

Organic Chemistry



Aldehydes and Ketones *2nd Stage*

Part II Reactions

Dr. Munther A. M. Ali

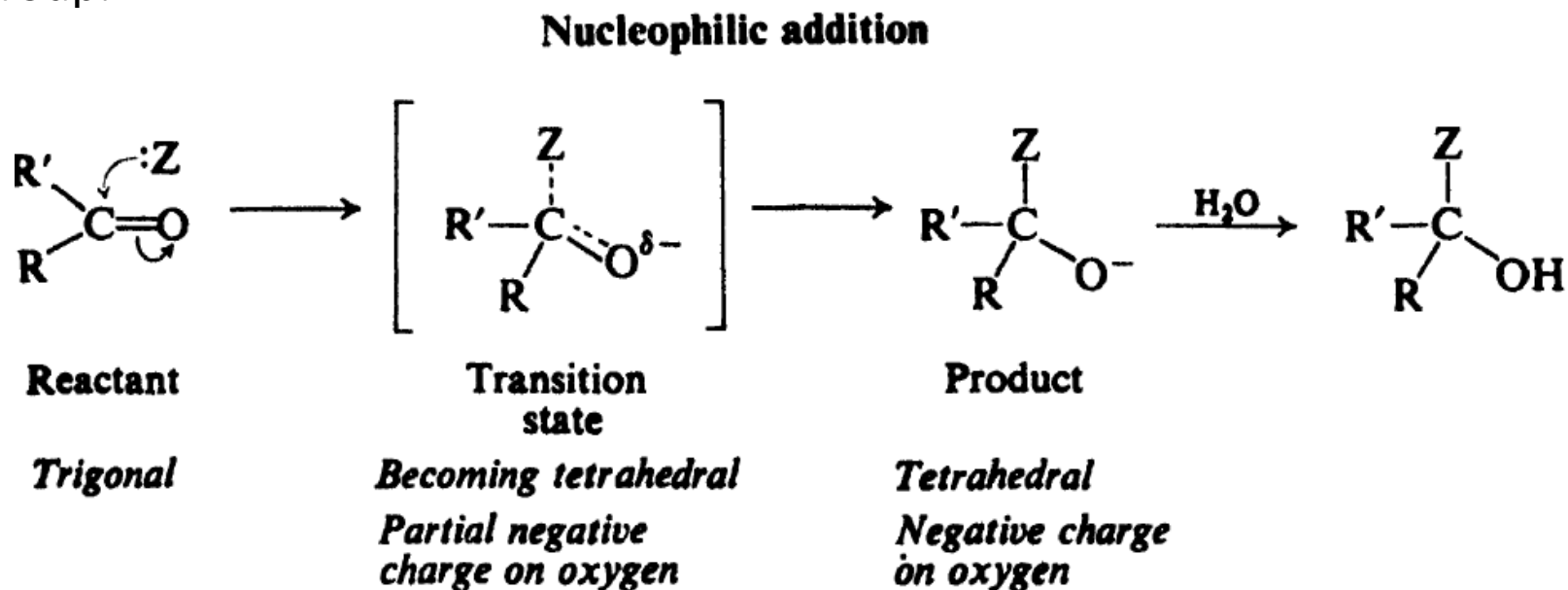
Reactions. Nucleophilic addition

The carbonyl group, C=O, governs the chemistry of aldehydes and ketones. It does this in two ways:

(a) by providing a site for nucleophilic addition, and (b) by increasing the acidity of the hydrogen atoms attached to the alpha carbon.

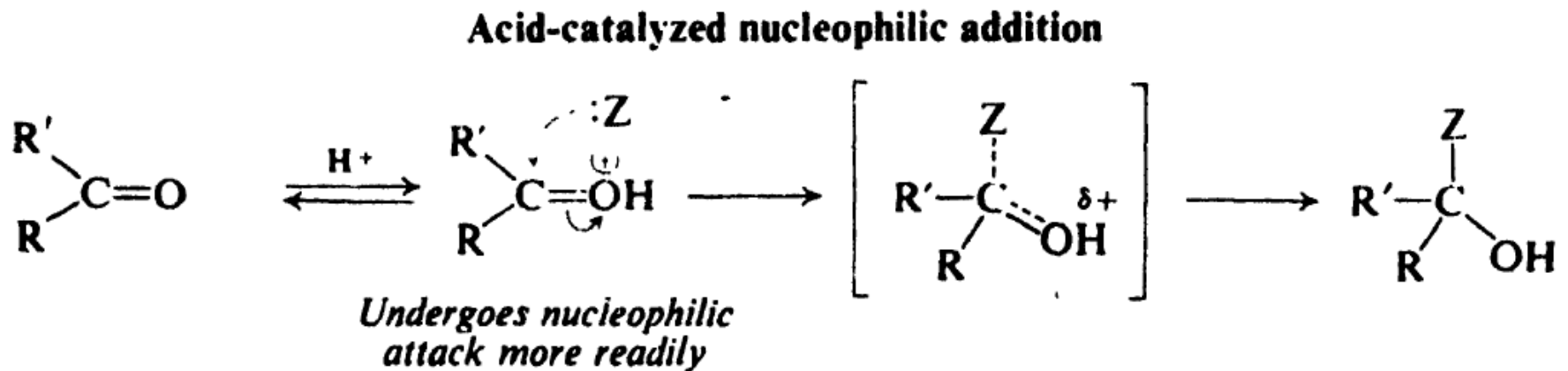
The carbonyl group contains a carbon-oxygen double bond; since the mobile π electrons are pulled strongly toward oxygen, carbonyl carbon is electron-deficient and carbonyl oxygen is electron-rich.

Because it is flat, this part of the molecule is open to relatively unhindered attack from above or below, in a direction perpendicular to the plane of the group.



What is the effect of acid?

If acid is present, hydrogen ion becomes attached to carbonyl oxygen. This prior protonation **lowers the *Fact* for nucleophilic attack**, since it permits oxygen to acquire the π electrons without having to accept a negative charge. Thus nucleophilic addition to aldehydes and ketones can be catalyzed by acids (sometimes, by Lewis acids).

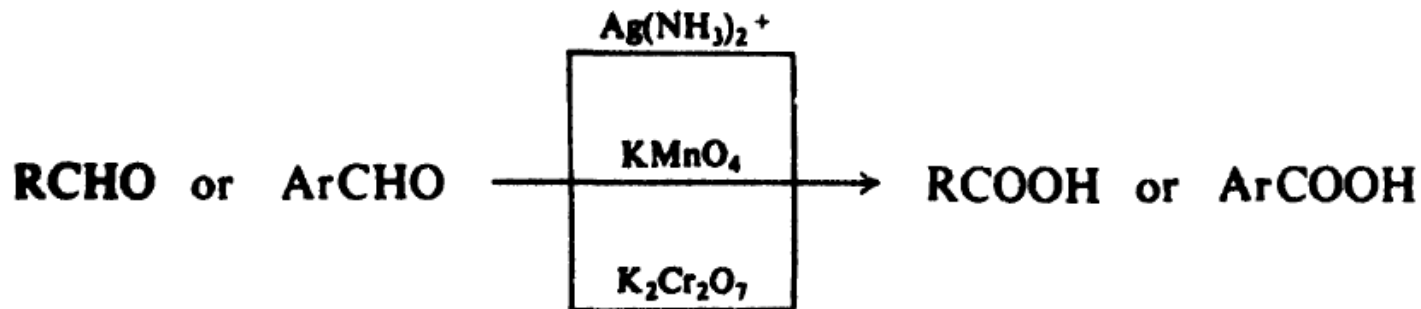


Reactions of aldehydes and ketones

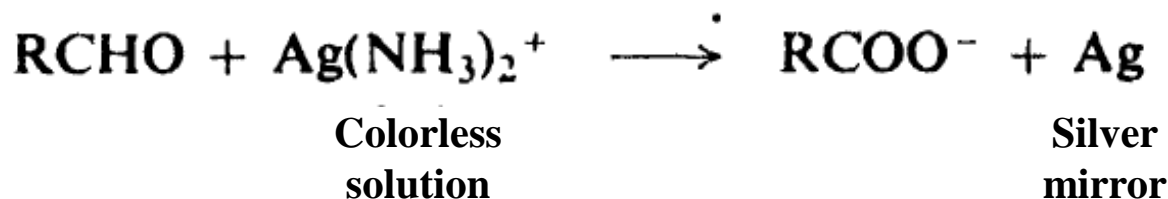
1. Oxidation

(a) Oxidation of aldehydes

Aldehydes are easily oxidized to carboxylic acids; ketones are not. This process is due to their difference in structure, an aldehyde has a hydrogen atom attached to the carbonyl carbon, and a ketone has not.



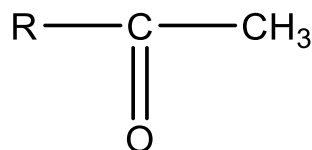
Tollens' reagent contains the silver ammonia ion, $\text{Ag}(\text{NH}_3)_2^{2+}$. Oxidation of the aldehyde is accompanied by reduction of silver ion to free silver (in the form of a mirror under the proper conditions).



(b) Oxidation of methyl ketones (iodoform test)

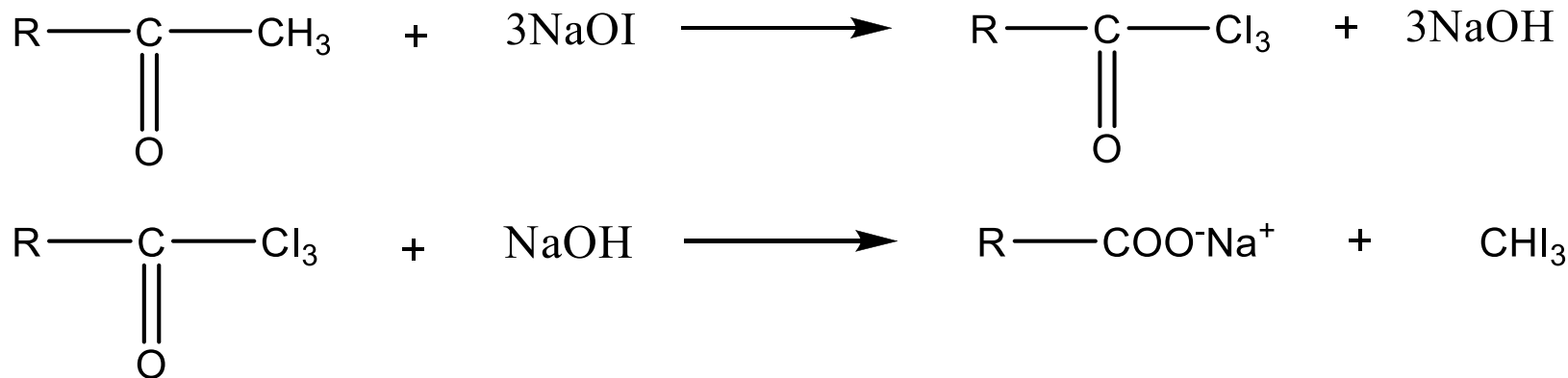
The ketone is treated with iodine and sodium hydroxide (sodium hypoiodite, NaOI).

