

Nicotine

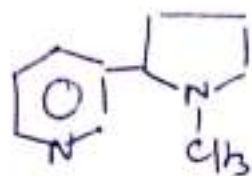
Most important, found in tobacco (*Nicotiana glauca*)
lethal dose for man is about 40mg. Other tobacco alkaloids
are nicotine (anabasine), nor nicotine, nicotylamine
The last one is responsible for aroma of tobacco smoke.

Isolation & properties -

Very tobacco leaves contain
5% nicotine combined with citric acid or malic acid
The stems & leaves containing nicotine are powdered &
extracted with water. The product is extracted with
alkali when the alkaloids are liberated. The free
nicotine is obtained by steam distillation & then
purified through oxalate.

It is colorless, low boiling
liquid (p.n. 246), but salt is dextro rotatory. Ractand
on exposure in air due to auto oxidation. It is
miscible ^{with} water in all proportions at temperature
below 60°C. Very deadly poison (dose 30-35mg),
kill the man within few second owing to paralysis of
nervous system including respiratory control centres.

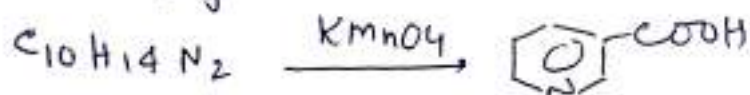
There is lot of evidence that smoking of cigarette
increases heart beat & thus causes constriction of
blood vessels with the result the blood pressure
increased & hence the blood pressure is disturbed.
In large amount it is used as insecticide & in the
presence preparation of nicotinic acid & niacin



Constitution -

(1) Molecular formula - $C_{10}H_{14}N_2$

- (2) Both nitrogen atoms are found to be present as tertiary one & one of them is found to be N-methyl gp.
- (3) On oxidation it gives nicotinic acid (pyridine-3-carboxylic acid) indicating the presence of that nicotine is 3-substituted pyridine

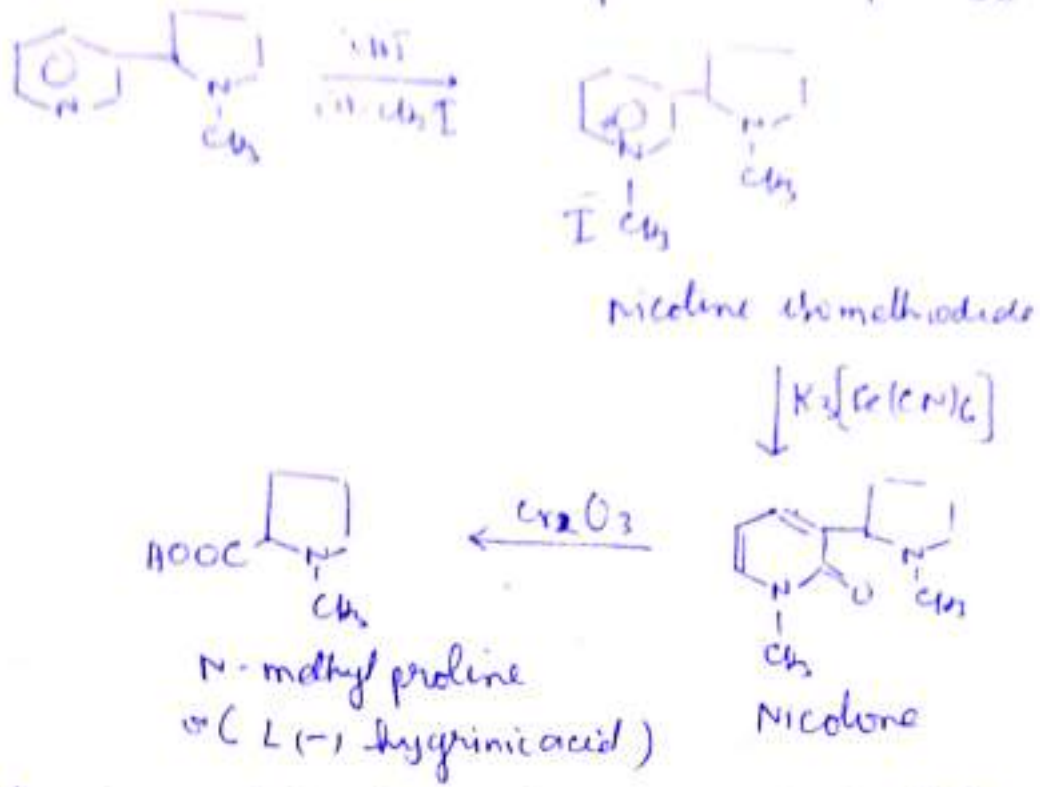


By subtracting the molecular formula of pyridine nucleus (C_5H_4N) from the nicotine molecular formula. The side chain present at 3 position of pyridine nucleus has formula $C_5H_{10}N$.

