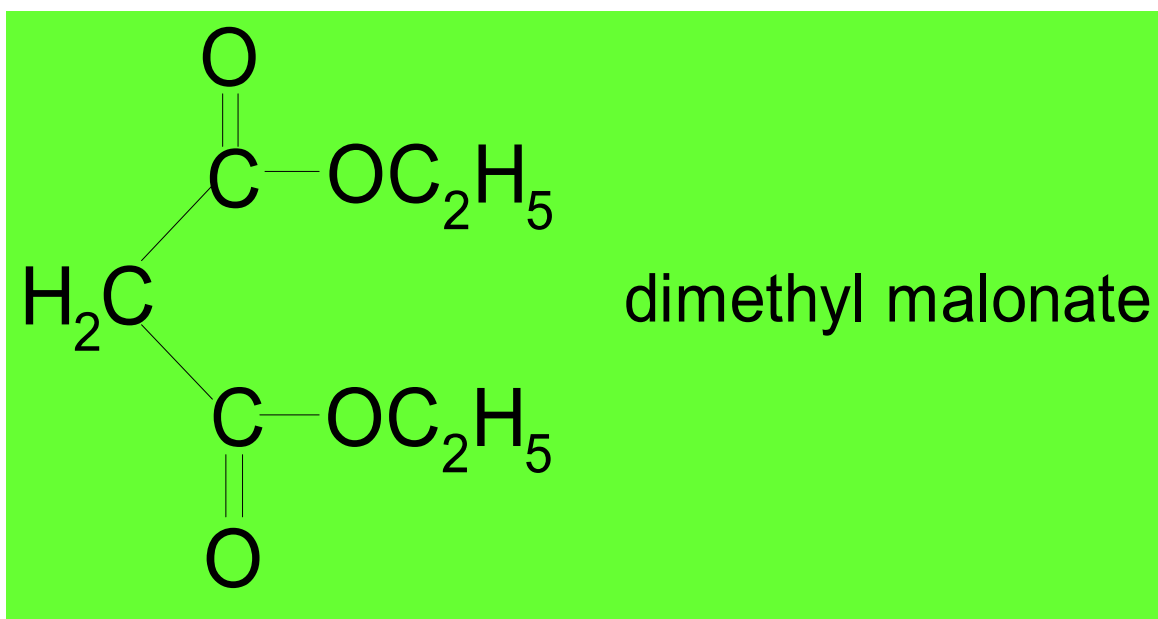


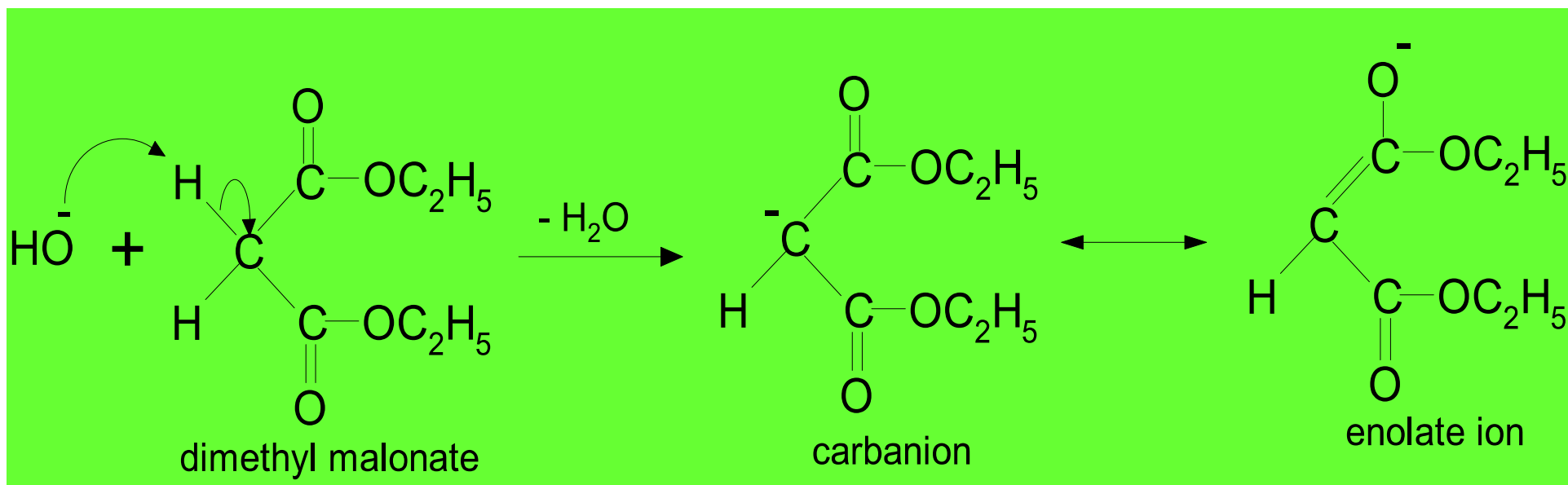
Organic Synthesis Via Enolate

- A methylene group ($-\text{CH}_2-$) which is attached from both sides by electron withdrawing groups (e.g. $-\text{CHO}$, $>\text{C}=\text{O}$, $-\text{COOH}$, $-\text{COOR}$, $-\text{CN}$, $-\text{X}$ etc.) is called active methylene group.

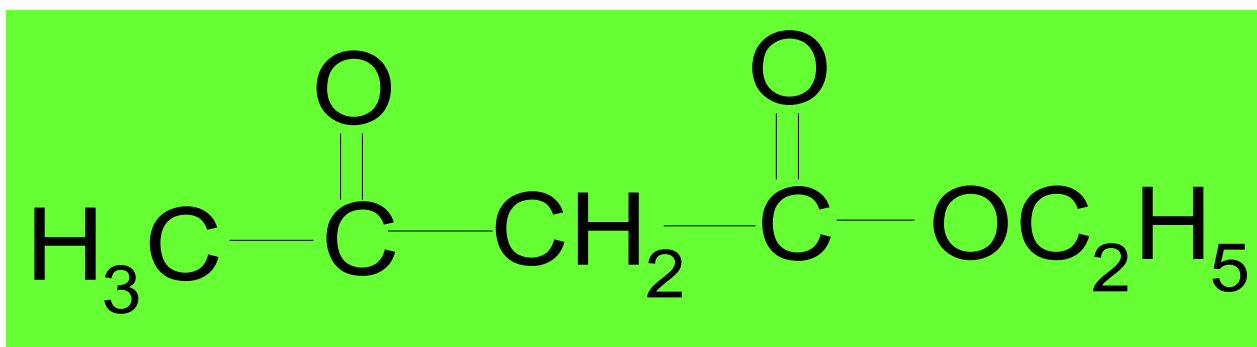


Acidity of α -hydrogen

- The hydrogen atoms of active methylene group are **acidic in nature**.
- The compounds containing active methylene group when treated with base, loses hydrogen atoms to form **carbanion**.
- This carbanion is stabilized by another resonating structure called as **enolate ion**.

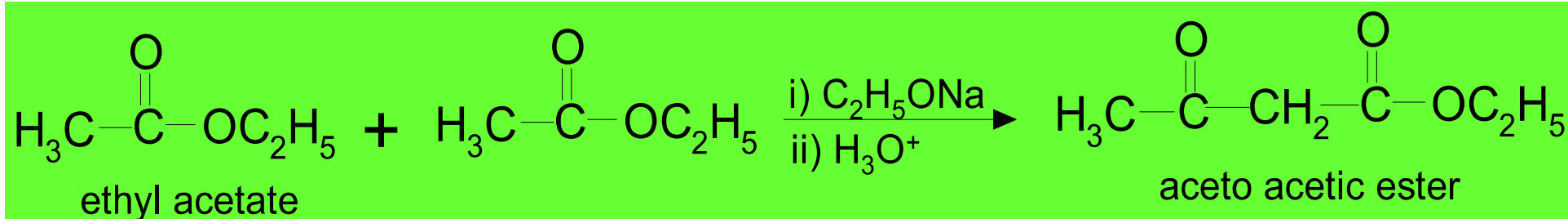


Aceto Acetic Ester (AAE) or Ethyl Aceto Acetate (EAA)

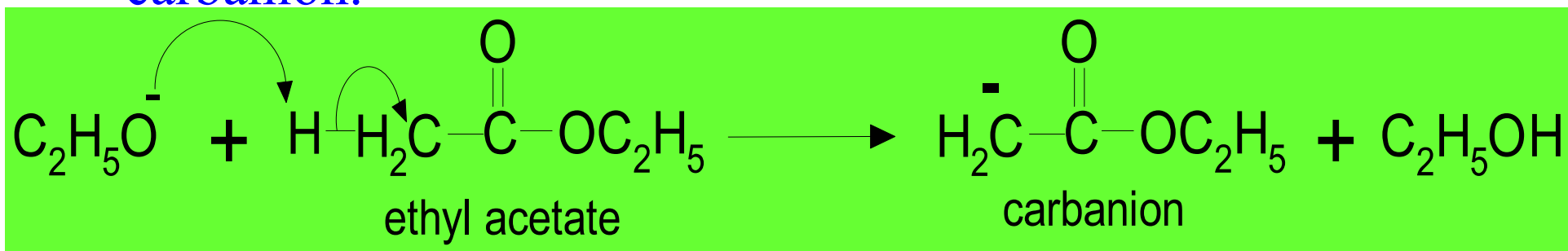


Preparation of AAE (Claisen Condensation)

