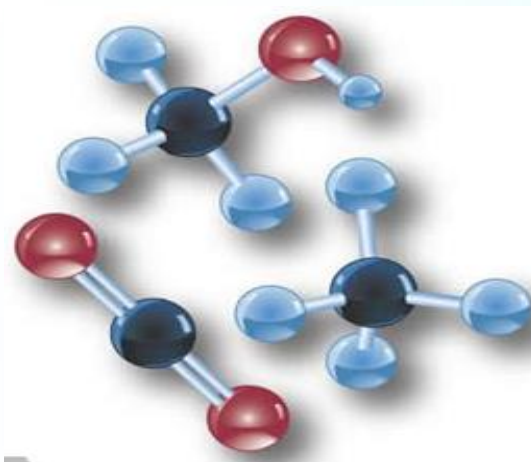




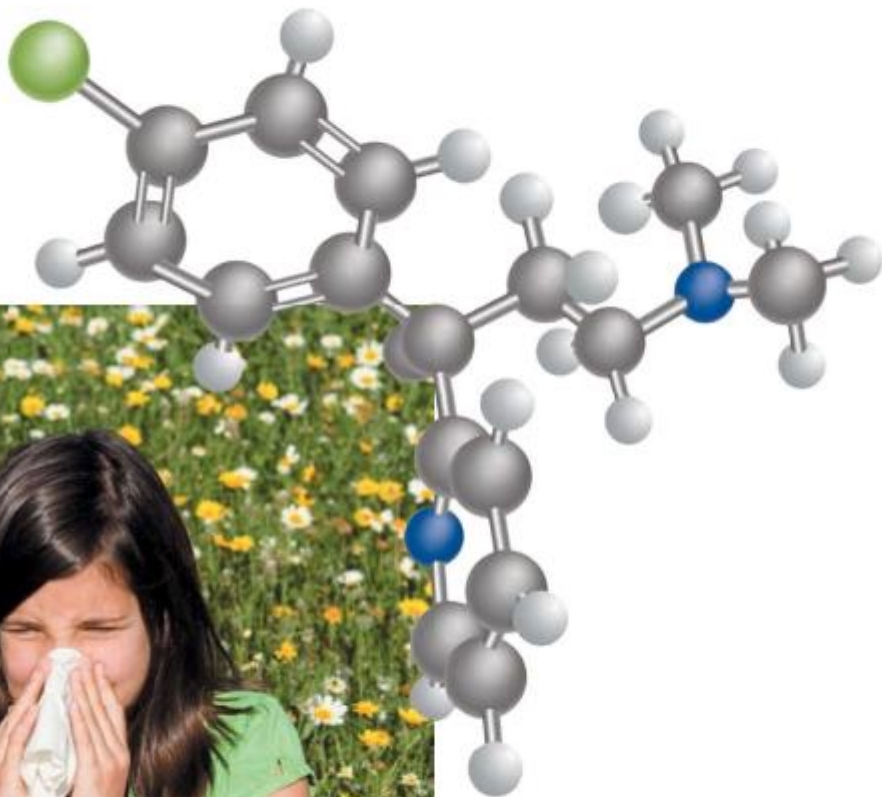
Organic Chemistry



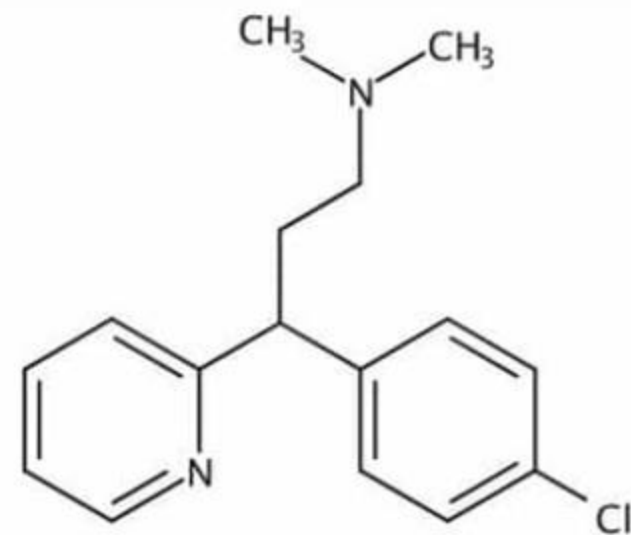


10

Amines



Chlorphenamine, an organic amine, is an antihistamine used to prevent some of the symptoms of allergies. Inset: A model of chlorphenamine. (© mandygodbehear/iStockphoto)



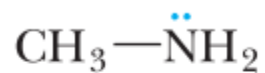
氯苯那敏



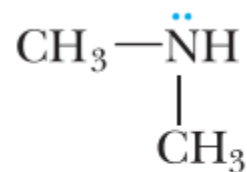
Naming aldehydes and ketones using IUPAC rules



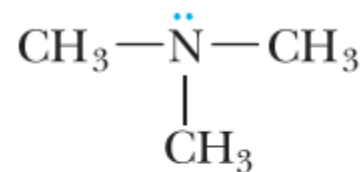
Ammonia



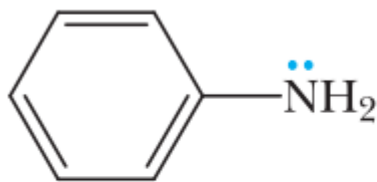
Methylamine
(a 1° amine)



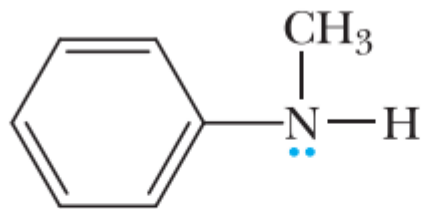
Dimethylamine
(a 2° amine)



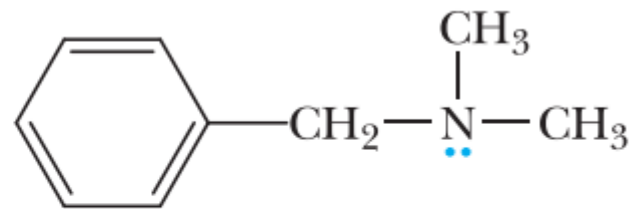
Trimethylamine
(a 3° amine)



Aniline
(a 1° aromatic amine)



N-Methylaniline
(a 2° aromatic amine)



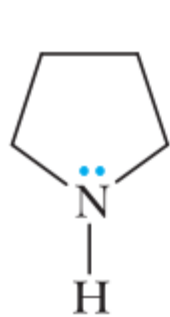
Benzyldimethylamine
(a 3° aliphatic amine)



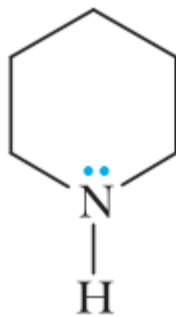
- ◆ The stem names of amines are derived from those of **the parent alkanes**, defined **by the longest continuous chain** (LCC) of carbon atoms that contains the functional group.
- ◆ For **an amine**, **drop the *-e* from the alkane name and add the ending *-amine***.
- ◆ To indicate the position of a substituent on amines, **number the chain in the manner that gives the amino carbon atom the lowest possible number**. In cyclic amines, it is understood that the amino carbon atom is C1.



氨的分类与命名

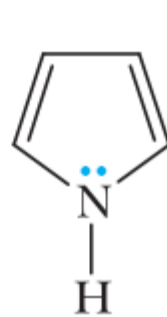


Pyrrolidine

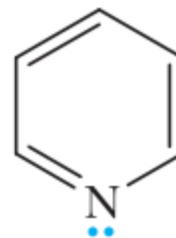


Piperidine

(heterocyclic aliphatic amines)

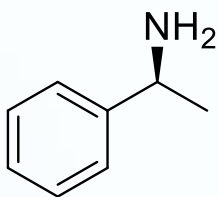


Pyrrole

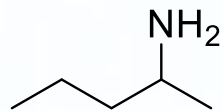


Pyridine

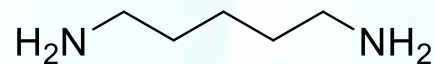
(heterocyclic aromatic amines)



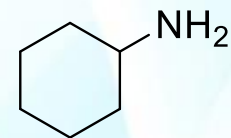
(S)-1-phenylethan-1-amine



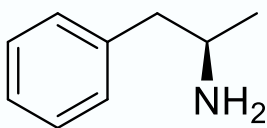
pentan-2-amine



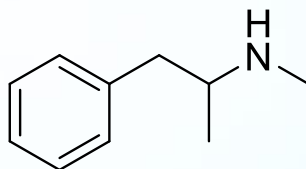
pentane-1,5-diamine



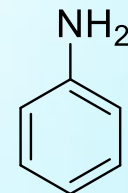
cyclohexanamine



(R)-1-phenylpropan-2-amine



N-methyl-1-phenylpropan-2-amine



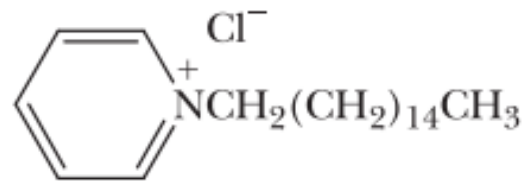
aniline



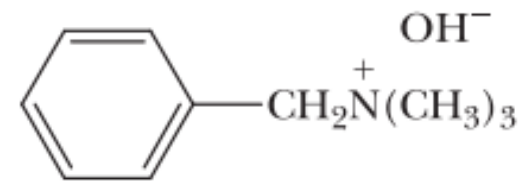
氨的分类与命名



Tetramethylammonium
chloride



Hexadecylpyridinium chloride
(Cetylpyridinium chloride)



Benzyltrimethylammonium
hydroxide

氨
Ammonia



胺
Amine



铵
Ammonium



An N—H----N hydrogen bond is weaker than an O—H----O hydrogen bond, because the difference in electronegativity between nitrogen and hydrogen ($3.0 - 2.1 = 0.9$) is less than that between oxygen and hydrogen ($3.5 - 2.1 = 1.4$). We can illustrate the effect of intermolecular hydrogen bonding by comparing the boiling points of methylamine and methanol:

	CH ₃ NH ₂	CH ₃ OH
molecular weight (g/mol)	31.1	32.0
boiling point (°C)	-6.3	65.0

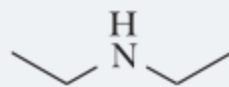
解释原因



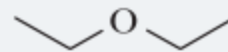
Butylamine
bp 78 °C



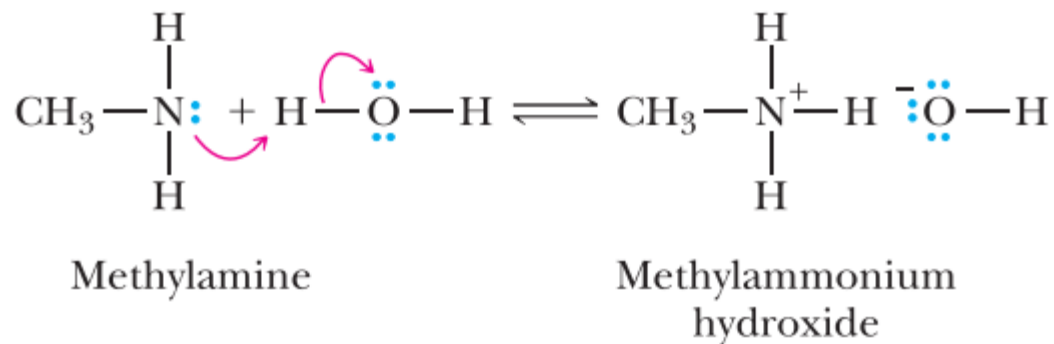
t-Butylamine
bp 46 °C



Diethylamine
bp 55 °C



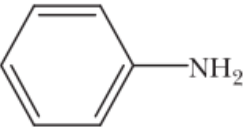
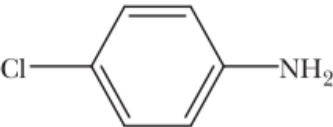
Diethyl ether
bp 34.6 °C

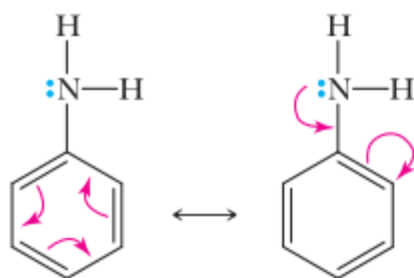


1) 脂肪胺碱性 > 氨分子

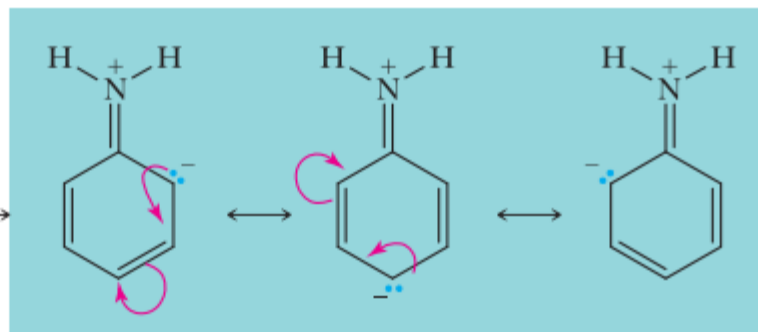
2) 芳香胺碱性 < 脂肪胺

原因：芳香胺上N原子的孤对电子可以共振到pi体系，相对减弱了可以结合质子的电荷的能力

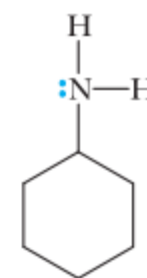
Amine	Structure	pK _b	pK _a
Ammonia	NH ₃	4.74	9.26
Primary Amines			
methylamine	CH ₃ NH ₂	3.36	10.64
ethylamine	CH ₃ CH ₂ NH ₂	3.19	10.81
cyclohexylamine	C ₆ H ₁₁ NH ₂	3.34	10.66
Secondary Amines			
dimethylamine	(CH ₃) ₂ NH	3.27	10.73
diethylamine	(CH ₃ CH ₂) ₂ NH	3.02	10.98
Tertiary Amines			
trimethylamine	(CH ₃) ₃ N	4.19	9.81
triethylamine	(CH ₃ CH ₂) ₃ N	3.25	10.75
Aromatic Amines			
aniline		9.37	4.63
4-methylaniline (p-toluidine)		8.92	5.08
4-chloroaniline		9.85	4.15
4-nitroaniline		13.0	1.0



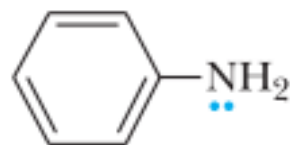
Two Kekulé structures



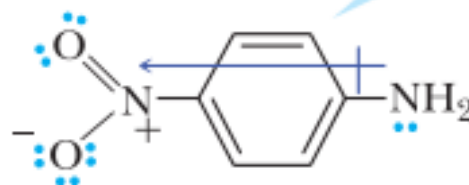
Interaction of the electron pair on nitrogen with the pi system of the aromatic ring reduces the availability of the electron pair to participate in a reaction with an acid



