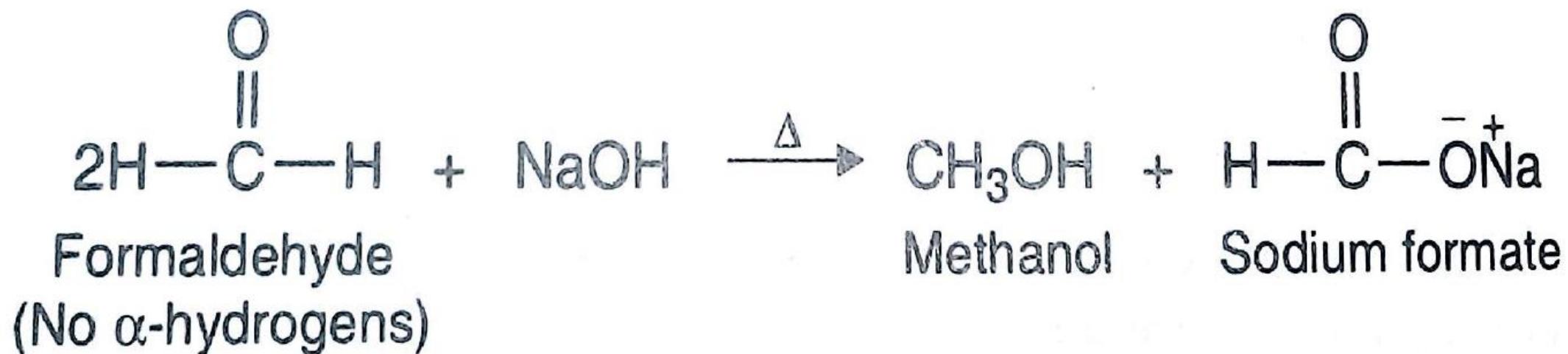


NAME REACTIONS

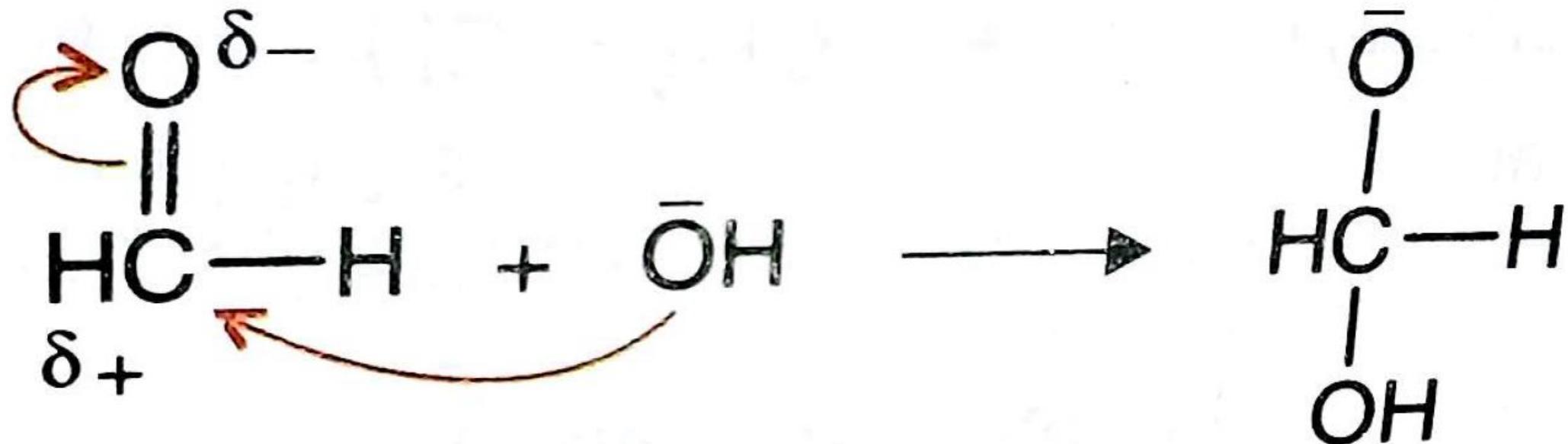
Cannizzaro Reaction

The Cannizzaro reaction involves the treatment of an aldehyde ([without alpha-hydrogens](#)) with concentrated NaOH or KOH. Aldehydes when heated with NaOH, undergo a **disproportion reaction**. One half of aldehyde molecules are oxidized to a carboxylic acid and one half to an alcohol. The Cannizzaro reaction, named after its discoverer [Stanislao Cannizzaro](#).

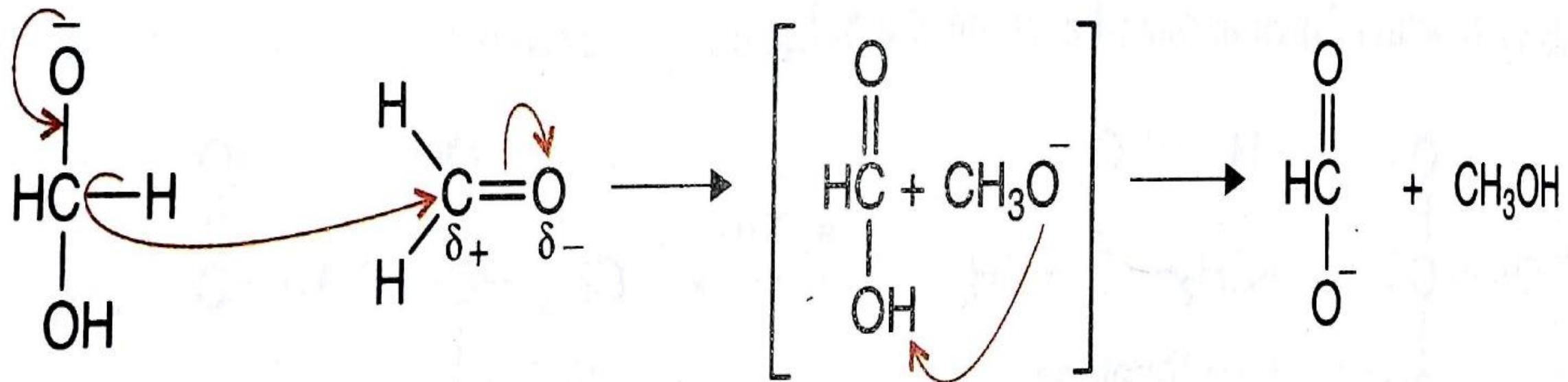


Mechanism

Step-1: Attack of OH^- on the carbonyl carbon



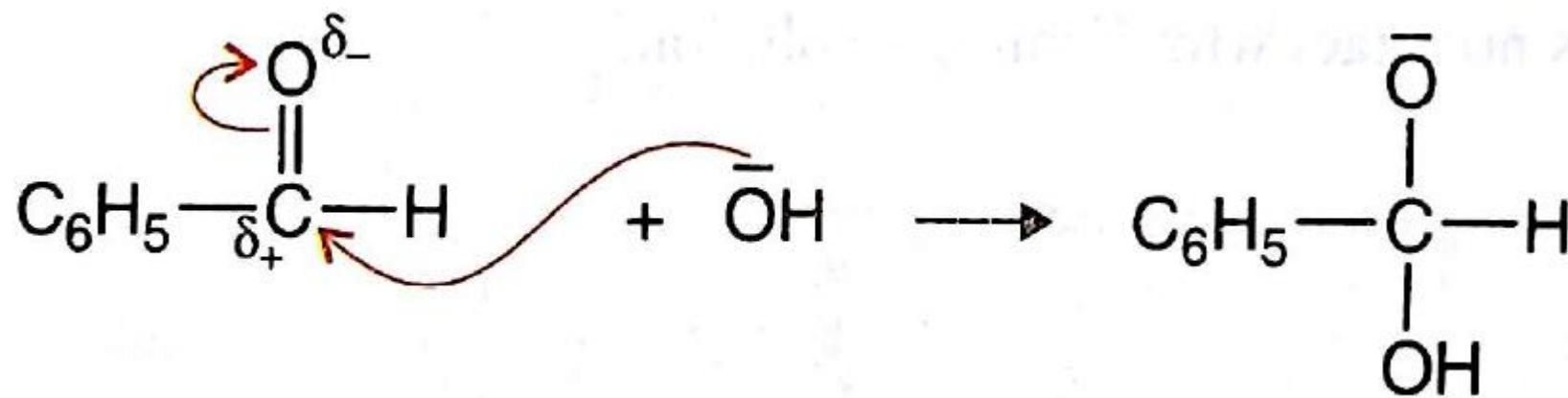
Step-2: Hydride-ion transfer



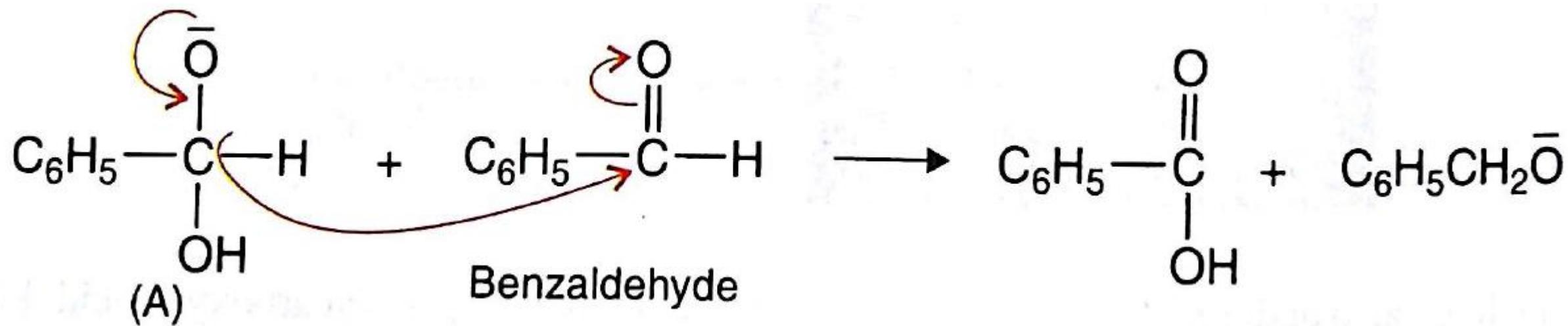


Mechanism:???

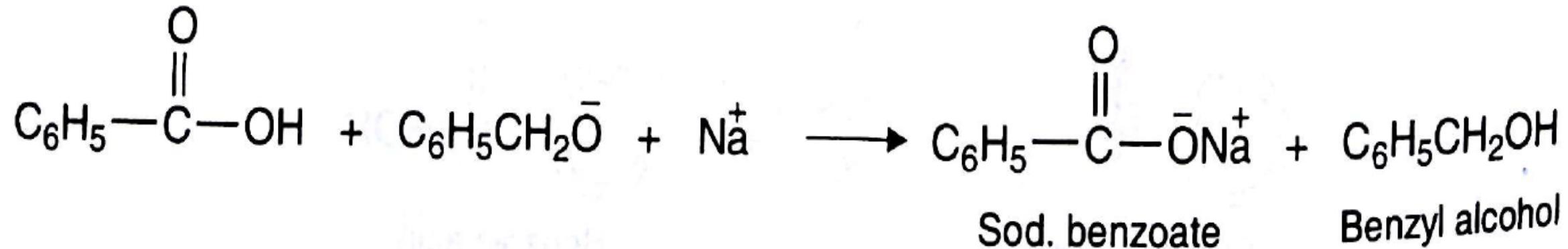
Step-1: Attack of OH^- on the carbonyl carbon



Step-2: Hydride ion transfer

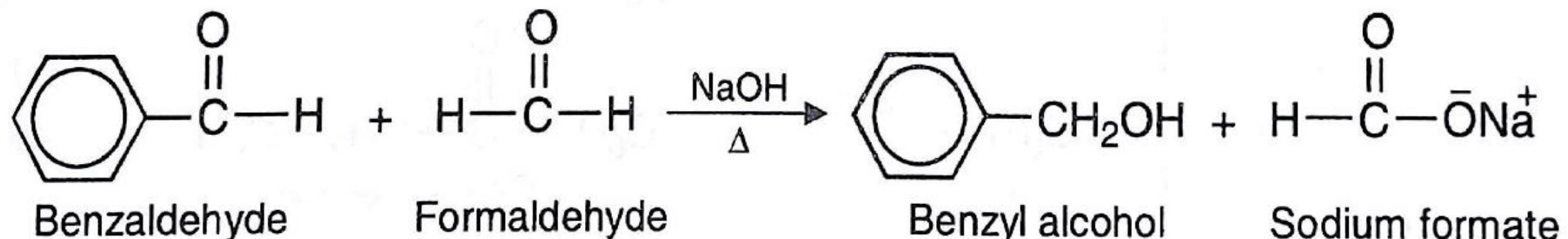


Step-3: Acid-base reaction



Crossed Cannizzaro reaction

When two different aldehydes, each lacking alpha-hydrogen are heated in an alkaline solution, the reaction is said to be crossed Cannizzaro reaction. For example, when benzaldehyde and formaldehyde is heated in the presence of NaOH, a mixture of benzyl alcohol and sodium formate is formed.

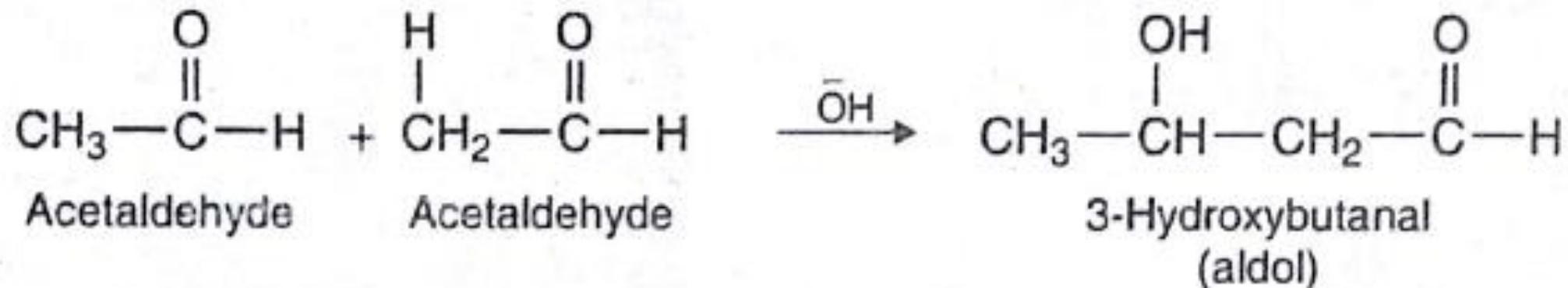


Under ideal conditions the reaction produces only 50% of the alcohol and the carboxylic acid (it takes two aldehydes to produce one acid and one alcohol). **To avoid the low yields, it is more common to conduct the crossed Cannizzaro reaction, in which a sacrificial aldehyde is used in combination with a more valuable chemical.** In this variation, the reductant is formaldehyde, which is oxidized to sodium formate and the other aldehyde chemical is reduced to the alcohol. In this scenario, each of the two separate aldehydes can be converted completely to its corresponding product rather than losing 50% of a single reactant to each of two different products.

Aldol Condensation

Aldehydes containing alpha-hydrogens undergo self-addition in the presence of a base to form products called **aldols**. The reaction is called aldol condensation. The term aldol is derived from the combination of the words **Aldehyde** and **Alcohol**, the two functional groups present in the product. When two acetaldehyde molecules combine with each other in the presence of dilute NaOH, it form aldol (3-hydroxybutanal).

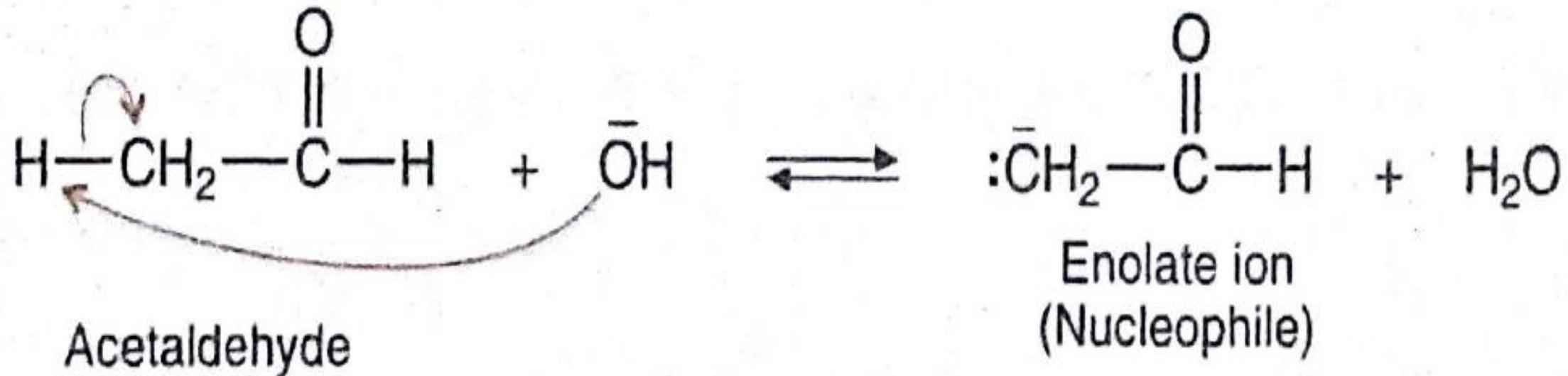
Chemical Reaction



Mechanism

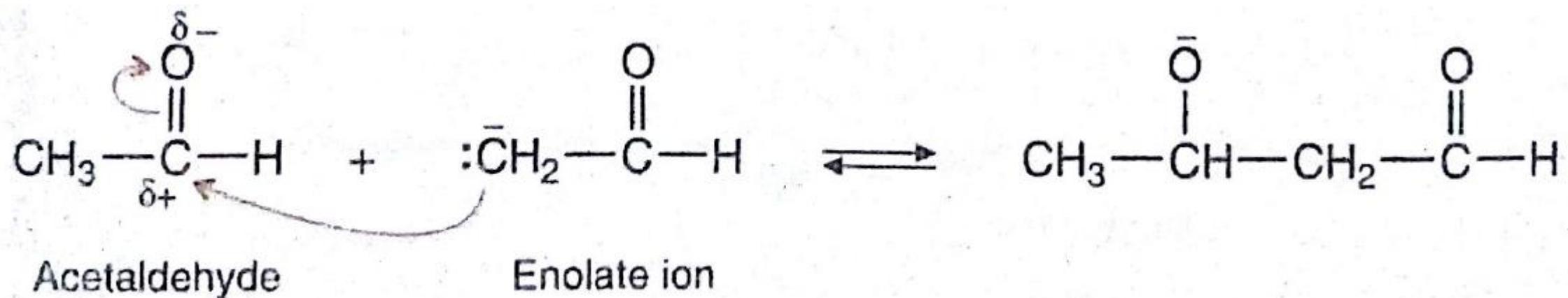
The reaction is reversible and involves the following steps

