Aldehydes: Although higher aldehydes are also used, but formaldehyde is the common component during Mannich Rx.

Mechanism:

The lone pair of electrons of nitrogen attacks on the carbonyl group of formaldehyde to form an ion which is protonated and finally eliminates a molecule of water to produce the ion I. The ion I, is then attacked by the carbanion II, derived from acetophenone, to yield the Mannich base. The base is usually isolated as hydrochloride.

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

$(C_2H_5)_2\overset{+}{N}H-CH_2OH \xrightarrow{-H_2O} (C_2H_5)_2\overset{+}{N}=CH_2 \longleftrightarrow (C_2H_5)_2N-\overset{+}{C}$

I

(ii) $C_6H_5.CO.CH_3 \xrightarrow{-H^+} C_6H_5.CO\bar{C}H_2$

II

(iii) $(C_2H_5)_2N-\overset{+}{C}H_2 \quad C_6H_5.CO.\bar{C}H_2 \longrightarrow C_6H_5CO.CH_2.CH_2.N(C_2H_5)_2$

(Mannich base)

Synthetic applications

(1) Synthesis of alkaloids: →

(a) Synthesis of tropinone and atropine: The synthesis consists of two Mannich reactions to form an intermediate I which easily looses two molecules of ~~water~~ carbondioxide to give tropinone.

(4)

$CH_2 \cdot CHO$ + $H_2N \cdot CH_3$ + CH_2COO^-, CO, CH_2COO^- — Two Mannich (−2H₂O)

(Succindialdehyde) (Acetone dicarboxylate)

$CH_2-CH-CH\,COO^-$, $N\,CH_3$, CO, $CH_2-CH-CH\,COO^-$ —(−2CO₂)→ $CH_2-CH-CH_2$, $N\,CH_3$, CO, $CH_2-CH-CH_2$

I — Tropinone

(i) Zn–Hg (Reduction)

(ii) $C_6H_5-CH(CH_2OH)COOH$.

(esterification with tropic acid)

$CH_2-CH-CH_2$, $N\,CH_3$, $CH\,OCO\,CH\cdot C_6H_5$, $CH_2-CH-CH_2$, CH_2OH.

(Atropine)

(4) Synthesis of Pseudopelletierine :→

H_2C ⟨ CH_2-CHO, CH_2-CHO + $H_2N\,CH_3$ + CH_2COOH, CO, CH_2COOH — Two Mannich reaction → −2CO₂

CH_2 ⟨ CH_2-CH-H_2C, $N\,CH_3$, CH_2-CH-H_2C ⟩ CO.

Pseudopelletierine

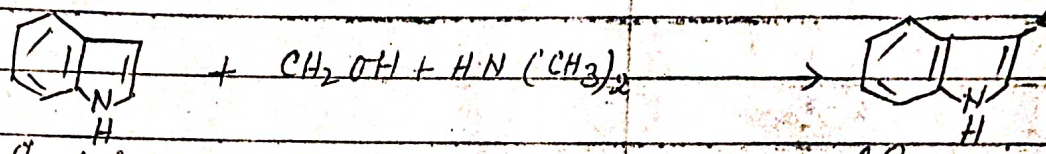
(2) Preparation of α:β unsaturated carbonyl compounds— Mannich base hydrochloride, those derived from aliphatic compounds ~~those~~ eliminates an amine hydrochloride to form unsaturated product. e.g.

$C_6H_5CO\,CH_2\cdot CH_2\cdot NH(CH_3)_2^+\,Cl^- \xrightarrow{\text{Heat}}$

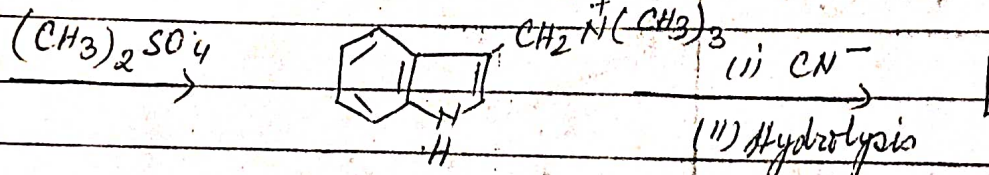
$C_6H_5\cdot CO\cdot CH=CH_2^+(CH_3)_2\,\overset{+}{N}H_2\,Cl^-$