(4) Position & nature of side chain -

- (i) Nicotine absorbs only three ^{molar} moles of hydrogen to form hexa-hydro derivative suggesting that side chain is saturated since three moles of hydrogen are required by pyridine nucleus of nicotine.
- (ii) Since nitrosation of pyridine moiety is present as =N- the other nitrogen atom present in the side chain must possess a methyl gp (N^{CH_3}) hence side chain can be extended as $C_4H_7.NCH_3$.

Written as below which explains all the reactions



(6) The proposed structure also explains the following two Pinner observations. Definitely the above structure was proposed on the observations of Pinner (1892, 1893)

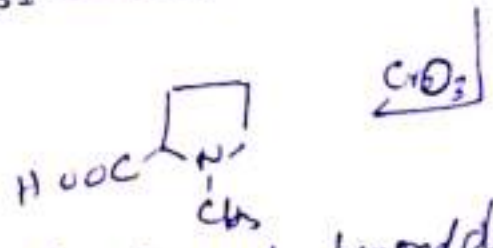
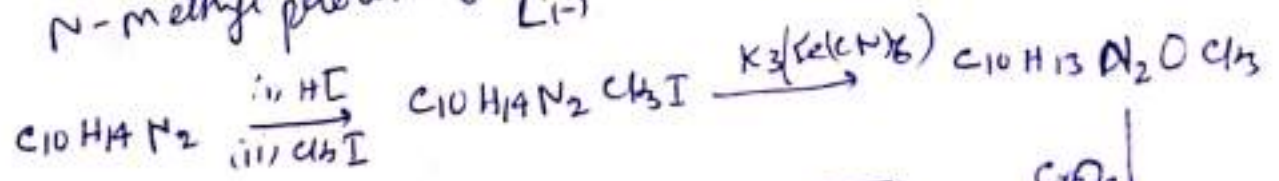
(i) Nicotine on treatment with Br_2 in acetic acid gives hydrobromide perbromide along with other products. The hydrobromide perbromide ($\text{C}_{10}\text{H}_{10}\text{Br}_2\text{N}_2 \cdot \text{HBr} \cdot \text{Br}_2$) which when treated with aqueous H_2SO_5 (Sulphurous acid) is converted into dibromonicotinine $\text{C}_{10}\text{H}_{10}\text{Br}_2\text{N}_2$. This on heating the mixture with $\text{H}_2\text{SO}_5 + \text{H}_2\text{SO}_4$ at $130^\circ - 140^\circ\text{C}$ forms 3-acetylpyridine, oxalic acid + methylamine.

(iii) Nicotine forms addition product nicotine zinc chloride with ZnCl₂. This addition product on heating with lime gives pyridine + pyrrole + methylamine.



This step clearly indicates that side chain is pyrrole derivative. From the point (4) it is clear that the side is saturated it means it is pyrrolidine nucleus and the side chain contain N-methyl gp. It means the side chain is N-methyl pyrrolidine.

iv) On the treatment with ~~conc~~ HI ~~at 150°C~~ followed by ~~etc~~ (Hofmann degradation) Nicotine yields which is formed. which on reaction with ethyl iodide gives nicotine ethyl iodide which on oxidation with $\text{Fe}(\text{K}_2\text{Cr}_2\text{O}_7)$ K ferricyanide followed by dichromate oxidation gives N-methyl proline (hygrinic acid Kern, 1925, 26, 1-)

