



B.Sc. Third Year V Semester

CHEMISTRY

Paper XII [Organic + Inorganic]

Organic Chemistry



ALKALOIDS



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ALKALOIDS

Origin, History & Introduction

- ❑ The term ‘**alkaloids**’ (alkali-like) is commonly used to designate basic heterocyclic nitrogenous compounds of plant origin that are physiologically active.
- ❑ The term alkaloids, **Pflanzenkalein** was coined by **Meissner**, a German pharmacist in 1819.
- ❑ The mankind has been using alkaloids for various purposes like *poisons, medicines, poultices, teas etc.* The French chemist, **Derosne** in 1803, isolated **Narcotine**.
- ❑ **Konigs (1880)** : Firstly all organic bases isolated from plant naturally occurring organic bases contain pyridine ring.
- ❑ **Ladenberg** : Natural occurring plant compound having one nitrogen atom in heterocyclic ring.
- ❑ **Robinson & Skarup**: Basic compounds of plant origin in which at least one nitrogen atom forms part of cyclic compound & have physiologically active.
- ❑ **Alkaloids = Alkali like substances (combine with acid & neutralized forming a salt)**

Definitions: The term “alkaloid” (alkali-like) is commonly used to designate basic heterocyclic nitrogenous compounds of plant origin that are physiologically active. **OR**

Alkaloids are cyclic organic compounds containing nitrogen in a negative state of oxidation with limited distribution among living organisms. **OR**

Alkaloids are applied to basic nitrogen plant product mostly optically active possessing nitrogen heterocyclic as their structural units with a pronounced psychological (therapeutic) action derived from amino acid.

EX. Morphine, quinine, strychnine, ephedrine, nicotine, cocaine etc.

Whole alkaloids are poisonous, but used medicinally in very small quantity.

Many of them possess curative properties of great value in medicine.

❑ Distribution and Occurrence:

- Rare in lower plants.
- Dicots are more rich in alkaloids than Monocots.
- Families rich in Alkaloids: Apocynaceae, Rubiaceae, Solanaceae, Papaveraceae.
- Families free from Alkaloids: Rosaceae, Labiatae



❑ Distribution in Plant:

- All Parts e.g. Datura.
- Barks e.g. Cinchona
- Seeds e.g. Nux vomica
- Roots e.g. Aconite
- Fruits e.g. Black pepper
- Leaves e.g. Tobacco
- Latex e.g. Opium





Classification



- **True (Typical) alkaloids** that are derived from amino acids and have nitrogen in a heterocyclic ring. e.g Atropine
- **Protoalkaloids** that are derived from amino acids and do not have nitrogen in a heterocyclic ring. e.g Ephedrine
- **Pseudo alkaloids** that are not derived from amino acids but have nitrogen in a heterocyclic ring. e.g Caffeine
- **False alkaloids** are non alkaloids give false positive reaction with alkaloidal reagents.


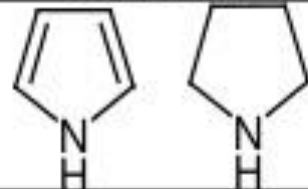

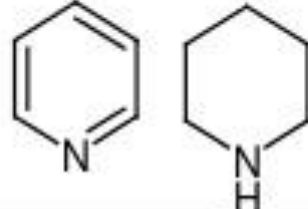

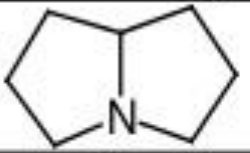



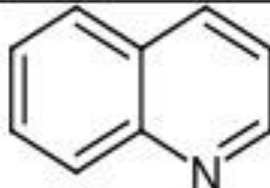

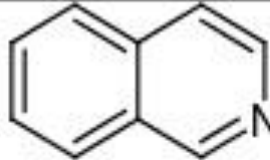


Classification of Alkaloids

Chemical Classification

A) True alkaloids

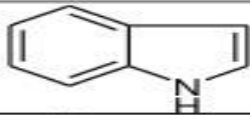


Sr. no.	Type	Structure	Examples
1.	Pyrrole and pyrrolidine 		e.g. Hygrine, coca species
	Pyridine and piperidine 		e.g. Arecoline, anabesine, lobeline, conine, trigonelline
	Pyrrolizidine 		e.g. Echimidine, senecionine, seneciphylline
	Tropane 		e.g. Atropine, hyoscyne, hyoscyamine, cocaine, pseudopelletirine
5.	Quinoline 		e.g. Quinine, quinidine, cinchonine, cupreine, camptothecine
6.	Isoquinoline 		e.g. Morphine, codeine, emetine, cephaline, narcotine, narceine, d-tubocurarine





Indole



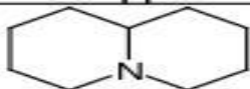
e.g. Erotamine, ergotametriene, reserpine, vincristine, vinblastine, strychnine, brucine

