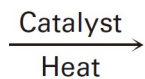
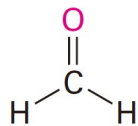
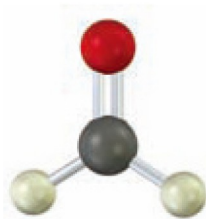
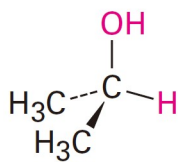


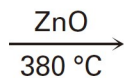
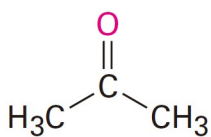
Methanol



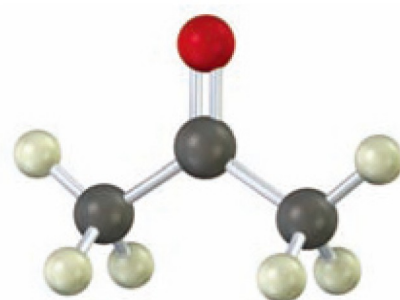
Formaldehyde



2-Propanol



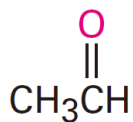
Acetone



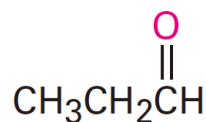
# 19

## 醛和酮：亲核加成反应

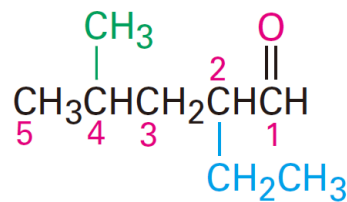
## 19.1 命名



**Ethanal**  
(acetaldehyde)

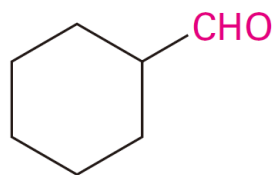


**Propanal**  
(propionaldehyde)

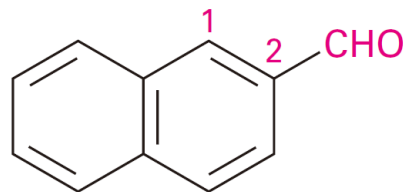


**2-Ethyl-4-methylpentanal**

For cyclic aldehydes in which the  $\text{-CHO}$  group is directly attached to a ring, the suffix *-carbaldehyde* is used.

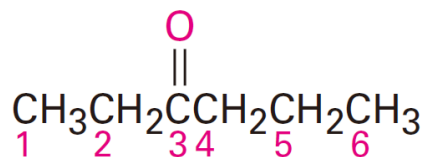


**Cyclohexanecarbaldehyde**

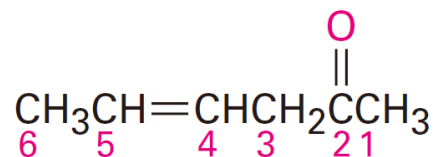


**2-Naphthalenecarbaldehyde**

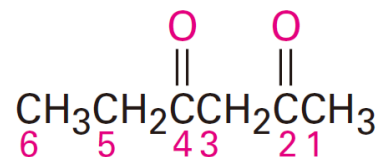
## 19.1 命名



**3-Hexanone**  
(New: Hexan-3-one)

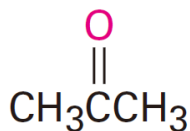


**4-Hexen-2-one**  
(New: Hex-4-en-2-one)

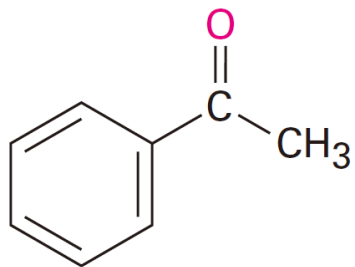


**2,4-Hexanedione**  
(New: Hexane-2,4-dione)

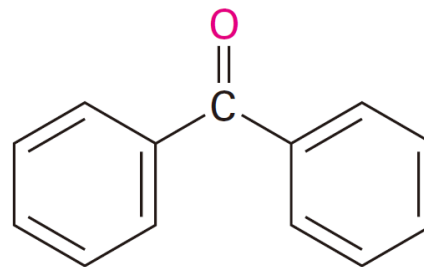
A few ketones are allowed by IUPAC to retain their common names.



**Acetone**



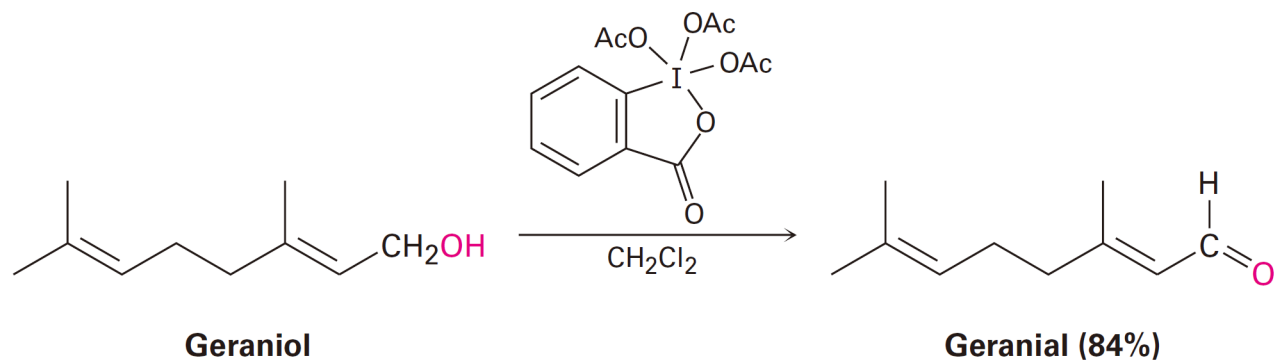
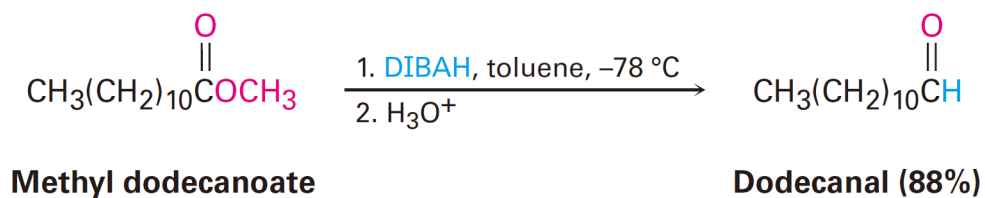
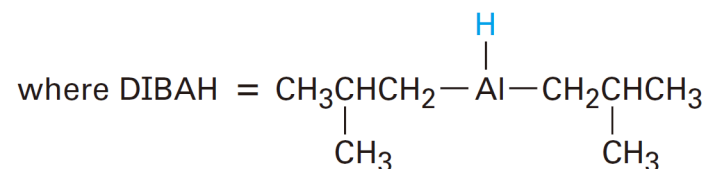
**Acetophenone**



**Benzophenone**

## 19.2 制备

### • 醛的制备



### Problem 19.3

How would you prepare pentanal from the following starting materials?

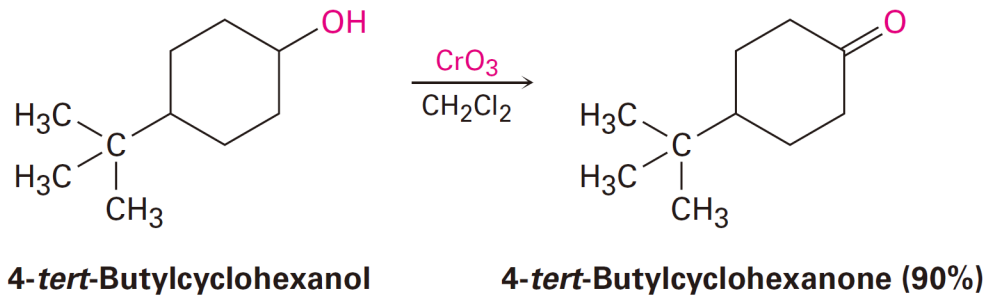
- (a)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$       (b)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$   
(c)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$       (d)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$



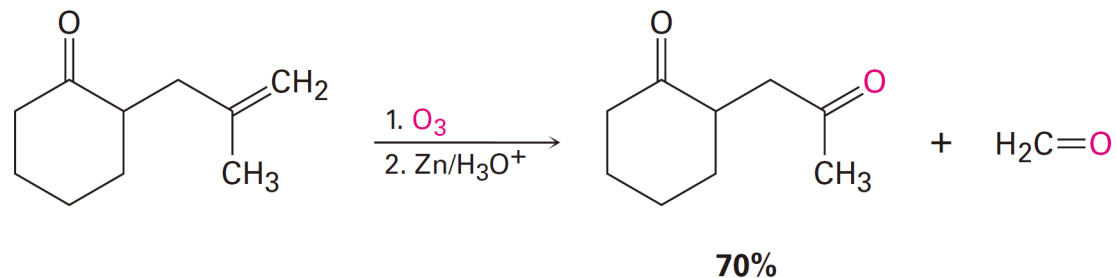
## 19.2 制备

### • 酮的制备

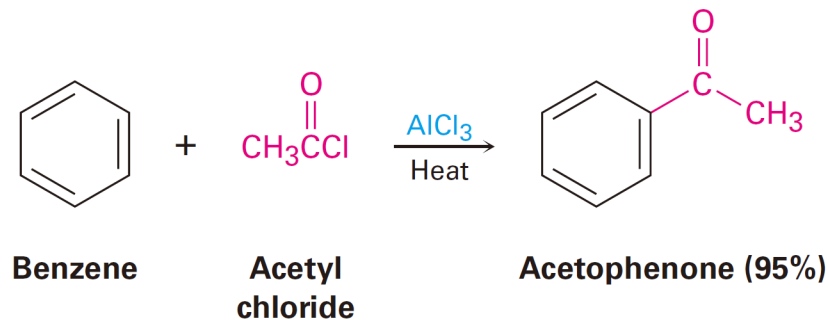
1



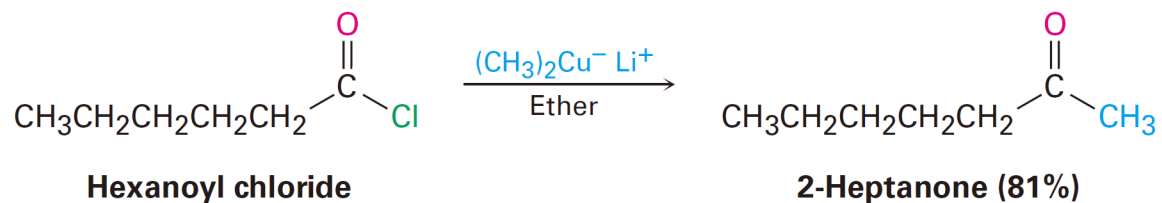
2



3



4



## 19.2 制备

- 课堂练习

### **Problem 19.4**

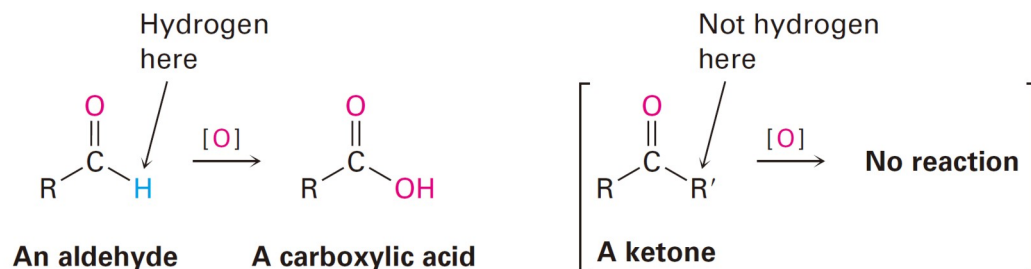
How would you carry out the following reactions? More than one step may be required.

- (a) 3-Hexyne  $\rightarrow$  3-Hexanone
- (b) Benzene  $\rightarrow$  *m*-Bromoacetophenone
- (c) Bromobenzene  $\rightarrow$  Acetophenone
- (d) 1-Methylcyclohexene  $\rightarrow$  2-Methylcyclohexanone

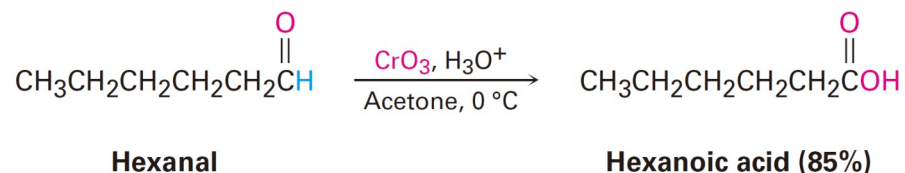


## 19.3 氧化

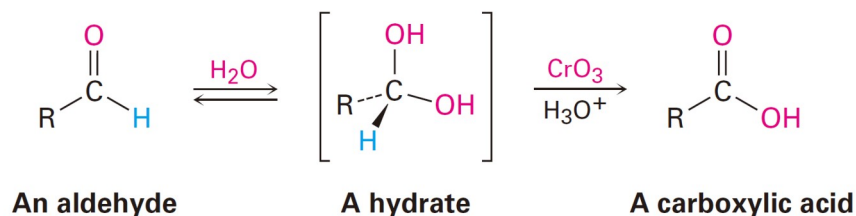
- 醛被氧化为羧酸，酮通常不易氧化（酮的氧化通常不用做制备方法）。



Many oxidizing agents, including  $\text{KMnO}_4$  and hot  $\text{HNO}_3$ , convert aldehydes into carboxylic acids, but  $\text{CrO}_3$  in aqueous acid is a more common choice. The oxidation occurs rapidly at room temperature and generally results in good yields.



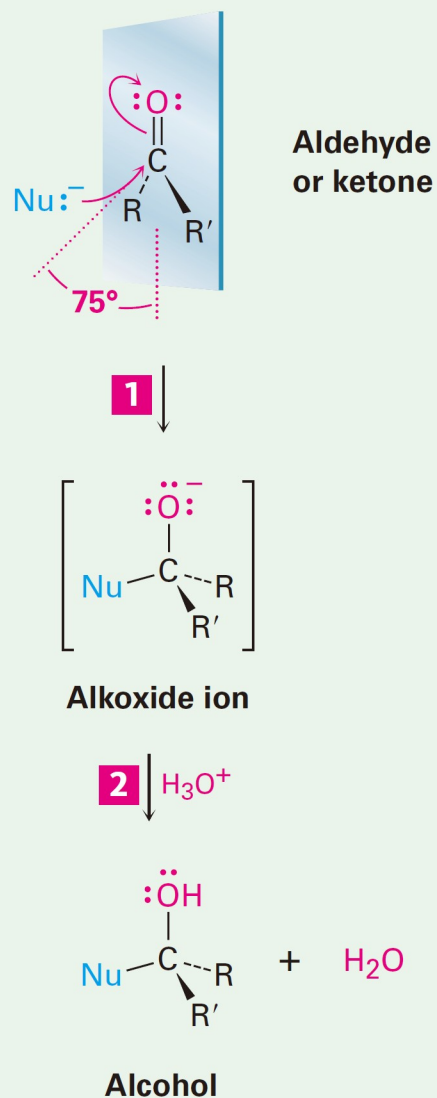
Aldehyde oxidations occur through intermediate 1,1-diols, or *hydrates*, which are formed by a reversible nucleophilic addition of water to the carbonyl group. Even though formed to only a small extent at equilibrium, the hydrate reacts like any typical primary or secondary alcohol and is oxidized to a carbonyl compound (**Section 17.7**).