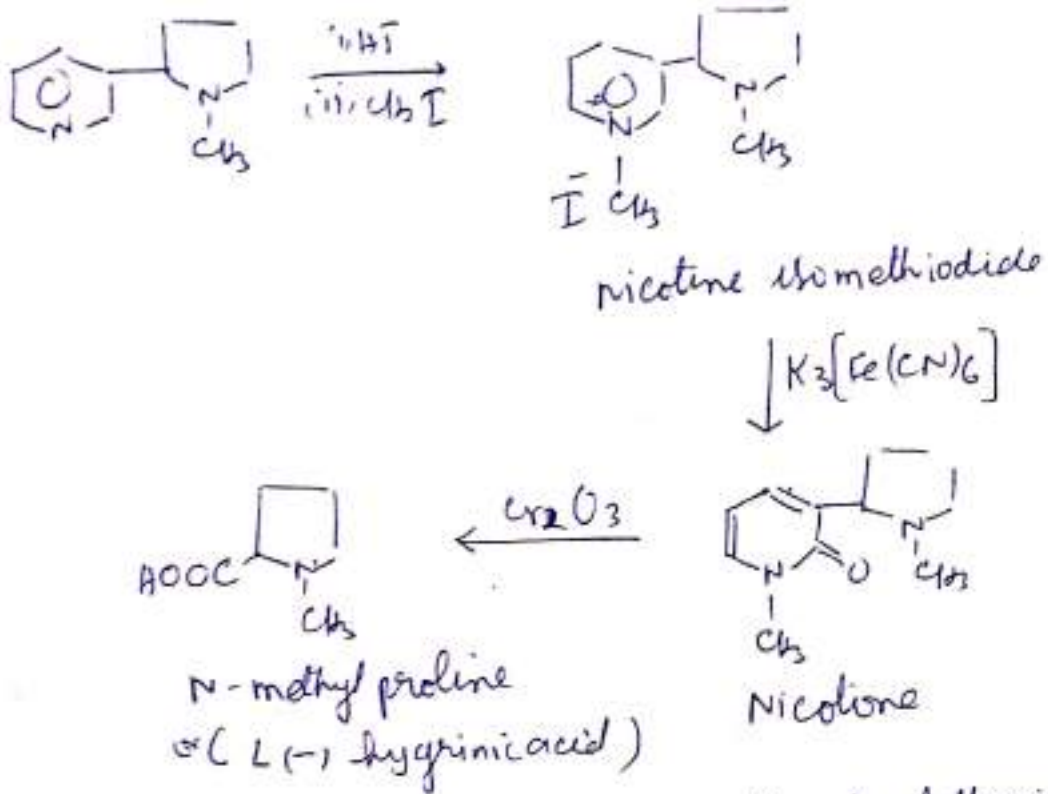


The formation of N-methyl proline suggest beyond doubt that the pyrrolidine unit is attached to position 3 of pyridine nucleus by means of α -position

