Amine Molecules are Weak Bases

- Amines are relatives of ammonia, $\text{NH}_3$, in which the hydrogen atoms on nitrogen have been replaced by one or more non-carbonyl substituent groups.
- Aliphatic amines in which alkyl groups replace hydrogen are slightly more basic than ammonia.
- Aromatic amines in which one or more of the substituent groups is an arene, are considerably less basic than ammonia.
- Heterocyclic amines have the nitrogen atom within a ring. The ring may be aliphatic or aromatic.
- Heterocyclic aliphatic amines are stronger bases than ammonia.
- Heterocyclic aromatic amines are considerably weaker bases than ammonia. In these rings the nitrogen atom contributes one or two electrons to the aromatic sextet of electrons.

Aliphatic & Aromatic Amines

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Aromatic versus Aliphatic Amines

- Aliphatic Amines have the amino-group attached by tetrahedral carbon:
  - $\text{NH}_3$ and $\text{C}_2\text{H}_5\text{NH}$: primary, first order
  - $\text{C}_2\text{H}_5\text{CH}_2\text{NH}$ and $\text{C}_2\text{H}_5\text{N}\text{H}_2$: secondary, second order
  - $\text{C}_2\text{H}_5\text{NCH}_3$: tertiary, third order

- Aromatic amines have the amino-group bonded to a benzene ring:
  - Aniline, $\text{C}_6\text{H}_4\text{NH}_2$,
  - N-methylaniline, $\text{C}_6\text{H}_4\text{NHCH}_3$,
  - N,N-dimethylaniline, $\text{C}_6\text{H}_4\text{N(CH}_3)_2$.

- Aliphatic amines can have aromatic rings as long as the nitrogen is attached by tetrahedral carbon.
Heterocyclic Aliphatic/Aromatic Amines

Heterocyclic aliphatic amines – the nitrogen is incorporated into a ring and is connected by two tetrahedral carbons.

\[
\begin{align*}
&\text{N-methylpyrrolidine} \\
&\text{piperidine} \\
&\text{3* heterocyclic aliphatic amine}
\end{align*}
\]

Heterocyclic aromatic amines – the nitrogen is incorporated into an aromatic ring – N contributes to the aromatic sextet.

\[
\begin{align*}
&\text{pyridine} \\
&\text{pyrimidine} \\
&\text{imidazole} \\
&\text{purine}
\end{align*}
\]

Naming of Amines

- IUPAC names for aliphatic amines follow that for alcohols. Drop the final -e of the parent alkane and replace it with -amine.
- Use a number to locate the amino group on the parent chain.
- Name unsymmetrical secondary and tertiary amines as N-substituted primary amines. In this case take the largest group bonded to nitrogen as the parent amine.
- Name the smaller group(s) bonded to nitrogen, and show that their location is bonded to nitrogen by using the prefix N- before the listing of that substituent.

\[
\begin{align*}
&\text{N, N-dimethylaniline} \\
&\text{propanamine} \\
&\text{N-methylpropanamine}
\end{align*}
\]

Naming of Amines

- IUPAC nomenclature retains the common name aniline for \(\text{C}_6\text{H}_5\text{NH}_2\), the simplest aromatic amine.
- Name simple derivatives of aniline by using locator numbers starting with the amino group, or locate substituents by using the prefixes ortho (o), meta (m), and para (p).
- Several derivatives of aniline have common names that are still widely used; among them is toluidine.
- If another substituent overrides with a special name locate the amine substituent with a locator number starting at the other substituent.

\[
\begin{align*}
&\text{aniline} \\
&\text{2-methylaniline} \\
&\text{2-aminobenzoic acid}
\end{align*}
\]
Naming of Amines

Common Names

- For most aliphatic amines, list the groups bonded to nitrogen in alphabetical order in one word ending in the suffix –amine.

- Because amines are bases they react with strong acids to form ammonium salts. In these salts nitrogen has four bonds, has a positive charge and is associated with an anion.

Properties of Amines

- Amines are polar, hydrogen bond with water, and 1° and 2° with each other, but more weakly than alcohols.
- Amines have lower boiling points than alcohols of similar molecular weight, they are also soluble in water if the substituent group part is not too large and non-polar. C₆-C₈ = miscible to slightly soluble, C₉ and higher are insoluble.
- Amines are basic in water, the pH will go to higher values.
- Amines readily react with acid. The resulting ammonium ion are much more soluble than the parent amines.

