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Topic - Nicotine (Alkaloid)  
Paper - M.Sc. CHCC-EC-Ic  
Semester - IV (Organic special)

### Introduction:

Nicotine is a tobacco alkaloid and is very important plant product occurring in *Nicotiana tabacum* and in some other *Nicotianan* species. Although it is distributed in whole plant but its highest concentration is found in the leaves. Although tobacco is the commercial source of Nicotine, it also occurring is also observed in many flowering plants.

Fresh Nicotine is a colourless hygroscopic liquid which is discoloured when it becomes in the contact of air.

The natural Nicotine is laevorotatory but its salt is dextrorotatory.

### Constitution of Nicotine

Following are the different steps for the elucidation of the structure of Nicotine:

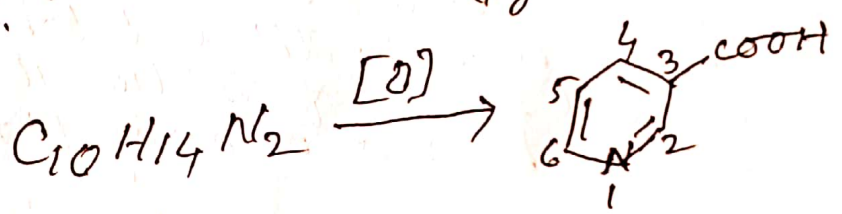
1. The elemental analysis and the molecular weight determination, the suggested molecular formula of the compound is  $C_{10}H_{14}N_2$ .

2. The double bond ring equivalent for the compound is five which is calculated as:-

$$\begin{aligned}
 DBRE &= (a + \frac{c}{2} + 1) - \frac{1}{2}b \\
 &= (10 + \frac{2}{2} + 1) - \frac{1}{2} \times 14 \\
 &= 12 - 7 = 5
 \end{aligned}$$

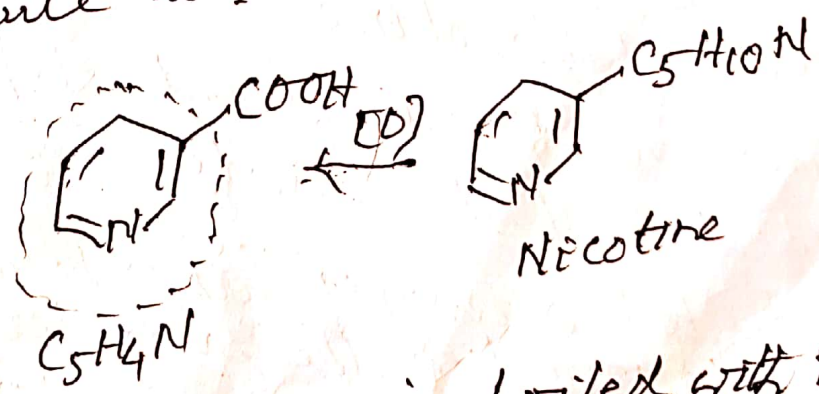
This indicates that the compound is either polycyclic or having at least one aromatic ring.

3. On chromic acid or  $KMnO_4$ , it is oxidized into Nicotinic acid (pyridine-3-carboxylic acid).



This indicates that Nicotine is a pyridine derivative with a side chain at position number 3.

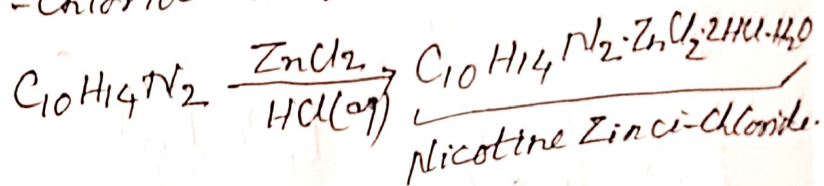
Hence, we can express the molecule as:



4. When nicotine is boiled with hydroiodic acid ( $150^\circ$ ),  $CH_3I$  is released (Heizig-Mayer test). This indicates that the side chain

contains N-CH<sub>3</sub> residue.

5. Nicotine forms an addition product with Zinc-chloride with ZnCl<sub>2</sub>:



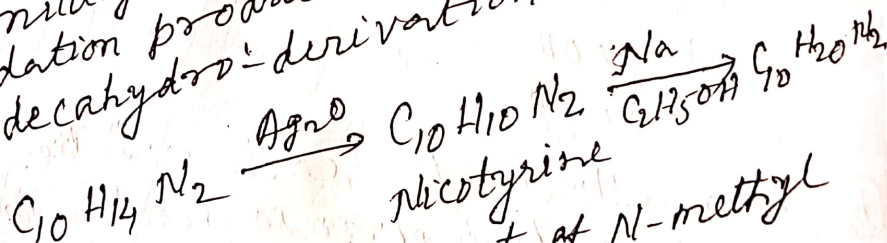
This addition product when distilled with soda-lime, gives pyridine, pyrrole and methyl amine.

