كيمياء عضوية (IV) (١ ٤ ٤ ك)

Natural Products النواتج الطبيـــعية

4th Year Students Faculty of Science
(Chemistry group)

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قسم الكيمياء – كلية العلوم

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Alkaloids	Definition of alkaloids -Extraction of alkaloids -General Properties
	Structure –elucidation of alkaloids *Classification of alkaloids (Phenyl ethyl amine –Pyrrolidine – pyridine –(pyridine, pyrrolidine group) –quinoline –isoquinoline-* Tropine alkaloids Phenanthrene Group)
Terpenoids	Definition –Extraction -*Structure elucidation -Classification –monoterpenoids* – Cyclic Monoterpenoids(Limonene-Menthol-Camphor)-Sesquiterpenoids-Diterpenoids-Triterpenoid-tetraterpenoids –Polyterpenoids (rubber)
Steroids	Definition of steroids Classification Determination of ring A in cholesterol and cholic acid Determination of the nucleus - Blanc Rule 1-Sterols (cholesterol **)** 2-Vitamin D(vitamin D2) 3-Bile Acids (cholic acid) 4- Steroidal Hormones or Sex Hormones(progesterone) 5- Adrenocortical hormones (cortisone)

تعريف النواتج الطبيعية –التقسيم
Definition of Natural Product -Classification

Natural products are organic compounds produced by living organisms, such as human organs, plants, animal organs, sea organisms and micro-organisms, as a result of the metabolism.

According to their physiological influence and according to their structural composition, and they are studied in groups as follows:

1. القلويدات (اشباه القلويات)Alkaloids
2. التربينات Terpenes
3. الاستيرويدات Steroids
4. الفلافونويدات والانثوسيانينات Flavonoids and anthocyanins
5. الكومارينات Coumarins
6. الفينانثرينات Phenanthrens
7. المضادات الحيوية Antibiotics
8. الفيتامينات Vitamins

And there are some interactions, for example, vitamin A, which is classified as diterpens . As for the modern classification, it is as follows It is classified into a smaller number of sects, namely :

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

ALKALOIDS --- القلويـدات

Definition of alkaloids

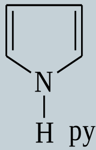
-All organic bases isolated from plants, and it covers wide variety of compounds.

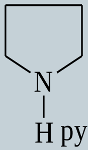
-(Konigs)suggested that alkaloids should be defined as [naturally occurring organic bases which contain a pyridine ring] ,this definition include a limited number of compounds.

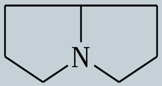
-(Ladenburg definition): natural plant compounds having a basic character and containing at least one nitrogen atom in heterocyclic ring .

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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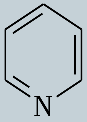
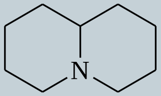
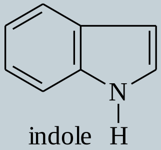
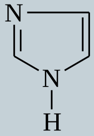
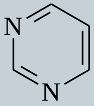
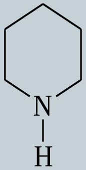

pyridine

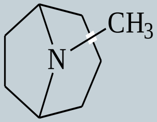

nor-hipinane

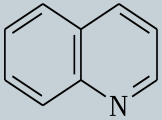

indole
(benzopyrrole)

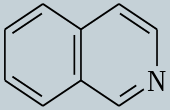

imidazole

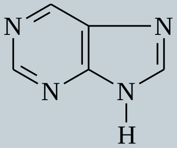

pyrimidine

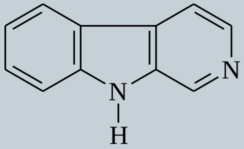

piperidine

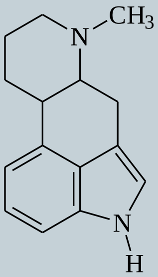

tropane
(piperidine-pyrrolidine)


quinoline


isoquinoline


purine


carboline


indole + hydroquinolin

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

Functional nature of oxygen طبيعة ذرة الأكسجين

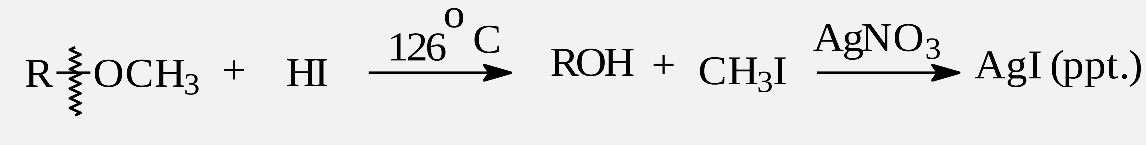
(A) Phenolic hydroxyl group (=C-OH) : The phenolic hydroxyl group is characterized by alkali solubility followed by reprecipitation by carbon dioxide, a colour reaction with ferric chloride, acylation to an ester and alkylation to an ether. The number of phenolic hydroxyl groups is estimated by acetylation.

(B) Alcoholic hydroxyl group (-C-OH) : The alcoholic hydroxyl group is generally indicated by its acylation reaction along with the negative tests for phenolic group. It is further confirmed by characteristics like dehydration, oxidation, and absorption spectrum in the infrared. The three possible alcoholic groups are usually differentiated by their oxidation reactions.

(C) Carboxyl group (-COOH) : The carboxyl group is indicated by its solubility in weak bases, like $NaHCO_3$, NH_3, *etc.*, esterification with alcohols, and specific absorption in the infrared. The groups are generally estimated quantitatively either by acid-alkali titration or by silver salt method.

Functional nature of oxygen

(D) Alkoxyl group (-OR) : The alkoxyl groups, generally methoxy ($-OCH_3$) and sometimes ethoxy ($-OC_2H_5$) occur frequently in the alkaloids. It is detected as well as estimated by Zeisel method which involves boiling of the alkaloid with concentrated hydroiodic acid at its boiling point (126°C) when the alkoxy groups are converted into alkyl halides which can be easily estimated as silver iodide by treatment with ethanolic silver nitrate.



$$R{-}OCH_3 + HI \xrightarrow{126\,^{o}C} ROH + CH_3I \xrightarrow{AgNO_3} AgI\ (ppt.)$$

The number of moles of silver iodide is equivalent to the number of alkoxyl groups in the alkaloid.

(E) The related group, **methylene dioxy ($-O-CH_2-O-$)** is estimated on the basis that it liberates formaldehyde when treated with hydrochloric or sulphuric acid; thus the quantitative estimation of formaldehyde will give the number of methylene dioxy groups.

F)**Oxo group** the presence of an oxo group is readily determined by formation of an oxime ,semi carbazone and phenylhydrazone .

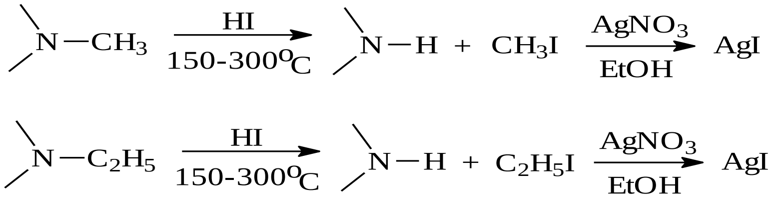
Alkaloids

Determination of the structure - The nature of N

a)The general reaction of alkaloid with acetic anhydride,methyl iodide and nitrous acid show the nature of the nitrogen

b)Distillation with aqu.pot.hydroxide gives information about the nature and number of alkyl groups attached to nitrogen

c) The N-alkyl groups are frequently estimated by Herzig Meyer method



d)Hydrolysis show the presence of an amide ,lactam ---in the alkaloid structure .

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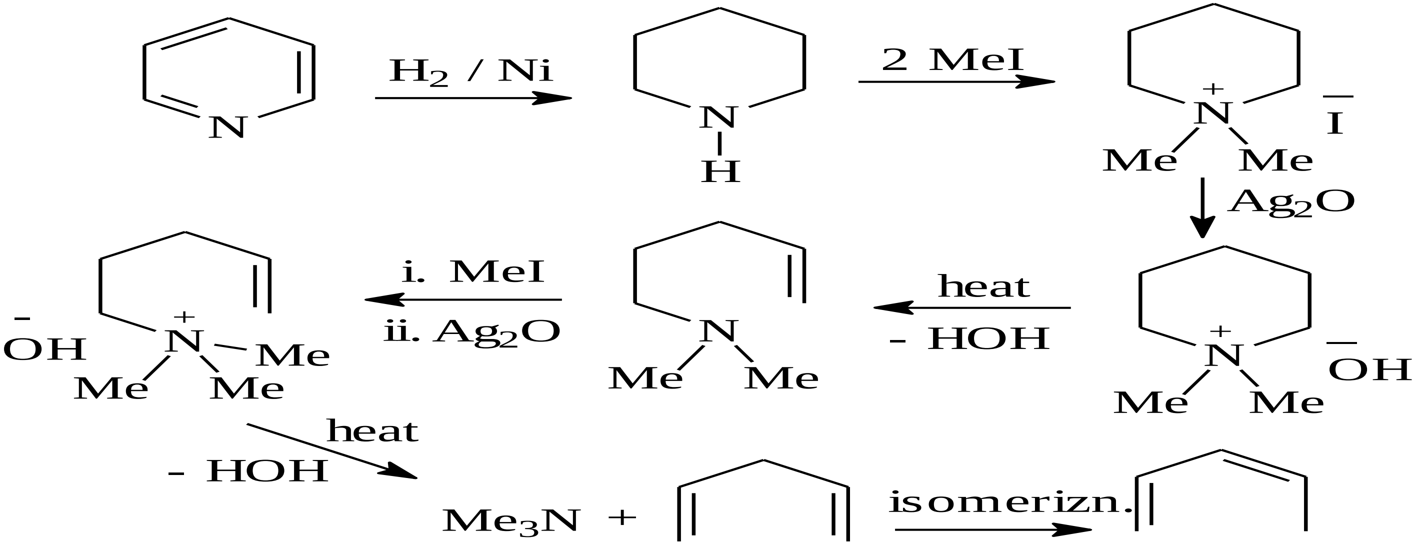
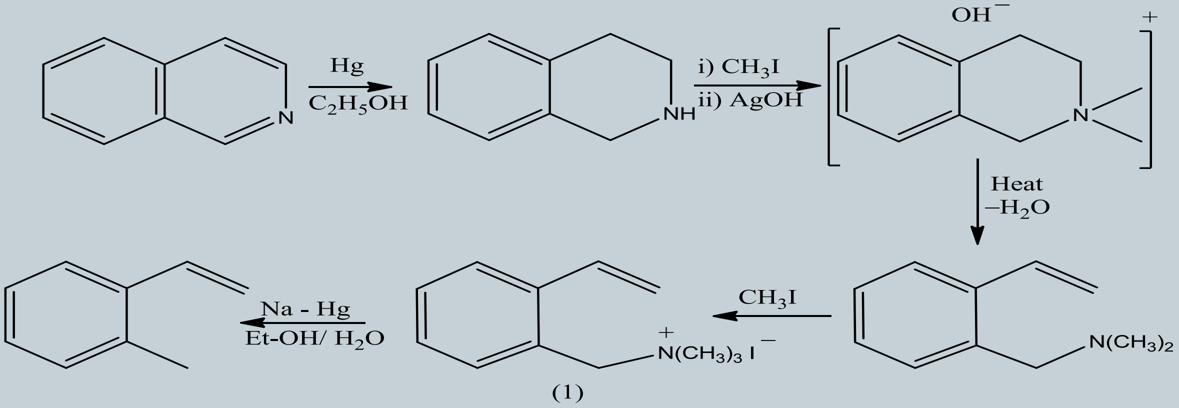
Determination of the structure
Functional nature of nitrogen

e)Hofmann exhaustive methylation **:**

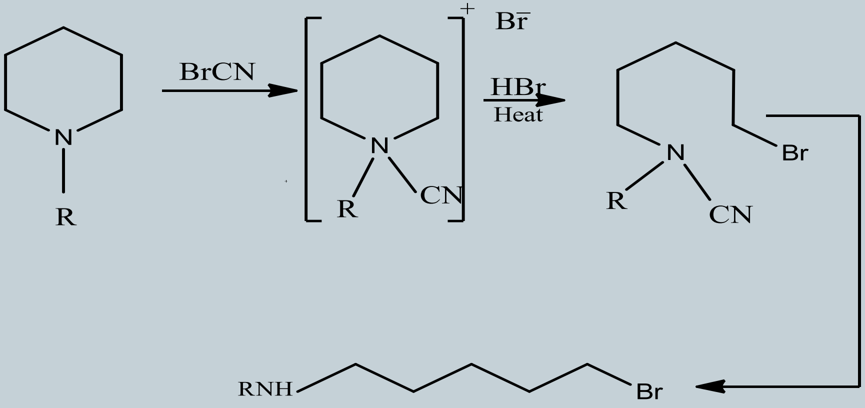


Functional nature of nitrogen

Emid modification

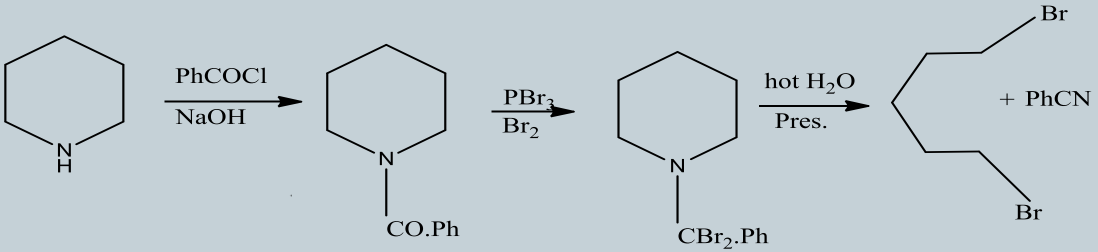


Von Braun methods for tertiary cyclic amines

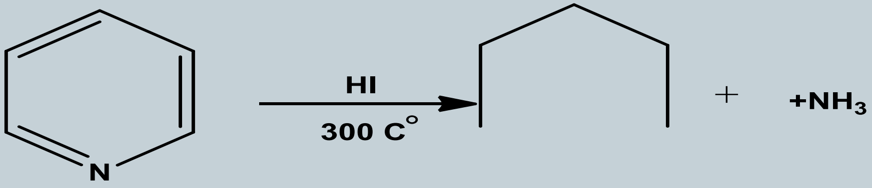


Functional nature of nitrogen

Von Braun methods for secondary cyclic amines



By using hydro iodic acid



Determination of the structure

4-Detection of the unsaturation : by addition of bromine and halogen acids or by reduction by means of sodium amalgam ,sodium and ethanol and hydrochloric acid etc----- .

5- Oxidation:
a)Mild oxidation (hydrogen peroxide-ozone- iodine in ethanolic solution ---)
b)Moderate oxidation (acid or alkaline pot.permenganate-chromium trioxide in acetic acid--) c)Vigorous oxidation (pot.dichromate in sulphuric acid–conc.nitric acid -chromium trioxide in sulphuric acid ---)
6- Alkali fusion: fusion with solid potassium hydroxide and investigation of the products .
7-Distillation with Zinc dust and investigation of the products .
8-Physical methods : (IR –NMR-MS-UV- X ray)
9- Synthesis :
Finally, the structure proposed by degradative methods is confirmed by the synthesis.

Classification of alkaloids

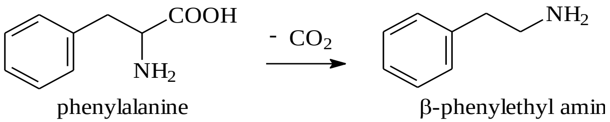
Phenylethyl amine alkaloids

Classification of alkaloids

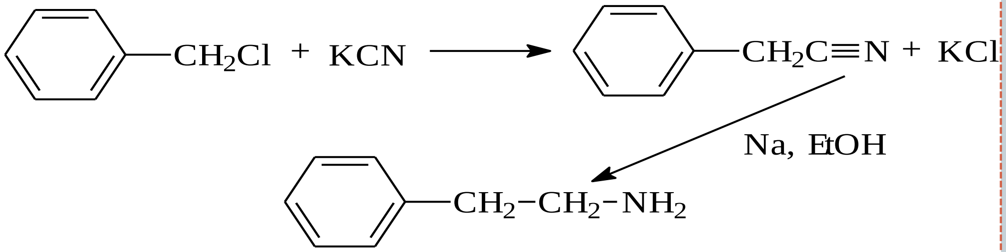
(1) Phenylethyl amine alkaloids
(2) Pyrrolidine alkaloids
(3) Pyridine or piperidine alkaloids
(4) Pyridine-pyrrolidine alkaloids
(5) Tropane alkaloids
(6) Quinoline alkaloids
(7) Isoquinoline alkaloids
(8) Phenanthrene alkaloids
(9) Indole alkaloids

Phenyl ethyl amine group

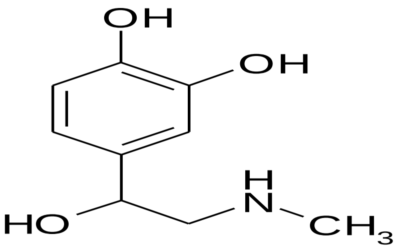
Many compounds of this group are known some natural and other synthetic .The physiological action is to increase the blood pressure .They are referred to as the blood - pressure drugs.



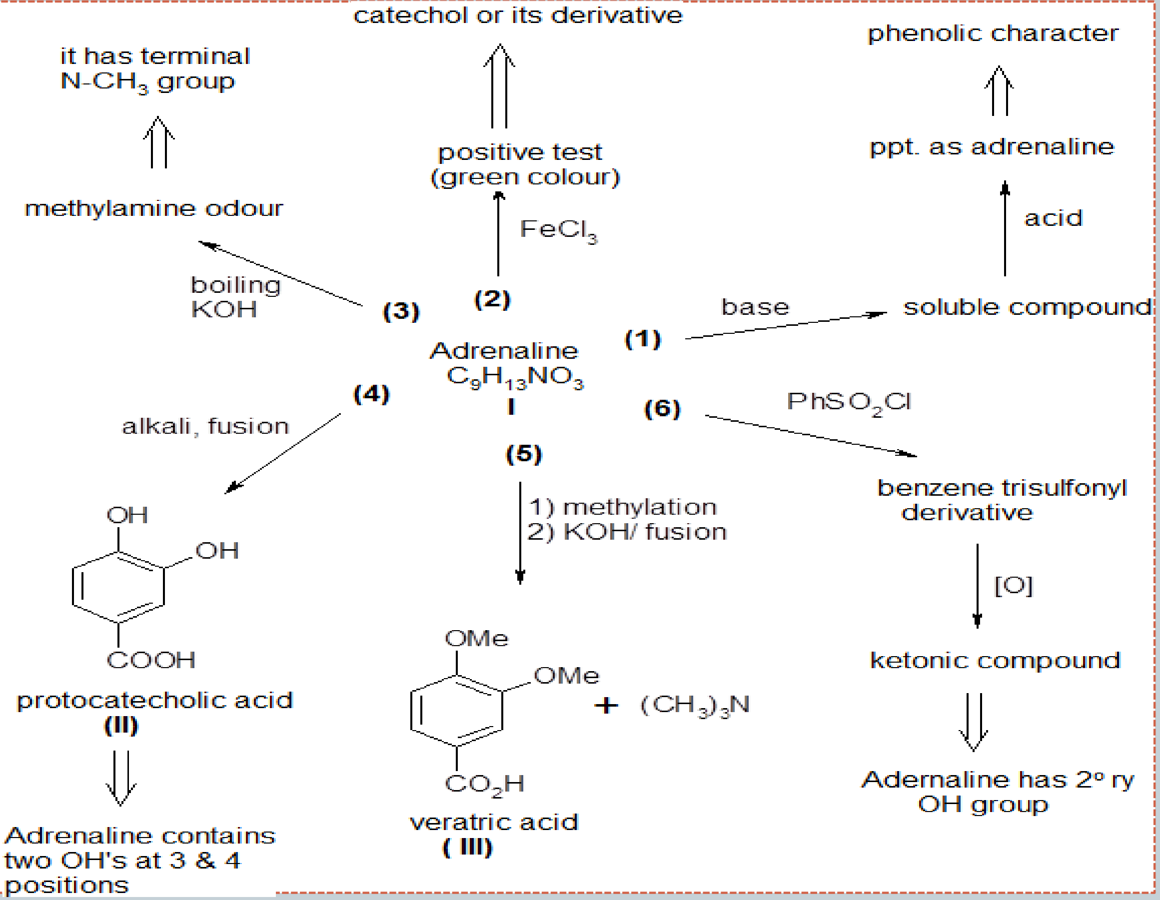
Synthesis of Beta phenyl ethyl amine



($C_9H_{13}NO_3$) Adrenaline الأدرينالين



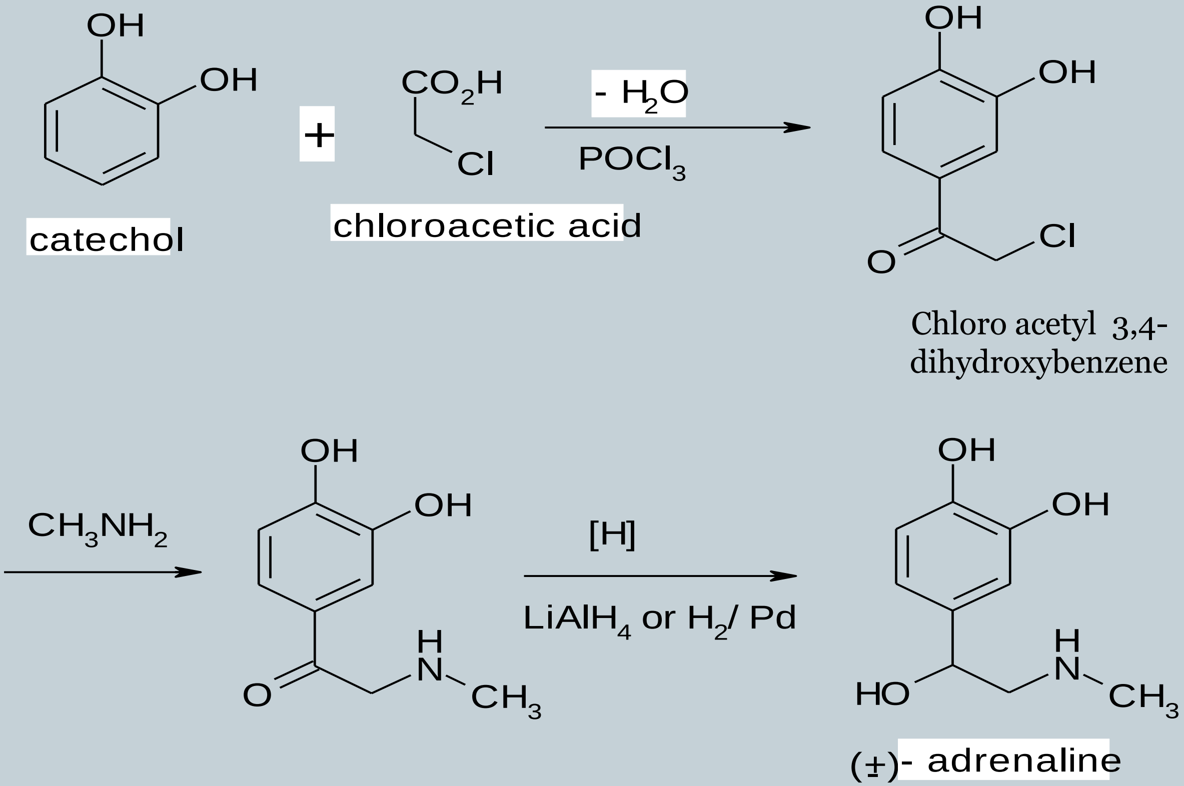
adrenaline
I



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.