Step-1: Formation of enolate ion



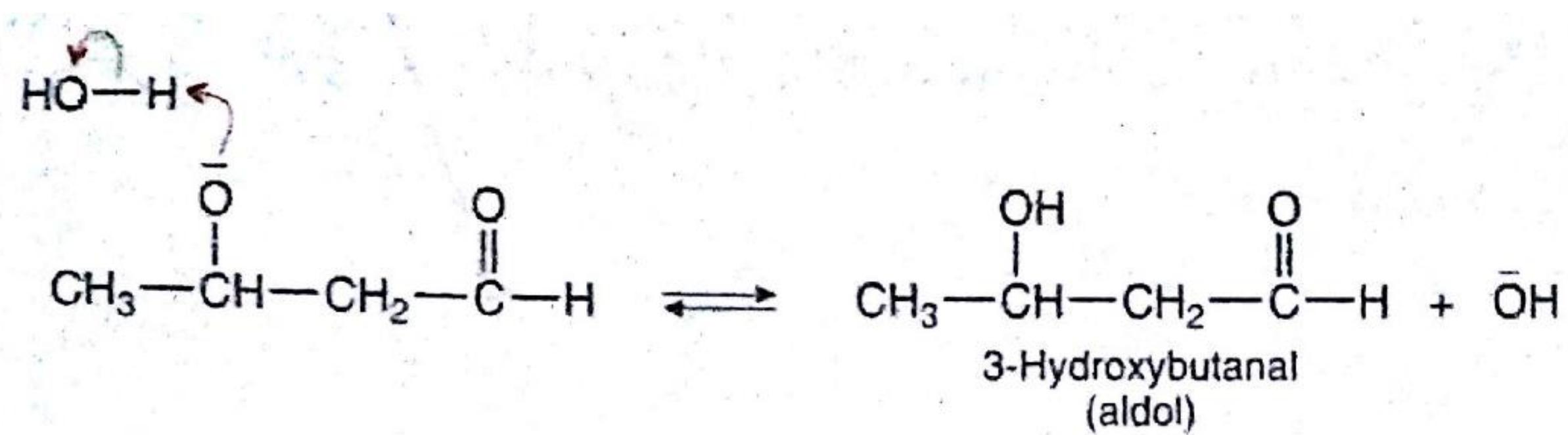
Step-2:

The enolate ion attacks the carbonyl carbon of another un-ionized aldehyde molecule

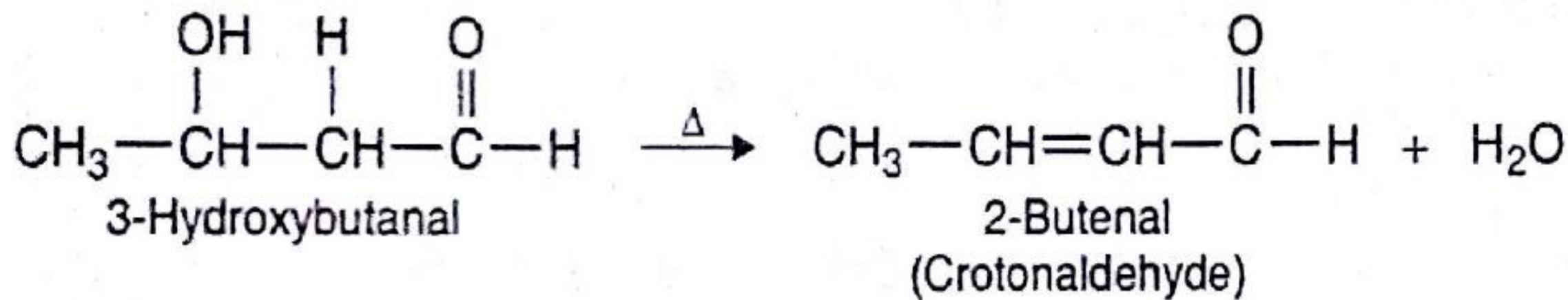


Step-3:

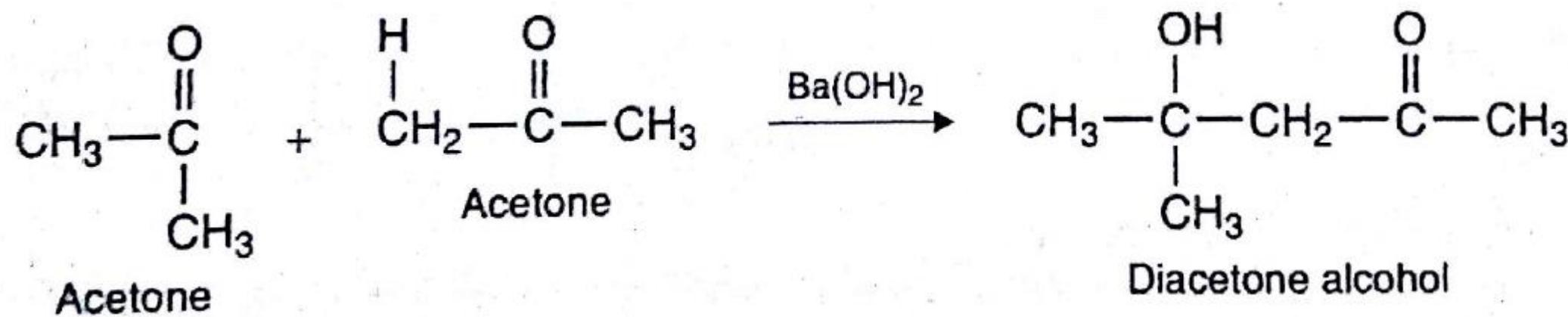
The negative oxygen in the product accepts a proton from water to give aldol



Aldols can easily be dehydrated either by heating or by treatment with dilute acid to form α,β -unsaturated aldehydes.



Ketones containing α -hydrogens also undergo aldol condensation to form **ketols**. For example, two acetone molecules combine with each other in the presence of barium hydroxide to form **diacetone alcohol** (4-hydroxy-4-methyl-2-pentanone).

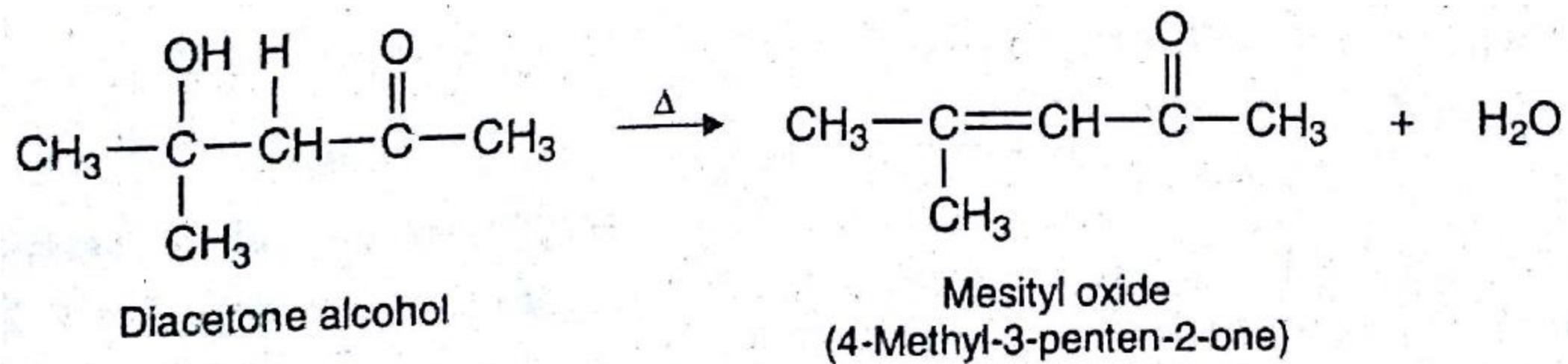


Mechanism:?????

Dehydration product????

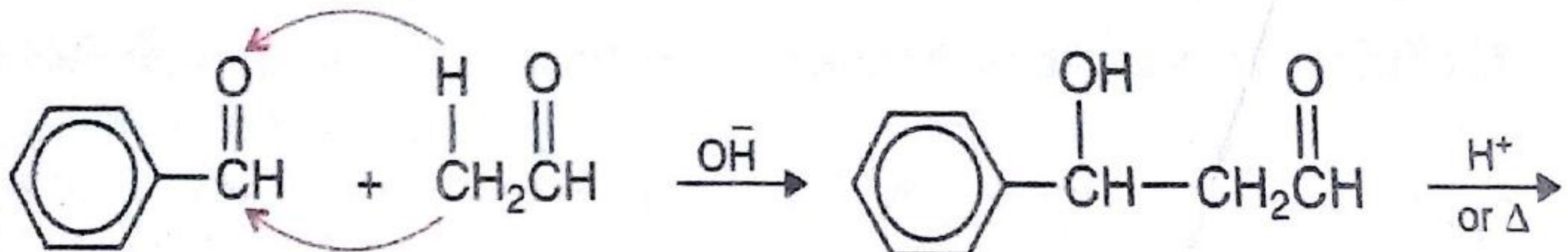
Dehydration product

Ketols are also easily dehydrated by heating or by treatment with dilute acid to form α,β -unsaturated ketones.

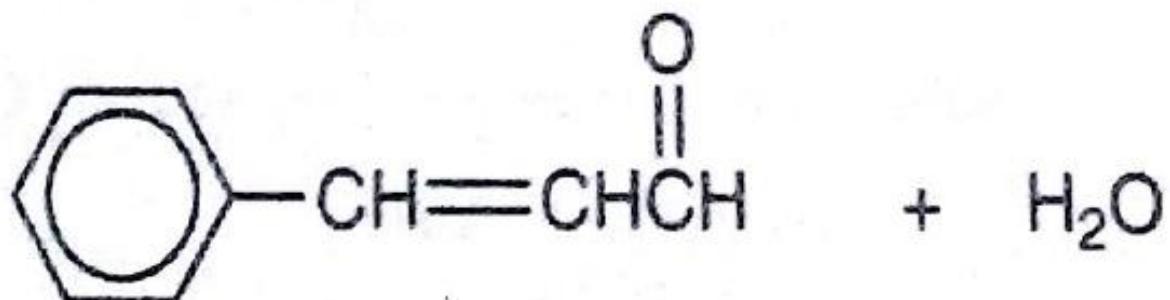


Mixed Aldol Condensation

The reaction of two different carbonyl compounds (one of which must contain α -H) in the presence of a base is known as mixed aldol condensation. For example, acetaldehyde react with benzaldehyde (which has no α -H) in the presence of a base to form cinnamaldehyde



Benzaldehyde



Cinnamaldehyde

Key points in aldol condensation

1. The product is a larger molecule that contains newly formed C-C bond.
2. The products contains two functional groups; one carbonyl group and one hydroxyl group.
3. The hydroxyl group is always attached to the beta carbon, which is two carbons away from the carbonyl group.
4. An aldol condensation is a condensation reaction in organic chemistry in which an enol or an enolate ion reacts with a carbonyl compound to form a β -hydroxyaldehyde or β -hydroxyketone, followed by dehydration to give a conjugated enone.

Grignard Reactions

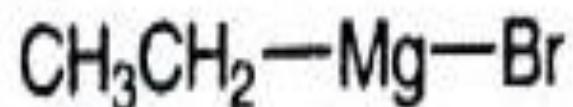
Of all the organometallic compounds known, organomagnesium halides (RMgX) or Grignard reagents are the most important. They are so named after **Victor Grignard** discovered them and developed their use as synthetic agents. **Grignard reagents occupy pride of place in organic synthesis by virtue of their versatility and wide application. Almost all classes of organic compounds can be prepared from them.** Grignard earned one-half of a Nobel Prize in 1912 for his remarkable contribution to synthetic organic chemistry.

General formula:

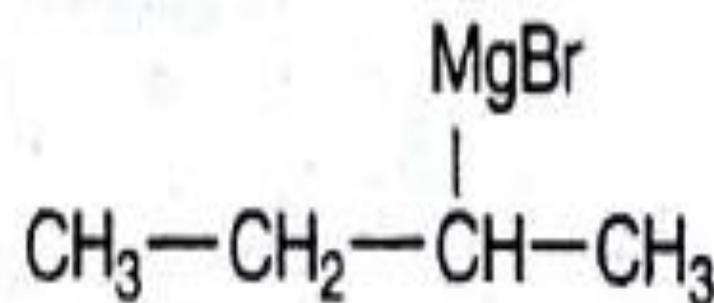


Where R = alkyl, alkenyl, alkynyl or aryl group

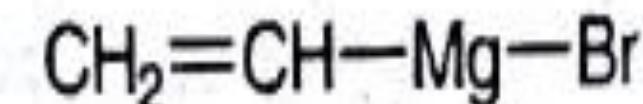
X = Cl, Br or I. **Organomagnesium fluorides are not known**



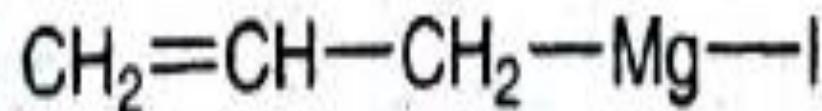
Ethylmagnesium bromide



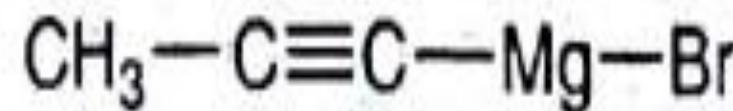
2-Butylmagnesium bromide



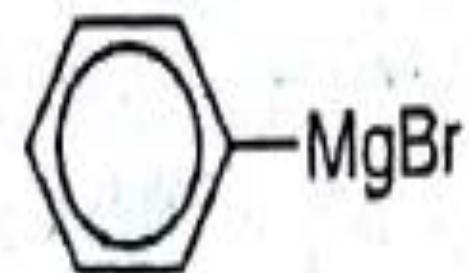
Vinylmagnesium bromide



Allylmagnesium iodide



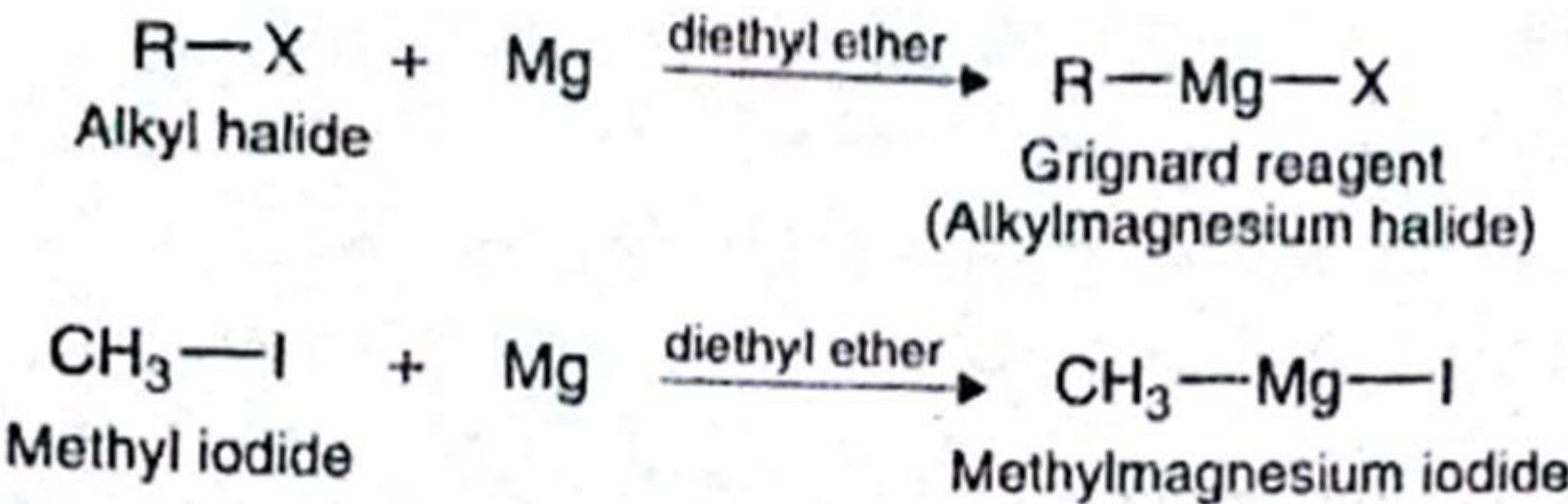
Propynylmagnesium bromide



Phenylmagnesium bromide

Preparation

These are prepared by the action of alkyl halides on magnesium metal in the presence of dry ether (anhydrous diethyl ether).

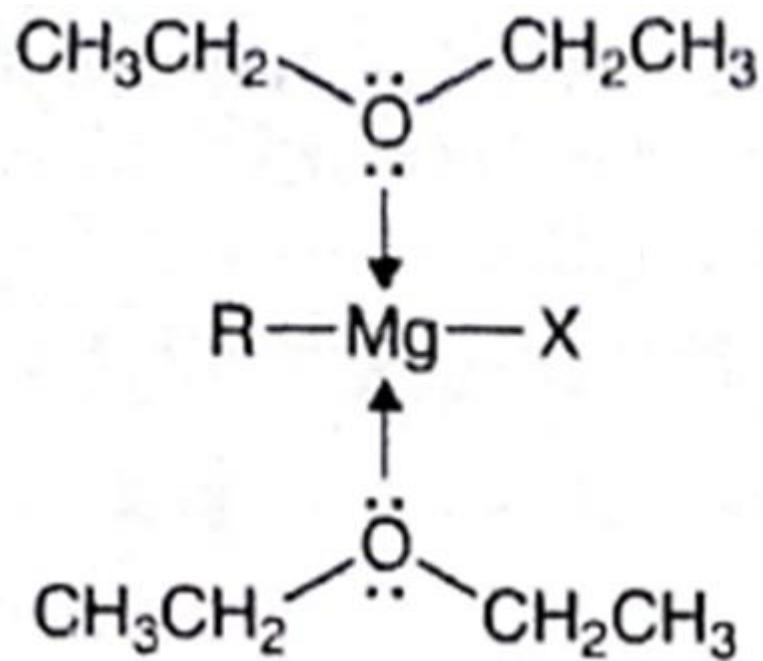


The order of ease of formation of Grignard reagent is **RI > RBr > RCl**.

In the preparation of Grignard reagents care must be taken that all the apparatus and reactants are absolutely dry. The moisture or any other impurities present will react with the Grignard reagent produced. Thus even traces of moisture or impurities prevents the formation of Grignard reagent.

Role of Ether

Grignard reagents are usually prepared in diethyl ether ($\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$). The two ether oxygen atoms stabilize the reagent by making complex with reagent.