(5) On the basis of above point. Nicotine may be

②

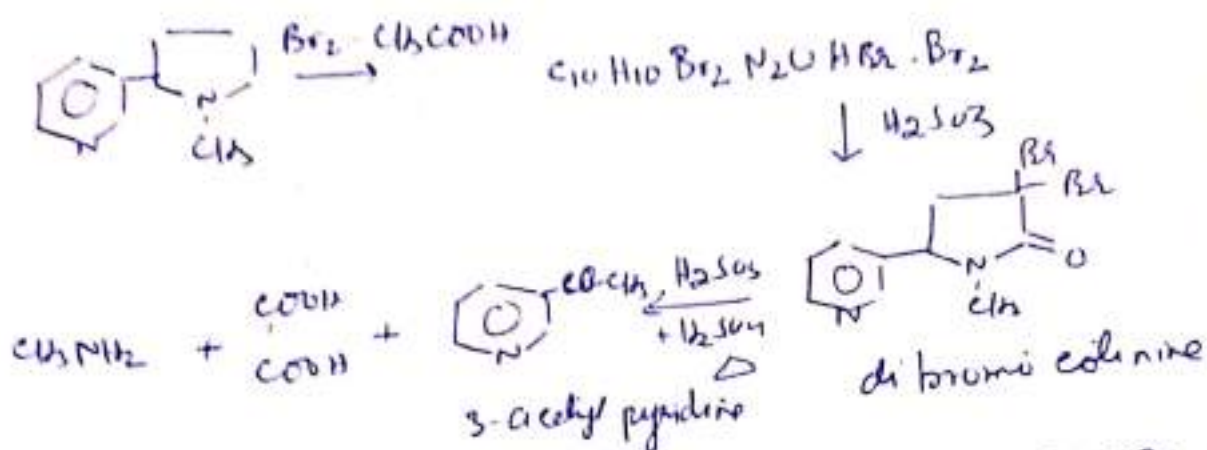
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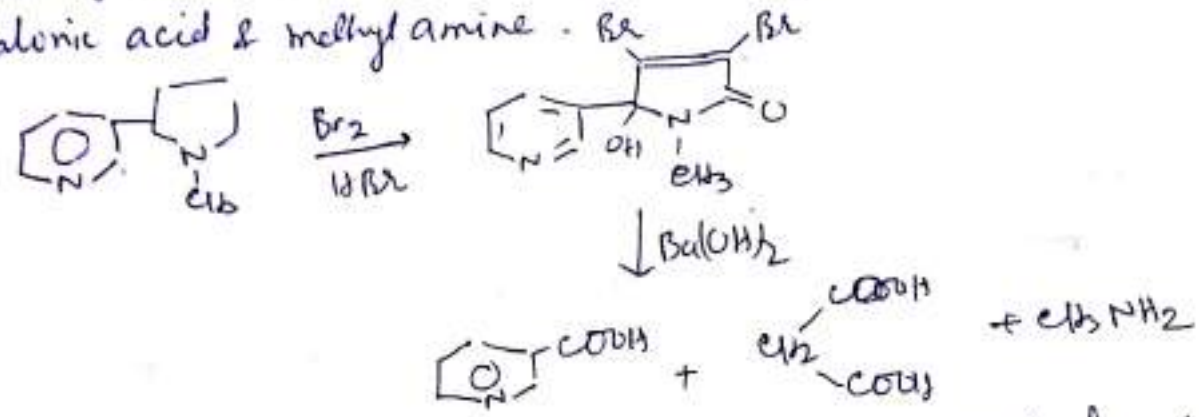
(6) The proposed structure also explains the following two Pinner observations. - Actually the above structure was proposed on the observations of Pinner (1892, 1893)

(ii) Nicotine on treatment with Br_2 in acetic acid gives hydrobromide perbromide along with other products. The hydrobromide perbromide ($\text{C}_{10}\text{H}_{10}\text{Br}_2\text{N}_2\text{O} \cdot \text{HBr} \cdot \text{Br}_2$) which when treated with aqueous H_2SO_4 (sulphurous acid) is converted into dibromo nicotinic acid $\text{C}_{10}\text{H}_{10}\text{Br}_2\text{N}_2\text{O}$. This on heating the mixture with $\text{H}_2\text{SO}_4 + \text{H}_2\text{SO}_4$ at $130^\circ - 140^\circ\text{C}$ forms 3-acetylpyridine, oxalic acid + methylamine.

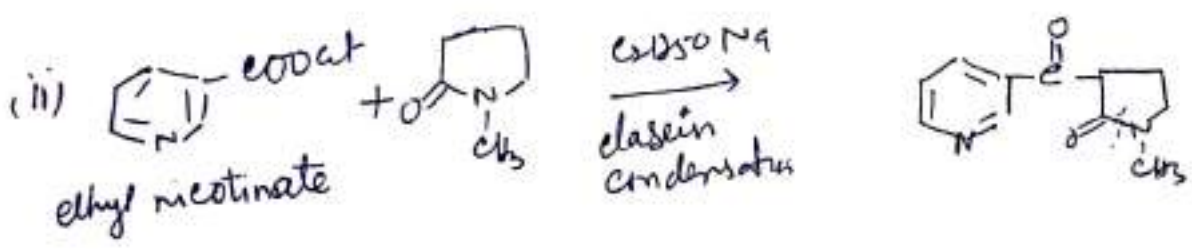
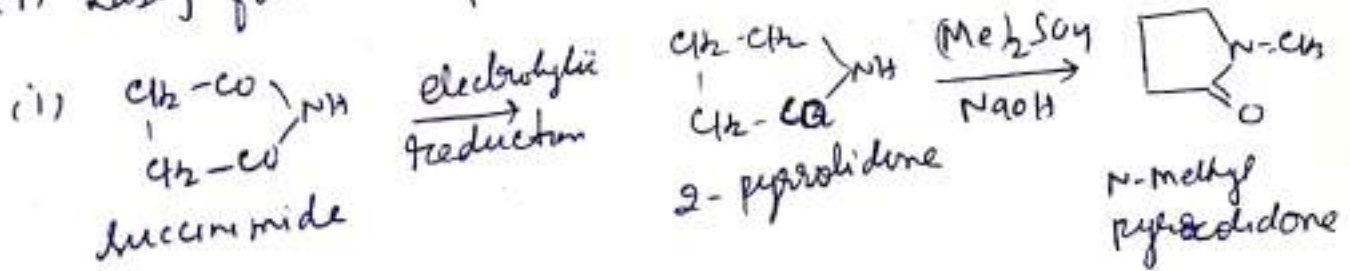
P.T.O