Imidazole



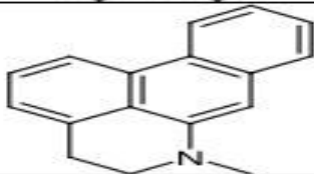
e.g. Pilocarpine, isopilocarpine, pilosine

Norlupinane



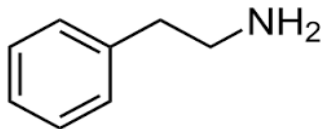
e.g. Cystisine, laburinine

Piporphine (reduced isoquinoline naphthalene)

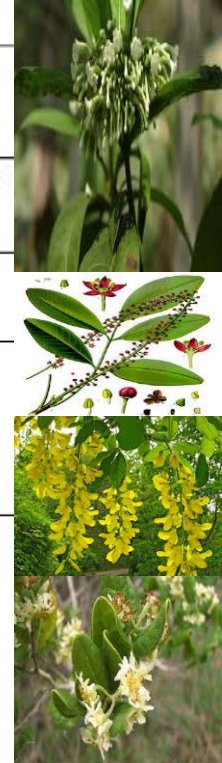


e.g. Boldine

Phenyl ethyl Amine

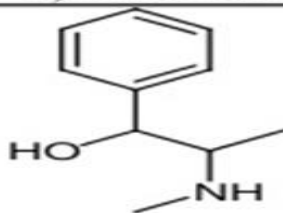


e.g. adrenaline
ephedrine
2-phenyl ethyl amine



B) PROTOALKALOID

1. Alkylamine

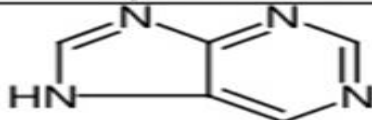


Ephedrine, Pseudoephedrine



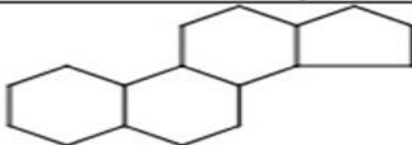
C) Pseudoalkaloid

1. Purine



e.g. Caffeine, thophylline, theobromine

Steroidal



e.g. Solanidine, conessine, protoveratrine

Diterpene



e.g. Aconitine, aconine, hypoaconine



Nomenclature

- ❑ Structure of Alkaloids are Complex material.
- ❑ Their botanical sources, Papaverine from *papaversevefinifar*.
- ❑ Their physiological action, Morphine.
- ❑ After name of chief investigators, Prefixes, epi, iso, neo, psedo, ine, palleterine after Pelletier
- ❑ **Trivial names** should end by '**ine**'. These names may refer to: The genus of the plant, such as Atropine from *Atropa belladona*. The **plant species**, Cocaine from *Erythroxyton coca*.
- ❑ **Common name** of the drug, such as *Ergotamine* from ergot. The name of **discover** such as Pelletierine that was discovered by **Pelletier** .
- ❑ The **physiological action** , such as emetine that acts as emetic. **Morphine** acts as **narcotic**.
- ❑ A prominent **physical character** such as Hygrine that is hygroscopic.

Prefixes & Suffixes

- ❖ **Prefixes:** '**Nor**' designates N-demethylation or N-demethoxylation,
Ex. Norpseudoeephedrine and nornicotine.
'**Apo**' designates dehydration Ex. Apomorphine.
'**Iso-, pseudo-, neo-, and epi-**' indicate different types of isomers.
- ❖ **Suffixes:** '**-dine**' designates isomerism as quinidine and cinchonidine.
'**-ine**' indicates, in case of ergot alkaloids, a lower pharmacological activity
Ex. Ergotamine is less potent than ergotamine.

General Properties of Alkaloids

❑ **State:** All alkaloids are colorless crystalline solids, a few are liquid & volatile:
Cocaine , Nicotine.

❑ **Physiological action:** Bitter taste.

❑ **Solubility :** Insoluble in water.

Readily soluble in organic solvent
Benzene, Alcohol, Chloroform.

❑ **Optical activity:** Alkaloids are optically active mostly,
All are levorotatory.

❑ **Basic nature:** Gives strong alkaline solution.
All forms salt of acids.

Due to presence of 1/2 nitrogen in tertiary form.

❑ **Precipitation:** Ppt form there acid solution by number of substances called alkaloid reagents like picric acid, tannic acid, potassium mercuric iodide.

❑ **Purification:** By quantitative analysis method & precipitate in different shapes & identification of alkaloids.
By qualitative analysis.