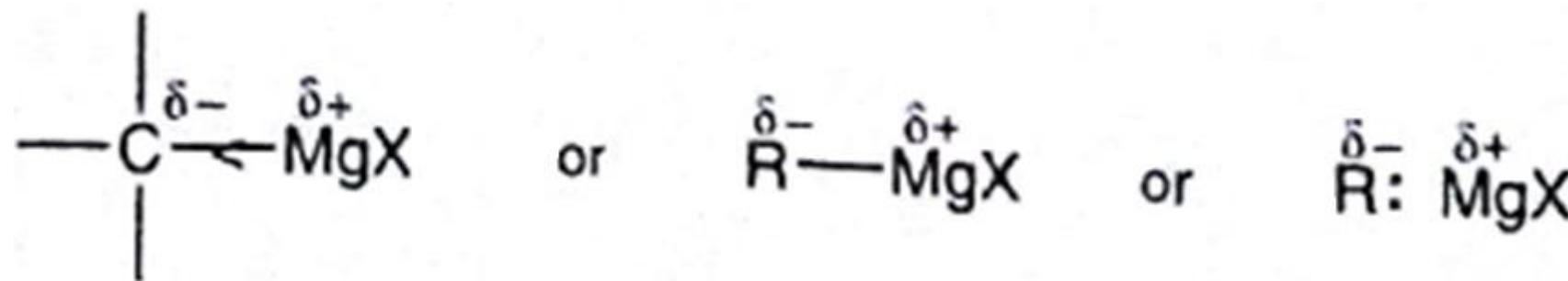
Properties

Physical Properties

- Non-volatile, colorless solid
- They are seldom isolated in free state because of its explosive nature. Therefore, for synthetic purposes the Grignard reagent are always prepared and used in ether solution

Chemical Properties

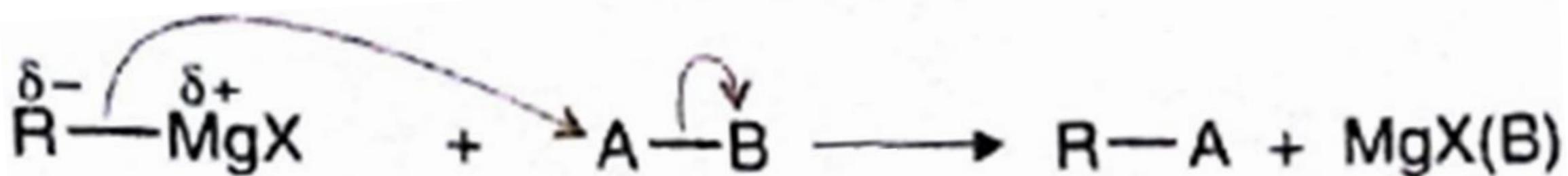
The C-Mg bond in Grignard reagent is covalent but highly polar. The carbon atom is more electronegative than magnesium. The electrons are drawn towards carbon atom as a result of which carbon atom has partial negative charge and the magnesium has positive charge.



The alkyl groups in Grignard reagents being electron rich can act as carbanions or nucleophiles. They would attack polarized molecules at points of low electron density. Thus the characteristic reactions of Grignard reagent are **nucleophilic substitution and nucleophilic addition reactions**.

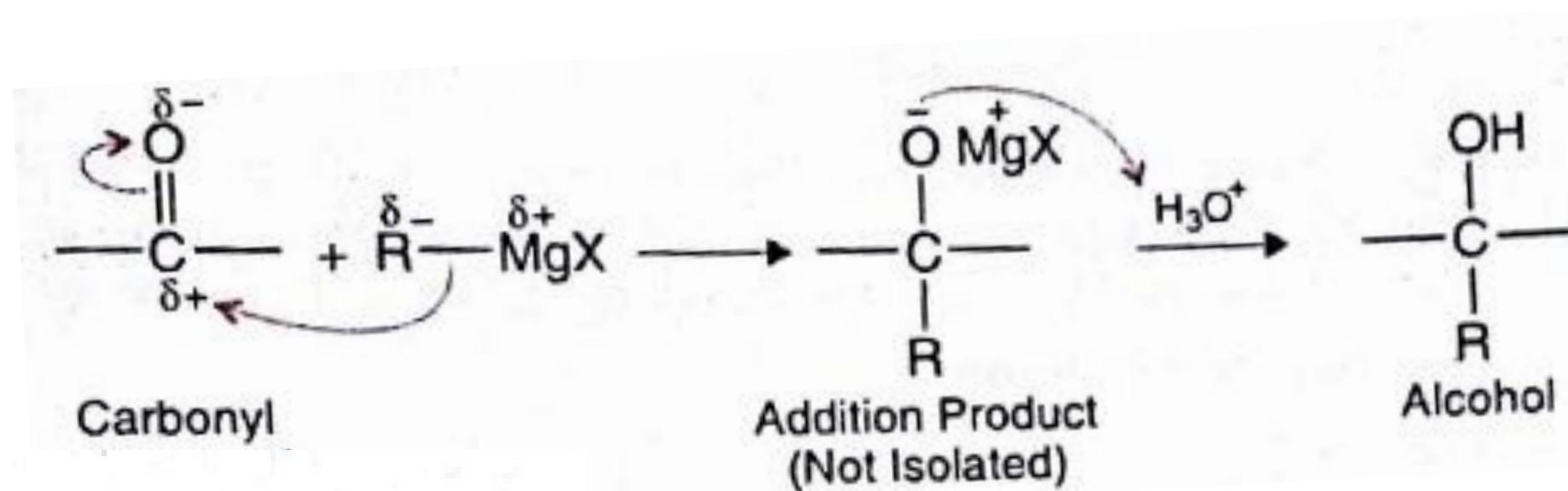
Nucleophilic Substitution

Grignard reagents undergo nucleophilic substitution by the following general mechanism.



Nucleophilic Addition

Carbonyl compounds are attacked by Grignard reagents to form addition products, which on acid-hydrolysis yields alcohols, acids, esters etc. **Addition always proceed such that the positive part of Grignard reagent (MgX) combines with the oxygen atom of the carbonyl group. The negative part (R) of Grignard reagent goes to the carbon atom of the carbonyl group.**

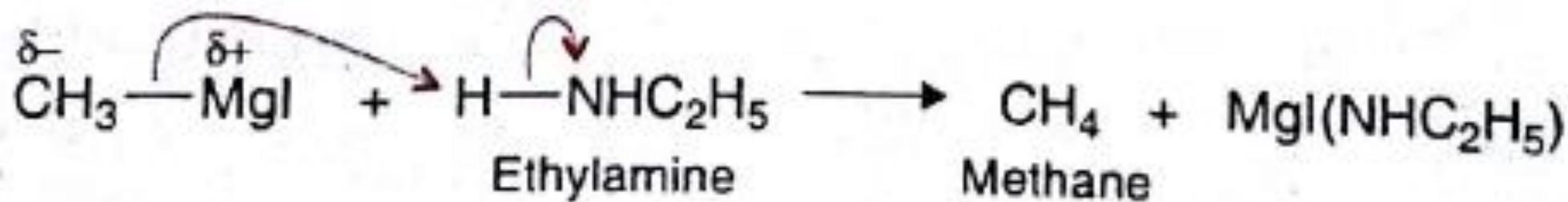
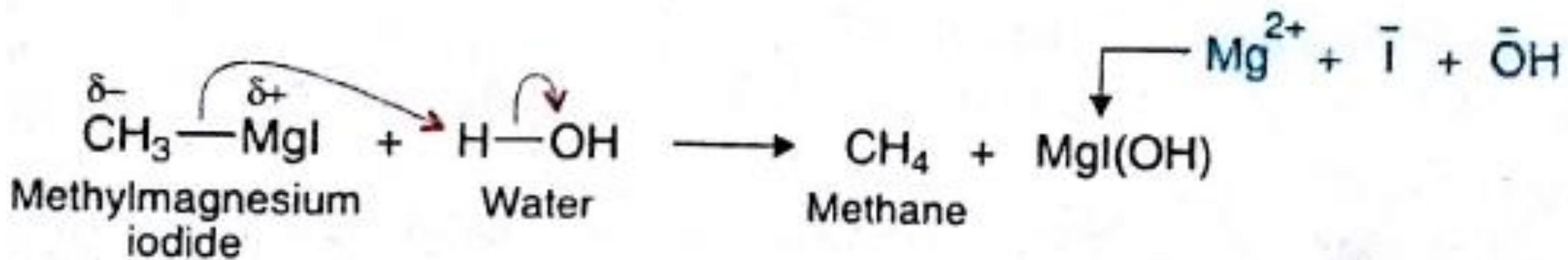


Grignard Reactions

Grignard reagents react with a variety of compounds yielding almost the entire range of organic substances. The following reactions illustrates the synthetic importance of Grignard reagent.

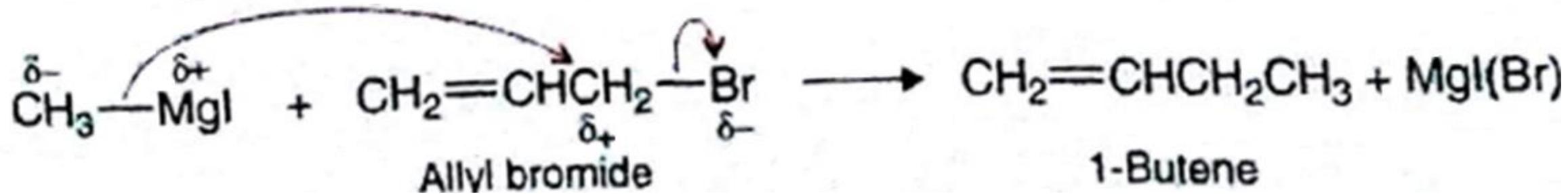
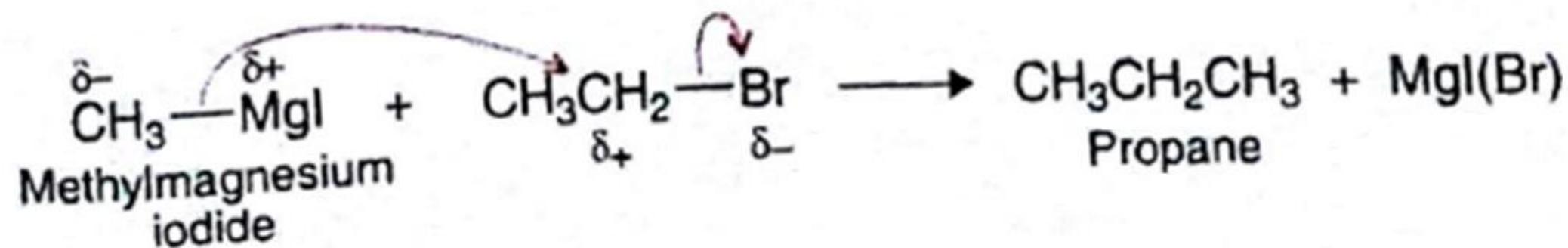
1. Reaction with compounds containing active Hydrogens

Active hydrogens are those that are more acidic than alkanes. Thus compounds like water, alcohols, and amines which contain active hydrogens react with Grignard reagents to form alkanes.



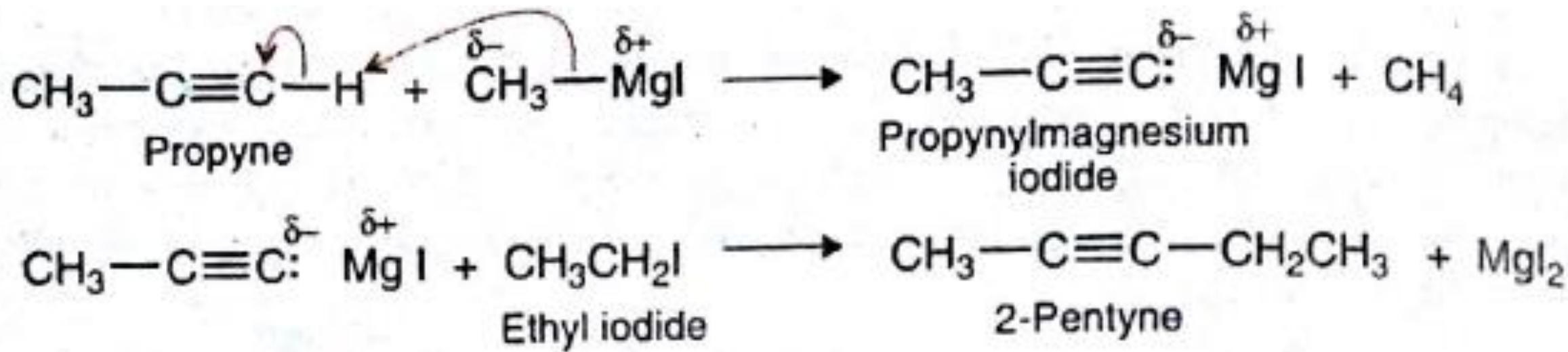
2. Reaction with alkyl halides

Grignard reagent react with alkyl halides to form higher alkanes or alkenes



3. Reaction with alkynes

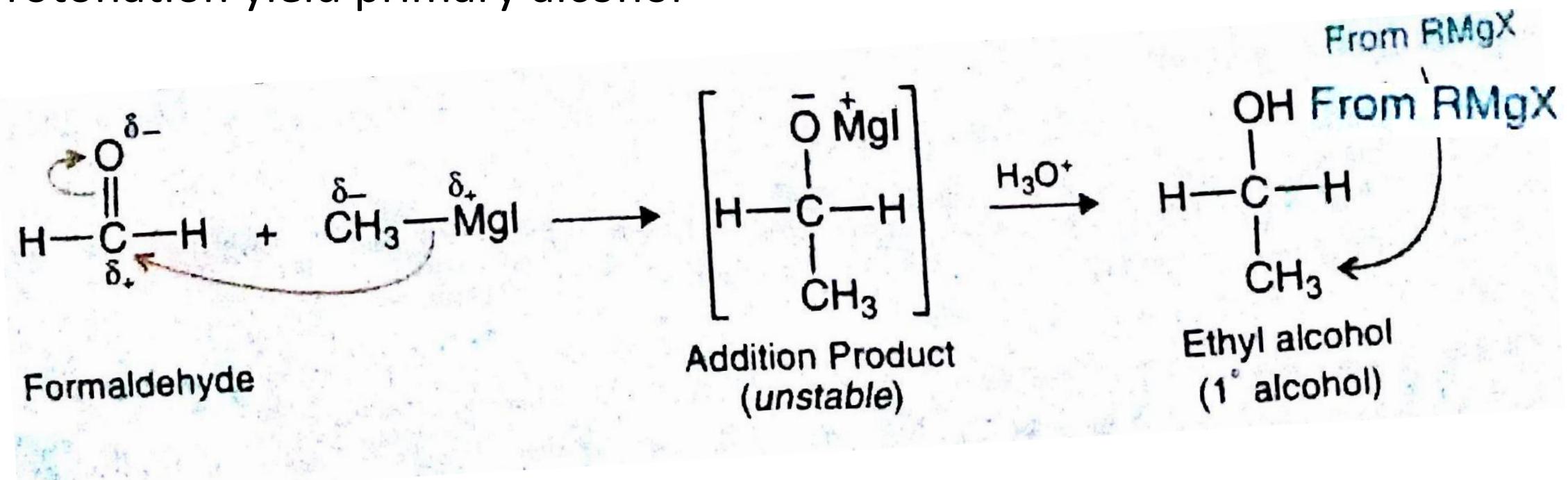
Terminal alkynes (1-alkynes) react with Grignard reagents to form alkynylmagnesium halides which on subsequent treatment with alkyl halides form higher alkynes.



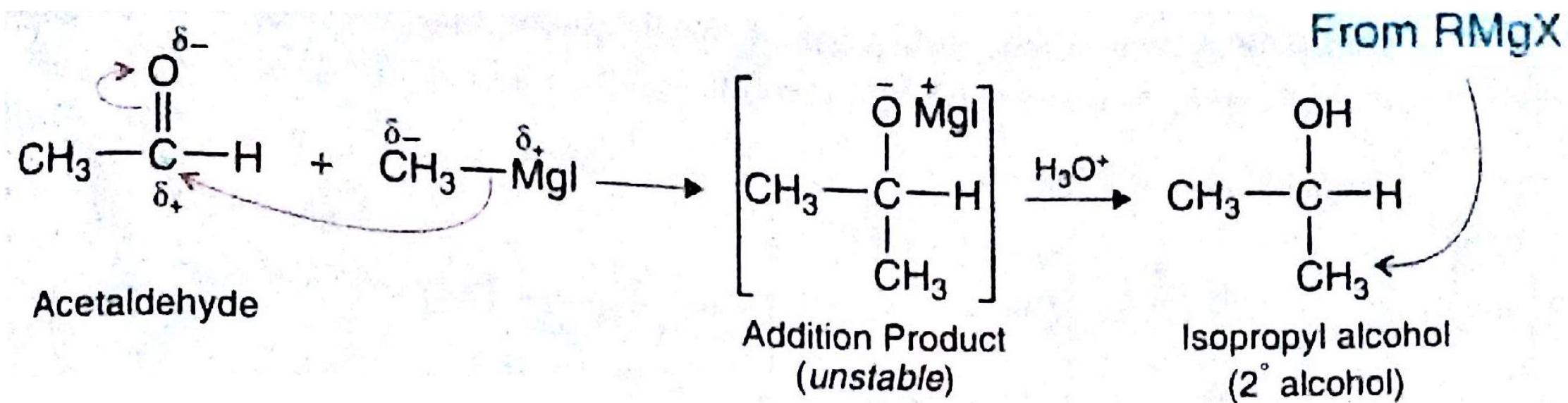
4. Reaction with Aldehydes

When GR react with aldehydes it results in the formation of Primary or secondary alcohols.

