



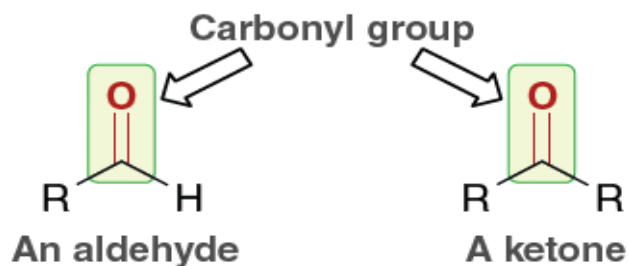
# Aldehydes and Ketones

## Part 1

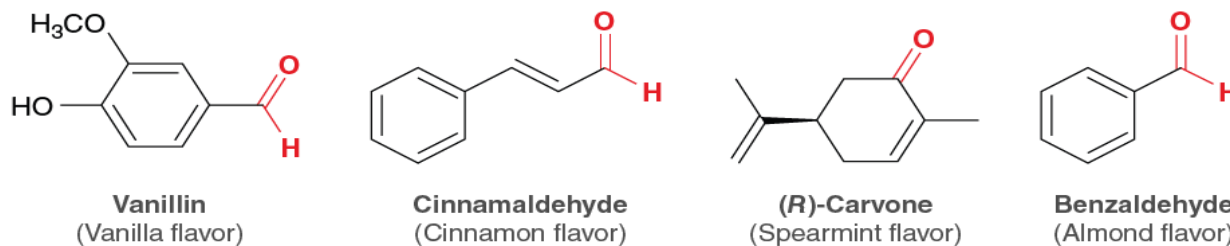
*Organic Chemistry*  
*Pharmacy College / 2<sup>nd</sup> Stage*  
*Dr. Sham Wali Qurban*

# 19.1 Introduction to Aldehydes and Ketones

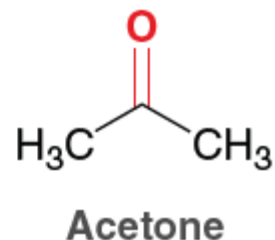
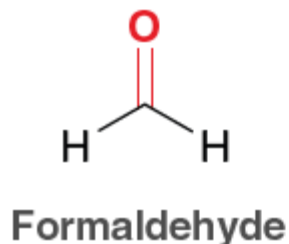
Aldehydes ( $\text{RCHO}$ ) and ketones ( $\text{R}_2\text{CO}$ ) are similar in structure in that both classes of compounds possess a  $\text{C}=\text{O}$  bond, called a *carbonyl group*:



Aldehydes and ketones are responsible for many flavors and odors that you will readily recognize:



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



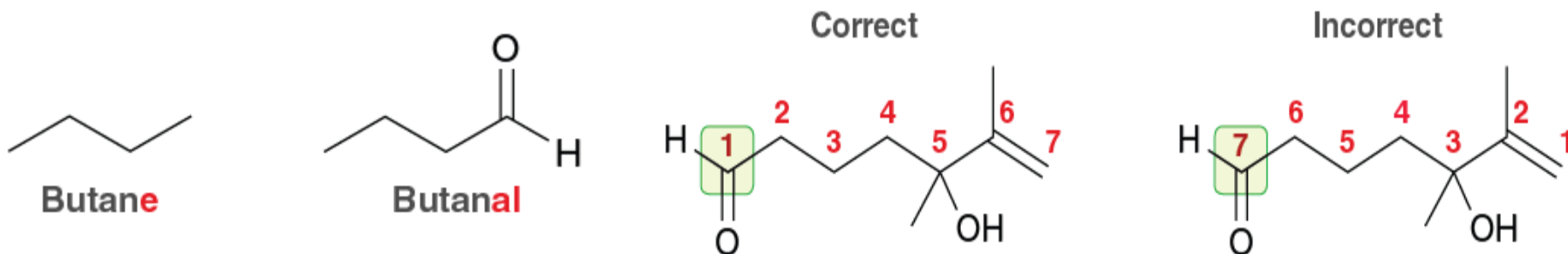
- **Formaldehyde** is used as a preservative in some vaccine formulations,
- while **acetone** is used as a solvent and is commonly found in nail polish remover.
- Aldehydes and ketones are also used as building blocks in the syntheses of commercially important compounds, including **pharmaceuticals 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.

# 19.2 Nomenclature

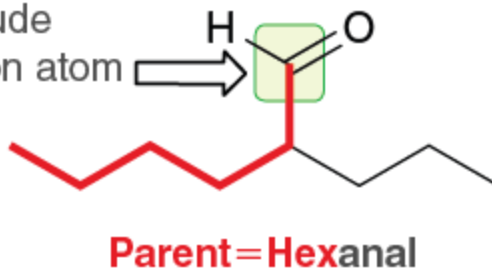
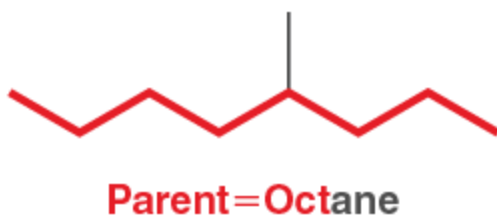
- Nomenclature of Aldehydes**

**Aldehydes** are also named using the same four-step procedure. When applying this procedure for naming aldehydes, the following guidelines should be followed:

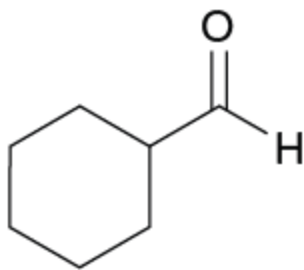
- When naming the parent, the suffix **“-al”** indicates the presence of an aldehyde group:



The parent must include this carbon atom

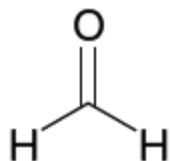


A cyclic compound containing an aldehyde group immediately adjacent to the ring is named as a carbaldehyde:

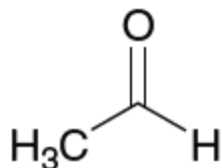


Cyclohexanecarbaldehyde

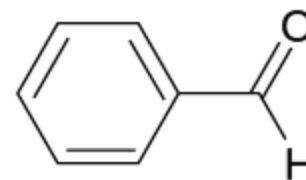
- **The International Union of Pure and Applied Chemistry (IUPAC)** nomenclature also recognizes the common names of many simple aldehydes, including the following examples:



Formaldehyde



Acetaldehyde

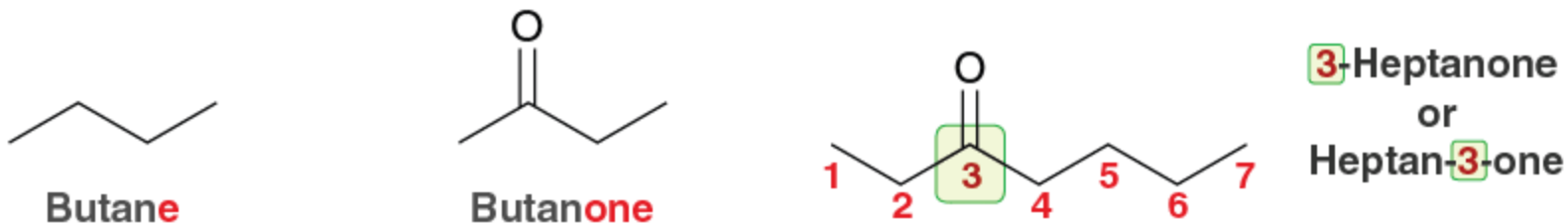


Benzaldehyde

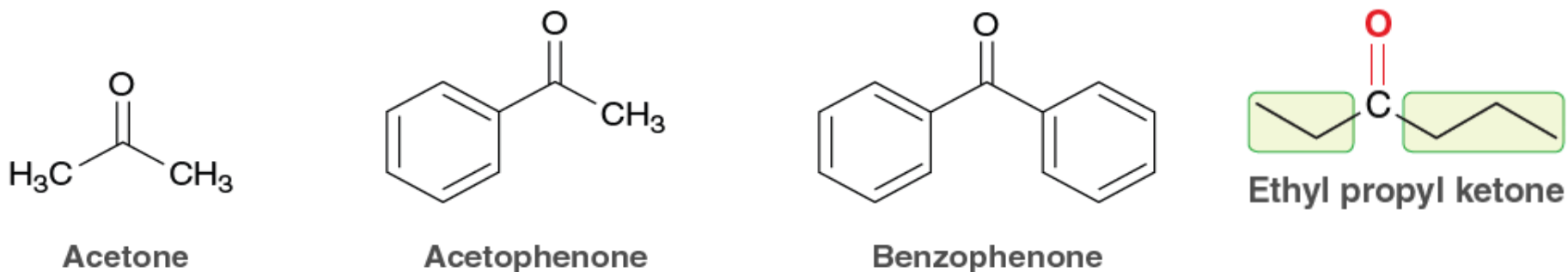


- **Nomenclature of Ketones**

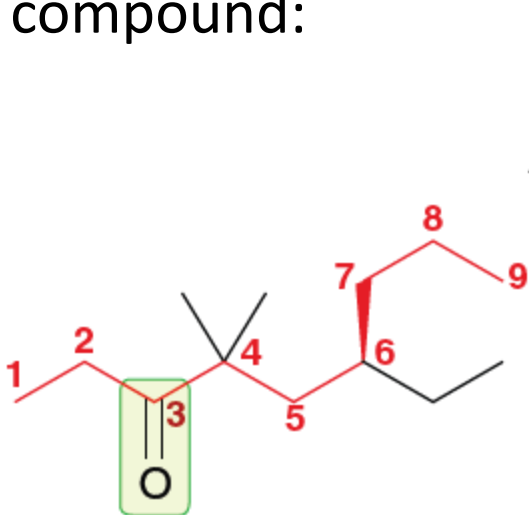
**Ketones**, like aldehydes, are named using the same four-step procedure. When naming the parent, the suffix “**-one**” indicates the presence of a ketone group:



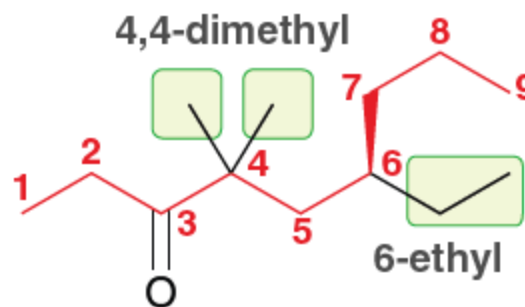
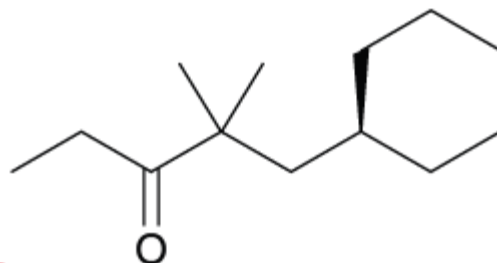
**IUPAC** nomenclature recognizes the common names of many simple ketones, including the following examples:



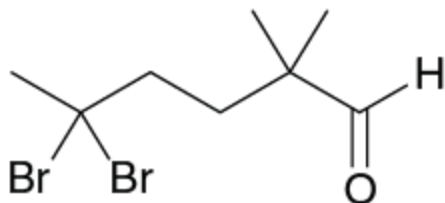
**19.1** Provide a systematic (IUPAC) name for the following compound:



3-Nonanone

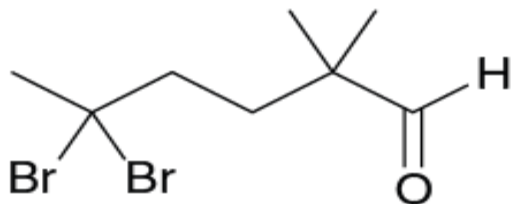


**(R)-6-ethyl-4,4-dimethyl-3-nonanone.**



**(S)-3,3-Dibromo-4-ethylcyclohexanone**

**19.1 Assign a systematic (IUPAC) name to each of the following compounds:**



**19.2 Draw the structure of each of the following compounds:**

**(S)-3,3-Dibromo-4-ethylcyclohexanone**

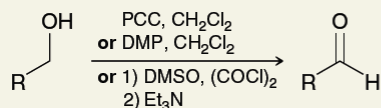


# 19.3 Preparing Aldehydes and Ketones: A Review

**TABLE 19.1** A SUMMARY OF ALDEHYDE PREPARATION METHODS COVERED IN PREVIOUS CHAPTERS

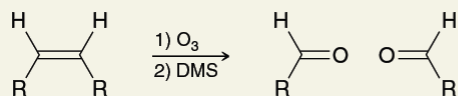
REACTION	SECTION
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<b>Oxidation of Primary Alcohols</b>	12.10
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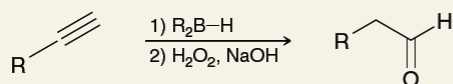
When treated with a strong oxidizing agent, primary alcohols are oxidized to carboxylic acids. Formation of an aldehyde requires a mild oxidizing agent, such as the oxidizing agents shown above, that will not further oxidize the resulting aldehyde.

<b>Ozonolysis of Alkenes</b>	8.13
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Ozonolysis will cleave a C=C double bond. If either carbon atom bears a hydrogen atom, an aldehyde will be formed.

<b>Hydroboration-Oxidation of Terminal Alkynes</b>	9.7
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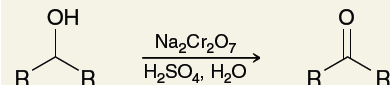


Hydroboration-oxidation results in an *anti*-Markovnikov addition of water across a  $\pi$  bond, followed by tautomerization of the resulting enol to form an aldehyde.

**TABLE 19.2** A SUMMARY OF KETONE PREPARATION METHODS COVERED IN PREVIOUS CHAPTERS

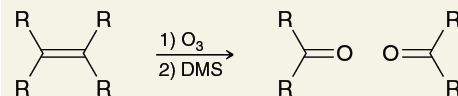
REACTION	SECTION
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<b>Oxidation of Secondary Alcohols</b>	12.10
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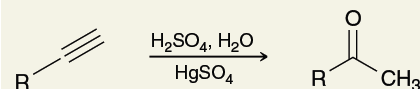
A variety of strong or mild oxidizing agents can be used to oxidize secondary alcohols. The resulting ketone does not undergo further oxidation.

<b>Ozonolysis of Alkenes</b>	8.13
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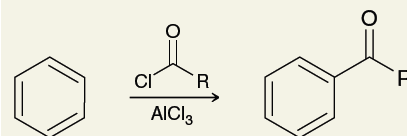
Tetrasubstituted alkenes are cleaved to form ketones.

<b>Acid-Catalyzed Hydration of Terminal Alkynes</b>	9.7
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This procedure results in a Markovnikov addition of water across the  $\pi$  bond, followed by tautomerization to form a methyl ketone.

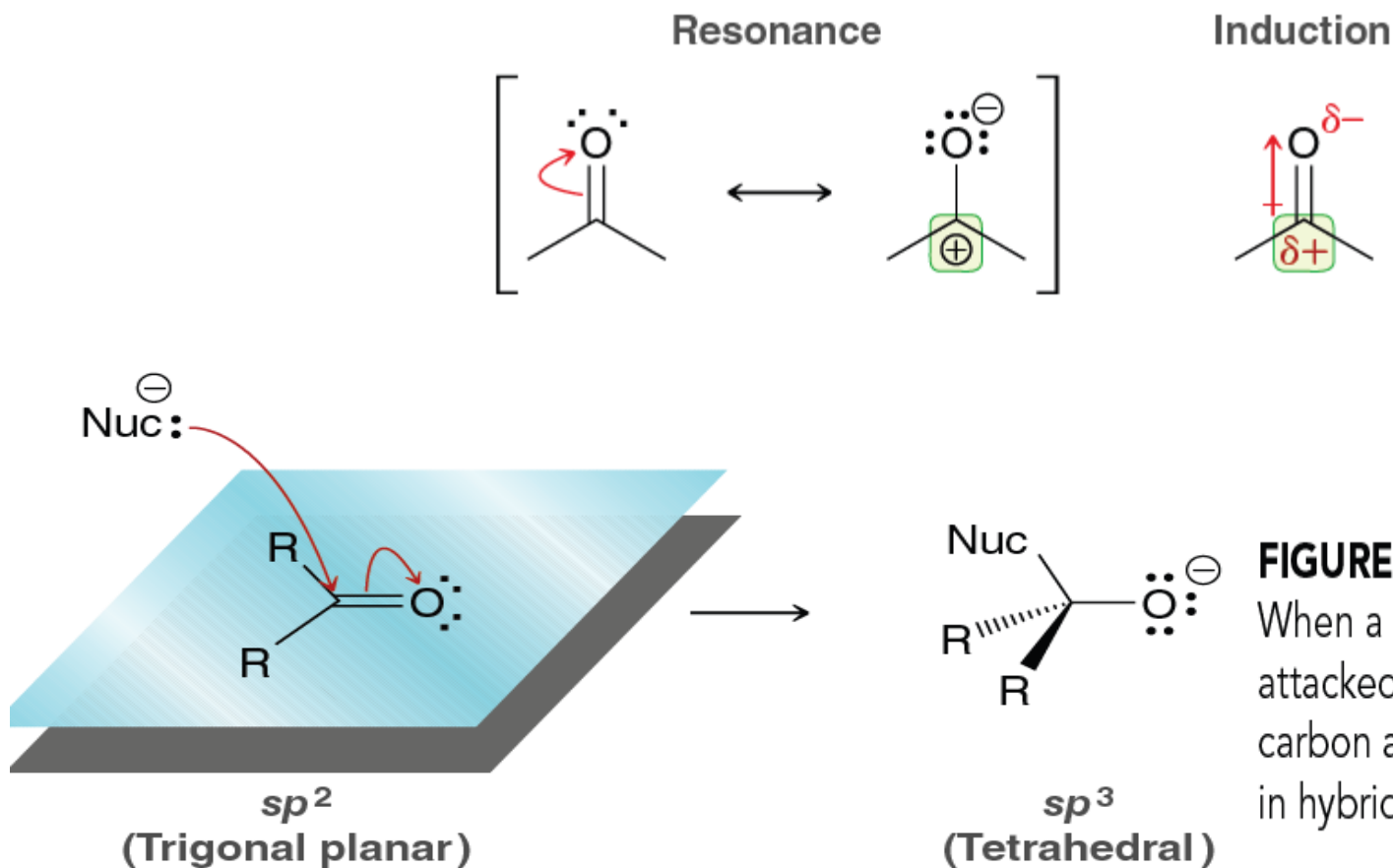
<b>Friedel-Crafts Acylation</b>	18.6
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Aromatic rings that are not too strongly deactivated will react with an acyl halide in the presence of a Lewis acid to produce an aryl ketone.