Extraction of Alkaloids

1. Stass otto method

Powdered plant material

Defatted with non-polar solvent

Defatted plant material

Moist with water and treated with NH_3 , Dil. Lime solution (*Free Alkaloid*)

Extracted with organic solvent like chloroform, ether

Extract, Concentrate it

Dissolved in Dil. Acid (*Alkaloidal salt*)

Aqueous phase

Organic phase impurities

Basified with ammonia or sodium
Bi-carbonate or Dil. KOH

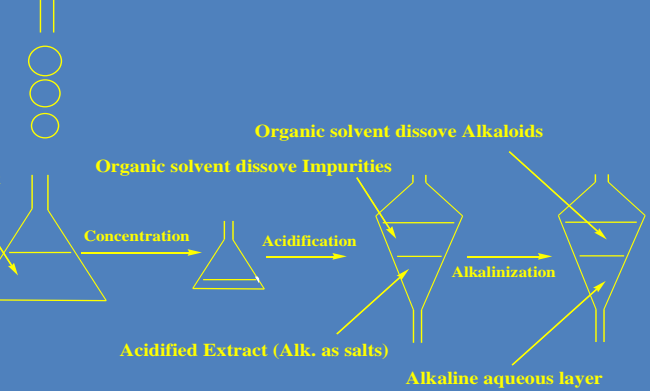
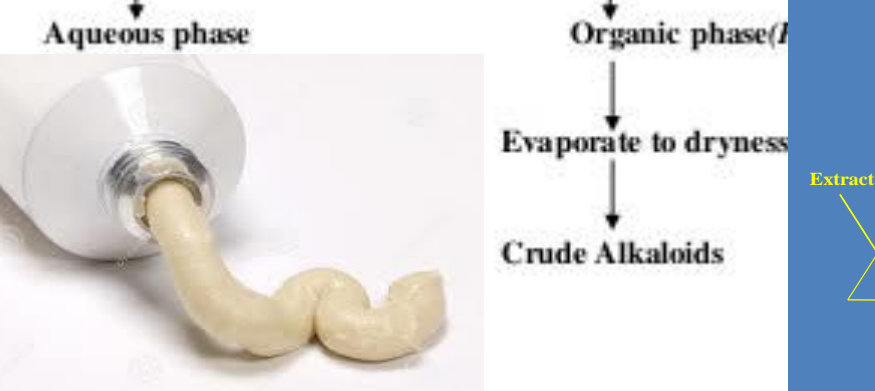
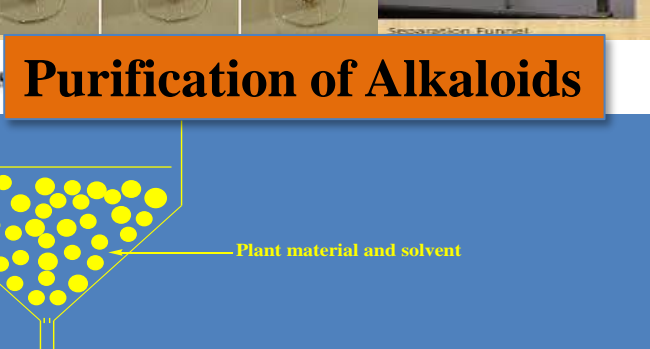
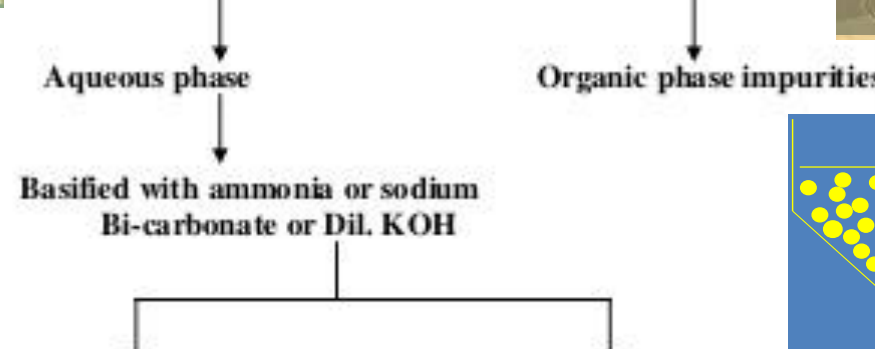
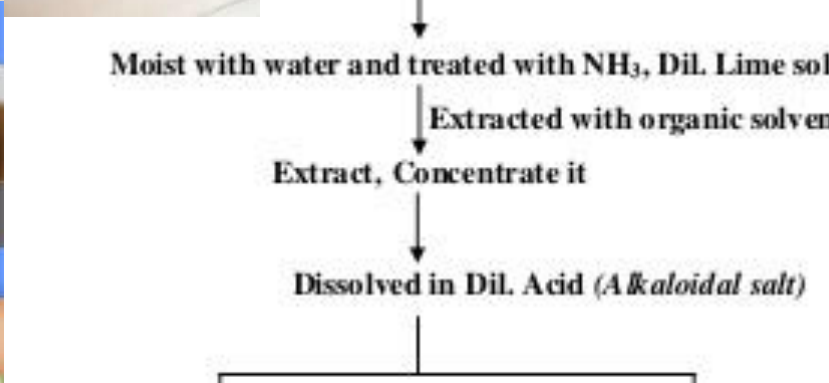
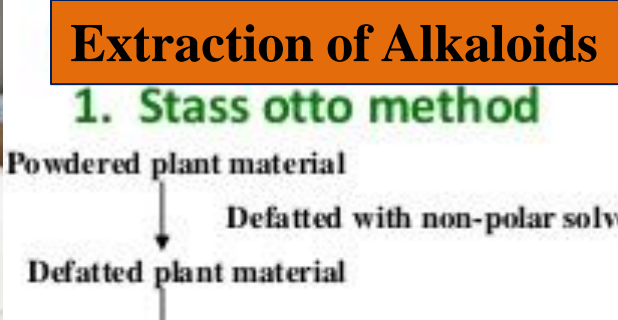
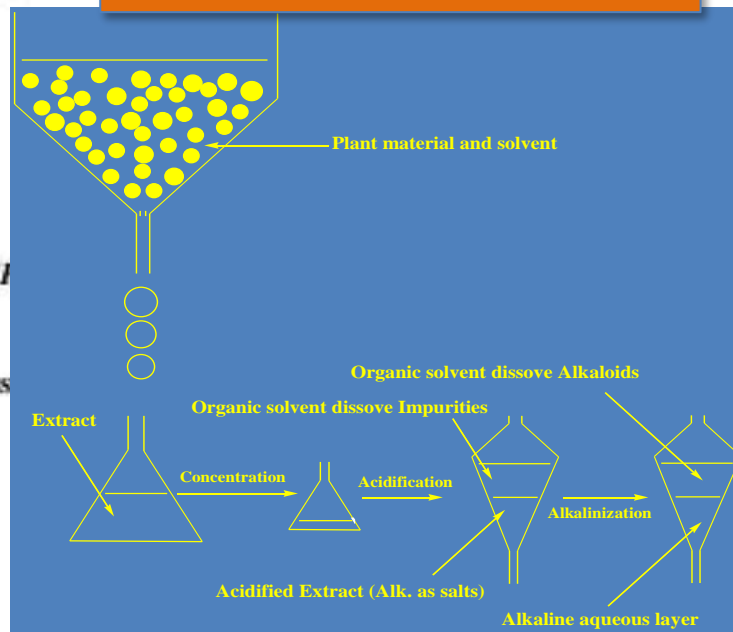
Aqueous phase

