Quadrant II – Transcript and Related Materials

Programme: T. Y. B. Sc.

Subject: Chemistry

Paper Code: CHC 107

Paper Title: Organic Chemistry

Unit: 2- Alkaloids

Module Name: Hofmann Exhaustive Methylation (HEM)

Module No: 11

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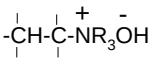
Hoffman's Exhaustive Methylation (HEM):-

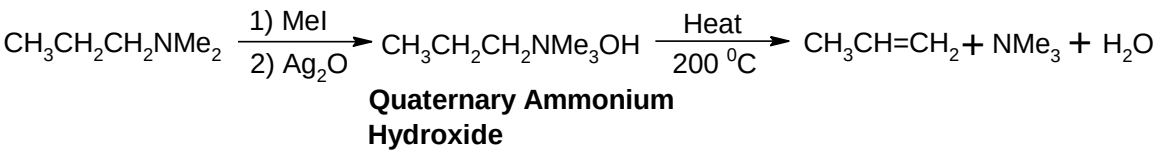
Consists of opening of Heterocyclic rings of alkaloid with the elimination of nitrogen to give a carbon fraction, and the nature of carbon skeleton is thereby obtained

Identification of alkene in the degradation reaction can provide valuable information about the structure of the parent amine

The availability of a β-H is a requirement for this reaction

The compounds which contain the structural unit 

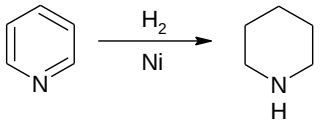
eliminate a trialkylamine on pyrolysis at 200 ^{0}C or above to yield an olefin



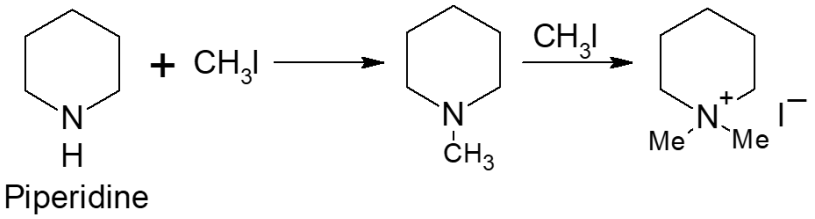
Degradation of Alkaloids

Step 1 - Hydrogenation of heterocyclic ring of an alkaloid

(if it is unsaturated)

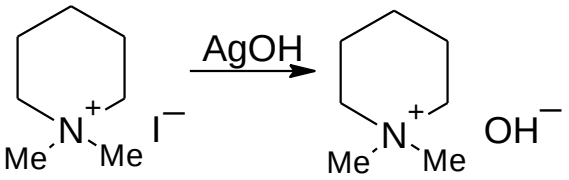


Step 2 - Exhaustive methylation of the primary, secondary or tertiary amine with excess methyl iodide - **yields quaternary methylammonium iodide**

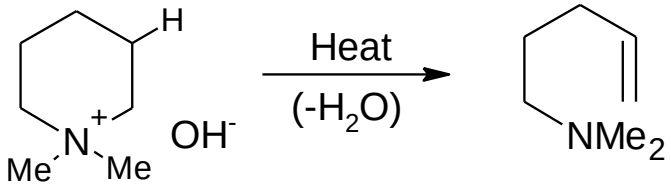


Piperidine

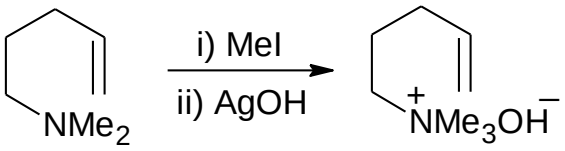
Step 3 - Treatment with silver oxide and water – To convert quaternary methylammonium iodide into quaternary methylammonium hydroxide



