CHEMISRY OF NATURAL PRODUCTS

FOR 2nd YEAR BIOLOGY STUDENTS

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2023/2024

Contents

- Introduction
- Classification of natural products
- Terpenoids
- Steroids
- Alkaloids
- Biosynthesis of natural products

المحاضرة الاولي

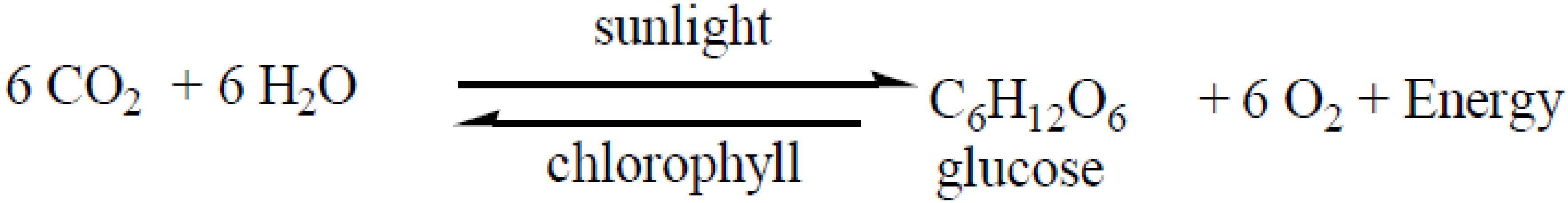
Introduction

- Natural products are chemical compounds or substance produced by a living organism that is found in nature.
- In the broadest sense, natural products include any substance produced by life.
- **Natural Products** is define as organic compounds and other chemicals synthesised by plants through metabolic processes aided by sunlight, involving CO2, H2O vapour and chlorophyll.
- Generally, natural products are characterised by specific functions they perform in plants and animals.
- Categories of natural Products are called metabolites.

Primary metabolites

A- Primary metabolites are usually found in all living organisms such as plants and animals. They form the nucles of living material e.g. mevalonic acids and nucleotides.

- Acetyl-coenzyme A (AScOA), Nucleotides and Mevalonic acids (MVA) constitutes primary metabolites from which secondary metabolites are derivable. A complex web of enzymecatalyzed reactions may involve the use of inorganic compounds such as H2O, CO2, solar energy through the process known as **Photosynthesis**. The reaction scheme is shown below.



$$6\,CO_2 + 6\,H_2O \underset{\text{chlorophyll}}{\overset{\text{sunlight}}{\rightleftharpoons}} \underset{\text{glucose}}{C_6H_{12}O_6} + 6\,O_2 + \text{Energy}$$

Secondary metabolites

B- Secondary metabolites are chemicals synthesized by plants but are not directly used by them, but are used indirectly by man as a source of pharmaceutical preparations. Secondary metabolites are generally built from primary metabolites. Examples are steroids, terpenoids, alkaloids, and others.

- Some secondary metabolites are synthesised via biosynthesis and or biogenesis.
- Higher plants synthesised chemical compounds *in vivo* and degrade them by means of series of chemical reactions, each aided by enzymes, by a process known as **metabolism**

What is difference between biosynthesis and biogenesis?

What biosynthesis means?

the production of a chemical compound by a living organism.

What biogenesis means?

Biogenesis refers to all living things that come from other living things.

- is that biogenesis is the principle that living organisms are produced only from other living organisms while biosynthesis is (biochemistry) the synthesis of organic compounds within a living organism, especially the synthesis of large compounds from small ones.

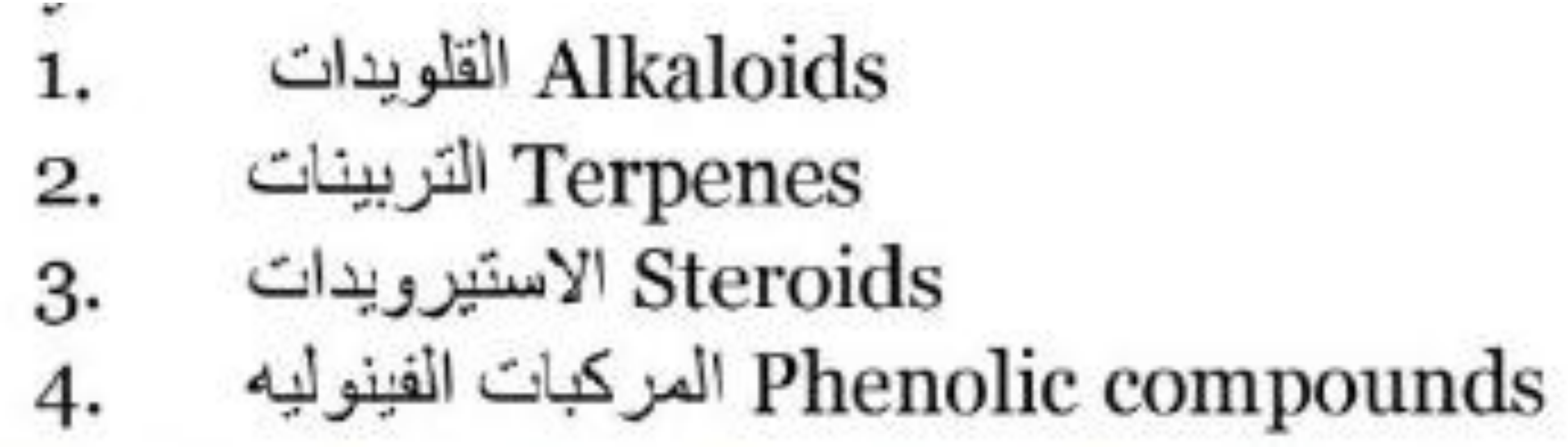
What are "Natural Products"?

Chemical characteristics

- Naturally-occurring small organic compounds
  - including heterocyclic compounds, and peptides.
  - does not include proteins, carbohydrates, and nucleic acids.
- MW: ~150 ~ <800 amu ("small molecule")
- Methods of extraction and purification are generally similar to the techniques used for organic compounds

  (e.g., TLC, column chromatography, HPLC, GC)
- Methods of structural determination
  - NMR, MS, IR, X-ray, UV

Classification of natural products



1. القلويدات Alkaloids
2. التربينات Terpenes
3. الاستيرويدات Steroids
4. المركبات الفينوليه Phenolic compounds

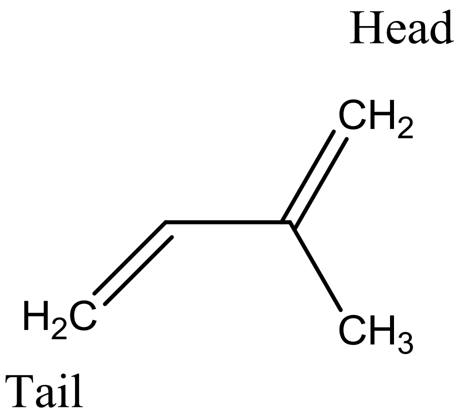
المحاضرة الثانية

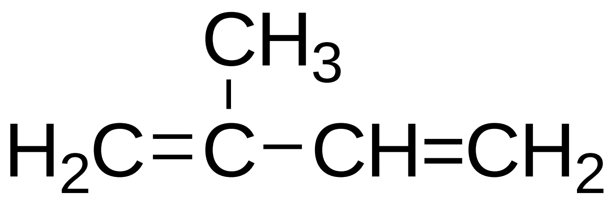
(I) Terpenoids

Terpenoids

- Terpenoids are naturally occurring organic compounds, mostly found in plants.
- Terpenoids are structurally related as they are all composed of isoprene units repeated twice or more.
- They can be either hydrocarbons or oxygenated compounds.

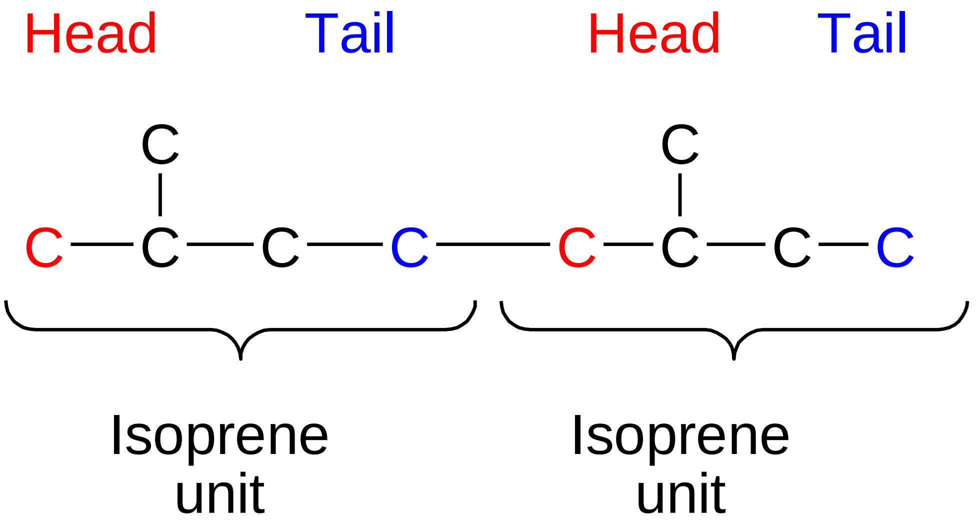
Isoprene Rule: All naturally occurring terpenoids consist of isoprene units $(C_5H_8)_n$ connected together in a head-to-tail arrangement.

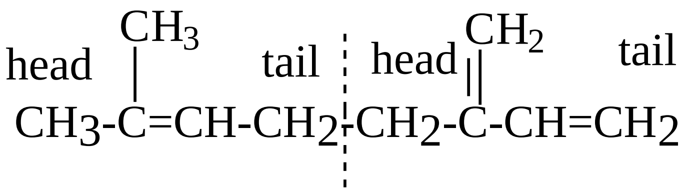




$$H_2C{=}\overset{CH_3}{\overset{|}{C}}{-}CH{=}CH_2$$

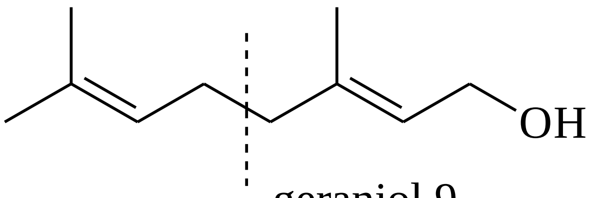
Isoprene





$$CH_3\text{-}\overset{CH_3}{\overset{|}{C}}{=}CH\text{-}CH_2\text{-}CH_2\text{-}\overset{CH_2}{\overset{\|}{C}}\text{-}CH{=}CH_2$$

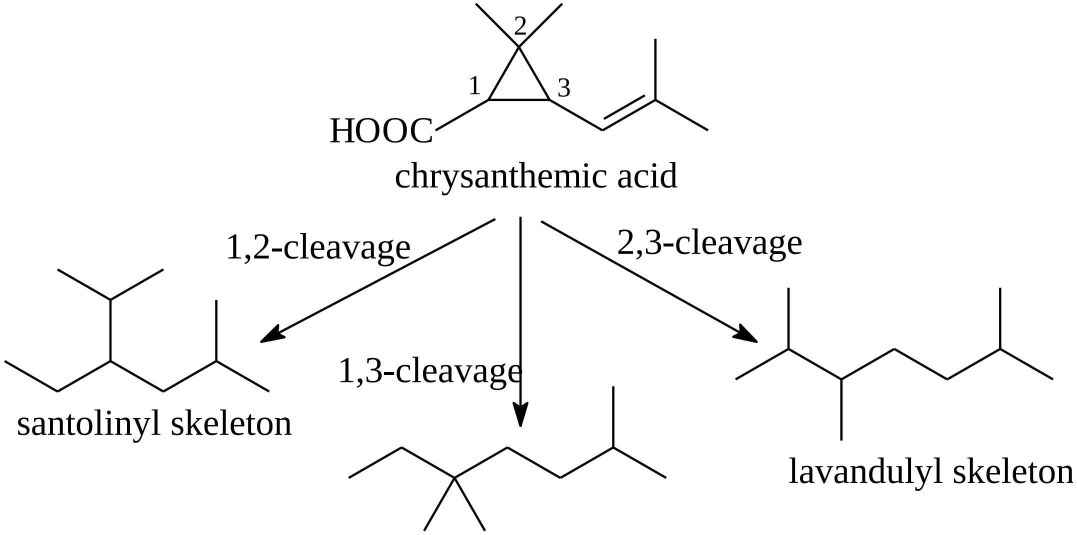
myrcene 8



geraniol 9

Exceptions of the Special Isoprene Rule

irregular monoterpenes



chrysanthemic acid

1,2-cleavage

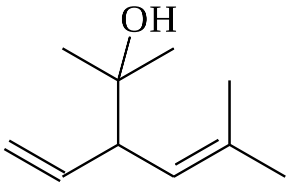
1,3-cleavage

2,3-cleavage

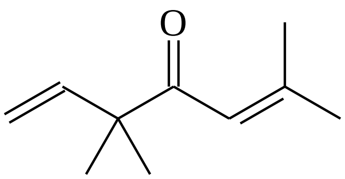
santolinyl skeleton

artemisyl skeleton

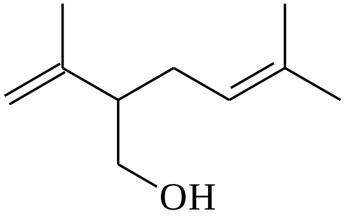
lavandulyl skeleton



santolina alcohol 10



artemisia ketone 11



lavandulol 12

Classification of Terpenoids:

Terpenoids are classified according to the number of isoprene units $(C_5H_8)_n$ into:

1- Hemiterpenes (n = 1), Ester and ether groups, C_5H_8

2- Monoterpenoids (n=2), Volatile oils, $C_{10}H_{16}$

3- Sesquiterpenoids (n=3), Volatile oils, $C_{15}H_{24}$

4- Diterpenoids (n=4), Gums and resins $C_{20}H_{32}$

5- Sesterterpenoids (n=5), Gums and resins, $C_{25}H_{40}$

6- Triterpenoids (n=6), Gums and resins, $C_{30}H_{48}$

7- Tetraterpenoids (n=8): $C_{40}H_{64}$ (Carotenoids)

8- Polyterpenoids (n is a large number) (Rubber)

Isolation of Mono- and Sesequiterpenes (essential oils)

There are four methods of extraction of the terpenoids

(i) Chromatography

(ii) Steam distillation

(iii) Extraction by means of volatile organic solvents

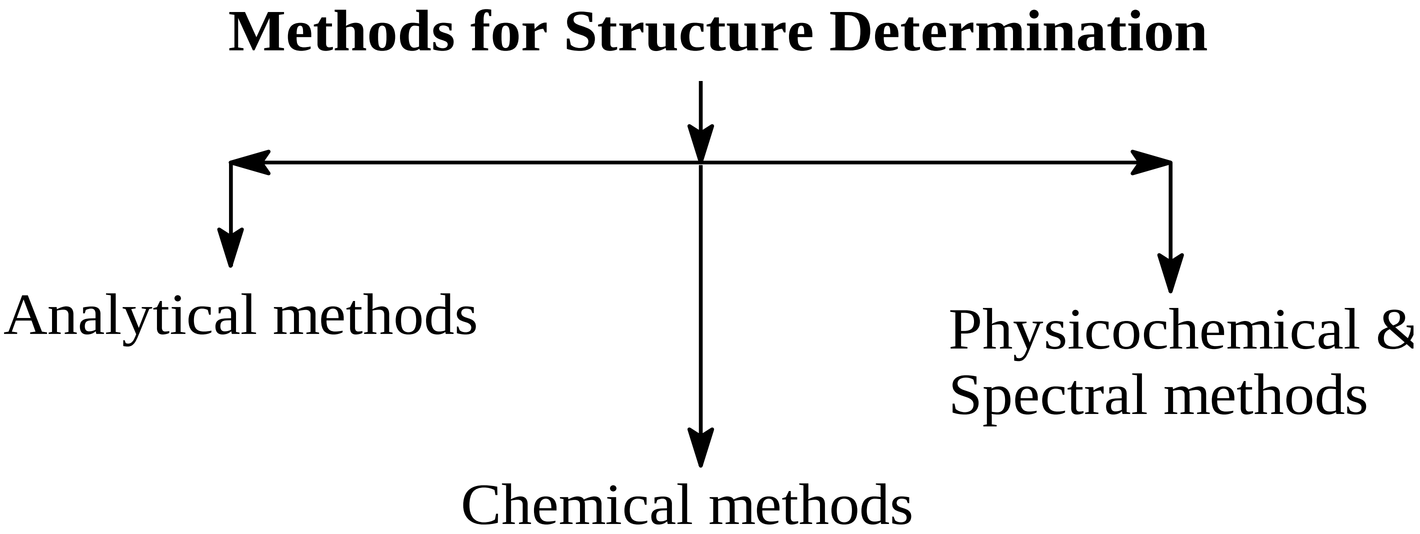
(iv) Adsorption on fats.