($C_9H_{13}NO_3$) الأدرينالين

Synthesis of adrenaline



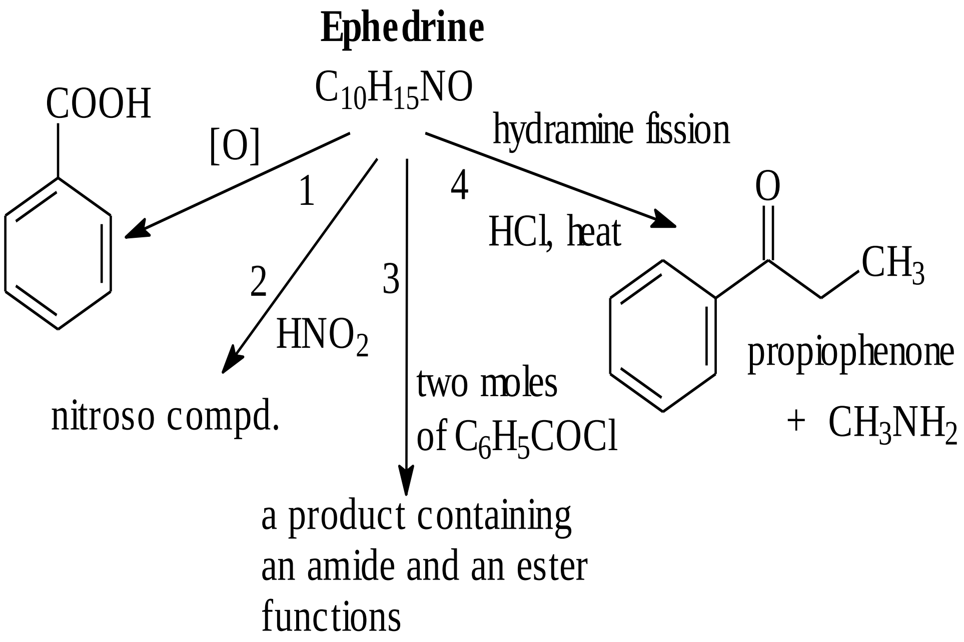
catechol

chloroacetic acid

Chloro acetyl 3,4-dihydroxybenzene

(±)- adrenaline

Ephedrine



Ephedrine

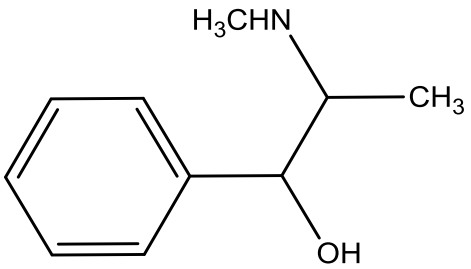
$C_{10}H_{15}NO$

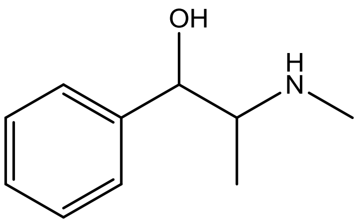
1 [O] → COOH

2 HNO_2 → nitroso compd.

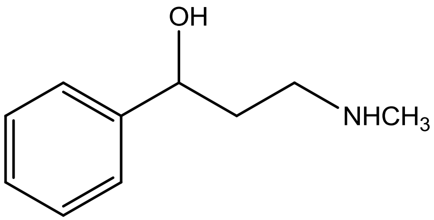
3 two moles of C_6H_5COCl → a product containing an amide and an ester functions

4 hydramine fission, HCl, heat → propiophenone + CH_3NH_2





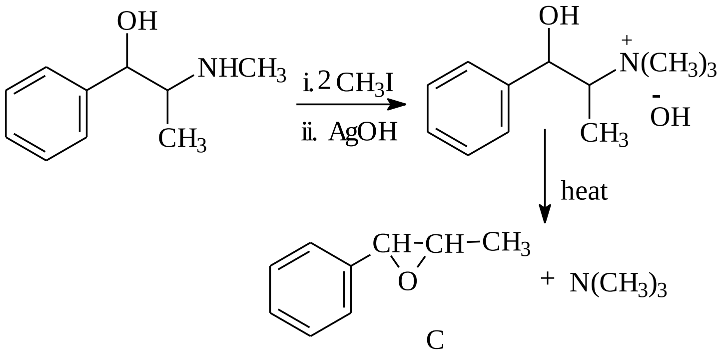
ephedrine 1



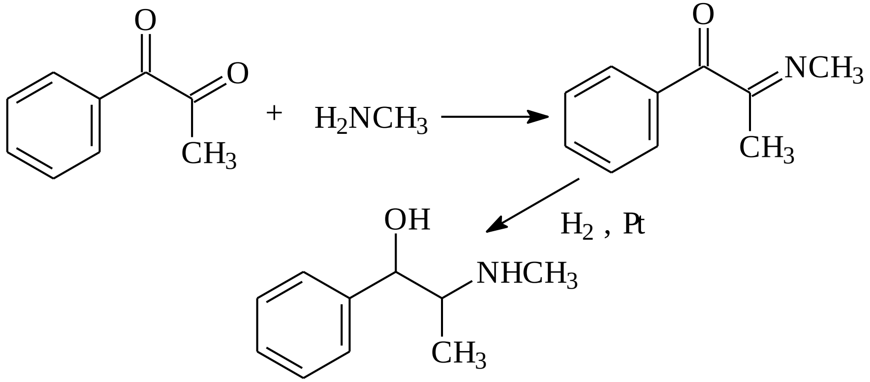
ephedrine 2

Ephedrine

Hofmann exhaustive methylation **:**



Synthesis of ephedrine

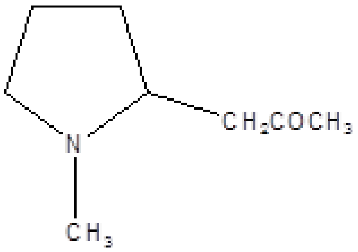


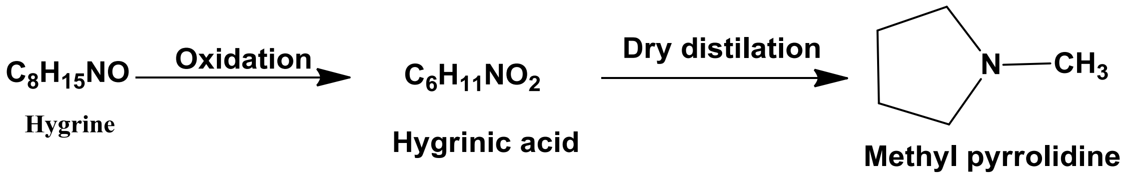
(Pyrrolidine group) قلويدات مجموعة البيروليدين

(Hygrine) الهيجرين $C_8H_{15}NO$

Confirmation of the structure

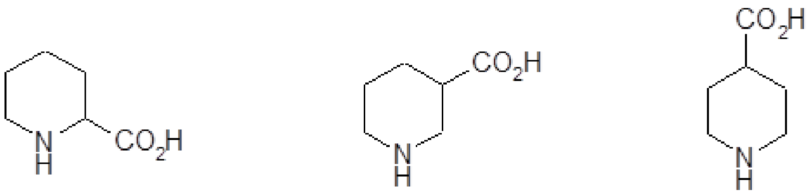
اثبات الشكل التركيبي للهيجرين :



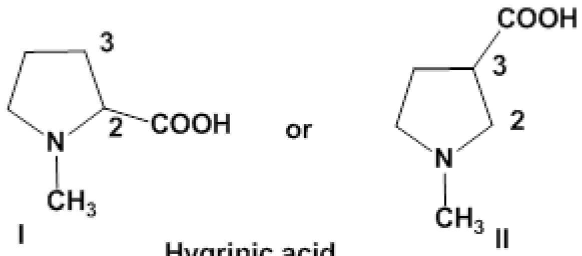


On oxidation of Hygrine ,Hygrinic acid is formed . Hygrinic acid was first believed to be a one from piperidine carboxylic acids but comparison with the three acids show ed this was incorrect.

اكسدة الهيجرين كونت حمض الهيجرينيك الذي كان يعتقد انه حمض من احماض البيبريدين الكربوكسيلية الثلاثة والمقارنة اثبتت عدم صحة هذا الافتراض .



piperidine carboxylic acids

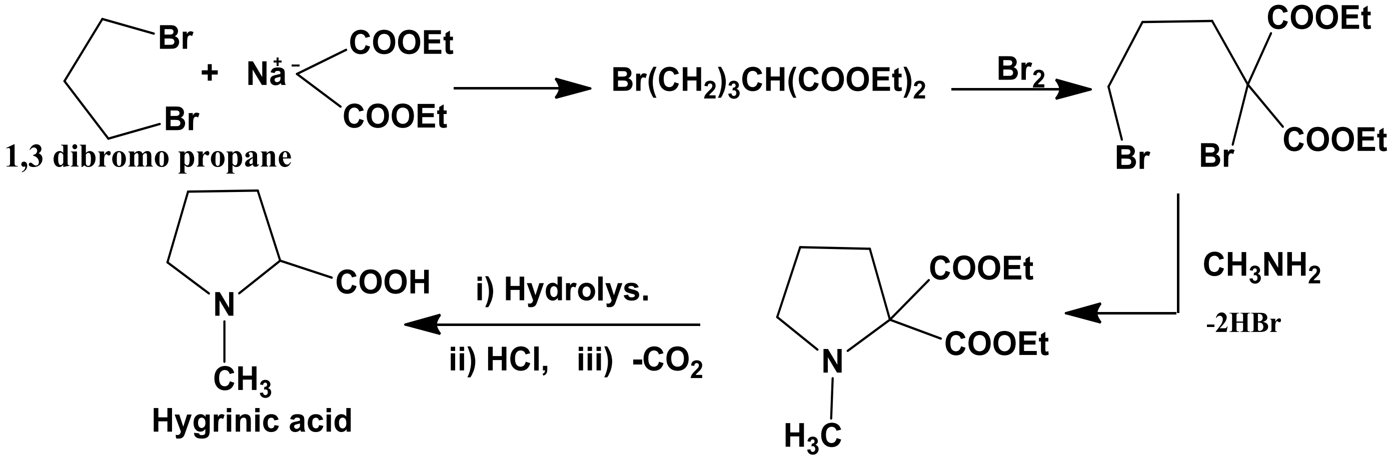


Hygrinic acid

(Hygrine) الهيجرين

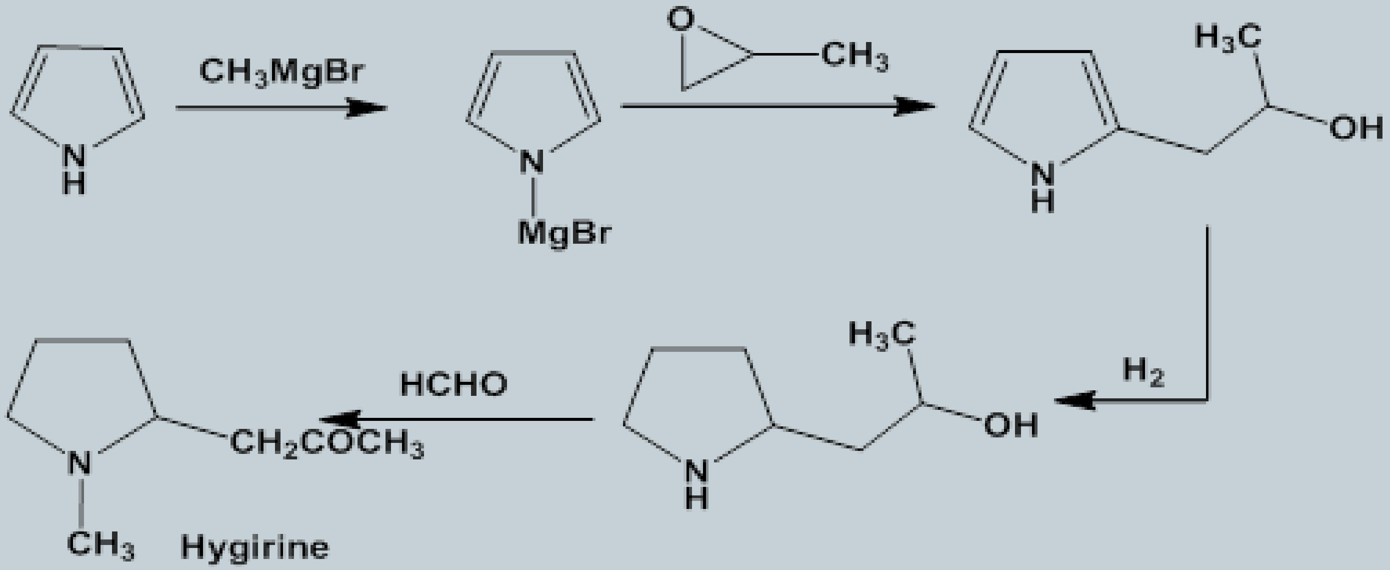
تحضير حمض الهيجرينيك

Synthesis of Hygrinic acid(N-methylpyrrolidine carboxylic acid)



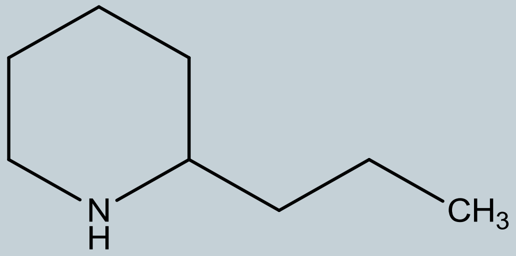
Synthesis of Hygrine تحضير الهيجرين

Synthesis of Hygrine
تحضير الهيجرين



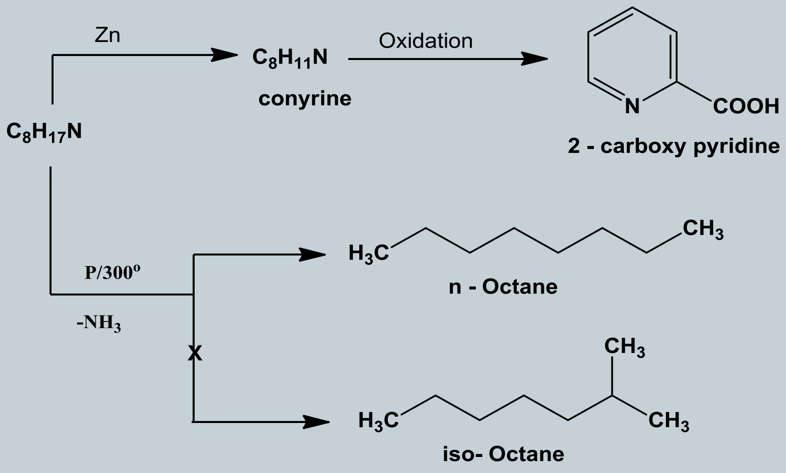
قلويدات مجموعة البيريدين

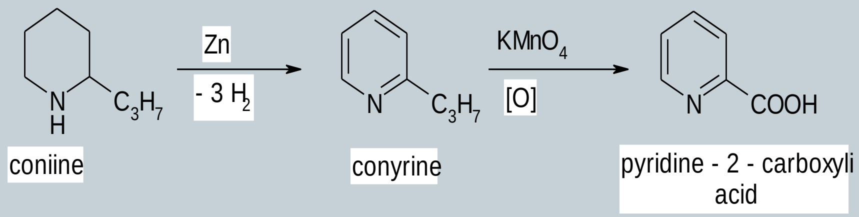
Pyridine alkaloids Coniine $C_8H_{17}N$ الكونيين

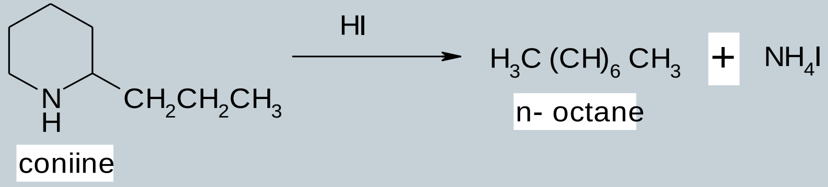


Confirmation of the structure اثبات الشكل التركيبي للكونيين

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 .



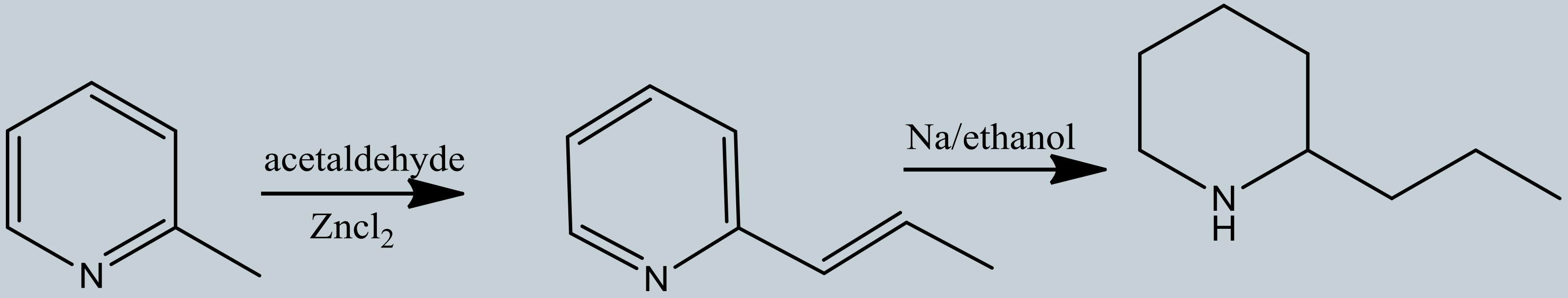




Coniine $C_8H_{17}N$

Synthesis of Coniine

تحضير كونيين



picoline

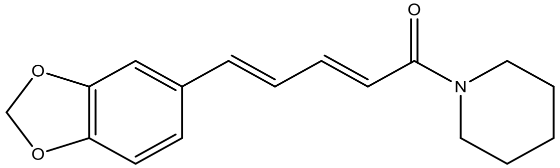
2- methyl pyridine

2-propenyl pyridine

Coniine

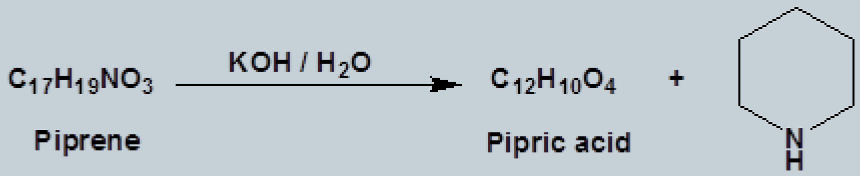
قلويدات مجموعة البيريدين - البيبـــرين $C_{17}H_{19}NO_3$

Pyridine alkaloids - Piperine



Confirmation of the structure

اثبات الشكل التركيبي للبيبرين



$C_{17}H_{19}NO_3 \xrightarrow{KOH / H_2O} C_{12}H_{10}O_4$ +

Piprene

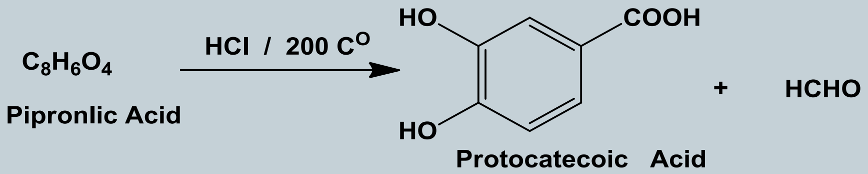
Pipric acid

$C_{12}H_{10}O_4 \xrightarrow{KMnO_4} C_8H_6O_3 \longrightarrow C_8H_6O_4$

Piperic acid

Pipronal

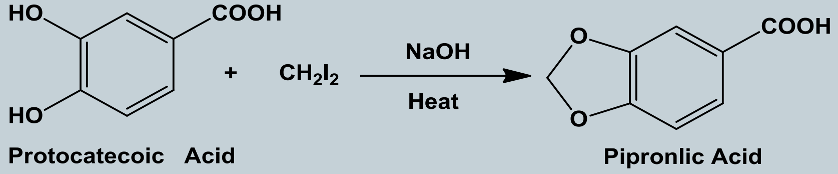
Pipronlic Acid



$C_8H_6O_4 \xrightarrow{HCl\ /\ 200\ C^{O}}$ + HCHO

Pipronlic Acid

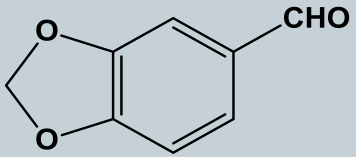
Protocatecoic Acid



+ CH_2I_2 $\xrightarrow[Heat]{NaOH}$

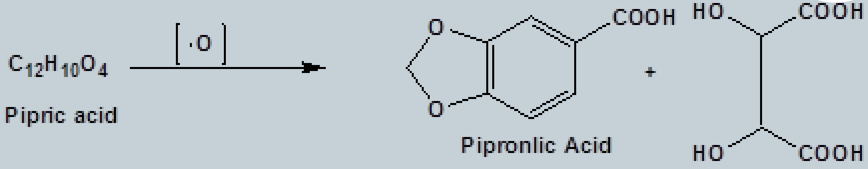
Protocatecoic Acid

Pipronlic Acid

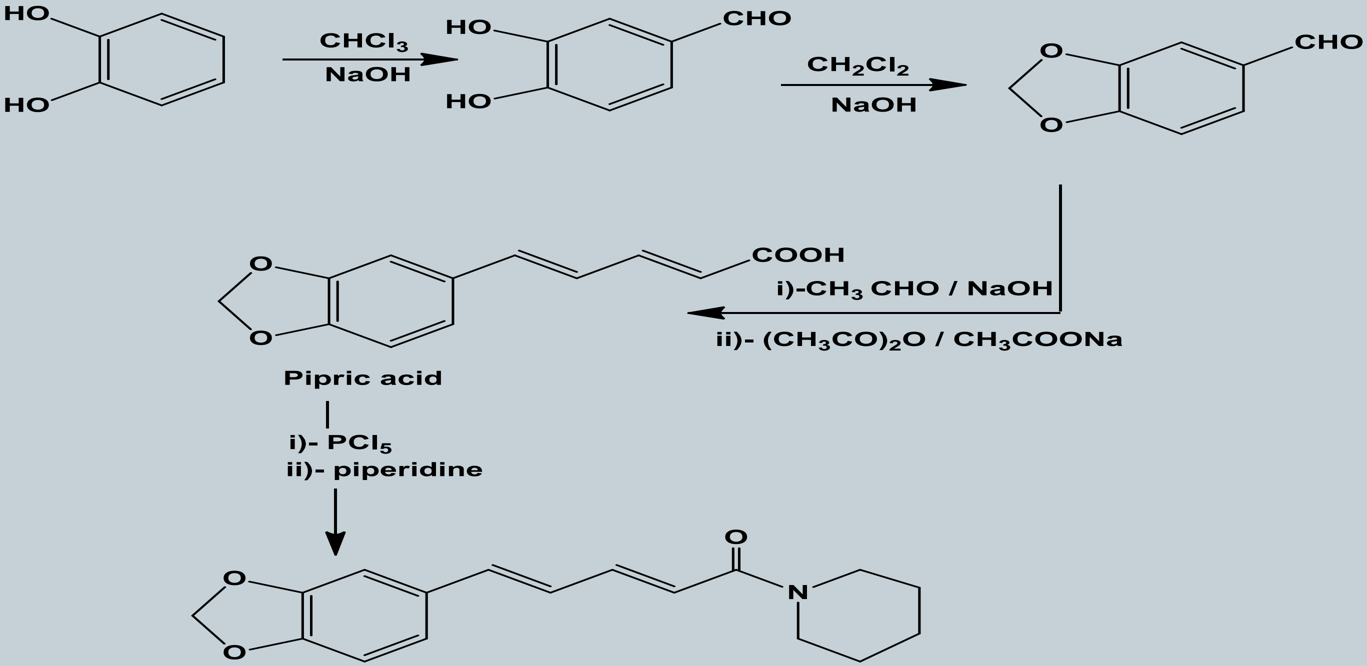


Pipronal

Piperine البيبرين

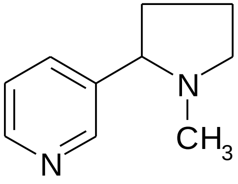


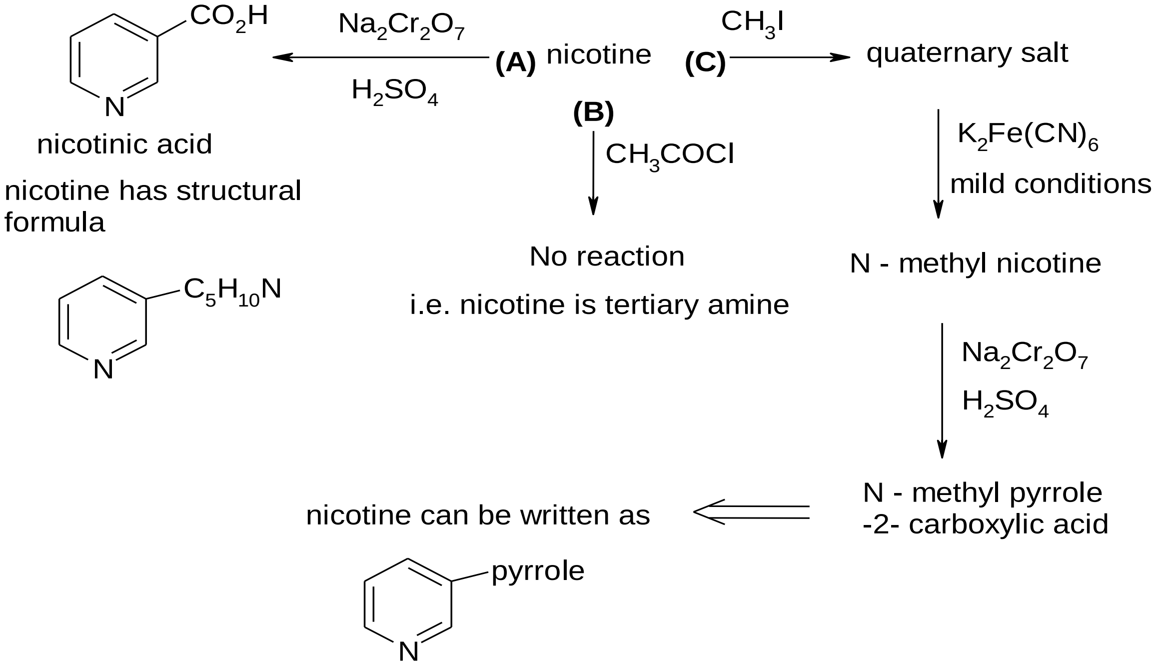
Synthesis of piperine



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

Confirmation of the structure
اثبات الشكل التركيبي للنيكوتين :


nicotine


CO_2H

nicotinic acid

nicotine has structural formula

$C_5H_{10}N$

$Na_2Cr_2O_7$

H_2SO_4

(A) nicotine **(C)**

CH_3I

quaternary salt

(B)

