

# *CHAPTER TWO*

## Amines

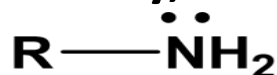
# Amines ( $R_3N$ )

- Amines are organic derivatives of ammonia in which one or more of the hydrogen of ammonia have been replaced by an organic (R) group.

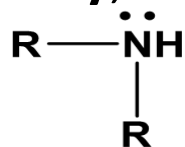
- **Classification of Amines**

- Amines are classified as

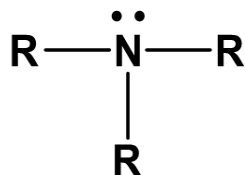
- **primary,**



- **secondary, and**



- **tertiary amines.**

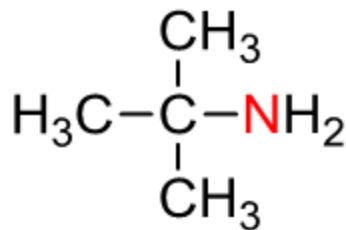
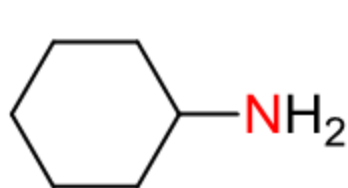


- The classification depends on how many alkyl groups are bonded to the nitrogen.
- Primary amines have one alkyl group bonded to the nitrogen, secondary amines have two, and tertiary amines have three.

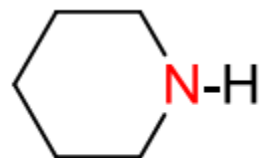
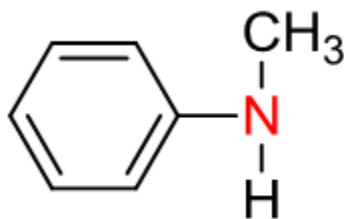
# Amines ( $R_3N$ )

## ○ Examples

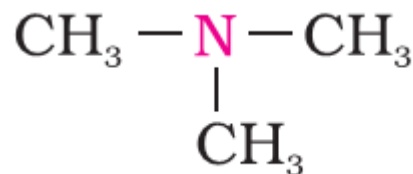
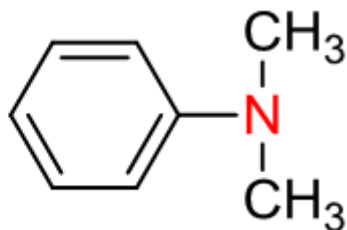
Primary  
Amines



Secondary  
Amines

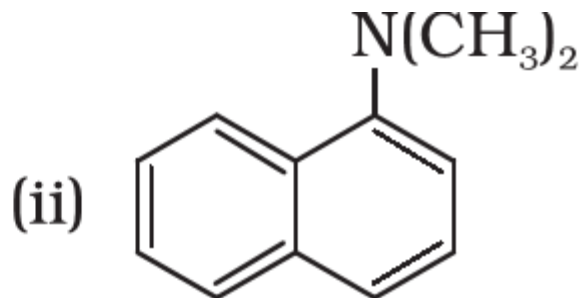
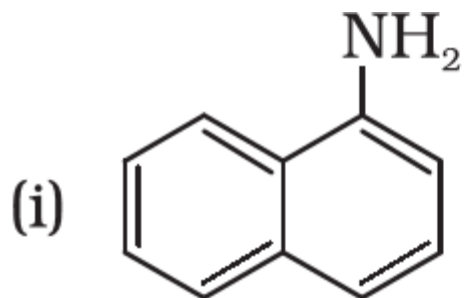


Tertiary  
Amines



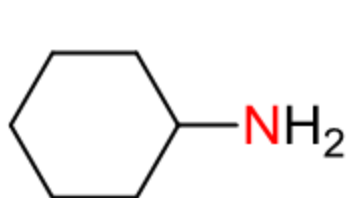
## Exercise

- Classify the following amines as primary, secondary or tertiary:

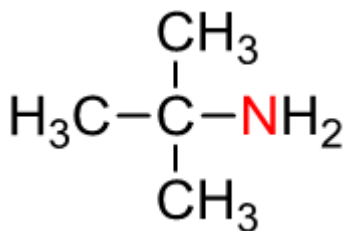


- Amines are further divided into
  - **aliphatic,**
  - **aromatic, and**
  - **heterocyclic amines:**

➤ **Aliphatic amine:** An amine in which nitrogen is bonded only to alkyl groups.



cyclohexanamine

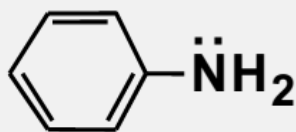


*t*-butylamine



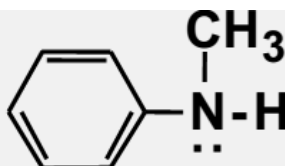
Ethylamine

➤ **Aromatic amine:** An amine in which nitrogen is bonded to one or more aryl groups.



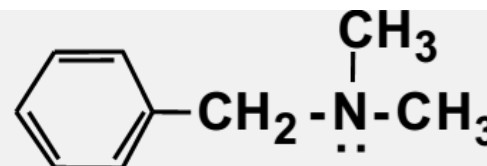
**Aniline**

(a 1° aromatic amine)



**N-Methylaniline**

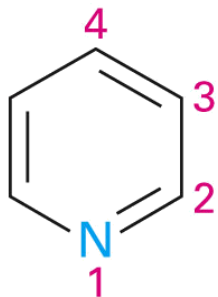
(a 2° aromatic amine)



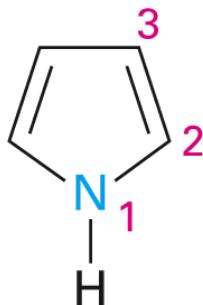
**Benzyldimethylamine**

(a 3° aliphatic amine)

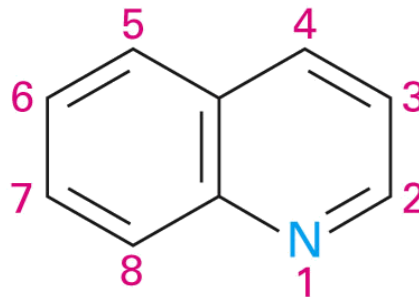
► **Heterocyclic amine:** An amine in which nitrogen is one of the atoms of a ring.



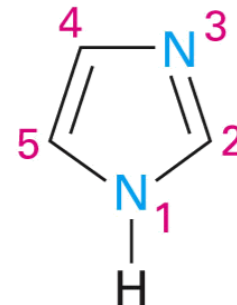
**Pyridine**



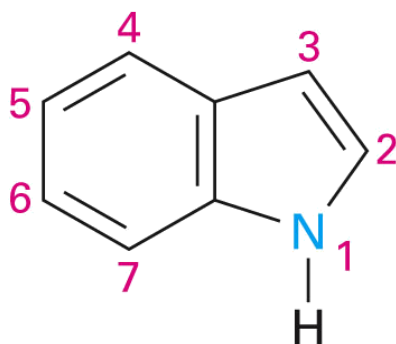
**Pyrrole**



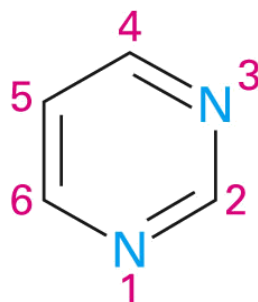
**Quinoline**



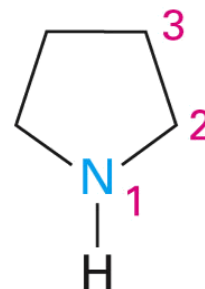
**Imidazole**



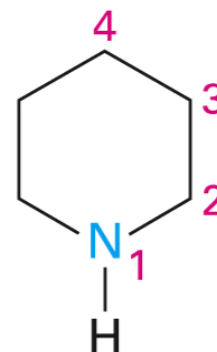
**Indole**



**Pyrimidine**



**Pyrrolidine**

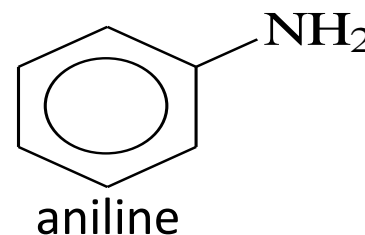
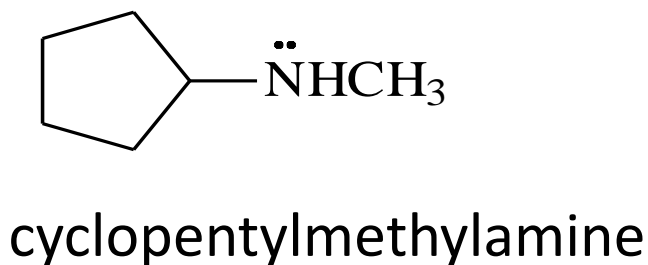
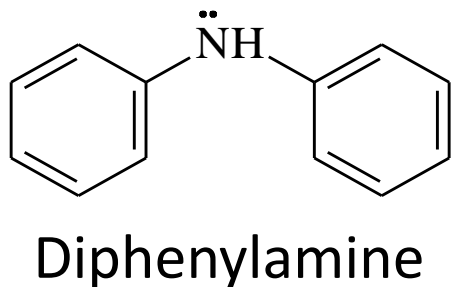
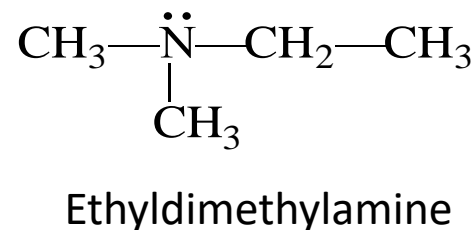
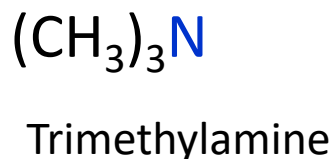
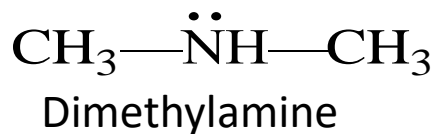


**Piperidine**

# Nomenclature of Amines

## Common names

- Name the alkyl or aryl groups bonded to nitrogen, then add suffix -*amine*.
- The entire name is written as **one word**.
- Amines **bearing two** or **three similar** alkyl or Aryl groups are indicated by the prefix **di-** or **tri-**
- Aromatic amines are called **Anilines**



# IUPAC NAMING FOR AMINES

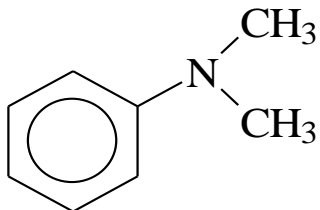
- Name the longest chain attached to the nitrogen.
- Replace the final *-e* of alkane with *-amine*.
- Number the chain so the carbon bonded to the nitrogen has the lowest possible number.
- Number the other substituents on the carbon chain.
- An italic "*N*" is used as a prefix for a substituent on nitrogen.
- Example



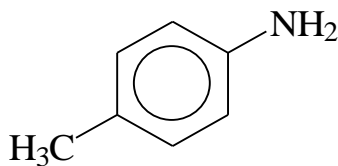
3-bromo-1-pentanamine



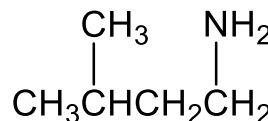
*N,N*-dimethyl-3-hexanamine



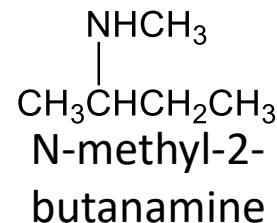
*N,N*-dimethylaniline



4-methylaniline

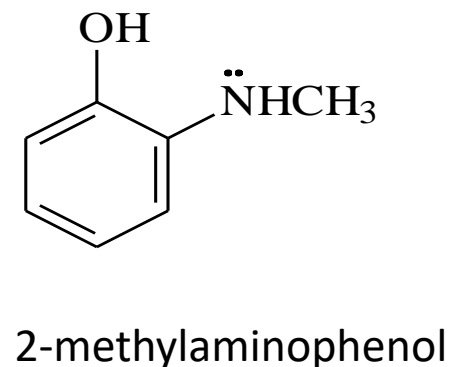
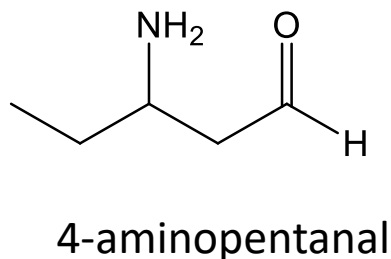
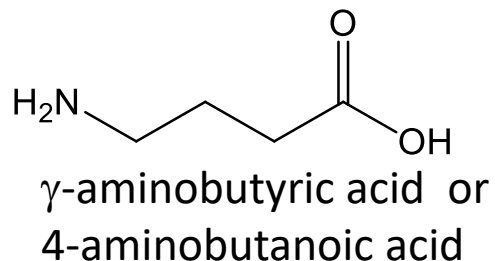


3-Methylbutanamine



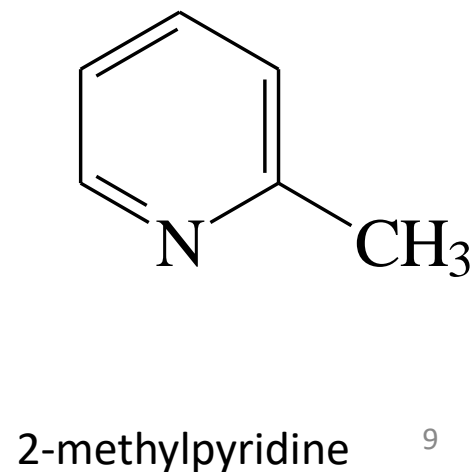
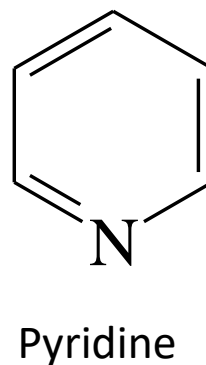
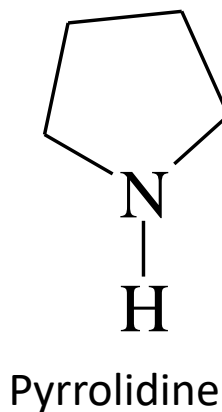
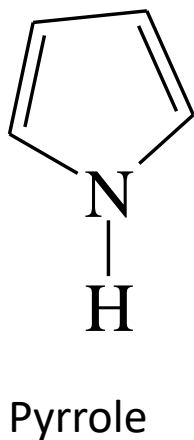
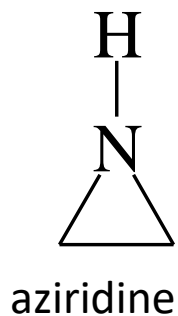


- On a molecule with a higher priority functional group the amine is named as a substituent.
- Example



## Naming Heterocyclic Amines

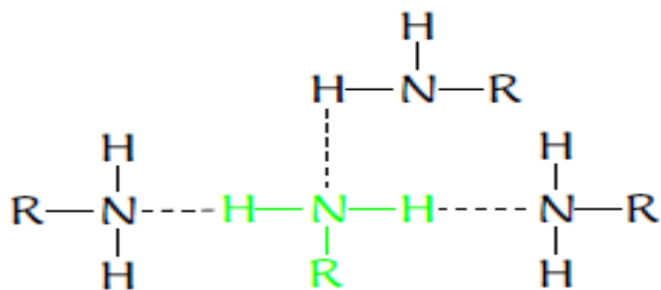
- The nitrogen is assigned the number 1.



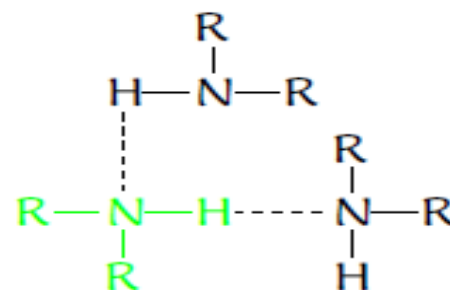
# Properties of Amines:

## Physical and chemical properties

- The N-H bond is not quite as polar as the O-H bond.
- N-H- - -N hydrogen bonds are weaker than O-H- - -O hydrogen bonds because the difference in electronegativity between N and H ( $3.0 - 2.1 = 0.9$ ) is less than that between O and H ( $3.5 - 2.1 = 1.4$ ).
- Primary amines ( $\text{RNH}_2$ ) & secondary amines ( $\text{R}_2\text{NH}$ ) possess N-H bonds & can thus form hydrogen bonds to each other, accounting for their higher boiling points:
- The hydrogen bonds are not as strong as those of alcohols, so amine boiling points are somewhat lower than those of alcohols.



1° amines



2° amines

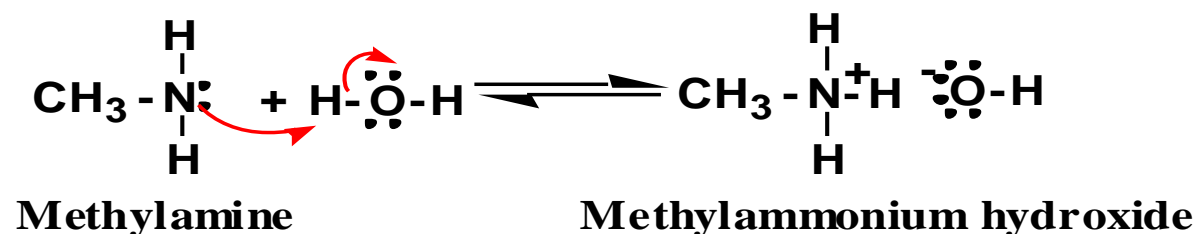
- Tertiary amines ( $R_3N$ ) have no N-H bonds, cannot form hydrogen bonds to each other, & thus, have **lower boiling points** than the other **two classes of amines**.

### **Solubility and Odor**

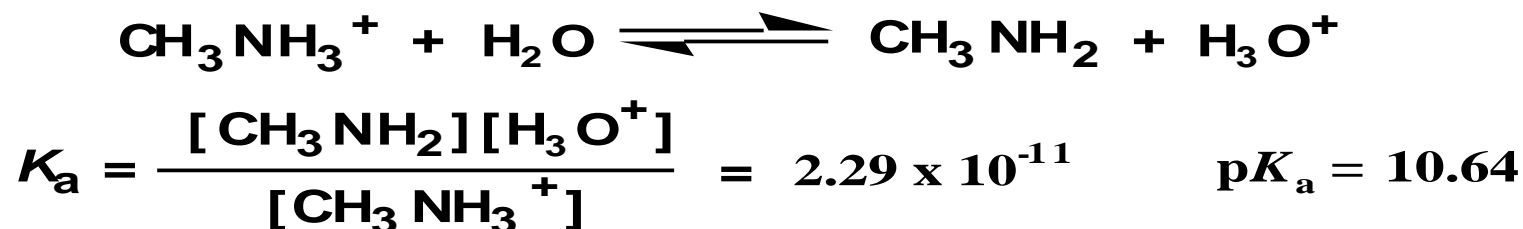
- Amines that have **fewer than six or seven** carbon atoms are soluble in water. Primary and secondary amines are **more soluble** than **tertiary** because they have **more H-bonding with water**
- Low molecular-weight amines tend to have sharp, penetrating odors similar to ammonia. Higher molecular-weight amines often smell like rotting fish, and are often found in decaying animal tissues.

# Basicity of amines

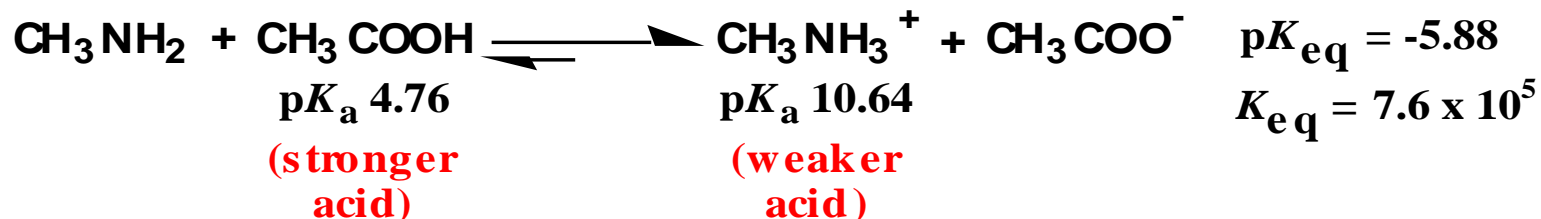
- Amines are more “willing” to share nitrogen’s lone electron pair with a hydrogen ion.
- nitrogen is less electronegative than oxygen, it makes a stronger bond with hydrogen, making it a stronger base in most cases.
- All amines are weak bases, and aqueous solutions of amines are basic.



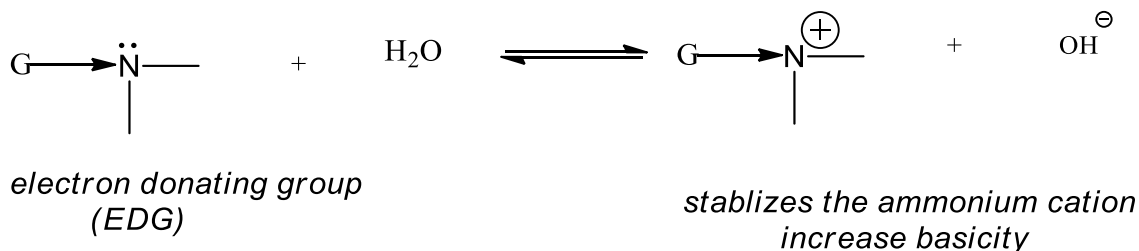
- It is common to discuss their basicity by reference to the acid ionization constant of the conjugate acid.



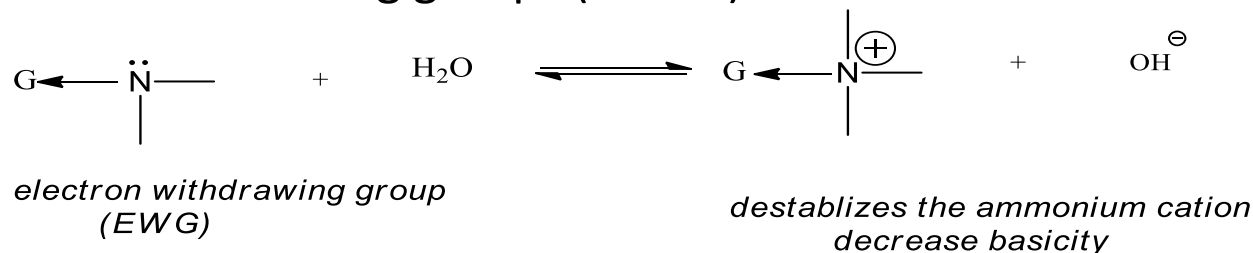
- Using values of  $pK_a$ , we can compare the acidities of amine conjugate acids with other acids.



