EUNOIA JUNIOR COLLEGE H2 CHEMISTRY (9729) ORGANIC CHEMISTRY

TEACHERS' COPY (2018 JC2)

NITROGEN COMPOUNDS

Name:

Civics Group: _____

Learning Outcomes

At the end of the lectures, you should be able to:

- (a) describe the formation of amines as exemplified by ethylamine (through amide and nitrile reduction) and by phenylamine (through the reduction of nitrobenzene)
- (b) describe the reaction of amines in the formation of salts
- (c) describe and explain the basicity of primary, secondary and tertiary amines in the gaseous phase (interpret as Lewis bases)
- (d) explain the relative basicities of ammonia, ethylamine and phenylamine in aqueous medium, in terms of their structures
- (e) describe the reaction of phenylamine with aqueous bromine
- (f) describe the formation of amides from the condensation reaction between RNH₂ and R'COCl
- (g) describe the acid/base properties of amino acids and the formation of zwitterions
- (h) describe the formation of peptide (amide) bonds between α -amino acids and, hence, explain protein formation
- (i) describe the hydrolysis of proteins

Recommended References:

- 1. A-Level Chemistry (4th ed), E.N. Ramsden
- 2. Organic Chemistry (6th ed), R.T. Morrison, R.N. Boyd
- 3. Organic Chemistry Structure and Reactivity (4th ed), S.N. Eğe
- 4. Organic Chemistry (5th ed), F.A. Carey
- 5. <u>http://www.chemguide.co.uk/organicprops/aminemenu.html</u>

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1 Introduction on Amines

- 1.1 Structure & Classification
- General formula of primary (1°) amines : RNH₂
- Functional Group : primary or secondary or tertiary amine
- Amines may be classified as primary (1°), secondary (2°) or tertiary (3°) depending on the <u>number of alkyl/aryl groups attached to the N atom</u>.



1.2 Nomenclature

- Many **aliphatic amines** are named by specifying the alkyl groups attached to the N atom, following by the ending **-amine**.
- Many **aromatic amines** are named as derivatives of the simplest aromatic amine, e.g. *phenylamine* (aniline).

Examples:

	Alkylamines	Arylamines
CH ₃ CH ₂ NH ₂ ethylamine	CH ₃ CHCH ₂ CH ₂ CH ₃ I NH ₂ 2-pentylamine	phenylamine
Cyclohexylamine	(phenylmethyl)amine / benzylamine	NH ₂ Br CH ₂ CH ₃ 5-bromo-2-ethylphenylamine
H ^{W, N} CH ₃ CH ₃	$CH_3 \overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{\overset{$	

- For polyfunctional amines with other functional groups of higher priority,
 - treat the amine group as a substituent and add the prefix *-amino* to the parent compound
- E.g.

H₂NCH₂COOH

2-aminoethanoic acid

4-aminophenol

- 1.3 Physical Properties of Amines
- (a) Boiling Point
 - Amines have **higher boiling points** than hydrocarbons with similar *M*_r due to **stronger intermolecular hydrogen bonding**.



IIIIIIIII Hydrogen bonds

 However, amines have <u>lower</u> boiling points than <u>alcohols</u> of similar M_r due to the <u>intermolecular hydrogen bonds</u> in amines being <u>weaker</u> than those in alcohols since the <u>N-H bond is less polar than O-H bond</u>.

Compound	Mr	b.p./ °C
CH ₃ CH ₂ CH ₂ NH ₂ (amine)	59	48.6
CH ₃ CH ₂ CH ₂ OH (alcohol)	60	97

Quick Check

Arrange the following compounds in order of increasing boiling points.