Method (ii) is the one most widely used. More recently, chromatography (in its various forms) has been used both for isolation and separation of terpenoids.

Methods for Separation of mixtures

- Fractional distillation
- thin layer chromatography
TLC
- column chromatography
CC
- high pressure liquid chromatograp
HPLC
- Other methods

General Methods for Structure Determination of Terpenoids



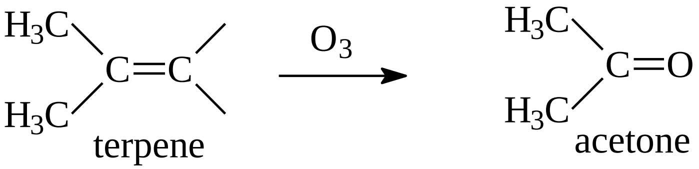
Methods for Structure Determination

Analytical methods

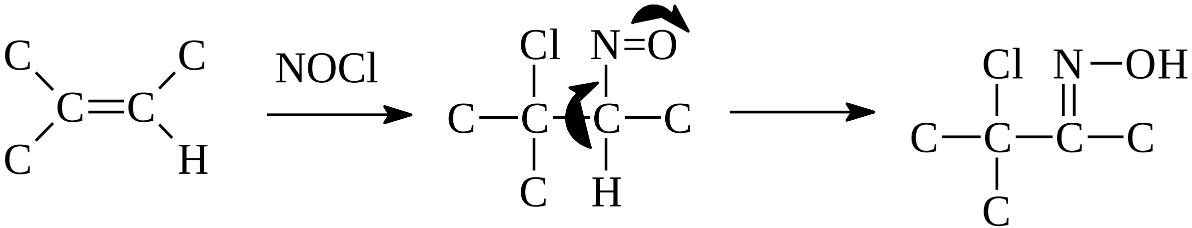
Chemical methods

Physicochemical & Spectral methods

- **Analytical methods**
- Determination of % of C,H and O by molecular formula
- Degrees of unsaturation
- Estimation of groups
- · Active hydrogen
- Terpene + $LiAlH_4 \rightarrow H_2$ ----- estimated



- Chemical methods
- Functional groups
- Unsaturation
- · by bromination (Br_2)
- · by nitrosyl chloride NOCl



nitrosyl chloride
intense blue colour

oxime

General methods of determining structure of terpenoids

1-After extraction and separation then purification of sample ,the molecular formula is ascertained by usual methods (qualitative and quantitative analysis – empirical formula-determination of M.Wt).

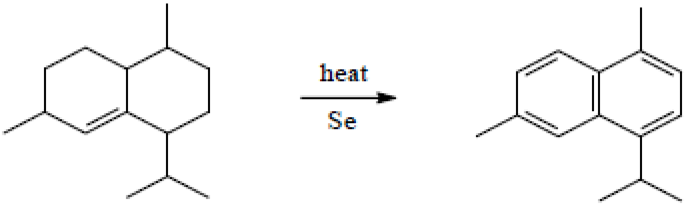
2-If the terpenoid is optically active ,its specific rotation is measured.

3-The nature of functional oxygen atom if it is present (hydroxyl-carbonyl -carboxyl --------- etc).

4-The presence of unsaturation olefinic bonds is ascertained by means of bromine and catalytic hydrogenation.

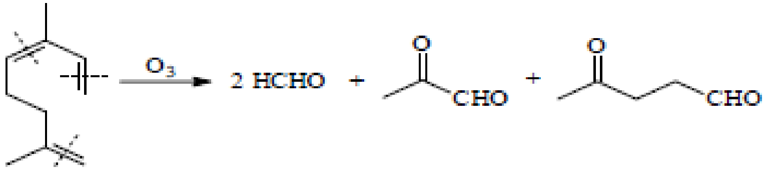
5-Conjugated and isolated double bonds are differentiated by Diel's Alder reaction also by using UV spectroscopy.

6-Dehydrogenation by heating the terpene with S or Se converts the terpene into aromatic derivative which is easily identified.

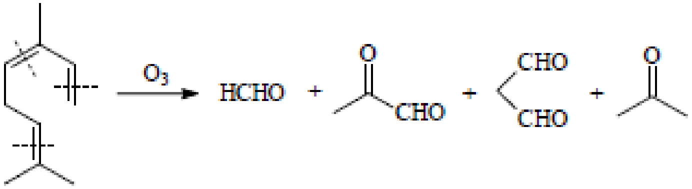


7- Ozonolysis is an example of oxidative degradation methods (O_3, $KMnO_4$, CrO_3 & OsO_4),this method produced two type of products, acetone arising from the terminal isopropylidene group($Me_2C=$) and formaldehyde arising from isopropenyl group($CH_2=CMe$) or terminal methylene group($CH_2=$).

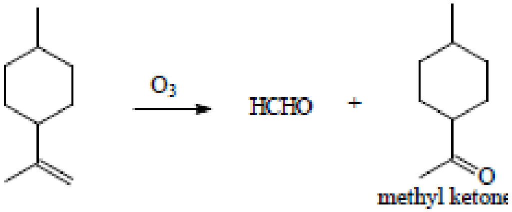
(i)



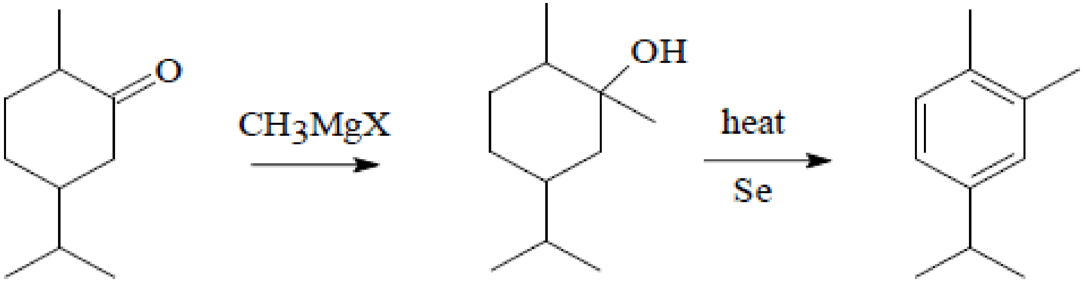
(ii)



(iii)



8-Grignard reagent useful for detecting the position of carbonyl group in terpenoids.

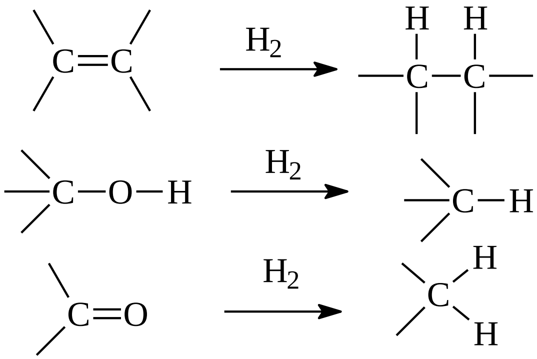


9-Infrared spectroscopy (IR) is useful by detecting the presence of hydroxyl group ,carbonyl group -------- etc , NMR (^{1}H-NMR & ^{13}C-NMR give information about the nature and the number of hydrogen and carbon, Ultraviolet spectroscopy (UV),mass spectrometry and X-Ray analysis are very useful for elucidating structure and stereochemistry of terpenoids.

10- A final confirmation of the proposed structure is usually achieved by synthesizing the compound and comparing the spectral data with those of an authentic sample.

- Physical and spectral methods
- a) Molecular refraction
- (b) Optical rotation
- c) IR absorption
- d) NMR (^{1}H-NMR & ^{13}C-NMR)
- e) X-Ray
- F) UV (ultraviolet absorption)

11- Hydrogenation of the substance to the parent hydrocarbon leads to the cyclic nature of the terpene (acyclic, monocyclic, bicyclic, ... etc).



saturated hydrocarbones

- · <u>Hydrocarbon</u> C_nH_{2n+2} -------------- Acyclic
- C_nH_{2n} -------------- Monocyclic
- C_nH_{2n-2} ------------- Bicyclic
- C_nH_{2n-4} -------------- Tricyclic
- C_nH_{2n-6} -------------- Tetracyclic

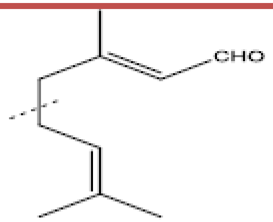
المحاضرة الثالثة

Monoterpenoids التربينات الأحادية

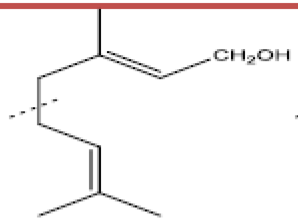
Monoterpenoids are classified into three groups (acyclic,monocyclic,bicyclic)

Acyclic Monoterpenoids

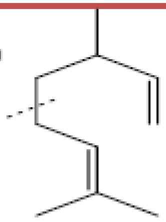
The carbon skeleton being formed by the head to tail of two isoprene units.



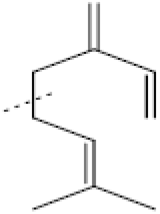
Citral



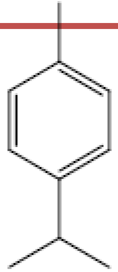
Geraniol



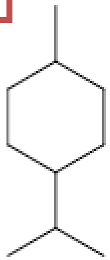
Ocimene



Myrcene



P-cymene

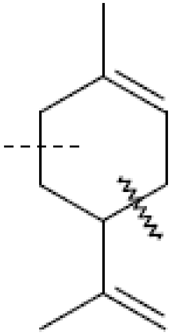


P-menthane

Monocyclic monoterpenoids contain a six membered ring and most natural monocyclic monoterpenoids are derivatives of p-cymene and the parent substance is named P-menthane.

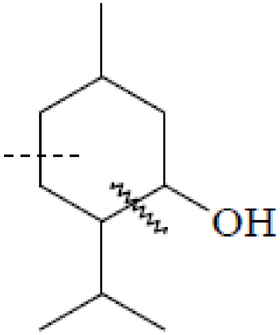
Bicyclic monoterpenoids contain a six membered ring and a three,four or five membered ring .

Monocyclic monoterpenoids

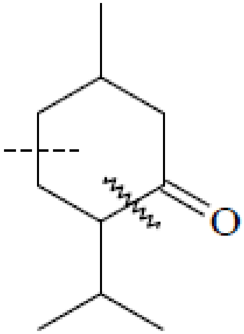


Limonene

occurs in lemon
and orange oils



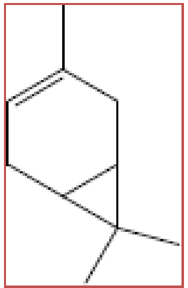
Menthol



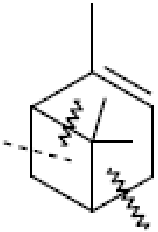
Menthone

both occur in pepermint oil

Bicyclic monoterpenoids

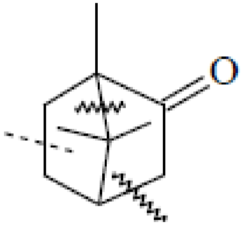


carene



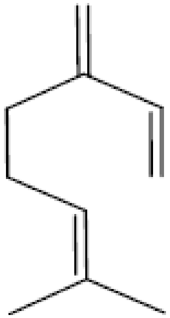
α-Pinene

occurs in turpentine oil



Camphor

occurs in camphor tr



$(C_{10}H_{16}$)Myrcene المـايرسيـــــن

IUPAC name: 7-methyl-3-methylene-octa-1,6-diene

Myrcene occurs in verbena and bay oils ,myrcene is optically inactive and highly unsaturated.

Structure of myrcene is supported by :

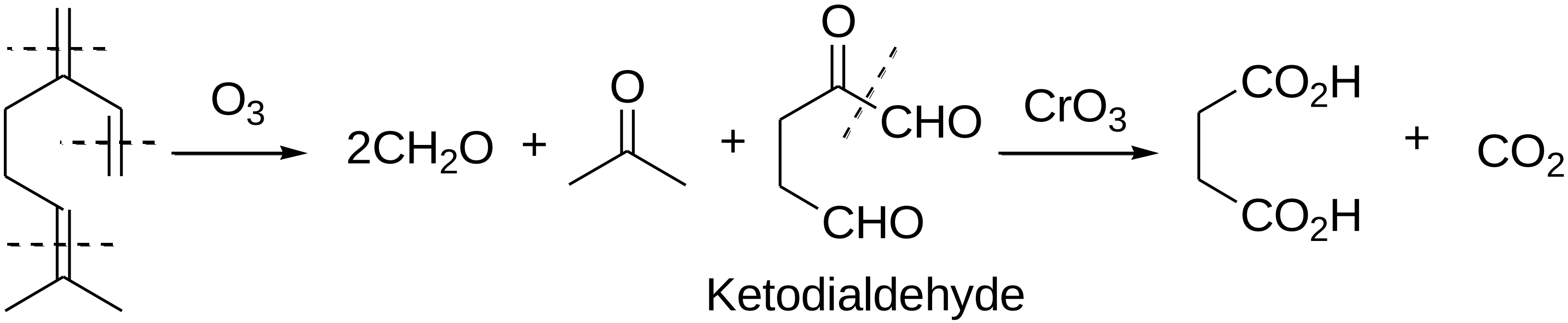
1-Molecular formula is $C_{10}H_{16}$.