- The conjugate base of a weak acid is a strong base:
  - ✓ Higher  $pK_a$  = weaker acid = stronger conjugate base
- The conjugate base of a strong acid is a weak base
  - ✓ Lower  $pK_a$  = stronger acid = weaker conjugate base
- Basicity of alkyl amines is increased by factors which stabilize the ammonium cation, thus electron donating groups (EDG's) make stronger bases

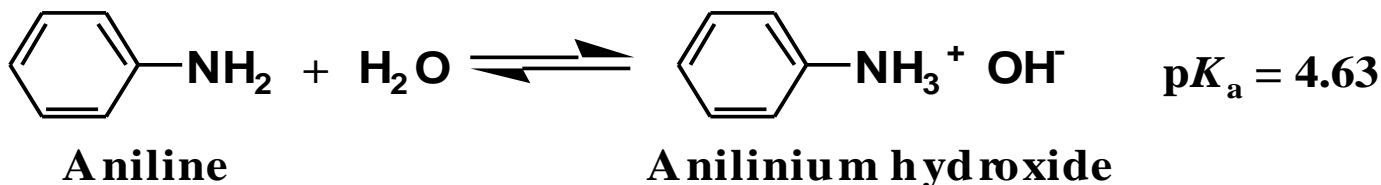
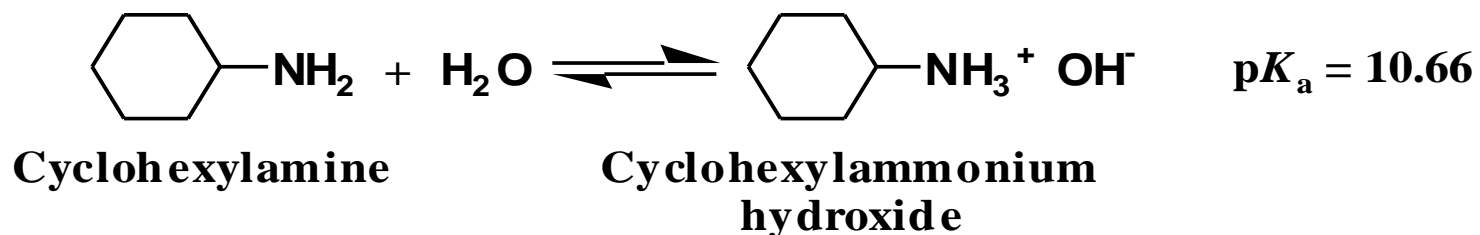


- Electron withdrawing groups (EWG's) make weaker bases



## Basicity-Aromatic Amines

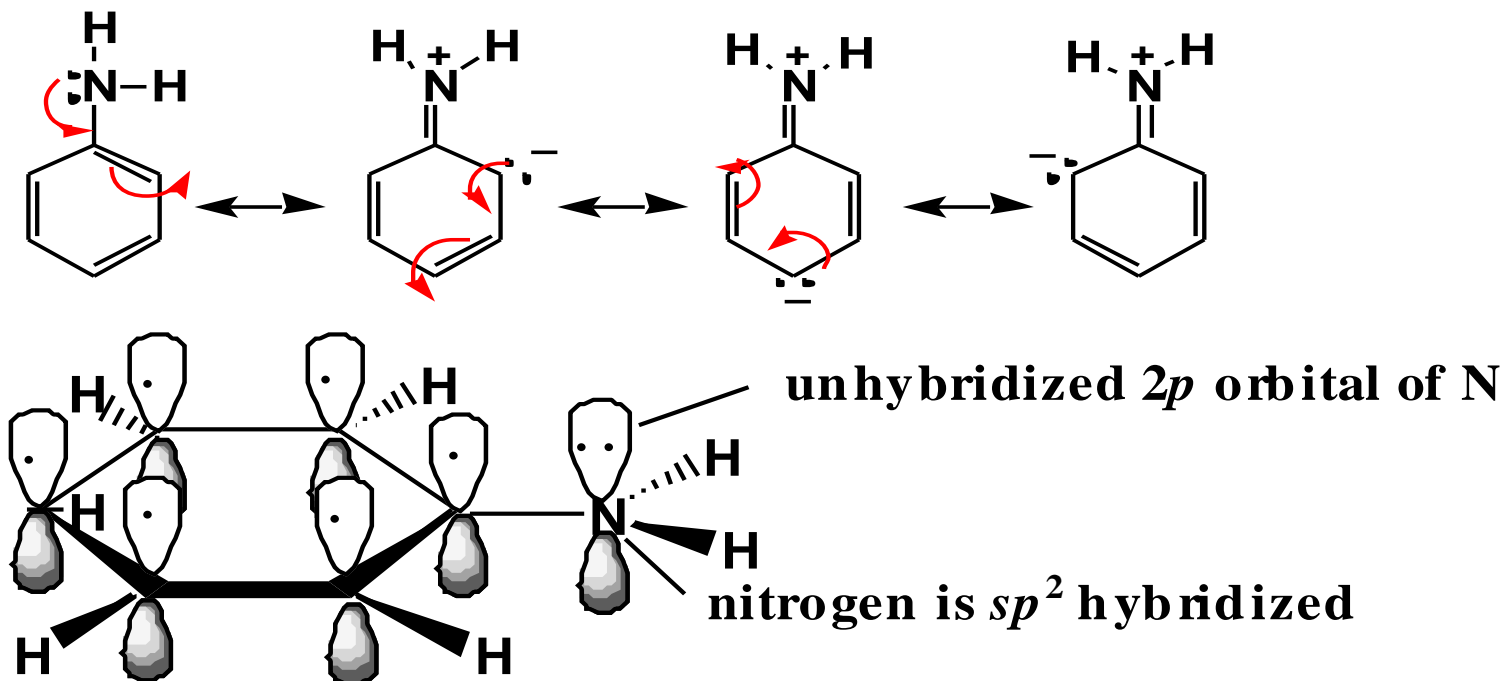
- Aromatic amines are considerably weaker bases than aliphatic amines.



- Aromatic amines are weaker bases than aliphatic amines because of two factors:
  - Resonance stabilization of the free base, which is lost on protonation.

- Aromatic amines are weaker bases than aliphatic amines because of two factors:

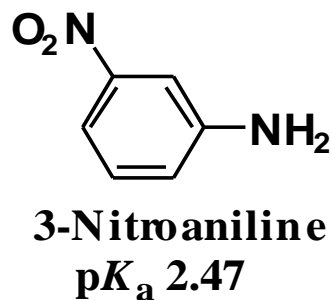
- ◆ Resonance stabilization of the free base, which is lost on protonation.



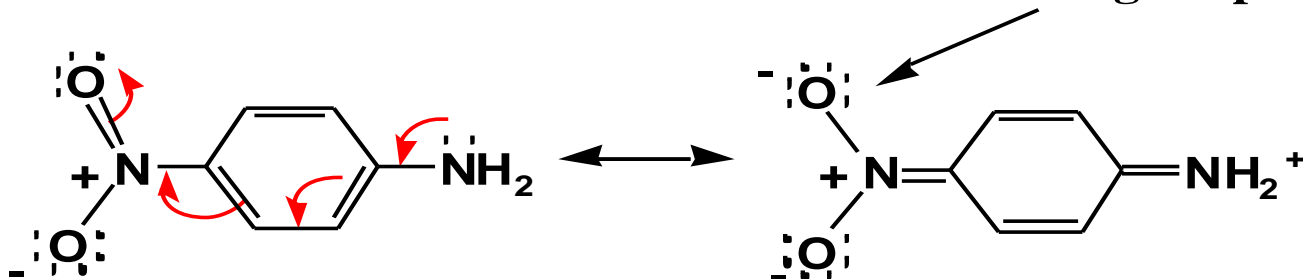
- ◆ The greater electron-withdrawing inductive effect of the  $sp^2$ -hybridized carbon of an aromatic amine compared with that of the  $sp^3$ -hybridized carbon of an aliphatic amine.

## Basicity-Aromatic Amines

- Electron-releasing groups, such as alkyl groups, increase the basicity of aromatic amines.
- Electron-withdrawing groups, such as halogens, the nitro group, and a carbonyl group decrease the basicity of aromatic amines by a combination of resonance and inductive effects.
- Example:-3-nitroaniline is a stronger base than 4-Nitroaniline.

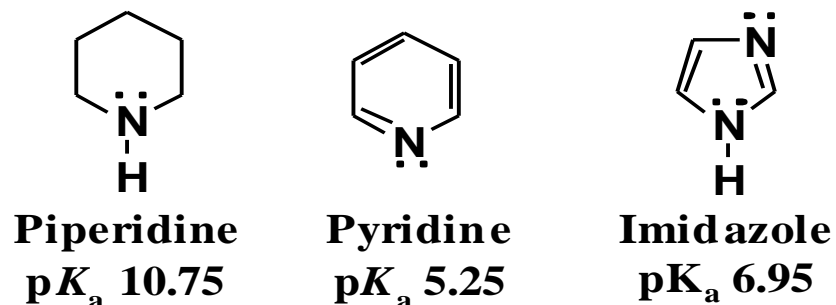


**delocalization of the nitrogen lone pair onto the oxygen atoms of the nitro group**

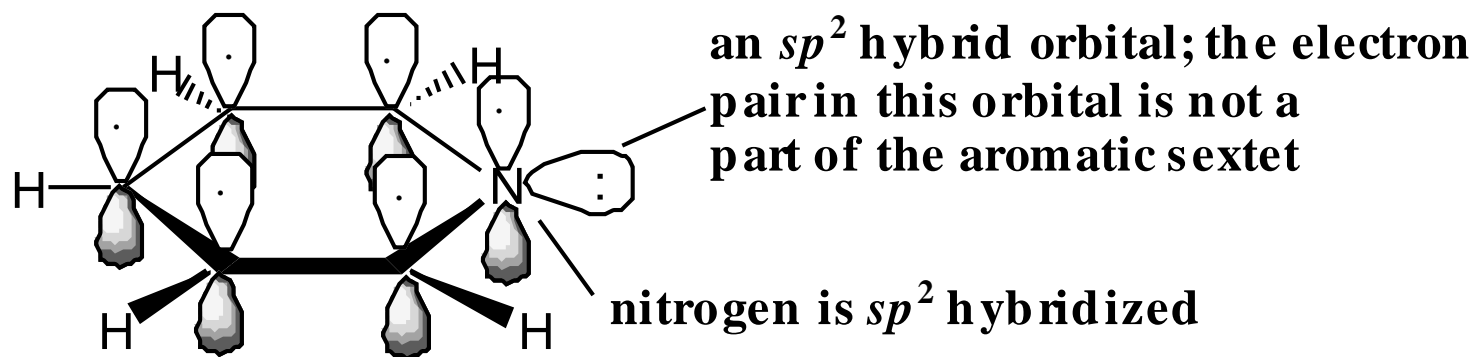




- Heterocyclic aromatic amines are weaker bases than heterocyclic aliphatic amines.



- In pyridine, the unshared pair of electrons on N is not part of the aromatic sextet.



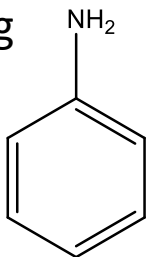
- Pyridine is a weaker base than heterocyclic aliphatic amines because the free electron pair on N lies in an  $sp^2$  hybrid orbital (33%  $s$  character) and is held more tightly to the nucleus than the free electron pair on N in an  $sp^3$  hybrid orbital (25%  $s$  character).

- because of the +I effect from the R group, alkylamines are more strong basic than ammonia

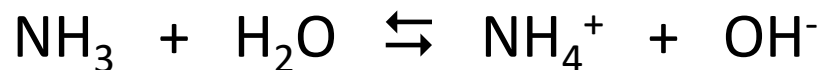
➤ Eg  $\text{CH}_3\text{NH}_2$  is strong base than  $\text{NH}_3$

- because of a slight -R (resonance) effect from the aromatic ring, anilines are less basic than ammonia

➤ Eg  $\text{NH}_2$  is weak base than ammonia

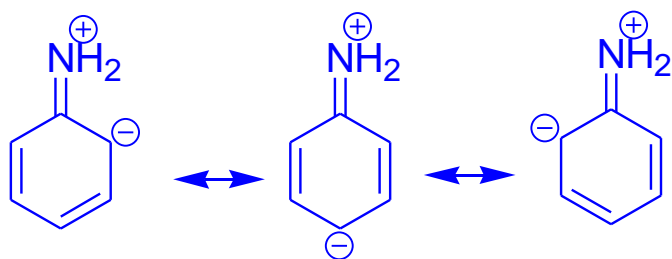
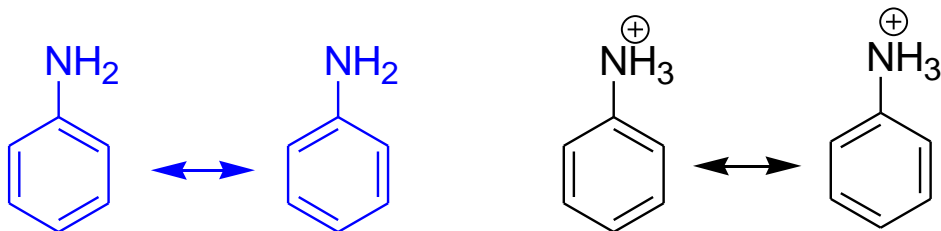
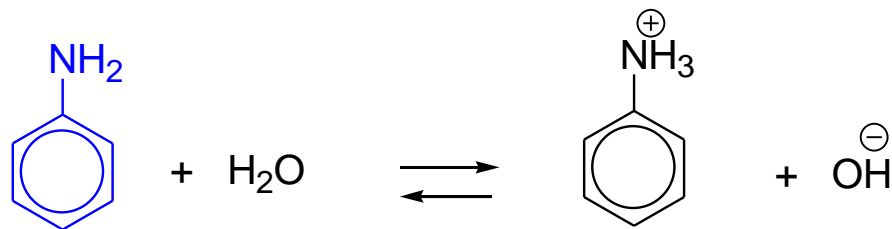


○**Question** :- Why are aliphatic amines more basic than ammonia?



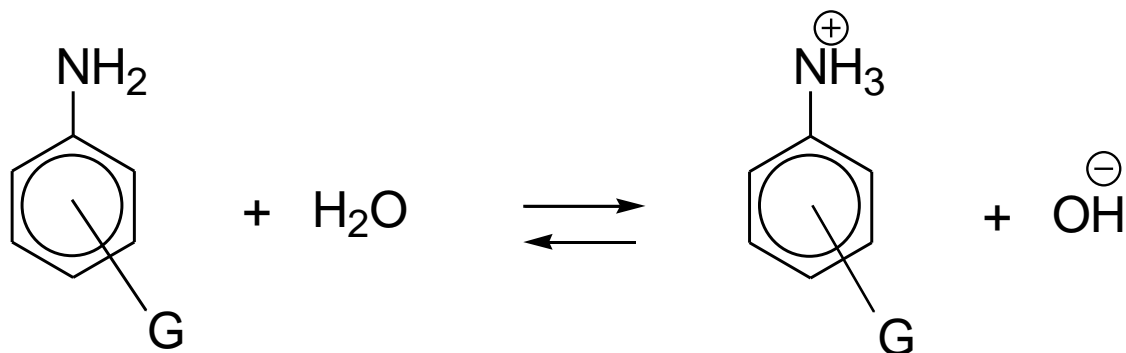
○**Answer** :- The alkyl group, -R, is an electron donating group. The donation of electrons helps to stabilize the ammonium ion by decreasing the positive charge, lowering the  $\Delta H$ , shifting the ionization farther to the right and increasing the basicity.

Questions :- Why are aromatic amines less basic than aliphatic amines?



**Answer** :- resonance stabilization of the free base, increases the  $\Delta H$ , shifts the ionization to the left, decreasing base strength.

## Effect of substituent groups on base strength:



○ **Electron donating groups** will stabilize the anilinium ion, decreasing the  $\Delta H$ , shifting the ionization farther to the right and making the compound a **stronger base**.

○ **Electron withdrawing groups** destabilize the anilinium ion, increasing the  $\Delta H$ , shifting the ionization towards the reactants, making the compound a **weaker base**.

## Common substituent groups:

-NH<sub>2</sub>, -NHR, -NR<sub>2</sub>

-OH

-OR

-NHCOCH<sub>3</sub>

-C<sub>6</sub>H<sub>5</sub>

-R

-H

-X

-CHO, -COR

-SO<sub>3</sub>H

-COOH, -COOR

-CN

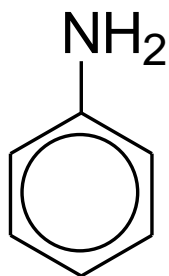
-NR<sub>3</sub><sup>+</sup>

-NO<sub>2</sub>

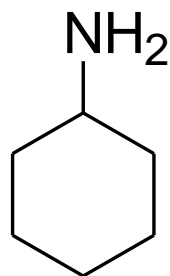
electron donating  
groups

electron withdrawing  
groups

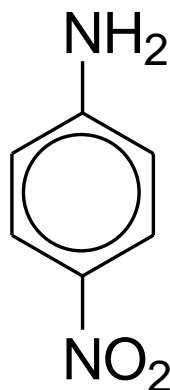
**Exercise :-** Number the following in decreasing order of base strength (let #1 = most basic, etc.



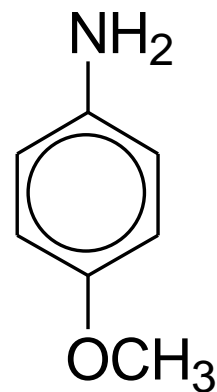
4



1



5



3



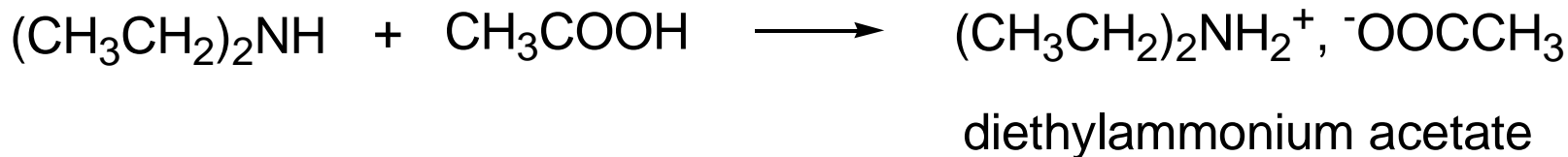
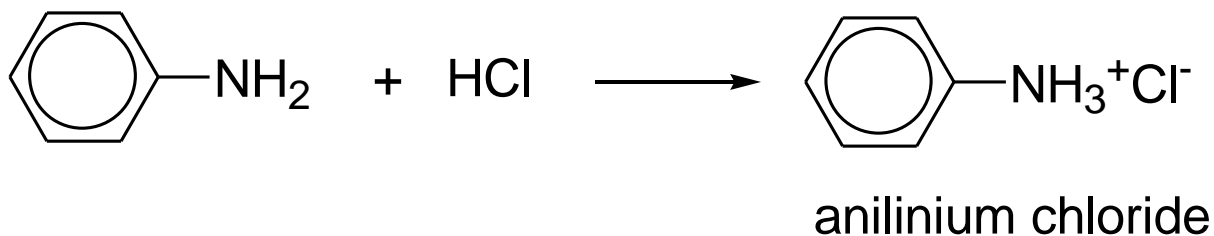
2

# REACTION OF AMINES

## 1. Amines reacts with acids

- When an amine is protonated, an *amine salt* is produced.
- The amine salt consists of two parts: the cationic ammonium ion, and the anionic counter ion.

### ○ Examples



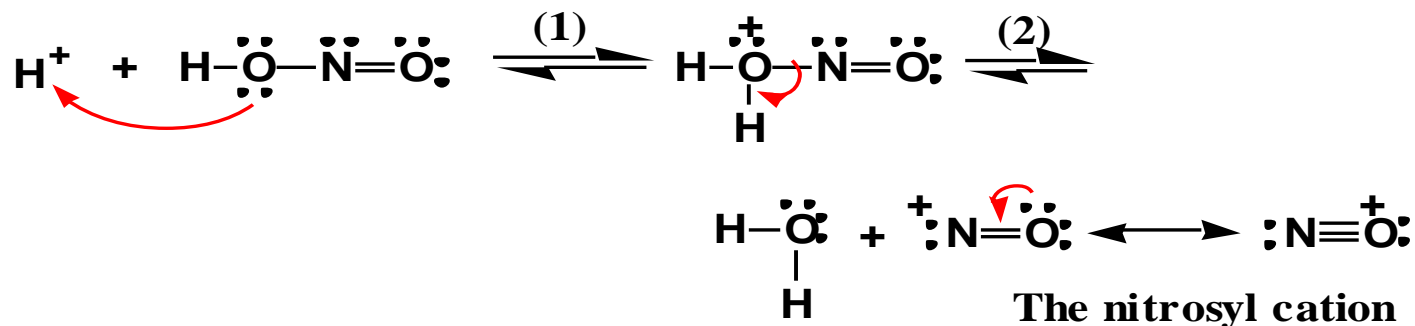


## 2. Amine reacts with HNO<sub>2</sub>

- Nitrous acid, a weak acid, is most commonly prepared by treating NaNO<sub>2</sub> with aqueous H<sub>2</sub>SO<sub>4</sub> or HCl.

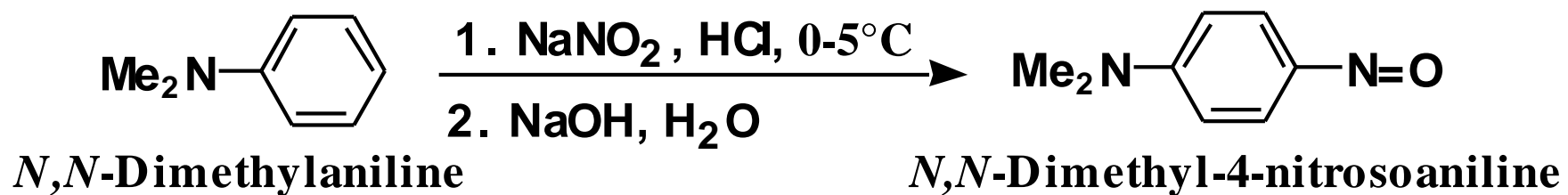


- In its reactions with amines, nitrous acid:
  - Participates in proton-transfer reactions.
  - A source of the nitrosyl cation, NO<sup>+</sup>, a weak electrophile.
- NO<sup>+</sup> is formed in the following way.
  - Step 1: Protonation of HONO.
  - Step 2: Loss of H<sub>2</sub>O.