# 19.4 Introduction to Nucleophilic Addition Reactions

The electrophilicity of a carbonyl group derives from resonance effects as well as inductive effects:



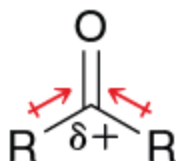
**FIGURE 19.1**

When a carbonyl group is attacked by a nucleophile, the carbon atom undergoes a change in hybridization and geometry.

In general, **aldehydes are more reactive than ketones toward nucleophilic attack**. This observation can be explained in terms of both steric and electronic effects:

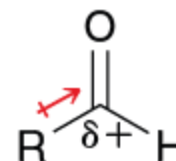
1. ***Steric effects.***

2. ***Electronic effects.***



A ketone

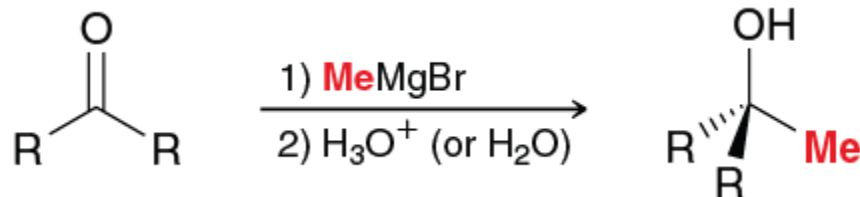
has **two** electron-donating alkyl groups that stabilize the partial positive charge



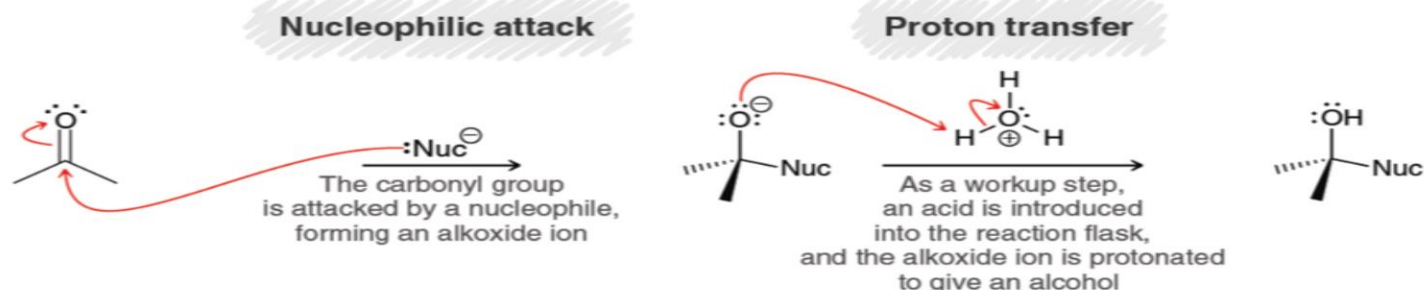
An aldehyde

has **only one** electron-donating alkyl group that stabilizes the partial positive charge

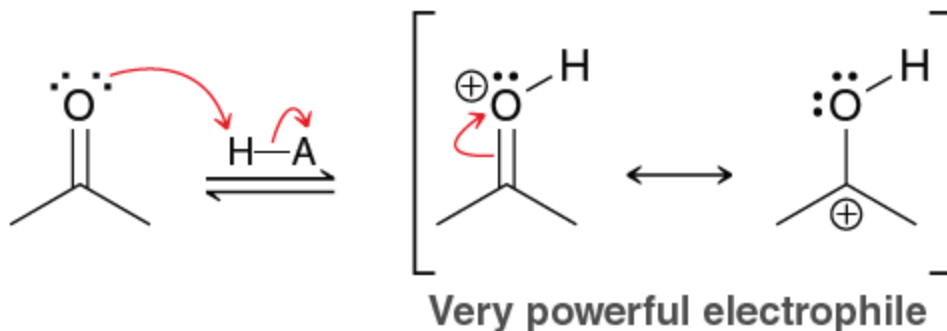
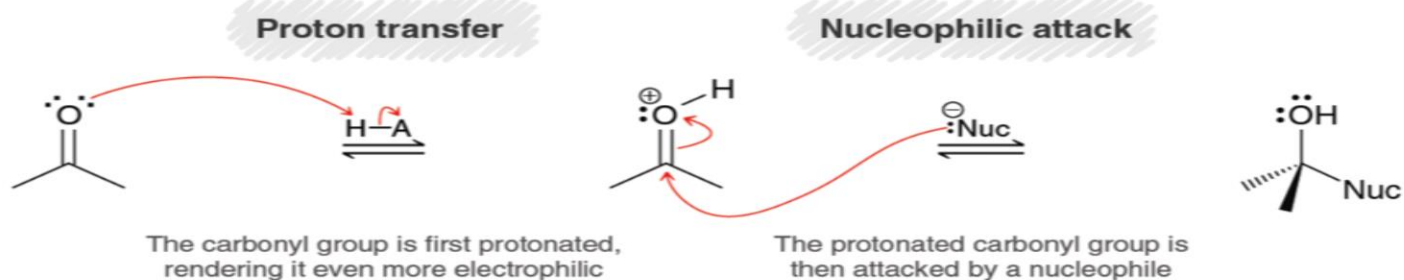
The  $\delta+$  charge of an aldehyde is less stabilized than a ketone. As a result, aldehydes are more electrophilic than ketones and therefore more reactive.



## MECHANISM 19.1 NUCLEOPHILIC ADDITION UNDER BASIC CONDITIONS

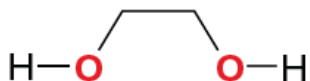
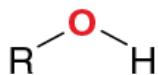
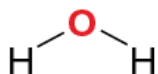


## MECHANISM 19.2 NUCLEOPHILIC ADDITION UNDER ACIDIC CONDITIONS

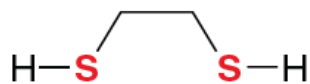
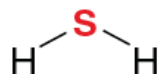


# Various nucleophiles that can attack a carbonyl group.

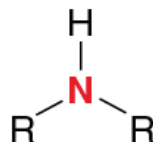
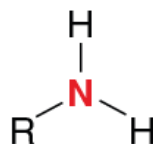
## Oxygen Nucleophiles



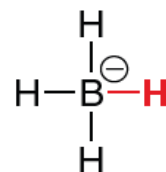
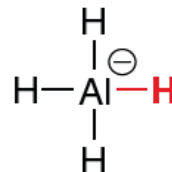
## Sulfur Nucleophiles



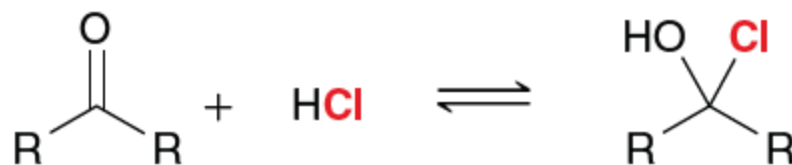
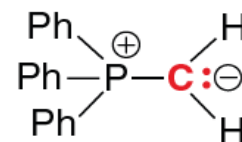
## Nitrogen Nucleophiles



