



**GOVERNMENT OF ANDHRA PRADESH**  
**COMMISSIONERATE OF COLLEGIATE EDUCATION**



# Named reactions in Carbonyl Compounds- Aldol and Cannizzaro reactions

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## 1. Learning Outcomes

After studying this topic, student will be able to

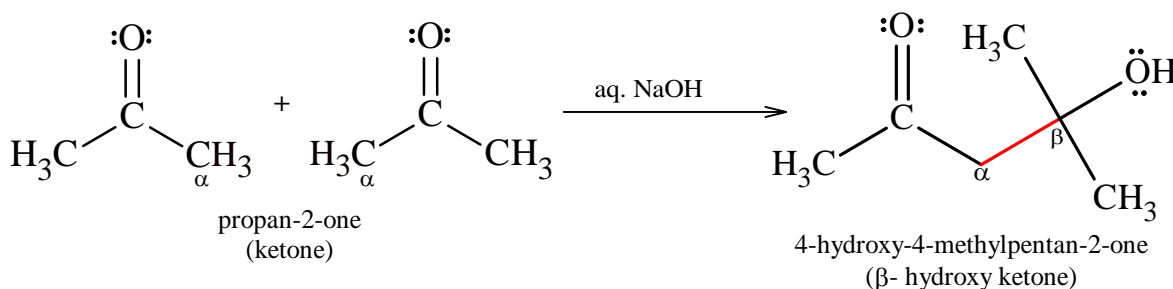
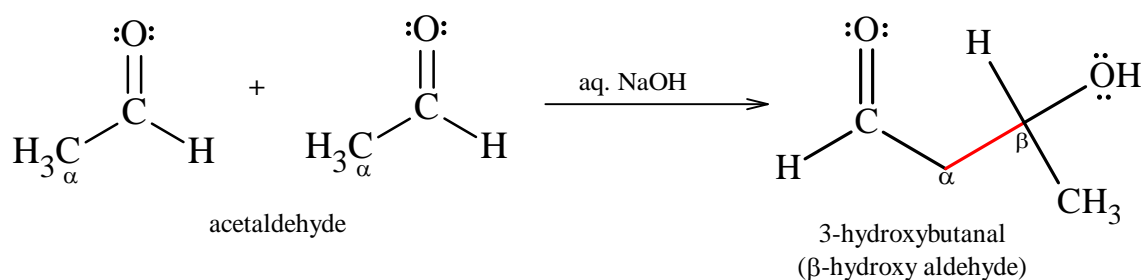
1. Write down the Aldol and Cannizzaro reactions.
2. Describe the mechanism of Aldol condensation in base.
3. Describe the crossed Aldol condensation.
4. Describe the intramolecular Aldol condensation.
5. Describe the mechanism of Cannizzaro reaction.

## 2. Introduction

Aldol reaction provide a good way to form carbon–carbon bonds. Removal of a hydrogen atom from the  $\alpha$ -carbon (**Note:** The carbon atom adjacent to the carbonyl carbon is referred to as  $\alpha$ -carbon and the hydrogen atoms present on  $\alpha$ -carbon are termed as  $\alpha$ -hydrogens) of a carbonyl compound with base produces the corresponding  $\alpha$ -carbanion, which is resonance stabilized via enolate anion. The Cannizzaro reaction is also a base-catalyzed reaction in which disproportionation of an aldehyde with no  $\alpha$ -hydrogen atoms produces corresponding salt of carboxylic acid and alcohol.

## 3. Aldol Reaction

- Aldehydes and ketones undergo an aldol reaction.
- An addition reaction between two aldehydes, two ketones, or an aldehyde and a ketone in presence of aqueous base (dil. NaOH, Ba(OH)<sub>2</sub>, K<sub>2</sub>CO<sub>3</sub>) resulting in the formation of a  $\beta$ -Hydroxy aldehyde or a  $\beta$ -hydroxy ketone (commonly known as Aldol ("*aldehyde alcohol*")) is called Aldol reaction.

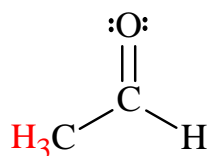


- The successive loss of water from  $\beta$ - Hydroxy aldehyde or a  $\beta$ -hydroxy ketone produces an  $\alpha$ ,  $\beta$ -unsaturated aldehyde or ketone.
- Both the aldol reaction and dehydration steps may be promoted by base or acid.
- For our discussion, we will restrict ourselves to base catalyzed aldol reactions.

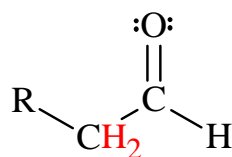
### 3.1 Characteristics of Aldol Reaction

1. An aldol reaction is a nucleophilic addition in which a carbanion is the nucleophile.
2. One molecule of aldehyde or ketone becomes a carbanion which is an electron rich nucleophile.
3. Another molecule serves as the electrophile because its carbonyl carbon is electron deficient.
4. Presence of  $\alpha$ -hydrogen in aldehyde or ketone is the essential condition for Aldol reaction, since only such carbonyl compounds can form carbanions (nucleophiles), which then attacks second carbonyl carbon (which acts as an electrophile) to form the product.

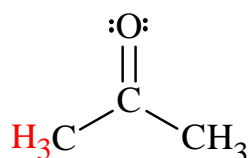
Some examples of the aldehydes and ketones that undergo aldol reaction are given below:



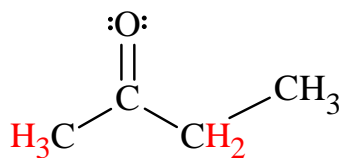
Acetaldehyde



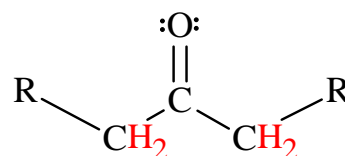
Where R= -H or -CH<sub>3</sub> or -phenyl group



Acetone



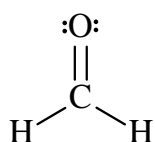
butan-2-one



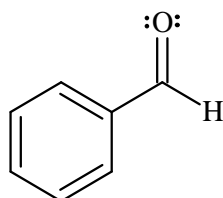
Where R= -H or -CH<sub>3</sub> or -phenyl group

[Note: Hydrogen atoms marked in red colour are  $\alpha$ -hydrogens]

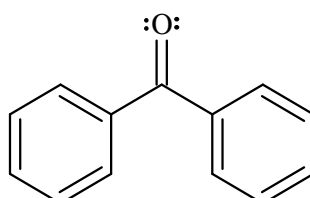
Aldehydes or ketones, not having  $\alpha$ -hydrogen atom, do not undergo aldol reaction.



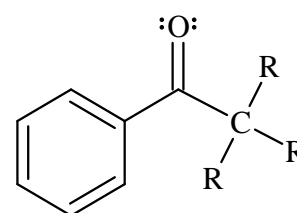
formaldehyde



benzaldehyde



diphenylmethanone



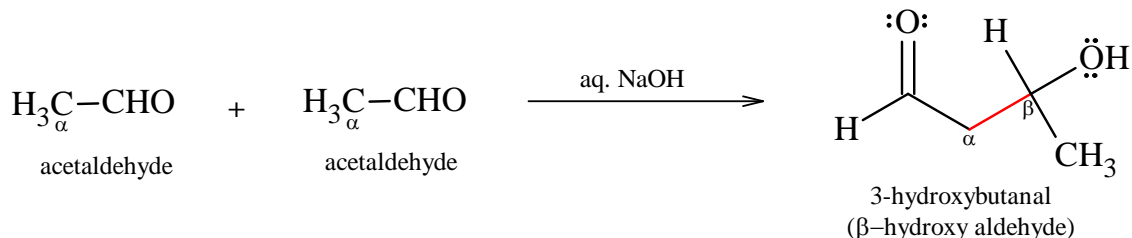
R= -CH<sub>3</sub>/-C<sub>6</sub>H<sub>5</sub>

Since there is no availability of  $\alpha$ -hydrogen atoms in the above compounds, these do not undergo aldol reaction. However, in the presence of concentrated base, they undergo Cannizzaro reaction.

