenoids 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 structure of degradation products.
- 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} | Tetracyclic |

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 limonene 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 ($\sim 3400\text{cm}^{-1}$) or an oxo group (saturated $1750-1700\text{cm}^{-1}$). 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.

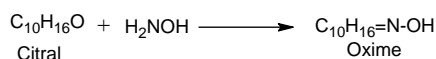
Citral

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.

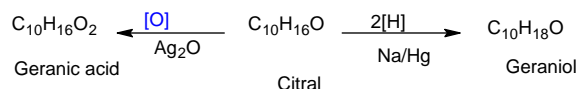
Constitution:

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.

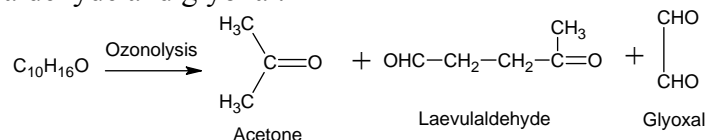


On reduction with Na/Hg it gives an alcohol called geraniol and on oxidation with silver oxide it give a monocarboxylic acid called Geranic acid without loss of any carbon atom.



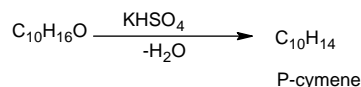
Both these reactions reveal that the oxo group in citral is therefore an aldehyde group. Citral reduces Fehling's solution, further confirming the presence of an aldehydic group.

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

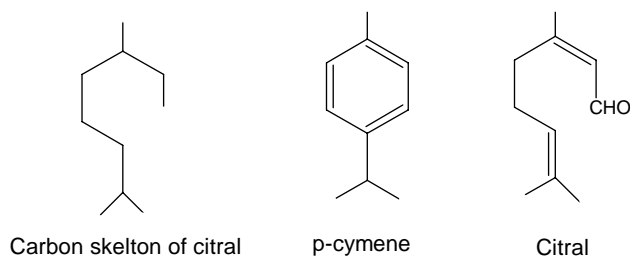


Formation of the above products shows that citral is an acyclic compound containing two double bonds. The corresponding saturated hydrocarbon of citral (molecular formula $\text{C}_{10}\text{H}_{22}$) corresponds to the general formula $\text{C}_n\text{H}_{2n+2}$ for acyclic compounds, indicating that citral must be an acyclic compound.

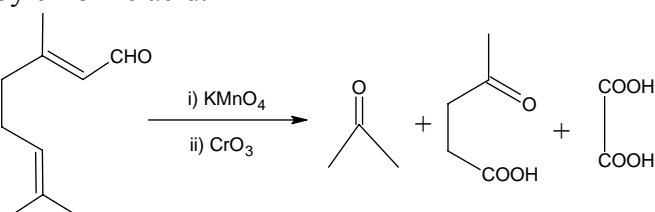
iv) Formation of p-cymene and the product obtained from the ozonolysis reveals that citral is formed by the joining of two isoprene units in the head-to-tail fashion.



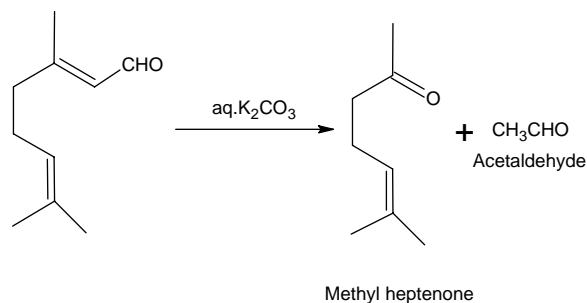
v) On the basis of the above facts, the following structure was proposed for citral.



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



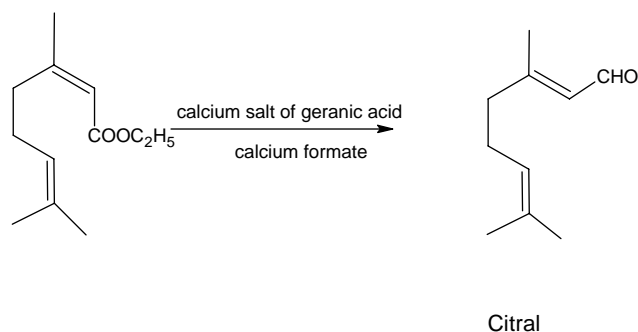
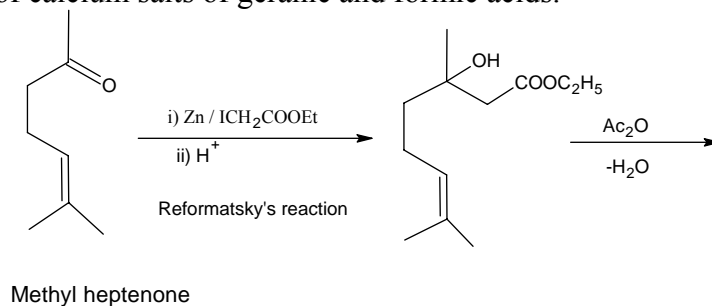
Verley found that citral on boiling with aqueous potassium carbonate yielded 6-methylhept-5-ene-2-one and acetaldehyde. The formation of these can only be explained on the basis of the proposed structure;



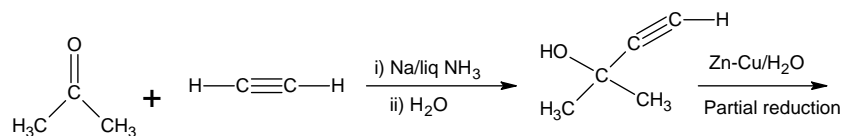
It appears that citral is product of aldol condensation of these two.