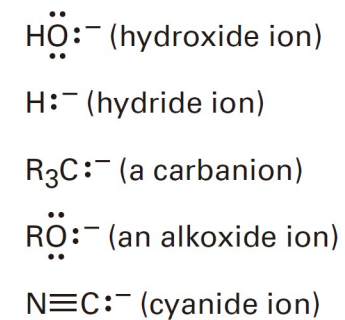
## 19.4 亲核加成

**1** An electron pair from the nucleophile adds to the electrophilic carbon of the carbonyl group, pushing an electron pair from the C=O bond onto oxygen and giving an alkoxide ion intermediate. The carbonyl carbon rehybridizes from  $sp^2$  to  $sp^3$ .

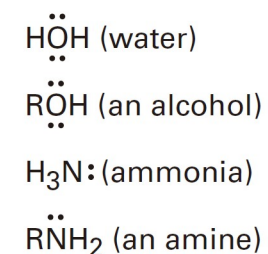
**2** Protonation of the alkoxide anion intermediate gives the neutral alcohol addition product.



Some negatively charged nucleophiles



Some neutral nucleophiles

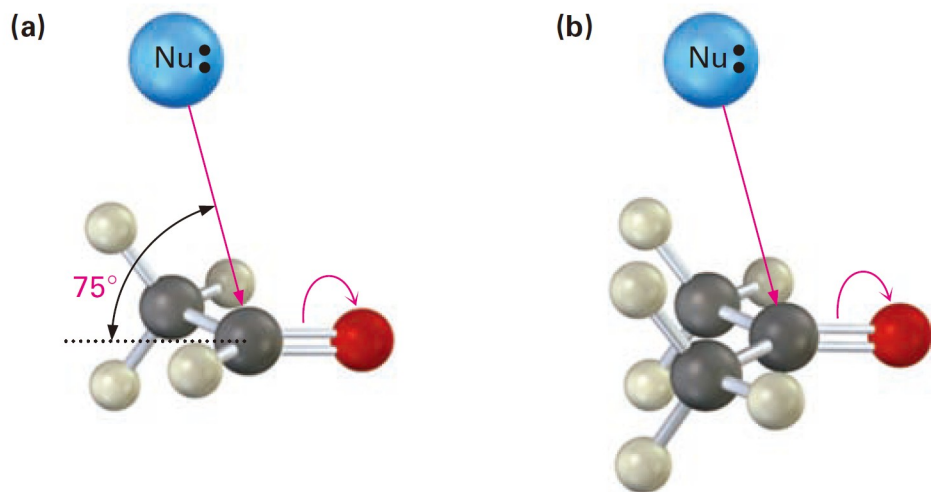


## 19.4 亲核加成

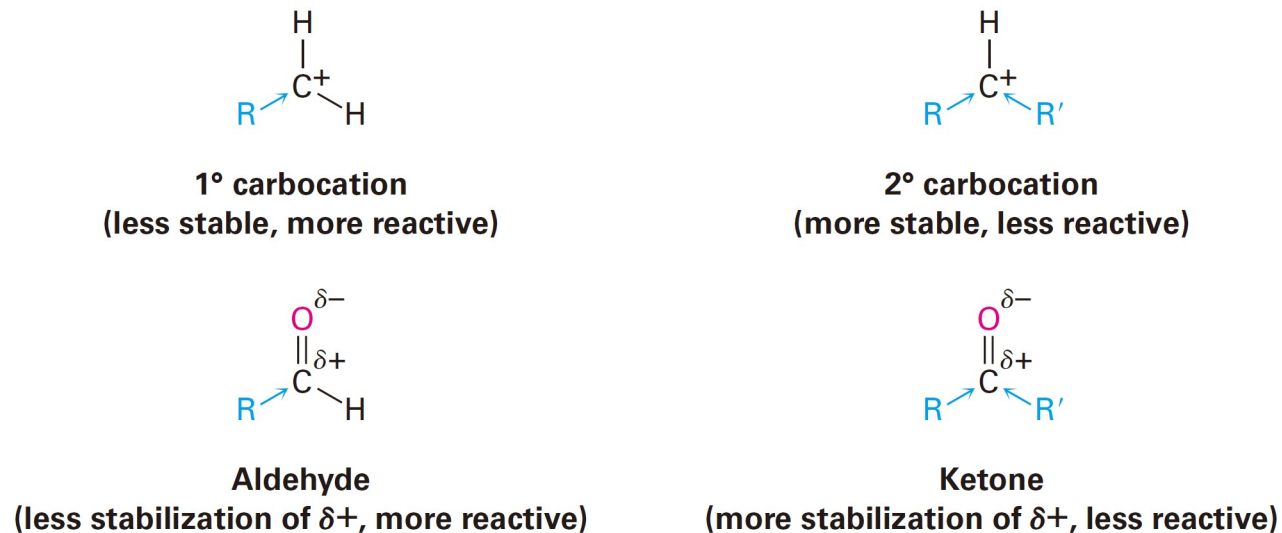
- 比较醛和酮的反应性

Aldehydes are generally more reactive than ketones in nucleophilic addition reactions for both steric and electronic reasons.

位阻

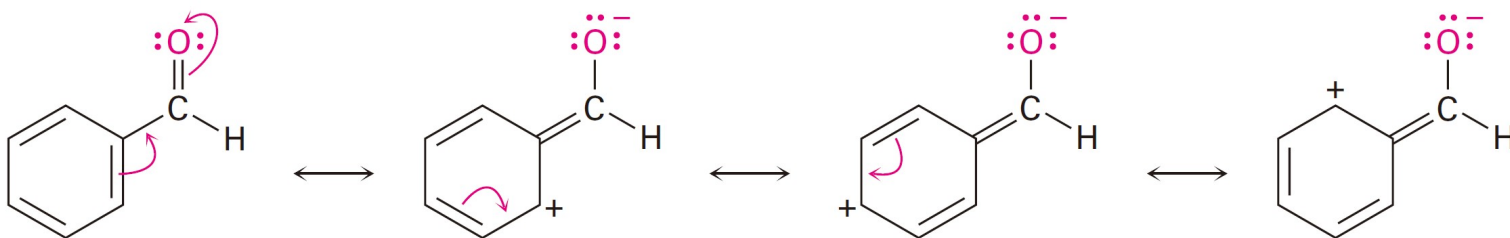
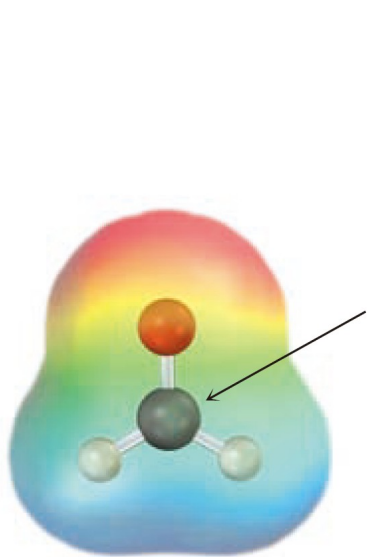


电性

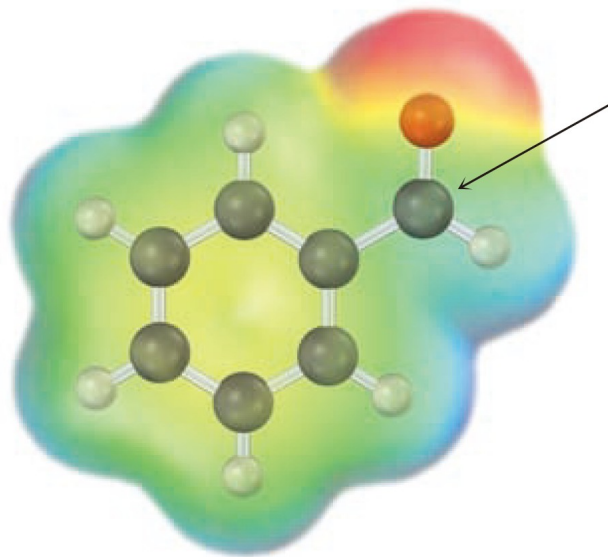


## 19.4 亲核加成

- 芳香醛酮比烷基醛酮更稳定，在亲核加成反应中反应性相对弱。



Formaldehyde



Benzaldehyde

## 19.4 亲核加成

- 课堂练习

### **Problem 19.5**

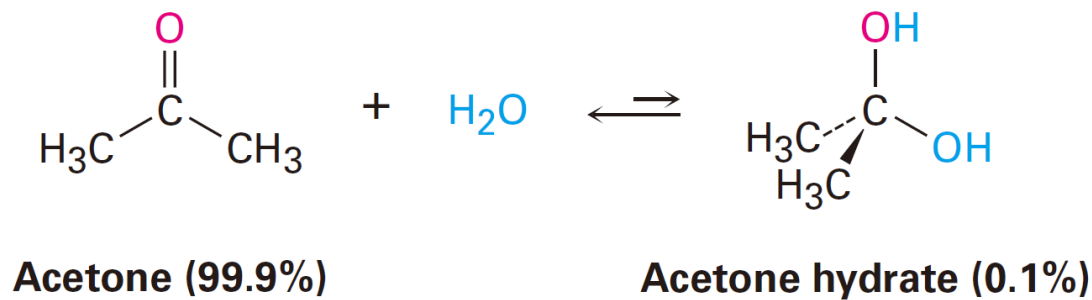
Treatment of an aldehyde or ketone with cyanide ion ( $\text{:C}\equiv\text{N}^-$ ), followed by protonation of the tetrahedral alkoxide ion intermediate, gives a *cyanohydrin*. Show the structure of the cyanohydrin obtained from cyclohexanone.

### **Problem 19.6**

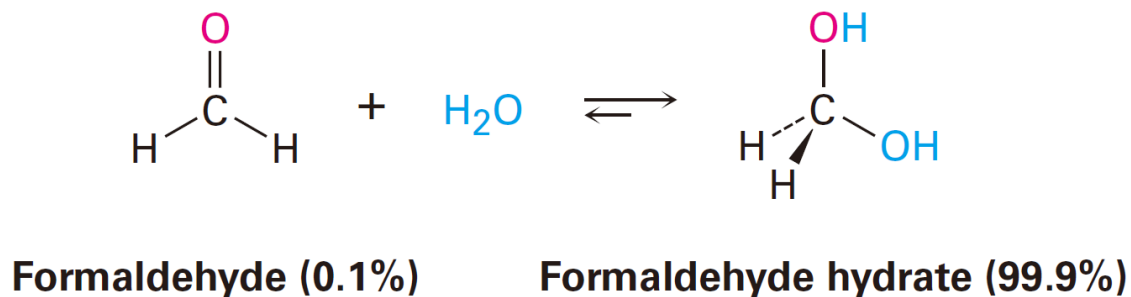
*p*-Nitrobenzaldehyde is more reactive toward nucleophilic additions than *p*-methoxybenzaldehyde. Explain.



## 19.5 水作为亲核试剂



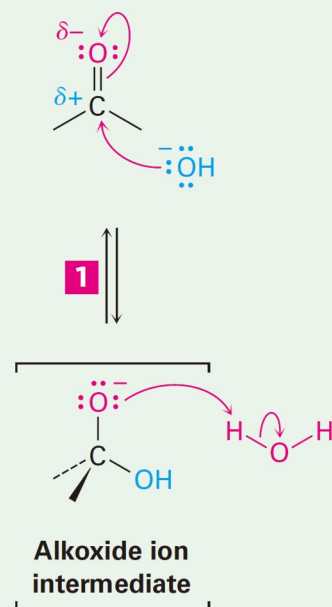
The position of the equilibrium between a gem diol and an aldehyde or ketone depends on the structure of the carbonyl compound. The equilibrium generally favors the carbonyl compound for steric reasons, but the gem diol is favored for a few simple aldehydes. For example, an aqueous solution of formaldehyde consists of 99.9% gem diol and 0.1% aldehyde at equilibrium, whereas an aqueous solution of acetone consists of only about 0.1% gem diol and 99.9% ketone.



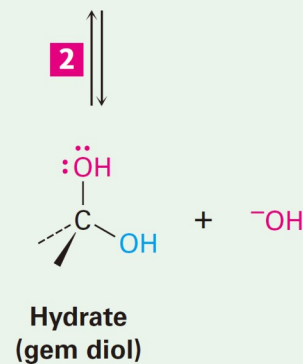
## 19.5 水作为亲核试剂

### (a) Basic conditions

- 1** The negatively charged nucleophile  $\text{OH}^-$  adds to the electrophilic carbon and pushes  $\pi$  electrons from the  $\text{C}=\text{O}$  bond onto oxygen, giving an alkoxide ion.



- 2** The alkoxide ion is protonated by water to give the neutral hydrate as the addition product and regenerating  $\text{OH}^-$ .

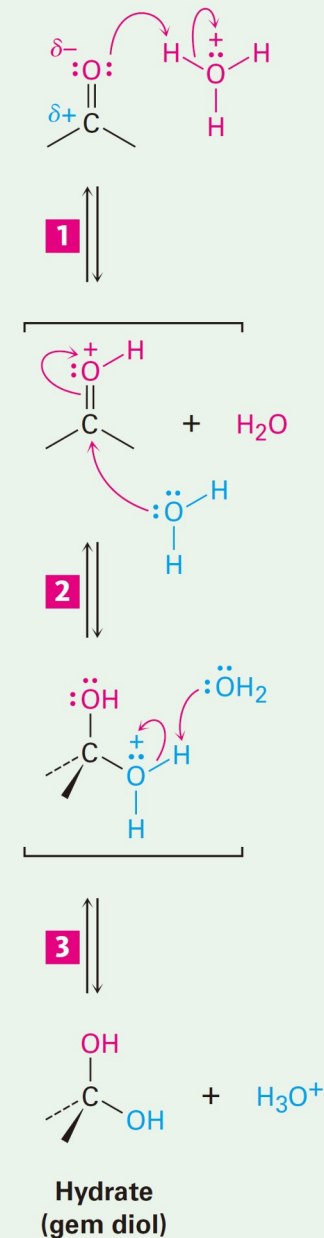


### (b) Acidic conditions

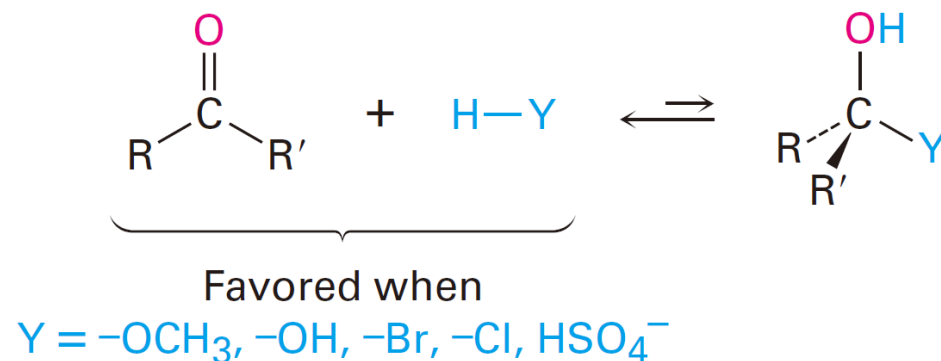
- 1** The carbonyl oxygen is protonated by acid  $\text{H}_3\text{O}^+$ , making the carbon more strongly electrophilic

- 2** The neutral nucleophile  $:\text{OH}_2$  adds to the electrophilic carbon, pushing the  $\pi$  electrons from the  $\text{C}=\text{O}$  onto oxygen. The oxygen becomes neutral, and the nucleophile gains the + charge.