CH_3COCl

No reaction

i.e. nicotine is tertiary amine

$K_2Fe(CN)_6$

mild conditions

N - methyl nicotine

$Na_2Cr_2O_7$

H_2SO_4

N - methyl pyrrole -2- carboxylic acid

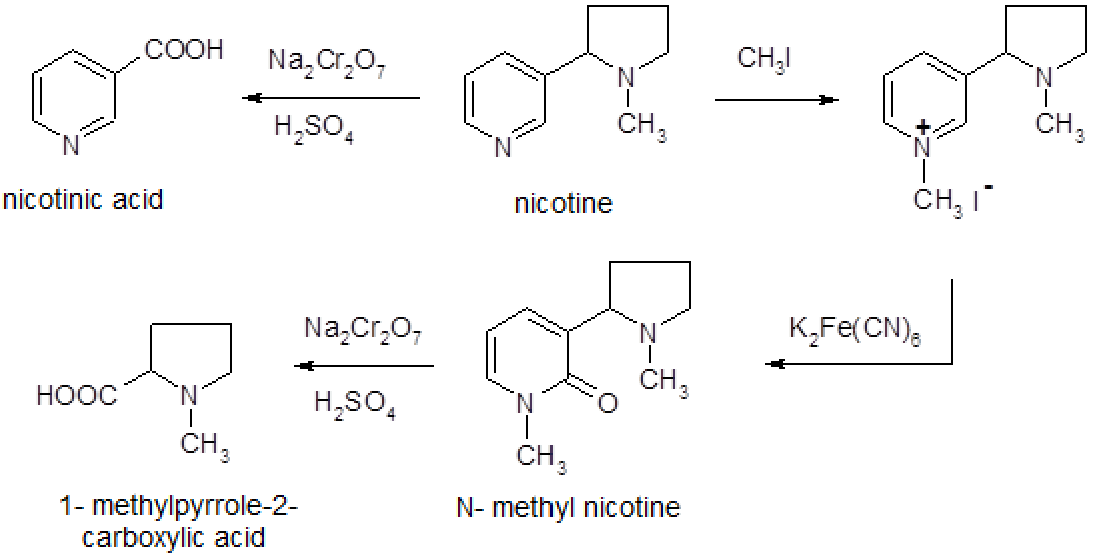
nicotine can be written as

pyrrole

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

Confirmation of the structure

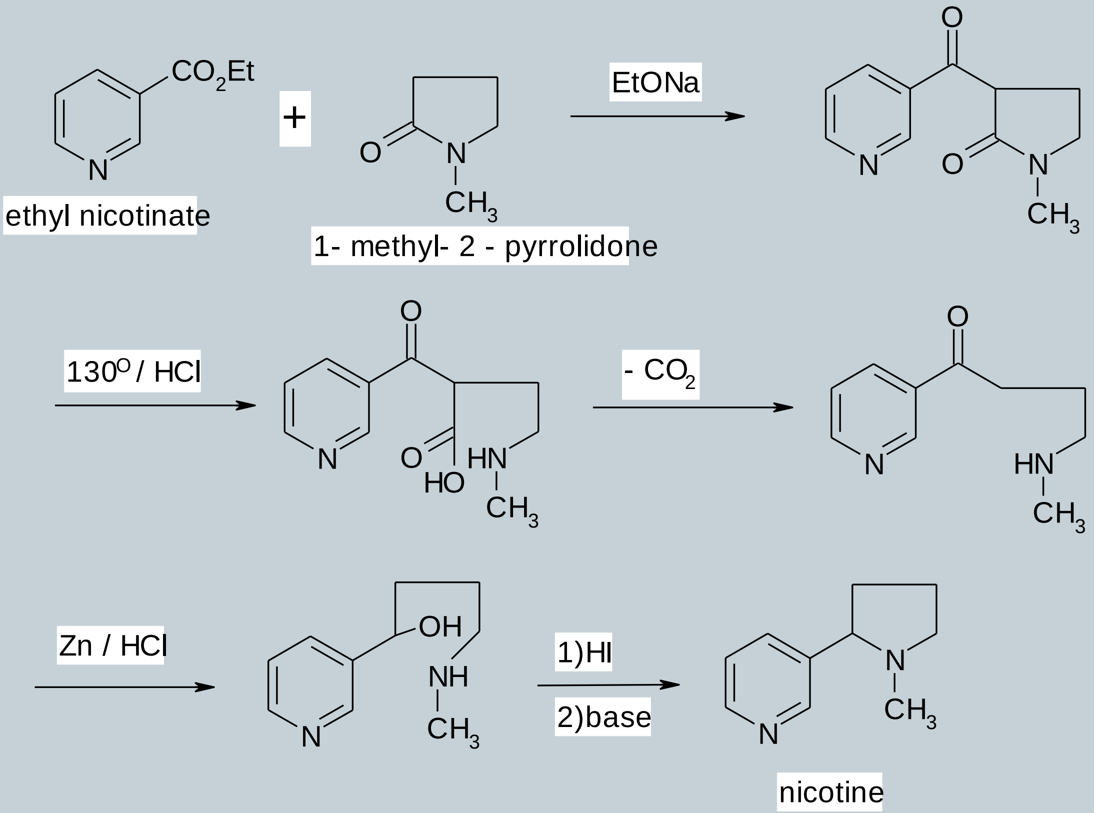
اثبات الشكل التركيبي للنيكوتين



Synthesis of Nicotine تحضير النيكوتين

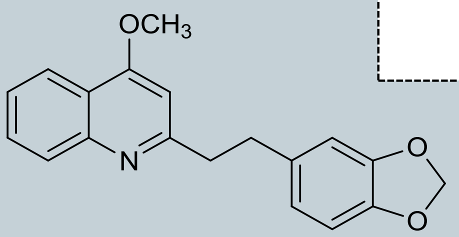
Synthesis of Nicotine *Spath and Bretsvchneider*

تحضير االنيكوتين طريقة سباث و برتشنيدر

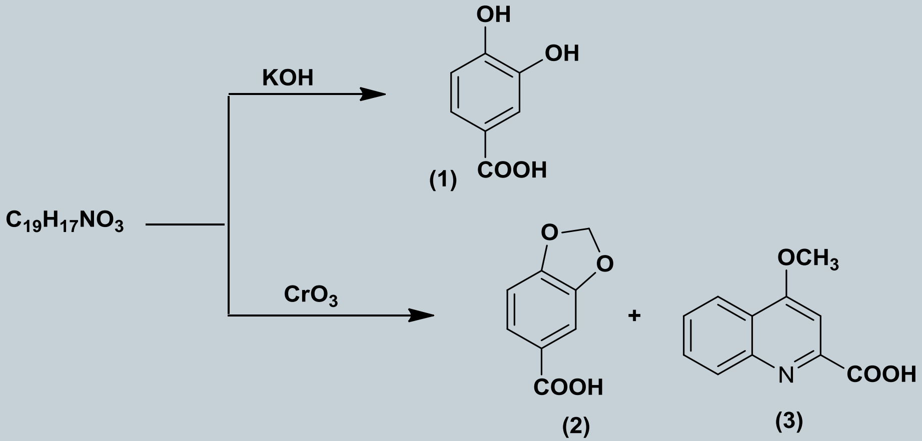


قلويدات مجموعةالكينولين الكسبارين $C_{19}H_{17}O_3N$

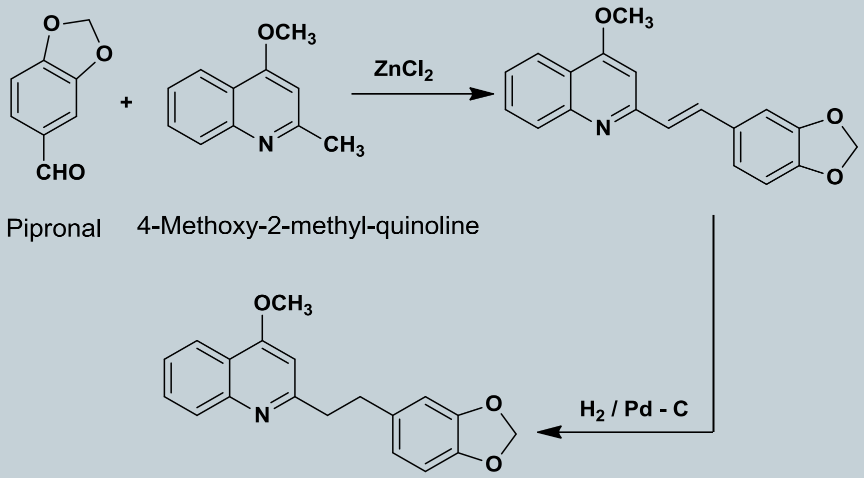
Quinoline alkaloids *Cusparine*



Confirmation of the structure اثبات الشكل التركيبي للكسبارين



Synthesis of cusparine تحضير كسبارين



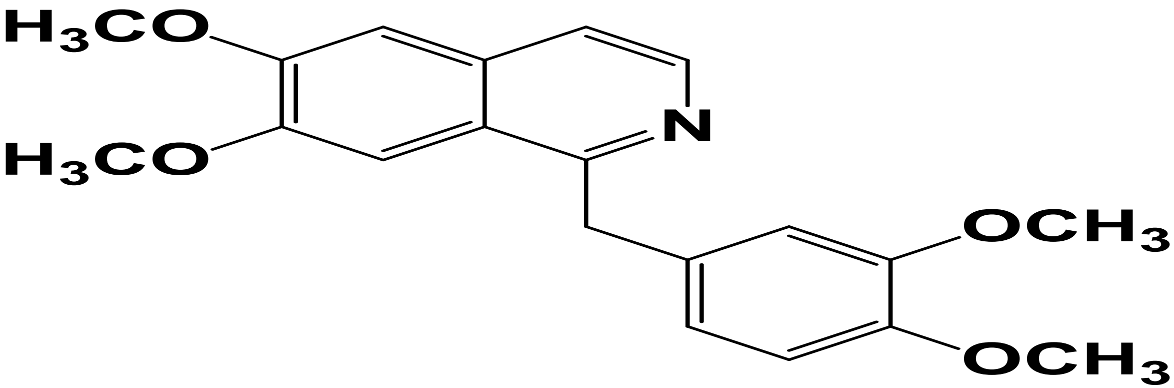
NATURAL PRODUCTS
ISOQUINOLINE ALKALOIDS

Dr. Awatef M. Elmaghraby

ISOQUINOLINE ALKALOIDS

($C_{2O}H_{21}NO_4$) Papaverine البابافيريــن

The alkaloids of this group contain in their main composition an isoquinoline nucleus. Most of the members of this group have a physiological toxic effect and cause many diseases for many tissues of the body, especially cancer, and they also have a strong destructive effect on the nervous system of the person.



Papaverine is a solid with a melting point of 147 ° C).

Golds-chmiedt et al established the structure as follow:

Papaverine
Determination of the structure

1-It has been proven that M.F $C_{20}H_{21}NO_4$

2-Papaverine is optically inactive , since it does not contain any chiral center (asymmetric carbon atom).

3- Since papaverine adds one molecule of methyl iodide to form a quaternary iodide salt, this indicates the presence of nitrogen in the tertiary state.

4- Papaverine contains four methoxy groups (Zeisel method).

$$C_{20}H_{21}NO_4 + 4\ HI \longrightarrow C_{16}H_{13}NO_4 + 4CH_3I$$

بابافيرين Papaverine

papaveroline بابافيرولين

Determination of the structure

5-Oxidation by cold dilute permanganate papaverinol is obtained ,thus more vigorous oxidation with hot dilute permanganate a ketone papaveraldine is obtained so papaverinol is a sec. alcohol and papaverine must be contain a methylene group(-CH_2-). The prolonged action of permanganate oxidize the ketone to papaverinic acid .

$$(C_{19}H_{19}NO_4)CH_2 \xrightarrow{[O]} (C_{19}H_{19}NO_4)CH\text{-}OH \xrightarrow{[O]} (C_{19}H_{19}NO_4)C{=}O$$

Papaverine	papaverinol	papaveraldine
بابافيرين	بابافيرينول	بابافيرالدين

6-When oxidized with hot permanganate ,papaverine (or the oxidized product)is broken down into small fragments:

1-Veratric acid

2- Meta hemipinic acid

3-Pyridine 2,3,4-tricarboxylic acid

4- 6,7-dimethoxyisoquinoline -1- carboxylic acid

Determination of the structure

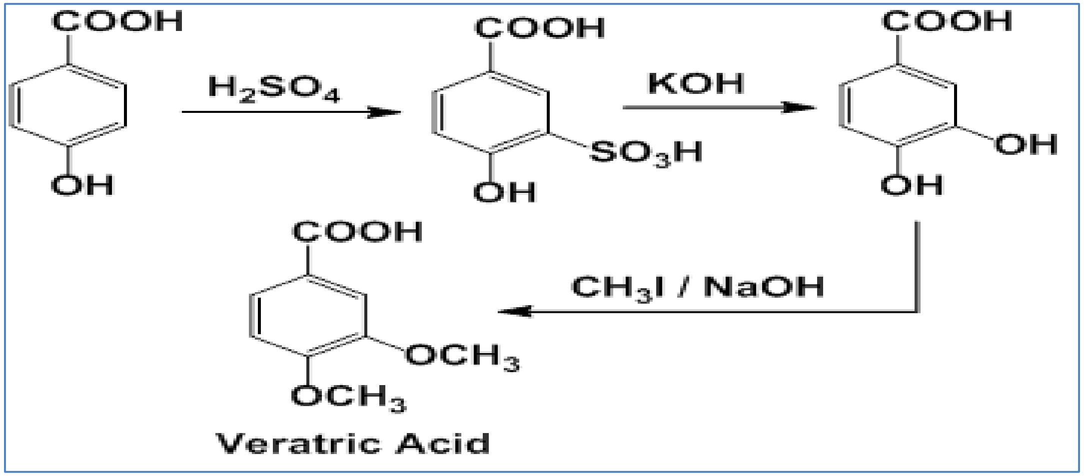
Now, let us consider the evidence for the structure of these compounds :

1- Veratric acid

a) Veratric acid contains one carboxyl group and two methoxy group

b) Decarboxylation of veratric acid veratrol is obtained. Since this is dimethoxy benzene ,so veratric acid is dimethoxy benzoic acid .

c) The position of the carboxyl with respect to methoxy groups established by the following synthesis :



So veratric acid is 3,4 dimethoxy benzoic acid.

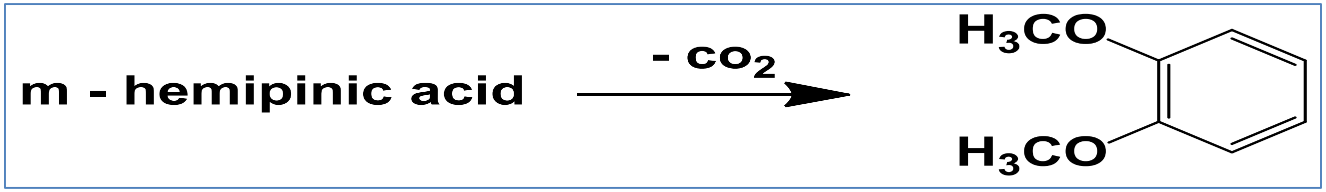
Determination of the structure

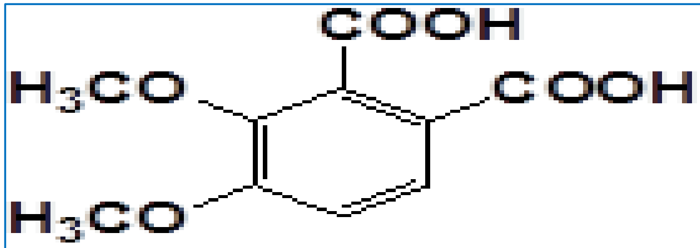
2-Metahemipinic acid:

a) This is dicarboxylic acid and decarboxylation with calcium oxide, veratrol is formed .

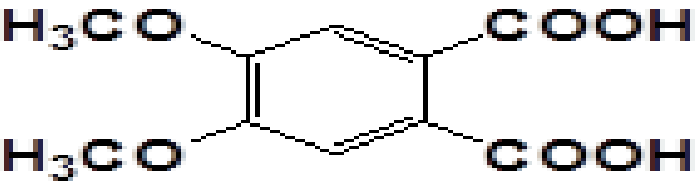
b) Meta hemipinic acid contains two methoxy group .

c) The meta hemipinic acid is either (1) or (2)





[1]

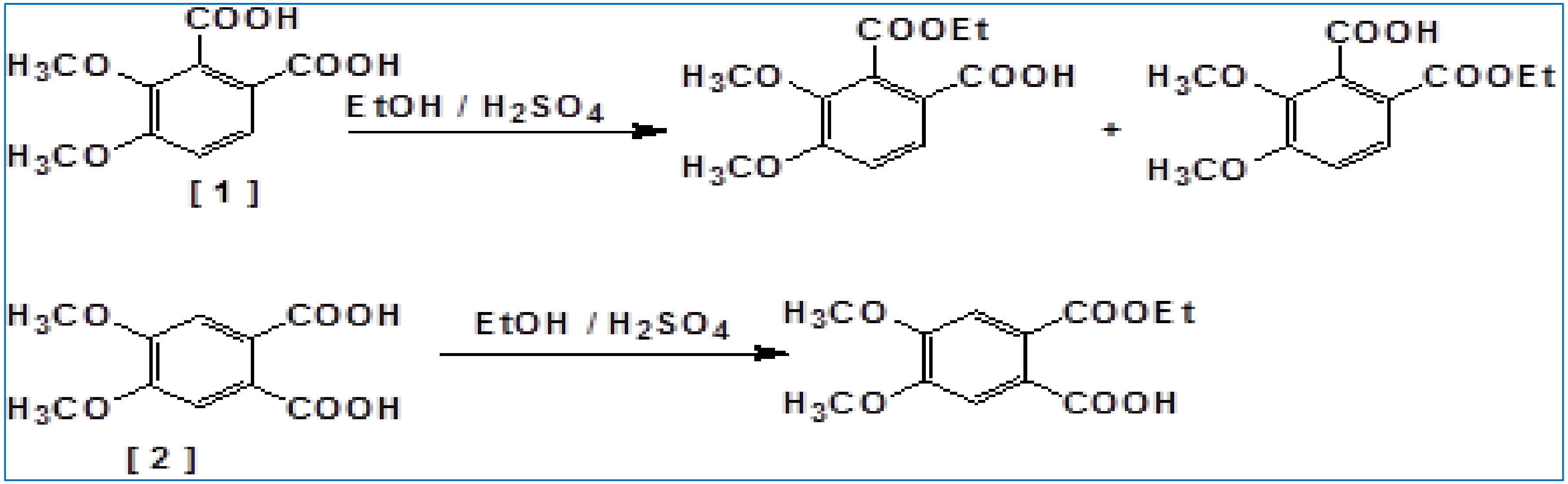


[2]

Determination of the structure

d)Heating the acid with acetic anhydride an anhydride is formed, so the two carboxyl group must be in the ortho position .

e)Meta hemipinic acid forms only mono ester (2) permits the formation of mono ester so the structure (2) is meta hemipinic acid.



Determination of the structure

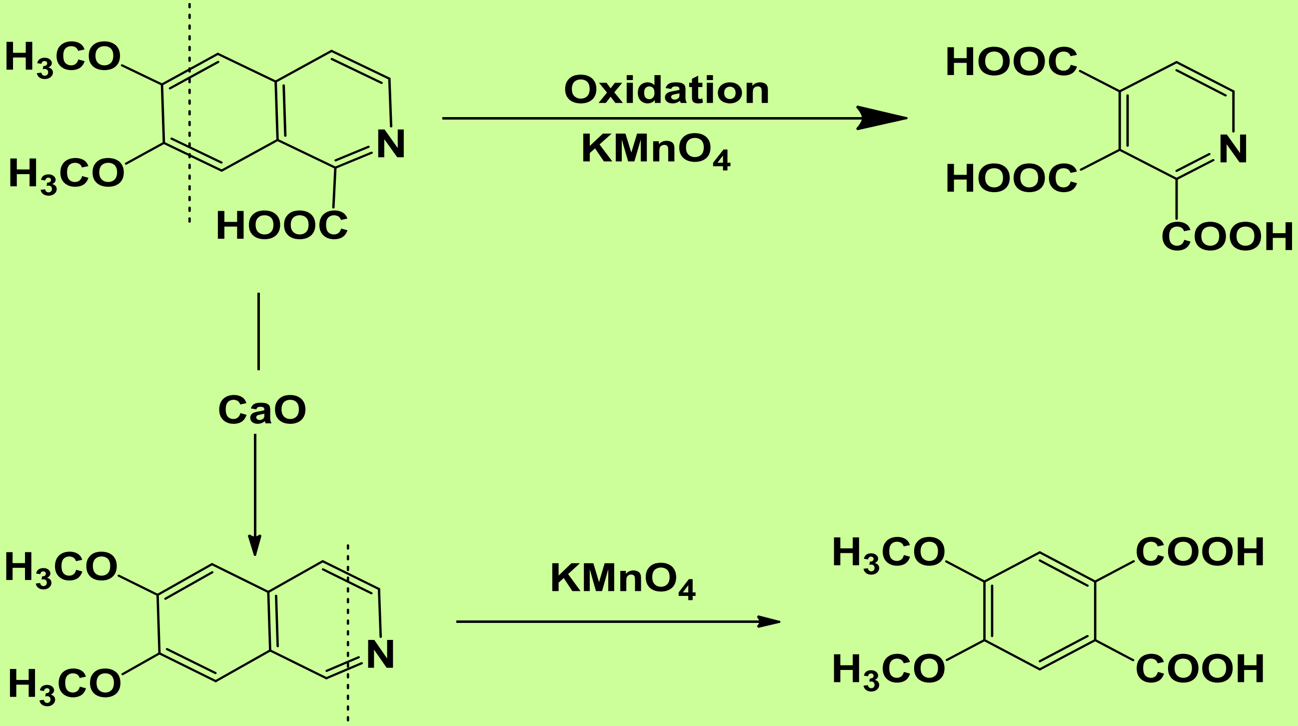
3-pyridine 2,3,4-tricarboxylic acid

a) It contains three carboxylic groups .

b) Decarboxylation gives pyridine .

The position of three carboxyl group is established by the following synthesis starting with lipidine(4-methyl quinoline).

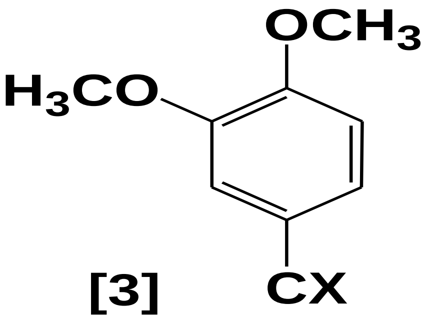
4- 6,7-dimethoxyisoquinoline -1- carboxylic acid



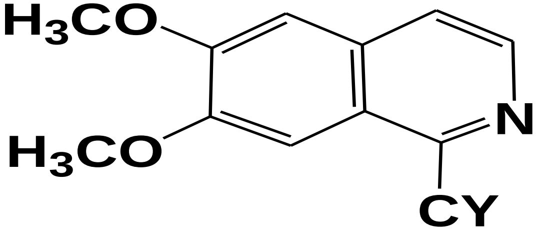
Elucidation of the structure

1-Separation of veratric acid indicates the presence of group [3] in papaverine.

2- The separation of the 6,7 dimethoxyi soquinoline - 1 - carboxylic acid indicates the presence of group [4] in the molecule..



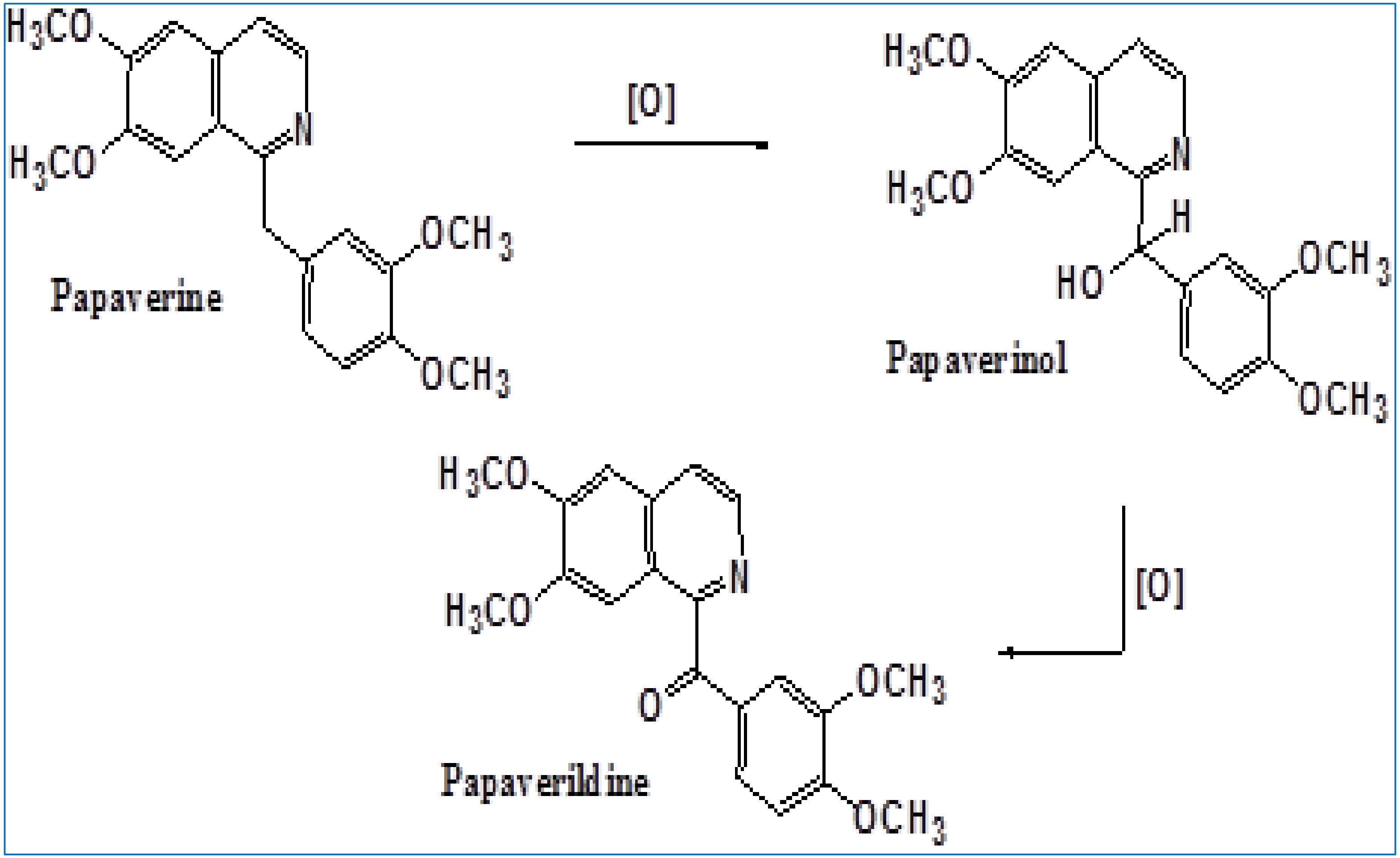
[3]



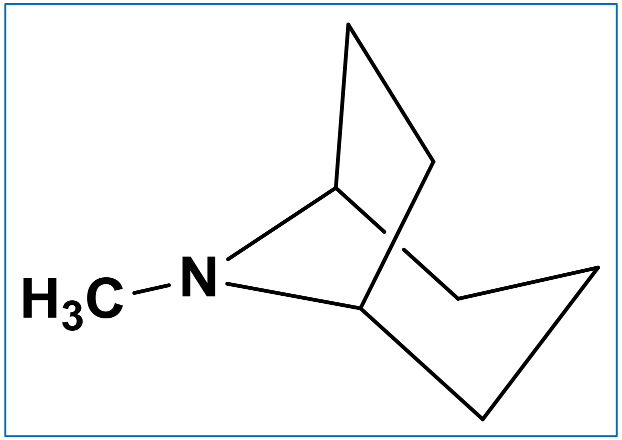
[4]

3- Given that the total number of carbon atoms in groups [3] and [4] is 21 carbon atoms, and papaverine contains only 20 carbon atoms. So, there must be a repeat carbon atom in each of the CX and CY groups. Given that the compound contains a group of CH2 (methylene), then it is likely that it is the same as the duplicated carbon atom.