Organic phase(*Impurities*)

Evaporate to dryness

Crude Alkaloids

Purification of Alkaloids



➤ Alkaloids are usually found in parts of the plants, plant material dried, finally powder & treated with water → acidified HCl/H₂SO₄ → salt → water → extract → hydrochlorides of alkaloids → dyestuff product → alkali → soluble in water ppt → volatile alkaloids → acidified → extract → alkali → steam distillation → purified crude product → special methods → crystallization → free compounds or their salts

General Physiological Action of Alkaloids

❑ There is great discovery & complexity of a chemical structure of alkaloids. Many of these alkaloids act as important drugs, some alkaloids stimulate CNS while other cause paralysis.

EX. : Quinine : Antimalarial, Opium : Stimulant, analgesic, narcotics, miotic

Cocaine : Local anesthetics, Atropine : Dilates the pupil of eye (Datura)

Reserpine: Lower the blood pressure, Indole : Antihypertensive & tranquilizers,

Ephedrine : Sympathomimetic (stimulate), adrenergic receptors

Colchicines: Suppressant for gout (Sandhirog)

Caffeine : Stimulant, several carbonated beverages, diuretic

Tea: Stimulant (due to caffeine), Astringent (tannin)

Morphine: Depressant, sedatives, anti tissue, analgesic

Paparavine: Powerful narcotics, depresses respiratory mechanism

Veratrum viride: Antihypertensive, cardiac depressant, insecticides

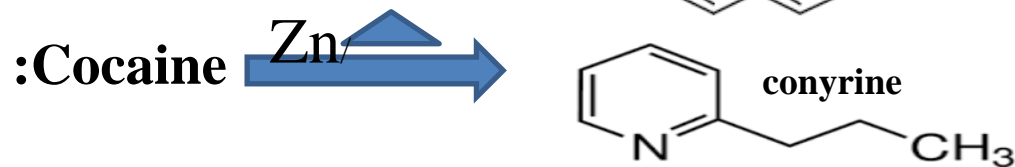
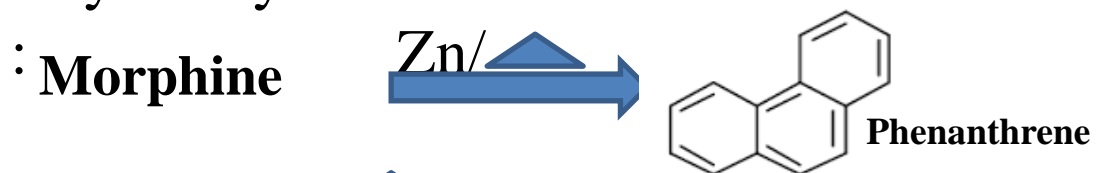
(European helle bore) IPECAC: EXPECTORANT

General Structure Determination of Alkaloids

❑ **Determination of M.F.** : Qualitative & Quantitative Analysis

❑ **Determination of Functional group Analysis:** UV shows **unsaturation**
 : IR spectroscopy, OH,
 : COOH, C=O, Acetyl derivative

❑ **Nature of carbon skeleton:** By catalytic reactions



Indicates presence of Quinoline, pyridine ring.