The formation of the pyrrole ring indicates that the side of pyridine may be pyrrole type of ring with N-methyl residue.

6. When reduced with Na-C<sub>2</sub>H<sub>5</sub>OH, nicotine forms only hexahydro derivative. This indicates that the double bonds are only present in the pyridine ring.

Hence the side chain may be N-methylpyrrolidine unit.

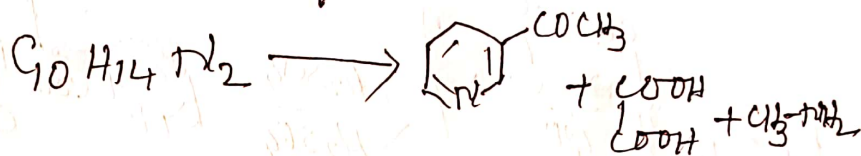
The fact is confirmed when the nicotine is mildly oxidised with Ag<sub>2</sub>O. This oxidation product on reduction is converted into decahydro-derivation.



7. Point of Attachment of N-methyl pyrrolidine with the pyridine ring:-  
It can be expressed in two ways

The final point of attachment can be expressed as:

(a) When nicotine is allowed to react with  $\text{Br}_2$  in acetic acid followed by  $\text{H}_2\text{SO}_3$  treatment, it is converted into dibromocotinine. Finally the formed compound when heated with  $\text{H}_2\text{SO}_3/\text{H}_2\text{SO}_4$ , 3-acetylpyridine, oxalic acid and methyl amine are formed.



