Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

CHEM 109

CHAPTER 8: AMINES

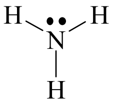
Learning Objectives

At the end of this chapter, students will able to:

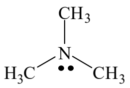
- Recognize and name amines.
- Predict the reactivity of amines as bases and nucleophiles
- Recognize the basic properties (structure, physical and chemical properties) of amines.
- know the different methods for the preparation of amines.
- Know the chemical reactions of amines.

Structure and Classification of Amines

- **Amines** are compounds that derived from ammonia by replacement of one, two, or three hydrogens by alkyl or aryl groups.



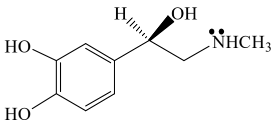
Ammonia



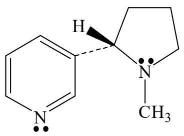
Trimethyl amine

Nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic

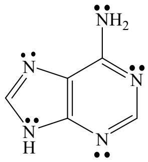
- Amines occur naturally in plants and animals.



Adrinaline
(Epinephrine)



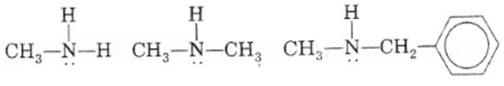
Nicotine



Adenine
(Vitamin B4)

Structure and Classification of Amines

- **Aliphatic amines** contain *only alkyl* groups bonded directly to the nitrogen atom.



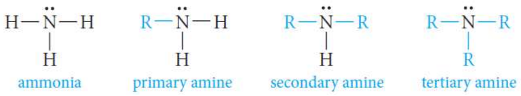
Aliphatic amines

- **Aromatic amines** are those in which one or more aryl groups are bonded directly to nitrogen.

Aromatic amines

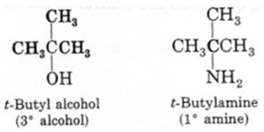
Classification and Structure of Amines

- The relation between **ammonia and amines** is illustrated by the following structures:



- **Amines** are classified as **primary**, **secondary**, **or tertiary**, *depending on whether one, two, or three organic groups are attached to the nitrogen*.

- **NOTE:**



t-Butyl alcohol (3° alcohol)

t-Butylamine (1° amine)

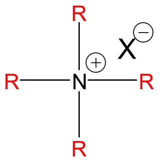
  - *t*-butyl alcohol is a tertiary alcohol (because three carbons are attached to the carbinol carbon).
  - *t*-butyl amine is a primary amine (because only one carbon is attached directly to the nitrogen atom).

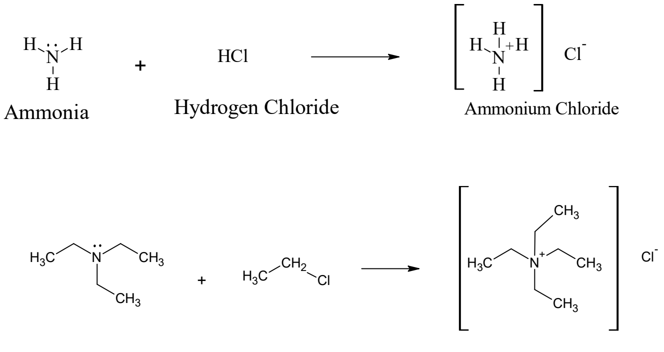
Classification and Structure of Amines

- **Quaternary Ammonium Ions:**

A nitrogen atom with four attached groups is positively charged

Compounds are quaternary ammonium salts





Tetraethyl Ammonium Chloride

Nomenclature of Amines

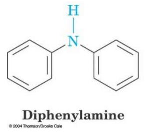
Common Names

Amines are named by specifying the alkyl groups attached to the nitrogen and adding the suffix –*amine* (*Alkylamine*).

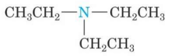
$CH_3CH_2NH_2$ ethylamine (primary)

$(CH_3CH_2)_2NH$ diethylamine (secondary)

$(CH_3CH_2)_3N$ triethylamine (tertiary)



Diphenylamine

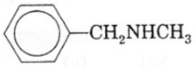


$$CH_3CH_2-\underset{\displaystyle CH_2CH_3}{\underset{|}{N}}-CH_2CH_3$$

Triethylamine

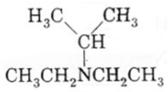
CH_3NH_2 Methylamine

$CH_3NHCH_2CH_3$ Ethylmethylamine



Benzylmethylamine

CH_3NHCH_3 Dimethylamine



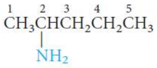
Diethylisopropylamine

IUPAC Names

Nomenclature of Amines

- The amino group, $-NH_2$, is named **as a substituent.**

$CH_3CH_2NH_2$ aminoethane

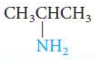


$$\overset{1}{C}H_3\overset{2}{C}H\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H_3 \quad (NH_2 \text{ on } C2)$$