## 3.2 Mechanism of Aldol Reaction

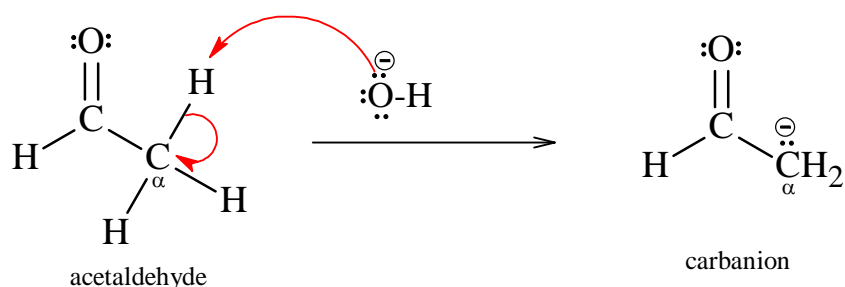
In the Aldol reaction, two molecules of an aldehyde or ketone react with each other in the presence of an aqueous base to form  $\beta$  - hydroxy carbonyl compound.

**Example:** Treatment of acetaldehyde with an aqueous base produces 3-hydroxybutanal, a  $\beta$ - hydroxy aldehyde.

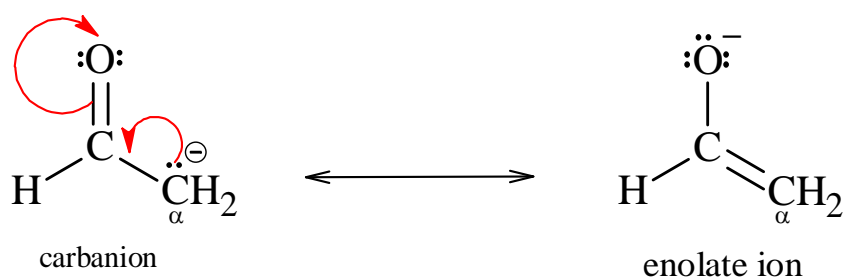


The Mechanism of the aldol reaction occurs in three steps. Carbon- carbon bond formation occurs in step-2 of the mechanism when the nucleophilic enolate reacts with the electrophilic carbonyl carbon.

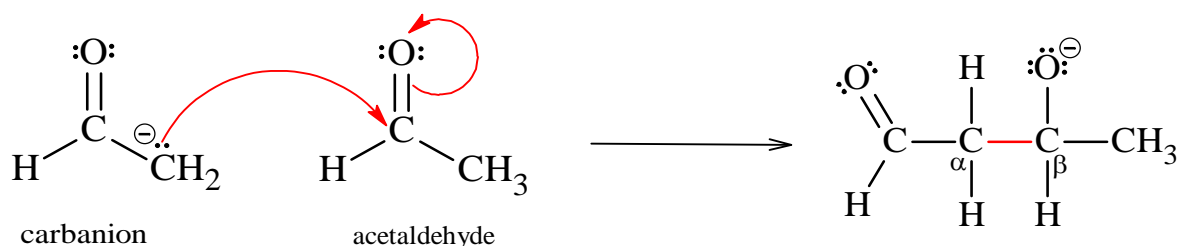
**Step 1:** Attack of a base removes a proton from the  $\alpha$ -carbon ( $\text{C}_\alpha$ ) of the aldehyde or ketone to generate a “carbanion”.



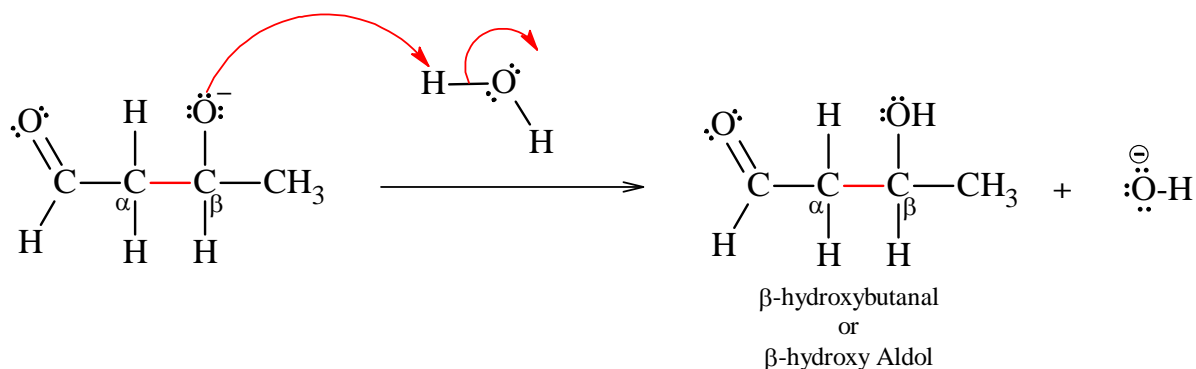
The carbanion that is formed in step 1 is resonance stabilized with an enolate ion as shown below:



**Step 2:** Nucleophilic carbanion (formed in step 1) attacks the electrophilic carbonyl carbon of a second molecule of aldehyde, thus forming a new carbon- carbon bond. This joins the  $\alpha$ -carbon of one aldehyde to the carbonyl carbon of a second aldehyde.