## Hydrogen Nucleophiles



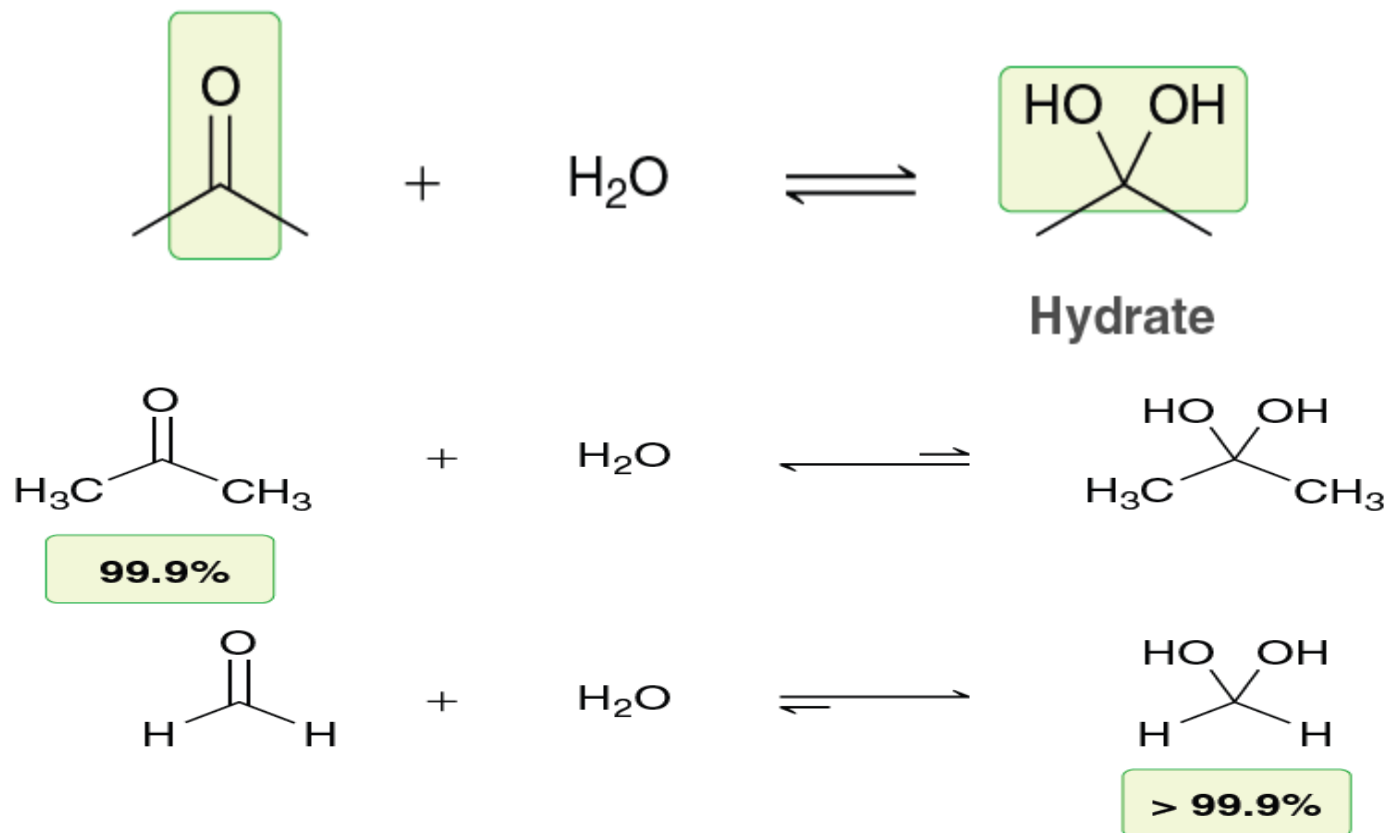
## Carbon Nucleophiles



# 19.5 Oxygen Nucleophiles

- Hydrate Formation

When an aldehyde or ketone is treated with water, the carbonyl group can be converted into a **hydrate**:



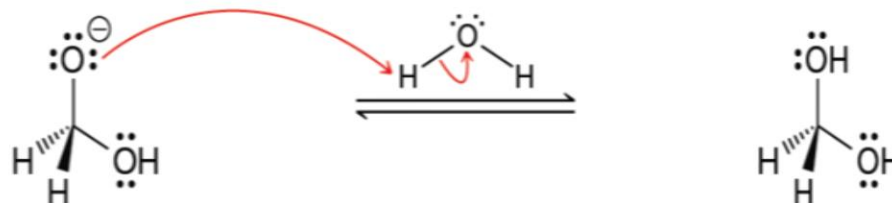
## MECHANISM 19.3 BASE-CATALYZED HYDRATION

### Nucleophilic attack



The carbonyl group is attacked by hydroxide, forming an anionic intermediate

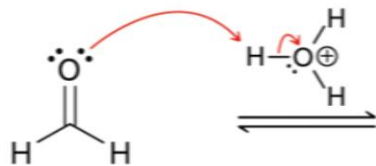
### Proton transfer



The anionic intermediate is protonated by water to form the hydrate

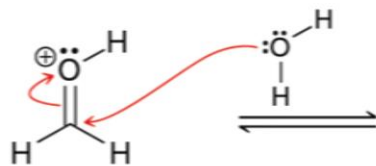
## MECHANISM 19.4 ACID-CATALYZED HYDRATION

### Proton transfer



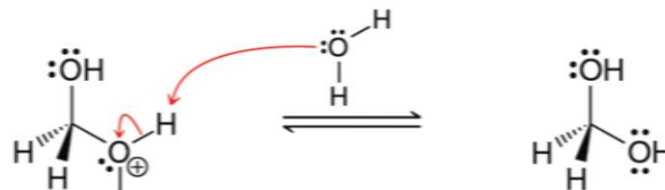
The carbonyl group is protonated, rendering it more electrophilic

### Nucleophilic attack



The protonated carbonyl group is attacked by water, forming an oxonium intermediate

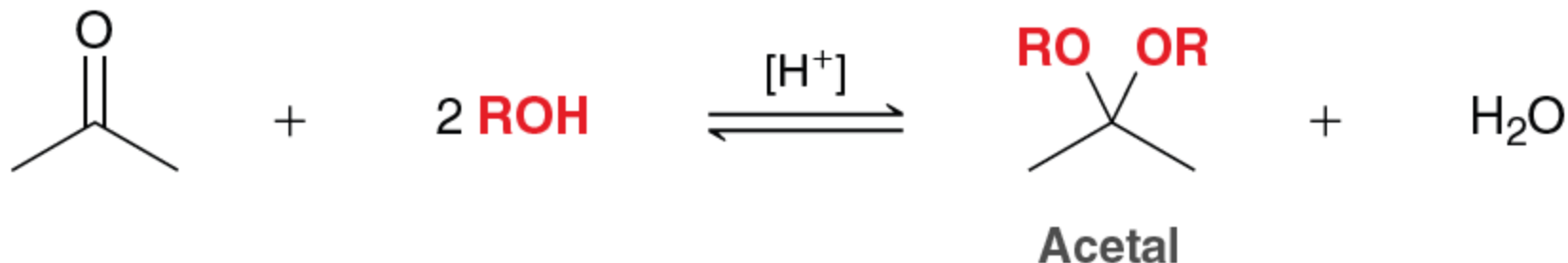
### Proton transfer



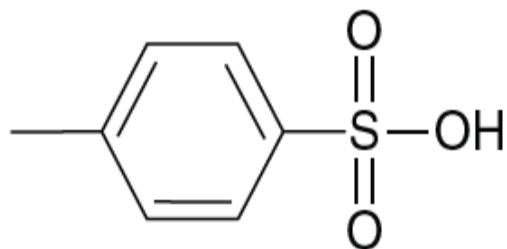
The oxonium intermediate is deprotonated by water to form the hydrate



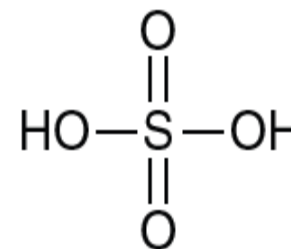
## Acetal Formation



- The brackets surrounding the  $\text{H}^+$  indicate that the acid is a catalyst.



*p*-Toluenesulfonic acid  
(TsOH)



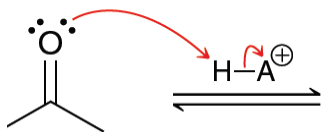
Sulfuric acid

When the starting compound is a ketone, the product can also be called a "ketal." **Acetal** is a more general term,

Common acids

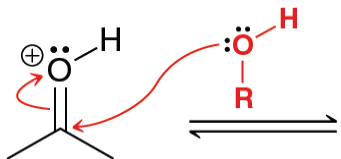
# MECHANISM 19.5 ACETAL FORMATION

## Proton transfer



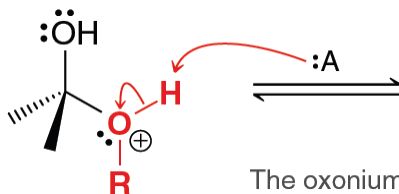
The carbonyl group is protonated, rendering it more electrophilic

## Nucleophilic attack

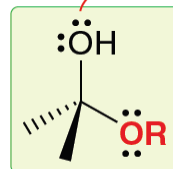


The alcohol attacks the protonated carbonyl to generate an oxonium intermediate

## Proton transfer

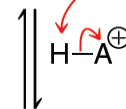


The oxonium intermediate is deprotonated to form a hemiacetal

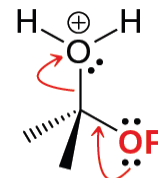


Hemiacetal

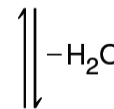
## Proton transfer



The OH group is protonated, thereby converting it into an excellent leaving group

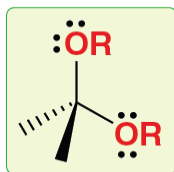


## Loss of a leaving group



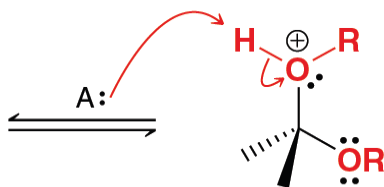
Water leaves to regenerate the C=O double bond