A ketone of the structure

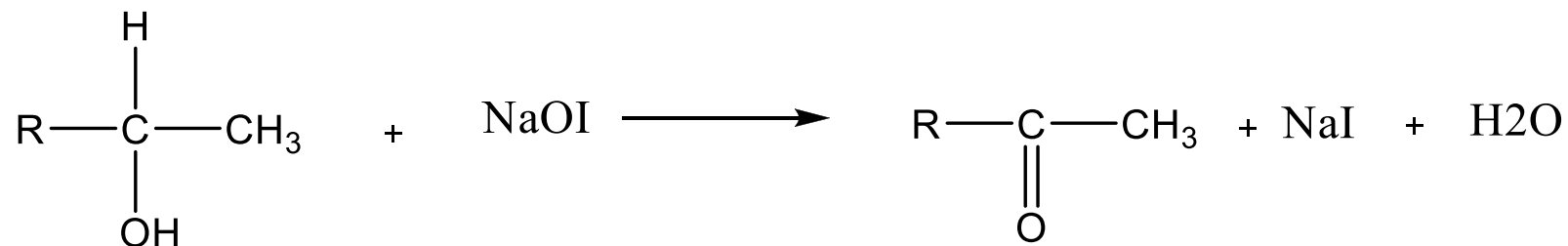


yields a yellow precipitate of iodoform (CHI_3).

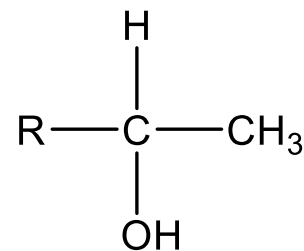
The reaction involves halogenation and cleavage:



Hypohalites can not only halogenate but also oxidize:



As a result, an alcohol of the structure

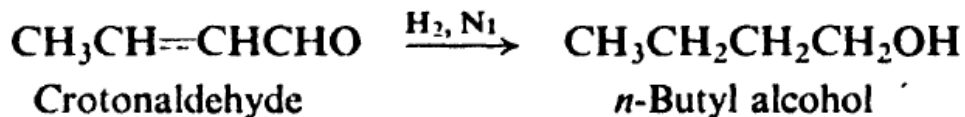
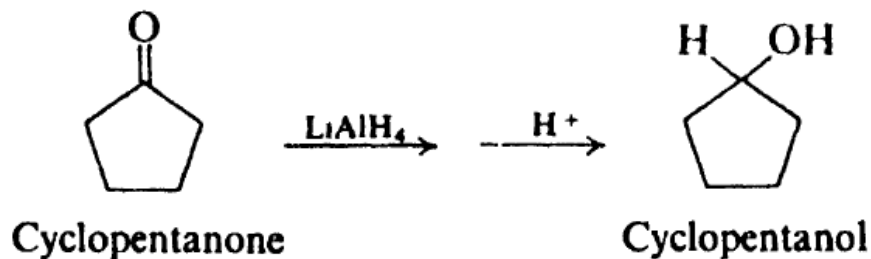


oxidize to a methyl ketone, and hence gives a positive test.

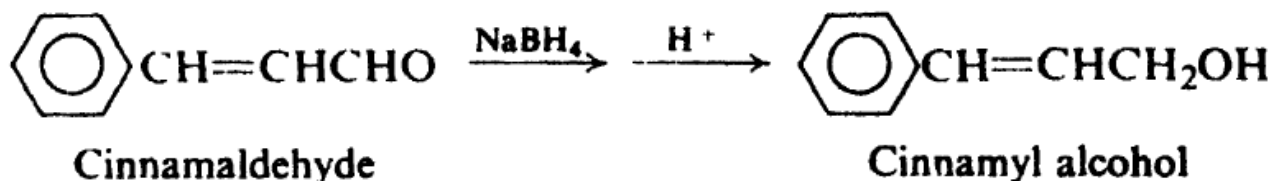
2. Reduction

(a) Reduction to alcohols.

Aldehydes can be reduced to primary alcohols, and ketones to secondary alcohols, either by catalytic hydrogenation (H_2 , Ni) or by use of chemical reducing agents like lithium aluminum hydride, LiAlH_4 .

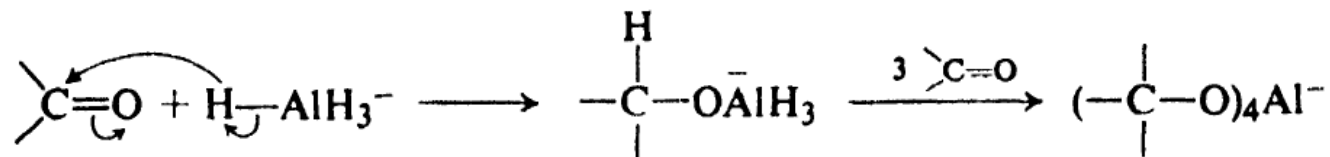


Sodium borohydride, NaBH_4 , does not reduce carbon-carbon double bonds, not even those conjugated with carbonyl groups, and is thus useful for the reduction of such **unsaturated carbonyl compounds** to unsaturated alcohols.



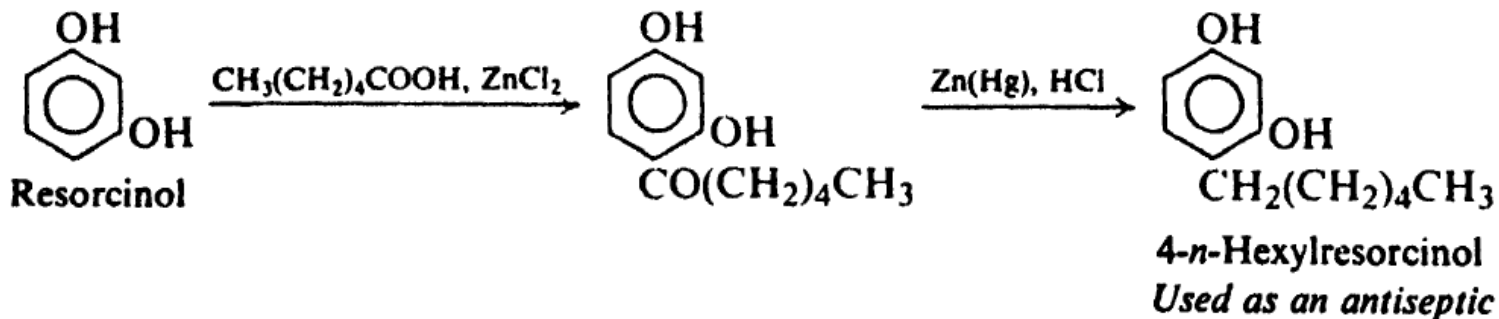
Mechanism of alcohol formation:

nucleophilic addition, this time the nucleophile is hydrogen transferred with a pair of electrons as a **hydride ion, H⁻** from the metal to carbonyl carbon



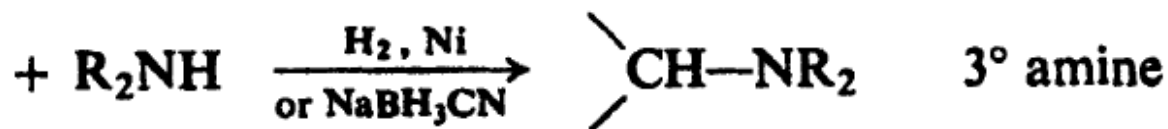
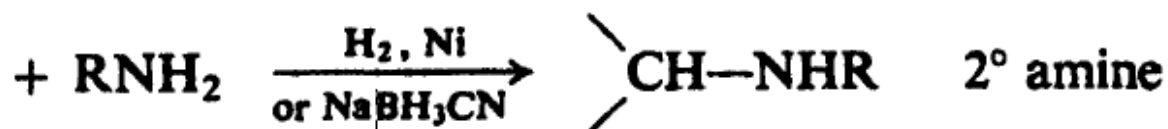
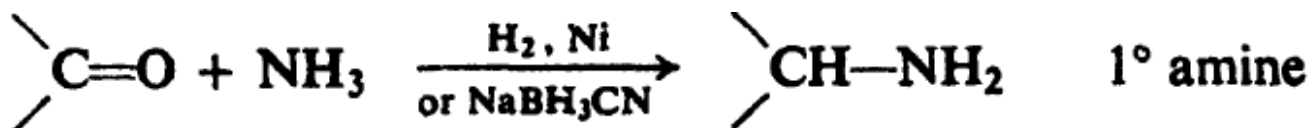
(b) Reduction to hydrocarbons.

Aldehydes and ketones can be reduced to hydrocarbons by the action (a) of **amalgamated zinc and concentrated hydrochloric acid**, the **Clemmensen reduction**; or (b) of **hydrazine, NH₂NH₂**, and a strong base like **KOH** or **potassium *tert*-butoxide**, the **Wolff-Kishner reduction**.



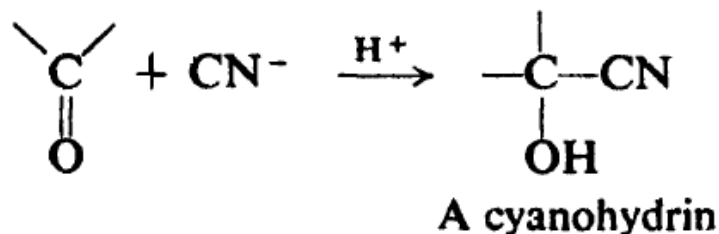
(c) Reductive amination.

Reduction of aldehydes and ketones in the presence of ammonia or amine to the corresponding amines .