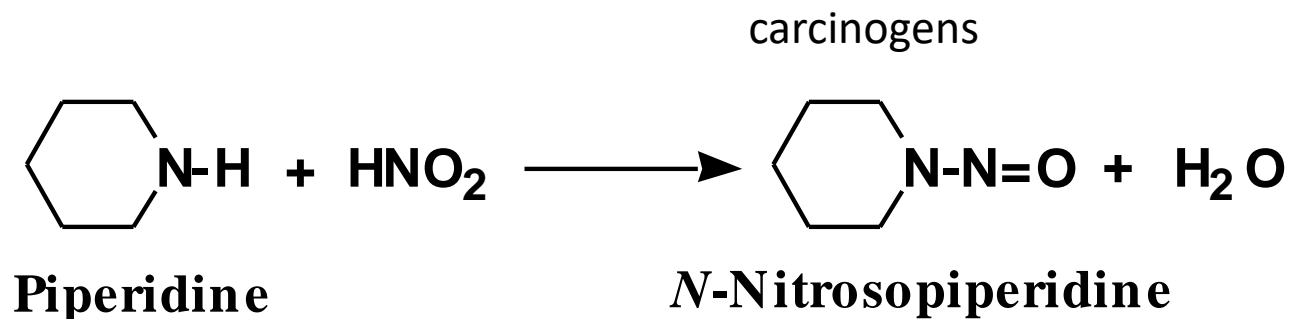
## Tertiary Amines with $\text{HNO}_2$

- 3° Aliphatic amines, whether water-soluble or water-insoluble, are protonated to form water-soluble salts.
- 3° Aromatic amines:  $\text{NO}^+$  is a weak electrophile and participates in Electrophilic Aromatic Substitution.
- **Example**

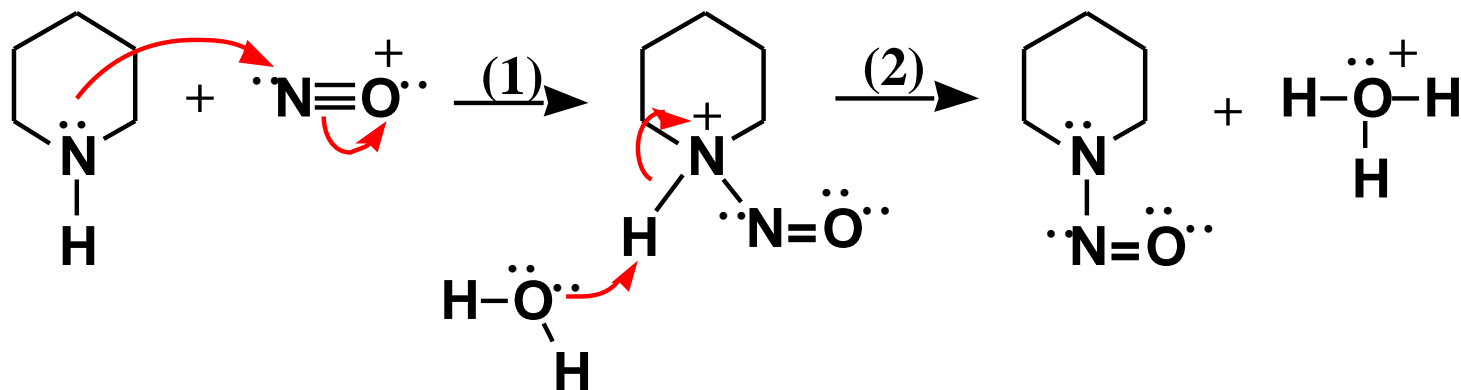


## Secondary Amines with HNO<sub>2</sub>

- 2° Aliphatic and aromatic amines react with NO<sup>+</sup> to give *N*-nitrosamines.
- Example



Mechanism:



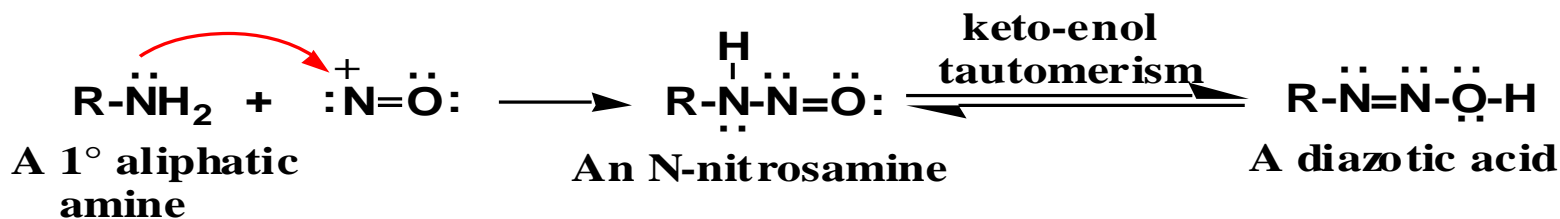
## RNH<sub>2</sub> with HNO<sub>2</sub>

- 1° aliphatic amines give a mixture of unrearranged and rearranged substitution and elimination products, all of which are produced by way of a diazonium ion and its loss of N<sub>2</sub> to give a carbocation.
- Diazonium ion:** An RN<sub>2</sub><sup>+</sup> or ArN<sub>2</sub><sup>+</sup> ion

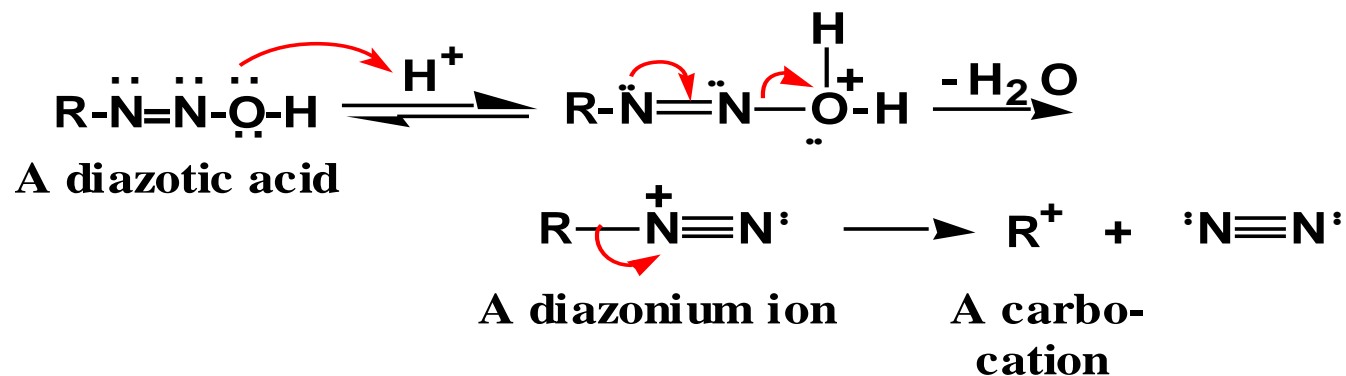
### 1° RNH<sub>2</sub> with HNO<sub>2</sub>

- Formation of a diazonium ion.

Step 1: Reaction of a 1° amine with the nitrosyl cation.

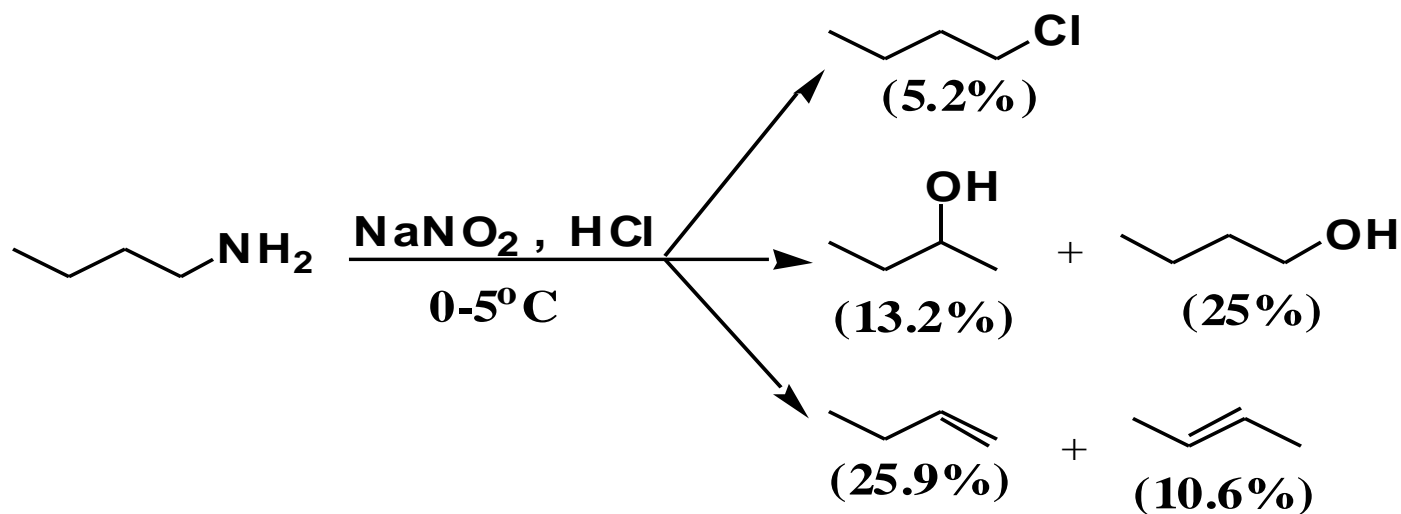


Step 2: Protonation followed by loss of water.



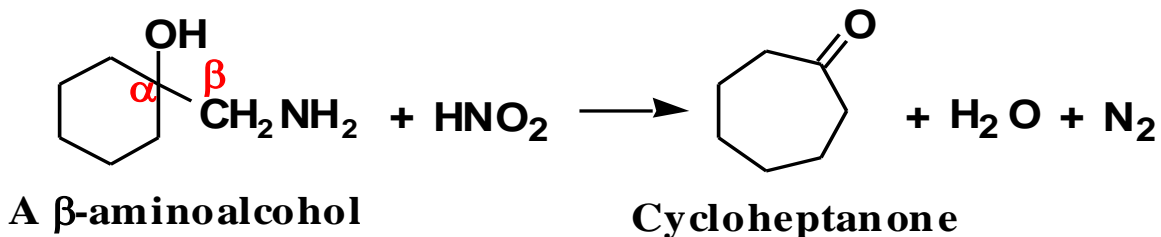
# 1° RNH<sub>2</sub> with HNO<sub>2</sub> (Aliphatic)

- Aliphatic diazonium ions are unstable and lose N<sub>2</sub> to give a carbocation which may:
  1. Lose a proton to give an **alkene**.
  2. React with a nucleophile to give a **substitution product**.
  3. **Rearrange** and then react by Steps 1 and/or 2.

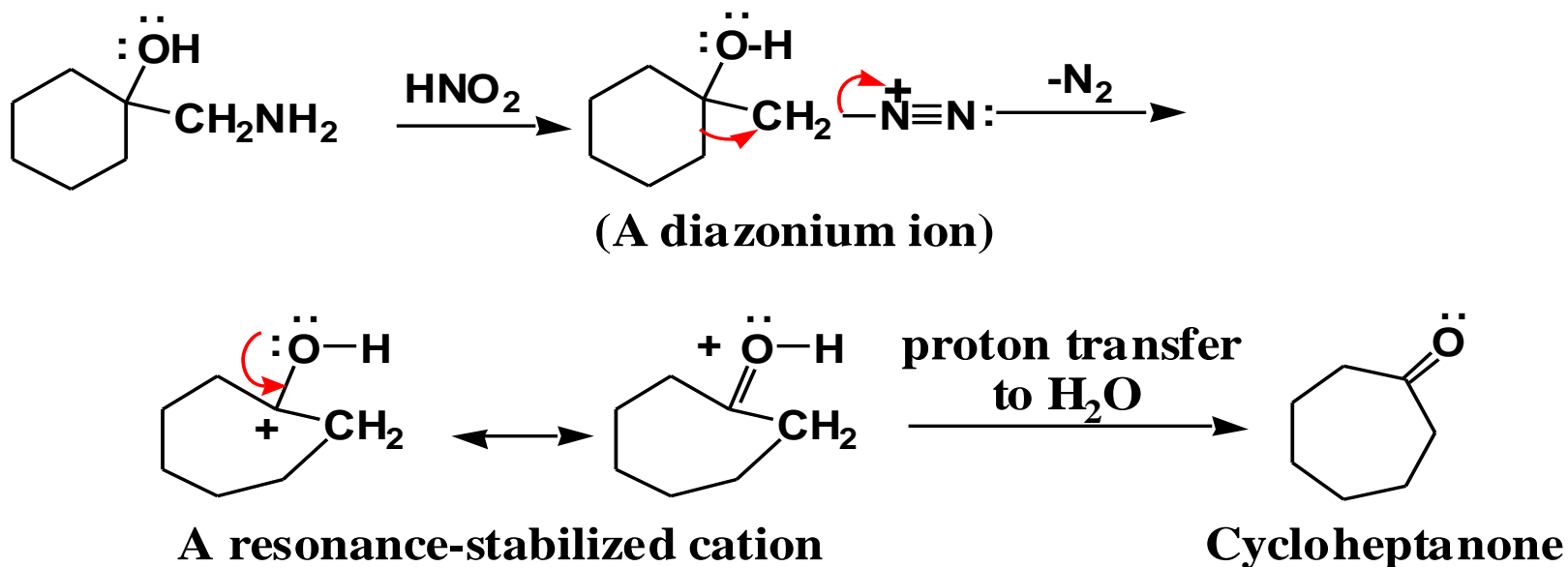


# 1° RNH<sub>2</sub> with HNO<sub>2</sub>

◆ **Tiffeneau-Demjanov reaction:** Treatment of a β-aminoalcohol with HNO<sub>2</sub> gives a ketone and N<sub>2</sub>.



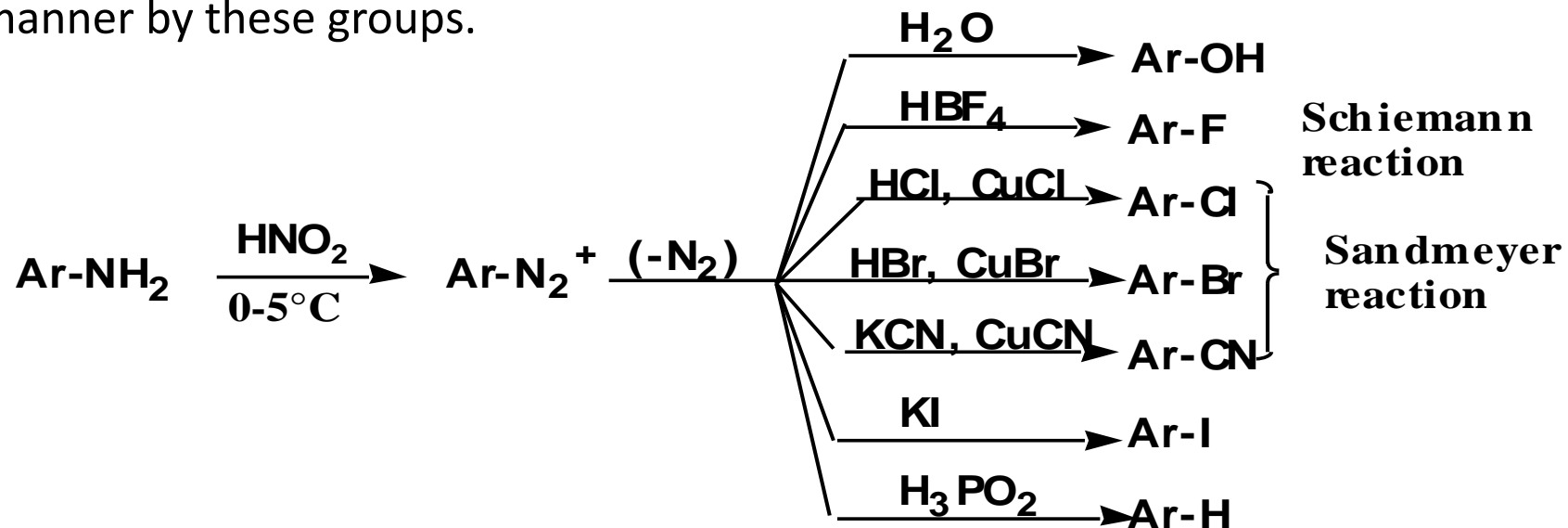
## ◆ Mechanism



◆ Which is similar to pinacol rearrangement

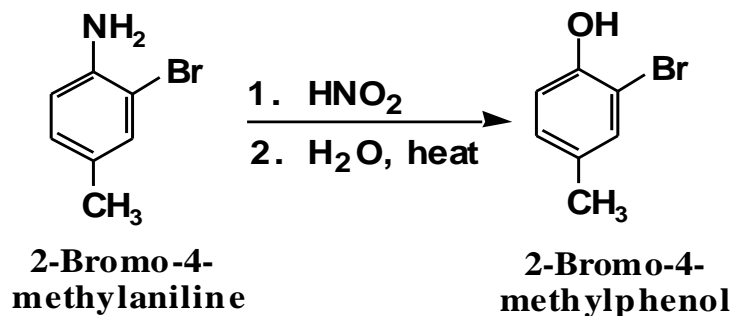
# 1° Primary Amines with HNO<sub>2</sub> (Aromatic)

- The -N<sub>2</sub><sup>+</sup> group of an arene diazonium salt can be replaced in a regioselective manner by these groups.

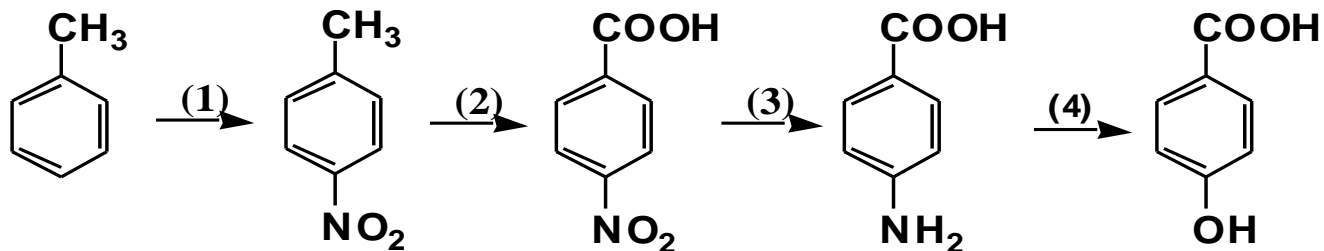


## 1° ArNH<sub>2</sub> with HNO<sub>2</sub>

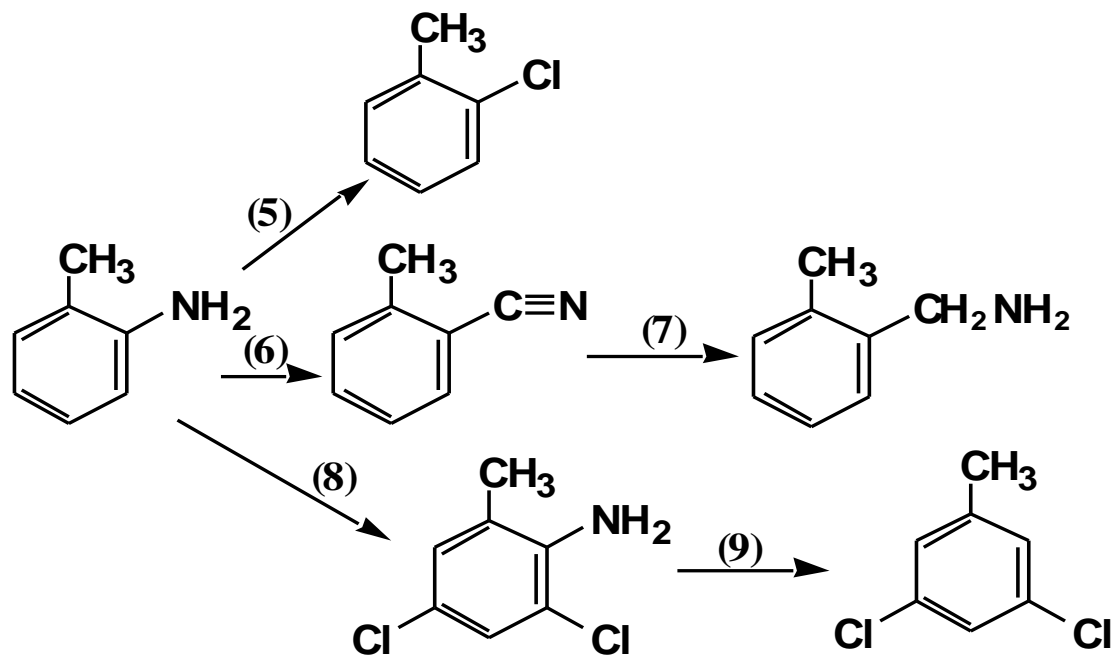
- A 1° aromatic amine converted to a phenol.



**Exercise :** What reagents will fulfill the following conversion?



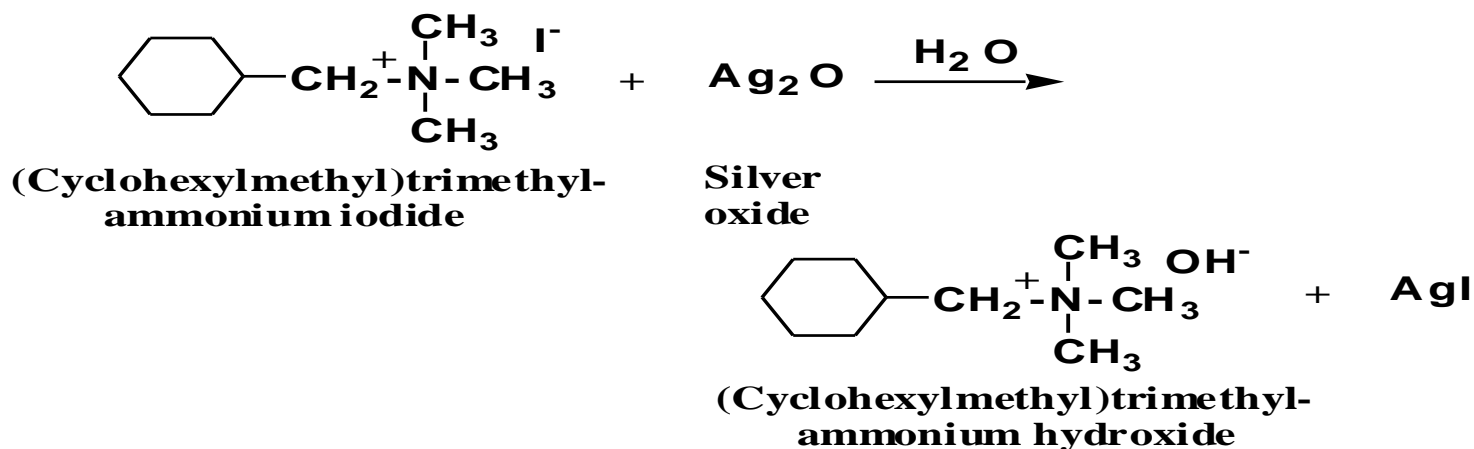
**Exercise :** Show how to bring about each conversion.



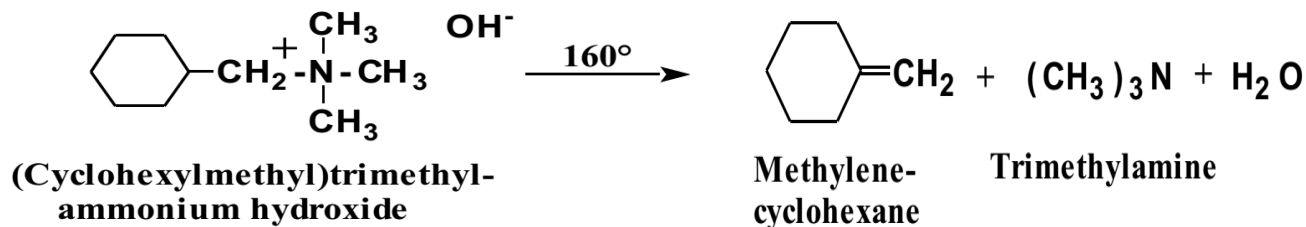


◆ **Hofmann elimination:** Thermal decomposition of a quaternary ammonium hydroxide to give an alkene.

➤ Step 1: Formation of a 4° ammonium hydroxide.

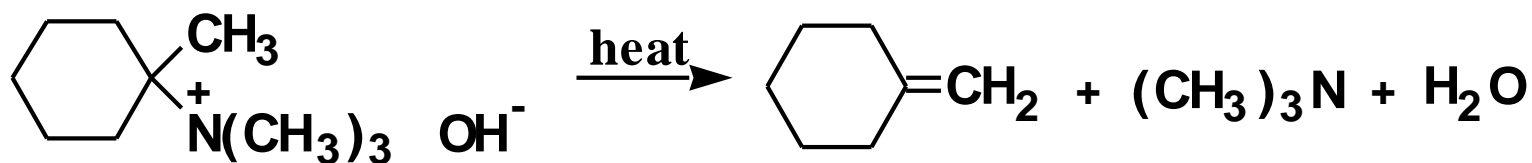


➤ Step 2: Thermal decomposition of the 4° ammonium hydroxide.



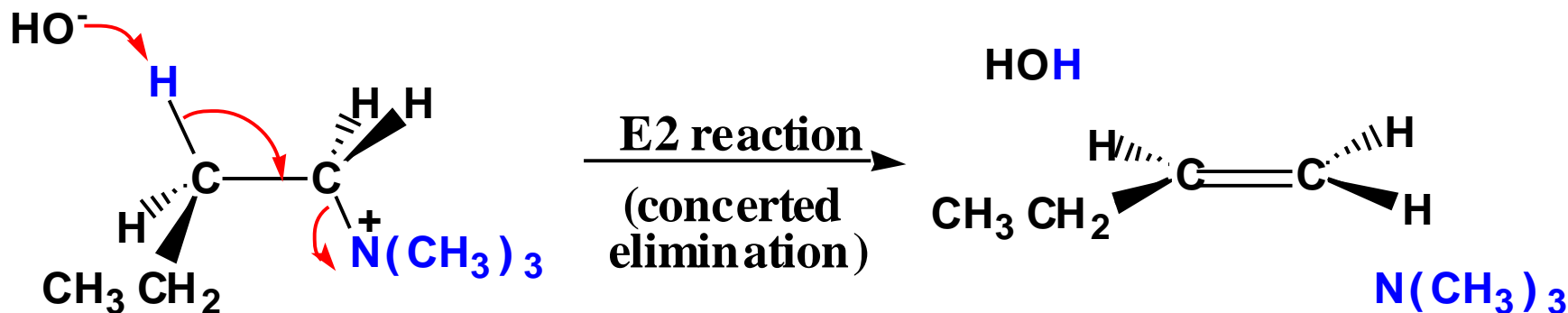
# Hofmann Elimination

- ◆ Hofmann elimination is regioselective - the major product is the least substituted alkene.



