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Cannizzaro Reaction

Assistant Lecturer

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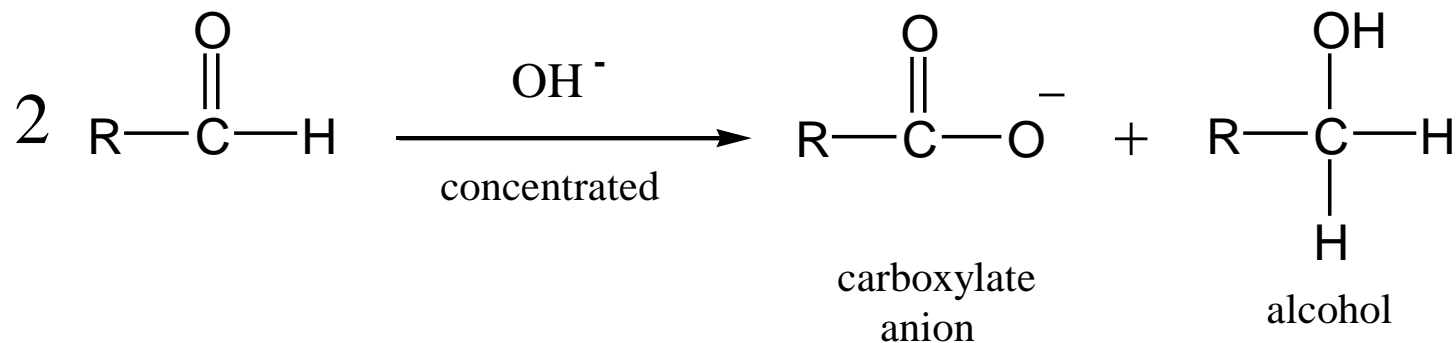
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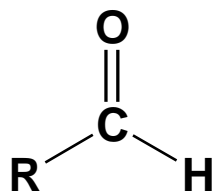
Part I

Cannizzaro Reaction

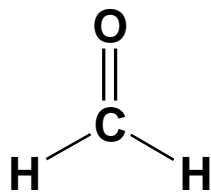
In the presence of concentrated alkali, aldehydes containing no α - hydrogens undergo self oxidation & reduction (Redox) reaction to yield a mixture of an alcohol & a salt of carboxylic acid.



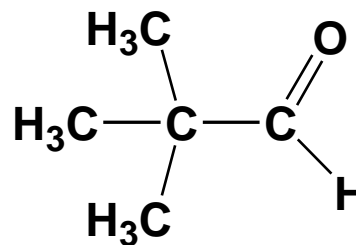
Examples:



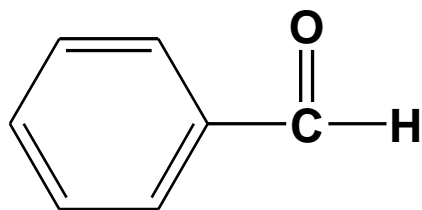
Aldehyde



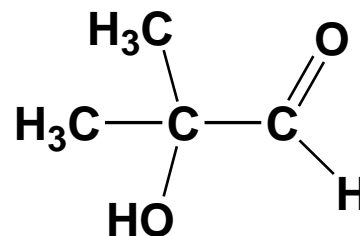
Formaldehyde
(Methanal)



