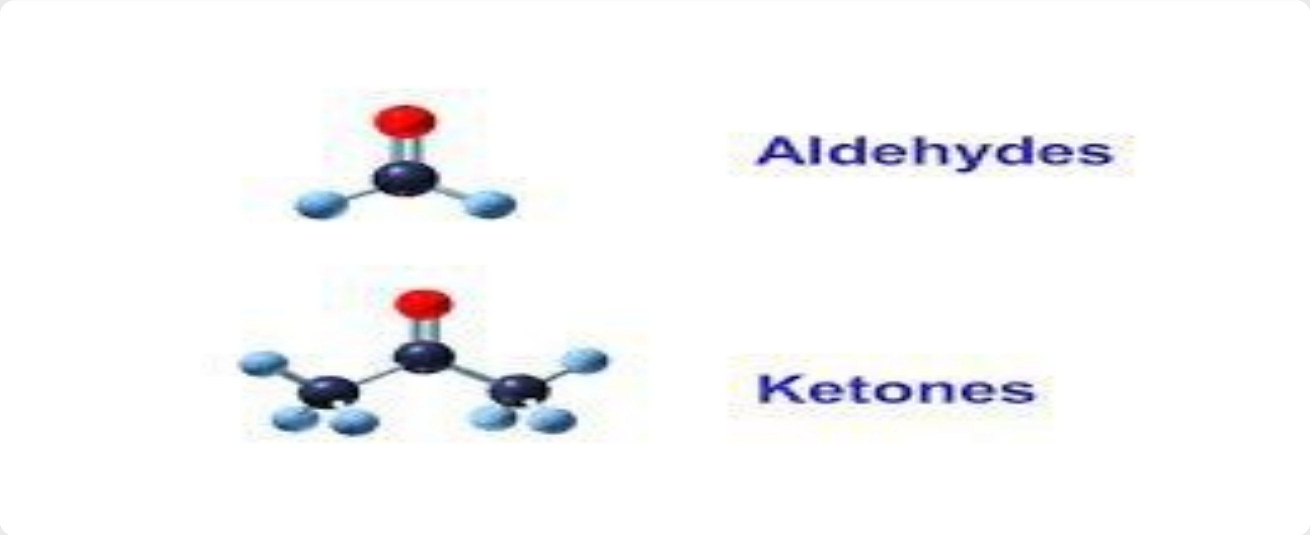
Unıversıty of Zakho
Colleage basic education Department
of general science 2nd stage
(2020-2021)

- ***Reactıon of Aldehydes and Ketones***



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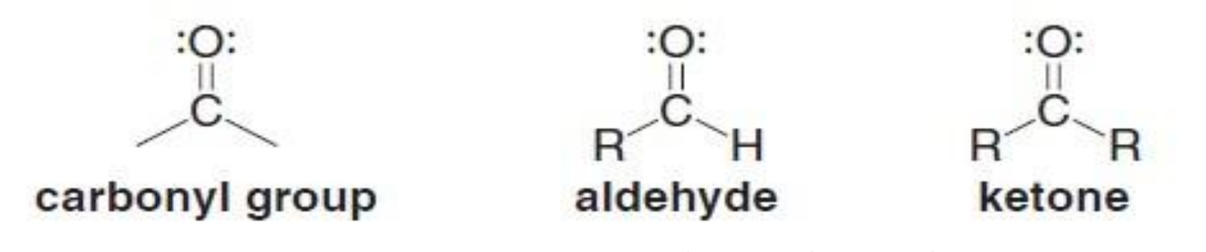
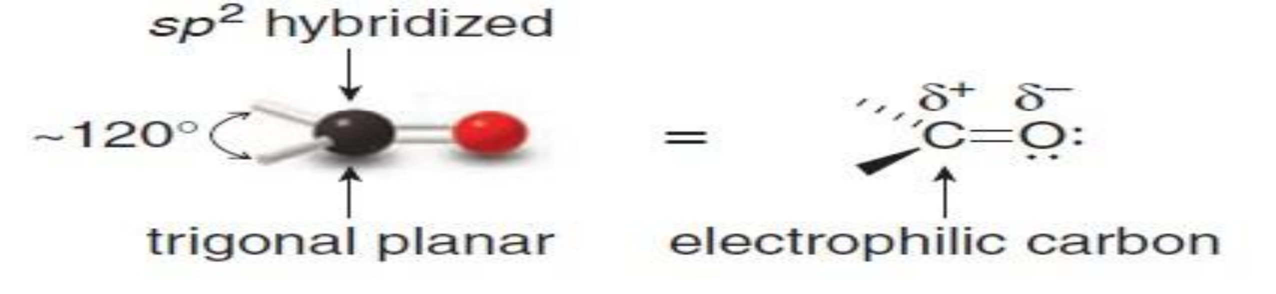
1-1 Introduction of Aldehydes and ketones (1)

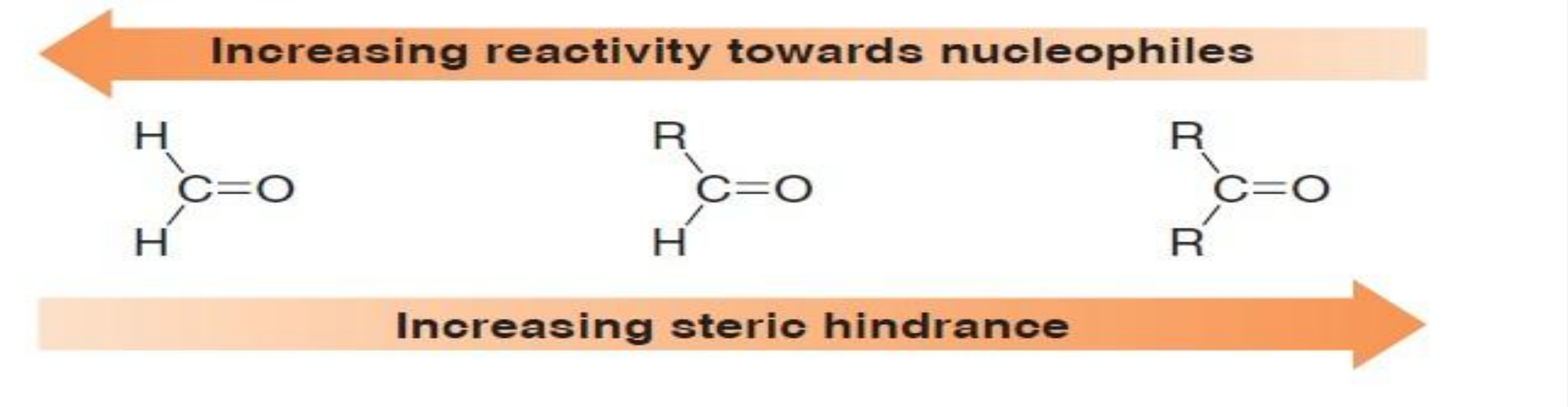
aldehydes and ketones contain a carbonyl group. An aldehyde contains at least one H atom bonded to the carbonyl carbon, whereas a ketone has two alkyl or aryl groups bonded to it



An aldehyde is often written as RCHO. Remember that the H atom is bonded to the carbon atom, not the oxygen. Likewise, a ketone is written as RCOR, or if both alkyl groups are the same, R2CO. Each structure must contain a C—O for every atom to have an octet.: v Two structural features determine the chemistry and properties of aldehydes and ketones.