- ◆ **Hofmann's rule:** Any  $\beta$ -elimination that occurs preferentially to give the least substituted alkene as the major product is said to follow Hofmann's rule.

# Mechanism

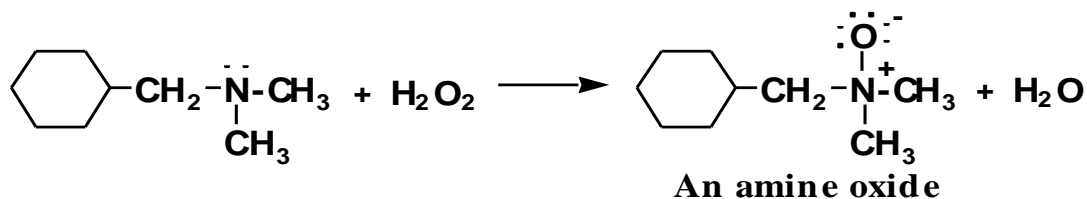


- The regioselectivity of Hofmann elimination is determined largely by steric factors, namely the bulk of the  $-\text{NR}_3^+$  group.
- Hydroxide ion preferentially approaches and removes the least hindered hydrogen and, thus, gives the least substituted alkene.
- Bulky bases such as  $(\text{CH}_3)_3\text{CO}^-\text{K}^+$  give largely Hofmann elimination with **haloalkanes**.

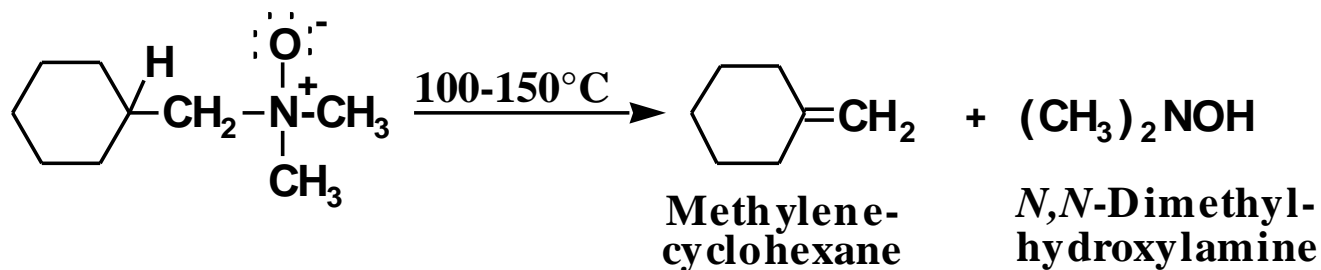
# Cope Elimination

◆ **Cope elimination:** Thermal decomposition of an amine oxide.

✓ Step 1: Oxidation of a 3° amine gives an amine oxide.

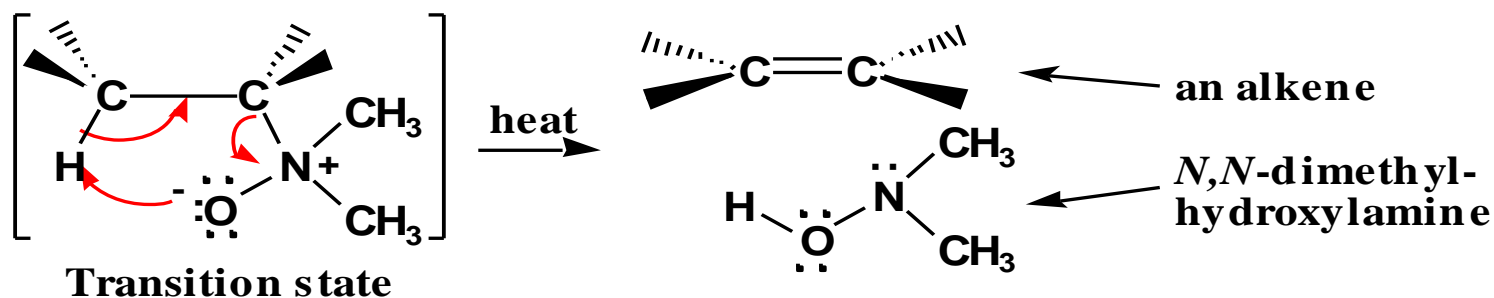


✓ Step 2: If the amine oxide has at least one β-hydrogen, it undergoes thermal decomposition to give an alkene.

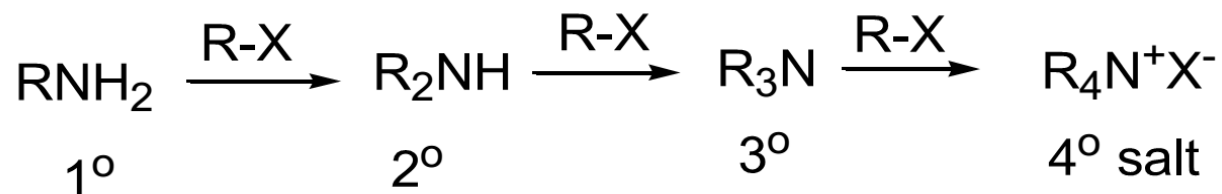


- Cope elimination shows syn stereoselectivity but little or no regioselectivity.
- Mechanism: a cyclic flow of electrons in a six-membered transition state.

## Mechanism

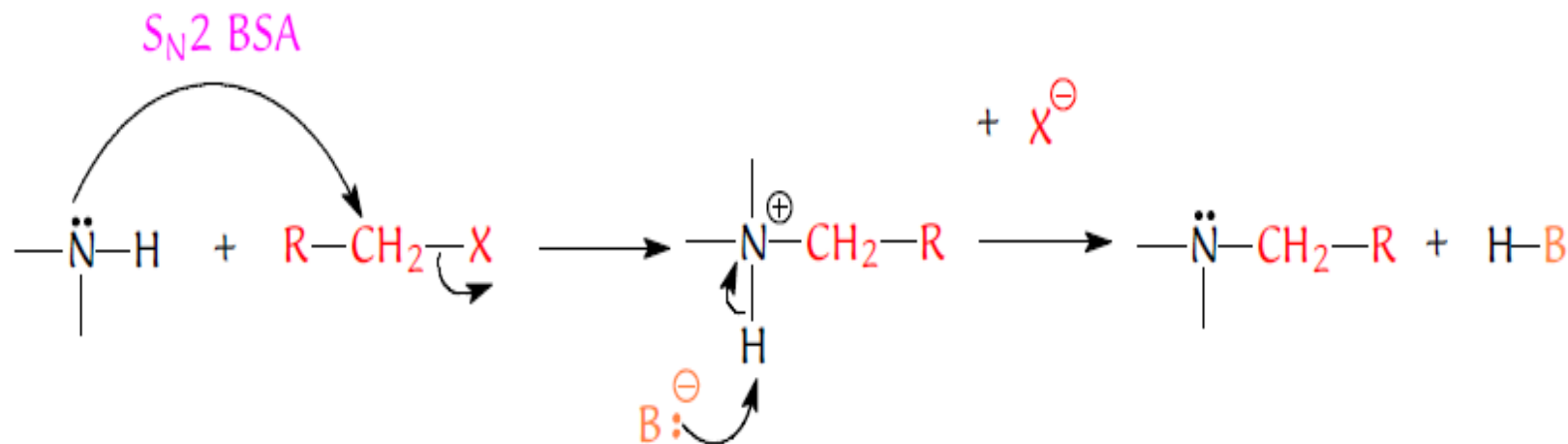


## 2. Alkylation (ammonolysis of alkyl halides) (ES at nitrogen)

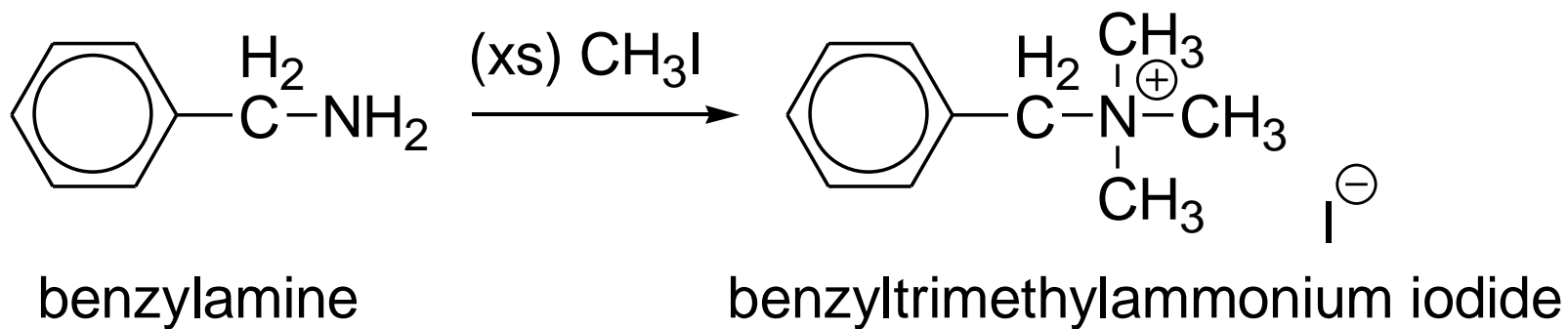
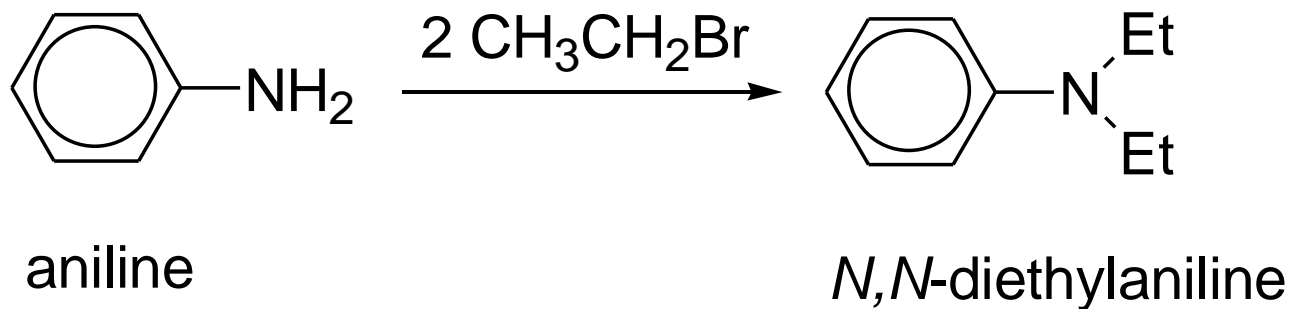
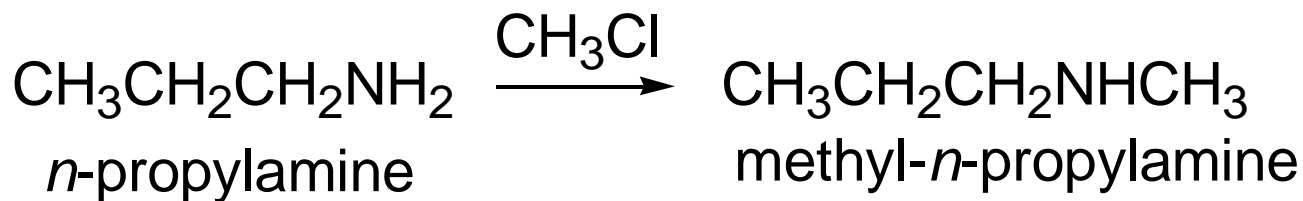


$S_N2$ : R-X must be  $1^\circ$  or  $CH_3$

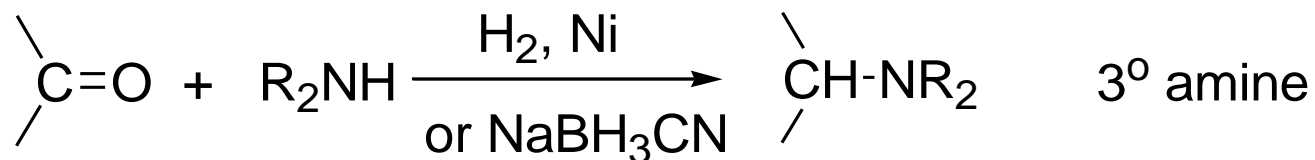
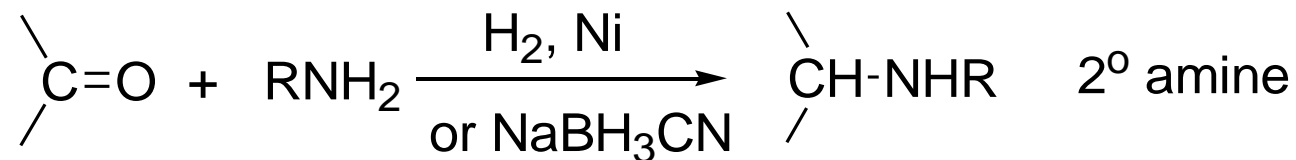
# Mechanism



## Examples



### 3. Reductive amination (EAS at nitrogen)

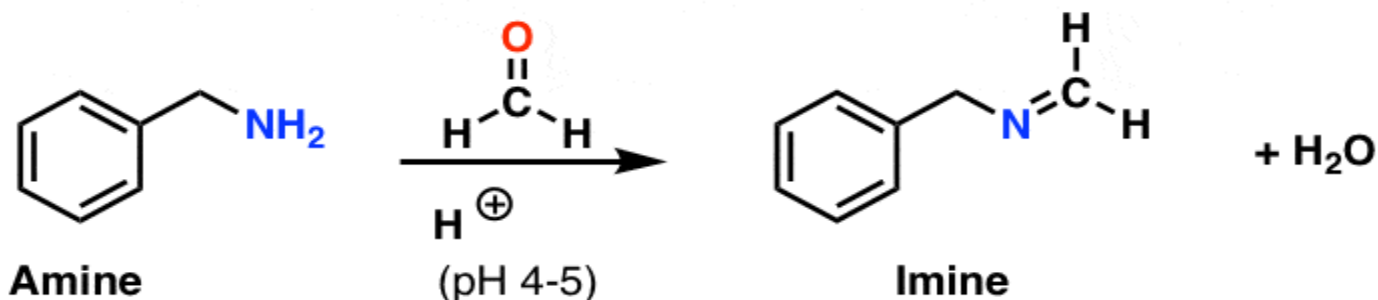




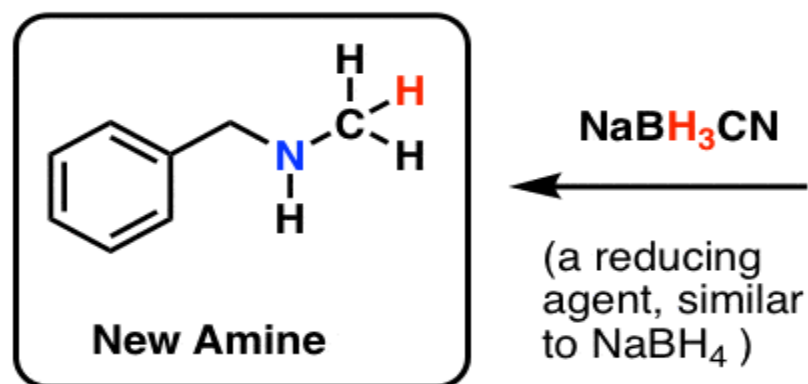
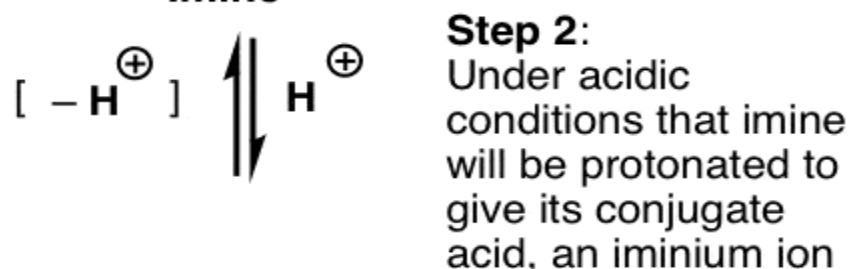
## A Better Way To Do It: Reductive Amination

A more versatile way to form N-C bonds is to use a process called **reductive amination**. This involves transforming the amine into an imine, and then reducing the imine.

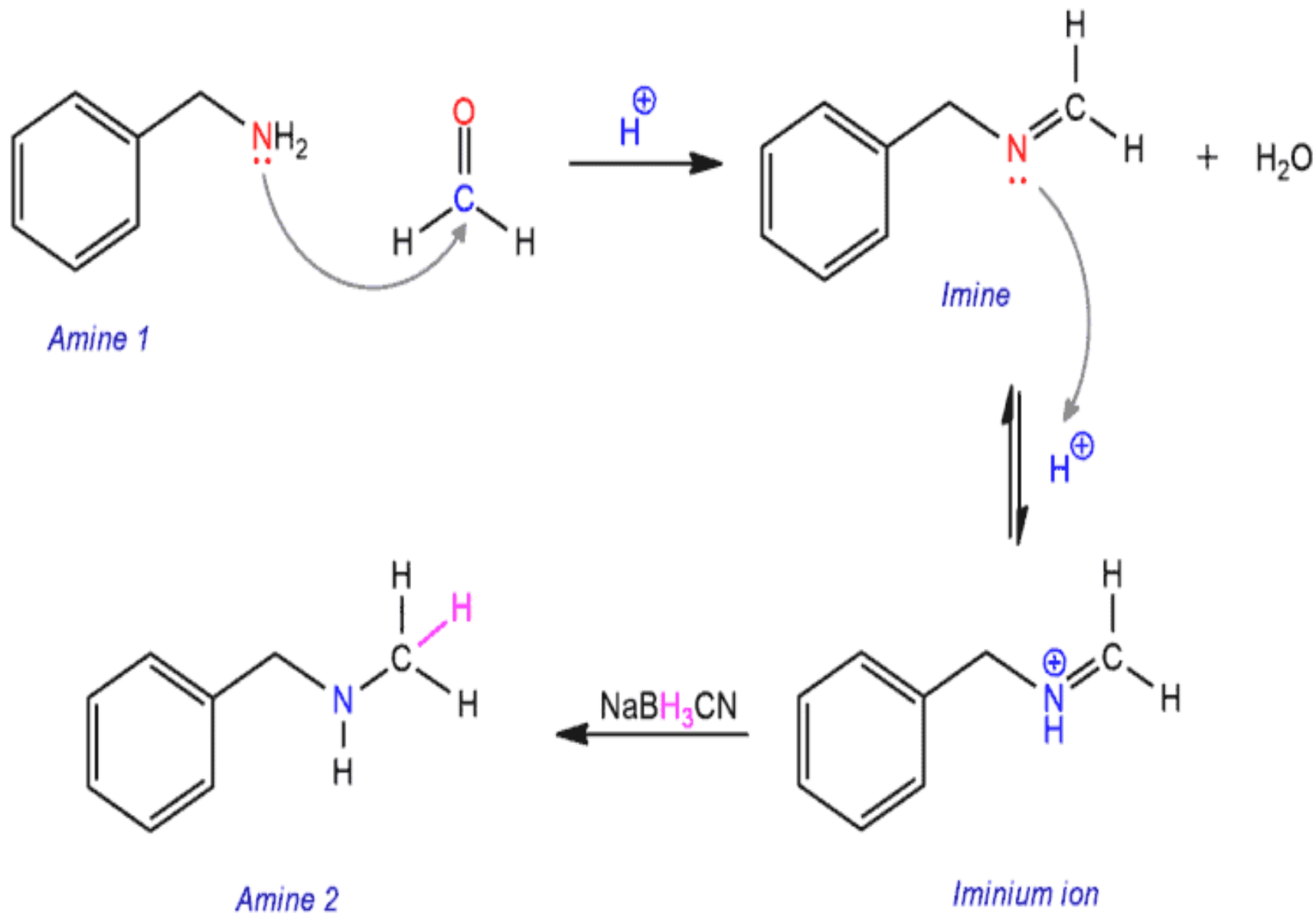
**Step 1:** Form an imine. We need to add a single carbon to our amine, so we add a carbonyl group with a single carbon - methanal (formaldehyde)



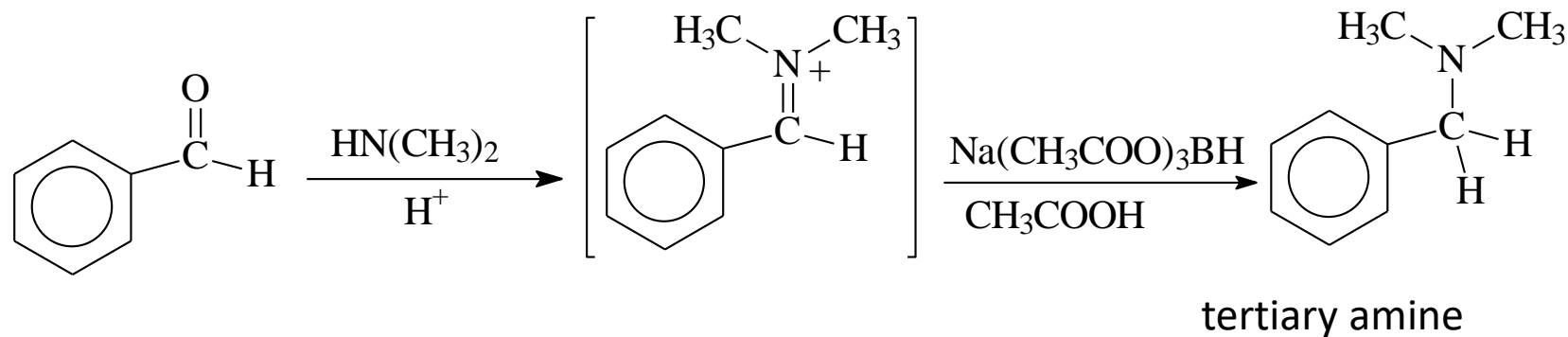
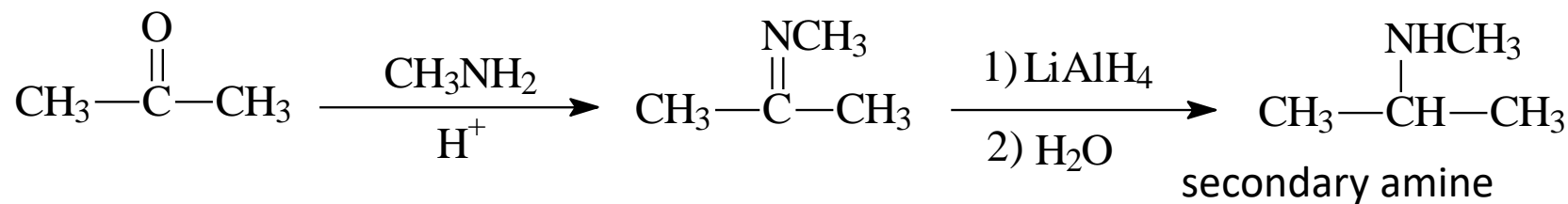
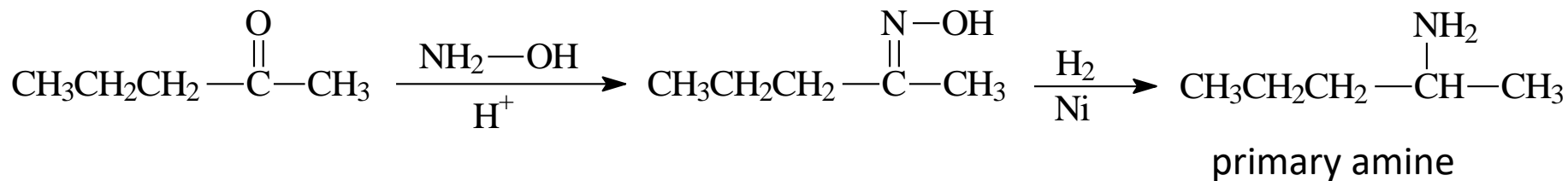
**Step 3:** In the presence of a reducing agent like  $\text{NaBH}_3\text{CN}$  the iminium will be reduced to give a new amine