2,2-Dimethylpropanal



Benzaldehyde



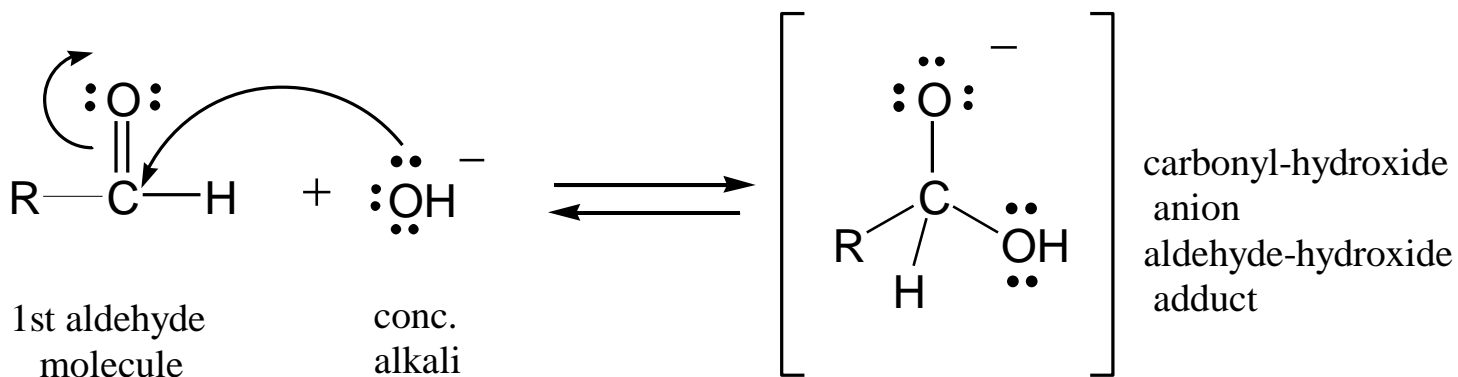
2-Hydroxy-2-methylpropanal

Mechanism of the reaction


Three proposed mechanisms,

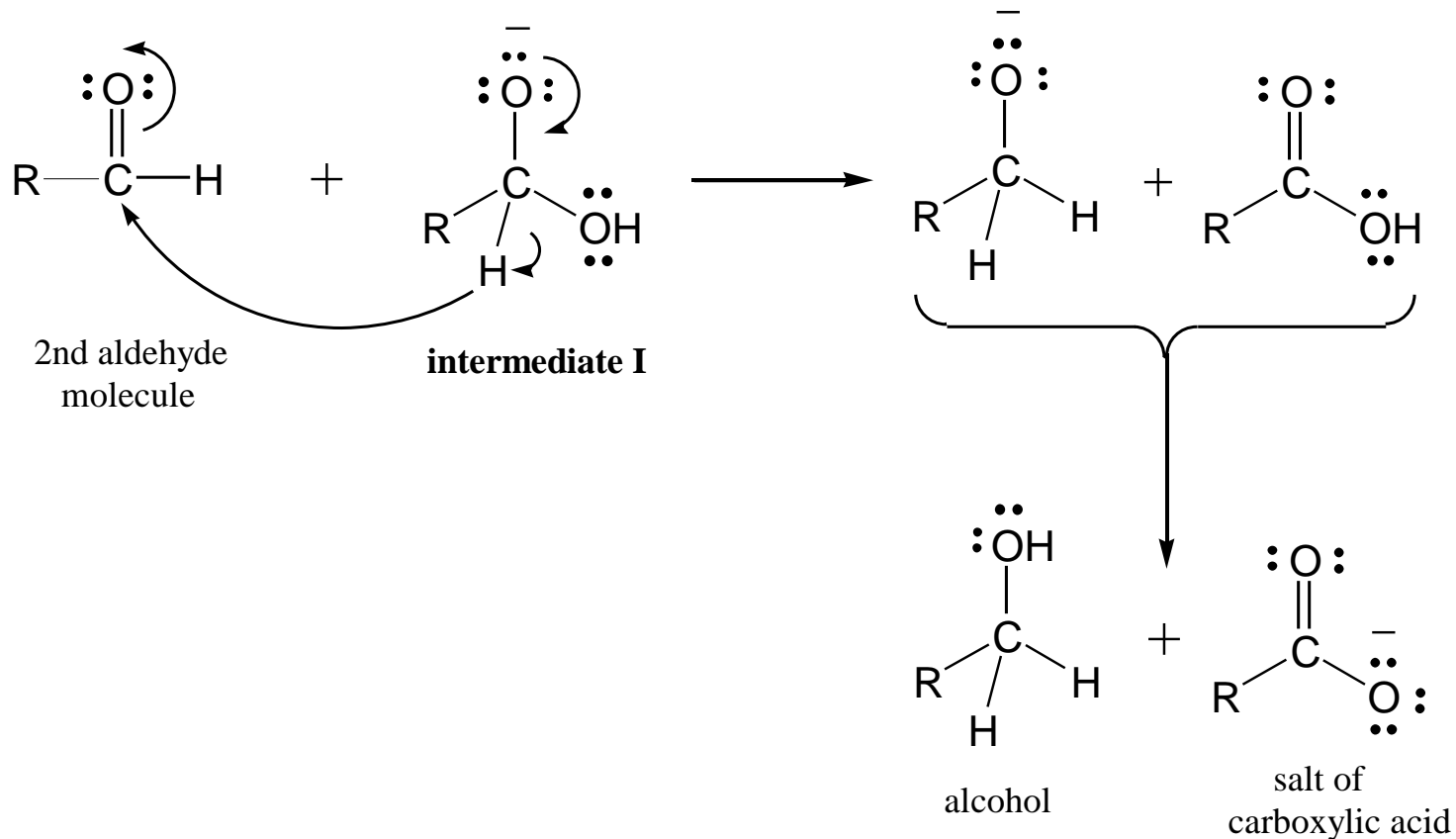
1st Mechanism:

 **Step I Nucleophilic addition of an OH⁻ ion to the 1st aldehyde molecule gives a tetrahedral intermediate I .**



Tetrahedral intermediate
intermediate I

 **Step II Hydride shift:** The tetrahedral intermediate I, expels a hydride ion* as a leaving group** and is thereby oxidized. A second aldehyde molecule accepts the hydride ion in another nucleophilic addition step and is thereby reduced.