## Proton transfer



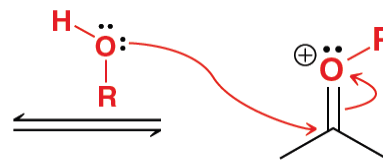
Acetal

## Proton transfer

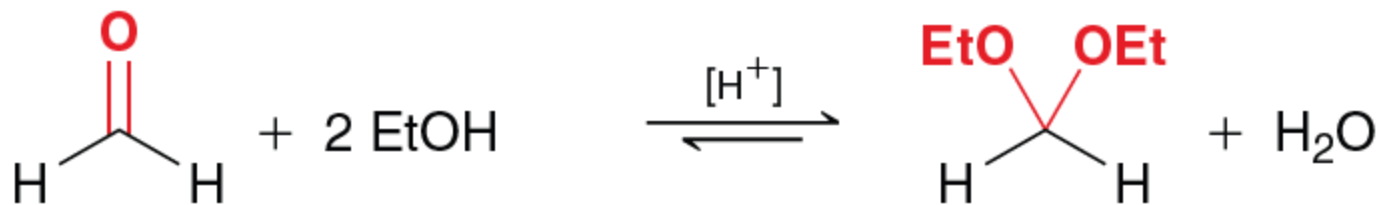


The oxonium intermediate is deprotonated, generating an acetal

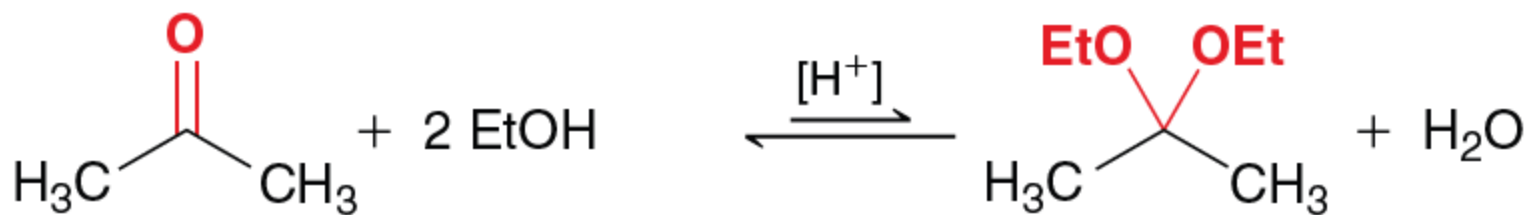
## Nucleophilic attack



The second molecule of the alcohol attacks the C=O double bond to generate another oxonium intermediate

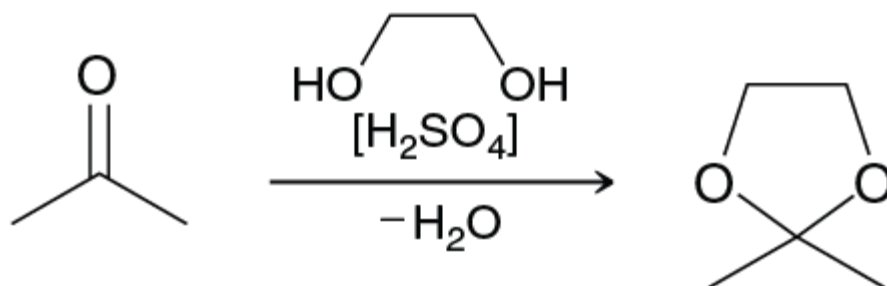
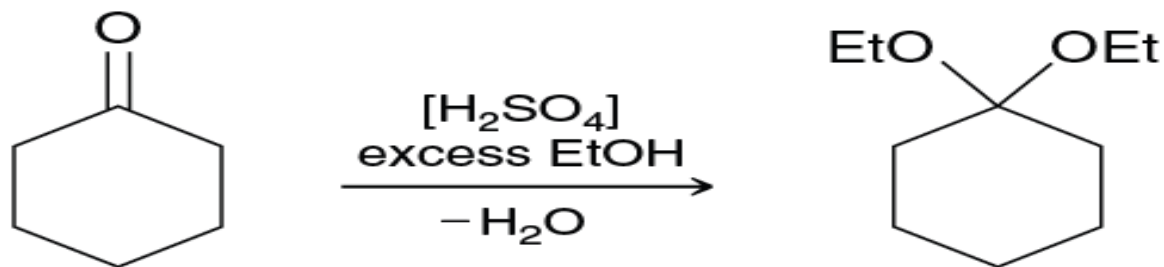
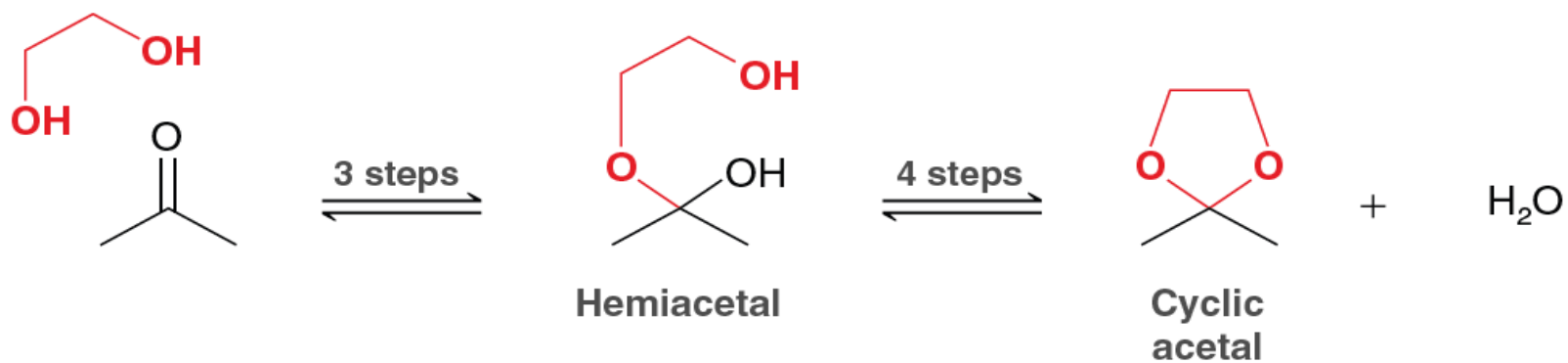


**Products are favored  
at equilibrium**

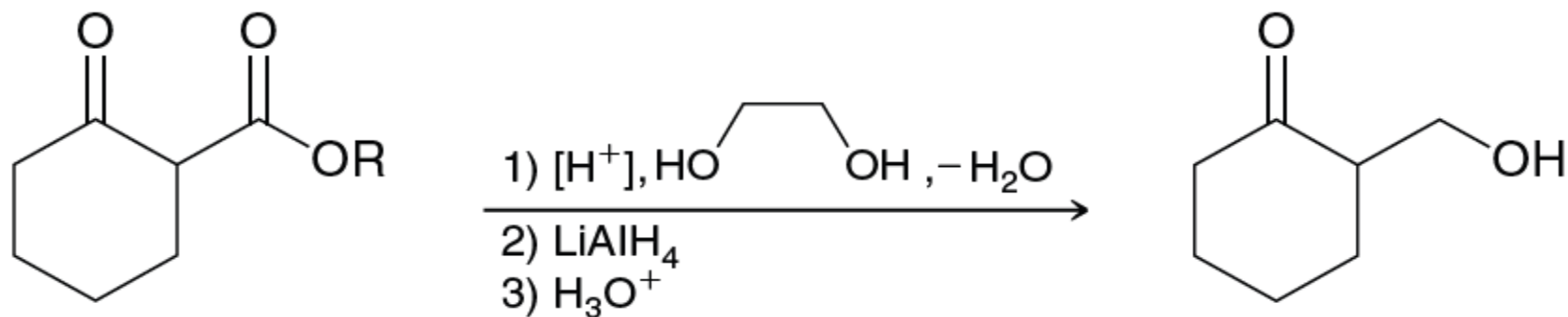
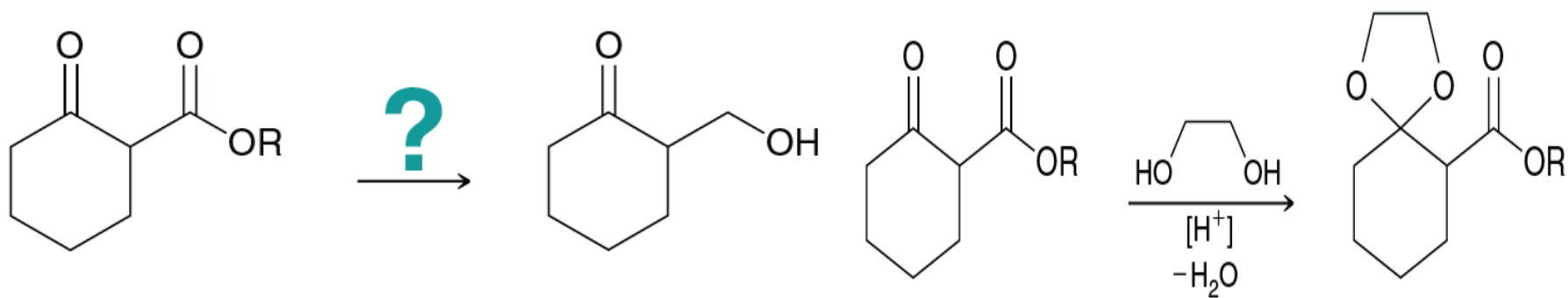
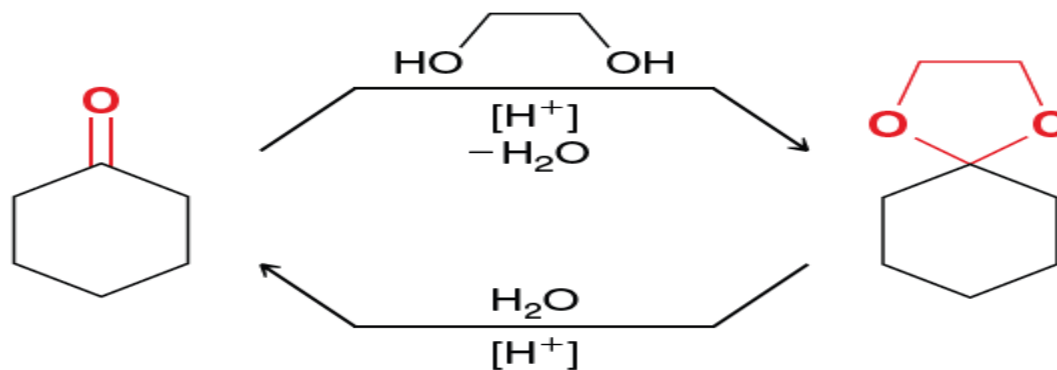