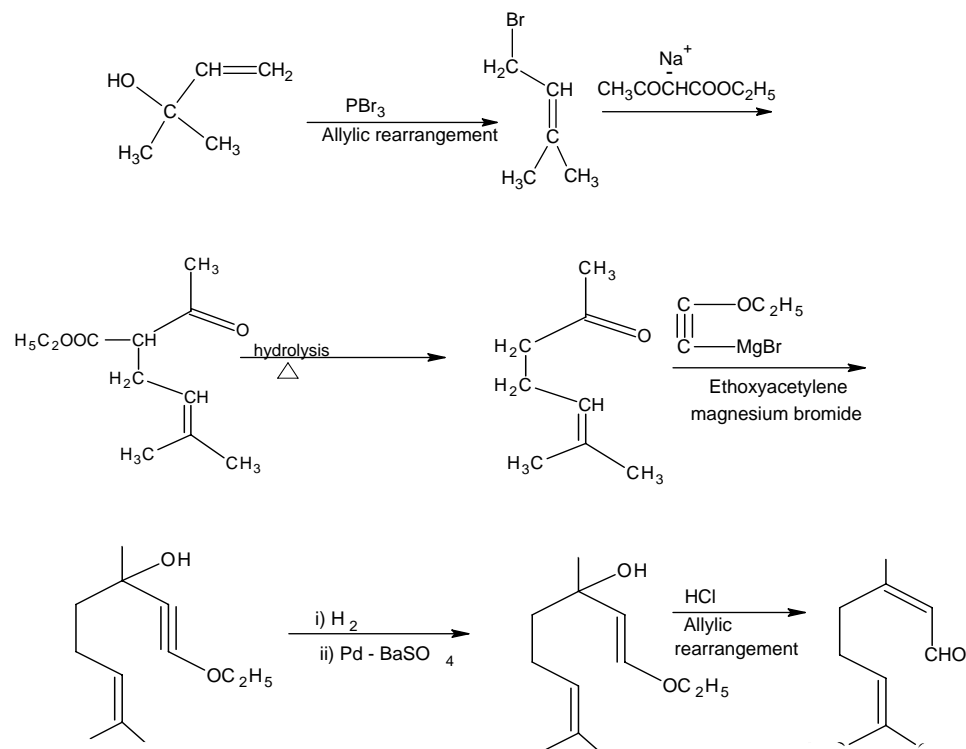
Synthesis: Finally the structure of citral was confirmed by its synthesis.

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.

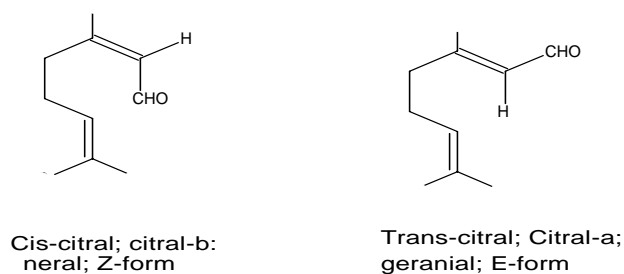


b) Arens-Van Drop's Synthesis: This synthesis involves condensation of acetone with acetylene in the presence of liquid ammonia. Condensation product is then reduced and treated with PBr_3 , allylic rearrangement takes place. The rearranged product so obtained is treated with sodium salt of acetoacetic 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.





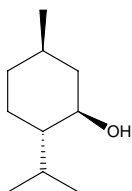
Isomerism of citral: Two geometrical isomers occur in nature.



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

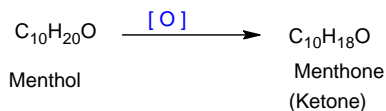
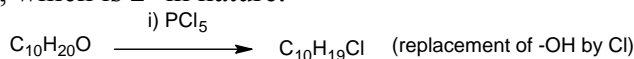
Menthol is the major constituent of *Mentha Piperita*. It is used as an antiseptic and anesthetic. Menthol (also called peppermint camphor or mint camphor) is the major constituent of peppermint oil and is responsible for its odour and taste and the cooling sensation when applied to the skin. It is ingredient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



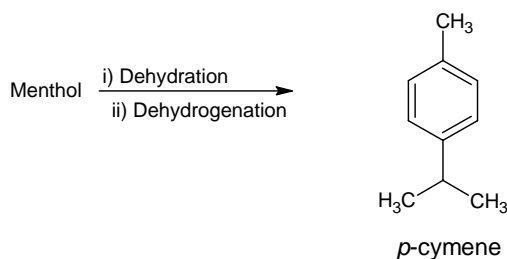
Structure elucidation:

1. Mol formula was determined as $C_{10}H_{20}O$

2. Menthol forms esters readily with acids and oxidized to yield ketone it means that it must possess alcoholic group, which is 2° in nature.