Notes :

*** A hydride ion is the anion of hydrogen , H^- , have nucleophilic, reducing or basic properties.**

**** The strong electron - donating character of O^- greatly facilitate the ability of the aldehydic hydrogen to leave with it's electron pair .**

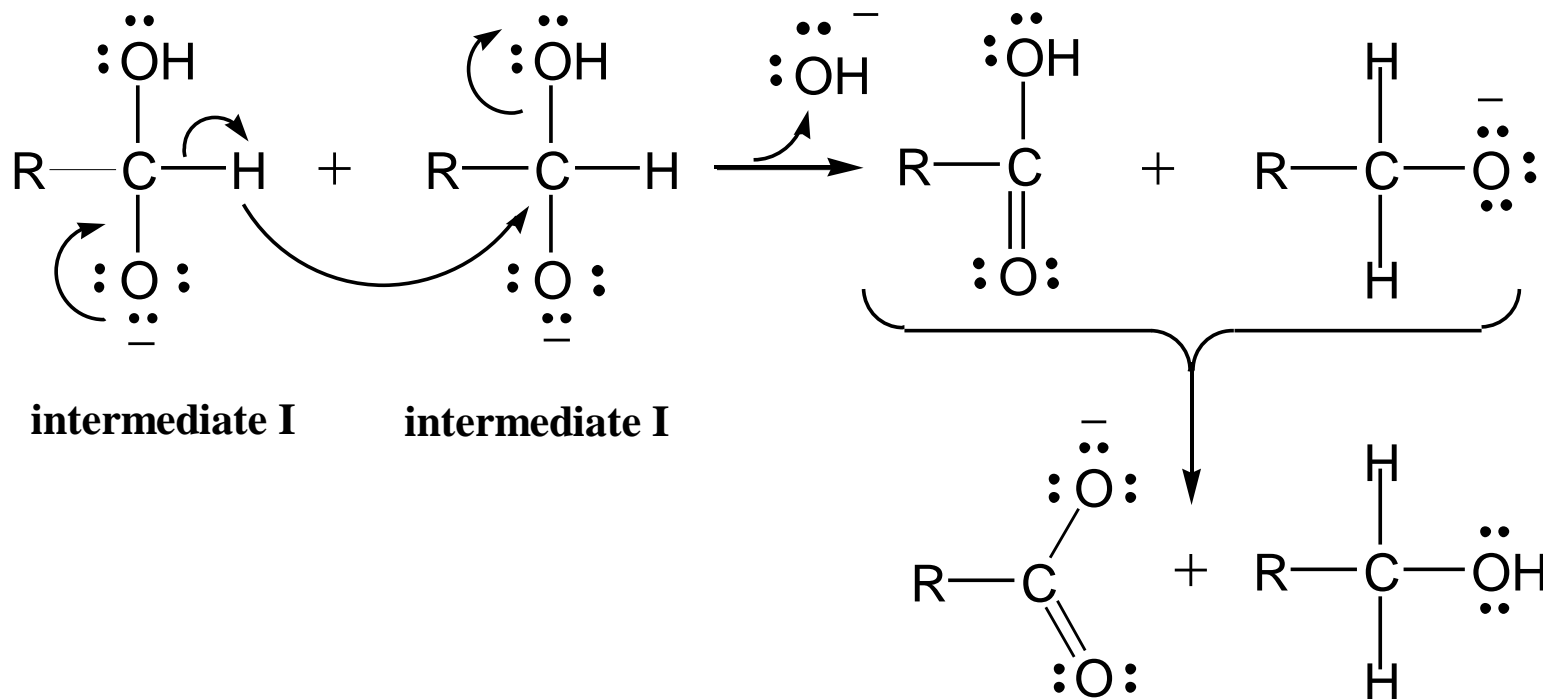
2nd Mechanism :

 **Step I Generation of the Intermediate I; Nucleophilic addition of OH^- ion to an aldehyde molecule to give a carbonyl-hydroxide anion (intermediate I) as in the 1st mechanism.**

 **Step II** A hydride ion from one carbonyl – hydroxide anion (I) is added to another carbonyl – hydroxide anion (I).

In the last step , the alkoxide anion receives a proton from the carboxylic acid.