2-Catalytic hydrogenation of myrcene gave saturated alkane$C_{10}H_{22}$ (isodecane) thus myrcene is an open chain and contains three double bond .

3-Since myrcene forms adduct with maleic anhydride, thus two of the double bond are conjugated .

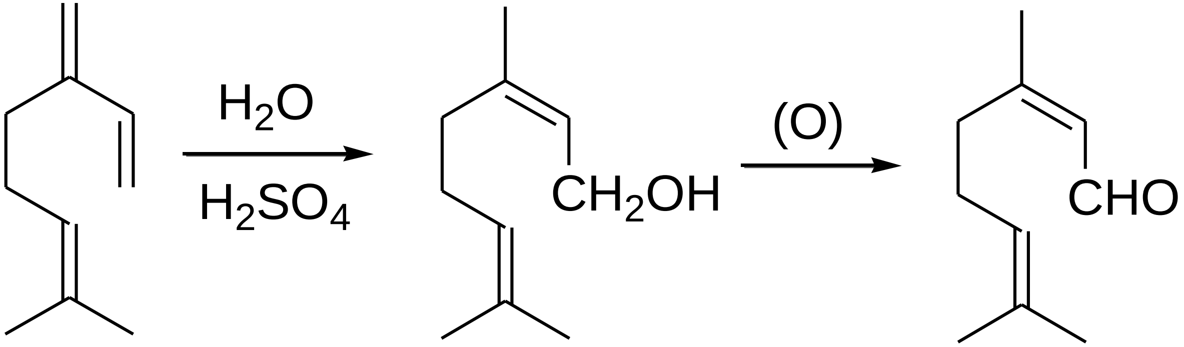
4-Ozonolysis of myrcene produces acetone ,two molecule of formaldehyde and ketodialdehyde which oxidized with chromic acid to give succinic acid and carbon dioxide.

The process of ozonolysis can be represented as shown:



Ketodialdehyde

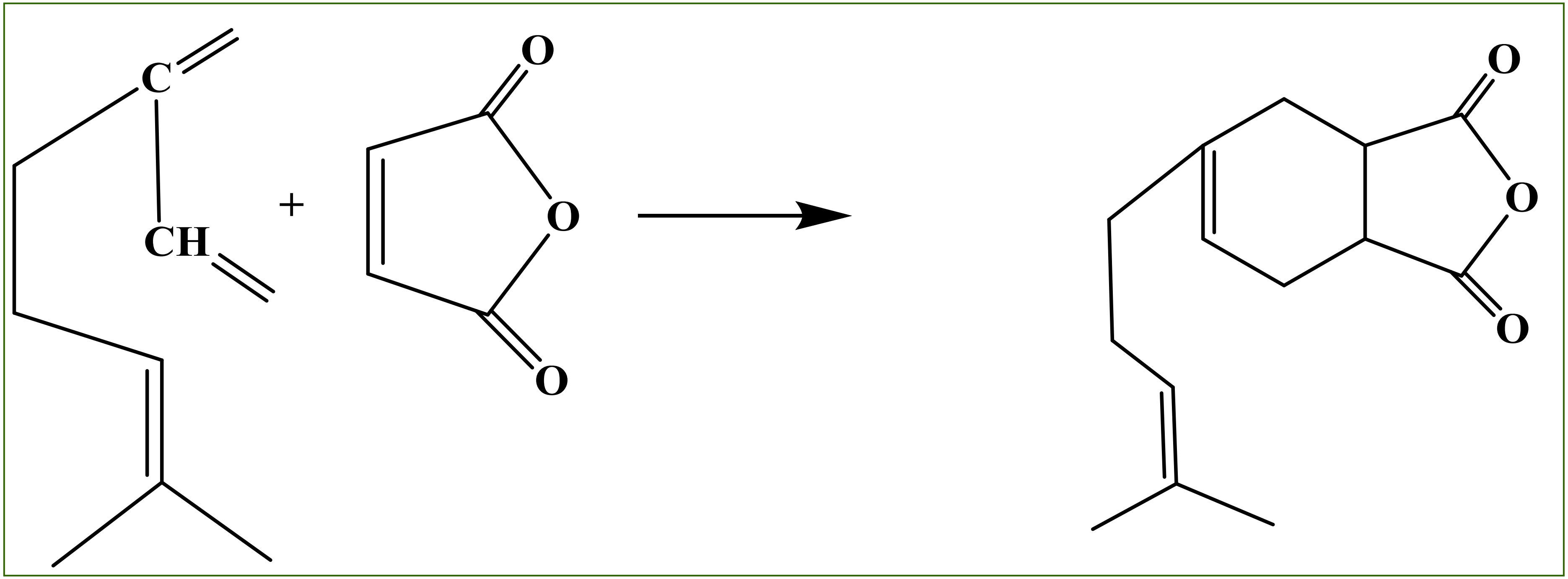
This structure for myrcene is supported by the fact that on hydration (under the influence of sulphuric acid), myrcene form an alcohol which, on oxidation gives citral:



Citral

Diel's-Alder reaction of Myrcene

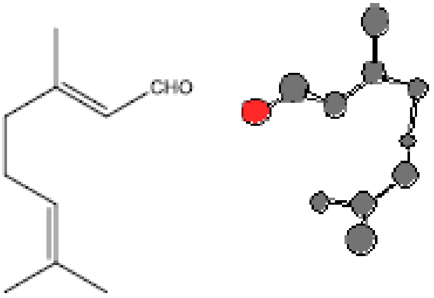
- Furthermore, since myrcene forms an adduct with maleic anhydride, two of the double bonds are conjugated.

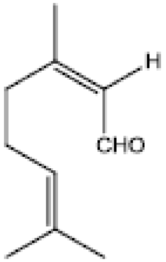


Citral ($C_{10}H_{16}O$)

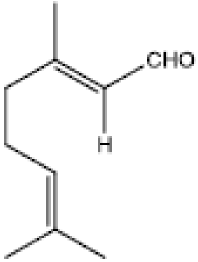
3,7 dimethyl 2,6 -octadienal

Citral occurs to an extent 60-80 per cent in lemon grass oil
Structure of citral was supported by:

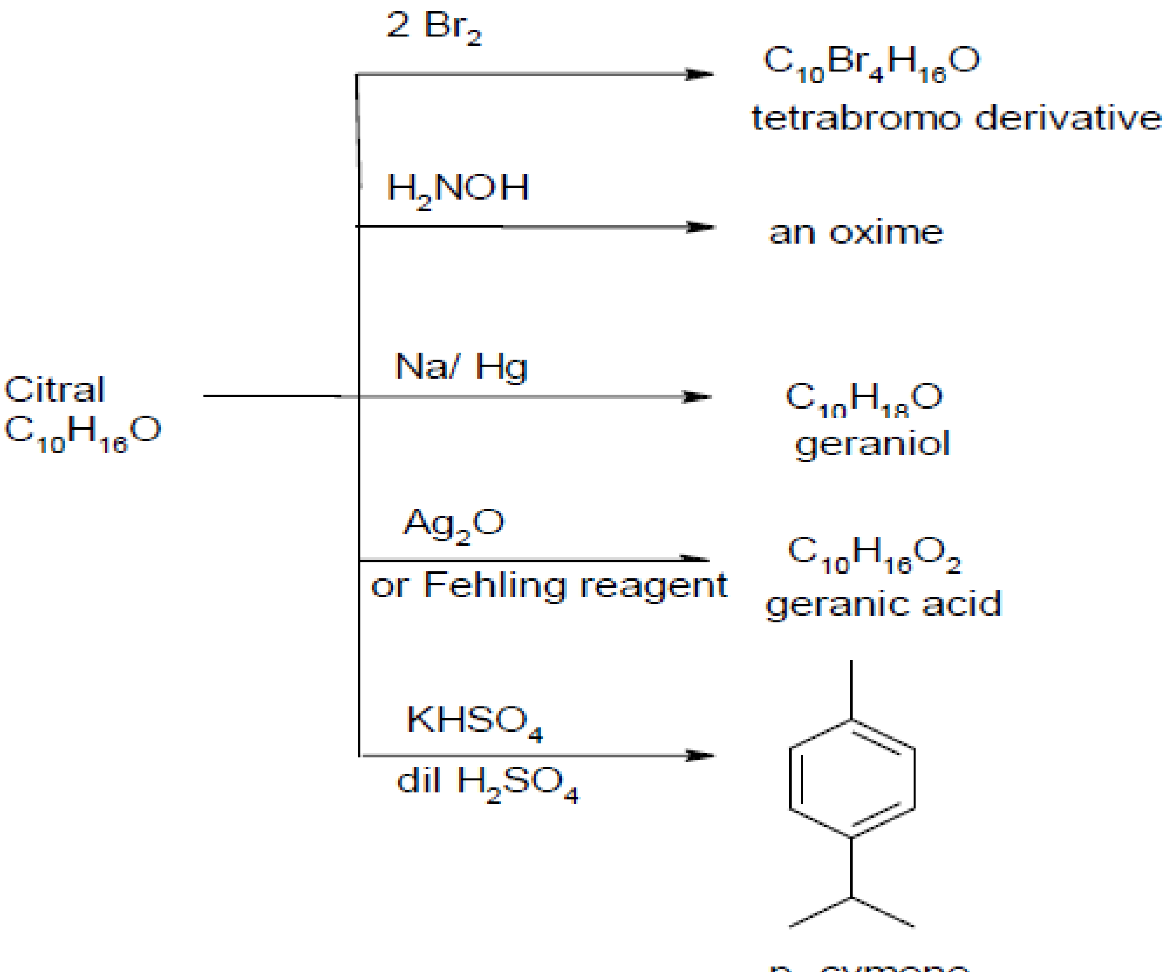




cis form
citral b or neral



trans form
citral a or geranial



Citral $C_{10}H_{16}O$

$\xrightarrow{2\,Br_2}$ $C_{10}Br_4H_{16}O$ tetrabromo derivative

$\xrightarrow{H_2NOH}$ an oxime

$\xrightarrow{Na/\,Hg}$ $C_{10}H_{18}O$ geraniol

$\xrightarrow[\text{or Fehling reagent}]{Ag_2O}$ $C_{10}H_{16}O_2$ geranic acid

$\xrightarrow[\text{dil } H_2SO_4]{KHSO_4}$ p- cymene

1-It has been proven by analysis that Molecular formula is **$C_{10}H_{16}O$** .

2-It added two molecule of bromine thus citral contains two double bond .

3-It forms oxime derivative with hydroxyl amine citral contains oxo group.

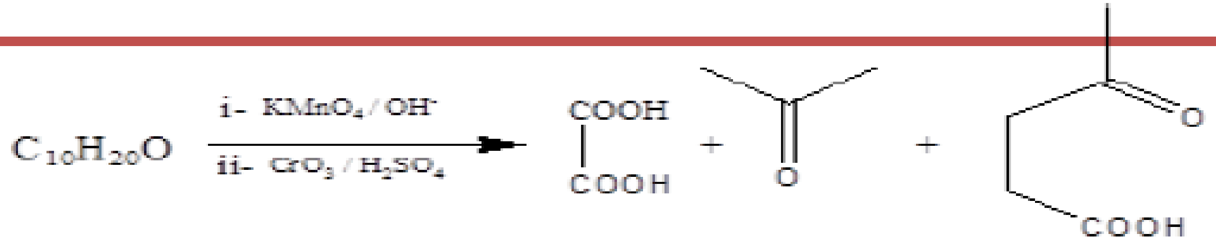
4-Citral can be reduced by sodium amalgam to an alcohol geraniol.

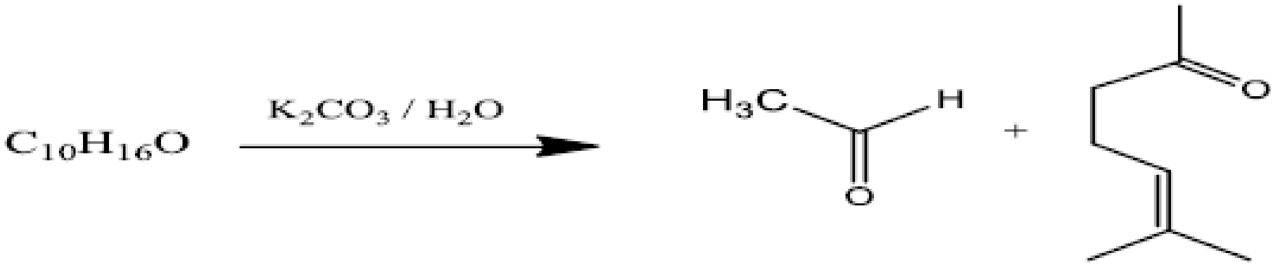
5-Citral oxidized with silver oxide to geranic acid since there is no loss of carbon oxidation to acid ,the oxo group in citral is t here an aldehyde group .

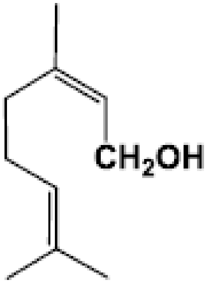
6-On heating with potassium hydrogen sulphate citral forms p-cymene ,this reaction was used to determine the position of methyl and isopropyl groups .

7-Oxidation of citral with alkaline permanganate,f ollowed by chromic acid ,gives acetone, oxalic acid and levulinic acid.

8-Citral with aqueous potassium carbonate gives acetaldehyde and 6-methylhept-5-en-2one .

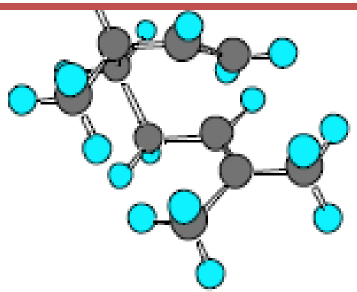


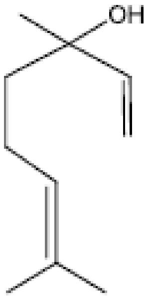




Geraniol

$(C_{10}H_{18}O)$ Linalool اللينـــالـول





3,7-Dimethyl -octa-1,6-diene 3 -ol

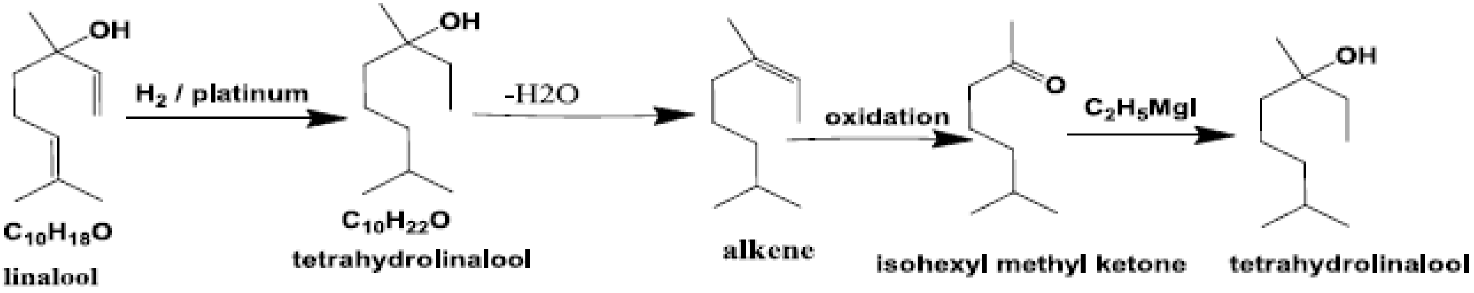
Structure of Linalool : $(C_{10}H_{18}O)$ b.p:198-199C

1- It is an optically active the (-)form occurs in rose oil and the (+) form in orange oil.