Alkaloids reduction, LiAlH_4 gives unsaturation test, bromine/ KMnO_4 in
 Unsaturation addition reaction, *Indicates presence of unsaturation.*

❑ **Nature of Nitrogen:** May be, in heterocyclic ring, amino, amido,
 N-alkyl amino group etc.

Alkaloids

$\xrightarrow{\text{Anhydride/iodide}}$

Nitrous acid (HNO_2)



This indicates alkaloids, pri., sec., or ter. Nitrogen present.



Hersing Mayer method (-N- Me group)



:This shows – N-methyl group present.

Hofmann Elimination:



Like Pyridine on reduction, Piperidine heat silver iodide gives piperylene
:This shows heterocyclic ring with nitrogen atom.

Nature of Oxygen Atom: a. -OH group,

-OH, -C=O, -COOH, -OCH₃, -OR, -COOR.



b. -COOH group,

Determined by solubility test using NaHCO_3 , elimination of CO_2

:Indicates carboxylic group present.

c. > C=O group,

Determined by phenyl hydrazine to form phenyl hydrazone

:Indicates carbonyl group present.

d. -OCH₃ group, Zeisel method

Alkaloids $\xrightarrow{\text{HI / boil}}$ methyl iodide

:Indicates methoxy group present.

e. Active hydrogen attached, -OH, -NH, hetero atom

Alkaloids $\xrightarrow{\text{G.R.}}$ Alkane (methane)

:Indicates -OH, -NH, hetero atom in ring.

Physical Methods: UV spectra. gives information about unsaturation.

IR no. of functional group

NMR no. of protons

Mass molecular weight

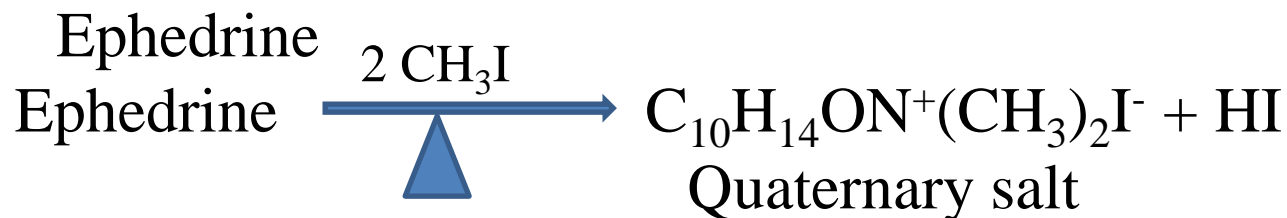
Synthetic Methods: *Support for determination of structure of alkaloids .*

Constitution of Ephedrine

I) **On Elemental Analysis**, Molecular weight determination shows molecular formula of ephedrine is $C_{10}H_{15}NO$

II) **Nature of nitrogen:**

a) It reacts with nitrous acid to form nitroso compound & also quaternary salt with two moles of CH_3I

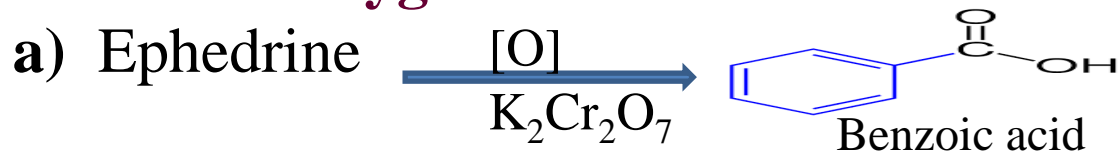


∴ *This indicate ephedrine is sec. amine.*

b) It also reacts with HI at 300°C gives one mole of CH_3I

∴ *Ephedrine also indicate sec. amine.*

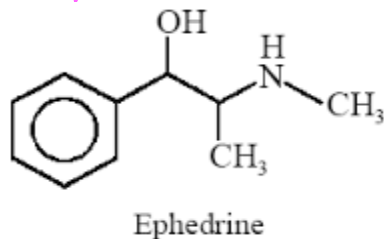
III) **Nature of oxygen /carbon skeleton**



∴ *It indicate one benzene ring with side chain.*

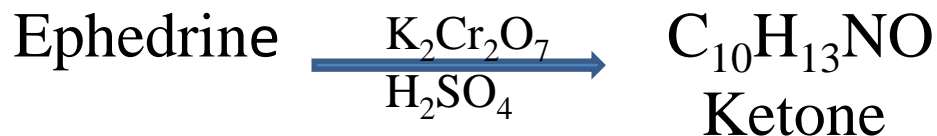
b) On benzoylation ephedrine gives dibenzene derivative.

- This indicate presence of oxygen atom in the form of $-OH$ group
Ephedrine structure may be.