2-aminopentane

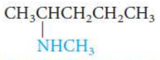
- Amines can be named as **alkanamines.**

$CH_3CH_2CH_2NH_2$ propanamine



$$\underset{\displaystyle NH_2}{CH_3\underset{|}{C}HCH_3}$$

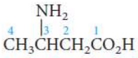
2-propanamine



$$CH_3\underset{\displaystyle NHCH_3}{\underset{|}{C}H}CH_2CH_2CH_3$$

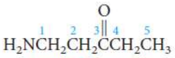
N-methyl-2-pentanamine

- When **other functional groups** are present, the amino group, $-NH_2$, is named as a substituent.



$$\overset{4}{C}H_3\overset{\displaystyle NH_2}{\overset{|}{\overset{3}{C}}}H\overset{2}{C}H_2\overset{1}{C}O_2H$$

3-aminobutanoic acid



$$H_2N\overset{1}{C}H_2\overset{2}{C}H_2\overset{O}{\overset{\|}{\overset{3}{C}}}\overset{4}{C}H_2\overset{5}{C}H_3$$

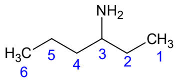
1-amino-3-pentanone

$CH_3NH\overset{2}{C}H_2\overset{1}{C}H_2OH$ 2-methylaminoethanol

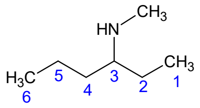
IUPAC Names

Nomenclature of Amines

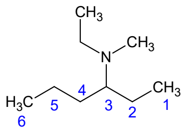
When different alkyl groups are attached to the nitrogen; they are named in alphabetical order



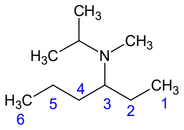
3-Hexanamine



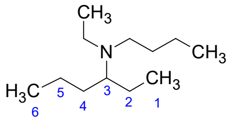
N-Methyl-3-hexanamine



N-Ethyl-N-methyl-3-hexanamine



N-Ethyl-N-isopropyl-3-hexanamine

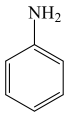


N-butyl-N-ethyl-3-hexanamine

IUPAC Names

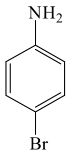
Nomenclature of Amines

- **Aromatic amines** are named as derivatives of aniline.
- In the CA system, aniline is called benzenamine.



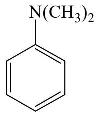
Aniline

(Benzenamine)



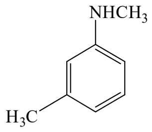
p-Bromoaniline

(4-Bromobenzenamine)



N,N-Dimethylaniline

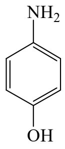
(4-Dimethylbenzenamine)



m-Methyl-N-methylaniline

OR: *N*-Methyl-*m*-toluidine

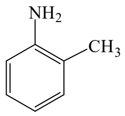
(N-methyl-3-methylbenzenamine)



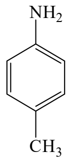
p-Aminophenol

p- Hydroxyaniline

(4-Aminophenol)



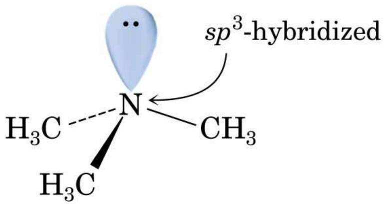
o-Toluidine



p-Toluidine

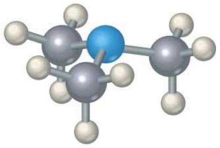
Structure and Bonding in Amines

Bonding to N is similar to that in ammonia: N is *sp*^{3}-hybridized C–N–C bond angles are close to 109° tetrahedral value



Trimethylamine

© 2004 Thomson/Brooks Cole



Physical Properties of Amines

Boiling Point

- **Methylamine and ethylamine are gases**, but primary amines with three or more carbons are liquids.
- **Primary amines** boil well above alkanes with comparable molecular weights, but below comparable alcohols.

  *Intermolecular N-H· · ·N hydrogen bonds are important and raise the boiling points of primary and secondary amines but are not as strong as the **O-H · · · · O** bonds of alcohols.*

  The reason for this is that nitrogen is not as electronegative as oxygen.

alkane	CH_3CH_3 (30) bp −88.6°C	$CH_3CH_2CH_3$ (44) bp −42.1°C
amine	CH_3NH_2 (31) bp −6.3°C	$CH_3CH_2NH_2$ (45) bp +16.6°C
alcohol	CH_3OH (32) bp +65.0°C	CH_3CH_2OH (46) bp +78.5°C

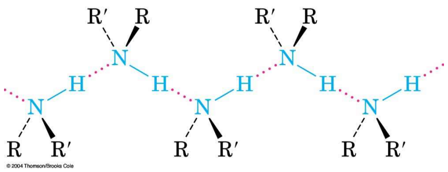
- **Tertiary amines** are also polar compounds, but because hydrogen is not bonded to nitrogen, these amines are incapable of intermolecular hydrogen bonding.