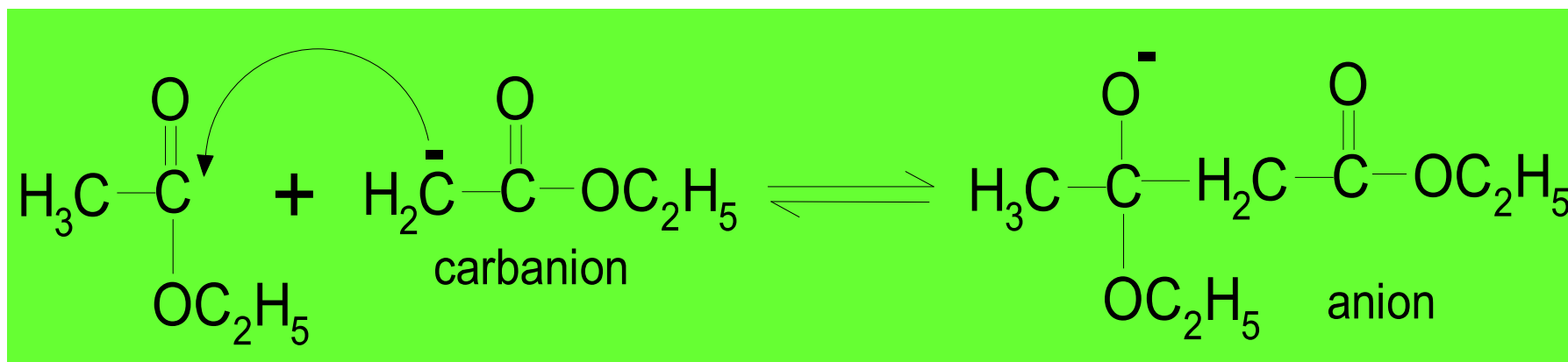
- Ethyl acetate on refluxion with sodium ethoxide gives aceto acetic ester.



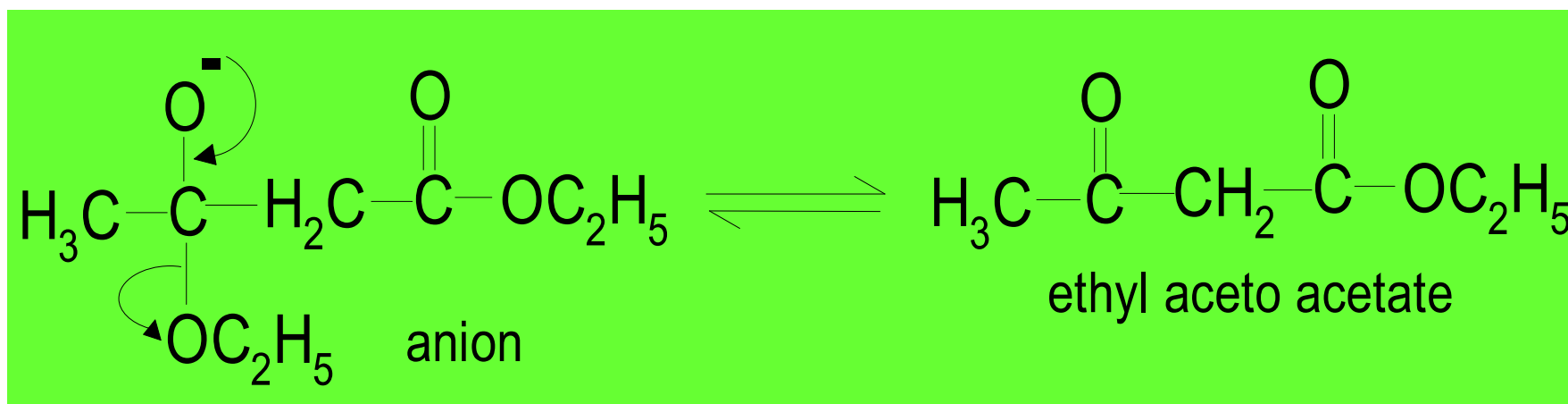
- This base catalyzed condensation of ester containing α -hydrogen atom is called Claisen condensation.
- Mechanism:** It involves following steps.
 - a) Base abstract α -H atom from ethyl acetate to form carbanion.



- b. This carbanion attacks on carbonyl carbon of another ethyl acetate molecule to form anion.

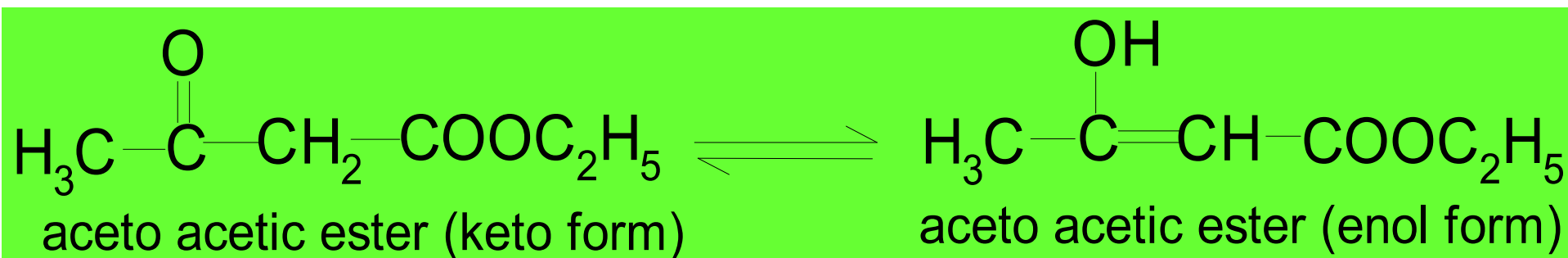


- c. This anion loses ethoxide ion to form ethyl aceto acetate.



Keto-Enol Tatuomerism

- Ethyl aceto acetate exists as an equilibrium mixture of two **functional forms** as keto and enol. These two forms are constantly interconvert into one another.
- This phenomenon in which two structural isomers spontaneously interconvert and exist in dynamic equilibrium is called **tatuomerism**.

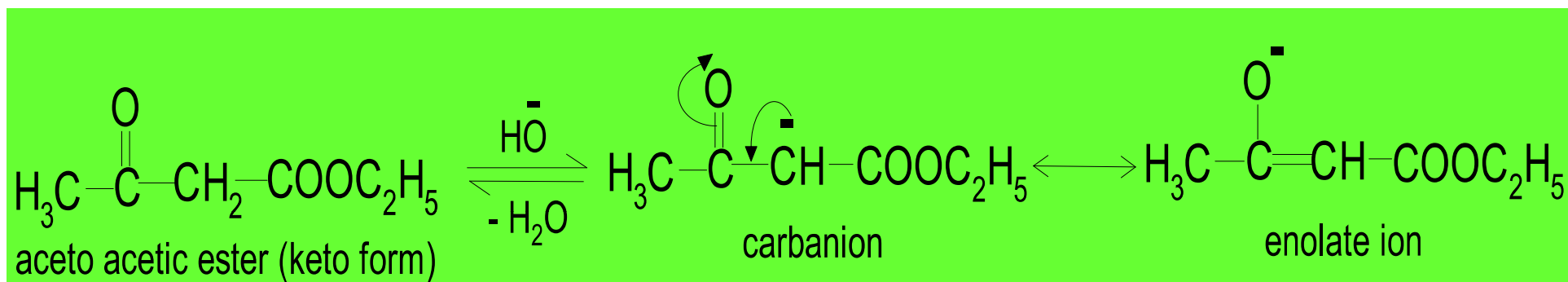


- The tatuomer which containing carbonyl group is called **keto form** while other tatuomer which containing hydroxyl group attached to double bonded carbon is called **enol form**. The tatuomerism is called **keto-enol tatuomerism**

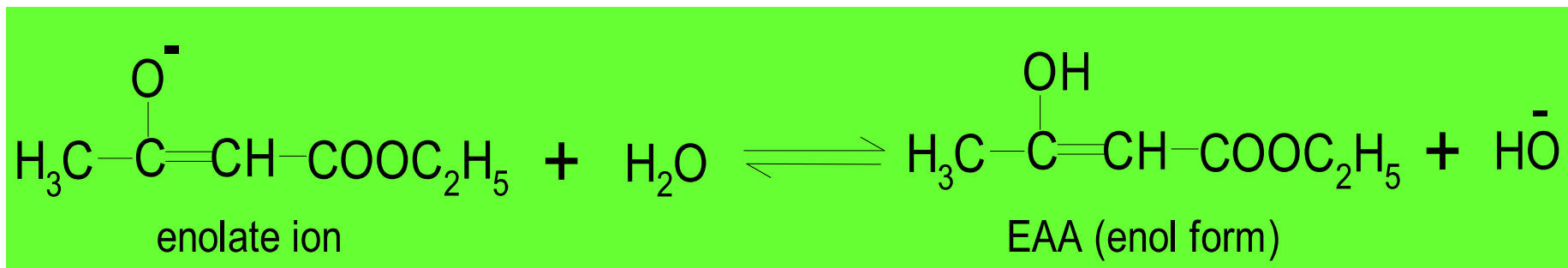
- **Mechanism:** Keto and enol forms are isomers which are easily interconvertible in presence of small amount of acid or base.

