Class - B. Sc. Part III

Subject - chemistry (organic)

Paper - VII

Topic - Mannich reaction

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4. Mannich Reaction

"This is the Condensation between a compd. containing at least one active hydrogen atom. Formaldehyde and ammonia a primary or secondary amine (preferably as the hydrochloride)"

$$C_6H_5COCH_3 + CH_2O + R_2NH\cdot HCl \longrightarrow C_6H_5COCH_2\cdot CH_2\cdot NR_2HCl + H_2O$$

Acetophenone, Formaldehyde, ammonic → Mannich Base

↓

[In this reaction the replacement of the active hydrogen atom by an amino methyl group or substituted amino methyl group is not change the product formed in this reaction is called a Mannich Base"]

Mechanism:- [There is uncertainly of mechanism of Mannich reaction. A possibility is that the lone pair electron of N_2 attacks on the Carbonyl group of formaldehyde to form an ion which is protonated and finally eliminates a molecule of water to produce the ions]. The ion I is then attacked by the Carbonion II, derived from acetophenone to yield the mannich base. The base is usually isolated as hydrochloruch.

(i) $(C_2H_5)\ddot{N}H + CH_2=\ddot{O} \longrightarrow (C_2H_5)_2\overset{+}{N}H\cdot -CH_2-\ddot{O}^- \xrightarrow{H^+}$

$(C_2H_5)_2\underset{H}{\overset{+}{N}}-CH_2-OH \xrightarrow[-H_2O]{} [(C_2H_5)_2\overset{+}{N}=CH_2 \longleftrightarrow (C_2H_5)_2\ddot{N}-CH_2]$

Carbonion

(ii) $C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2-H \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2 + H^+ \longleftrightarrow C_6H_5-\overset{\ddot{O}}{\overset{|}{C}}=CH_2$

Carbonion II

$(C_6H_5)N-\overset{+}{C}H_2 + \ddot{C}H_2-\overset{O}{\overset{\|}{C}}-C_6H_5 \longrightarrow (C_6H_5)_2N-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-C_6H_5$

Mannich base

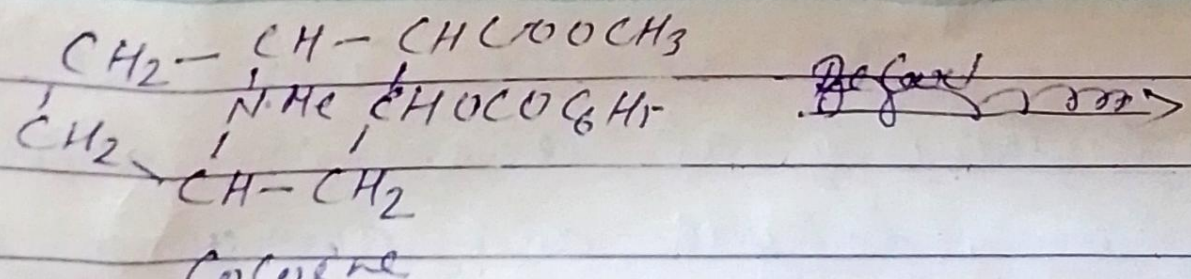
Application:-

(i) **Synthesis of Cocaine**

$$\begin{matrix} CH_2\cdot CHO \\ CH_2\cdot CHO \end{matrix} + H_2N\cdot CH_3 + \begin{matrix} CH_2COOCH_3 \\ CO \\ CH_2-COO^- \end{matrix} \xrightarrow[-2H_2O]{\text{Two mannich reaction}}$$

$$\begin{matrix} CH_2-CH-CHCOOCH_3 \\ | \quad N-CO-COO^- \\ CH_2-CH-CHCOOCH_3 \end{matrix} \xrightarrow[-CO_2]{\text{Decarboxylation}} \begin{matrix} CH_2-CH-CH\cdot COOCH_3 \\ | \quad N\cdot Me \quad CO \\ CH_2-CH-CH_2 \end{matrix}$$

Reduction



Cocaine