No resonance is possible with alkylamines

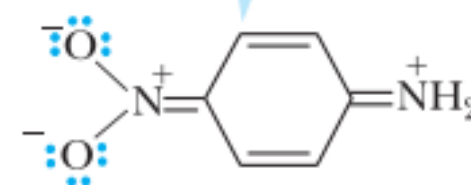


Aniline
 pK_b 9.37



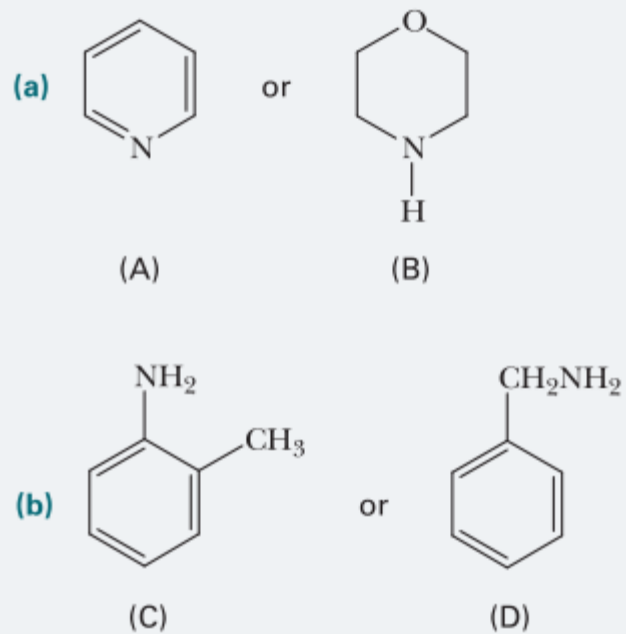
4-Nitroaniline
 pK_b 13.0

$-\text{NO}_2$ reduces the availability of the electron pair on nitrogen to participate in a reaction with an acid via both an inductive effect and a resonance effect

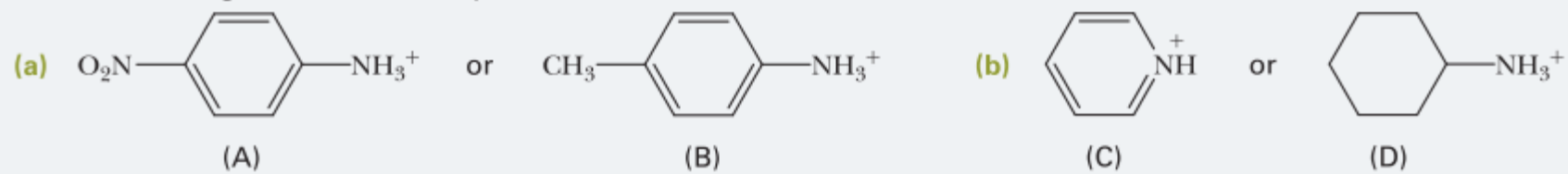


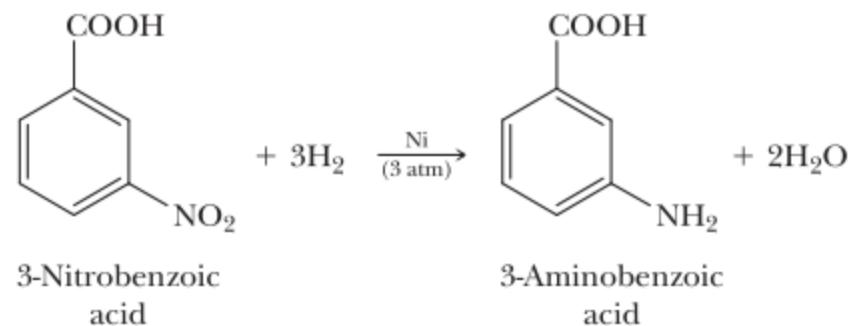


Select the stronger base in each pair of amines:



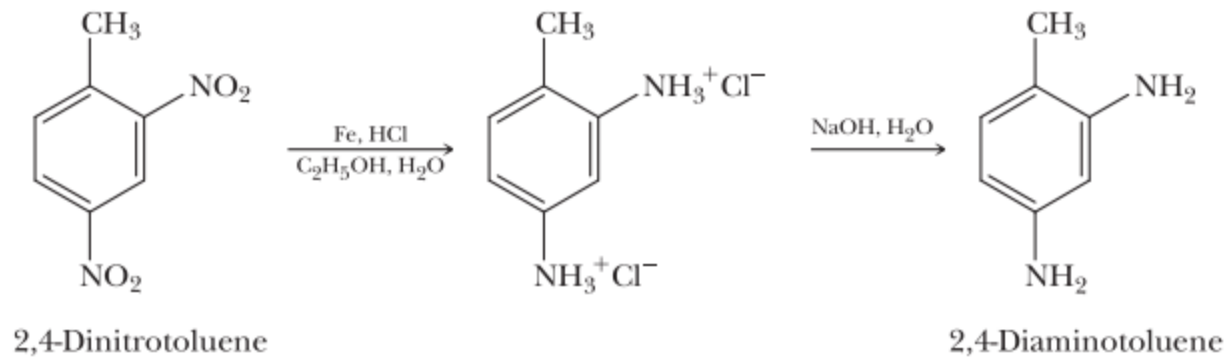
Select the stronger acid from each pair of ions:





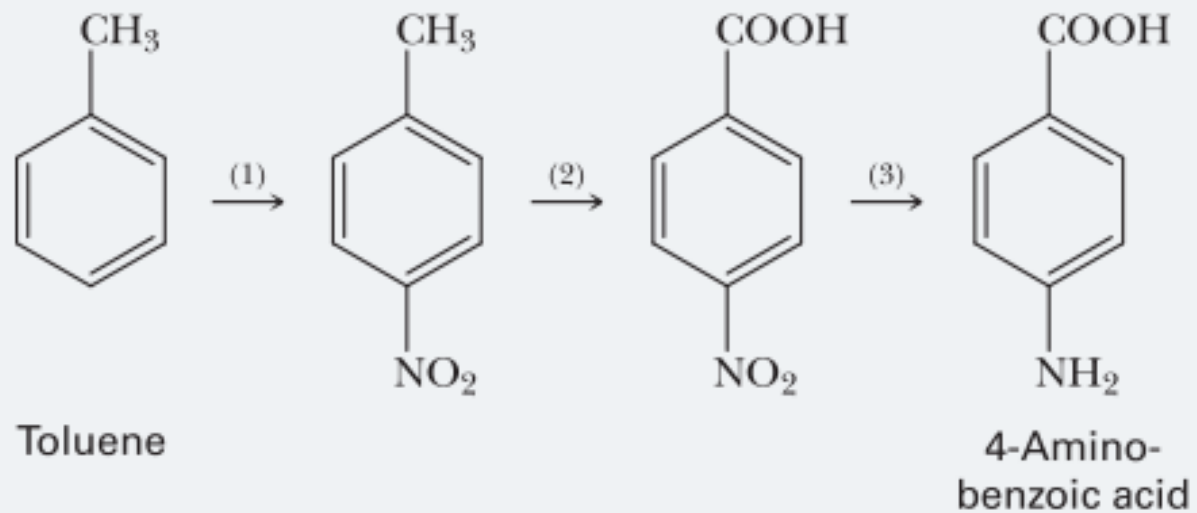
This method has the potential disadvantage that other susceptible groups, such as a carbon-carbon double bond, and the carbonyl group of an aldehyde or ketone, may also be reduced. Note that neither the —COOH nor the aromatic ring is reduced under these conditions.

Alternatively, a nitro group can be reduced to a primary amino group by a metal in acid:



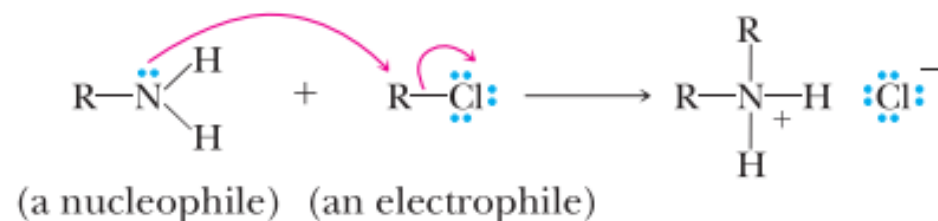


Show the reagents that will bring about each step in this conversion of toluene to 4-aminobenzoic acid:

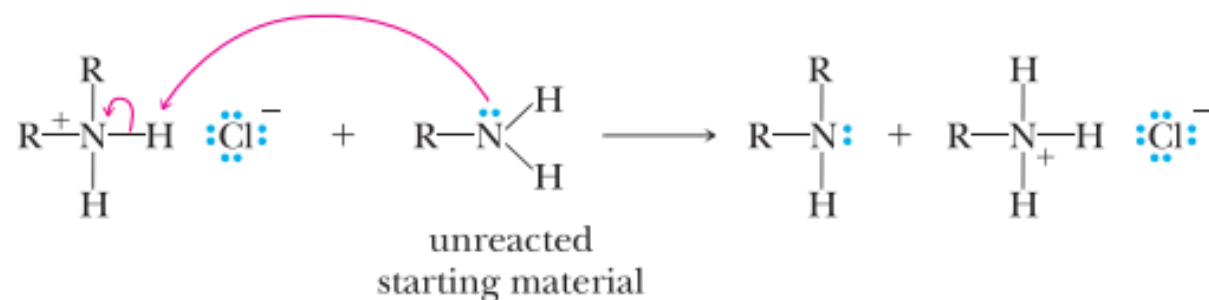




Step 1: Reaction of an electrophile and a nucleophile to form a new covalent bond. The nitrogen atom of an amine displaces chlorine in a haloalkane to yield an ammonium chloride ion.

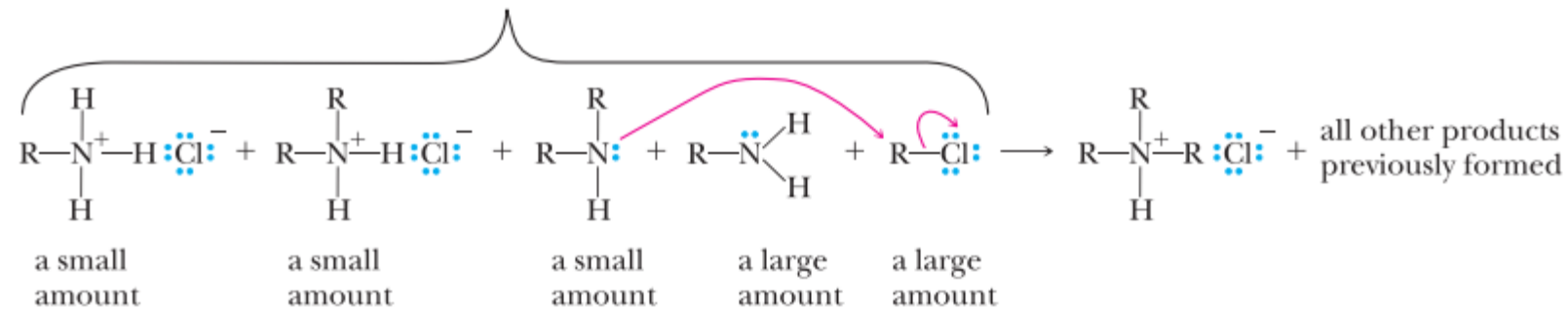


Step 2: Take a proton away. At the beginning of this reaction, when only a few product molecules are formed, plenty of amine starting material (a weak base) remains to react with the hydrogen of the ammonium salt to yield a secondary amine and another ammonium chloride ion.





compounds remaining in the reaction mixture



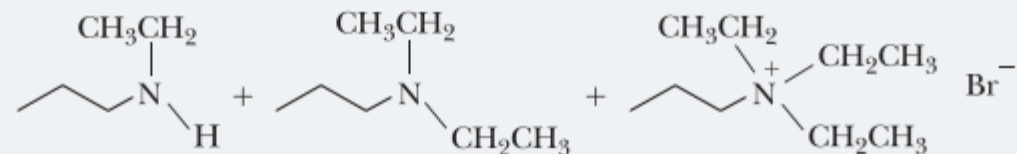
Determine all possible nitrogen-based products that can be formed in the following reaction:



STRATEGY

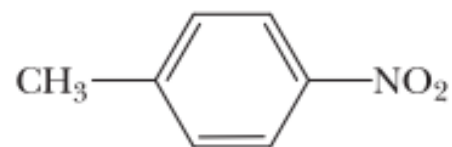
Keep in mind that the reaction of amines with haloalkanes often results in multiple nitrogen-based products with one or more alkyl groups from the haloalkane forming a bond with the nitrogen atom of the original amine.

SOLUTION





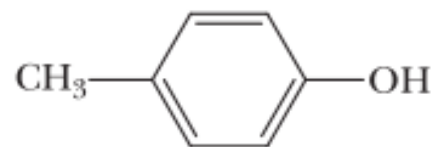
10.34 Suppose that you have a mixture of the following three compounds:



4-Nitrotoluene
(*p*-Nitrotoluene)



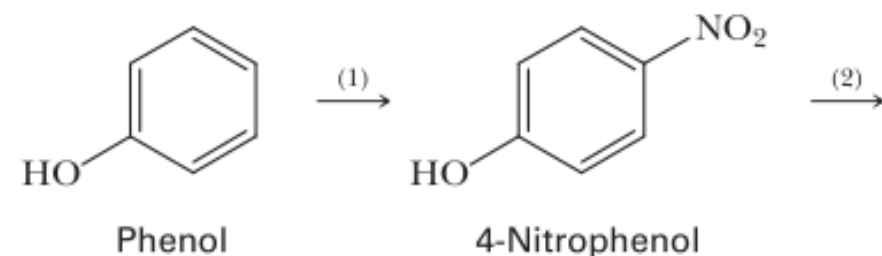
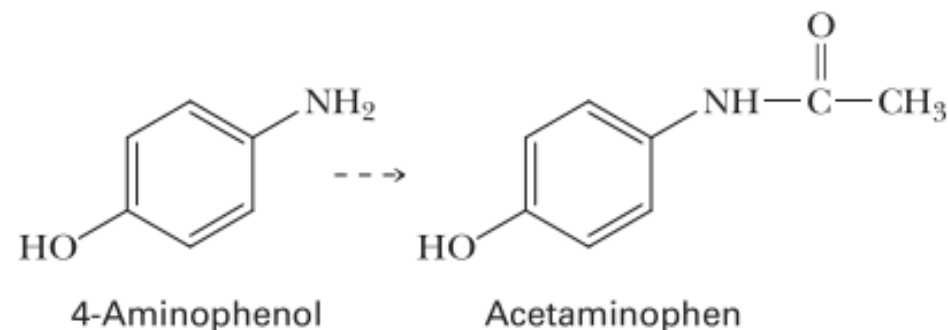
4-Methylaniline
(*p*-Toluidine)



4-Methylphenol
(*p*-Cresol)

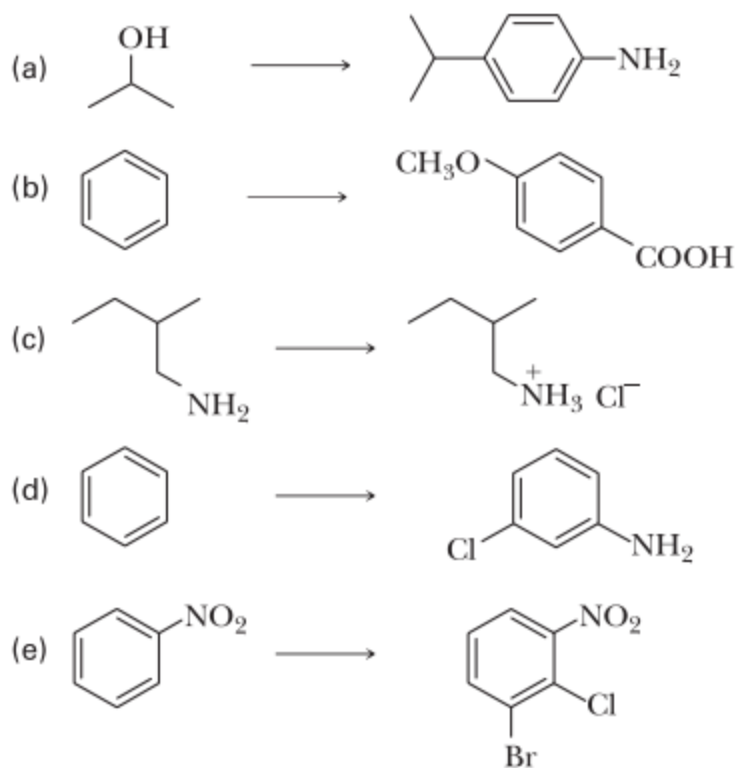
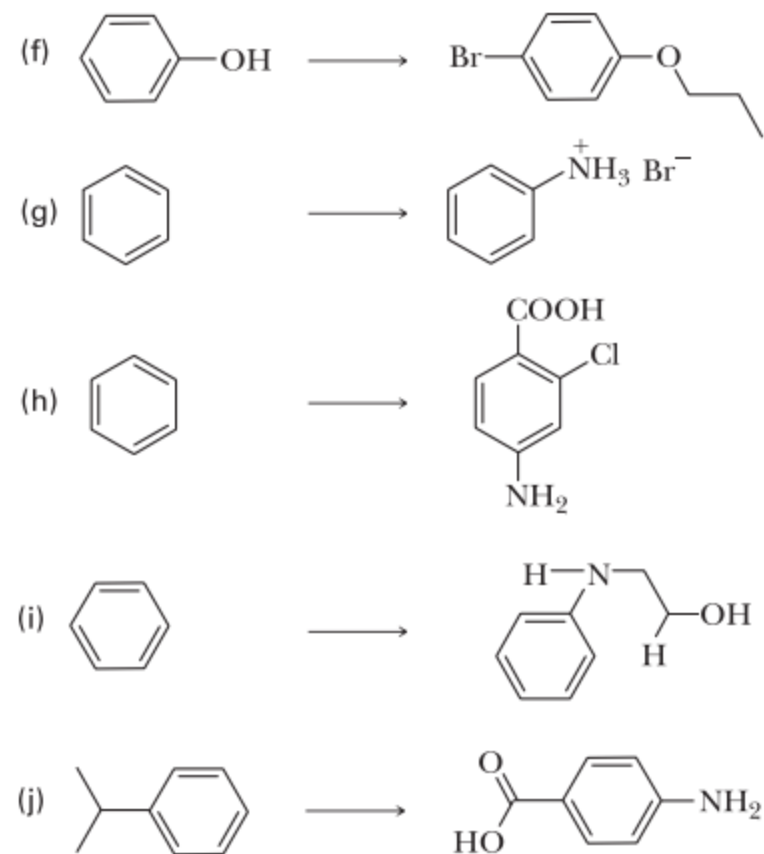
Devise a chemical procedure based on their relative acidity or basicity to separate and isolate each in pure form.

