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# Chemistry

## SUB. CODE- BSCC2402

*For B.Sc. 4<sup>th</sup> Semester*

(Alkaloids)  
Module-VI

*Structure Elucidation and Synthesis of Hygrine*

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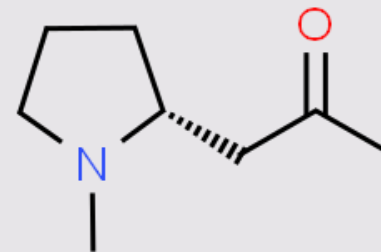
## Hygrine: Occurrence

**Hygrine**, is a pyrrolidene alkaloid with molecular formula  $C_8H_{15}NO$ .

It is a natural product **occurring** in the coca leaves along with cocaine. It is a thick oil having pungent smell and odour. Boiling point 193 -195 °C.



Coca leaves



- Hygrine is used as a sedative, hypnotic, laxative and diuretic.

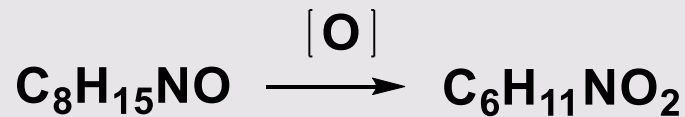


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## STRUCTURE ELUCIDATION

- Mol formula was determined as  $C_8H_{15}NO$  and it shows the presence of a keto group and a tertiary N-atom.
- On oxidation with Chromic acid, hygrinic acid is formed.



- On dry distillation, hygrinic acid gives N-methyl pyrrolidine. This shows that hygrinic acid is an N-methyl pyrrolidine carboxylic acid.
- Hygrinic acid undergoes decarboxylation very rapidly indicating that the  $-COOH$  group is present at 2-position.
- This structure is confirmed by Wilstatter synthesis.

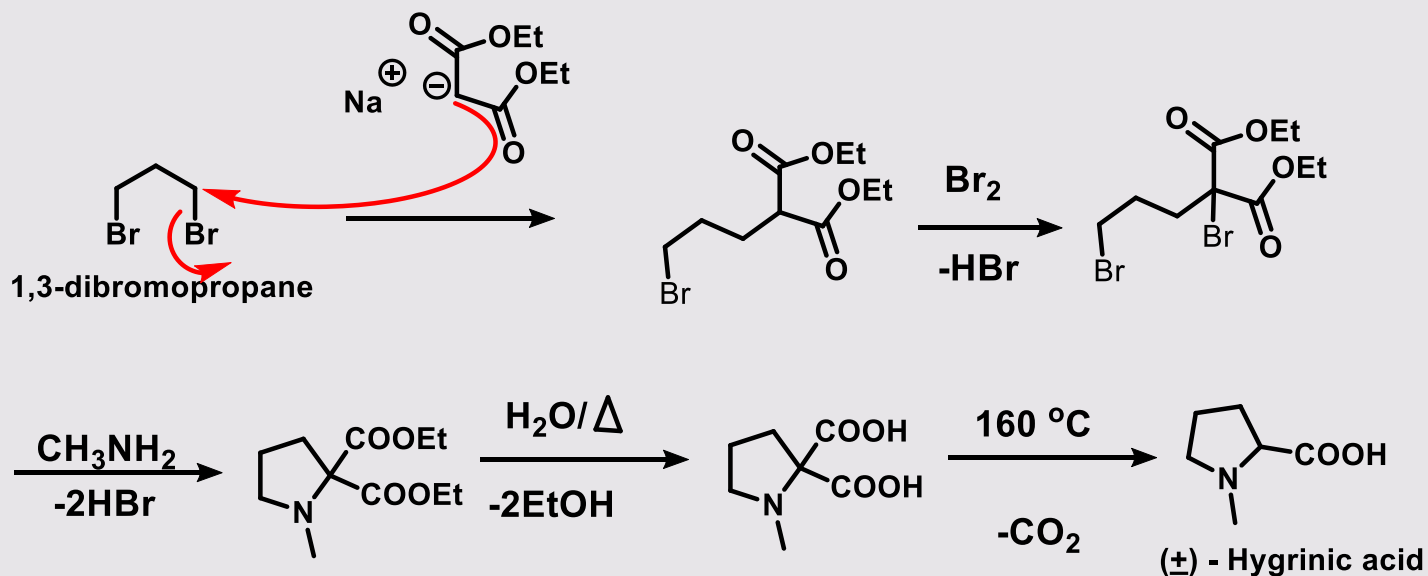


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# STRUCTURE ELUCIDATION

## Willstatter Hygrinic acid synthesis



Formation of Hygrinic acid on oxidation of hygrine shows that in hygrine a side chain of  $\text{C}_3\text{H}_5\text{O}$  must be present at C-2 position of N-methyl pyrrolidine nucleus.