- **The carbonyl group is sp2 hybridized and trigonal planar, making it relatively uncrowded.**
- **The electronegative oxygen atom polarizes the carbonyl group, making the carbonyl carbon electrophilic. As a result, aldehydes and ketones react with nucleophiles. The relative reactivity of the carbonyl group is determined by the number of R groups bonded to it. As the number of R groups around the carbonyl carbon increases, the reactivity of the carbonyl compound decreases, resulting in the following order of reactivity:**

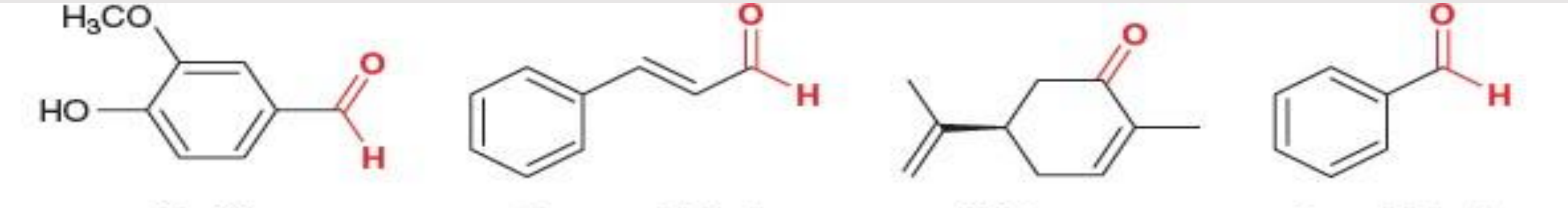


- Increasing the number of alkyl groups on the carbonyl carbon decreases reactivity for both steric and electronic reasons, as discussed in Section 20.2B.

1-1,1 Aldehydes and Ketones (2)

Aldehydes (RCHO) and ketones (R2CO) are similar in structure in that both classes of compounds possess a CRO bond, called a carbonyl group

- The carbonyl group of an aldehyde is flanked by a hydrogen atom, while the carbonyl group of a ketone is flanked by two carbon atoms. Aldehydes and ketones are responsible for many flavor and odors that you will readily recognize:



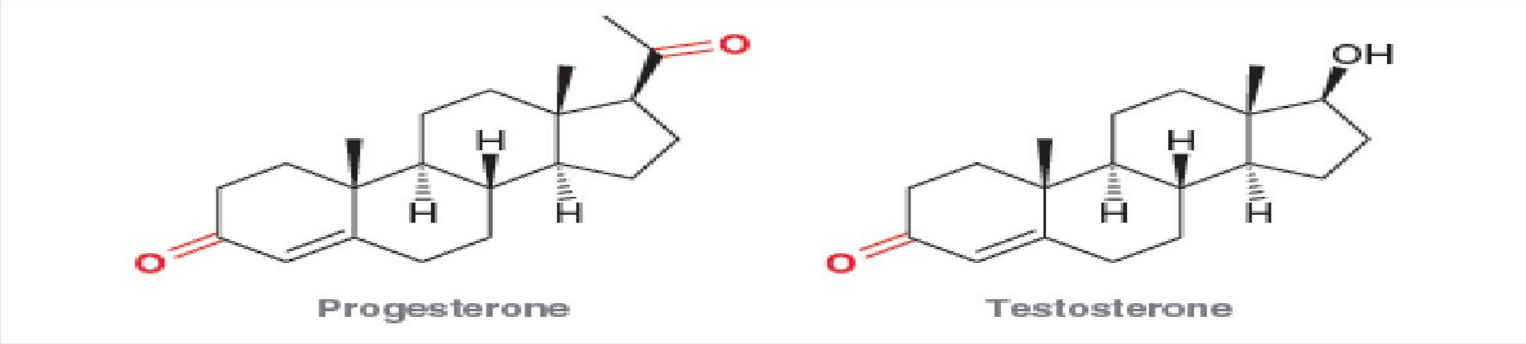
Vanillin (Vanilla flavor)

Cinnamaldehyde (Cinnamon flavor)

(*R*)-Carvone (Spearmint flavor)

Benzaldehyde (Almond flavor)

Many important biological compounds also exhibit the carbonyl group, including progesterone and testosterone, the female and male sex hormones



- Simple aldehydes and ketones are industrially important; for example:

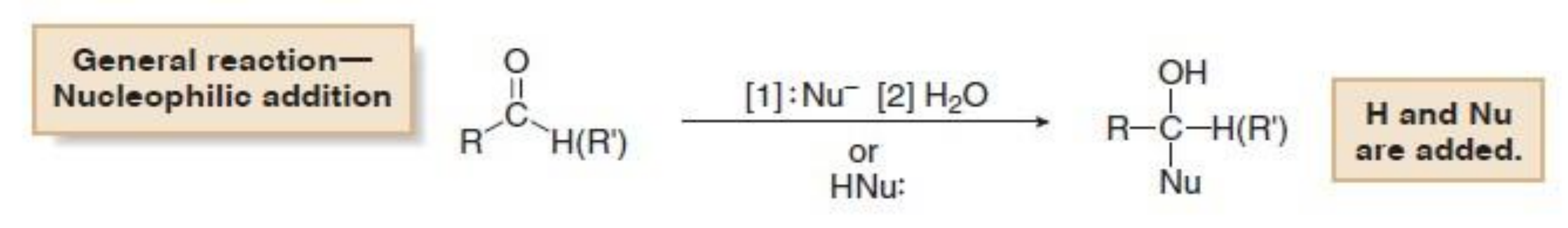
Acetone is used as a solvent and is commonly found in nail polish remover, while formaldehyde is used as a preservative in some vaccine formulations. Aldehydes and ketones are also used as building blocks in the syntheses of commercially important compounds, including pharmaceuticals and polymers. Compounds containing a carbonyl group react with a large variety of nucleophiles, affording a wide range of possible products. Due to the versatile reactivity of the carbonyl group, aldehydes and ketones occupy a central role in organic chemistry.

1-2 Reactions of Aldehydes and Ketones— General Considerations (1)

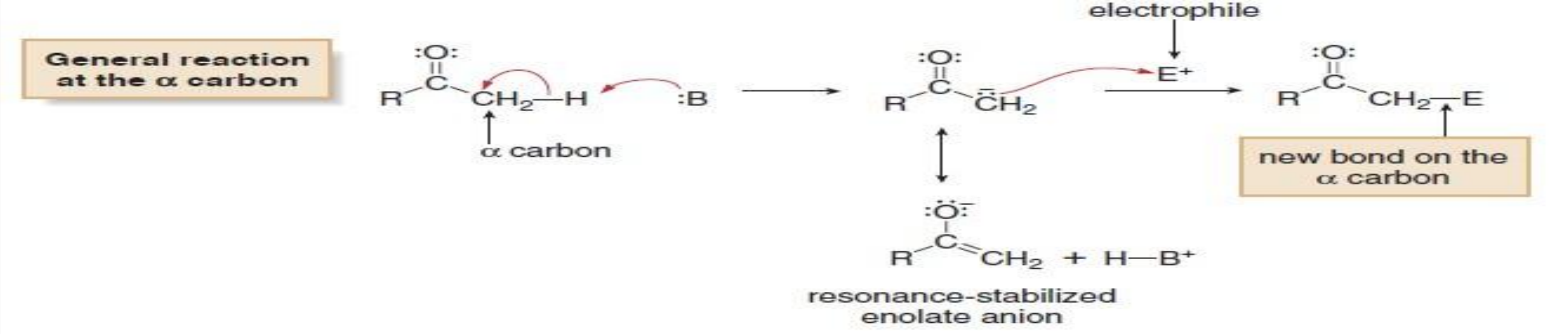
Let’s begin our discussion of carbonyl reactions by looking at the two general kinds of reactions that aldehydes and ketones undergo.