2- It adds on two molecule of hydrogen in catalytic hydrogenation ,and give negative with maleic anhydride it must be contain two (non conjugated) double bond .

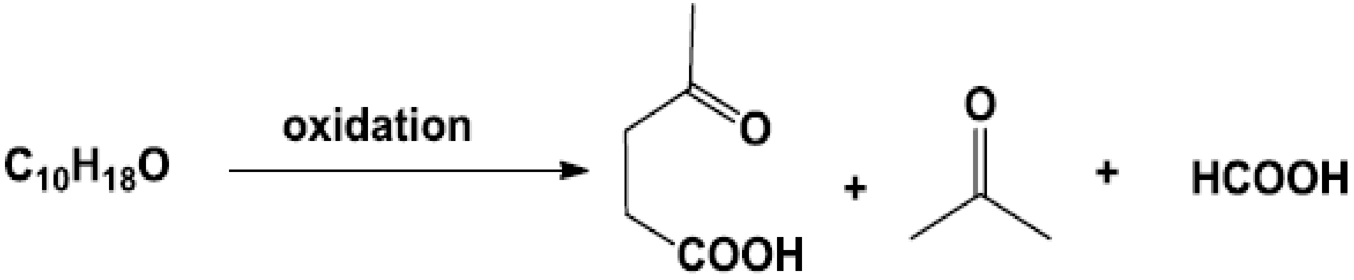
3-It is converted into geranyl acetate by heating with acetic anhydride and converted into linalool by heating with steam at 200C under pressure , also linalool isomerizes in the presence of acid to geraniol .

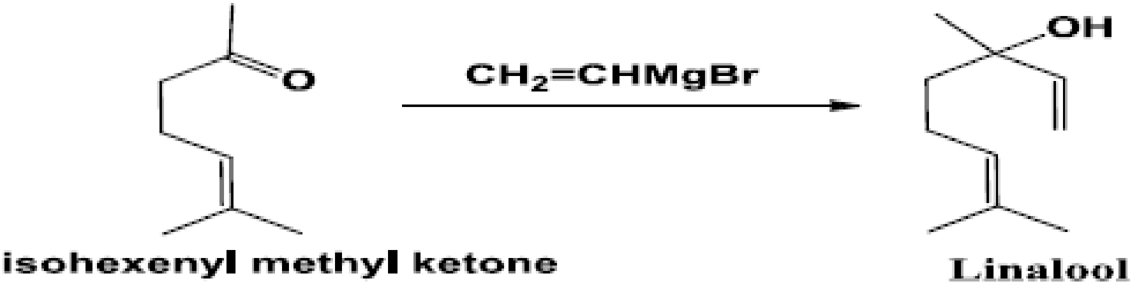
4-It has a tertiary alcoholic group and the position confirmed as follow:



5-Oxidation of linalool by pot. Permenganate converted it into levulinic acid ,acetone and formic acid .

6-Normant has synthesized linalool in one step by the action of vinyl magnesium bromide with 6-methyl -5-heptene-2-one(isohexenyl methyl keton).

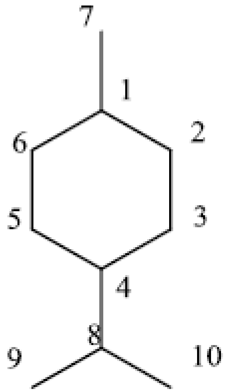


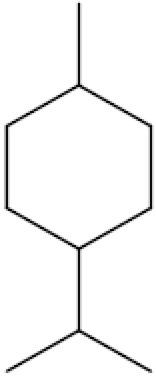


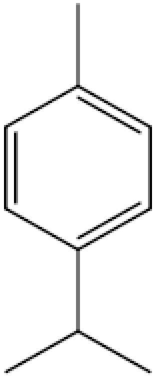
المحاضرة الرابعة

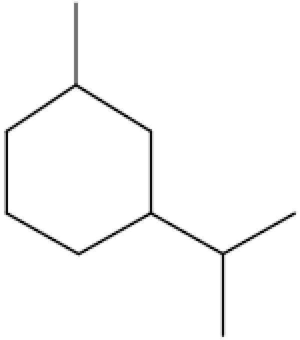
Monocyclic Monoterpenoids

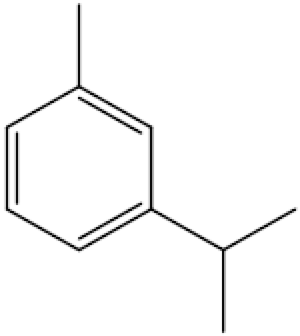
Monocyclic Monoterpenes is subdivided into two groups the larger group with carbon skeleton which are related to P-cymene(4-isopropyl toluene), the smaller group with carbon skeleton are related to m-cymene.

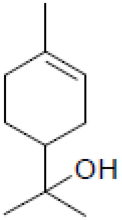


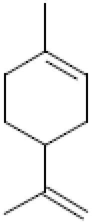

P-menthane

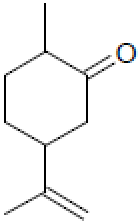

P-cymene

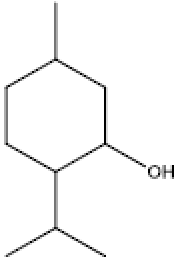

m-menthane

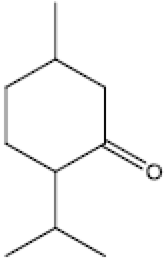

m-cymene

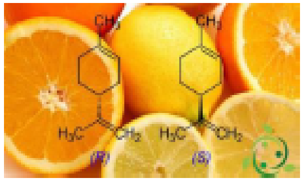

α – terpineol


limonene

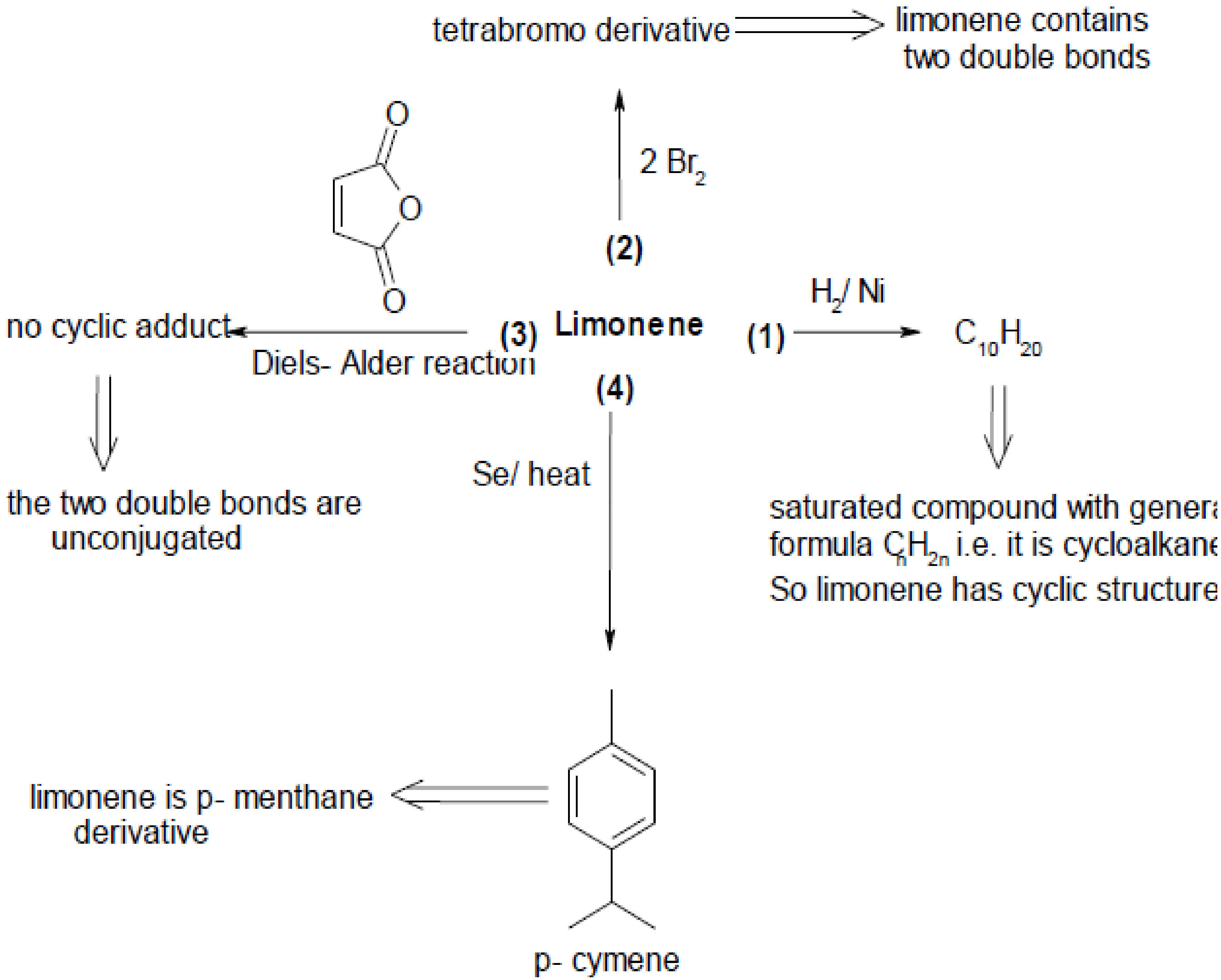

carvone


Menthol


Menthone



Structure of Limonene was supported by



tetrabromo derivative ⟹ limonene contains two double bonds

(2) $2\ Br_2$

(3) Diels- Alder reaction → no cyclic adduct

⟹ the two double bonds are unconjugated

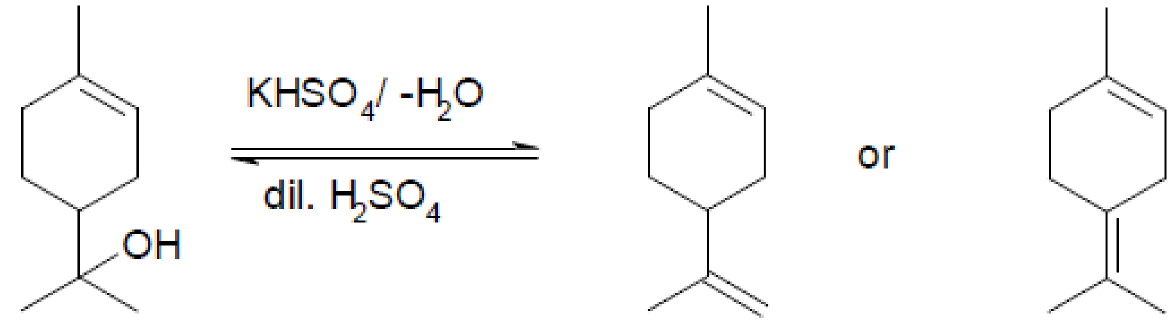
Limonene

(1) H_2/Ni → $C_{10}H_{20}$

⟹ saturated compound with genera
formula C_nH_{2n} i.e. it is cycloalkane
So limonene has cyclic structure

(4) Se/ heat

p- cymene ⟹ limonene is p- menthane derivative



α – terpineol

I

التركيب البنائي الصحيح
لليمونين لأنه نشط ضوئيا

II

مستبعد لأنه تركيب بنائي
غير نشط ضوئيا

5-limonene may be prepared by dehydrating α- terpineol by using potassium hydrogen sulphate ($KHSO_4$) ,and on shaking with dilute sulphuric limonene may be converted to α- terpineol .

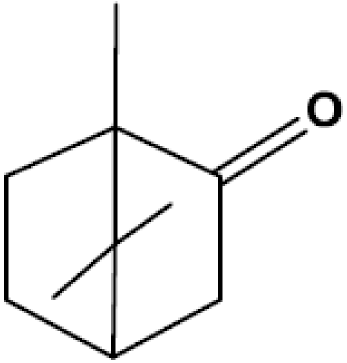
6-The carbon skeleton and the position of double bond in limonene are known ,but the other double bond remains uncertain (may be C8-C10 or C4-C8).

7-Structure (I) contains a chiral center(C4)and hence can exhibit optical activating .

Structure (II) is symmetric and so cannot be optically active. Therefore (I) must be **Limonene**

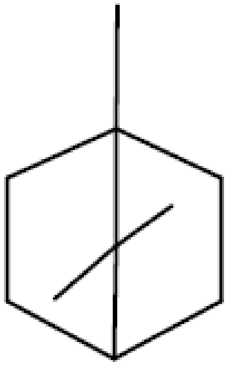
التربينات الأحادية ثنائية الحلقة

Bicyclic monoterpenoids



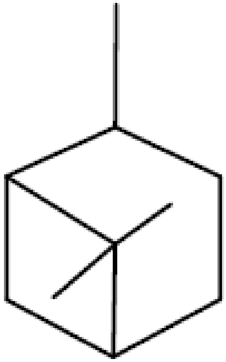
camphor

6+5



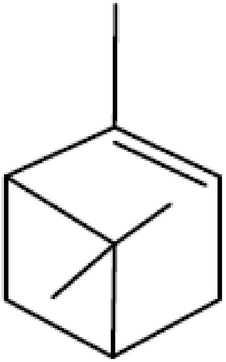
camphane
bornan

6+5



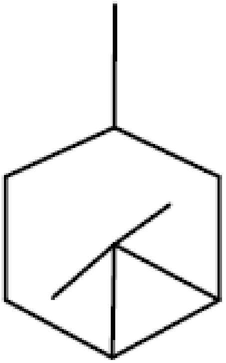
Pinane

6+4



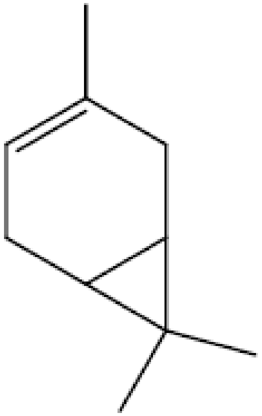
Pinene

6+4

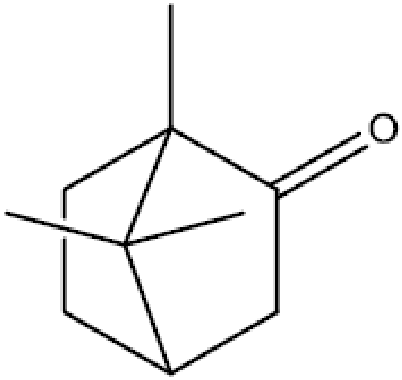


carane

6+3



Carene
6+3



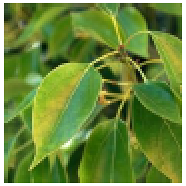
Camphor الكافور

Camphor occurs in the camphor tree of Japan . It is an optically active solid with m.p 180 ° C the(-)and (+)forms occur naturally and racemic camphor is the usual form of synthetic camphor .