***10.36** 4-Aminophenol is a building block in the synthesis of the analgesic acetaminophen. Show how this building block can be synthesized in two steps from phenol (in Chapter 15, we will see how to complete the synthesis of acetaminophen): (**See Example 10.9**)





10.44 Test your cumulative knowledge of the reactions learned thus far by completing the following chemical transformations. *Note: Some will require more than one step. (See Example 10.9)*

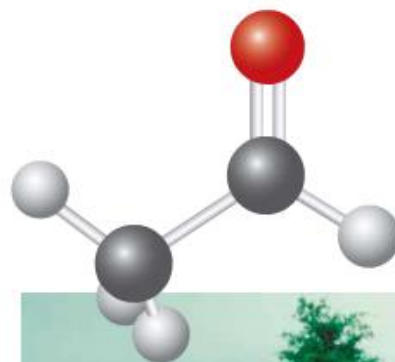




12

Aldehydes and Ketones

Ethanol from alcoholic beverages is first metabolized to acetaldehyde before being broken down further in the body. The reactivity of the carbonyl group of acetaldehyde allows it to bind to proteins in the body, the products of which lead to tissue damage and organ disease. Inset: A model of acetaldehyde. (Novastock/Stock Connection/Glow Images)



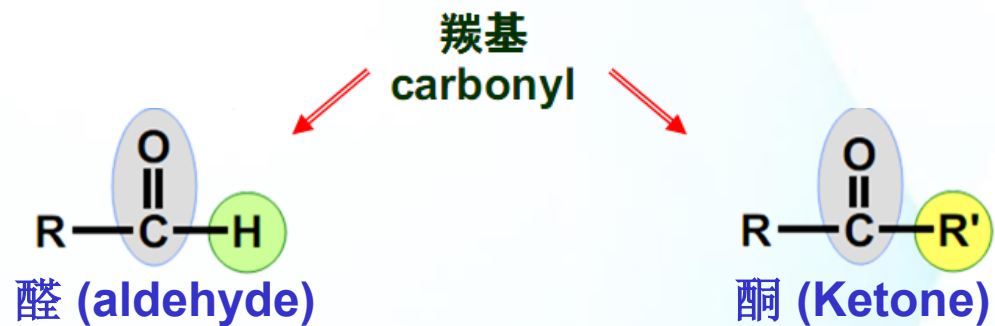


KEY QUESTIONS

- 12.1** What Are Aldehydes and Ketones?
- 12.2** How Are Aldehydes and Ketones Named?
- 12.3** What Are the Physical Properties of Aldehydes and Ketones?
- 12.4** What Is the Most Common Reaction Theme of Aldehydes and Ketones?
- 12.5** What Are Grignard Reagents, and How Do They React with Aldehydes and Ketones?
- 12.6** What Are Hemiacetals and Acetals?
- 12.7** How Do Aldehydes and Ketones React with Ammonia and Amines?

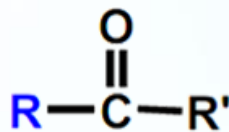
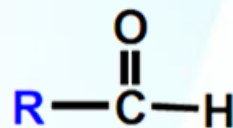


分类

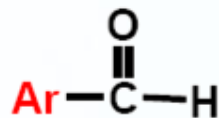
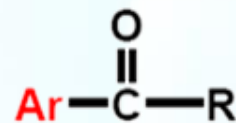


羰基化合物

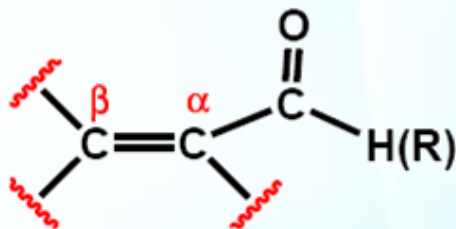
脂肪族醛、酮



芳香族醛、酮



α, β -不饱和醛、酮



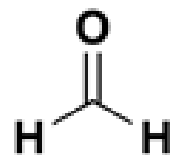


The following are the IUPAC rules for naming aldehydes and ketones:

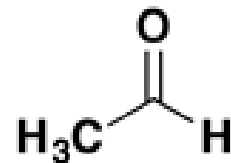
- ◆ The stem names of aldehydes and ketones are derived from those of **the parent alkanes**, defined **by the longest continuous chain** (LCC) of carbon atoms that contains the functional group.
- ◆ For **an aldehyde**, **drop the *-e* from the alkane name and add the ending *-al***.
- ◆ For a **ketone**, drop the *-e* from the alkane name and add the ending ***-one***.
- ◆ To indicate the position of a substituent on an aldehyde, the carbonyl carbon atom is always considered to be C1; it is unnecessary to designate this group by number.
- ◆ To indicate the position of a substituent on a ketone, **number the chain in the manner that gives the carbonyl carbon atom the lowest possible number**. In cyclic ketones, it is understood that the carbonyl carbon atom is C1.



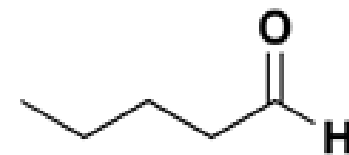
Naming aldehydes and ketones using IUPAC rules



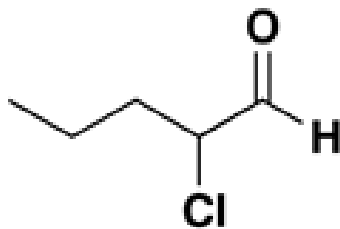
methanal
(formaldehyde)



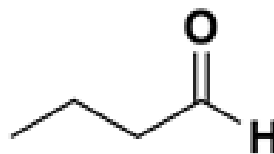
ethanal
(acetaldehyde)



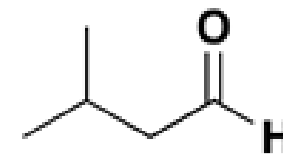
pentanal
(valeraldehyde)



2-chloropentanal
(α -chlorovaleraldehyde)



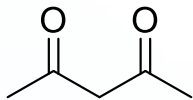
butanal
(butyraldehyde)



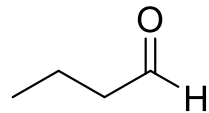
3-methylbutanal
(isovaleraldehyde)



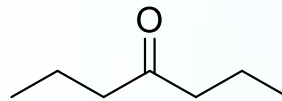
Naming aldehydes and ketones using IUPAC rules



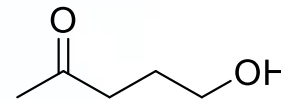
Pentane-2,4-dione



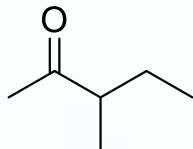
Butanal



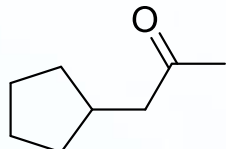
Heptan-4-one



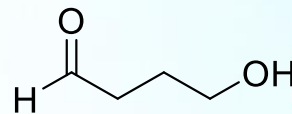
5-Hydroxypentan-2-one



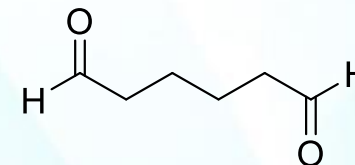
3-methylpentan-2-one



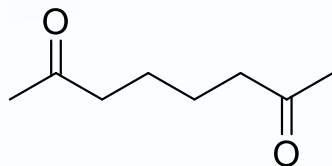
1-cyclopentylpropan-2-one



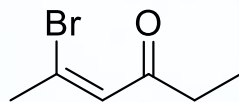
4-hydroxybutanal



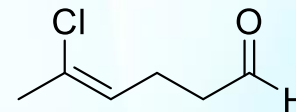
Hexane-1,6-dial



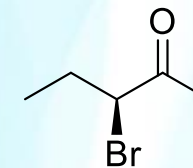
octane-2,7-dione



(Z)-5-bromohex-4-en-3-one

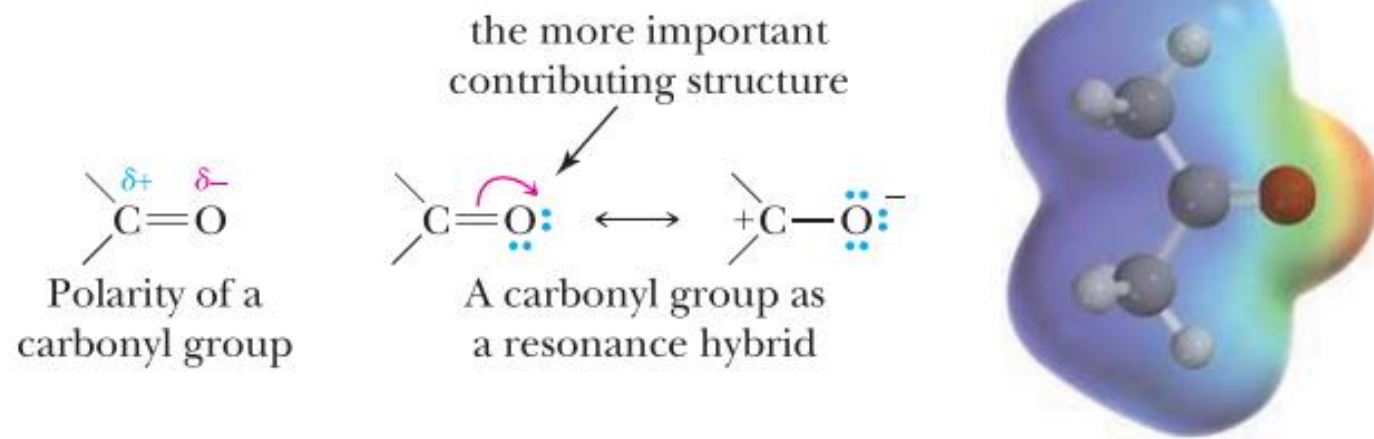


(Z)-5-chlorohex-4-enal



(S)-3-bromopentan-2-one

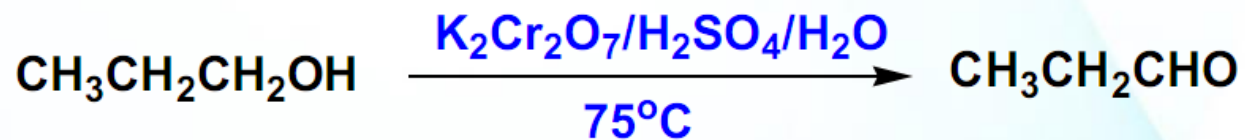
结构



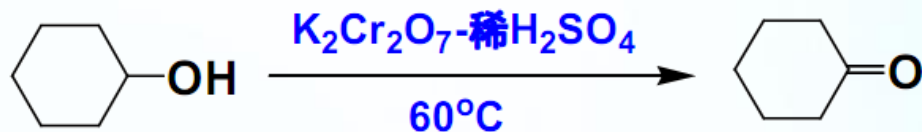
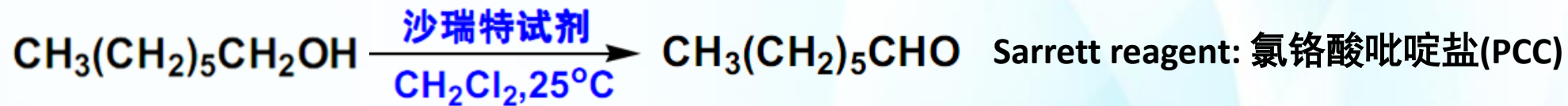
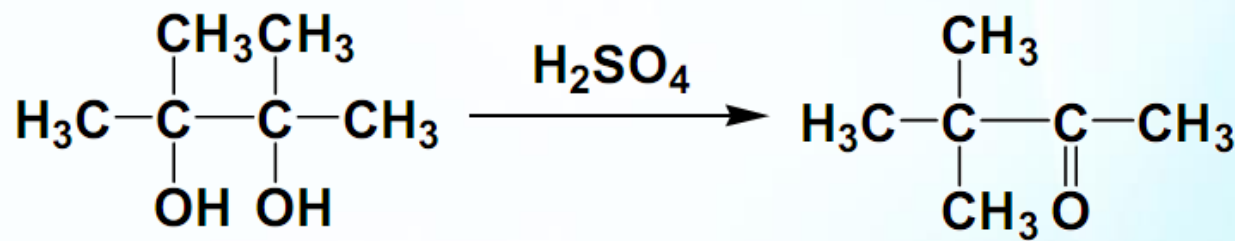
- C=O双键是由一个 σ 键和一个 π 键组成的
- C=O是一个极性基团，具有偶极矩



① 由醇制备

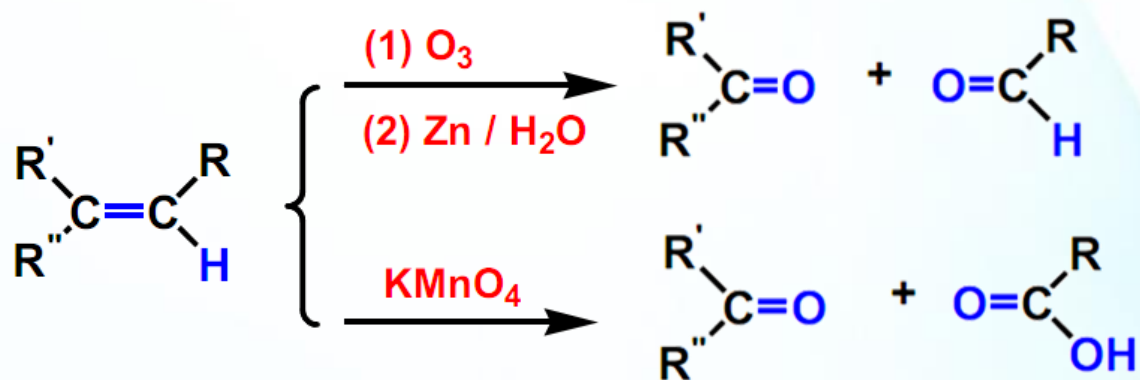
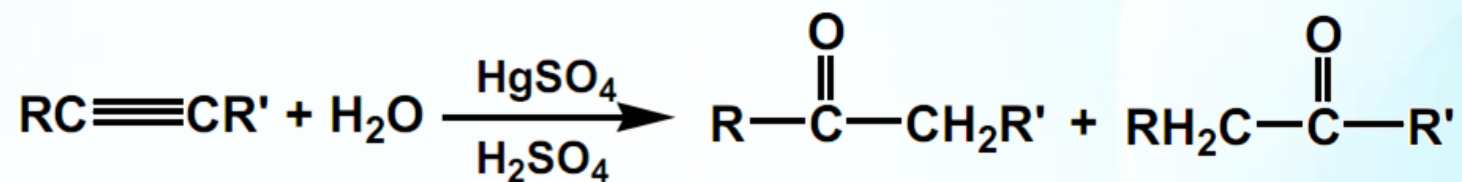