A. Base Catalyzed Keto-Enol Tautomerism:

- In first step, Base abstract proton from EAA to form **carbanion** which is resonance stabilized.

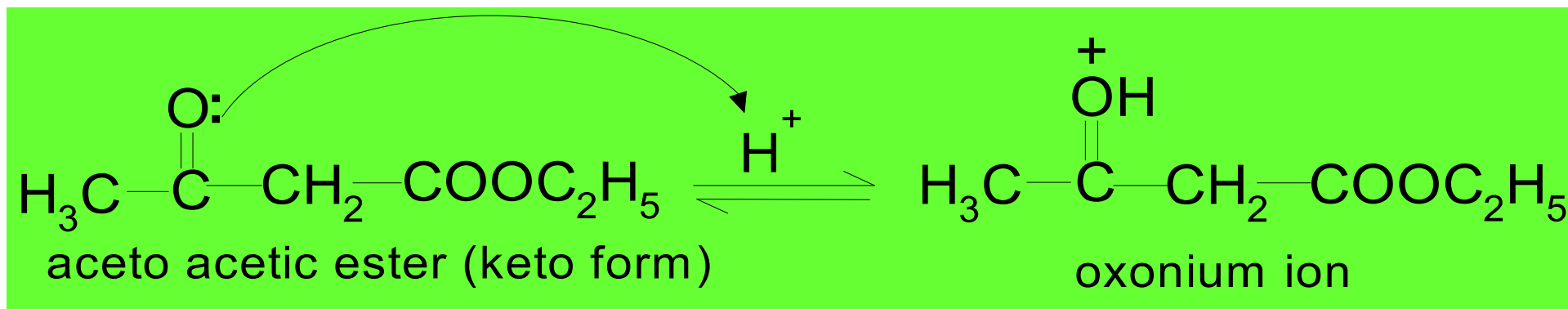


- In second step, enolate ion takes proton from water molecule to form **enol** form of EAA.

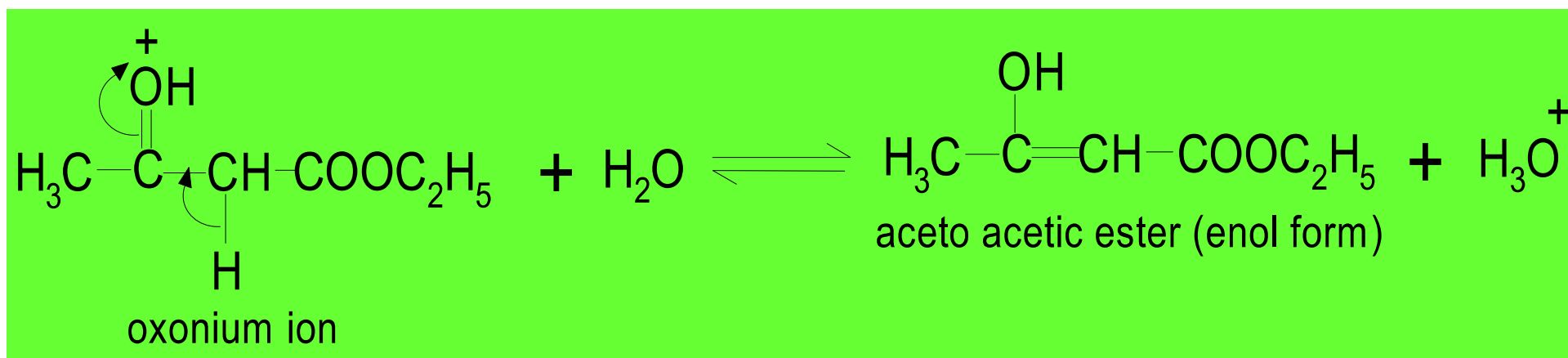


B. Acid Catalyzed Keto-Enol Tautomerism

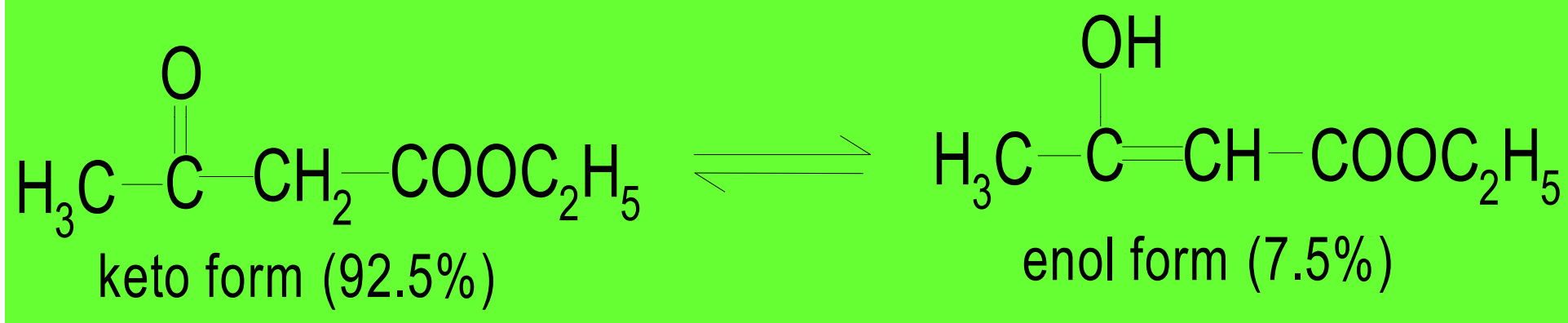
- In first step, carbonyl oxygen takes proton from acid to form **oxonium ion**.



- In second step, oxonium ion loses proton to form **enol form**.



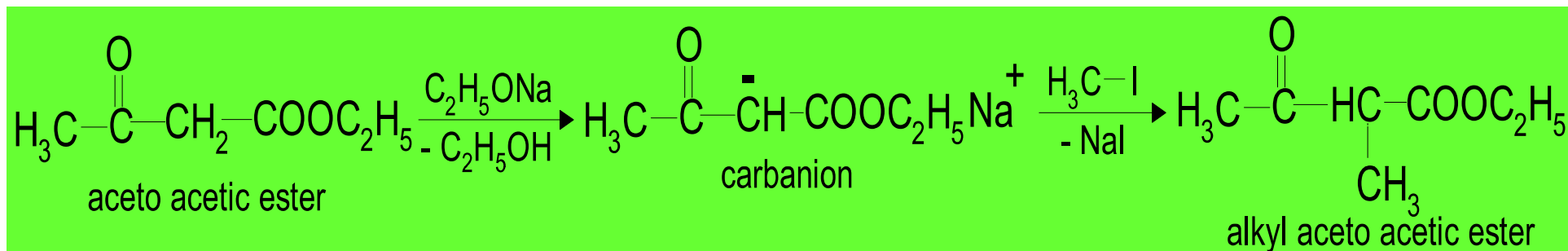
In EAA, there is comparatively more percentage of keto form.



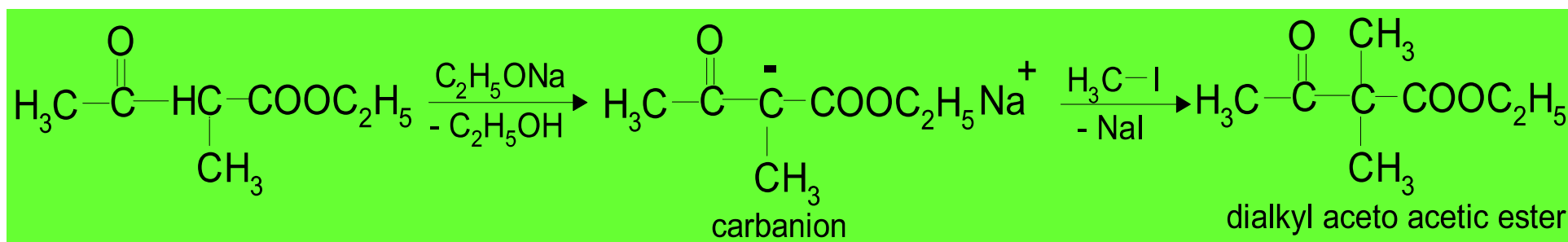
Synthetic Applications of EAA

1. Synthesis of alkyl aceto acetic ester:-

- Aceto acetic ester when treated with sodium ethoxide gives carbanion which on further treatment with alkyl halide gives corresponding **alkyl derivative**.

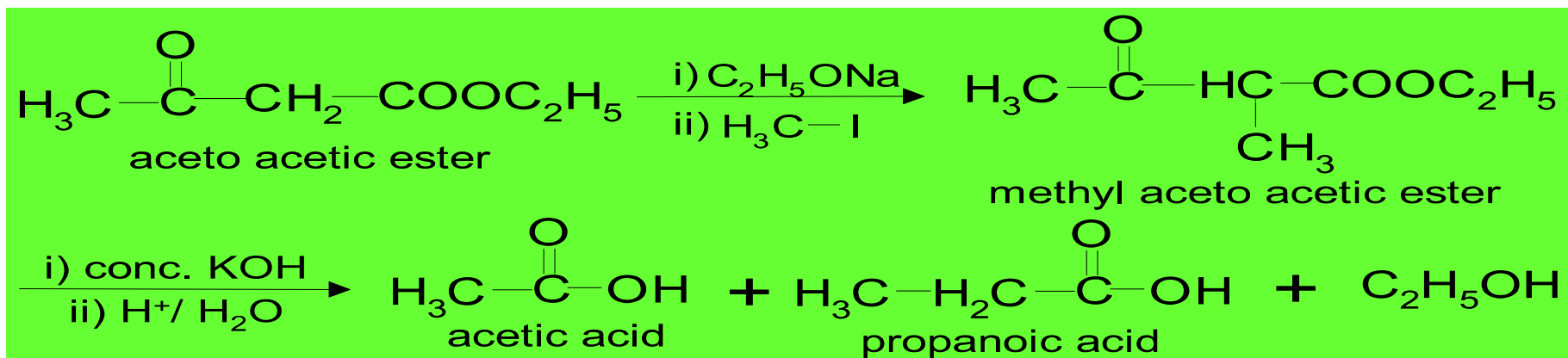


- This alkyl aceto acetic ester again on treatment with sodium ethoxide followed by reaction with alkyl halide gives **dialkyl aceto acetic ester**.