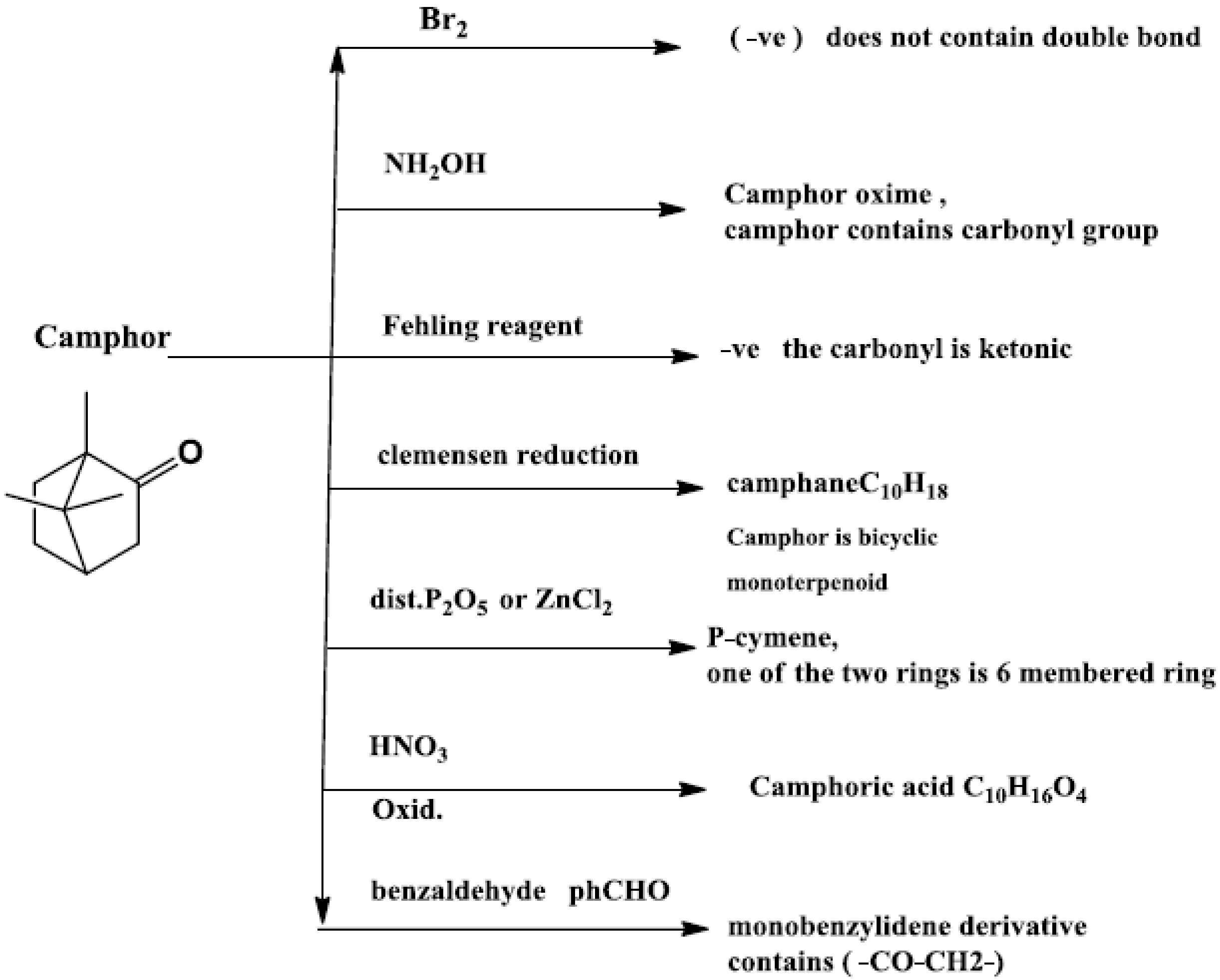
Camphor used in manufacture of cellulose as well as has many medical uses, including that it is used as a disinfectant and as a local anesthetic, and in the laboratories it is used as a solvent in experiments determining the molecular weight of organic compounds.

Structure of camphor was supported by :

1-The molecular formula of camphor is $C_{10}H_{16}O$,and the general reactions show that it is saturated .



Structure of Camphor



Camphor

Br_2 → (-ve) does not contain double bond

NH_2OH → Camphor oxime , camphor contains carbonyl group

Fehling reagent → -ve the carbonyl is ketonic

clemensen reduction → camphane$C_{10}H_{18}$

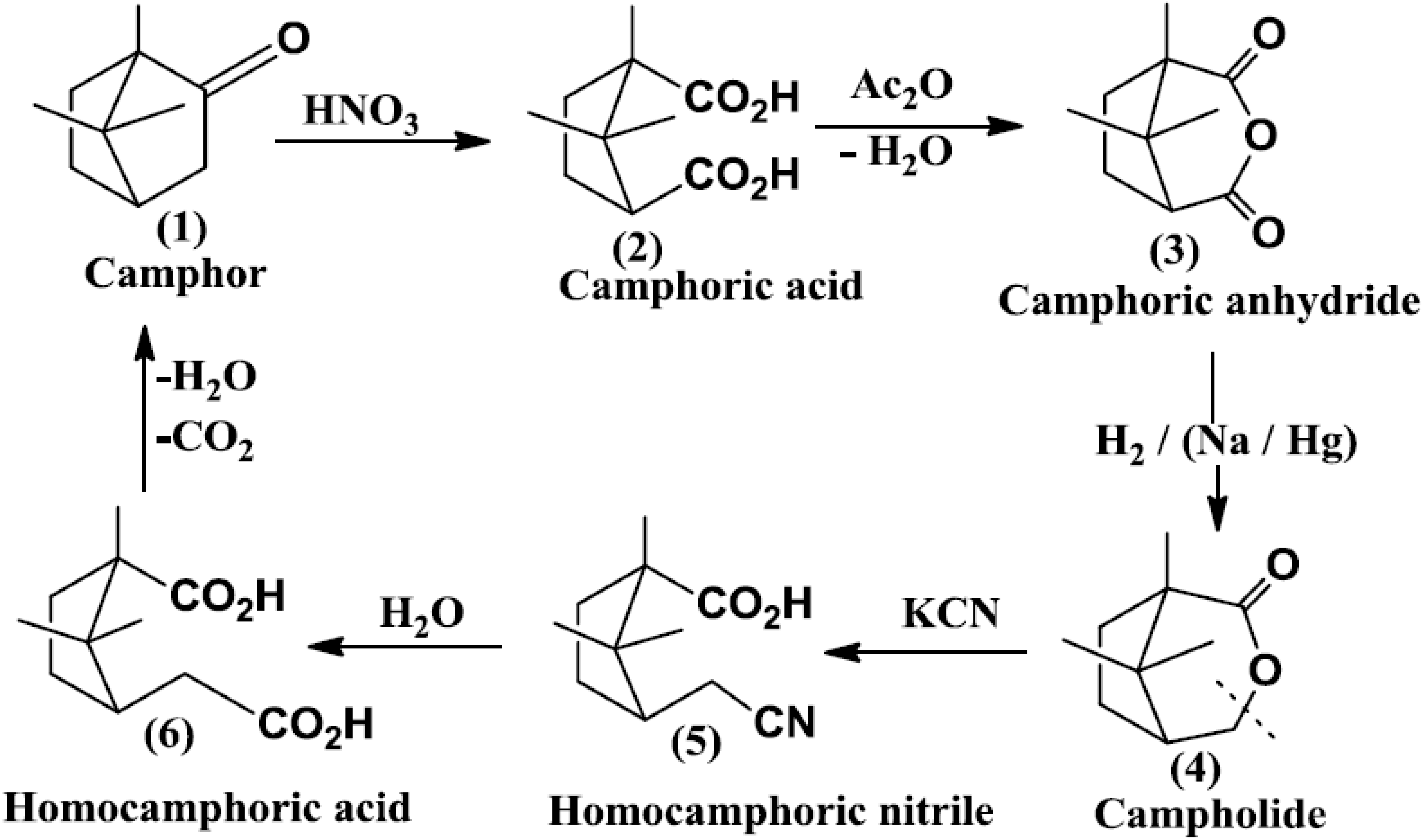
Camphor is bicyclic monoterpenoid

dist.P_2O_5 or $ZnCl_2$ → P-cymene, one of the two rings is 6 membered ring

HNO_3 Oxid. → Camphoric acid $C_{10}H_{16}O_4$

benzaldehyde phCHO → monobenzylidene derivative contains (-CO-CH2-)

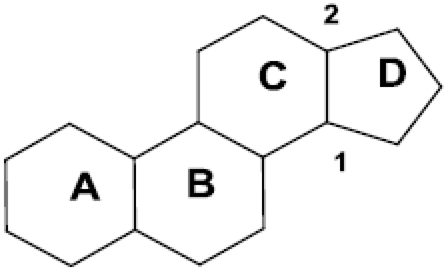
Structure of Camphor



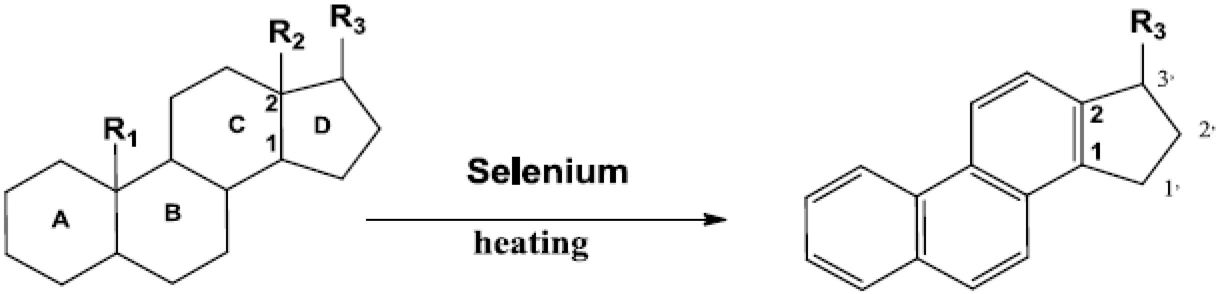
Steroids

Definition of steroids

Saturated natural products possessing the tetracyclic carbon skeleton ,ring **A,B,C** are six membered ring while ring **D** is five membered ring, the side chain R1, R2 and R3. R1 may be absent when ring **A** is aromatic ,R1 and R2 are generally methyl groups . The side chain R3 may be absent .



Perhydro-1,2-cyclopentanophenanthrene



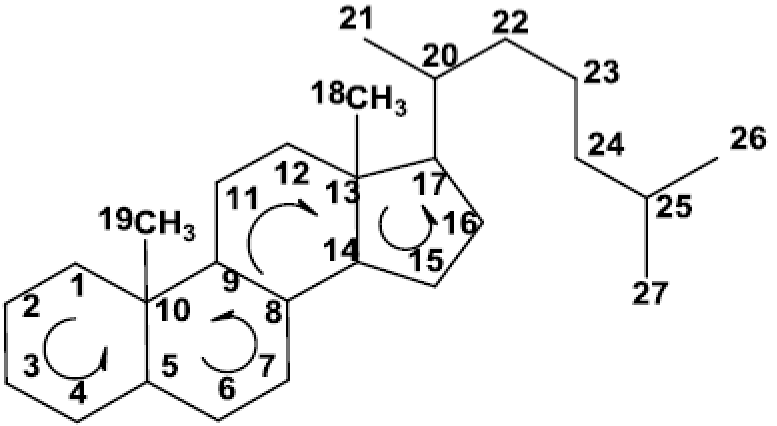
Steroid

R_3=Me (Diels hydrocarbon)
3'-methyl-1:2-cyclopentenophenanthrene
R_3 = H 1: 2-cyclopentenophenanthrene

A steroid could be defined, in another way, as any compound which gives Diel's hydrocarbon(beside other products) when distilled with selenium.

Classification of Steroids

The carbon skeleton of the hydrocarbon cholestane is given which shows the correct numbering of the system .



Cholestane

Classification of Steroids

1- Sterols (cholesterol)

2-Vitamin D(vitamin D2)

3-Bile Acids (cholic acid)

4- Steroidal Hormones or Sex Hormones(progesterone)

5- Adrenocortical hormones (cortisone)

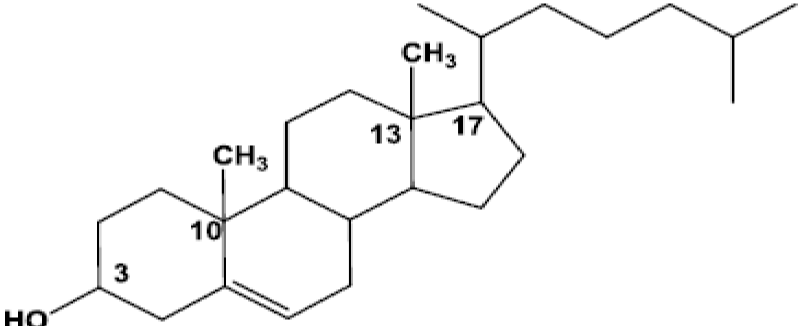
6-Cardiotonic glycosides

7- Saponins and Sapogenins

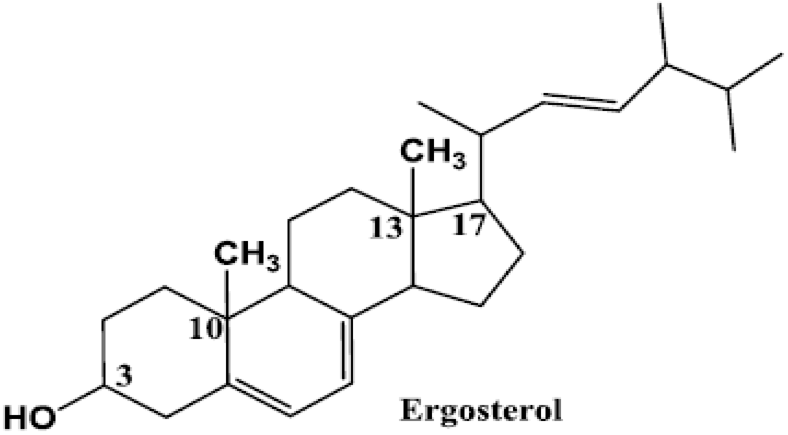
Sterols

Sterols are steroid alcohol containing an aliphatic side chain they are crystalline, widely Distributed in nature .

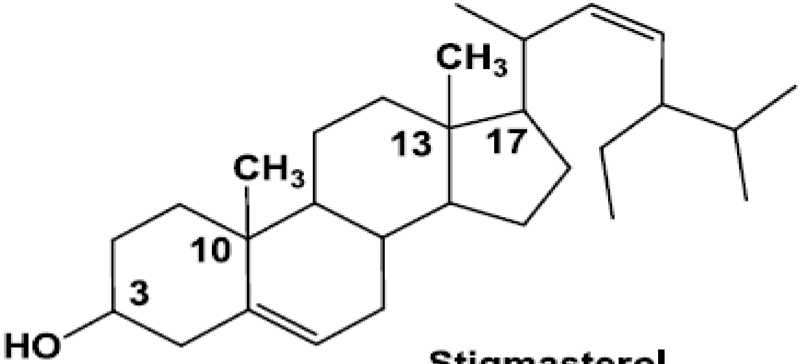
Sterols may be classified on the basis of occurrence as Zoo sterols(animal), Phytosterol (plants), mycosterol (yeast and fungi) and marine sterols(sponges).