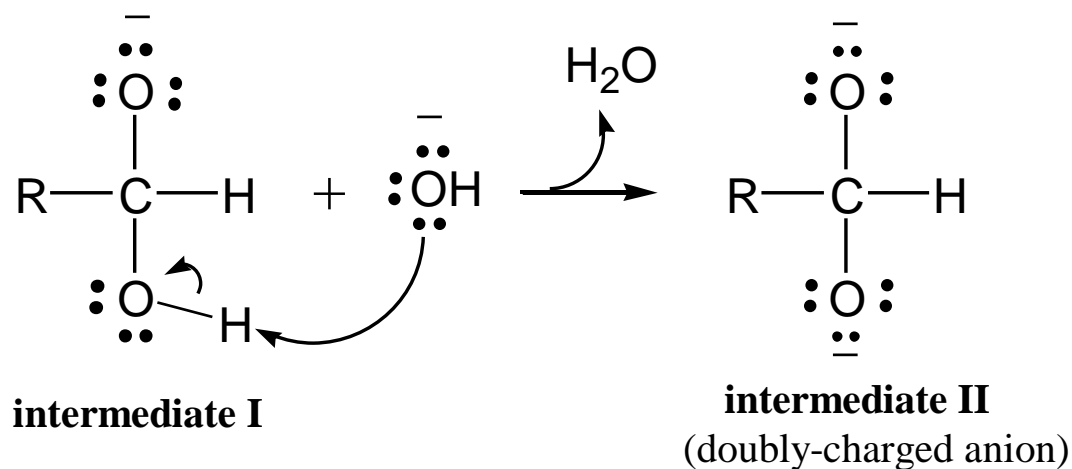
The acid can be recovered by acidifying the mixture.




3rd Mechanism:

 **Step I** Nucleophilic addition to give intermediate I as in the 1st mechanism.

 **Step II** Deprotonation of the intermediate I to give a dianion intermediate II.

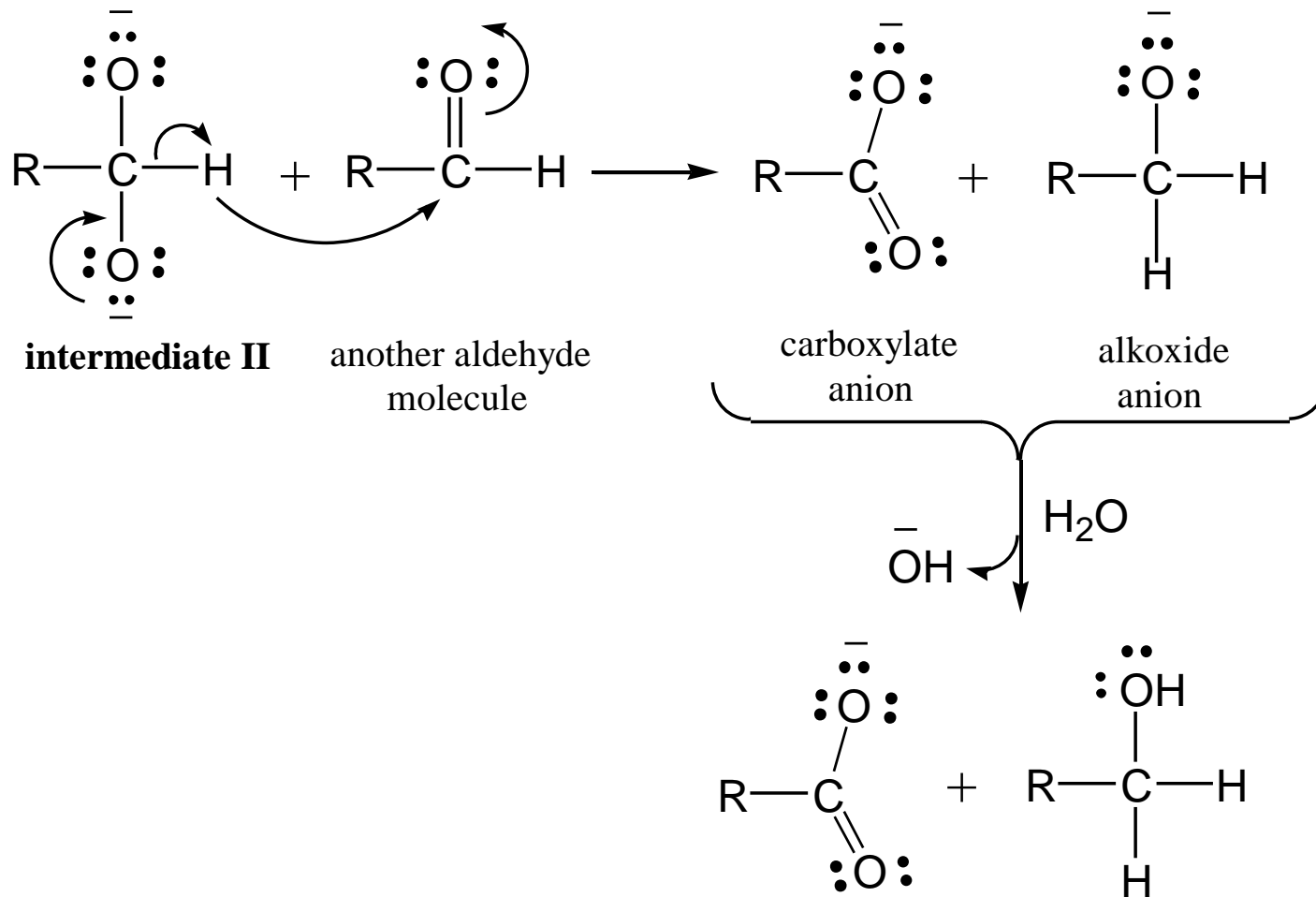


 **Step III** The unstable intermediate II releases a hydride anion which attacks another molecule of the aldehyde. In this process the dianion intermediate converts to a carboxylate anion and the aldehyde to an alkoxide anion.

The alkoxide anion then picks up a proton from water to provide the alcohol final product [□], while the carboxylate anion is converted to the carboxylic acid product after acid work-up ^{□□}.

□ The alkoxide anion is more basic than water, so it can pick up a proton from water.

□□ The carboxylate anion is less basic than water, thus it can not pick up a proton from water and require an acid work up to protonate.



Worked example :

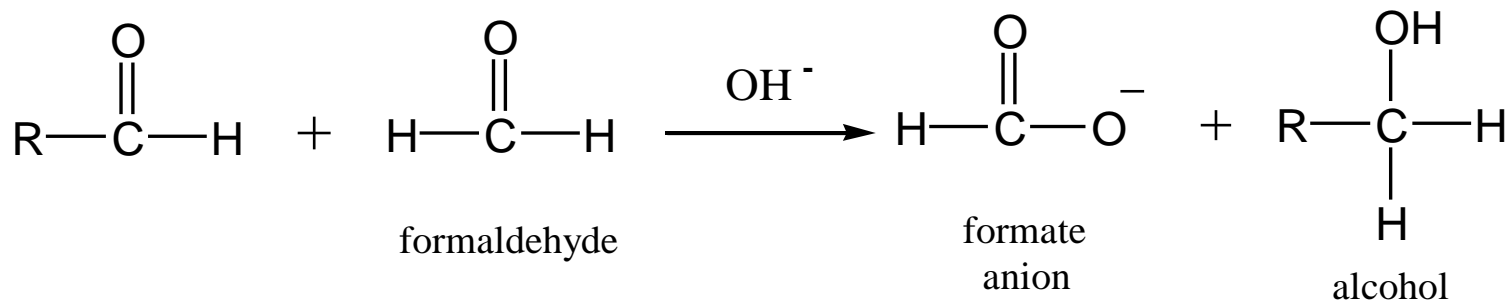
How can you prove that the hydrogen comes from another equivalent of aldehyde and not from the medium , (i.e. Involvement of a hydride shift in the mechanism of Cannizzaro reaction) ?

Solution:

When the reaction was run in D_2O instead of H_2O , the recovered alcohol contained no α deuterium .