If we assume that C-x and C-y are one and the same carbon atom of the (X-CH_2 –Y) group, then the following structure of papaverine accounts for all the facts.



Fused pyrrolidine-pyridine group
Tropine alkaloids
قلويدات البيروليدين- بيريدين المتكاثفة
[قلويدات التروبين]



نواة التروبين

Tropine nucleus

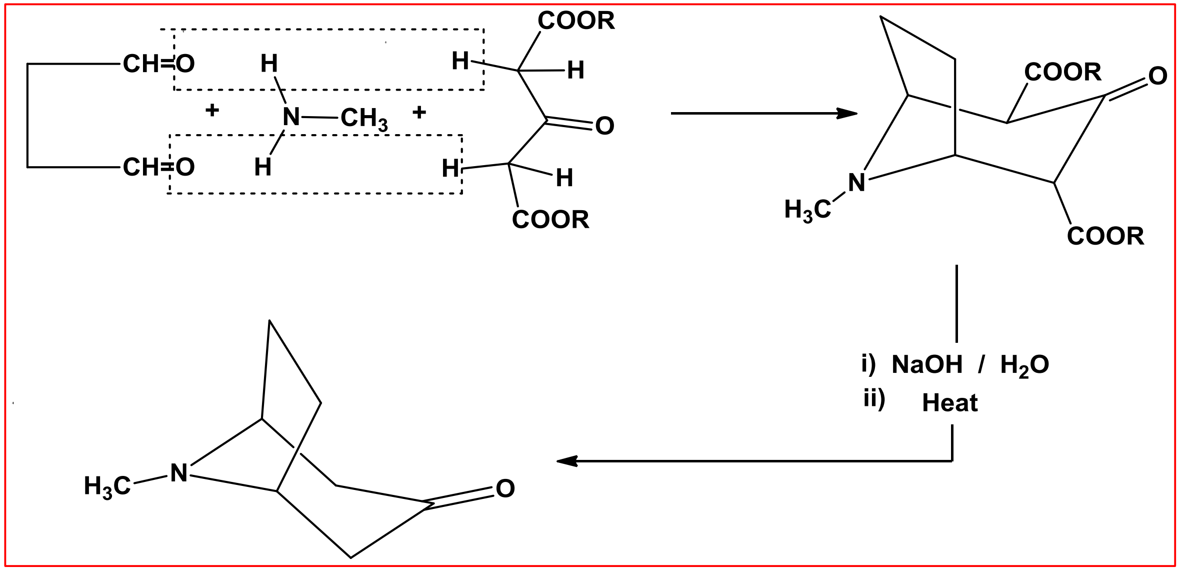
8-methyl-8-azabicyclo[3.2.1]octane

Tropine alkaloids [8-methyl-8-azabicyclo[3.2.1]octane occur in (atropa belladonna).

The most important alkaloids that can be obtained from these sources are atropine drugs, high amino acid, scopolamine, etc.

The heterocyclic tropic alkaloids as they consist of the fusion of the pyridine nucleus with the pyrrole nucleus. It is also possible to attribute all of these alkaloids. To the compound tropan.

Tropinone can be synthesized via heating succinaldehyde,methyl amine and alkyl acetondicarboxylate in the presence of hydrochloric acid as follow (Robinson method)



طريقة روبنسون Robinson’s method

نبات ست الحسن
(atropa belladonna الاتروبابلادونا)

(hyoscyamus السكران
nizer)

الداتورا الصفراوية
Datura stramonium

Tropinone can be reduced to give tropanol (sec.alcohol) also it can be add hydrogen cyanide to give the cyanohydrine derivative which hydrolyzed into the corresponding hydroxy acid,.In this way it has been possible to create many of these compounds, which have such a structural structure for the purpose of studying their physiological effect.

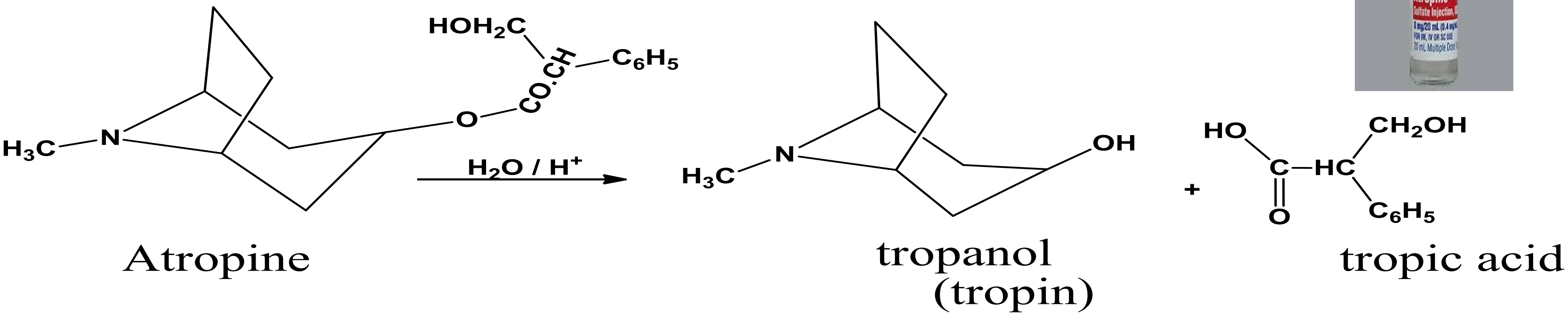
سير روبرت روبنسون جائزه نوبل ١٩٤٧ لتحقيقاته فى المنتجات
النباتية ذات الأهمية البيولوجية، وخصوصا القلويدات"

Atropine الأتروبيـــن:

Atropine is occurs in (atropa belladonna) together with hyoscyamine, atropine solid m.p118 ^{o}C

-It has been proven that molecular formula $C_{17}H_{23}NO_3$

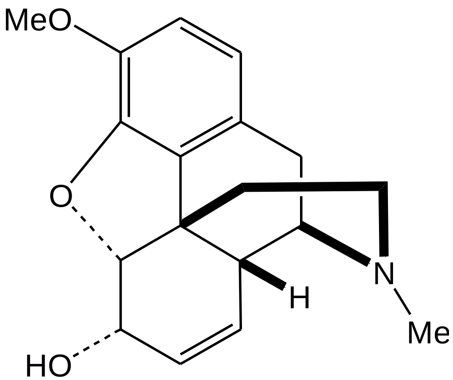
-Atropine is hydrolyzed to tropic acid and tropine(tropanol),thus atropine is the tropanoyl ester of tropic acid ,atropine can be synthesized by heating of tropic acid with tropanol in the presence of hydrogen chloride. It is known that it is used in ophthalmology, since its solution with a concentration of ½ - 1% in oil causes an expansion in the eye (diffusive effect).



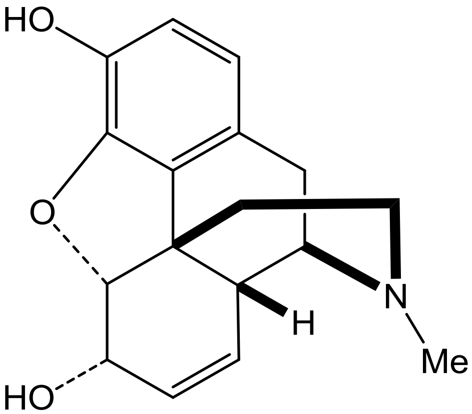
Phenanthrene Group

قلويدات الفينانثرين

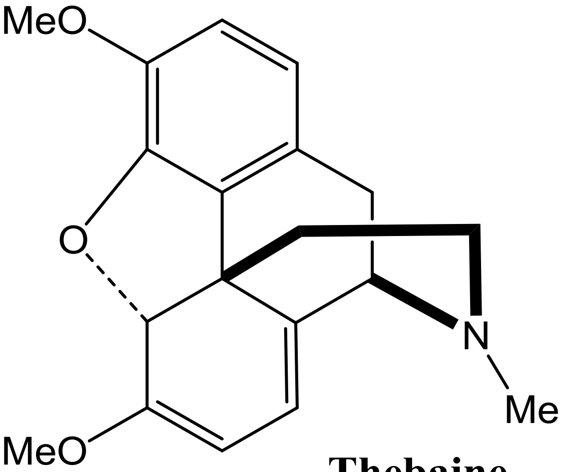
Morphine, Codeine and Thebaine those are the three important opium alkaloids containing the Phenanthrene nucleus.



Codeine



Morphine

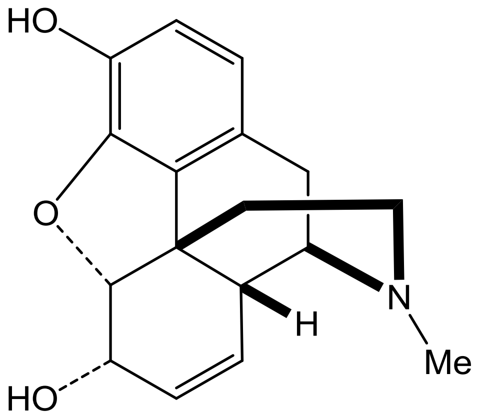


Thebaine

قلويد الكودين

قلويد المورفين

قلويد الثيبايين



Morphine

Morphine المورفين

Morphine is the chief alkaloid in opium and was the first alkaloid to be isolated ,the chemical structure was supported by:

1- It has been proven that molecular formula $C_{17}H_{19}NO_3$ (after purification, Qualitative and quantitative analysis, determination of empirical formula)

2- Routine tests confirmed that nitrogen in the tertiary state .

3- Acetylation of morphine gives morphine diacetate (Heroin),two hydroxyl groups are present in the molecule.

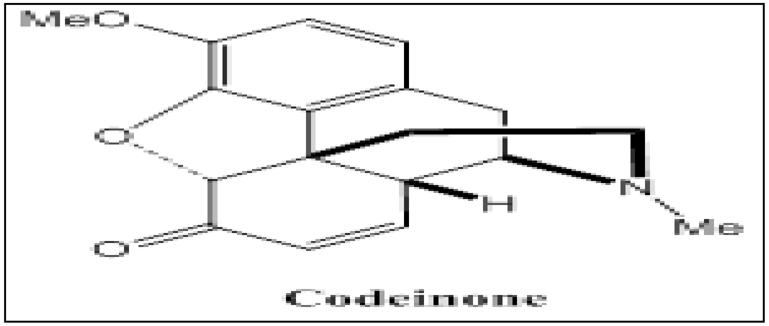
4-Morphine gives the ferric chloride test for phenols and dissolves in aqueous sodium hydroxide to form mono sodium salt ,and this is reconverted into morphine by the action of carbon dioxide,thus one of the hydroxyl groups is phenolic.

5--**Morphine with halogen acids converted morphine into mono halogeno derivative, one hydroxyl group being replaced by halogen atom thus the second hydroxyl is secondary alcoholic hydroxyl group.**

6-Morphine is methylated by heating with methyl iodide and aqueous potassium hydroxide to give Codeine, therefore follow that it is only the phenolic hydroxyl group in morphine has been methylated.

7- Oxidation of codeine by using chromic acid to give Codeinone ,(a ketone).Thus the hydroxyl group in codeine(and this one in morphine) is secondary alcoholic, and so codeine is the monomethyl (phenolic)ether of morphine .

8-When morphine is distilled with zinc dust phenanthrene and other bases are produced .This suggests that phenanthrene nucleus is present.



Codeinone

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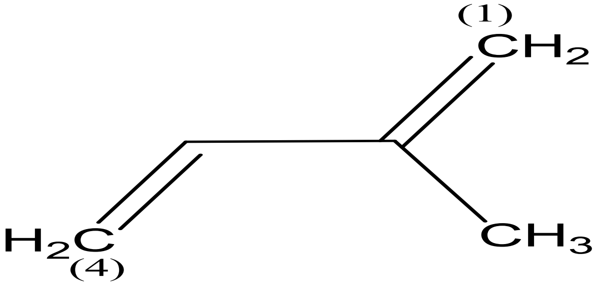
Natural Product Terpenoids

The terpenoids form a group of compounds most of them occur in the plant kingdom. The distinctive aroma of many flowers and roses, as well as the colors of the fruits of some plants, such as carrots, tomatoes, etc., are attributed to terpenoids (terpenes). Terpenoids comprise most of the Kingdom's vegetable products and are involved in the synthesis of many volatile oils. They are also used to make perfumes, medicines and food flavors. This family also belongs to the natural rubber that we obtain as a white liquid from the rubber tree.

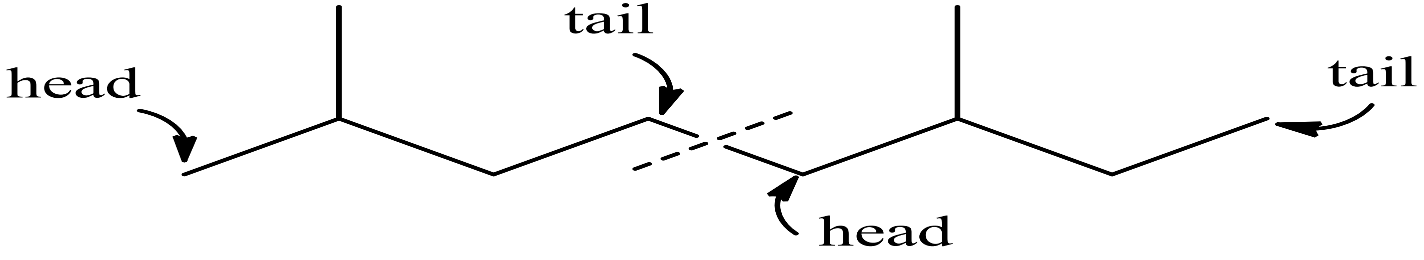


isoprene (2-methyl 1,3 butadiene

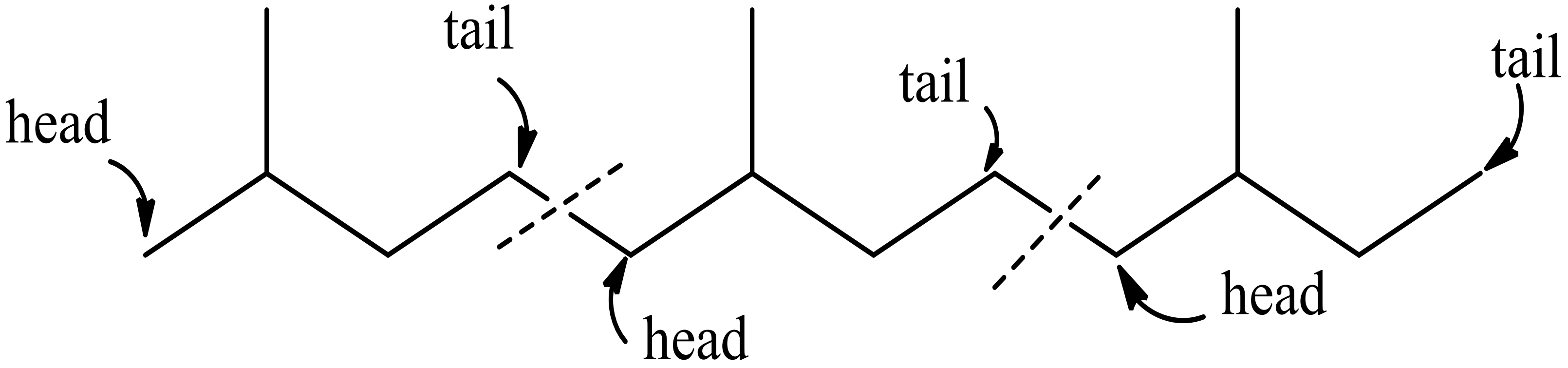
Classification of Terpenoids
M.F$(C_5H_8)_n$

The thermal decomposition of almost all terpenoids gives isoprene as one of the products ,this led to suggestion that:
The skeleton structures of all naturally occuring terpenoids can built up of isoprene units this is known as the isoprene rule
Ingold pointed out that isoprene units in natural terpenoids were joined head to tail .
Several exceptions occur ,e.g.the carotenoids joined tail to tail .

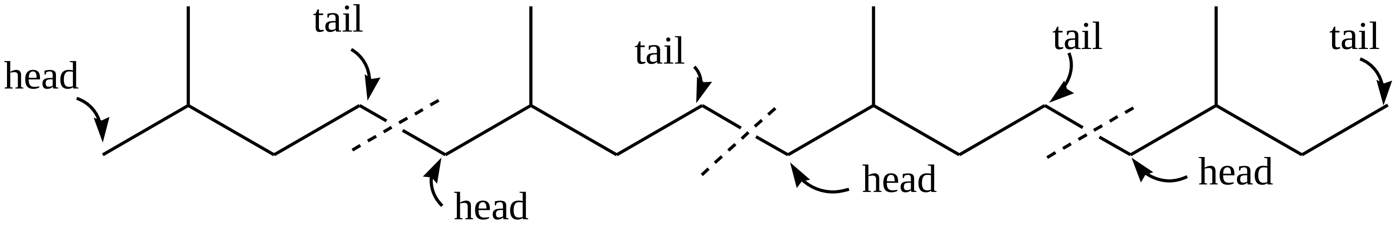
n	Number of carbon	Class	Formula	examples
٢	١٠	Monoterpenes	$C_{10}H_{16}$	**Volatile oils**
٣	١٥	Sesquiterpenes	$C_{15}H_{24}$	**Volatile oils**
٤	٢٠	Diterpenens	$C_{20}H_{32}$	**Gums and resins**
٥	٢٥	Sesterterpenes	$C_{25}H_{40}$	**Gums and resins**
٦	٣٠	Triterpenes	$C_{30}H_{48}$	**Gums and resins**
٨	٤٠	Tetraterpens	$C_{40}H_{64}$	**Carotenoids**
>٨	>٤٠	Polyterpenes	$(C_5H_8)_n$	**Natural rubber**



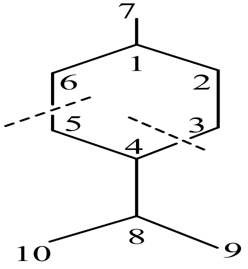
open chain monoterpenoid



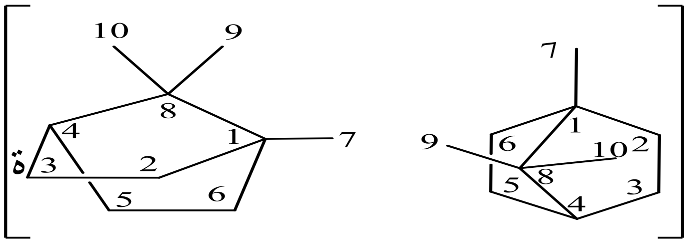
open chain sesquiterpenoids



Open chain diterpenoid **تربيـن ثنائي مفتوح السلسلـة**



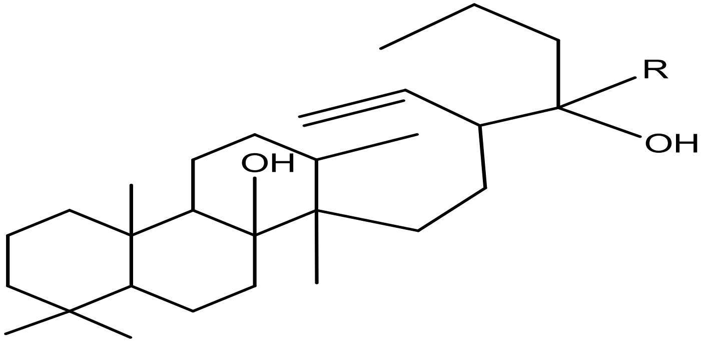
monocyclic monoterpenoid



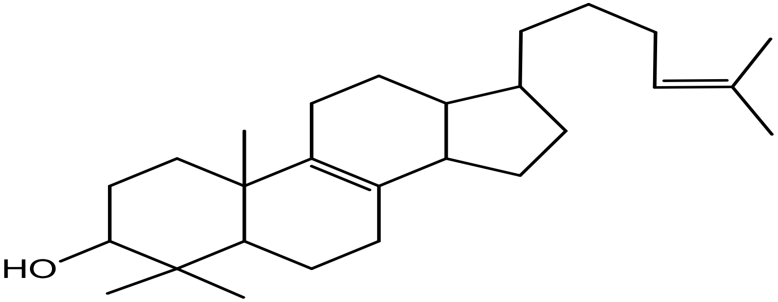
bicyclic monoterpenoid

تربيـن احادي أحـادى الحلقة

تربيـن أحـادى ثنائي الحلقة ملتحـم



fused tricyclic triterpenoid



fused tetracyclic triterpenoid

تربين ثلاثى رباعي الحلقة ملتحم   تربين ثلاثي ثلاثى الحلقة ملتحم

Separation and Extraction of Monoterpenoids and Sesquiterpenoids

1-Expression
2- Steam distillation
3- Extraction by means of volatile organic solvents
4- Adsorption on fats.

Steam distillation or extraction with volatile organic solvents is one of the most important multiple methods used to extract terpenes from plants, and the method of steam distillation is the most commonly used method, especially when extracting monoterpenes , sesquiterpenes and some diterpenes.

The method of extracting is summarized in grinding the vegetable parts well and then distilling them with steam. Volatile oils by fractional distillation. One of the methods widely used to separate terpenoids is the thin layer (TLC) or column method (CC) or HPLC, and the column method (on silica gel) is one of the most suitable methods of color separation for high terpenes such as di ,tri,and tetraterpenoids.

Methods for
Separation of mixtures

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

If the compound is decomposes due to the high temperature, it may be extract by means of several organic solvents, where the petroleum ether is used for extraction at a low temperature (50 ° C) and for a period sufficient to extract all types of terpenes, or at least most of them, The ether is then distilled at reduced pressure to maintain the terpenes without decomposition . Then the volatile oil mixture is separated by fractional distillation under reduced pressure or by column .chromatography

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).

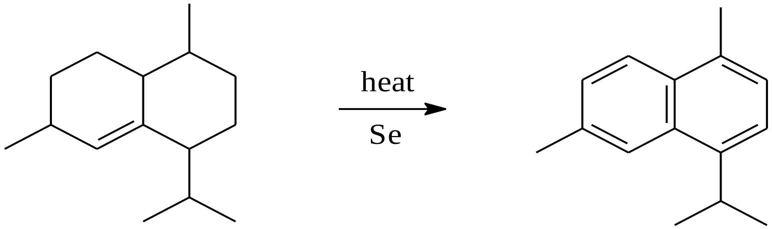
2-If the terpenoid is optically active ,its specific rotation is measured.

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

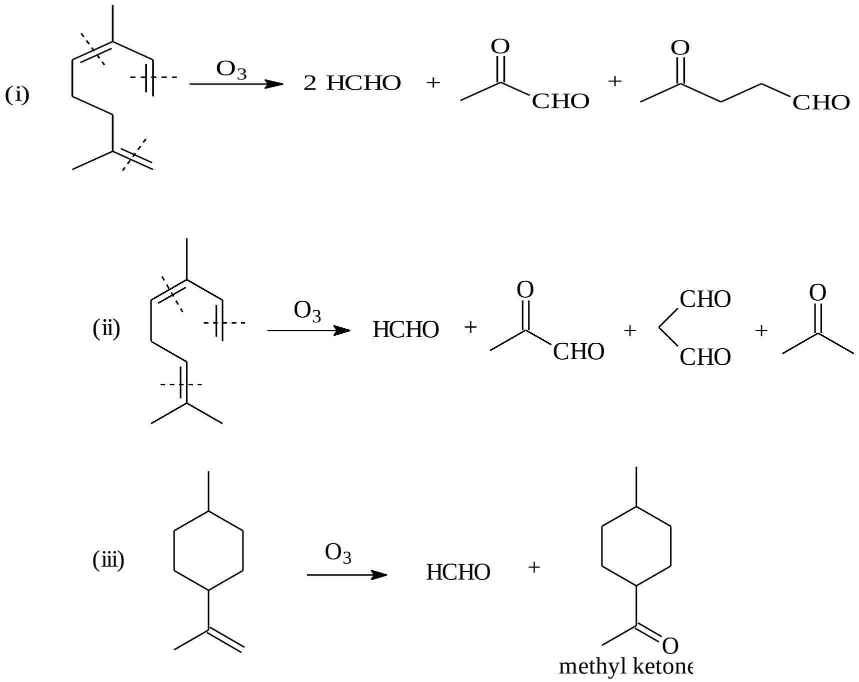
4-The presence of unsaturation olefinic bonds is ascertained by means of bromine and catalytic hydrogenation.

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

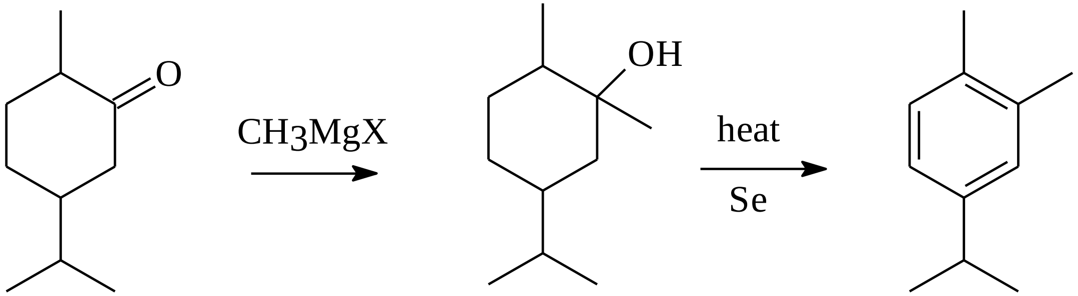
6-Dehydrogenation by heating the terpene with S or Se converts the terpene into aromatic derivative which is easily identified.



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($CH_2=$).



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.

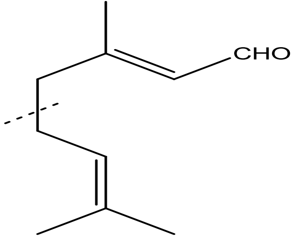
10- A final confirmation of the proposed structure is usually achieved by synthesizing the compound and comparing the spectral data with those of an authentic sample.

Monoterpenoids التربينـات الأحادية

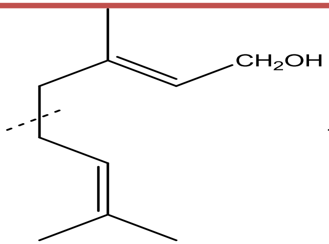
Monoterpenoids are classified into three groups (acyclic,monocyclic,bicyclic)

Acyclic Monoterpenoids

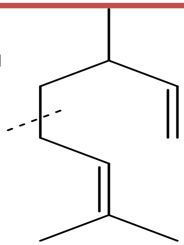
The carbon skeleton being formed by the head to tail of two isoprene units.