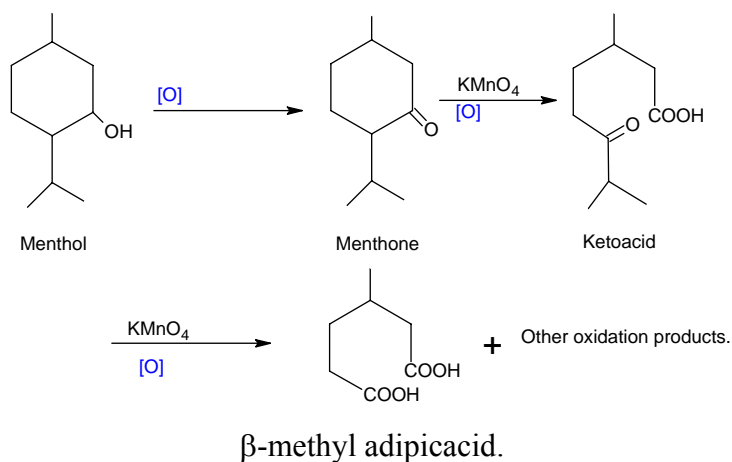


3. On dehydration followed by dehydrogenation it yields *p*-cymene.

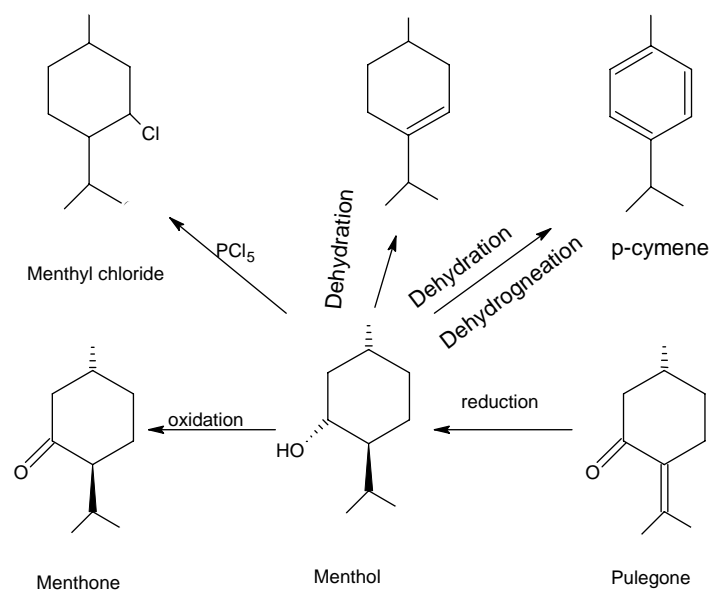


It shows the presence of *p*-Cymene nucleus in menthol.

4. Menthone on oxidation with $KMnO_4$ yields ketoacid $C_{10}H_{18}O_3$ which readily oxidized to 3-methyladipic acid. These reactions can be explained by considering the following structure of menthol.