  Their boiling points are Lower than primary and secondary amines of identical molecular weights and Higher than those of alkanes of similar molecular weight.

Physical Properties of Amines

Solubility in Water

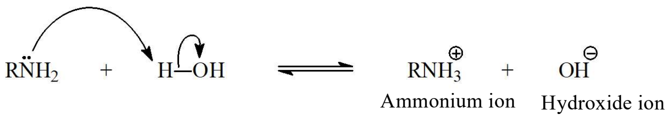
- **All** **three classes of amines** can form hydrogen bonds with the -OH group of water (that is, O-H· · ·N).
- **Primary and secondary amines** can also form hydrogen bonds with the oxygen atom in water: N-H· · ·O.
- **Amines** with up to six carbons show appreciable solubility in water.



© 2004 Thomson/Brooks Cole

The Basicity of Amines

- ○ **The** **unshared pair of electrons** on the nitrogen atom dominates the chemistry of amines.
- ○ Because of this electron pair, **amines are both basic and nucleophilic**.
- ○ Aqueous solutions of amines are basic because of the following equilibrium:



- ○ The most convenient way to measure the basicity of an amine (RNH_2) is to look at the acidity of the corresponding ammonium ion (RNH_3^+)

$$K_b = \frac{[RNH_3^{\oplus}]\,[OH^{\ominus}]}{[RNH_2]} \qquad pK_b = -\log K_b$$

- ○ Typical amines have K_b values = 10^{-3} to 10^{-4}

The Basicity of Amines

	K_b
Aliphatic amines	$10^{-3} – 10^{-4}$
Ammonia	1.8×10^{-5}
Aniline	10^{-9} or less

- Electron-donating groups increase the basicity of amines.
- Electron-withdrawing groups decrease their basicity.

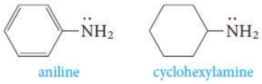
- Amines are stronger bases than alcohols, ethers, or water

The Basicity of Amines

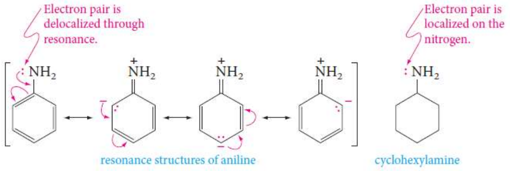
	Structure	Basicity	Acidity of conjugate acid
compound		pK_b	pK_a
Ammonia	NH_3	4.7	9.3
Primary Amines			
Methylamine	CH_3NH_2	3.4	10.6
Ethylamine	$CH_3CH_2NH_2$	3.2	10.8
Isopropylamine	$(CH_3)_2CHNH_2$	3.4	10.6
tert-Butylamine	$(CH_3)_3CNH_2$	3.6	10.4
Aniline	$C_6H_5NH_2$	9.4	4.6
Secondary amines			
Dimethylamine	(CH3)2NH	3.3	10.7
Diethylamine	(CH3CH2)2NH	2.9	11.1
N-Methylaniline	C6H5NHCH3	9.2	4.8
Tertiary amines			
Trimethylamine	(CH3)3N	4.3	9.7
Triethylamine	(CH3CH2)3N	3.2	10.8
N,N-Dimethylaniline	C6H5N(CH3)2	8.9	5.1

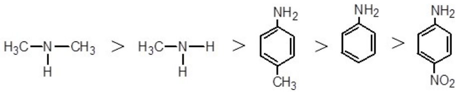
The Basicity of Amines

- **Aromatic amines are much weaker than aliphatic amines or ammonia.**
  - **Example:** aniline is less basic than cyclohexylamine.



The reason is the resonance delocalization of the unshared electron pair that is possible in aniline, but not in cyclohexylamine:

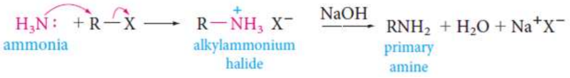




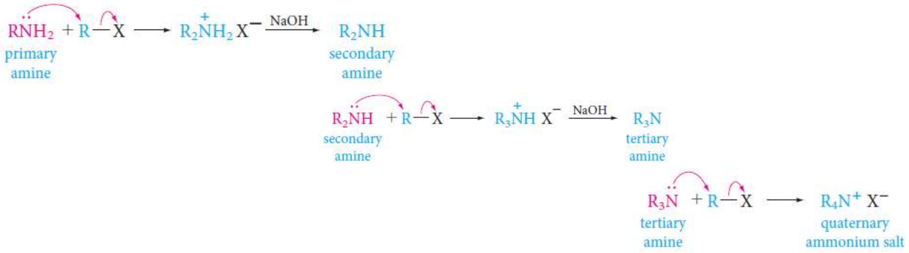
Preparation of Amines

1) Alkylation of Ammonia

- **Ammonia** reacts with alkyl halides to give amines via a two-step process.
  - *The first step is a nucleophilic substitution reaction.*
  - *The free amine can then be obtained from its salt by treatment with a strong base*


$$H_3\ddot{N}: + R{-}X \longrightarrow R{-}\overset{+}{N}H_3\ X^- \xrightarrow{NaOH} RNH_2 + H_2O + Na^+X^-$$