IV) Nature of $-OH$ group:

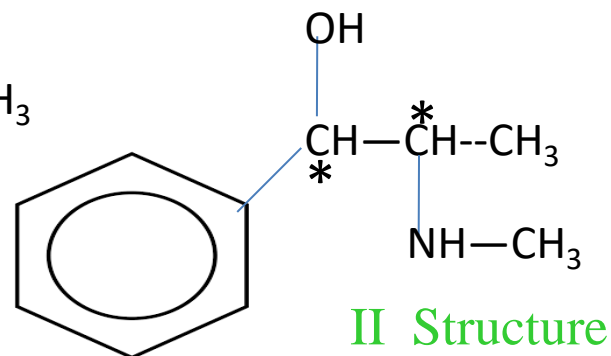
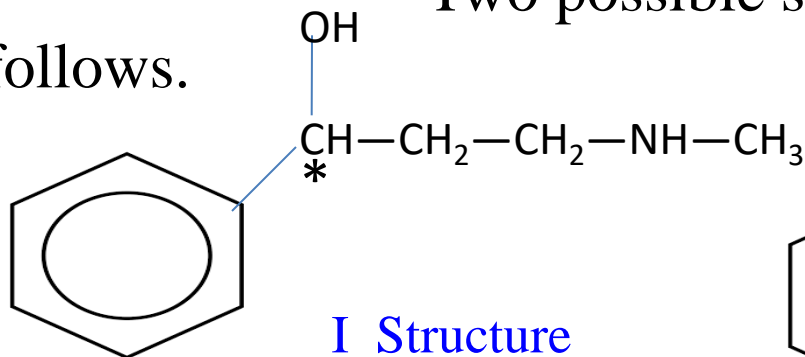
It reacts with benzoylation gives the dibenzene derivative of ketene containing same number of carbon atom.



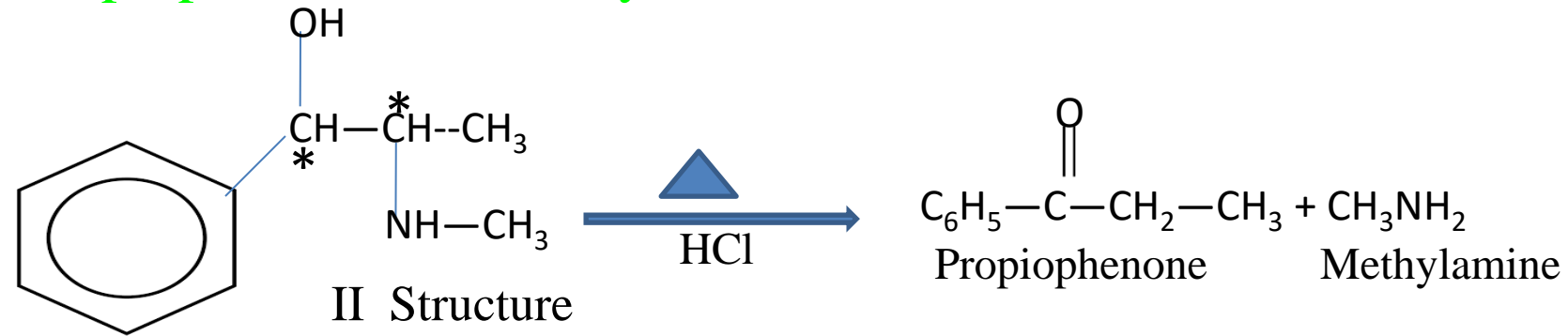
- It indicate presence of $-OH$ group in sec. position .

V) Nature of Side Chain:

Two possible structure of side chain in ephedrine are as follows.

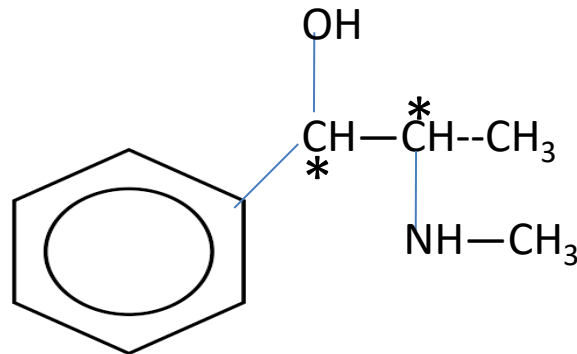


Ephedrine on heating conc. HCL under goes hydramine fusion is form Propiophenone and methylamine



Structure II is correct structure of ephedrine because of I structure cannot shows propiophenone & methylamine products.