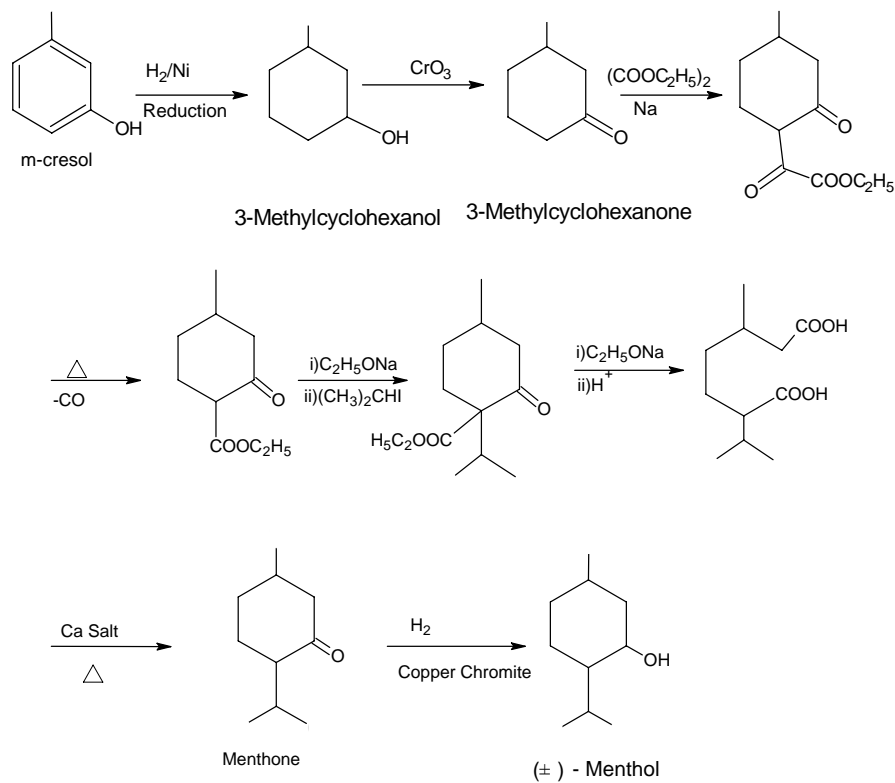


5. Menthol was converted to *p*-Cymene [1-methyl-4-isopropylbenzene], which was also obtained by dehydrogenation of pulegone. Pulegone on reduction yielded menthone which on further reduction yielded menthol. Pulegone is P-menth-4-(8)-en-3-one.



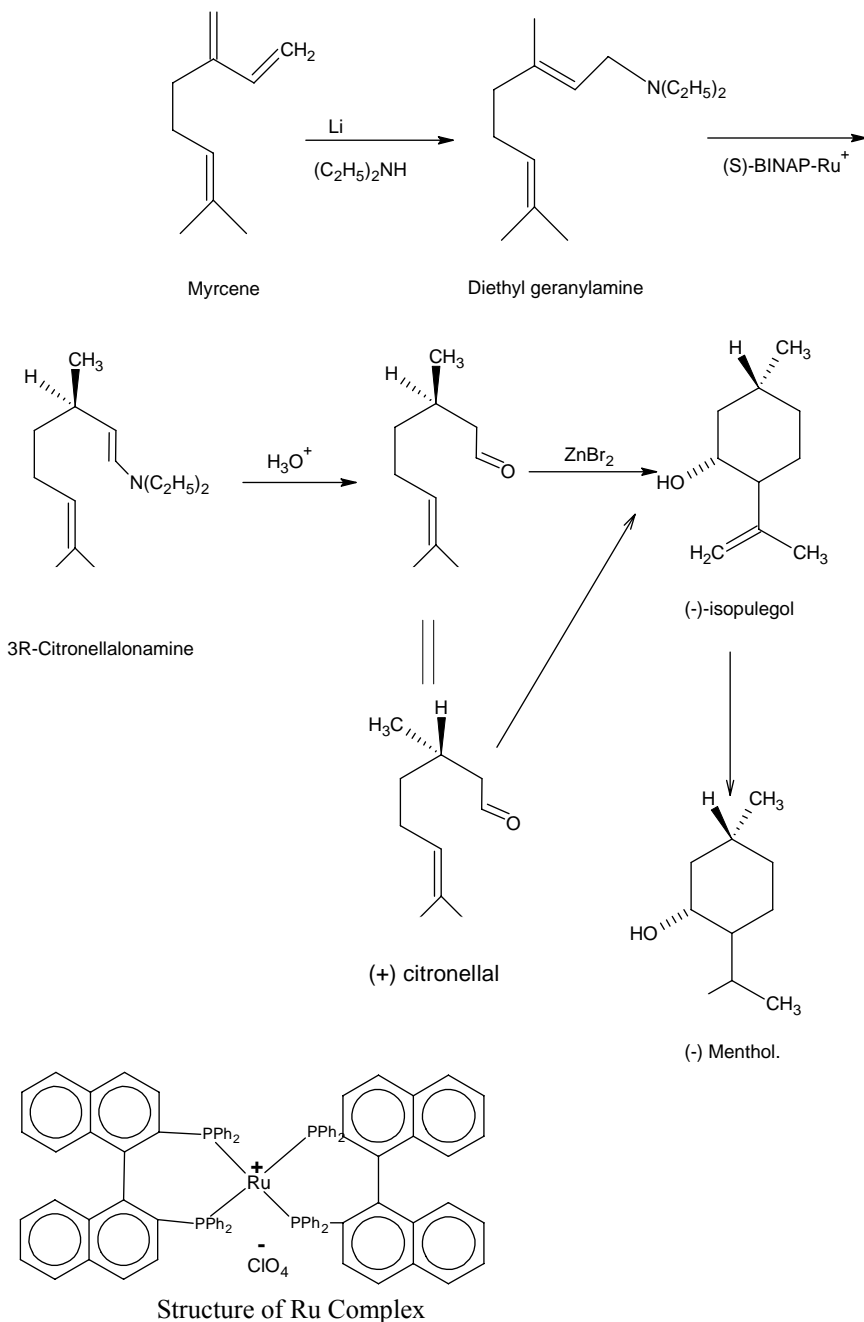
Thus the correlation of pulegone with menthol proved the structure of menthol.

Finally the structure of menthone and menthol have been confirmed by the synthesis given by Kotz and Hese from m-cresol.



Synthesis of menthol from Myrcene:

In early 1980's Takasago developed an elegant synthesis of (-) menthol from Myrcene.