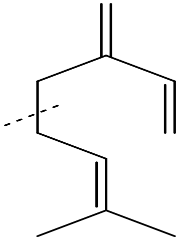
Citral



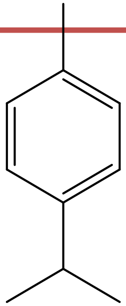
Geraniol



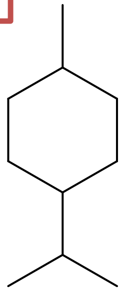
Ocimene



Myrcene



P-cymene

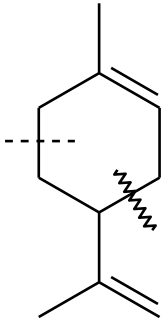


P-menthane

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.

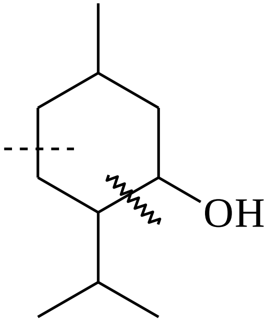
Bicyclic monoterpenoids contain a six membered ring and a three,four or five membered ring .

Monocyclic monoterpenoids

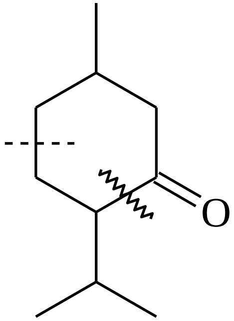


Limonene

occurs in lemon
and orange oils



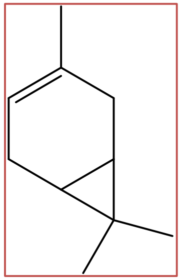
Menthol



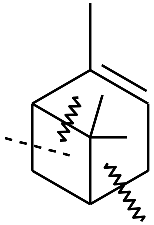
Menthone

both occur in pepermint oil

Bicyclic monoterpenoids

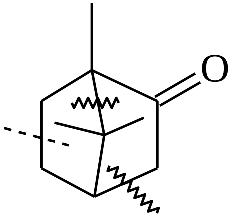


carene



α-Pinene

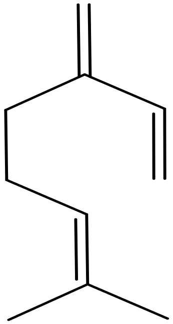
occurs in turpentine oil



Camphor

occurs in camphor tr

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



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

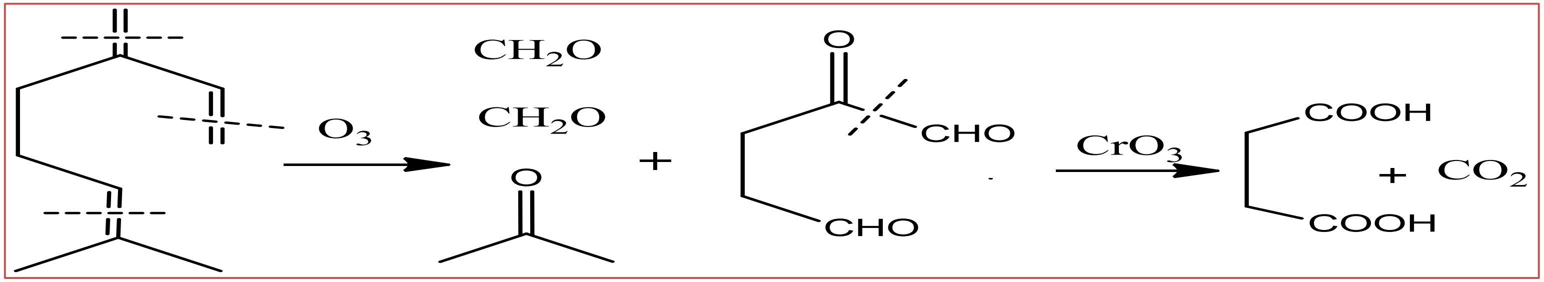
Structure of myrcene is supported by :

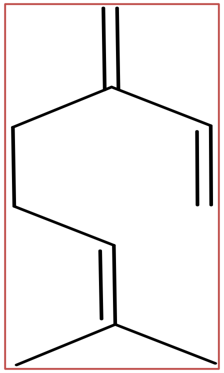
1-Molecular formula is $C_{10}H_{16}$.

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 .

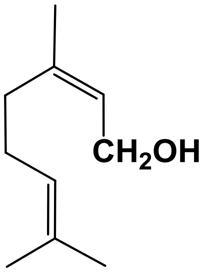
4-Ozonolysis of myrcene produces acetone ,two molecule of formaldehyde and ketodialdehyde which oxidized with chromic acid to give succinic acid and carbon dioxide.



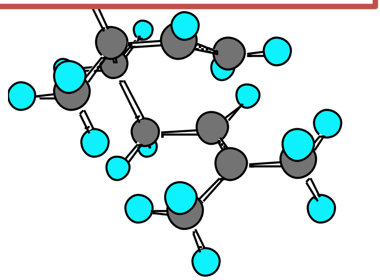


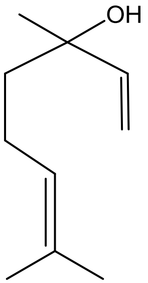
7-methyl-3-methylene-octa-1,6-diene

$(C_{10}H_{18}O)$ Linalool اللينالول



Geraniol





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

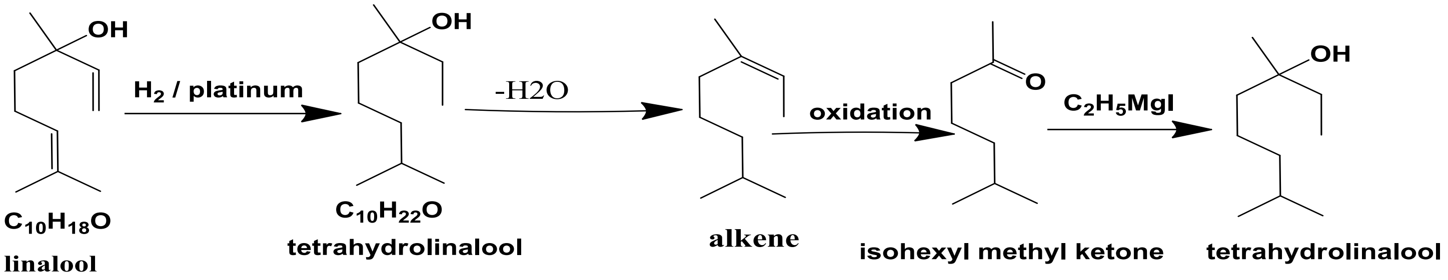
Structure of Linalool : $(C_{10}H_{18}O)$ b.p:198-199C

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 .

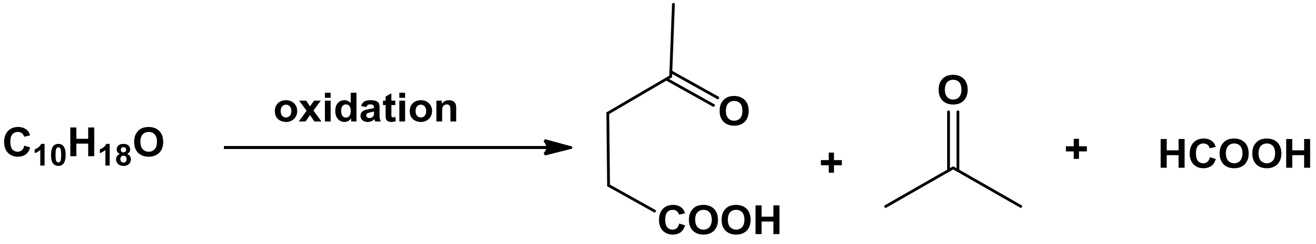
3-It is converted into geranyl acetate by heating with acetic anhydride and converted into linalool by heating with steam at 200C under pressure , also linalool isomerizes in the presence of acid to geraniol .

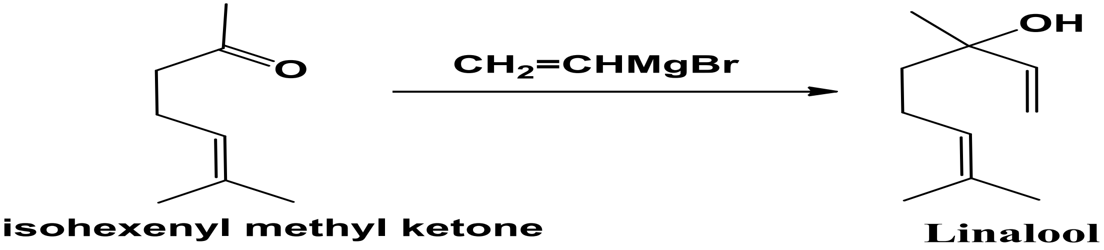
4-It has a tertiary alcoholic group and the position confirmed as follow:

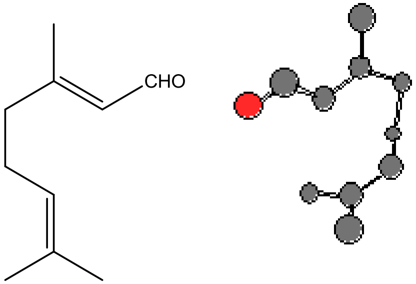


5-Oxidation of linalool by pot. Permenganate converted it into levulinic acid ,acetone and formic acid .

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).





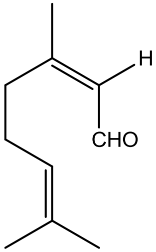


Citral ($C_{10}H_{16}O$)

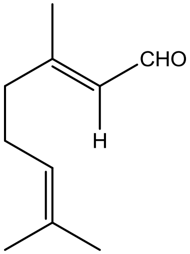
3,7 dimethyl 2,6 -octadienal

Citral occurs to an extent 60-80 per cent in lemon grass oil

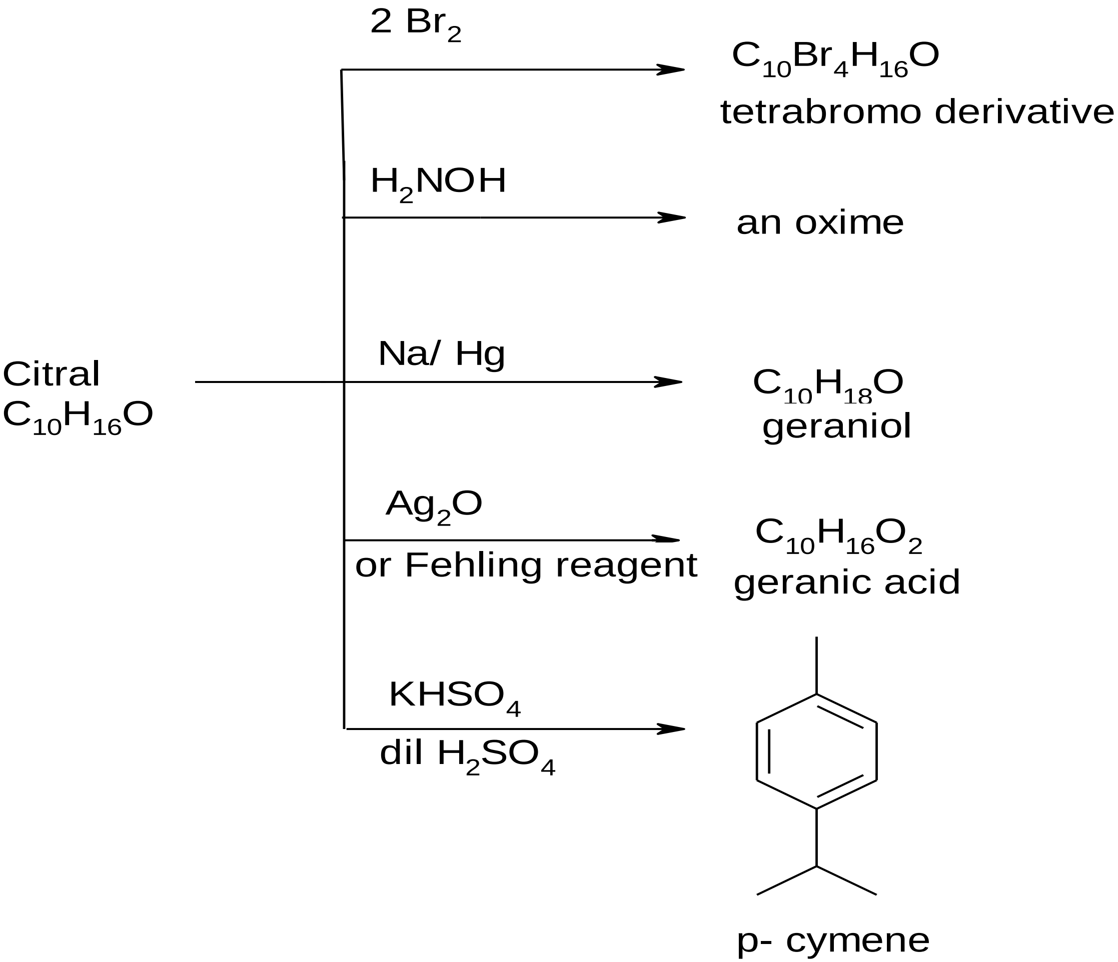
Structure of citral was supported by:



cis form
citral b or neral



trans form
citral a or geranial



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

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

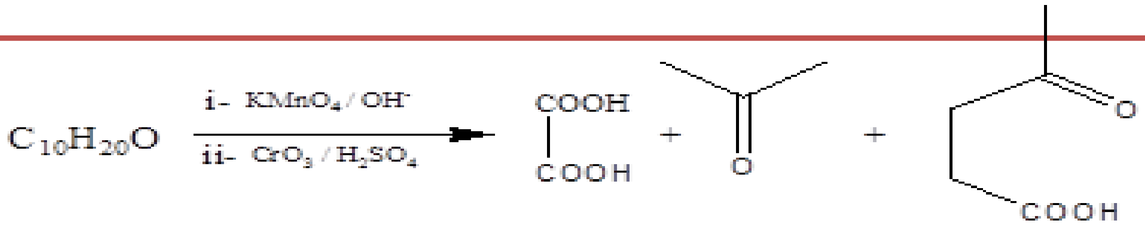
H_2NOH → an oxime

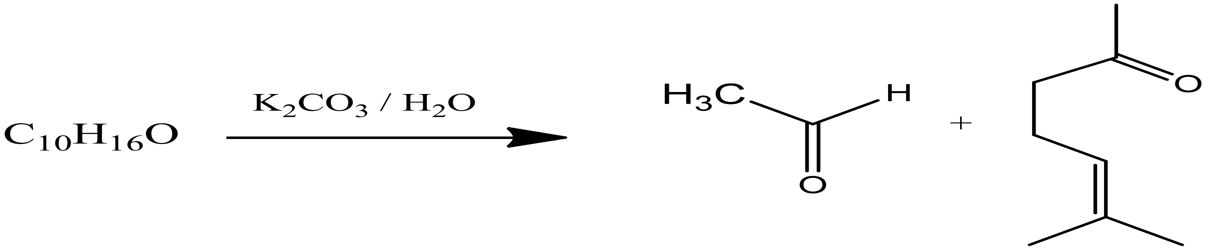
Na/ Hg → $C_{10}H_{18}O$ geraniol

Ag_2O or Fehling reagent → $C_{10}H_{16}O_2$ geranic acid

$KHSO_4$ dil H_2SO_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 .



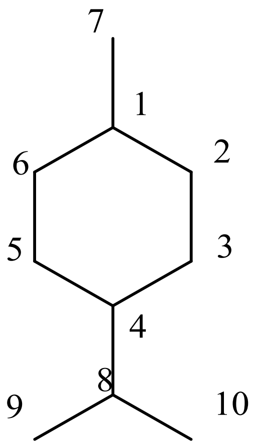


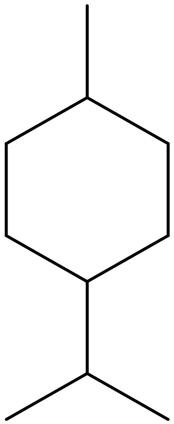
Natural Products
Terpenoids
Cyclic Monoterpenoids
Limonene-Menthol-Camphor

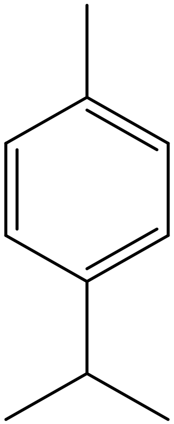
استاذ المادة
د /عواطف محمد المغربي
استاذ الكيمياء العضوية م
قسم الكيمياء – كلية العلوم

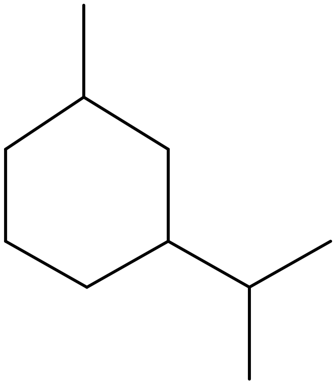
Monocyclic Monoterpenoids

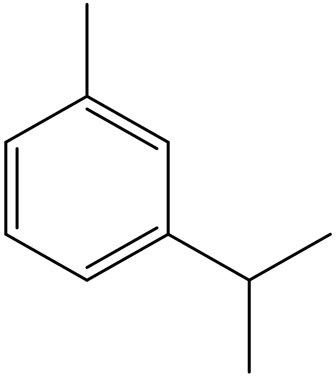
Monocyclic Monoterpenes is subdivided into two groups the larger group with carbon skeleton which are related to P-cymene(4-isopropyl toluene), the smaller group with carbon skeleton are related to m-cymene.

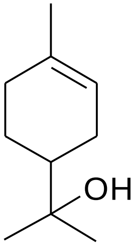



P-menthane

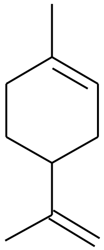

P-cymene

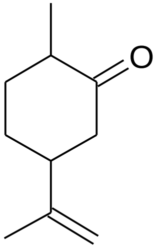

m-menthane


m-cymene

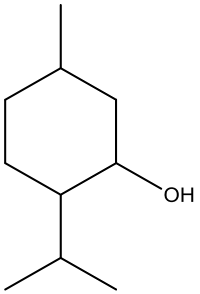


α – terpineol

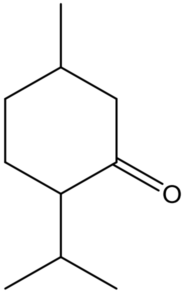

limonene



carvone



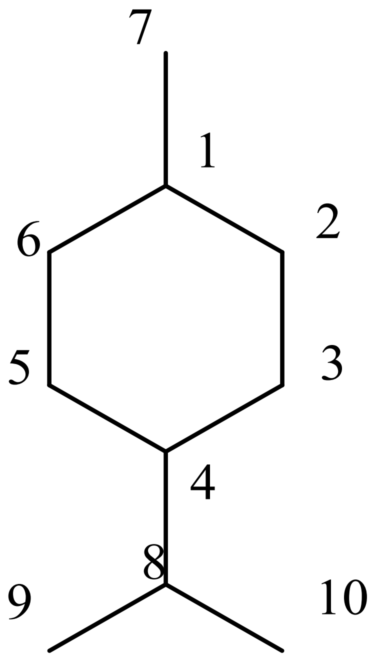
Menthol

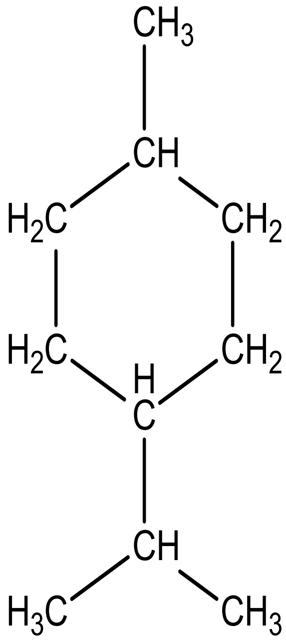


Menthone

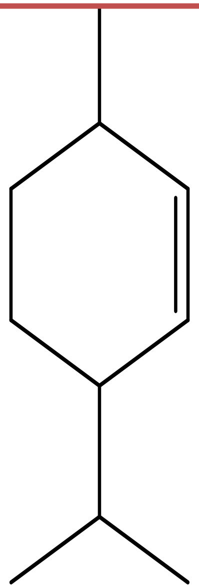
Nomenclature

The fully saturated compound p- methyl isopropylcyclohexane, hexahydro p-cymene or **p- menthane** $C_{10}H_{20}$ is used as parent substance.

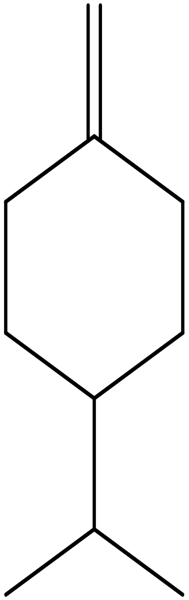




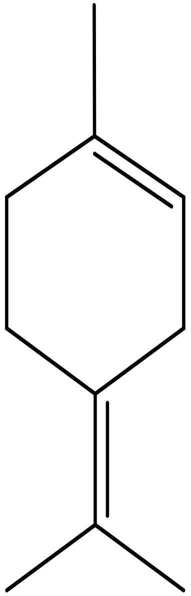
P-menthane



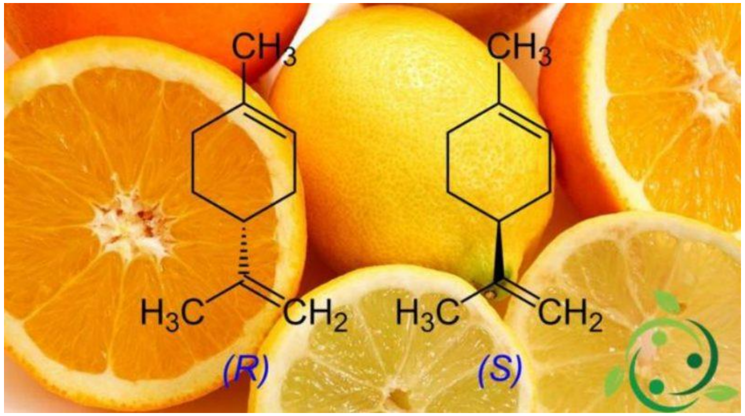
P-menthene-2
2-P-menthene
P-meth-2-ene

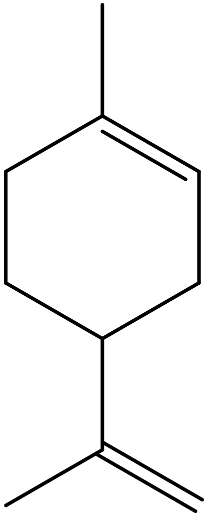


P-mentha-1(7) ene



P-meth-1,4(8)diene





Limonene

$C_{10}H_{16}$ الليـمونيـن

P-menth1,8(10)diene

Limonene

٨، ١ بارامينثادايين

Limonene is optically active, (+) form in lemon,orange oils (-)form in peppermint oil and racemic mixture(dipentene) in turpentine oil b.p 175-176°C

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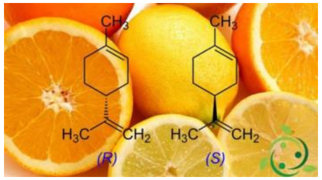
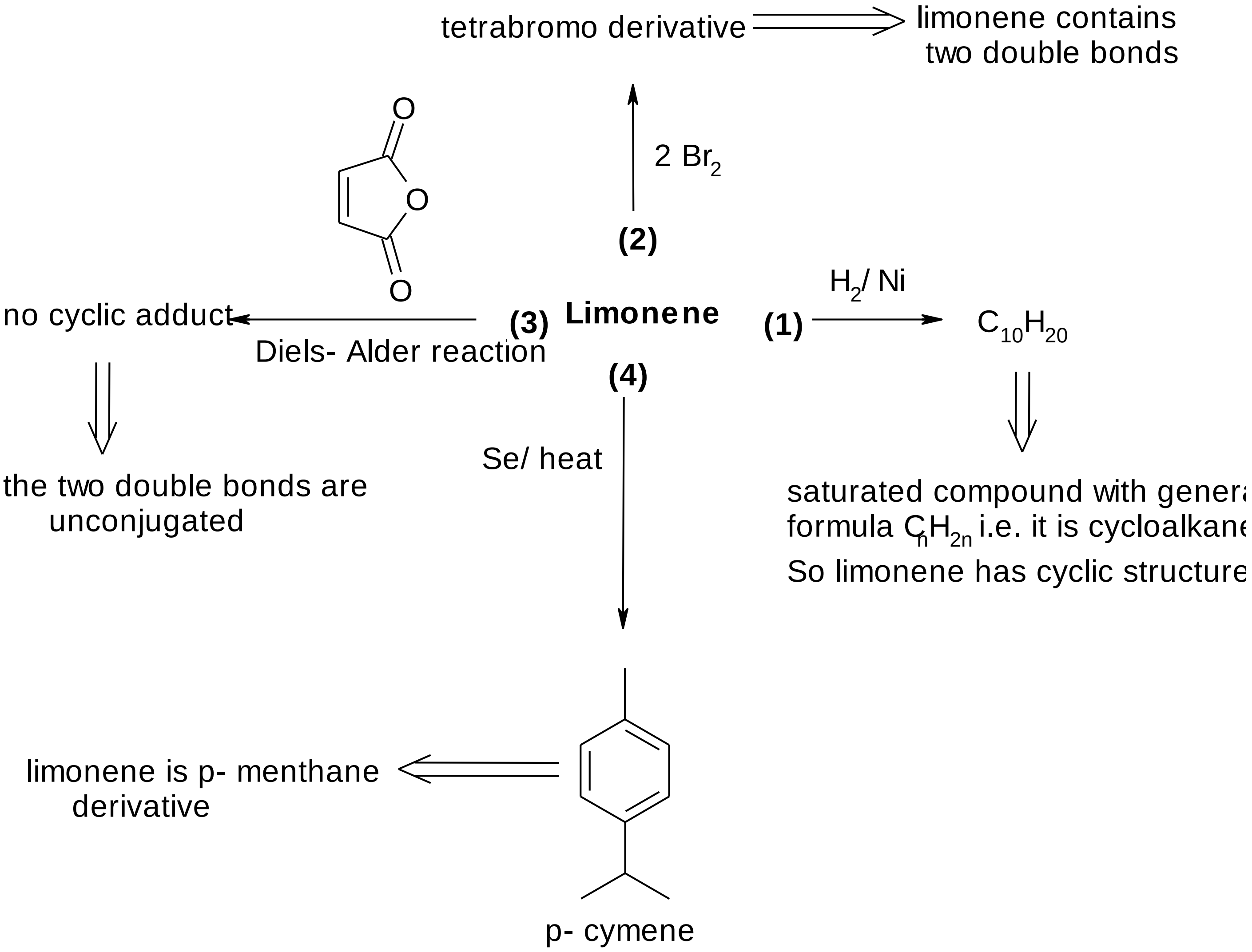


Structure of Limonene was supported by



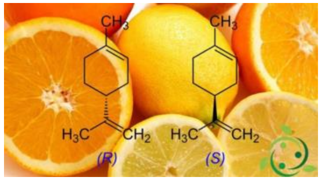
Limonene

(1) $\xrightarrow{H_2/\ Ni}$ $C_{10}H_{20}$ ⟹ saturated compound with genera formula C_nH_{2n} i.e. it is cycloalkan So limonene has cyclic structur

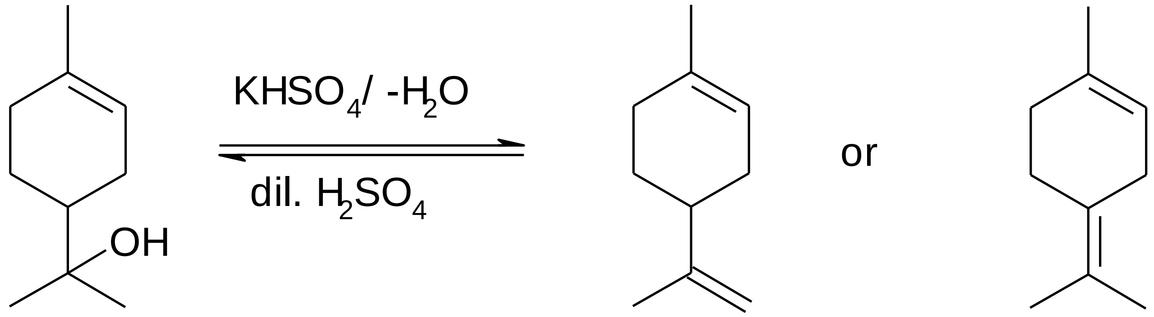
(2) $\xrightarrow{2\ Br_2}$ tetrabromo derivative ⟹ limonene contains two double bonds

(3) Diels- Alder reaction → no cyclic adduct ⟹ the two double bonds are unconjugated

(4) $\xrightarrow{Se/\ heat}$ p- cymene ⟹ limonene is p- menthane derivative



Structure of Limonene



α – terpineol

I

التركيب البنائي الصحيح
لليمونين لأنه نشط ضوئيا

II

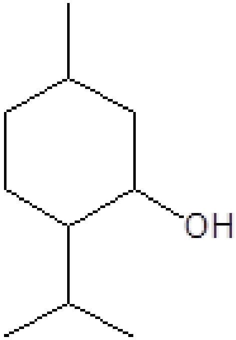
مستبعد لأنه تركيب بنائي
غير نشط ضوئيا

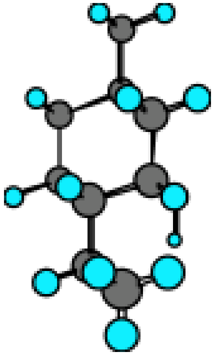
5-limonene may be prepared by dehydrating α- terpineol by using potassium hydrogen sulphate ($KHSO_4$) ,and on shaking with dilute sulphuric limonene may be converted to α- terpineol .