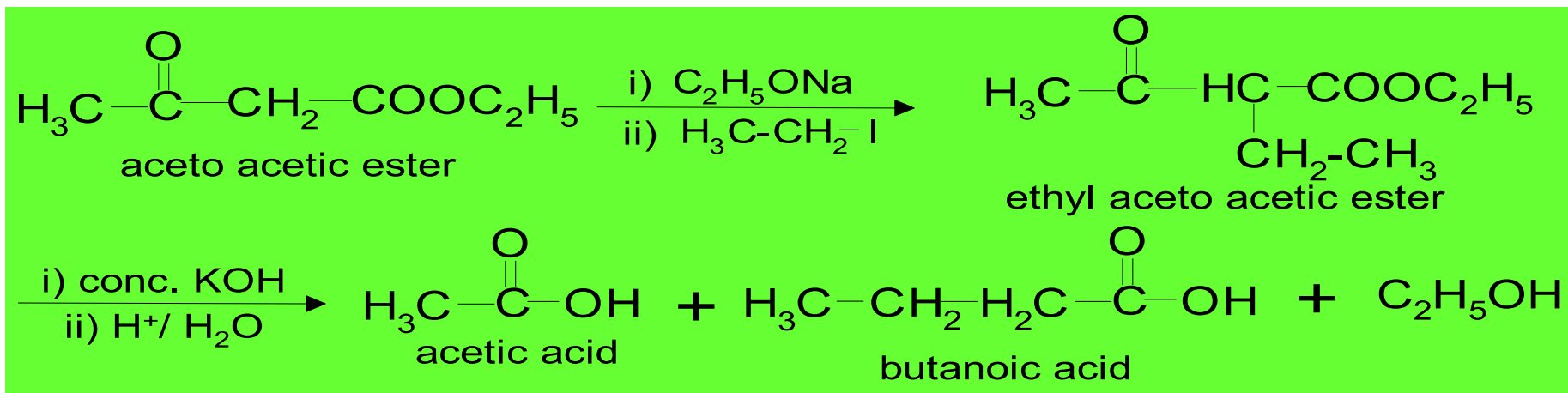


2. **Synthesis of Mono-carboxylic acid:** - Higher carboxylic acids prepared by alkylating EAA followed by hydrolysis.

- EAA when treated with sodium ethoxide and methyl iodide gives methyl EAA which on further hydrolysis gives **propanoic acid**.

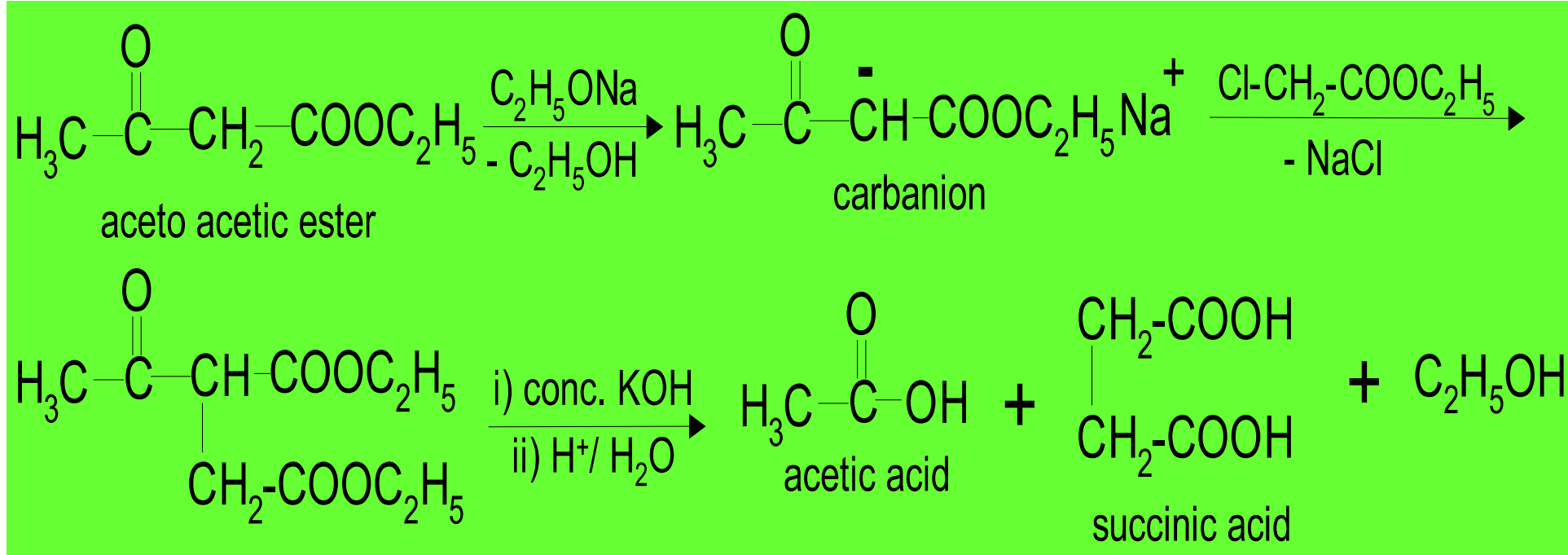


- EAA when treated with sodium ethoxide and ethyl iodide gives ethyl EAA which on further hydrolysis gives **butanoic acid**.



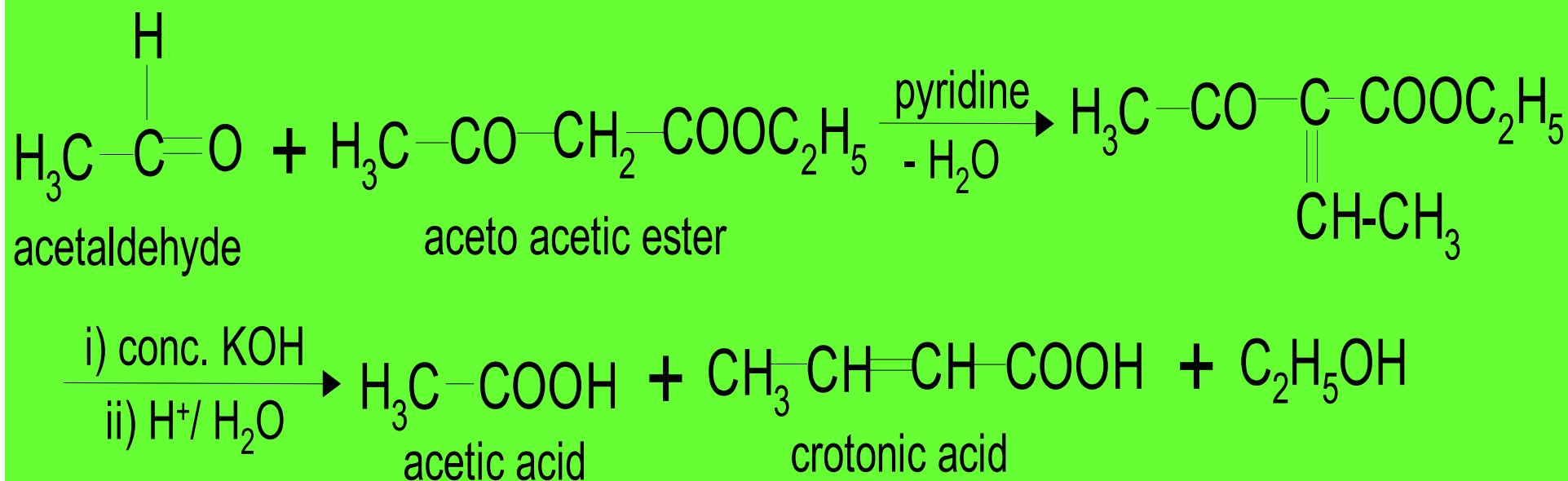
3. Synthesis of Dicarboxylic Acid: -

- Aceto acetic ester on treatment with sodium ethoxide gives carbanion which on condensation with halo ester followed by hydrolysis gives corresponding dicarboxylic acid.
- Aceto acetic ester on treatment with sodium ethoxide gives carbanion which on condensation with ethyl chloro acetate followed by hydrolysis gives succinic acid.