Also support synthesis of ephedrine method for II structure

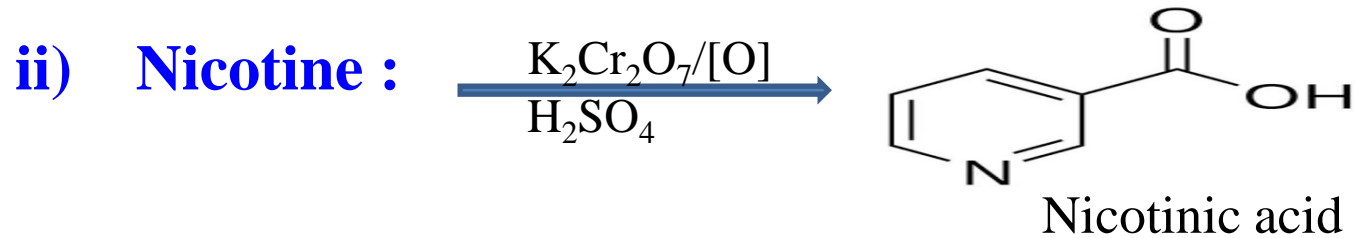


Structure of Ephedrine.

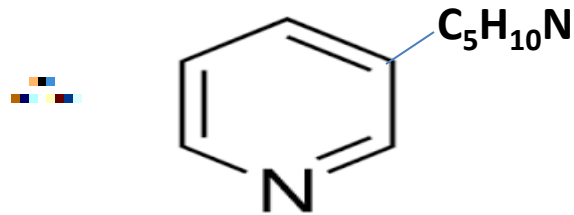




Constitution of Nicotine

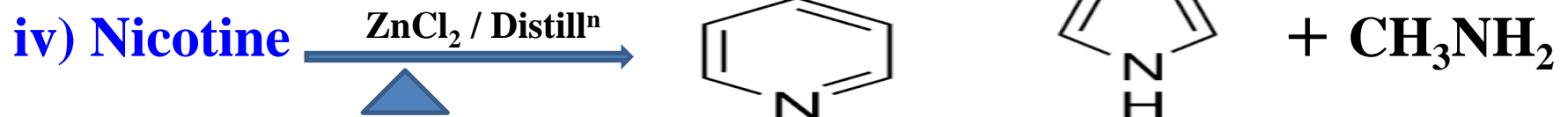
i) **Molecular Formula:** $C_{10}H_{14}N_2$

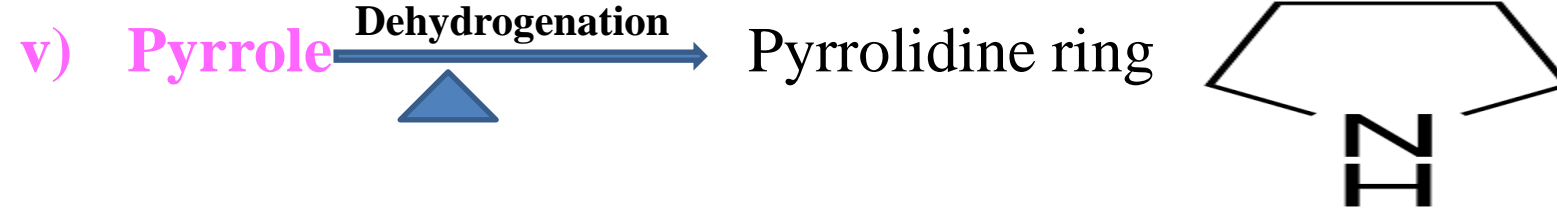


 *It Indicates pyridine ring & side chain .*



 *One nitrogen in pyridine ring.*
 *One nitrogen in secondary position.*





 *Pyrrolidine structure in side chain .*



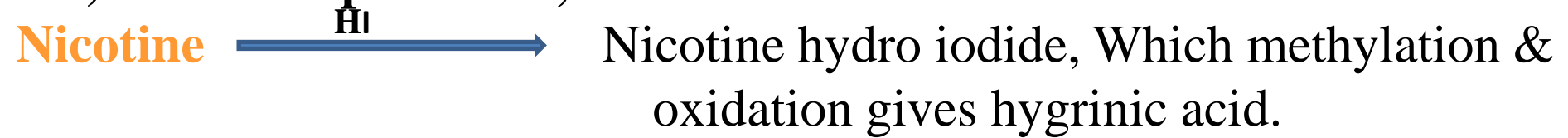
 *Reduces pyridine ring indicates nicotine is saturated comp.*

vii) **Hersing Mayer method,**




 *Indicates – N-CH₃ group present in side chain.*

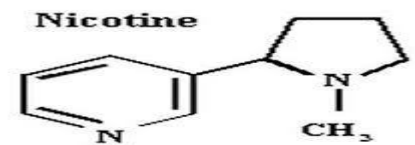
viii) **Karrer Explanation,**



 Indicates attached – N – pyrrolidine ring is present in side chain.