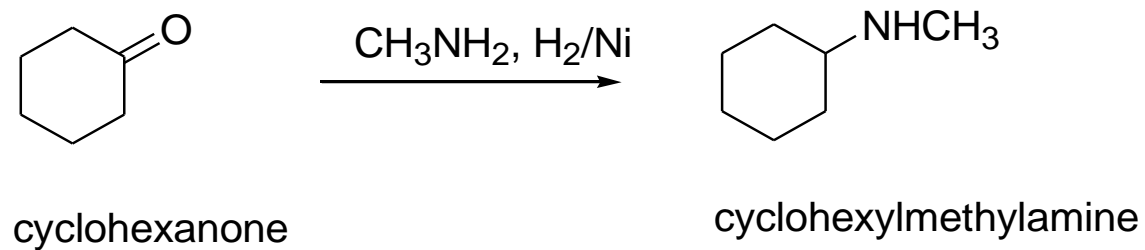
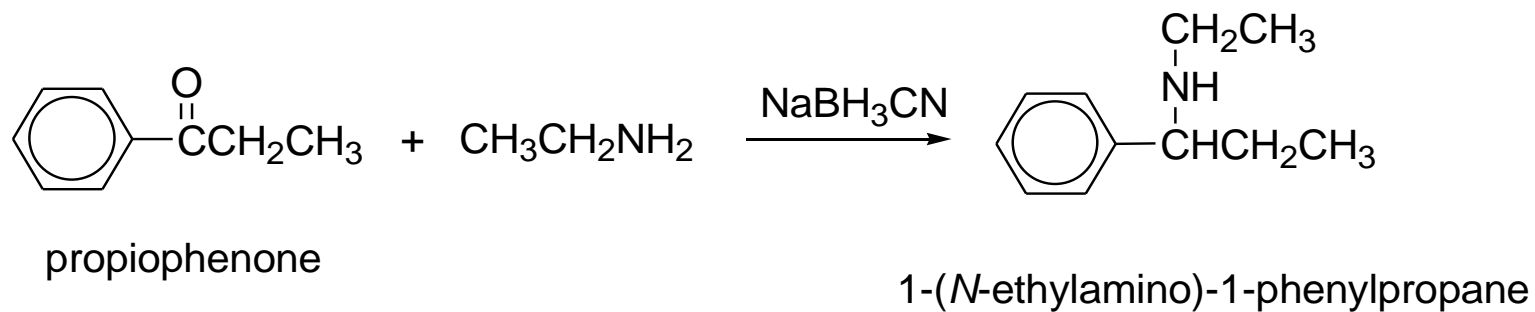


# Mechanism



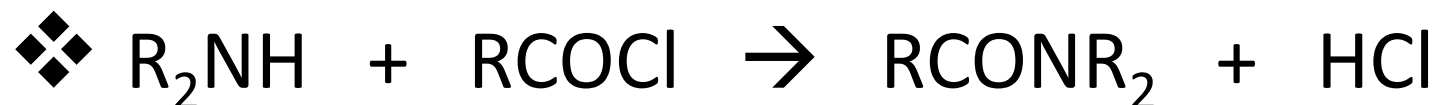
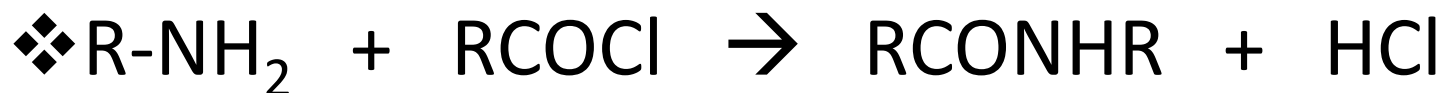
## Examples



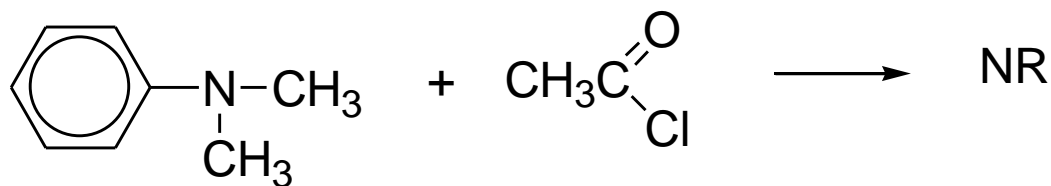
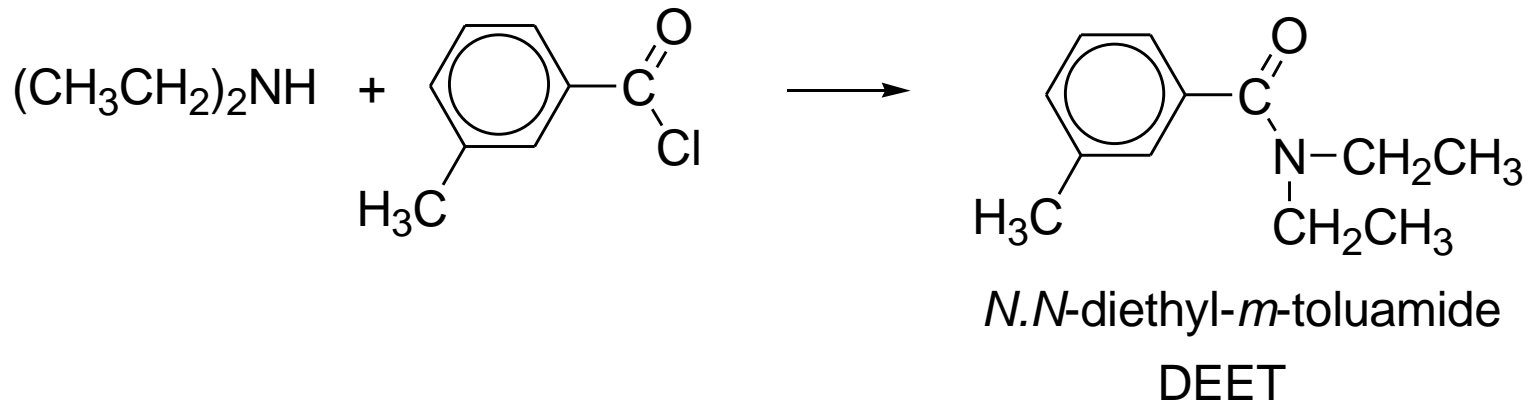
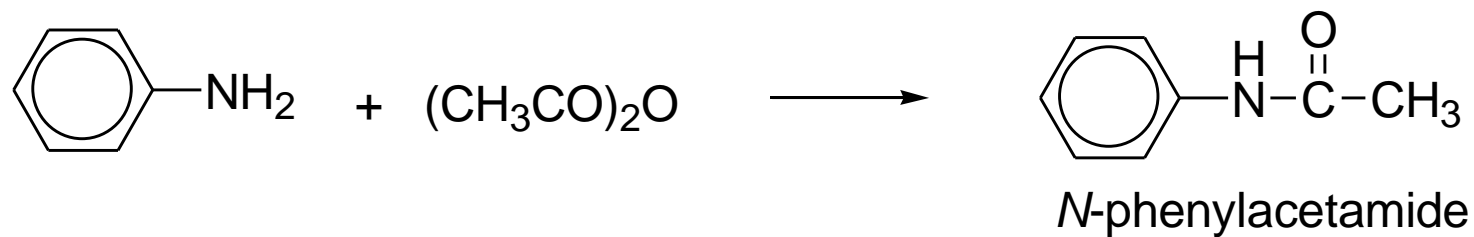


## Amines are converted into amides (Acylation)

❖ Aminolysis (/am·i·nol·y·sis/ amino meaning "contains  $\text{NH}_2$  group", and lysis meaning "to unbind") is **any chemical reaction in which a molecule is split into two parts by reacting with ammonia or an amine.** .

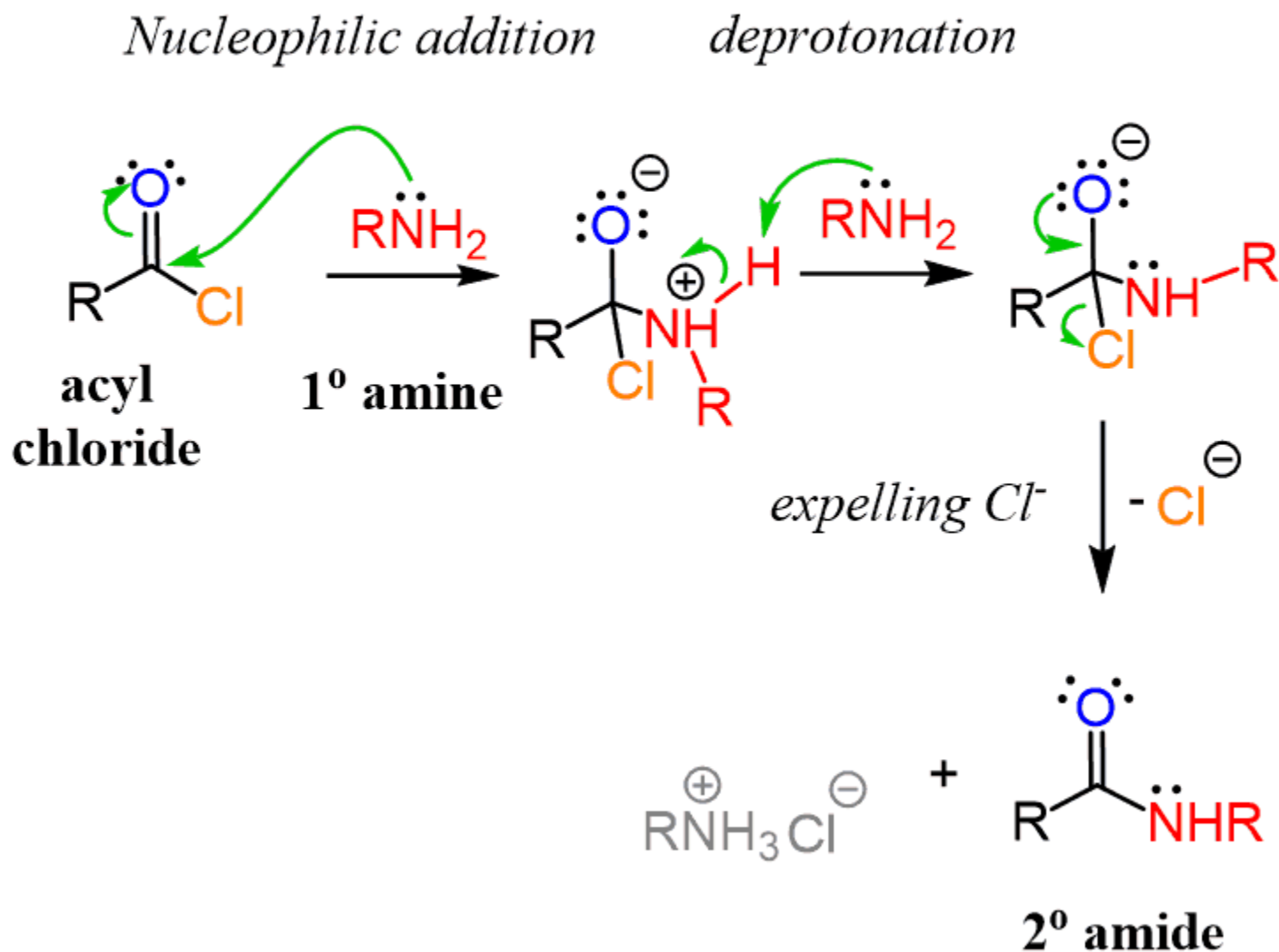


# Examples



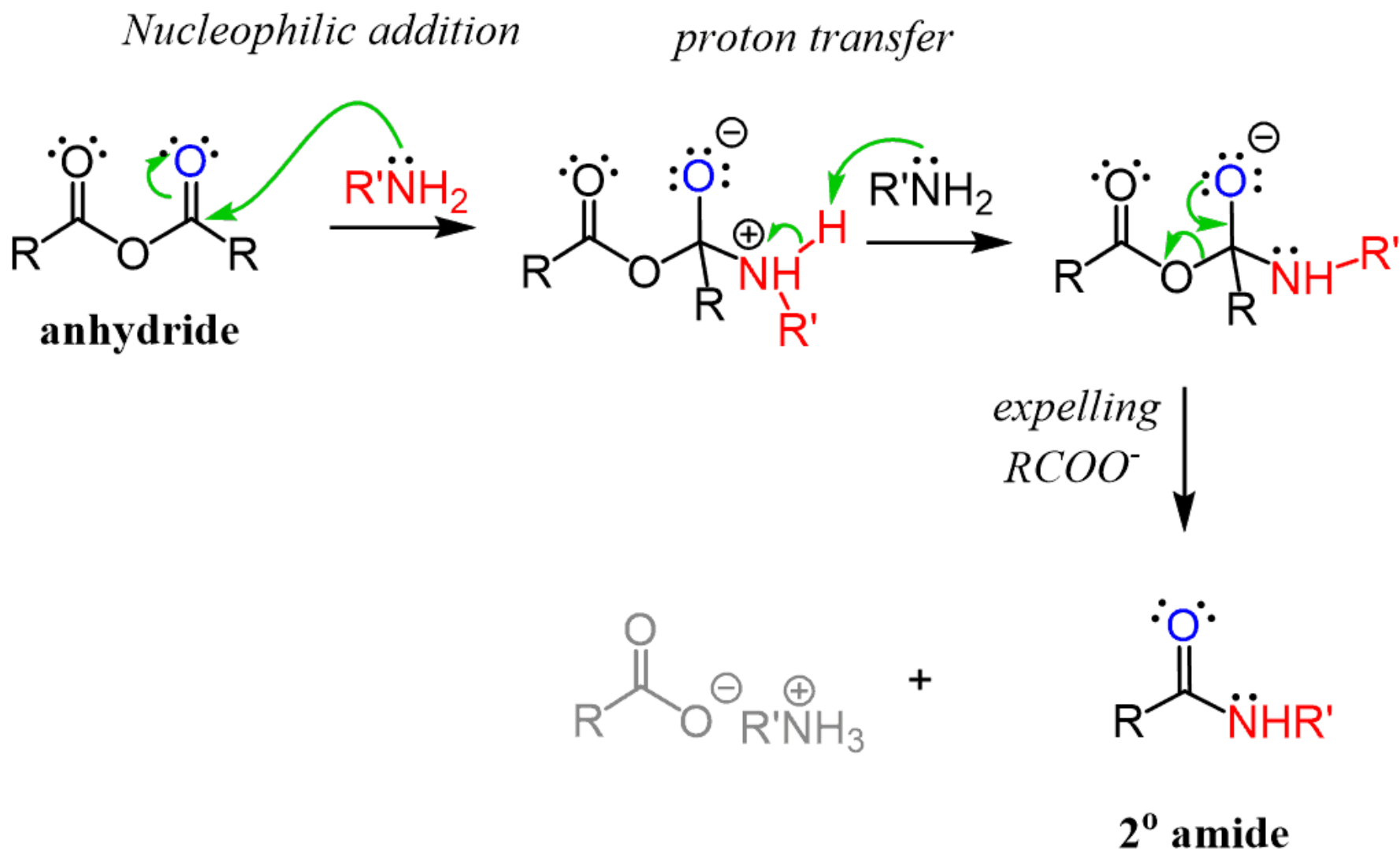
# Mechanism Aminolysis of acid chlorides

## Reaction of Acyl Chlorides with Amines



# Mechanism Aminolysis of acid Anhydrides

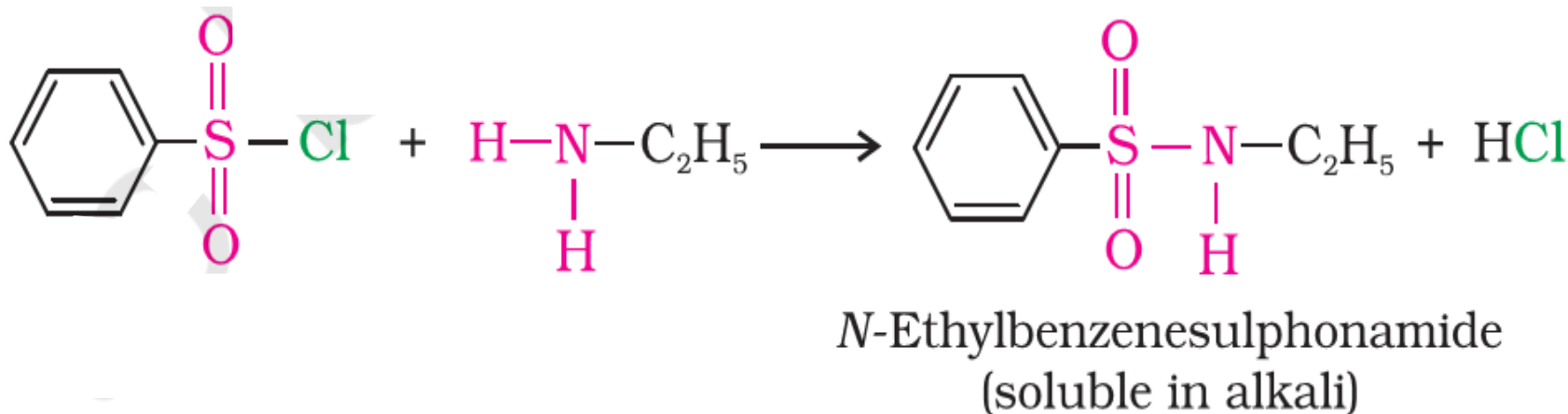
## Reaction of Anhydrides with Amines





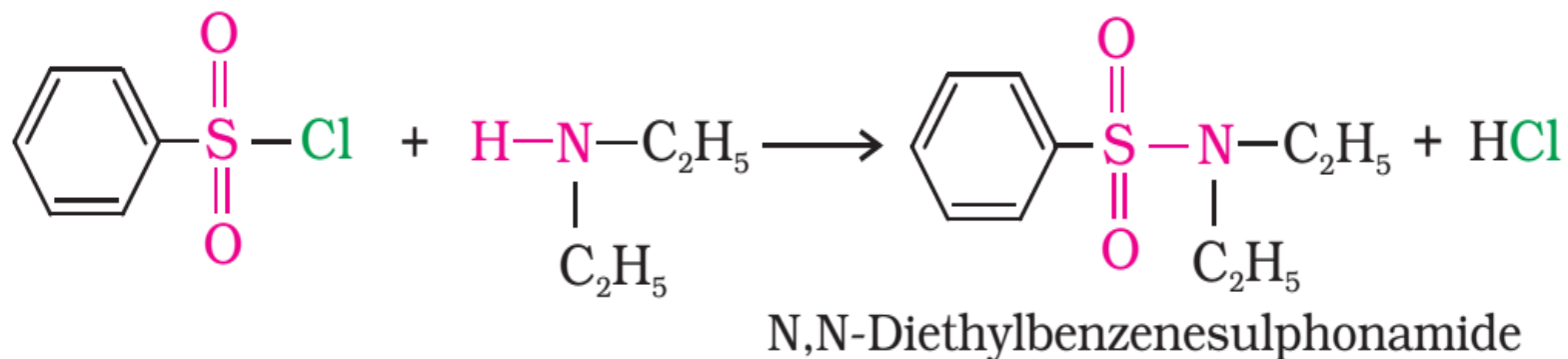
## 5. Amines are Converted into sulfonamides (EAS at nitrogen)

- Benzenesulphonyl chloride ( $\text{C}_6\text{H}_5\text{SO}_2\text{Cl}$ ), which is also known as Hinsberg's reagent, reacts with primary and secondary amines to form sulfonamides.
- I. The reaction of benzenesulphonyl chloride with primary amine yields N-ethylbenzenesulphonyl amide.



- The hydrogen attached to nitrogen in sulfonamide is strongly acidic due to the presence of strong electron withdrawing sulphonyl group. Hence, it is soluble in alkali.

- II. The reaction of benzenesulphonyl chloride with secondary amine, N,N-diethylbenzenesulphonamide is formed.



- Since N, N-diethylbenzene sulphonamide does not contain any hydrogen atom attached to nitrogen atom, it is not acidic and hence insoluble in alkali.
- III. Tertiary amines do not react with benzenesulphonyl chloride. This property of amines reacting with benzenesulphonyl chloride in a different manner is used for the distinction of primary, secondary and tertiary amines and also for the separation of a mixture of amines. However, these days benzenesulphonyl chloride is replaced by p-toluenesulphonyl chloride.

# Test for amines

- **Hinsberg Test:-** The reagent used in this test is **benzene sulfonyl chloride**. Amines reacts with benzene sulfonyl chloride in the alkaline medium.
- *Primary amines* reacts with benzene sulfonyl chloride to produce substituted sulfonamide which contains an acidic hydrogen and dissolve in basic medium.
- **Primary amine** + benzenesulfonyl chloride, KOH (aq) → clear solution and then gives a ppt upon acidification

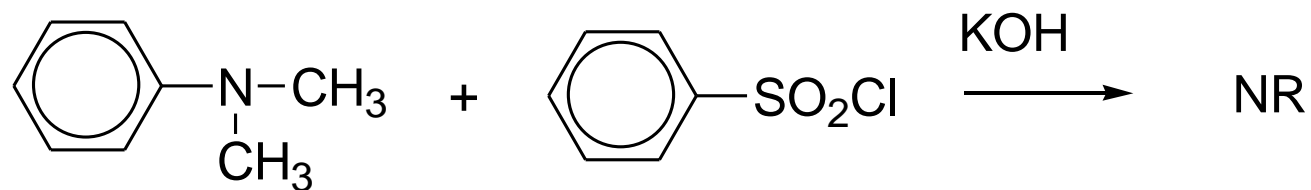
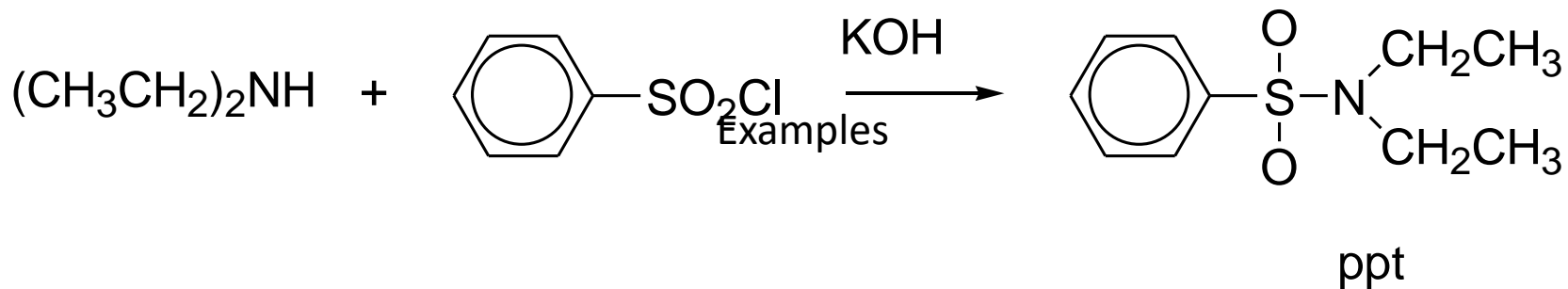
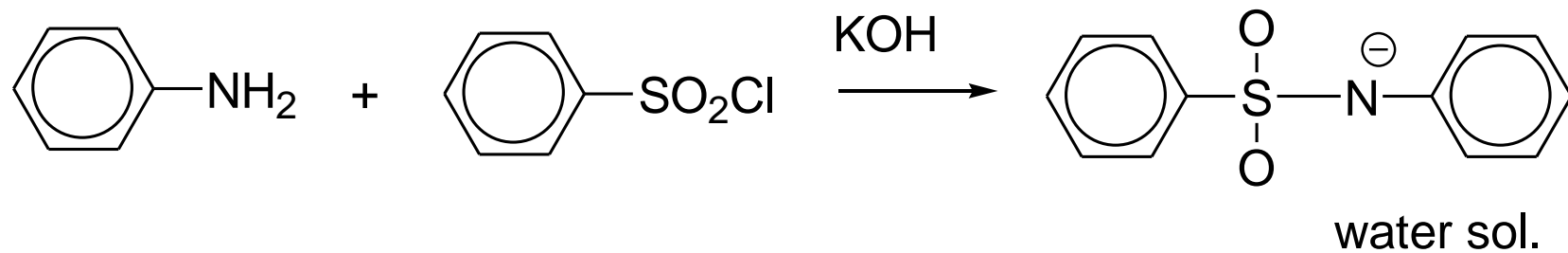
# Test for amines