Camphor

Camphor occurs in camphor tree of Formosa and Japan. It is optically active; the (+) and (-) forms occur in nature. It is solid having m.p. 180°C. It is obtained by steam distillation of wood, leaves or bark of camphor tree. It sublimes at room temperature.

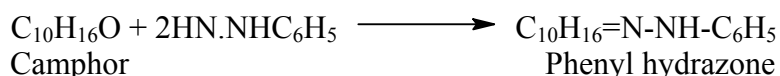
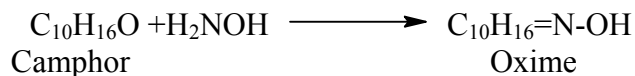
It is used in pharmaceutical preparation because of its analgesic, stimulant for heart muscles, expectorant and antiseptic properties. It is used in manufacture of celluloid, smokeless powder and explosives. It is also used as moth repellent.

Structure Determination:

I) Molecular formula: By usual method it was found to be $C_{10}H_{16}O$.

II) Saturated Nature: General reactions like formation of mono substituted products; mono bromo, monochloro camphor and molecular refraction show that it is saturated.

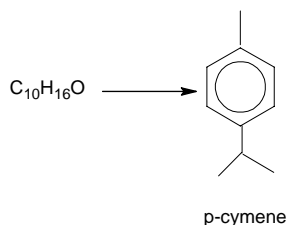
III) Nature of Oxygen atom present: Nature of Oxygen atom in camphor is found to be ketonic as it forms oxime with hydroxyl amine, and phenyl hydrazone with phenyl hydrazine.



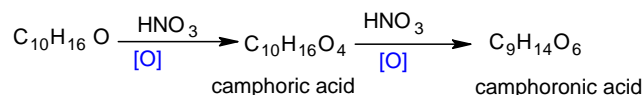
Camphor when oxidised with nitric acid yields a dicarboxylic acid called camphoric acid, without loss of carbon atoms. On reduction with sodium amalgam it gives secondary alcohol; borneol. Thus oxo function in camphor is cyclic ketone.

IV) Presence of Bicyclic system: Molecular formula of saturated hydrocarbon of camphor ($C_{10}H_{16}O$) corresponds to the general formula of a bicyclic compound (C_nH_{2n-2})

V) Presence of a Six membered ring: When distilled with zinc Chloride or phosphorous peroxide, it yields p-cymene. Formation of p-cymene confirms the presence of six-membered ring.



VI) Nature of Carbon frame: Bredt assigned the correct formula to camphor on the basis of above facts and also on the basis of oxidation products obtained from camphor. Oxidation of camphor with nitric acid gives camphoric acid, $C_{10}H_{16}O_4$ and further oxidation of camphoric acid gives camphoronic acid $C_9H_{14}O_6$.



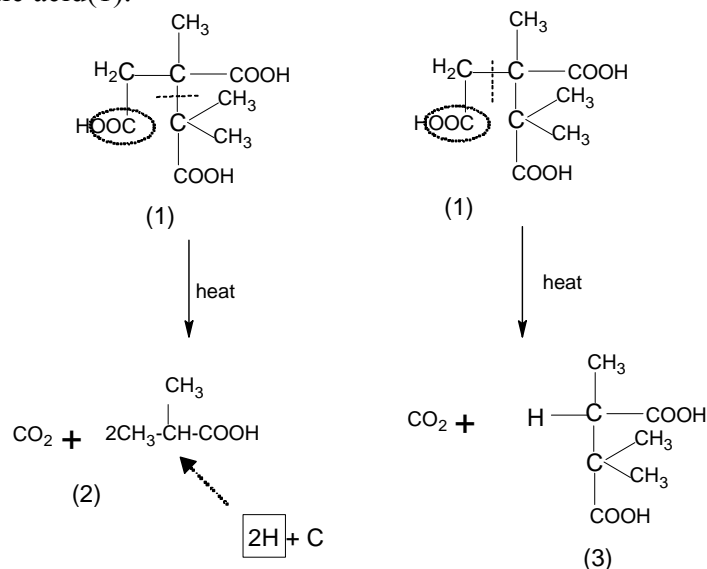
Camphoric acid is saturated dicarboxylic acid with the same number of carbon atoms as camphor, it suggest that keto group is present in one of ring and ring contain keto group is opened in the formation of camphoric acid . Thus camphoric acid should be a monocyclic compound.

Camphoronic acid is tricarboxylic acid. In order to determine the structure of camphor, the structures of camphoric acid and camphoronic acid should be known.

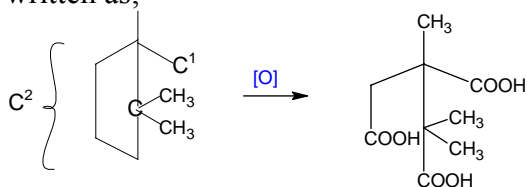
VII) Structure of Camphoronic acid and camphoric acid:

a) It was found to be saturated tricarboxylic acid, and on distillation at atmospheric pressure it gave (1) isobutyric acid (2) trimethyl succinic acid (3), carbon dioxide, and carbon. But it does not undergo decarboxylation under ordinary condition it shows that three carboxylic groups are attached to the different carbon atoms.