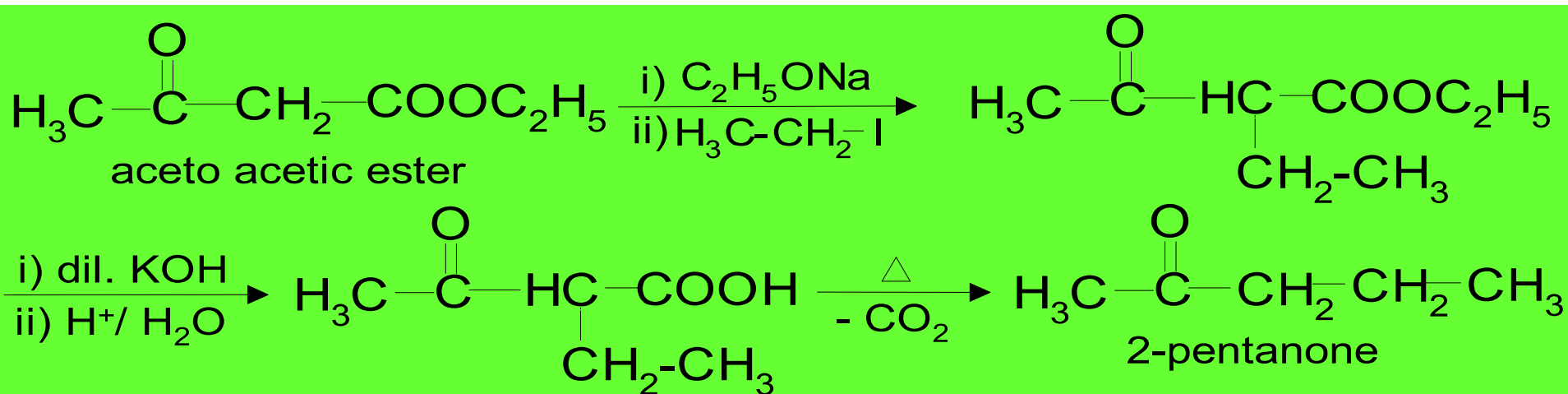
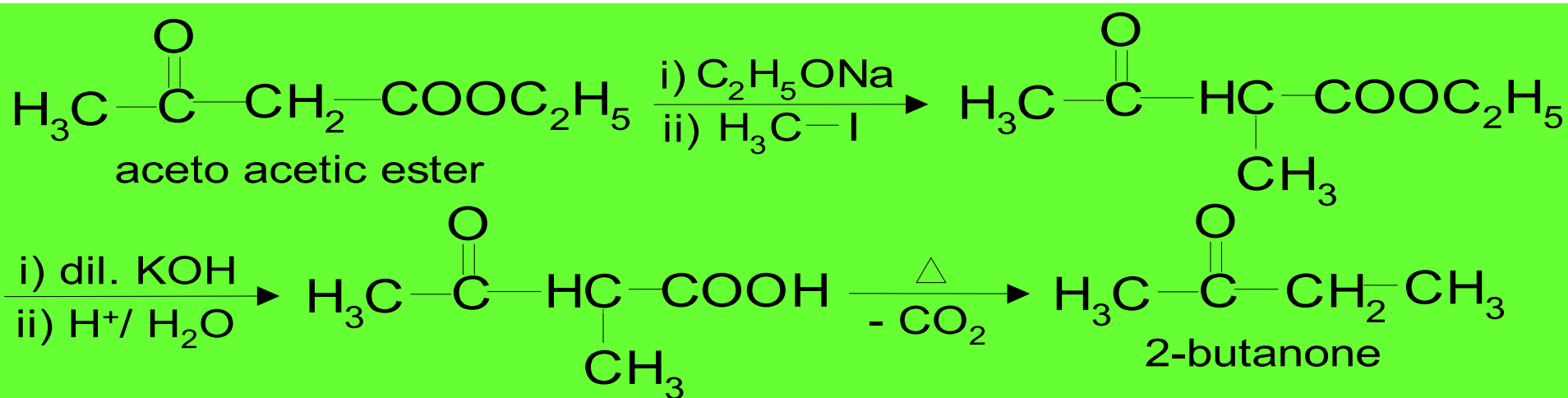
4. Synthesis of unsaturated acid:-

- AAE on condensation with **aldehyde** or **ketone** in presence of base (pyridine) gives intermediate which on further acid hydrolysis gives **α , β -unsaturated acid**.
- AAE on condensation with **acetaldehyde** in presence of base (pyridine) gives intermediate which on further acid hydrolysis gives **crotonic acid**.



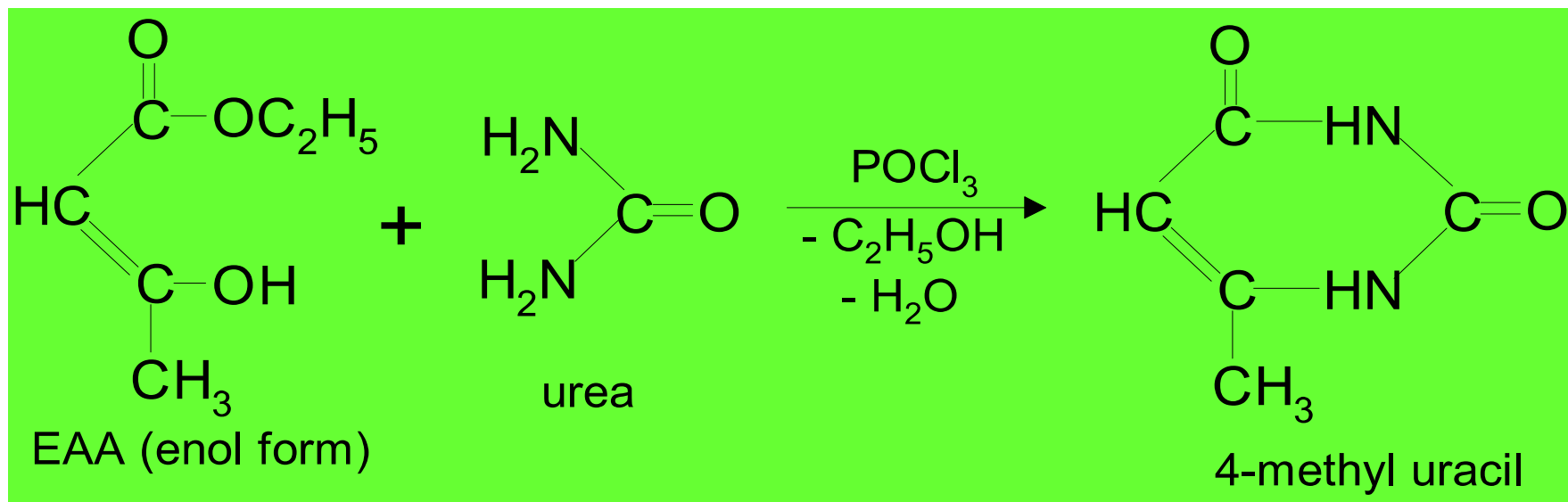
5. Synthesis of ketone: -

- AAE on alkylation gives corresponding alkyl aceto acetic acid which on hydrolysis gives corresponding carboxylic acid intermediate. This intermediate carboxylic acid further on decarboxylation gives ketone.

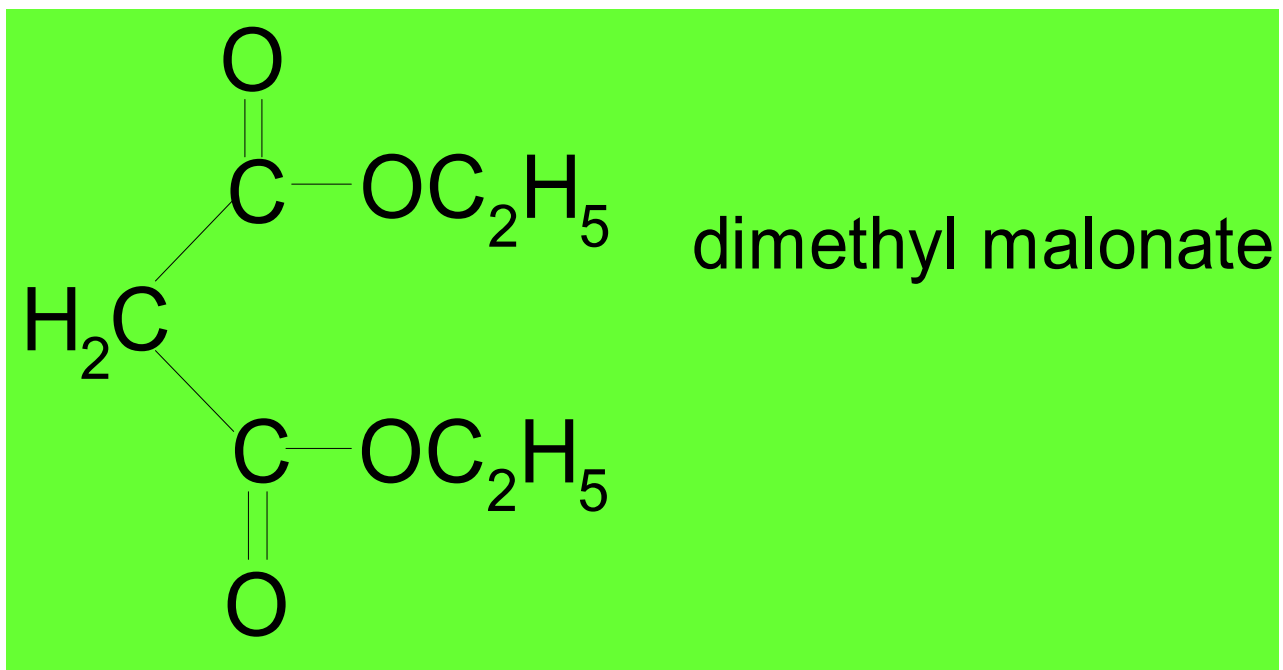


7. Synthesis of 4-methyl uracil: -

Enol form of EAA on condensation with urea in presence of phosphoryl chloride gives 4-methyl uracil.