**Reactants are favored  
at equilibrium**

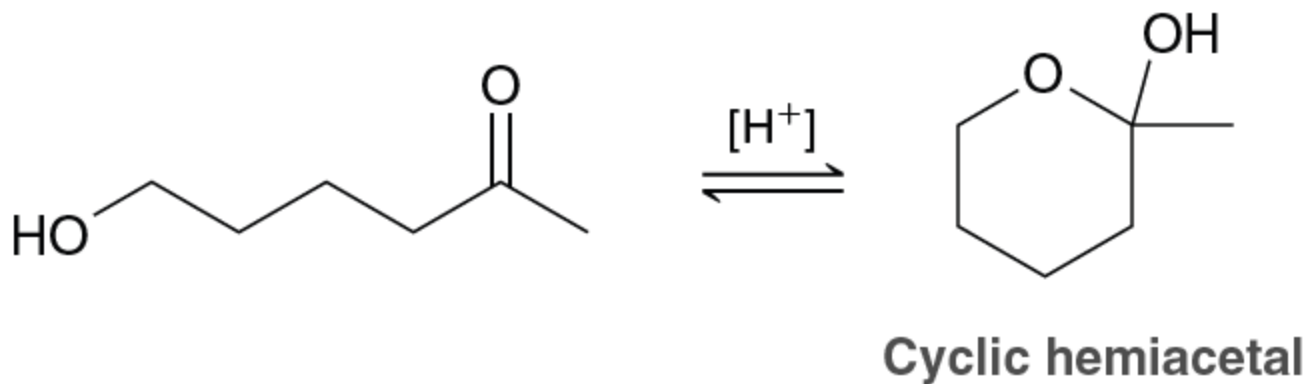
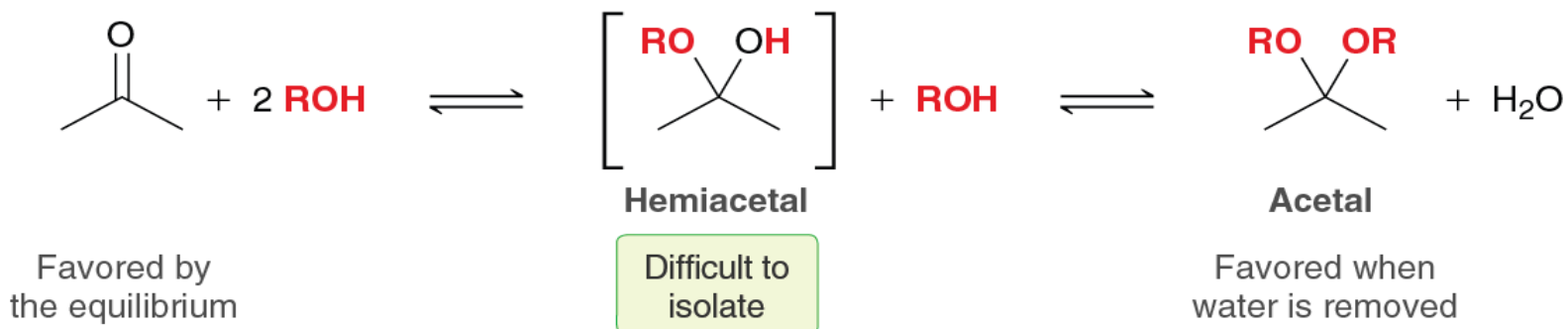
In such cases, formation of the acetal can be accomplished by removing one of the products (water) via a special distillation technique. By removing water as it is formed, the reaction can be forced to completion.



## Acetals as Protecting Groups



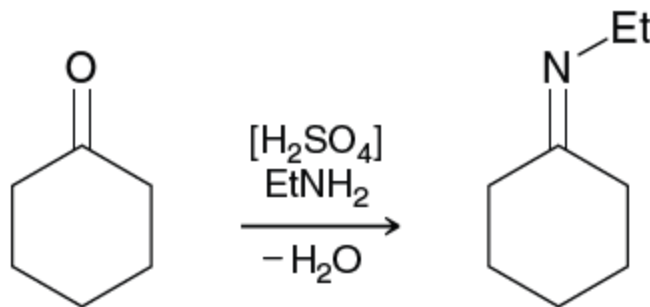
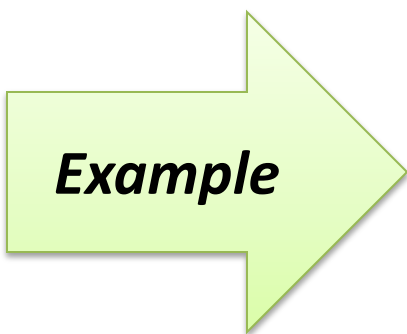
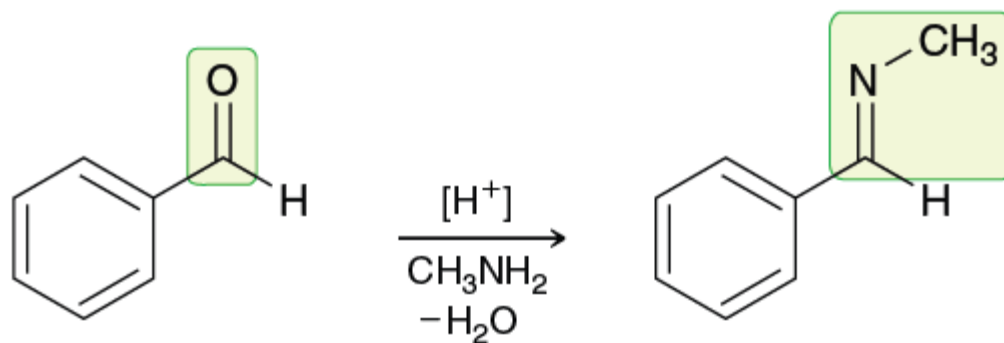
## Stable Hemiacetals



# 19.6 Nitrogen Nucleophiles

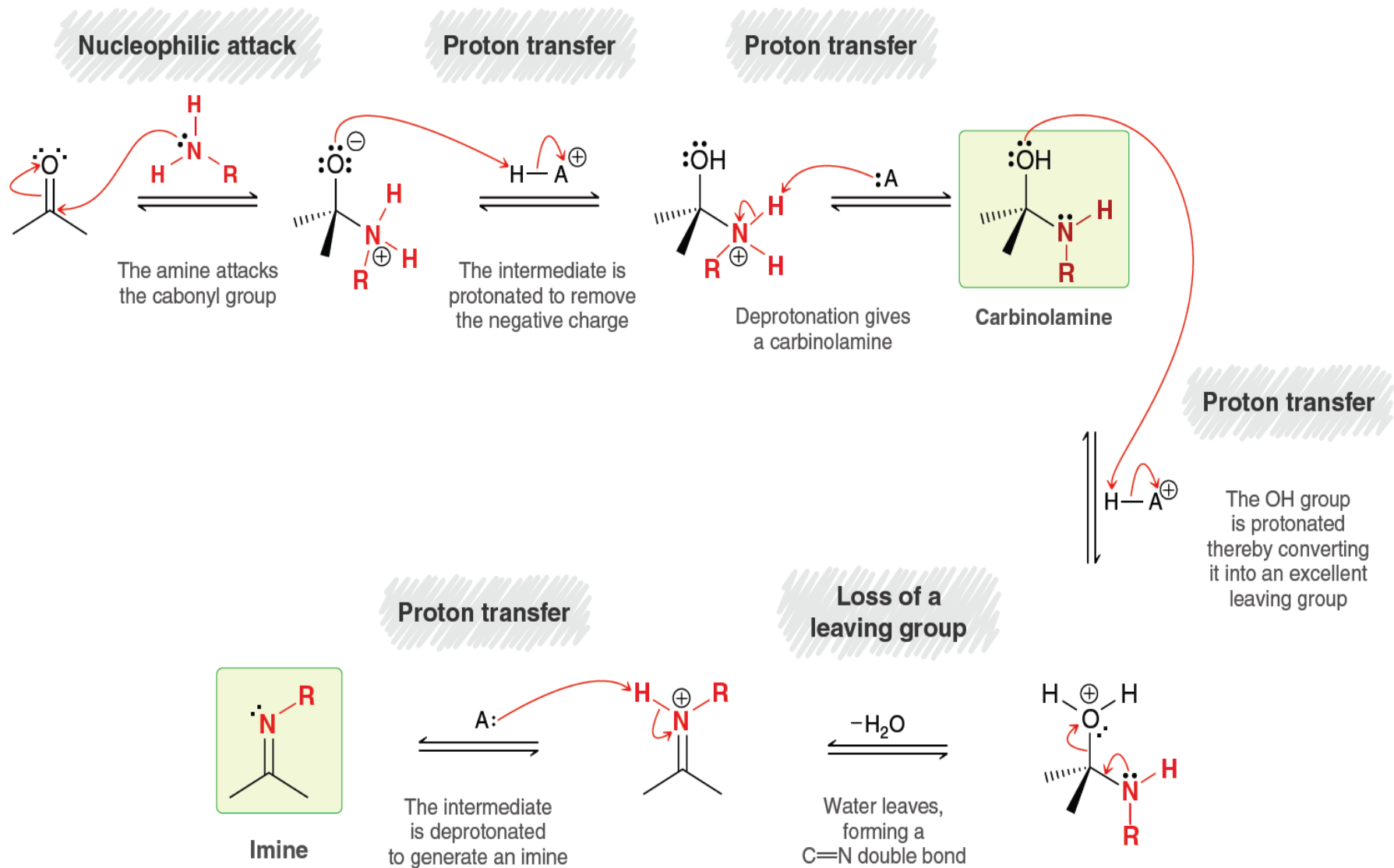
## Primary Amines

In mildly acidic conditions, an aldehyde or ketone will react with a primary amine to form an **imine**:

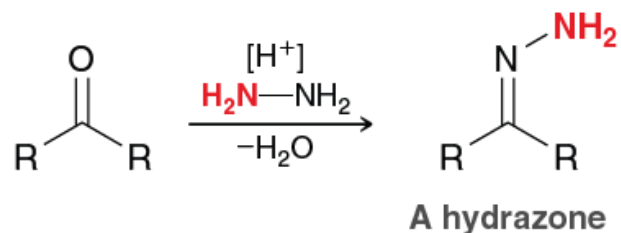
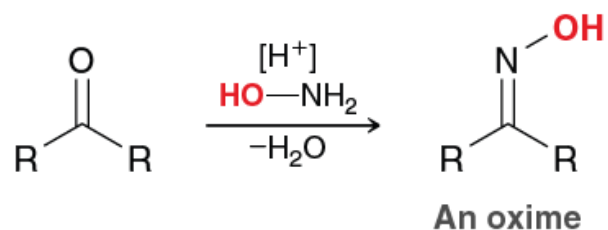




# MECHANISM 19.6 IMINE FORMATION

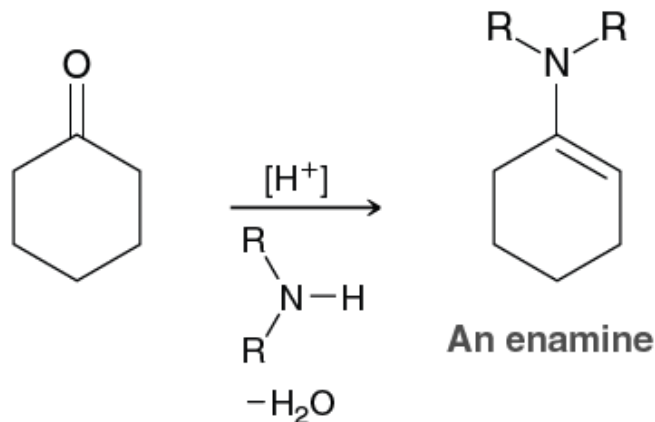


Many different compounds of the form  $\text{RNH}_2$  will react with aldehydes and ketones, including compounds in which **R** is not an alkyl group, for example:

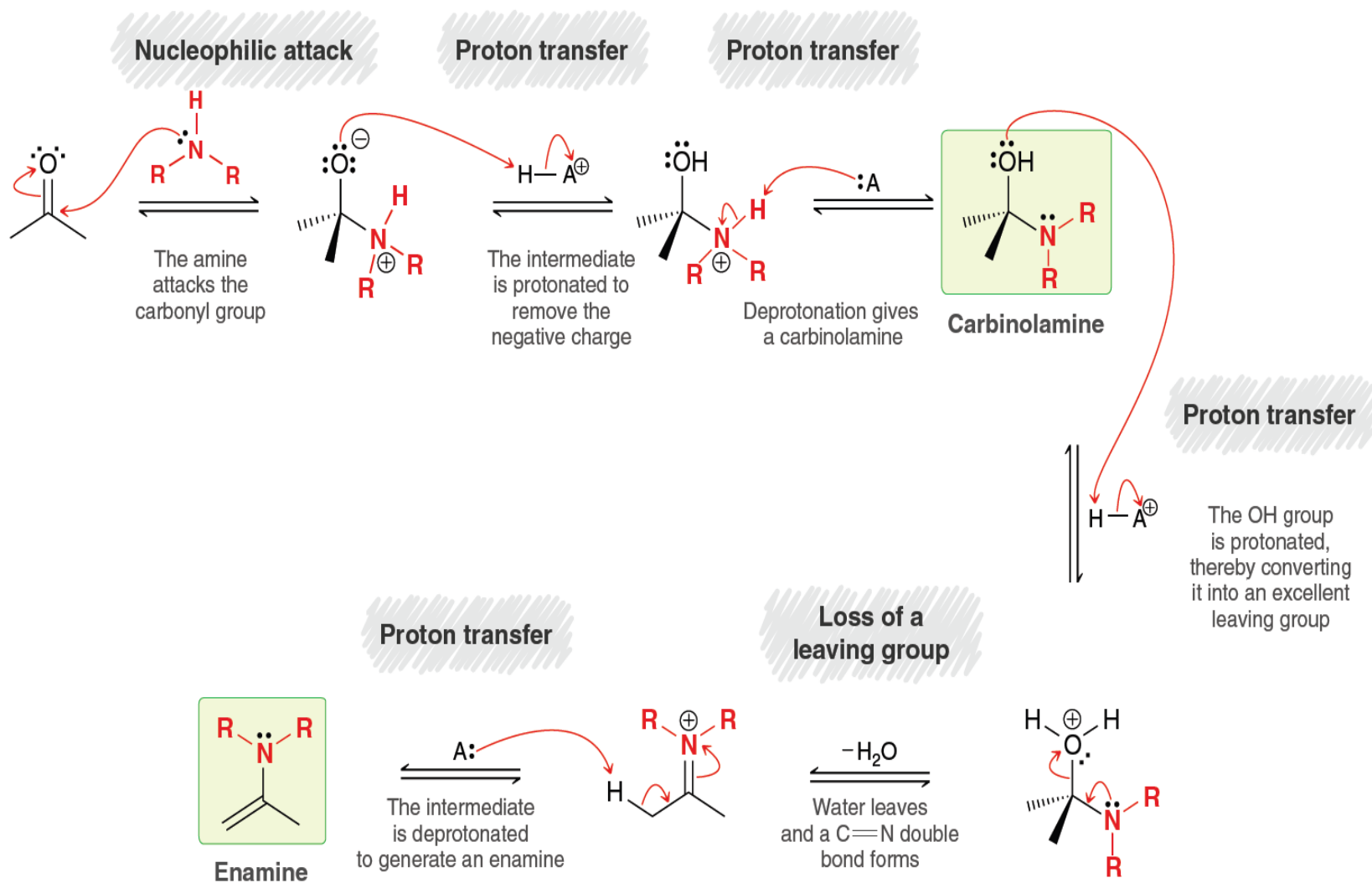


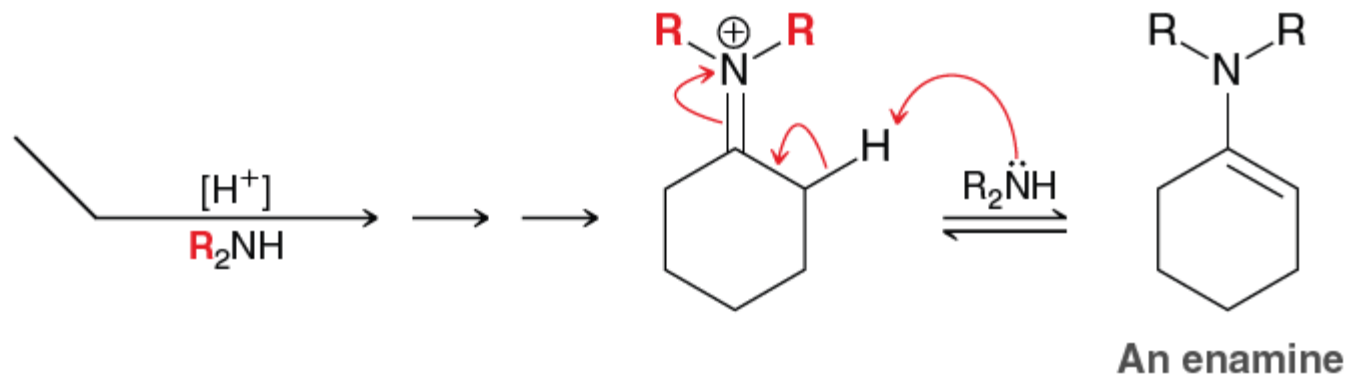
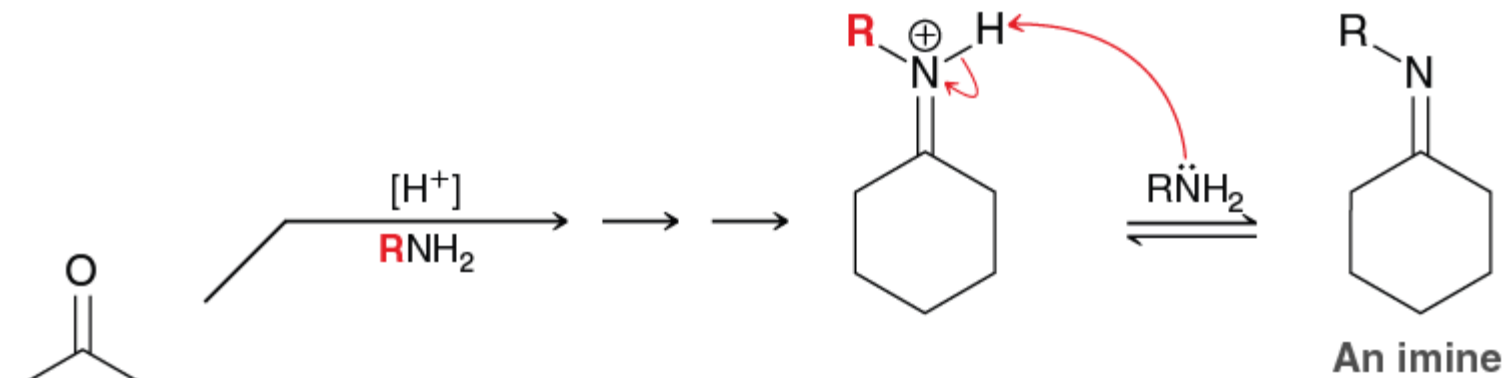
## Secondary Amines

