ACTIVE METHYLENE COMPOUNDS

ACETOACETIC ESTER

1. Keto Enol Tautomerism

Aldehydes or ketones having either $-CH_2-\overset{O}{\overset{\|}{C}}-$ or $-CH-\overset{O}{\overset{\|}{C}}-$ group has ability to exist in two structural isomers.

$$-CH_2-\overset{O}{\overset{\|}{C}}- \rightleftharpoons -CH=\overset{OH}{\overset{|}{C}}-$$

Keto form enol form

Ethyl aceto acetate or Aceto acetic ester exhibits keto enol tautomerism

Geuther in 1863 proposed enol form of Aceto acetic ester as

$$CH_3-\overset{OH}{\overset{|}{C}}=CH-\overset{O}{\overset{\|}{C}}-OC_2H_5$$

Frankland and Duppa in 1865 proposed keto form of Aceto acetic ester as

$$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5$$

Both the forms has their own evidences in the form of chemical reactions.

Later on it was proposed that both the forms of the compound exists in equilibrium in solution.

$$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5 \rightleftharpoons CH_3-\overset{OH}{\overset{|}{C}}=CH-\overset{O}{\overset{\|}{C}}-OC_2H_5$$

Keto form enol form

At equilibrium keto form exists in 92.3% where as enol form exists in 7.7%. Both the forms were isolated. Enol form has lower boiling point than keto form

Keto enol tautomerism refers to a chemical equilibrium between keto form and enol form. The interconversion of the two forms involves the transfer of alpha hydrogen atom and reorganisation of bonding electrons.

2. METHODS OF PREPARATION

a) Preparation of Aceto Acetic Ester (AAE) by Claisen condensation with mechanism

Condensation of an ester containing α-Hydrogen with same ester molecule or different ester in presence of base give β-Keto ester is known as claisen condensation.

Example:

Self condensation of Ethyl acetate in presence of $NaOEt$ (C_2H_5) (Sodium ethoxide) gives Ethyl acetoacetate (EAA)

$$CH_3COOC_2H_5 + CH_3COOC_2H_5 \xrightarrow{EtONa} CH_3COCH_2COOC_2H_5$$

Ethyl acetate Ethyl acetate Ethyl acetoacetate

Mechanism

1. $H-CH_2-COOC_2H_5 + C_2H_5O^{\ominus} \rightleftharpoons {}^{\ominus}CH_2COOC_2H_5 + C_2H_5OH$

2. $CH_3-C(=O)-OC_2H_5 + {}^{\ominus}CH_2COOC_2H_5 \rightarrow CH_3-C(-O^{\ominus})(-CH_2COOC_2H_5)-OC_2H_5 \longrightarrow$

$CH_3-C(=O)-CH_2-COOC_2H_5 + C_2H_5O^{\ominus}$

β-Keto Ester

Properties of Acetoacetic ester and alkyl derivative of Acetoacetic ester

a) Acid hydrolysis

Hydrolysis of alkyl derivative of Acetoacetic ester with Conc. alcoholic base (NaOH or KOH) under elevated temperature gives Carboxylic acid as product.

$$R\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}COOC_2H_5 \xrightarrow{\text{Conc NaOH}} R\text{-}CH_2\text{-}COOH + CH_3\text{-}COOH + C_2H_5OH$$

alkyl derivative of Acetoacetic ester Carboxylic acid Acetic acid Ethyl alcohol

Hydrolysis of Acetoacetic ester with Conc. alcoholic base (NaOH or KOH) under elevated temperature gives Acetic acid as product.

$$\underset{\text{Acetoacetic ester}}{CH_3\text{-}CO\text{-}CH_2\text{-}COOC_2H_5} \xrightarrow{\text{Conc NaOH}} \underset{\text{Acetic acid}}{CH_3\text{-}COOH} + \underset{\text{Acetic acid}}{CH_3\text{-}COOH} + \underset{\text{Ethyl alcohol}}{C_2H_5OH}$$

b) Ketonic hydrolysis

Hydrolysis of alkyl derivative of Acetoacetic ester with dilute aqueous base or acid under elevated temperature gives ketone as product. This reaction takes place in two steps

Step-I: Formation of keto acid

$$\underset{\text{alkyl derivative of Acetoacetic ester}}{R\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}COOC_2H_5} + H_2O \xrightarrow{H^+} \underset{\text{Keto acid}}{R\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}COOH} + \underset{\text{Ethyl alcohol}}{C_2H_5OH}$$