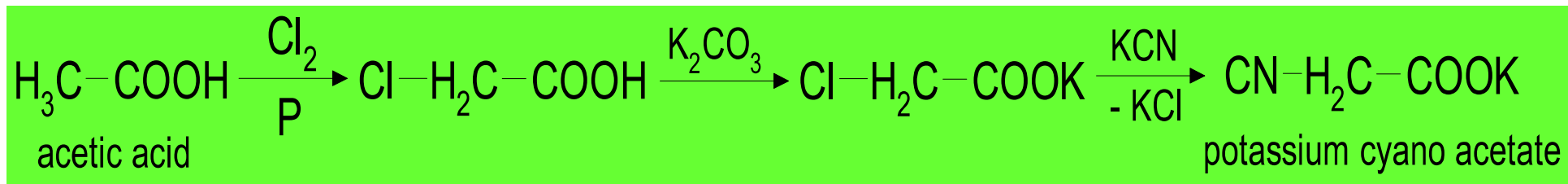


Diethyl Malonate (Malonic ester)

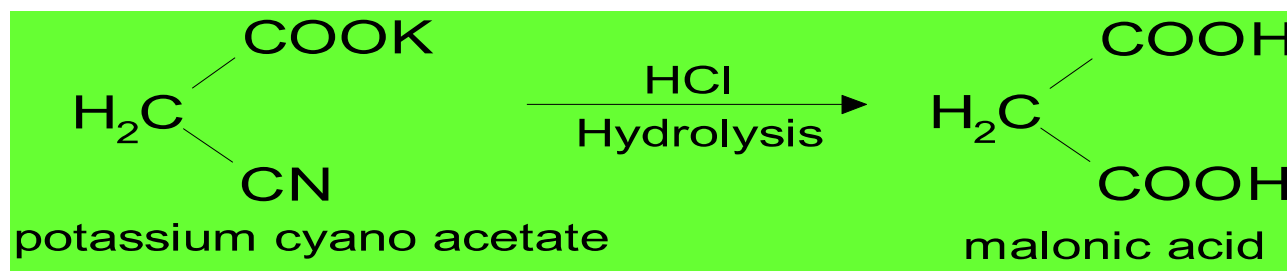


Preparation of diethyl Malonate: -Potassium cyano acetate on acidic hydrolysis gives malonic acid which on further esterification with ethyl alcohol gives diethyl malonate. It occurs in following steps.

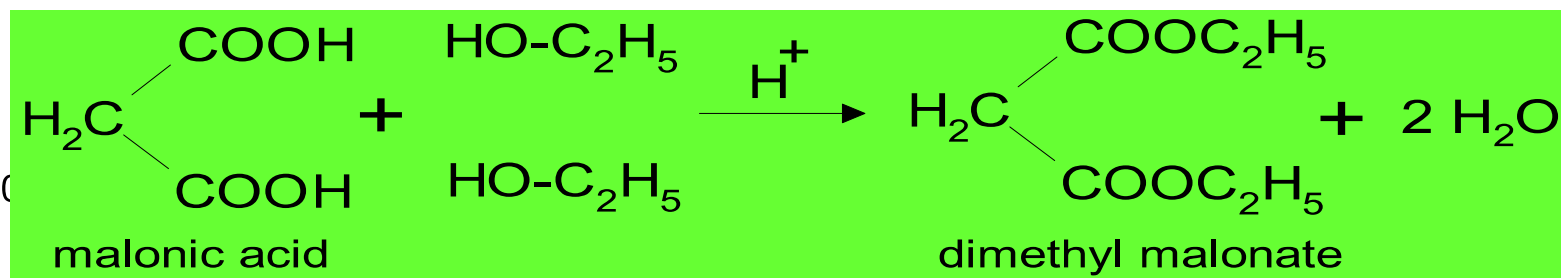
i. Potassium cyano acetate is prepared from acetic acid.



ii. Potassium cyano acetate on hydrolysis with HCl gives malonic acid.



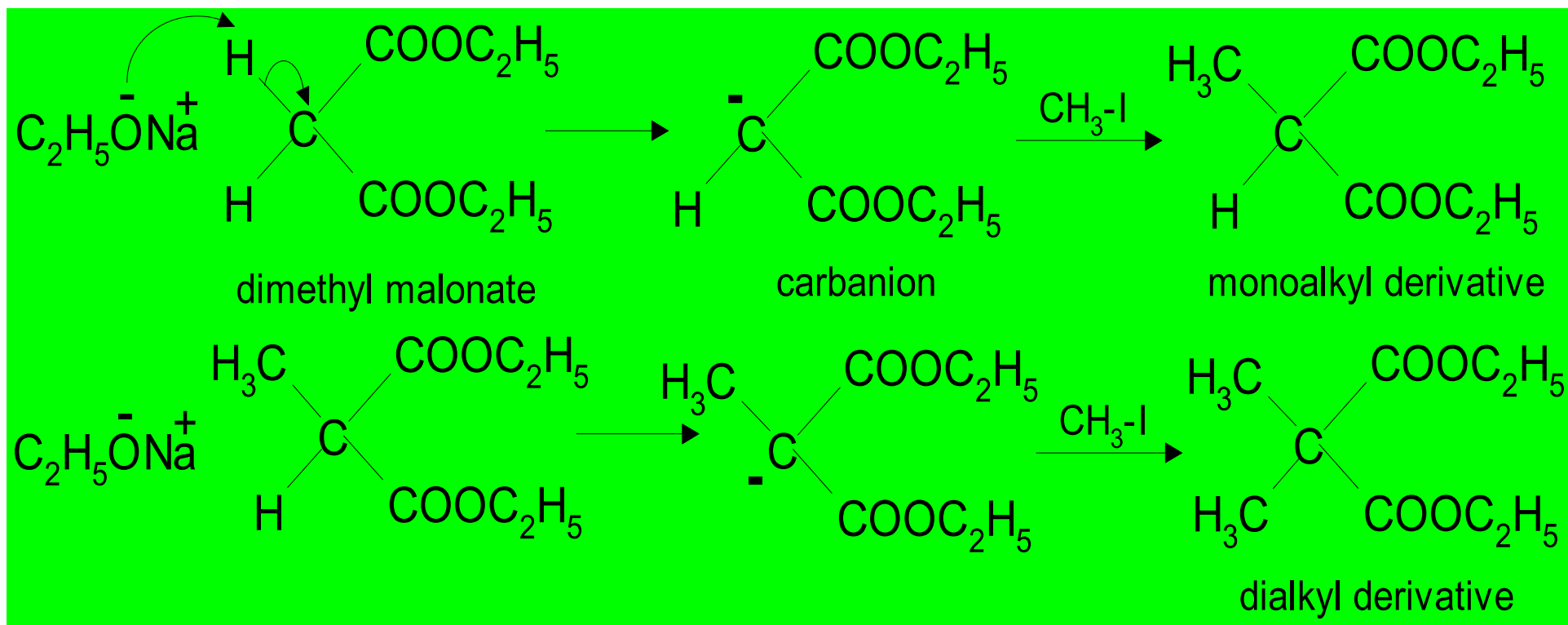
iii. Malonic acid on esterification with ethyl alcohol gives diethyl malonate.