Properties of Amines

- The N-H---N hydrogen bond is weaker than an O-H---O hydrogen bond 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).
- The effect of hydrogen bonding between molecules of comparable molecular weight can be seen by comparing the boiling points of ethane, methanamine, and methanol.

<table>
<thead>
<tr>
<th></th>
<th>CH₃CH₃</th>
<th>CH₃NH₂</th>
<th>CH₃OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>MW (amu)</td>
<td>30.1</td>
<td>31.1</td>
<td>32.0</td>
</tr>
<tr>
<td>bp (°C)</td>
<td>-88.6</td>
<td>-6.3</td>
<td>65.0</td>
</tr>
</tbody>
</table>

- Like ammonia, low-molecular-weight amines have very sharp, penetrating odors; for example, rotting fish = trimethylamine.
Hydrogen Bonds – Amines in Water

Hydrogen Bonds – Pure Amines – Except 3°

Can You Name these Amines?

Classify them as aromatic, aliphatic, and as primary, secondary or tertiary.
**Amines Are Relatives of Ammonia**

Amines are basic: (Aliphatic amines about as basic as ammonia)

\[
\begin{align*}
\text{Primary} & : \text{NH}_3 \\
\text{Secondary} & : \text{NH}_2^+ \\
\text{Tertiary} & : \text{NH}_3^+ \\
\end{align*}
\]

And make ammonium salts in acidic solution.

Note: N has 3 bonds in amines, but 4 bonds in ammonium ions.

---

**Ammonium Ions React with Base**

Ammonium salts are weakly acidic:

\[
\begin{align*}
\text{Primary} & : \text{NH}_4^+ + \text{OH}^- \rightarrow \text{NH}_3 + \text{H}_2\text{O} \\
\text{Secondary} & : \text{NH}_2^+ + \text{OH}^- \rightarrow \text{NH}_3 + \text{H}_2\text{O} \\
\text{Tertiary} & : \text{NH}_3^+ + \text{OH}^- \rightarrow \text{NH}_3 + \text{H}_2\text{O} \\
\end{align*}
\]

And react with hydroxide ion to regenerate the original amine + water.

---

**Reaction of Amines with Water**

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

**Reaction of Ammonium Ions with Water**

\[
\text{NH}_4^+ + \text{H}_2\text{O} \rightleftharpoons \text{NH}_3 + \text{H}_2\text{O}^-
\]
What is the form of amines in blood plasma?

pH of blood is 7.4, [OH\(^{-}\)] = 2.5 \times 10^{-7}

Ethylamine: \(K_b = 4.3 \times 10^{-4}\) = \[
\frac{[\text{CH}_3\text{CH}_2\text{NH}_3^+] [\text{OH}^-]}{[\text{CH}_3\text{CH}_2\text{NH}_2]}\]

\[
\frac{K_b}{[\text{OH}^-]} = \frac{[\text{CH}_3\text{CH}_2\text{NH}_3^+]}{[\text{CH}_3\text{CH}_2\text{NH}_2]} = \frac{4.3 \times 10^{-4}}{2.5 \times 10^{-7}} = 1720
\]

An aliphatic amine is mostly in the ammonium form in blood!

Pyridine: \(K_b = 1.5 \times 10^{-9}\) = \[
\frac{[\text{C}_5\text{H}_5\text{NH}_3^+] [\text{OH}^-]}{[\text{C}_5\text{H}_5\text{N}]}\]

\[
\frac{K_b}{[\text{OH}^-]} = \frac{[\text{C}_5\text{H}_5\text{NH}_3^+]}{[\text{C}_5\text{H}_5\text{NH}_2]} = \frac{1.5 \times 10^{-9}}{2.5 \times 10^{-7}} = 0.0060
\]

An aromatic amine is mostly in the amine form in blood!

Carboxylic Acids & Amines Give Salts

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_3^+ + \text{O}^2^- &\xrightarrow{10\%} \text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_3^- + \text{O}^2^- \\
\text{Amine} &\quad \text{Carboxylic Acid} &\quad \text{Ammonium Ion} &\quad \text{Carboxylate Anion}
\end{align*}
\]

Aminoacids exist \textit{in vivo} only in their ionized form!

What Products are Formed?

If No Reaction write – NR

\[\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_3^+ + \text{OH}^- &\rightarrow \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2 + \text{Na}^+ &\rightarrow \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_3^+ + \text{Cl}^- &\rightarrow \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2 + \text{HCl} &\rightarrow
\end{align*}\]