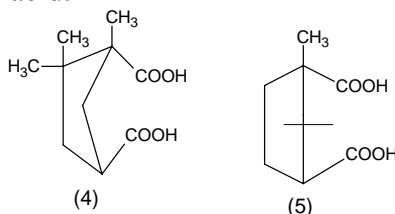
To explain the formation of carbon products Bredt suggested that camphoronic acid is a α,β -trimethyl tricarboxylic acid(1).



Above proposed structure for camphoronic acid is confirmed by its synthesis given by Perkin junior and Thorpe (1897). Camphoric acid was found to be saturated dicarboxylic acid. If above (1) structure of camphoronic acid should have three methyl groups. So camphoric acid is $(\text{CH}_3)_3\text{C}_5\text{H}_5(\text{COOH})_2$. The saturated hydrocarbon of this (C_5H_{10}) corresponds to the general formula C_nH_{2n} . Thus camphoric acid is cyclopentene derivative and oxidation of camphoric acid to camphoronic acid may be written as;

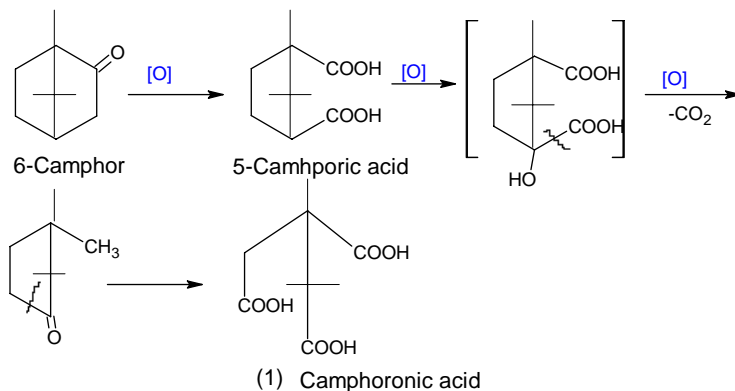


Camphoric anhydride form only one mono bromo derivative it means one α -hydrogen is there in camphoric acid. Thus the carbon atom of one carboxylic acid must be ^1C . But question arises what should be the position of other $-\text{COOH}$ group, when cyclopentane ring open on oxidation. It opens with loss of one carbon atom to give camphoronic acid. So two structure (4) and (5) could be proposed for camphoronic acid.

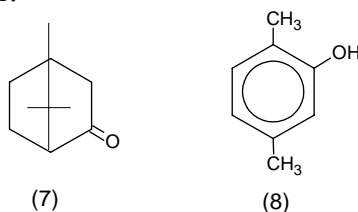


Structure (5) accounts for all the facts given in the foregoing discussion.

VI: Structure of Camphor: Brett therefore suggested that structure (5) was the structure camphoric acid and structure (6) was the structure of Camphor and proposed the following reaction.

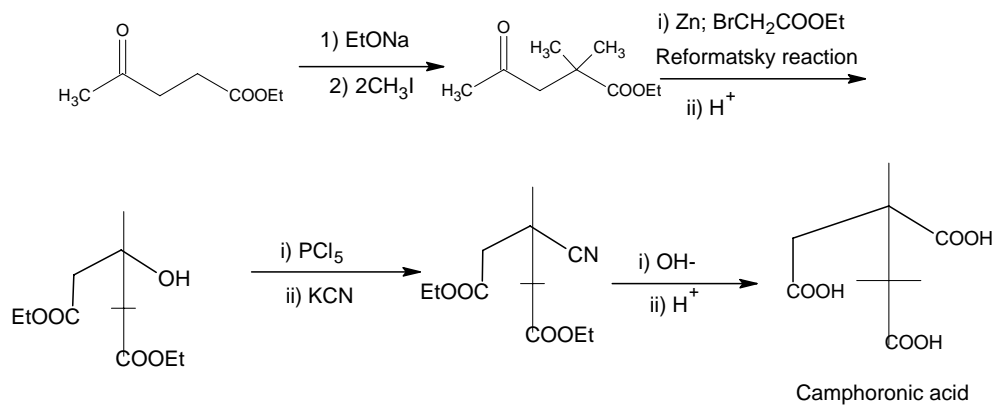


Brett also proposed structure (7) for the camphor, but he rejected (7) in favor of (6) because camphor gives carvacrol (8). When distilled with iodine formation of which can be explained by assuming structure (6) for camphor.

