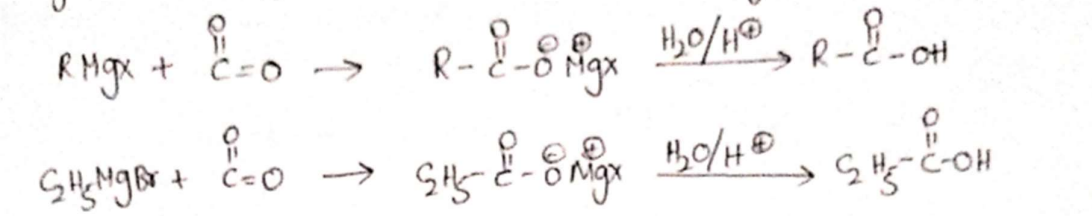
CARBOXYLIC ACIDS

Methods of preparation

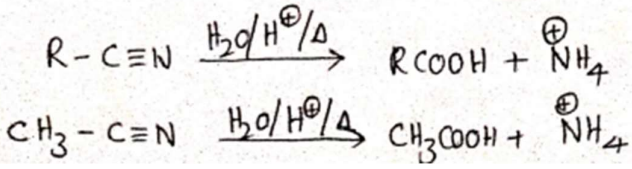
a) From Grignard's reagent

Grignard reagents reacts with Carbondioxide to yield Magnesium Carboxylates. These on acidification gives Carboxylic acids



b) From Cyanides or nitriles

Cyanides on hydrolysis in presence of acid or base catalyst to give Carboxylic acids

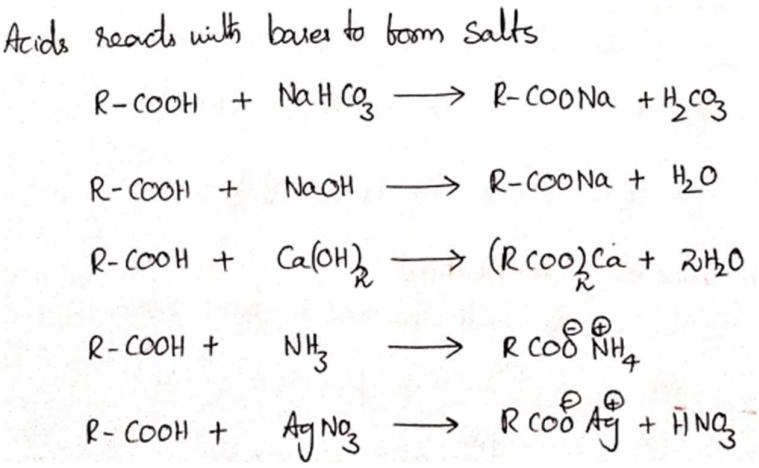


Chemical reactions

1. Reactions involving -H of -COOH group.

a) Formation of salts

Acids reacts with bases to form salts



2. Reactions involving -OH of -COOH group

a) Formation of esters

Carboxylic acids reacts with Alcohols to form Esters

$$R\text{-}COOH + HO\text{-}R' \xrightarrow{H^{\oplus}} R\text{-}COOR' \text{ (Ester)}$$

$$CH_3COOH + HO\text{-}C_2H_5 \xrightarrow{H^{\oplus}} CH_3COOC_2H_5$$

b) Formation of acid chlorides

Carboxylic acids reacts with PCl_3, PCl_5 or $SOCl_2$ to form Acid chloride

$$R\text{-}COOH \xrightarrow[\text{(or) } SOCl_2]{PCl_3 \text{ (or) } PCl_5} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl$$

$$CH_3\text{-}COOH \xrightarrow[\text{(or) } SOCl_2]{PCl_3 \text{ (or) } PCl_5} CH_3\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl$$

c) Formation of amides

Carboxylic acid reacts with 1° Amines to form Amide

$$R\text{-}COOH + H_2N\text{-}R' \longrightarrow R\text{-}CO\text{-}NH\text{-}R' \text{ (Amide)}$$

$$CH_3COOH + H_2N\text{-}C_2H_5 \longrightarrow CH_3\text{-}CO\text{-}NH\text{-}C_2H_5$$

d) Formation of anhydrides.