- nitrous acid test for amines
  - 1°-Amines + HONO (cold acidic solution) → Nitrogen Gas Evolution from a Clear Solution
  - 2°-Amines + HONO (cold acidic solution) → An Insoluble Oil (N-Nitrosamine)
  - 3°-Amines + HONO (cold acidic solution) → A Clear Solution (Ammonium Salt Formation)

# Test for amines

- A *secondary amine* forms a substituted sulfonamide which is insoluble in alkali because it does not have acidic hydrogen.
  - Secondary amine + benzenesulfonyl chloride, KOH (aq) → ppt
- A *tertiary amine* forms a substituted sulfonamide which is insoluble in alkali because it does not have an acidic hydrogen.
  - Tertiary amine + benzenesulfonyl chloride, KOH (aq) → no reaction

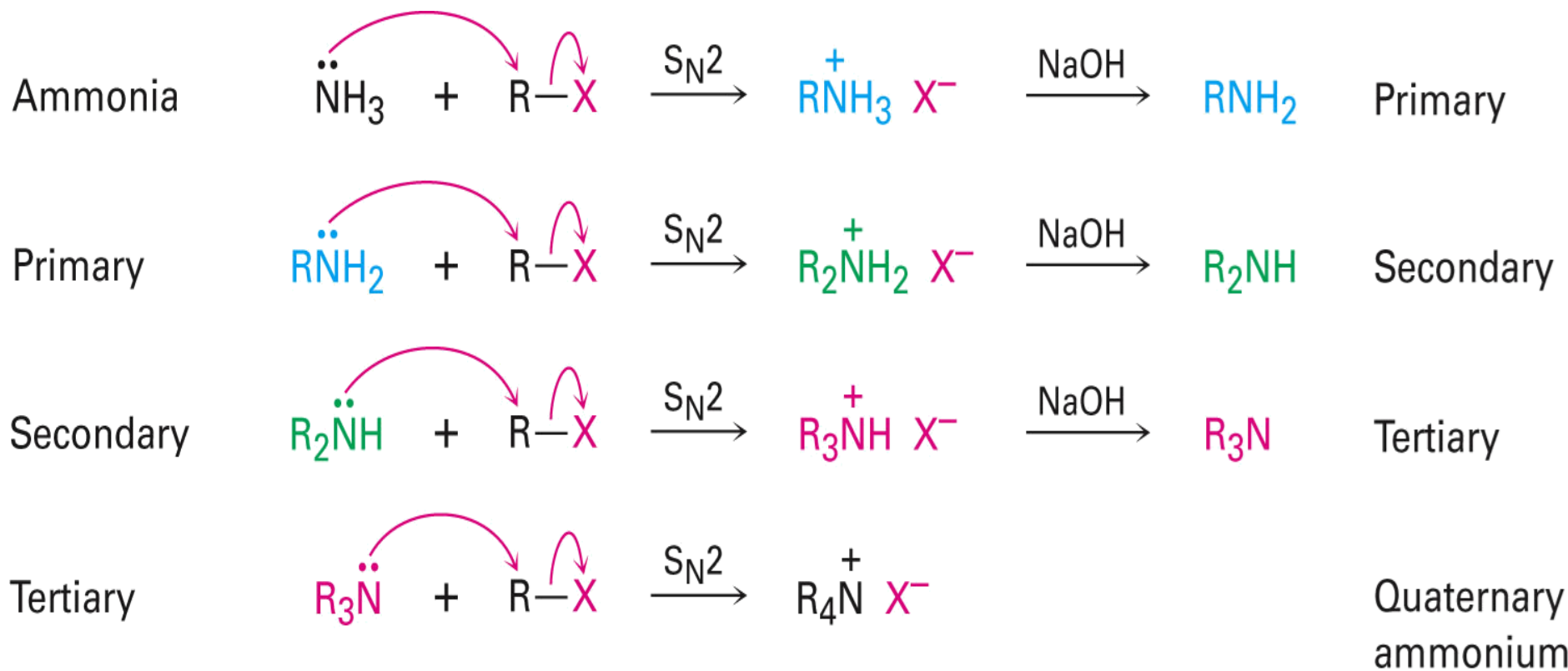
## Examples



# Preparation of amines

## 1. Alkylation of ammonia and amine

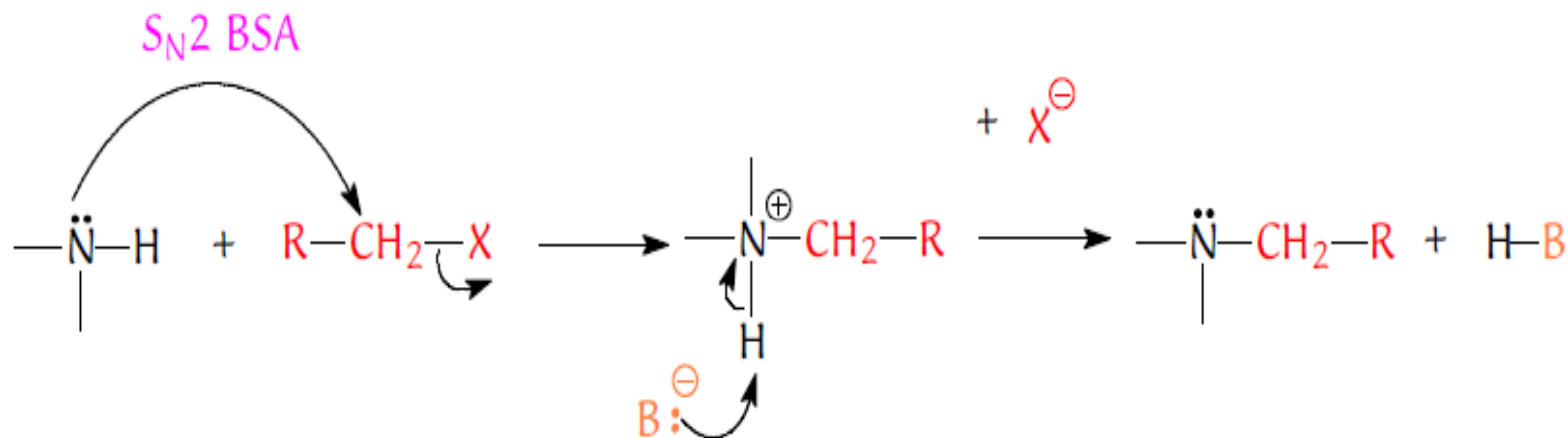
- Ammonia or an amine is treated with an alkyl halide; substituting an R group on the nitrogen



- R, R' can be alkyl or aryl

## Mechanism

- an  $S_N2$  back-side attack by the nucleophilic amine on the alkyl halide with  $X^-$  as leaving group (LG)

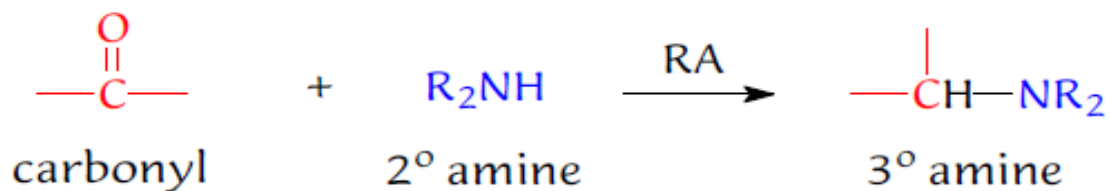
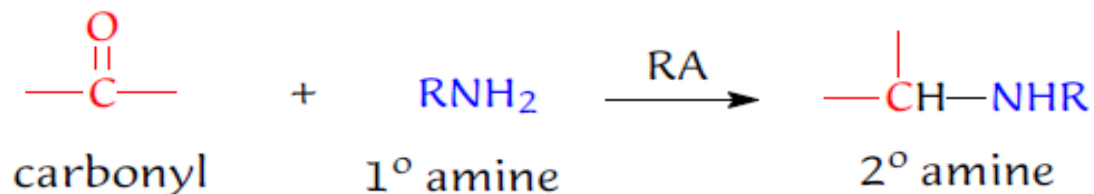
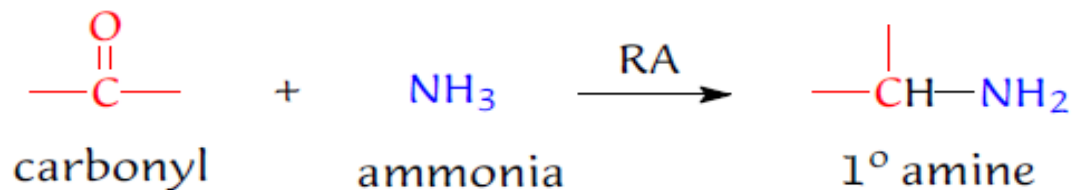


- note** - in the formation of a quaternary ammonium salt, there is no hydrogen to remove, hence, base is not required
- the alkylation reaction is difficult to control (over substitution occurs) & is therefore somewhat limited in its utility
- two useful applications which do provide good yields of a single product employ an excess of one of the reactants:



## 2. Reductive Amination

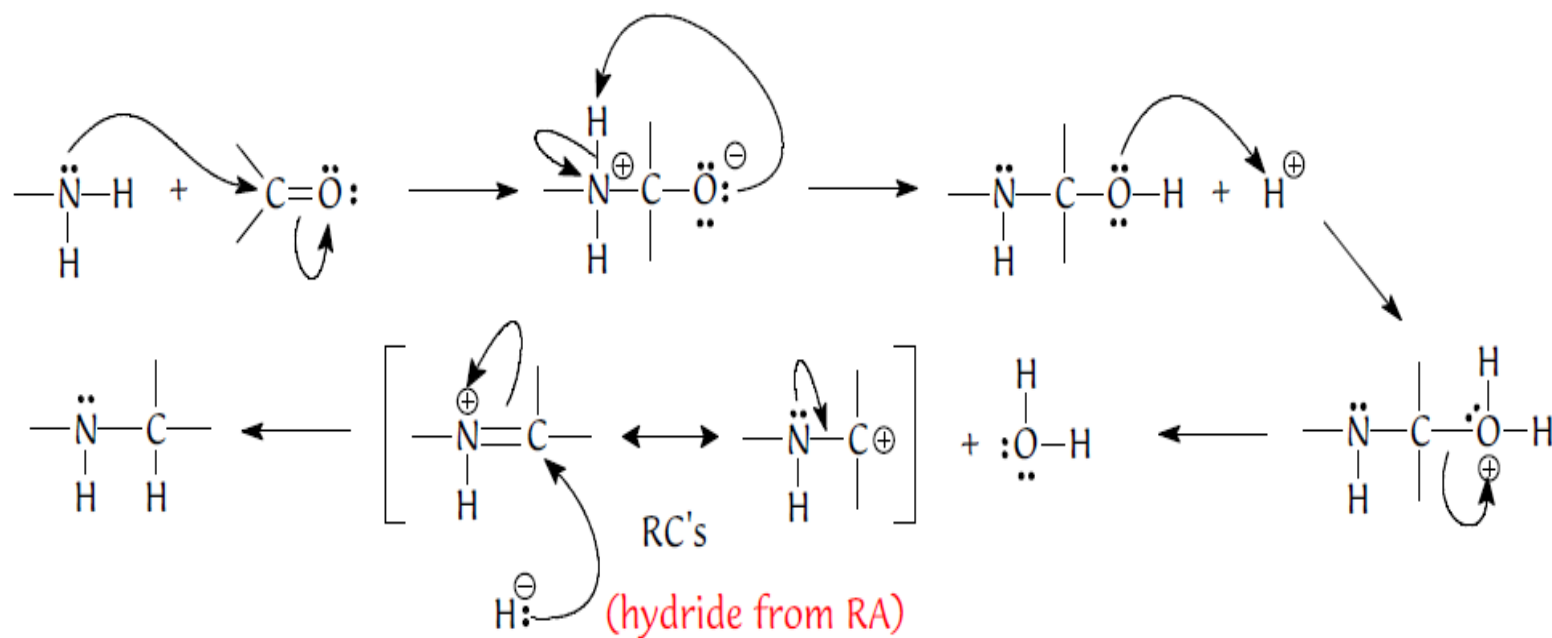
- reduction of the carbon-nitrogen double bond produces an amine with the same substitution level as provided by alkylation



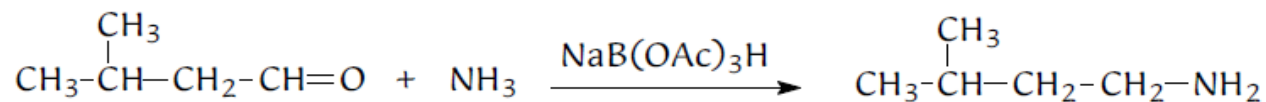
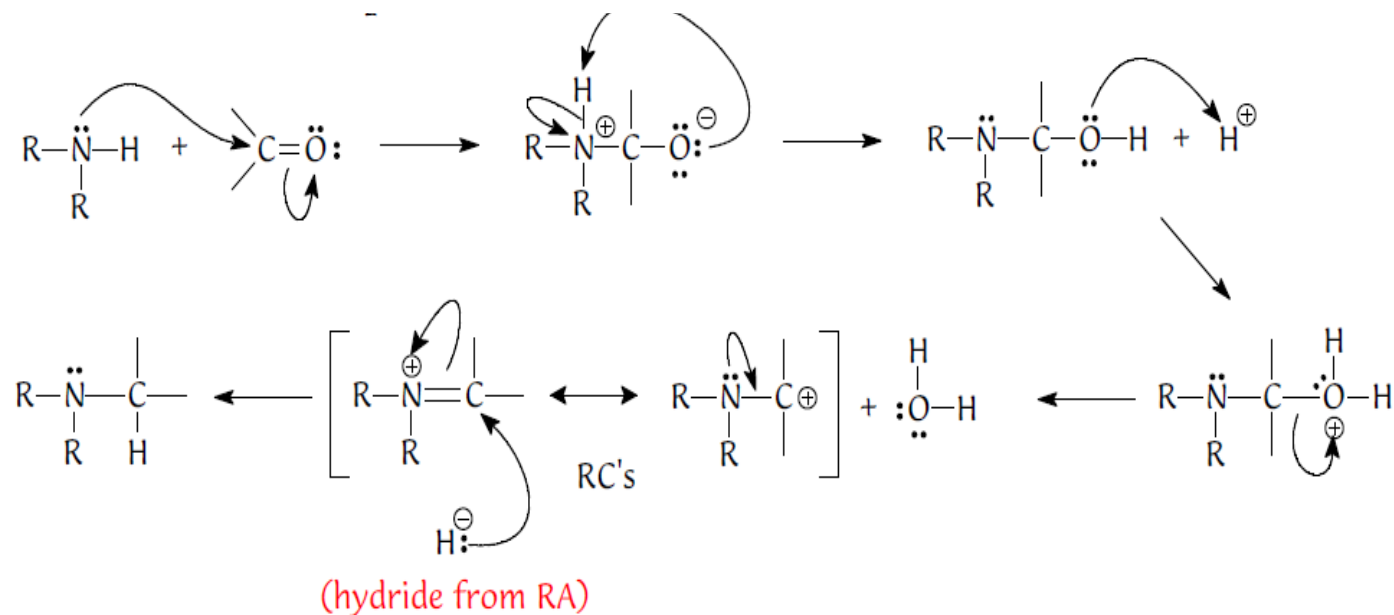
- R = Ar, also  $\text{NH}_3 = \text{NH}_2\text{OH}$ , also
- RA =  $\text{H}_2/\text{Ni}$  ;  $\text{H}_2/\text{Pd}$  ; ..... (Catalytic)  
=  $\text{NaBH}_3\text{CN}$ ,  $\text{NaB}(\text{OAc})_3\text{H}$ , ..... (Hydride)

## Mechanism

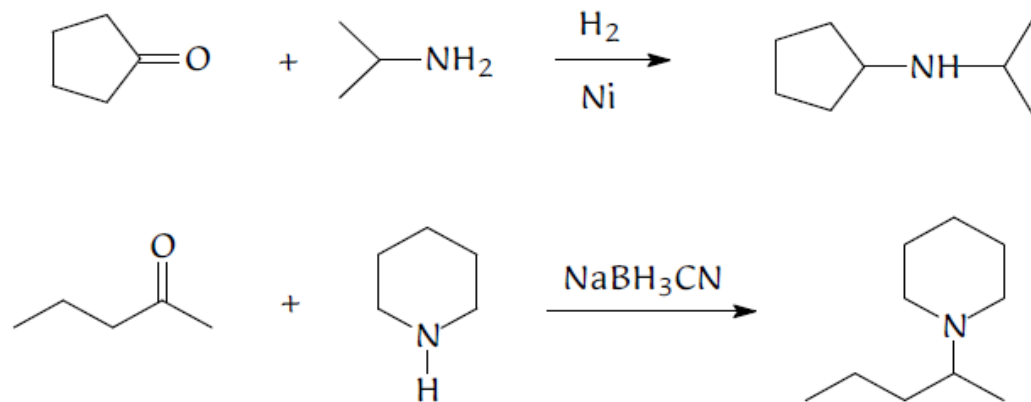
- The process varies slightly with the level of substitution on the nitrogen:
- 1) Ammonia (NH<sub>3</sub>) & primary amines (RNH<sub>2</sub>)



○ Secondary amines ( $R_2NH$ )

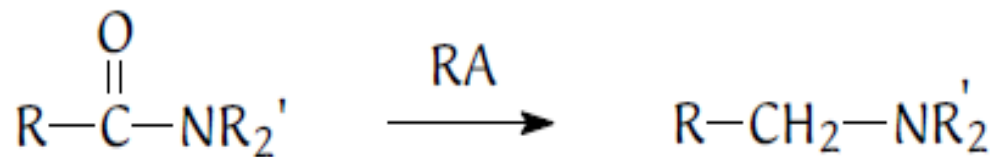


○ Example



### 3. Reduction of Amides

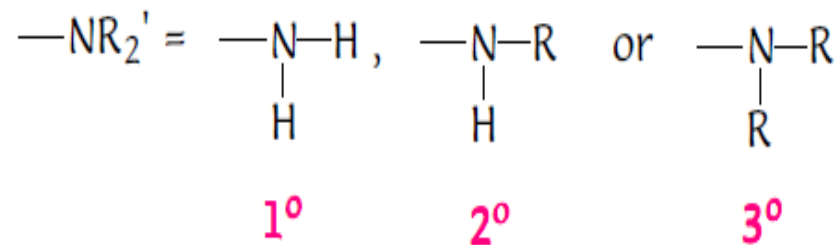
- amide can be converted to its corresponding amine by reduction:



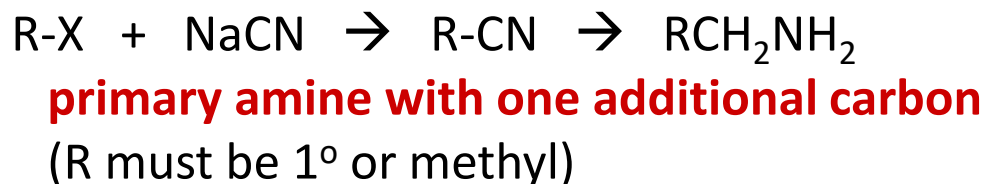
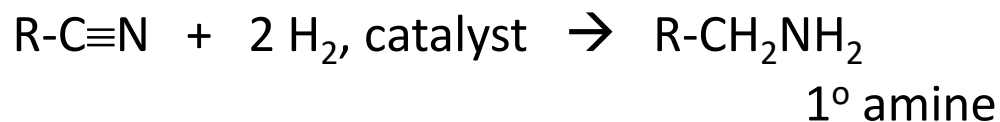
1°, 2° or 3° amide

1°, 2° or 3° amine

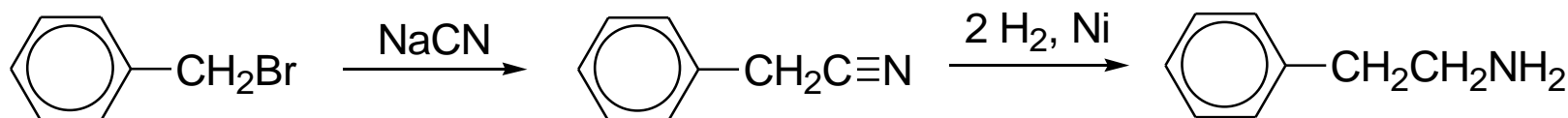
RA = LiAlH<sub>4</sub>, BH<sub>3</sub>/LB, .....



