BIO-ORGANIC CHEMISTRY
(Organic Chemistry for Biology Students)
(SQBS 1603)

Organic Compounds Containing Nitrogen

Dr Nik Ahmad Nizam Bin Nik Malek,
BSc (Ind. Chem.)(UTM), MSc (Chem)(UTM), PhD (Chem)(UTM), A.M.I.C
Senior Lecturer,
Department of Biotechnology and Medical Engineering
Faculty of Biosciences and Medical Engineering
Nitrogen-based functional group

- **Amine**: The amino group
  - $\text{RNH}_2$
  - $\text{R}_2\text{NH}$
  - $\text{R}_3\text{N}$

- **Amide**: The amide group
  - $\text{RCONH}_2$
  - $\text{RCONHR}$
  - $\text{RCONR}_2$
Amines

• The amino group
• Generic formula:
  – \( R\text{NH}_2 \)
  – \( R_2\text{NH} \)
  – \( R_3\text{N} \)
Naming amines

IUPAC name

\[ \text{Pentanamine} \]

5 C \( \rightarrow \) pentane
Naming amines

5 C → pentane → pentanamine

Methyl at position 3

3-methyl-pentanamine
IUPAC or systematic names of secondary and tertiary amines

- Secondary (2°) and tertiary (3°) amines having identical alkyl groups are named by using the prefix di- or tri- with the name of the primary amine.

- Example:

![Dipropyl-amine](image)

![Triethyl-amine](image)
Naming amines

• IUPAC or systematic names of secondary and tertiary amines
  – Secondary (2°) and tertiary (3°) amines having more than one kind of alkyl group are named as *N-substituted* primary amines.
Naming amines

Name the following 2° amine: \((\text{CH}_3)_2\text{CHNHCH}_3\)

1) Name the longest alkyl chain bonded to the N atom as the parent amine.
   - 3 C \(\rightarrow\) propanamine
   - Since the N atom bonded to the middle C (at position 2) \(\rightarrow\) 2-propanamine
Naming amines

2) Name the other groups on the N atom as alkyl group

- alphabetize the names when there is more than one substituent
- Precede each name with the prefix \( N- \).

\[
\text{N-methyl-2-propanamine}
\]
Physical properties of amines

• Physical property of primary amine

\[ \text{N (nitrogen) } \rightarrow \text{ electronegative atom } \rightarrow \text{ polar molecule} \]

Hydrogen bonding?
Physical properties of amines

- Hydrogen bonding between molecules of same compound.
- Up to 3 hydrogen bonds can occur for primary amine.
Physical properties of amines

- Hydrogen bonding with water.
- Up to 3 hydrogen bonds can occur for primary amine.
Physical properties of amines

- Secondary amine

- Hydrogen bonding between molecules of same compound.

- Up to 2 hydrogen bonds can occur for secondary amine.
Physical properties of amines

- Secondary amine

- Hydrogen bonding with water.
- Up to 2 hydrogen bonds can occur for secondary amine.
Physical properties of amines

- Tertiary amine

- No hydrogen bonding between molecules of same compound for tertiary amine.
Physical properties of amines

- Hydrogen bonding with water.
- Only 1 hydrogen bonds can occur for tertiary amine.
Physical properties of amines

- Comparison with other organic compounds – alcohol

Two lone pair can participate in 2 hydrogen bonds

One lone pair participates in only one hydrogen bond

Results:
- amines have lower melting and boiling points than alcohol.
The general rule

- For compounds of comparable size
  - The stronger the intermolecular forces (forces between molecules of same compounds) → the higher the boiling points.

- Compounds that can hydrogen bond have higher boiling points than compounds that are polar but cannot hydrogen bond.

- Polar compounds have higher boiling points than nonpolar compounds.
Physical properties of amines

• Which compound has the higher boiling point?

Butane
Methoxy-ethane
Ethyl-methyl-amine
Amines as bases

- Amines are proton acceptor

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

ammonia

\[ \text{RNH}_2 + \text{H}_2\text{O} \rightarrow \text{RNH}_3^+ + \text{H}_2\text{O} \]

primary amine
Reaction of amines with acids

- Amines react with acids such as HCl to form water-soluble salts.
- Amine gains a proton to form its conjugate acid (ammonium cation).
- A proton is removed from the acid to form its conjugate base.
- Example:

\[
\text{H}_3\text{C} \text{N} \text{CH}_3 + \text{H-Cl} \rightleftharpoons \text{H}_3\text{C} \text{N}^+ \text{CH}_2 \text{CH}_3 + \text{Cl}^-
\]
Amides

• The amide group

• Generic formula:
  – RCONH₂
  – RCONHR
  – RCONR₂
Amides

• Amide group closely resembles the carboxyl group of carboxylic acid
Amides

- Primary, secondary and tertiary amide
Naming amides

- In the IUPAC system, amides are identified by the suffix -amide.

