

CHEMICAL METHODS

- The alkaloids mostly contains one or more oxygen atoms, which may be present as hydroxyl, methoxy, methylenedioxy, carbonyl, carbonyl ester, lactone, amide, lactam, epoxide groups or ether linkage.
- i) Hydroxyl group**
Molecule contains hydroxyl group or -NH group then the number of these groups can be estimated by acetylation or Zerewitinoff's method.
- Acetylation's method**

$$\text{R-OH} + \text{CH}_3\text{-CO-Cl} \rightarrow \text{R-OCO-CH}_3$$

$$\text{R-NH-R}_1 + \text{CH}_3\text{-CO-Cl} \rightarrow \text{R-N(COCH}_3\text{)-R}_1$$
- Zerewitinoff's method**

$$\text{R-OH} + \text{MeMgI} \rightarrow \text{R-OMgI} + \text{CH}_4$$

$$\text{R-NH-R}' + \text{MeMgI} \rightarrow \text{R-N(MgI)-R}' + \text{CH}_4$$
- If hydroxyl group is present it may be Alcoholic or Phenolic.
Phenolic compounds are soluble in sodium hydroxide and are reprecipitated by carbon dioxide and give colouration with ferric chloride while alcoholic does not respond to these tests .

96

CHEMICAL METHODS Contd.....

- ii) Carbonyl group**
Ascertained by usual reactions with hydroxylamine, semicarbazide or 2,4-dinitrophenylhydrazine. The carbonyl group may be present as an aldehyde or a ketone. This distinction can be made from Tollen's reagent and silver mirror.
- iii) Carboxyl group**
Dissolved in bicarbonate or ammonia and reprecipitation with carbon dioxide indicates the presence of carboxyl group.
The formation of ester on treatment with alcohol in the presence of dehydrating agent.
- iv) Methoxy group**
Use Zeisel's method, which is similar to the Herzig-Meyer method



97

CHEMICAL METHODS Contd.....

- **v) Methylenedioxy group (-O-CH₂-O-)**

On heating with hydrochloric or sulfuric acid yields formaldehyde.

- **vi) Amide, lactam, ester, lactone groups**

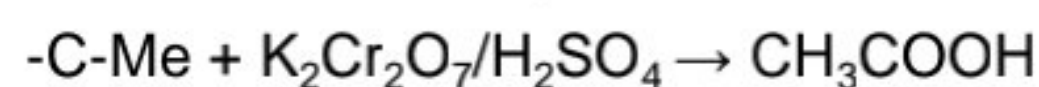
Be detected and estimated through acid or alkaline hydrolysis.

- **vii) Epoxide and ether linkage**

Be cleaved by the addition of hydrogen bromide or hydroiodic acid.

- **viii) Tertiary methyl group**

Estimated by Kuhn-Roth oxidation (K₂Cr₂O₇/H₂SO₄) to acetic acid, which is distilled off and titrated against standard base.



- **ix) Nature of nitrogen**

The acetylation or benzylation can distinguish tertiary amine from secondary amine, the former being inert whereas the latter gives acetate or benzoate derivative.

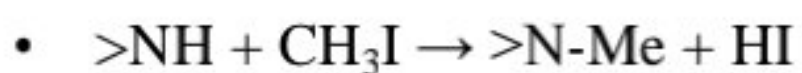
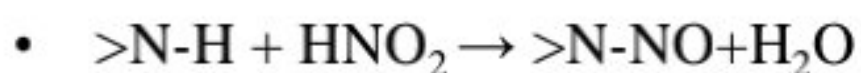
This distinction can also be done by treatment with HNO₂ or methyl iodide or oxidation with 30% hydrogen peroxide. 98

CHEMICAL METHODS Contd.....

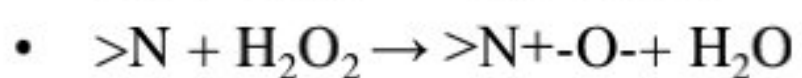
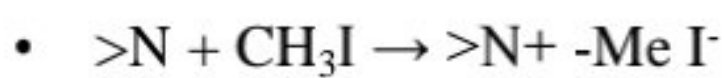
- **ix) Nature of nitrogen**

The presence of N-methyl group is often detected by distillation of amine with sodalime or estimated by the treatment with hydroiodic acid at 150-300 and conversion of methyl iodide produced to silver iodide as mentioned for estimation of methoxy groups.