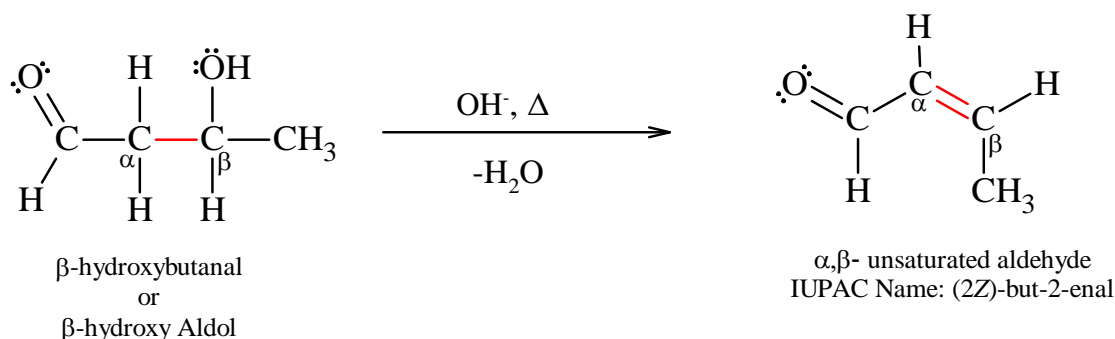


**Step 3:** Protonation of the product formed in step 2 gives the  $\beta$ -hydroxy aldehyde.

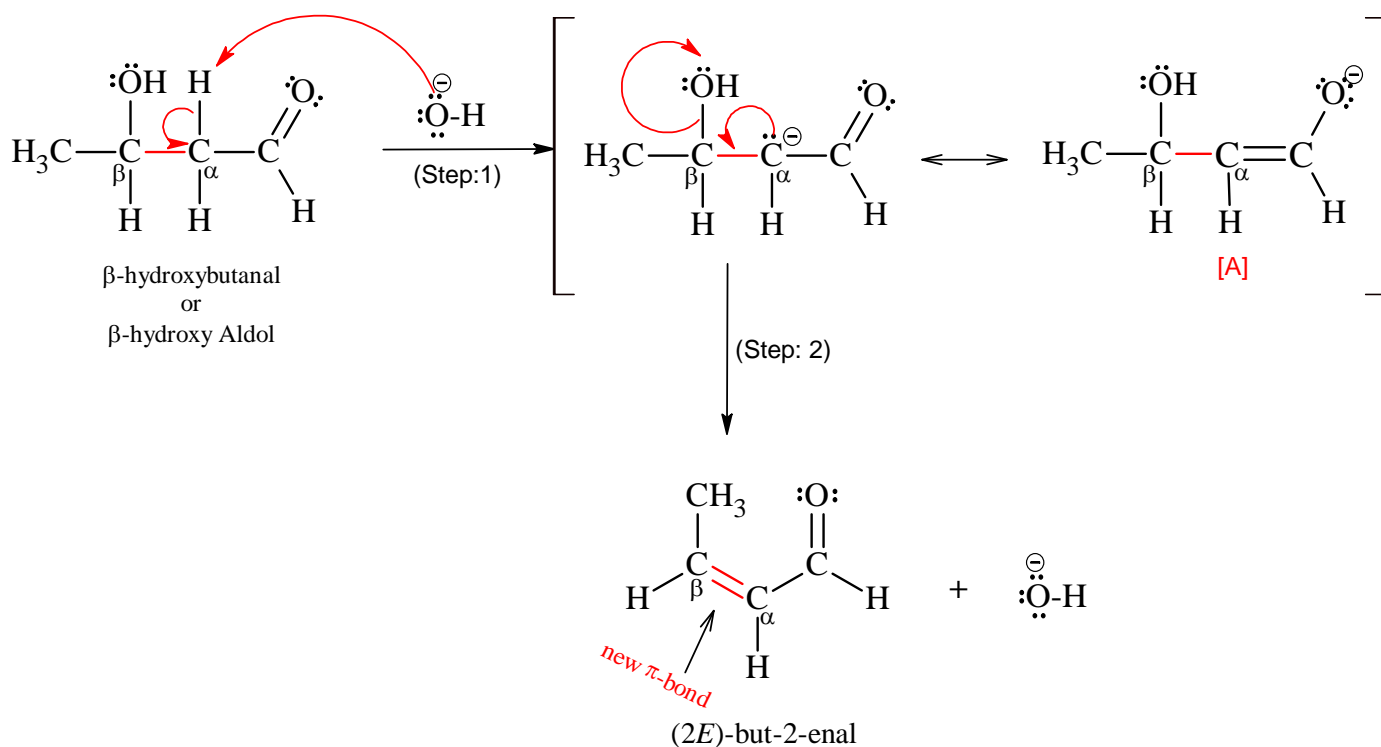


### 3.3. Dehydration of Aldol Product

The  $\beta$ -hydroxy carbonyl compound formed in the aldol reaction dehydrate more readily in the presence of base. It loses the  $\text{H}_2\text{O}$  molecule irreversibly to form an  $\alpha, \beta$ -unsaturated carbonyl compound.



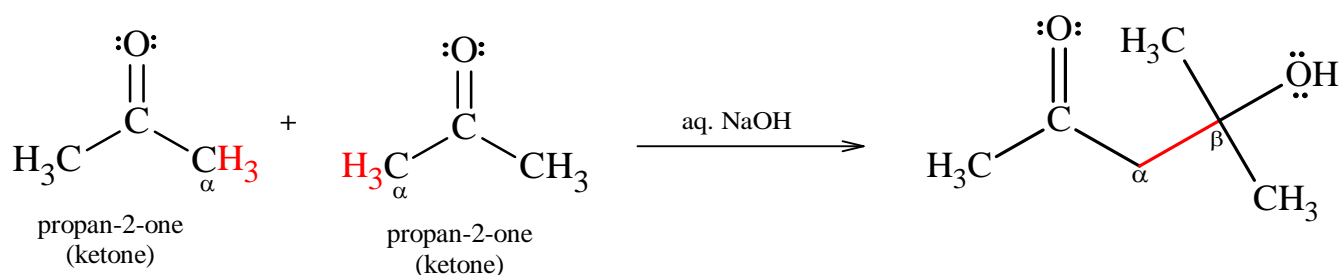
Mechanism of dehydration with base completes in two steps. In step (1), base removes a proton from the  $\alpha$ -carbon, thus forming a resonance stabilized enolate[A]. In step (2), the electron pair of the enolate forms the  $\pi$ -bond as  $\text{OH}^-$  is eliminated.



**Note:** If the mechanism involves steps 1 to 3 only, then it is termed as an **Aldol addition reaction (or simply an Aldol reaction)**. But if dehydration step takes place, then it becomes an **aldol condensation reaction** (because a water molecule is lost in the event).

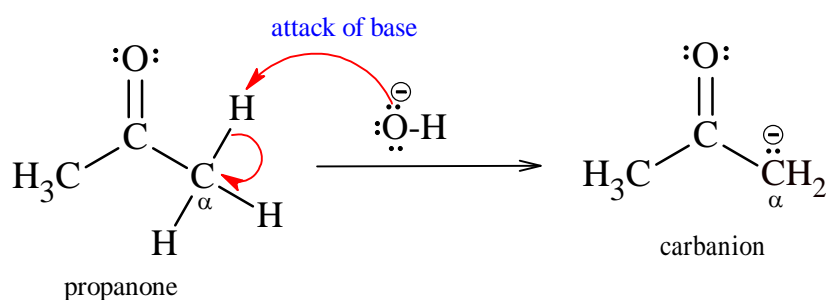
In case of Ketones the reaction mechanism follows as shown below:

**Example:** Formation of  $\beta$ -hydroxy ketone from acetone.

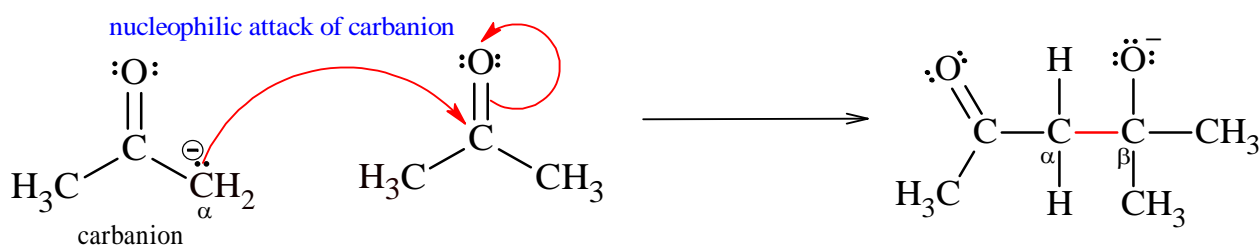


### Mechanism:

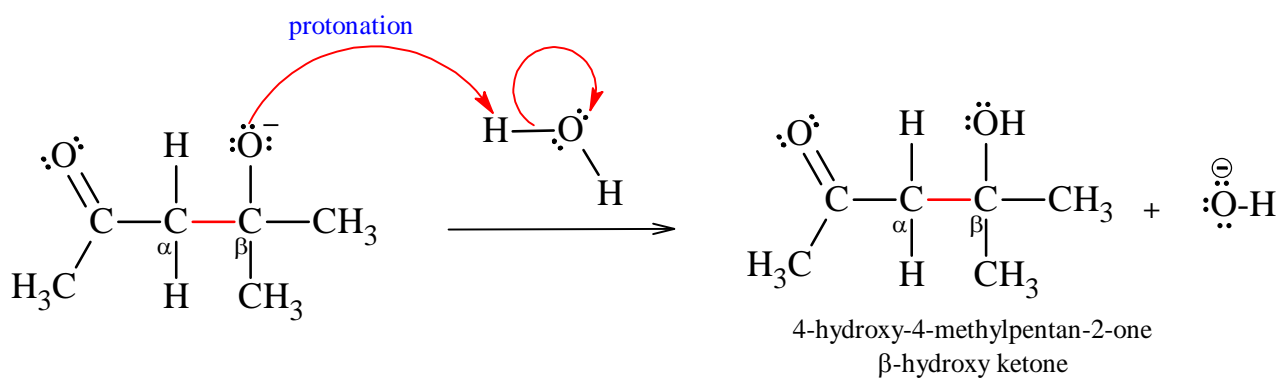
#### Step 1



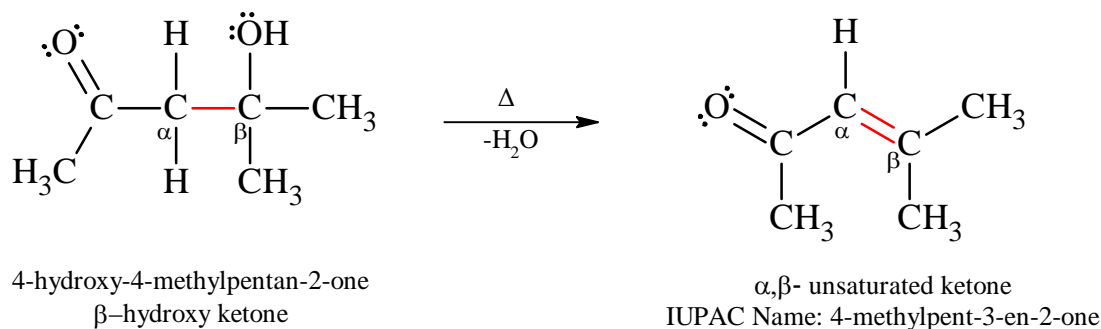
#### Step 2



#### Step 3



**Step 4:** A dehydration step to yield a  $\alpha, \beta$ -unsaturated ketone.



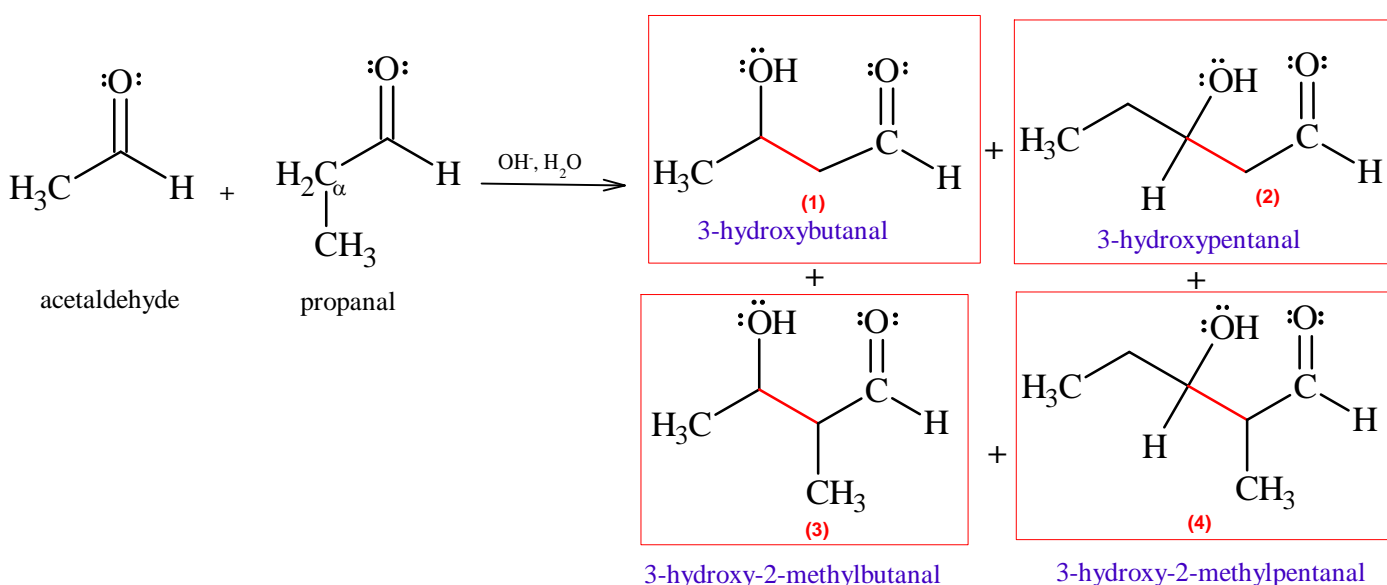
### 3.4. Crossed Aldol Reaction

In the aldol reactions discussed so far, the nucleophilic carbanion and the electrophilic carbonyl components have originated from the same aldehyde or ketone. Sometimes, it is possible to carry out an aldol reaction between two different carbonyl compounds.

Aldol reaction between two different carbonyl compounds is called a ***crossed aldol*** or ***mixed aldol reaction***.