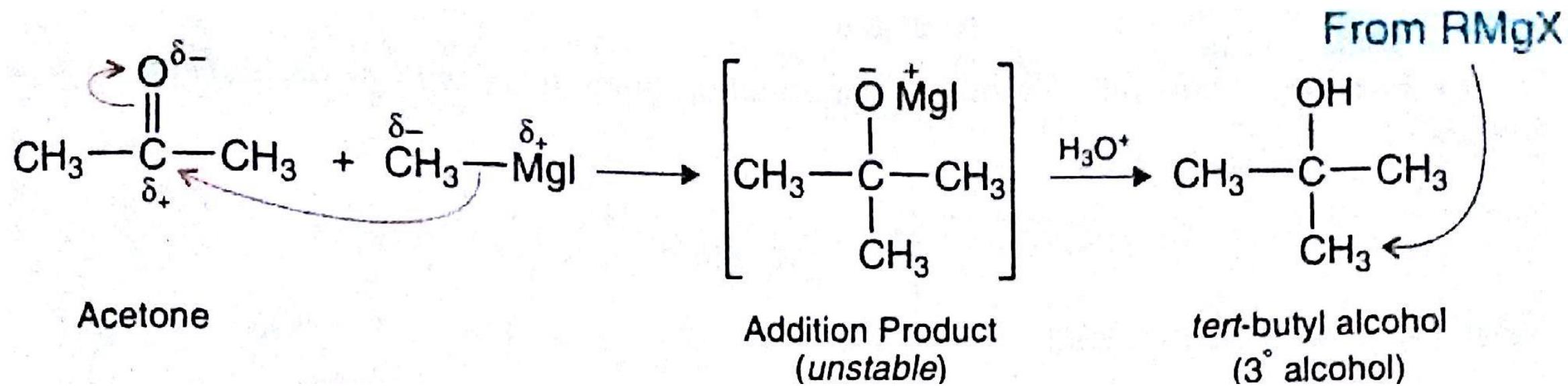
Formaldehyde reacts with GR to give addition products which on protonation yield primary alcohol



Other aldehydes react with GR to give addition products which on protonation yield secondary alcohol



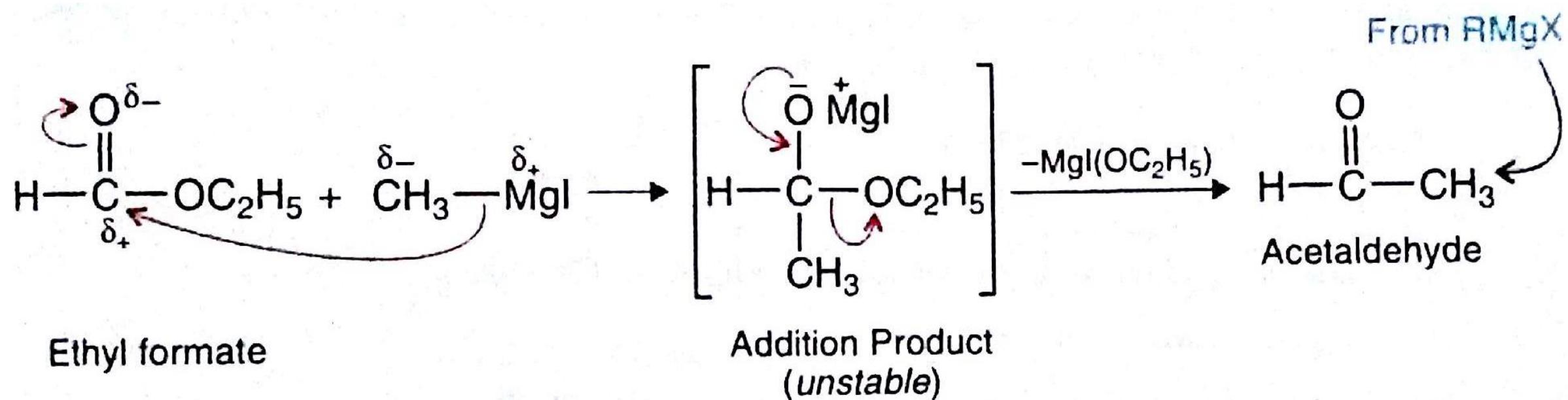
5. Reaction with Ketones



7. Reaction with Esters

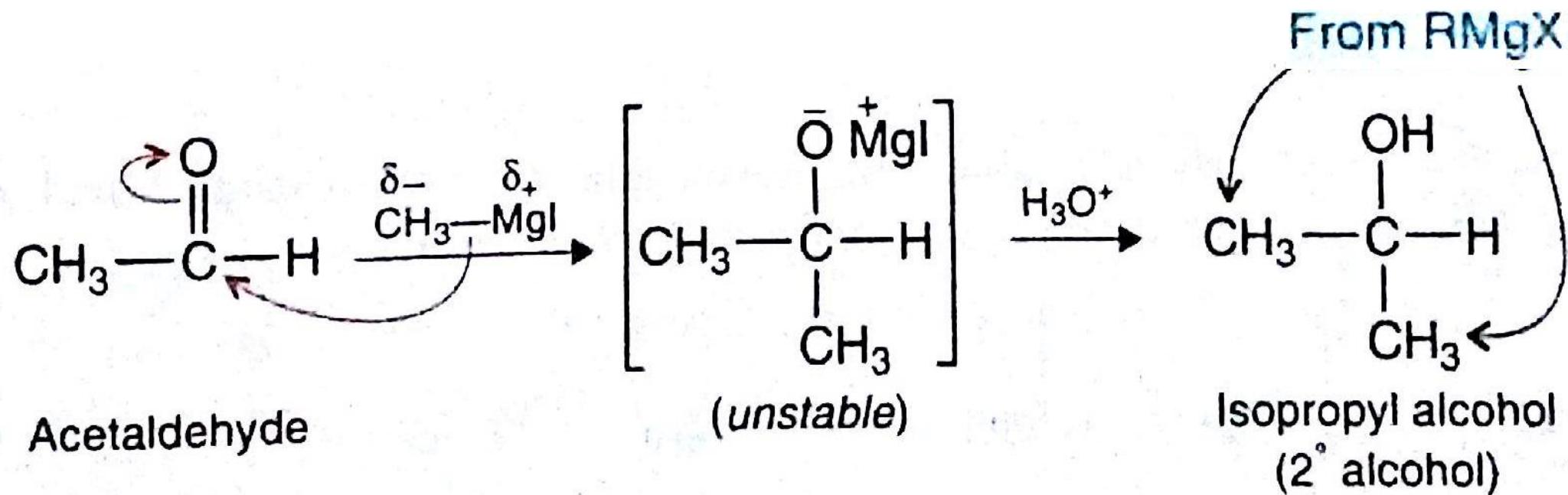
GRs react with formic esters to form secondary alcohol, while other esters yield tertiary alcohols. **Two steps process**

Step-1: (a) Ethyl formate reacts with GR to first form aldehydes

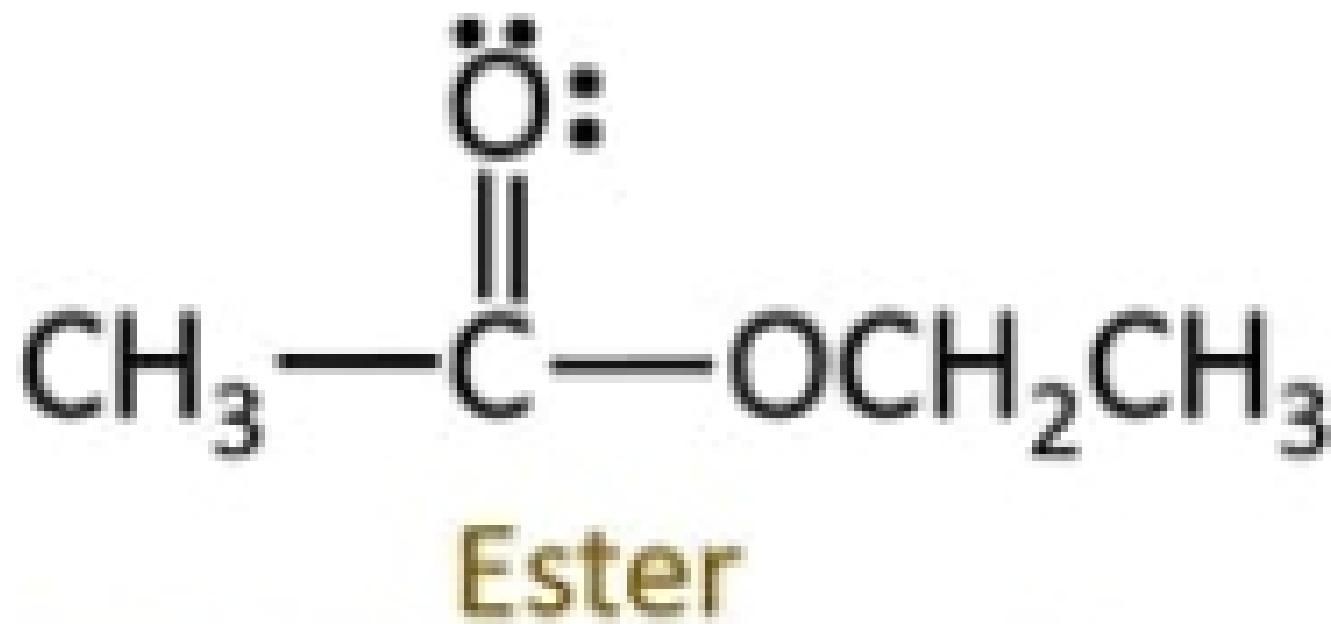


Step-2:

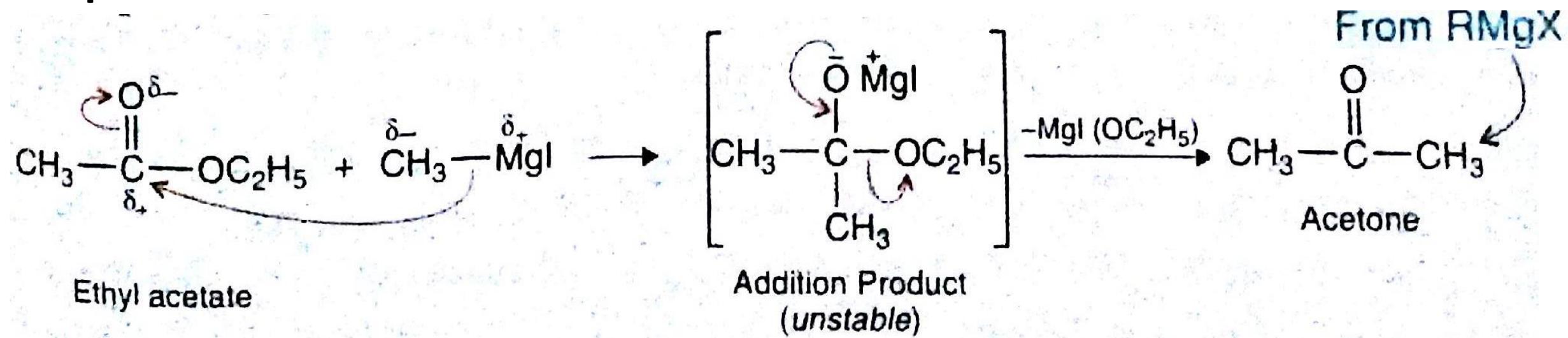
The aldehyde then reacts Grignard reagent to give an addition product which on protonation forms a secondary alcohol



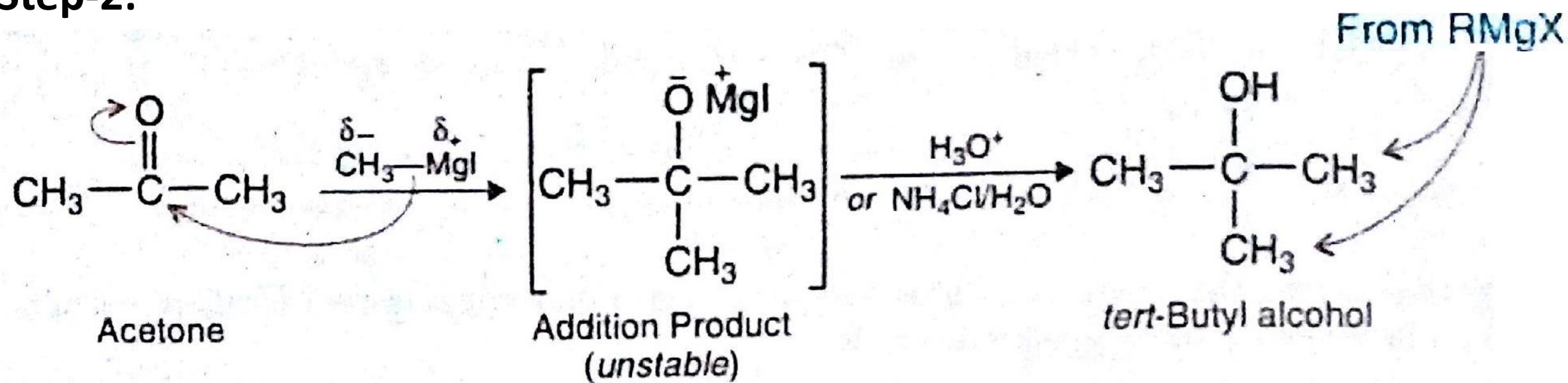
(b) Reaction with ethyl acetate



Step-1:

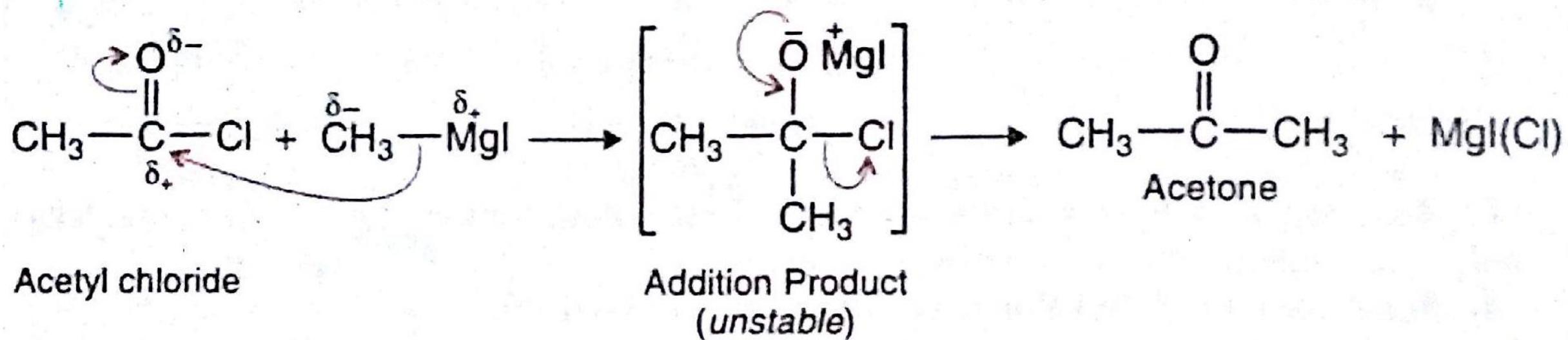


Step-2:



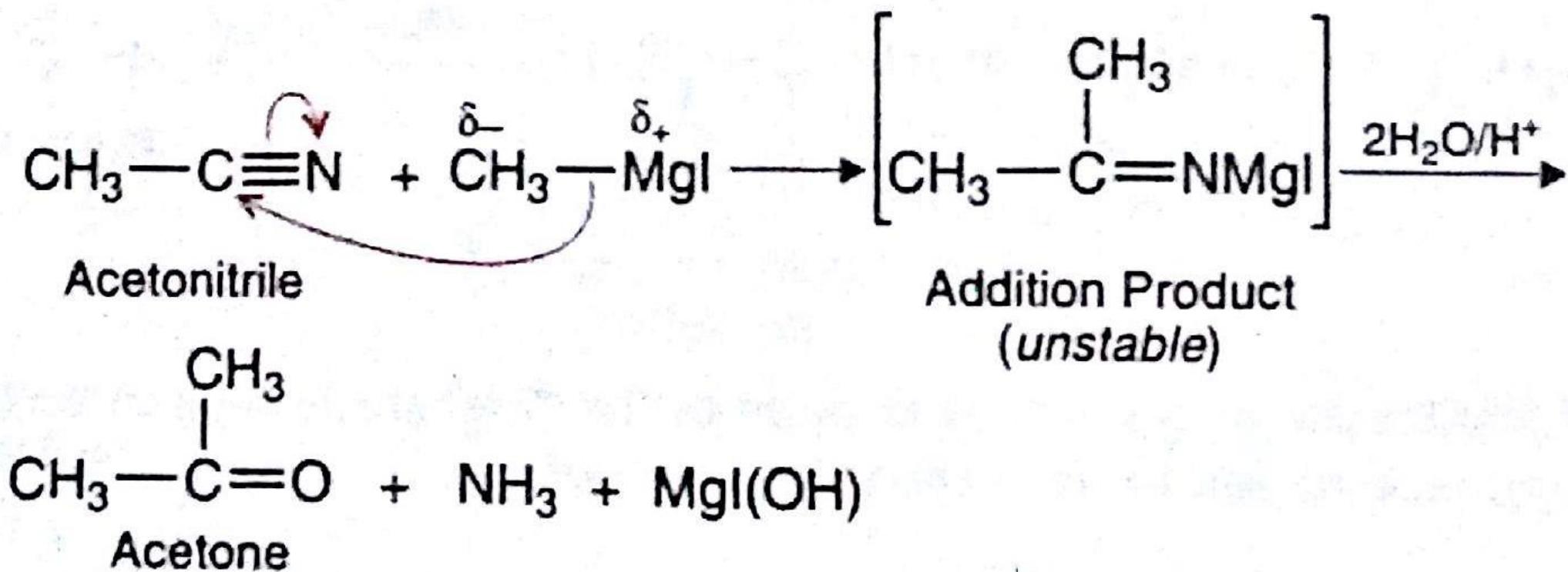
7. Reaction with Acid Chlorides

Grignard reagent reacts with acid chlorides to form ketones.



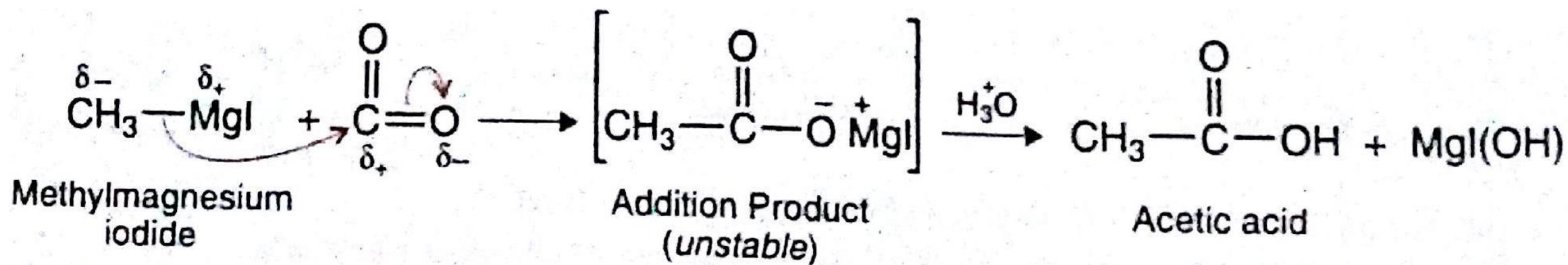
8. Reaction with Cyanides

Grignard reagent reacts with cyanides to give addition products which on hydrolysis with dilute HCl yield ketones.



9. Reaction with Carbon Dioxide

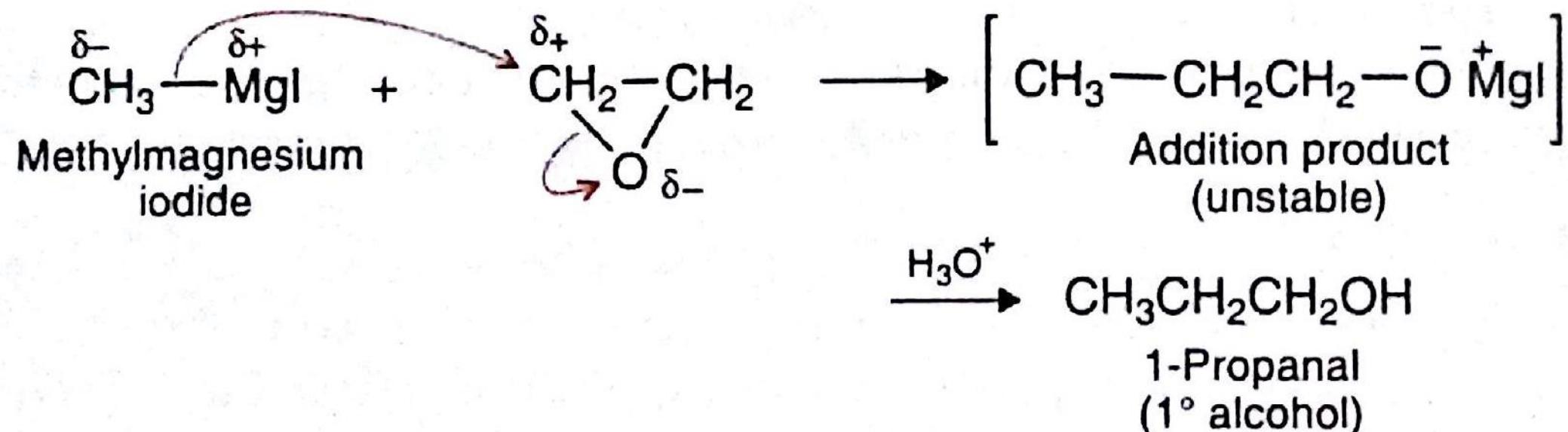
Grignard reagent reacts with cyanides to give addition products which on protonation yield carboxylic acids.