(3) Replacement of amino group :—

(a) Synthesis of Nitroauxin (indole β-acetic acid) :—

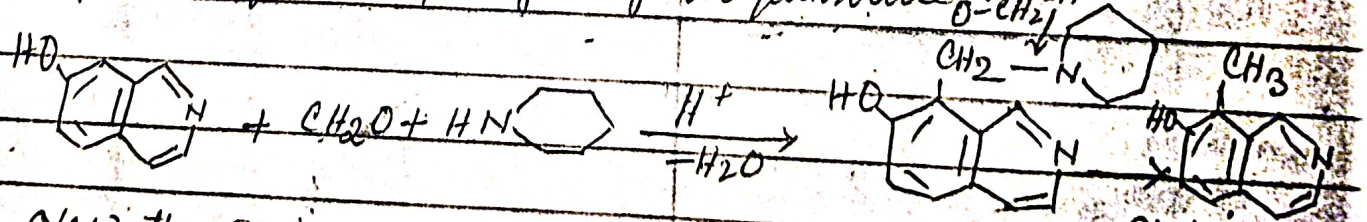


(Indole) (Gramine)



Nitroauxin

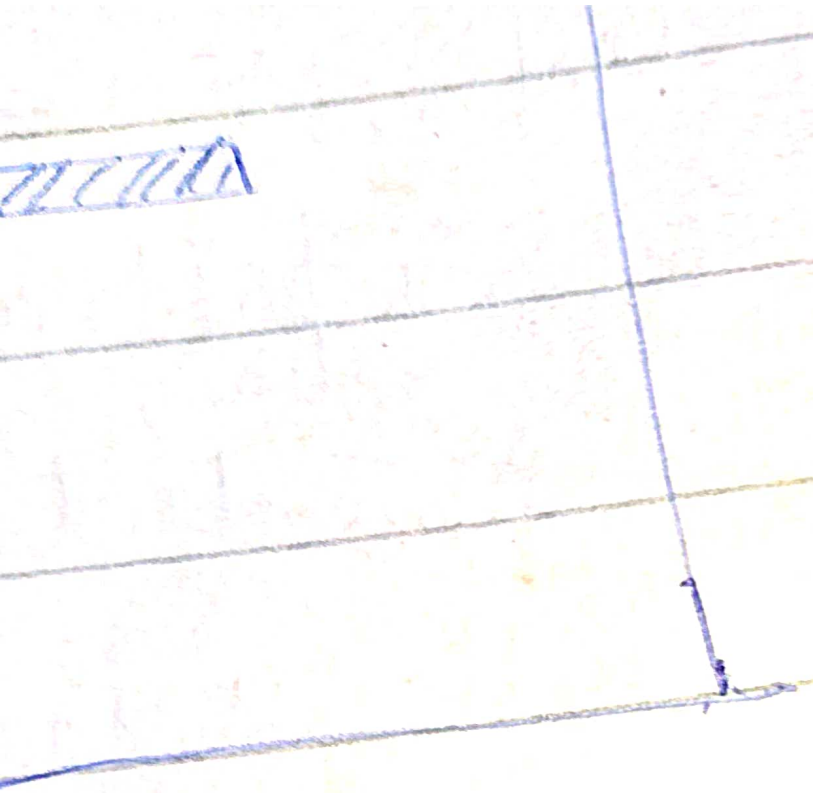
(b) Synthesis of quinine :— This reaction is applied in the synthesis of quinine to introduce a methyl group into the 8 position of 7-hydroxy-iso-quinoline. Mannich base is prepared from 7-hydroxy iso-quinoline.



Now the ~~quinine group~~ amino group of the base is replaced by hydrogen from methoxide ion, hydride ion transfer.

The distinction between true solution colloidal solution and suspension is given below.

PROPERTIES	TRUE SOLUTION	COLLOIDAL SOLS	SUSPENSION
Size of particle	10^{-7} cm or less	is between 10^{-7} to 10^{-4} cm	10^{-7} cm or greater
Visibility	The solute particles are not visible to the naked eye as well as a most powerful microscope.	The particles are visible with help of ultra microscope.	The particles are visible even to the naked eye.
Separation	The solute and solvent can not be separated even by ultra filtration.	The two phases can not be separated by ordinary filtration.	The solute and the solvent can be separated by ordinary separation.
Settling	The solute particles do not settle on standing.	The particles can settle by centrifugation.	The particles settle under gravity.
Diffusion	The true sols diffuse rapidly through parchment membrane.	The diffuse slowly through a parchment membrane.	The solute particles can not diffuse through a parchment membrane.
Tyndal Effect	True solution does not show Tyndal effect.	colloidal solution shows Tyndal effect.	They also show Tyndal effect.
Brownian movement	True solution does not show Brownian movement.	Colloidal solution shows Brownian movement.	The Brownian movement is slow and not at all.



mill is shown in the above
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directions. A slurry conta
e material is placed
plates. Finer dispersion an
ent diluent during gri
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