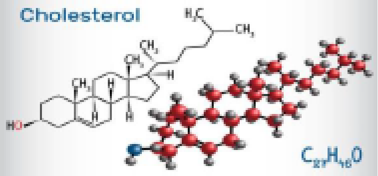
Cholesterol
Zoo sterol



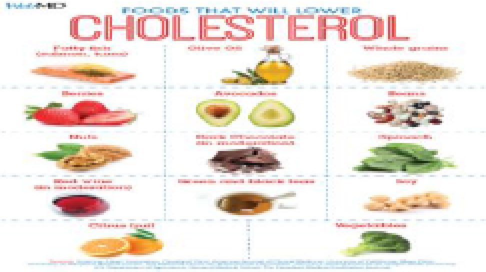
Ergosterol
mycosterol
occurs in yeast

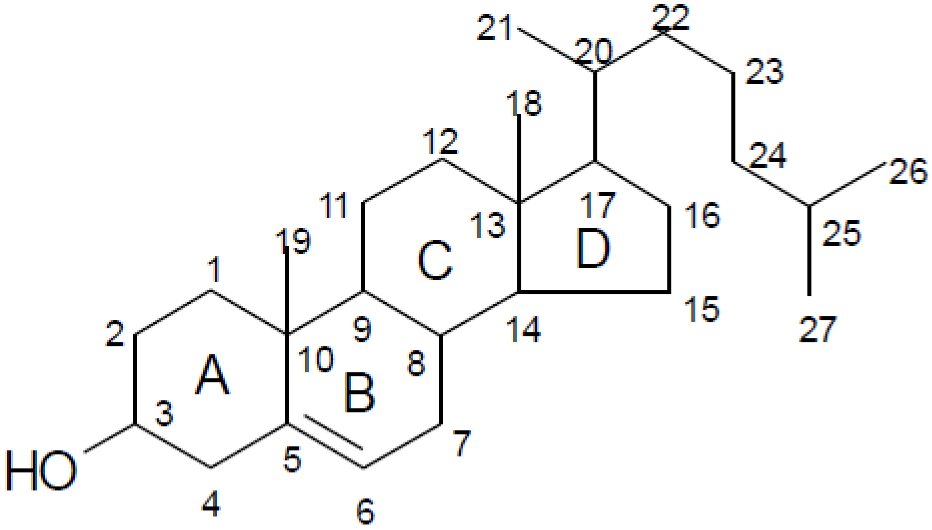


Stigmasterol
Phytosterol
obtained from soya bean oil



كوليسترول Cholesterol





characteristic features :-

1- The nucleus of cholesterol is tetracyclic composed of three six-membered rings (A, B and C) and one five-membered (D) ring.

2- There is a secondary OH group at C-3, and a double bond at C-5 (between C-5 and C-6).

3- There are two angular methyl groups at C-10 and C-13, and a saturated side-chain C_8H_{17} at C-17.

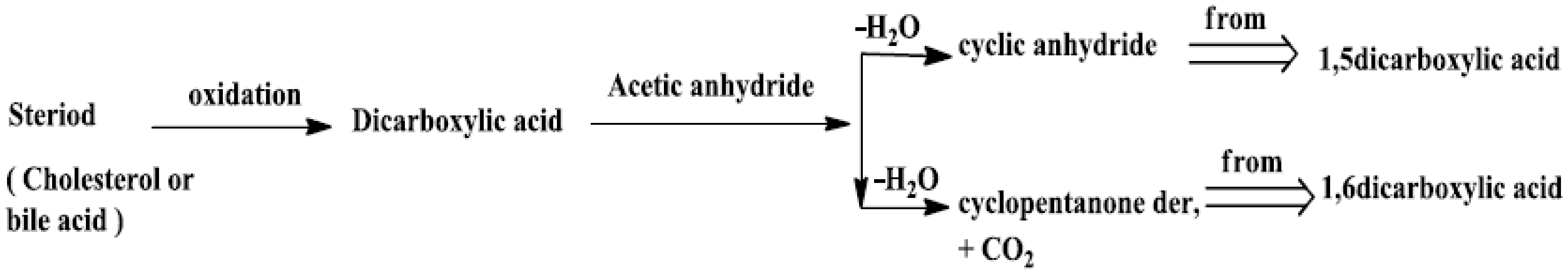
Determination of the nucleus - Blanc Rule

All the steroids possess the same tetracyclic carbon skeleton (cyclopentaneperhydrophenanthrene) ,it has been confirmed by heating steroid with selenium which gives cyclopentenophenanthrene derivative.

The rings of the steroid nucleus were opened by oxidation to give dicarboxylic acid and the relative position of the two carboxyl groups were determined by the application of

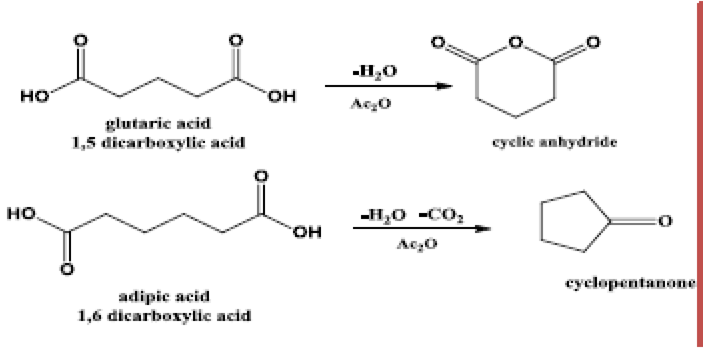
Blanc rule:

Heating with acetic anhydride,1,5-dicarboxylic acids forms cyclic anhydride and 1,6-dicarboxylic acids form cyclopentanones with elimination of carbon dioxide



Steriod (Cholesterol or bile acid) —oxidation→ Dicarboxylic acid —Acetic anhydride→

- $-H_2O$ → cyclic anhydride ⟹ from 1,5dicarboxylic acid
- $-H_2O$ → cyclopentanone der, + CO_2 ⟹ from 1,6dicarboxylic acid

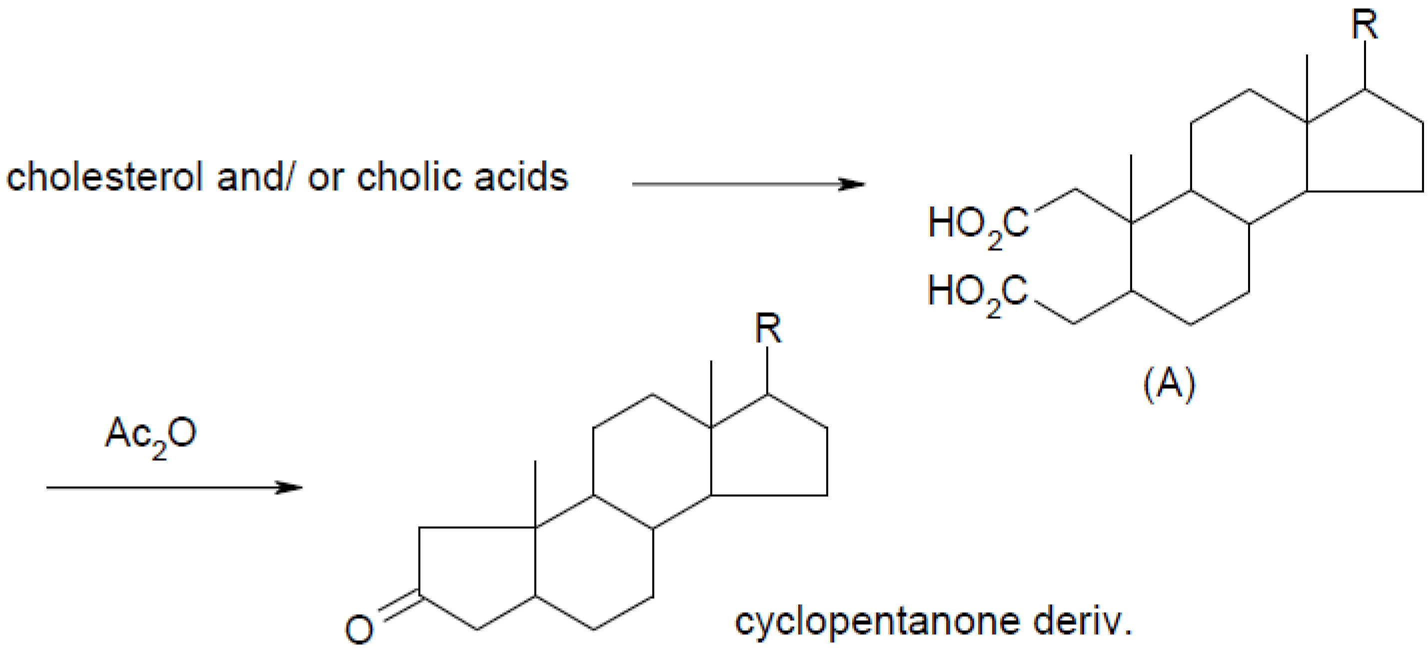


كل الستيرويدات تتكون من هيكل كربوني رباعي الحلقة (سيكلوبنتان بير هيدرو فينانترين) وهذا تم اثباته عند تسخين الستيرويد مع السيلينيوم ليعطي مشتق سيكلوبنتينوفينانترين .

ولإثبات حجم كل حلقة في الستيرويدات تجري الاكسدة للستيرويد فتفتح الحلقات لتعطي احماض ثنائية الكربوكسيل ولمعرفة طبيعة هذه الاحماض تطبق قاعدة بلانك والتي تنص علي :

عند التسخين مع اسيتيك انهيدريد الاحماض ١،٥ داي كربوكسيليك تكون انهيدريد حلقي مع فقد ماء اما الاحماض ١،٦داي كربوكسيليك فتكون سيكلوبنتانون مع فقد ثاني اكسيد الكربون بالإضافة لفقد الماء.

Determination of ring A in cholesterol and cholic acid

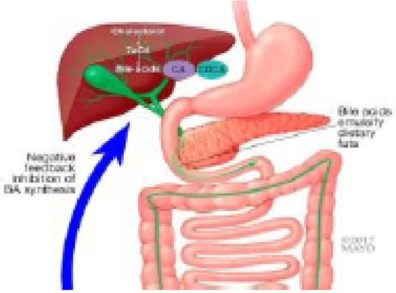


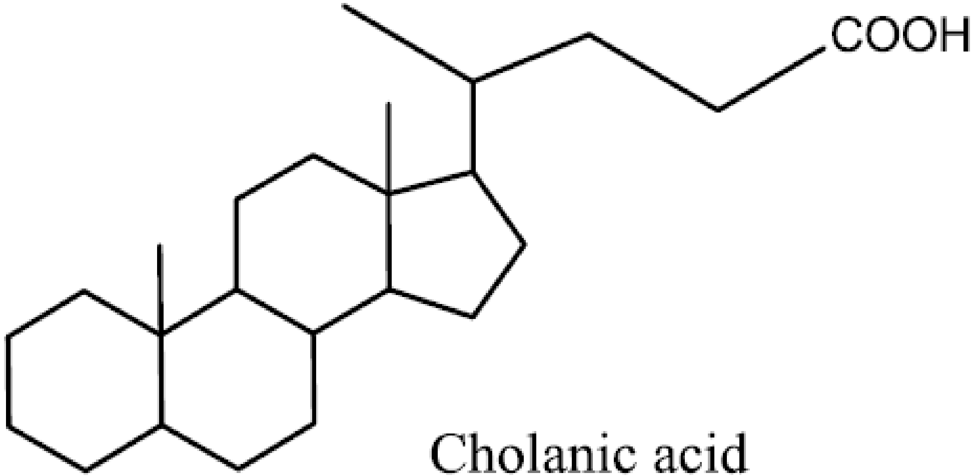
(A)

cyclopentanone deriv.

Cholesterol and cholic acid were converted into the dicarboxylic acid by oxidation which gave a cyclopentanone derivative by heating with acetic anhydride according to blanc rule and the acid 1,6 dicarboxylic acid and ring A is six membered ring (R is the appropriat side chain).

Bile acids



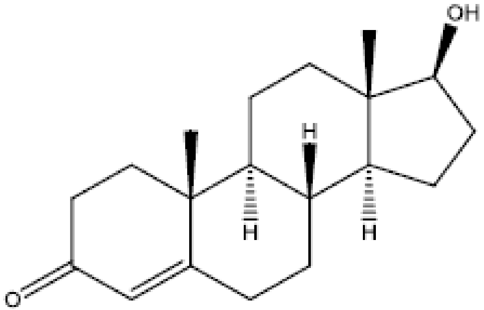


Cholanic acid

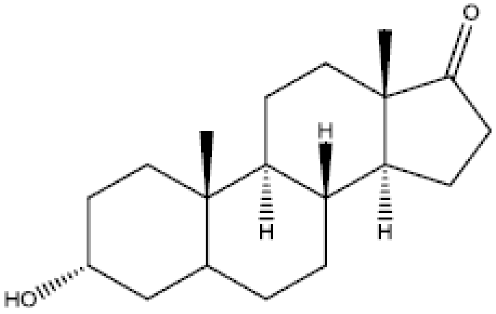
The natural bile acids are generally hydroxy derivatives of cholanic acid .They are produced in the liver either synthetically or by degradation of cholesterol and occur in bile as water soluble sodium salts of peptide conjugate with glycine or taurine.

Sex Hormones

1-Androgens (Male Hormones)(androsterone –testosterone)

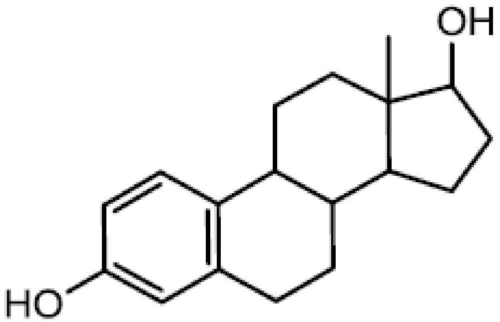


Testosterone

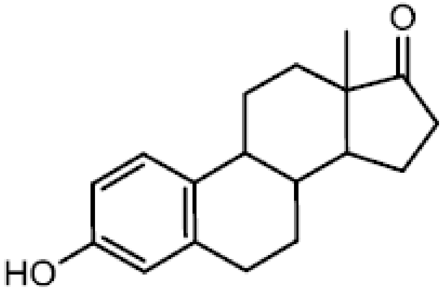


Androsterone

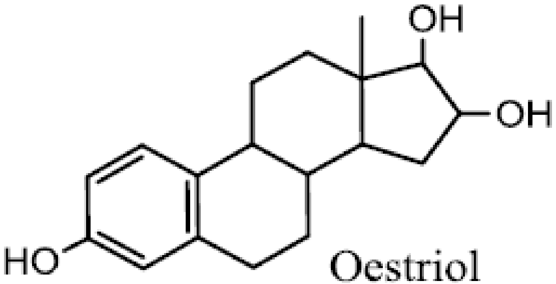
2-Oestrogens (Female Hormones)



Oestradiol



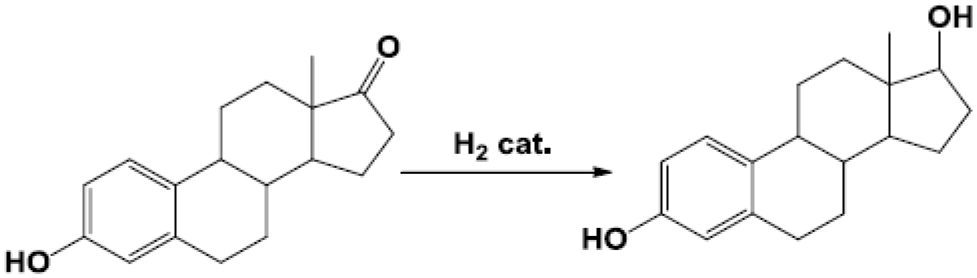
Oestrione



Oestriol

Oestrogens (Female Hormones) all of them contain phenolic hydroxyl group at C3 and may be prepared from dehydroepiandrosterone(D.E.A) which can be synthesized from cholesterol.