Step-II: Formation of ketone

$$\underset{\text{Keto acid}}{R\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}COOH} \xrightarrow{\Delta} \underset{\text{Ketone}}{R\text{-}CH_2\text{-}CO\text{-}CH_3} + \underset{\text{Carbondioxide}}{CO_2}$$

Hydrolysis of Acetoacetic ester with dilute aqueous base or acid under elevated temperature gives acetone as product. This reaction takes place in two steps

Step-I: Formation of keto acid

$$\underset{\text{Acetoacetic ester}}{CH_3\text{-}CO\text{-}CH_2\text{-}COOC_2H_5} + H_2O \xrightarrow{H^+} \underset{\text{Acetoacetic acid}}{CH_3\text{-}CO\text{-}CH_2\text{-}COOH} + \underset{\text{Ethyl alcohol}}{C_2H_5OH}$$

Step-II: Formation of ketone

$$\underset{\text{Acetoacetic acid}}{CH_3\text{-}CO\text{-}CH_2\text{-}COOH} \xrightarrow{\Delta} \underset{\text{Acetone}}{R\text{-}CH_2\text{-}CO\text{-}CH_3} + \underset{\text{Carbondioxide}}{CO_2}$$

3. Synthetic applications of AAE

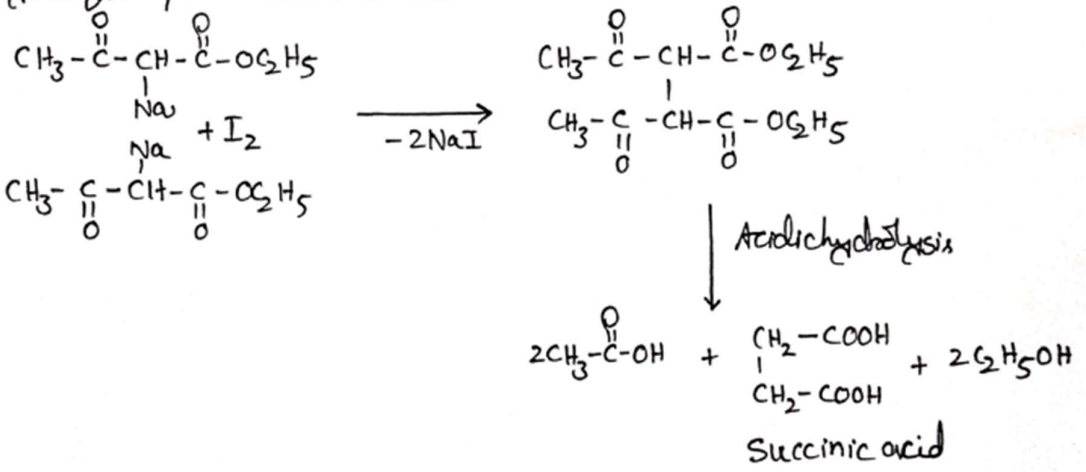
a) Preparation of mono carboxylic acids

Acetoacetic ester undergo acidic hydrolysis in presence of Concentrated alcoholic potash gives acetic acid and Ethyl alcohol.

$$\underset{\text{Acetoacetic ester}}{CH_3\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}OC_2H_5} \xrightarrow{\text{Alc KOH}/H_2O} \underset{\text{Acetic acid}}{2CH_3COOH} + C_2H_5OH$$

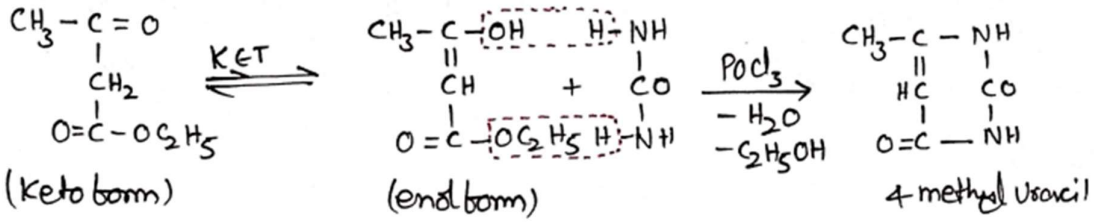
b) Preparation of di carboxylic acids

Sodio aceto acetic ester on reacting with iodine followed by acidic hydrolysis yields Succinic acid



c) Preparation of Heterocyclic compounds

Aceto acetic ester undergo condensation with Urea in presence & $POCl_3$ gives 4-methyl Uracil



MALONIC ESTER / DIETHYL MALONATE

Methods of preparation

1.) From Acetic acid

Acetic acid on reaction with Cl_2 in presence of Red P gives chloro acetic acid, which on reaction with K_2CO_3 gives Potassium Chloro acetate, which on reaction with Potassium Cyanide (KCN) gives potassium cyano acetate. Then dry Hcl is passed through the solution of potassium cyano acetate gives malonic acid which on reaction with Hcl in presence of Ethyl alcohol gives malonic ester.

$$CH_3COOH \xrightarrow{Cl_2/Red\,P} Cl-CH_2-COOH \xrightarrow{K_2CO_3} CH_2(Cl)(COOK) \xrightarrow{KCN}$$

Acetic acid — Chloro acetic acid — Pot. Chloro acetate

$$CH_2(CN)(COOK) \xrightarrow{Hcl/H_2O} CH_2(COOH)_2 \xrightarrow{C_2H_5OH/Hcl} CH_2(COOC_2H_5)_2$$

Pot. Cyano acetate — Malonic acid — Malonic ester

Properties

1. Synthesis of Aliphatic Carboxylic acids (Mono Carboxylic acids)

Mono Carboxylic acids are prepared form malonic ester.

A) synthesis of propanoic acid

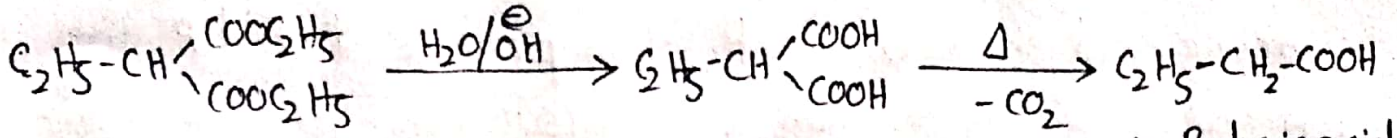
Methyl malonic ester on hydrolysis gives methyl malonic acid. This methyl malonic acid on decarboxylation gives propanoic acid.

$$CH_3-CH(COOC_2H_5)_2 \xrightarrow{\ominus OH/H_2O} CH_3-CH(COOH)_2 \xrightarrow[-CO_2]{\Delta} CH_3-CH_2-COOH$$

Methyl malonic ester — methyl malonic acid — Propanoic acid

synthesis of n-Butyric acid

Ethyl malonic ester on hydrolysis gives Ethyl malonic acid which on decarboxylation gives n-Butyric acid.



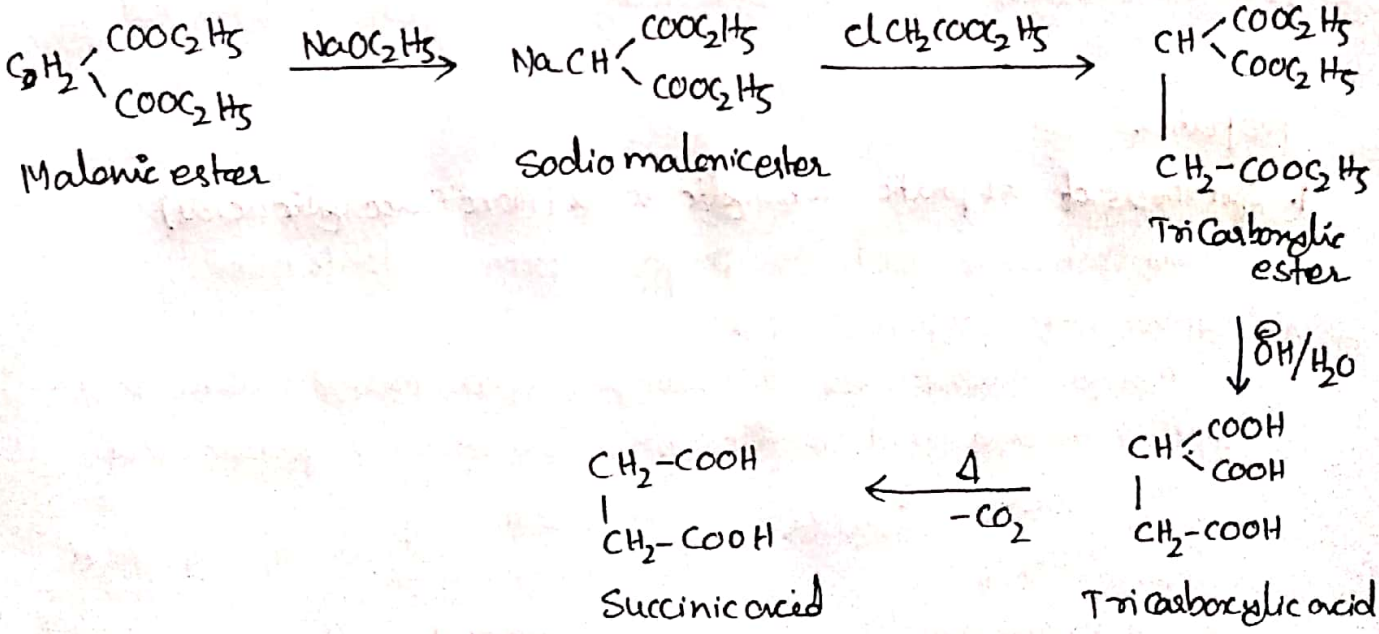
Ethyl malonic ester — Ethyl malonic acid. — n-Butyric acid