[1] Reaction at the carbonyl carbon

electrophilic carbonyl carbon makes aldehydes and ketones susceptible to nucleophilic addition reactions. The elements of H and Nu are added to the carbonyl group.



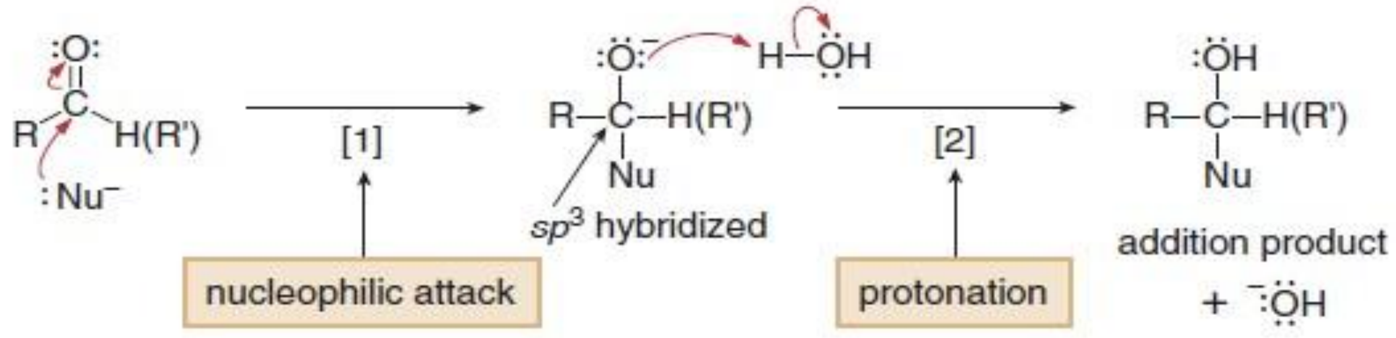
- [2] Reaction at the carbon
- Enolates are nucleophiles, and so they react with electrophiles to form new bonds on the ` carbon
- Aldehydes and ketones react with nucleophiles at the carbonyl carbon.
- Aldehydes and ketones form enolates that react with electrophiles at the ` carbon.



1-3 The General Mechanism of Nucleophilic Addition (1)

Two general mechanisms are usually drawn for nucleophilic addition, depending on the nucleophile (negatively charged versus neutral) and the presence or absence of an acid catalyst.
With negatively charged nucleophiles, nucleophilic addition follows the two-step process

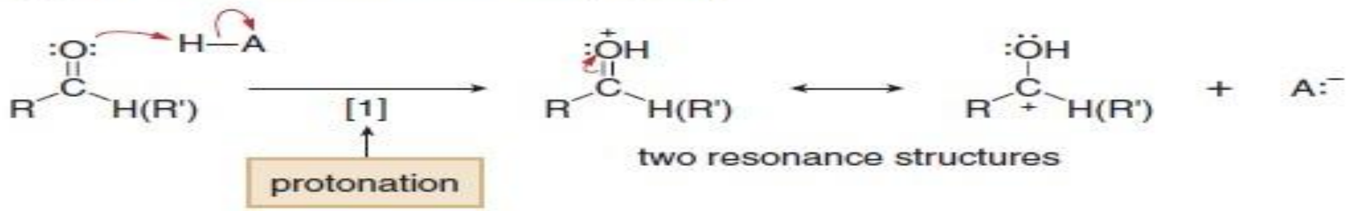
General Mechanism—Nucleophilic Addition (1)



- In Step [1], **the nucleophile attacks the carbonyl group,** cleaving the π bond and moving an electron pair onto oxygen. This forms an sp^3 hybridized intermediate with a new C – Nu bond.
- In Step [2], **protonation of the negatively charged O atom by H_2O** forms the addition product.

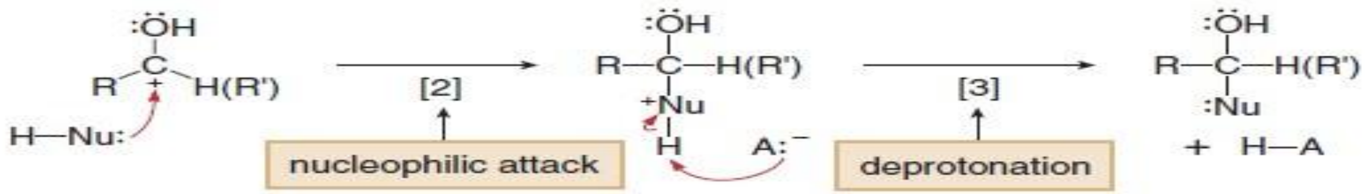
General Mechanism—Acid-Catalyzed Nucleophilic Addition (1)

Step [1] Protonation of the carbonyl group



- Protonation of the carbonyl oxygen forms a resonance-stabilized cation that bears a full positive charge.

Steps [2]–[3] Nucleophilic attack and deprotonation



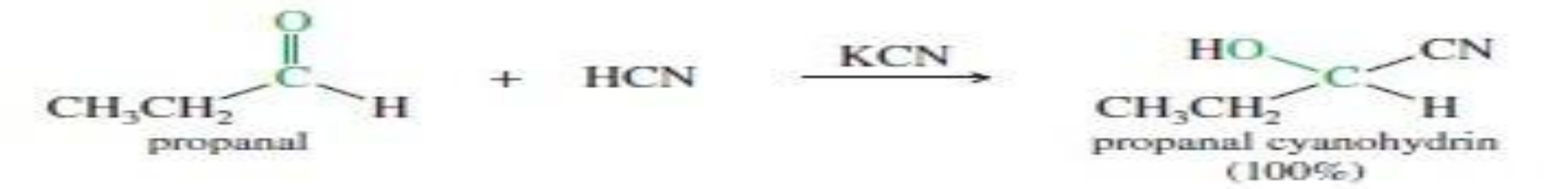
- In Step [2], the nucleophile attacks, and then deprotonation forms the neutral addition product in Step [3].
- The overall result is the addition of H and Nu to the carbonyl group.