Compound	Mr
(CH ₃) ₃ N	59
(CH ₃) ₃ CH	58
CH ₃ CH ₂ CH ₂ NH ₂	59

Answer: $(CH_3)_3CH < (CH_3)_3N < CH_3CH_2CH_2NH_2$

Compound	Polarity	Type of intermolecular forces of attraction
(CH ₃) ₃ N	Polar	Permanent dipole – permanent dipole attraction
(СН3)3СН	Non-polar	Instantaneous dipole – induced dipole attraction
CH ₃ CH ₂ CH ₂ NH ₂	Polar	Hydrogen bonding

(b) Solubility in water

Amines with **small molecular size** are soluble in water. *Reason*: Amines can form <u>hydrogen bonds</u> with water molecules.



hydrogen bond

However, as the <u>alkyl group(s) becomes bulkier/heavier</u>, the <u>solubility in water</u> <u>decreases</u> because of the <u>greater hydrophobic nature of the R group.</u>

Pen down your notes/ questions/ thoughts on this section in the space below



Example Ammonolysis of 2-bromopropane:

 $(CH_3)_2CHBr + NH_3 \longrightarrow (CH_3)_2CHNH_2 + HBr$

Note:

• If an <u>excess of NH</u>₃ is used, the main product formed is the <u>1° amine</u>. Side-products can include the 2° and 3° amines as well as the quaternary ammonium salt.



Predict with reasoning, the solubility of the end-product of the reaction in water.

Answer: The ammonium salt is soluble in water. The **ionic** quaternary ammonium salt can **form ion-dipole interactions** with water molecules which **releases energy that cause the detachment of ions from the crystal lattice for solvation**.

2.4 Reduction of Nitrobenzenes



Reagents & Conditions: Sn in excess concentrated HCl, heat, followed with addition of NaOH (aq), r.t.p.

Type of reaction: Reduction

Note:

- Fe can be used in place of Sn as the reducing agent.
- The first formed product in Step 1 is $C_6H_5NH_3^+Cl^-$ or $(C_6H_5NH_3^+)_2SnCl_6^{2-}$.
- Aqueous NaOH is added for *acid-base reaction* with the acidic $C_6H_5NH_3^+$ to form the required phenylamine product in Step 2.
- $LiAlH_4$ in dry ether cannot be used as the nitrobenzene is reduced to other

unintended products, *i.e.* azo compounds,

3 Basicity of Amines

- In the <u>gaseous phase</u>, amines behave like a Lewis base *i.e.* <u>electron-pair donor</u>.
- In <u>aqueous medium</u>, amines behave like a Bronsted Lowry base *i.e.* proton acceptor.

3.1 Lewis Theory

- Lewis Theory of acids and bases states that:
 - An **Lewis acid** is a substance that can accept a pair of electrons from a Lewis base to form a dative bond i.e. **a Lewis acid is an electron-pair acceptor.**
 - A **Lewis base** is a substance that that can donate a pair of electrons to a Lewis acid to form a dative bond i.e. **a Lewis base is an electron-pair donor.**
- In the <u>gaseous phase</u>, amines behave like a Lewis base.

Relative gas-phase basicity of primary, secondary and tertiary amines

• Basicity of tertiary amine > secondary amine > primary amine > ammonia



Order of base strength:

trimethylamine	>	dimethylamine	>	methylamine	>	ammonia
most basic						least basic

<u>Reason</u>

- From methylamine to trimethylamine, the degree of alkyl substitution in amine increases. (*i.e.* from primary to tertiary amine)
- The <u>increase in number of electron-donating alkyl groups increases</u> the <u>electron density of the lone electron pair on N atom</u> of the amine. Hence, the <u>lone electron pair on N atom</u> is <u>more available for donation</u> to form a <u>stronger</u> <u>dative bond</u>
- Thus basicity of tertiary amine > secondary amine > primary amine > ammonia.
- The same order basicity is seen in the reaction of amines with other Lewis acids, such as A1C13:



3.2 Bronsted-Lowry Theory

• Amines are **weak bases** in aqueous medium due to the ability of the <u>lone pair of</u> <u>electrons on N atom</u> to <u>accept a proton</u>.

e.g. $CH_3CH_2NH_2(aq) + H_2O(l) + H_2O(l) + CH_3CH_2NH_3^+ (aq) + OH^-(aq)$ ethylamine ethylammonium

(i) Relative basicity of ammonia, ethylamine and phenylamine in water

Comparing the K_b , base dissociation constant:

Compounds	<i>K</i> ₀ / mol dm ⁻³
Ethylamine	5.6 × 10 ⁻⁴
Ammonia	1.8 × 10 ⁻⁵
Phenylamine	$4.3 imes 10^{-10}$

Order of base strength: **ethylamine > ammonia > phenylamine** most basic least basic

<u>Reasons</u>

Why is ethylamine a stronger base than ammonia?