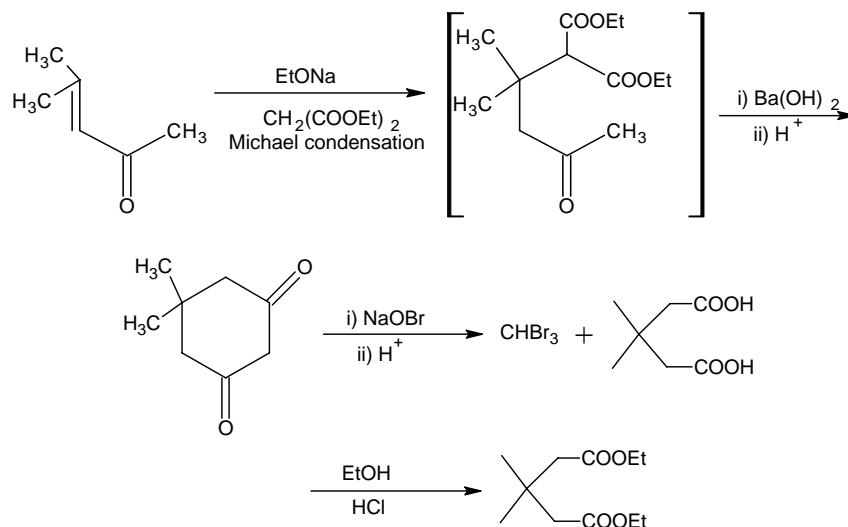


VII) Synthesis: Finally structure was confirmed by the synthesis. All the deductions of Brett were confirmed by the synthesis of Camphoronic acid, camphoric acid and Camphor.

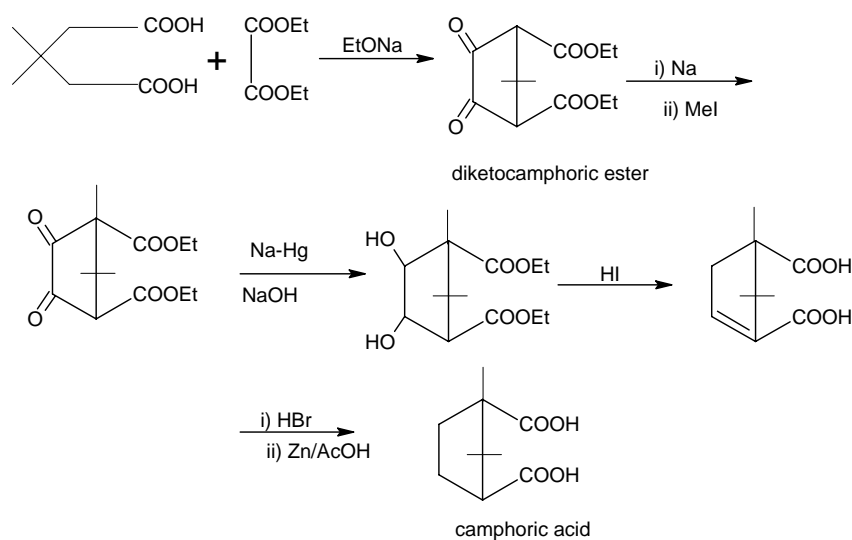
a) synthesis of (\pm) -Camphoronic acid: This synthesis is given by Perkin junior and Thorpe(1987), In this synthesis first ethyl acetoacetate is converted to its dimethyl derivative, which undergoes Reformatsky reaction with ethyl acetate. The product so obtained is converted into halide and then into cyanide. Last product is hydrolysed to give camphoronic acid.



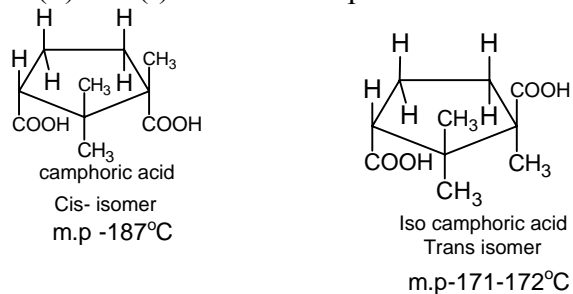
b) Synthesis of (±) –Camphoric acid: This is given by Komppa (1903). He first synthesized 3,3- dimethyl glutaric acid from mesityl oxide and ethyl malonate as follows:



Komppa(1903) then prepared camphoric acid from 3,3-dimethylglutaric acid as follows:

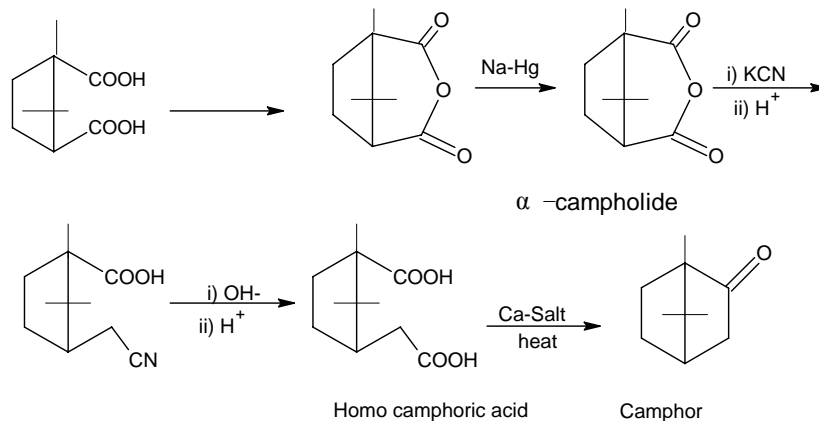


Camphoric acid can exist in two geometrical isomeric forms, cis and trans, neither of these has any element of symmetry. Thus four optical isomers are possible for camphoric acid. All exist and corresponds to the (+) and (-) forms of camphoric acid and iso camphoric acid.