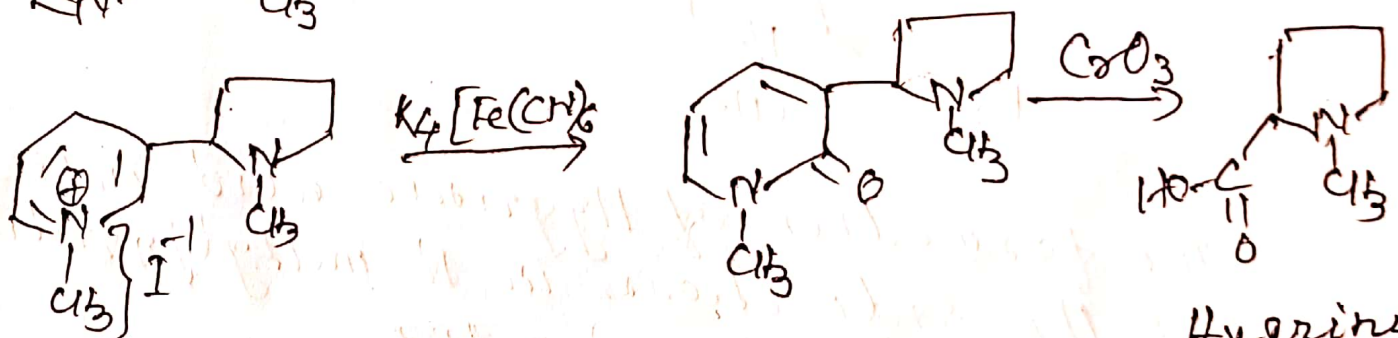
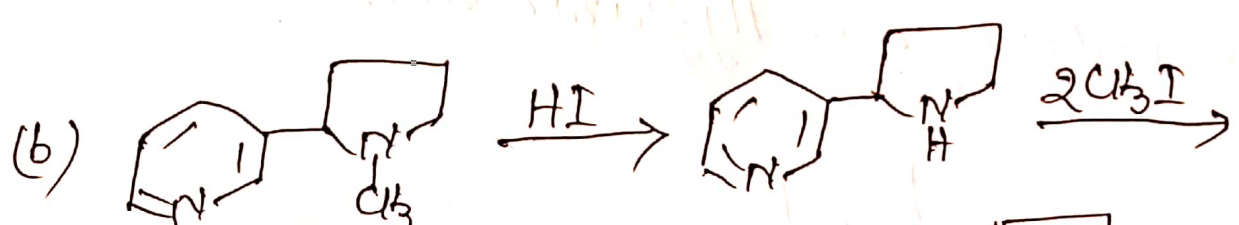
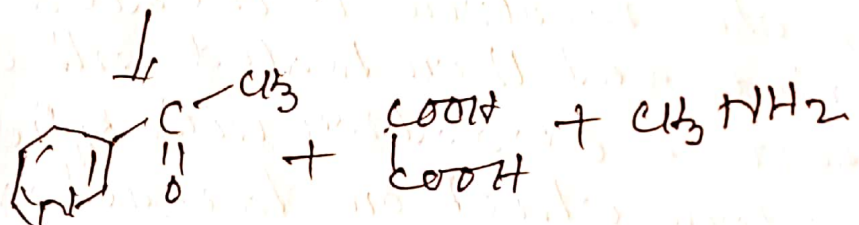
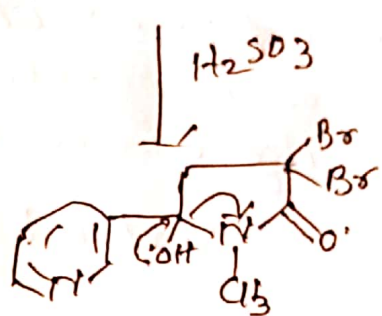
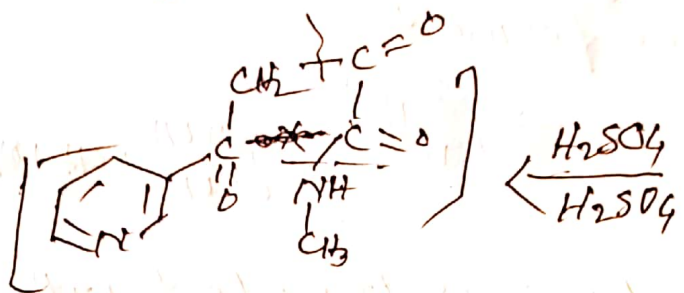
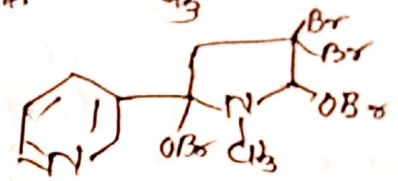
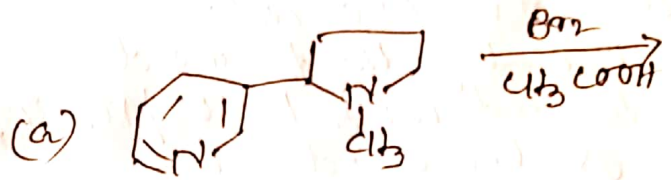
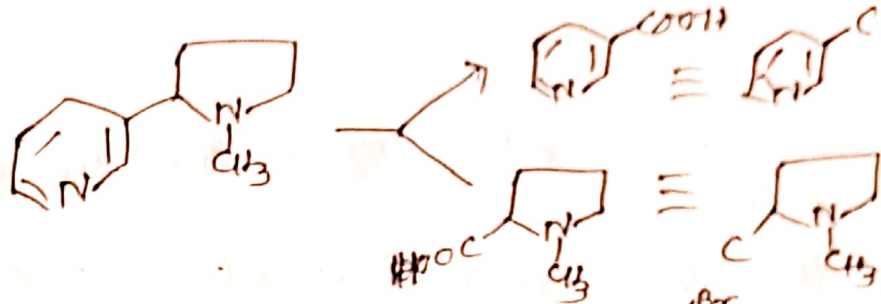
(b) Finally when nicotine is treated with HI (boiled) and then heated with  $\text{CH}_3\text{I}$ . The product on oxidation with  $\text{K}_4[\text{Fe}(\text{CN})_6]$  gives nicotone, which on chromic acid oxidation gives Hygrinic acid.



The formation of Hygrinic acid indicates that the side chain in N-methylpyrrolidine is at position number two.

These two reactions can easily be explained if the structure of Nicotine is proposed as: -

5.