 $CH_3CH_2\dot{N}H_2(aq) + H_2O(l)$ $\dot{f}^{\uparrow} CH_3CH_2NH_3^+(aq) + OH^-(aq)$

 $\ddot{N}H_3(aq) + H_2O(l) \ddagger \ddot{T} NH_4^+(aq) + OH^-(aq)$

- The <u>electron-donating ethyl group (CH₃CH₂-) increases</u> the <u>electron density</u> of the lone electron pair on N atom of ethylamine. Hence, the <u>lone electron</u> pair on N atom is more available for donation to a proton.
- However, ammonia does not have any electron-donating group attached to its N atom. Hence, ammonia is a weaker base than ethylamine.

Why is phenylamine a weaker base than ammonia?



- In phenylamine, the lone pair of electrons on the nitrogen atom is delocalised into the benzene ring.
- Hence the lone pair on N atom is less available for donation to a proton.



Note:

In general, for amines:

- electron-donating groups increase the basicity of amines
- electron-withdrawing groups decrease the basicity of amines
- (ii) Effect of substituents on basicity
 - (a) Electron-donating substituents cause an increase in basicity
 - *Effect:* In the **presence of electron donating group, the lone electron pair on N atom** is **more available** to accept H⁺ ions. Hence, the amine compound is **more basic.**

 $\mathsf{R}-\mathbf{\mathring{N}H}_{2}(\mathsf{aq}) + \mathsf{H}_{2}\mathsf{O}(l) \stackrel{\circ}{\ddagger} \stackrel{\circ}{\twoheadrightarrow} \mathsf{R}-\mathsf{N}\mathsf{H}_{3}^{+}(\mathsf{aq}) + \mathsf{O}\mathsf{H}^{-}(\mathsf{aq})$

The bulkier the R group \rightarrow the greater the electron-donating effect

(b) Electron-withdrawing substituents cause a decrease in basicity

Effect: In the **presence of electron withdrawing group, the lone pair on N atoms** is **less available** to accept H⁺ ions. Hence, the amine compound is **less basic**.



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3 factors determining the extent of effect

1 Number of electron-withdrawing groups

<u>More</u> electron-withdrawing groups \Rightarrow <u>greater</u> electron-withdrawing effect

2 Strength of the electron-withdrawing groups

The more electronegative the atom \Rightarrow greater electron-withdrawing effect

3 Distance of the electron-withdrawing groups from **aliphatic/alicyclic** amine

<u>Nearer</u> to the <u>amine group</u> \Rightarrow <u>greater</u> electron-withdrawing effect

Quick Check

State and explain the relative basic strength of phenylamine, 4-chlorophenylamine and 4-methylphenylamine







phenylamine

4-chlorophenylamine

4-methylphenylamine

Format for Phrasing of Answers Related to Basicity Question

Order of basicity: 4-methylphenylamine > phenylamine > 4-chlorophenylamine

Equations to represent basicity



4-methylphenylamine

• The <u>electron donating –CH₃ group increases the electron density of the lone pair on</u> <u>N atom</u>. Hence, the <u>lone pair on N atom</u> is <u>more available for donation to a proton</u>

 \Rightarrow 4-methylphenylamine is the <u>strongest</u> base.

4-chlorophenylamine

The electron withdrawing chloro group decreases the electron density of the lone pair on N atom. Hence, the lone pair on N atom is less available for donation to a proton.

 \Rightarrow 4-chlorophenylamine is the *weakest* base.

Concept on Comparison of Acidity and Basicity of Salts [conjugate acid and bases]

Quick Check (H2 Chemistry N07/I/29)

1 Which salt will be the most acidic in aqueous solution?

Α $C_2H_5NH_3^+Cl^-$ В C6H5NH3⁺Cl⁻ С NH₄+C*l*-K+Cl-D

Explanation:

For Option C: KCl is neutral since it dissolves in water to form $K^+(aq)$ and $Cl^-(aq)$.