## 4. Reduction of nitriles

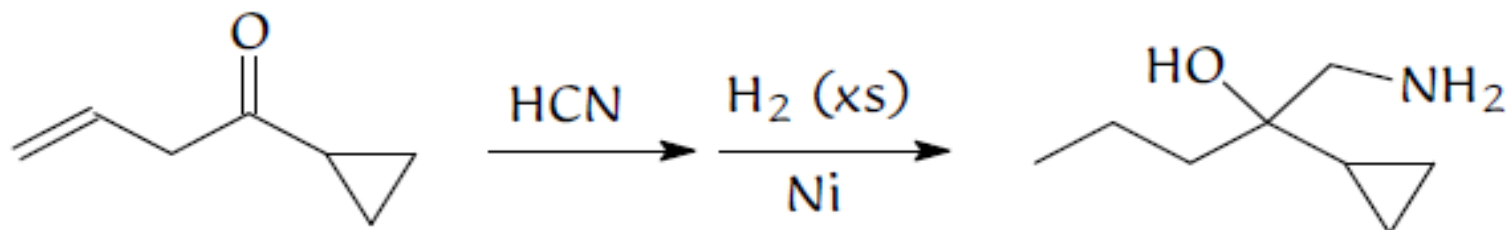
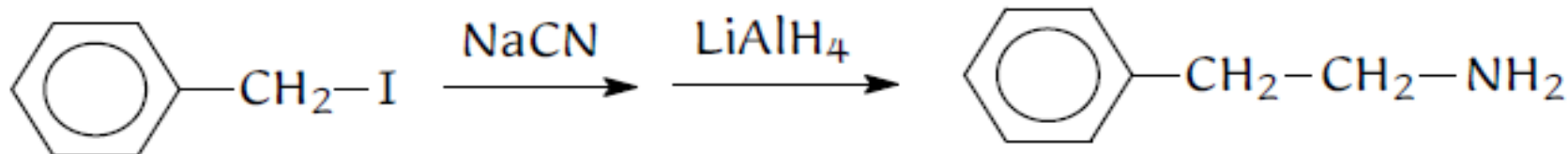


### Example



benzyl bromide

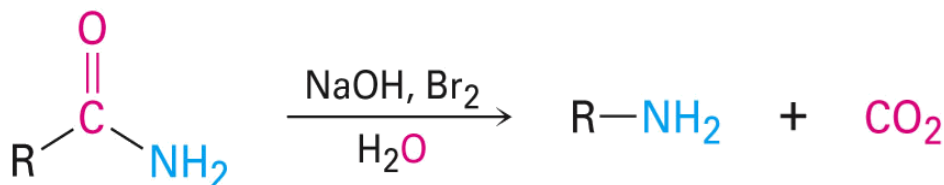
1-amino-2-phenylethane



# Curtius and Hofmann Rearrangements

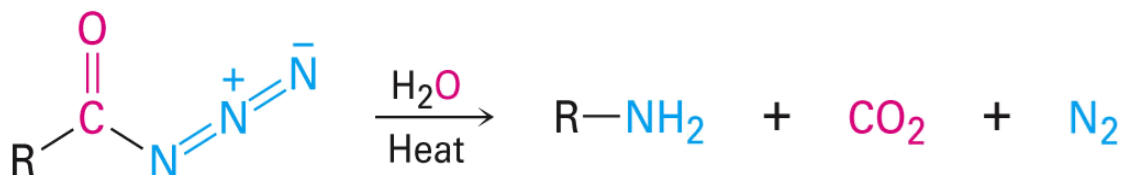
- Carboxylic acid derivatives can be converted into primary amines with loss of one carbon atom by both the Hofmann rearrangement and the Curtius rearrangement
- General reaction

**Hofmann  
rearrangement**



**An amide**

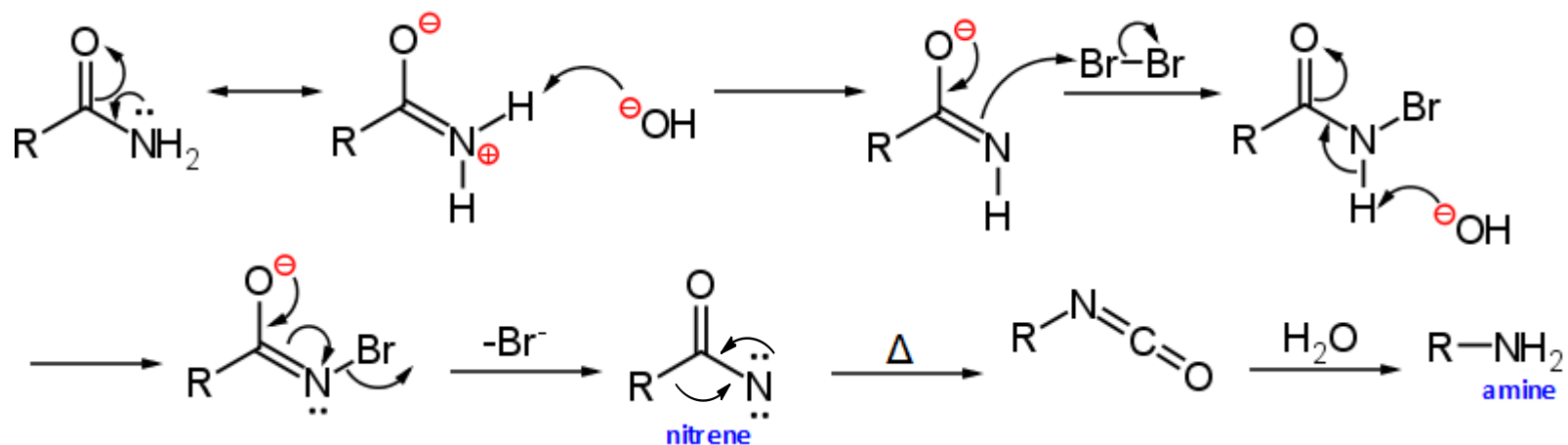
**Curtius  
rearrangement**



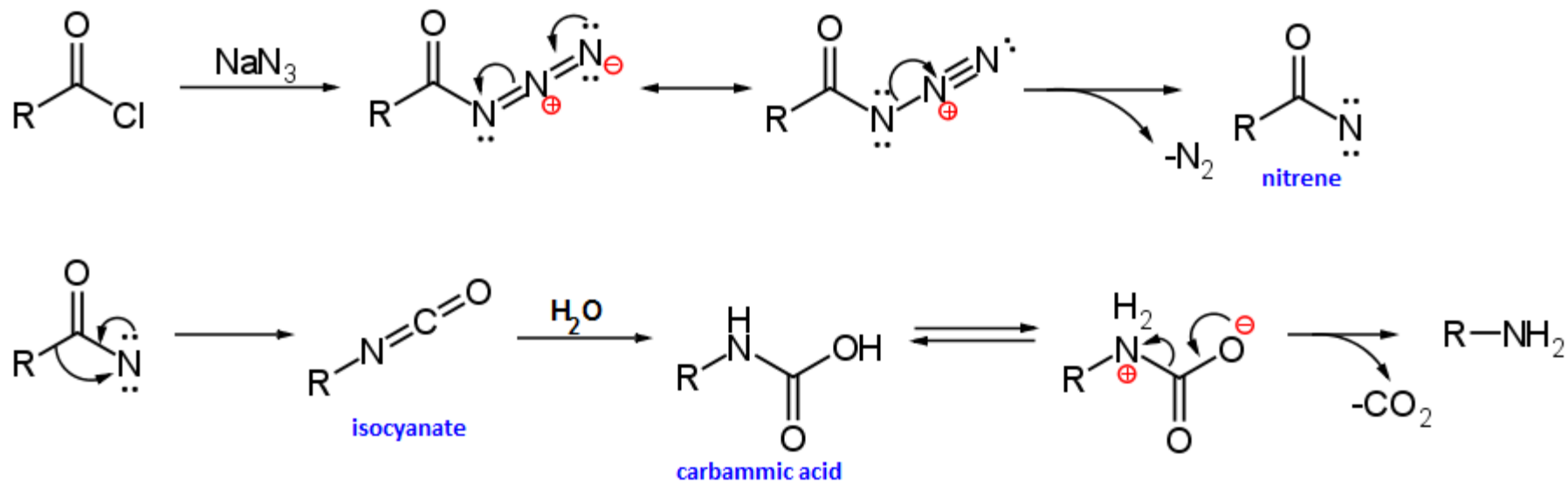
**An acyl azide**

# ○ Mechanisms

## Hofmann rearrangement

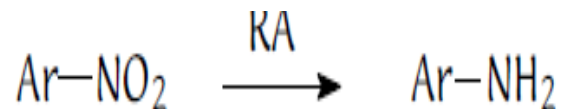


## Curtius rearrangement



## 6. Reduction of Aromatic Nitro Compounds

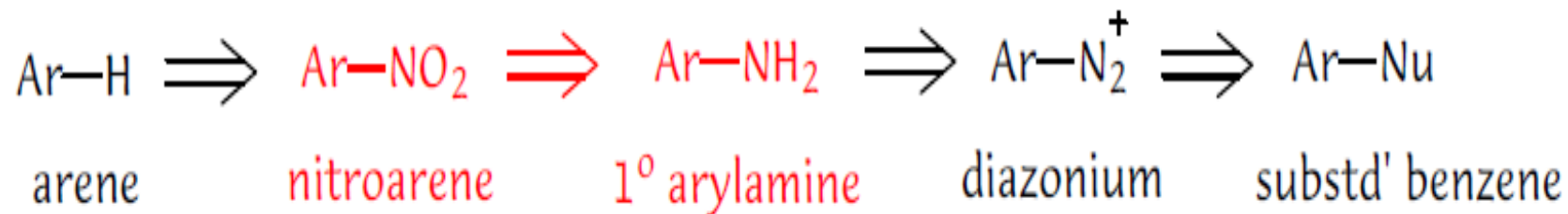
- This reductive method provides facile access to primary arylamines



- Nitroarene = 1° aromatic amine
- RA = Sn/H<sup>+</sup>; Fe/H<sup>+</sup>; Zn/H<sup>+</sup>; .....(chemical)  
= H<sub>2</sub>/Ni; H<sub>2</sub>/Pd; ..... (Catalytic)

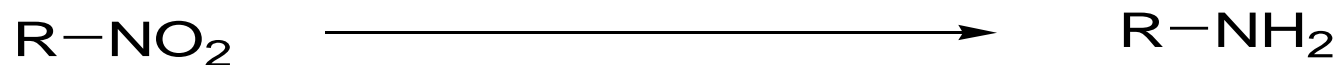
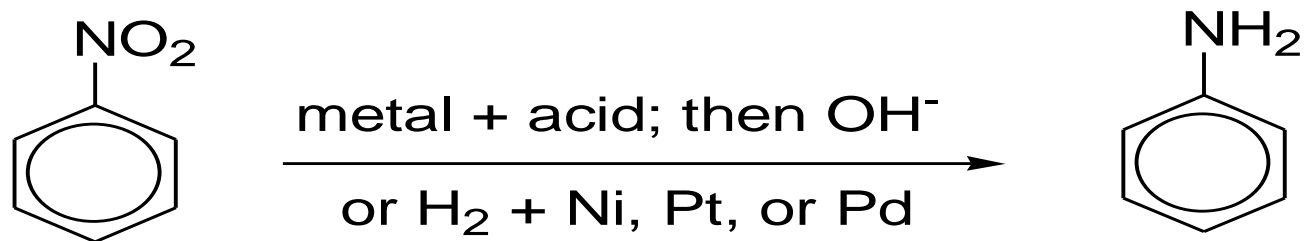
- **Mechanism**

- the “dissolving metal” provides the electrons & the acid provides the hydrogens for a free radical process which replaces the nitro group O's with H's

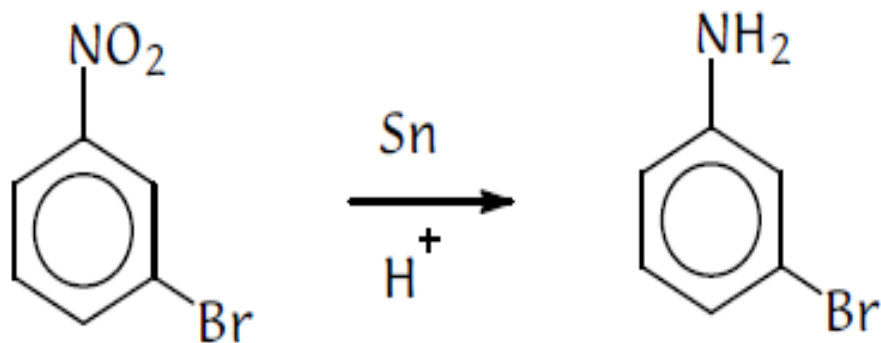


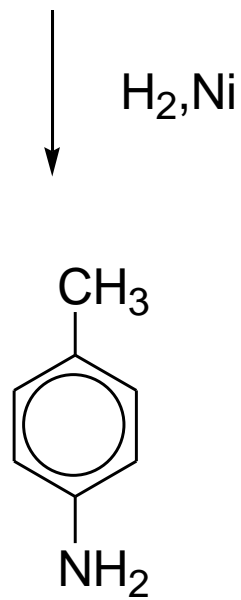
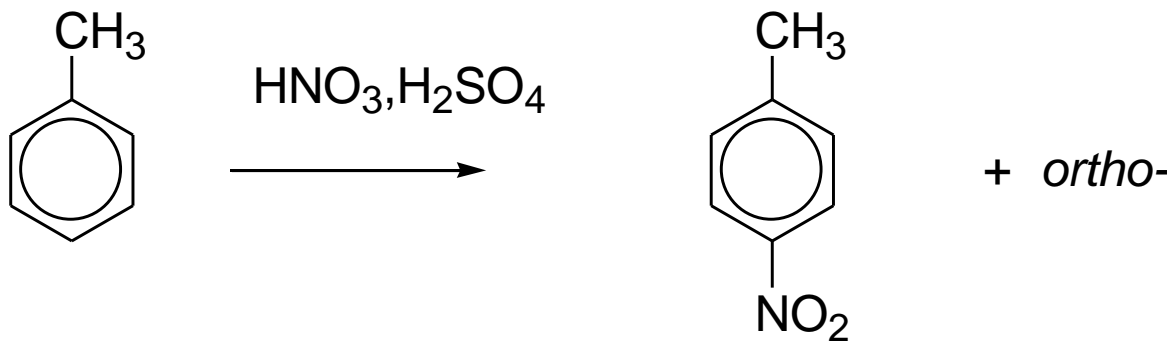


## Examples



Chiefly for primary **aromatic** amines.

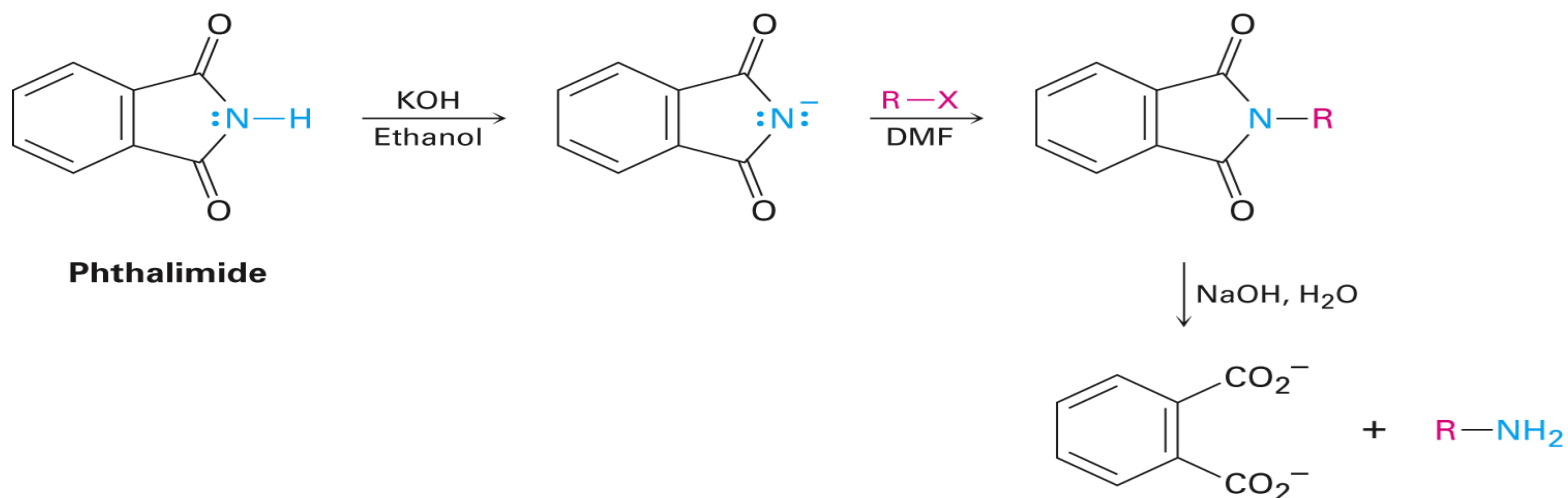




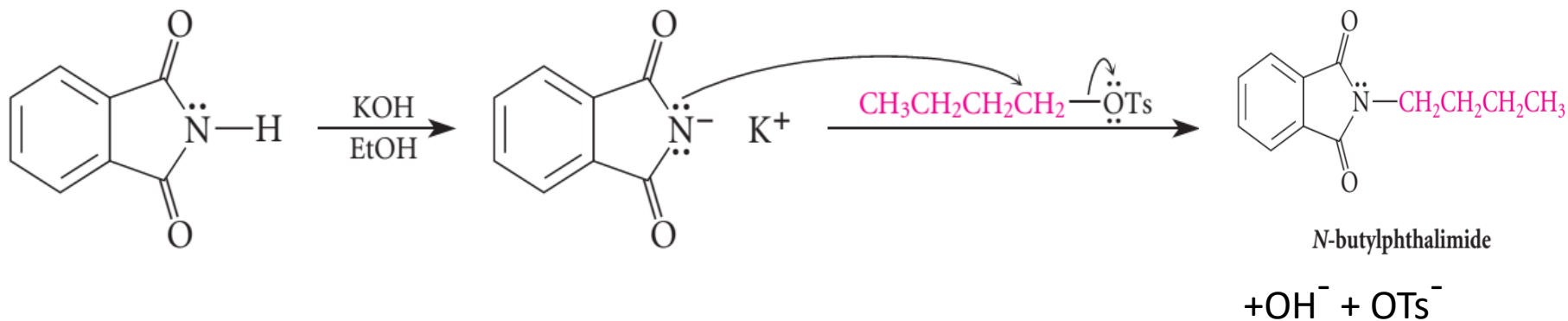
*p*-toluidine

## 7. Gabriel Synthesis of Primary Amines

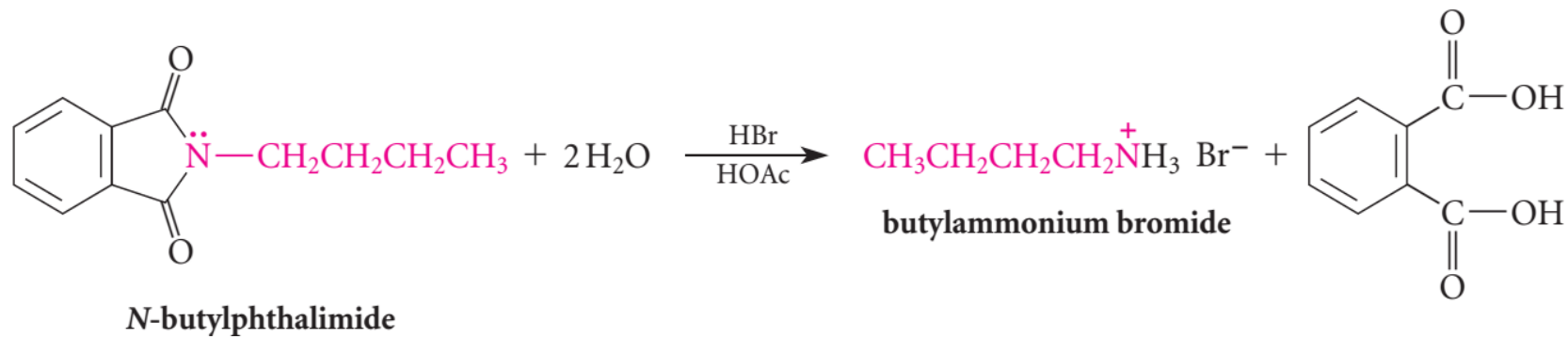
- The Gabriel synthesis produces primary amines via potassium phthalimide



### Mechanism

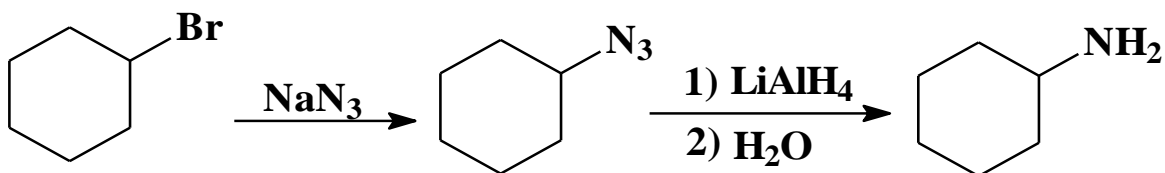


Cont'd



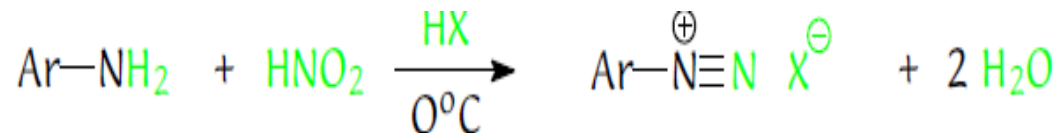
## 8. Azide reduction (1°)

- Azide ion,  $\text{N}_3^-$ , is a good nucleophile.
- React azide with unhindered 1° or 2° halide or tosylate ( $\text{S}_{\text{N}}2$ ).
- Alkyl azides are explosive! Do not isolate.



## Diazotization of Amines (reaction with nitrous acid) see slide 25-31

- Amines react with nitrous acid ( $\text{HNO}_2$ ) to produce diazonium salt



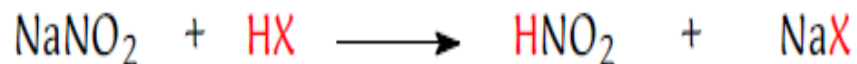
1° aromatic amine

arene diazonium salt

$\text{HX} = \text{HCl}, \text{H}_2\text{SO}_4 \dots$

$\text{Ar} = \text{R}$ , also

- Unstable nitrous acid is generated in situ from sodium nitrite & an acid:



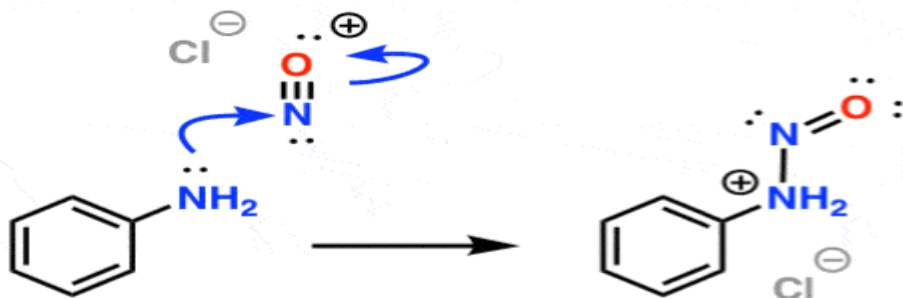
# Mechanism

- The electrophilic nitrosonium cation is attacked by the nucleophilic aniline to initiate diazotization

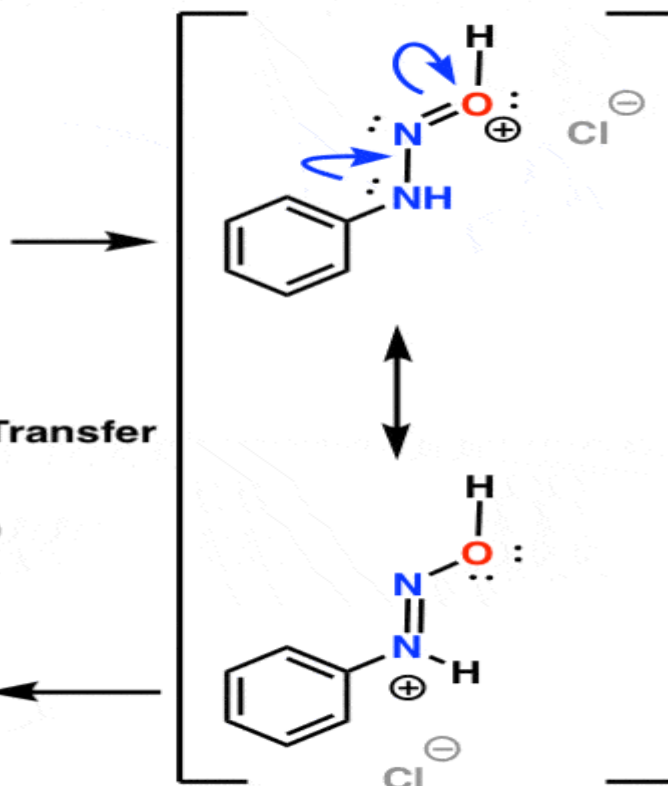


## Mechanism: Formation of Diazonium Ions From Aromatic Amines

### Step 1: Addition to nitrosonium ion

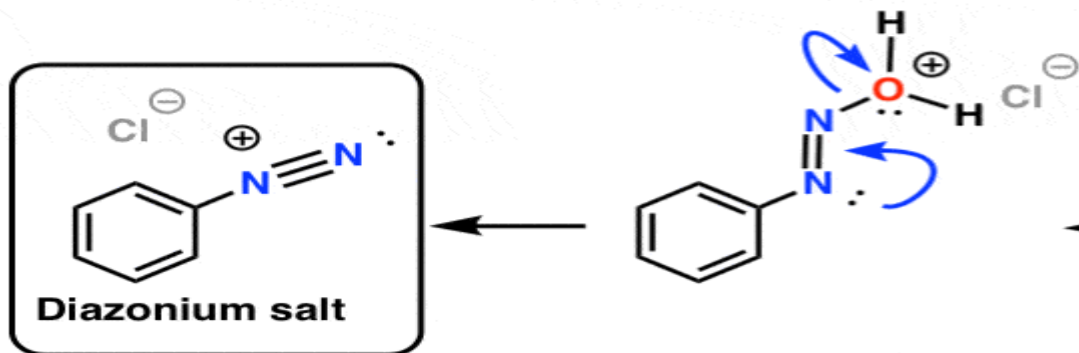


### Step 2: Proton Transfer



### Step 4: Elimination of H<sub>2</sub>O

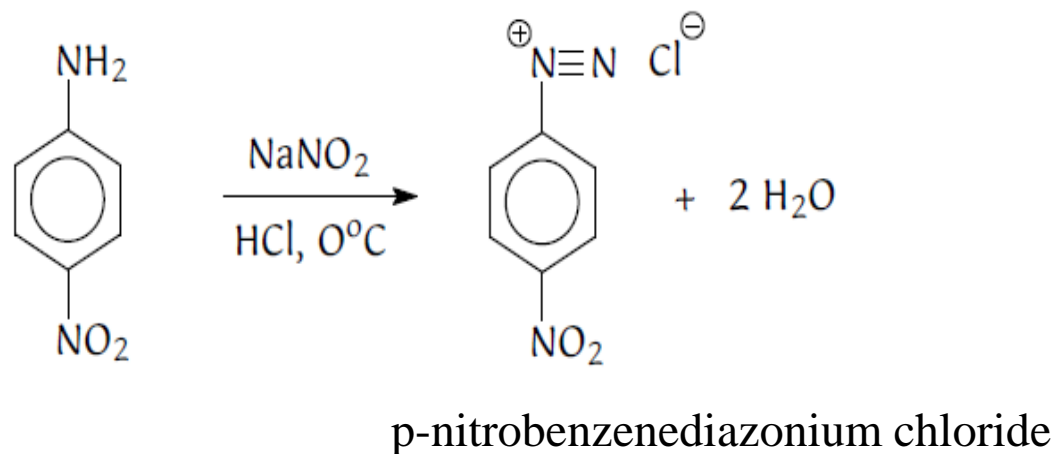
### Step 3: Proton Transfer



Diazonium salt

+ H<sub>2</sub>O

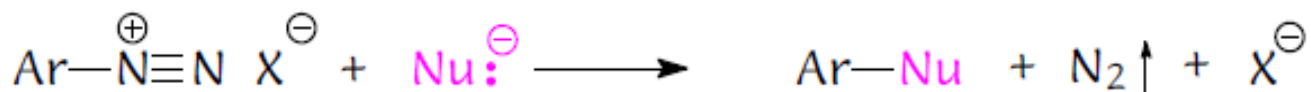
○ Example



## Reactions of Arenediazonium Compounds

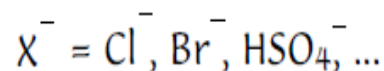
- Arenediazonium cations are very reactive because the diazonium nitrogen ( $-\text{N}_2^+$ ) is an extremely effective leaving group
- arenediazonium salts readily undergo nucleophilic aromatic substitution in which the diazonium moiety is replaced by a wide variety of functional groups