1-4 Formation of Cyanohydrins (4)

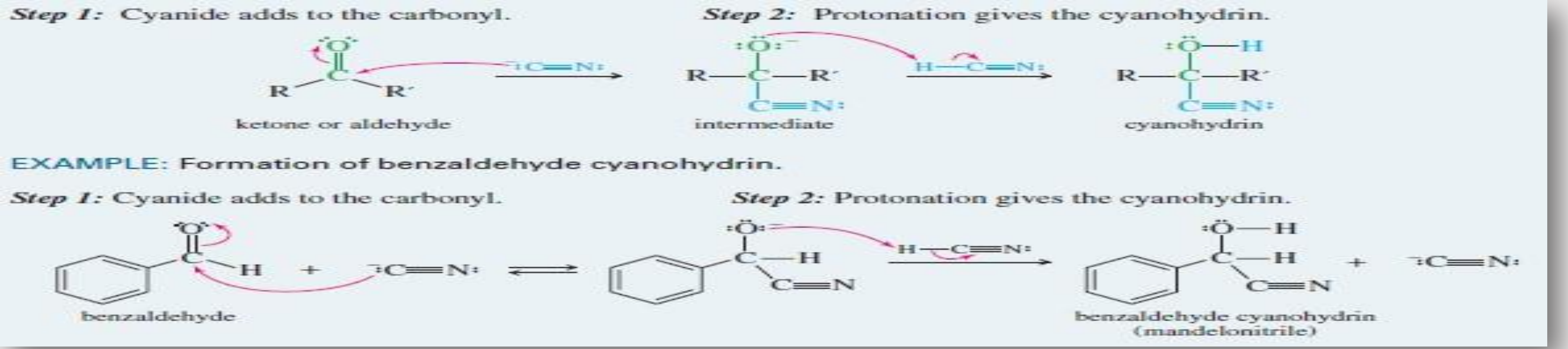
Hydrogen cyanide is a toxic, water-soluble liquid that boils at 26 °C. Because it is mildly acidic, HCN is sometimes called hydrocyanic acid. The conjugate base of hydrogen cyanide is the cyanide ion Cyanide ion is a strong base and a strong nucleophile. It attacks ketones and aldehydes to give addition products called cyanohydrins. The mechanism is a base-catalyzed nucleophilic addition, as shown in Mechanism 18-4. Cyanide ion attacks the carbonyl group, forming an alkoxide ion that protonates to give the cyanohydrin.

$(H-C\equiv N)$

$$H-C\equiv N: + H_2O \rightleftharpoons H_3O^+ + {}^-:C\equiv N: \quad pK_a = 9.2$$



• Mechanısm -Formation of Cyanohydrins


Step 1: Cyanide adds to the carbonyl.

Step 2: Protonation gives the cyanohydrin.

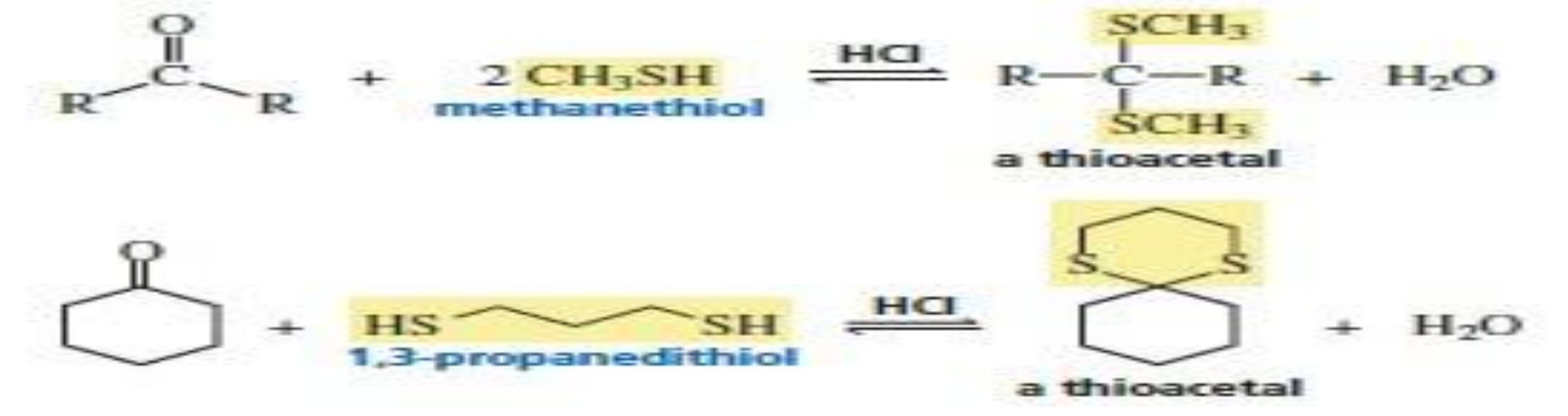
EXAMPLE: Formation of benzaldehyde cyanohydrin.

Step 1: Cyanide adds to the carbonyl.

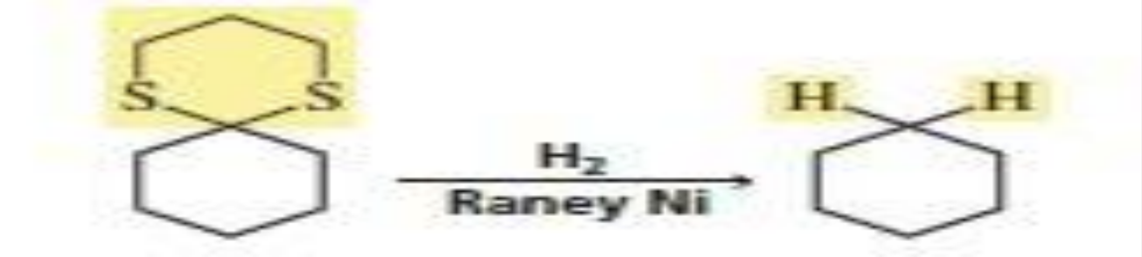
Step 2: Protonation gives the cyanohydrin.

1-5 Reactions Of Aldehydes And Ketones With Sulfur Nucleophiles (3)

Aldehydes and ketones react with thiols (the sulfur analogues of alcohols) The mechanism for the addition of a thiol is the same as the mechanism for the addition of an alcohol Thioacetal formation is useful in organic synthesis because a thioacetal is desulfurized when it reacts with H2 and Raney nickel. Desulfurization replaces the C—S bonds with C—H bonds.



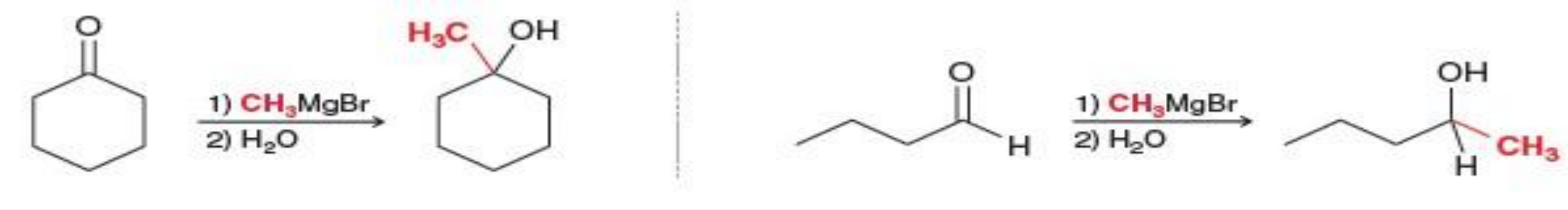
Thus, thioacetal formation followed by desulfurization provides a way to convert a carbonyl grou into a methylene group.