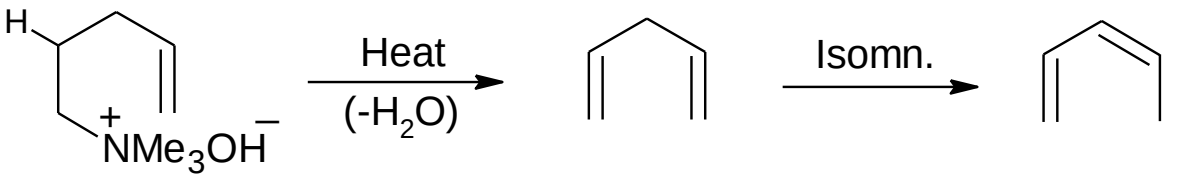
Step 4 - The quaternary methylammonium hydroxide is heated between 100-200 °C – To eliminate water molecule



Steps 1st, 2nd and 3rd are repeated – Process is continued until the nitrogen atom is eliminated from heterocyclic ring

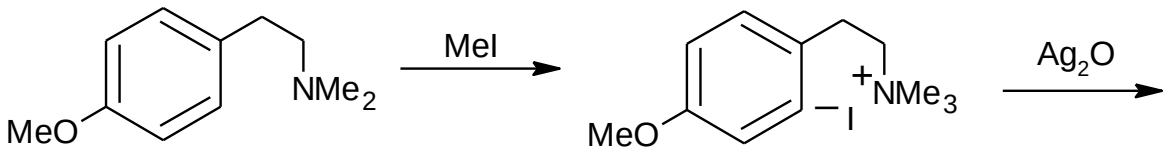


Results in an unsaturated hydrocarbon which isomerises to a conjugated diene

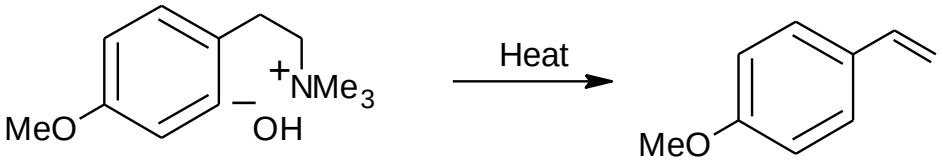


Piperyline

The Hofmann's Degradation method can be applied to Hordenine methyl ether to yield p-methoxy styrene



Hordenine methyl ether



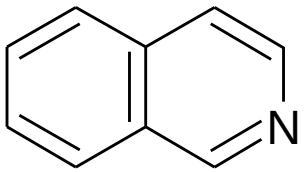
p-methoxy styrene

Although the general procedure is to heat the quaternary ammonium hydroxide at about 200 0C - the reaction may be Carried out by refluxing an aqueous or ethanolic solution of potassium hydroxide containing the methiodide or methosulphate of the base.

Limitations

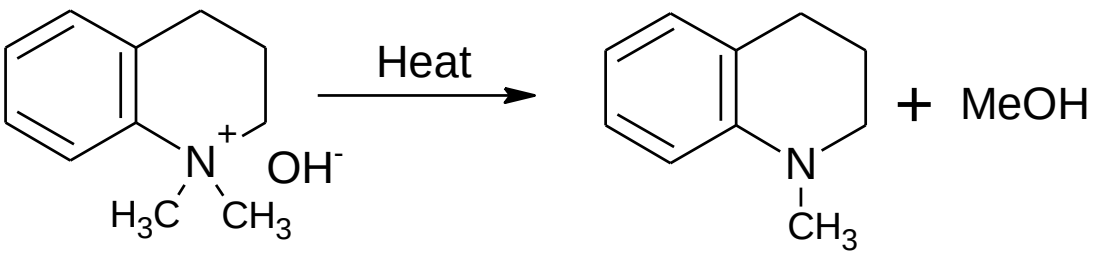
1. HEM fails if there is no beta hydrogen available for elimination as water. In such case the Emde modification may be used

Eg - Isoquinoline



2. Even though the compound contains a beta hydrogen atom, the exhaustive methylation method may fail

Eg – Tetrahydroquinoline


Heat
N+
OH-
H3C
CH3
N
CH3
+ MeOH