(Oestrogens)

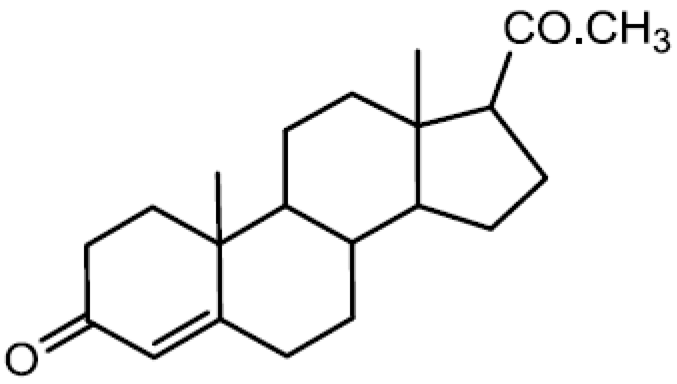


Oestrone

Oestradiol

Oestrone may be reduced to oestradiol by catalytic hydrogenation or by lithium aluminium hydride .

3- (Gestogens)
Progesterone



Progesterone

These are essential hormones which responsible for pregnancy.

Progesterone is α,β-unsaturated ketone and synthesized from both D.E.A and Ergosterol .

ALKALOIDS --- القلويـدات

Definition of alkaloids

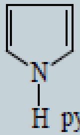
-All organic bases isolated from plants, and it covers wide variety of compounds.

-(Konigs)suggested that alkaloids should be defined as [naturally occurring organic bases which contain a pyridine ring] ,this definition include a limited number of compounds.

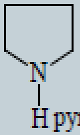
-(Ladenburg definition): natural plant compounds having a basic character and containing at least one nitrogen atom in heterocyclic ring .

Alkaloids have clear physiological effects, and are chemically related to pyrrole, pyridine, quinoline and isoquinoline, which are different heterocyclic rings, some of which are highly toxic, and some are used as medical drugs such as quinine used to treat malaria, morphine to remove pain or cocaine as a local anesthetic and atropine in surgery and ophthalmology.

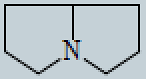
Different heterocyclic rings related to alkaloids



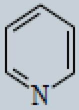
pyrrole



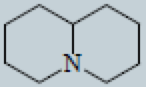
pyrrolidine



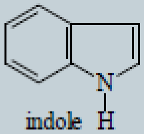
pyrrolizidine



pyridine

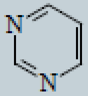


nor-hipinane

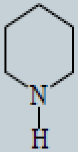


indole
(benzopyrrole)

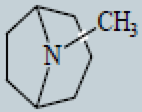
imidazole



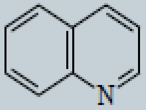
pyrimidine



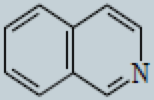
piperidine



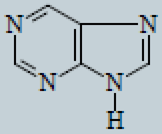
tropane
(piperidine-pyrrolidine)



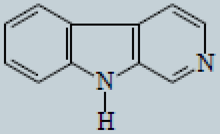
quinoline



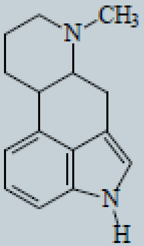
isoquinoline



purine



carboline



indole + hydroquinoline

Extraction of alkaloids استخلاص القلويدات

- Alkaloids are generally found in plants in the form of salts combined with some organic acids such as malic or citric acid .
- .Alkaloids are found mainly in fruits and seeds, as well as in tree bark.
- We extract the alkaloids from the plants by carefully cutting the plants, then adding a solution of hydrochloric or sulfuric acid to form their corresponding mineral salts.
- In this process, the alkaloids (bases) are liberated from the organic acids, and then the alkaloids are dissolved in the form of solutions of salts of hydrochloric or sulfuric acid with sugars and some other compounds found in the tissues of plants.
- As the alkaloids do not dissolve in water, they can be precipitated from chloride or sulfuric salts by adding bases such as sodium or potassium hydroxide.
- In the case of volatile alkaloids such as nicotine, the salt solution or the raw material is treated with the addition of alkali (sodium hydroxide) and treated by steam distillation, then the alkaloids are extracted by organic solvents such as, chloroform or other organic solvents.
- The mixture of alkaloids is separated by various methods into pure substances .

General Properties الخواص العامـــة

. Alkaloids are colorless, in crystalline form, and do not dissolve in water, but dissolve in organic solvents, such as, chloroform, ethyl alcohol ... etc.

But there are liquid alkaloids that can be mixed with water, such as coniine and nicotine, and some have a yellow color like piperine.

Most alkaloids have a bitter taste and optically active .

It generally contains one or two nitrogen atoms in a tertiary state in a ring.

Most alkaloids also contain an oxygen.

الطرق العامة لتعيين تركيب القلويدات

Structure –elucidation of alkaloids

1-The first step in determining the structure of a pure alkaloid consists in ascertaining its molecular formula and optical rotatory power.

2- Functional nature of oxygen

The oxygen atom may be present in the form of alcoholic or phenolic hydroxyl (-OH), methoxyl (-OCH_3), acetoxyl $OCOCH_3$), benzoxyl (- COC_6H_5), carboxyl (-COOH) or carbonyl (C=O) group, various oxygen functional groups can be characterized according to the following characteristics

Classification of alkaloids

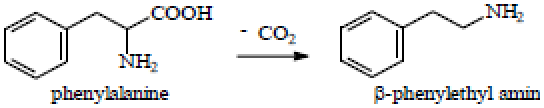
Phenylethyl amine alkaloids

Classification of alkaloids

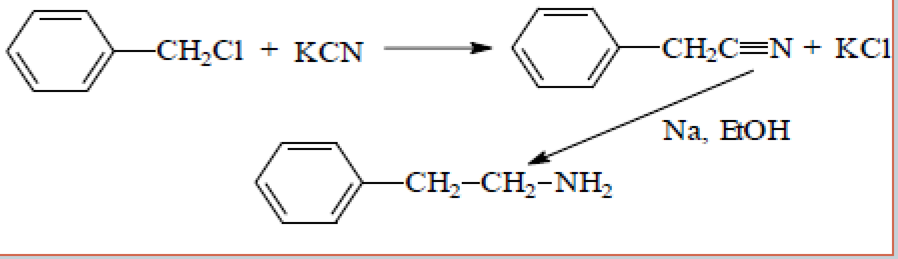
(1) Phenylethyl amine alkaloids
(2) Pyrrolidine alkaloids
(3) Pyridine or piperidine alkaloids
(4) Pyridine-pyrrolidine alkaloids
(5) Tropane alkaloids
(6) Quinoline alkaloids
(7) Isoquinoline alkaloids
(8) Phenanthrene alkaloids
(9) Indole alkaloids

Phenyl ethyl amine group

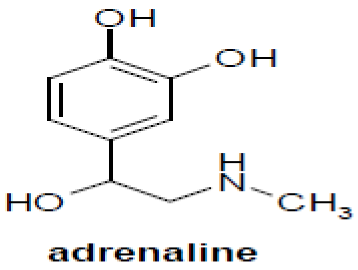
Many compounds of this group are known some natural and other synthetic .The physiological action is to increase the blood pressure .They are referred to as the blood - pressure drugs.



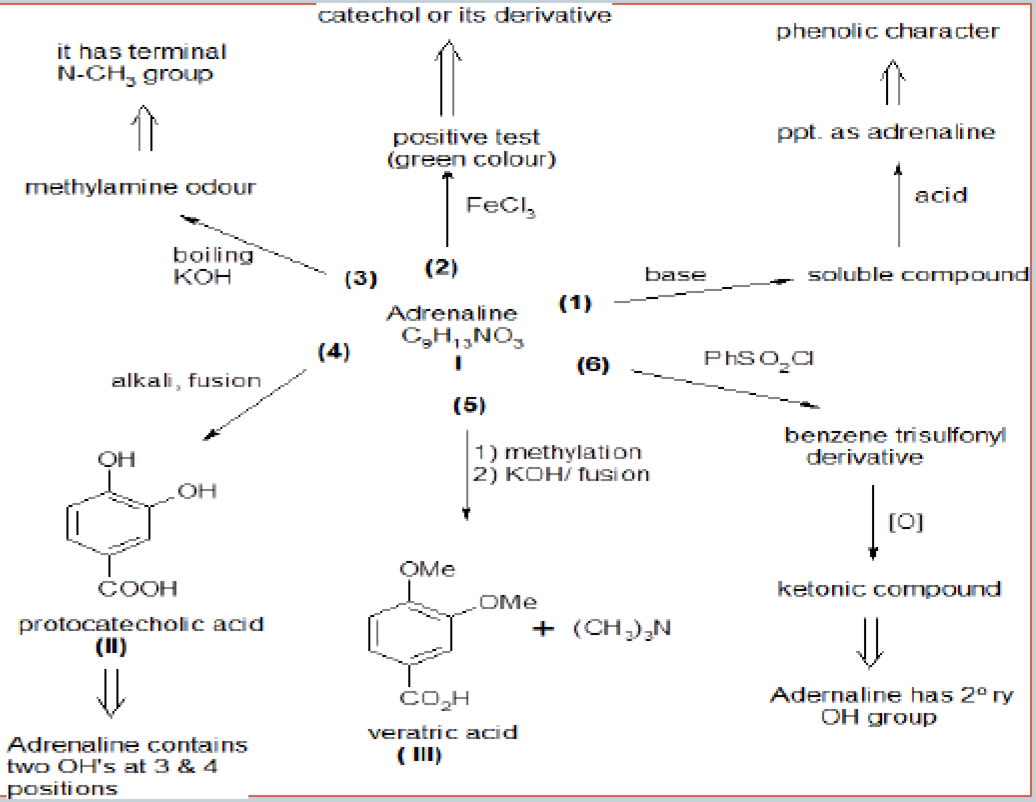
Synthesis of Beta phenyl ethyl amine



($C_9H_{13}NO_3$) Adrenaline الأدرينالين



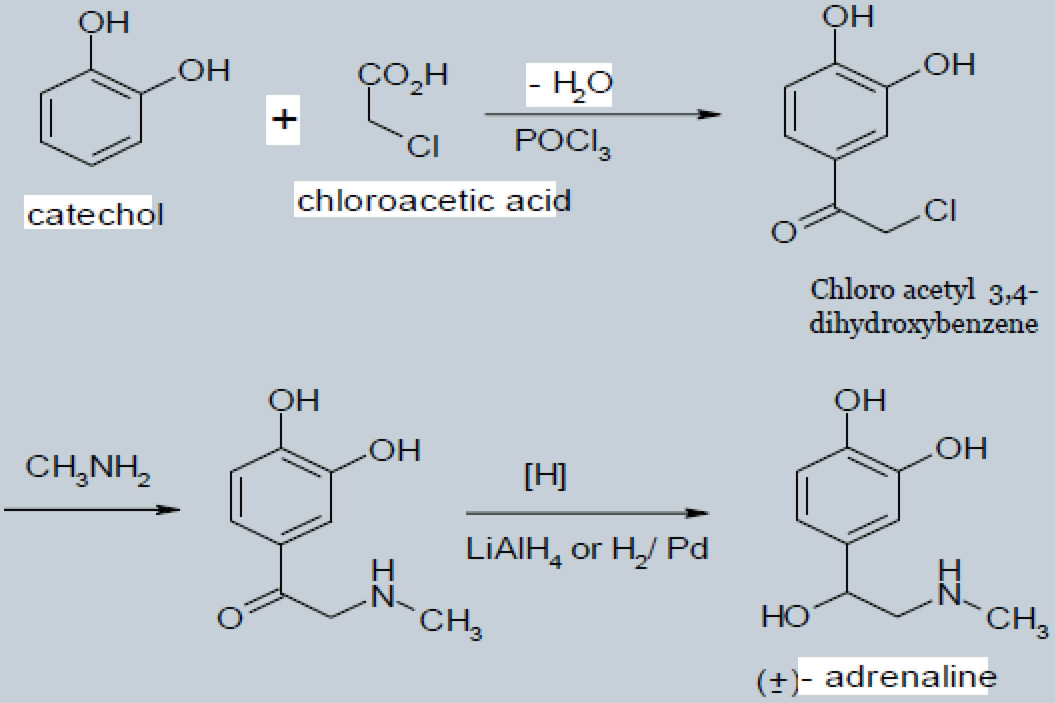
adrenaline
I



It is a non-steroid hormone. Adrenaline was the first hormone to be isolated in a crystalline form ,adrenaline is active only when given by injection , it raises blood pressure ,is used locally to stop hemorrhage.

الأدرينالين ($C_9H_{13}NO_3$)

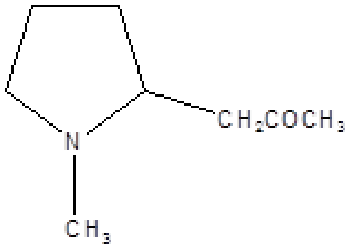
Synthesis of adrenaline

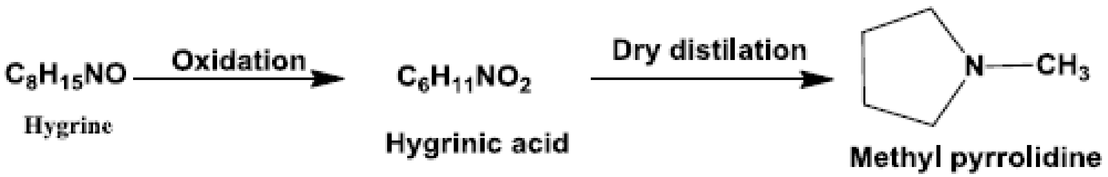


(Pyrrolidine group) قلويدات مجموعة البيروليدين
(Hygrine) الهيجرين $C_8H_{15}NO$

Confirmation of the structure

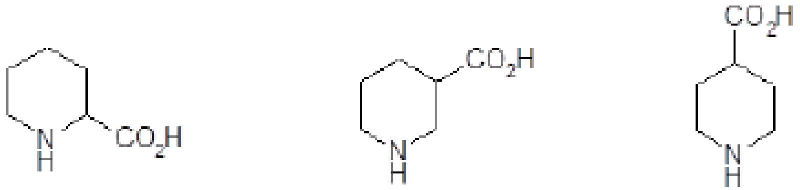
اثبات الشكل التركيبي للهيجرين :



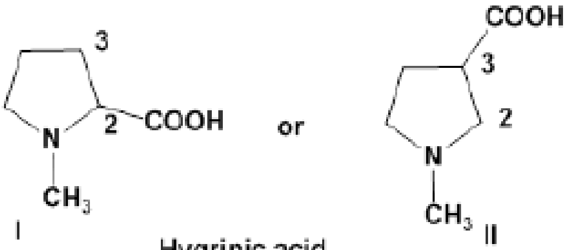


On oxidation of Hygrine ,Hygrinic acid is formed . Hygrinic acid was first believed to be a one from piperidine carboxylic acids but comparison with the three acids show ed this was incorrect.