1-6 Reaction Of Aldehydes And Ketones With Carbon Nucleophiles

(2)

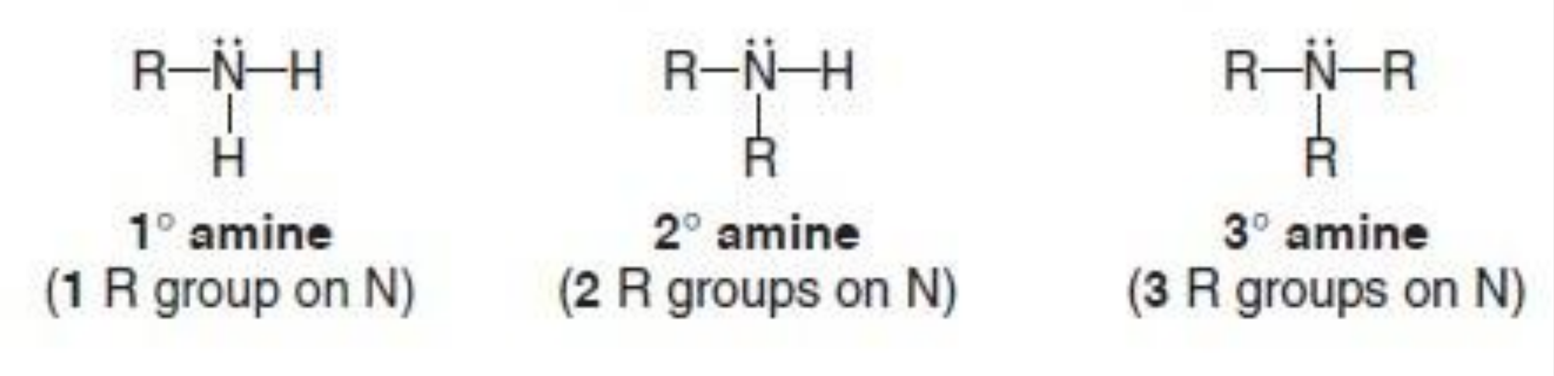
Grignard Reagents When treated with a Grignard reagent, aldehydes and ketones are converted into alcohols, accompanied by the formation of a new C|C bond:



The mechanism of action for these reagents has been heavily investigated and is fairly complex

1-7 Addition of 1° Amines (Formation of Imine) (1)

We now move on to the reaction of aldehydes and ketones with nitrogen and oxygen hetero atoms. Amines, for example, are organic nitrogen compounds that contain a nonbonded electron pair on the N atom. Amines are classified as 1°, 2°, or 3° by the number of alkyl groups bondedto the nitrogen atom

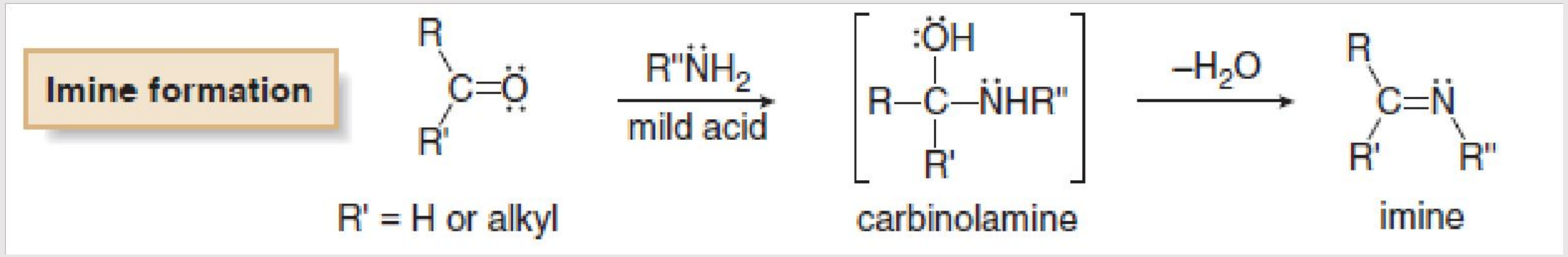


1° amine (1 R group on N)

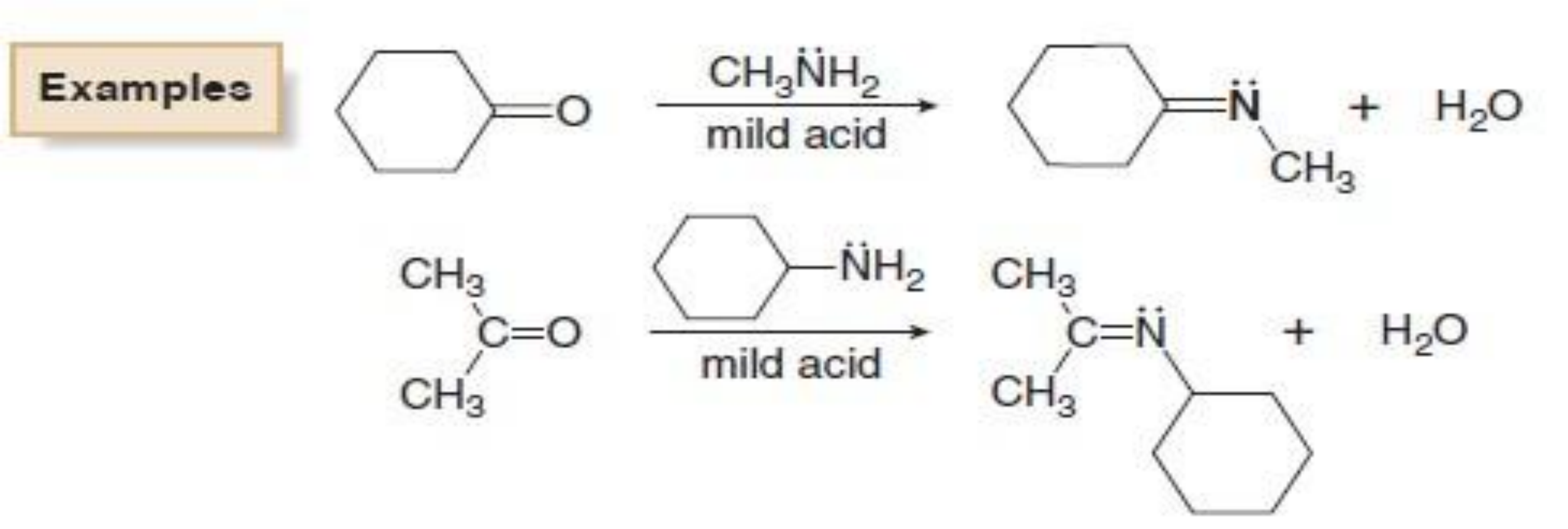
2° amine (2 R groups on N)

3° amine (3 R groups on N)