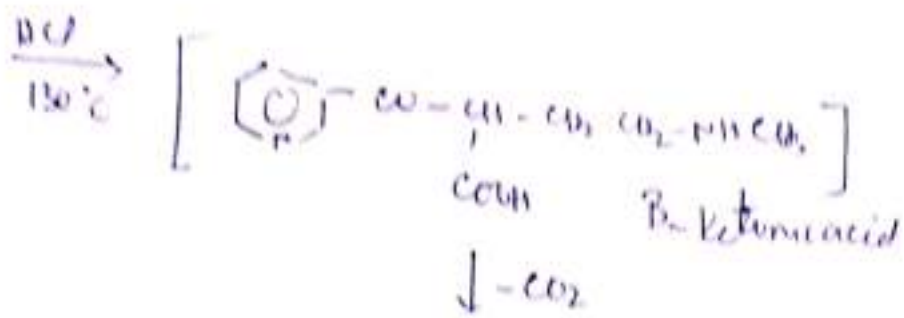


(ii) Nicotine on treatment with Br_2 in presence of HBr gives dibromu colinine ticonine ($C_{10}H_8Br_2N_2O_2$). which on heating with $Ba(OH)_2$ soln at $100^\circ C$ affords nicotinic acid, malonic acid & methylamine.



(7) Lasby formula is proved synthesis: Spath & Breilschneider (1928)



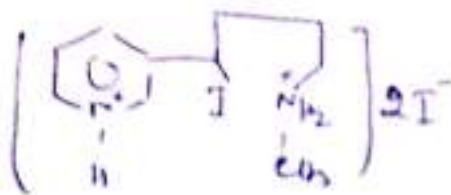


$\downarrow -\text{CO}_2$

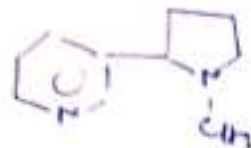


\downarrow Zn dust Reduction $\text{C}=\text{O} \rightarrow \text{C}-\text{OH}$
 $\text{C}_2\text{H}_5\text{OH} - \text{NaOH}$

\swarrow HCl
 100°C



$\xrightarrow{\text{NaOH}}$

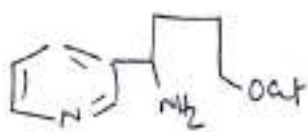
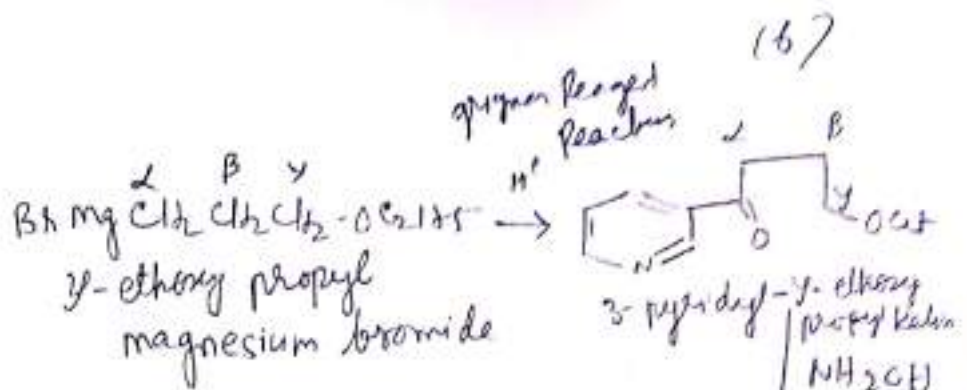
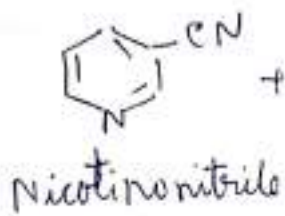