اكسدة الهيجرين كونت حمض الهيجرينيك الذي كان يعتقد انه حمض من احماض البيريدين الكربوكسيلية الثلاثة و المقارنة اثبتت عدم صحة هذا الافتراض .



piperidine carboxylic acids

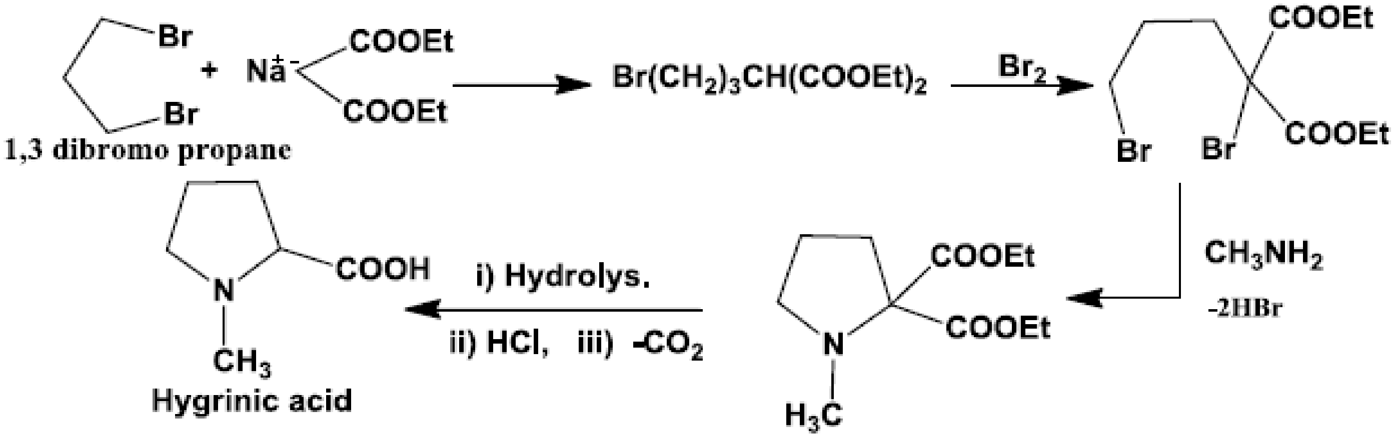


Hygrinic acid

(Hygrine) الهيجرين

تحضير حمض الهيجرينيك

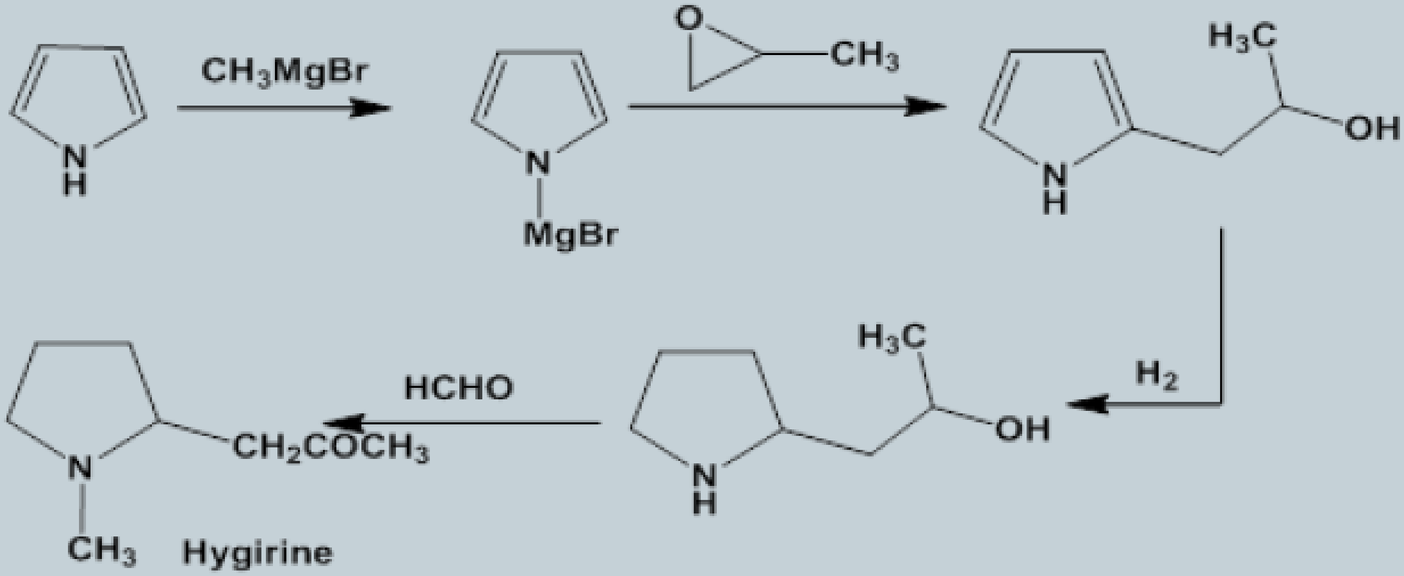
Synthesis of Hygrinic acid(N-methylpyrrolidine carboxylic acid)



Synthesis of Hygrine تحضير الهيجرين

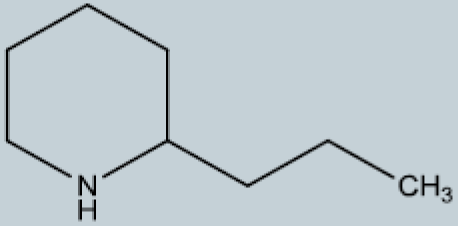
Synthesis of Hygrine

تحضير الهيجرين



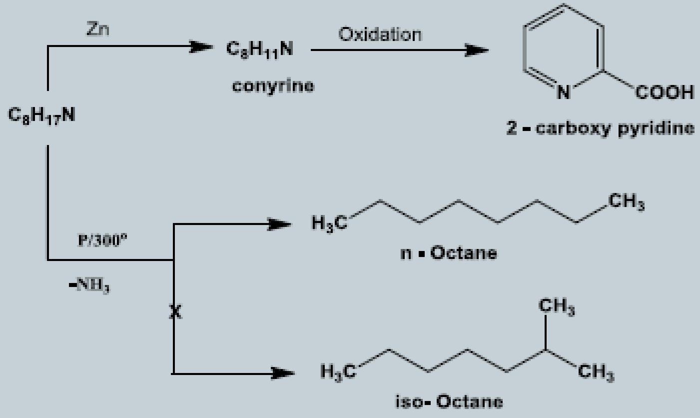
قلويدات مجموعة البيريدين

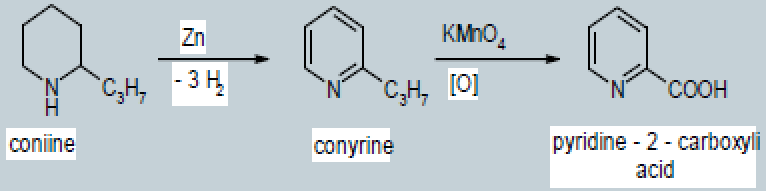
Pyridine alkaloids Coniine $C_8H_{17}N$ الكونيين

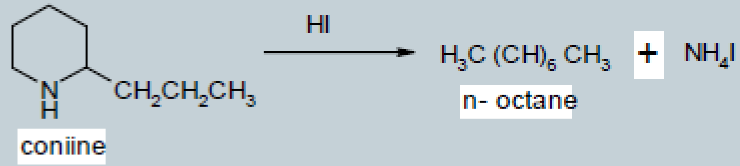


Confirmation of the structure اثبات الشكل التركيبي للكونيين

1-M.F $C_8H_{17}N$
2-Dry dist. with zinc dust coniine is converted into conyrine
3- Pyridine 2-carboxylic acid (α-picolinic acid)was obtained via oxidation of conyrine
4- Coniine is may be piperidine with side chain with three carbon atom
5- the side chain either n-propyl or iso propyl ,it may be n-produces n- propyl (heating coniine with hydroiodic acid octane not iso –octane,so Coniine is 2-n-propylpiperidine which confirmed by synthesis .



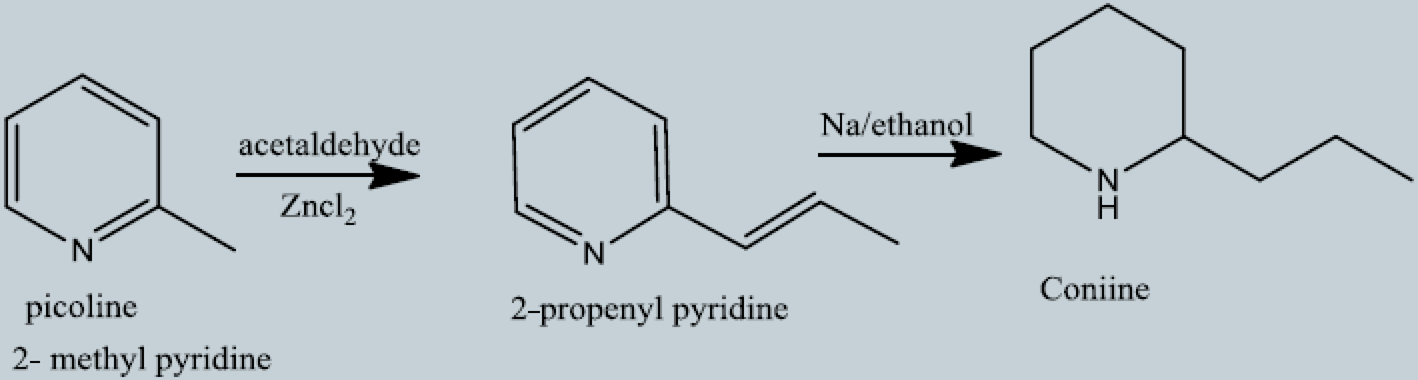




Coniine $C_8H_{17}N$

Synthesis of Coniine

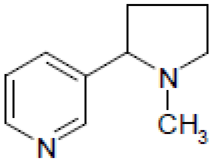
تحضير كونيين



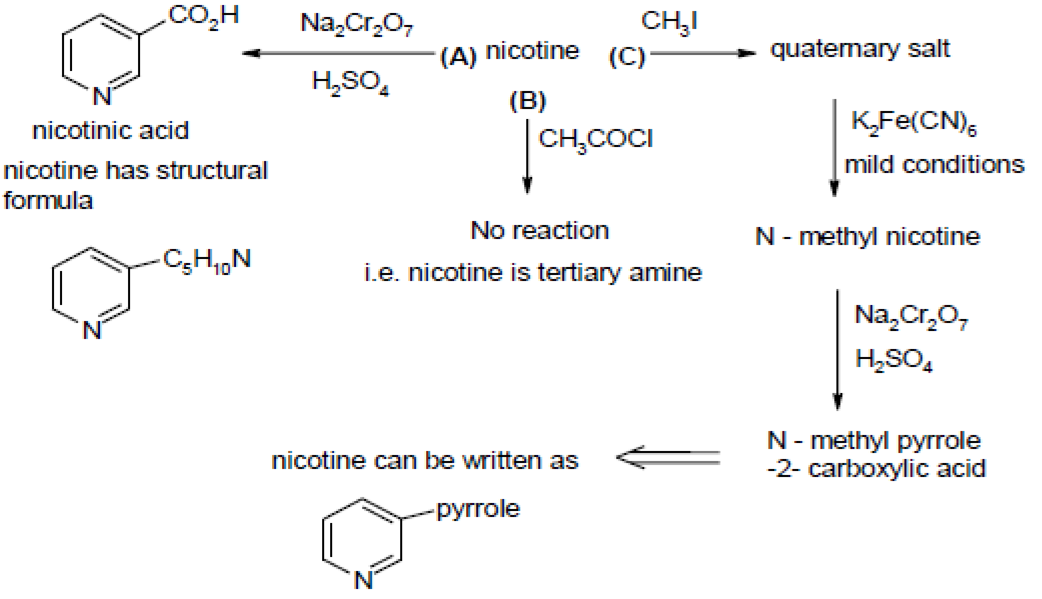
(Pyrrolidine-pyridine group) قلويدات مجموعة البيروليدين بيريدين
Nicotine($C_{10}H_{14}N_2$) النيكوتـين

Confirmation of the structure

اثبات الشكل التركيبي للنيكوتين :



nicotine



nicotinic acid

nicotine has structural formula

No reaction

i.e. nicotine is tertiary amine

N - methyl nicotine

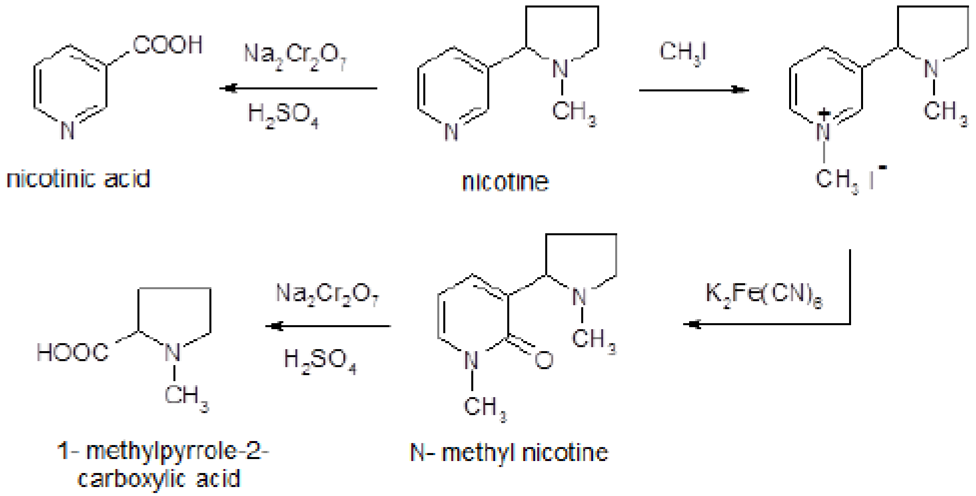
N - methyl pyrrole -2- carboxylic acid

nicotine can be written as

Nicotine $(C_{10}H_{14}N_2)$ النيكوتيــن

Confirmation of the structure

اثبات الشكل التركيبي للنيكوتين



Synthesis of Nicotine تحضير النيكوتين

Synthesis of Nicotine ***Spath and Bretsvchneider***
تحضير االنيكوتين طريقة سباث و برتشنيدر