- 3** Water deprotonates the intermediate, giving the neutral hydrate addition product and regenerating the acid catalyst  $\text{H}_3\text{O}^+$ .



## 19.5 水作为亲核试剂



### Problem 19.7

When dissolved in water, trichloroacetaldehyde exists primarily as its hydrate, called chloral hydrate. Show the structure of chloral hydrate.

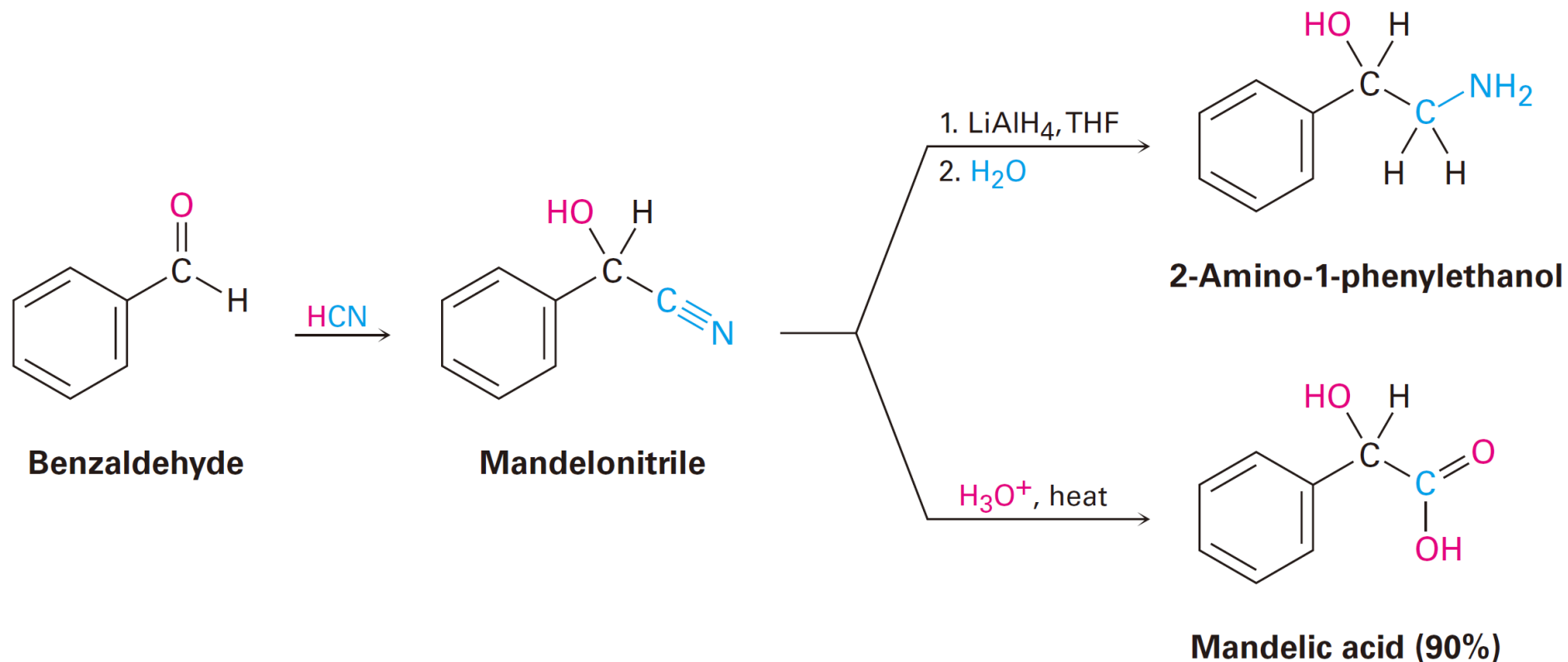
### Problem 19.8

The oxygen in water is primarily (99.8%)  $^{16}\text{O}$ , but water enriched with the heavy isotope  $^{18}\text{O}$  is also available. When an aldehyde or ketone is dissolved in  $^{18}\text{O}$ -enriched water, the isotopic label becomes incorporated into the carbonyl group. Explain.



## 19.6 HCN 作为亲核试剂

- 很有用，增加一个碳的新方法。



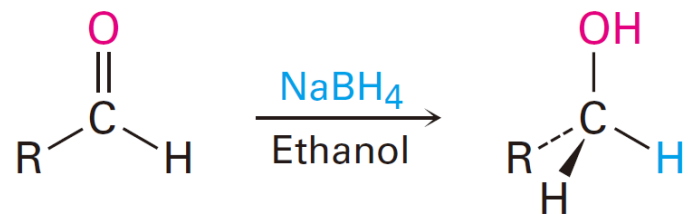
### Problem 19.9

Cyclohexanone forms a cyanohydrin in good yield but 2,2,6-trimethylcyclohexanone does not. Explain.



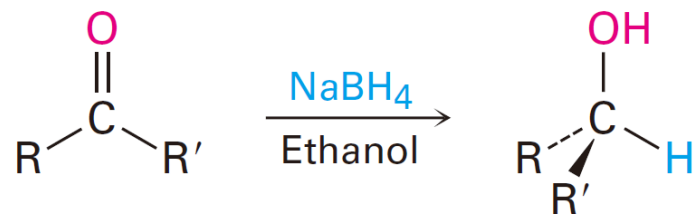
## 19.7 负氢和格氏试剂作为亲核试剂

- 构建碳碳键最重要的方法之一



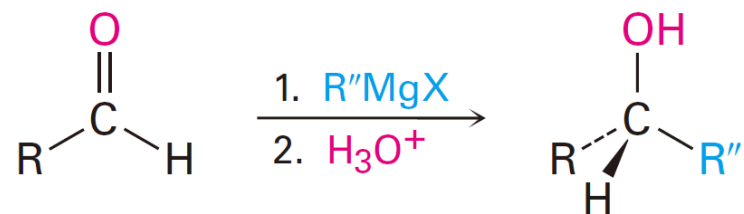
Aldehyde

1° Alcohol



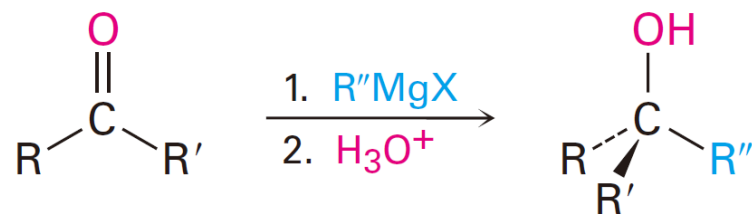
Ketone

2° Alcohol



Aldehyde

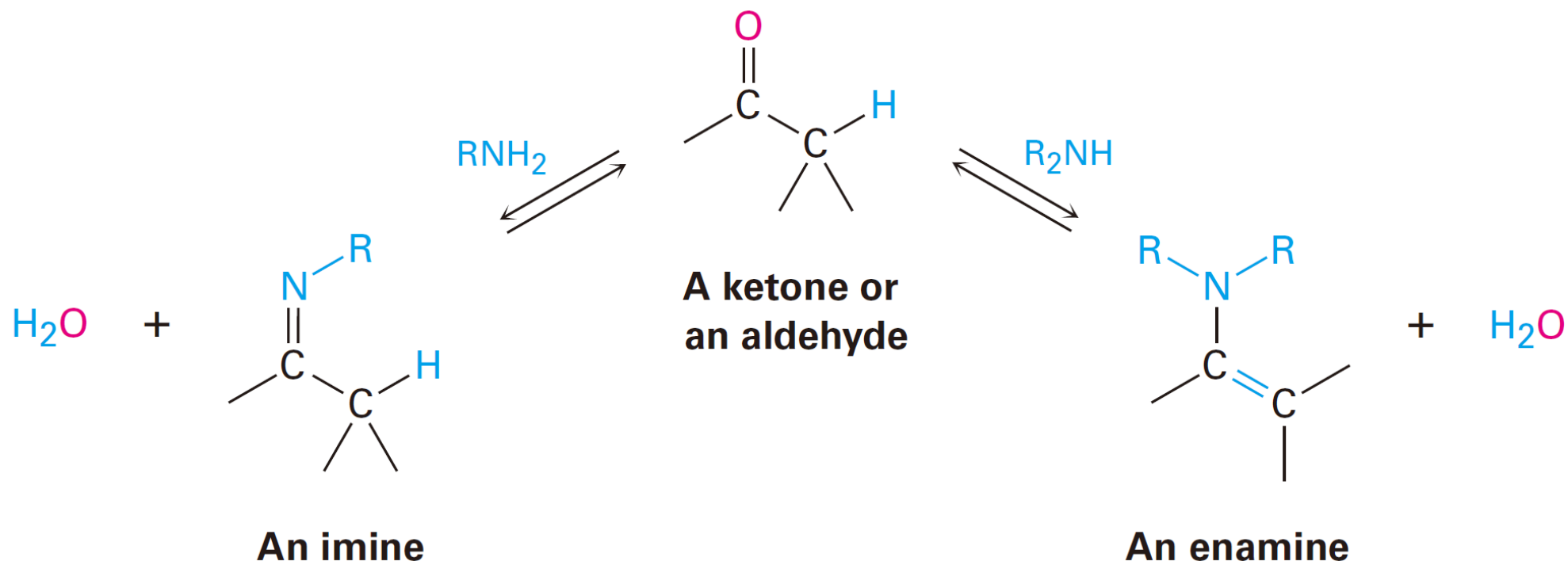
2° Alcohol



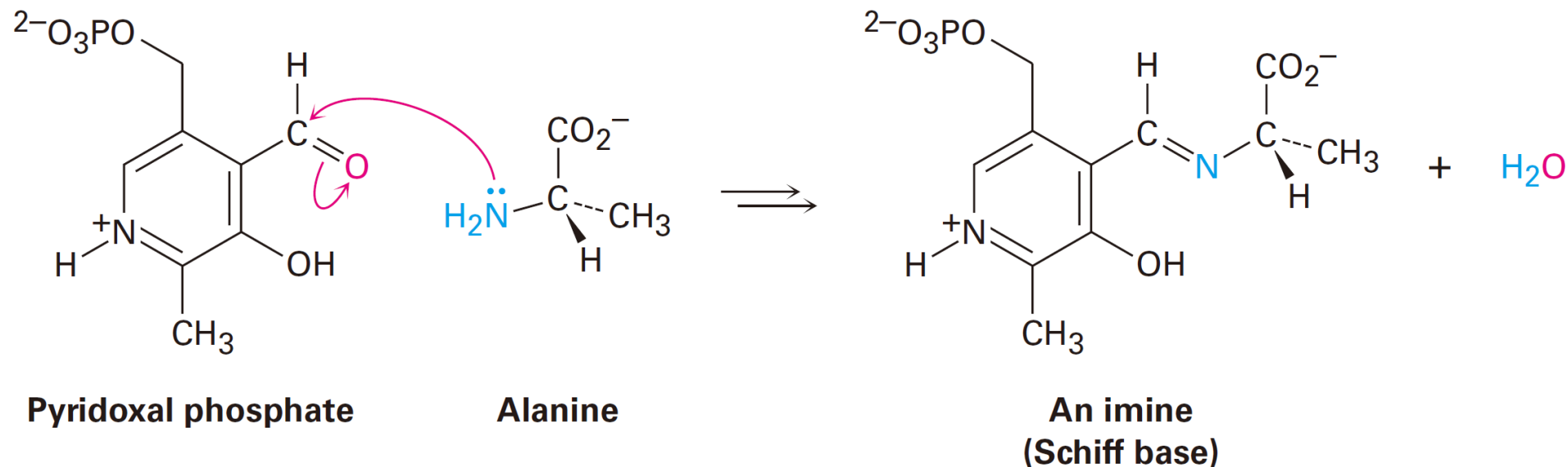
Ketone

3° Alcohol

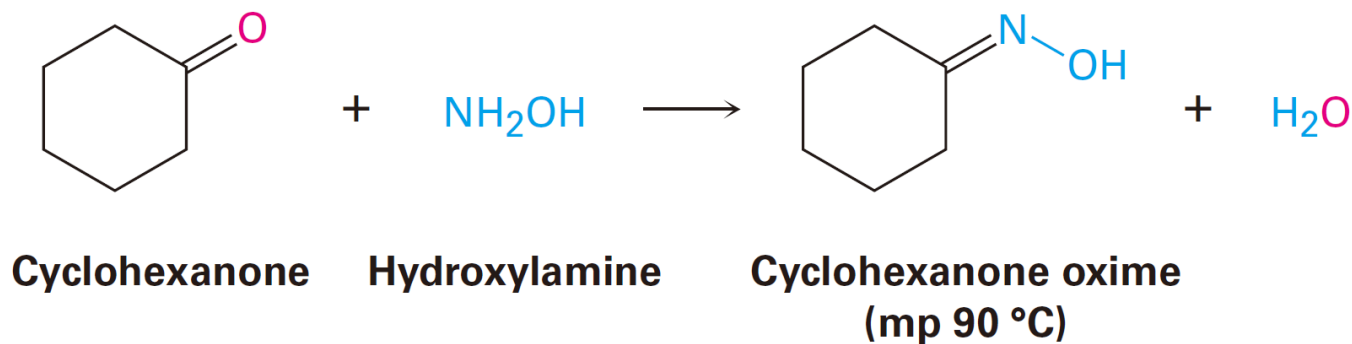
## 19.8 胺作为亲核试剂



## 19.8 胺作为亲核试剂

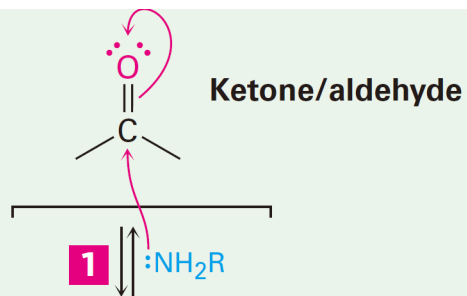


### Oxime

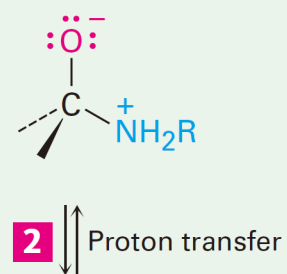
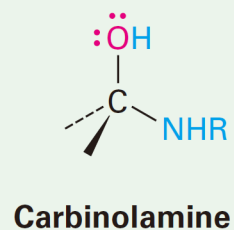


## 19.8 胺作为亲核试剂

**1** Nucleophilic attack on the ketone or aldehyde by the lone-pair electrons of an amine leads to a dipolar tetrahedral intermediate.



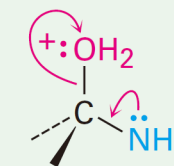
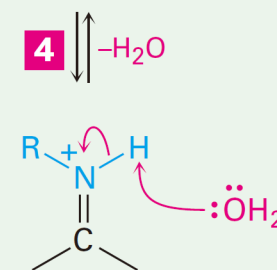
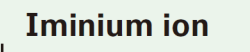
**2** A proton is then transferred from nitrogen to oxygen, yielding a neutral carbinolamine.



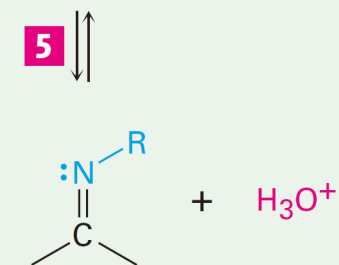
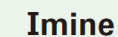
**3** Acid catalyst protonates the hydroxyl oxygen.



**4** The nitrogen lone-pair electrons expel water, giving an iminium ion.



**5** Loss of H<sup>+</sup> from nitrogen then gives the neutral imine product.



## 19.8 胺作为亲核试剂

### Problem 19.10

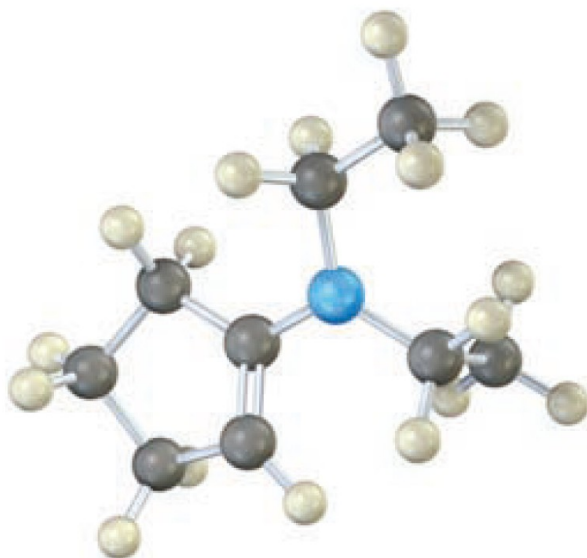
Show the products you would obtain by acid-catalyzed reaction of cyclohexanone with ethylamine,  $\text{CH}_3\text{CH}_2\text{NH}_2$ , and with diethylamine,  $(\text{CH}_3\text{CH}_2)_2\text{NH}$ .

### Problem 19.11

Imine formation is reversible. Show all the steps involved in the acid-catalyzed reaction of an imine with water (hydrolysis) to yield an aldehyde or ketone plus primary amine.

### Problem 19.12

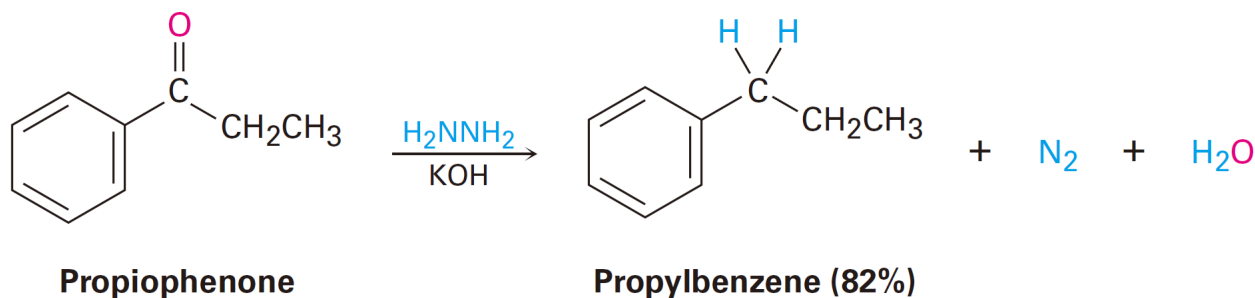
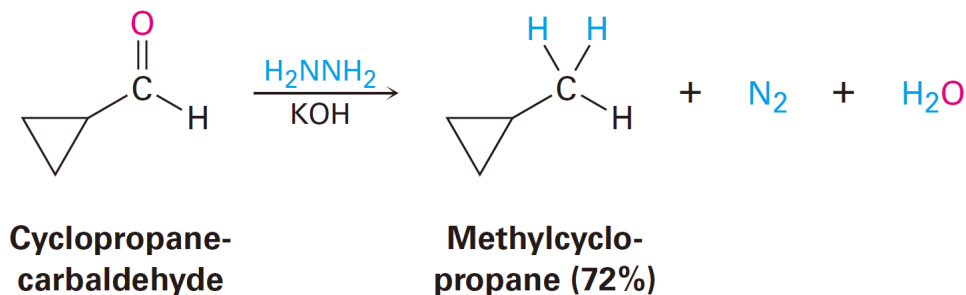
Draw the following molecule as a skeletal structure, and show how it can be prepared from a ketone and an amine.



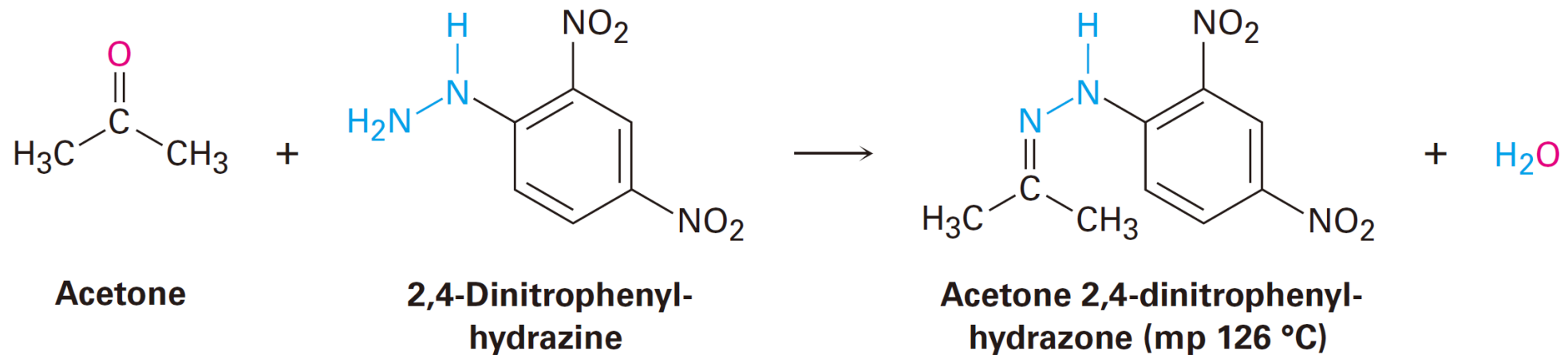
## 19.9 肼作为亲核试剂

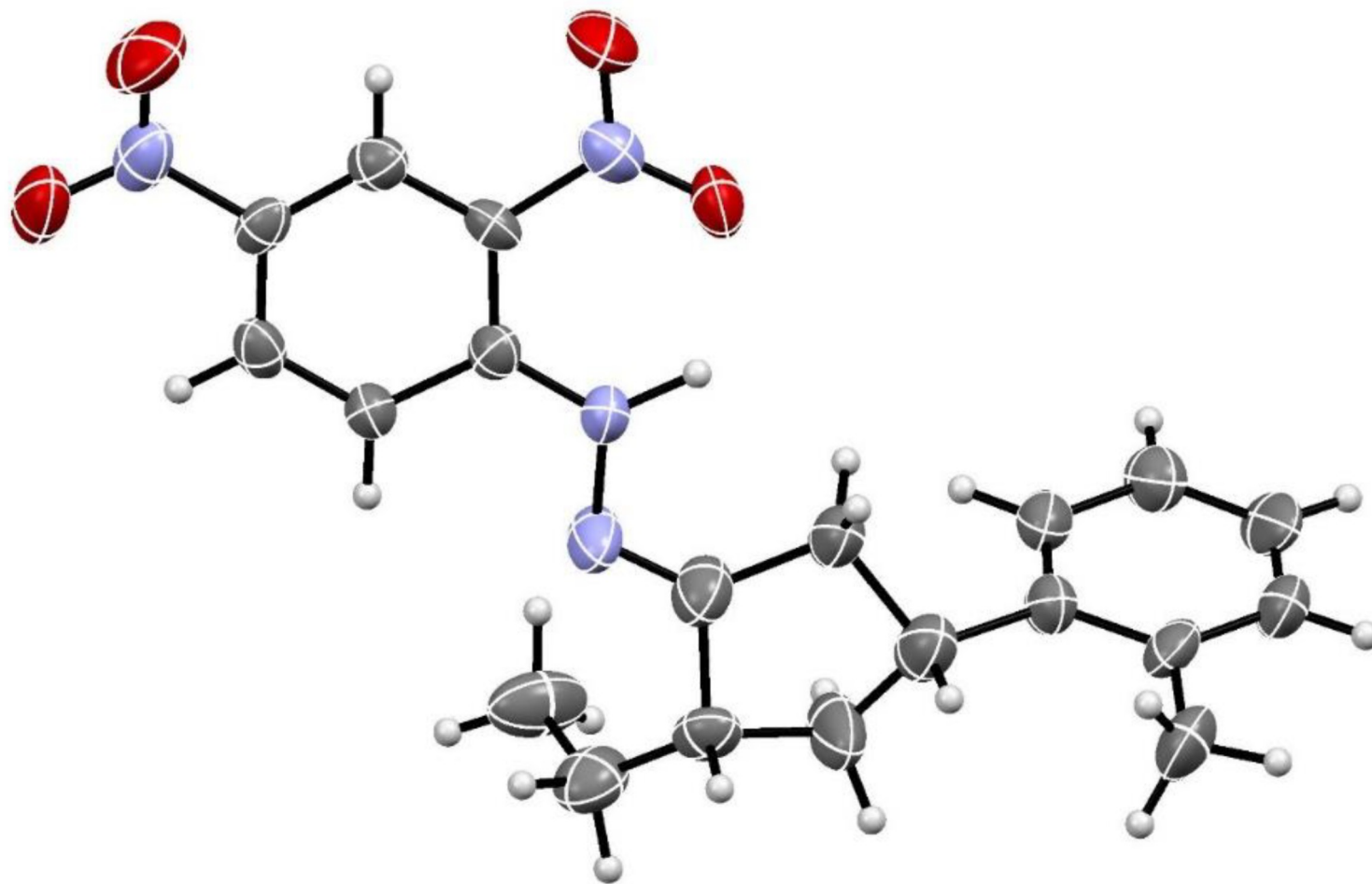
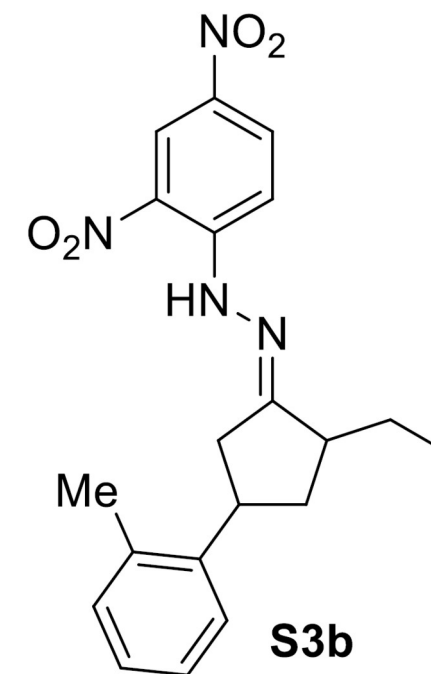
- 沃尔夫 - 凯惜纳 - 黄鸣龙还原反应

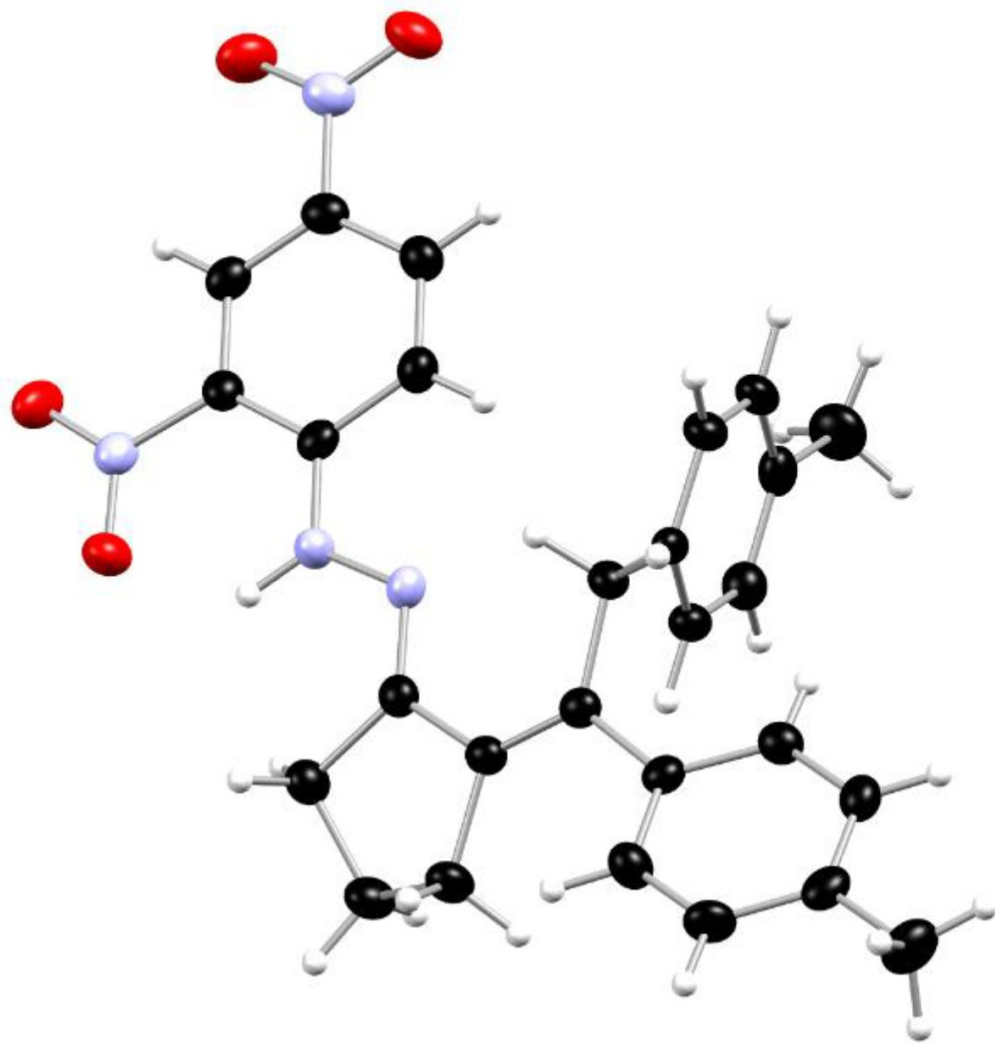
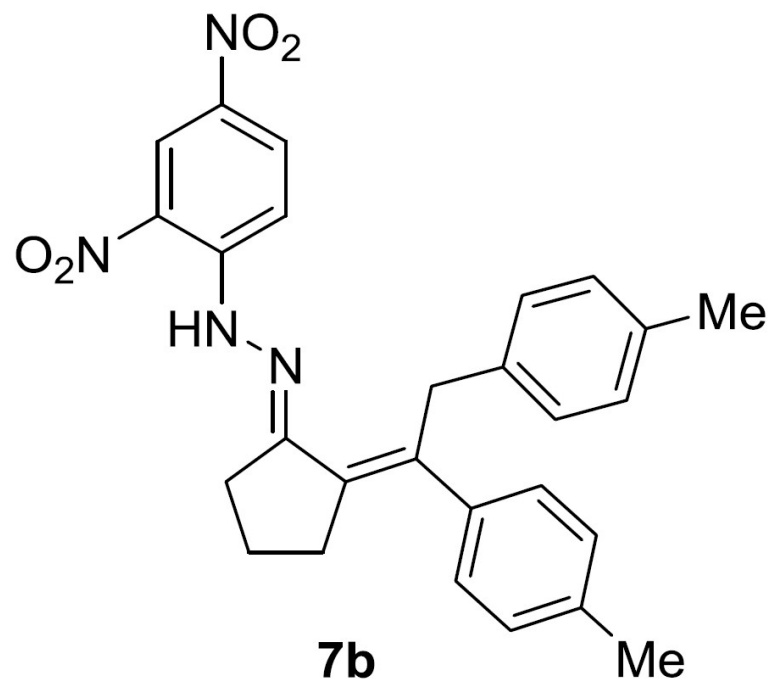
A useful variant of the imine-forming reaction just discussed involves the treatment of an aldehyde or ketone with hydrazine,  $\text{H}_2\text{NNH}_2$ , in the presence of KOH. Called the **Wolff-Kishner reaction**, the process is a useful and general method for converting an aldehyde or ketone into an alkane,  $\text{R}_2\text{C}=\text{O} \rightarrow \text{R}_2\text{CH}_2$ .



**2,4-Dinitrophenyl-  
hydrazone**

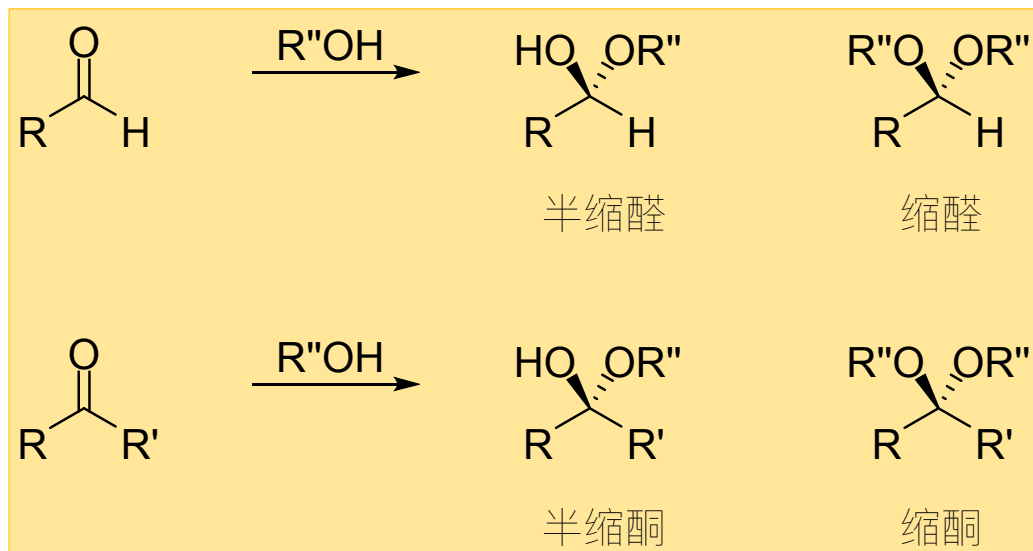
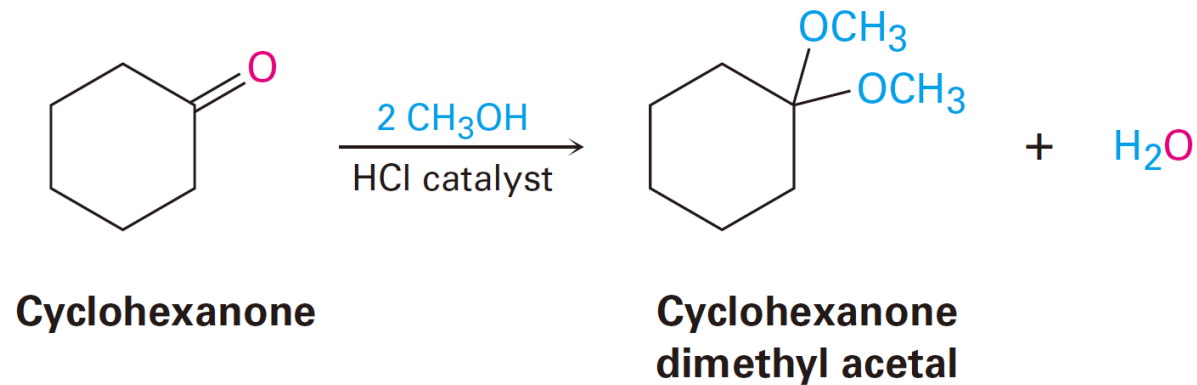
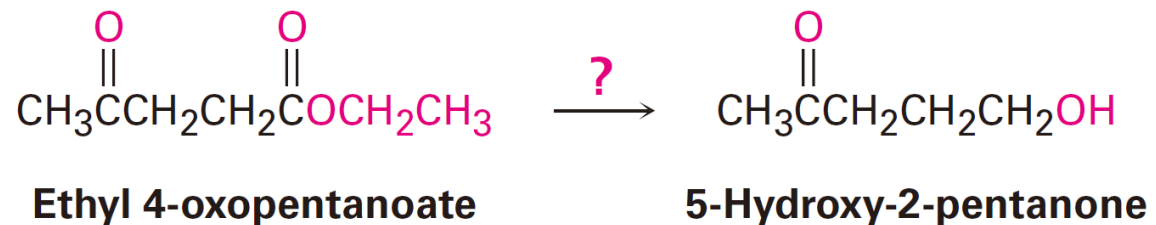




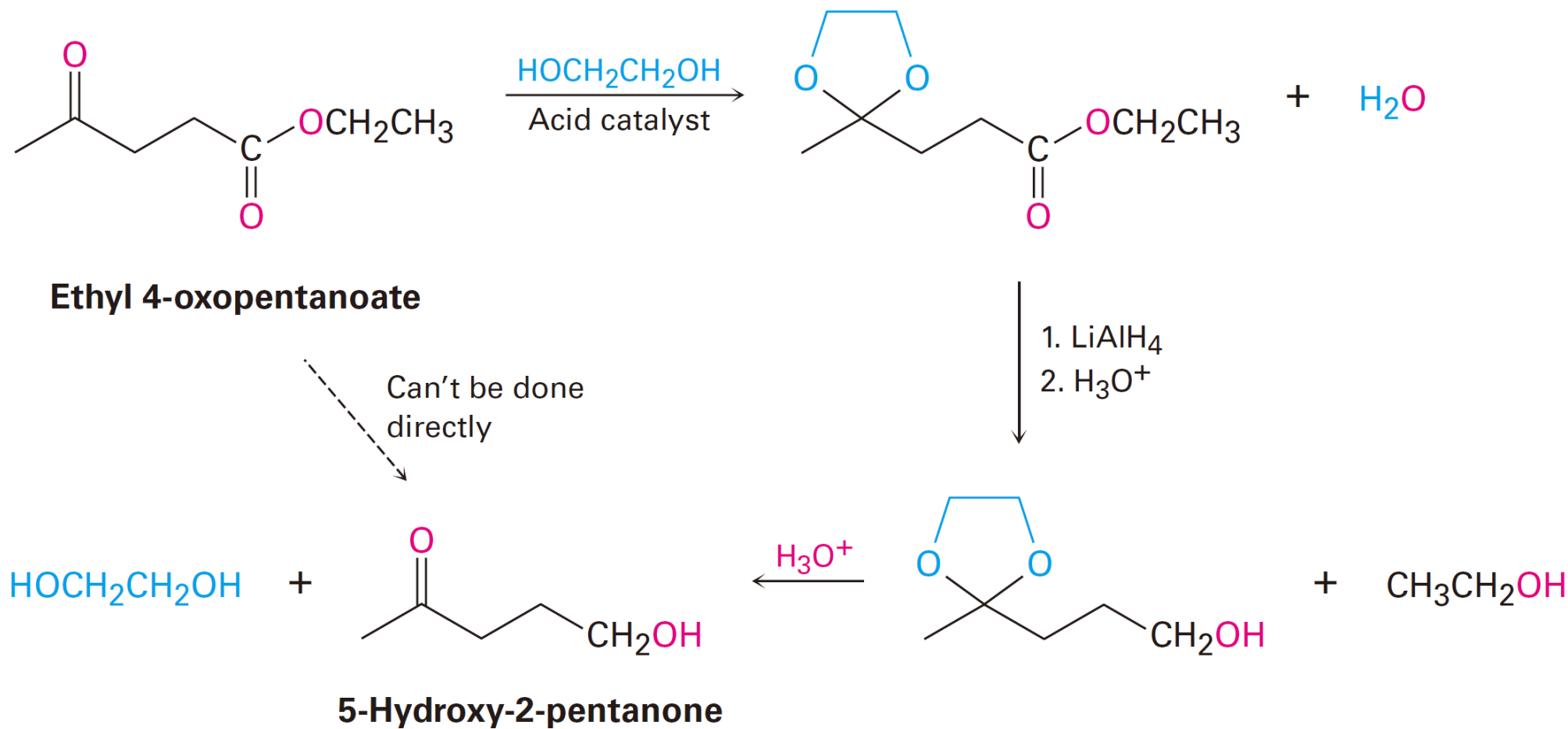


## 19.10 醇作为亲核试剂

- 作为醛和酮的保护基——(半)缩醛、(半)缩酮

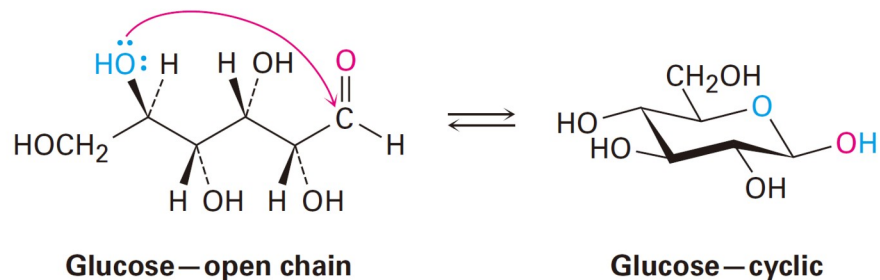


## 19.10 醇作为亲核试剂



## 19.10 醇作为亲核试剂

Acetal and hemiacetal groups are particularly common in carbohydrate chemistry. Glucose, for instance, is a polyhydroxy aldehyde that undergoes an *internal* nucleophilic addition reaction and exists primarily as a cyclic hemiacetal.

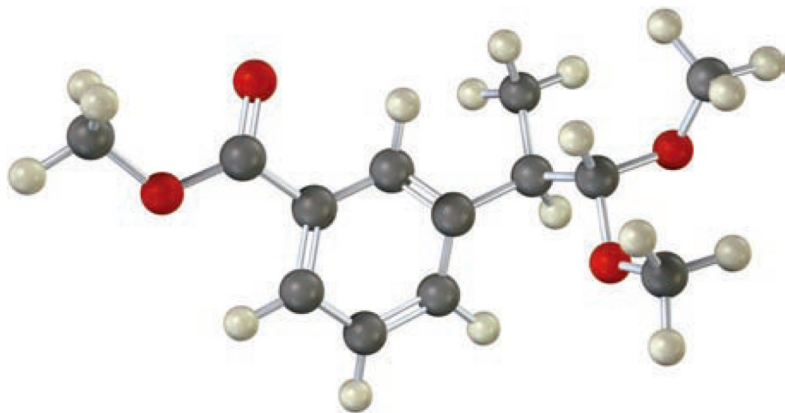


### Problem 19.14

Show all the steps in the acid-catalyzed formation of a cyclic acetal from ethylene glycol and an aldehyde or ketone.

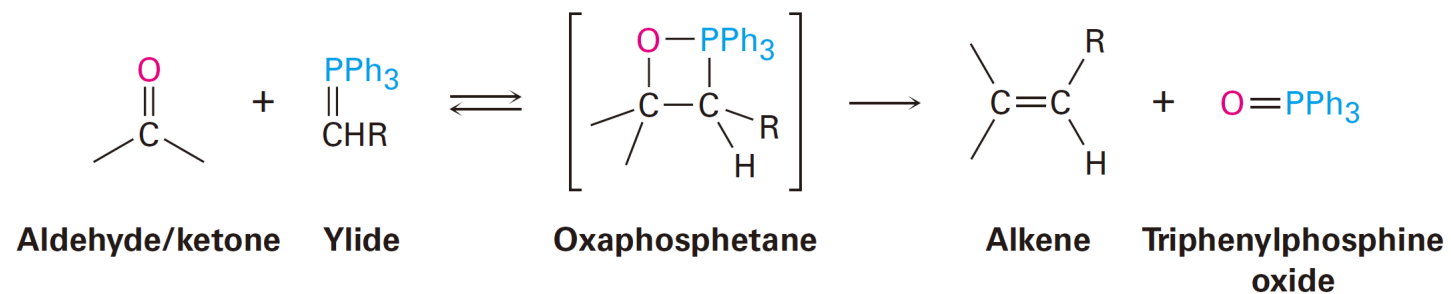
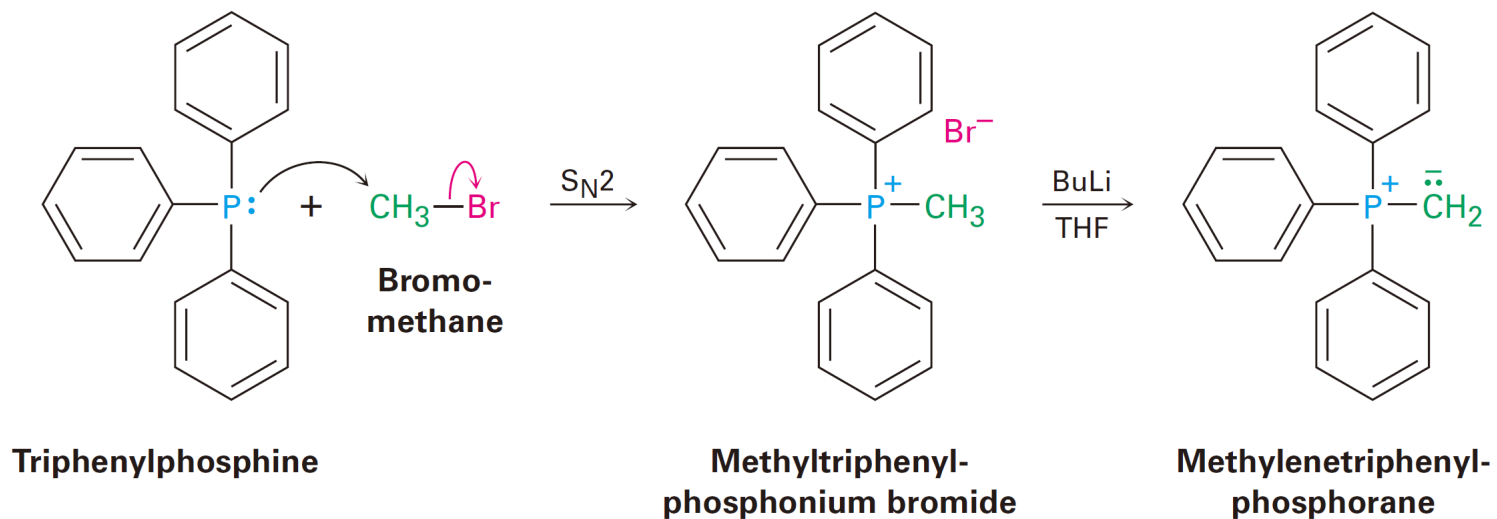
### Problem 19.15

Identify the carbonyl compound and the alcohol that were used to prepare the following acetal:



## 19.11 磷叶立德作为亲核试剂

- Wittig 反应



## 19.11 膦叶立德作为亲核试剂

- 1979 诺贝尔化学奖

### The Nobel Prize in Chemistry 1979



Photo from the Nobel Foundation archive.

Herbert C. Brown

Prize share: 1/2



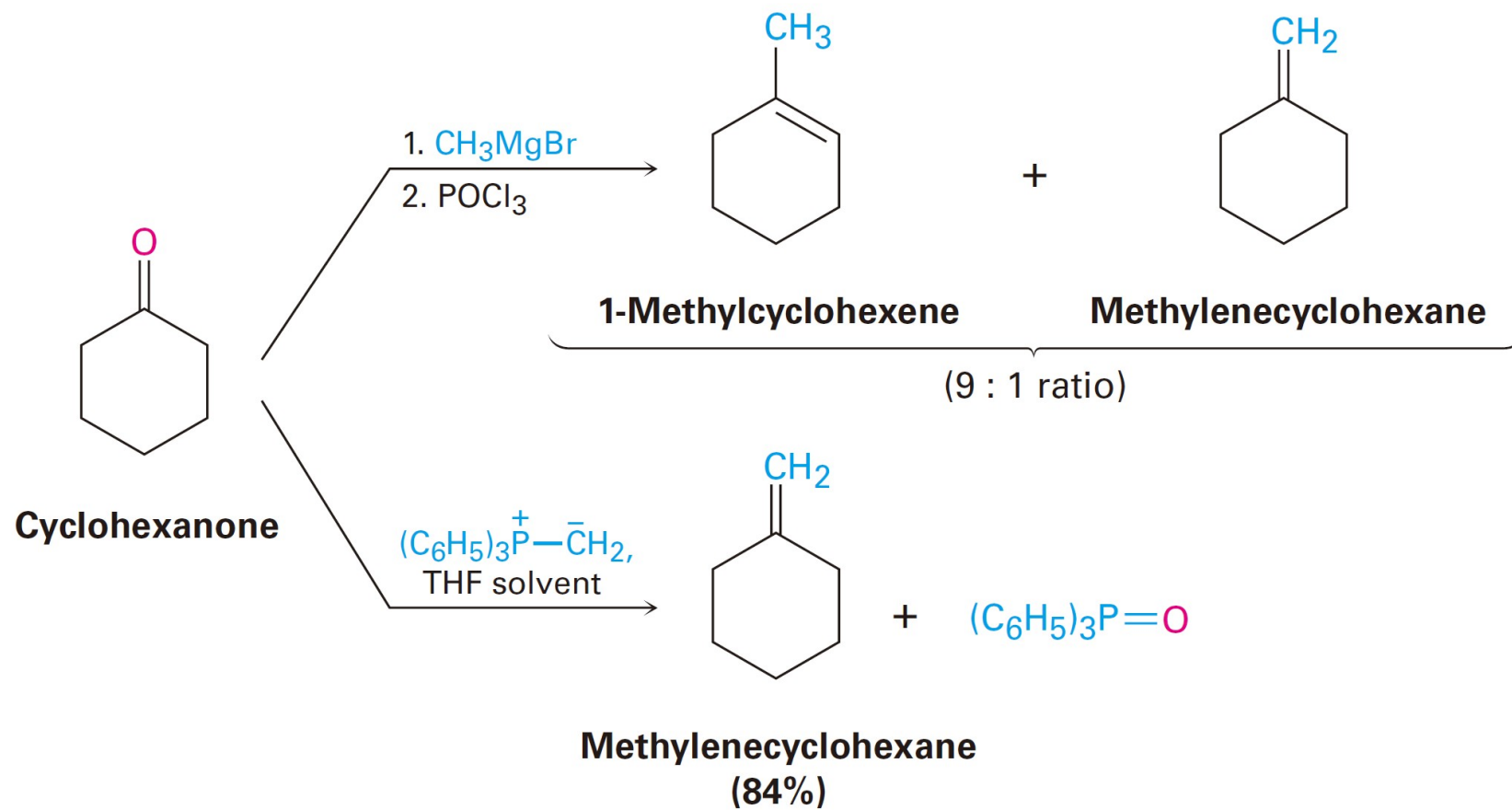
Photo from the Nobel Foundation archive.

Georg Wittig

Prize share: 1/2

The Nobel Prize in Chemistry 1979 was awarded jointly to Herbert C. Brown and Georg Wittig "for their development of the use of boron- and phosphorus-containing compounds, respectively, into important reagents in organic synthesis."

## 19.11 磷叶立德作为亲核试剂



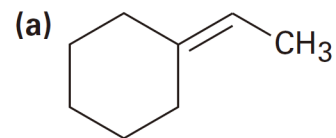
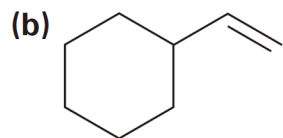
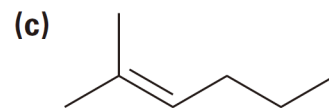
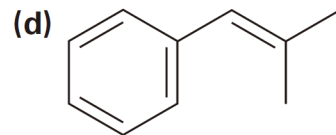
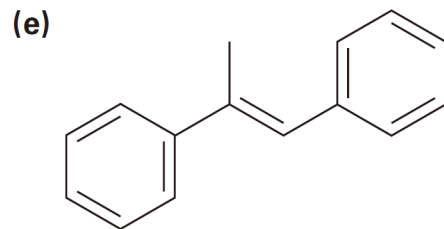
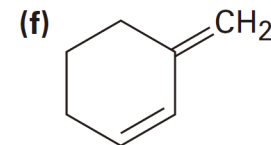


## 19.11 磷叶立德作为亲核试剂

### • 课堂练习

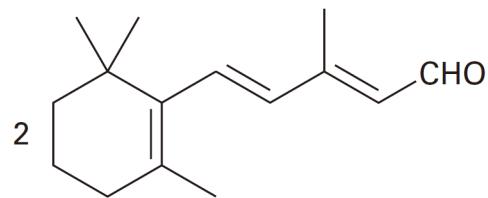
#### Problem 19.16

What carbonyl compound and what phosphorus ylide might you use to prepare each of the following compounds?

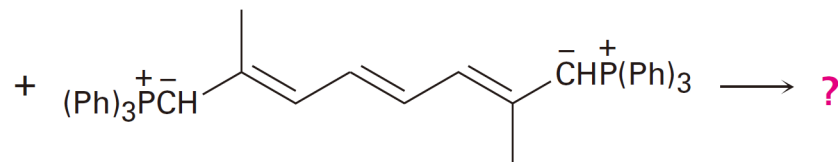


#### Problem 19.17

$\beta$ -Carotene, a yellow food-coloring agent and dietary source of vitamin A can be prepared by a *double* Wittig reaction between 2 equivalents of  $\beta$ -ionylideneacetaldehyde and a *diylide*. Show the structure of the  $\beta$ -carotene product.



$\beta$ -Ionylideneacetaldehyde

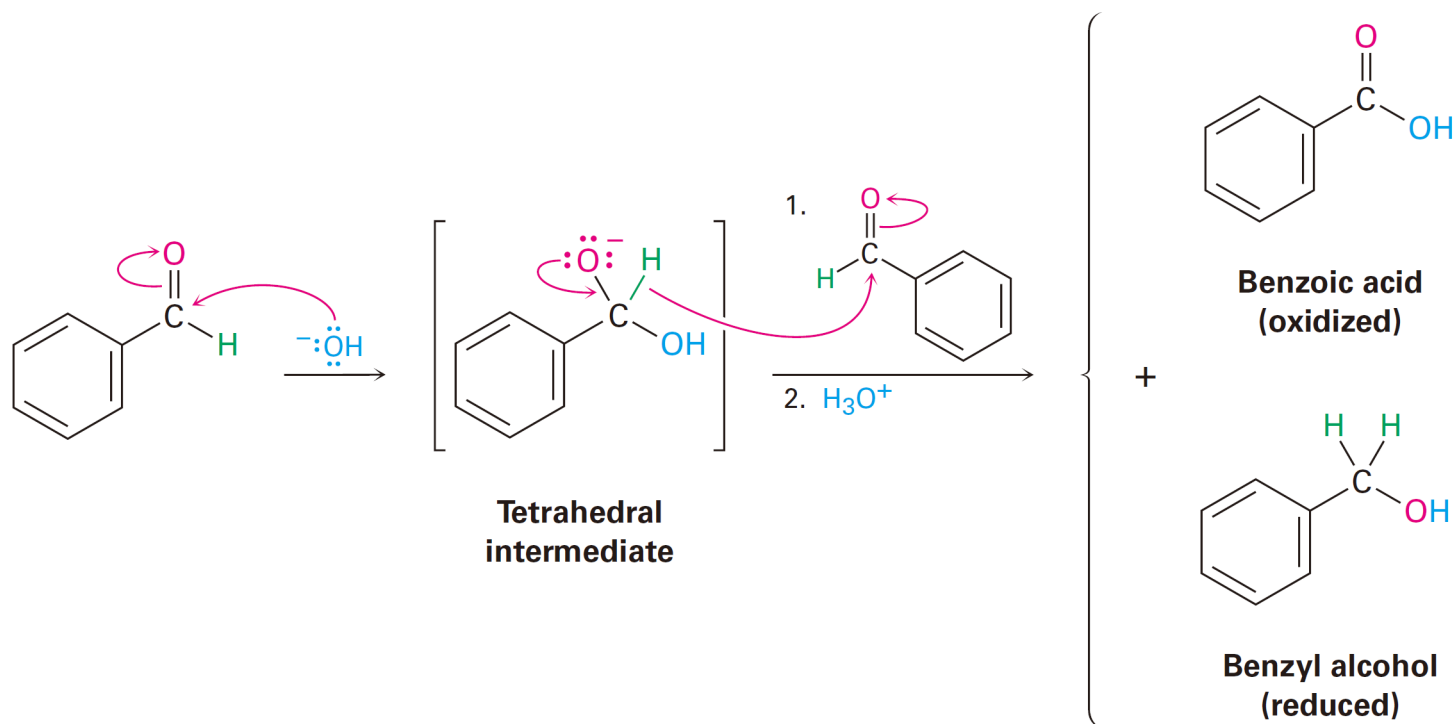


A diylide

## 19.12 生物还原

- 坎尼扎罗反应

The **Cannizzaro** reaction takes place by nucleophilic addition of  $\text{OH}^-$  to an aldehyde to give a tetrahedral intermediate, *which expels hydride ion as a leaving group* and is thereby oxidized. A second aldehyde molecule accepts the hydride ion in another nucleophilic addition step and is thereby reduced. Benzaldehyde, for instance, yields benzyl alcohol plus benzoic acid when heated with aqueous NaOH.



## 19.12 生物还原

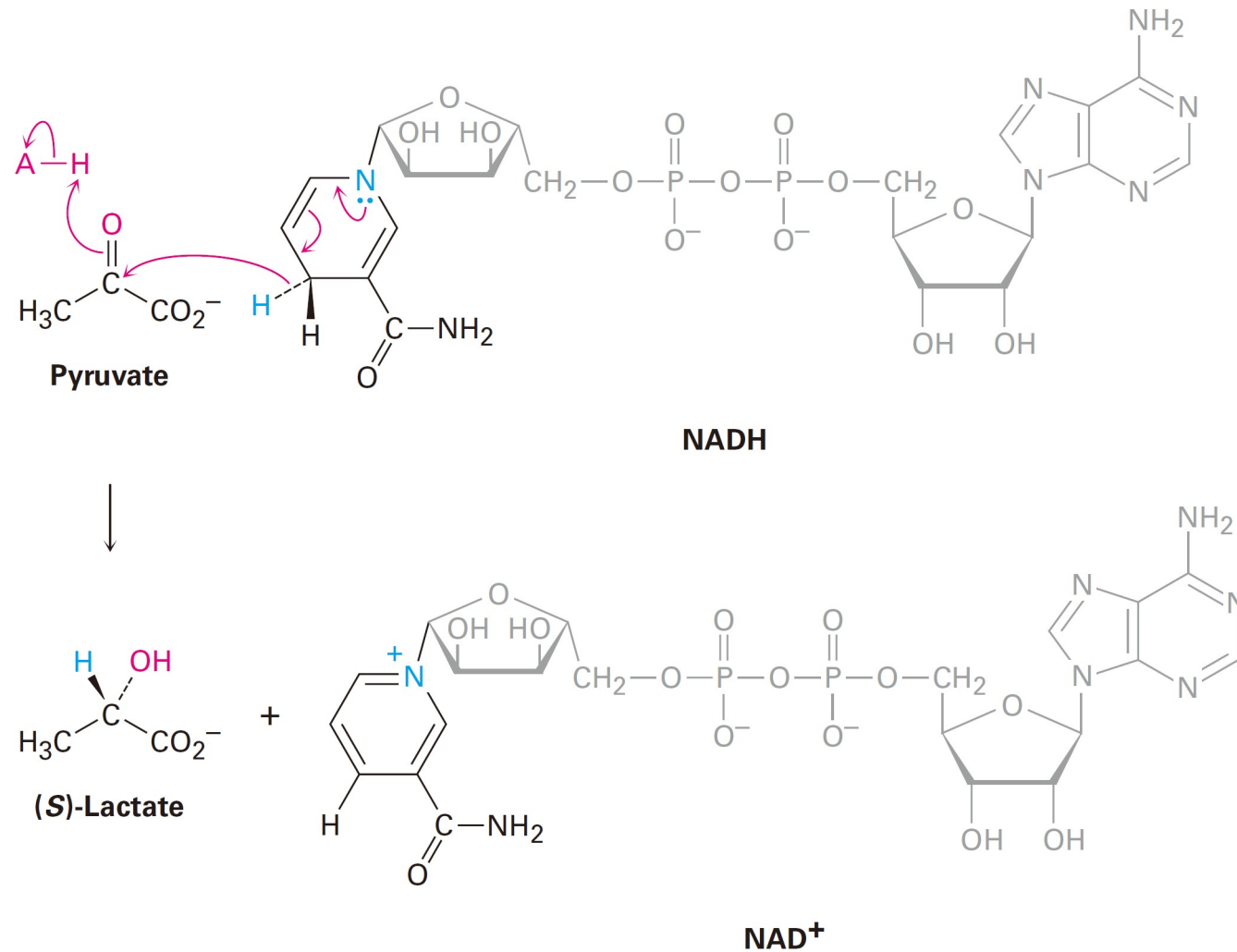
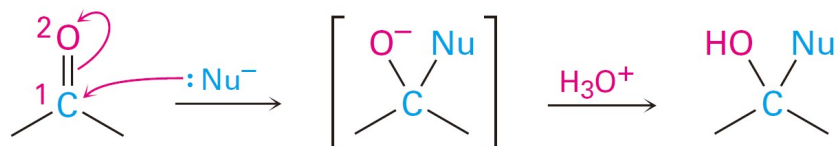


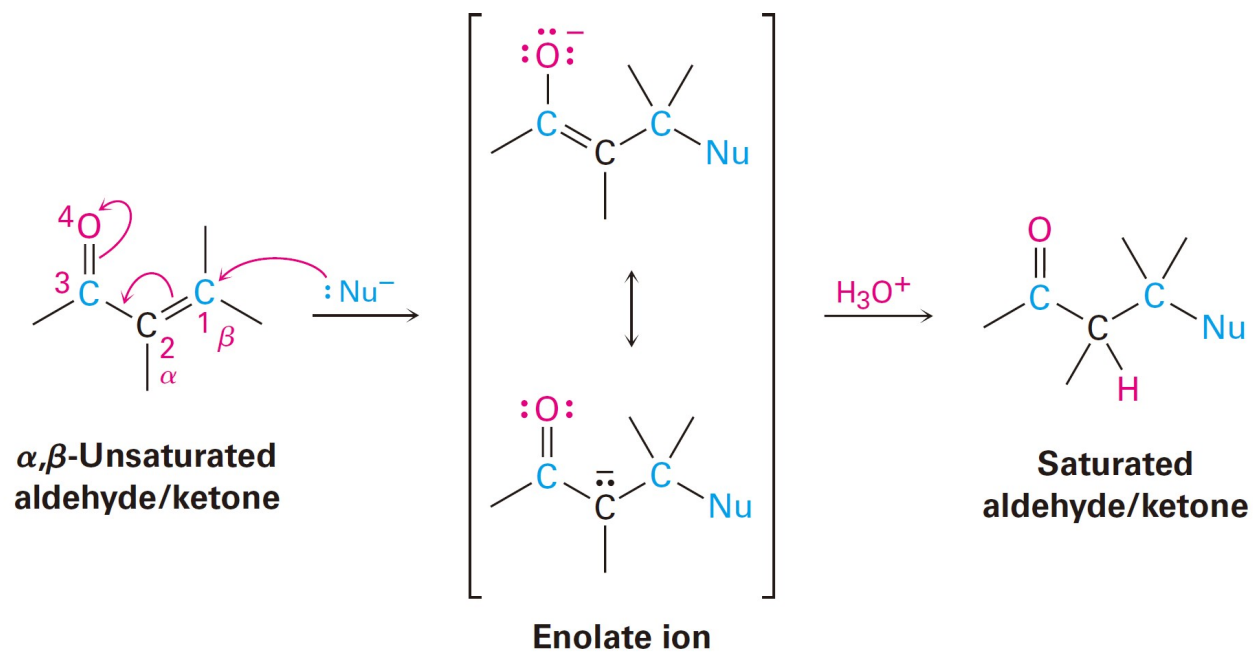
**Figure 19.12** Mechanism of biological aldehyde and ketone reductions by the coenzyme NADH. The key step is an expulsion of hydride ion from NADH and donation to the carbonyl group.

# alpha, beta- 不饱和醛酮的共轭加成

## Direct (1,2) addition



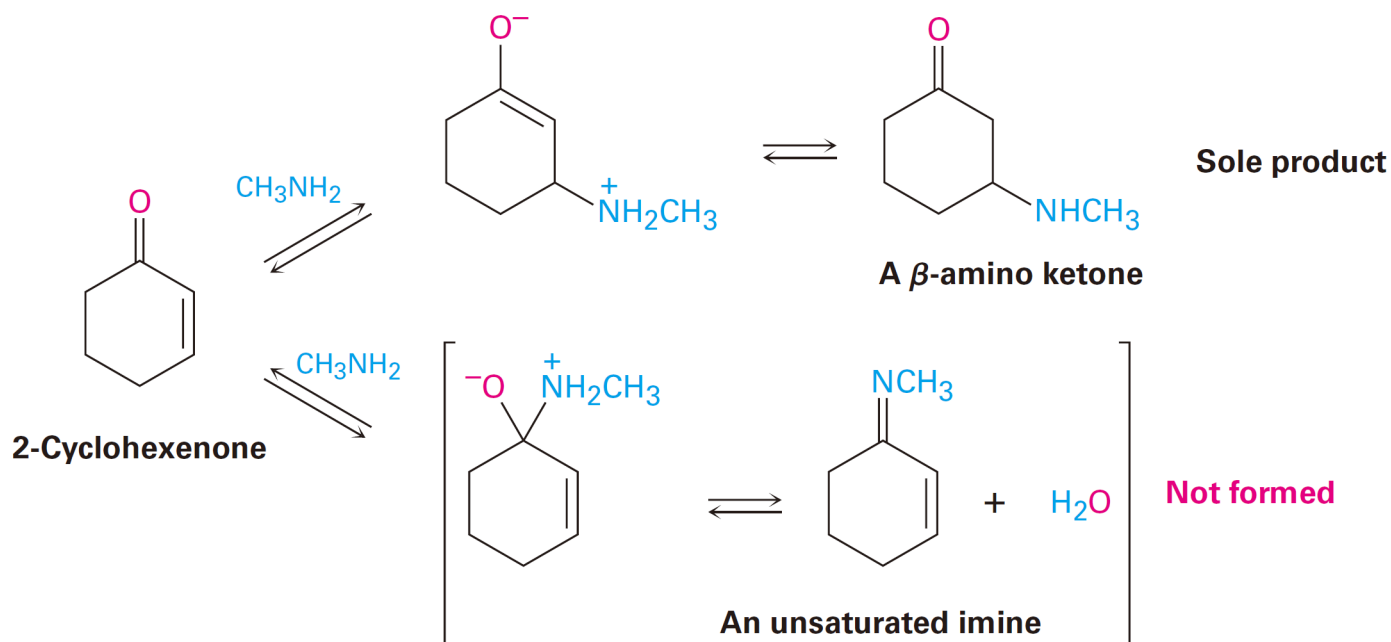
## Conjugate (1,4) addition



# alpha, beta- 不饱和醛酮的共轭加成

## Conjugate Addition of Amines

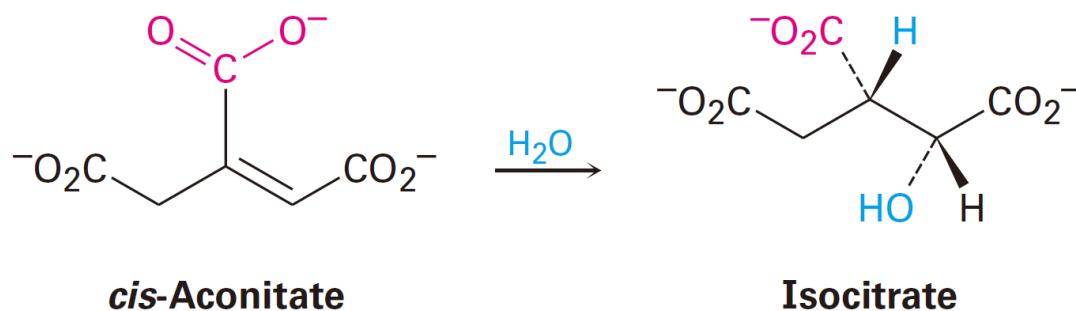
Both primary and secondary amines add to  $\alpha,\beta$ -unsaturated aldehydes and ketones to yield  $\beta$ -amino aldehydes and ketones rather than the alternative imines. Under typical reaction conditions, both modes of addition occur rapidly. But because the reactions are reversible, they generally proceed with thermodynamic control rather than kinetic control (**Section 14.3**), so the more stable conjugate addition product is often obtained to the complete exclusion of the less stable direct addition product.



## alpha, beta- 不饱和醛酮的共轭加成

### Conjugate Addition of Water

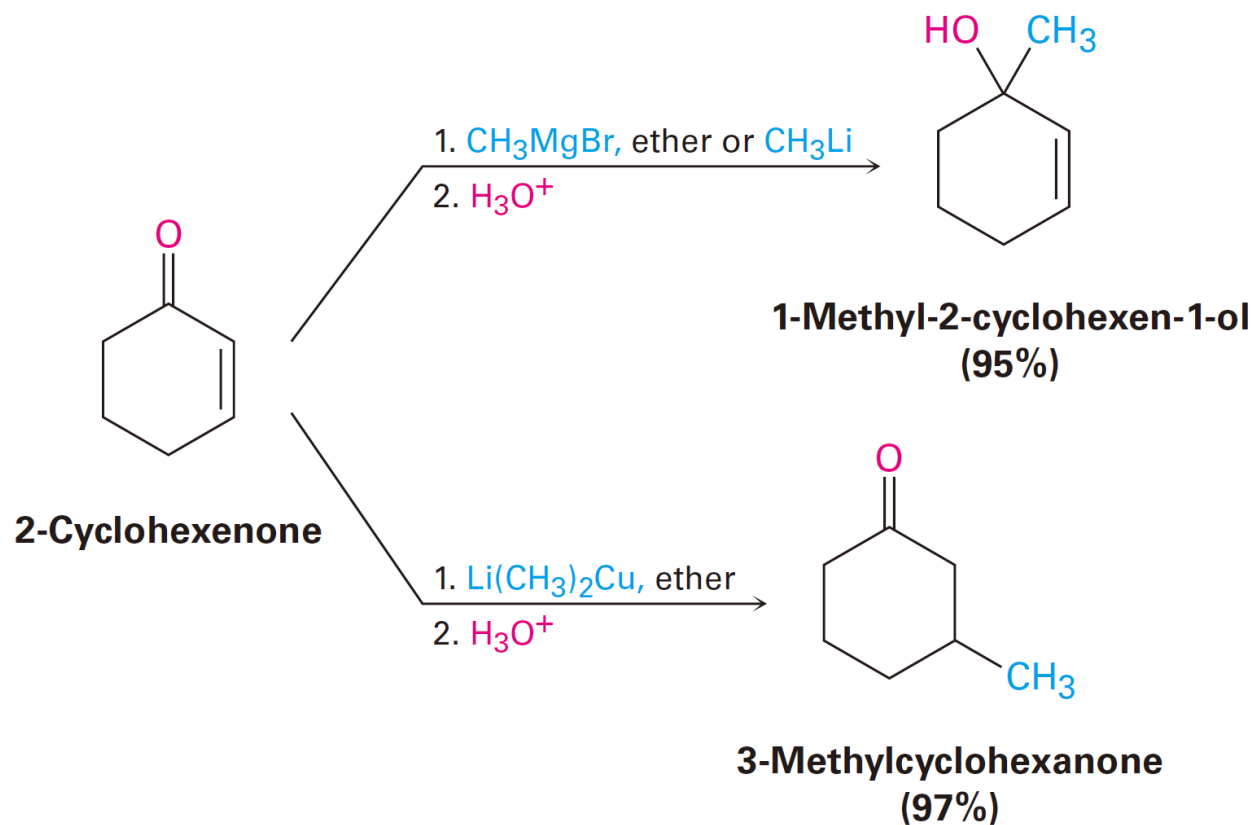
Water can add reversibly to  $\alpha,\beta$ -unsaturated aldehydes and ketones to yield  $\beta$ -hydroxy aldehydes and ketones, although the position of the equilibrium generally favors unsaturated reactant rather than saturated adduct. Related additions to  $\alpha,\beta$ -unsaturated carboxylic acids occur in numerous biological pathways, such as the citric acid cycle of food metabolism in which *cis*-aconitate is converted into isocitrate by conjugate addition of water to a double bond.



## alpha, beta- 不饱和醛酮的共轭加成

### Conjugate Addition of Alkyl Groups: Organocopper Reactions

The conjugate addition of an alkyl or other organic group to an  $\alpha,\beta$ -unsaturated ketone (but not aldehyde) is one of the more useful 1,4-addition reactions, just as direct addition of a Grignard reagent is one of the more useful 1,2 additions.

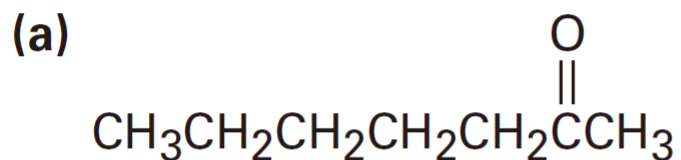
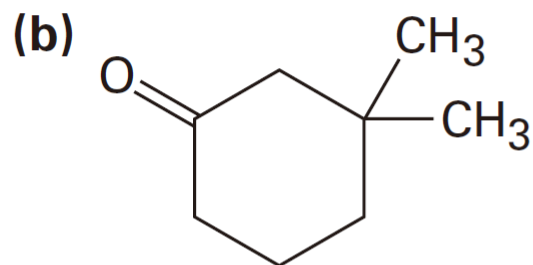
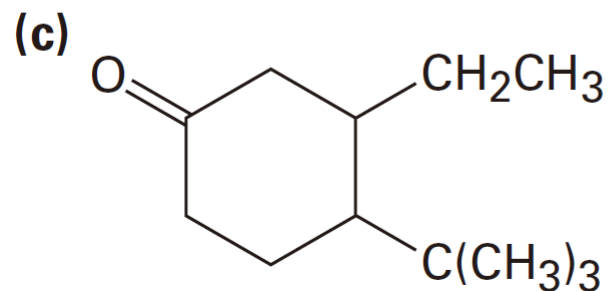
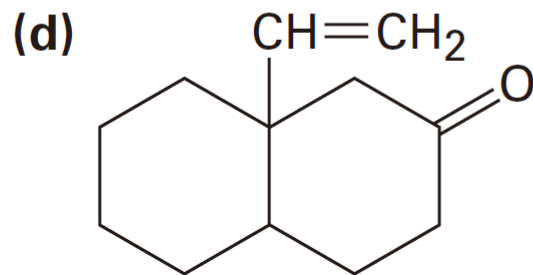


## alpha, beta- 不饱和醛酮的共轭加成

- 课堂练习

### Problem 19.22

How might conjugate addition reactions of lithium diorganocopper reagents be used to synthesize the following compounds?



## 19.14 波谱分析

- 红外

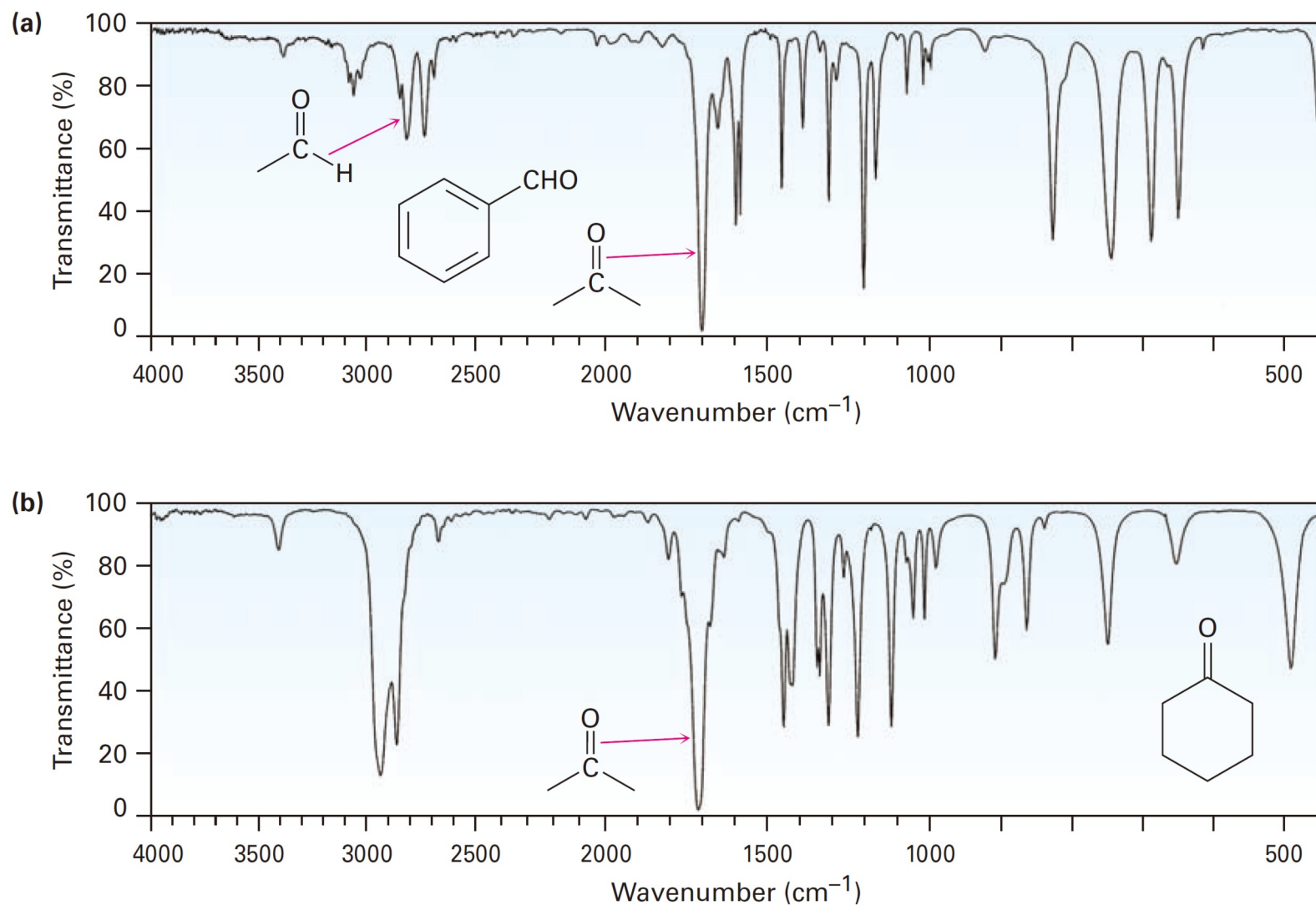


**Figure 19.14** Infrared spectra of (a) benzaldehyde and (b) cyclohexanone.

## 19.14 波谱分析

- 课堂练习

### **Problem 19.23**

How might you use IR spectroscopy to determine whether reaction between 2-cyclohexenone and lithium dimethylcopper gives the direct addition product or the conjugate addition product?

### **Problem 19.24**

Where would you expect each of the following compounds to absorb in the IR spectrum?

**(a)** 4-Penten-2-one

**(b)** 3-Penten-2-one

**(c)** 2,2-Dimethylcyclopentanone

**(d)** *m*-Chlorobenzaldehyde

**(e)** 3-Cyclohexenone

**(f)** 2-Hexenal



## 19.14 波谱分析

### • 核磁

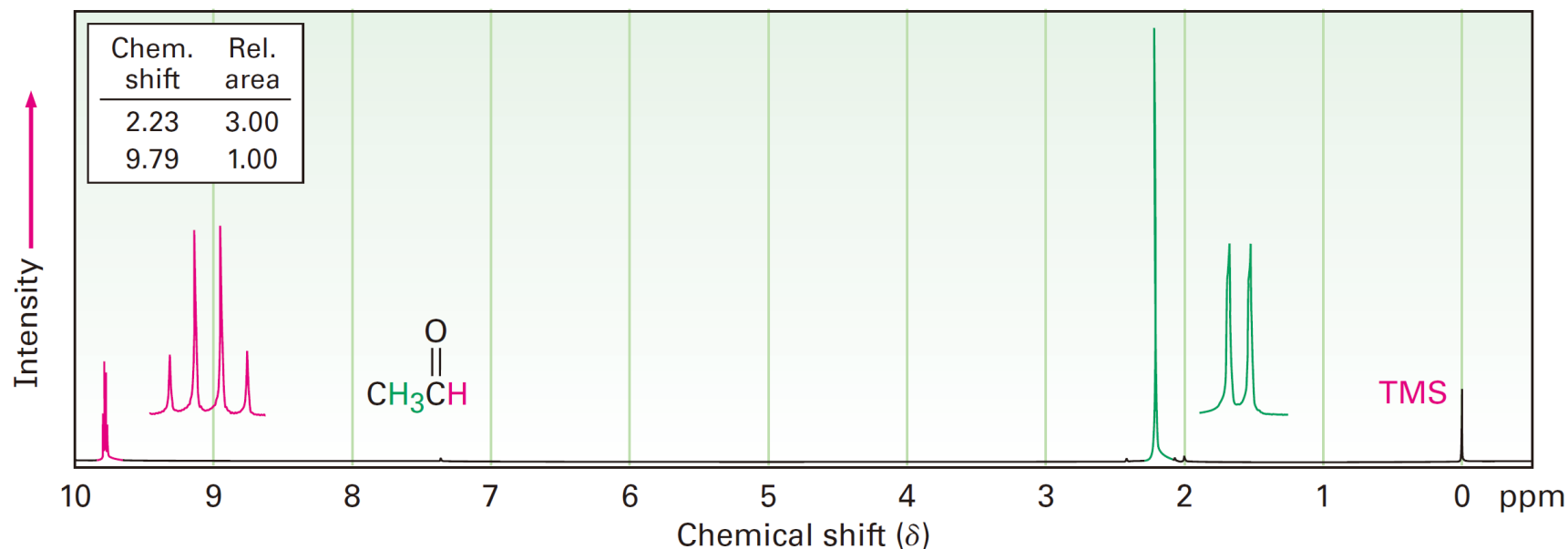
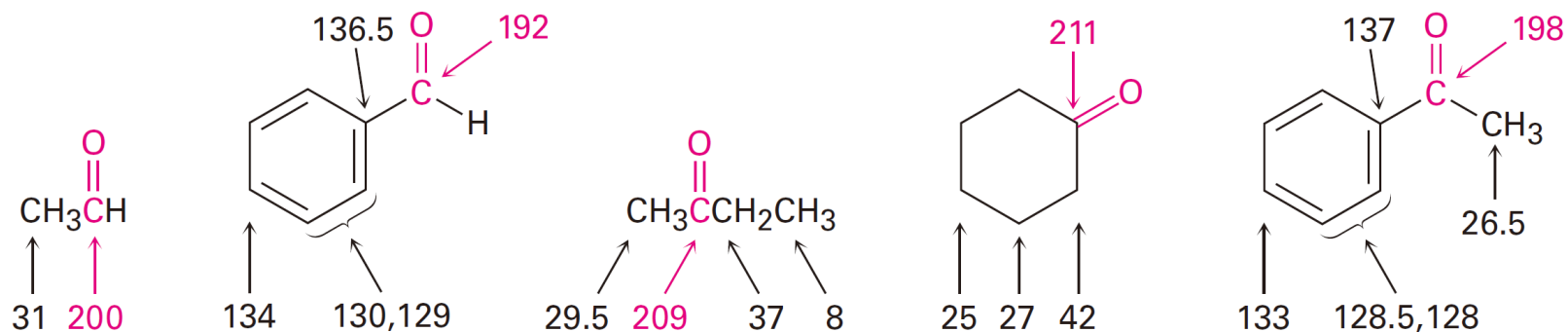
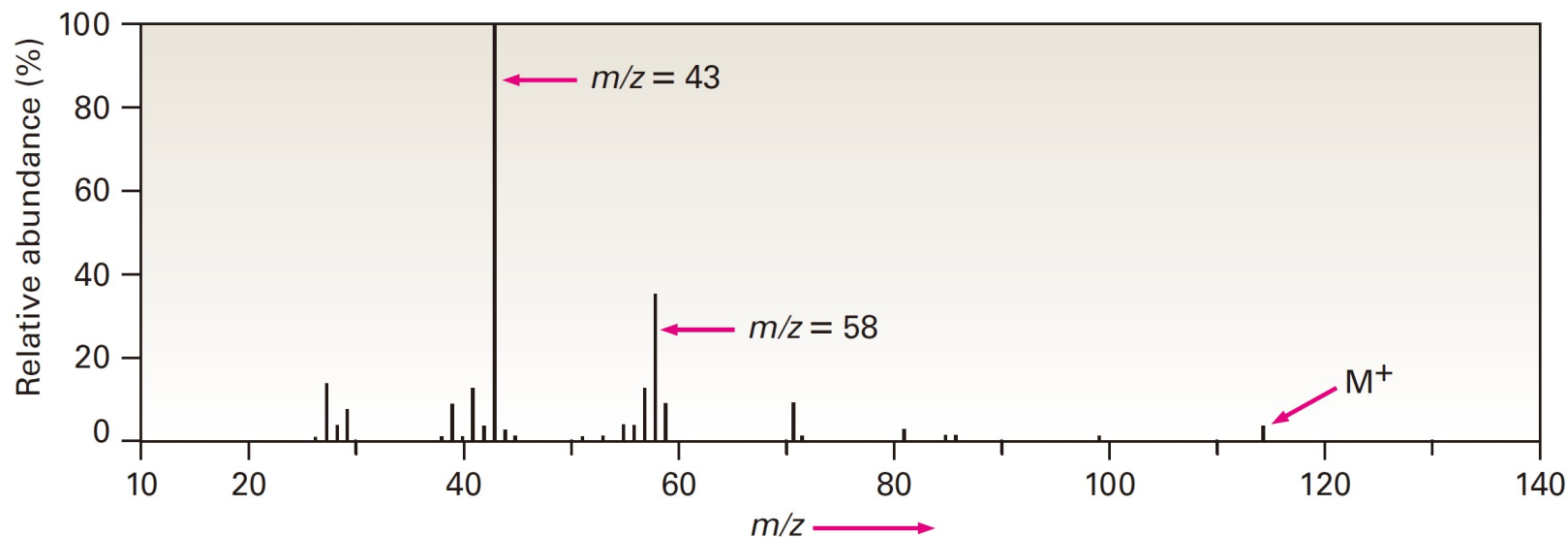
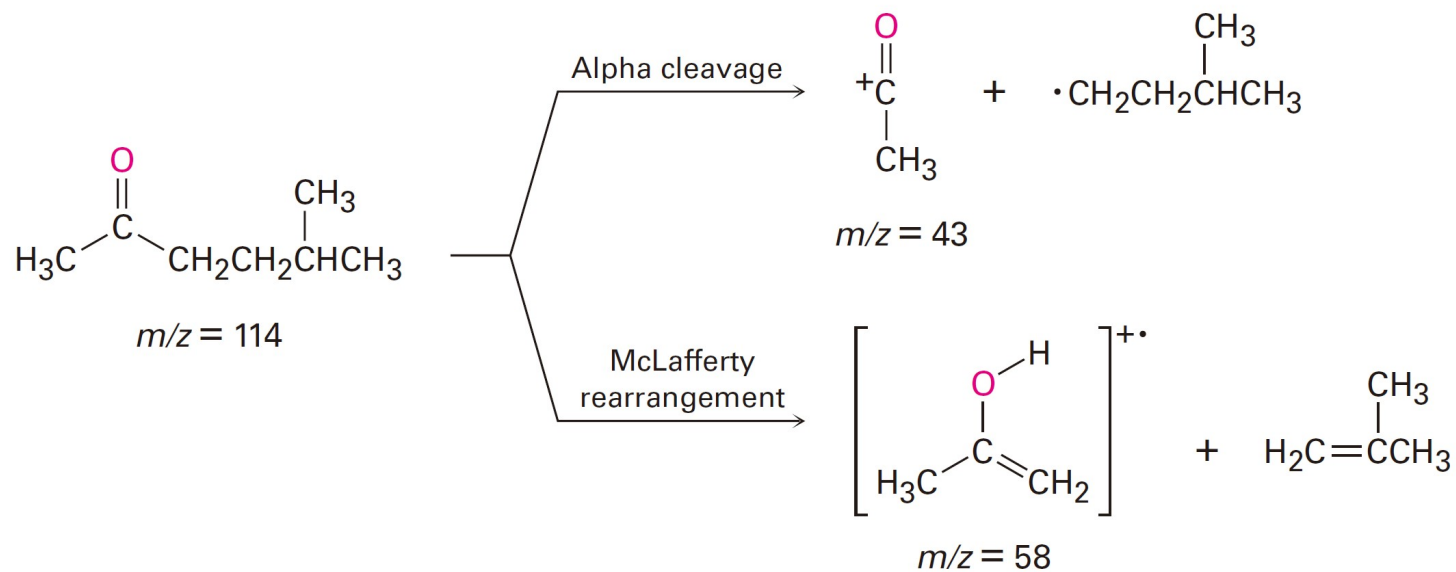


**Figure 19.15**  $^1\text{H}$  NMR spectrum of acetaldehyde. The absorption of the aldehyde proton appears at 9.8  $\delta$  and is split into a quartet.



## 19.14 波谱分析

### • 质谱



# 作业

- 19.47, 19.54, 19.55, 19.60, 19.61, 19.62, 19.63, 19.66, 19.68, 19.71, 19.73