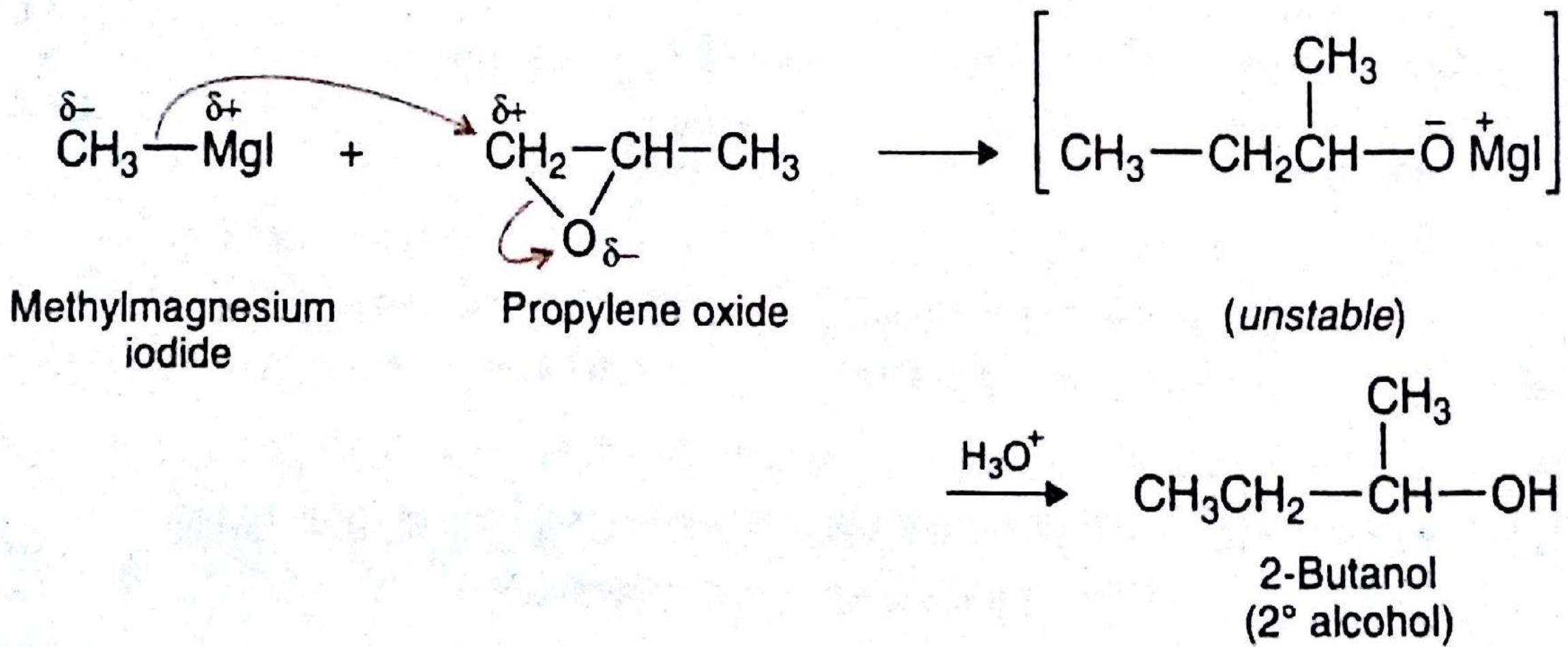
10. Reaction with Epoxide (Oxiranes)

Grignard reagents are powerful nucleophiles and can react with partial positive carbons of epoxides. The reaction results in ring opening and formation of an alcohol.

Formation of 1-propanol

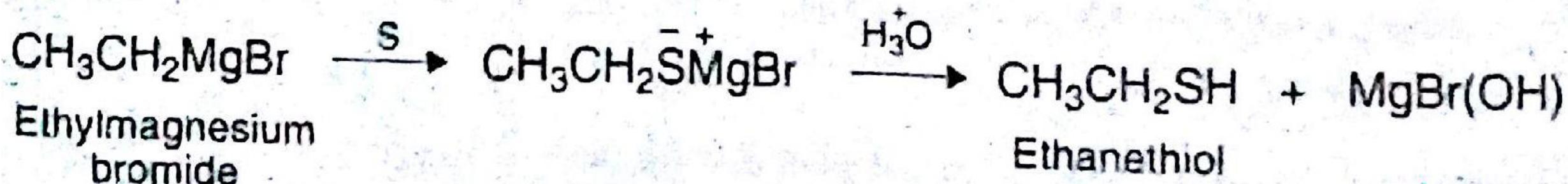


Formation of 2-Butanol

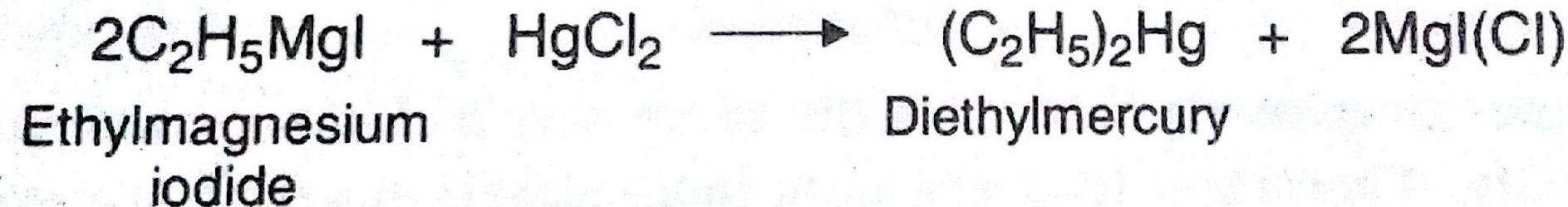
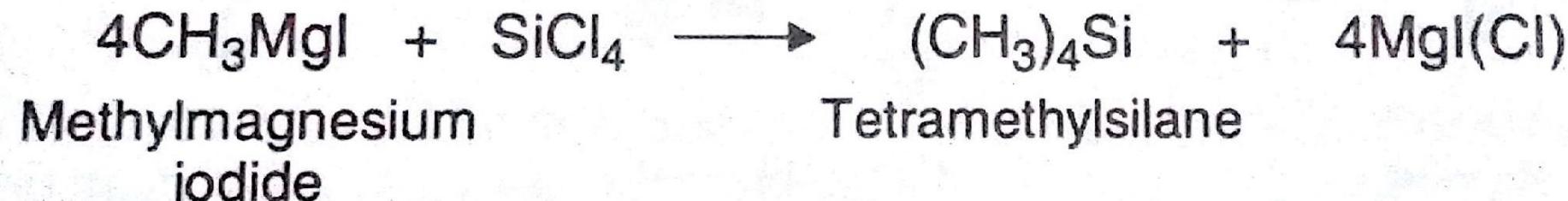
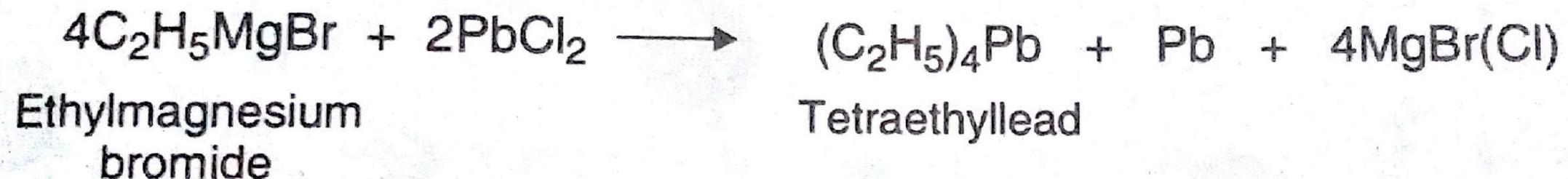


11. Reaction with Sulfur

Grignard reagent reacts with sulfur to give a product which on protonation gives the corresponding thioalcohol.



12. Reaction with inorganic halides to form other organometallic compounds



Friedel-Crafts Reaction

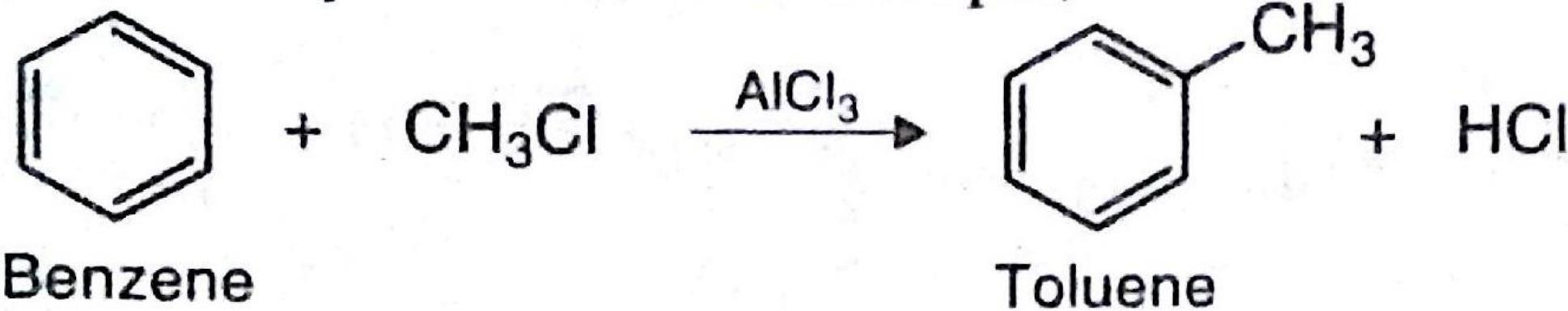
1. Friedel-Crafts Alkylation

One of the most useful electrophilic aromatic substitution reactions is alkylation—the introduction of an alkyl group onto the benzene ring. Called the **Friedel–Crafts alkylation reaction**.

The reaction is carried out by treating the aromatic compound with an alkyl chloride (RCl), in the presence of $AlCl_3$ to generate a carbocation electrophile, R^+ . $AlCl_3$ catalyzes the reaction by helping the alkyl halide to dissociate in much the same way that $FeBr_3$ catalyzes aromatic brominations by helping Br_2 dissociate. Loss of H^+ then completes the reaction

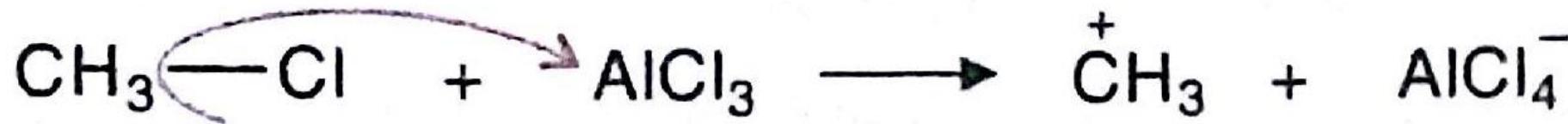
Chemical Reaction

Benzene reacts with alkyl halide in the presence of aluminium chloride to form alkylbenzene

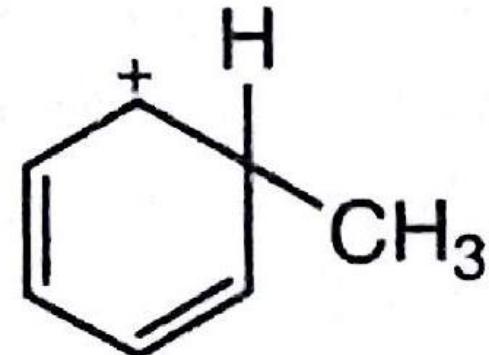
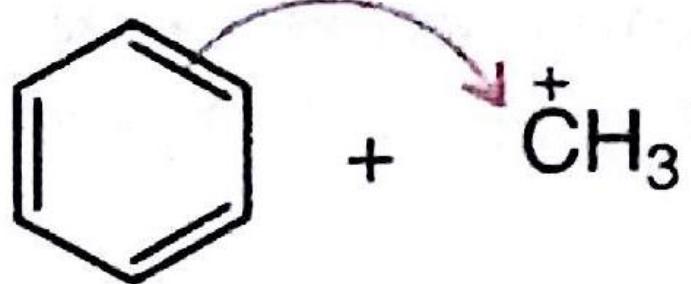


Mechanism

Step-1: Formation of electrophile

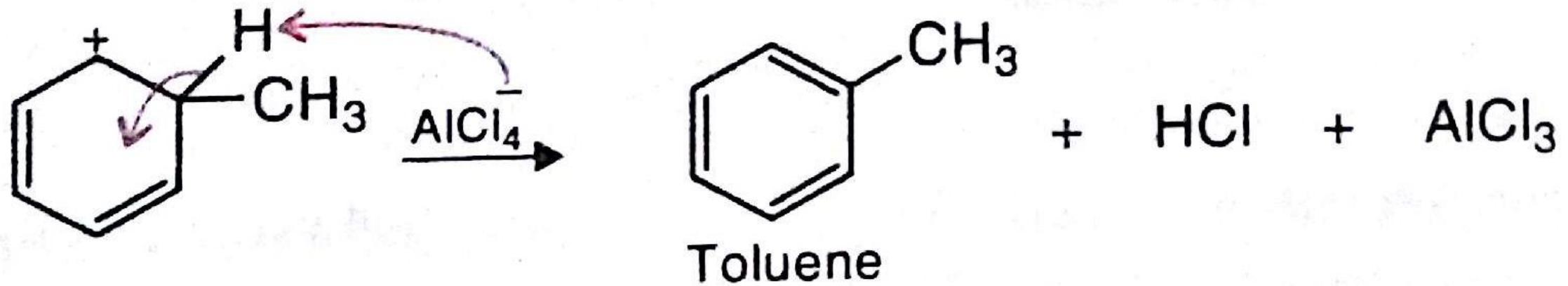


Step-2: The electrophile attacks the benzene ring to give a carbocation



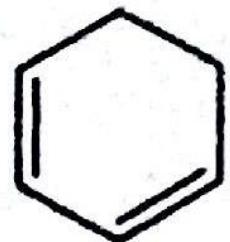
Carbocation
(Plus two more
resonance structures)

Step-3: Loss of proton gives alkyl benzene



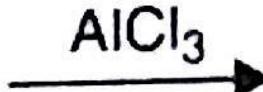
Write the mechanism

Example-1

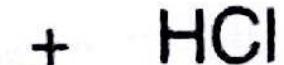


Benzene

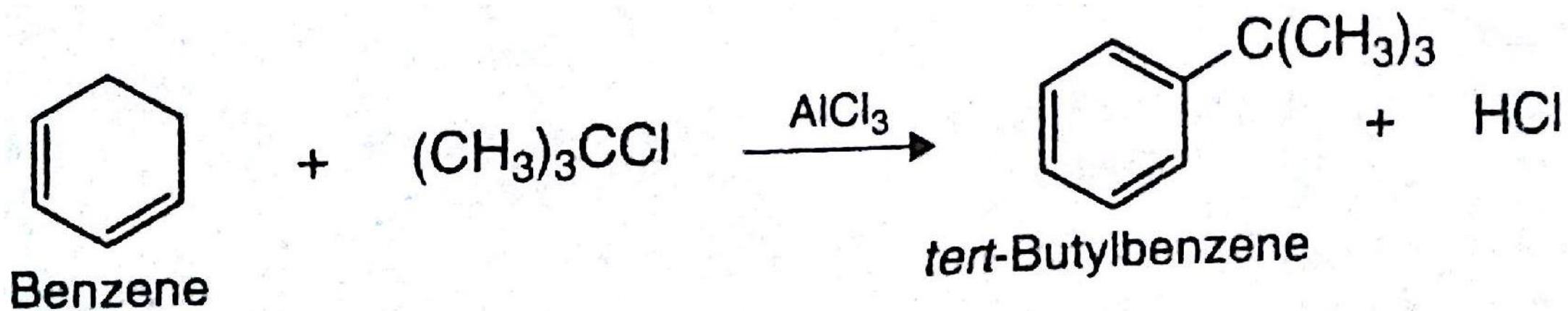
+



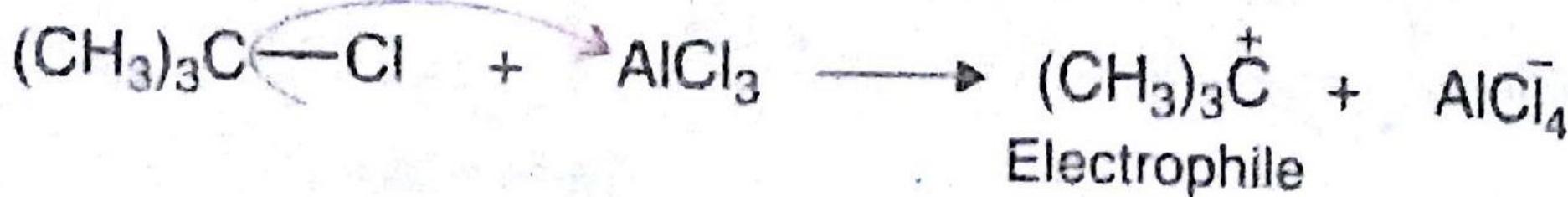
Ethylbenzene



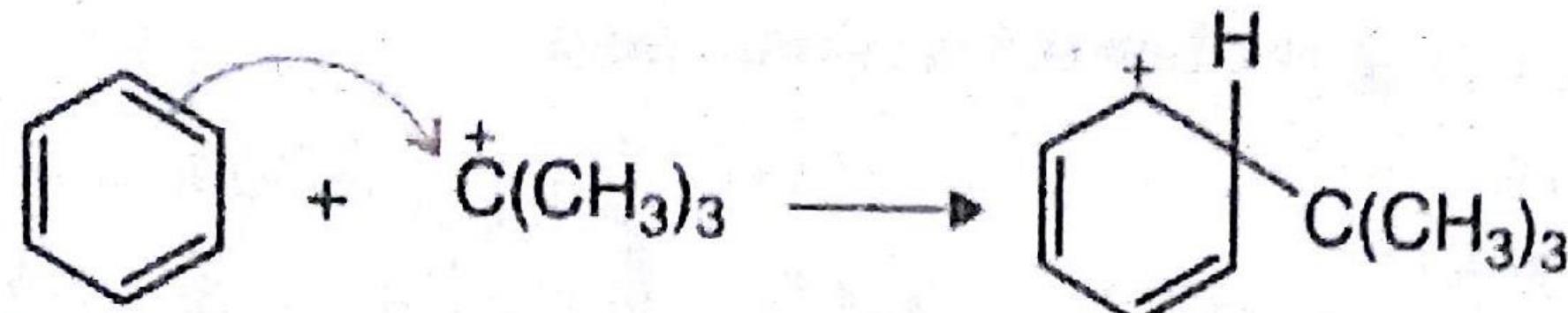
Example-2



Mechanism: Step-1



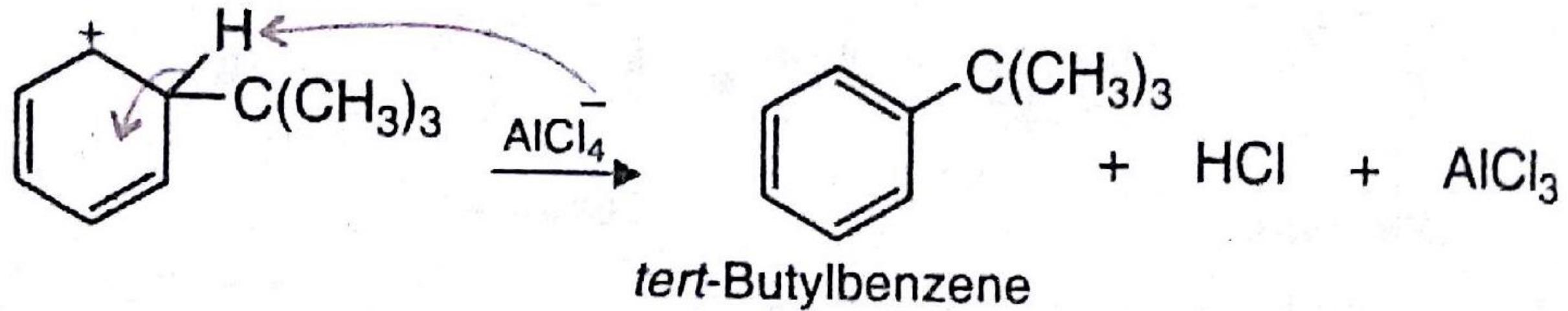
Step-2



Benzene

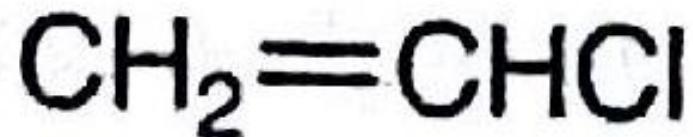
Carbocation
(Plus two more
resonance structures)

