Structure & Classification

Classification

- 1°, 2°, or 3° amines: Amines in which 1, 2, or 3 hydrogens of NH₃ are replaced by alkyl or aryl groups.

\[ \text{NH}_3 \quad \text{CH}_3-\text{NH}_2 \quad \text{CH}_3-\text{NH} \quad \text{CH}_3-\text{N}==\text{CH}_3 \]

Ammonia  Methylamine  Dimethylamine  Trimethylamine
(a 1° amine) (a 2° amine) (a 3° amine)

Table of Contents

1. Structure & Classification
2. Nomenclature
3. Physical Properties and Structure of Amines
4. Basicity of Amines: Amine Salts
5. PKa and pKb
6. Reactions with acids
7. Amines as nucleophiles
Structure & Classification

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

![Pyridine, Piperidine, Pyrrole, Pyridine](images)

- Example: Classify each amino group by type.

![Structures of (S)-Cocaine, (S)-Nicotine, and (S)-Cocaine](images)

**Aliphatic Amines**: Replace the suffix of the parent alkane by -amine.

- Butanamine
- (S)-1-Phenylethanamine
- 1,6-Hexanediamine

Nomenclature
- The IUPAC system retains the common name aniline.

- Aniline
- 4-Nitroaniline
- 4-Methylaniline
- 3-Methoxyaniline

- NH₂
- NH₂
- NH₂
- NH₂
- NH₂
- NO₂
- CH₃
- OCH₃
Nomenclature
• Among the various functional groups discussed in the text, -NH₂ group has one of the lowest priorities.

H₂N−CH₂OH  2-Aminoethanol
H₂N−COOH  2-Aminobenzoic acid

Nomenclature
• Common names for most aliphatic amines are derived by listing the alkyl groups bonded to nitrogen in one word ending with the suffix -amine.

CH₃NH₂  Methylamine
 tert-Butylamine
CH₃(CH₂)₃NH₂  1-Methylcyclopentylamine
CH₃(CH₂)₃N⁺H⁻  Triethylammonium

Nomenclature
• When four groups are bonded to the nitrogen atom, we name the compound as a salt of the corresponding amine.

(CH₃)₄N⁺Cl⁻  Tetramethylammonium chloride
CH₃(CH₂)₃CH₂N⁺H⁻  Hexadecylpyridinium chloride
CH₃(CH₂)₃N⁺(CH₃)₃  Benzyltrimethylammonium chloride

Physical Properties
• Amines are polar compounds, and both 1° and 2° amines form intermolecular hydrogen bonds.

- 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).

<table>
<thead>
<tr>
<th></th>
<th>CH₃NH₂</th>
<th>CH₃OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>molecular weight (g/mol)</td>
<td>31.1</td>
<td>32.0</td>
</tr>
<tr>
<td>boiling point (°C)</td>
<td>-6.3</td>
<td>65.0</td>
</tr>
</tbody>
</table>
Basicity

• All amines are weak bases, and aqueous solutions of amines are basic.

\[
\text{CH}_3\text{NH}_2 + \text{H}_2\text{O} \rightleftharpoons \text{CH}_3\text{NH}_3^+ + \text{OH}^-
\]

\[
K_{eq} = \frac{[\text{CH}_3\text{NH}_3^+][\text{OH}^-]}{[\text{CH}_3\text{NH}_2][\text{H}_2\text{O}]}
\]

Methylation
Methylammonium hydroxide

Basicity

• It is also common to discuss the basicity of amines by reference to the ionization constant \(K_a\) of its conjugate acid.

\[
\text{CH}_3\text{NH}_3^+ + \text{H}_2\text{O} \rightleftharpoons \text{CH}_3\text{NH}_2 + \text{H}_3\text{O}^+
\]

\[
K_a = \frac{[\text{CH}_3\text{NH}_2][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{NH}_3^+]}
\]

\[pK_a = 10.64\]

– For any acid-conjugate base pair.

\[pK_a + pK_b = 14.00\]

Basicity

• Using values of \(pK_a\), we can predict the position of equilibrium in acid-base reactions.

\[\text{CH}_3\text{NH}_2 + \text{CH}_3\text{COOH} \rightleftharpoons \text{CH}_3\text{NH}_3^+ + \text{CH}_3\text{COO}^-\]

\[pK_a = 4.76\]

Stronger

\[pK_b = 10.64\]

Stronger

Weaker

Weaker

Acid

Base

Acetic acid is the stronger acid and, therefore, the position of this equilibrium lies to the right.

Basicity

• Aliphatic amines have about the same base strength, \(pK_b\) 3.0 – 4.0 and are slightly stronger bases than \(\text{NH}_3\).
Basicity

Aromatic amines are considerably weaker bases than aliphatic amines.

- Electron-withdrawing groups, such as halogen, nitro, and carbonyl, decrease the basicity of aromatic amines by decreasing the availability of the electron pair on nitrogen.

- Example: Select the stronger base in each pair of amines.

Basicity

Aromatic amines are weaker bases than aliphatic amines because the resonance stabilization of the free base is lost on protonation.

Two Kekulé structures

Interaction of the electron pair on nitrogen with the π 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.
Guanidine

- Guanidine ($pK_b 0.4$) is the strongest base among neutral organic compounds.

$$\text{H}_2\text{N}↔\text{C}↔\text{NH}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{N}↔\text{C}↔\text{NH}_2 + \text{OH}^- \quad pK_b = 0.4$$

Guanidine Guanidinium ion

- Its basicity is due to the resonance delocalization of the positive charge over the three nitrogen atoms.

$$\text{H}_2\text{N}↔\text{C}↔\text{NH}_2 \leftrightarrow \text{H}_2\text{N}↔\text{C}↔\text{NH}_2 \leftrightarrow \text{H}_2\text{N}↔\text{C}↔\text{NH}_2$$

Three equivalent contributing structures

Reaction with Acids

- All amines, whether soluble or insoluble in water, react quantitatively with strong acids to form water-soluble salts.

Amines as Nucleophiles

- Reaction of an amine with an alkyl halide can be used to form a new covalent bond.

**Step 1:** Reaction of a nucleophile with an electrophile to form a new covalent bond.

(a nucleophile) (an electrophile)

Amines as Nucleophiles

- **Step 2:** Take a proton away. Converts the amine salt to a free amine.

(unreacted starting material)