For Option A, B, D:

RNH2 + H2O 🔫	► RNH ₃ ⁺ + OH ⁻ conjugate acid
asicity:	$C_2H_5NH_2 > NH_3 > C_6H_5NH_2$
acidity of the conjugate acid:	$C_{2}H_{5}NH_{3}^{+} < NH_{4}^{+} < C_{6}H_{5}NH_{3}^{+}$

Since ba

Hence, cidity of the cor ijugate

(Answer: **B**)

Concept: The stronger the base, the weaker the conjugate acid.

2 Which salt will be the most basic in aqueous solution?

Α C₆H₅O⁻Na⁺ В CH₃CH₂O⁻Na⁺ С CH₃COO⁻ Na⁺ D CCl₃COO⁻ Na⁺

Explanation:

Option A Option B Option C Option D	$C_6H_5O^- + H_2O$ $CH_3CH_2O^- + H_2O$ $CH_3COO^- + H_2O$ $CCI_3COO^- + H_2O$		C ₆ H ₅ OH CH ₃ CH ₂ OH CH ₃ COOH CC <i>l</i> ₃ COOH	+ OH ⁻ + OH ⁻ + OH ⁻ + OH ⁻	
Since acidity:	$CH_3CH_2OH < C$	3H₅OH < CH ₃ O	COOH < CCl	COOH	
Hence, basic	ity of the conjugate	base: CH ₃ Cl	$H_2O^- > C_6H_5O$	⁻ > CH₃COO ⁻	> CC/3COO-
(Answer: B)					

Concept: The stronger the acid, the weaker the conjugate base.

Gas-Phase versus Ageuous Basicity of amines

• Despite the <u>gas-phase</u> basicity of the methyl amines being in the order (page 8):

t	trimethylamine	>	dimethylamine	>	methylamine	>	ammonia	a
$\Delta H_{\rm protonat}$	ion -938		-923		-896		-858	kJ mol⁻¹
	most basic						least basi	ic

• In <u>aqueous</u> solution, the basicity as measured by the $\mathbf{p}K_{\mathbf{b}}$ is of the order:

	dimethylamine	>	methylamine	>	trimethylamine	>	ammonia
р <i>К</i> ь	3.27		3.38		4.22		4.74
	most basic						least basic

- In the aqueous phase, the substituted ammonium cations get stabilised not only by electron-donating effect of the alkyl group (+I) but also by solvation with water molecules *via* hydrogen bonding.
 - The greater the size of the ion, lesser will be the solvation and the less stabilised is the ion. The order of stability of ions are as follows:

which is **opposite** to the inductive effect based order.

- In addition, when the alkyl group is small, like –CH₃ group, there is no **steric hindrance** to H-bonding. In case the alkyl group is bigger than CH₃ group, there will be steric hindrance to H-bonding.
 - Hence aqueous basicity of the ethyl substituted amines follows the order:

	diethylamine	>	triethylamine	>	ethylamine	>	ammonia
р <i>К</i> ь	3.00		3.25		3.29		4.74
	most basic						least basic

• Hence, there is a subtle interplay of the *inductive effect*, *solvation effect* and *steric hindrance* of the alkyl group which decides the basic strength of <u>alkyl amines in the</u> <u>aqueous state</u>.

4. Reactions of Amines

4.1 Formation of Salts

General Equation:	$R - NH_2 + H^+ \longrightarrow R - NH_3^+$			
Reagents & Conditions:	HC <i>l</i> (aq) or H ₂ SO ₄ (aq), r.t.p.			
Type of reaction:	Acid-base reaction or neutralisation			

Example: Reaction of phenylamine with hydrochloric acid



4.2 Acylation of Amines



Reagents & Conditions:	Anhydrous acyl chloride, RCOC <i>l</i> , r.t.p
Type of Reaction:	Nucleophilic acyl substitution
Application:	Reaction of acyl halide with NH ₃ / amines is the ONLY method to synthesise amides

E.g. Reaction of ethylamine with ethanoyl chloride



4.3 Electrophilic Substitution of Phenylamine

$$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

substitution as the **–NH**² group activates the ring towards electrophilic substitution. This is due to lone electron pair on N atom being delocalised into the benzene ring hence increasing the electron density in the ring.