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**





المنثول
Menthol
$C_{10}H_{20}O$

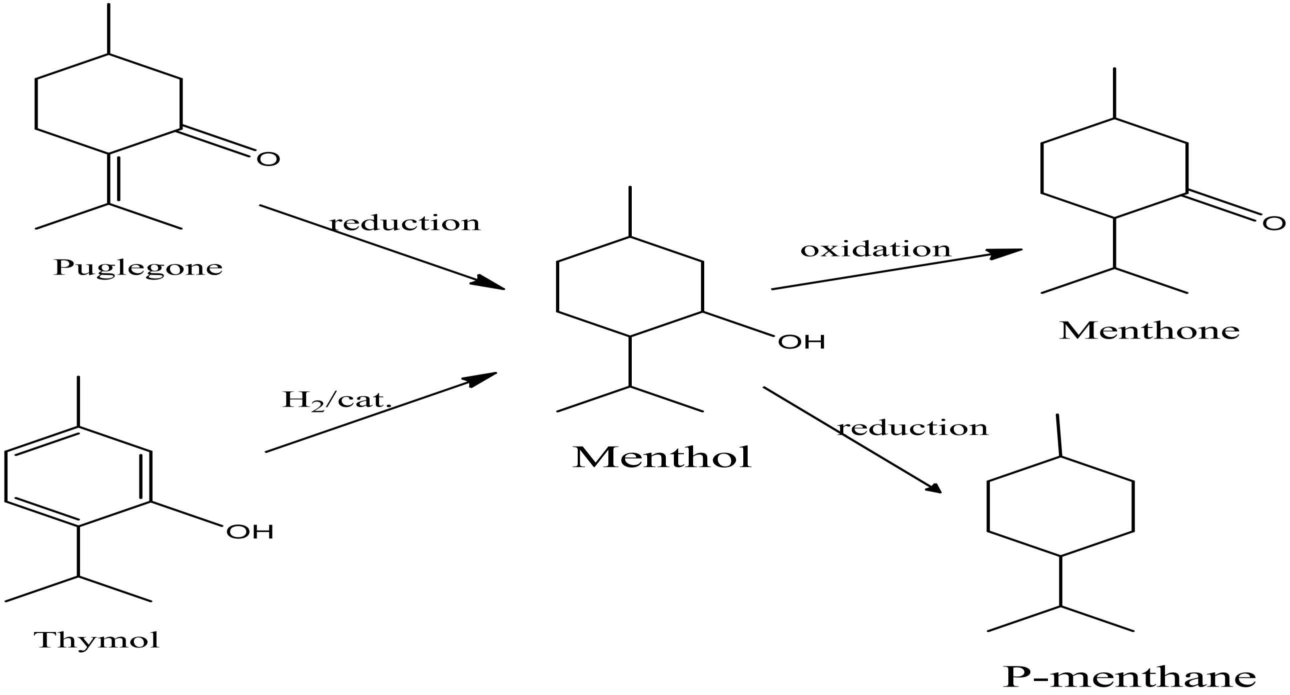
Menthol is optically active compound ,(-)form occurs in peppermint oil.

Menthol has medical uses :as anti-inflammatory ,analgesic, used in dental care as a topical antibacterial agent.

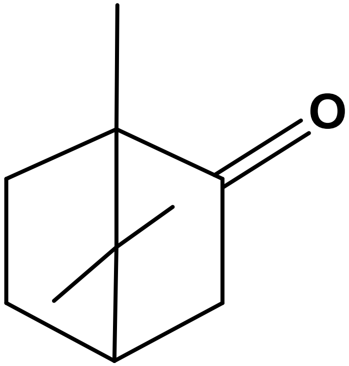
3-Hydroxy-4-Isopropyl-1-methyl cyclohexane , which is one of the most important monocyclic alcohols and contains three chiral carbon atoms (1,3,4), so that it can have eight enantiomers.

Structure of Menthol was supported by

1-It has been proven that molecular formula is $C_{10}H_{20}O$ and menthol is saturated compound .
2-The nature of oxygen atom is alcoholic (menthol forms ester).
3 -Oxidation of menthol gives menthone (a ketone)thus menthol is secondary alcohol.
4-Reduction using hydrogen iodide give p-menthane thus menthol contains this carbon skeleton.
5-Pulegone gives menthol on reduction .
6-Menthol can be synthesized by catalytic hydrogenation of thymol(3-hydroxy p-cymene)

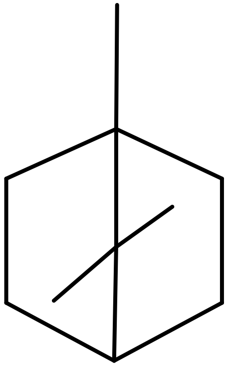


التربينات الأحادية ثنائية الحلقة
Bicyclic monoterpenoids



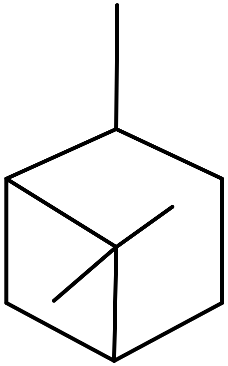
camphor

6+5



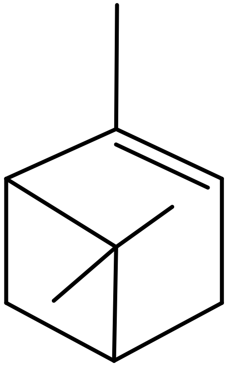
camphane
bornan

6+5



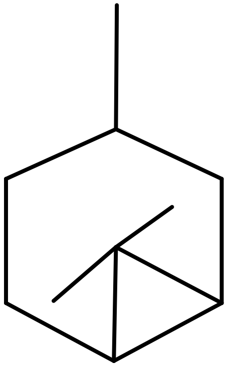
Pinane

6+4



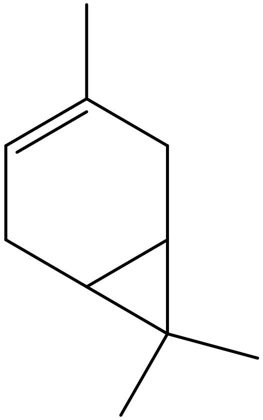
Pinene

6+4



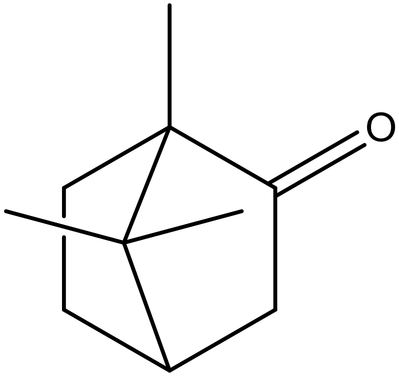
carane

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 .

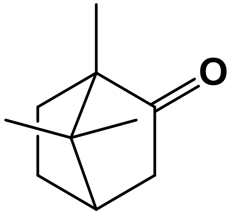
Camphor used in manufacture of cellulose as well as has many medical uses, including that it is used as a disinfectant and as a local anesthetic, and in the laboratories it is used as a solvent in experiments determining the molecular weight of organic compounds.

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



$\xrightarrow{Br_2}$ (-ve) does not contain double bond

$\xrightarrow{NH_2OH}$ Camphor oxime , camphor contains carbonyl group

$\xrightarrow{\text{Fehling reagent}}$ -ve the carbonyl is ketonic

$\xrightarrow{\text{clemensen reduction}}$ camphane$C_{10}H_{18}$

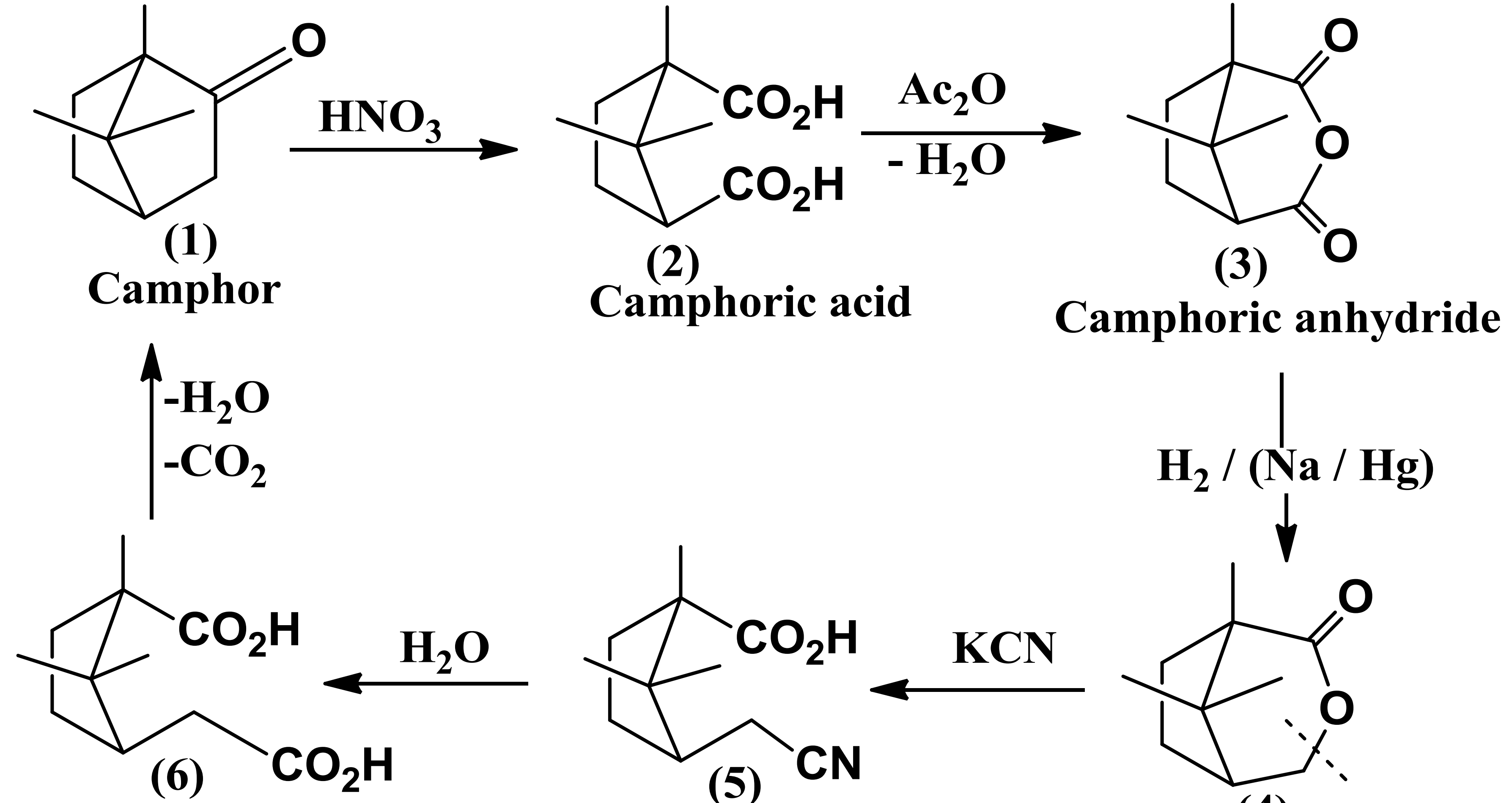
Camphor is bicyclic monoterpenoid

$\xrightarrow{\text{dist.}P_2O_5 \text{ or } ZnCl_2}$ P-cymene, one of the two rings is 6 membered ring

$\xrightarrow[\text{Oxid.}]{HNO_3}$ Camphoric acid $C_{10}H_{16}O_4$

$\xrightarrow{\text{benzaldehyde phCHO}}$ monobenzylidene derivative contains (-CO-CH2-)

Structure of Camphor



(1) Camphor

(2) Camphoric acid

(3) Camphoric anhydride

(4) Campholide

(5) Homocamphoric nitrile

(6) Homocamphoric acid

جامعة جنوب الوادي

كلية العلوم بقنا

النواتج الطبيـــعية

التربينات النصف ثلاثية والثنائية والرباعية والعديدة

Sesquiterpenoids,diterpenoids ,tetraterpenoidand poly terpenoids

د /عواطف محمد المغربي
قسم الكيمياء – كلية العلوم

التربينات النصف ثلاثيــة (السيسكوتربينات) Sesquiterpenoids

The sesquiterpenoids are naturally occuring compounds containing fifteen carbon atoms, in general they form the higher boiling point fraction of the essential oils and may be acyclic or cyclic hydrocarbons ,alcohols , ketones or lactones ,the sesquiterpenoids structure is built up from three isoprene units but there are some exceptions.

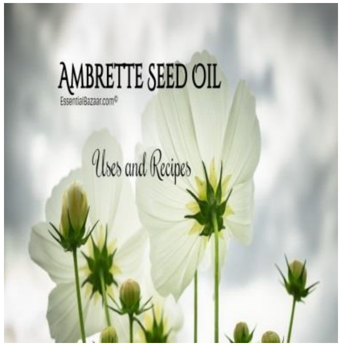
The sesquiterpenoids are classified into four groups :

1-Acyclic sesquiterpenoids contain four double bonds (farnesene) .

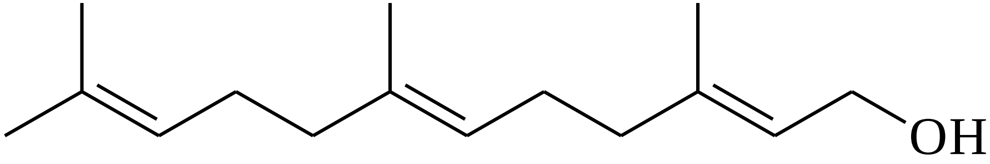
2-Monocyclic sesquiterpenoids contain three double bonds (zingiberene from ginger oil) .

3-Bicyclic sesquiterpenoids contain two double bonds (selinene occurs in celery oil).

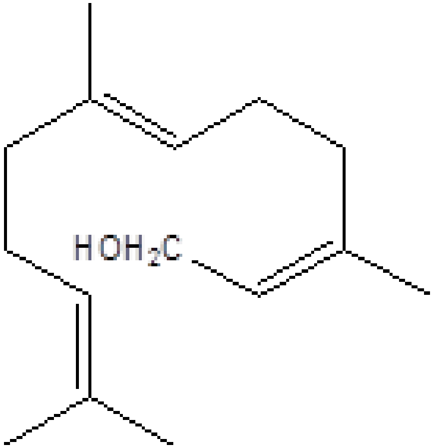
4-Tricyclic sesquiterpenoids contain one double bond (cedrol in sedar wood oil) .



($C_{15}H_{26}O$)Farnesol الفارنيسول



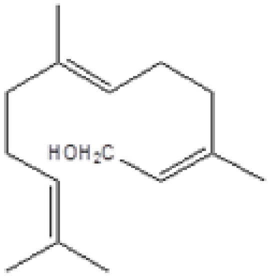
Farnesol
occurs in oil of ambrette seeds



Farnesol considered acyclic sesquiterpenoid contains 15 carbon atom and the carbon skeleton can be formed by the union of three isoprene units.

Farnesol is a primary alcohol ,it is used in perfume manufacture and it occurs in ambrette seeds.

الفارنيسول($C_{15}H_{26}O$)Farnesol
Determination of structure



Farnesol

catalytic hydrogenation

$3H_2$

(+ve) saturated alcohol Hexahydro - farnesol thus it contains 3 double bond

maleic anhydride

(-ve) the double bonds are unconjugated

Analysis

Molecular Formula $C_{15}H_{26}O$

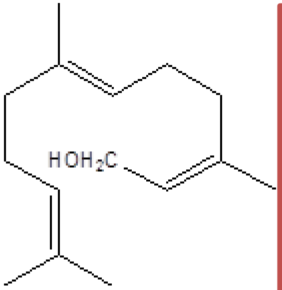
Oxidation

chromic acid

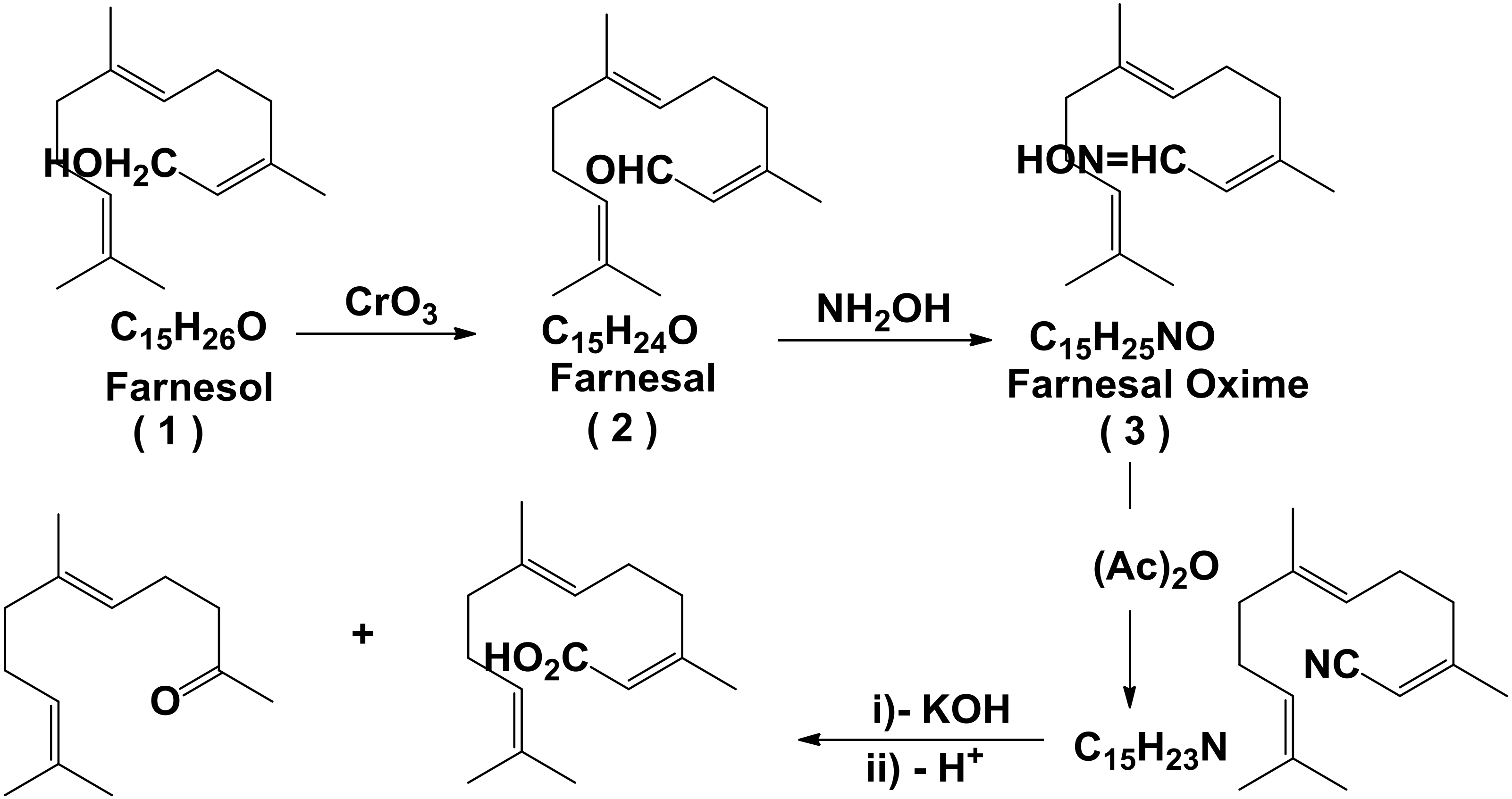
Farnesal $C_{15}H_{24}O$, farnesol is primary alcohol

Ozonolysis

acetone+2mole of Laevulaldehyde +glycolaldehyde



($C_{15}H_{26}O$)Farnesol Determination of structure



$C_{15}H_{26}O$
Farnesol
(1)

$\xrightarrow{CrO_3}$

$C_{15}H_{24}O$
Farnesal
(2)

$\xrightarrow{NH_2OH}$

$C_{15}H_{25}NO$
Farnesal Oxime
(3)

$(Ac)_2O$

$C_{15}H_{23}N$
farnesal cyanide
(4)

i)- KOH
ii) - H^+

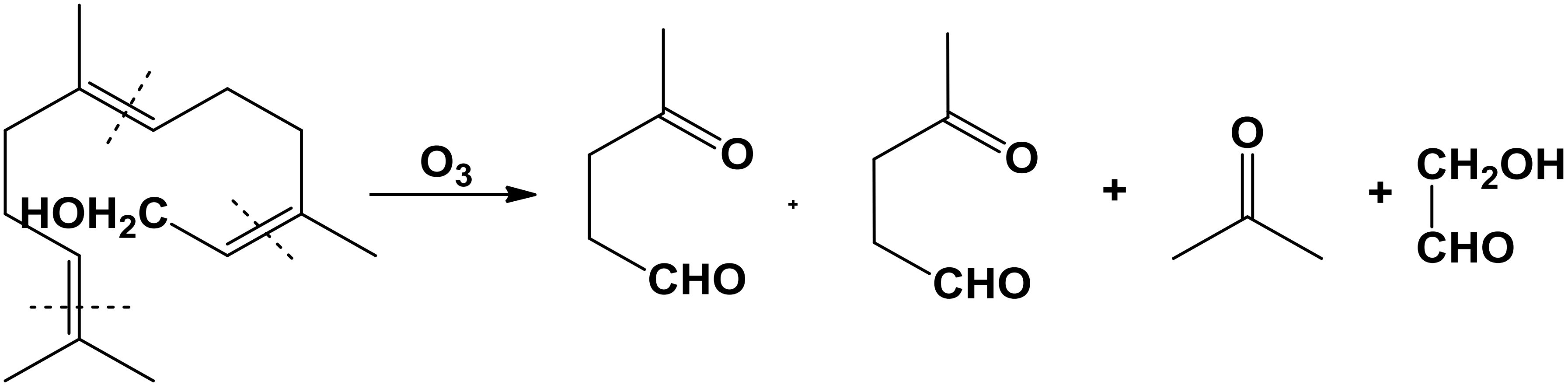
Farnesenic acid
(5)

+

Geranylacetone
(6)

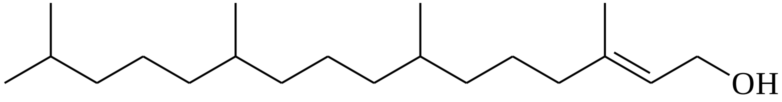
$C_{15}H_{26}O$ Farnesol

Determination of structure

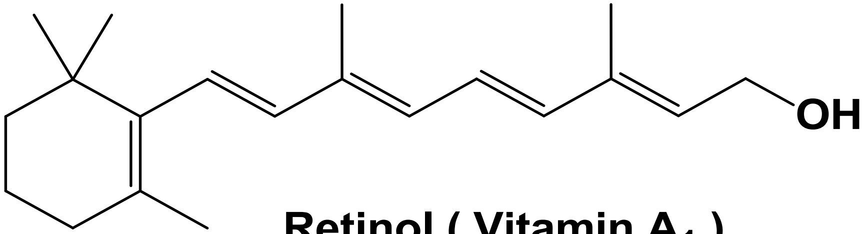


التربينات الثنائية (الداي تربينات)
Diterpenoids

The diterpenoids are naturally occurring compounds containing 20 carbon atoms and four isoprene units ,which distributed in plants kingdom. Diterpenoids are classified on the basis of the number of carbon ring present into acyclic (phytol) monocyclic (vitaminA1and vitaminA2) , dicyclic, tricyclic and tetracyclic diterpenoid .