Carboxylic acids undergo dehydration to form acid anhydride

$$\underset{\text{Acid.}}{R\text{-}COOH} + \underset{\text{Acid}}{HO\text{-}\overset{O}{\overset{\|}{C}}\text{-}R} \xrightarrow[-H_2O]{P_2O_5,\ \Delta} \underset{\text{Anhydride}}{R\text{-}CO\text{-}O\text{-}CO\text{-}R}$$

$$CH_3\text{-}COOH + HOOC\text{-}CH_3 \xrightarrow[-H_2O]{P_2O_5,\ \Delta} \underset{\text{Acetic anhydride}}{CH_3\text{-}CO\text{-}O\text{-}CO\text{-}CH_3}$$

3. Reactions involving entire -COOH group

a) Degradation of carboxylic acids by Huns - Diecker's reaction

Treatment of silversalt of acid with Bromine in presence of CCl_4 to give alkyl or Aryl Bromide

$$R\text{-}COOH + NaOH \longrightarrow RCOONa \xrightarrow{AgNO_3} R\text{-}COO^{\ominus}Ag^{\oplus} \xrightarrow[\Delta]{Br_2/CCl_4} R\text{-}Br + CO_2 + AgBr$$

$$CH_3\text{-}COOH + NaOH \longrightarrow CH_3COONa \xrightarrow{AgNO_3} CH_3COO^{\ominus}Ag^{\oplus} \xrightarrow{Br_2/CCl_4} CH_3\text{-}Br + CO_2 + AgBr$$

Mechanism

i) $R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O^{\ominus}Ag^{\oplus} \xrightarrow{Br\text{-}Br} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}Br + AgBr$

Hypo bromite

ii) $R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}Br \xrightarrow{\Delta} \left[R^{\bullet} + \overset{O}{\overset{\|}{C}}\text{-}O^{\bullet} + Br^{\bullet}\right] \longrightarrow R^{\bullet} + CO_2$

$$R^{\bullet} + Br\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-}R \longrightarrow R\text{-}Br + R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O^{\bullet}$$

b) Decarboxylation by Schmidt reaction

Carboxylic acids on treatment with Hydrazoic acid gives primary amine

$$R\text{-}COOH \xrightarrow[\text{Conc } H_2SO_4]{N_3H/\Delta} R\text{-}NH_2 + N_2 + CO_2$$

$$CH_3COOH \xrightarrow[\text{Conc } H_2SO_4]{N_3H/\Delta} CH_3NH_2 \text{ (Methyl amine)}$$

Mechanism

i $Ar\text{-}\overset{O}{\overset{\|}{C}}\text{-}OH \overset{H^{\oplus}}{\rightleftharpoons} \left[Ar\text{-}\overset{O^{\oplus}\text{-}H}{\overset{\|}{C}}\text{-}OH \longleftrightarrow Ar\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{\oplus}{O}H_2\right] \longrightarrow Ar\text{-}\overset{O}{\overset{\|}{C}}^{\oplus} + H_2O$

ii) $Ar\text{-}\overset{O}{\overset{\|}{C}}^{\oplus} + H\text{-}\overset{\ominus}{N}\text{-}\overset{\oplus}{N}\equiv N \longrightarrow Ar\text{-}\overset{O}{\overset{\|}{C}}\text{-}\underset{H}{N}\text{-}\overset{\oplus}{N}\equiv N \xrightarrow{-N_2} \overset{O}{\overset{\|}{C}}=\underset{H}{\overset{\oplus}{N}}\text{-}Ar \longrightarrow \overset{O}{\overset{\|}{C}}=N\text{-}Ar \xrightarrow{H_2O} Ar\text{-}NH_2$

c) Arndt-Eistert synthesis

Conversion of an acid into its next higher homologue or to a derivative of the homologous acid, such as amide or ester.

$$RCOOH \xrightarrow{SOCl_2} RCOCl \xrightarrow{CH_2N_2} RCOCHN_2$$

Carboxylic acid — Acid chloride — α-Diazo ketone

$$RCOCHN_2 \xrightarrow{Ag_2O/H_2O} RCH_2COOH \text{ (Carboxylic acid)}$$
$$RCOCHN_2 \xrightarrow{Ag_2O/R'OH} RCH_2COOR' \text{ (Ester)}$$
$$RCOCHN_2 \xrightarrow{Ag_2O/NH_3} R\text{-}CH_2CONH_2 \text{ (Amide)}$$

Mechanism

i) Carboxylic acid is converted into its acid chloride using Thionyl chloride ($SOCl_2$).

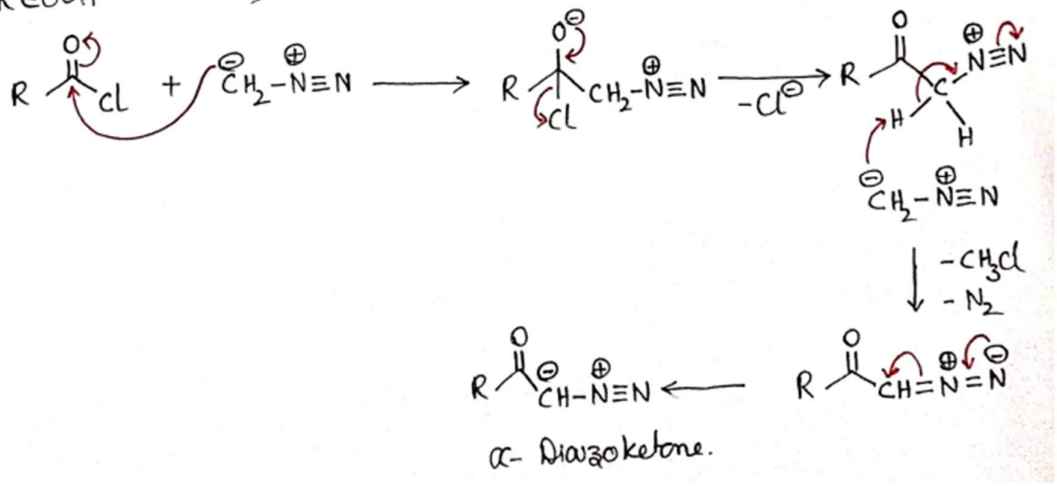
ii) Acid chloride reacts with Diazomethane gives α-diazo ketone (1)

iii) α-Diazo ketone (1) eleminates N_2 molecule and rearranges to ketene (2) in presence of Ag_2O (or) hν

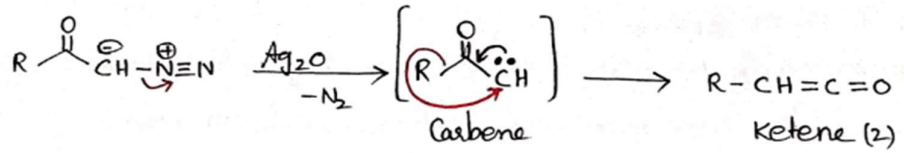
iv) Ketene is converted into an acid (or) amide (or) ester

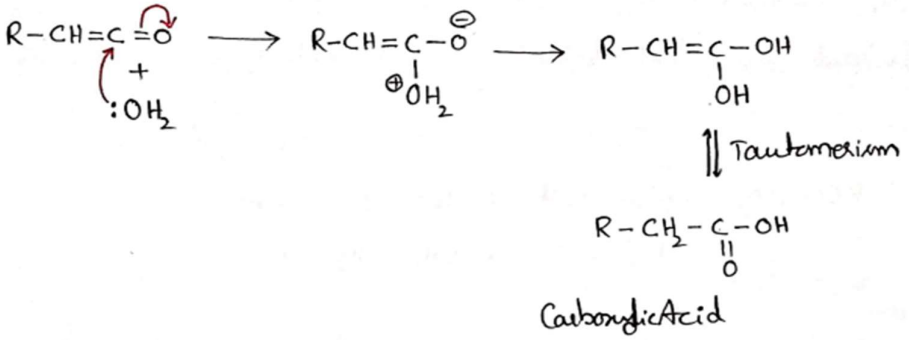
i) $RCOOH \xrightarrow{SOCl_2} RCOCl$ (Acid chloride)

ii)



α-Diazoketone.

iii) 

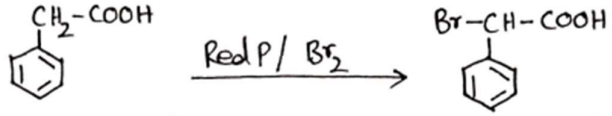
iv) 

d) Halogenation by Hell- Volhard- Zelinsky reaction

Preparation of α- chloro (or) bromo carboxylic acids by the action of chlorine (or) Bromine on mono carboxylic acids having α- hydrogens in presence of Red phosphorus.