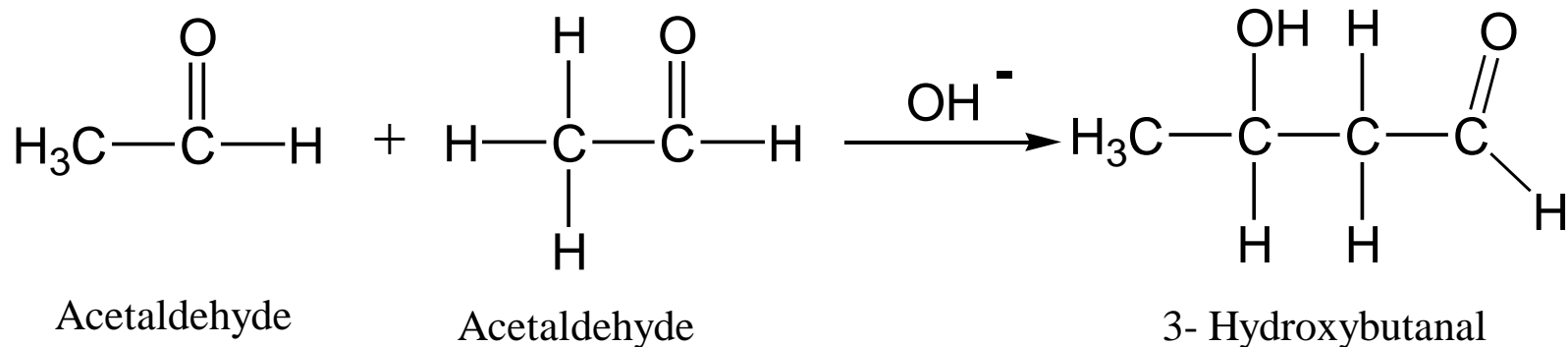
Crossed Cannizzaro Reaction

In general, a mixture of aldehydes undergoes a Cannizzaro reaction to yield all possible products. If one of the aldehydes is formaldehyde, the reaction yields almost exclusively salt of formic acid and the alcohol corresponding to the other aldehyde. Such a reaction is called a *Crossed Cannizzaro Reaction*.



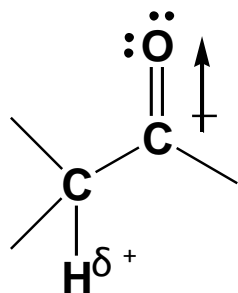
Aldol Condensation

Aldehydes or ketones with an α - hydrogen (acidic *) undergo *Aldol Condensation (carbonyl condensation reaction)* under the influence of dilute base or acid, 2 molecules of aldehyde or ketone combine to form a β - hydroxy aldehyde or β - hydroxy ketone in such a way that the α - carbon of the 1st becomes attached to the carbonyl carbon of the 2nd.

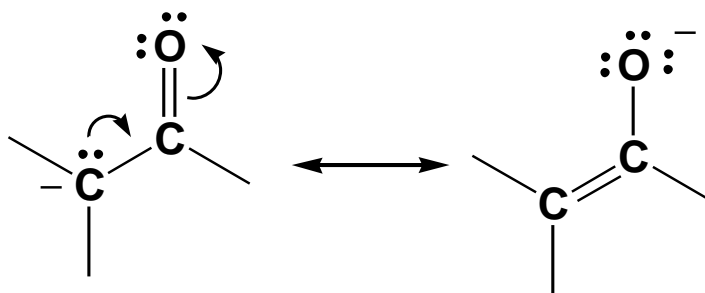


* *Two factors* – one **inductive** , the other **resonance** – combine to make an α hydrogen of an aldehyde or ketone relatively acidic.

The electron – withdrawing inductive effect of the carbonyl group increases the positive character of the α -H, & resonance stabilizes the conjugate base.



Inductive effect increase
positive character of hydrogen



Electron delocalization
stabilizes conjugate base

The resonance of the conjugate base of an aldehyde or ketone is called an enolate ion . Of the two resonance structures shown for the conjugate base, the major contributor is the one with the negative charge on oxygen.

Synthesis of Benzoic acid and Benzyl alcohol

BENZALDEHYDE, C_7H_6O , (C_6H_5CHO)

Molar mass = 106.12 g mol⁻¹.

It's a colorless or yellowish liquid.

It has a characteristic pleasant almond - like odor .

BENZOIC ACID, $C_7H_6O_2$, (C_6H_5COOH)

Molar mass = 122.12 g mol⁻¹.

Melting point = 121 – 123 °C.

It is a colorless plate or needle like crystals with a faint, pleasant odor.

Sparingly soluble in water but soluble in hot or boiled water.

Reacts with sodium bicarbonate to give CO_2 gas.

Benzoic acid and it's salts are used as food preservatives.

Also used externally in the form of lotions , ointments (e.g. Whitfield ointment), mouth washes, etc.