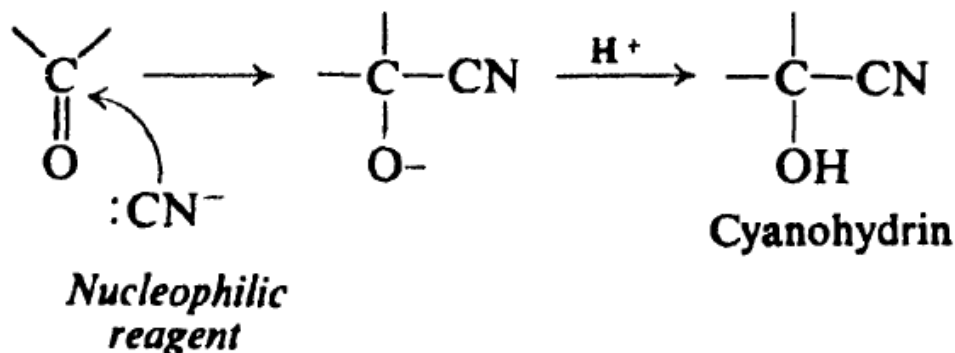


3. Addition of cyanide

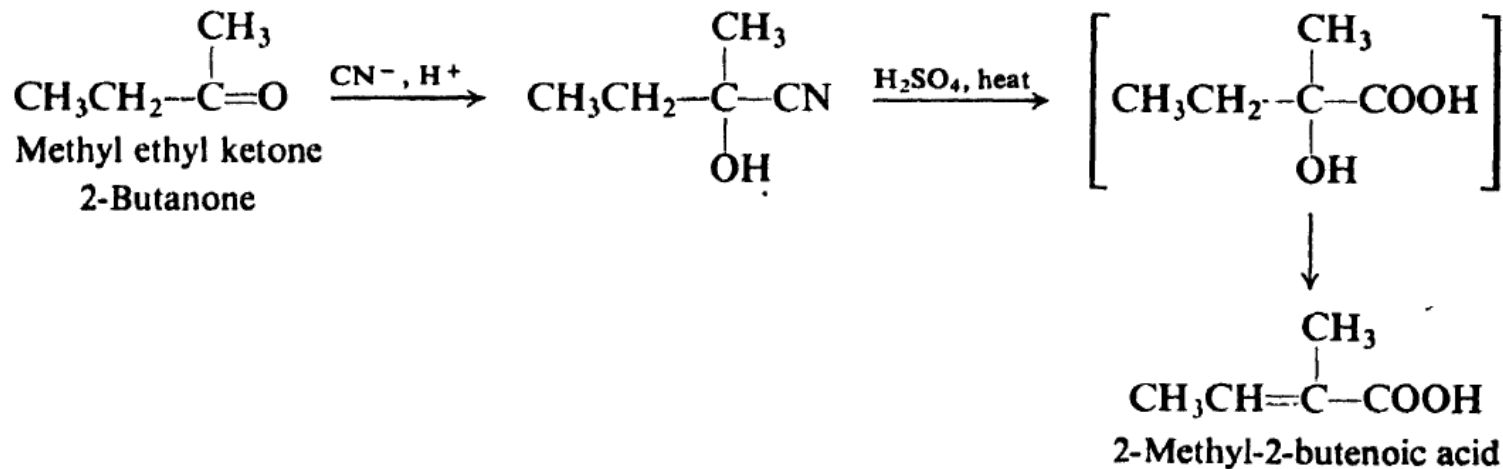
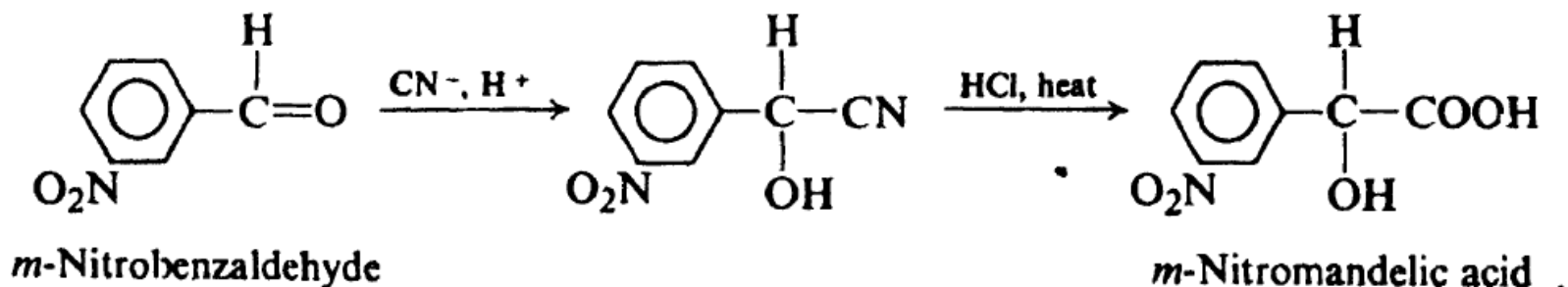
The elements of **HCN** add to the **carbonyl group** of aldehydes and ketones to yield compounds known as **cyanohydrins**:



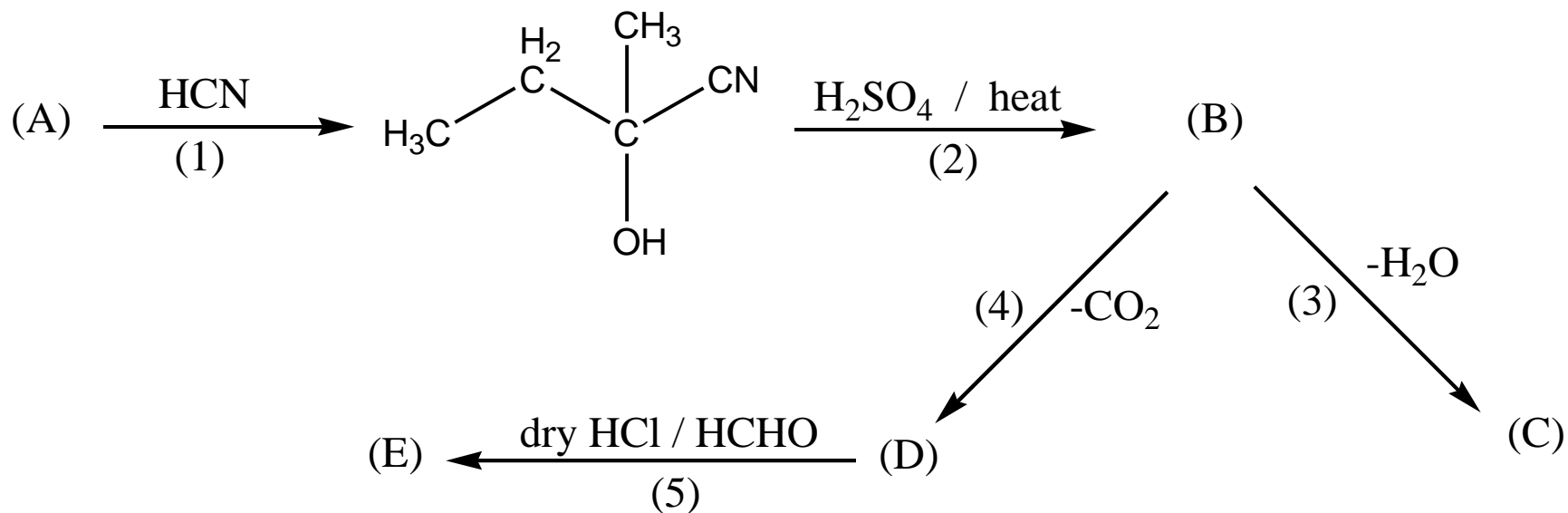
Addition appears to involve **nucleophilic attack** on carbonyl carbon by the strongly basic cyanide ion; subsequently (or possibly simultaneously) oxygen accepts a hydrogen ion to form the cyanohydrin product :



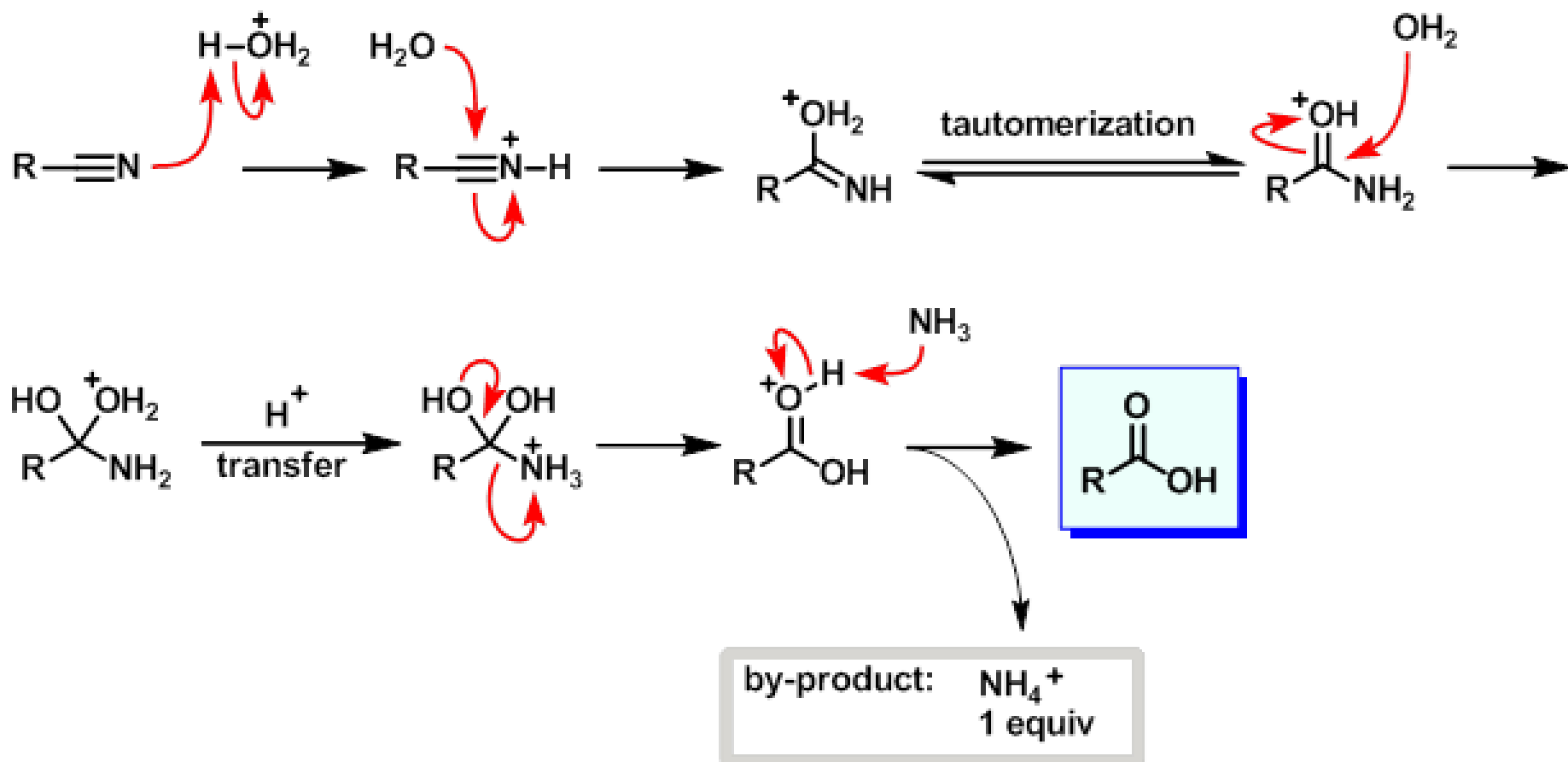
Cyanohydrins are nitriles, they undergo **hydrolysis**; in this case the products are **α -hydroxyacids** or **unsaturated acids**.
For example:



Give the chemical structure instead of A, B, C, D and E and the name of reaction instead of 1, 2, 3, 4 and 5:

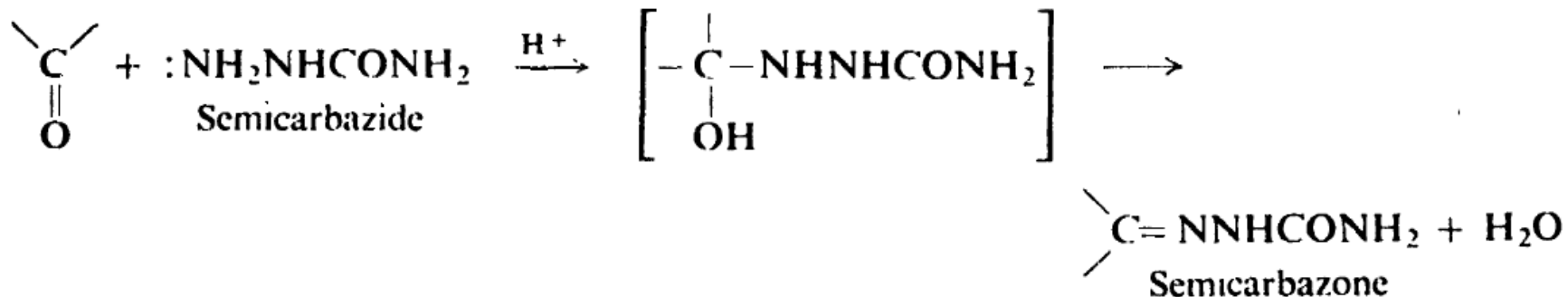
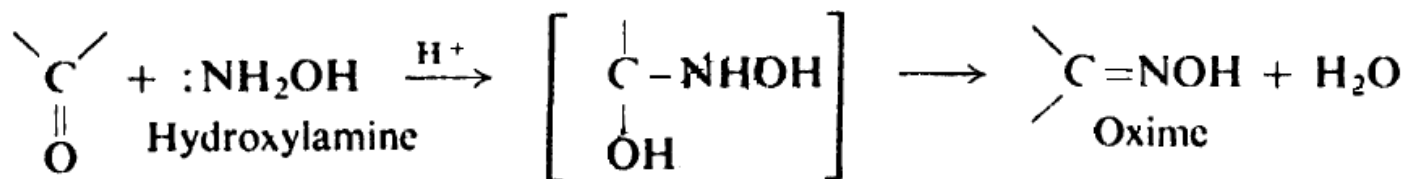