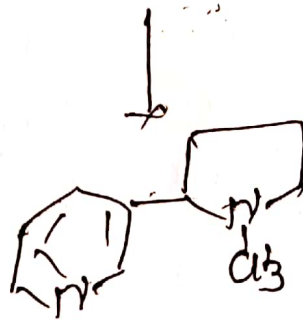
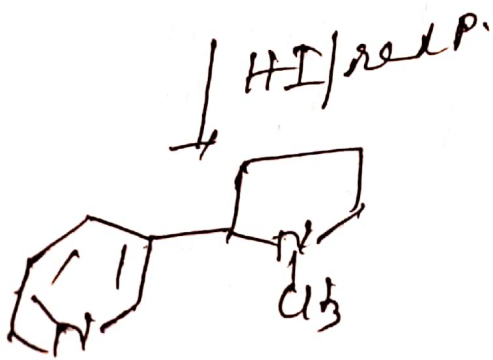
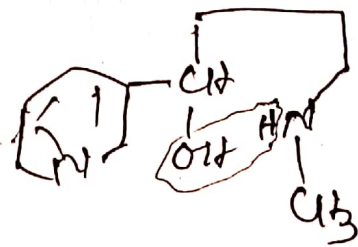
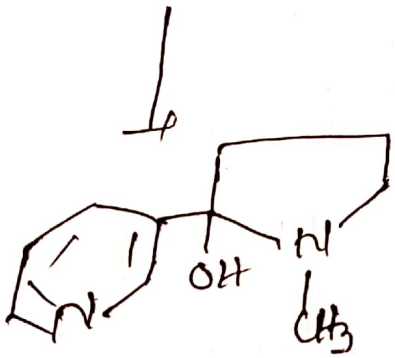
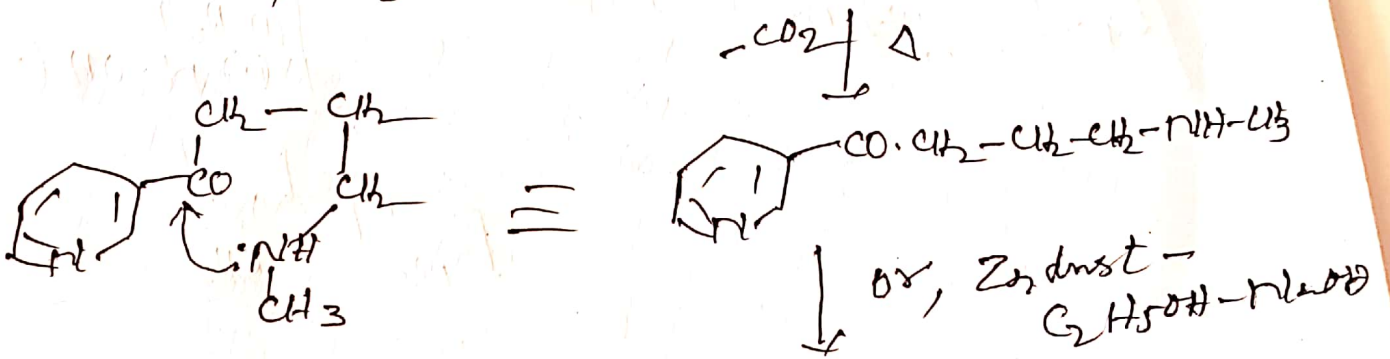
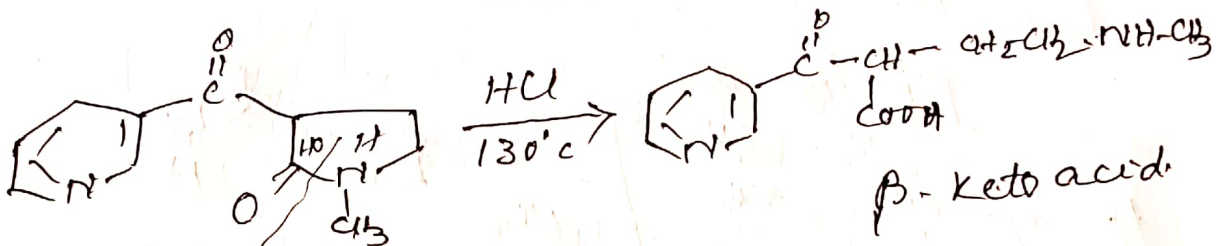
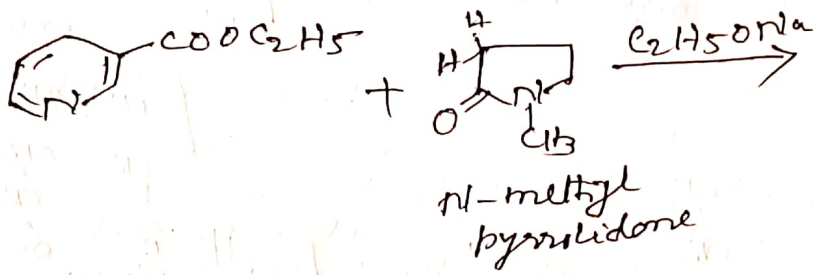


Hygrinic acid.

(8) Finally the structure of nicotine is confirmed by its synthesis -

② From Ethyl nicotinate.

6.



(±) Nicotine.

⑥ From Nicotroutrile (Craig synthesis) 7