Quick Check

Phenol and phenylamine reacts similarly with Br_2 (aq) to give the same observations. How can phenol and phenylamine be distinguished?

Test:	Add aqueous neutral FeC13 solution separately to each unknown compound.
Observation:	Phenol forms a <u>violet complex</u> .
	Phenylamine <u>does not form a violet complex</u> .

4.4 Reactions of Primary Amides, Ammonium Salts and Amines with Aqueous NaOH

• Add aqueous NaOH to a primary amide, ammonium salt or amine, and heat

Compound	Reagents & Conditions	Observations				
Primary Amide RCONH ₂	Aqueous NaOH, heatPungent gas evolved turned moist re- paper blue.					
		NH₃ gas evolved only for primary amides of the following structure:				
		$RCONH_2 + NaOH \rightarrow RCO_2^-Na^+ + NH_3$				
Ammonium Salt, $NH_4^+X^-$	Aqueous NaOH, heatPungent gas evolved turned moist re paper blue. NH3 gas evolved.					
		$NH_4^+X^-$ + NaOH \longrightarrow NaX + NH ₃ + H ₂ O				
Amine RNH2	Aqueous NaOH, heat	No NH ₃ gas evolved.				
		However, note that lower amines are volatile liquids/gases with a fishy smell that turns moist red litmus paper blue.				

4.5 Distinguishing Test between Aliphatic and Aromatic Amines

- Add <u>aqueous CuSO4</u> to the amine at room temperature.
 - A copper(II) complex is formed with the amine, blue in the case of aliphatic amines and green for aromatic amines:

$$\begin{bmatrix} \mathsf{Cu}(\mathsf{H}_2\mathsf{O})_6 \end{bmatrix}^{2+} + 4 \operatorname{RNH}_2 \rightarrow \begin{bmatrix} \mathsf{Cu}(\mathsf{RNH}_2)_4 (\mathsf{H}_2\mathsf{O})_2 \end{bmatrix}^{2+} + 4 \operatorname{H}_2\mathsf{O} \\ & \text{blue} \\ \begin{bmatrix} \mathsf{Cu}(\mathsf{H}_2\mathsf{O})_6 \end{bmatrix}^{2+} + 4 \operatorname{ArNH}_2 \rightarrow \begin{bmatrix} \mathsf{Cu}(\mathsf{ArNH}_2)_4 (\mathsf{H}_2\mathsf{O})_2 \end{bmatrix}^{2+} + 4 \operatorname{H}_2\mathsf{O} \\ & \text{green} \end{bmatrix}$$

5 Introduction on Amino Acids

- Amino acids are **building blocks of proteins**. Of the 20 amino acids needed to make up our proteins, eight cannot be synthesised in our bodies. These eight are called essential amino acids and must be part of our diet.
- An amino acid contains at least 1 carboxylic acid group (–CO₂H) and 1 amino group (–NH₂).
- The C atom to which the $-CO_2H$ group is bonded to is called α -carbon.
- Definition of α -amino acid : An amino-acid where both the –NH₂ and the –COOH group are directly bonded to the same C atom (α -carbon)





 The side chain, R, varies considerably in the 20 naturally occurring α-amino acids (see Annex). The composition of the R group confers an individual set of properties to each amino acid, which affects the properties of the proteins in which they are found.

If the **R** group contains **one or more carboxyl group**, –COOH: <u>acidic</u> amino acid.

If the **R** group contains **one or more amino group**, –NH₂: **<u>basic</u> amino acid**.

If the **R** group contains **neutral group(s)**: <u>**neutral**</u> amino acid.

• All α -amino acids that can be found in our bodies have at least 1 chiral C centre (except aminoethanoic acid (glycine) where R = H) with no plane of symmetry, thereby exhibiting enantiomerism.