橙红色
变绿色



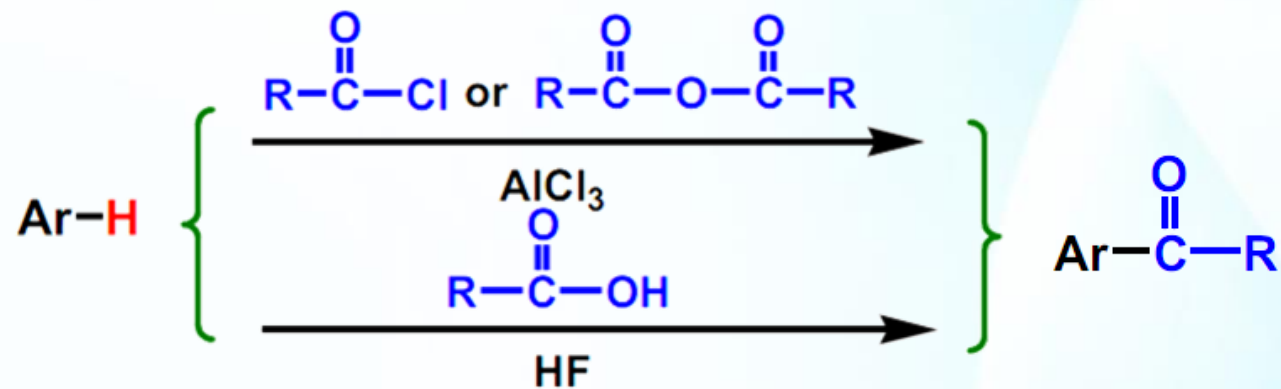


② 由不饱和烃制备



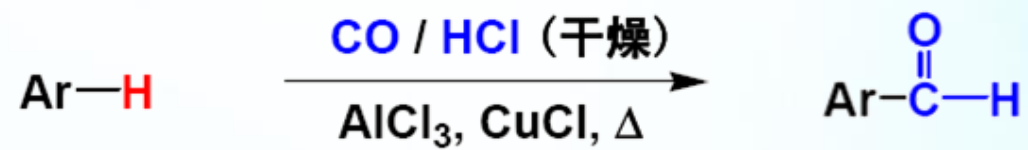


③ Friedel-Crafts 酰化反应合成芳酮



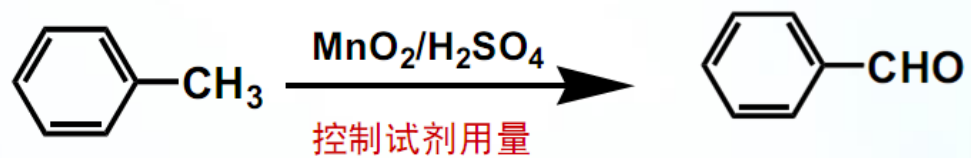
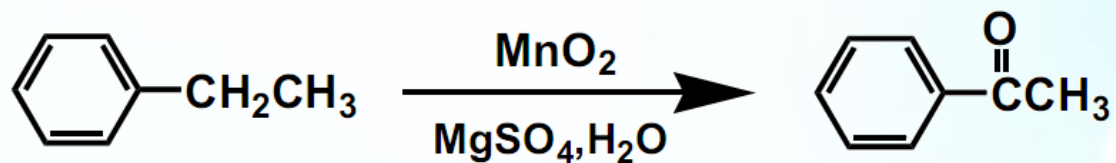
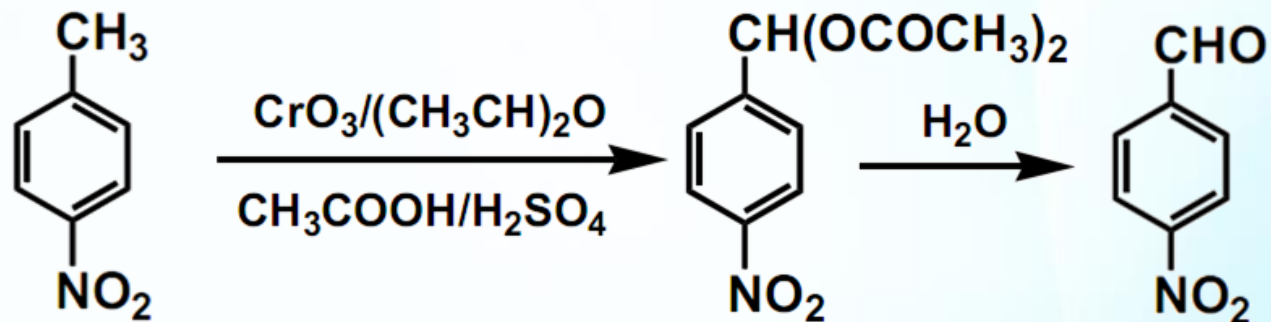


④ Gattermaan-Koch反应合成芳醛





⑤ 芳烃侧链的氧化





- 醛酮的沸点比相应相对分子质量的烷烃高
(偶极矩增加了分子间的吸引力)
- 羰基能与水形成氢键，故低级醛酮能与水混溶，高级醛酮溶解度随分子量增加而下降
- 醛酮分子间不能形成氢键，故沸点低于醇
- 脂肪族醛酮相对密度小于1，芳香族醛酮相对密度大于1



第七章 醛和酮

本章内容

7.1 醛、酮的结构和命名

7.2 醛、酮的制法

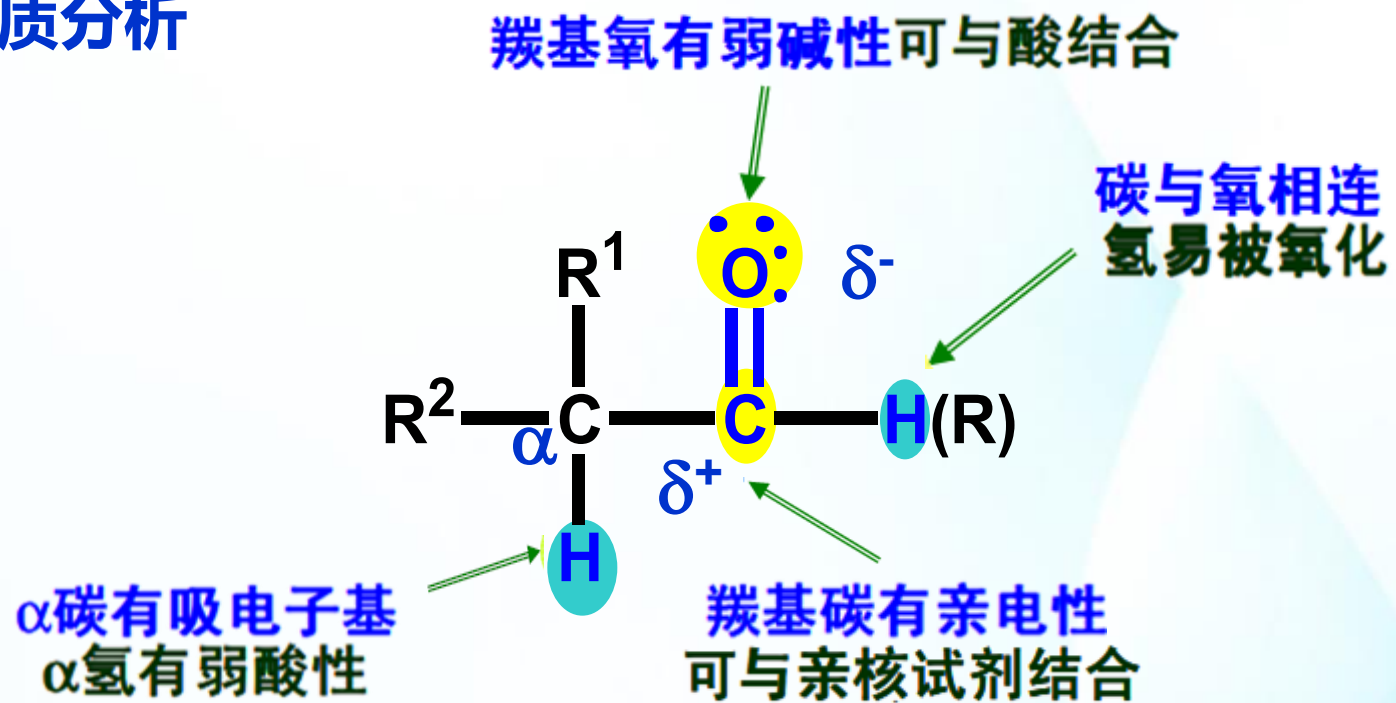
7.3 醛、酮物理性质

7.4 醛、酮化学性质

7.5 重要的醛、酮

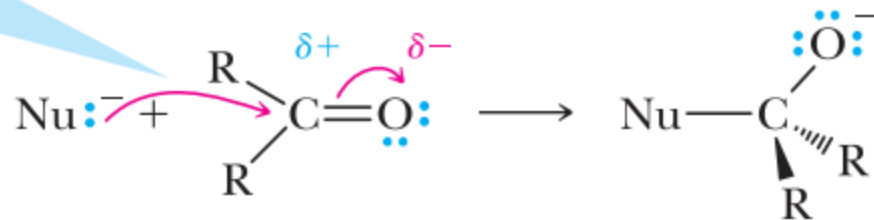


性质分析





this is the common mechanism pattern: **Reaction of a nucleophile and an electrophile to form a covalent bond**

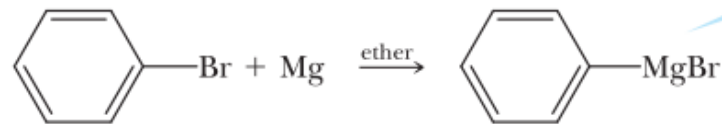


Tetrahedral carbonyl addition intermediate



1-Bromobutane

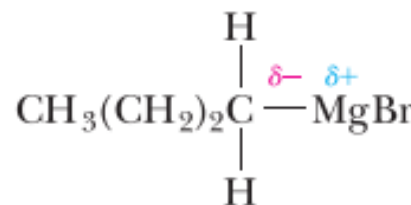
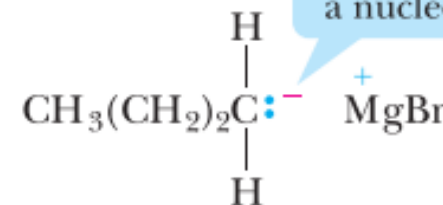
Butylmagnesium bromide



Bromobenzene

Phenylmagnesium bromide

in a Grignard reagent, the magnesium atom has inserted itself between the bromine and carbon atom

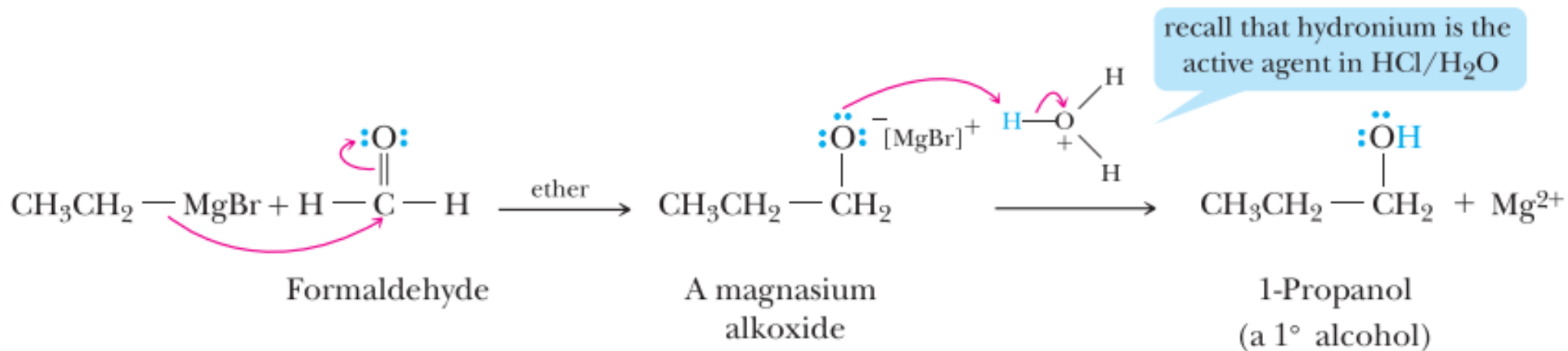


carbon is a nucleophile



Addition to Formaldehyde Gives a 1° Alcohol

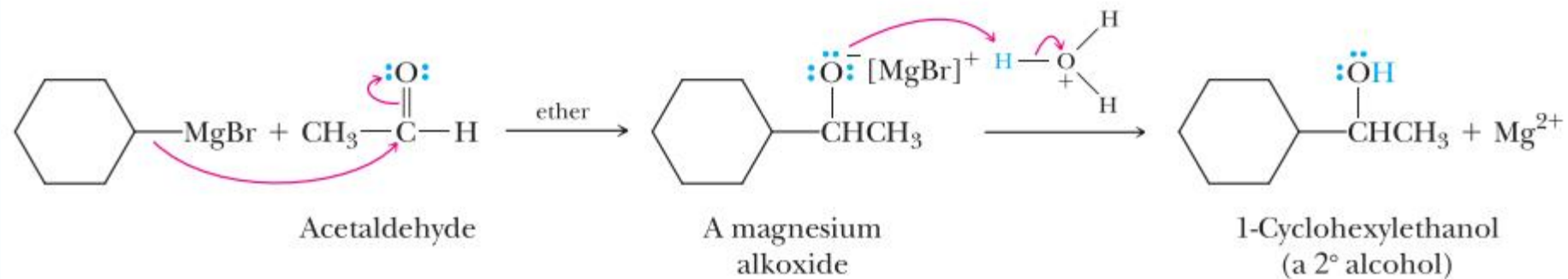
Treatment of a Grignard reagent with formaldehyde, followed by hydrolysis in aqueous acid, gives a primary alcohol:





Addition to an Aldehyde (Except Formaldehyde) Gives a 2° Alcohol

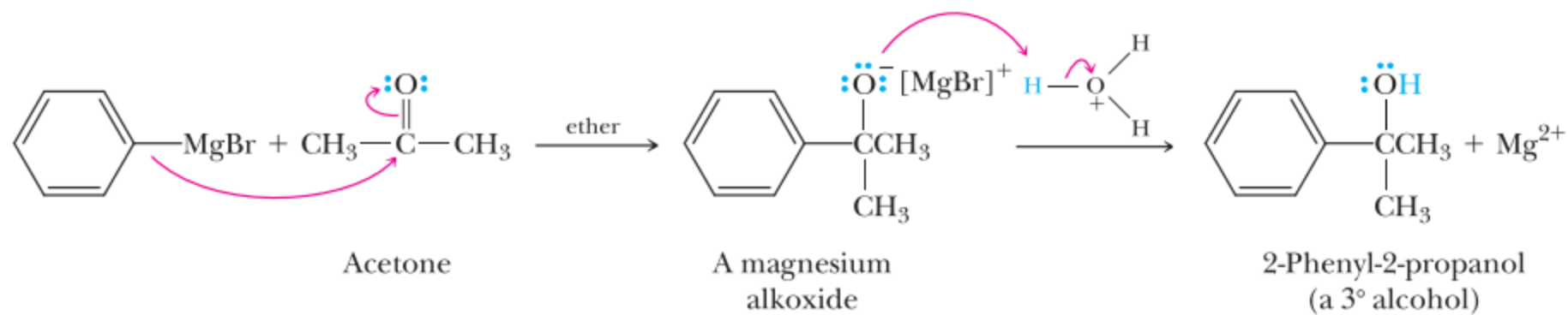
Treatment of a Grignard reagent with any aldehyde other than formaldehyde, followed by hydrolysis in aqueous acid, gives a secondary alcohol:

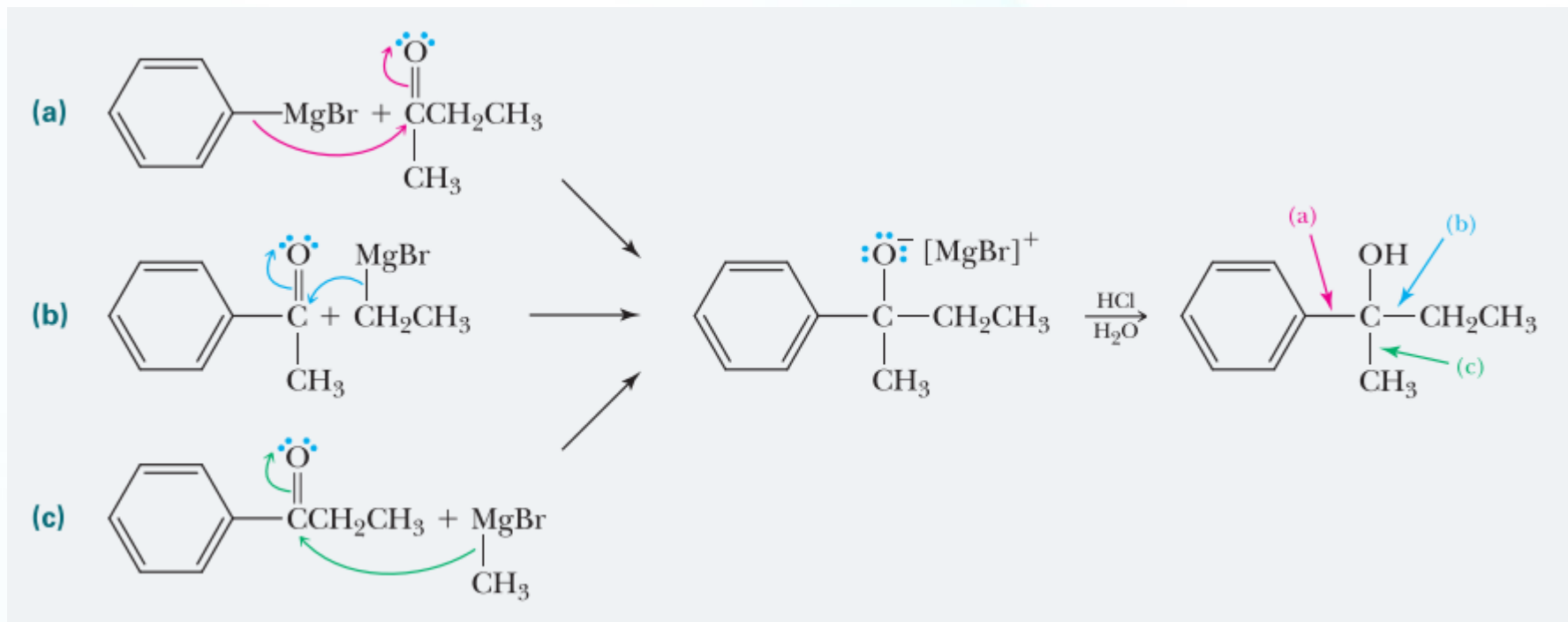




Addition to a Ketone Gives a 3° Alcohol

Treatment of a Grignard reagent with a ketone, followed by hydrolysis in aqueous acid, gives a tertiary alcohol:

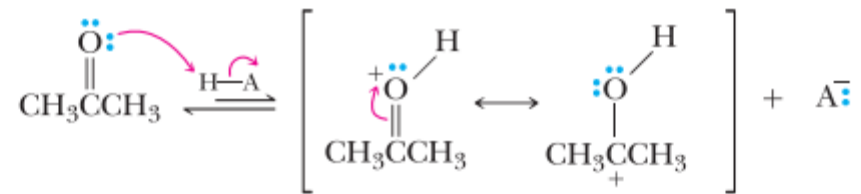






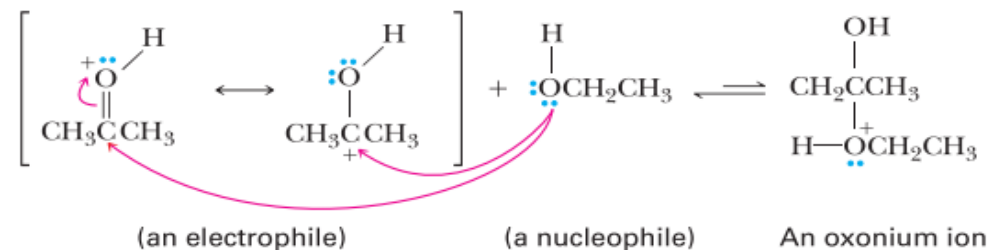
Acid-Catalyzed Formation of a Hemiacetal

STEP 1: Add a proton. Proton transfer from H—A to the carbonyl gives a resonance-stabilized cation. The more significant resonance structure places the positive charge on the carbon:

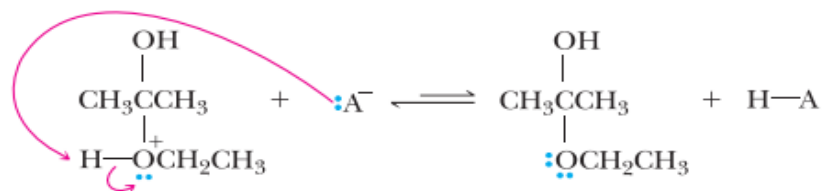


A resonance-stabilized cation

STEP 2: Reaction of an electrophile and a nucleophile to form a new covalent bond. Addition of the alcohol to the resonance-stabilized cation gives an oxonium ion. *Note:* The attack of the alcohol can be to either contributing structure:



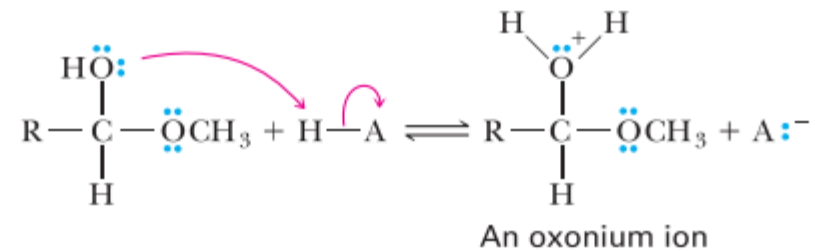
STEP 3: Take a proton away. Proton transfer from the oxonium ion to A⁻ gives the hemiacetal and regenerates the acid catalyst:



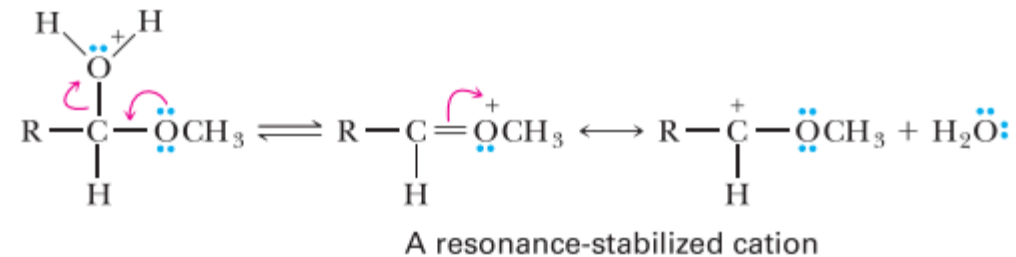


Acid-Catalyzed Formation of an Acetal

STEP 1: Add a proton. Proton transfer from the acid, $\text{H}-\text{A}$, to the hemiacetal OH group gives an oxonium ion:

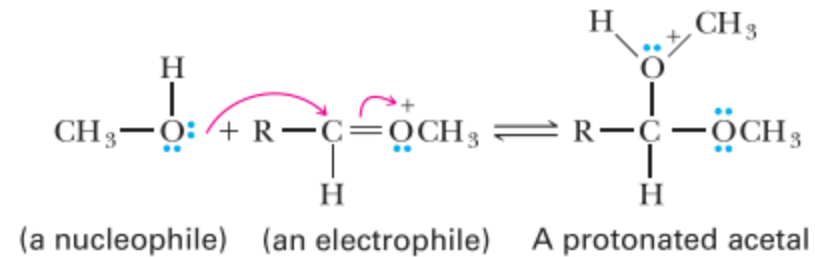


STEP 2: Break a bond to form a stable ion or molecule. Loss of water from the oxonium ion gives a resonance-stabilized cation:

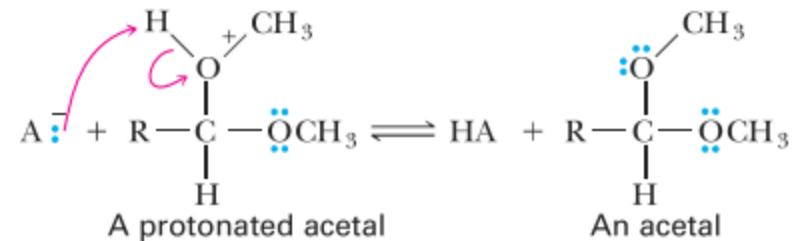




STEP 3: Reaction of an electrophile and a nucleophile to form a new covalent bond. Reaction of the resonance-stabilized cation (an electrophile) with methanol (a nucleophile) gives the conjugate acid of the acetal:



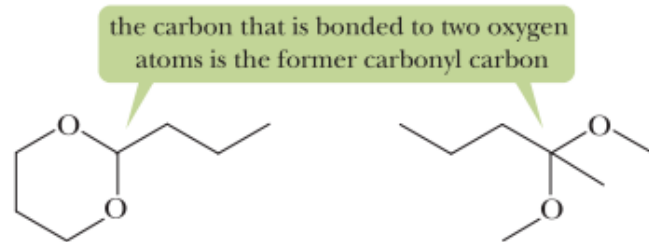
STEP 4: Take a proton away. Proton transfer from the protonated acetal to A^- gives the acetal and generates a new molecule of $\text{H}-\text{A}$, the acid catalyst:



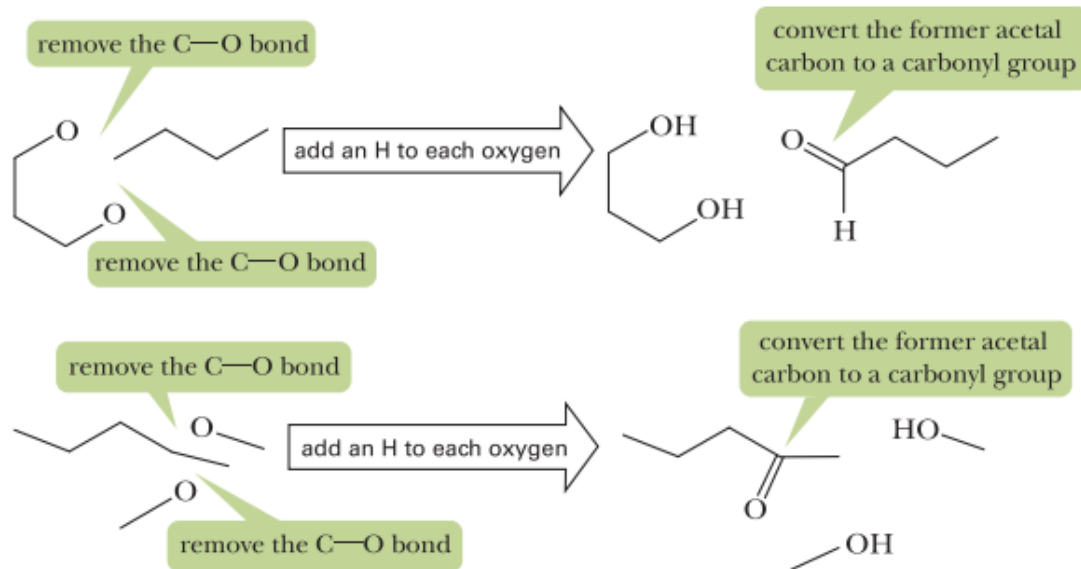
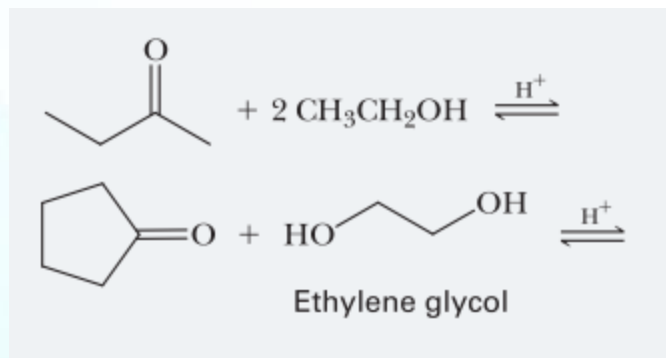


Determine the Reactants Used to Synthesize a Hemiacetal or Acetal

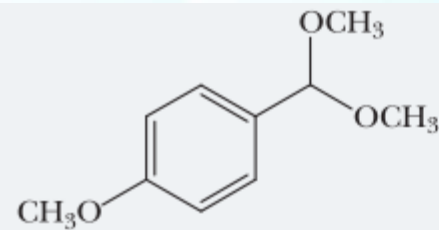
- (a) Identify the carbon atom that is bonded to two oxygen atoms. This carbon atom is the carbonyl carbon that was converted to the carbon of the acetal or hemiacetal group.



- (b) Remove both C—O bonds and add back a hydrogen to each oxygen to obtain the alcohol reagent(s) used. Then convert the carbon identified in (a) to a carbonyl group.