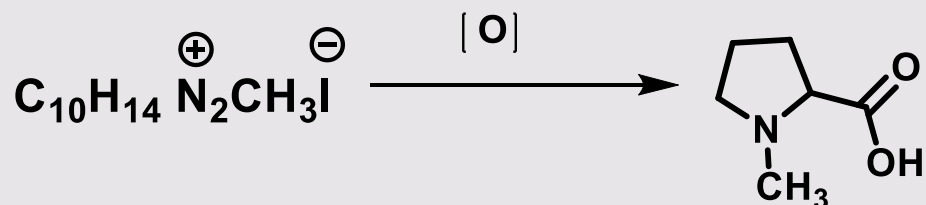


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## STRUCTURE ELUCIDATION

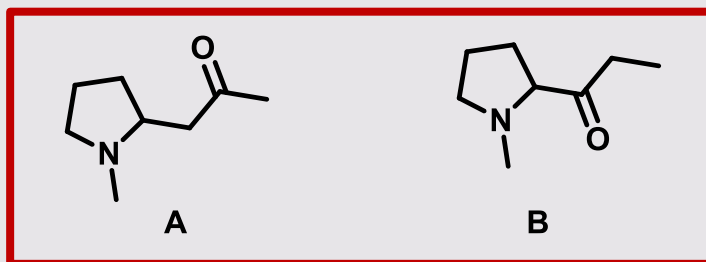
- Upon oxidation, this side chain nicotine methiodide gives hygrinic acid.



N-methyl-pyrrolidine-2-carboxylic acid

Hygrinic acid

- This suggests that 2-position of N-methylpyrrolidine ring is attached to 3-position of pyridine nucleus.
- Upon drastic oxidation, the side chain gives only one carbon containing carboxylic acid (hygrinic acid). So the side chain must contain a keto group.
- The structures proposed for Hygrine by Hess (1913) are A and B.



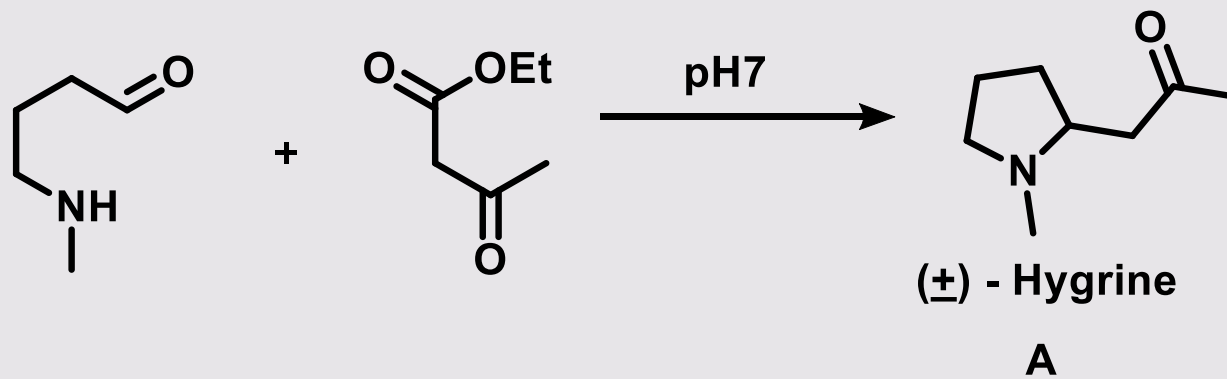


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## STRUCTURE ELUCIDATION

- Structure A for Hygrine is finally confirmed by its synthesis from the condensation reaction of  $\gamma$ -methylaminobutyraldehyde with ethyl acetoacetate at pH 7.



- The product resembles in structure to natural Hygrine and give all the reactions discussed earlier.



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# References

1. K.D Sharma and Y. R. Sharma, Kalyani Publishers, Unit-III page-319;
2. University Chemistry, Vol-IV, Dr. U. N. Dash, Dr. K. K. Ojha, Himalaya Publishing house, Unit V, page-411