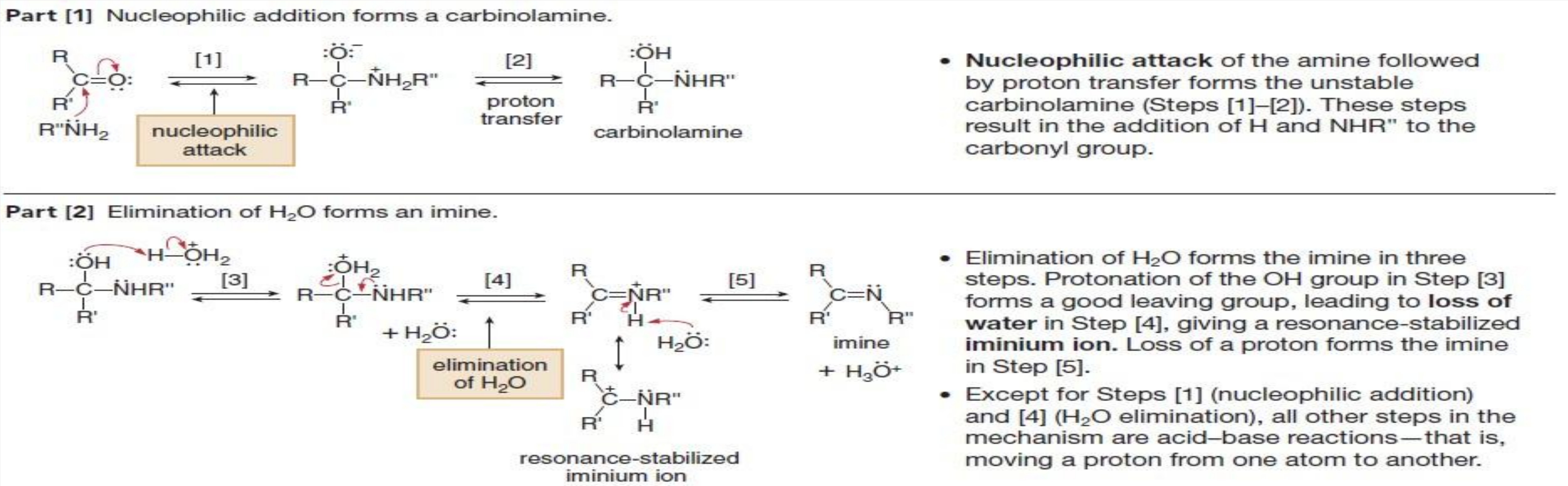
replacement of C— O by C–NR



- **Because the N atom of an imine is surrounded by three groups (two atoms and a lone pair), it is sp2 hybridized, making the C –N– R" bond angle ~120° (not 180°). Imine formation is fastest when the reaction medium is weakly acidic**



MECHANISM- Imine Formation from an Aldehyde or Ketone



Part [1] Nucleophilic addition forms a carbinolamine.

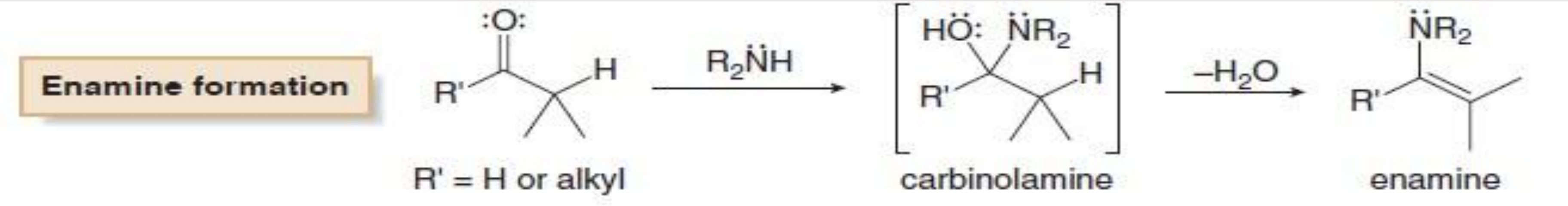
- **Nucleophilic attack** of the amine followed by proton transfer forms the unstable carbinolamine (Steps [1]–[2]). These steps result in the addition of H and NHR" to the carbonyl group.

Part [2] Elimination of H_2O forms an imine.

- Elimination of H_2O forms the imine in three steps. Protonation of the OH group in Step [3] forms a good leaving group, leading to **loss of water** in Step [4], giving a resonance-stabilized **iminium ion.** Loss of a proton forms the imine in Step [5].
- Except for Steps [1] (nucleophilic addition) and [4] (H_2O elimination), all other steps in the mechanism are acid–base reactions—that is, moving a proton from one atom to another.

1-8 Addition of 2° Amin(Formation of Enamines) (1)

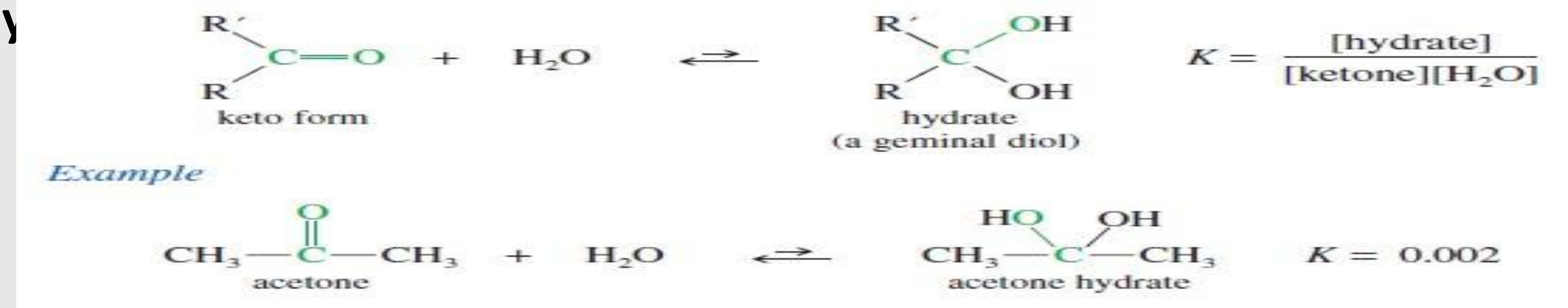
A 2° amine reacts with an aldehyde or ketone to give an enamine. Enamines have a nitrogen atom bonded to a double bond (alkene + amine = enamine)



1-9 Hydration of Ketones and Aldehydes

(4)

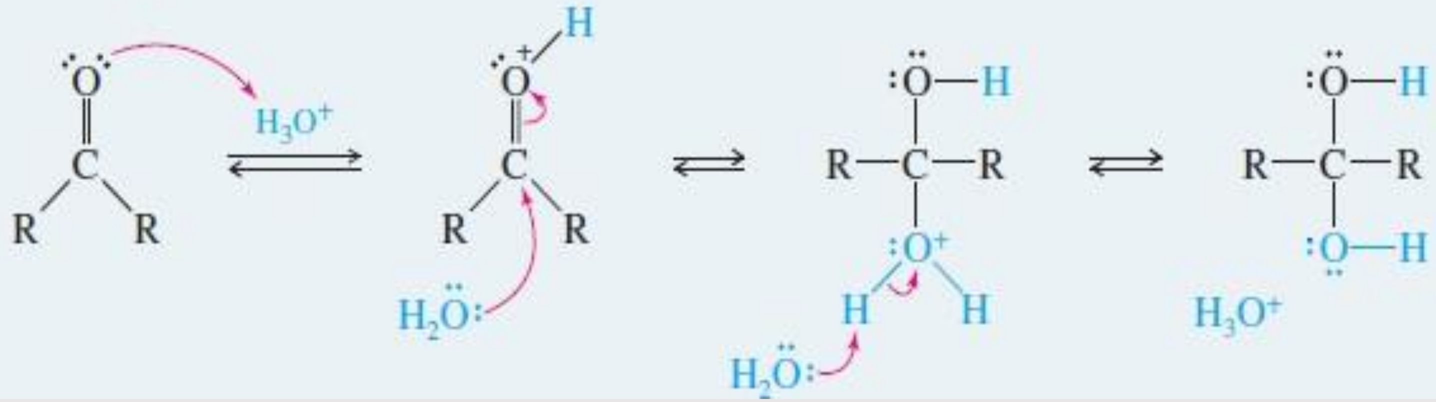
In an aqueous solution, a ketone or an aldehyde is in equilibrium with its hydrate, a geminal diol. With most ketones, the equilibrium favors the unhy