Mechanism of acidic hydrolysis of cyanohydrin

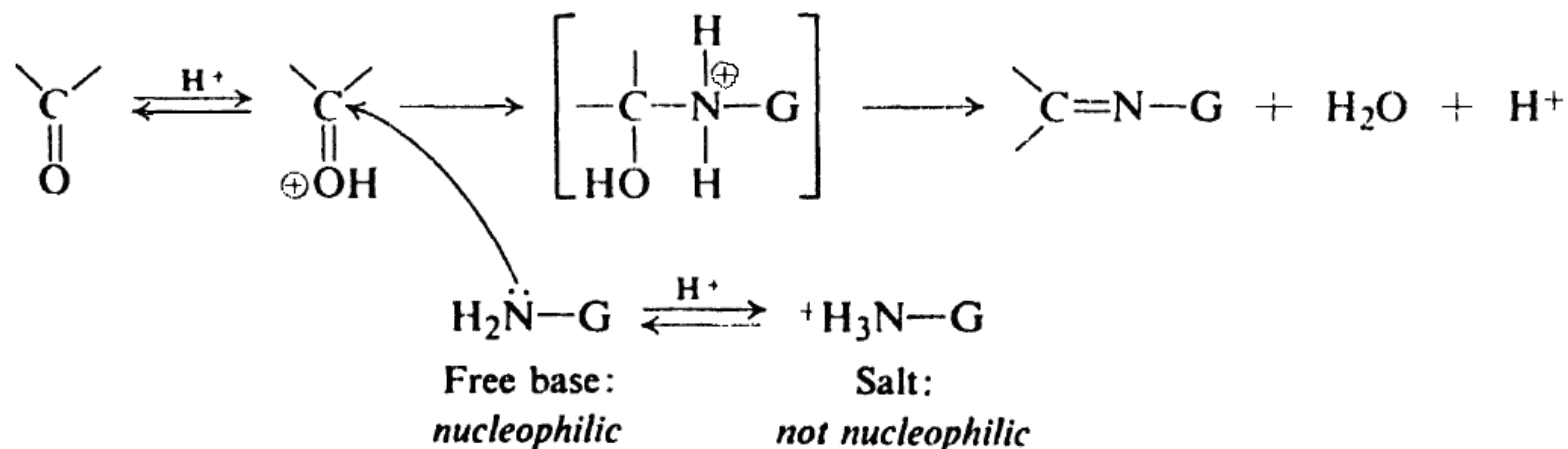


4. Addition of derivatives of ammonia

Ammonia derivatives add to the carbonyl group to form derivatives containing C=N (azomethine, Imine)

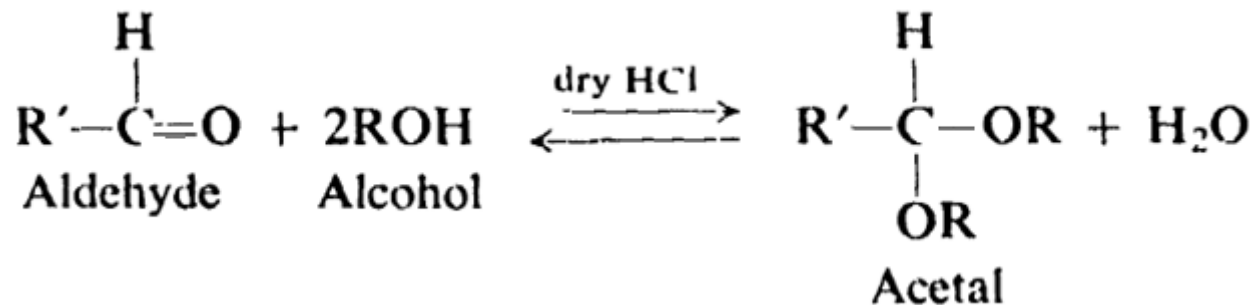


The solution must be acidic enough for an appreciable fraction of the carbonyl compound to be protonated

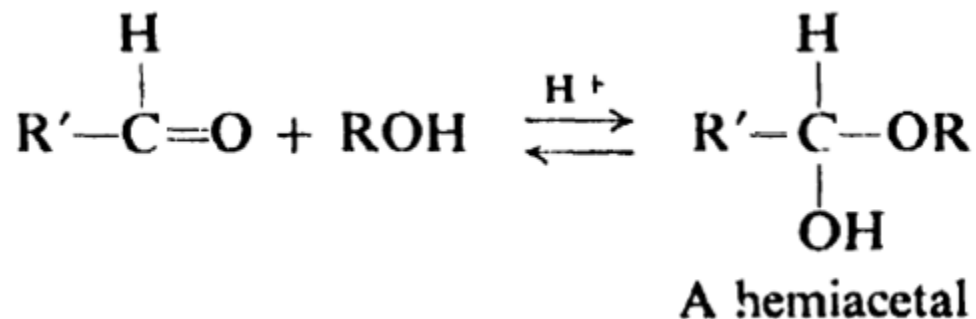


5- Addition of alcohols. Acetal formation.

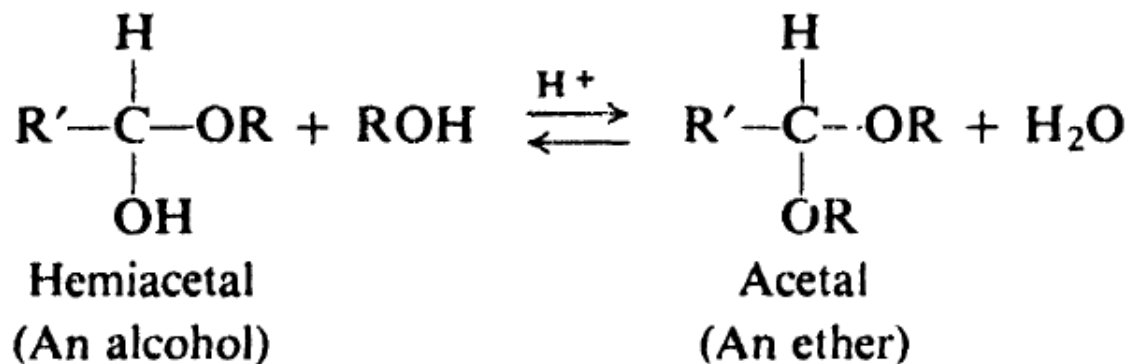
Alcohols add to the carbonyl group of aldehydes in the presence of anhydrous acids to yield acetals:



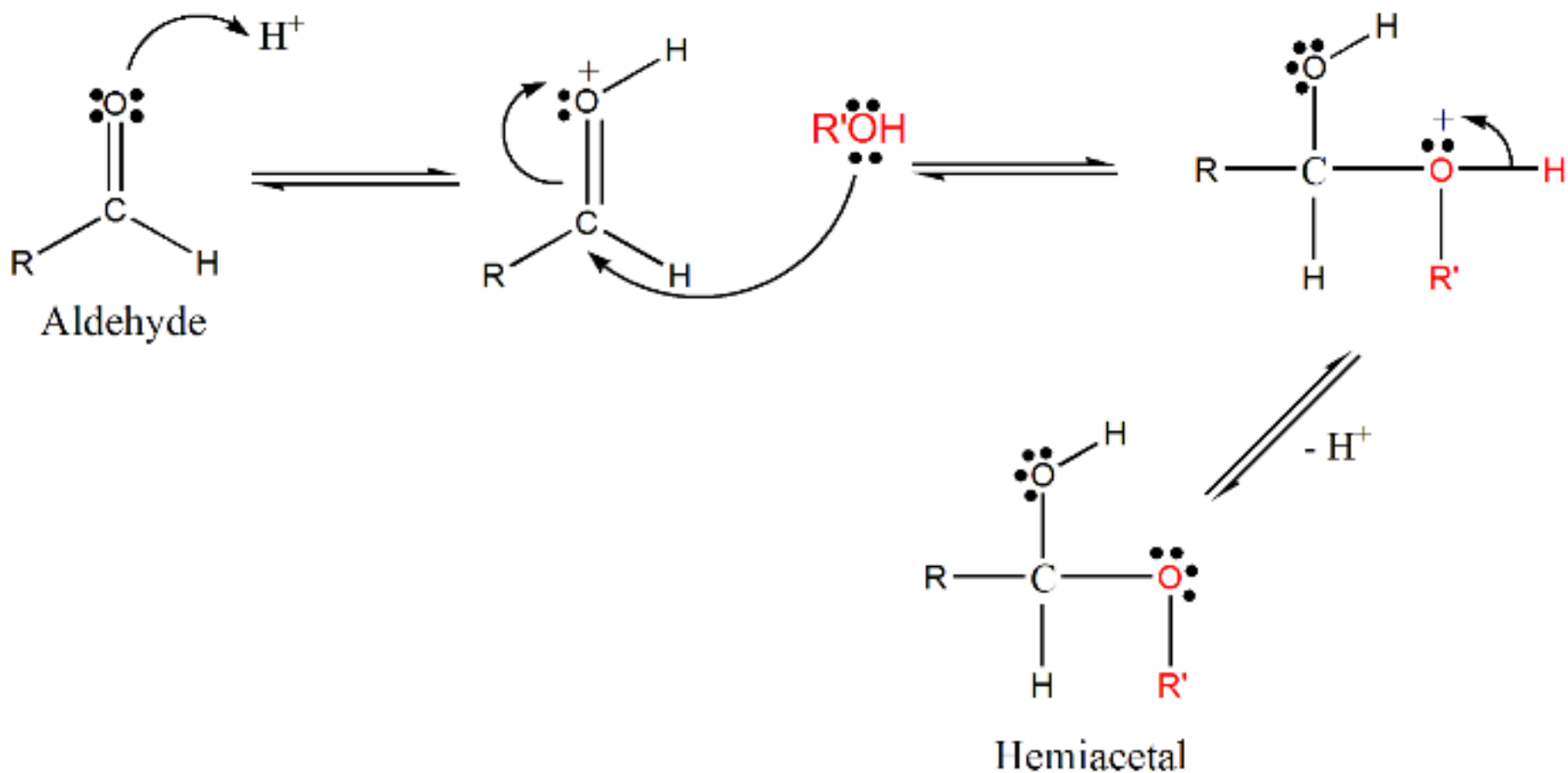
The **mechanism** including formation of **hemiacetal** (alcohol) by the addition of the nucleophilic alcohol molecule to the carbonyl group. **What is the mechanism of hemiacetal formation.**



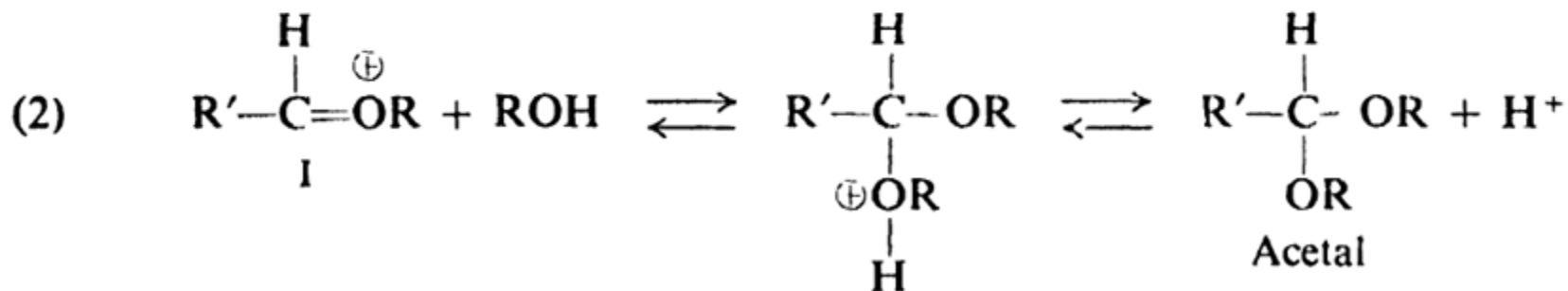
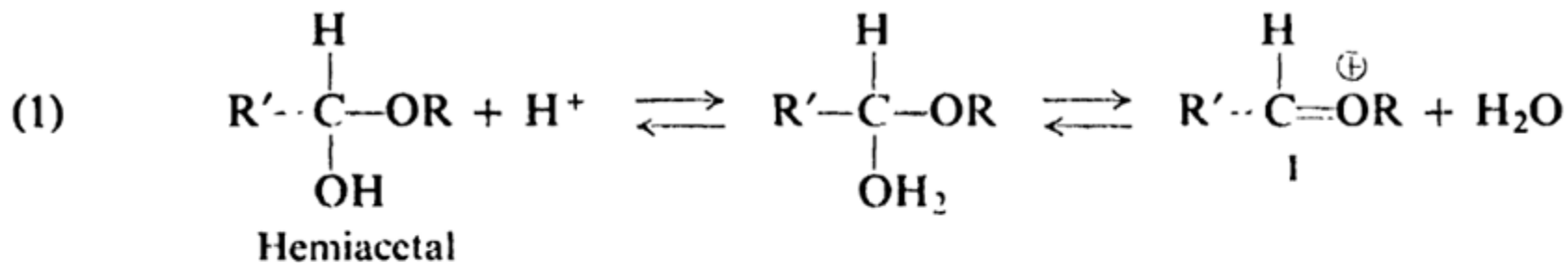
In the presence of acid the hemiacetal, acting as an alcohol, reacts with more of the solvent alcohol to form the **acetal**, an **ether**:



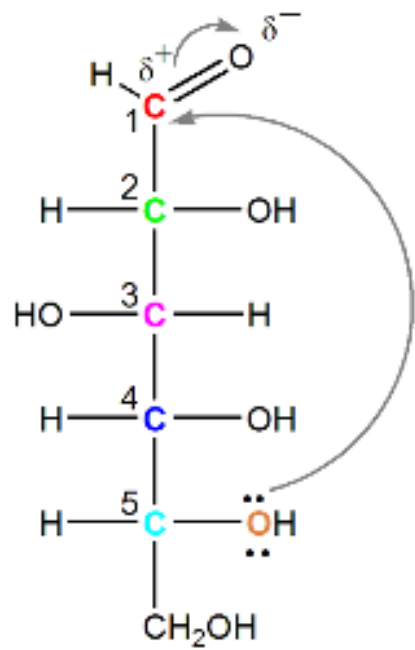
The mechanism of hemiacetal formation



The mechanism of reaction involves the formation (step 1) of the ion I, which then combines (step 2) with a molecule of alcohol to yield the protonated acetal.

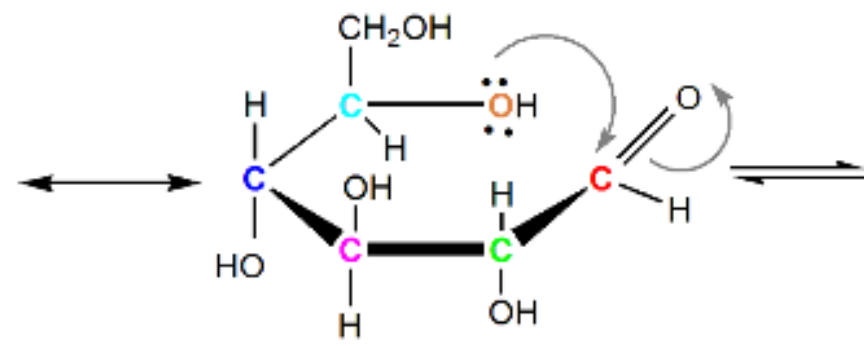


Glucose has an aldehyde group and five hydroxyl groups. Glucose can form an intramolecular cyclic hemiacetal.

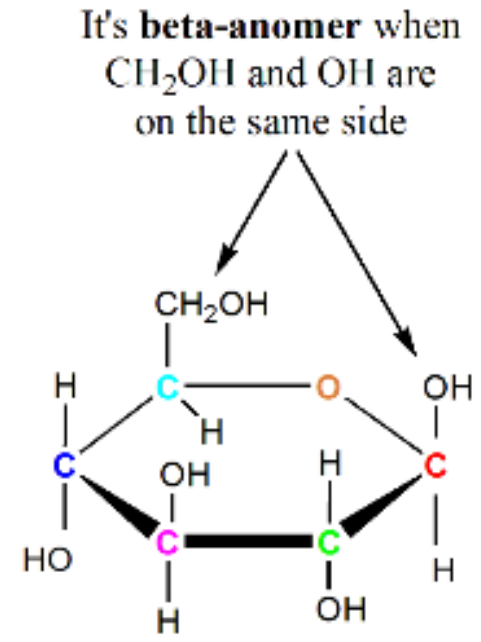


up on the ring
down on the ring

D-Glucose
Fischer projection



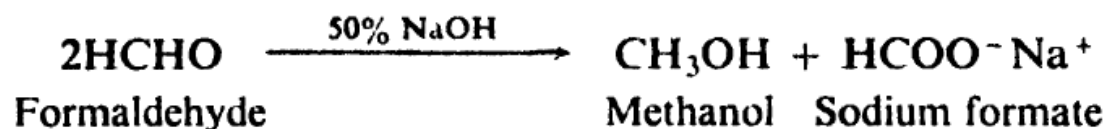
Groups on left side of Fischer projection are facing upwards, while groups on right side are facing downwards in this representation



β-D-Glucopyranose
(hemiacetal of D-glucose)
Haworth projection

6- Cannizzaro reaction

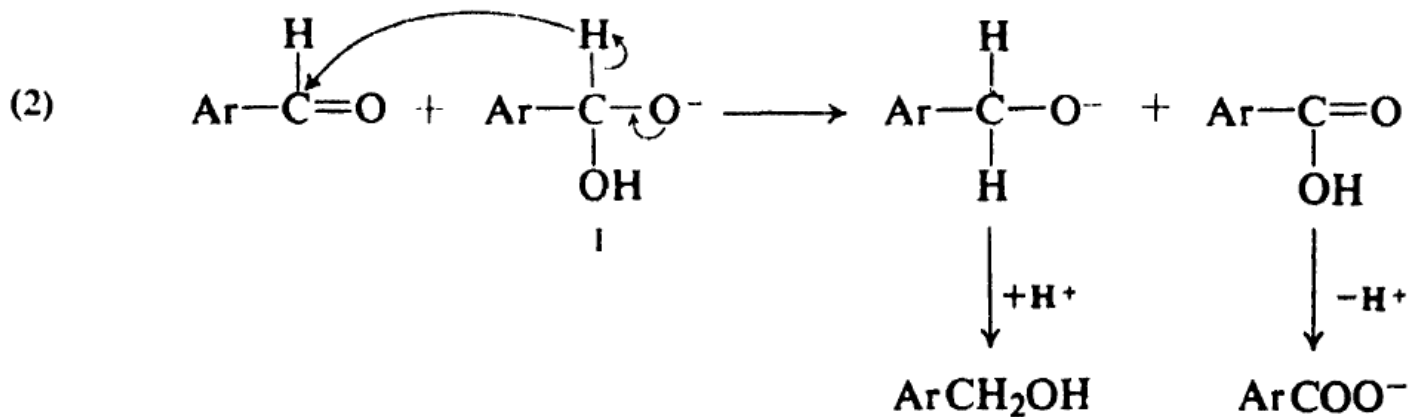
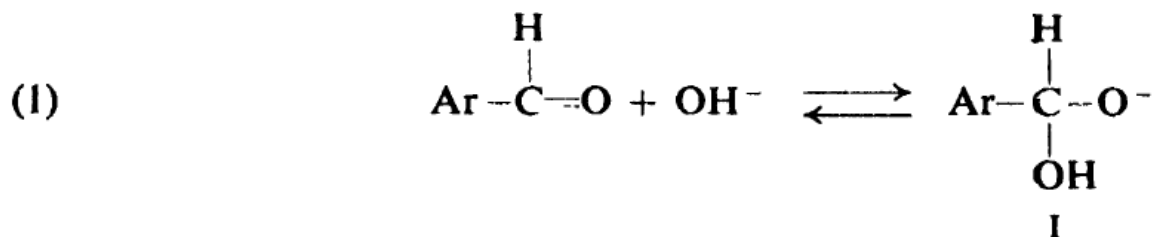
In the presence of **concentrated alkali**, **aldehydes containing no α -hydrogen** undergo self-oxidation-and-reduction to yield a mixture of an alcohol and a salt of a carboxylic acid.



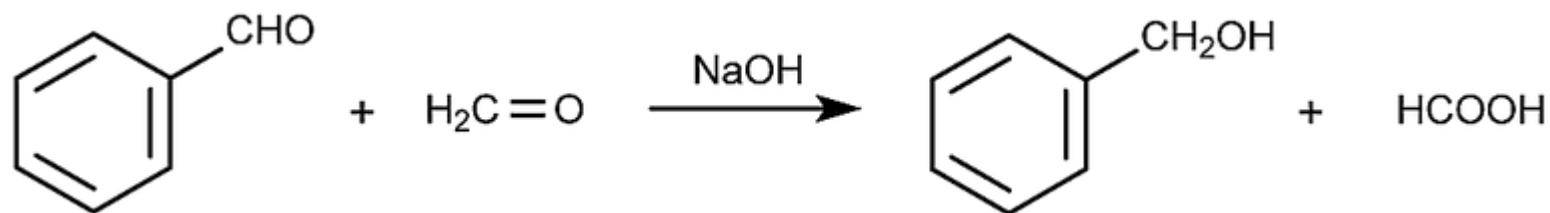
The mechanism includes two successive additions,

- * addition of hydroxide ion (step 1) to give intermediate I
- * addition of a hydride ion from I (step 2) to a second molecule of aldehyde.

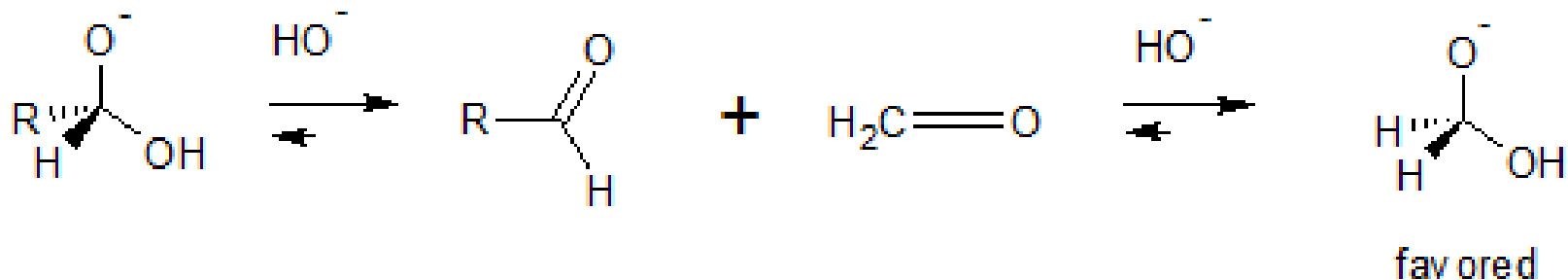
The presence of the negative charge on I aids in the loss of hydride ion.



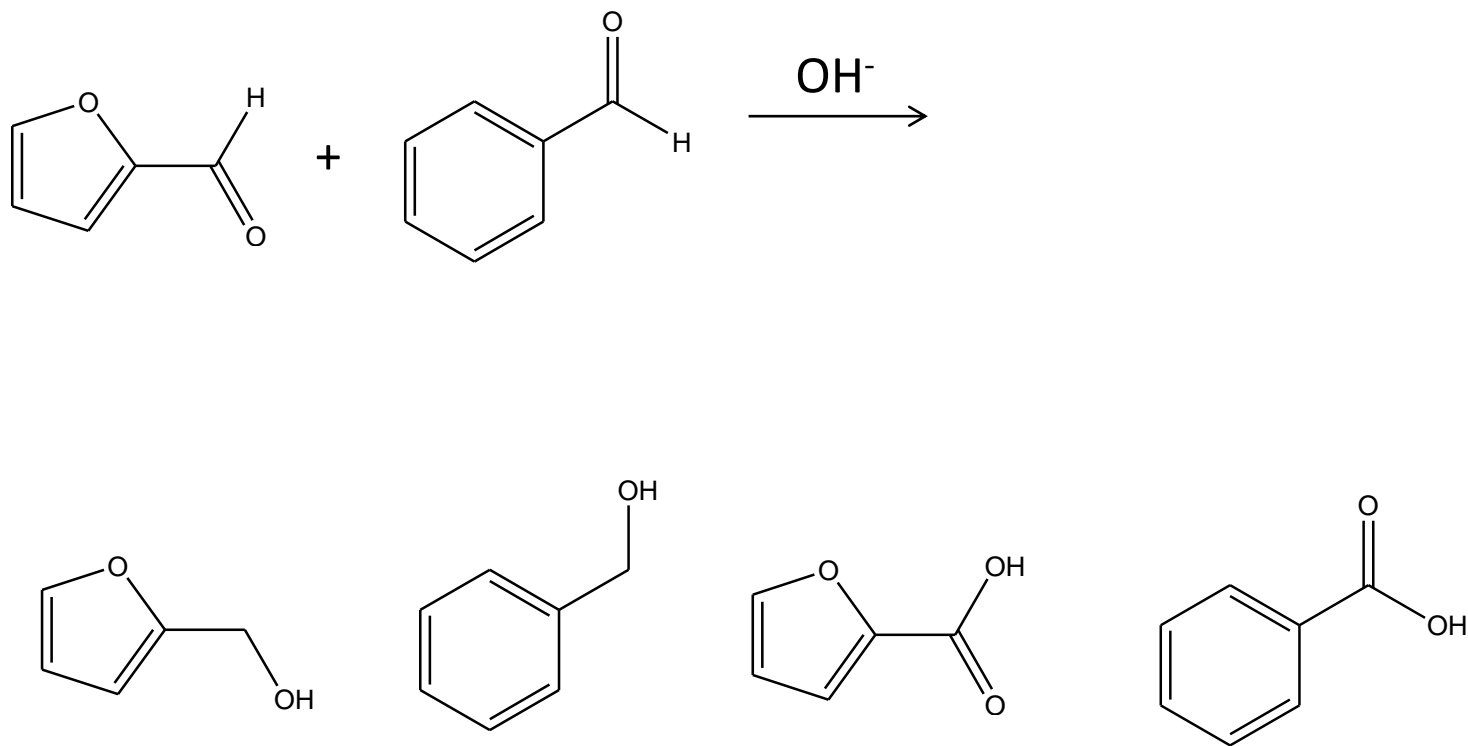
Crossed Cannizzaro Reaction



In the case of Crossed Cannizzaro with formaldehyde, **the formaldehyde carbonyl is extremely reactive** and the equilibrium will lie strongly on the side of the formaldehyde tetrahedral intermediate, and consequently most of the other aldehyde will remain present as the aldehyde.



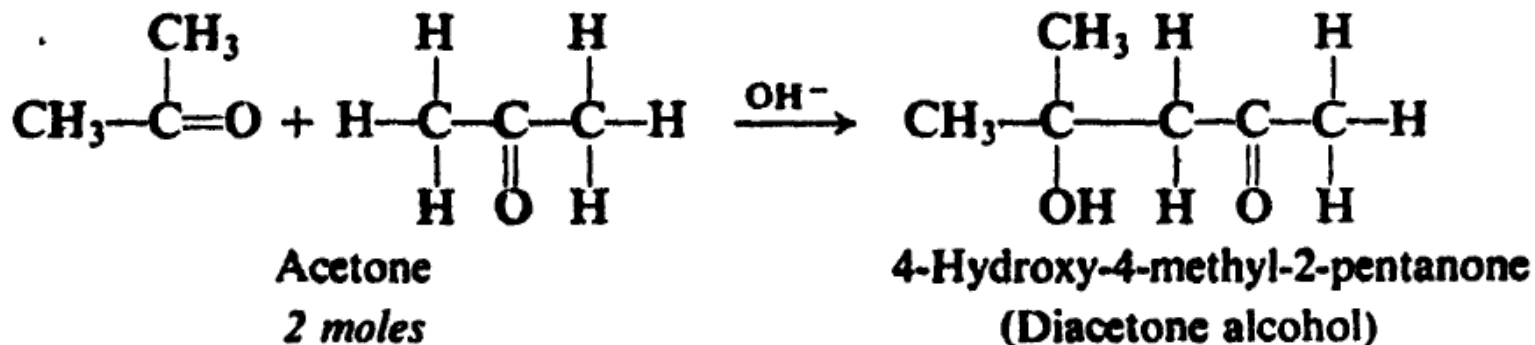
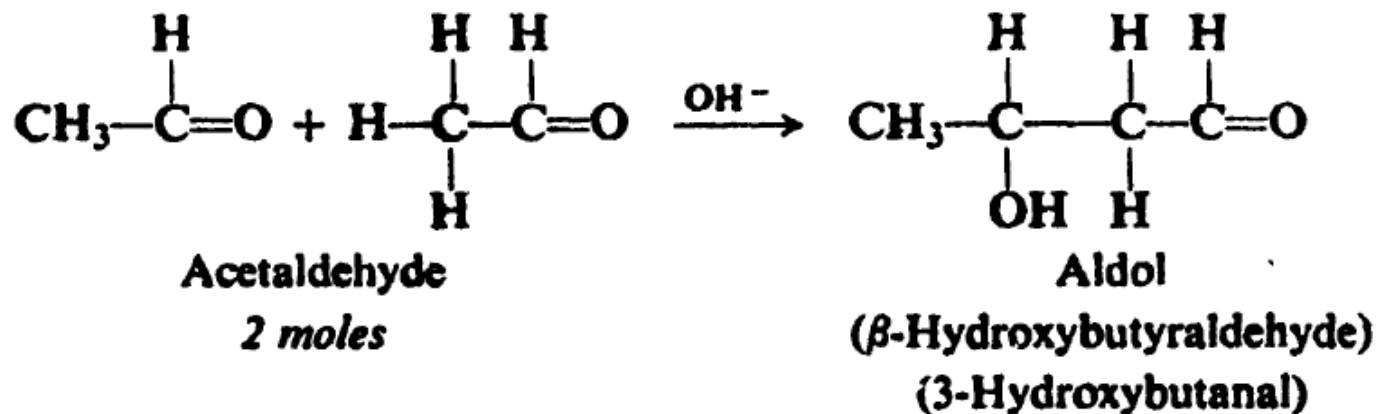
Furfural and benzaldehyde



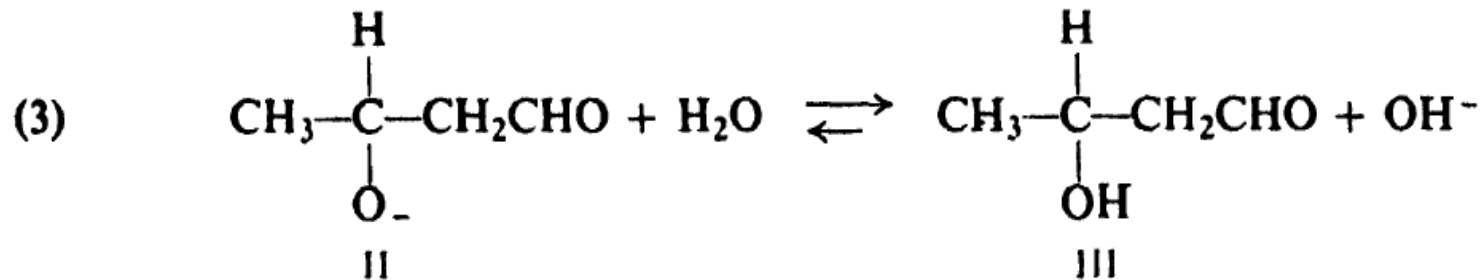
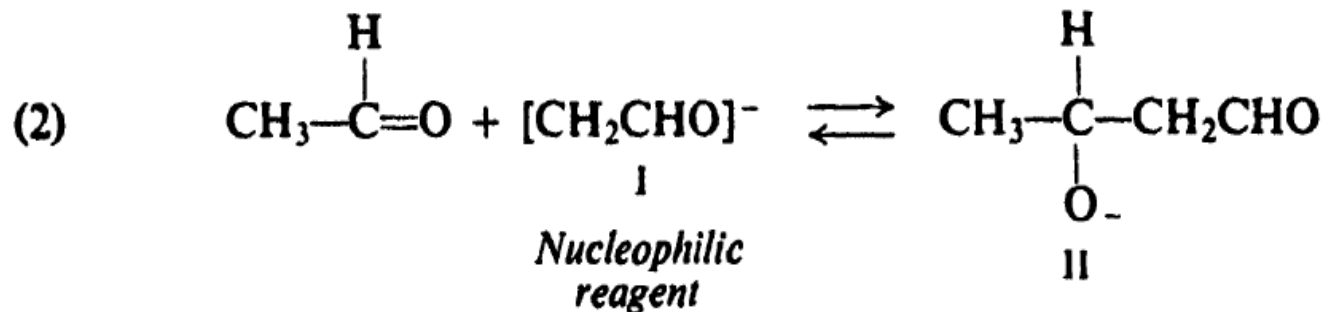
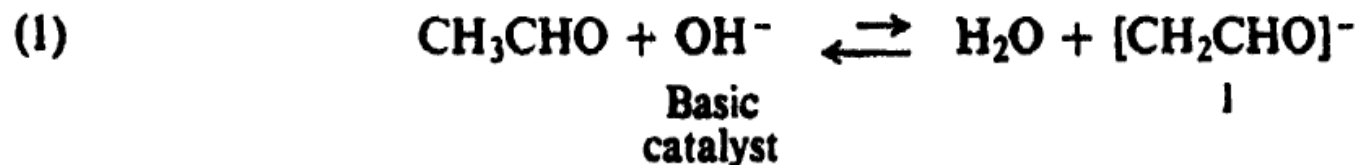
Furfuryl alcohol + benzyl alcohol + Furoic acid + benzoic acid

7- Aldol condensation

Under the influence of **dilute base or dilute acid**, two molecules of an aldehyde or a ketone containing α -hydrogen may combine to form a β -hydroxyaldehyde or β -hydroxyketone.

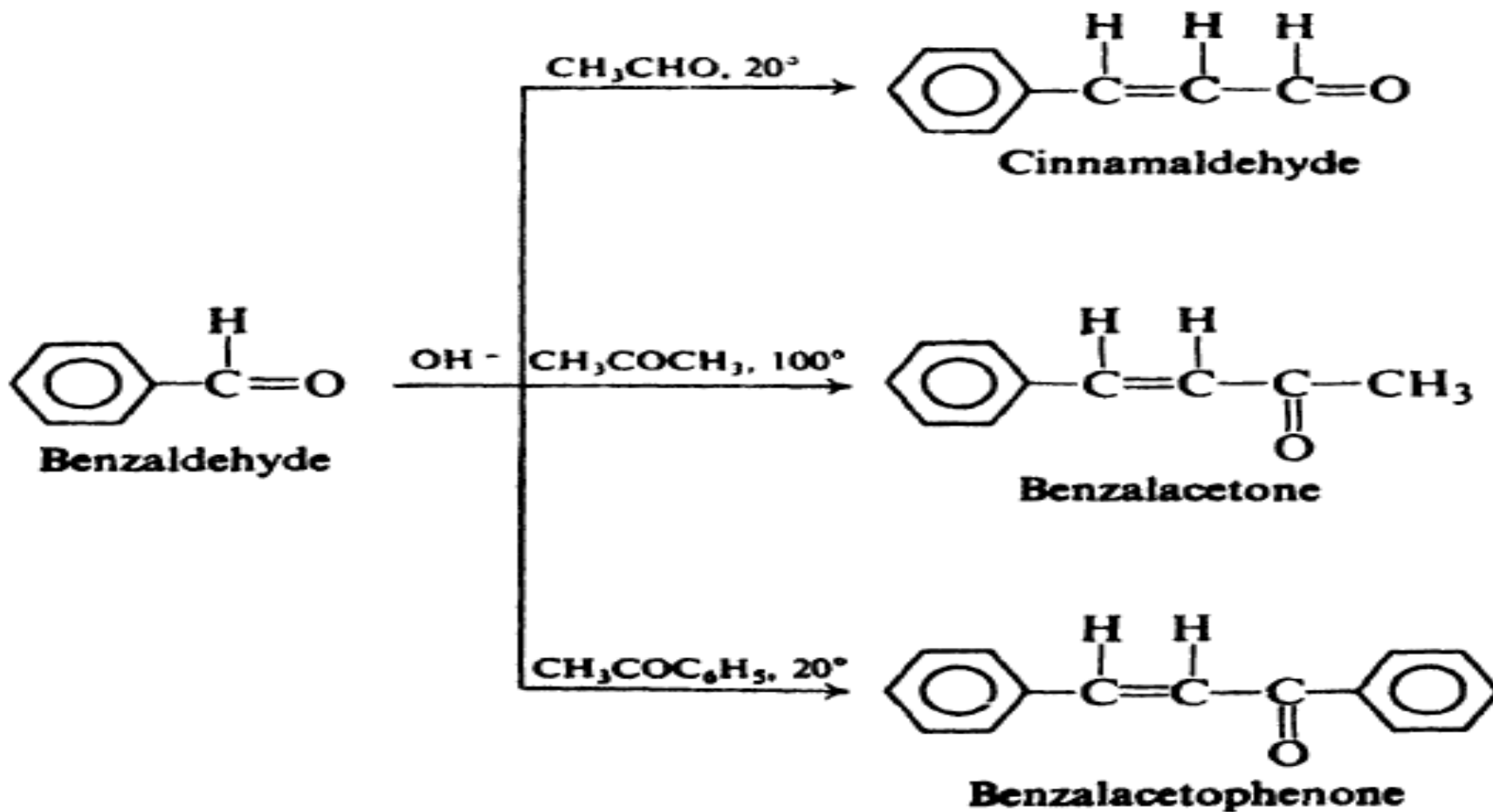


Hydroxide ion abstracts (step 1) a hydrogen ion from the α -carbon of the aldehyde to form **carbanion I**, which attacks (step 2) carbonyl carbon to form ion II. An alkoxide (II) abstracts (step 3) a hydrogen ion from water to form the β -hydroxyaldehyde III, regenerating hydroxide ion



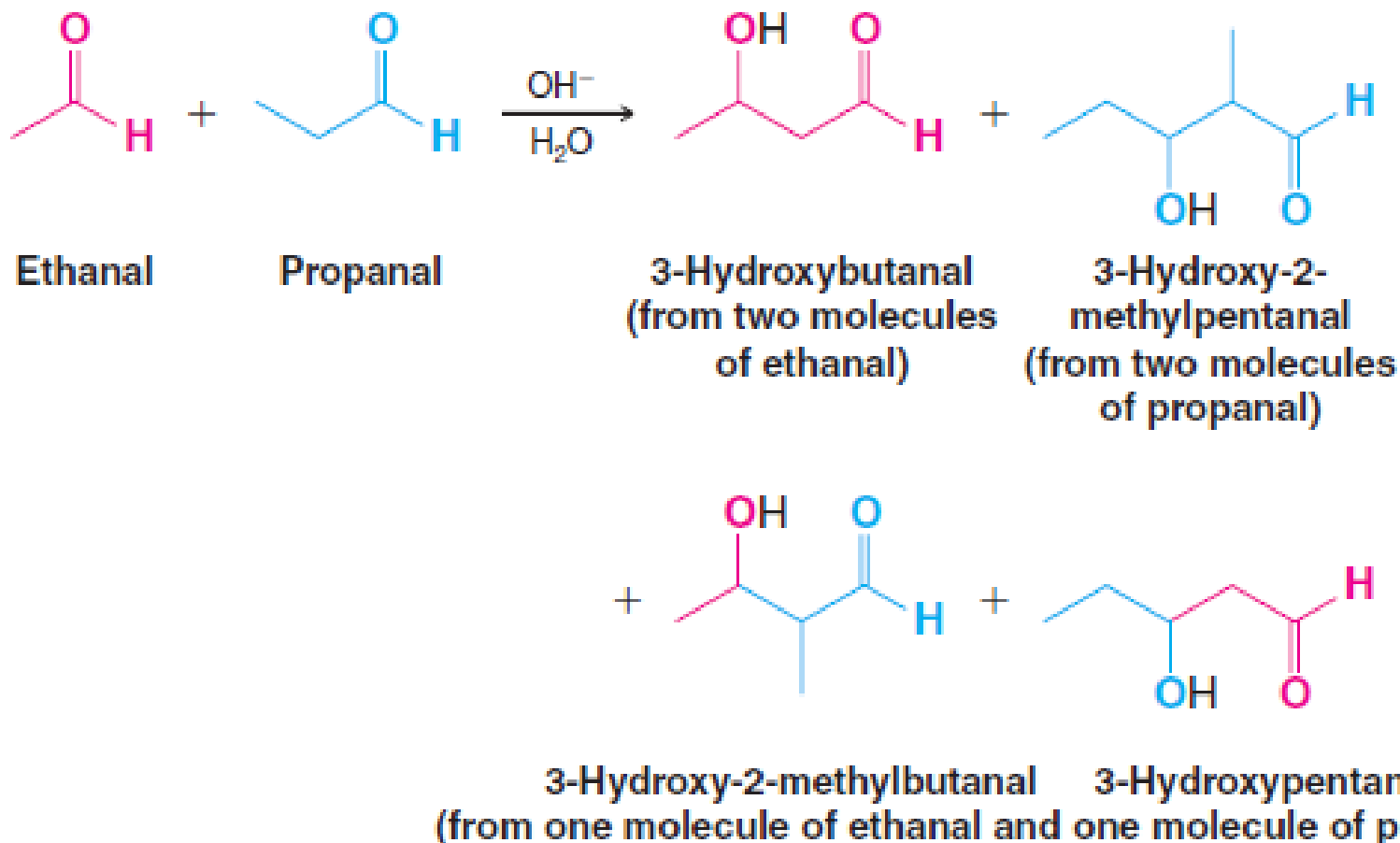
Crossed aldol condensation

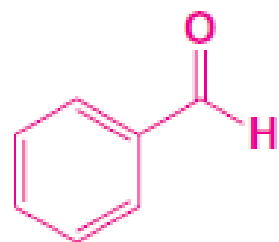
An aldol condensation between two different carbonyl compounds,



Crossed aldol condensation

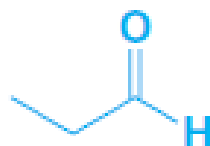
An aldol condensation between two different carbonyl compounds,



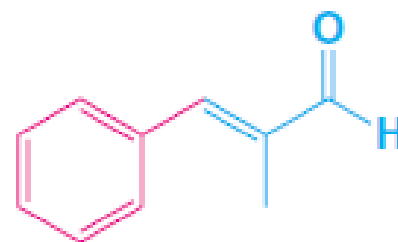


Benzaldehyde

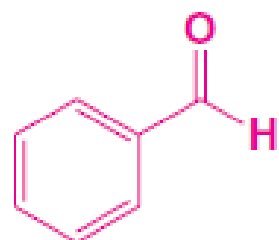
+



Propanal

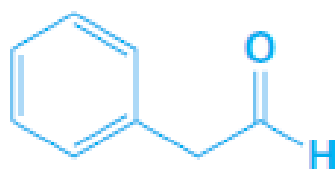


2-Methyl-3-phenyl-2-propenal
(α -methylcinnamaldehyde)
(68%)

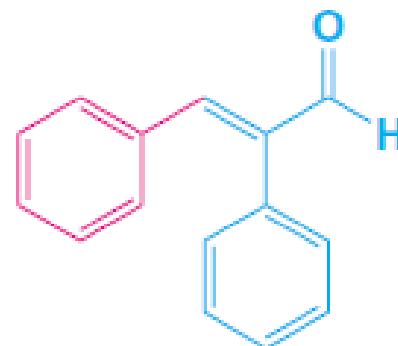


Benzaldehyde

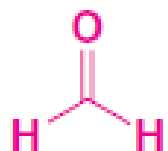
+



Phenylacetaldehyde

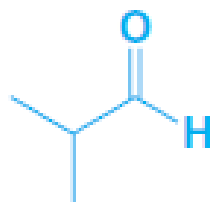


2,3-Diphenyl-2-propenal

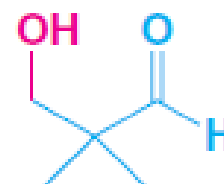
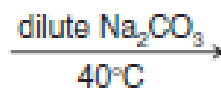


Formaldehyde

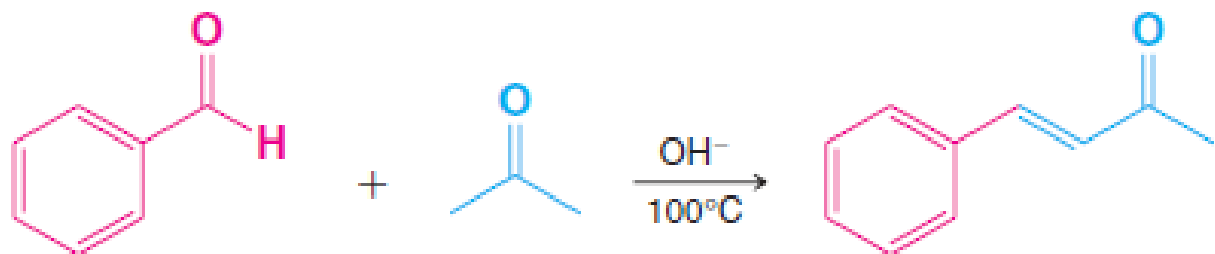
+



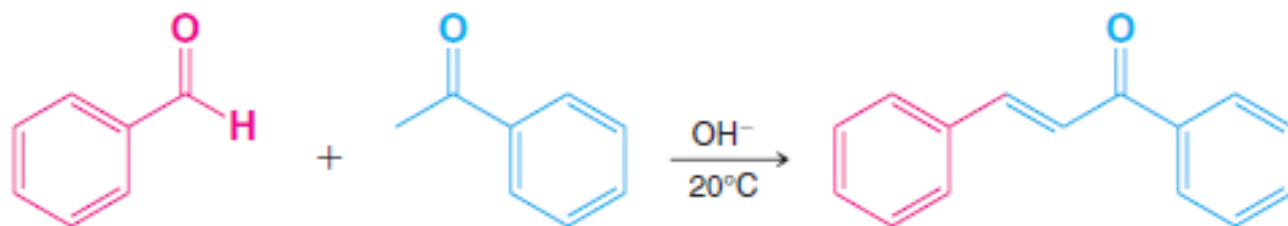
2-Methylpropanal



3-Hydroxy-2,2-
dimethylpropanal
(>64%)

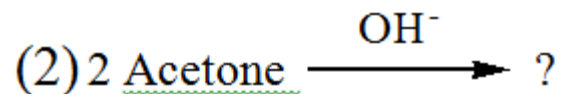


**4-Phenylbut-3-en-2-one
(benzalacetone)
(70%)**



**1,3-Diphenylprop-2-en-1-one
(benzalacetophenone)
(85%)**

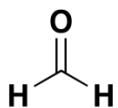
Q/ Give the product for the following reactions:



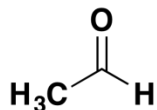
Q/ Give the mechanism of reactions (1) and (2).

Q/ Give the mechanism of aldol condensation under the influence of dilute acid.

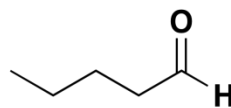
Q/ Are these compounds subjected to Cannizzaro reaction or aldol condensation in the presence of alkaline medium, give the products:



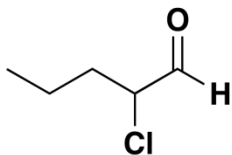
methanal
(formaldehyde)



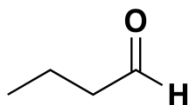
ethanal
(acetaldehyde)



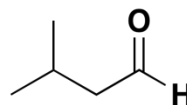
pentanal
(valeraldehyde)



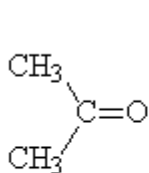
2-chloropentanal
(α -chlorovaleraldehyde)



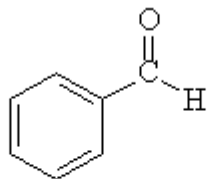
butanal
(butyraldehyde)



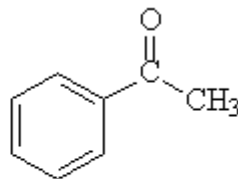
3-methylbutanal
(isovaleraldehyde)



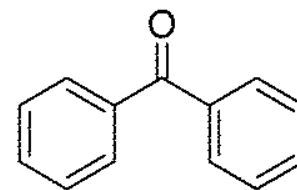
acetone
(propanone)



benzaldehyde



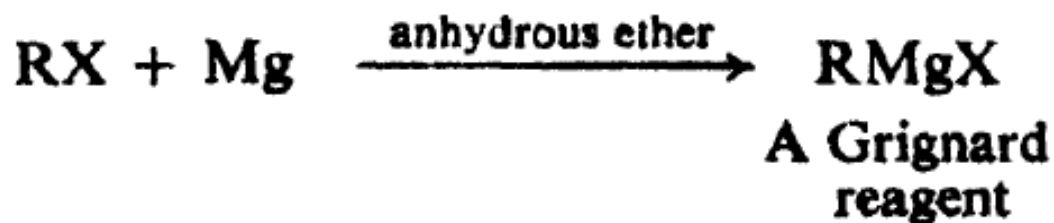
acetophenone



(b) benzophenone

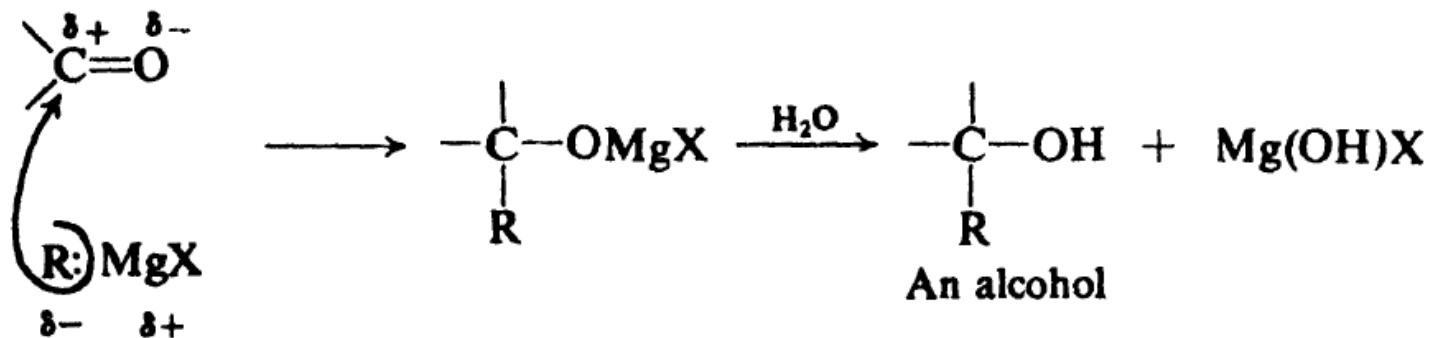
8- Addition of Grignard reagents.

The Grignard reagent has the formula RMgX , and is prepared by the reaction of **metallic magnesium with the appropriate organic halide**. This halide can be alkyl (1, 2, 3), allylic, aralkyl (e.g., benzyl), or aryl (phenyl or substituted phenyl).



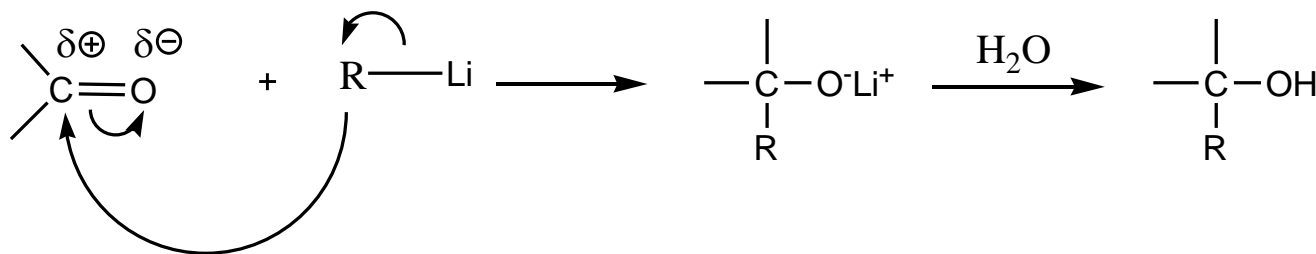
Grignard reagent reacts with **aldehydes and ketones** to yield **alcohols**.

Mechanism



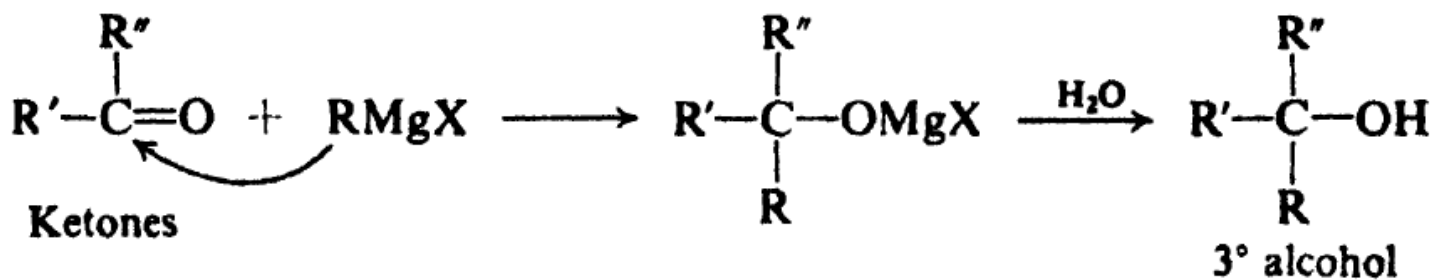
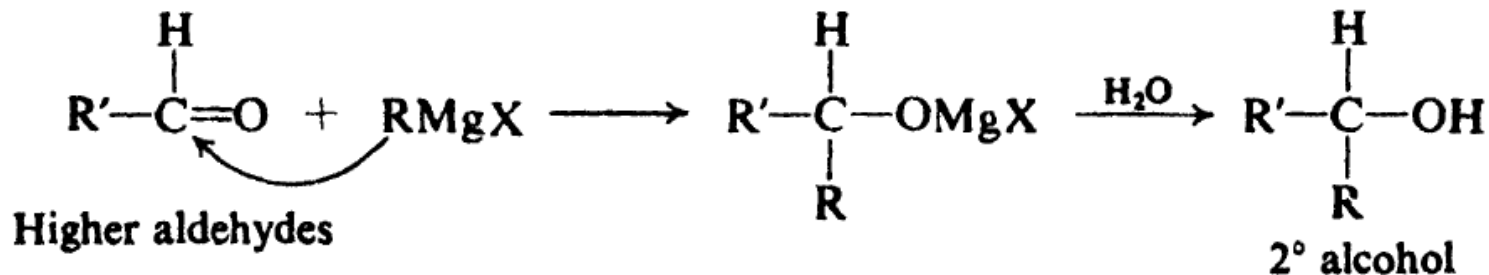
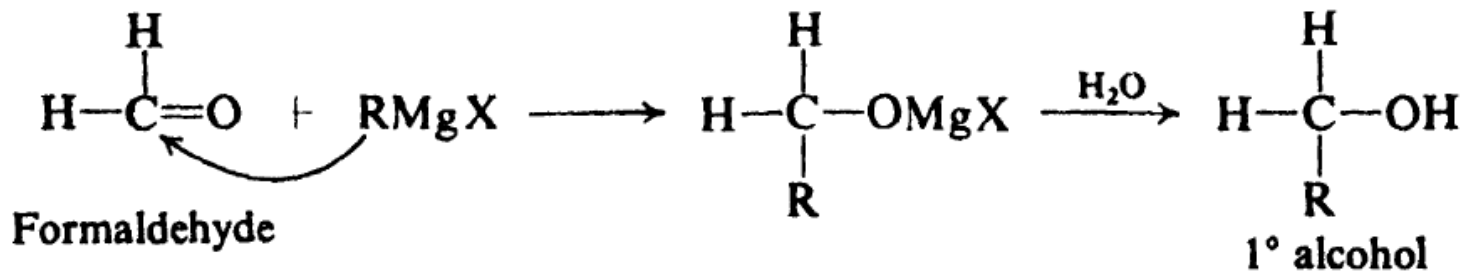
The **carbon-magnesium bond** of the Grignard reagent is a **highly polar bond**, carbon being negative relative to electropositive magnesium. It is not surprising, then, that in the **addition to carbonyl compounds**, the organic group becomes attached to carbon and magnesium to oxygen. The product is the magnesium salt of the weakly acidic alcohol and is easily converted into the alcohol itself by the addition of the stronger acid, water.

Organolithium compounds are used instead of Grignard because, give less unwanted side reactions and lithium is more electropositive than magnesium,



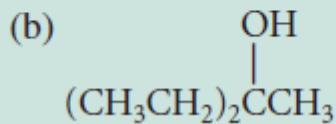
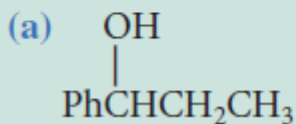
Products of the Grignard synthesis

The class of alcohol that is obtained from a Grignard synthesis depends upon the type of carbonyl compound used: formaldehyde, $HCHO$, yields primary alcohols; other aldehydes, $RCHO$, yield secondary alcohols; and ketones, R_2CO , yield tertiary alcohols.



Problem

19.22 Show how ethyl bromide can be used as a starting material in the preparation of each of the following compounds. (*Hint: How are Grignard reagents prepared?*)



(c) 1-butanol