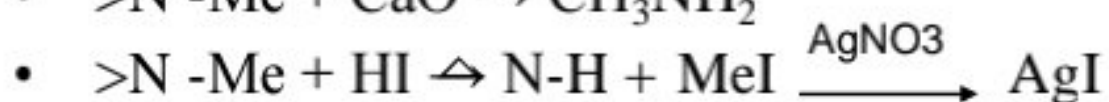
- **Secondary amine**



- **Tertiary amine**



- **N-Methyl group**



DEGRADATION OF ALKALOIDS

The following methods are used to find out structural fragments of alkaloid molecules:

- ☐ i. **Hofmann exhaustive methylation.**
- ☐ ii. **Emde's degradation.**
- ☐ iii. von Braun's method.
- ☐ iv. Hydrolysis.
- ☐ v. Alkali fusion.
- ☐ vi. Dehydrogenation.

100

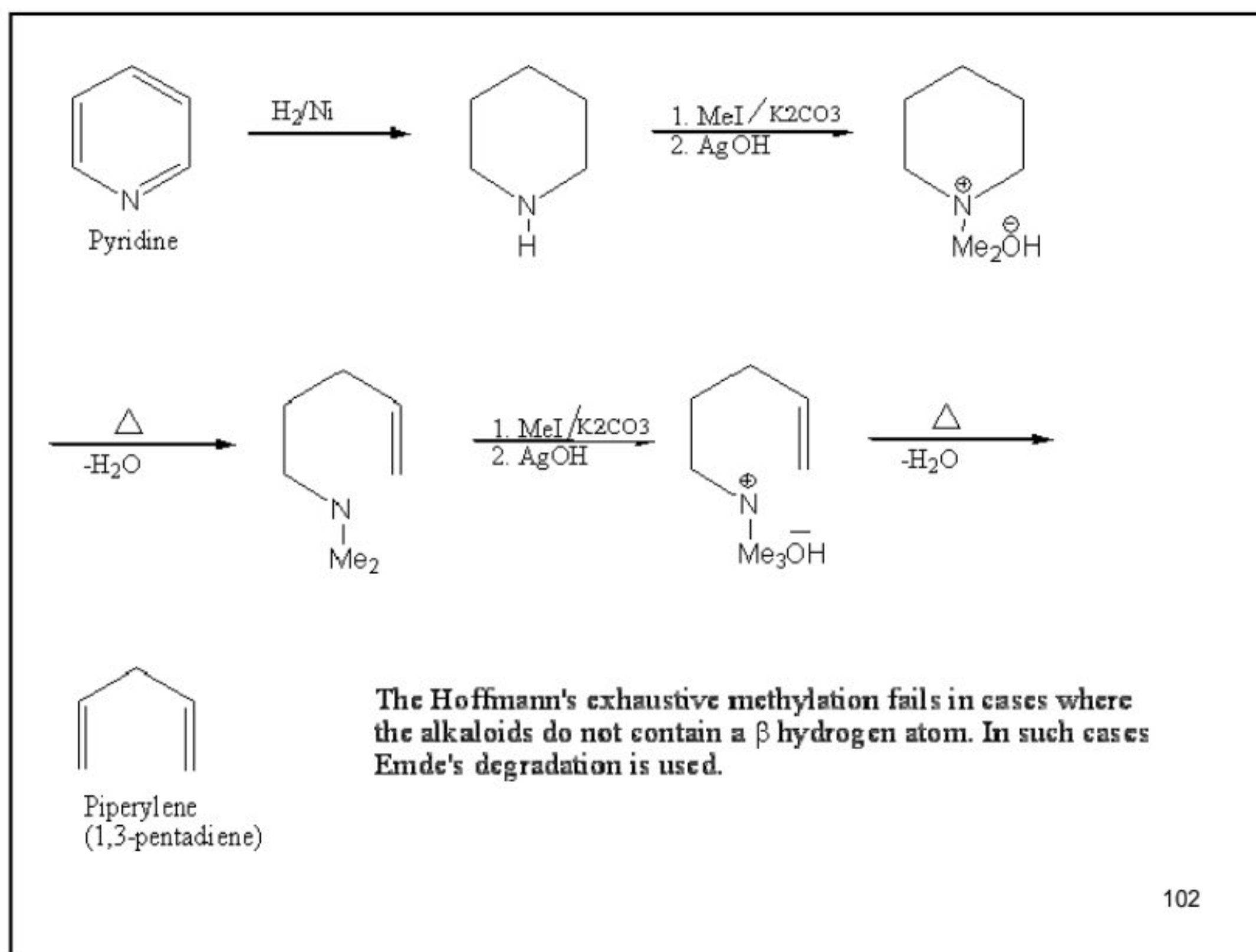
☐ DEGRADATION OF ALKALOIDS

Now we discuss the mainly used methods of Hofmann degradation and Emde's degradation.

i. Hofmann exhaustive methylation

- It consists in opening of the heterocyclic ring with elimination of 'N' to give a carbon fraction.
- In this method, the alkaloid is first hydrogenated (if it is unsaturated) and then converted into quaternary methyl ammonium hydroxide, which on heating loses a molecule of water.
- The hydroxyl group is eliminated from tetra methyl ammonium hydroxide and the hydrogen atom from the β position with respect to the 'N' atom resulting in ring opening at the 'N' atom on the same side from which the β hydrogen was eliminated.
- The process is repeated on the formed product till the 'N' is eliminated & an unsaturated hydrocarbon is left which isomerizes to a conjugated diene