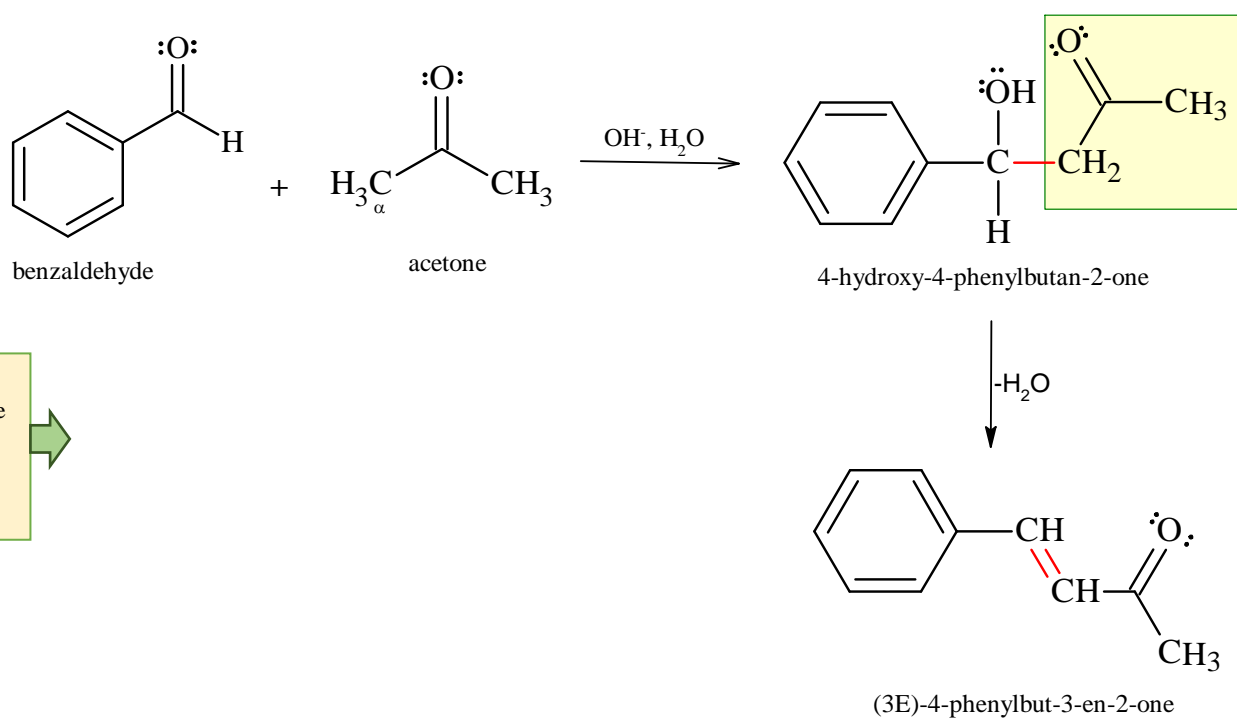
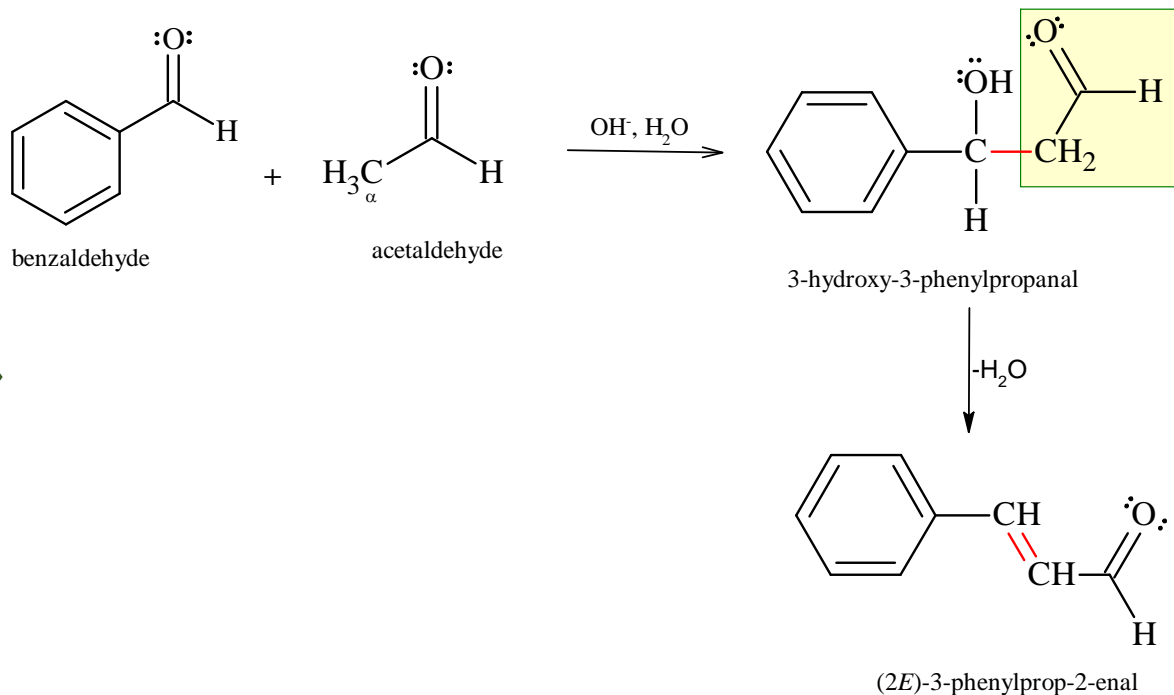
For example, when two different aldehydes having  $\alpha$ -hydrogen atoms, are combined in an aldol reaction, four different  $\beta$ -hydroxy carbonyl compounds are formed. Four products (no single product as in case of self-aldol reaction) are formed because both aldehydes can lose an acidic  $\alpha$ -hydrogen atom and form a nucleophilic carbanion in the presence of base. Both enolates can then react with both carbonyl compounds as shown in the following scheme.

Reaction between an acetaldehyde and a propanal



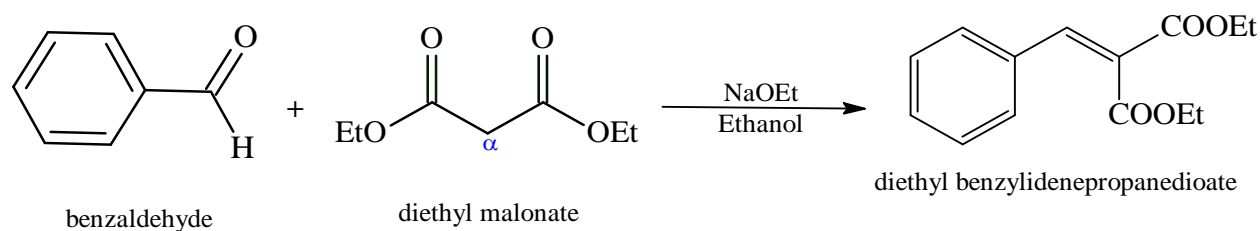
**Conclusion:** When two different aldehydes have  $\alpha$ -hydrogens, a crossed aldol reaction is synthetically not useful. But, when one of the two carbonyl compounds have no  $\alpha$  hydrogens, a crossed aldol reaction leads to one product (synthetically useful).

For example, the reaction of benzaldehyde ( $C_6H_5CHO$ ) which acts as an electrophile with either acetaldehyde ( $CH_3CHO$ ) or acetone ( $CH_3COCH_3$ ) which acts as nucleophile in the presence of base form single  $\alpha, \beta$  - unsaturated carbonyl compound after dehydration.

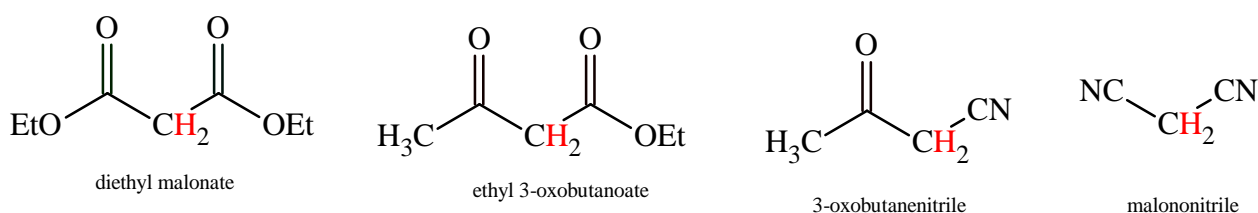


A crossed aldol reaction occurs readily when one carbonyl component has specifically acidic  $\alpha$ -hydrogen atoms.

For example: Crossed aldol reaction between an aldehyde or ketone and a  $\beta$ -dicarbonyl (or similar) compound.