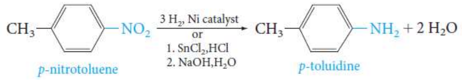
- **Primary, secondary, and tertiary amines** can be similarly alkylated.


$$R\ddot{N}H_2 + R{-}X \longrightarrow R_2\overset{+}{N}H_2\ X^- \xrightarrow{NaOH} R_2NH$$
$$R_2\ddot{N}H + R{-}X \longrightarrow R_3\overset{+}{N}H\ X^- \xrightarrow{NaOH} R_3N$$
$$R_3\ddot{N} + R{-}X \longrightarrow R_4N^+\ X^-$$

Preparation of Amines

2) Reduction of Nitro Groups

- The best route to **aromatic primary amines** is by reduction of the corresponding nitro compounds.



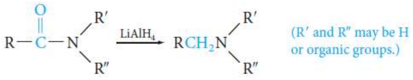
3) Reduction of Nitriles

- **Reduction of nitriles** (cyanides) gives primary amines.

$$R-C\equiv N \xrightarrow[\text{or } H_2,\ Ni]{LiAlH_4} RCH_2NH_2$$

4) Reduction of Amides

- **Amides** can be reduced to amines with lithium aluminum hydride.



(R′ and R″ may be H or organic groups.)

Reactions of Amines

1) Reactions with Acids: Salt Formation

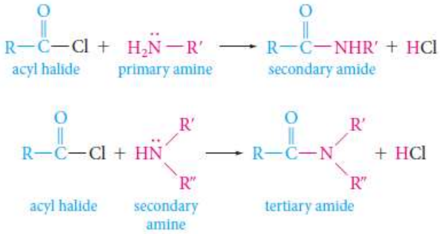
Amines react with strong acids to form alkylammonium salts.

$$R-\ddot{N}H_2 + HCl \longrightarrow R\overset{+}{N}H_3\ \ Cl^-$$

primary amine — an alkylammonium chloride

2) Acylation of Amines: Amides Formation

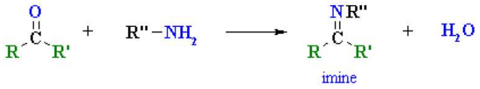
Primary and secondary amines react with acyl halides to form amides.



Reactions of Amines

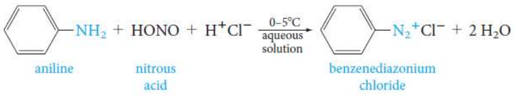
3) Imines Formation

Primary amines, R-NH_2 or ArNH_2, undergo nucleophilic addition with aldehydes or ketones in an acidic buffer to give substituted imines.



4) Aromatic Diazonium Salts

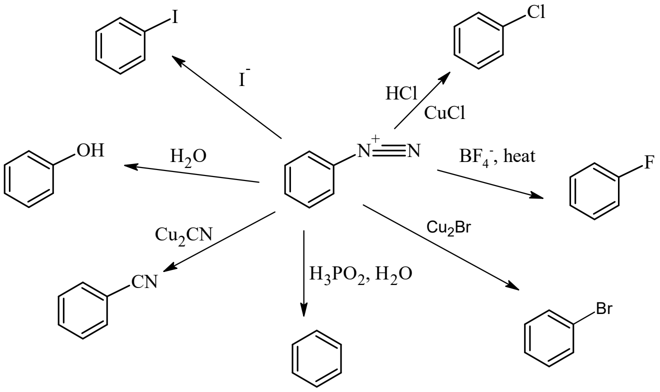
- Primary aromatic amines react with nitrous acid at 0°C to yield aryldiazonium ions.
  The process is called ***diazotization***.



Reactions of Amines

5) Aromatic Diazonium Salts

- They are useful in synthesis because the diazonio groum (-N_2^+) can be replaced by nucleophiles; the other product is nitrogen gas.



Uses of Amines

- Amines are largely used in pharmaceutical industry.
- Morphine and Demerol are used as analgesics that are pain killers.
- Novocaine is used as anesthetic and Ephedra is a very common decongestant.
- We use tetramethyl ammonium iodide for disinfecting drinking water.
- They find large applications in man-made dyes.