Class – B.Sc. Part - III
Subject - chemistry (organic)
Paper - VII
Topic – Claisen condensation.

Claisen condensation

The condensation of an ester and another hydrogen containing ester, ketone or nitrile to form a β-ketoester, ketone or nitrile respectively is known as claisen condensation. This reaction is catalysed by sodium ethoxide, sodamide, triphenylmethyl sodium etc. e.g.- The condensation of ethyl acetate in presence of ethoxide ion to form ethyl acetoacetate.

$$2\,CH_3COOC_2H_5 \xrightarrow{C_2H_5ONa} \underset{\text{Ethyl acetoacetate}}{CH_3COCH_2COOC_2H_5} + \underset{}{C_2H_5OH}$$
Ethyl acetate

$$CH_3COOC_2H_5 + CH_3COCH_3 \xrightarrow{C_2H_5ONa} \underset{\text{Acetyl acetone}}{CH_3CO\cdot CH_2\cdot COCH_3}$$
Ethyl acetate Acetone

Mechanism :– The ethoxide ion, from sodium ethoxide removes a proton from a molecule of ethyl acetate to give the carbanion I. The carbanion adds to the

carbonyl group of the second molecule of the ester or ketone and forms anion II, which loses ethoxide ion to yield the β-keto ester. The β-keto ester having a CH_2 group between two carbonyl groups, ionizes even more readily than ethyl acetate and thus the enolate anion III is form which is stabilised by mesomerism, is formed. Acidification of anion III regenerates the β-keto ester.

$$CH_3COOC_2H_5 + C_2H_5O^- \xrightleftharpoons{-C_2H_5OH}$$

$$\left\{ \bar{C}H_2-\underset{\underset{O}{\|}}{C}OC_2H_5 \longleftrightarrow CH_2=\underset{\underset{O^-}{|}}{C}OC_2H_5 \right\}$$

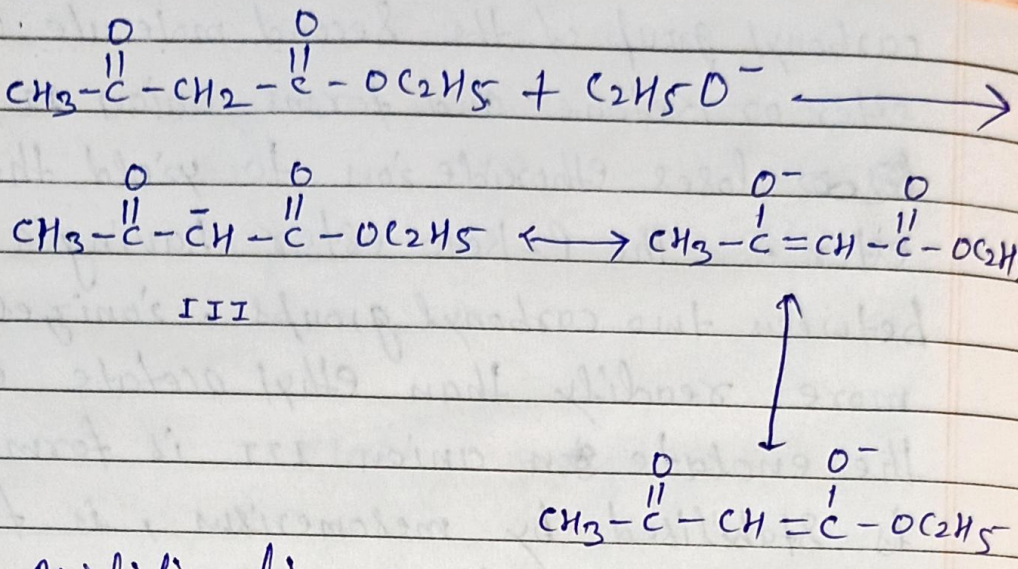
I

$$CH_3-\overset{\overset{O}{\|}}{C}-OC_2H_5 + \bar{C}H_2COOC_2H_5 \rightleftharpoons CH_3-\overset{\overset{O^-}{|}}{C}-CH_2COOC_2H_5$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad OC_2H_5$$

II

$$\Big\downarrow\Big\uparrow -C_2H_5O^-$$

$$CH_3-\underset{\underset{O}{\|}}{C}-CH_2-COOC_2H_5$$



Acidification:

$$CH_3COCHCOOC_2H_5 + HCl \longrightarrow CH_3COCH_2COOC_2H_5 + Cl^-$$

The last step of the reaction is an essential feature of the reaction as it helps to force the equilibrium of the first step to the right. The importance of this step can be proved by the fact that condensation can't be affected with sodium ethoxide when the expected product (β-keto ester) does not contain a C-H bond adjacent to both carbonyl and carboxyalkyl gr. and therefore can't form an anion analogous to III. e.g. ethylisobutyrate does not undergo claisen condensation in the presence of C_2H_5ONa because the β-keto ester does not contain a C-H bond of the above mentioned type, necessary to displace the equilibrium to right.

$$2(CH_3)_2CHCOOC_2H_5 \xrightarrow{C_2H_5ONa} (CH_3)_2CHCO\cdot\overset{(CH_3)_2}{\overset{|}{C}}\cdot COOC_2H_5$$

However, ethylisobutyrate can also be made to undergo claisen condensation in presence of either a very strong base or a base that reacts irreversibly in place of C_2H_5ONa because in the former case the second product of the acid-base reaction escapes as a gas and thus the first step of the condensation proceeds only to the right.

$$(CH_3)_2CHCOOC_2H_5 + (C_6H_5)_3CNa, NaNH_2 \text{ or } NaH$$

$$\downarrow$$

$$(CH_3)_2\cdot\bar{C}COOC_2H_5 + (C_6H_5)_2CH, NH_3 \text{ or } H_2$$

$$(CH_3)_2CHCOOC_2H_5 + (CH_3)_2\cdot\bar{C}COOC_2H_5 \xrightarrow{-OC_2H_5^-}$$

$$(CH_3)_2CH\cdot CO\cdot\overset{(CH_3)_2}{\overset{|}{C}}\cdot COOC_2H_5$$

3-Ketopentanoate

The aldol condensation and claisen condensation resemble each other in the sense that both involve nucleophilic attack by a carbanion on an electron-deficient carbonyl carbon. However in aldol condensation nucleophilic attack leads to addition, the typical reaction of aldehydes and Ketones while in the claisen condensation.

nucleophilic attack leads to substitution, the typical reaction of acyl compounds.