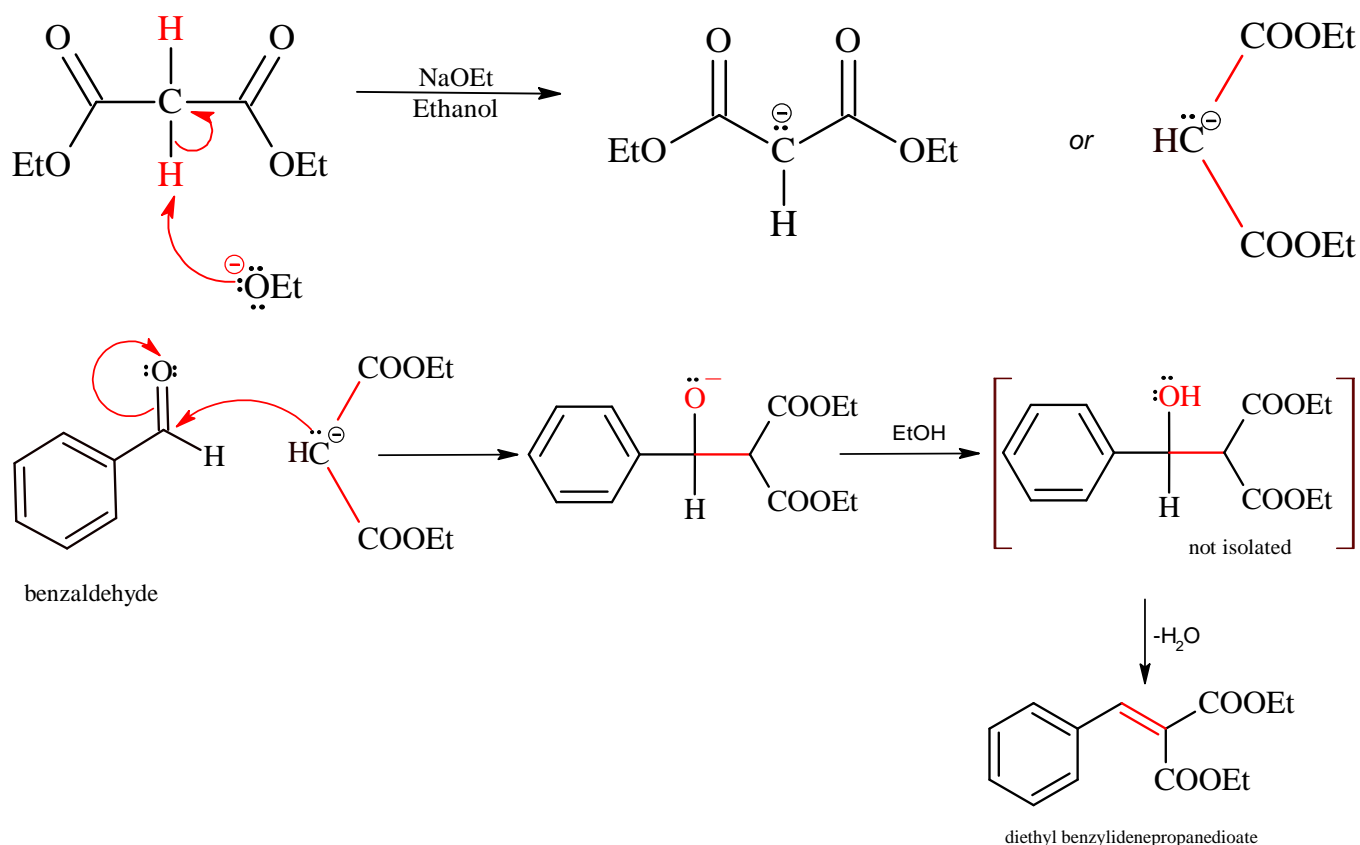
$\beta$ -dicarbonyl compounds are sometimes called active methylene compounds because they are more reactive towards base than other carbonyl compounds.



The  $\alpha$ -hydrogens between two carbonyl groups of a  $\beta$ -dicarbonyl compounds are highly acidic and hence they are easily removed in presence of base than other  $\alpha$ -hydrogen atoms.

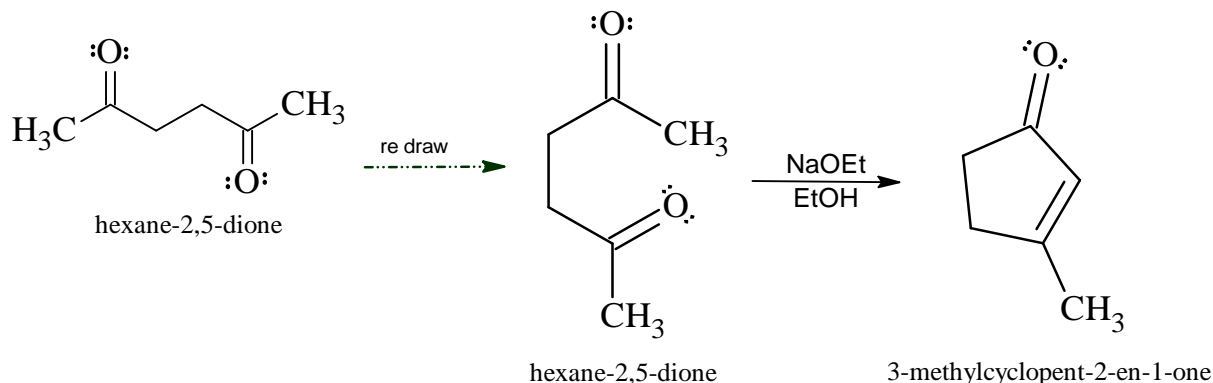
As a result, the  $\beta$ -dicarbonyl compound always become the enolate component of this aldol reaction.

### Mechanism



### 3.5. Intramolecular Aldol Reaction

Di carbonyl compounds undergo aldol reactions to make five and six member rings. The enolate formed from one carbonyl group is the nucleophile and the carbonyl carbon of another carbonyl group is the electrophile. For example, treatment of 2,5 hexadione with base forms a five membered ring.



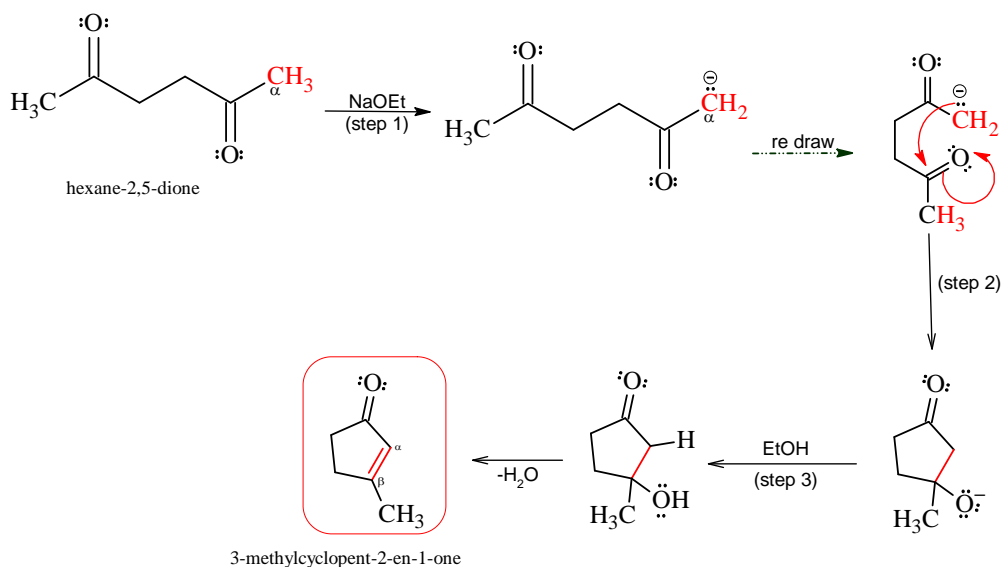
The steps in this process shown in mechanism are not different from the general mechanism of aldol reaction and dehydration discussed previously.

**Step 1: Formation of enolate:** In this step deprotonation of the methyl group with base forms a nucleophilic enolate which is redrawn to more clearly show the intramolecular reaction in step 2.

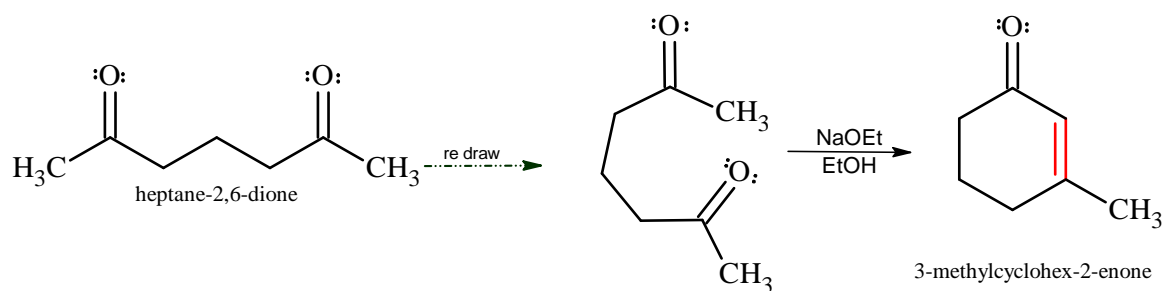
**Step 2: Nucleophilic attack of enolate:** In this step the nucleophilic enolate attacks the electrophilic carbonyl carbon in the same molecule forming a new carbon-carbon sigma bond. This generates the five membered ring.