Synthetic Applications of Malonic Ester

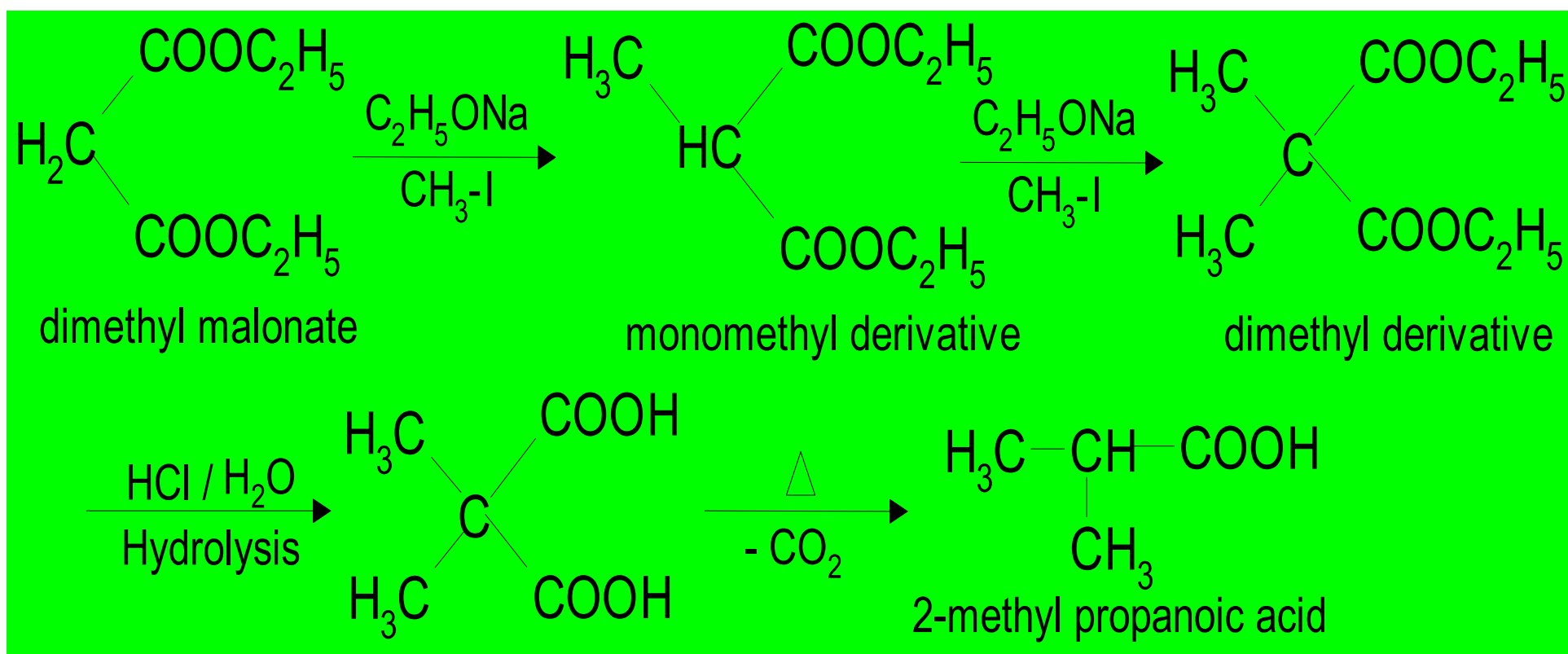
1. Synthesis of alkyl Derivative: -

- Diethyl malonate on treatment with sodium ethoxide gives carbanion which when treated with alkyl halide gives **mono alkyl derivative**. This mono alkyl derivative further on treatment with sodium ethoxide followed by reaction with alkyl halide gives **dialkyl derivative**.



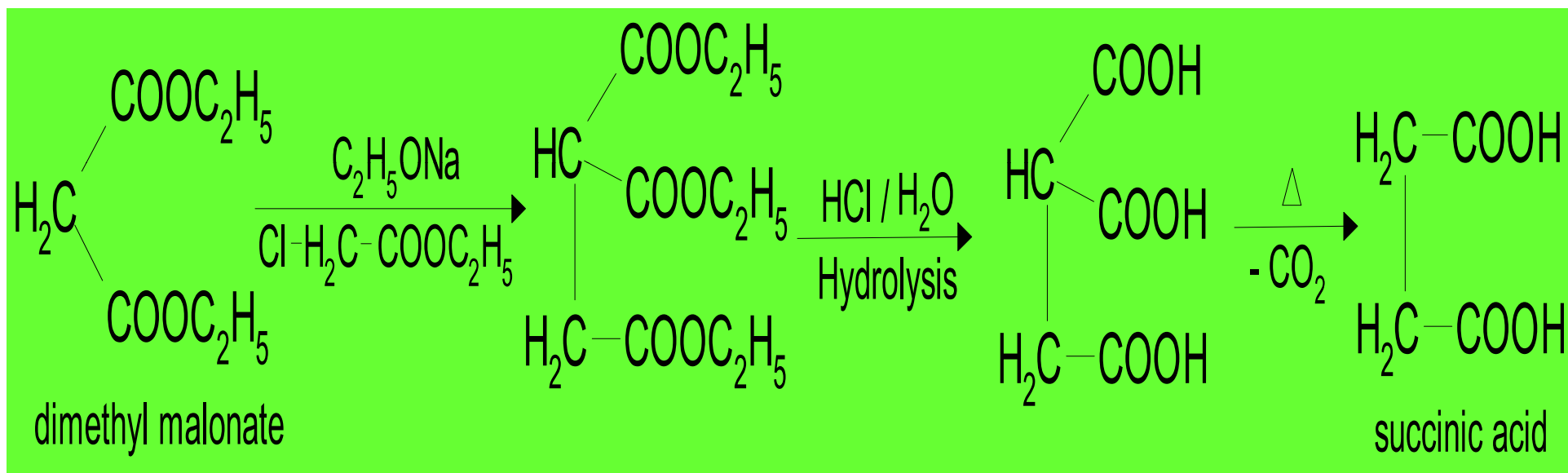
2. Synthesis of Mono-carboxylic acid: -

- Malonic ester on alkylation gives dimethyl derivative of malonic ester which on acid hydrolysis followed by decarboxylation gives **2-methyl propanoic acid**.

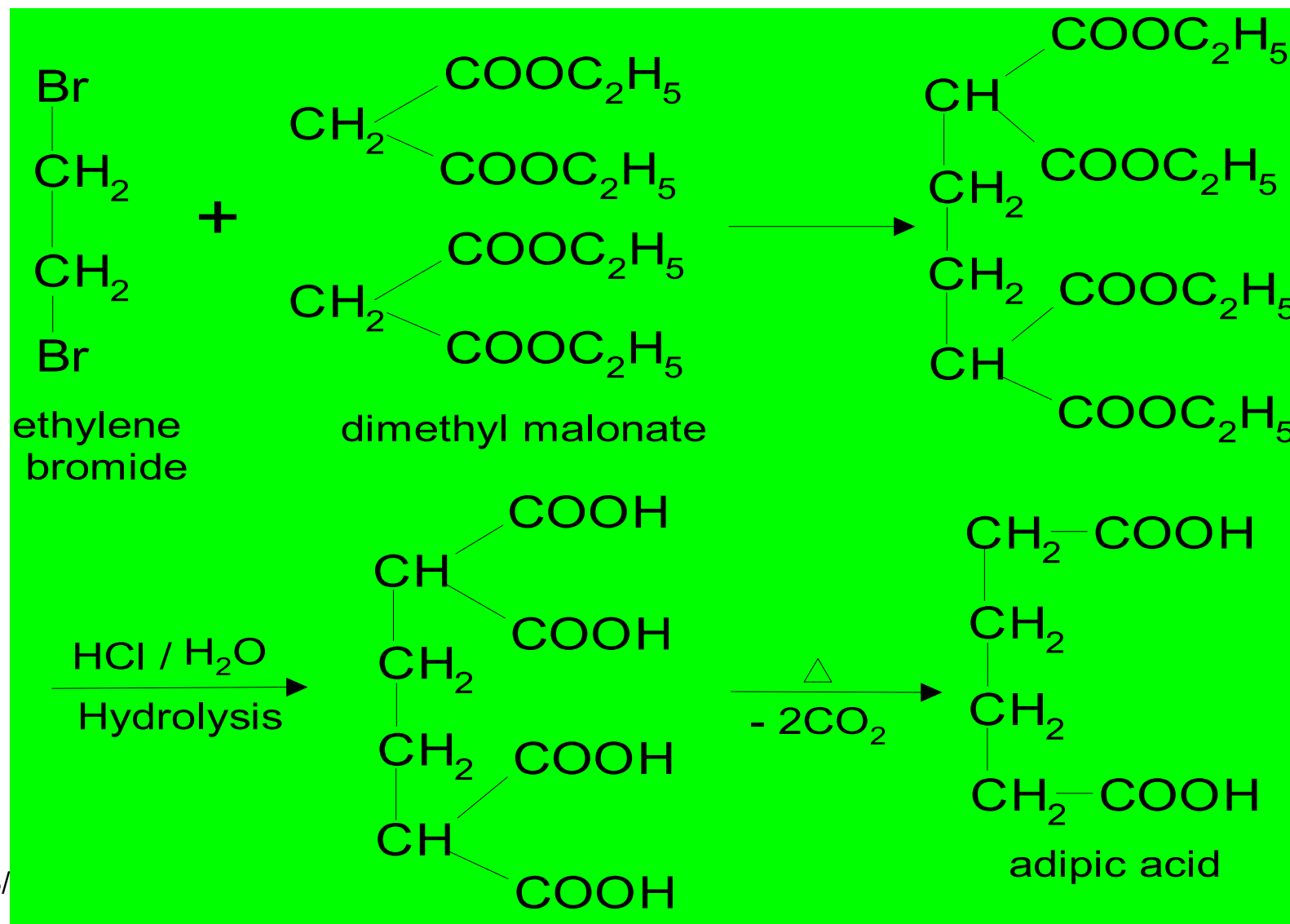


3. Synthesis of Dicarboxylic acid: -

- Malonic ester on treatment with sodium ethoxide & ethyl chloro- acetate gives intermediate which on hydrolysis followed by decarboxylation gives **succinic acid**.