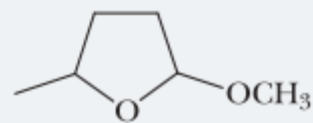
(a)

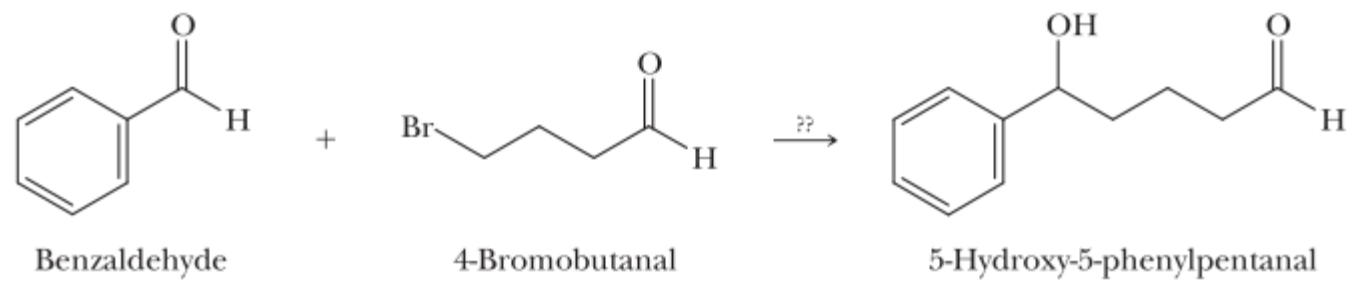
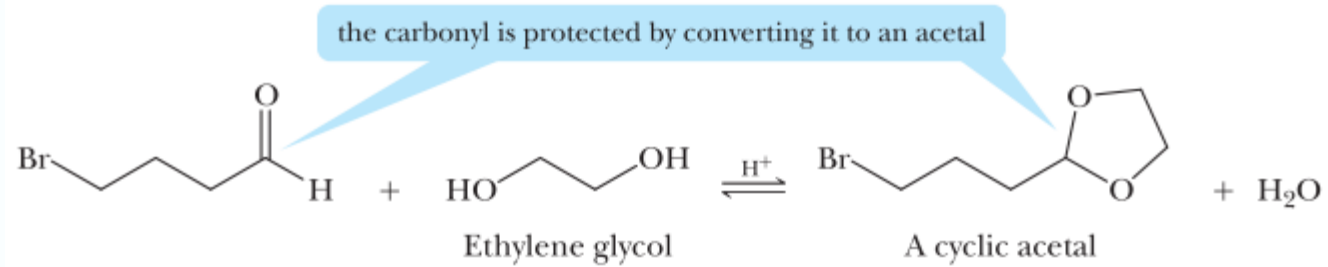


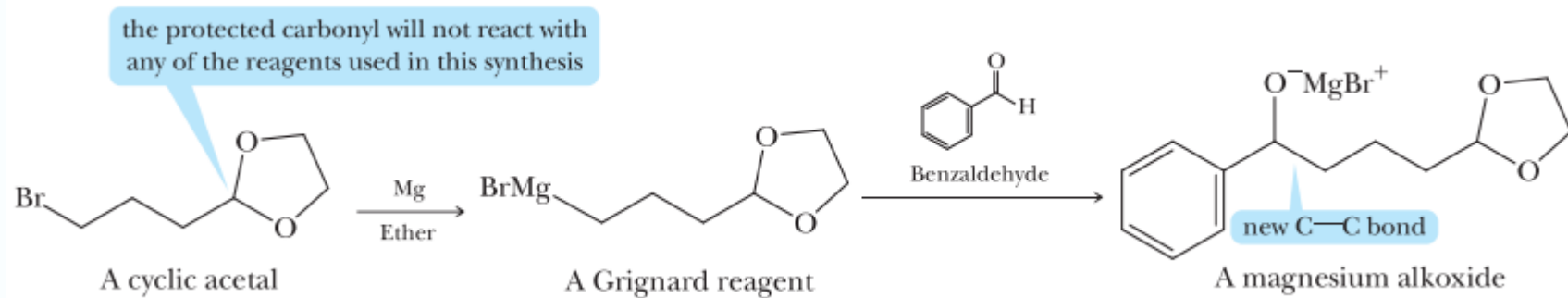
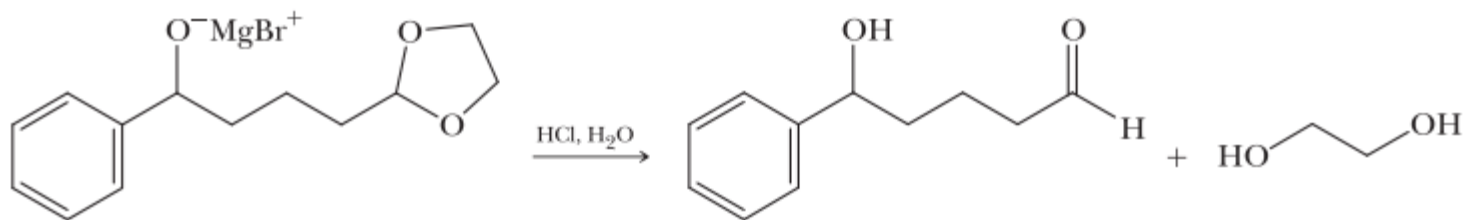
(b)



(c)







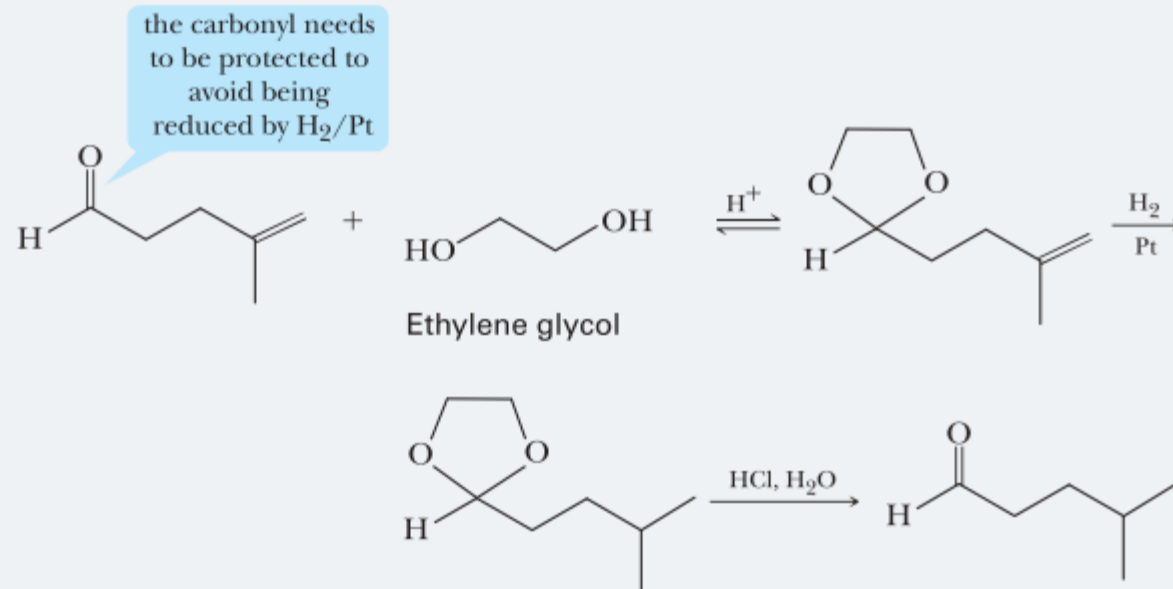


Propose a method for the following transformation. *Note:* Catalytic hydrogenation adds H_2 across $\text{C}=\text{O}$ double bonds as well as across $\text{C}=\text{C}$ double bonds.

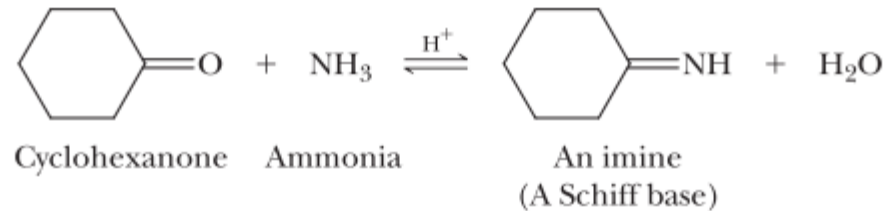


SOLUTION

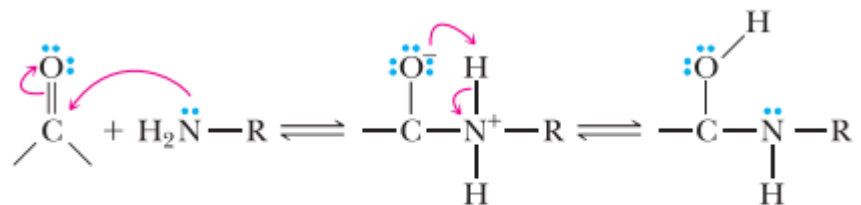
It is important to protect the carbonyl group. Otherwise, it will be reduced to an alcohol by H_2/Pt :



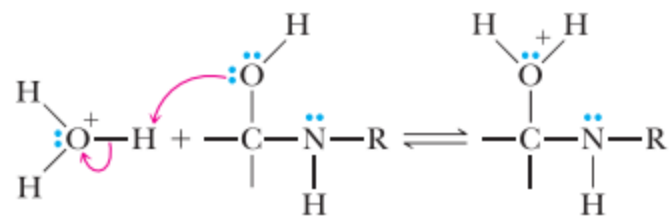
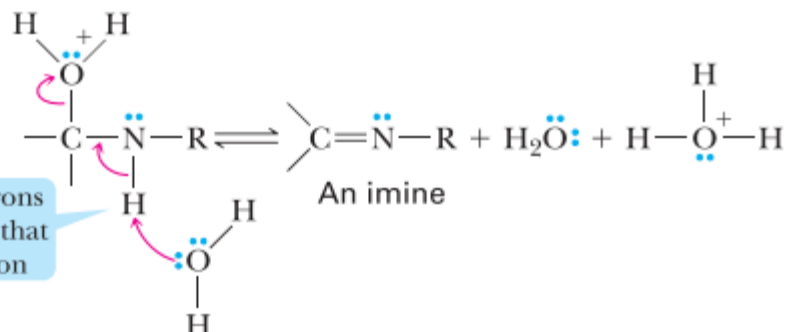
Ammonia, primary aliphatic amines (RNH_2), and primary aromatic amines (ArNH_2) react with the carbonyl group of aldehydes and ketones in the presence of an acid catalyst to give a product that contains a carbon–nitrogen double bond. A molecule containing a carbon–nitrogen double bond is called an **imine** or, alternatively, a **Schiff base**:


$$\text{Cyclohexane ring}=\text{NCH}_3 \xrightarrow[\text{H}_2\text{O}]{\text{HCl}} \text{Cyclohexane ring}=\text{O} + \text{NH}_3^+\text{CH}_3\text{Cl}^-$$

An imine (A Schiff base) Cyclohexanone Ammonium salt



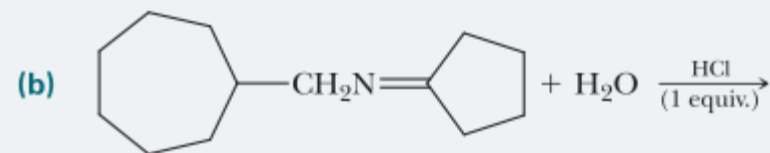
A tetrahedral carbonyl
addition intermediate



the flow of electrons
here is similar to that
in an E2 reaction

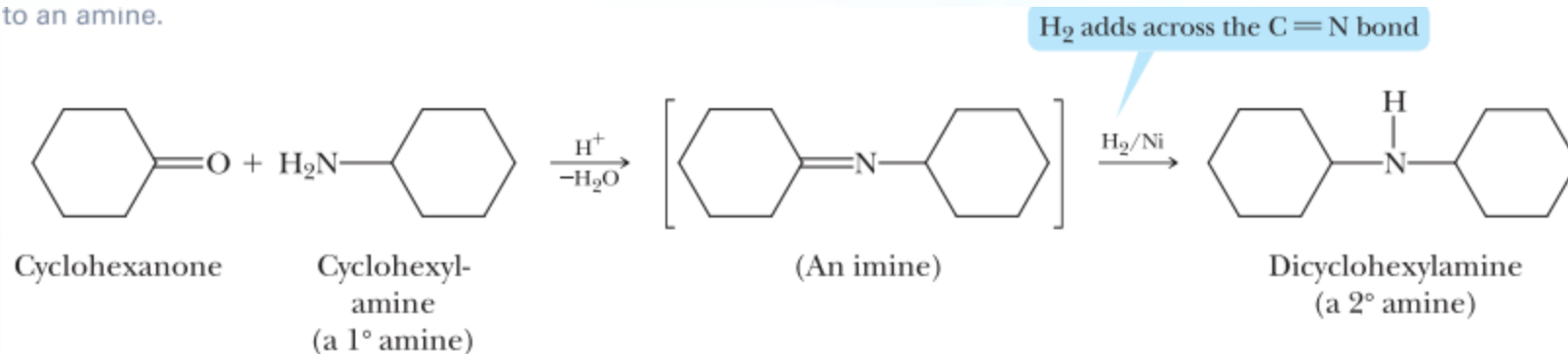
An imine

Predict the products formed in each reaction:

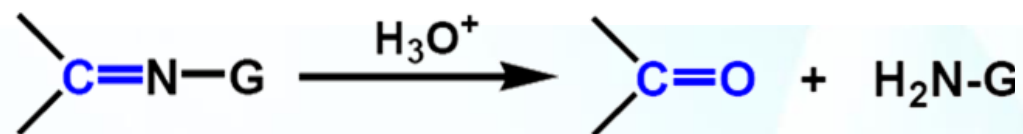




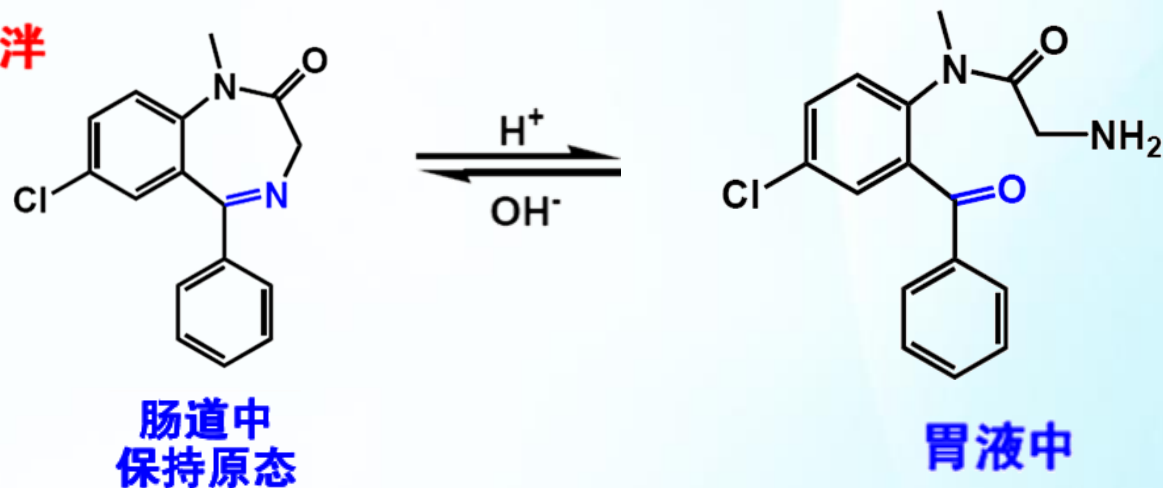
to an amine.



Conversion of an aldehyde or a ketone to an amine is generally carried out in one laboratory operation by mixing together the carbonyl-containing compound, the amine or ammonia, hydrogen, and the transition metal catalyst. The imine intermediate is not isolated.