101

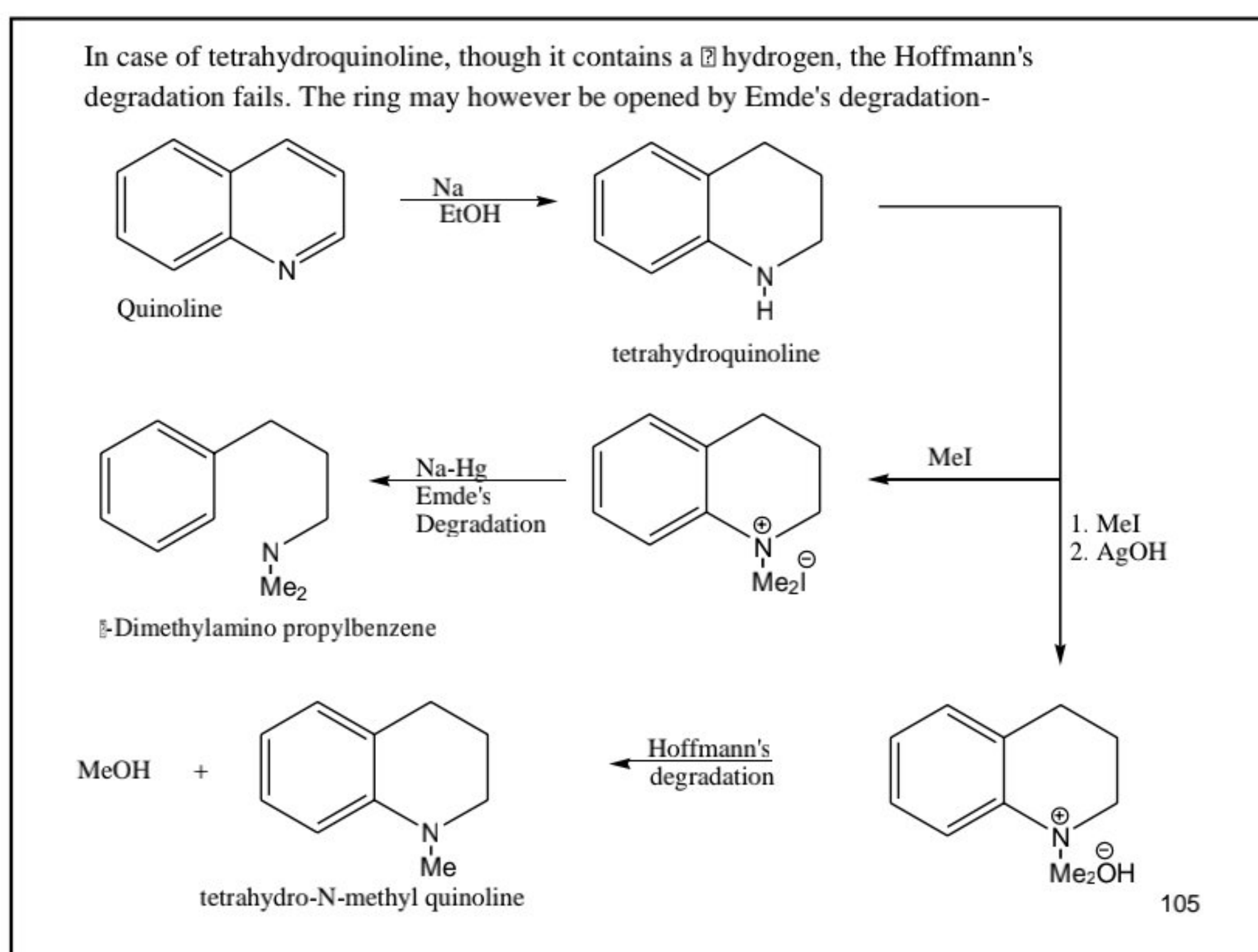