5.1 Nomenclature of Amino Acids

• Amino acids are named as derivatives of carboxylic acids.

Examples of some naturally occurring amino acids:



5.2 Bonding of Amino Acids

Definition of zwitterion

• Amino acids readily exist as electrically neutral dipolar ions called zwitterions.



How are zwitterions formed?

- The dipolar **zwitterion** is formed as a result of an **intramolecular acid-base reaction**, in which the **most acidic group** (usually a carboxylic acid) **donates a proton to the most basic group** (usually a amine group)
- Hence, amino acids are **<u>ionic</u>** in nature.

5.3 Physical Properties of Amino Acids

(a) Exist as crystalline solids with high melting points (above 200°C)

Reason: <u>High amount of energy</u> is required to overcome the <u>strong electrostatic</u> <u>forces of attraction between the zwitterions.</u>

Simplified structure of solid aminoethanoic acid:



www.ionic bonds

(b) Soluble in water

Amino acids are very soluble in water (and other polar solvents) but not in non-polar solvents.

Reason: The charged ends of the zwitterions can form strong <u>ion-dipole</u> interactions with the water molecules results in the <u>release of</u> <u>sufficient energy</u> that causes the <u>detachment of zwitterions from the</u> <u>crystal lattice for solvation</u>.

Amino acids can also form **hydrogen bonds** with water molecules.

ion-dipole attraction hydrogen bond $\mathcal{H}_{3}^{\delta^{+}}$ H₃N⁺CH₂COO⁻ $\mathcal{H}_{3}^{\delta^{+}}$ $\mathcal{H}_{3}^{\delta^{+}}$

(c) Amphoteric in nature \Rightarrow amino acids can act as <u>acids and bases</u>

<u>As an acid</u>: The <u> $-NH_3^+$ </u> group is responsible for its acidic properties.







Hence, amino acids (and zwitterions) can act as a buffer solution.

On addition of small amount of H+



(proton acceptor)

The <u>H⁺ is removed</u> and hence [H⁺] is slightly changed and pH remains fairly constant.

On addition of small amount of OH-



The <u>OH⁻ is removed</u> and hence [OH⁻] is slightly changed and pH remains fairly constant.

6 Reactions of Amino Acids

Due to the amphoteric nature of amino acids, they undergo <u>neutralisation</u> reactions at the respective $-COO^-$ or $-NH_3^+$ groups in the zwitterion form.

6.1 Reactions of the Acidic Group

Amino acids form **salts** with alkalis and carbonates due to the reaction of the $-NH_3^+$ group.

6.1.1 Reaction with Alkalis



Example: Reaction of aminoethanoic acid (glycine) with sodium hydroxide



6.1.2 Reaction with Carbonates (and Hydrogencarbonates)

$$2 H_{3} \overset{\oplus}{N} \overset{-}{\underset{R}{\overset{\cup}{\circ}}} - COO^{\ominus} + Na_{2}CO_{3} \longrightarrow 2 H_{2} N \overset{H}{\underset{R}{\overset{\cup}{\circ}}} - COO^{\ominus} Na^{\oplus} + CO_{2} + H_{2}O$$

Example: Reaction of aminoethanoic acid with sodium carbonate

$$2 H_{3}^{\oplus} \overset{H}{\overset{}_{H}} \overset{-}{\overset{}_{H}} \overset{-}{\overset{}_{H}} \overset{-}{\overset{}_{H}} COO^{\ominus} + Na_{2}^{2}CO_{3} \longrightarrow 2 H_{2}^{} N \overset{H}{\overset{}_{H}} \overset{-}{\overset{}_{H}} COO^{\ominus} Na^{\oplus} + CO_{2} + H_{2}^{} O$$

6.2 Reactions of the Basic Group

Amino acids form **salts** with acids due to the reaction of the **-COO⁻ group**.