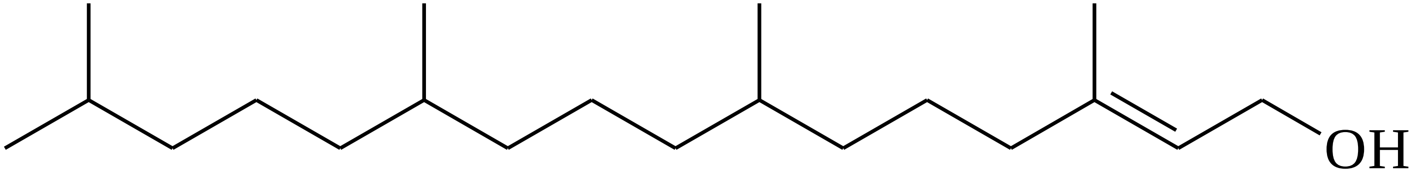


Phytol
is produced from hydrolysis of chlorophyll



Retinol (Vitamin A_1)

Phytol $C_{20}H_{40}O$



Phytol
is produced from hydrolysis of chlorophyll

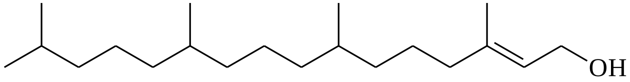
Phytol is an acyclic diterpenoid ,it is produced from hydrolysis of chlorophyll , and it forms a part of the molecules of vitamins E and K .

Determination of the structure

1-General reactions and analysis showed that molecular formula is $C_{20}H_{40}O$ and it is a primary alcohol .

2-On catalytic hydrogenation it forms dihydrophytol **$C_{20}H_{42}O$** so phytol is acyclic diterpenoid and contains one double bond.

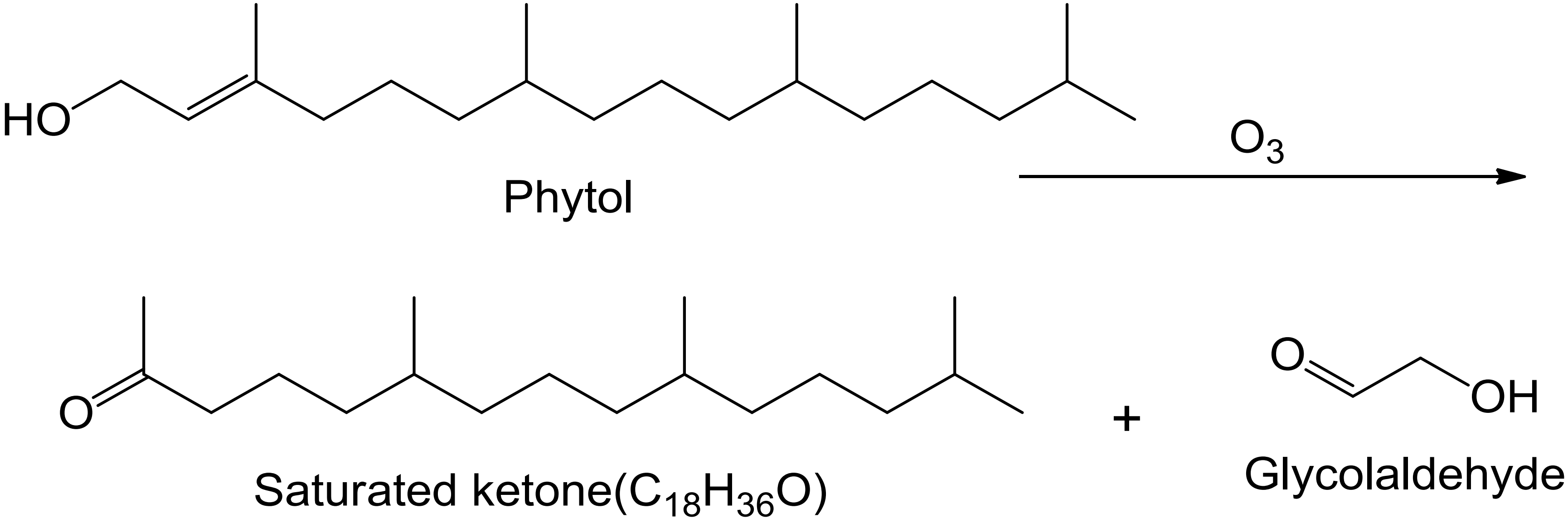
Phytol $C_{20}H_{40}O$
Determination of the structure



Phytol
is produced from hydrolysis of chlorophyll

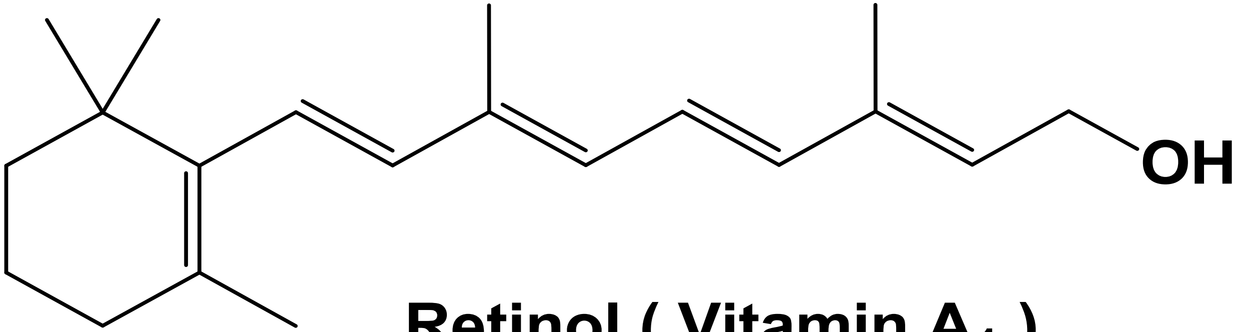
3-Ozonolysis of phytol gives glycol aldehyde and a saturated ketone $C_{18}H_{36}O$.

4-Phytol contains four isoprene units connected (head-tail).



Monocyclic Diterpenoids

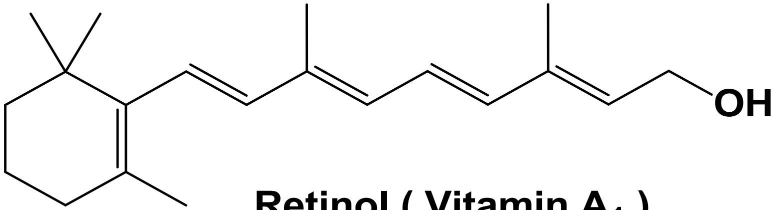
Retinol VitaminA$_1$ ($C_{20}H_{30}O$)



Retinol (Vitamin A$_1$)

- Retinol or Vitamin **A$_1$** is a monocyclic diterpenoid occurs in many flowers and carrots as a β-carotene which converted into vitamin A$_1$ by hydrolysis .
- Retinol occurs free and as esters in fats in fish liver and in blood,it was originally isolated as viscous yellow oil ,but later it was obtained as crystalline solid .
- Vitamin **A$_1$** is estimated by the blue color reaction it gives with a solution of antimony trichloride in chloroform .
- Vitamin **A$_1$** influences growth in animals and increased the resistance to disease . ***Night blindness*** is due to Vitamin **A$_1$** deficiency .

($C_{20}H_{30}O$) Retinol VitaminA_1



Retinol (Vitamin A_1)

Structure of Retinol was supported by

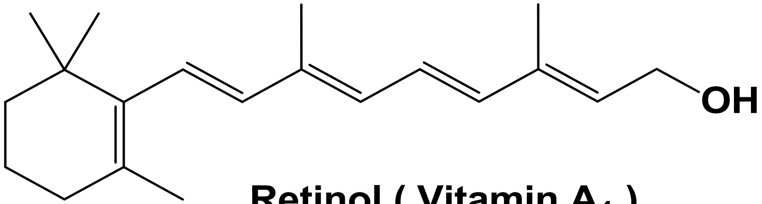
1-Routine tests confirmed that M. F **$C_{20}H_{30}O$** and it is a primary alcohol since mild oxidation it yields the corresponding aldehyde retinal **$C_{20}H_{28}O$.**

2-Catalytic hydrogenation converts it into perhydro vitamin A_1

$C_{20}H_{40}O$ thus it contains five double bond and vitamin A_1 must be monocyclic.

3-Ultra violet absorption measurements show the presence of conjugation, so it is a conjugated polyene alcohol .

Retinol VitaminA$_1$ ($C_{20}H_{30}O$)

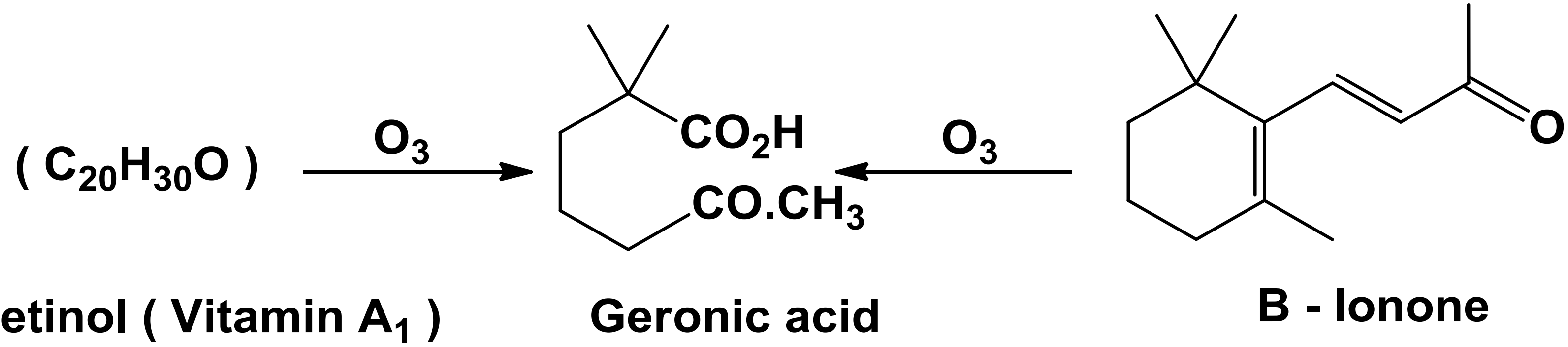


Retinol (Vitamin A$_1$)

4-Ozonolysis of retinol afforded one molecules of geronic acid which was isolated also from oxidative degradation of β-ionone nucleus .

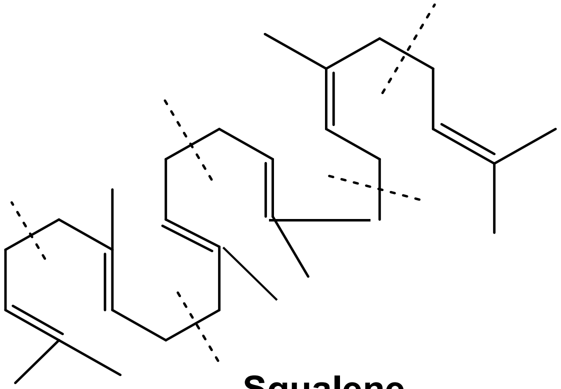
5-Application of isoprene rule led to confirmation of carbon skeleton .

6- The structure of retinol also can be confirmed by using β-ionone as a starting material in synthesis .

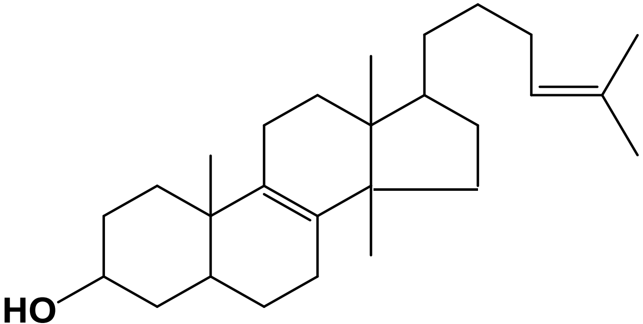


Triterpenoids
التربينات الثلاثية

- Triterpenoid compounds are widely distributed in nature mainly in plants where they found in resins and plant saps in the free state and as esters . A few have been found in animal sources as in the liver oils of certain fish .
- Triterpenoids contain 30 carbon atom and most of them have carbon skeleton which may be built up by the union of six isoprene units , they may be acyclic or cyclic.
- Squalene is acyclic triterpenoid occurs in the fraction of liver oil and also in various plant sources and it is an intermediate in the biosynthesis of cholesterol from acetic acid .
- Lanosterol is a very important tetracyclic triterpenoid which contains the steroid carbon skeleton.



Squalene



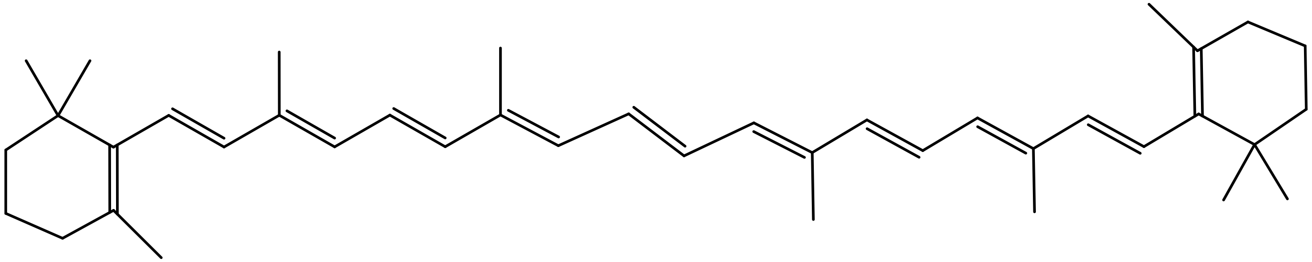
Lanosterol

Tetraterpenoids
التربينات الرباعية (التترا تربينات)

1- The tetraterpenoids more commonly referred to as the carotenoids , are compounds containing eight isoprene units and 40 carbon atoms , constitute a group of natural pigments which are widely distributed in plants and animals.

2- A characteristic reaction shown by carotenoids is the formation of deep blue color with antimony trichloride in chloroform solution .

3- β-Carotene was isolated from carrots and M.F **$C_{40}H_{56}$** , and isolated by extraction with light petroleum .



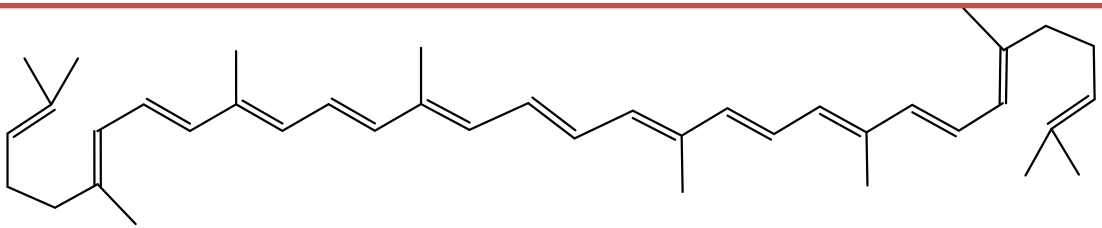
B - Carotene

التربينات الرباعية (التترا تربينات) الكاروتينات
(Carotenoids) Tetraterpenoids

4- Lycopene is a carotenoid that is the red tomato pigment .

5-Lycopene is considered the acyclic isomer of β-Carotene and β-Carotene shows vitamin A activity owing to the fact that it is converted into vitamin A in animal blood .

6—Carotenoids are polyenes , most of them the central portion of the molecules is composed of long conjugated chain comprised of 8 isoprene unites , the center two of which are joined tail to tail .

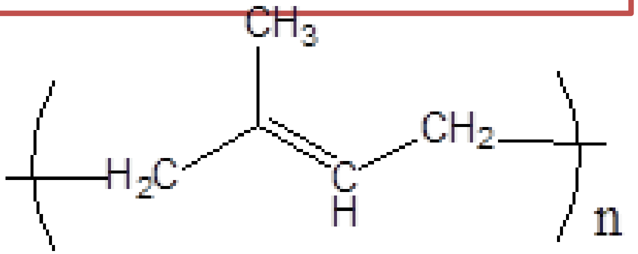


Lycopene $C_{40}H_{56}$

Poly terpenes- التربينات العديدة Rubber

- Poly terpenoids consist of several units of isoprene connected together in large chains .
- Natural rubber is the most important example ,rubber is obtained from latex which is an emulsion of rubber particles with water , it is obtained from the inner bark of many types of trees which grow in the tropic and sub tropics .
- Addition of acetic acid coagulate the rubber which is separate from the liquor either pressed into blocks or rolled into sheets finally dried in a current of warm air
- Crude latex rubber contains in addition to the actual rubber hydrocarbon , proteins, sugar, fatty acids and resins the amount of these substance depends on the source .

Poly terpenes-Rubber



Structure of natural rubber

1-The destructive distillation of rubber gives isoprene as one of the main products thus rubber is a polymer of isoprene and molecular formula **$(C_5H_8)_n$.**

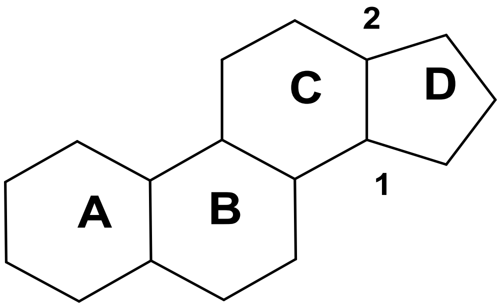
2-Rubber is unsaturated hydrocarbon , on catalytic hydrogenation at high temperature and pressure ,the product is ***hydro rubber which*** is an elastic solid which is fully saturated and resistant to oxidation.

3-Rubber reacts with hydrogen chloride or hydrogen bromide to give rubber hydrochloride or rubber hydrobromide formed by the addition of hydrogen halide to the double bonds ***(Markwnikoff) .***

Natural Products
Steroids

Dr. Awatef Mohamed El-maghraby
Chemistry Department
Faculty of Science
South Valley University

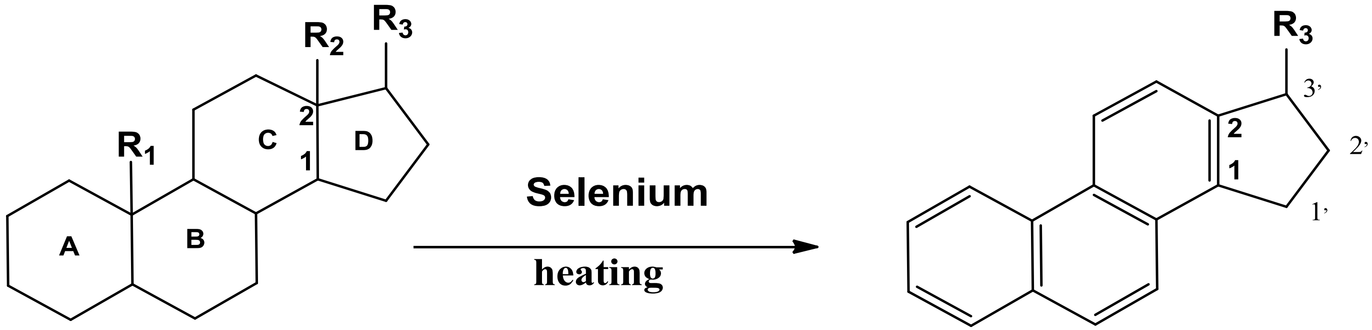
Steroids



Perhydro-1,2-cyclopentanophenanthrene

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 .



Steroid

R_3=Me (Diels hydrocarbon)

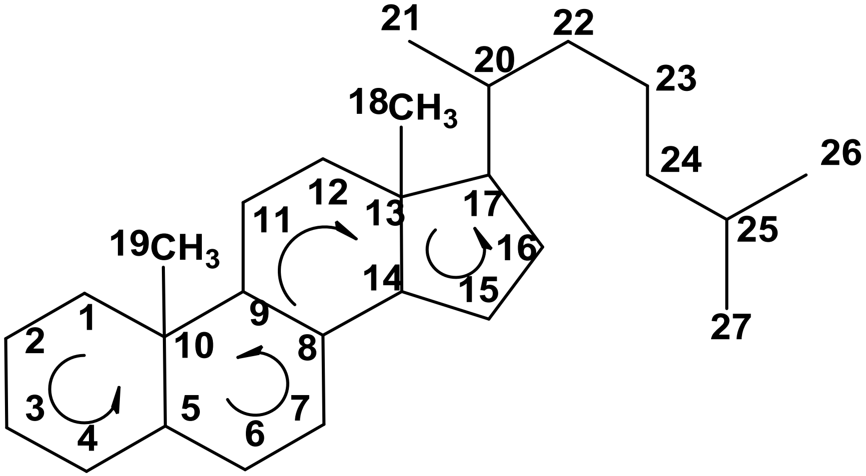
3'-methyl-1:2-cyclopentenophenanthrene

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)

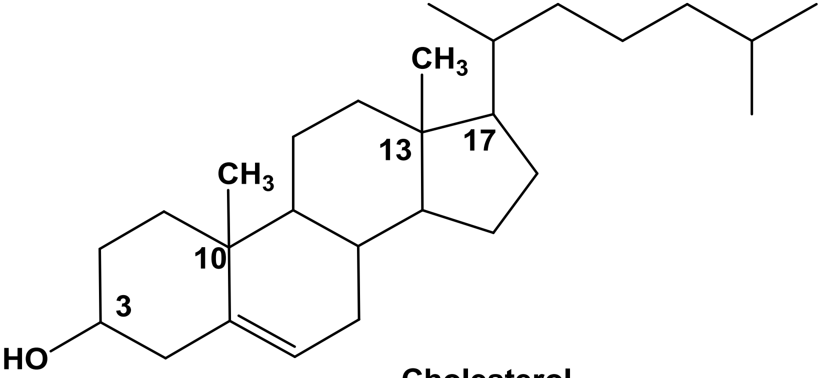
6-Cardiotonic glycosides

7- Saponins and Sapogenins

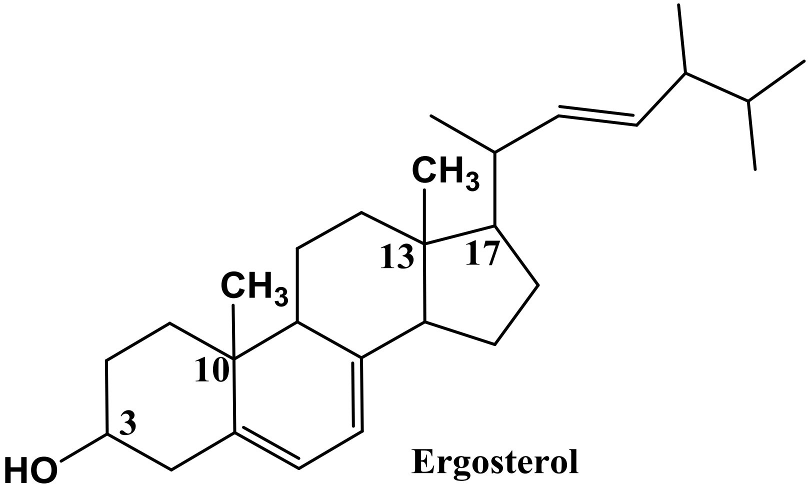
Sterols

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

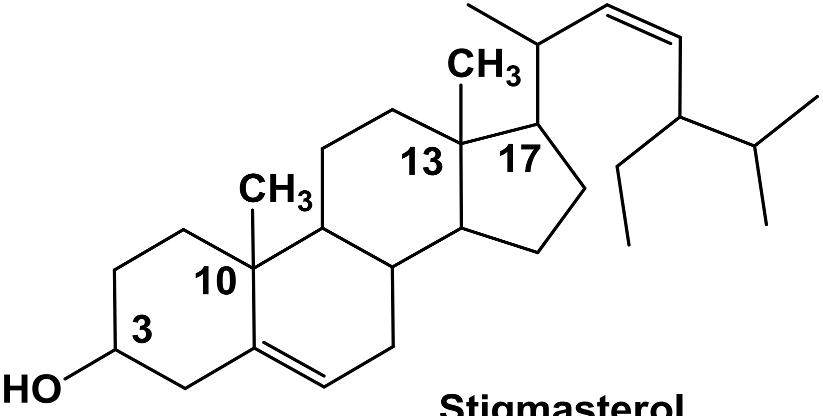
Sterols may be classified on the basis of occurrence as Zoo sterols(animal), Phytosterol (plants), mycosterol (yeast and fungi) and marine sterols(sponges).