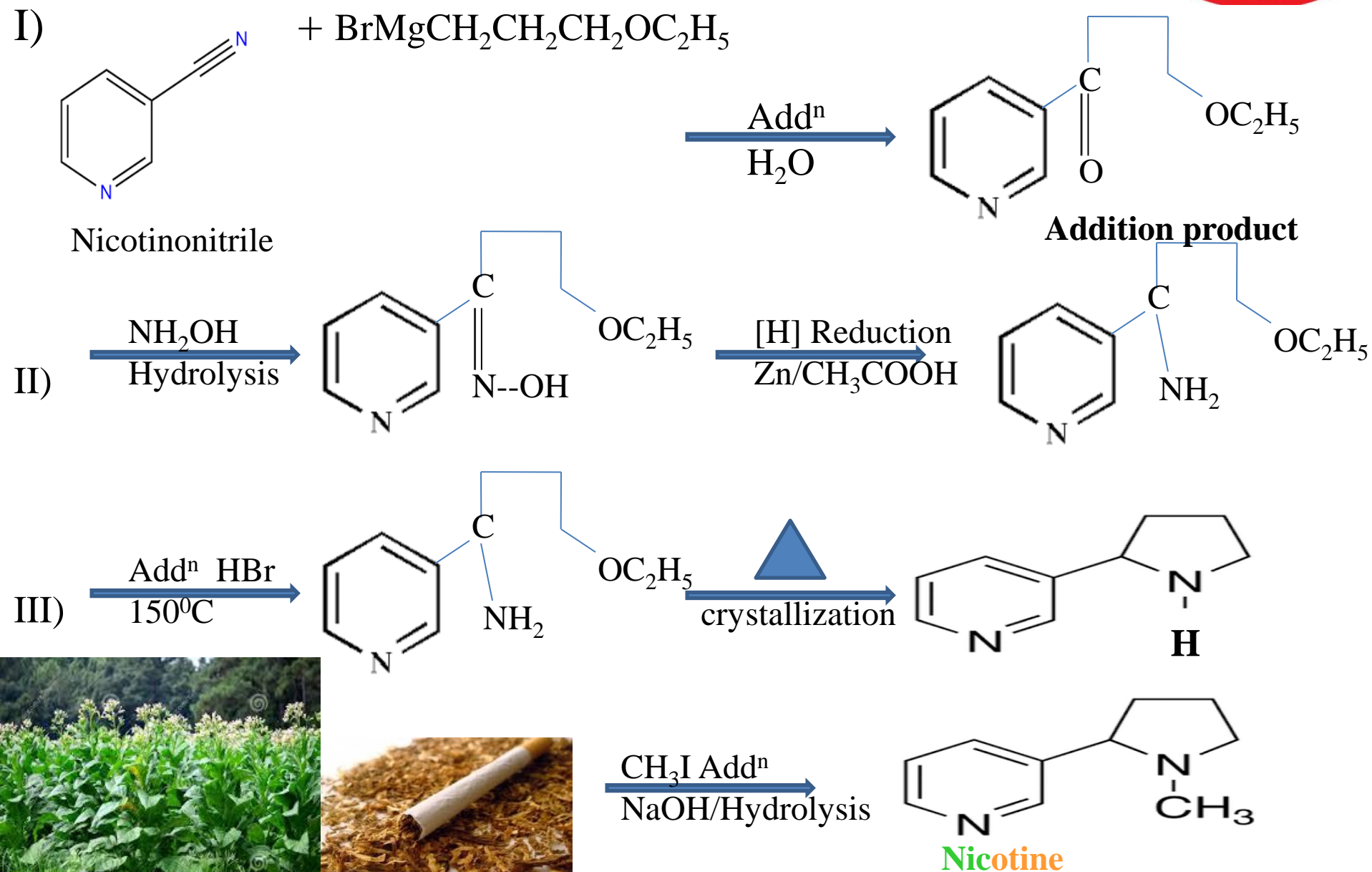
 **Nicotine** have –N – methylpyrrolidine ring structure present.

 *Structure of nicotine is.*

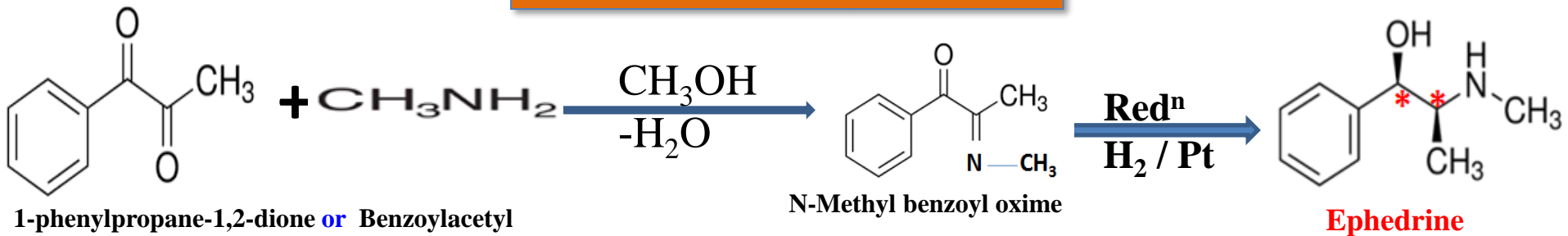




Synthesis of Nicotine



Synthesis of Ephedrine



झाडे लावा, झाडे जगवा,.....SUGGESTIONS
Save Earth, Save Life.

Created by, Dr. Subhash Lonkar

THANKS.....