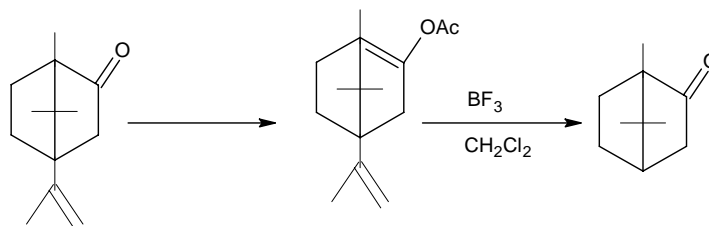


Synthesis of Camphor:

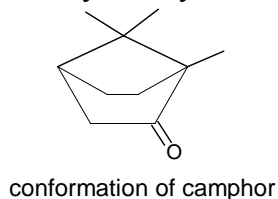
i) Haller gave this synthesis of camphor from camphoric acid which was synthesized by Komppa.



ii) Another two step synthesis of camphor from dehydro carvone was given by Money et al (1969).



Though camphor has two dissimilar chiral centers only one pair of enantiomers is possible, since only cis fusion of the gem dimethyl methylene to cyclohexane ring is possible. Boat conformation with cis fusion of gem dimethyl methylene is shown below;



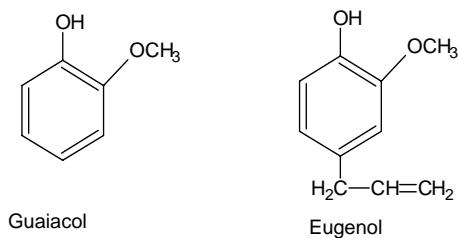
Commercially, Camphor is prepared from α -pinene.

Eugenol

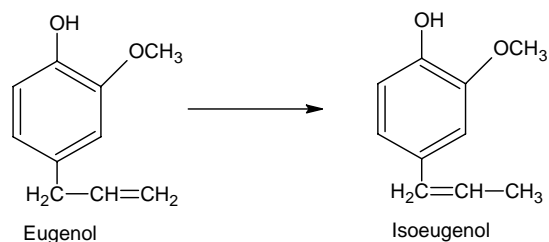
Eugenol is the principal ingredient of clove oil which gives the characteristic spicy fragrance to it. It also occurs in many other essential oils. Mainly eugenol is isolated from clove oil. Eugenol is used in perfumes, mouth washes etc. It is also used as an insect attractant and dental analgesic.

i) M.F = $C_{10}H_{12}O_2$

ii) Eugenol is phenolic ether (α -allyl guaiacol) having b.p-254°C. Guaiacol is also a phenolic ether containing one $-OCH_3$ group ortho to each other. In Eugenol one more allyl group is present other than a hydroxyl and methoxy group at 4th position. Thus structure of eugenol may be written as-

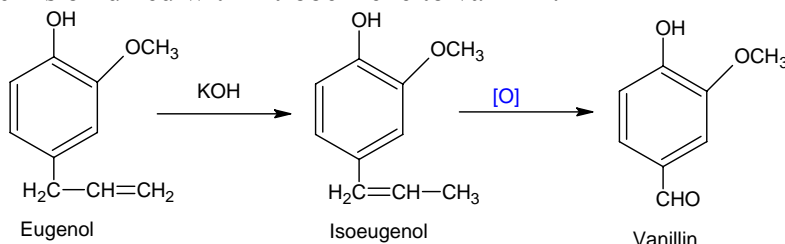


iii) On heating with ethanolic potassium hydroxide or with potassium hydroxide in diethylene, eugenol isomerises to isoeugenol which is 4-propenyl guaiacol.



Isoeugenol, b.p. 267.5°C, also occurs naturally.

iv) Presence and position of One -OH, one -OCH₃ and side chain in eugenol is also confirm by its conversion to vanillin which is p-Hydroxy-m-methoxybenzaldehyde. Eugenol first isomerises to isoeugenol which is oxidized with nitrobenzene to vanillin.



Side chain can also be oxidized with ozone. If the oxidation is carried out with acid dichromate, it is necessary to protect the hydroxyl group.

Vanillin may be prepared synthetically from guaiacol by means of Reimer-Tiemann or the Gattermann reaction.

Suggested Readings

- i) Organic Chemistry by I. L. Finar, vol. 2, 6th edition
- ii) Organic Chemistry by Paula Yurkanis Bruice, 3rd edition.
- iii) Organic Chemistry by Robert T. Morrison and Robert Neilson Boyd, 6th edition.
- iv) Chemistry of Natural Products by S. V. Bhat, B. A. Nagasampagi and M. Siva Kumar