**Step 3: Protonation followed by dehydration:** Protonation of the oxide in step 3 and loss of water form carbon-carbon  $\pi$ -bond.

Mechanism:



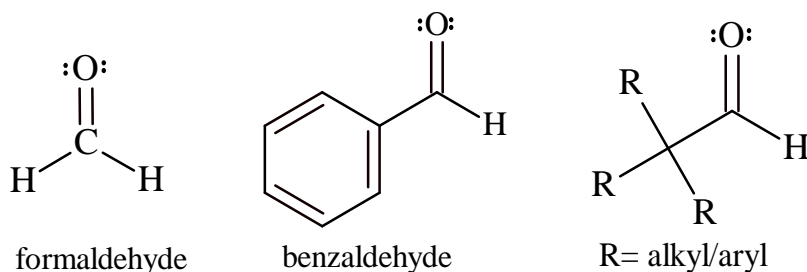
In a similar fashion six membered rings can be formed from the intramolecular aldol reaction of 1, 5 dicarbonyl compounds.



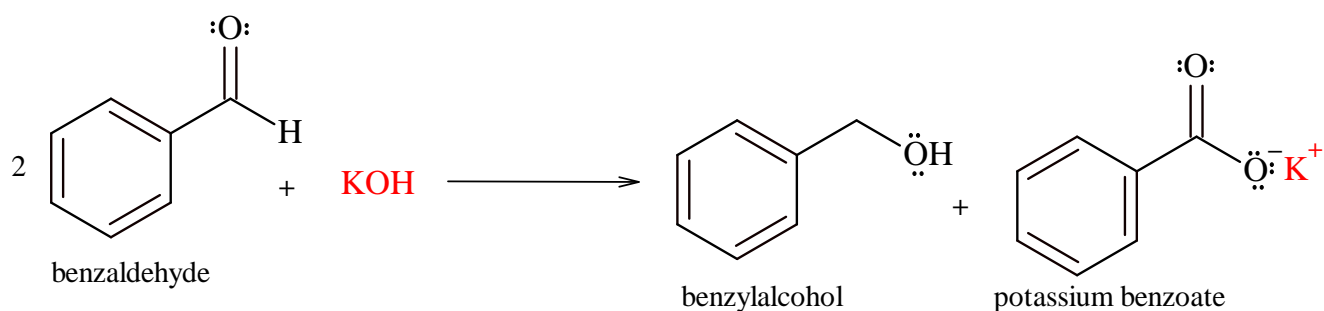
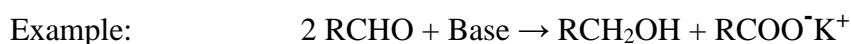
## 4. Cannizzaro Reaction

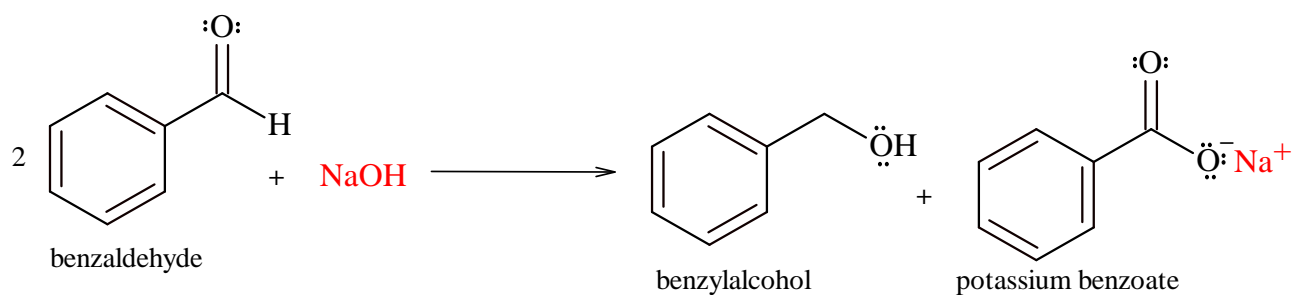
Aromatic aldehydes and aliphatic aldehydes with no  $\alpha$ -hydrogen atom gives the Cannizzaro reaction when treated with concentrated NaOH or other strong bases. In this reaction one molecule of aldehyde oxidises to form salt of carboxylic acid and another aldehyde is reduced to the primary alcohol. This simultaneous oxidation and reduction (Disproportionation) of aldehyde is known as Cannizzaro reaction. The Cannizzaro reaction is named after its discoverer Stanislao Cannizzaro. Cannizzaro first accomplished this transformation in 1853, when he obtained benzyl alcohol and potassium benzoate from the treatment of benzaldehyde with potash (potassium carbonate).

The aldehydes that undergo Cannizzaro reaction are given below:



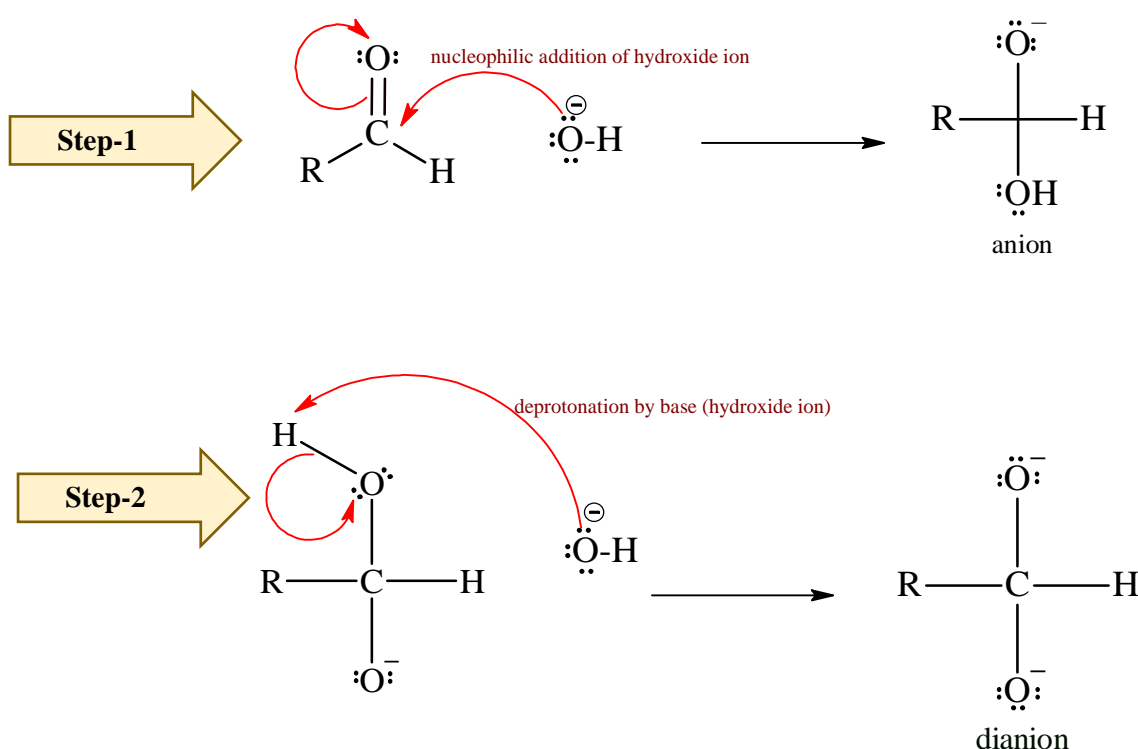
More typically, the reaction takes place with sodium or potassium hydroxide: The oxidation product is a salt of a carboxylic acid and the reduction product is an alcohol.