Step-3

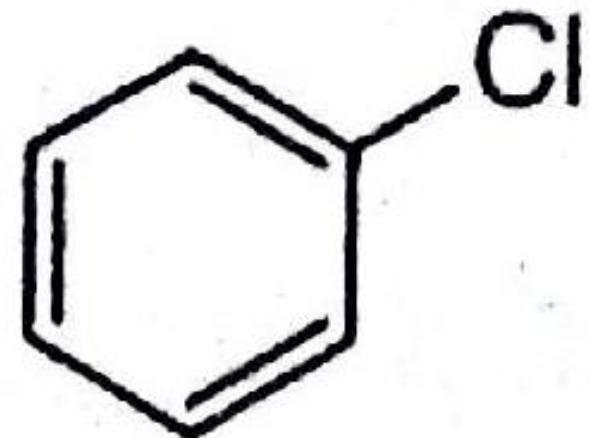


Other Facts about Friedel-Crafts Alkylation Reactions

Vinyl halides and aryl halides do not react in Friedel-Crafts alkylation.
Because the carbocations derived from vinyl halides and aryl halides are highly unstable and do not readily form.



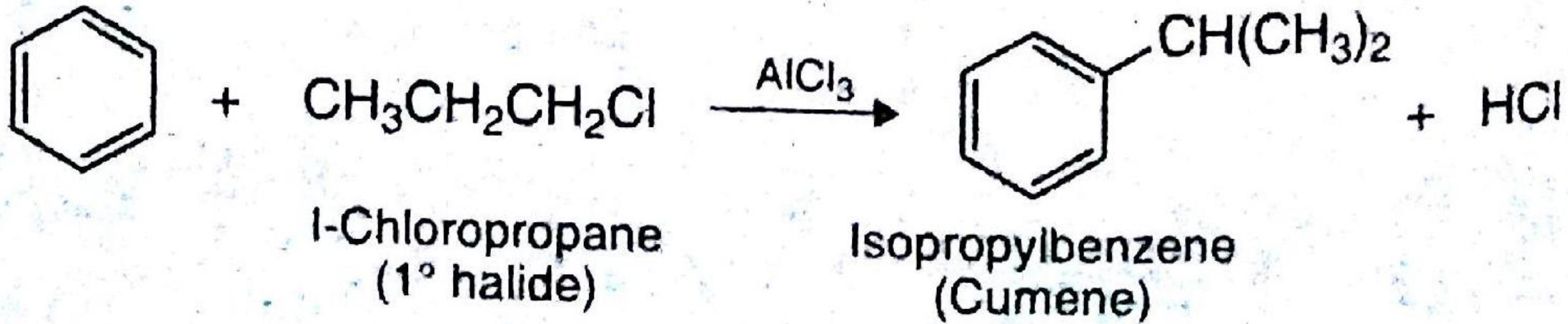
Vinyl halide



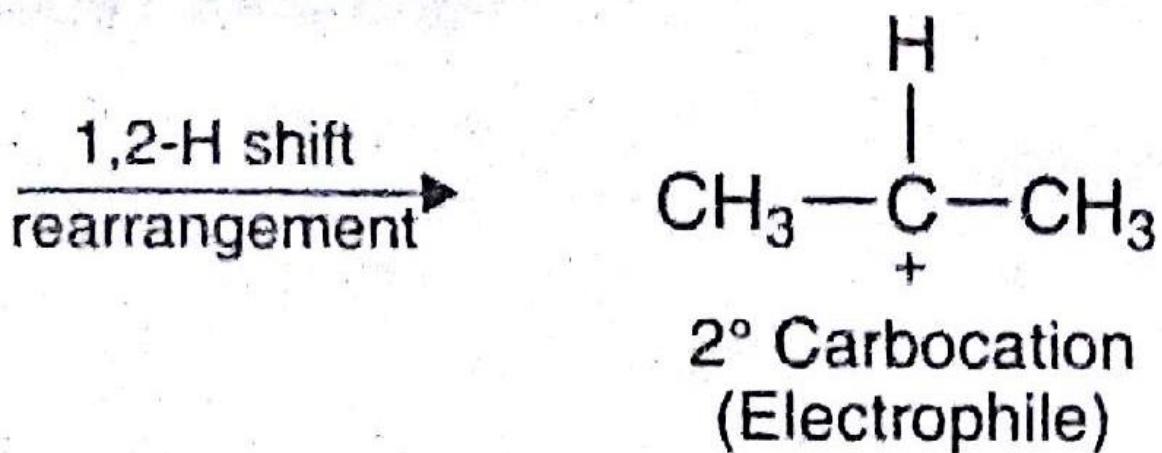
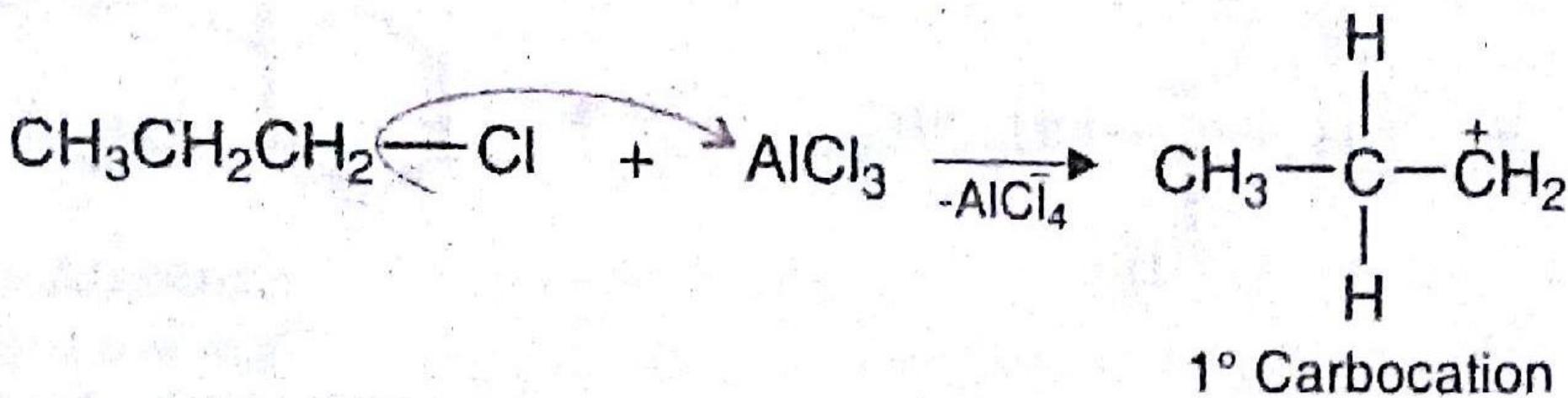
Aryl halide

Rearrangement can occur

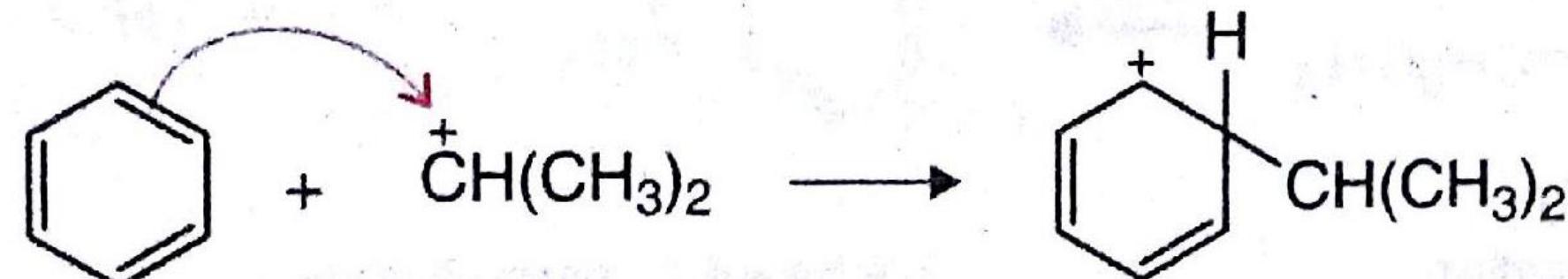
When primary and secondary alkyl halides are used as a starting material rearrangement can occur



Mechanism: Step-1



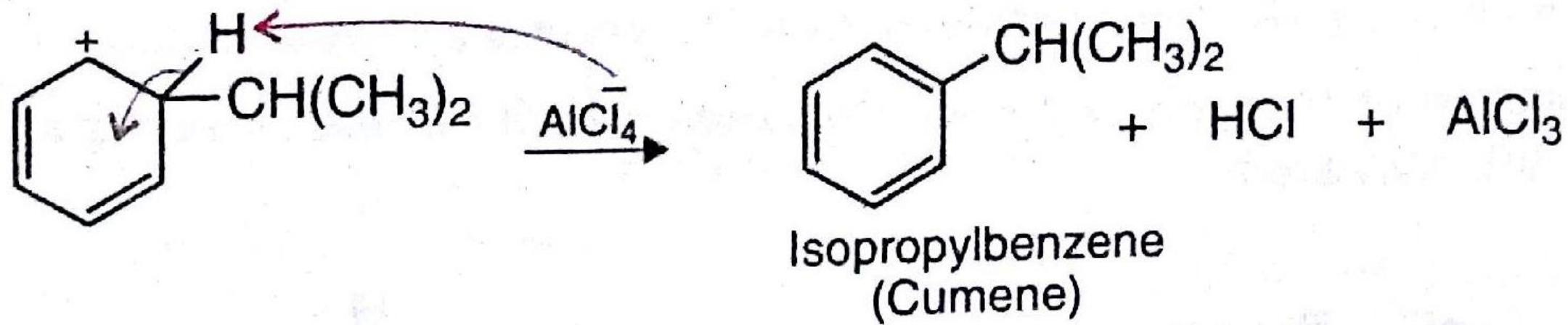
Step-2



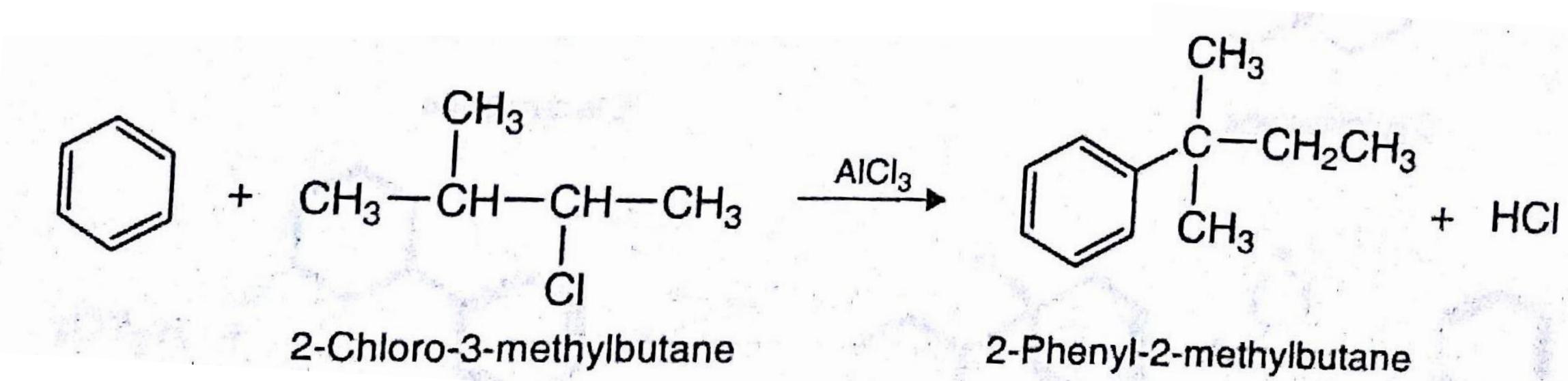
Benzene

Carbocation
(Plus two more
resonance structures)

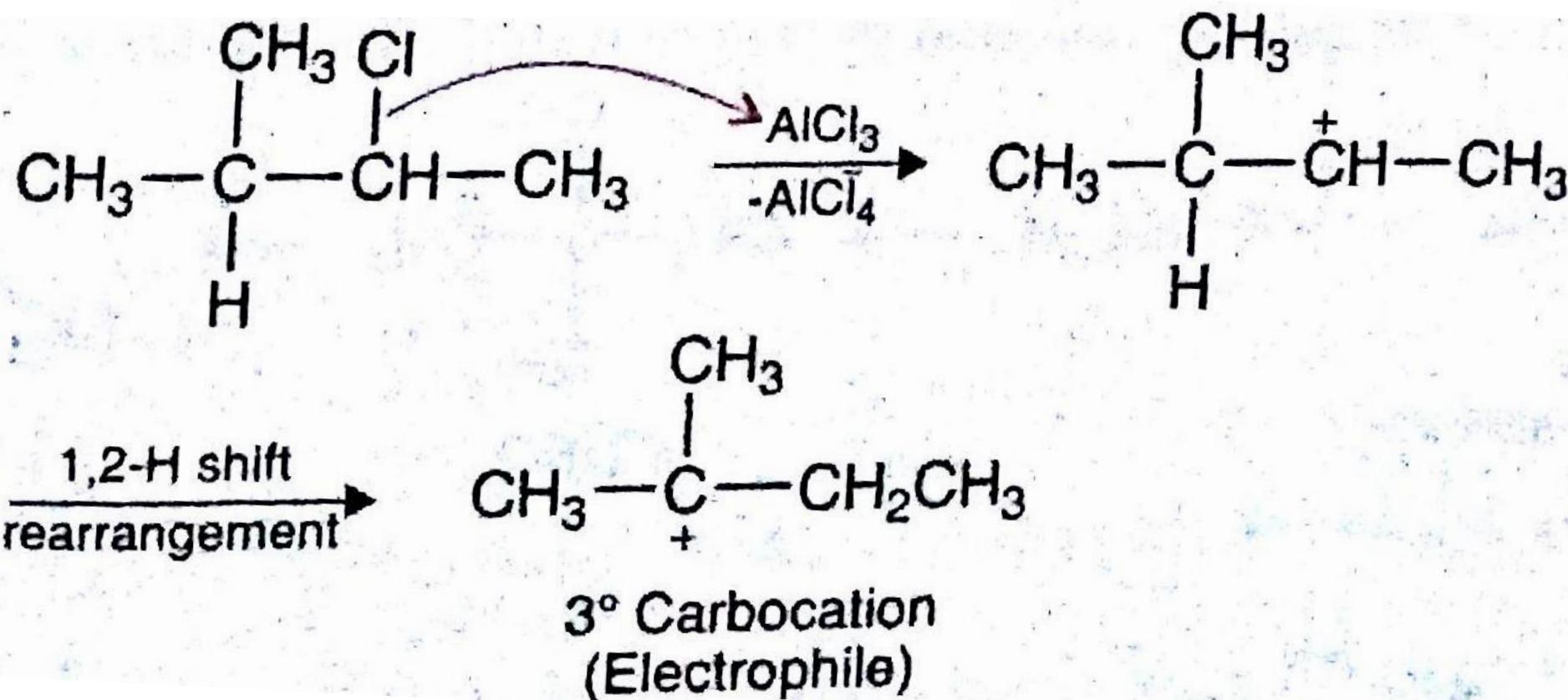
Step-3



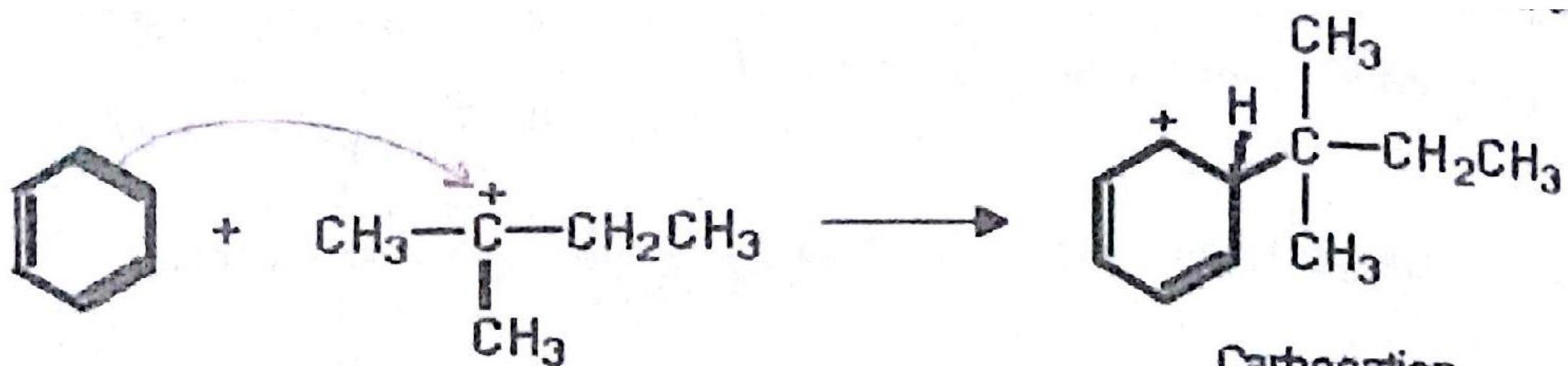
Example-2: Mechanism???