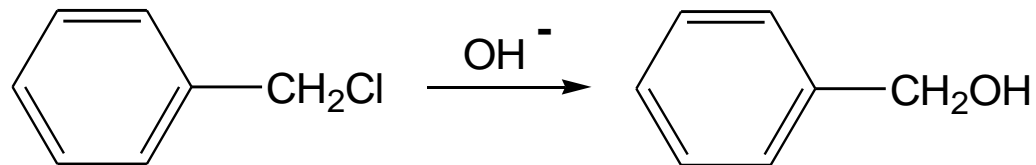
BENZYL ALCOHOL , C_7H_8O , ($C_6H_5CH_2OH$)

Molar mass = 108.14 g mol⁻¹.

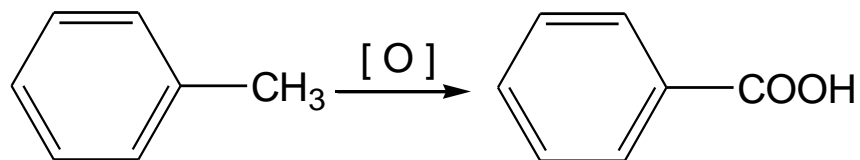
Boiling point = 204 – 207 ° C.

It is a colorless oily liquid with a mild pleasant aromatic odor, immiscible with water and completely miscible with alcohols and organic solvents as diethyl ether . It's a useful solvent due to its polarity , low toxicity and low vapor pressure (volatile with steam) . It has some local anesthetic properties so it is useful as an antipruritic and it is included in some dental remedies & injectibles . Used in pharmaceutical preparations for local application up to 10% in ointments as antipruritic and antiseptic.

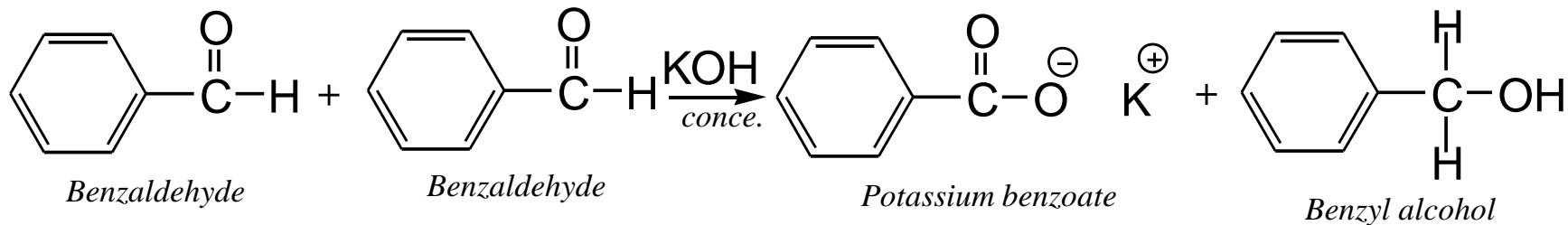
Benzyl alcohol can be prepared by hydrolysis of **benzyl chloride** with **NaOH**.



Benzoic acid can be prepared by the oxidation of **toluene**.



However, both **Benzoic acid** & **Benzyl alcohol** can be prepared in the laboratory by **Cannizzaro Reaction**, by the action of concentrated **NaOH** or **KOH** on **benzaldehyde**.



Name of Experiment: **CANNIZZARO REACTION.**

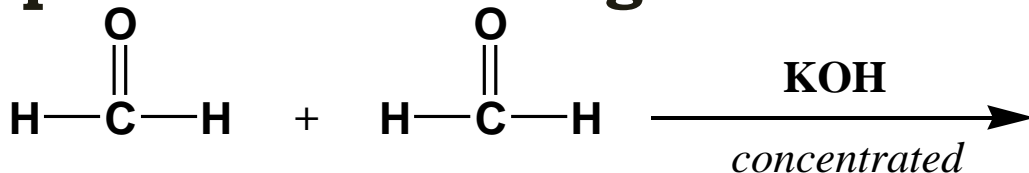
Aim of Experiment: **Synthesis of BENZOIC ACID and BENZYL ALCOHOL**

Procedure:

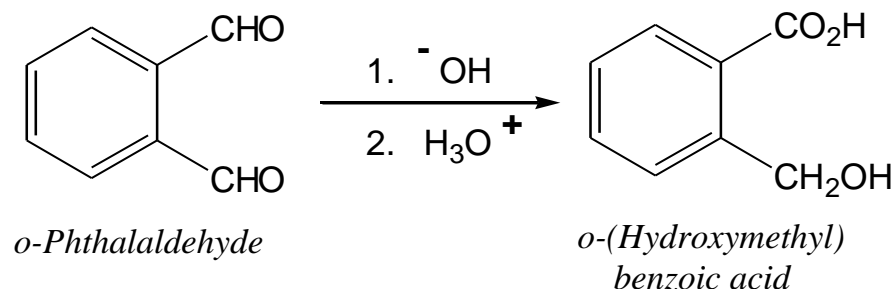
- 1- Dissolve 7.2 g of KOH in about 7 ml of H₂O contained in a beaker.**
- 2- Cool the solution to about 20 °C in an ice-water bath.**
- 3- Pour the solution into a 125 ml reagent bottle.**
- 4- Add 7.3 ml of pure benzaldehyde , cork the bottle securely and shake the mixture vigorously until it has been converted to a thick emulsion.**
- 5- Allow the mixture to stand overnight (in this case until the next laboratory period). By which time the reaction should have been completed.**

Post Lab. Exercises:

- 1- How would propanal react with KOH solution under the condition of this experiment? Answer the same question for the reaction of 2,2-dimethylpropanal.
- 2- Write an equation for the reaction of a mixture of benzaldehyde and 2,2-dimethylpropanal with concentrated KOH solution. Show all possible products.
- 3- Write a mechanism for the reaction of benzaldehyde with formaldehyde under strong basic conditions.
- 4- Complete the following reaction



5- When o-phthalaldehyde is treated with base , o- (hydroxymethyl) benzoic acid is formed. Show the mechanism of this reaction.

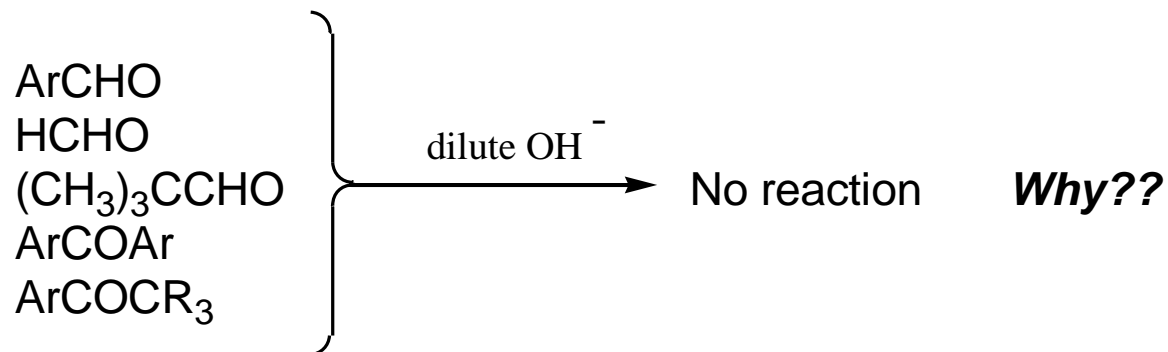


6- In the case of some aldehydes there is evidence that intermediate II is the hydride donor in the Cannizzaro reaction.

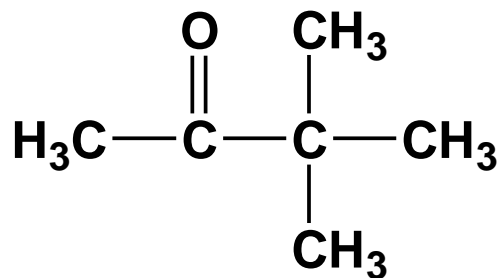
a- How would II be formed from I ?

b- Why would you expect II to be a better hydride donor than I ? (Hint : What is one product of the hydride transfer from II ?) .

7- Explain ,



8- Find the most acidic H in *tert*-Butyl methyl ketone & write a chemical equation for the proton-transfer process that occurs on reaction with hydroxide ion.



tert-Butyl methyl ketone

References

- * Robert T. Morrison , Robert N. Boyd: “ *Aldehydes and Ketones*” . **Organic Chemistry**, (6th) edition , Prentice - Hall Inc.
- * Carey, Francis A.: “ *Aldehydes and Ketones: Nucleophilic Addition to the Carbonyl Group* ” . **Organic Chemistry** (6th) edition, McGraw-Hill companies, Inc.
- * Samira Finjan Hassan, Amer Nadem, May Mohammed Jawad , **A Laboratory manual on Practical Medical Chemistry for 4th year students**, *University of Baghdad , College of Pharmacy , Department of Pharmaceutical Chemistry, 2010.*
- * Vogel, Arthur, *Textbook of Organic Chemistry*, 4th edition.
- * John E. McMurry, *Organic Chemistry*, 8th edition, 2012