(±) Nicotine

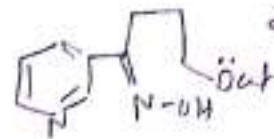
This was resolved by means of + tartaric acid. This synthetic nicotine is identical with natural compd

pyridine - pyrrolidine alkaloid

Craig (1935)



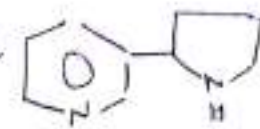
$\xleftarrow[\text{Reduction}]{\text{Zn / CH}_3\text{COOH}}$



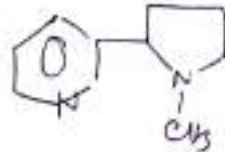
$\xrightarrow[\text{SM}_2]{\text{HBr (150-155}^\circ\text{C)}}$



$\xrightarrow{-\text{HBr}}$



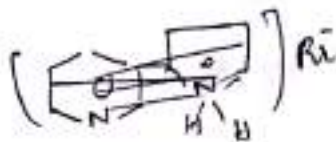
(±) Noh nicotine



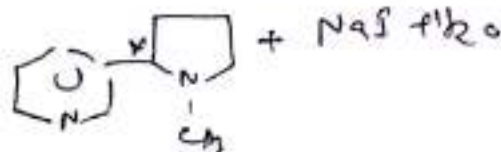
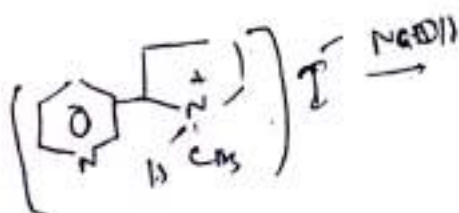
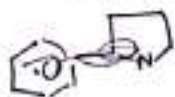
(±) Nicotine

$\xleftarrow[\text{ii. NaOH}]{\text{i. CH}_3\text{I}}$

Note -

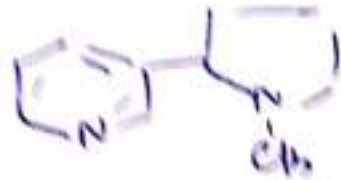


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Nicotine

Pyridine
pyrrolidine gp



- Nicotine

from tobacco leaves.

poisonous in Nature - 20-50mg ~~toxic~~

Human can stimulate the

central nervous system.

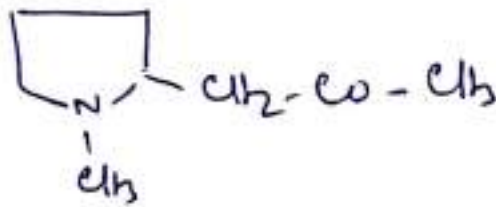
causes depression & increases blood

pressure.