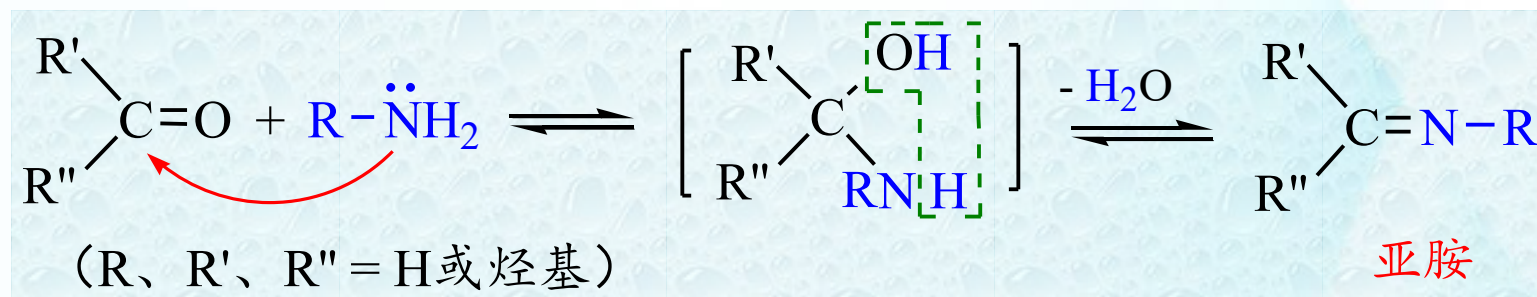
镇静催眠药物——地西洋



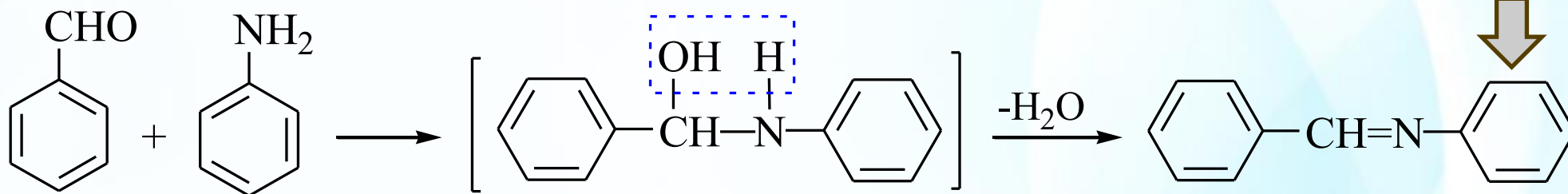


4. N-containing nucleophiles

(1) **Imine formation**: The reaction of ammonia or primary amines with aldehydes and ketones, under acid catalysis (pH=4~5), proceeds first via addition, followed by dehydration of the intermediate to form **imines**. Substituted imines derived from primary amines are also called **Schiff bases (席夫碱)**. The mechanism is an addition-elimination process.

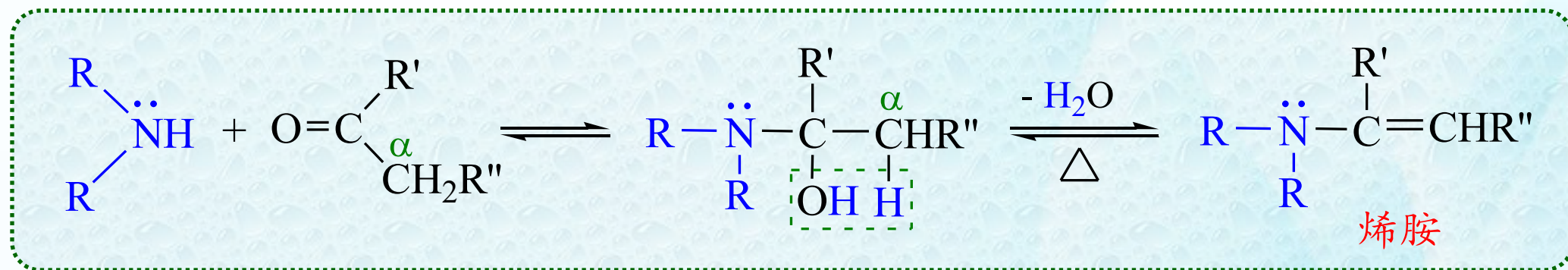
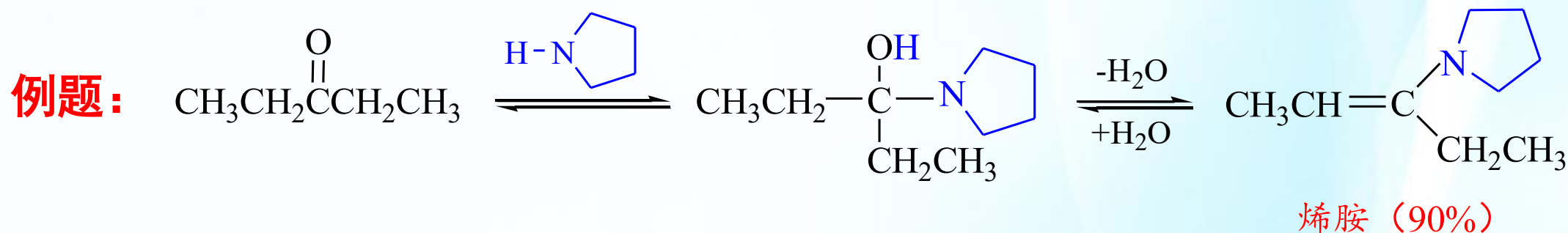


亚胺不稳定，但
芳醛与芳胺生成的
亚胺较稳定。



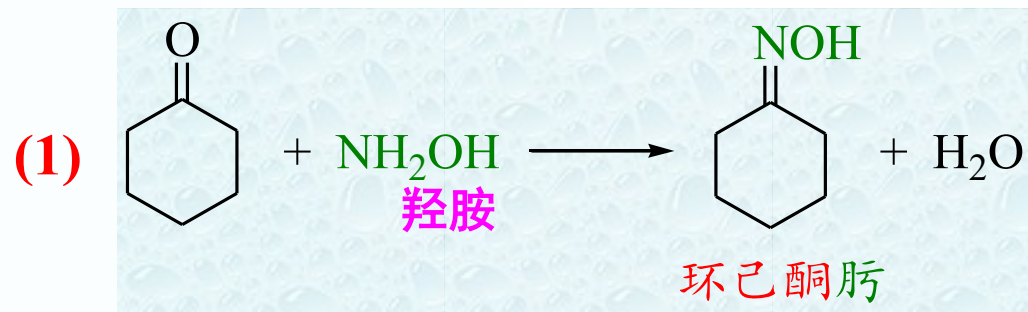
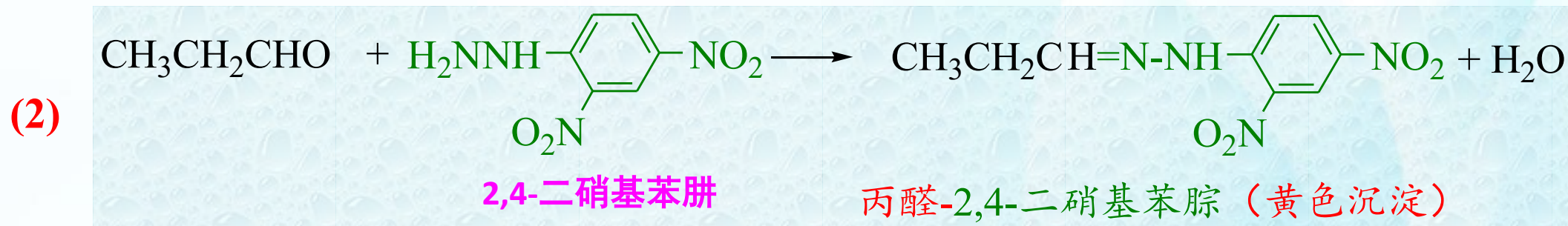
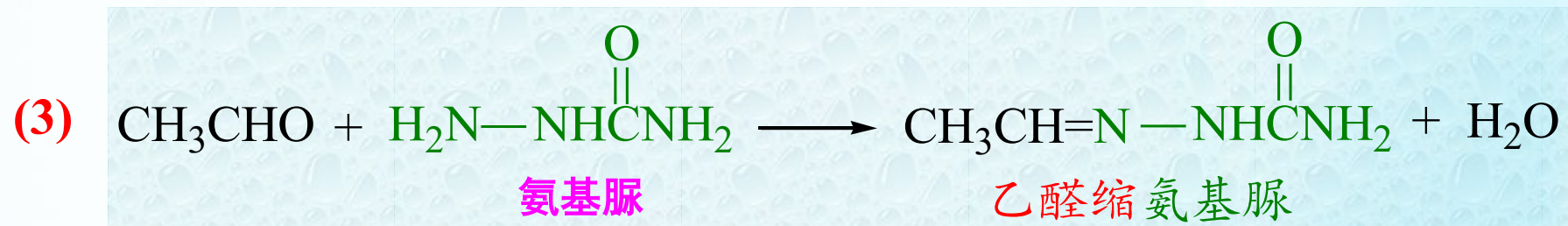
- Imines undergo **hydrolysis** in dilute acid to regenerate the original aldehyde/ketone and amine, making this a useful method for **carbonyl group protection**. Catalytic hydrogenation of imines is also an important route to secondary amines.

Secondary amines undergo nucleophilic addition with aldehydes/ketones that contain α -hydrogens. However, since there is no extra hydrogen on the nitrogen atom of the addition intermediate to dehydrate together with the newly formed hydroxyl group, the hydroxyl group can **only eliminate with a hydrogen on the adjacent α -carbon** to form a **carbon-carbon double bond**. The resulting product is called an **enamine**, and the formation of enamines is also reversible.



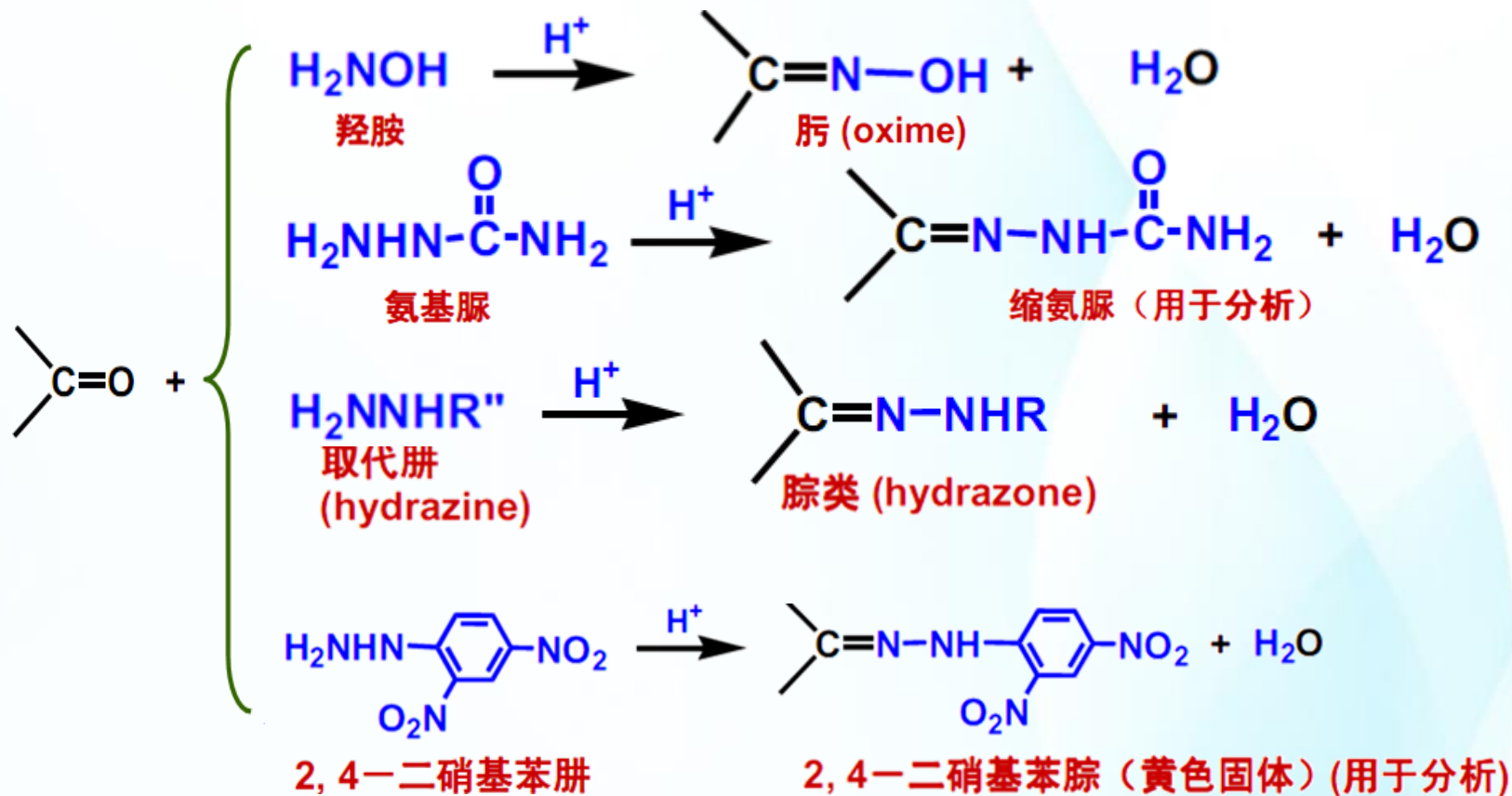


Certain amine derivatives (hydroxylamine, hydrazine, and semicarbazide, (羟胺、肼、氨基脒)) undergo addition-elimination (dehydration) condensation reactions with aldehydes and ketones to form imine derivatives





d) Reaction with amine derivatives

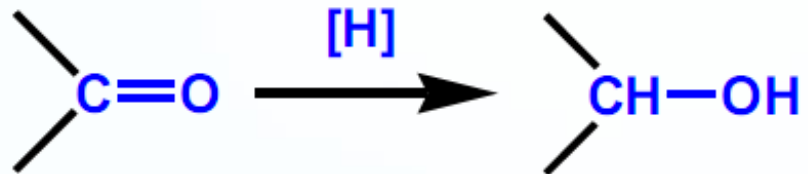




(5) Reduction Reactions of Aldehydes and ketones

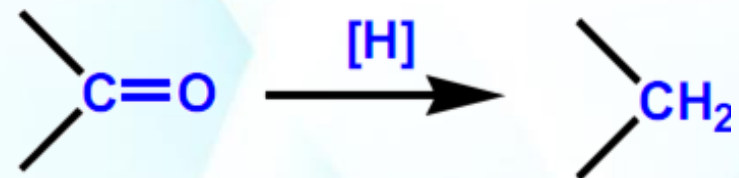
Two Types of Carbonyl Group Reduction

Reduction to hydroxyl group



- 氢化金属还原 (第III主族元素)
 $\text{LiAlH}_4, \text{NaBH}_4, \text{B}_2\text{H}_6$
- 催化氢化还原:
 H_2 , 加压 / Pt (or Pd, or Ni) / 加热
- Meerwein-Ponndorf 还原法:
 $(i\text{-PrO})_3\text{Al} / i\text{-PrOH}$
- 金属还原法: Na, Li, Mg, Zn

Reduction to methylene group

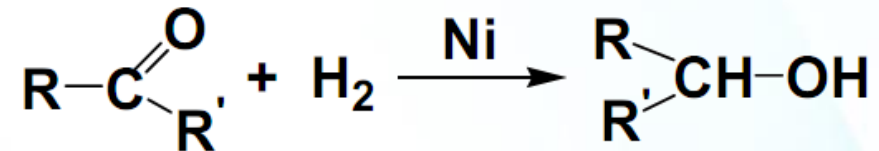
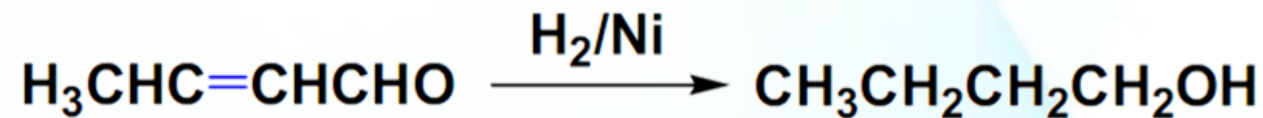


- Clemmensen还原
 $\text{Zn(Hg)} / \text{HCl}$
- Wolff-Kishner还原
 $\text{NH}_2\text{NH}_2 / \text{Na} / 200^\circ\text{C}$
黄鸣龙改良法
 $\text{NH}_2\text{NH}_2 / \text{NaOH} /$
 $(\text{HOCH}_2\text{CH}_2)_2\text{O} / \Delta$