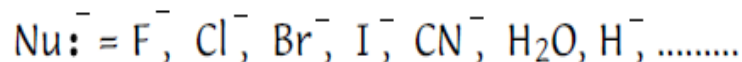


arene diazonium salt

substituted arene

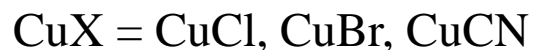
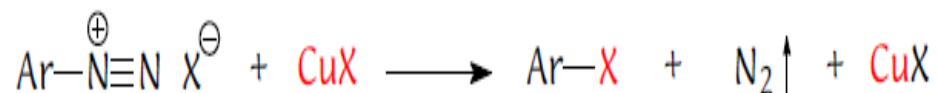


Ar = any substituted benzene

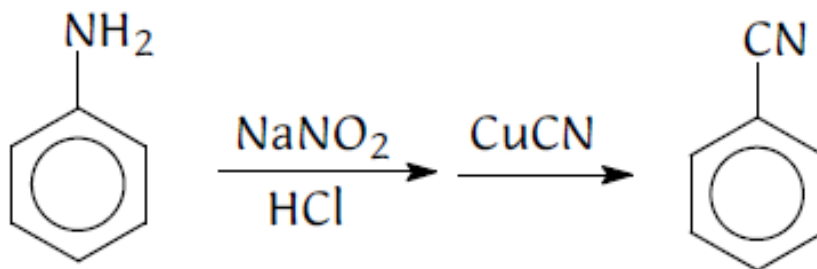


### Substitution with Chloride, Bromide & Cyanide

- known as the **Sandmeyer** reaction; the diazonium compound is allowed to warm up in the presence of the cuprous halide or cyanide of choice.

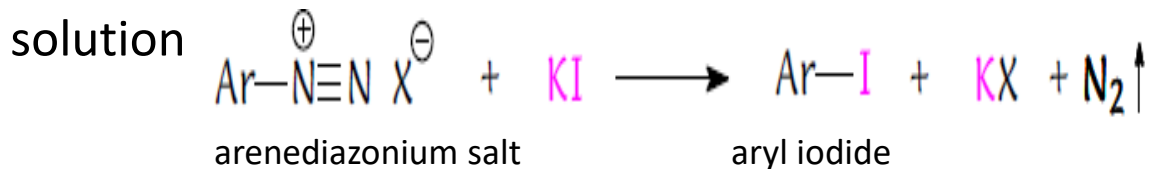


### Example



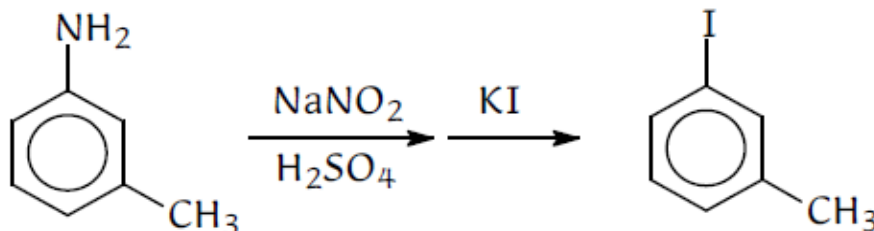
## Substitution with Iodide

- No copper catalyst is required; the diazonium is added directly to an iodide



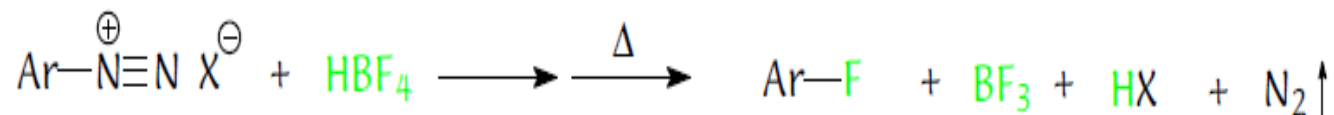
KI = NaI

- Example:



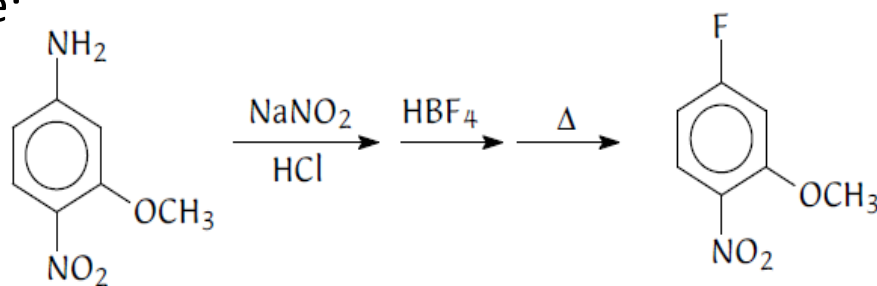
## Substitution with Fluoride

- The diazonium compound is treated with tetrafluoroboric acid ( $\text{HBF}_4$ ) & the resulting salt is decomposed with heating



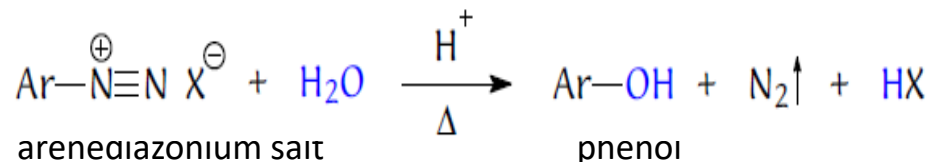
- The reaction proceeds through a diazonium fluoroborate salt which decomposes to the aryl fluoride upon heating

- Example:



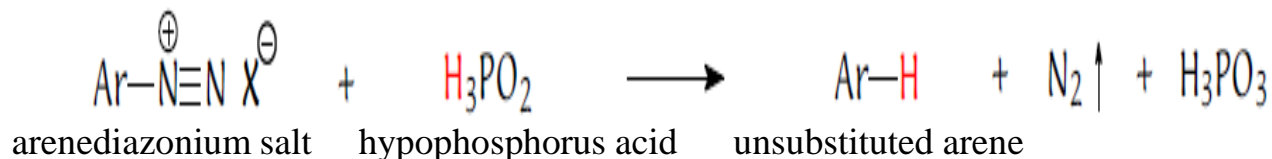
## Substitution with Hydroxide

- known as hydrolysis of a diazonium; the diazotization reaction mixture is simply allowed to warm up in the presence of added dilute acid.

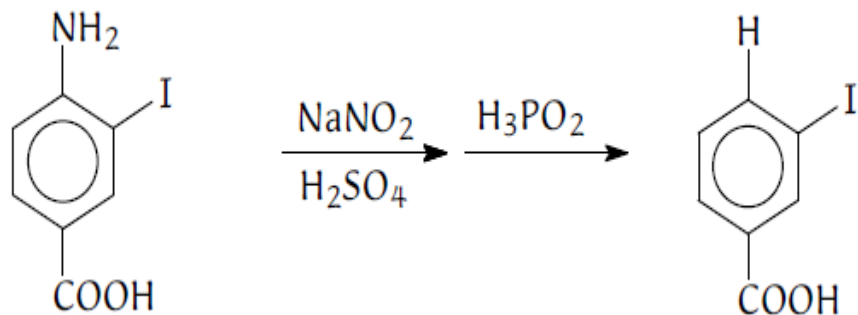


## Substitution with Hydride

- Also known as reduction of a diazonium; a reducing agent such as hypophosphorous acid (  $\text{H}_3\text{PO}_2$  ) replaces the diazonium group with a hydrogen

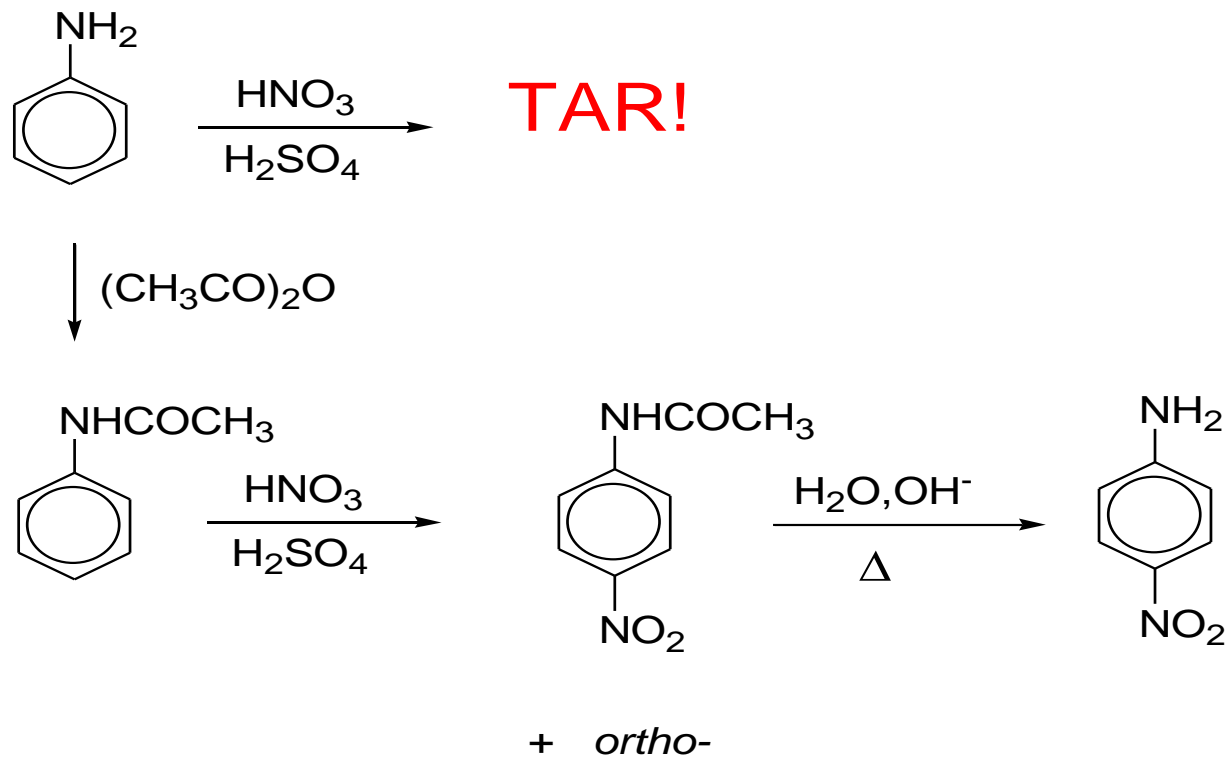


- reduction of a diazonium removes an amino group which may have served as a director or to block a position on the aromatic ring
- example:

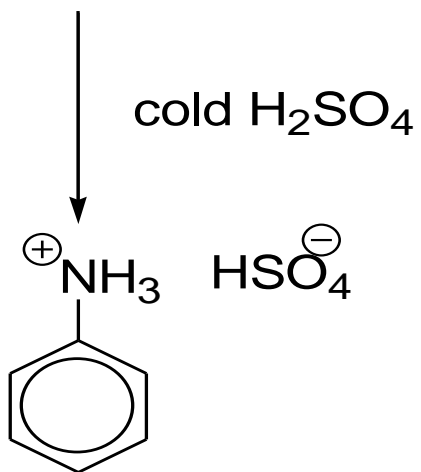
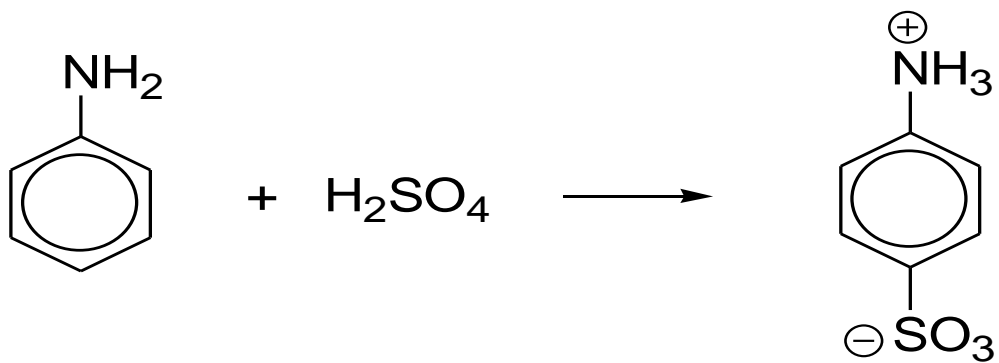


# Electrophilic Substitution at Nitrogen

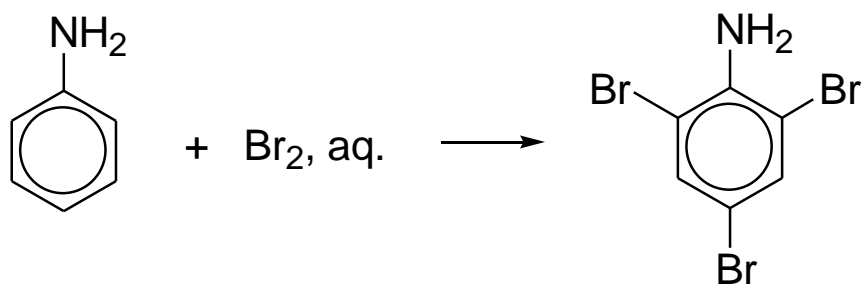
## a) nitration



**b) sulfonation**

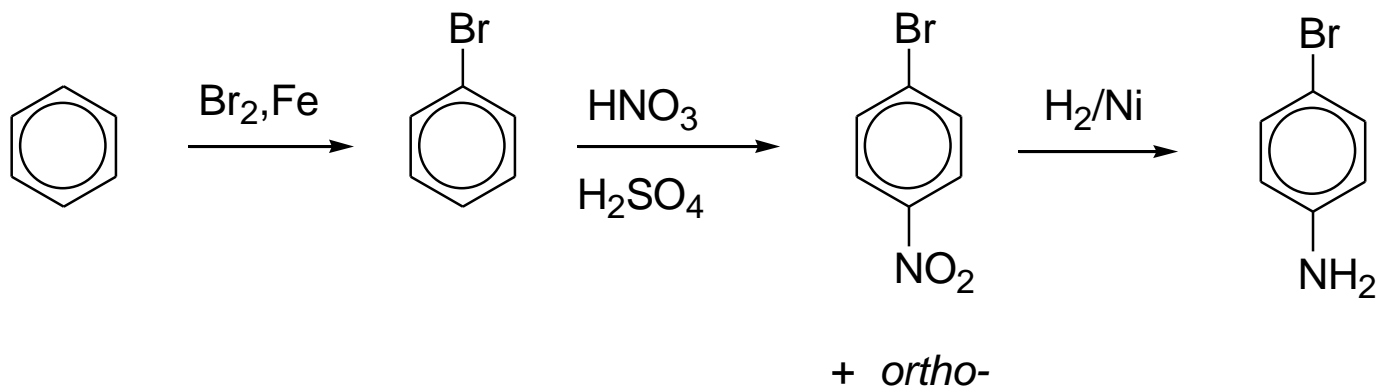


### c) halogenation



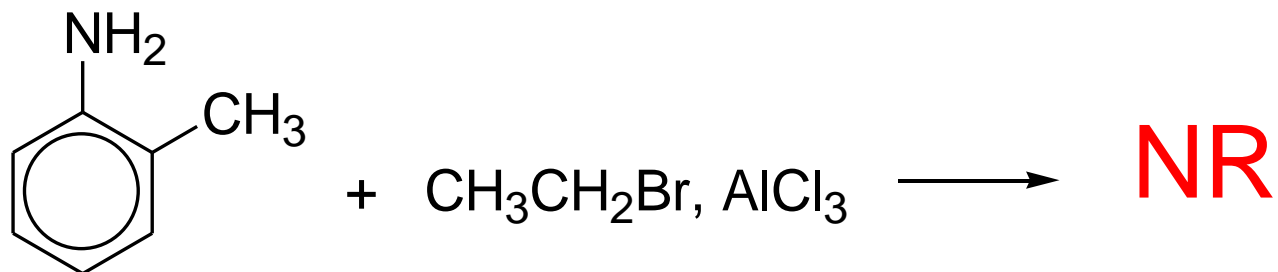
polyhalogenation!

no catalyst needed  
use polar solvent

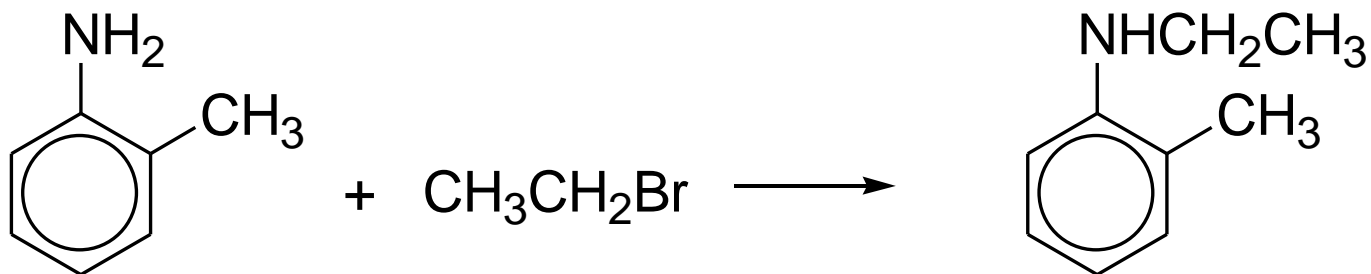


e) Friedel-Crafts alkylation

NR with  $\text{-NH}_2$ ,  $\text{-NHR}$ ,  $\text{-NR}_2$



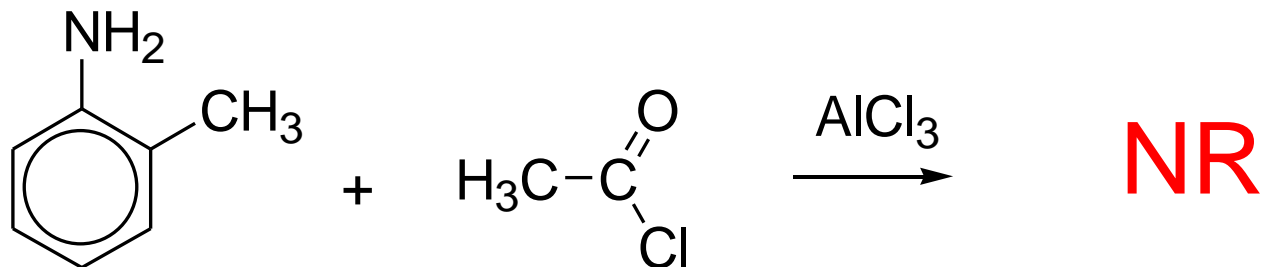
Do not confuse the above with the alkylation reaction:



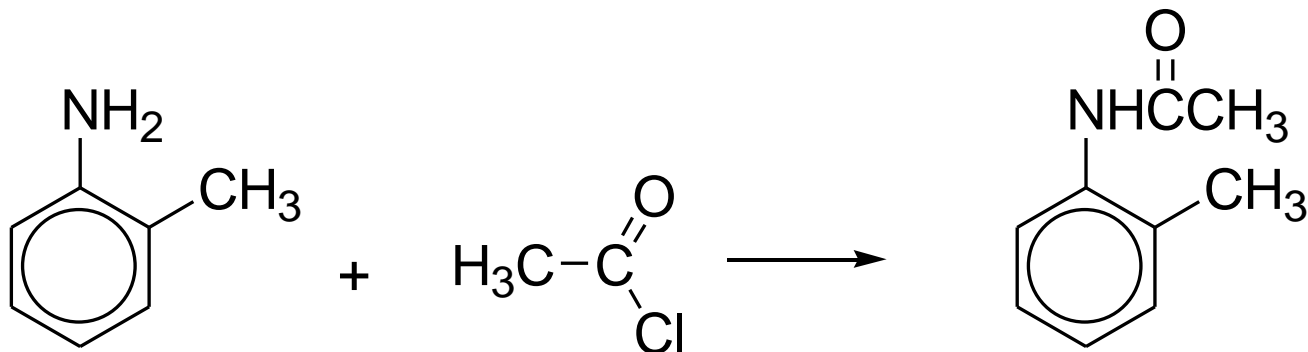


f) Friedel-Crafts acylation

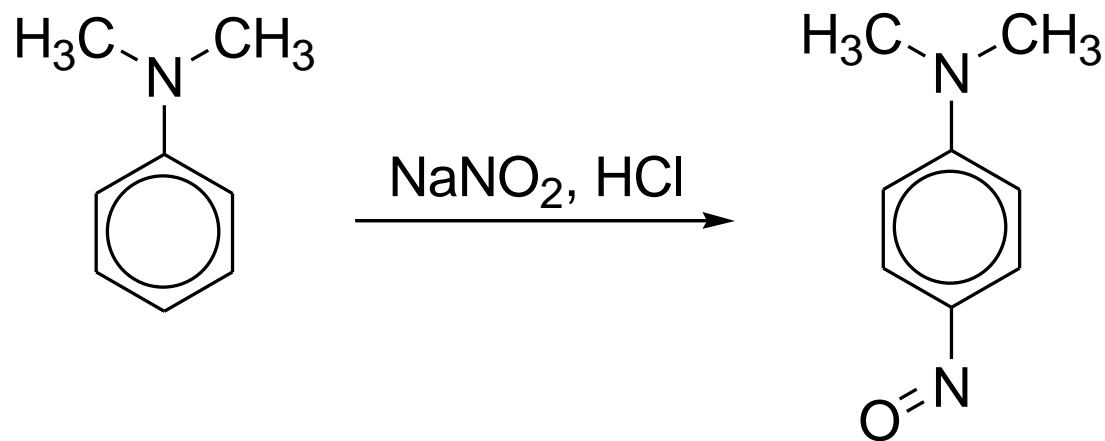
NR with  $\text{-NH}_2$ ,  $\text{-NHR}$ ,  $\text{-NR}_2$



Do not confuse the above with the formation of amides:



g) nitrosation



The ring is sufficiently activated towards EAS to react with the weak electrophile NO<sup>+</sup>

h) coupling with diazonium salts → azo dyes