- If primary amide
  - Replacing -oic acid ending (or -ic acid ending of a common name) with the suffix -amide
  - Examples
Naming amides

• Secondary (2°) and tertiary (3°) amides.
  – Acyl group: attach to carbonyl group.
  – Alkyl group: attach to N.
Naming amides

5 C → pentane → pentanamide

pentanamide

Primary (1°) amine
Naming amides

5 C $\rightarrow$ pentane $\rightarrow$ pentanamide

Methyl

Secondary (2°) amine

N-methylpentanamide
Naming amides

5 C → pentane → pentanamide

N,N-dimethylpentanamide
Physical properties of amides

• primary amide

N (nitrogen) and O (oxygen) $\rightarrow$ electronegative atom $\rightarrow$ polar molecule

Hydrogen bonding?
Physical properties of amides

- Hydrogen bonding between molecules of same compound.
- Up to 4 hydrogen bonds can occur for primary amide.
Physical properties of amides

- Hydrogen bonding between molecules of same compound.
- Up to 3 hydrogen bonds can occur for secondary amide.
Physical properties of amides

Tertiary amide

- No hydrogen bonding between molecules of same compound for tertiary amide.
Physical properties of amides

• Hydrogen bonding with water?
Physical properties of amides

- Hydrogen bonding with water.
- Up to 5 hydrogen bonds can occur for primary amide.
Physical properties of amides

- Hydrogen bonding with water.
- Up to 4 hydrogen bonds can occur for secondary amide.
Physical properties of amides

- Tertiary amide

- Hydrogen bonding with water.
- Up to 3 hydrogen bonds can occur for tertiary amide.
Formation of Amide

- Heating a carboxylic acid (RCOOH) with ammonia (NH$_3$) or an amine (R’NH$_2$ or R’$_2$NH) forms an amide.

\[
\text{Carboxylic acid} \quad + \quad \text{NH}_3 \quad \xrightarrow{\Delta} \quad \text{amide} \\
\text{Carboxylic acid} \quad + \quad \text{R’NH}_2 \quad \xrightarrow{\Delta} \quad \text{amide}
\]
Formation of Amide

- Reaction of RCOOH with NH₃ forms a 1° amide (RCONH₂)

\[
\begin{align*}
\text{H}_3\text{C}&-\text{C}-\text{OH} & + & \text{H-NH}_2 & \overset{\Delta}{\longrightarrow} & \text{H}_3\text{C}&-\text{C}&-\text{NH}_2 \\
\text{Acetic acid} & & & \text{Ammonia} & & \text{Acetamide} & \text{1° amide} & \text{H-OH}
\end{align*}
\]
Formation of Amide

- Reaction of RCOOH with R’NH₂ forms a 2° amide (RCONHR’)

Acetic acid + Methylamine $\xrightarrow{\Delta}$ N-Methyl-acetamide

$\text{H}_3\text{C} - \text{C} - \text{OH}$

$\text{H} - \text{N} - \text{CH}_3$

$\text{H}_3\text{C} - \text{C} - \text{NH}_2$

$\text{H}_3\text{C} - \text{C} - \text{NH}_2$
Formation of Amide

- Reaction of RCOOH with R’₂NH forms a 3° amide (RCONR’₂)

\[
\text{Acetic acid} + \text{Dimethyl-amine} \xrightarrow{\Delta} \text{N,N-Dimethyl-acetamide} + \text{H-OH}
\]

3° amide
Hydrolysis of Amide

• Treatment of an amide (RCONHR') with water in the presence of an acid catalyst (HCl) forms
  – a carboxylic acid (RCOOH)
  – An amine salts

\[
\text{H}_3\text{CH}_2\text{C} \quad \text{C} \quad \text{C} \quad \text{N} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{CH}_2\text{CH}_3 \quad \text{H} \quad \text{O} \quad \text{C} \quad \text{O} \\
\text{H}_3\text{CH}_2\text{C} \quad \text{C} \quad \text{O} \quad \text{H} \\
\text{H}_3\text{CH}_2\text{C} \quad \text{C} \quad \text{O} \quad \text{H} \quad \text{H} \quad \text{N} \quad \text{H} \quad \text{CH}_2\text{CH}_3 \quad \text{Cl}^-
\]

\[\text{N-Ethyl-propionamide} \quad \text{Propionic acid} \quad \text{Ethyl-ammonium; chloride}\]
Hydrolysis of Amide

- Amides are hydrolyzed in aqueous base to form
  - carboxylate anions
  - amines

\[ \text{H}_3\text{CCH}_2\text{C} \begin{array}{c} \text{C} \hline \text{NH} \end{array} \text{CH}_2\text{CH}_3 + \text{H-OH} \xrightarrow{\text{NaOH}} \text{H}_3\text{CCH}_2\text{C} \begin{array}{c} \text{C} \hline \text{O}^{-} \end{array} \text{Na}^+ + \text{H-} \begin{array}{c} \text{N} \hline \text{CH}_2\text{CH}_3 \end{array} \text{Ethylamine} \]

\( \text{N-Ethyl-propionamide} \)

\( \text{Sodium; propionate carboxylate anion} \)
REFERENCES


Dr Nik Ahmad Nizam Bin Nik Malek,
BSc (Ind. Chem.)(UTM), MSc (Chem)(UTM), PhD (Chem)(UTM), A.M.I.C
Senior Lecturer,
Department of Biotechnology and Medical Engineering,
Faculty of Biosciences and Medical Engineering,
Universiti Teknologi Malaysia.
Email: niknizam@fbb.utm.my, niknizam@utm.my
Website: http://www.staff.blog.utm.my/niknizam/