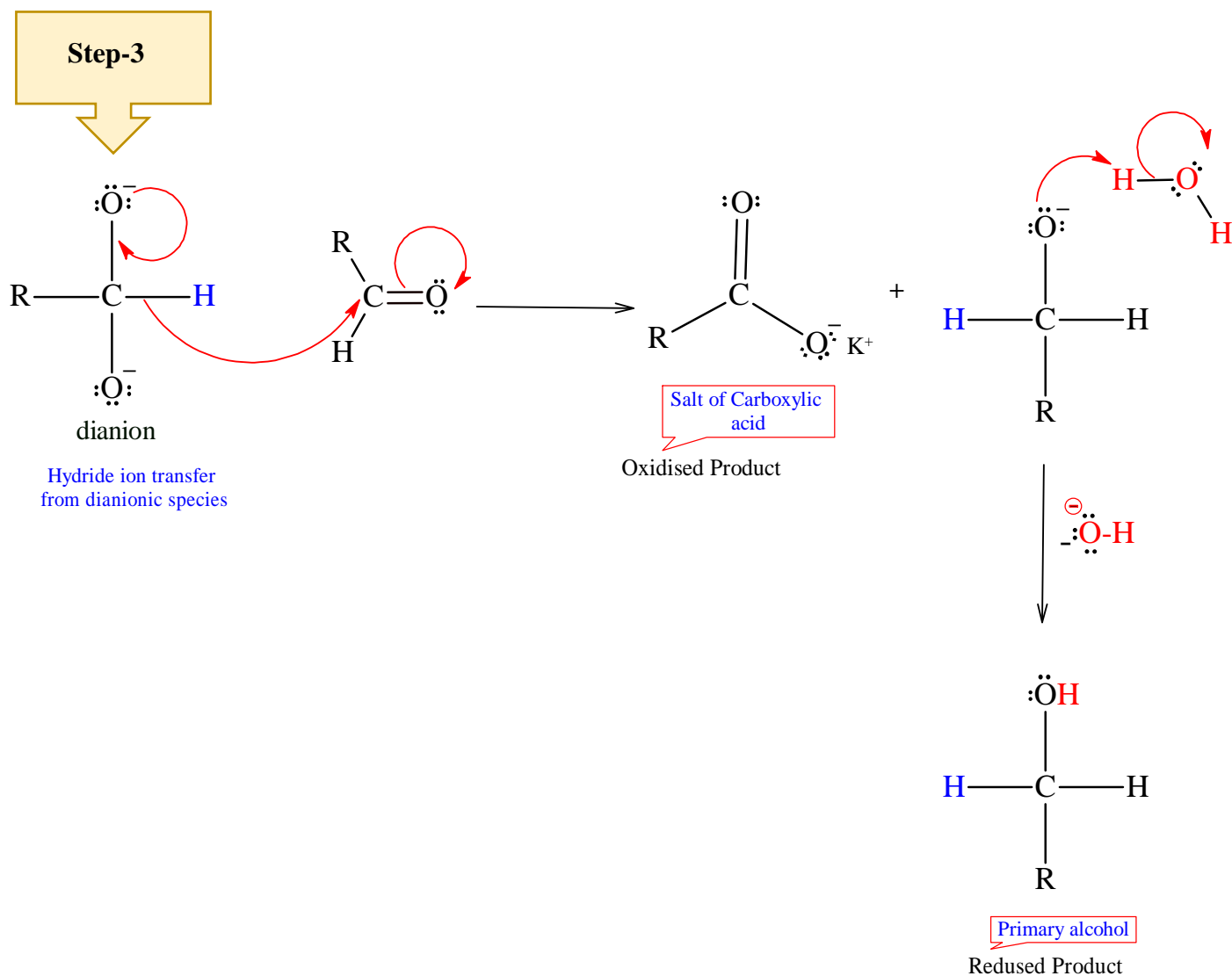




### 4.1. Mechanism of Cannizzaro Reaction

The reaction is initiated by the nucleophilic addition of hydroxide ion to the carbonyl group of an aldehyde molecule to give the anion (**Step-1**). In a strongly basic medium, the anion formed in step-1 can be deprotonated to give the di anionic species. (**Step-2**). These two anionic species are unstable. They attain stability by transferring hydride ion to the other aldehyde and gets oxidized to corresponding salt of carboxylic acid. The second molecule of aldehyde is there by reduced to alcohol. The strong electron- donating effect of two  $\text{O}^-$  substituents (in dianionic species) allows the transfer of a hydride ion  $\text{H}^-$  onto another aldehyde molecule. Thus, the key step of the Cannizzaro reaction is a *hydride transfer*.





The mechanism is supported by the result of experiments with D<sub>2</sub>O (Deuterium oxide) as solvent. The resulting primary alcohol obtained in the product does not contain carbon-carbon deuterium, indicating that the transferred hydrogen comes from a second substrate molecule, not from the solvent.

The applicability of the Cannizzaro reaction may be limited, if the aldehyde (non-enolizable) can undergo other reactions in the strongly basic medium. For example, an  $\alpha, \alpha, \alpha$ -trihalo acetaldehyde reacts according to the *haloform reaction*. Closely related to Cannizzaro reaction mechanism is the *benzylic acid rearrangement*, where an alkyl or aryl group migrates instead of the hydrogen.

## 5. Summary

1. The Aldol reaction between an aldehyde and another aldehyde or a ketone (having  $\alpha$  - hydrogens) is a good method for making carbon-carbon bonds.
2. An addition reaction between two aldehydes, two ketones, or an aldehyde and a ketone in presence of aqueous base resulting in the formation of a  $\beta$ - Hydroxy aldehyde (commonly known as Aldol) or a  $\beta$ -hydroxy ketone is called Aldol reaction.
3.  $\beta$ - hydroxy carbonyl compound loses water molecule more readily in base to form  $\alpha$ ,  $\beta$ - unsaturated carbonyl compound.
4. Reaction between two different carbonyl compounds in the presence of aqueous base is called “crossed aldol reaction”.
5. Intramolecular aldol reaction leads to the product having five or six membered rings (more stable).
6. This simultaneous oxidation and reduction of aldehyde (disproportionate reaction) is called the Cannizzaro reaction.
7. Aromatic and aliphatic aldehydes with no  $\alpha$ -hydrogens react with concentrated NaOH or other strong alkalis to give Cannizzaro reaction.

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## References:

1. Advanced Organic Chemistry: Reactions, Mechanisms, by Michael B. Smith; Jerry March, Fourth edition, John Wiley & Sons.
2. Writing Reaction Mechanisms in Organic Chemistry by Audrey Miller, Philippa H. Solomon, Third edition, Elsevier Science & Technology Books.
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5. Organic Chemistry by T. W. Graham Solomons, Craig B. Fryhle, Tenth edition, John Wiley & Sons.
6. Organic Chemistry (English, Paperback, 7<sup>th</sup> edition) by Paula Y Bruice, Pearson Education.
7. Organic Chemistry (English, Paperback, 3<sup>rd</sup> edition) by Janice Gorzynski Smith, McGraw-Hill.

## Web Links:

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2. [https://en.wikipedia.org/wiki/Aldol\\_condensation](https://en.wikipedia.org/wiki/Aldol_condensation)
3. [https://en.wikipedia.org/wiki/Cannizzaro\\_reaction](https://en.wikipedia.org/wiki/Cannizzaro_reaction)
4. [https://chem.libretexts.org/Bookshelves/Organic\\_Chemistry/Supplemental\\_Modules\\_\(Organic\\_Chemistry\)/Reactions/Organic\\_Reactions/Cannizzaro\\_Reaction](https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Reactions/Organic_Reactions/Cannizzaro_Reaction)
5. <http://www.chem.ucalgary.ca/courses/351/Carey5th/Ch18/ch18-3-4.html>