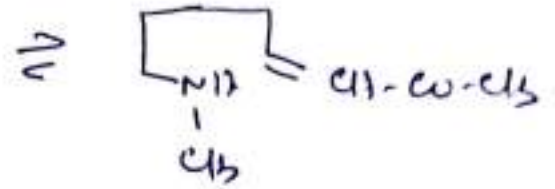
Smoking causes Asthma & lung cancer

Hydruine

pyrrolidine
gp



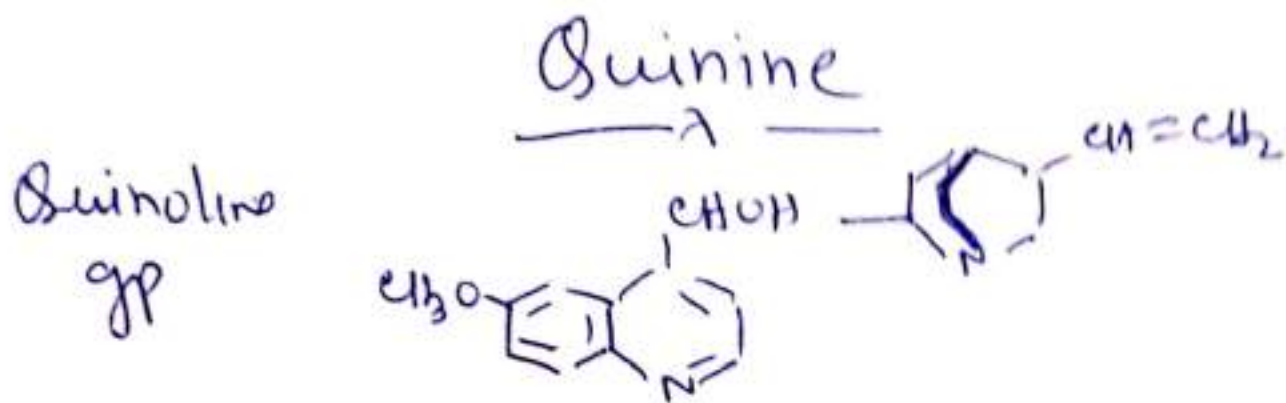
(-)-Hydruine



Racemises

Leaves of Peruvian coca shrub,
source of cocaine. Most volatile, coca
leaf alkaloids.

Precursor of Hyoscyamine &
scopolamine used for pharmaceutical product
scopolamine also known as Hyoscyne is
constituent of travel sickness tablets.



Febrifuge & as an antimalarial

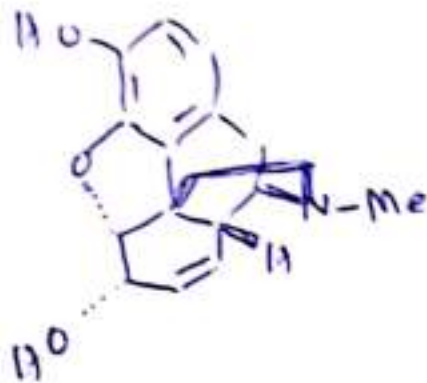
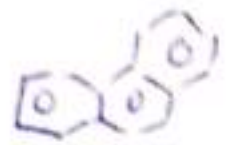
Quinoline Nucleus

Treatment - Plasmodium Vivax. (Amoeba) ^{Protozoan parasite.}

Plasmodium falciparum malaria.

Morphine

Phenanthrene gp



chief alkaloid in OPIUM.

diacetate of morphine - Heroin

Methylated morphine (phenol O) - Codeine

Narcosis (Sleep = sedation), Analgesic (No pain)

Narcotic analgesia -

Codeine less potent analgesic than morphine

Morphine is addictive. As medicine pain

relieving drug caused by serious injury, migraine,

It also causes respiratory depression on higher dose

Heroin - more potent analgesic than morphine

but shorter duration of action. Highly addictive.

Cocaine

pyrrolidine
nucleus gp

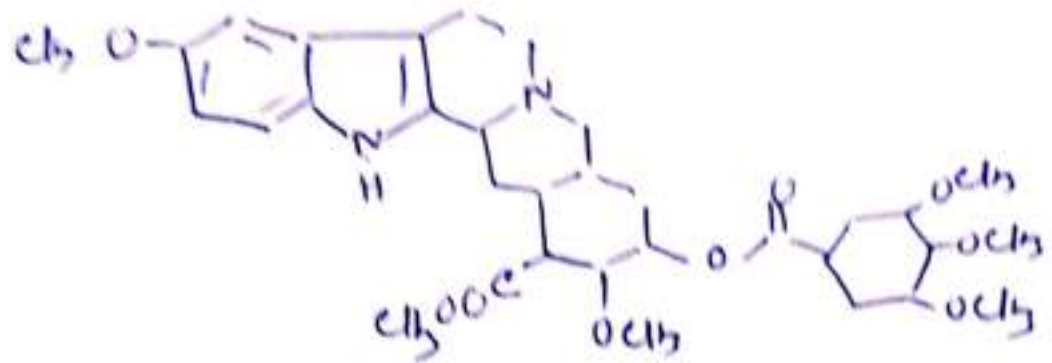


(-) cocaine

occurs in coca leaves, anaesthetic
property as local anaesthetic property
poisonous property - not used for long
prolong anaesthesia, a habit forming drug.

Reserpine

Indole
gp



use for embolism hypertension,
epilepsy, insomnia, fever etc
acts as tranquilizer

alkaloid of Rauwolfia species. Present
in Rauwolfia Serpentina also known as
Snake root.