Step-1:

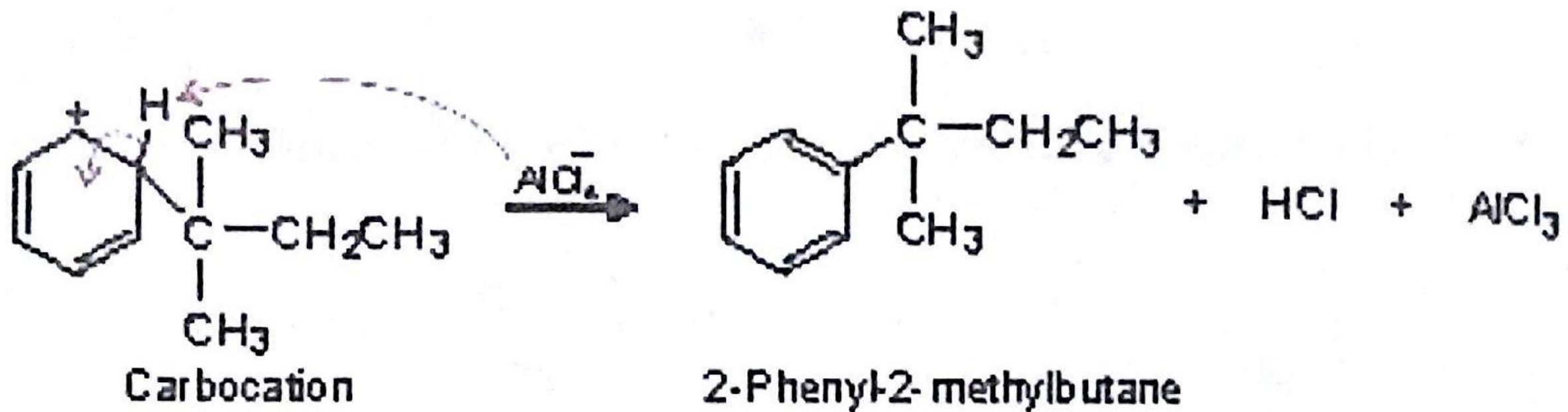


Step-2:



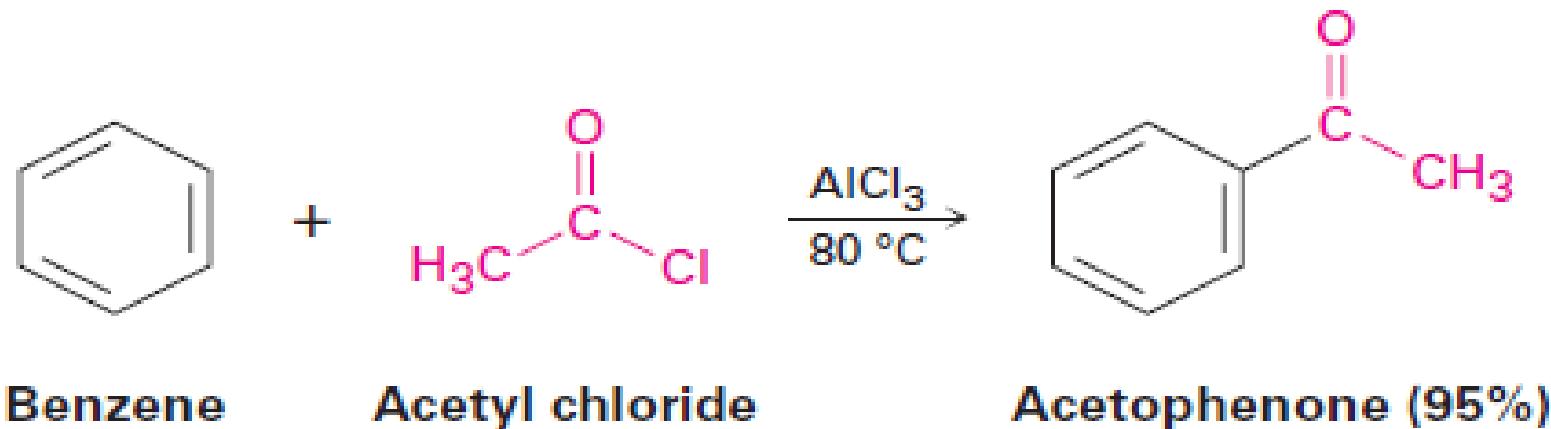
Carbocation
(Plus two more
resonance structures)

Step-3:

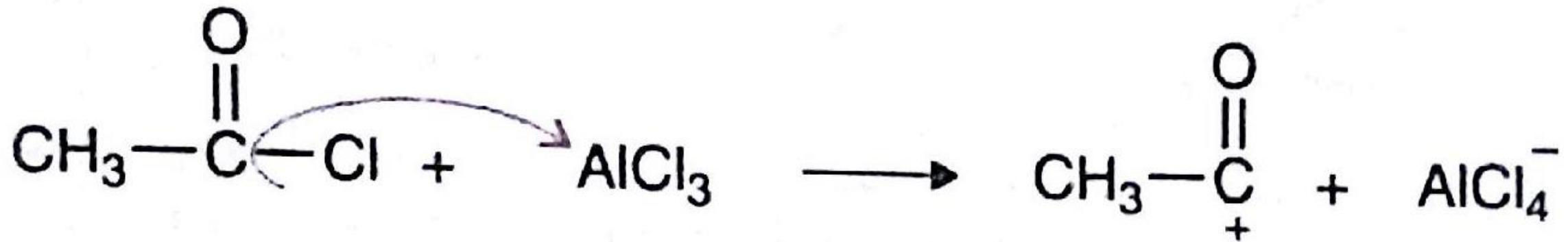


Friedel–Crafts Acylation

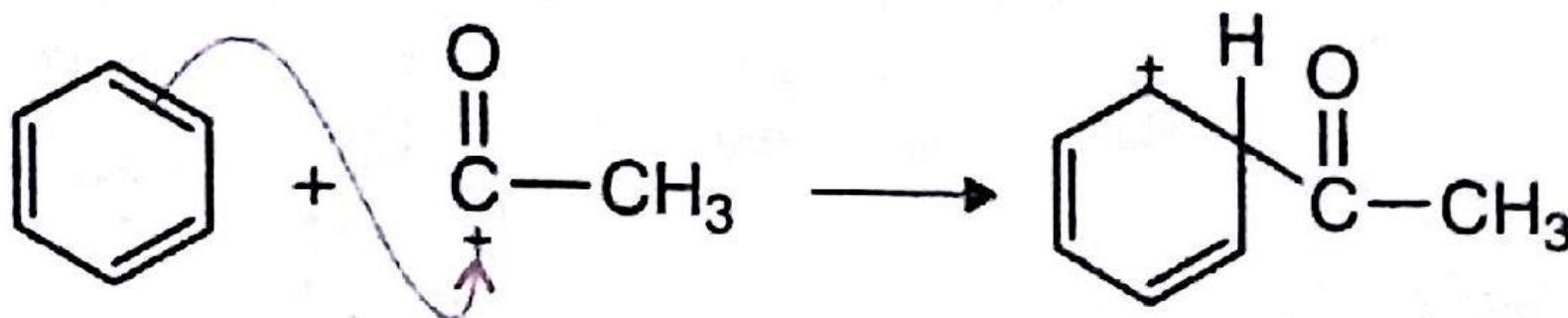
- When an aromatic compound is treated with a carboxylic acid chloride (RCOCl) in the presence of AlCl_3 , an acyl (a-sil) group ($\text{R}-\text{C}=\text{O}$) is introduced onto the ring. For example, reaction of benzene with acetyl chloride yields the ketone acetophenone.



Step-1: Formation of electrophile

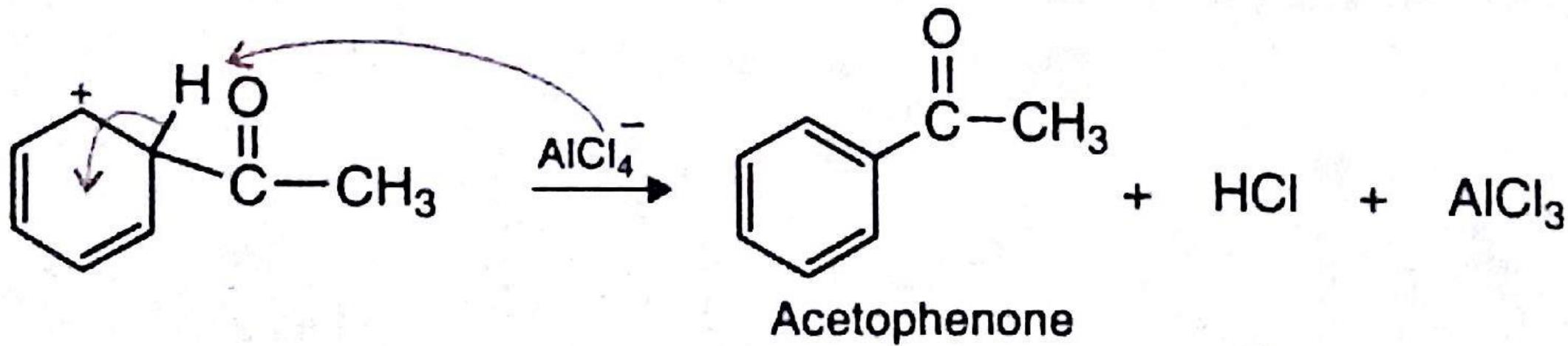


Step-2: Attack of Electrophile



Carbocation
(Plus two more
resonance structure)

Step-3: Loss of proton



Limitations of Friedel Crafts Reaction

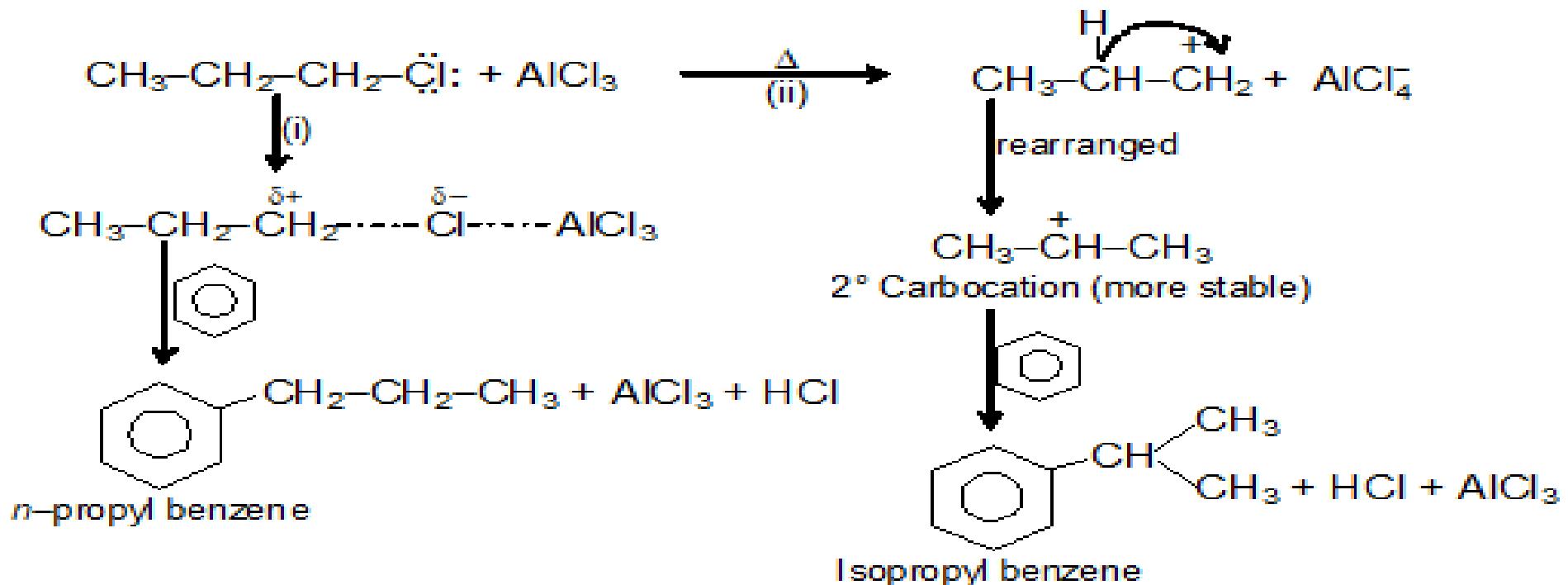
1. Rearrangement of Carbocation:

There are possibilities of carbocation rearrangements when you are trying to add a carbon chain greater than two carbons. The rearrangements occur due to hydride shifts and methyl shifts. For example, the product of a Friedel-Crafts Alkylation will show an iso-rearrangement when adding a three carbon chain as a substituent.

This rearrangement can be minimized if we do the reaction at very low temperature.

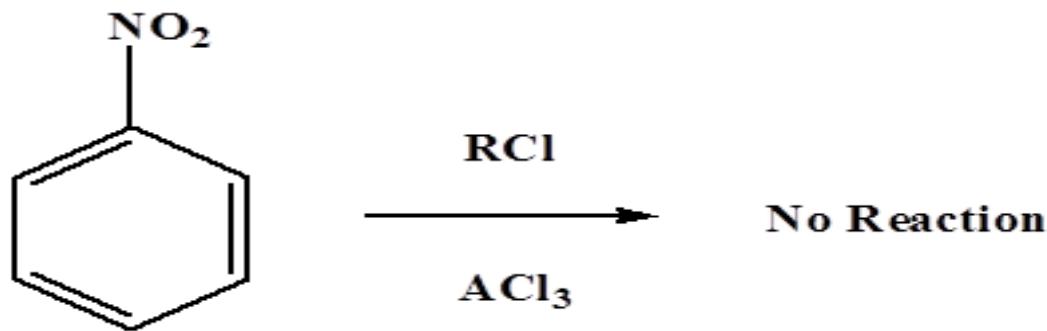


n-propylchloride gives isopropyl benzene.

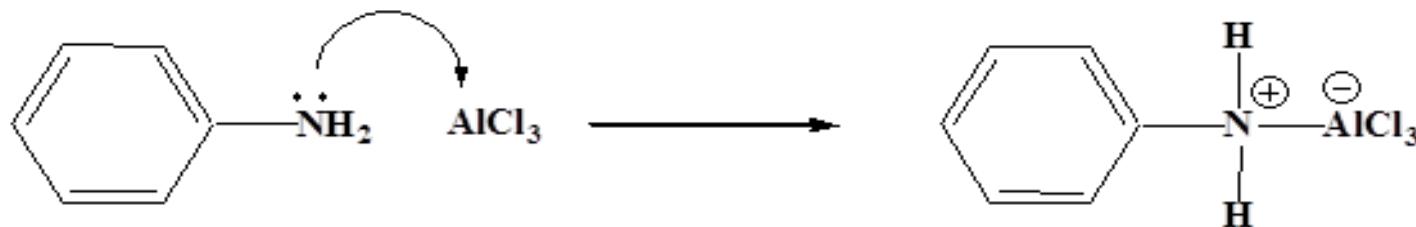


In the same way, isobutyl chloride gives t-butyl benzene.

2. Friedel - Crafts reactions do not occur when powerful electron-withdrawing groups (strong deactivators) are present on the aromatic ring.

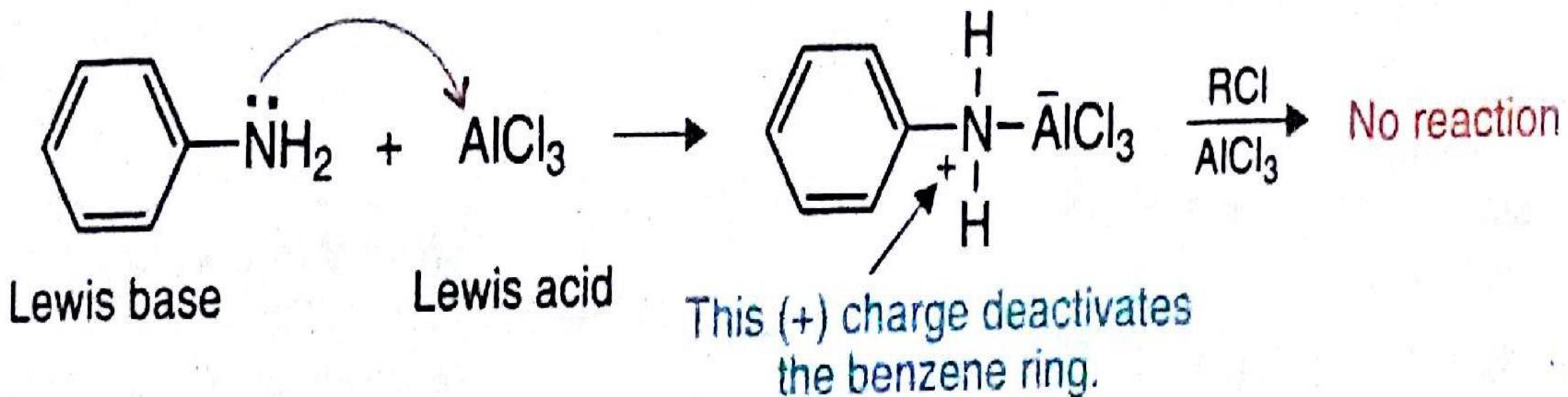


Friedel - Crafts reactions also do not occur when the ring bears strong activators such as $-\text{NH}_2$, $-\text{NHR}$, or $-\text{NR}_2$ groups. The lone pair electrons on the amines react with the Lewis acid AlCl_3 . This places a positive charge next to the benzene ring.

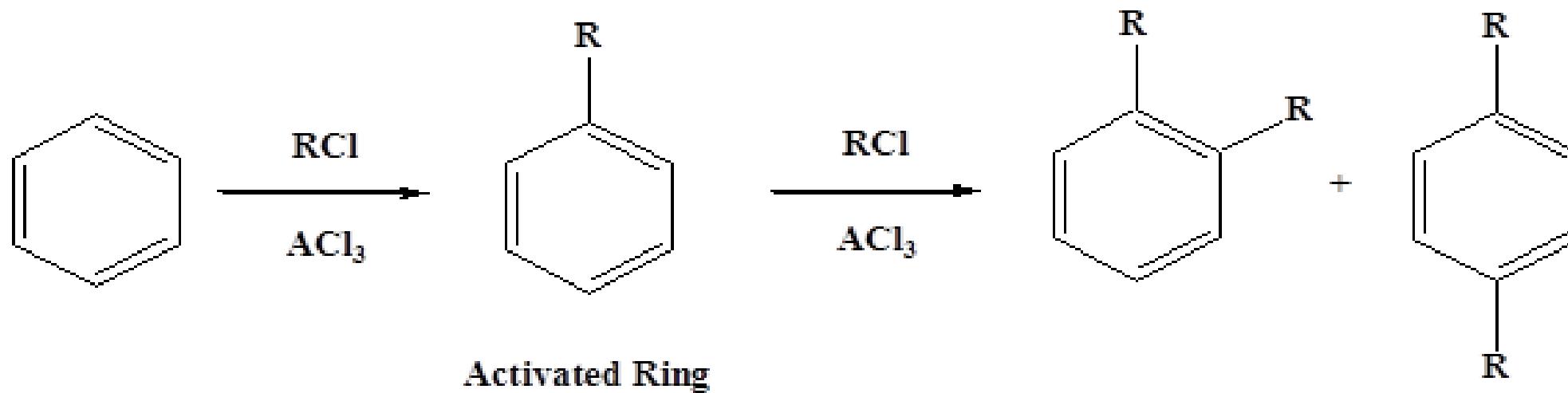


The positive charge strongly
deactivates the benzene ring

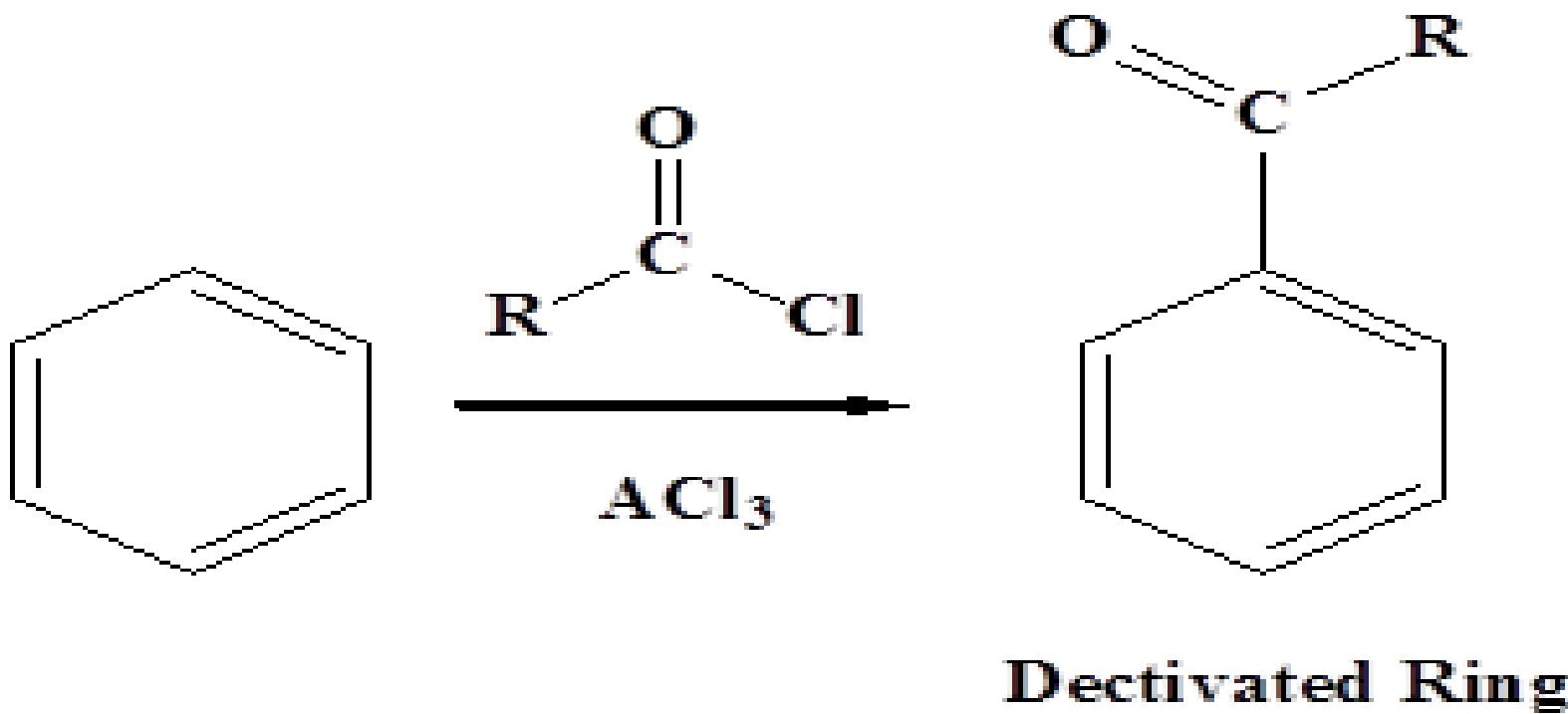
This product contains a positive charge adjacent to the benzene ring, so the ring is now strongly deactivated and therefore unreactive in Friedel-Crafts reactions.



3. Polyalkylations: Polyalkylations often occur because Alkyl groups are electron - releasing groups, and once one is introduced into the benzene ring it activates the ring toward further substitution. CH₃ group increases electron density through hyperconjugation.



Polysubstitution does not occur with Friedel-Crafts acylation,
because the acyl group ($\text{RCO}-$) by itself is an electron - withdrawing
group that deactivates the ring towards another electrophilic
substitution.



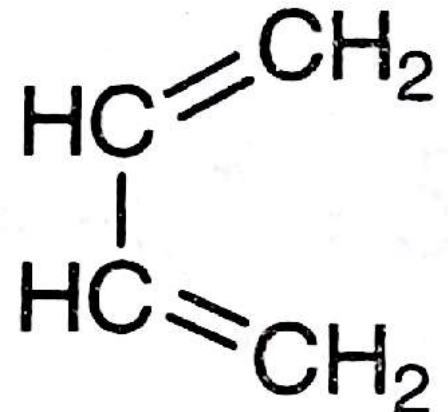
Diels-Alder Reaction

Diels-Alder Reaction

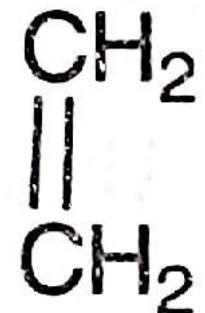
This reaction involves the treatment of a **diene** with an alkene or alkyne (**dienophile**) to give a product- (**Adduct**).

The net result is the formation of two new sigma bonds and one new pi-bond by the expense of three pi-bonds.

The simplest example of Diels-Alder reaction is the reaction of 1,3-butadiene with ethylene

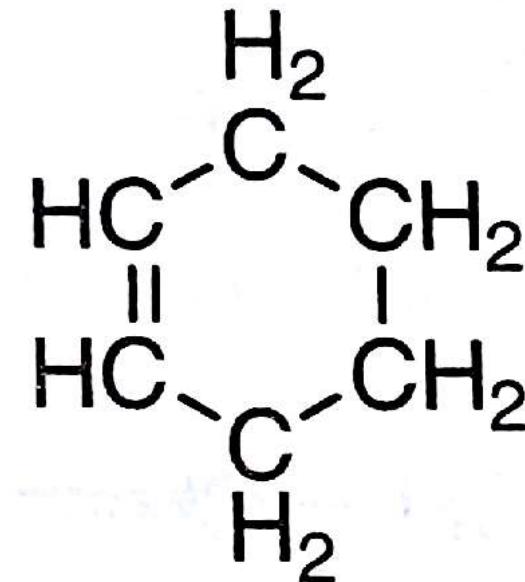


1,3-Butadiene
(Diene)

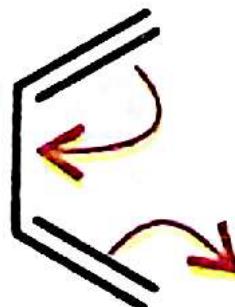


Ethylene
(Dienophile)

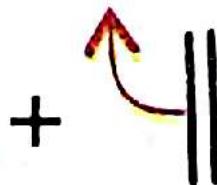
$\xrightarrow{200^\circ\text{C}}$



Cyclohexene
(Adduct)

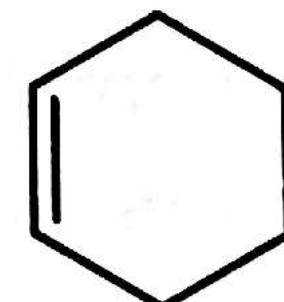


Diene



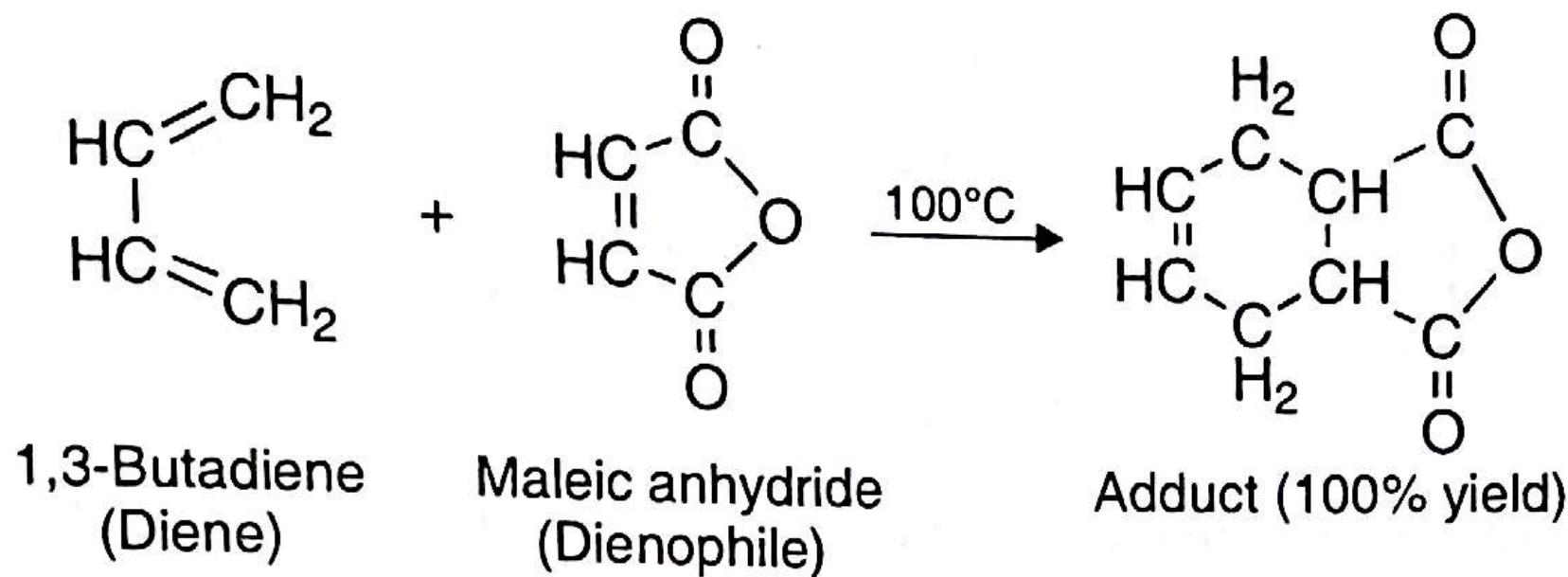
Dienophile

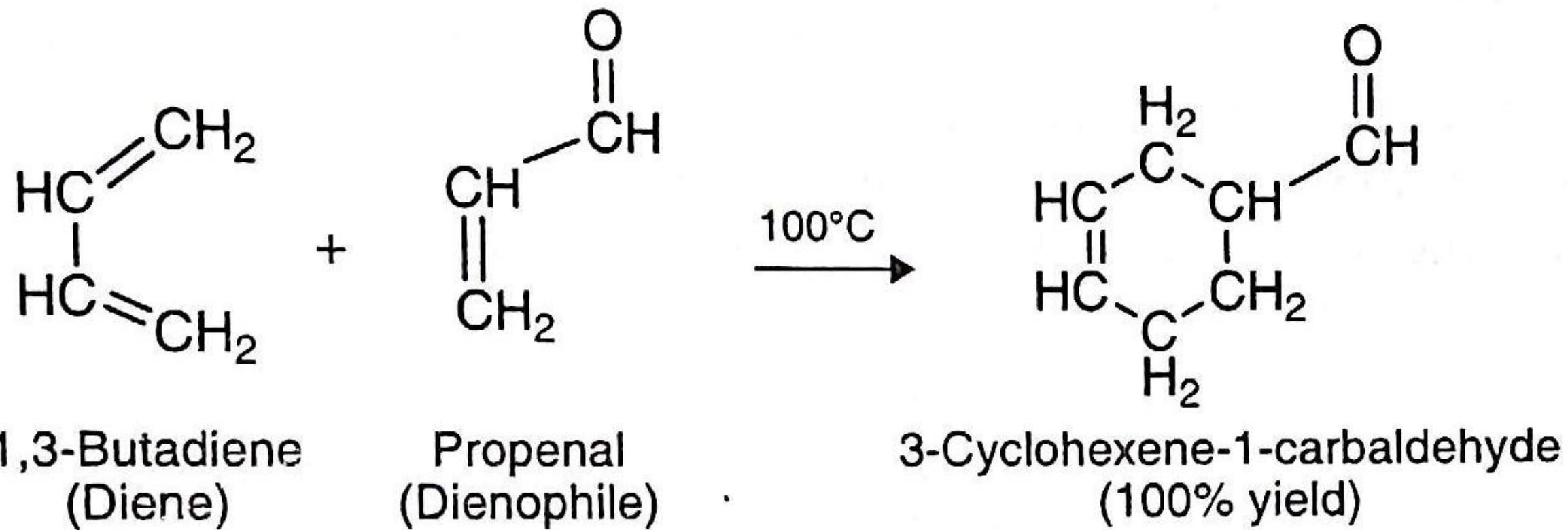
\longrightarrow



Adduct

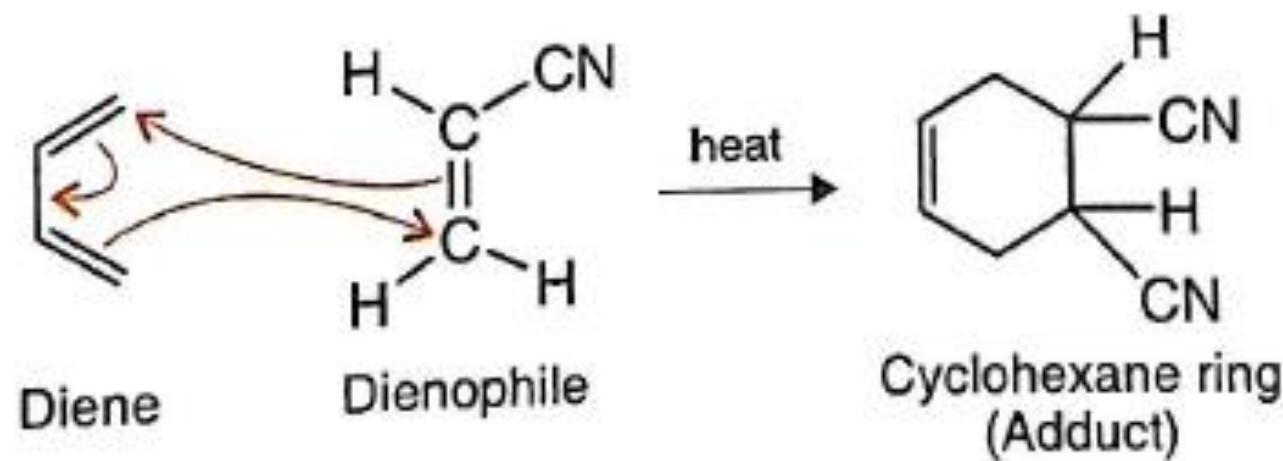
Dienophile can be a simple alkene, electron withdrawing groups such as CN, CHO, COR, -COOR, -COOH etc. Electron withdrawing groups facilitate the reaction





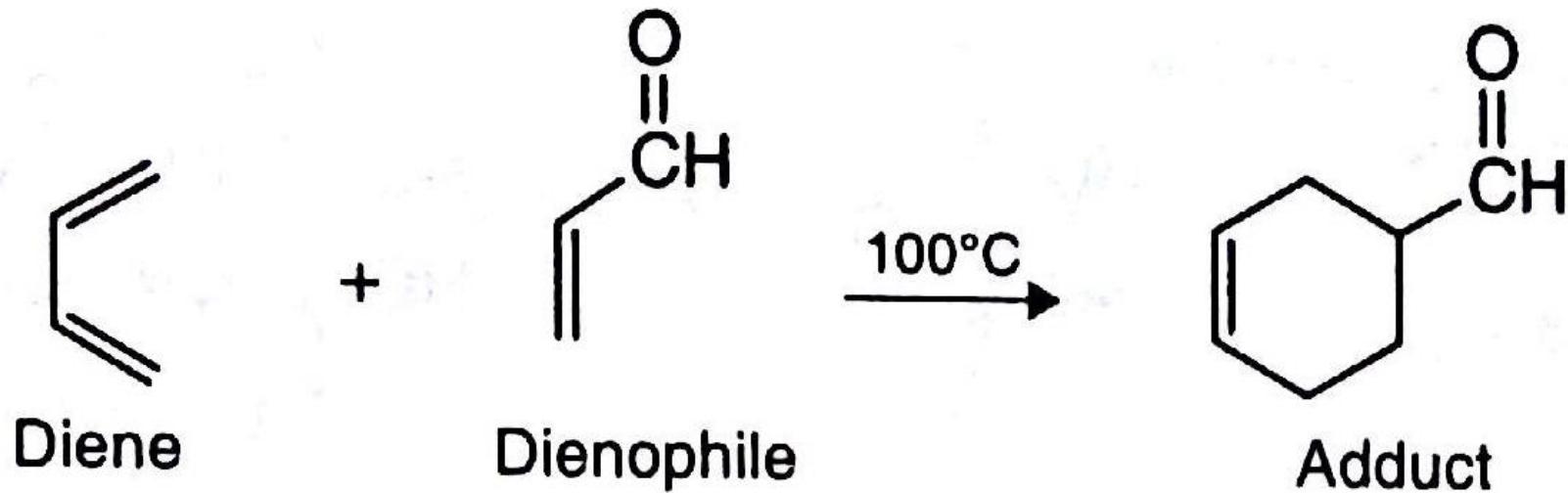
Mechanism

It is a one step concerted mechanism. A diene reacts with an electron-poor alkene to form a new cyclohexene ring.



Concerted means all the bond breaking and bond making occurs in one step.

More examples



POINTS TO REMEMBER

1. Alkenes and alkynes with electron withdrawing groups add to conjugated dienes to form six-membered rings. **This reaction has proved to be a useful synthetic tool, providing one of the best ways to make six-member rings.**
2. Also called **[4+2] cycloaddition** because the ring is formed by interaction of 4 pi electrons in the diene with 2 pi electrons of the alkene or alkyne.
3. The reaction is like a nucleophilic-electrophilic reaction. The diene is electron rich and the dienophile is electron poor. Simple dienes are sufficiently electron rich to be effective dienes for Diels-Alder reaction.
4. The Presence of electron releasing groups such as alkyl or alkoxy (-OR) may further enhance the reactivity of diene.
5. Good dienophiles commonly have electron withdrawing groups (carbonyl, cyano) groups to enhance their Diels-Alder reactivity.