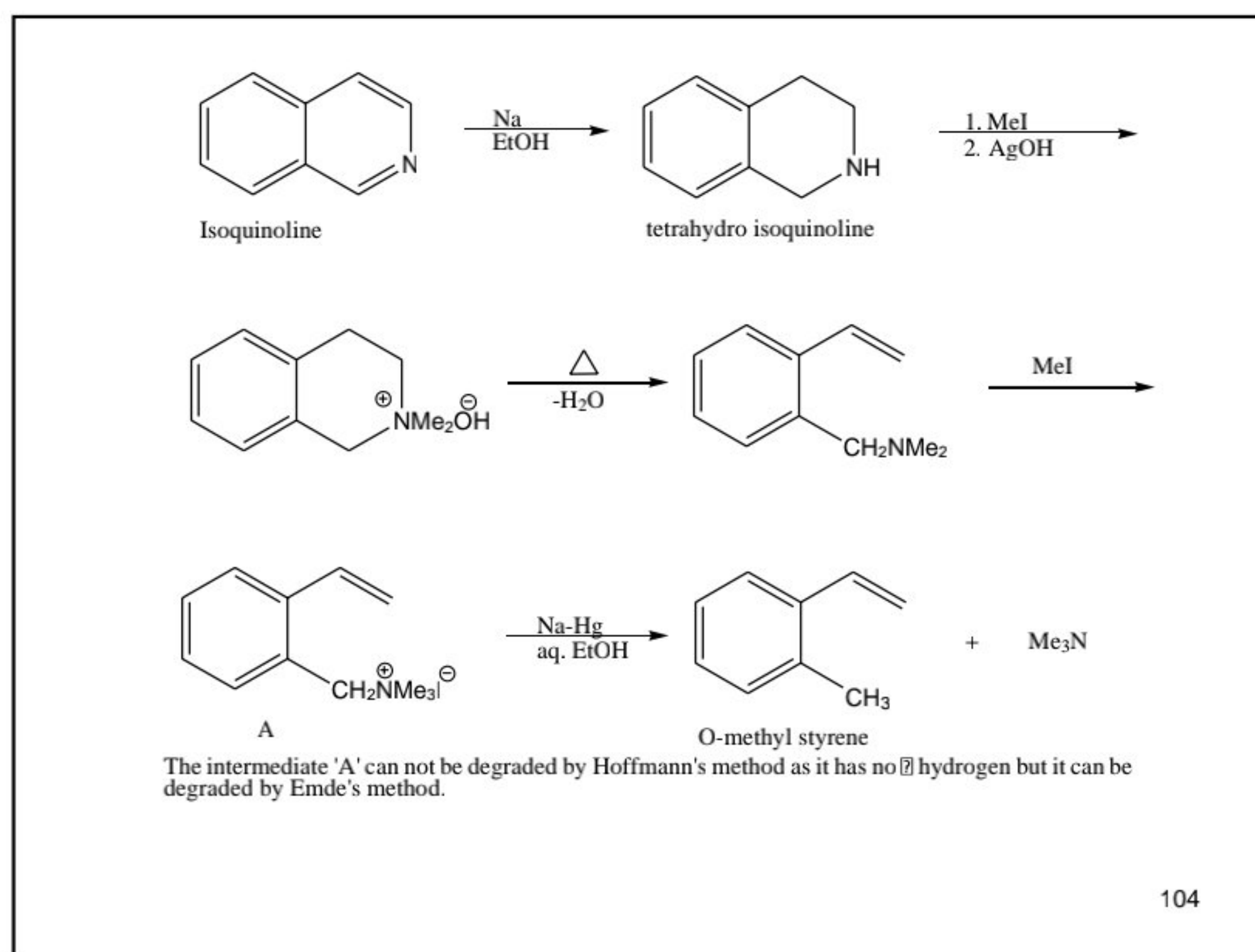