In acidic conditions, an aldehyde or ketone will react with a secondary amine to form an **enamine**:

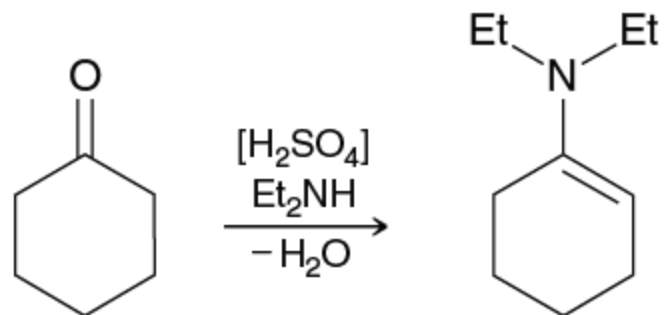


# MECHANISM 19.7 ENAMINE FORMATION



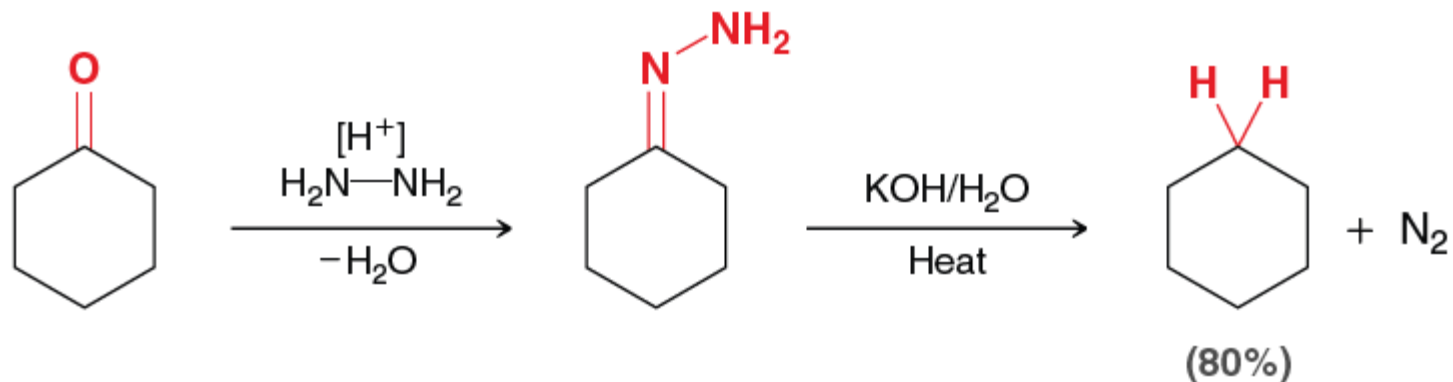
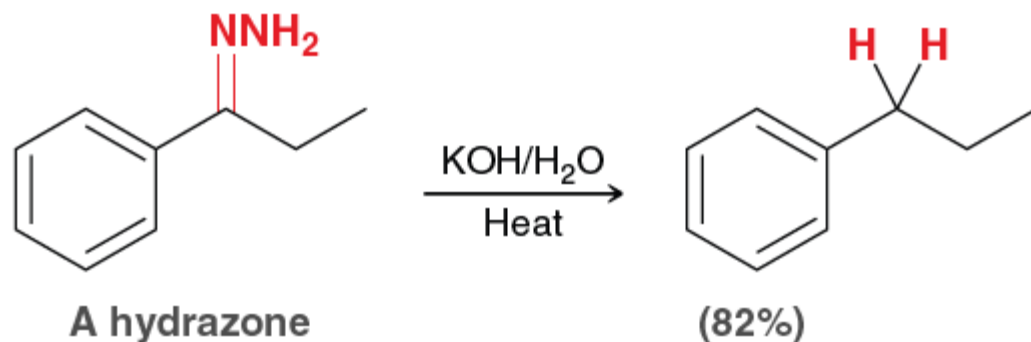


**Example**

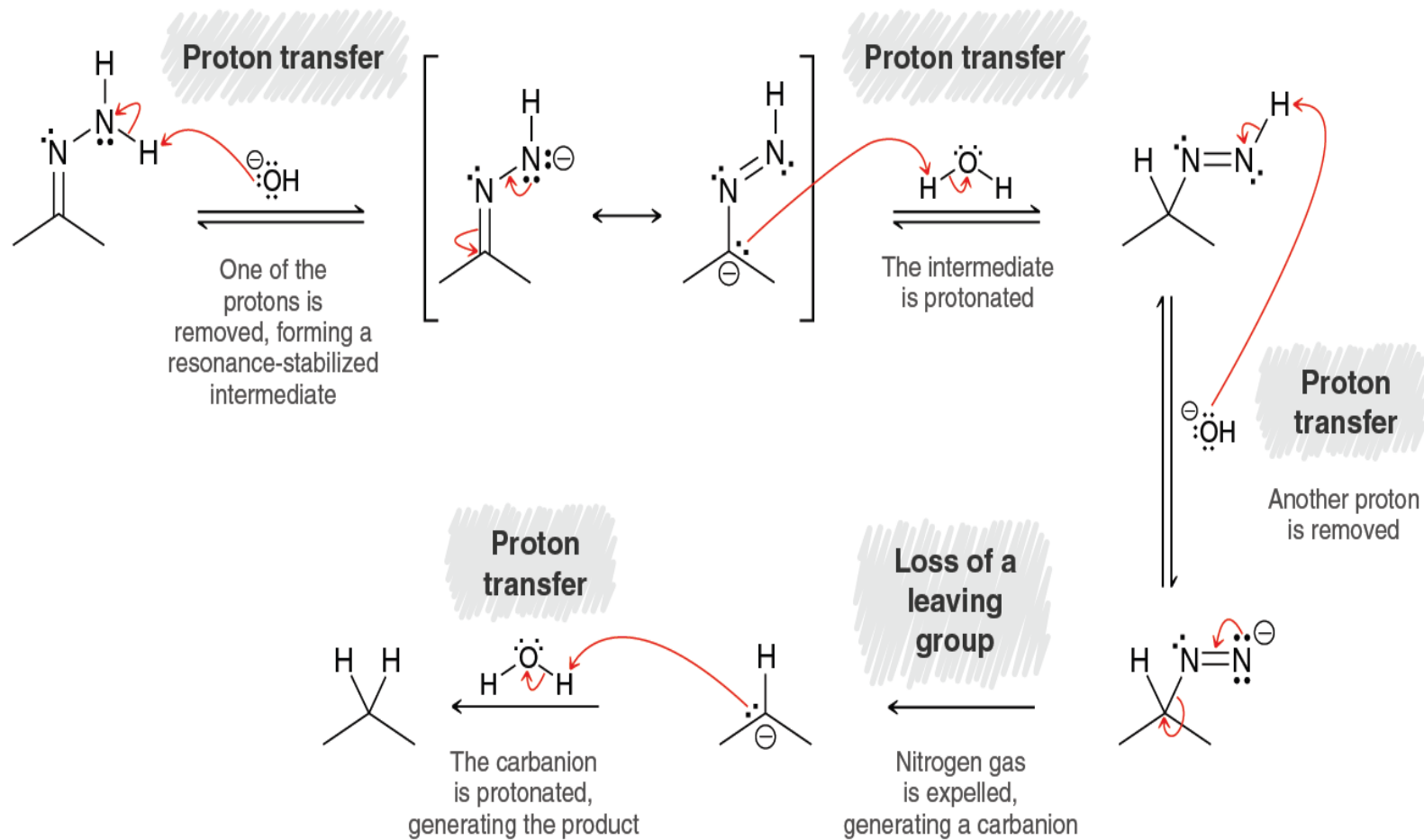


## Wolff–Kishner Reduction

we noted that ketones can be converted into **hydrazones**. This transformation has practical utility, because **hydrazones** are readily reduced under strongly basic conditions:



## MECHANISM 19.8 THE WOLFF-KISHNER REDUCTION



**19.22** Predict the product of the following two- step procedure and draw a mechanism for its formation:

