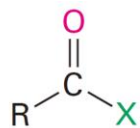
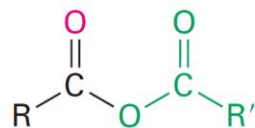


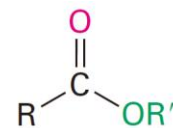
Carboxylic acid



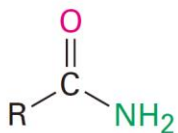
Acid halide  
(X = Cl, Br)



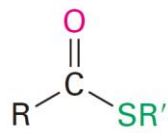
Acid anhydride



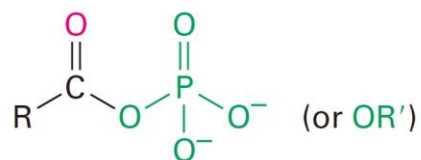
Ester



Amide



Thioester



Acyl phosphate

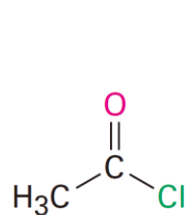
# 21

# 羧酸衍生物

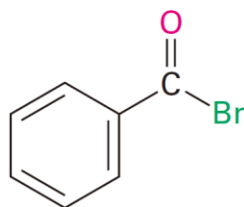


# 21.1 命名

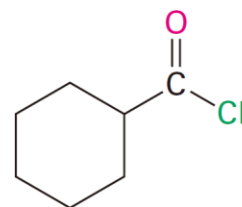
## 酰卤(酰氯, 酰溴)



Acetyl  
chloride

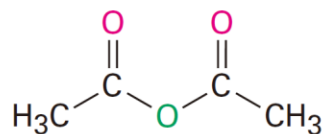


Benzoyl  
bromide

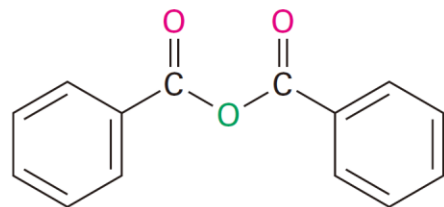


Cyclohexanecarbonyl  
chloride

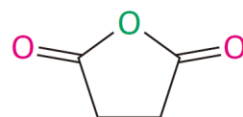
## 酸酐



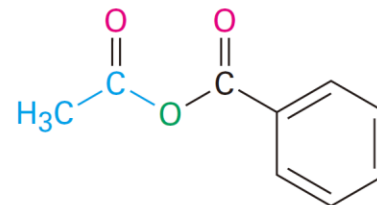
Acetic anhydride



Benzoic anhydride

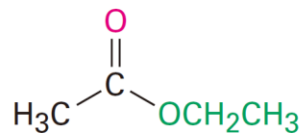


Succinic anhydride

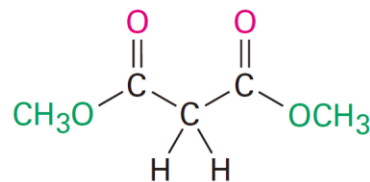


Acetic benzoic anhydride

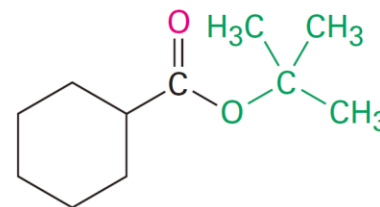
## 酯



Ethyl acetate



Dimethyl malonate

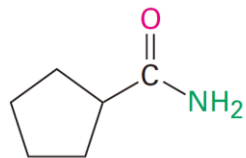


*tert*-Butyl cyclohexane-  
carboxylate

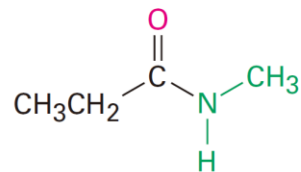


# 21.1 命名

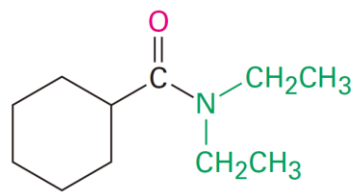
## 酰胺



Cyclopentane-carboxamide

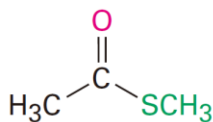


*N*-Methylpropanamide

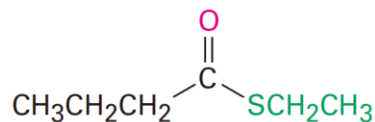


*N,N*-Diethylcyclohexanecarboxamide

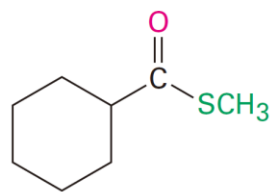
## 硫酯



Methyl thioacetate

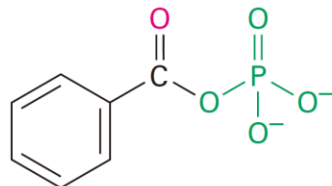


Ethyl butanethioate

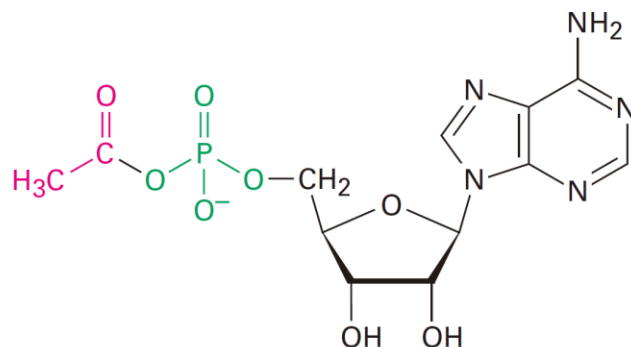


Methyl cyclohexane-carbothioate

## 酰基磷酸酯

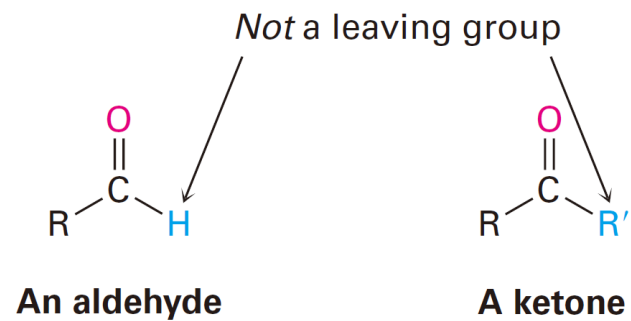


Benzoyl phosphate

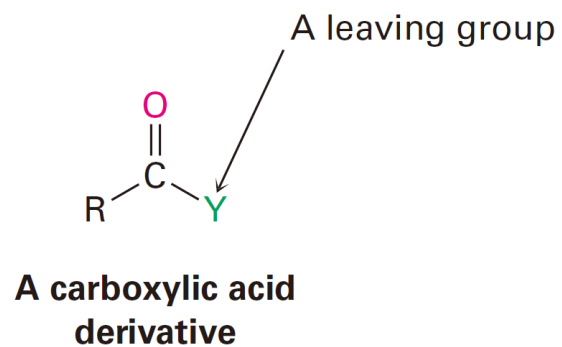
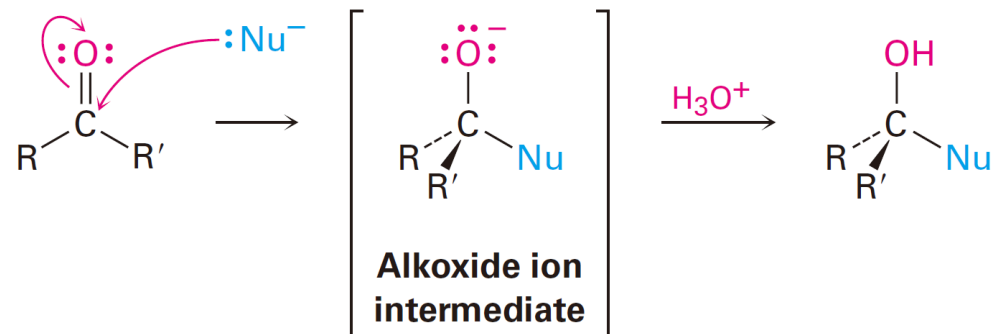


Acetyl adenosyl phosphate

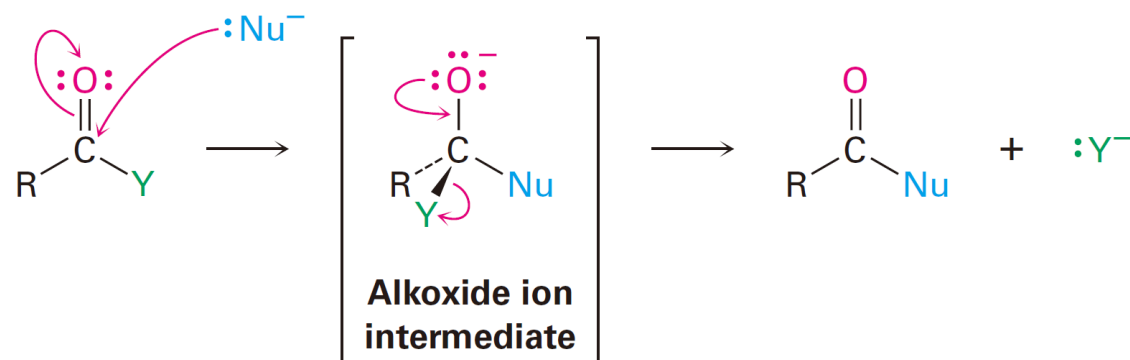
## 21.2 酰基亲核取代反应



(a) Aldehyde or ketone: nucleophilic addition

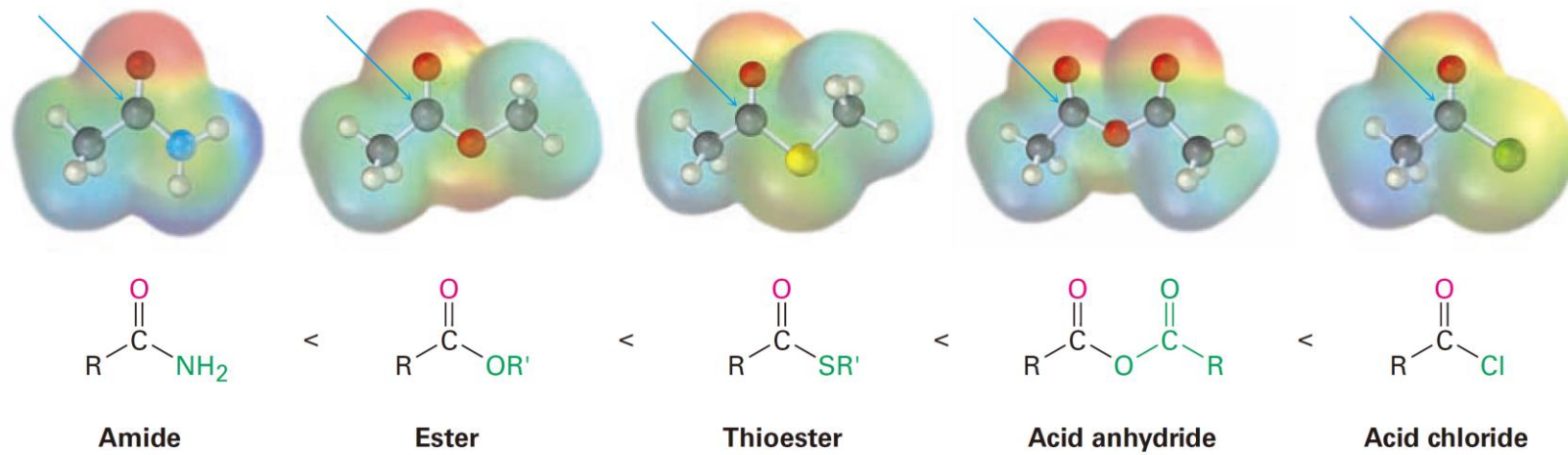
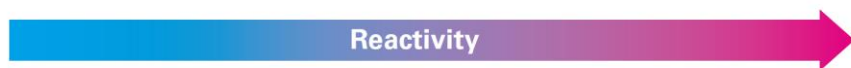
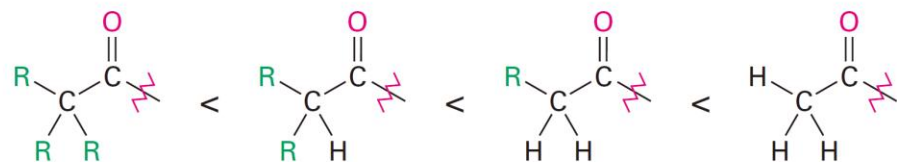


(b) Carboxylic acid derivative: nucleophilic acyl substitution



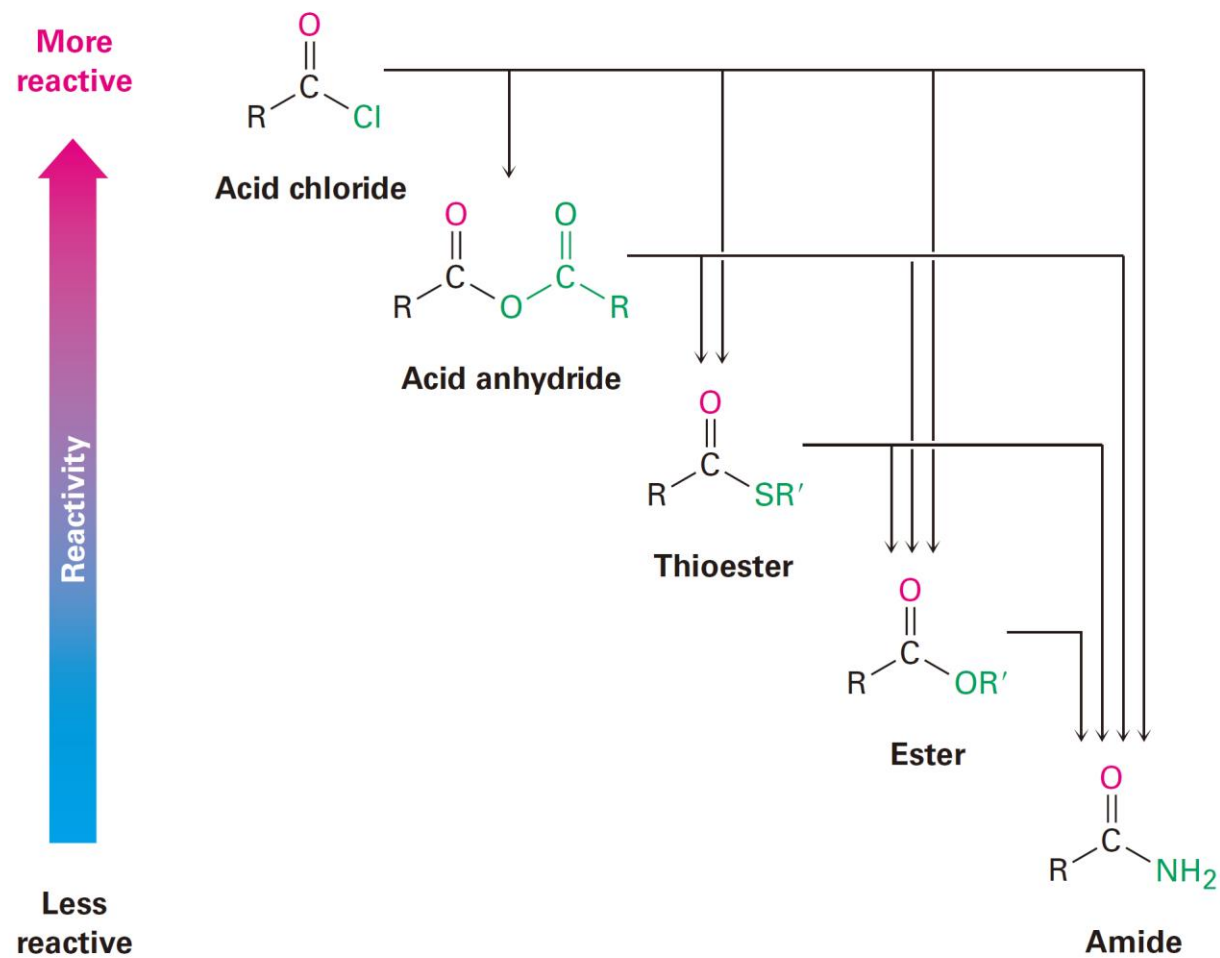
## 21.2 酰基亲核取代反应

- 相对反应活性比较：位阻和电性



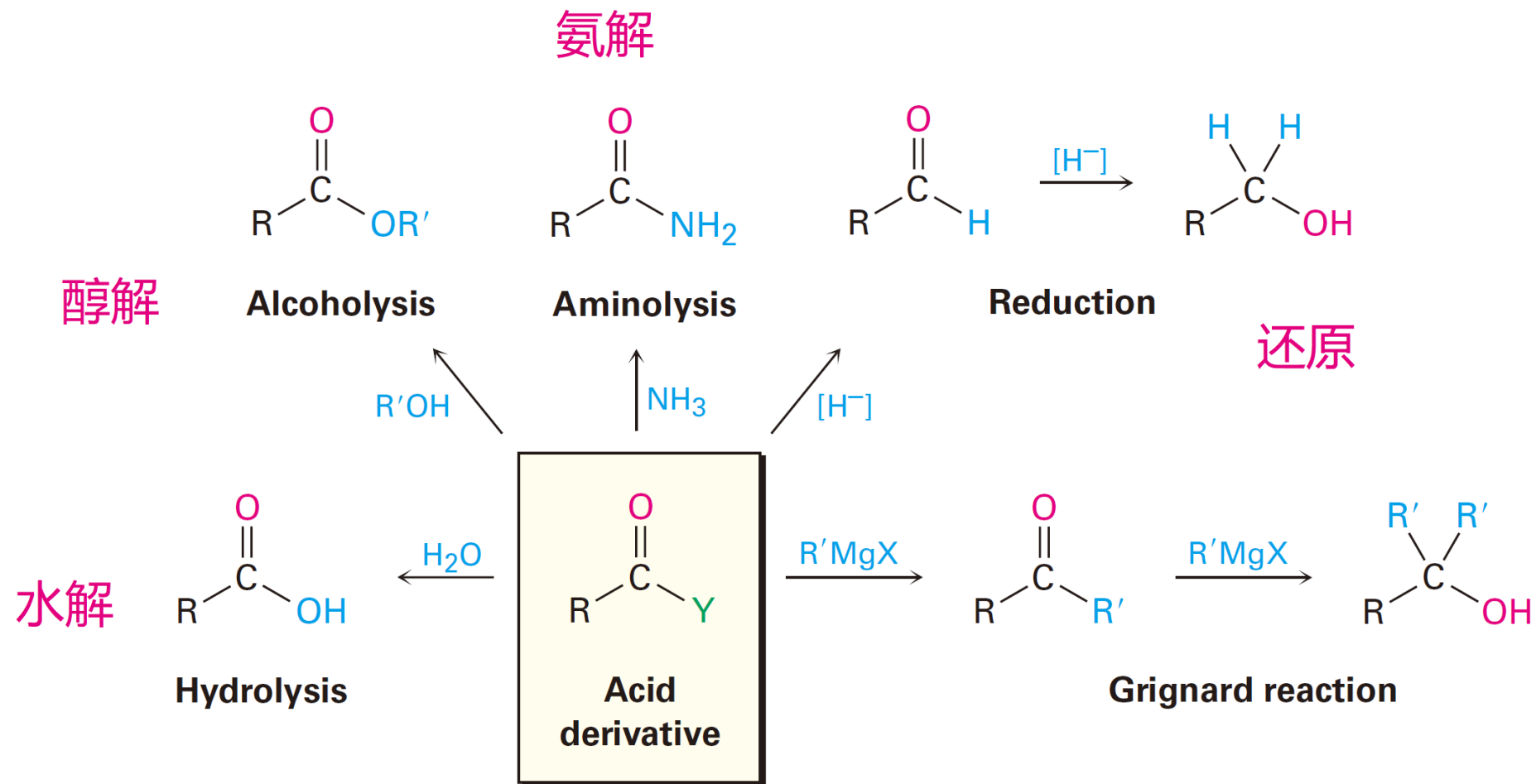
## 21.2 酰基亲核取代反应

- 转化关系：活性高的制备活性低的，这是一般情况。



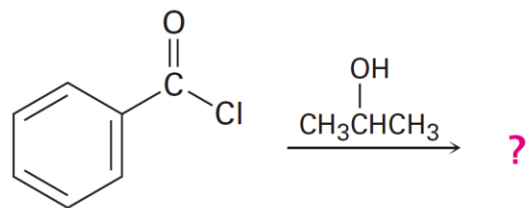
**Figure 21.2** Interconversions of carboxylic acid derivatives. A more reactive acid derivative can be converted into a less reactive one, but not vice versa.

## 21.2 酰基亲核取代反应



## 21.2 酰基亲核取代反应

- 例题

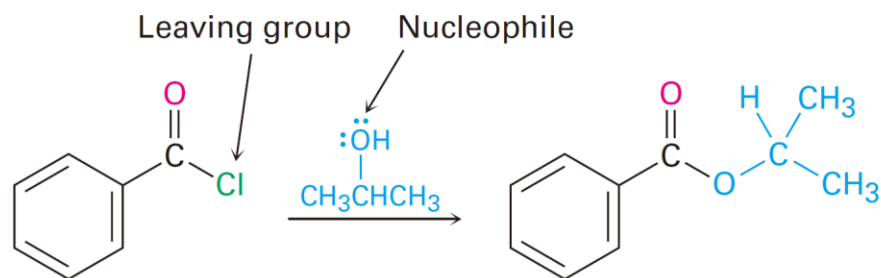


**Benzoyl chloride**

### Strategy

A nucleophilic acyl substitution reaction involves the substitution of a nucleophile for a leaving group in a carboxylic acid derivative. Identify the leaving group ( $\text{Cl}^-$  in the case of an acid chloride) and the nucleophile (an alcohol in this case), and replace one by the other. The product is isopropyl benzoate.

### Solution



**Benzoyl chloride**

**Isopropyl benzoate**

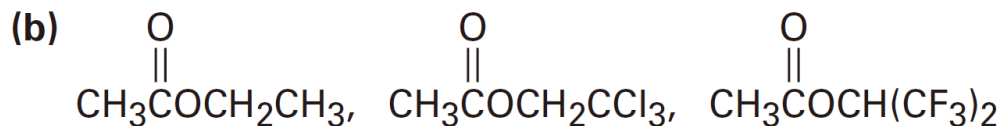
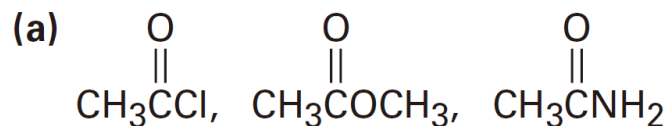


## 21.2 酰基亲核取代反应

### • 课堂练习

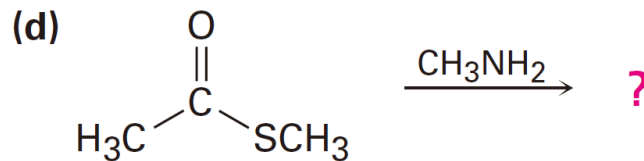
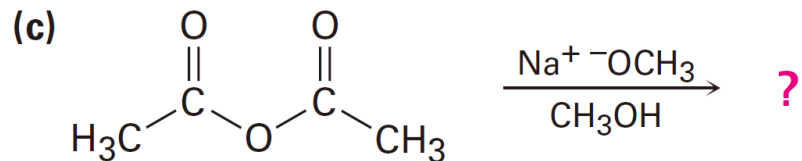
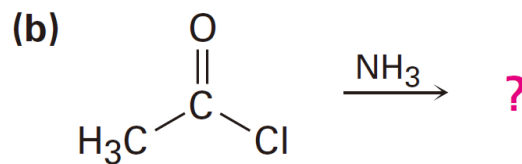
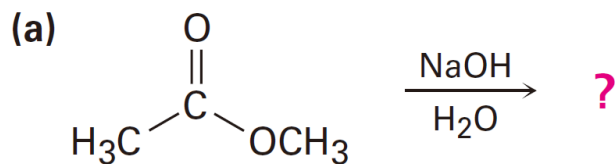
#### Problem 21.4

Rank the compounds in each of the following sets in order of their expected reactivity toward nucleophilic acyl substitution:



#### Problem 21.5

Predict the products of the following nucleophilic acyl substitution reactions:

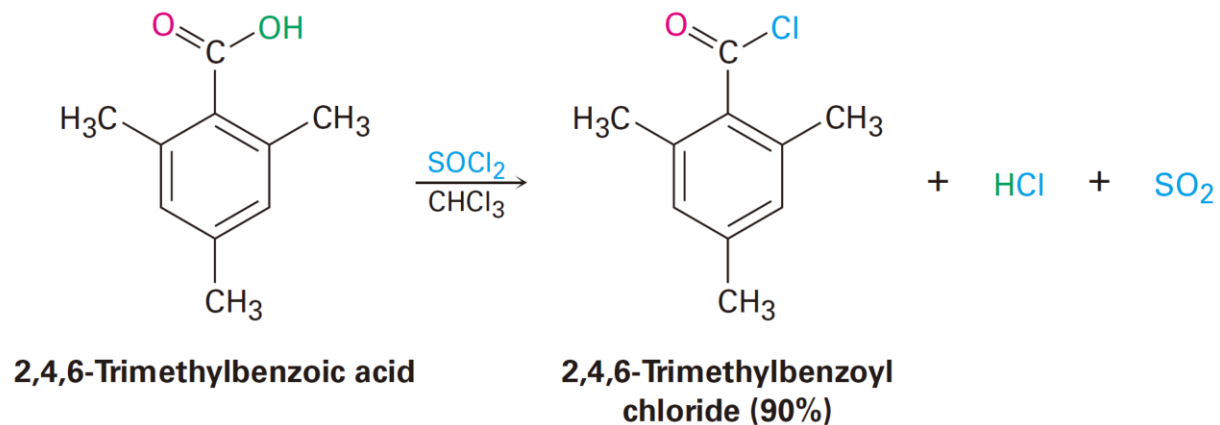


## 21.3 羧酸的酰基亲核取代反应

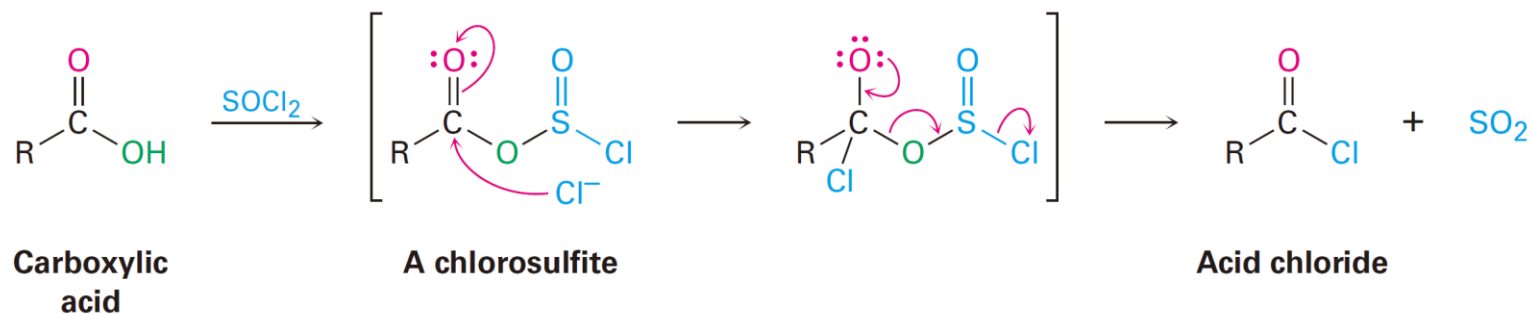
- 羧酸制备酰氯

### Conversion of Carboxylic Acids into Acid Chlorides

In the laboratory, carboxylic acids are converted into acid chlorides by treatment with thionyl chloride,  $\text{SOCl}_2$ .



机理

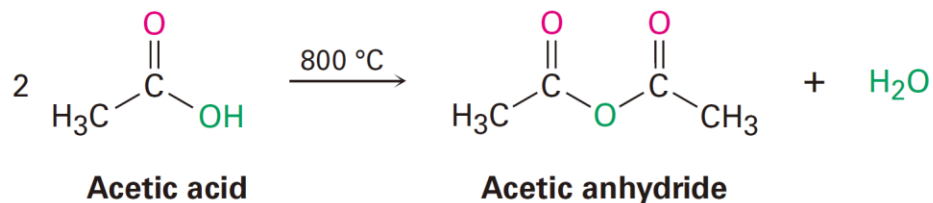


## 21.3 羧酸的酰基亲核取代反应

- 羧酸制备酸酐

### Conversion of Carboxylic Acids into Acid Anhydrides

Acid anhydrides can be derived from two molecules of carboxylic acid by heating to remove 1 equivalent of water. Because of the high temperatures needed, however, only acetic anhydride is commonly prepared this way.



生产 [\[编辑\]](#)

乙酸酐可由乙酸甲酯的孟山都法羰基化制得，常以铑和锂的碘化物作催化剂：<sup>[1]</sup>



该反应中，乙酸甲酯先被转化为碘甲烷和一个乙酸盐。然后碘甲烷的羰基化得到乙酰碘，和乙酸盐或乙酸反应生成产物。由于乙酸酐在水中不稳定，该反应需在无水环境中进行。相比之下，孟山都乙酸合成法虽然也涉及含铑催化剂催化羰基化碘甲烷，但起码有部分反应是在水溶液中的。

1922年，随着由乙酸酐合成的醋酸纤维需求量大大增加，瓦克（Wacker Chemie）发明了一种新的制取乙酸酐的方法，即以乙烯酮和乙酸反应来制取。该反应中的乙烯酮可由乙酸高温失水获得。

乙酸酐价格很便宜，在实验室中通常不需制取，直接购买使用。



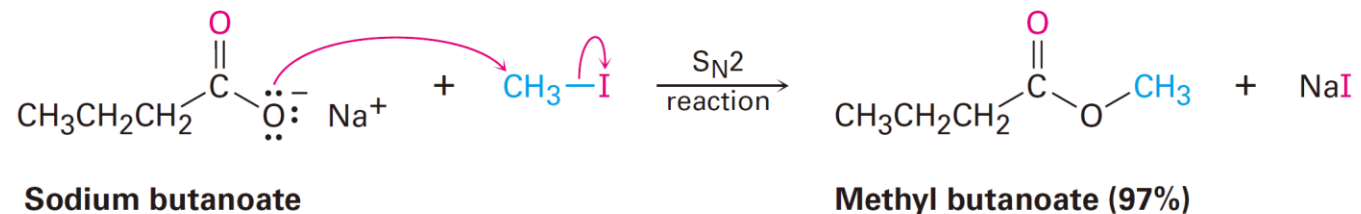
## 21.3 羧酸的酰基亲核取代反应

- 羧酸制备酯

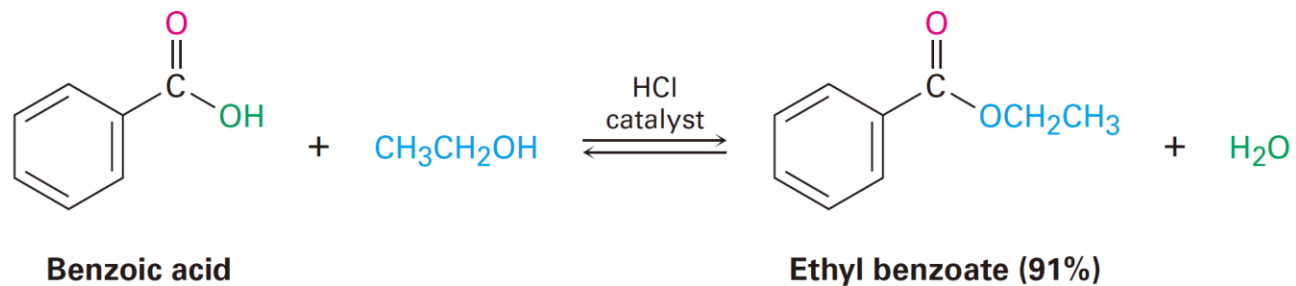
### Conversion of Carboxylic Acids into Esters

Perhaps the most useful reaction of carboxylic acids is their conversion into esters.

碱性条件



酸性条件

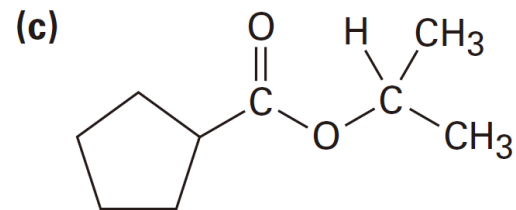
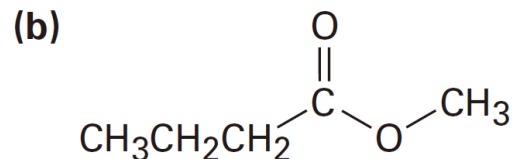
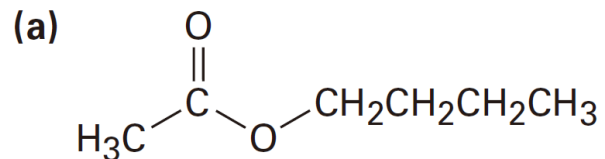


## 21.3 羧酸的酰基亲核取代反应

### • 练习

#### Problem 21.7

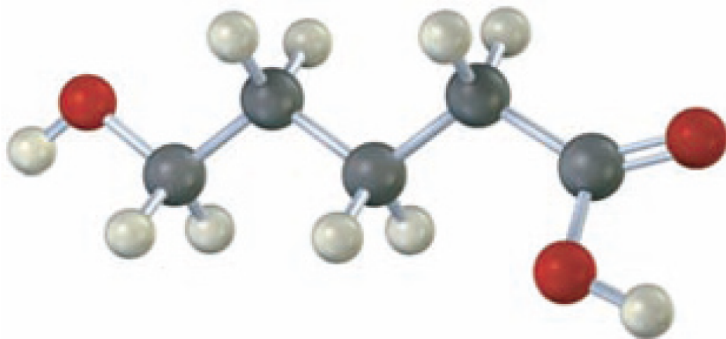
How might you prepare the following esters from the corresponding acids?



分子内酯化

#### Problem 21.8

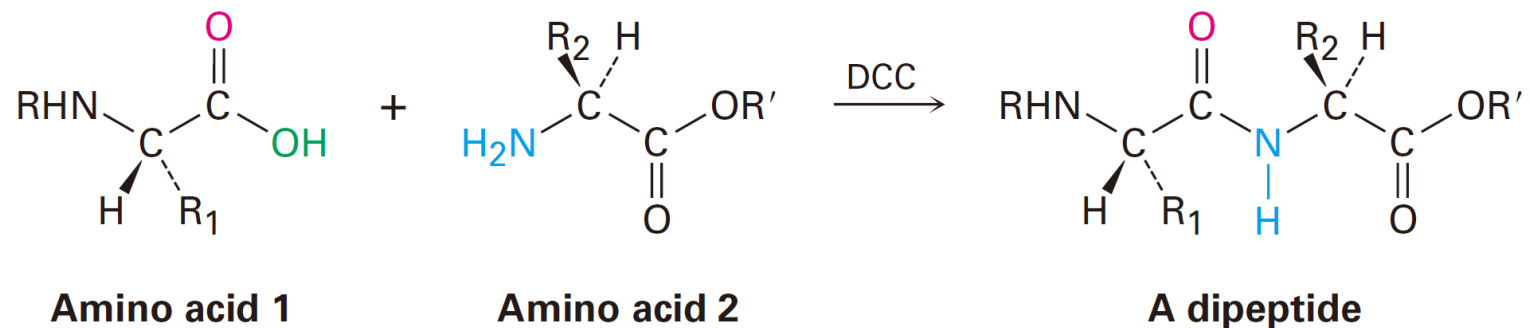
If the following molecule is treated with acid catalyst, an **intramolecular esterification** reaction occurs. What is the structure of the product? (*Intramolecular* means within the same molecule.)



## 21.3 羧酸的酰基亲核取代反应

- 羧酸制备酰胺

### Conversion of Carboxylic Acids into Amides

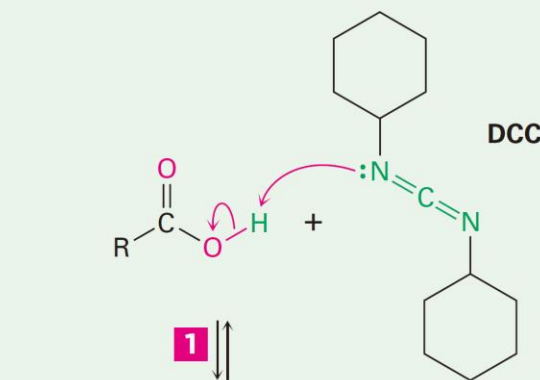


酰胺通常更难制备一些，需要脱水剂，如DCC

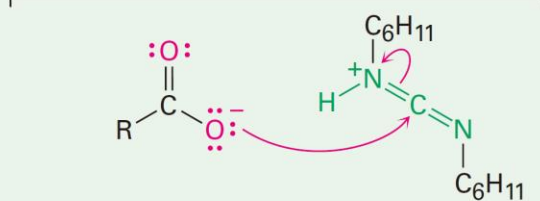
# 21.3 羧酸的酰基亲核取代反应

## • 反应机理

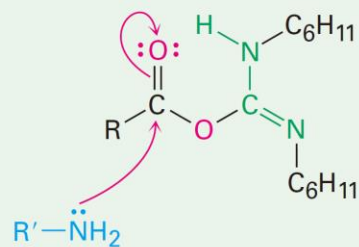
**1** Dicyclohexylcarbodiimide is first protonated by the carboxylic acid to make it a better acceptor.



**2** The carboxylate then adds to the protonated carbodiimide to yield a reactive acylating agent.

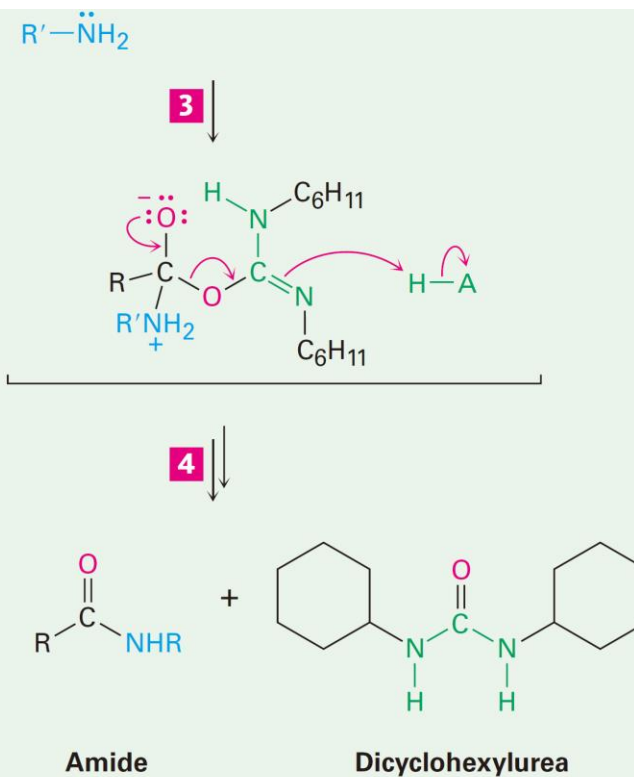


**3** Nucleophilic attack of the



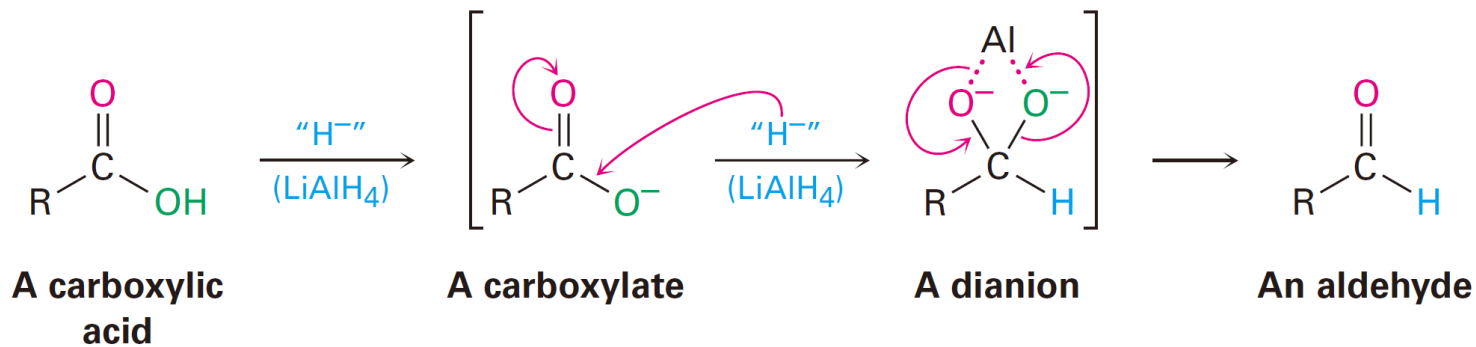
**3** Nucleophilic attack of the amine on the acylating agent gives a tetrahedral intermediate.

**4** The intermediate loses dicyclohexylurea and gives the amide.

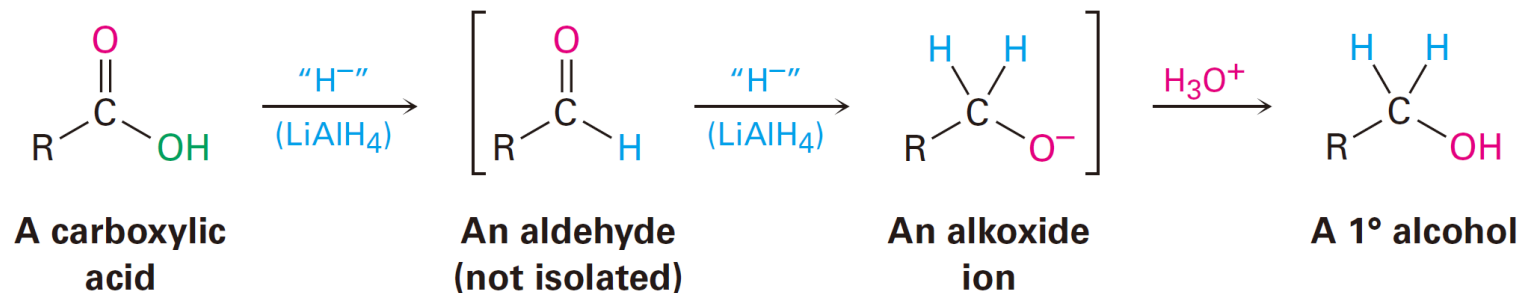


## 21.3 羧酸的酰基亲核取代反应

- 羧酸还原制备醇



中间产物：醛



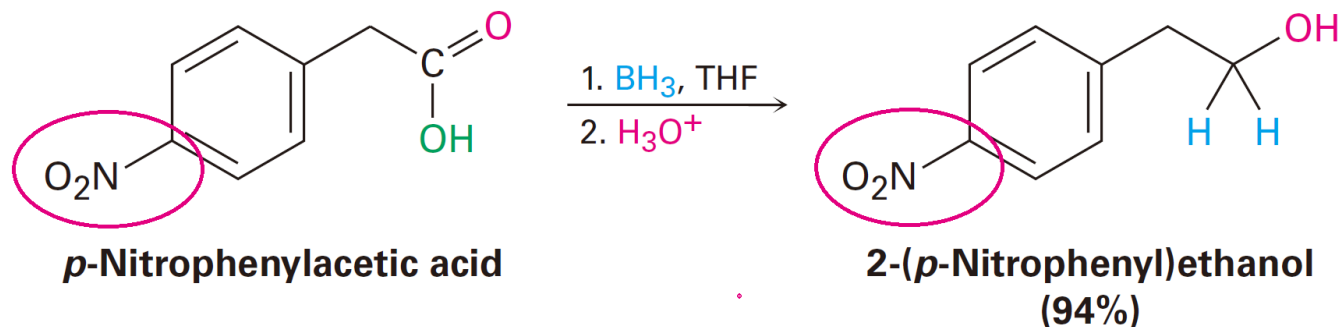
醛比羧酸更活泼，无法停留在醛，直接还原为一级醇。



## 21.3 羧酸的酰基亲核取代反应

- 羧酸还原制备醇

Alternatively, borane in tetrahydrofuran ( $\text{BH}_3/\text{THF}$ ) is a useful reagent for reducing carboxylic acids to primary alcohols. Reaction of an acid with  $\text{BH}_3/\text{THF}$  occurs rapidly at room temperature, and the procedure is often preferred to reduction with  $\text{LiAlH}_4$  because of its relative ease and safety. Borane reacts with carboxylic acids faster than with any other functional group, thereby allowing selective transformations such as that on *p*-nitrophenylacetic acid. If the reduction of *p*-nitrophenylacetic acid were done with  $\text{LiAlH}_4$ , both nitro and carboxyl groups would be reduced.



## 21.4 酰卤的化学反应

- 酰卤的制备

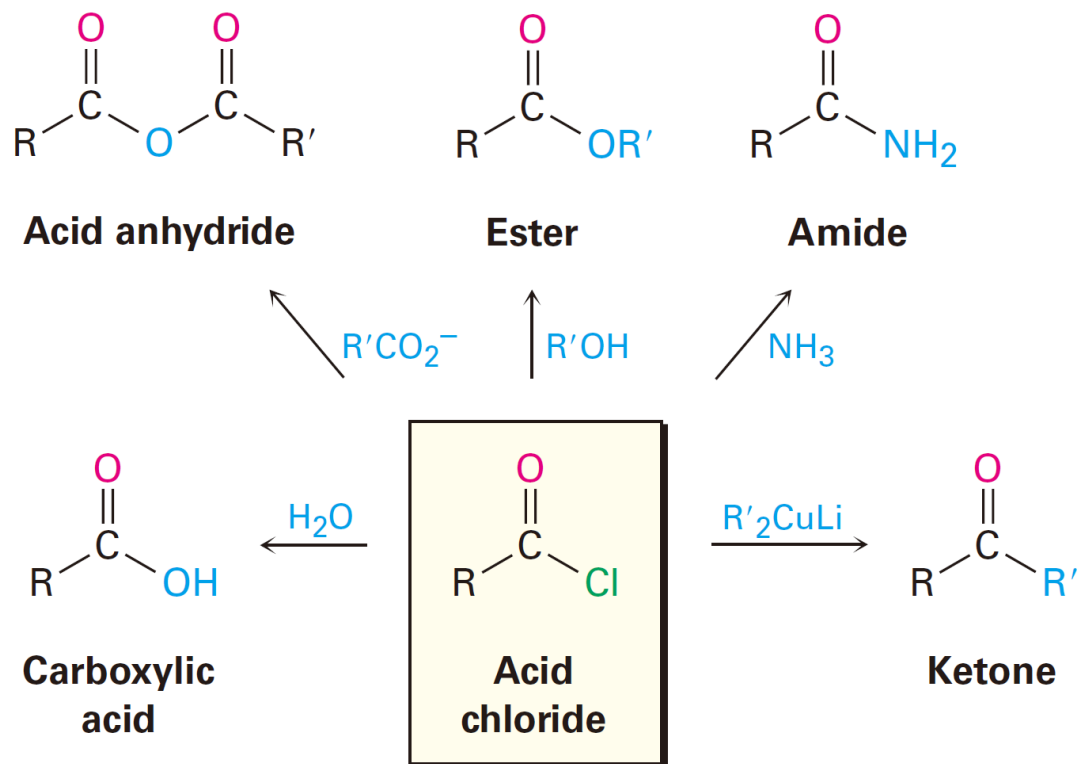
### Preparation of Acid Halides

Acid chlorides are prepared from carboxylic acids by reaction with thionyl chloride ( $\text{SOCl}_2$ ), as we saw in the previous section. Similar reaction of a carboxylic acid with phosphorus tribromide ( $\text{PBr}_3$ ) yields the acid bromide.



## 21.4 酰卤的化学反应

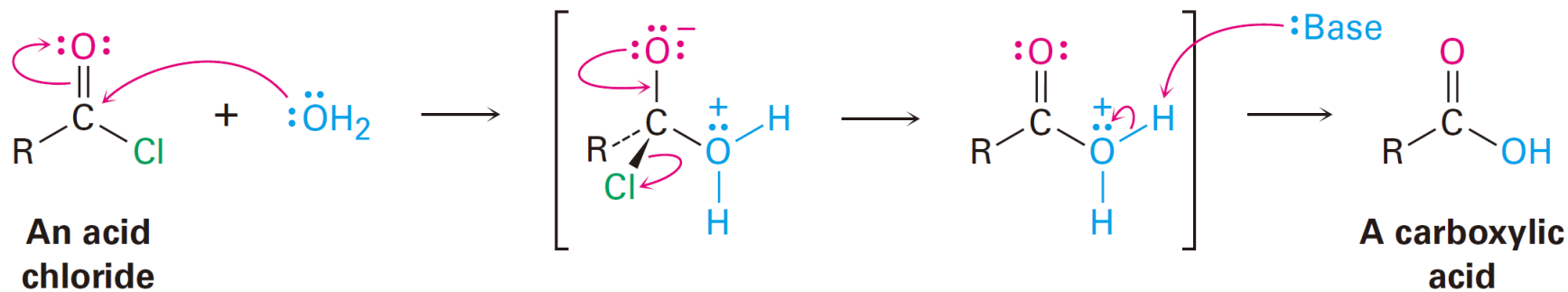
- 酰卤的化学反应总览



## 21.4 酰卤的化学反应

- 水解得酸

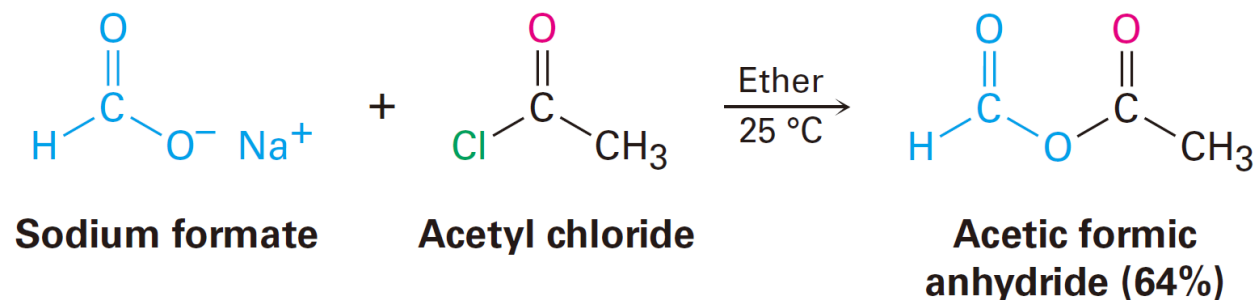
**Conversion of Acid Halides into Acids: Hydrolysis** Acid chlorides react with water to yield carboxylic acids. This hydrolysis reaction is a typical nucleophilic acyl substitution process and is initiated by attack of water on the acid chloride carbonyl group. The tetrahedral intermediate undergoes elimination of  $\text{Cl}^-$  and loss of  $\text{H}^+$  to give the product carboxylic acid plus  $\text{HCl}$ .



## 21.4 酰卤的化学反应

- 酸解得酸酐

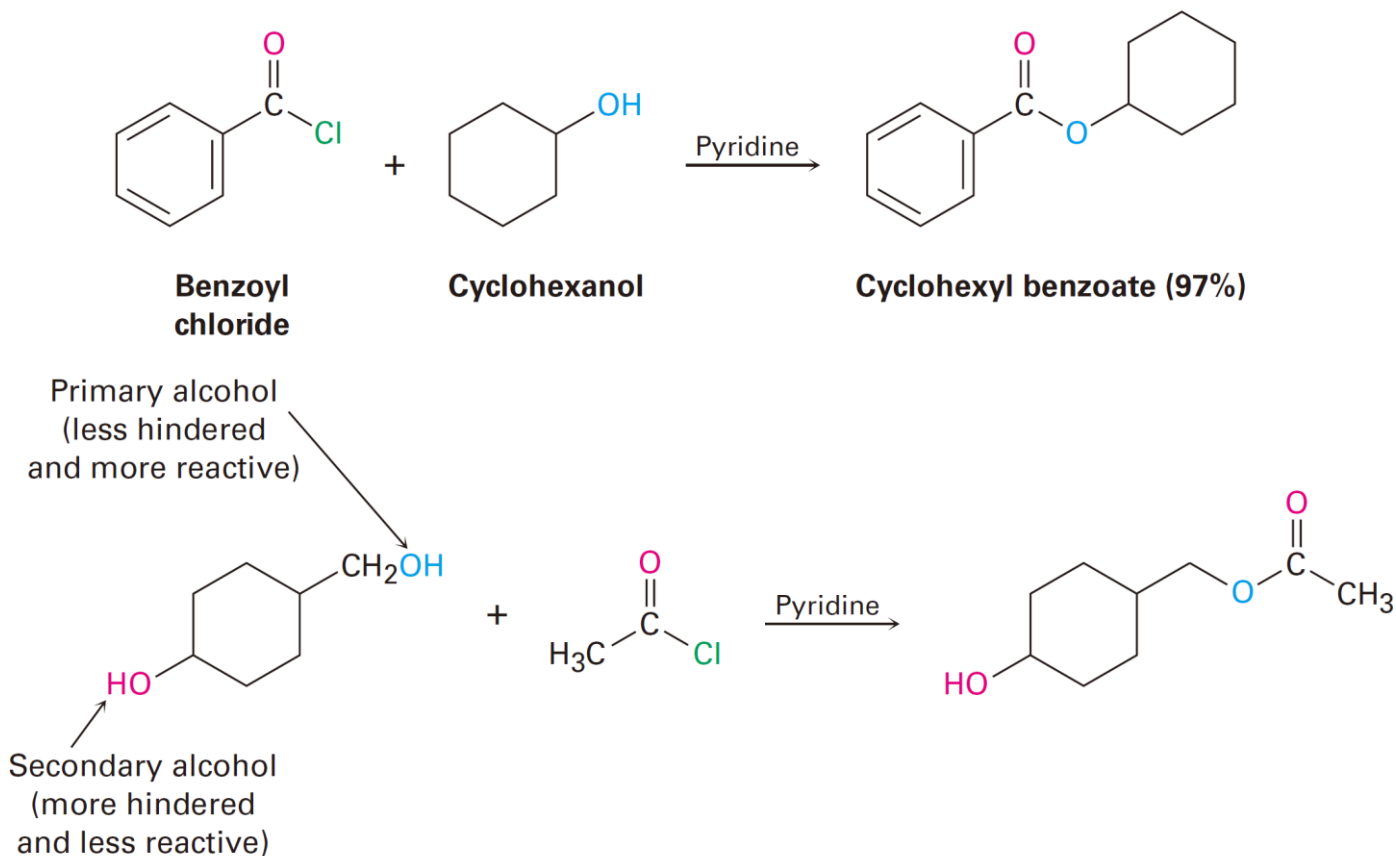
**Conversion of Acid Halides into Anhydrides** Nucleophilic acyl substitution reaction of an acid chloride with a carboxylate anion gives an acid anhydride. Both symmetrical and unsymmetrical acid anhydrides can be prepared.



## 21.4 酰卤的化学反应

- 醇解得酯

**Conversion of Acid Halides into Esters: Alcoholysis** Acid chlorides react with alcohols to yield esters in a process analogous to their reaction with water to yield acids. In fact, this reaction is probably the most common method for preparing esters in the laboratory. As with hydrolysis, alcoholysis reactions are usually carried out in the presence of pyridine or NaOH to react with the HCl formed.



## 21.4 酰卤的化学反应

- 课堂练习

### **Problem 21.10**

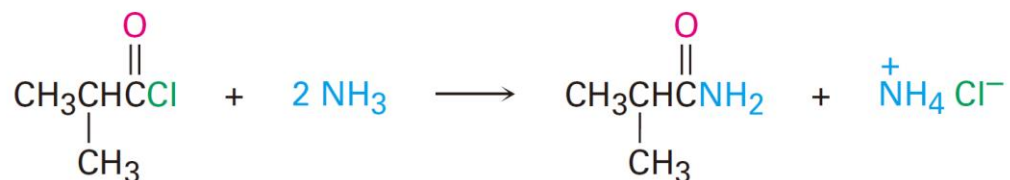
Which method would you choose if you wanted to prepare cyclohexyl benzoate—Fischer esterification or reaction of an acid chloride with an alcohol? Explain.



## 21.4 酰卤的化学反应

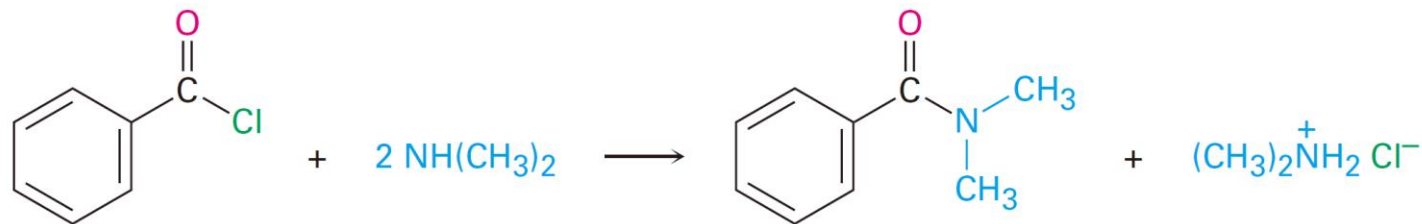
- 氨/胺解得酰胺

**Conversion of Acid Halides into Amides: Aminolysis** Acid chlorides react rapidly with ammonia and amines to give amides. As with the acid chloride-plus-alcohol method for preparing esters, this reaction of acid chlorides with amines is the most commonly used laboratory method for preparing amides. Both monosubstituted and disubstituted amines can be used, but not trisubstituted amines ( $R_3N$ ).



**2-Methylpropanoyl chloride**

**2-Methylpropanamide (83%)**



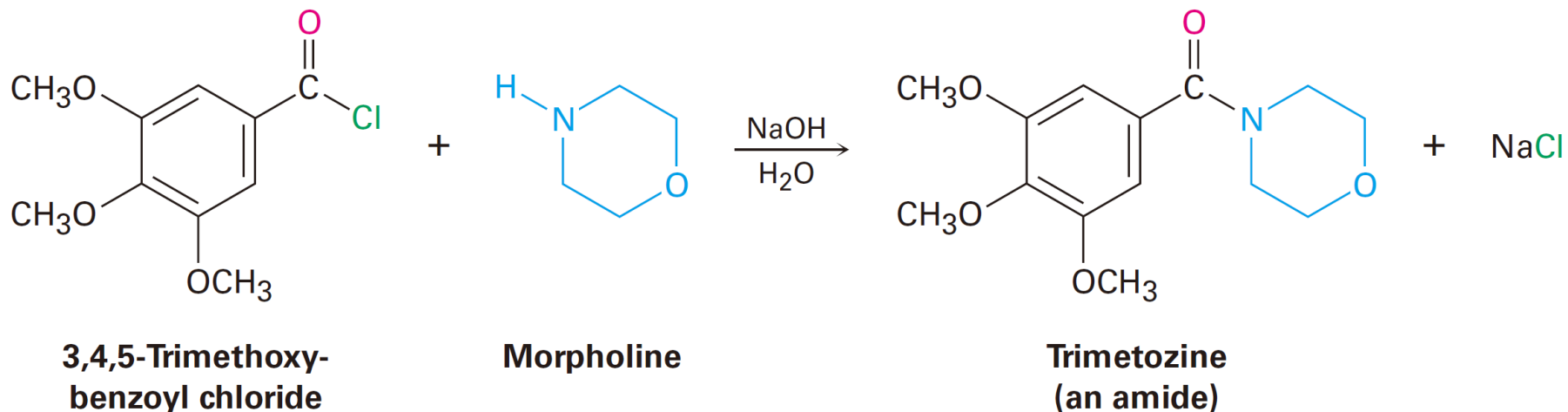
**Benzoyl chloride**

***N,N*-Dimethylbenzamide (92%)**



## 21.4 酰卤的化学反应

- 氨/胺解得酰胺



### **Problem 21.11**

Write the mechanism of the reaction just shown between 3,4,5-trimethoxybenzoyl chloride and morpholine to form trimetozine. Use curved arrows to show the electron flow in each step.

### **Problem 21.12**

How could you prepare the following amides using an acid chloride and an amine or ammonia?

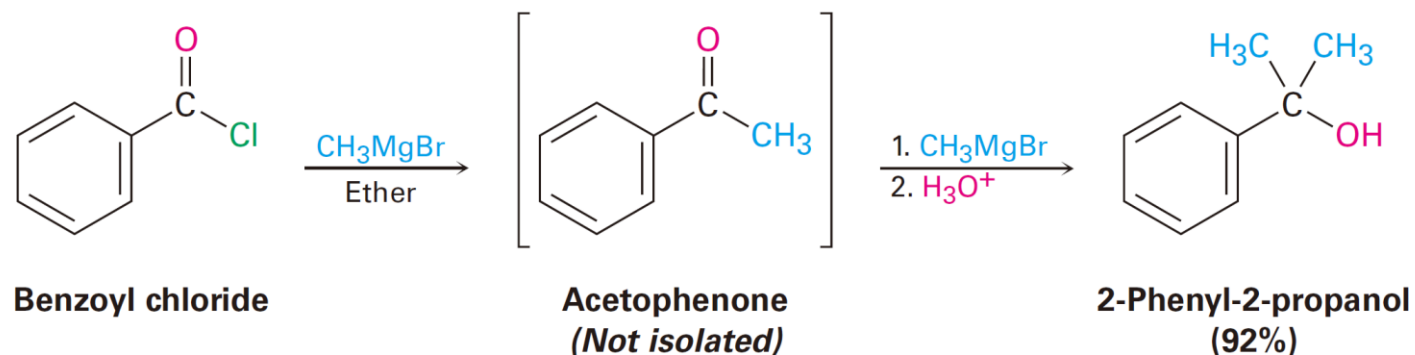
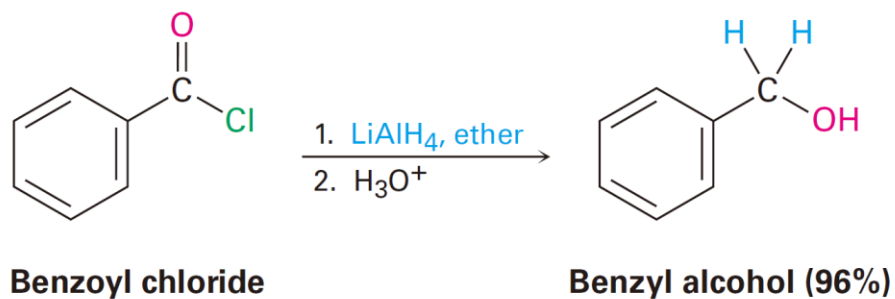
- (a)  $\text{CH}_3\text{CH}_2\text{CONHCH}_3$       (b) *N,N*-Diethylbenzamide      (c) Propanamide



## 21.4 酰卤的化学反应

- 还原或与格氏试剂反应得醇

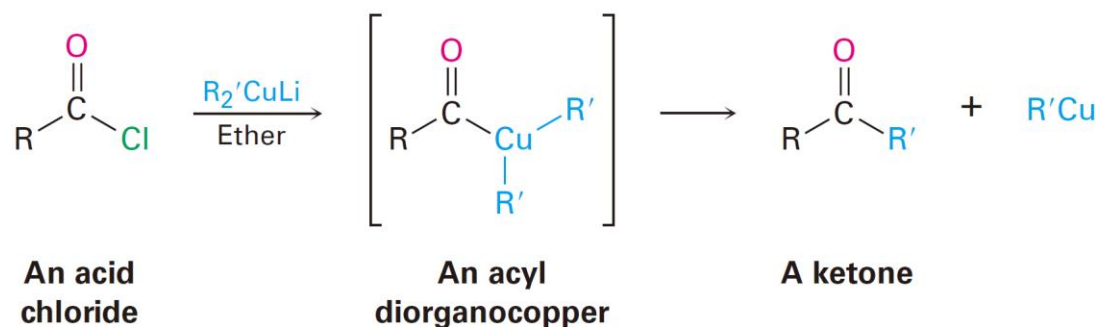
### Conversion of Acid Chlorides into Alcohols: Reduction and Grignard Reaction



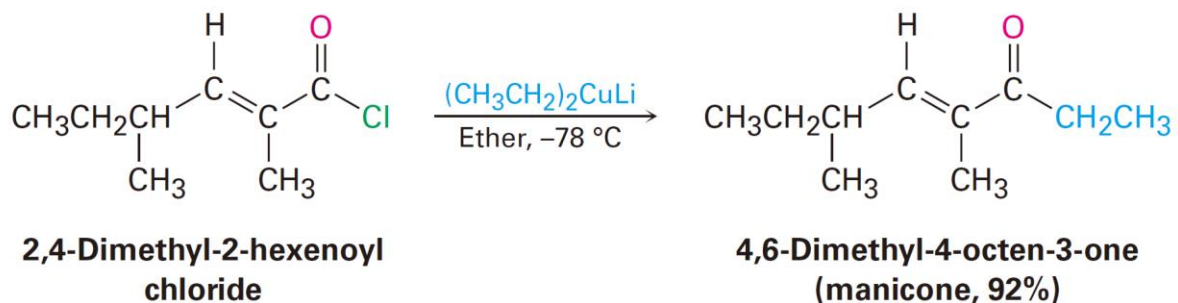
## 21.4 酰卤的化学反应

- 与铜锂试剂反应得酮

### Conversion of Acid Chlorides into Ketones: Diorganocopper Reaction



The reaction is generally carried out at  $-78\text{ }^{\circ}\text{C}$  in ether solution, and yields are often excellent. For example, manicone, a substance secreted by male ants to coordinate ant pairing and mating, has been synthesized by reaction of lithium diethylcopper with (*E*)-2,4-dimethyl-2-hexenoyl chloride.

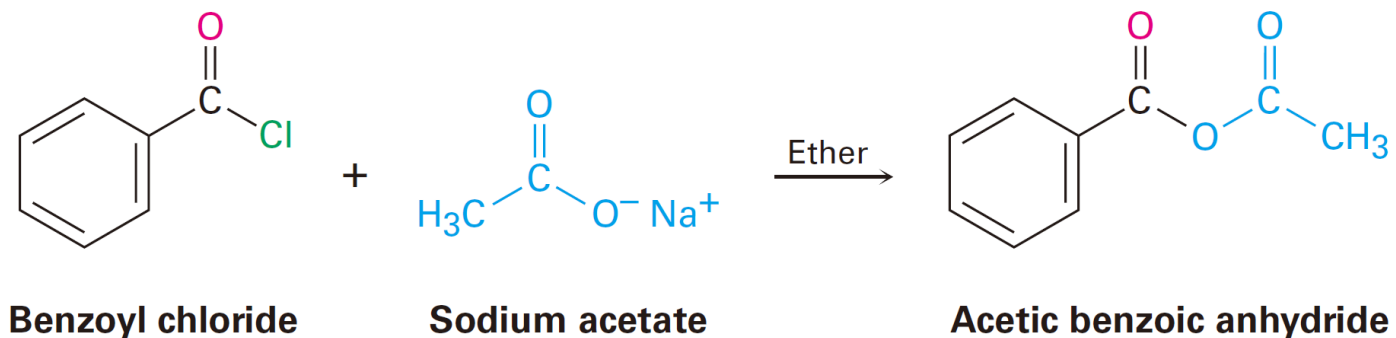


## 21.5 酸酐的化学反应

- 制备

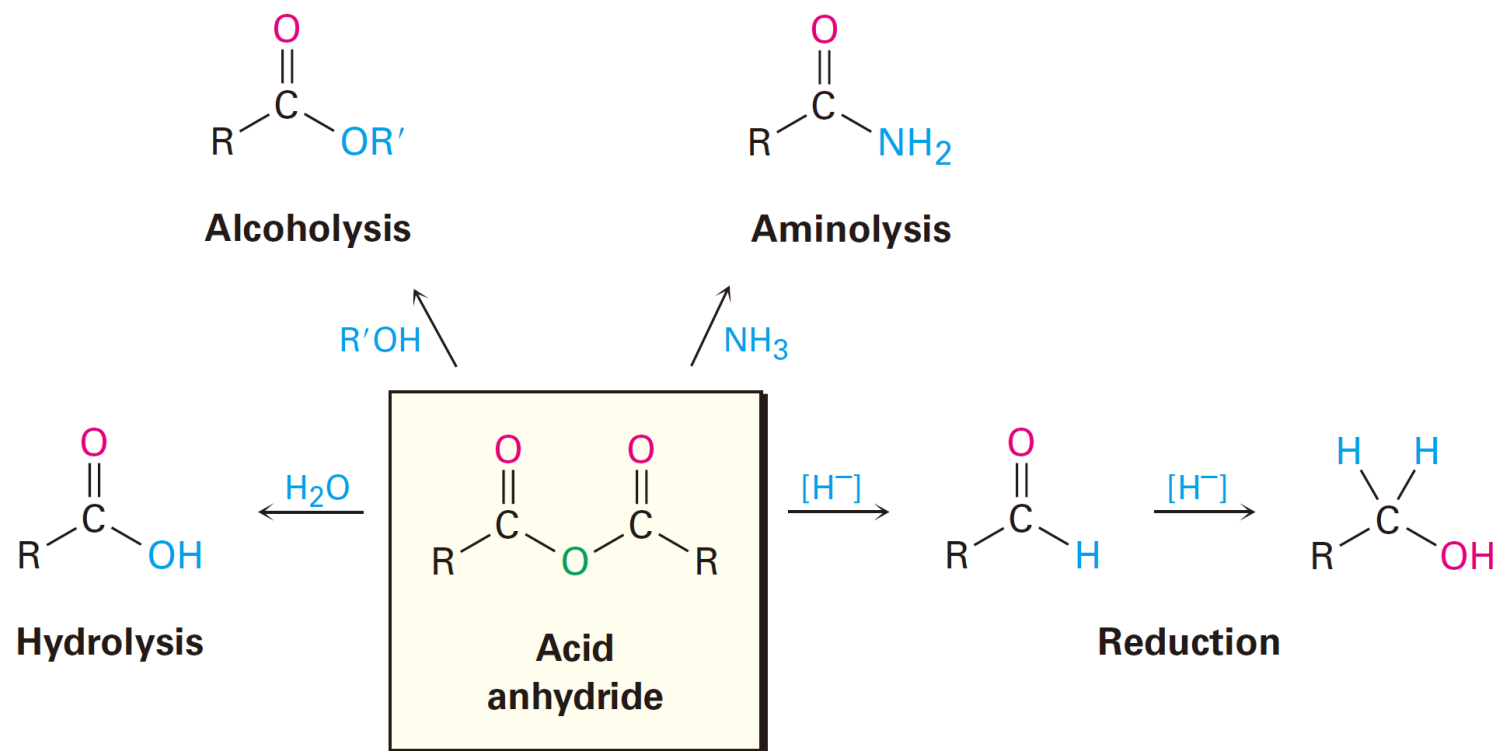
### Preparation of Acid Anhydrides

Acid anhydrides are typically prepared by nucleophilic acyl substitution reaction of an acid chloride with a carboxylate anion, as we saw in **Section 21.4**.



## 21.5 酸酐的化学反应

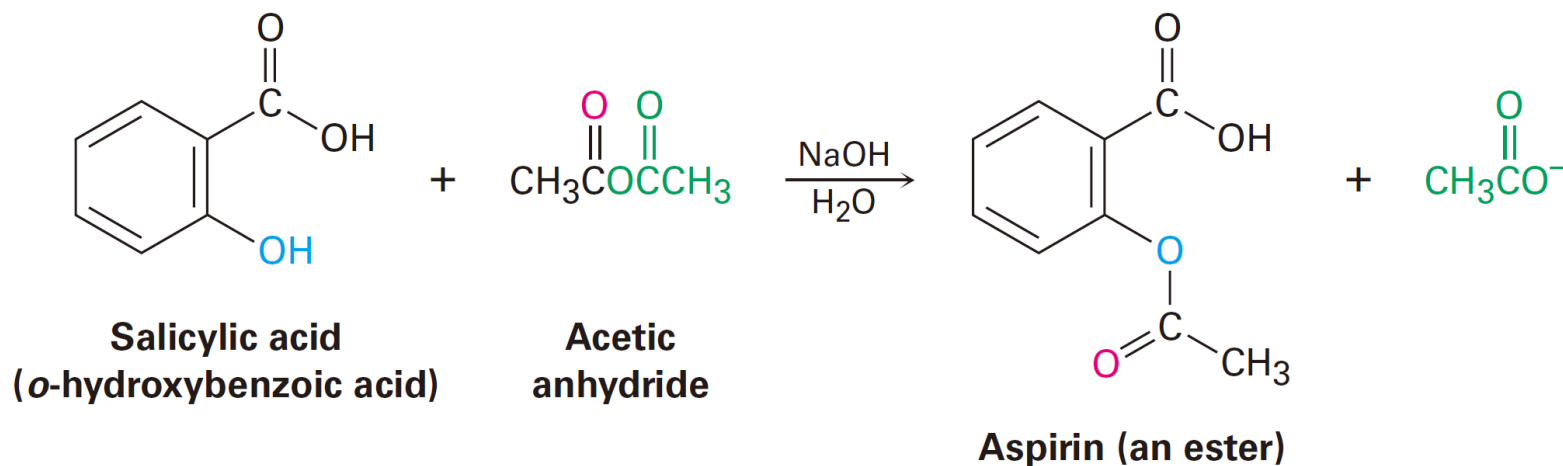
- 反应总览



## 21.5 酸酐的化学反应

- 醇解得酯

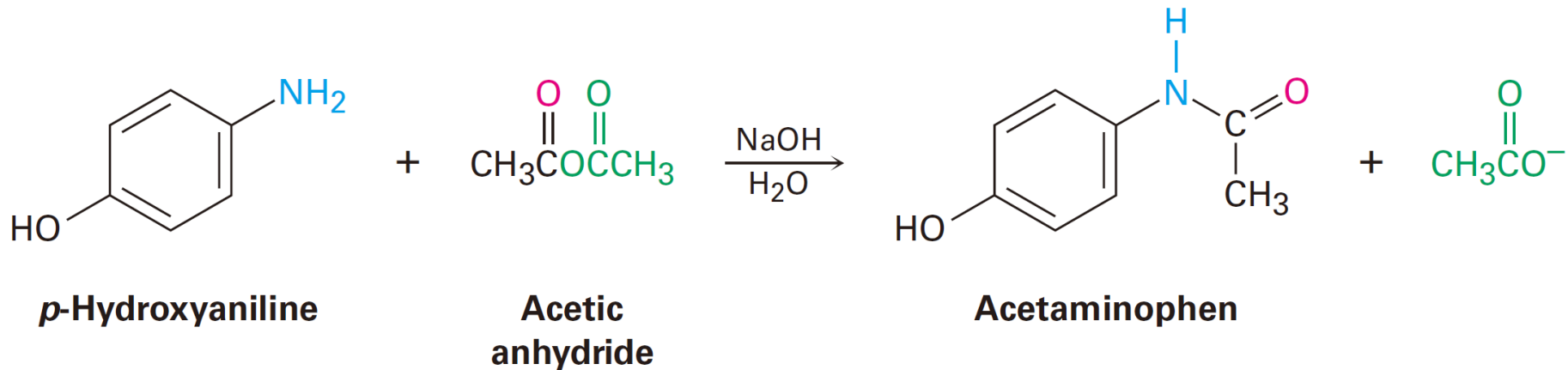
**Conversion of Acid Anhydrides into Esters** Acetic anhydride is often used to prepare acetate esters from alcohols. For example, aspirin (acetylsalicylic acid) is prepared commercially by the acetylation of *o*-hydroxybenzoic acid (salicylic acid) with acetic anhydride.



## 21.5 酸酐的化学反应

- 氨/胺解得酰胺

**Conversion of Acid Anhydrides into Amides** Acetic anhydride is also commonly used to prepare *N*-substituted acetamides from amines. For example, acetaminophen, a drug used in over-the-counter analgesics such as Tylenol, is



## 21.5 酸酐的化学反应

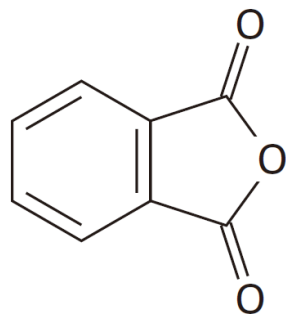
- 课堂练习

### **Problem 21.14**

Write the mechanism of the reaction between *p*-hydroxyaniline and acetic anhydride to prepare acetaminophen.

### **Problem 21.15**

What product would you expect from reaction of 1 equivalent of methanol with a cyclic anhydride, such as phthalic anhydride (1,2-benzenedicarboxylic anhydride)? What is the fate of the second “half” of the anhydride?

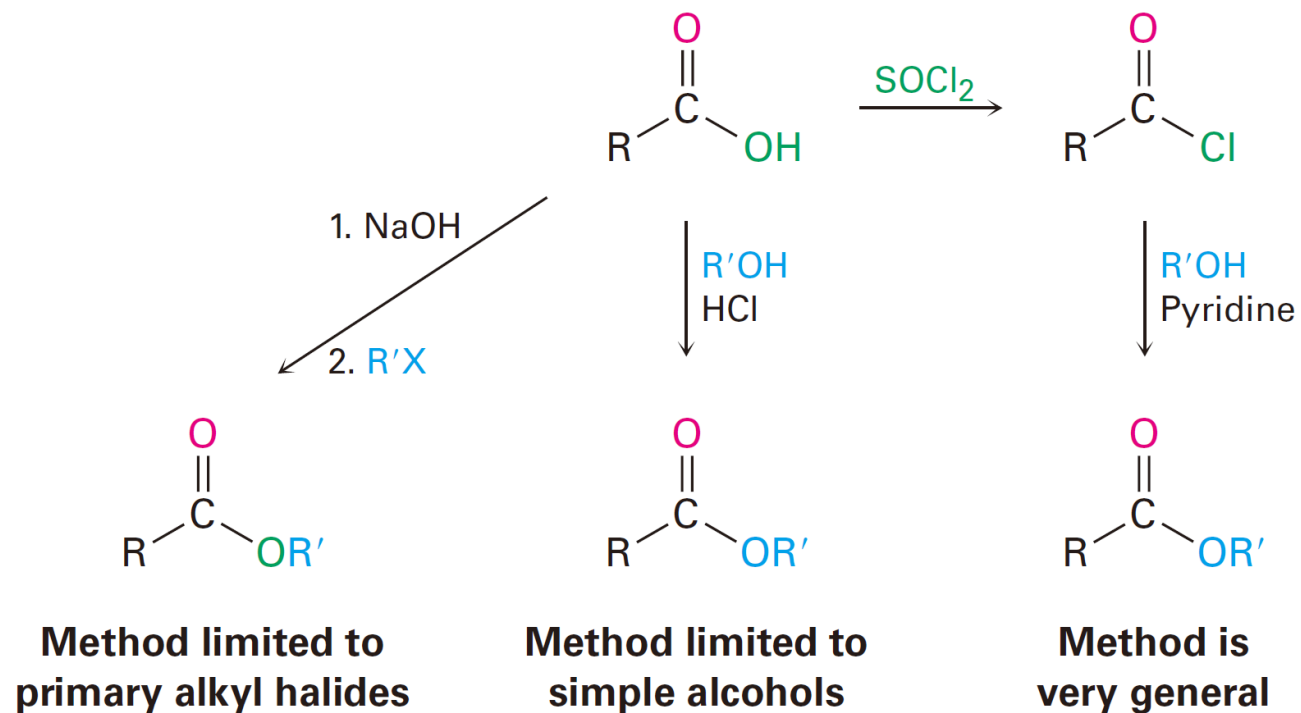


**Phthalic anhydride**

## 21.6 酯的化学反应

- 酯的合成

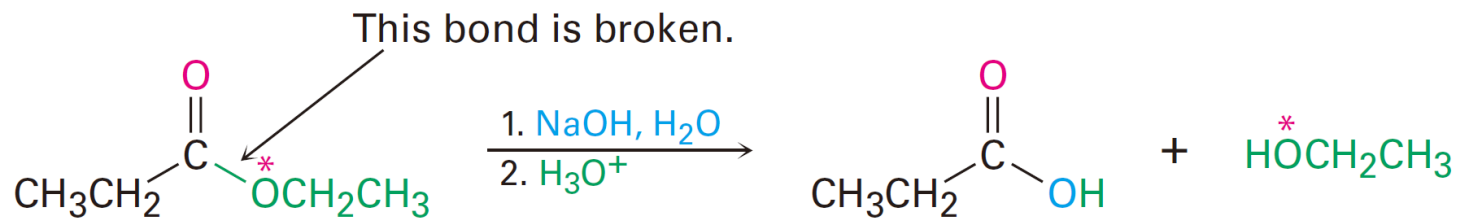
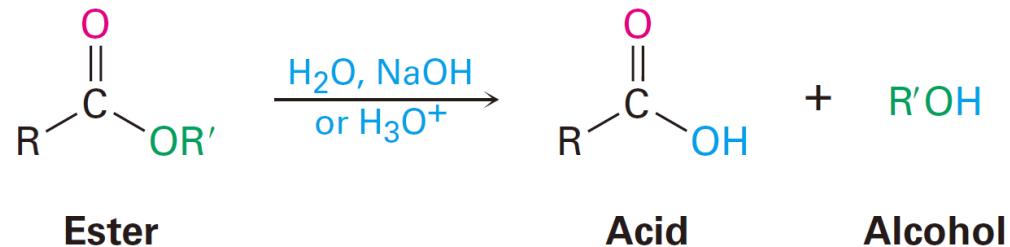
### Preparation of Esters



## 21.6 酯的化学反应

- 水解得酸

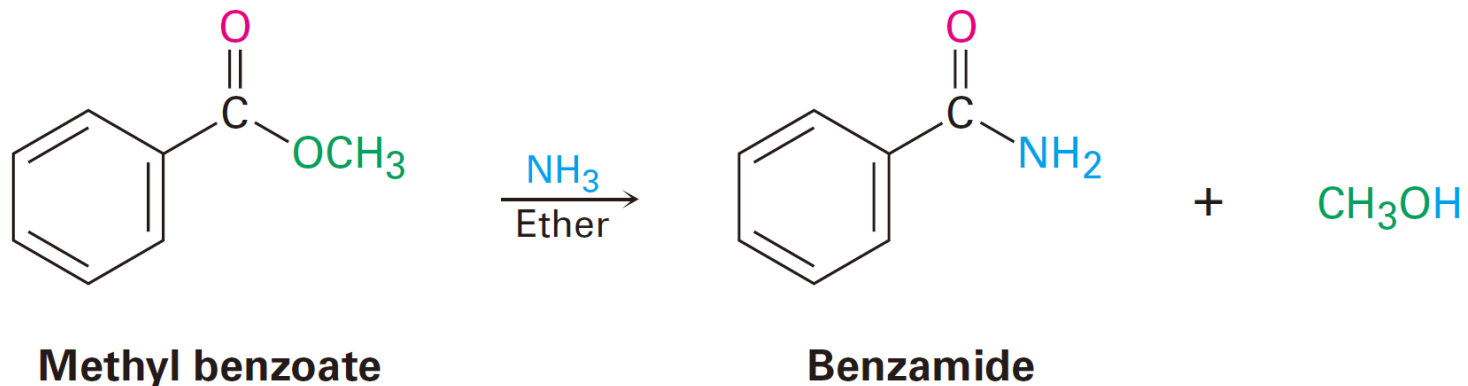
**Conversion of Esters into Carboxylic Acids: Hydrolysis** An ester is hydrolyzed, either by aqueous base or by aqueous acid, to yield a carboxylic acid plus an alcohol.



## 21.6 酯的化学反应

- 氨/胺解得酰胺

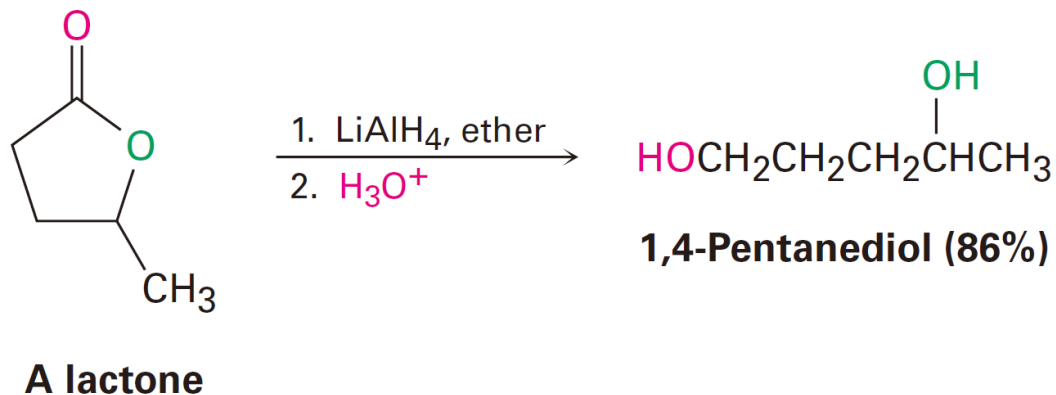
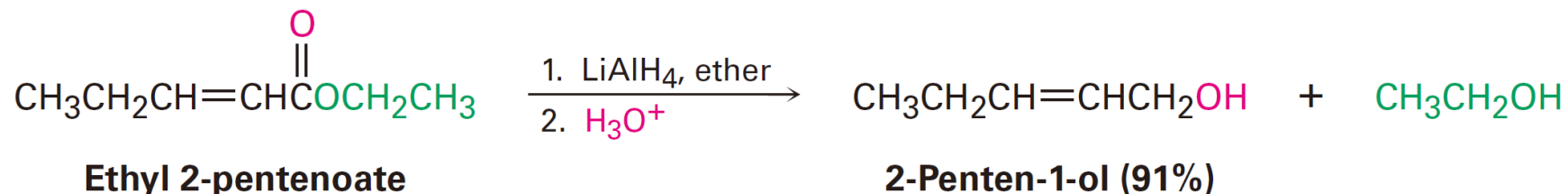
**Conversion of Esters into Amides: Aminolysis** Esters react with ammonia and amines to yield amides. The reaction is not often used, however, because it's usually easier to prepare an amide by starting with an acid chloride (**Section 21.4**).



## 21.6 酯的化学反应

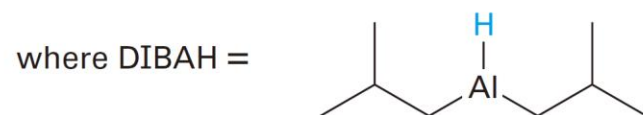
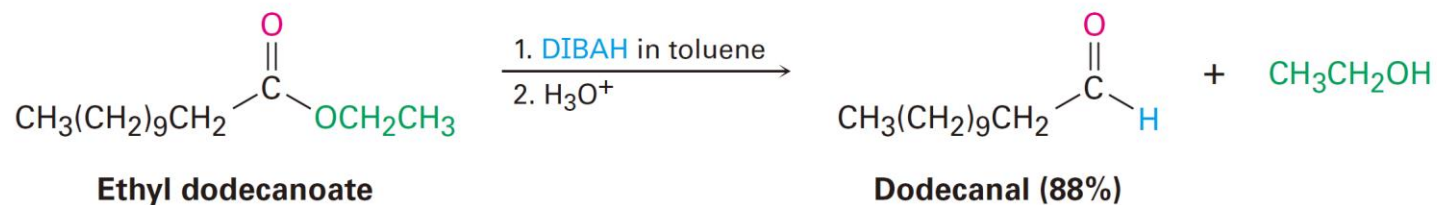
- 还原得醇

**Conversion of Esters into Alcohols: Reduction** Esters are easily reduced by treatment with  $\text{LiAlH}_4$  to yield primary alcohols (**Section 17.4**).



## 21.6 酯的化学反应

### • 课堂练习



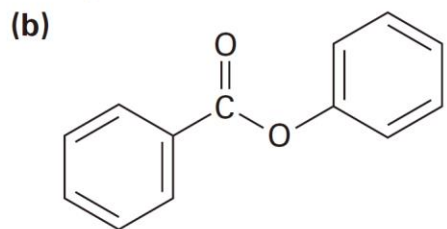
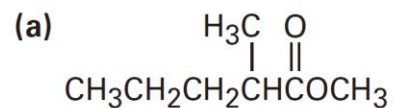
### **Problem 21.17**

What product would you expect from the reaction of butyrolactone with  $\text{LiAlH}_4$ ? With DIBAH?



### **Problem 21.18**

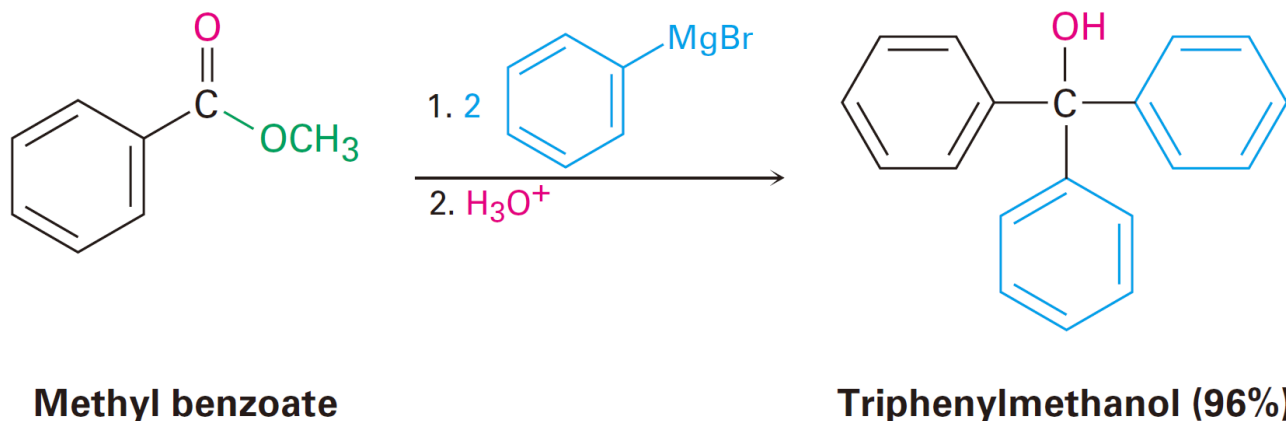
Show the products you would obtain by reduction of the following esters with  $\text{LiAlH}_4$ :



## 21.6 酯的化学反应

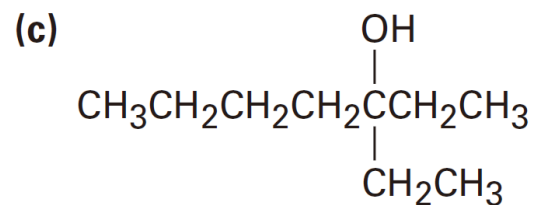
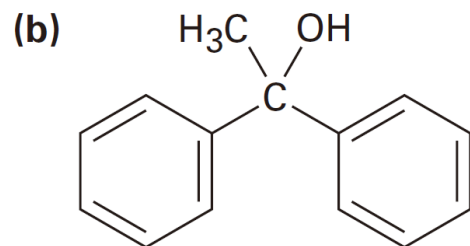
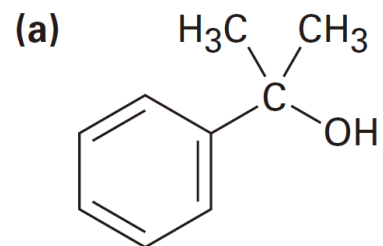
- 与格氏试剂反应得醇

### Conversion of Esters into Alcohols: Grignard Reaction



#### Problem 21.19

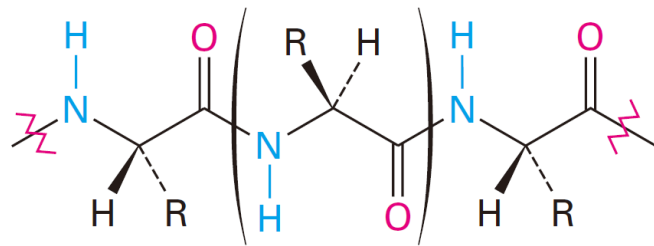
What ester and what Grignard reagent might you start with to prepare the following alcohols?



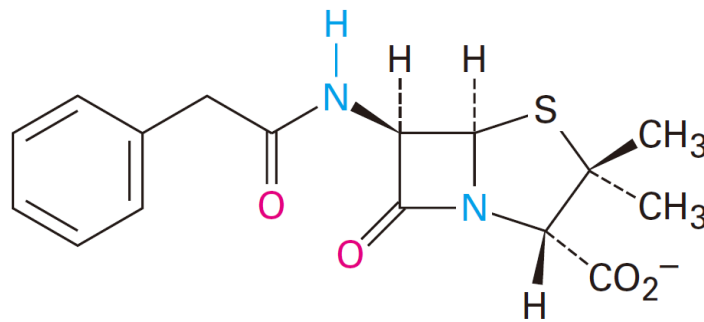
## 21.7 酰胺的化学反应

- 酰胺是重要生命活动物质的组成单元

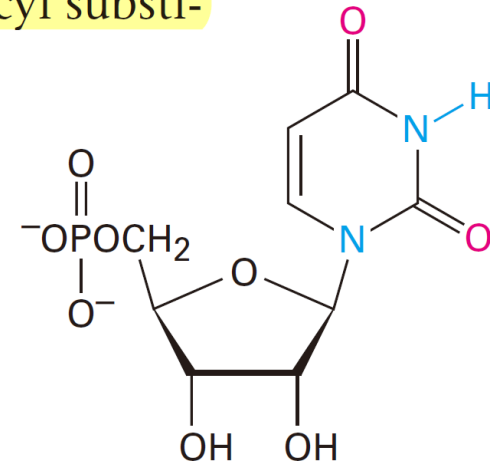
Amides, like esters, are abundant in all living organisms. Proteins, nucleic acids, and many pharmaceutical agents have amide functional groups. The reason for this abundance of amides is that they are stable to the aqueous conditions found in living organisms. Amides are the least reactive of the common acid derivatives and undergo relatively few nucleophilic acyl substitution reactions.



A protein segment



Benzylpenicillin  
(penicillin G)



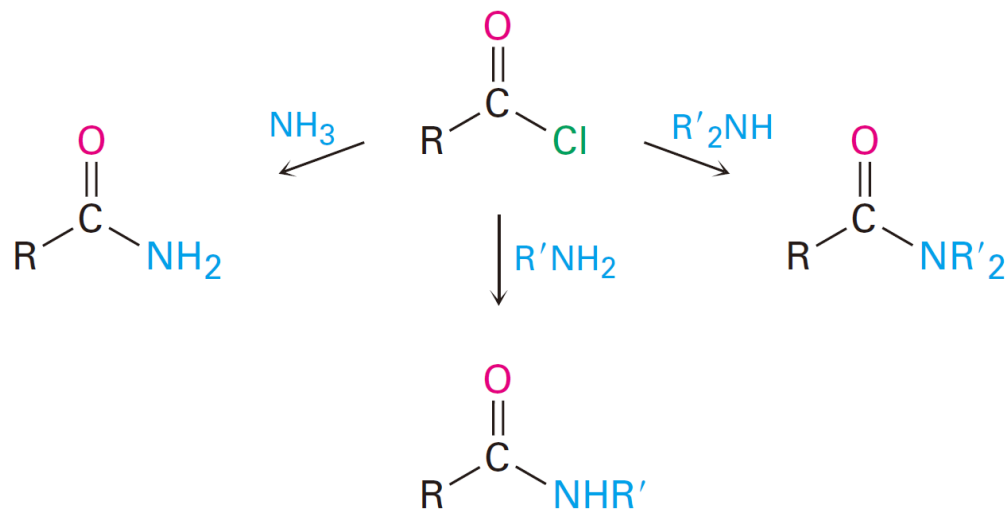
Uridine 5'-phosphate  
(a ribonucleotide)

## 21.7 酰胺的化学反应

- 酰胺的制备

### Preparation of Amides

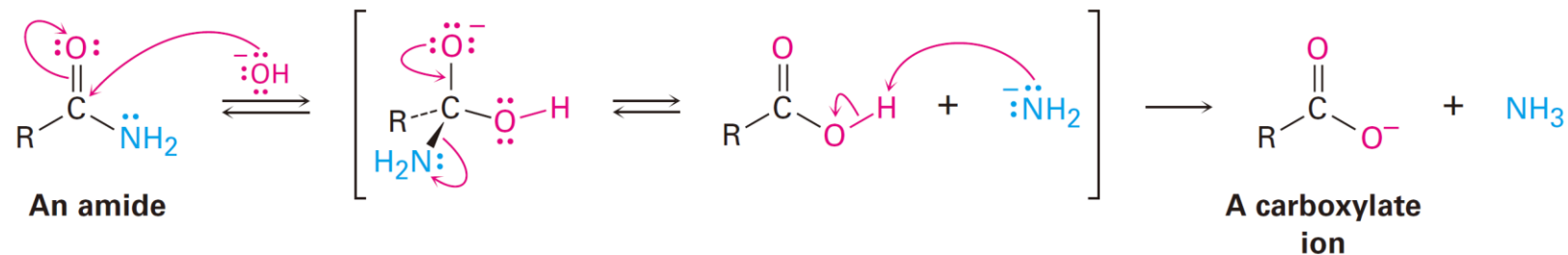
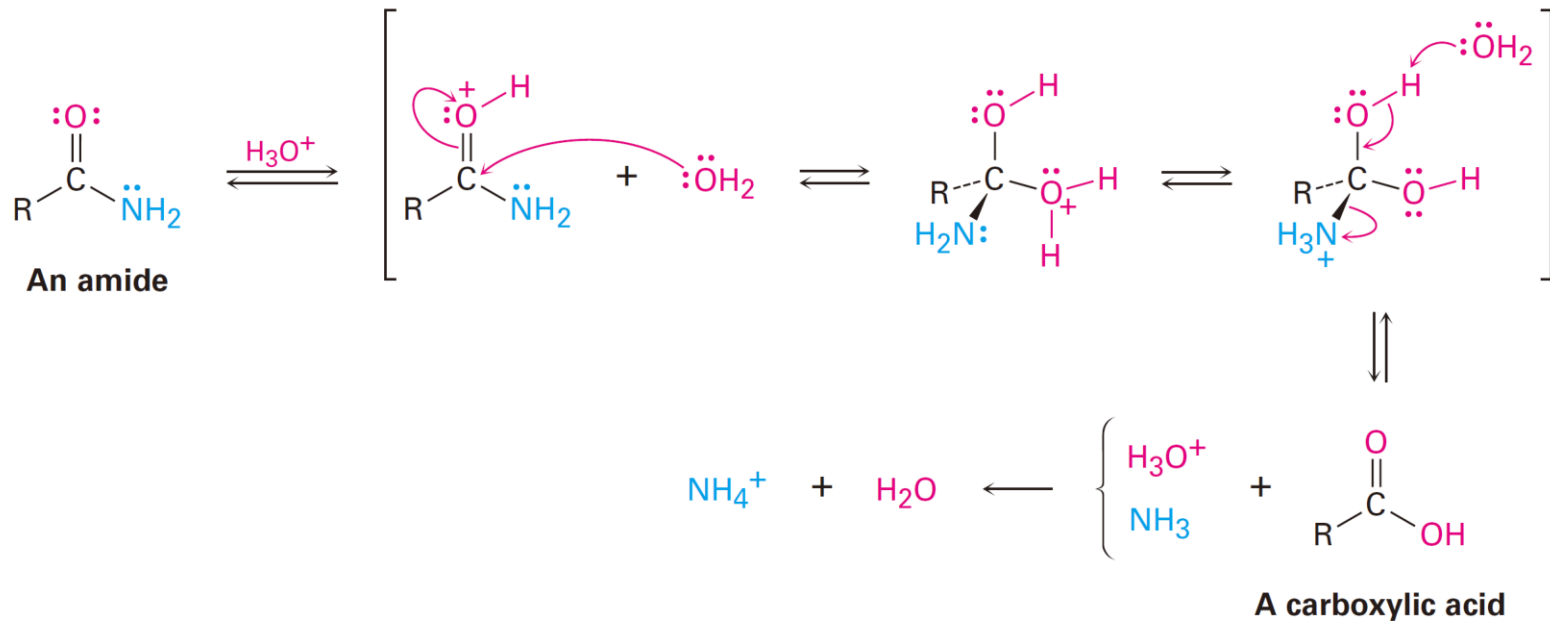
Amides are usually prepared by reaction of an acid chloride with an amine (**Section 21.4**). Ammonia, monosubstituted amines, and disubstituted amines all undergo the reaction.



## 21.7 酰胺的化学反应

- 水解得酸：酰胺的水解需要更加苛刻的反应条件——酰胺的稳定性

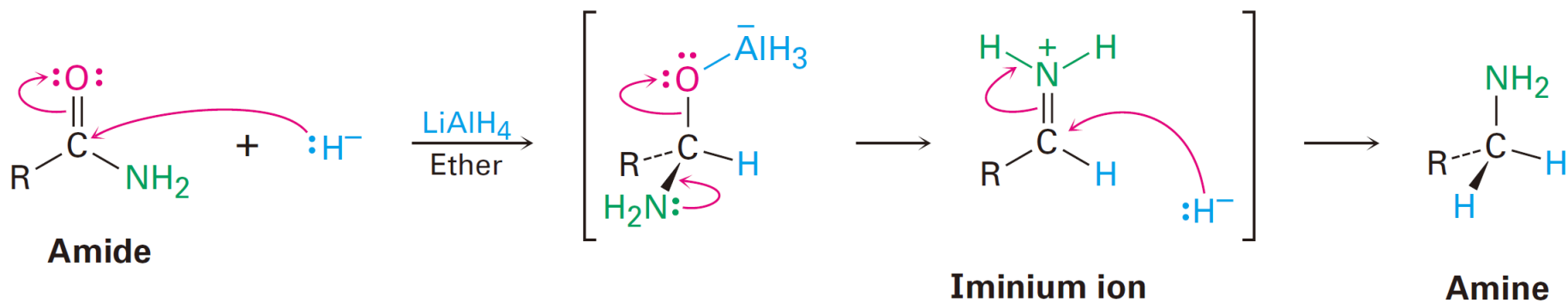
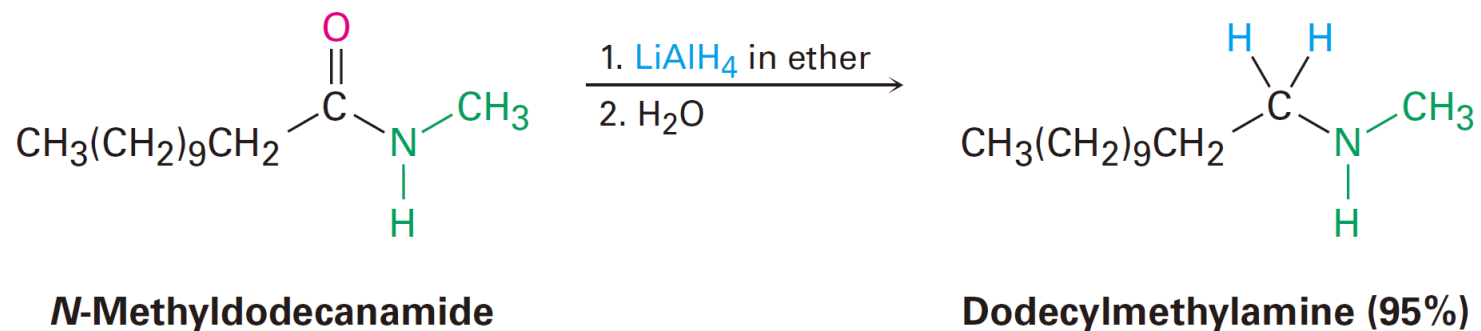
**Conversion of Amides into Carboxylic Acids: Hydrolysis** Amides undergo hydrolysis to yield carboxylic acids plus ammonia or an amine **on heating** in either aqueous acid or aqueous base.



## 21.7 酰胺的化学反应

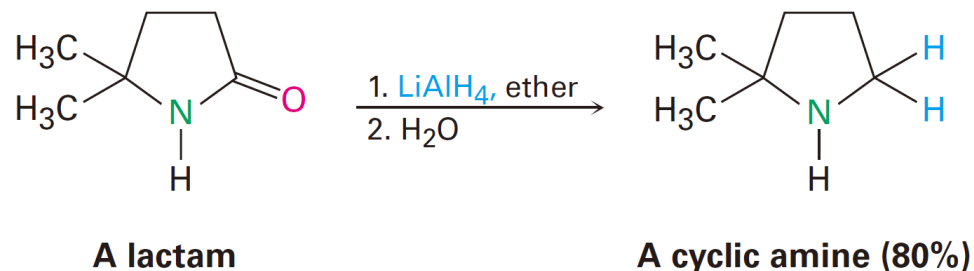
- 注意：与酯的还原对比，酰胺的还原有何不同？

### Conversion of Amides into Amines: Reduction



## 21.7 酰胺的化学反应

- 课堂练习



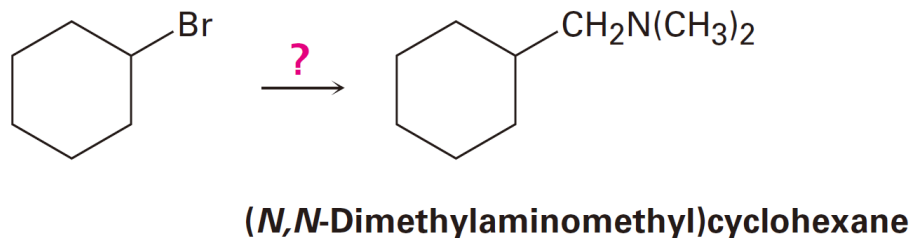
### Problem 21.20

How would you convert *N*-ethylbenzamide to each of the following products?

(a) Benzoic acid      (b) Benzyl alcohol      (c)  $\text{C}_6\text{H}_5\text{CH}_2\text{NHCH}_2\text{CH}_3$

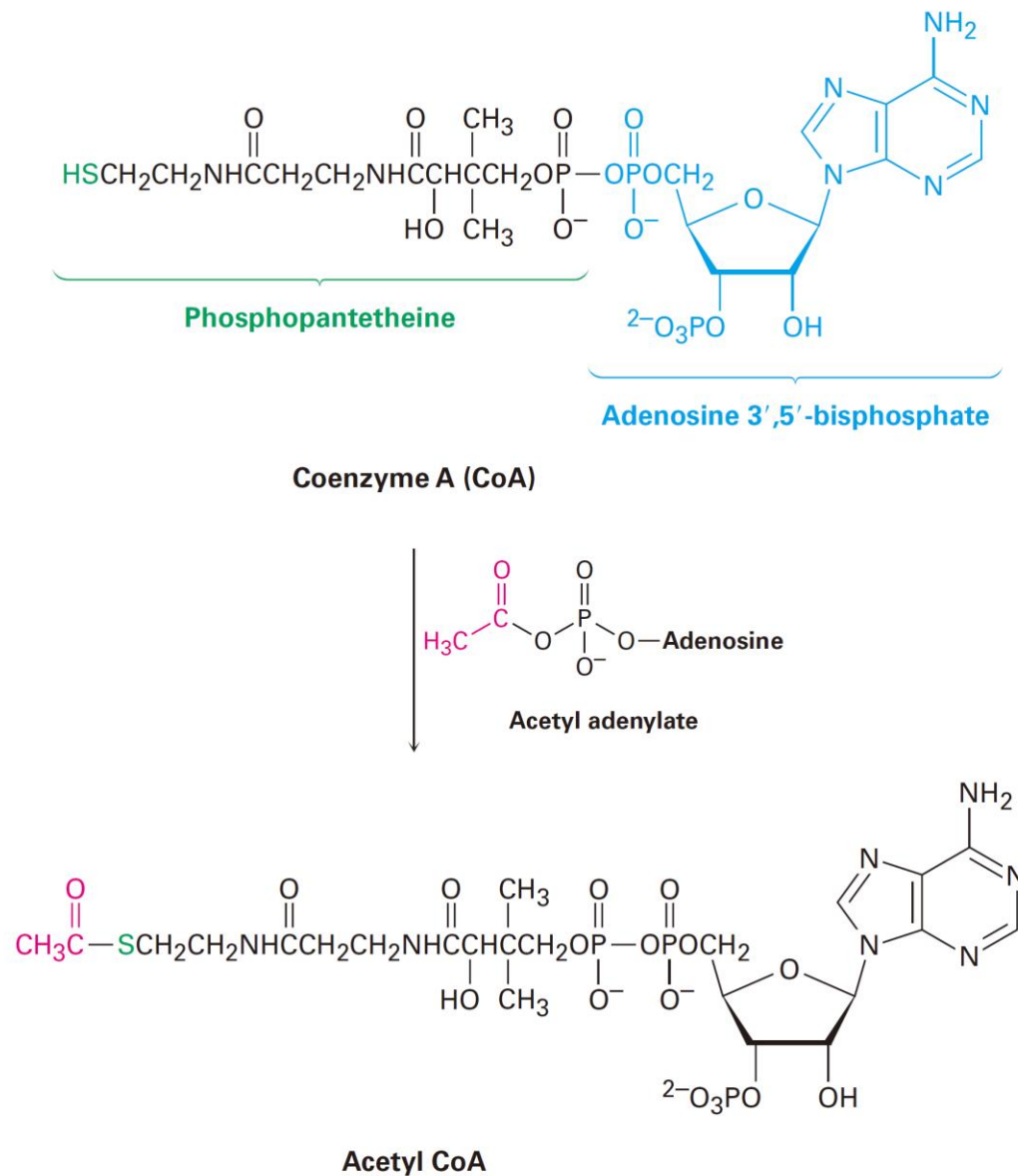
### Problem 21.21

How would you use the reaction of an amide with  $\text{LiAlH}_4$  as the key step in going from bromocyclohexane to (*N,N*-dimethylaminomethyl)cyclohexane? Write all the steps in the reaction sequence.



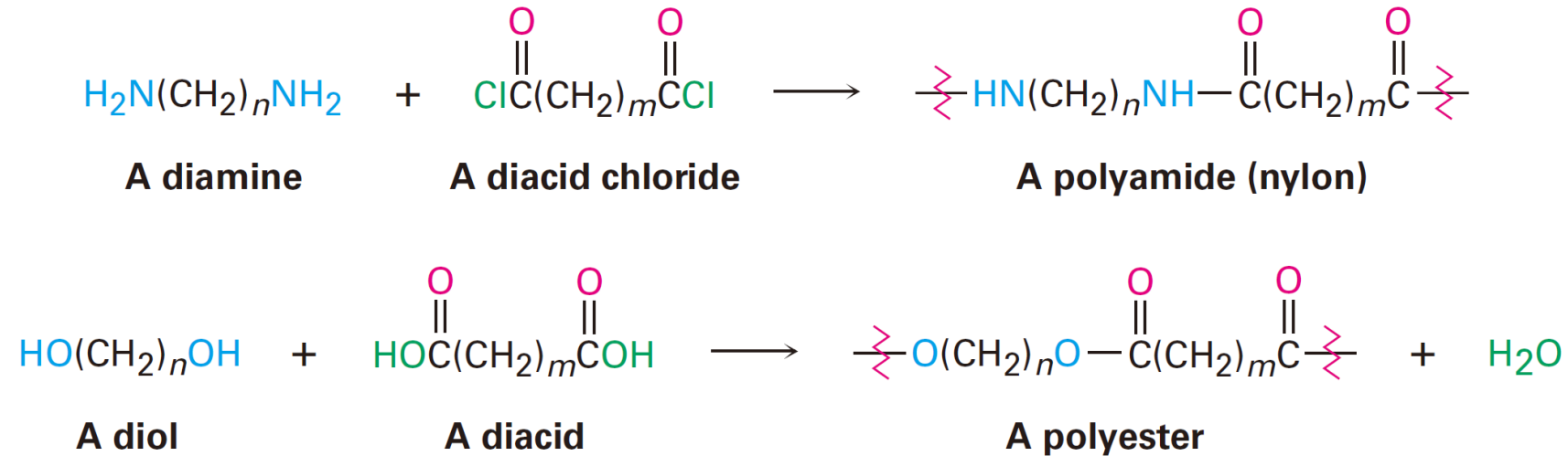
## 21.8 生物体内羧酸衍生物的反应

**Figure 21.9** Formation of the thioester acetyl CoA by nucleophilic acyl substitution reaction of coenzyme A (CoA) with acetyl adenylate.



## 21.9 聚酰胺和聚酯：逐步聚合反应

- 聚乙烯和聚酰胺聚合方式有何不同？



There are two main classes of synthetic polymers: *chain-growth polymers* and *step-growth polymers*. Polyethylene and other alkene and diene polymers like those we saw in **Sections 8.10 and 14.6** are chain-growth polymers because

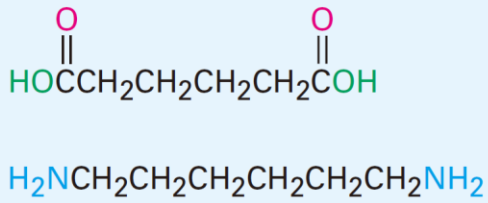
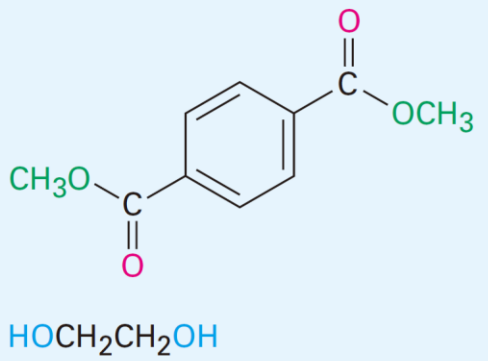
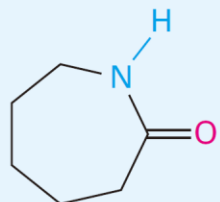
链增长聚合与逐步增长聚合



## 21.9 聚酰胺和聚酯：逐步聚合反应

- 一些用途广泛的高分子产品

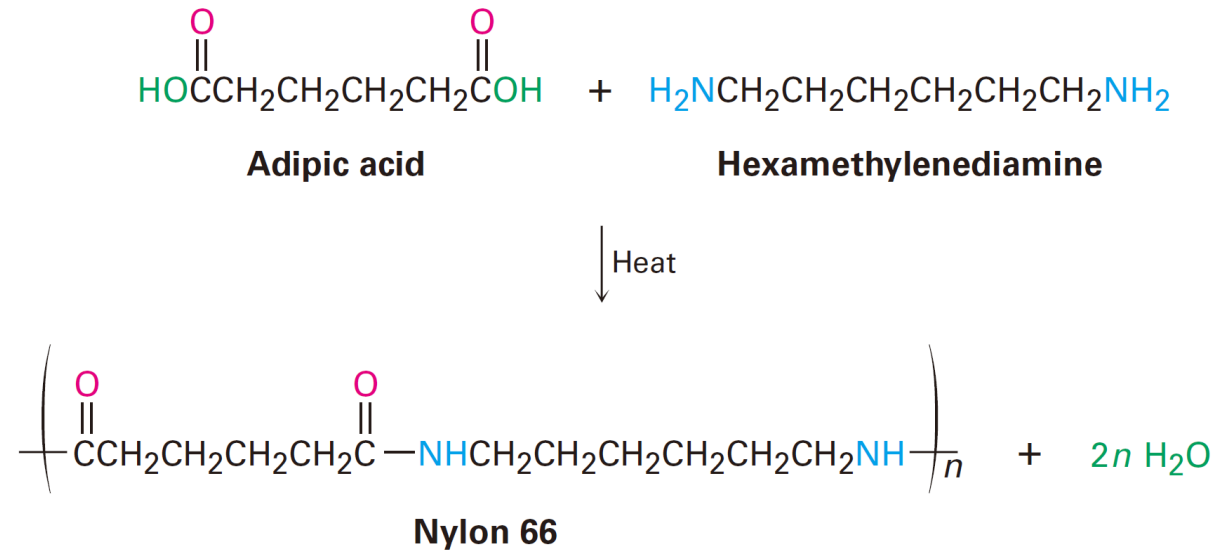
Table 21.2 Some Common Step-Growth Polymers and Their Uses

Monomers	Structure	Polymer	Uses
Adipic acid + Hexamethylenediamine		Nylon 66 尼龙66	Fibers, clothing, tire cord
Dimethyl terephthalate + Ethylene glycol		涤纶 Dacron, Mylar, Terylene	Fibers, clothing, films, tire cord
Caprolactam		尼龙6 Nylon 6, Perlon	Fibers, castings

## 21.9 聚酰胺和聚酯：逐步聚合反应

- 聚酰胺高分子：尼龙

### Polyamides (Nylons)



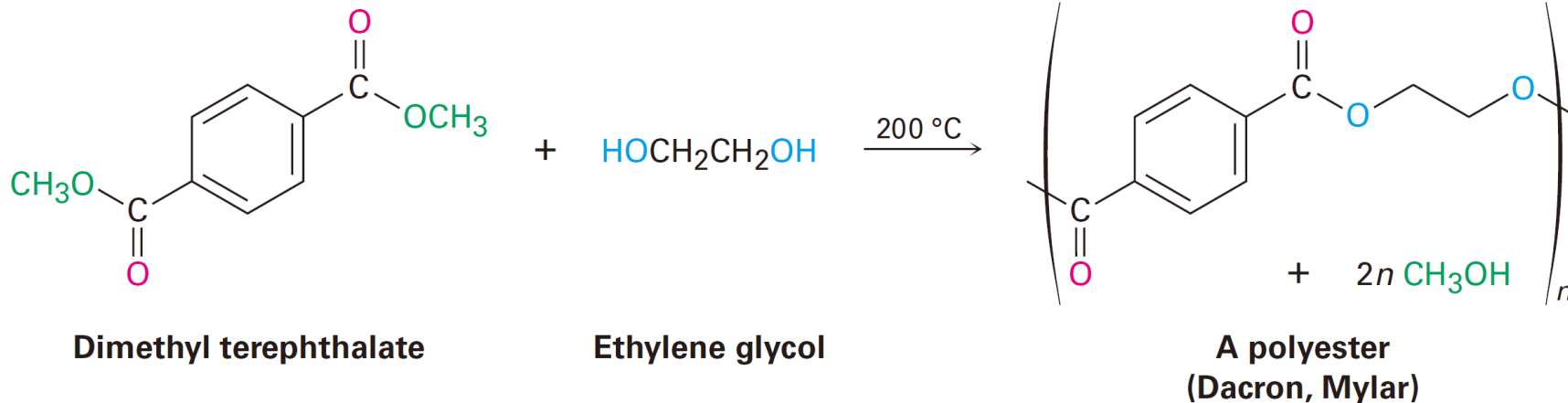
Nylons are used both in engineering applications and in making fibers. A combination of high impact strength and abrasion resistance makes nylon an excellent **metal substitute** for **bearings and gears**. As fiber, nylon is used in a variety of applications, from **clothing to tire cord to ropes**.

## 21.9 聚酰胺和聚酯：逐步聚合反应

- 聚酯高分子：涤纶

### Polyesters

The most generally useful polyester is that made by reaction between dimethyl terephthalate (dimethyl 1,4-benzenedicarboxylate) and ethylene glycol (1,2-ethanediol). The product is used under the trade name **Dacron** to make **clothing fiber** and tire cord and under the name Mylar to make recording tape. The tensile strength of poly(ethylene terephthalate) film is nearly equal to that of steel.

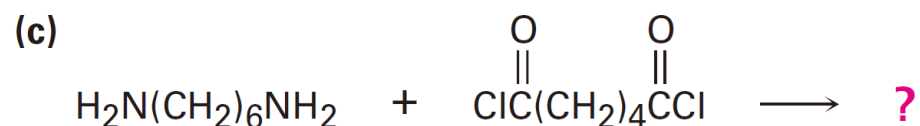
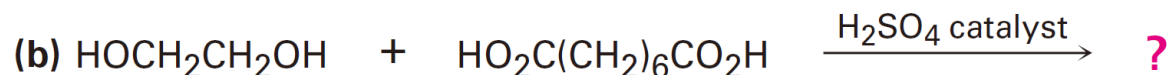
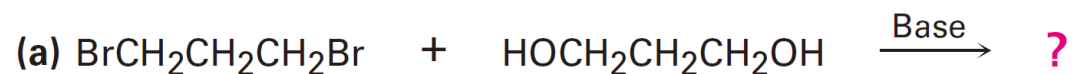


## 21.9 聚酰胺和聚酯：逐步聚合反应

- 课堂练习

### Problem 21.23

Draw structures of the step-growth polymers you would expect to obtain from the following reactions:



### Problem 21.24

Kevlar, a nylon polymer prepared by reaction of 1,4-benzenedicarboxylic acid (terephthalic acid) with 1,4-benzenediamine (*p*-phenylenediamine), is so strong that it's used to make bulletproof vests. Draw the structure of a segment of Kevlar.



## 21.10 光谱分析

- 红外分析：羰基化合物的红外最具特征

### Infrared Spectroscopy

All carbonyl-containing compounds have intense IR absorptions in the range 1650 to 1850  $\text{cm}^{-1}$ .

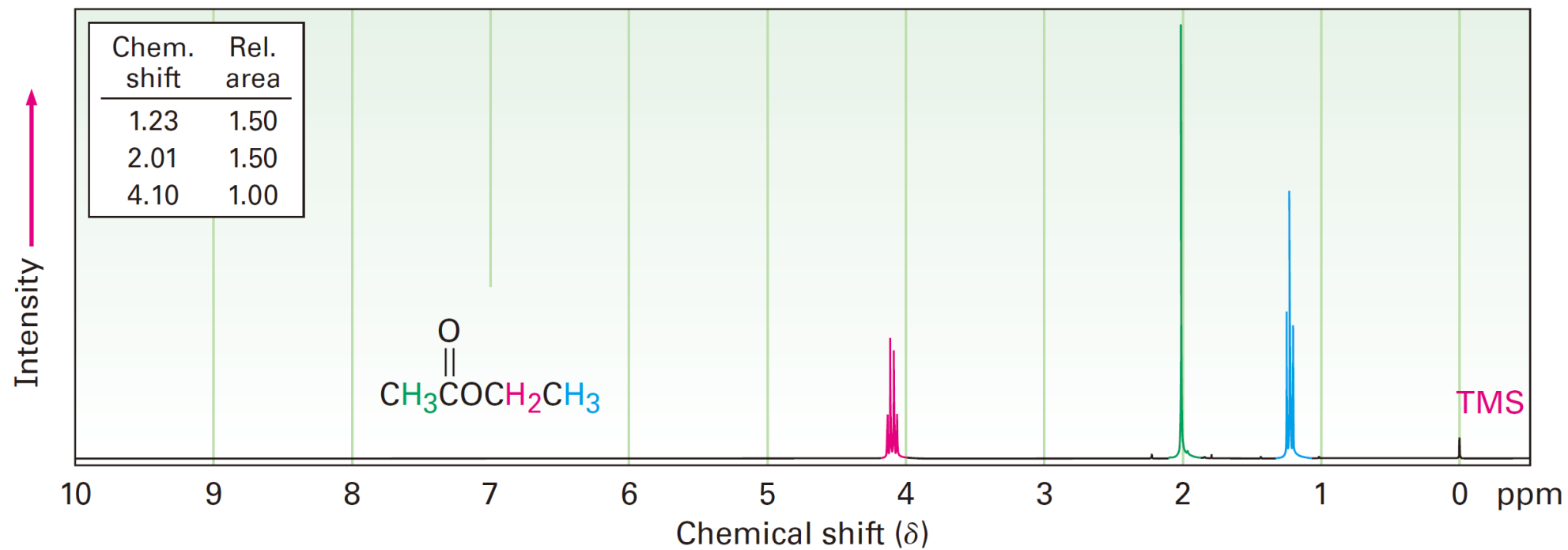
**Table 21.3** Infrared Absorptions of Some Carbonyl Compounds

Carbonyl type	Example	Absorption ( $\text{cm}^{-1}$ )
Saturated acid chloride	Acetyl chloride	1810
Aromatic acid chloride	Benzoyl chloride	1770
Saturated acid anhydride	Acetic anhydride	1820, 1760
Saturated ester	Ethyl acetate	1735
Aromatic ester	Ethyl benzoate	1720
Saturated amide	Acetamide	1690



## 21.10 光谱分析

- 核磁共振分析



**Figure 21.10** Proton NMR spectrum of ethyl acetate.

# 作业

- 21.39, 21.48, 21.53, 21.60, 21.61, 21.62, 21.63, 21.70