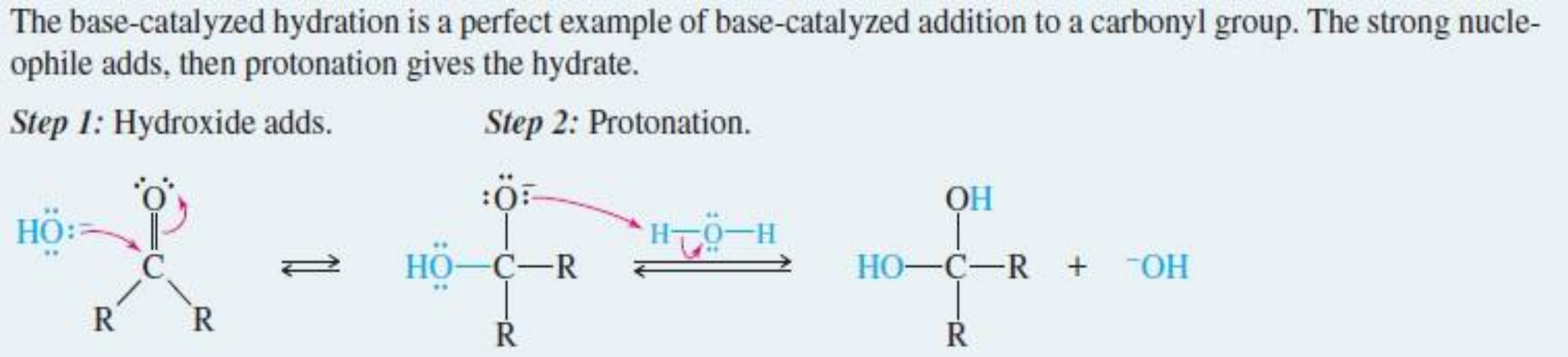
MECHANISM-Hydration of Ketones and Aldehydes In Acıd

The acid-catalyzed hydration is a typical acid-catalyzed addition to the carbonyl group. Protonation, followed by addition of water, gives a protonated product. Deprotonation gives the hydrate.

Step 1: Protonation. *Step 2:* Water adds. *Step 3:* Deprotonation.



In Base



The base-catalyzed hydration is a perfect example of base-catalyzed addition to a carbonyl group. The strong nucleophile adds, then protonation gives the hydrate.

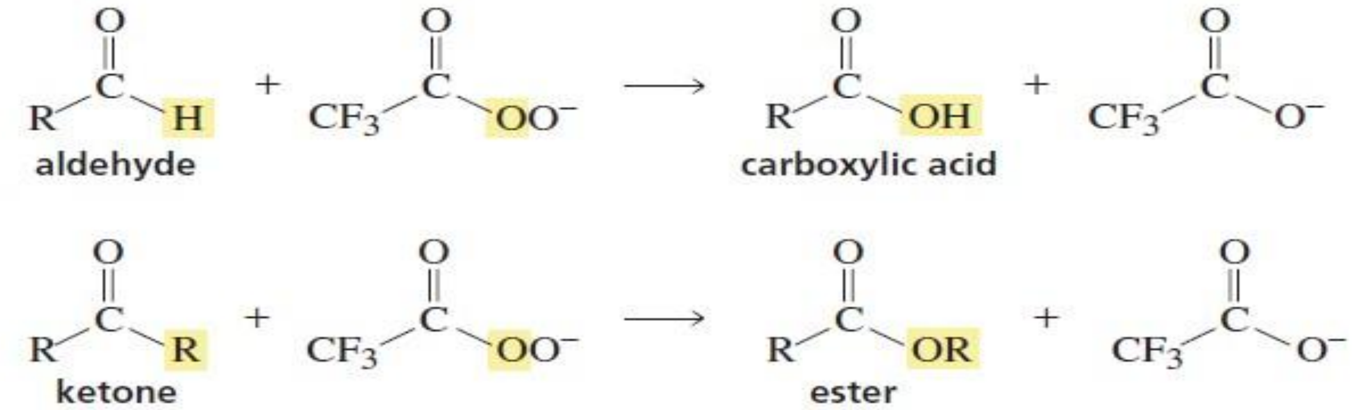
Step 1: Hydroxide adds.

Step 2: Protonation.

- **In basic conditions, a strong nucleophile usually adds directly to the carbonyl group. In acidic conditions, strong nucleophiles are rarely present. An acid (or Lewis acid) usually protonates the carbonyl to activate it toward attack by a weak nucleophile.**

1-10 REACTIONS OF ALDEHYDES AND KETONES WITH A PEROXYACID (3)

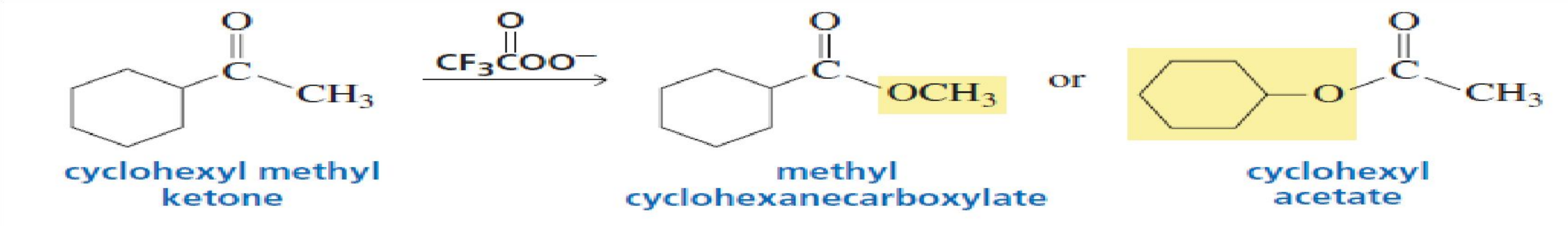
Aldehydes and ketones react with the conjugate base of a peroxyacid to form carboxylic acids and esters, respectively. Recall that a peroxyacid contains one more oxygen than a carboxylic acid and it is this oxygen that is inserted between the carbonyl carbon and the H of an aldehyde or the R of a ketone (see the top of the next page) The reaction is called a Baeyer–Villiger oxidation. It is an Oxidation reaction because the number of C¬O bonds increases. A particularly good reagent for a Baeyer–Villiger oxidation is peroxytrifluoroacetate ion



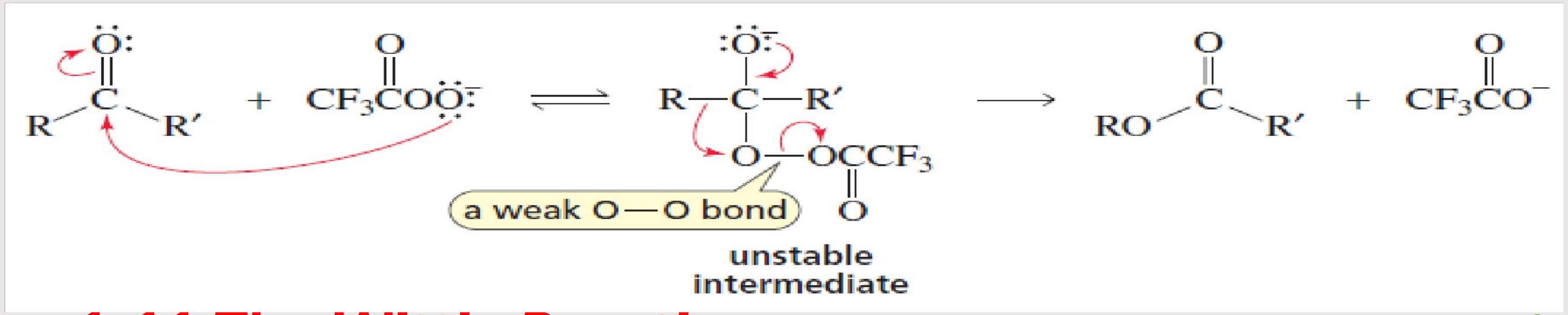
Aldehydes are oxidized to carboxylic acids by a peroxyacid.