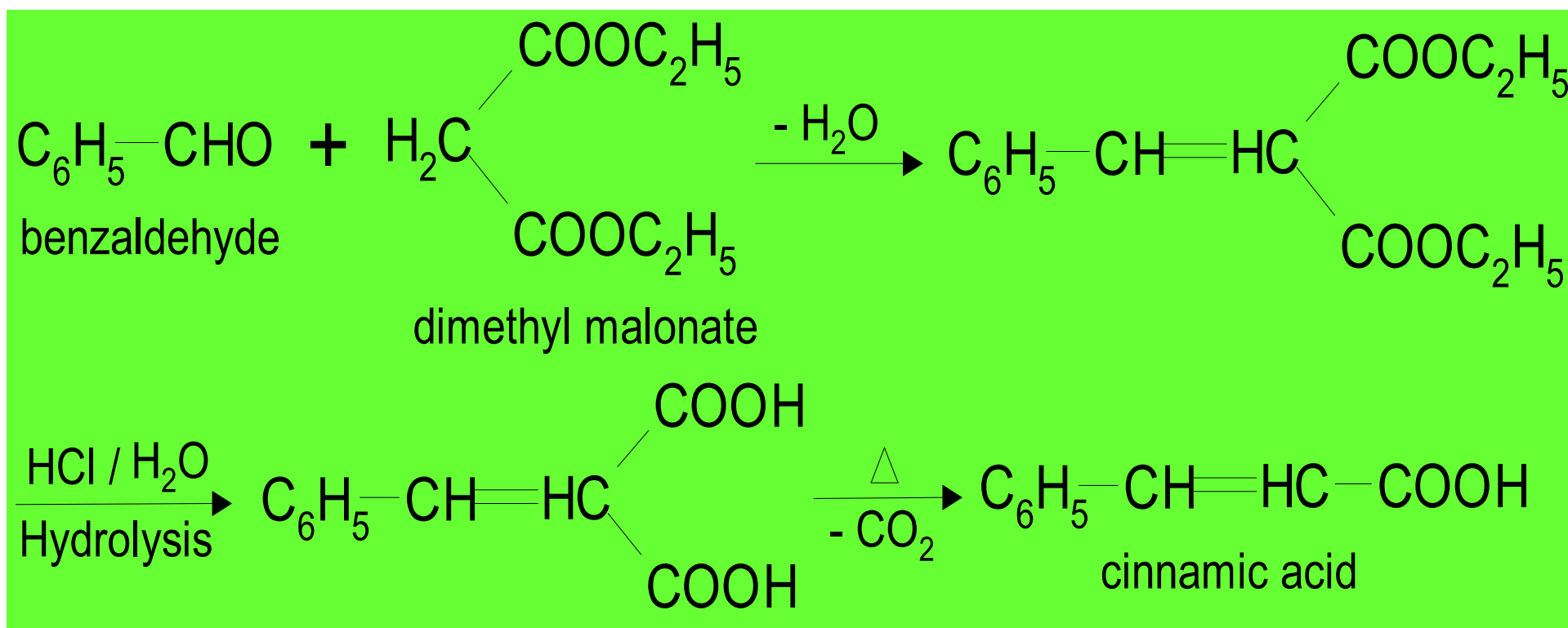


- Diethyl malonate on treatment with sodium ethoxide and ethylene dibromide gives intermediate. This intermediate on hydrolysis & followed by decarboxylation gives **adipic acid**.



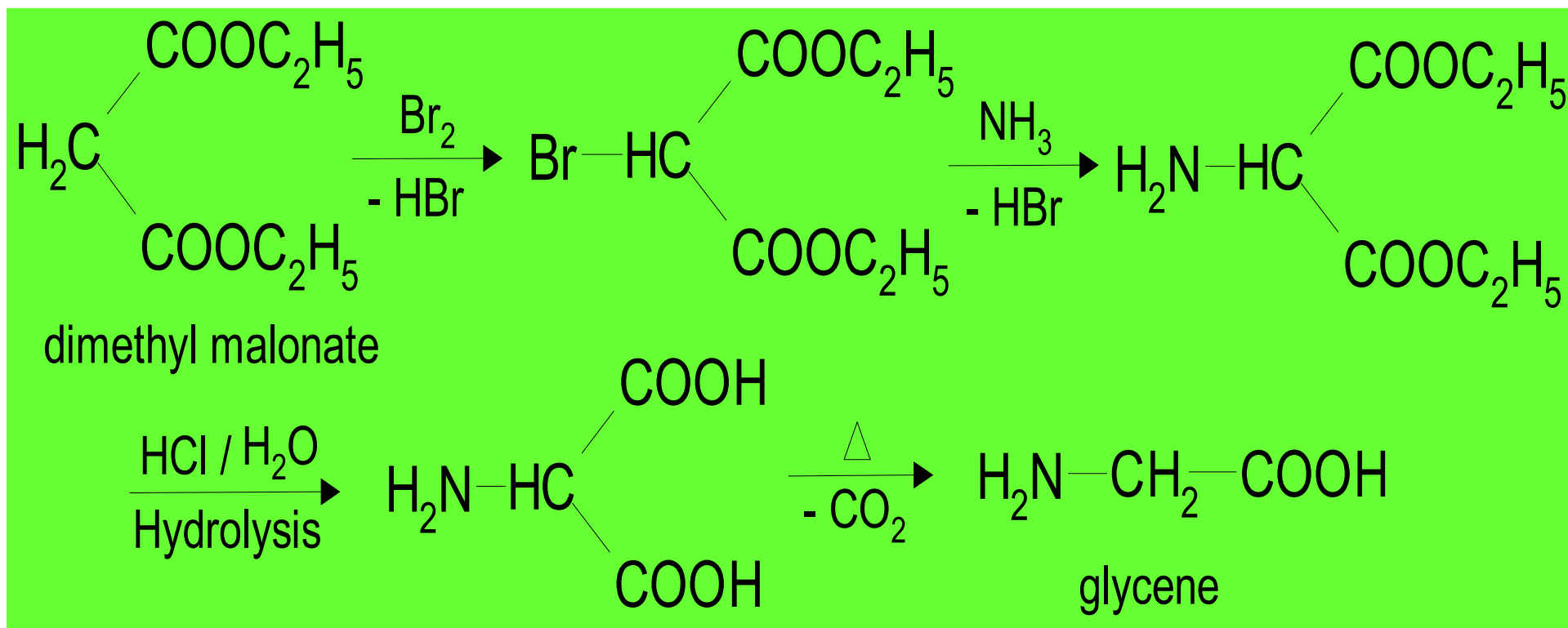
4. Synthesis of α, β -unsaturated acid:-

- Diethyl malonate on condensation with benzaldehyde gives condensed product which on further hydrolysis followed by decarboxylation gives α, β -unsaturated acid (cinnamic acid).



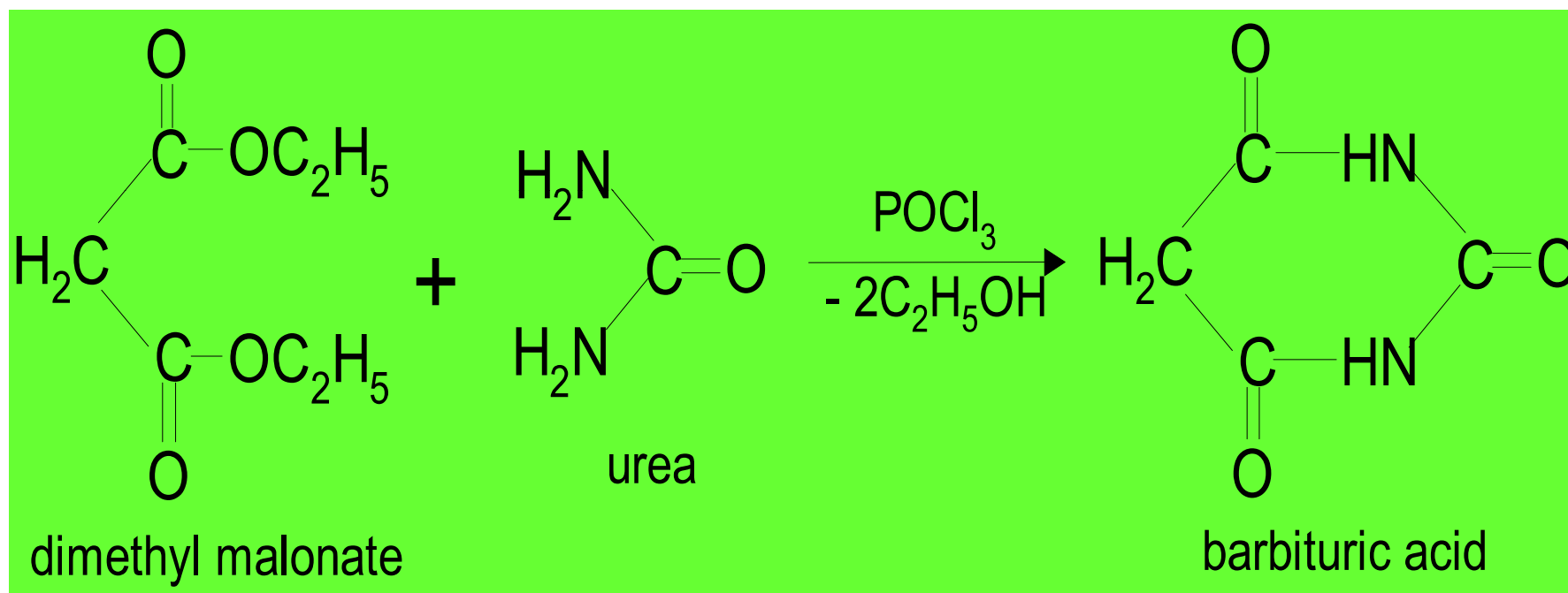
5. Synthesis of glycine (amino acetic acid): -

- Diethyl malonate on treatment with bromine gives diethyl bromo malonate which on treatment with ammonia gives diethyl amino malonate on hydrolysis followed by decarboxylation gives glycine.



6. Synthesis of Barbituric acid:-

- Malonic ester on condensation with urea gives barbituric acid.



THANK

YOU