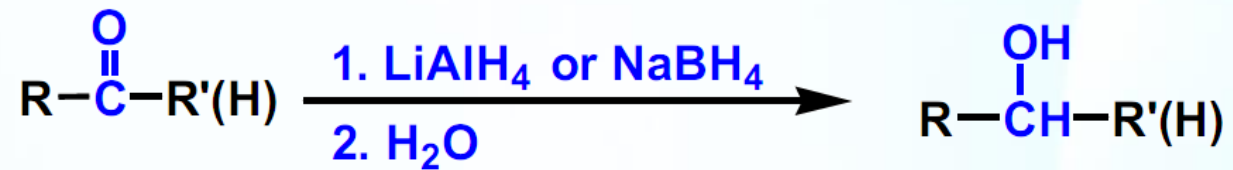
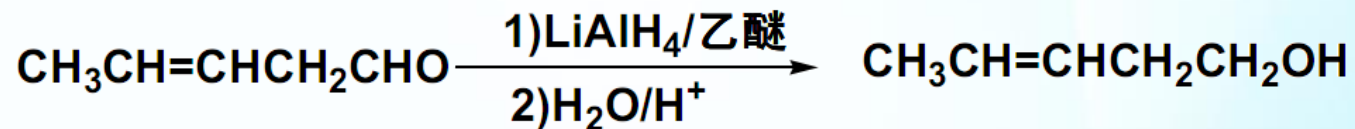


(5) Reduction Reactions of Aldehydes and ketones

Reduction to hydroxyl group



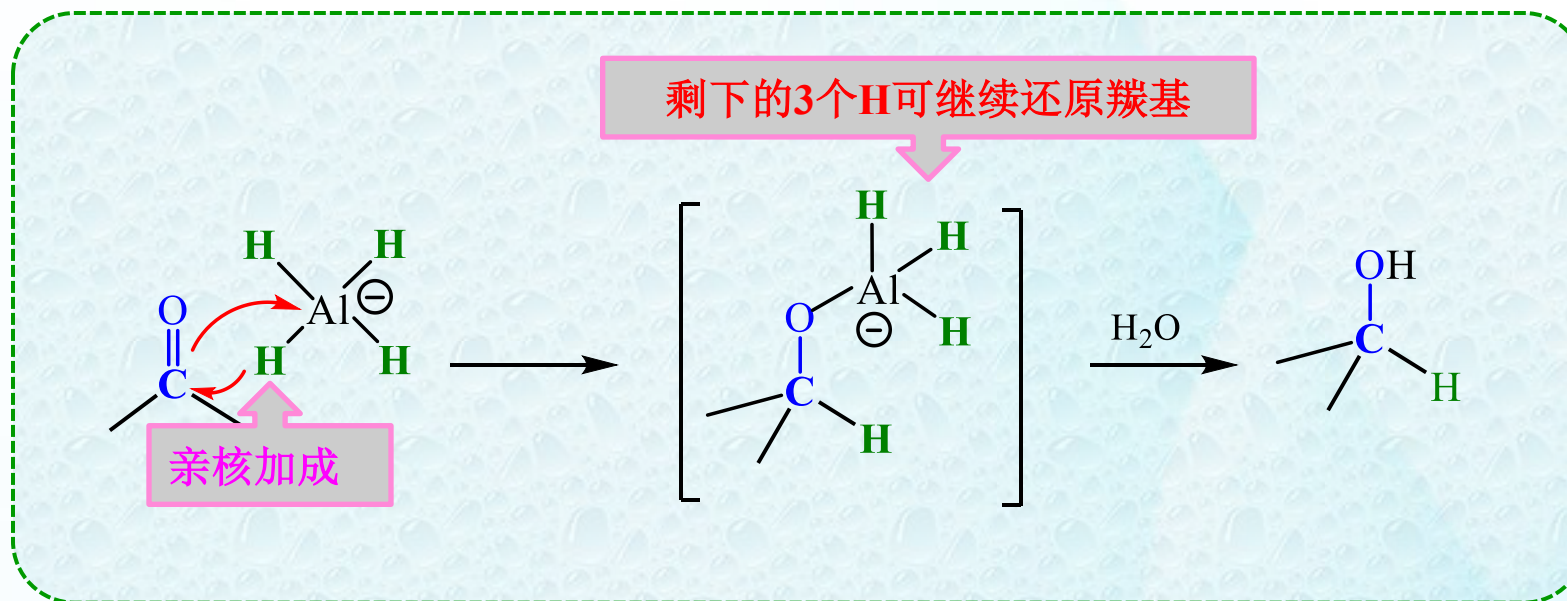
选择性还原剂: LiAlH_4 、 NaBH_4





(5) Reduction Reactions of Aldehydes and ketones

➤ NaBH_4 or LiAlH_4 are also called **hydride reagents**. Both can provide the nucleophile (H^-) to attack the carbonyl group, reducing aldehydes and ketones to primary or secondary alcohols:

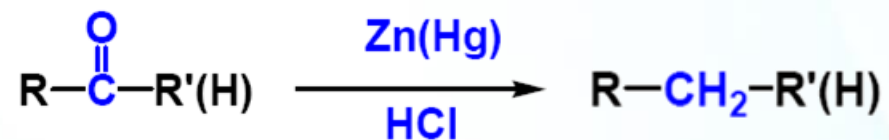
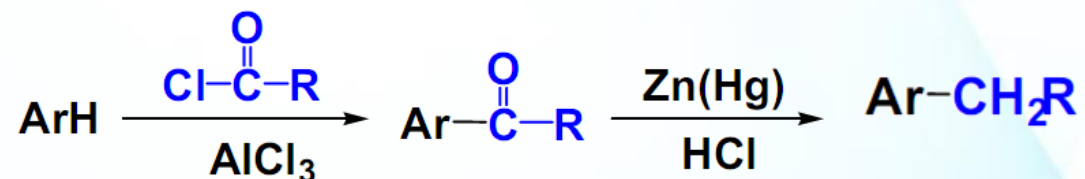


【拓展知识】 Generally, LiAlH_4 is a stronger reducing agent than NaBH_4 . Since the electronegativity of aluminum (1.61) is lower than that of boron (2.04), the electrons in the Al-H bond are more polarized toward hydrogen. This makes the hydrogen in the Al-H bond more negatively charged compared to that in the B-H bond, resulting in stronger reducing ability.



(5) Reduction Reactions of Aldehydes and ketones

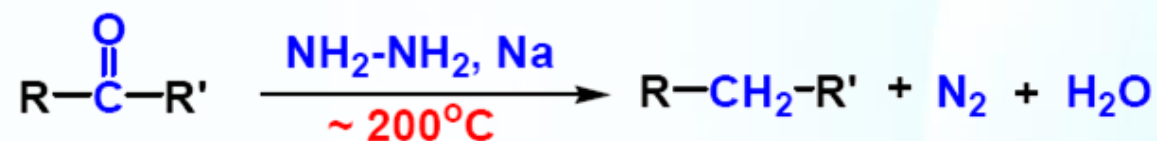
a) Clemmensen Reduction



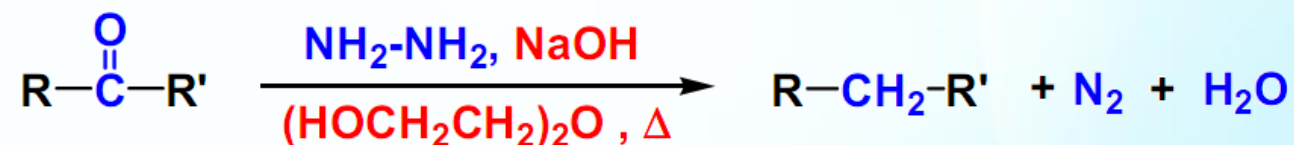
Friedel-Crafts反应

烷基苯

b) Wolff-Kishner, Huang-Minlon reduction



黄鸣龙改良法 (*Huang-Minlon modification*)

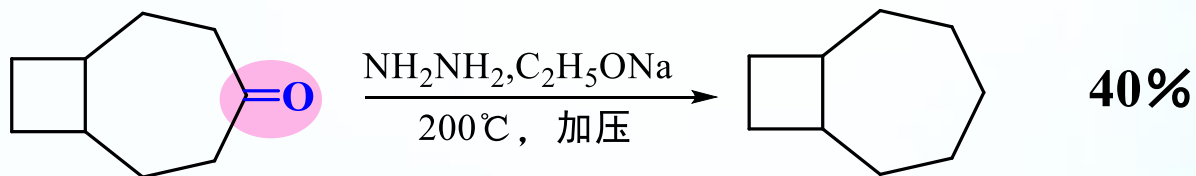




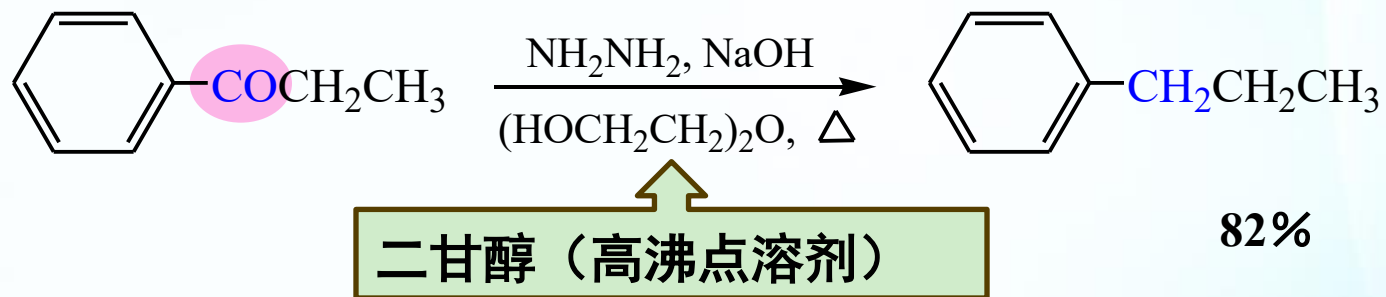
(5) Reduction Reactions of Aldehydes and ketones

The Wolff-Kishner reaction is suitable for aldehydes and ketones that are not sensitive to bases.

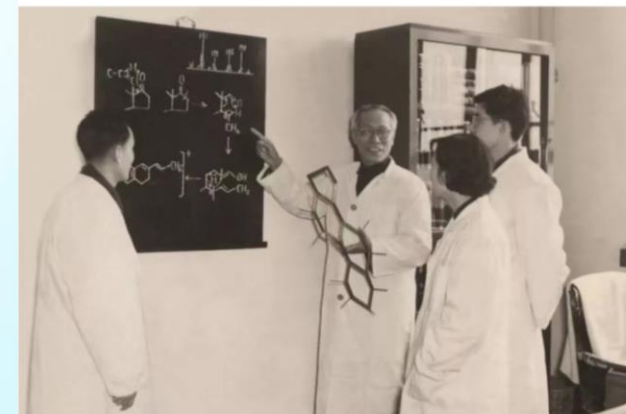
Examples



Huang Minlon's modification employs high-boiling di- or triethylene glycol, and any nitro groups present are reduced concurrently.



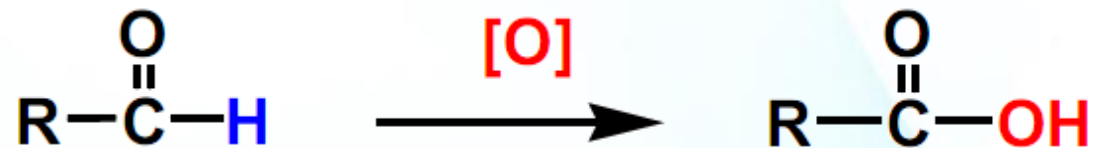
黄鸣龙指导青年科研人员实验



黄鸣龙为科研人员讲解质谱新技术



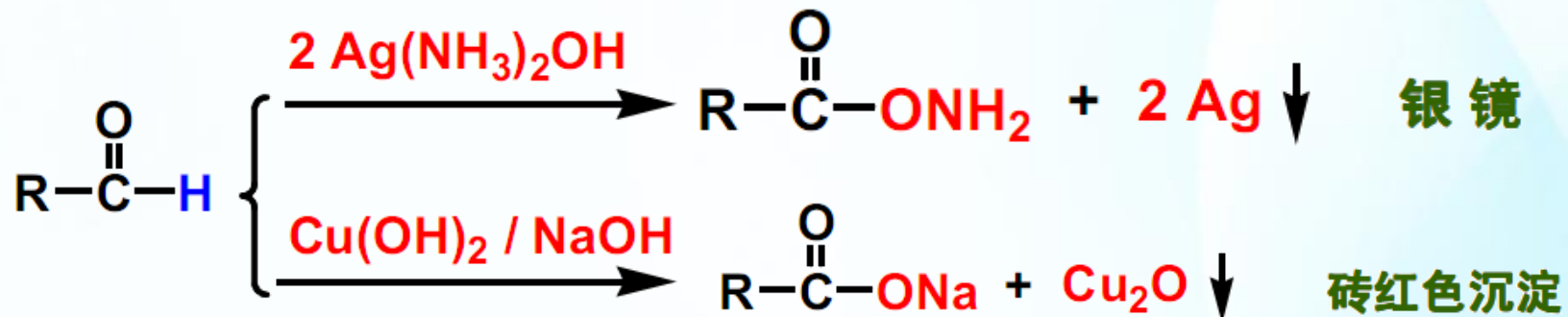
a) Oxidation Reactions of Aldehydes



温和氧化剂:

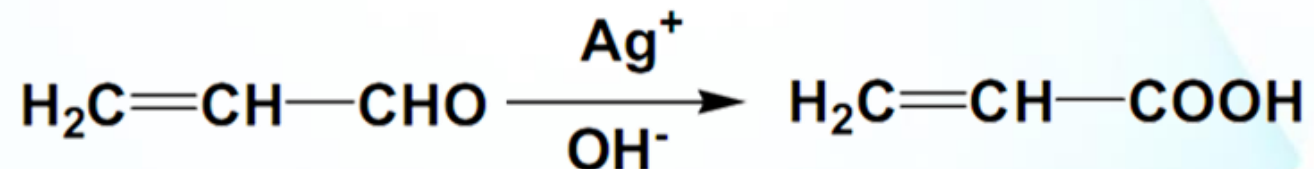
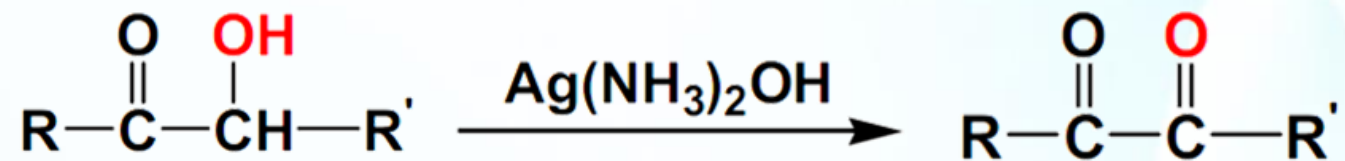
$\text{Ag}(\text{NH}_3)_2\text{OH}$ (Tollens 试剂, 银镜反应)

$\text{Cu}(\text{OH})_2/\text{NaOH}$ (Fehling试剂)





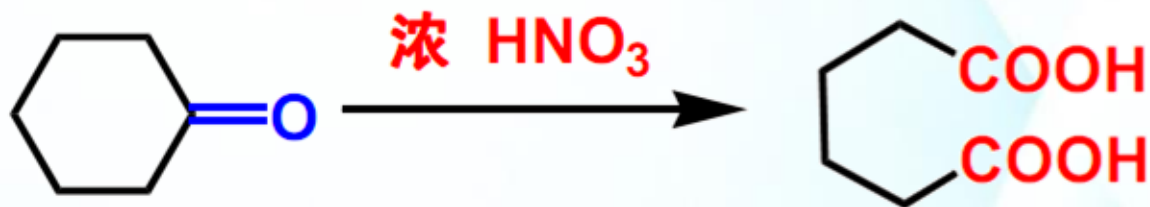
a) Oxidation Reactions of Aldehydes



- 醛类化合物的鉴定分析
- 制备羧酸类化合物
(优点: 不氧化C=C)
- 芳香醛不与斐林试剂反应



b) Oxidation of ketones



对称环酮的氧化（制备二酸）