Ketones are oxidized to esters by a peroxyacid.

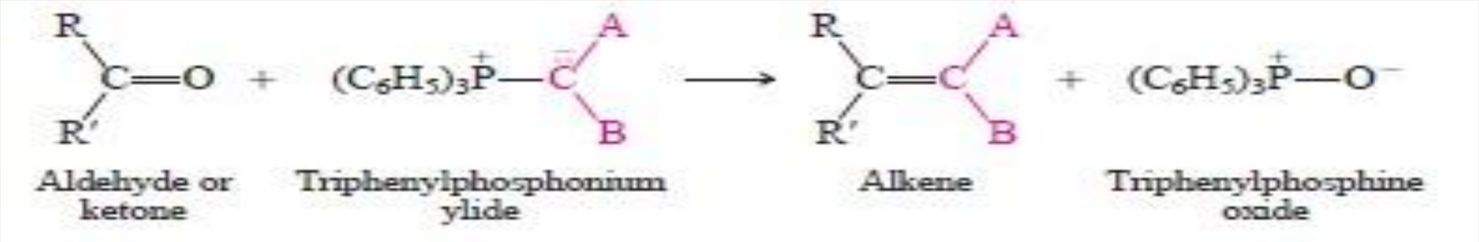
- **If the two alkyl substituents attached to the carbonyl group of the ketone are different, thenon what side of the carbonyl carbon is the oxygen inserted? For example, does the oxidation of cyclohexyl methyl ketone form methyl cyclohexanecarboxylate or cyclohexyl acetate?**



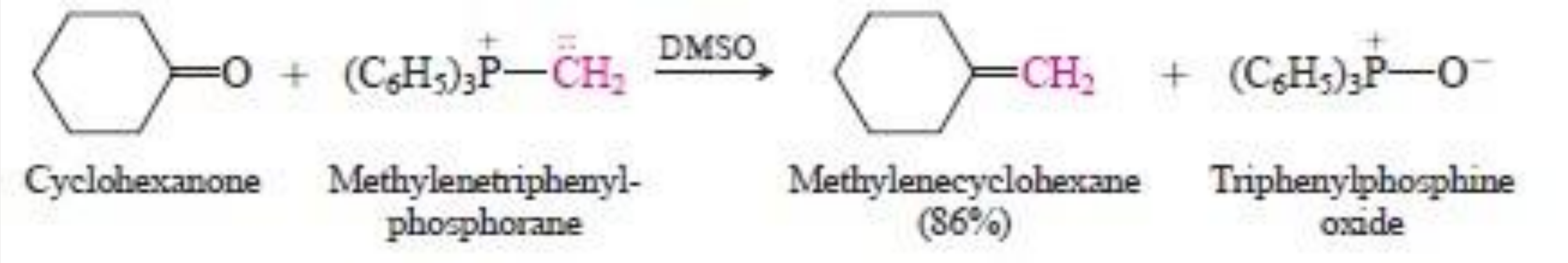
Mechanism For The Baeyer–villiger Oxidation



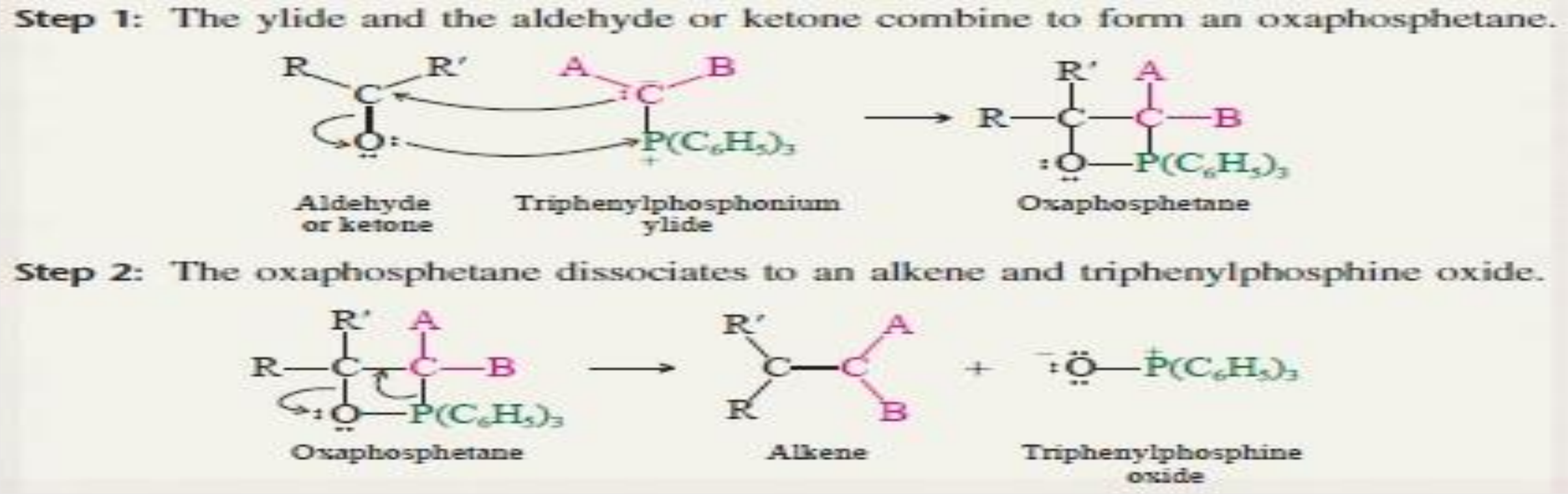
- **1-11 The Wittig Reaction** (5)
- **The Wittig reaction uses phosphorus ylides (called Wittig reagents) to convert aldehydes and ketones to alkenes**



Wittig reactions may be carried out in a number of different solvents; normally tetrahydrofuran (THF) or dimethyl sulfoxide (DMSO) is used.



MECHANISM-The Wittig Reaction



Step 1: The ylide and the aldehyde or ketone combine to form an oxaphosphetane.

Step 2: The oxaphosphetane dissociates to an alkene and triphenylphosphine oxide.

give an alkene and triphenylphosphine oxide. Presumably the direction of dissociation of the oxaphosphetane is dictated by the strong phosphorus–oxygen bond that results. The POO bond strength in triphenylphosphine oxide has been estimated to be greater than 540 kJ/mol (130 kcal/mol).