Example:

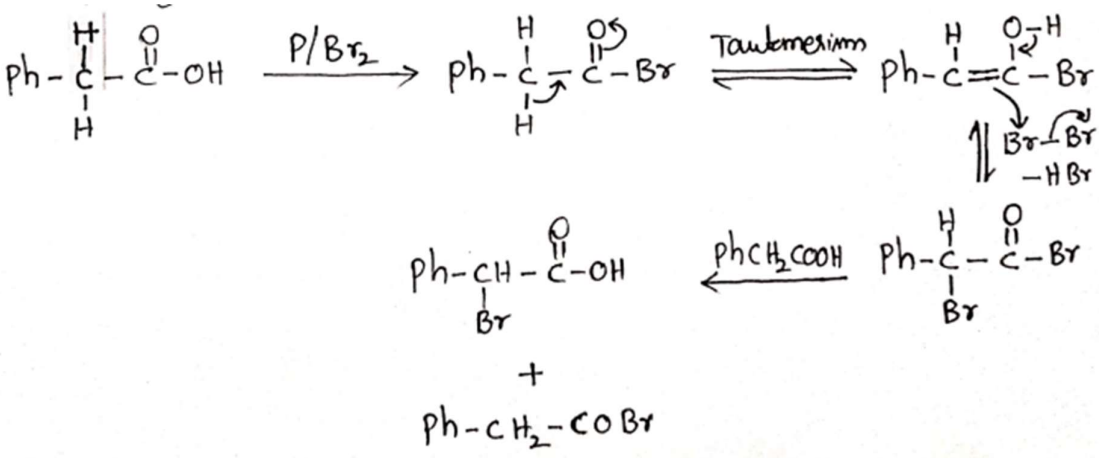
Preparation of α- Bromo phenyl acetic acid from phenyl acetic acid in presence of Red phosphorus and Bromine.



Phenyl acetic acid

α- Bromo phenyl acetic acid.

Mechanism



e) Mechanisms of acidic and alkaline hydrolysis of esters

ESTER HYDROLYSIS

Hydrolysis of Ester proceeds either by acid catalysed mechanism or by base catalysed mechanism.

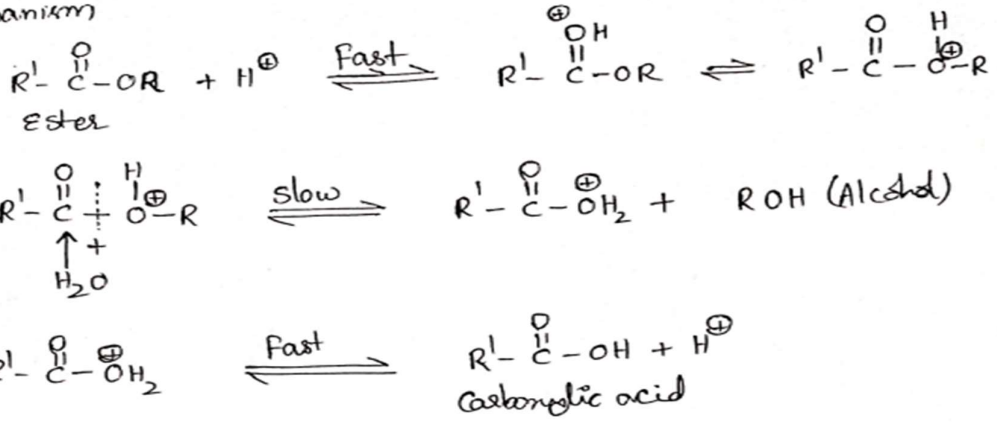
i) Ester hydrolysis by catalysed by acid is reversible

ii) Ester hydrolysis catalysed by Base is irreversible

1) Acid catalysed Ester hydrolysis

The first step of the mechanism is rapid protonation of Ester which is then solvolysed by a water molecule leading to the formation of protonated acid and an alcohol.

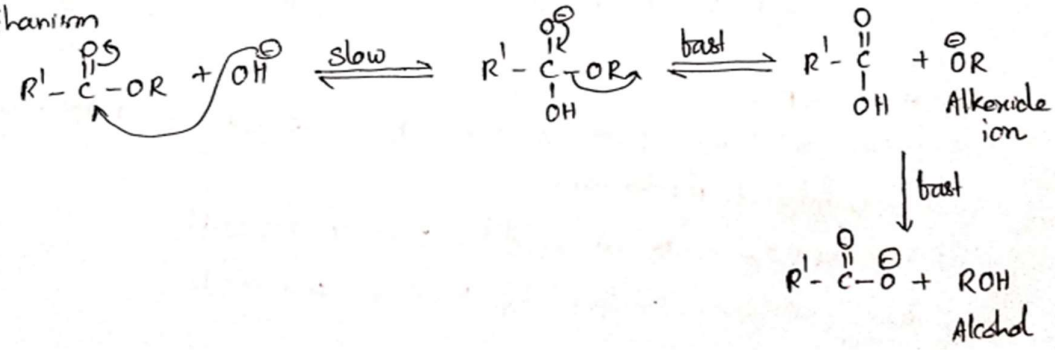
Mechanism



Base Catalysed Ester hydrolysis

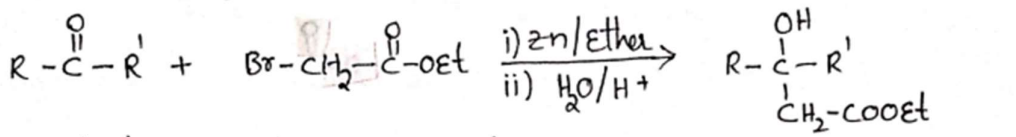
This reaction involves the nucleophilic attack of Hydroxide ion ($^{\ominus}OH$) on the Carbonyl group of the ester followed by rapid elemination of alkoxide ion. The next and the irreversible step is the transference of a proton from Carboxylic acid to the alkoxide ion

Mechanism



f) Reformatsky reaction

Reaction of α-halo esters (usually α-bromo esters) with Carbonyl Compounds (Aldehydes (or) Ketones) with zinc metal in an inert solvent (Ether / Benzene) gives β-hydroxy esters.

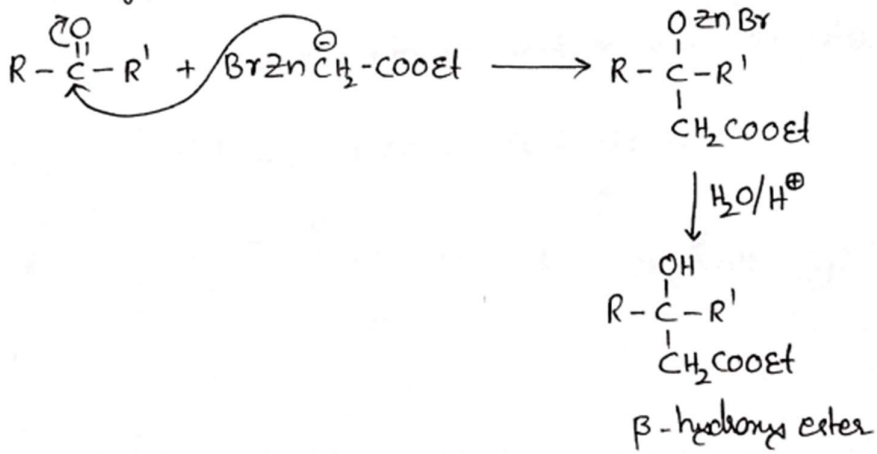


Aldehyde/ Ketone — Ethyl Bromo acetate — β-hydroxy ester

Mechanism:

i. In first step, addition of metallic zinc on α-Bromo ester (Ethyl Bromo acetate forming organo zinc compound.

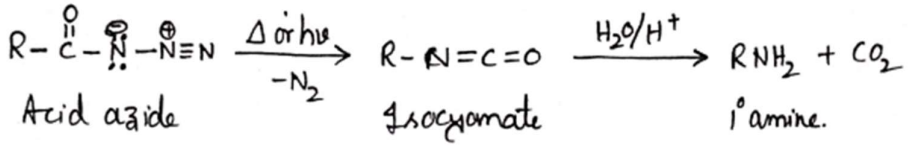
ii) Organo Zinc Compound reacts with Carbonyl group of aldehyde or Ketone gives β-hydroxy esters.



β-hydroxy ester

g) Curtius Rearrangement

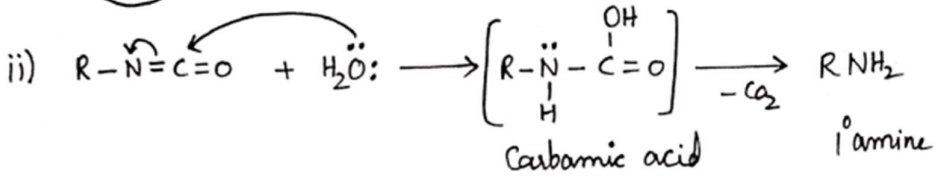
Thermal rearrangement of Acid azides to isocyanates in presence of aqueous solvents such as Chloroform is known as Curtius rearrangement



Isocyanate on hydrolysis gives 1° amines.

Mechanism:

i) 

ii) 

ACTIVE METHYLENE COMPOUNDS

1. Keto Enol Tautomerism

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

Condensation of an ester containing α-Hydrogen with some 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 $NaOC_2H_5$ (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

3. Synthetic applications of AAE

a) Preparation of mono carboxylic acids

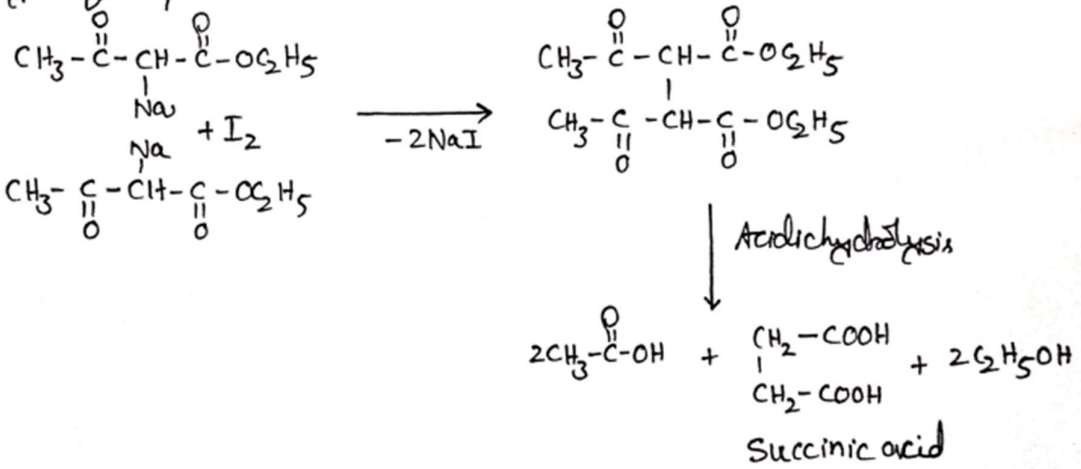
Acetoacetic ester undergo acidic hydrolysis in presence of Concentrated alcoholic potash gives acetic acid and Ethyl alcohol.

$$CH_3-C(=O)-CH_2-C(=O)-OC_2H_5 \xrightarrow{Alc\ KOH/H_2O} 2CH_3COOH + C_2H_5OH$$

Acetoacetic ester Acetic acid

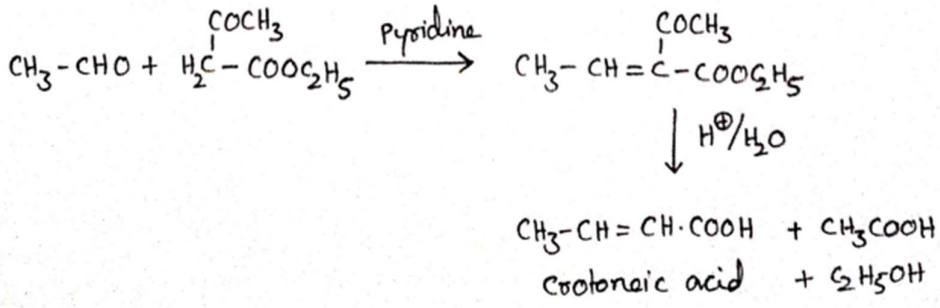
b) Preparation of di carboxylic acids

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



c) Preparation of α,β-unsaturated acids

Aceto acetic ester undergo condensation with aldehydes (or) Ketones gives condensed product, which on acidic hydrolysis gives α, β unsaturate acids



d) Preparation of Heterocyclic compounds

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