Cholesterol
Zoo sterol

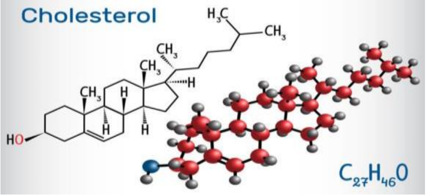


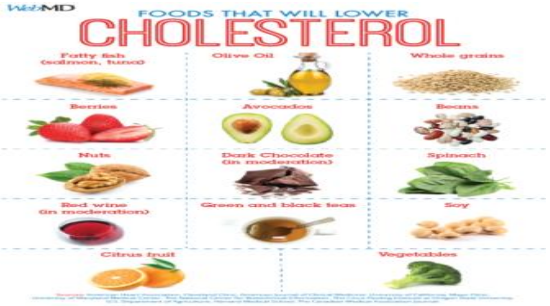
Ergosterol
mycosterol
occurs in yeast

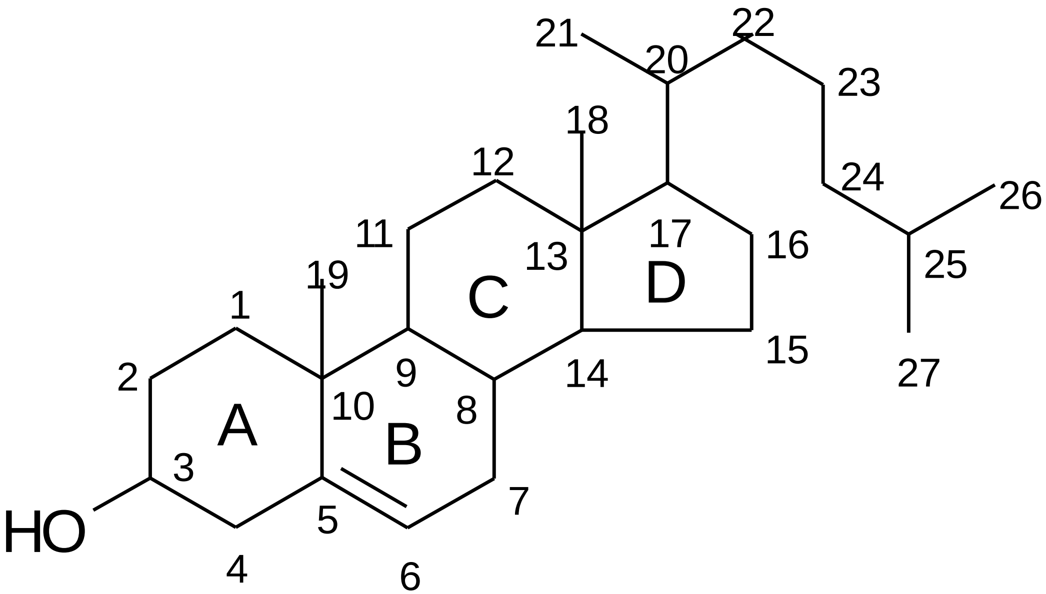


Stigmasterol
Phytosterol
obtained from soya
bean oil

كوليسترولCholesterol







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).

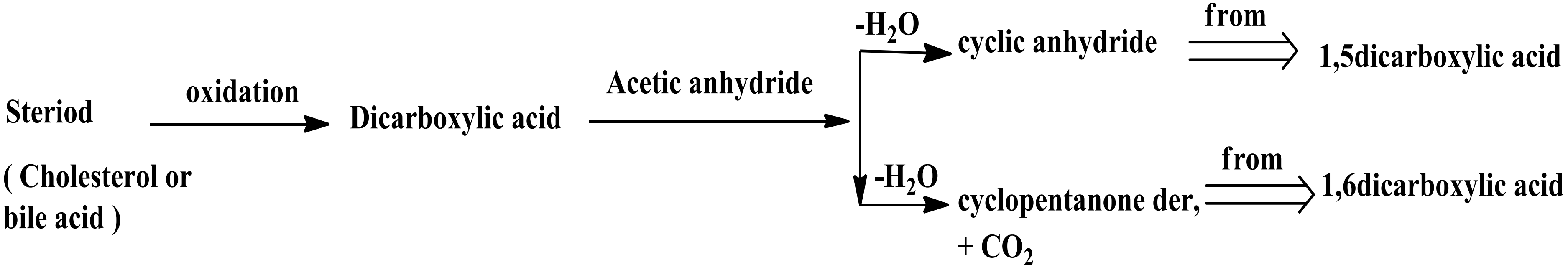
3- There are two angular methyl groups at C-10 and C-13, and a saturated side-chain C_8H_{17} at C-17.

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)

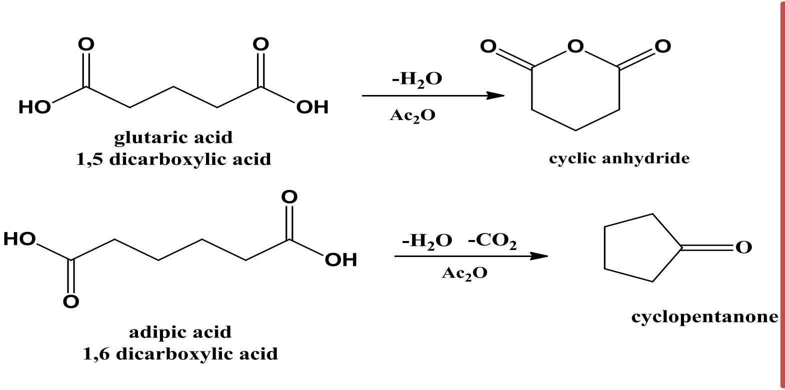
oxidation

Dicarboxylic acid

Acetic anhydride

$-H_2O$ cyclic anhydride from 1,5dicarboxylic acid

$-H_2O$ cyclopentanone der, $+ CO_2$ from 1,6dicarboxylic acid

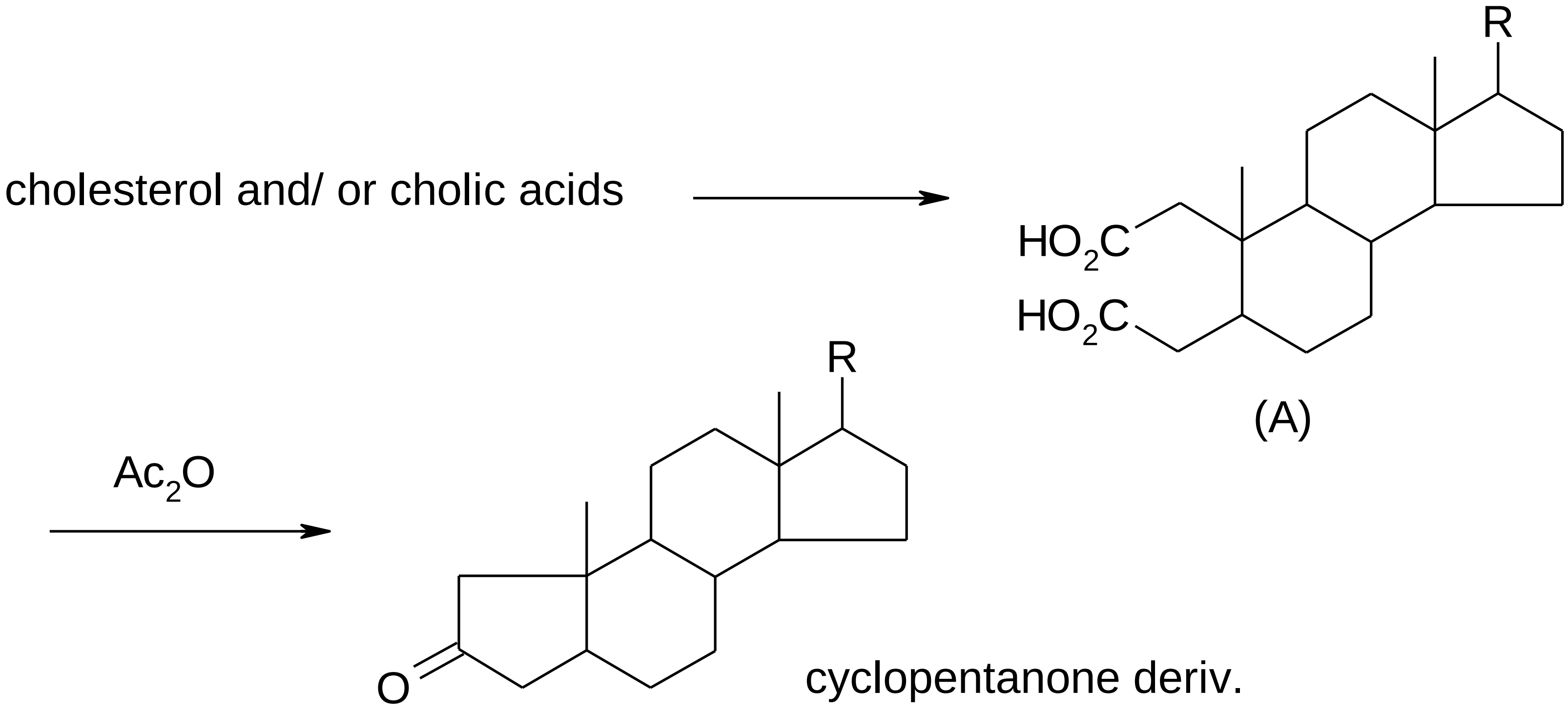


كل الستيرويدات تتكون من هيكل كربوني رباعي الحلقة (سيكلوبنتان بير هيدرو فينانثرين) وهذا تم اثباته عند تسخين الستيرويد مع السيلينيوم ليعطي مشتق سيكلوبنتينوفينانثرين .

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.

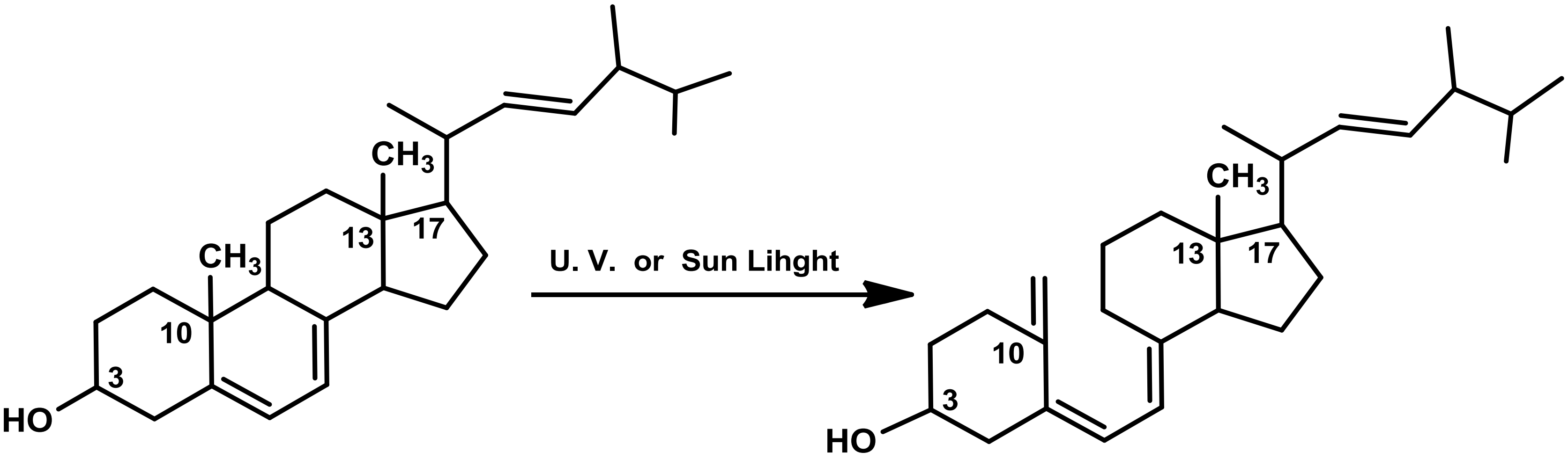
Determination of ring A in cholesterol and cholic acid



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).

Ergocalciferol
Vitamin D2

Conversion of Ergosterol into VitaminD_2

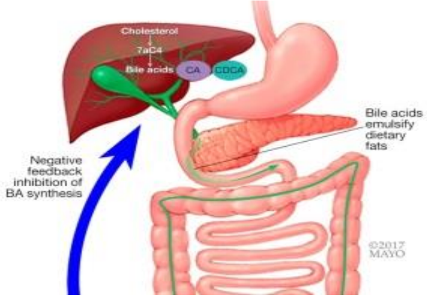


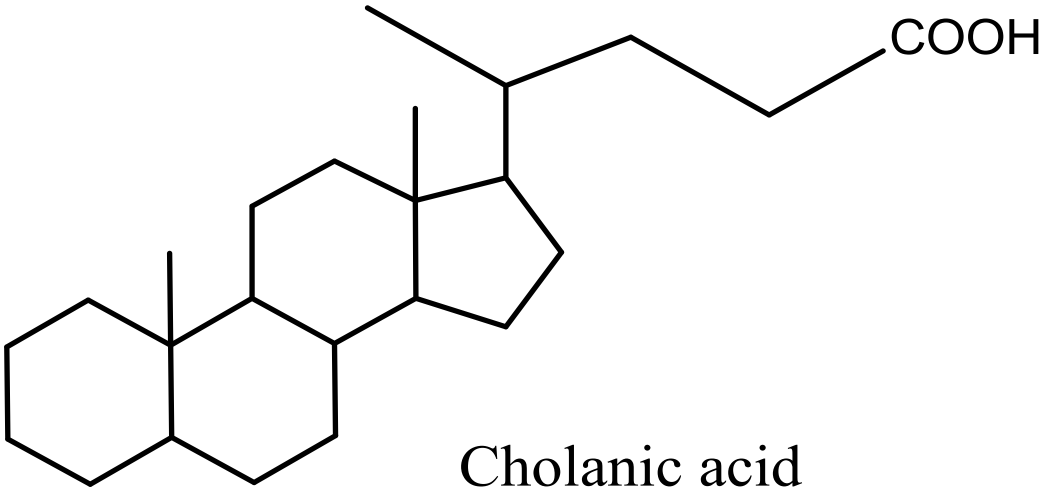
Ergosterol

Vitamin D_2

Vitamin D is anthracitic vitamin They are about seven compounds (Vitamin D1 - D7) with the ring B being opened. Vitamin D2 (or calciferol) is formed from ergosterol by the sunlight irradiation

Bile acids

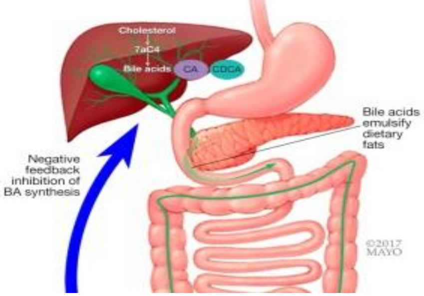


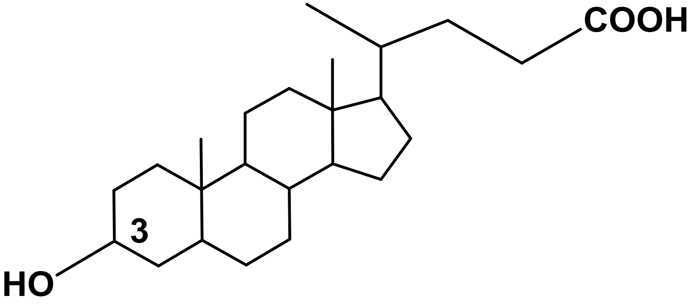


Cholanic acid

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.

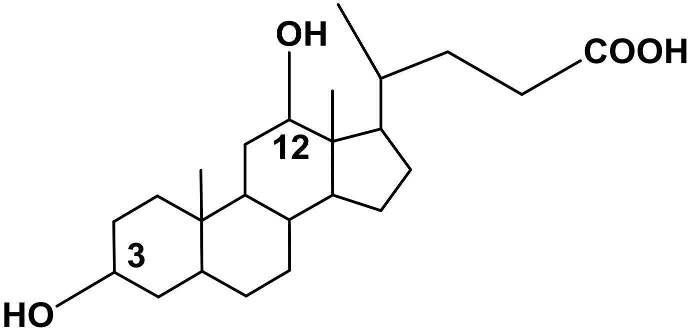
Bile acids





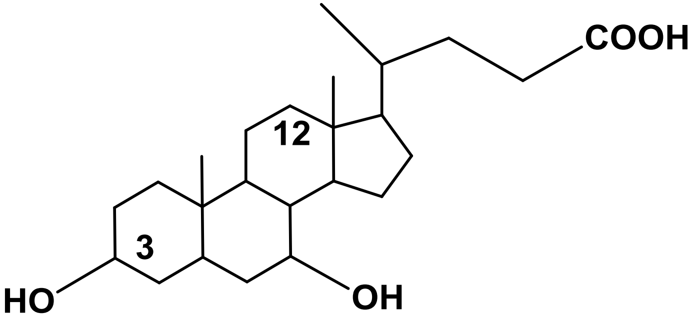
3-Hyrdroxycholanic acid

Lithocholic acid



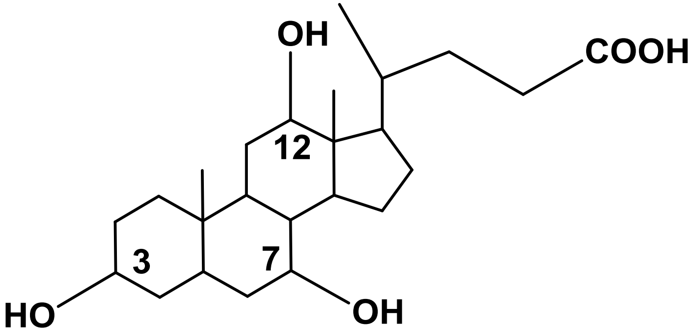
3,12-dihyrdroxycholanic acid

Deoxycholic acid



3,7-Dihyrdroxycholanic acid

Chenodeoxycholic acid

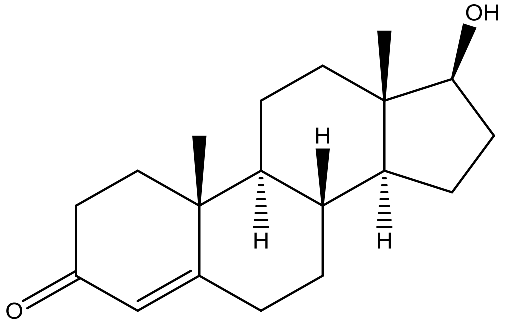


3,7,12-Trihyrdroxycholanic acid

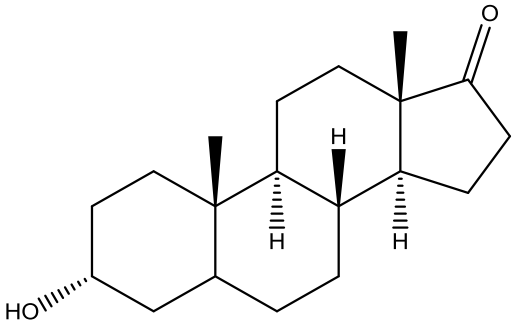
Cholic acid

Sex Hormones

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

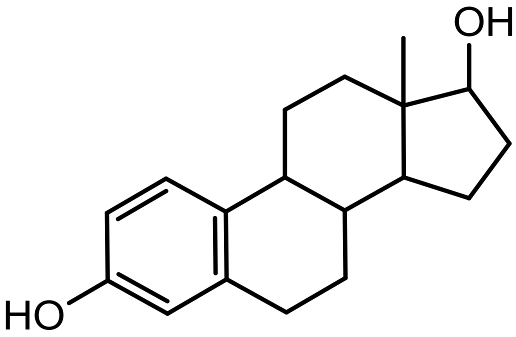


Testosterone

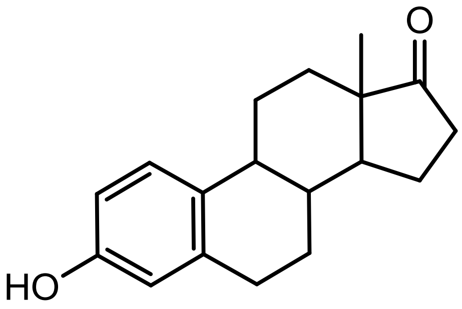


Androsterone

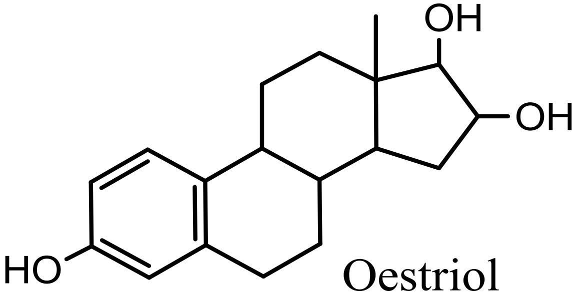
2-Oestrogens (Female Hormones)



Oestradiol



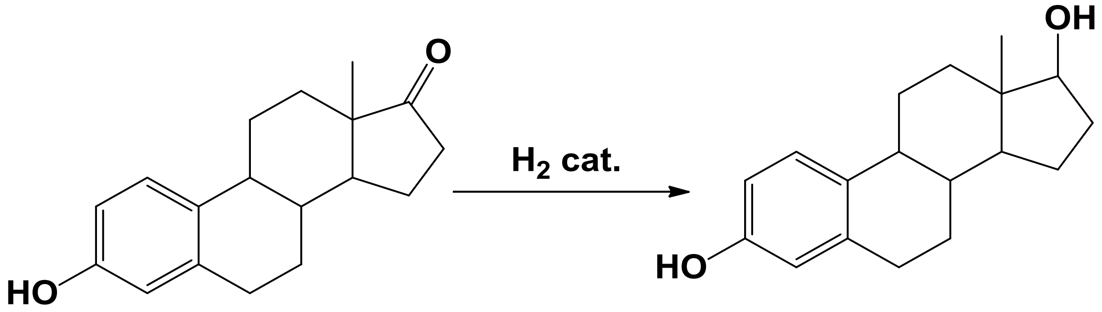
Oestrione



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)

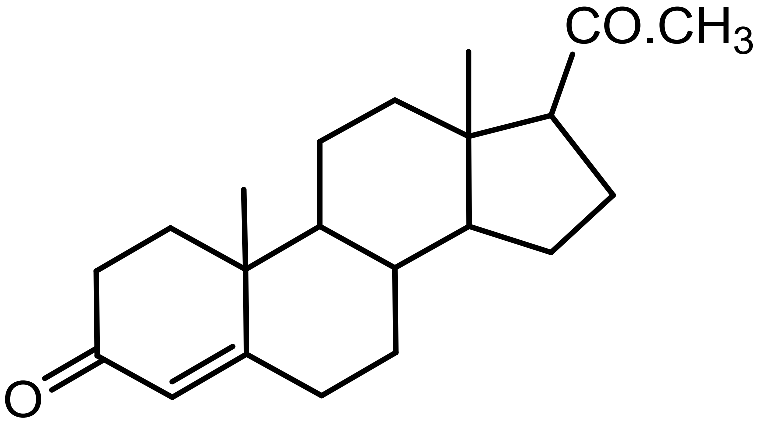


Oestrone

Oestradiol

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

3- (Gestogens)
Progesterone


Progesterone

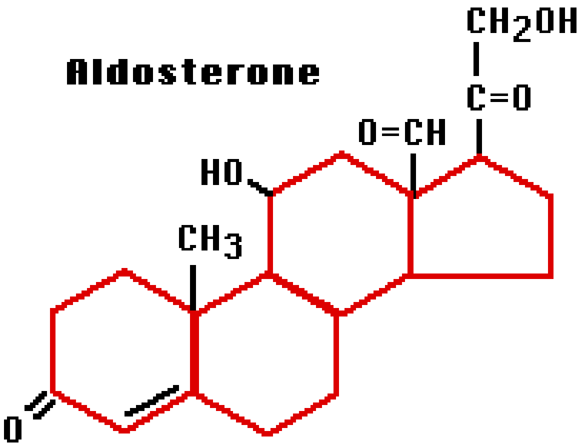
These are essential hormones which responsible for pregnancy.

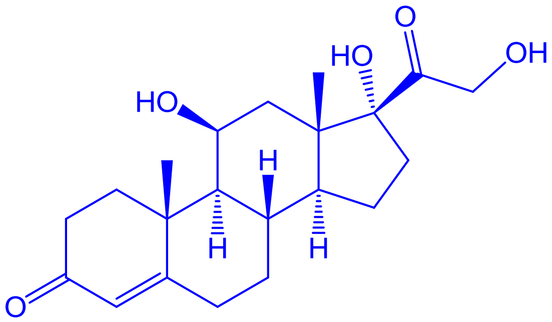
Progesterone is α,β-unsaturated ketone and synthesized from both D.E.A and Ergosterol .

Adrenocortical hormones

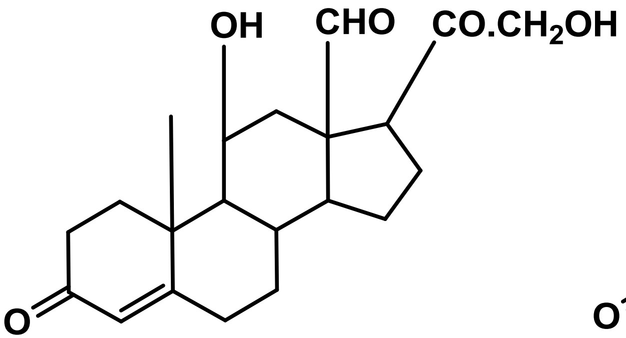
They are produced by the cortex of the adrenal glands ,their main functions are the control of carbohydrate and protein metabolism and control of balance of water and electrolytes.

Cortisone is also used in the treatment of allergies and immune diseases.

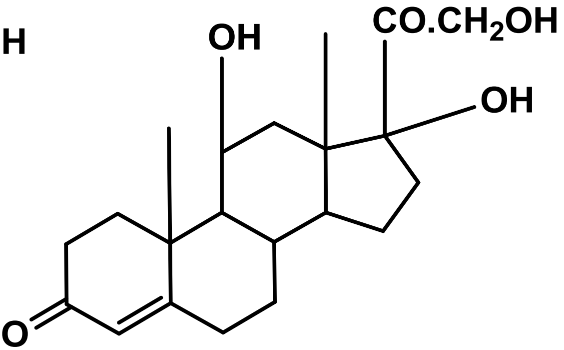




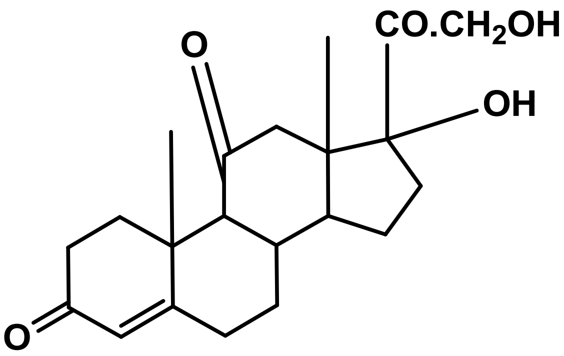
cortisol (stress hormone)



Aldosterone



Cortisol



Cortisone

References

1- I.L.FINAR Organic Chemistry VOL2