. synthesis of Dicarboxylic acids

Dicarboxylic acids were prepared from malonic ester.

A) synthesis of Succinic acid

Malonic ester on reaction with Sodium Ethoxide (C_2H_5ONa) gives Sodio malonic ester, which on reaction with chloro ester in particular Ethyl Chloro acetate gives Tricarboxylic ester which on hydrolysis gives Tri Carboxylic acid. Tricarboxylic acid undergo decarboxylation gives Succinic acid.



Malonic ester — Sodio malonic ester — Tri Carboxylic ester — Tri Carboxylic acid — Succinic acid

B) Synthesis of Adipic acid.

Malonic ester on reaction with strong base like Sodium Ethoxide (C_2H_5ONa) gives Sodio malonic ester. Two moles of sodio malonic ester reacts with 1,2 Dibromo ethane gives tetra Carboxylic ester which on hydrolysis gives tetra Carboxylic acid. Tetra Carboxylic acid on decarboxylation gives Adipic acid.

i) $CH_2(COOC_2H_5)_2 \xrightarrow{NaOC_2H_5} NaCH(COOC_2H_5)_2$

Malonic ester — Sodio malonic ester

ii) CH_2Br-CH_2Br (1,2 Dibromo Ethane) + 2 moles of Sodio malonic ester ($NaCH(COOC_2H_5)_2$) $\xrightarrow{-2\,NaBr}$ Tetra Carboxylic ester

Tetra Carboxylic ester $\xrightarrow{H_2O/\overset{\ominus}{O}H}$ Tetra Carboxylic acid

Tetra Carboxylic acid $\xrightarrow[-CO_2]{\Delta}$ Adipic acid ($CH_2(CH_2COOH)_2$)

3 Synthesis of α,β unsaturated acids = crotonic acid

Malonic ester on reaction with acetaldehyde in presence of Pyridine forms a product which on hydrolysis and followed by heating gives α,β unsaturated acid. (crotonic acid)

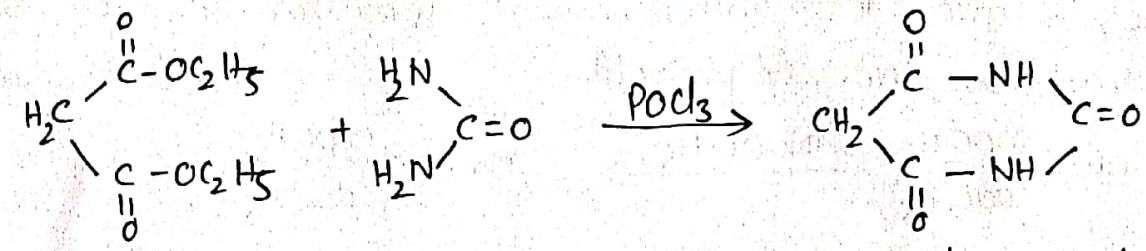
$CH_3CH=O + H_2C(COOC_2H_5)_2 \xrightarrow{\text{Pyridine}} CH_3-CH=C(COOC_2H_5)_2 \xrightarrow{H_2O/\overset{\ominus}{H}O}$

$CH_3-CH=C(COOH)_2 \xrightarrow[-CO_2]{\Delta} CH_3-CH=CH-COOH$

α,β unsaturated acid (Crotonic acid)

4. Reaction with Urea

Malonic ester on reaction with urea undergo condensation in presence of $NaOC_2H_5$ or $POCl_3$ gives malonyl urea or commonly called Barbituric acid.



Malonic ester + Urea → Barbituric acid