□ DEGRADATION OF ALKALOIDS

•ii. *Emde's degradation*

The alkaloid is converted to quaternary ammonium salt by refluxing with alkyl halide and the resulting salt is subjected to reductive cleavage by the treatment with sodium amalgam in alkanol or sodium in liquid ammonia or by catalytic hydrogenation.

Tetrahydroquinoline and tetrahydroisoquinoline quaternary salts undergo Emde's degradation.



☐ PHYSICAL METHODS

Recently physical methods are used, in conjunction with chemical reactions to elucidate structure of alkaloids and it is possible to determine a structure in a matter of days given a few milligrams(or less) of a pure compound.

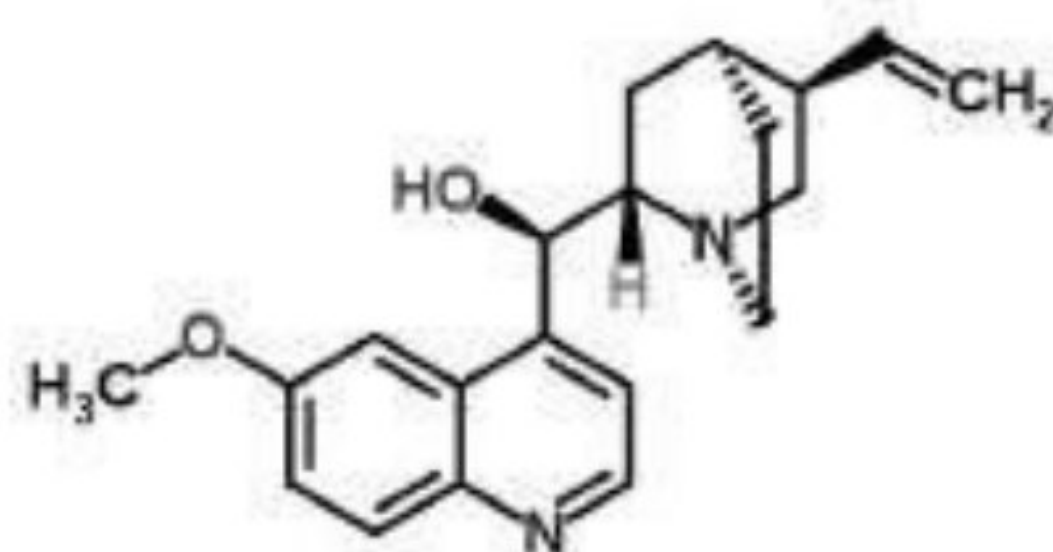
- Infrared spectrum : Gives information about many functional groups
- Ultraviolet spectra : Used to indicate the nature of unsaturation or aromatic rings
- NMR spectroscopy : More versatile for detecting many function groups, the nature of protons, carbons, heterocyclic rings etc

Mass spectra : The fragmentation gives the information

- about molecular weight and degradation of the skeleton.
- Single crystal X-ray analysis : Offers means for determining or confirming stereochemistry as well as distinguishing between alternate structures that appear to fit well for a particular
- alkaloid.

optical rotatory dispersion or circular dichroism: Further support

QUININE



107