6.2.1 Reaction with Acids

$$H_{3} \overset{\oplus}{N} \overset{H}{\underset{R}{\overset{\circ}{\to}}} \overset{H}{\underset{R}{\overset{\circ}{\to}}} + HC^{l} \longrightarrow C^{l^{\ominus}} H_{3} \overset{H}{\underset{R}{\overset{\circ}{\to}}} \overset{H}{\underset{R}{\overset{\circ}{\to}}} -COOH$$

Example: Reaction of aminoethanoic acid (glycine) with dilute hydrochloric acid

6.3 Formation of Peptides

- Amino acids are capable of undergoing self-condensation or condensation reaction with other amino acid molecules to form peptide/ amide linkages.
- The process involves the <u>elimination of a water molecule</u> between the carboxylic acid group of one amino acid molecule and the amino group of another molecule.

Example:



peptide bond

The peptide formed may vary in terms of the number of amino acids:

- <u>2 amino acids</u> joined together: <u>dipeptide</u> (only 1 peptide bond)
- <u>3 amino acids</u> joined together: <u>tripeptide</u> (only 2 peptide bonds)
- many amino acids joined together: polypeptide
- Polypeptides containing more than 40 amino acid residues are termed proteins.

6.4 Hydrolysis of Proteins

Hydrolysis of Peptide Bond

- In protein, peptide bonds can be broken by <u>hydrolysis</u> in presence of suitable <u>enzymes</u>, or <u>prolonged heating under reflux</u> in <u>acidic or alkaline solution.</u>
- There are 2 types of hydrolysis of peptide bonds.

Acidic Hydrolysis



Quick Check

The formulae of three amino acids are given.



Draw the displayed formula of the tripeptide, gly-pro-ala.

Solution



Note: By convention, the free NH_2 group is on the left and the free CO_2H group is on the right of the peptide chain.

<u>F.Y.I. only</u> Separation of Amino Acids

Amino acids, obtained from the hydrolysis of proteins / polypeptides, can be separated by a process known as **electrophoresis**. Different amino acids can exist as zwitterions, positive ions or negative ions, depending on the pH of the solution. To separate the amino acids, the pH of the solution is varied slightly over time and the different amino acids will migrate to the electrodes at different pH values.

Amino acids can also be separated by paper chromatography. The different amino acids are separated based on different solubilities in a solvent as well as their molecular masses. Amino acids which are more soluble will move faster, and lighter amino acids will move faster than heavier amino acids. A reagent, ninhydrin, is then used to indicate the position of amino acids by the observation of a blue or purple colouration.



Name	Abbrevi	ations	мw	Structure	p <i>K</i> ₄ α-CO₂H	p <i>K</i> ₄ α-NH₃⁺	p <i>K</i> ₄ side chain	p <i>I</i>	
Neutral Amino Acids									
Alanine	Ala	A	89	$ \begin{array}{c} O\\ H_3C\\ H_3C\\ H_3N\\ H \end{array} $	2.34	9.69	_	6.01	
Asparagine	Asn	N	132	$H_2N \underbrace{\begin{array}{c} 0 \\ H_2N \\ C \\ 0 \\ H_3N \\ H \end{array}}_{O H_3N H} O^{\Theta}$	2.02	8.80	_	5.41	
Cysteine	Cys	С	121	HS HS H ₃ N H	1.96	10.28	8.18	5.07	
Glutamine	GIn	Q	146	$H_2N \xrightarrow{C} H_3N \xrightarrow{\Theta} H$	2.17	9.13	_	5.65	
Glycine	Gly	G	75	O H H H ₃ N H	2.34	9.60	-	5.97	
Isoleucine	Ile	I	131	$H_{3}C \xrightarrow{H_{3}C} O^{\Theta}$	2.36	9.60	_	6.02	
Leucine	Leu	L	131	$ \begin{array}{c} $	2.36	9.60	-	5.98	
Methionine	Met	М	149	$H_{3}C^{-S} \xrightarrow[H_{3}N]{} H^{C} = 0^{\Theta}$	2.28	9.21	-	5.74	
Phenylalanine	Phe	F	165		1.83	9.13	-	5.48	
Proline	Pro	Ρ	115		1.99	10.60	-	6.30	
Serine	Ser	S	105		2.21	9.15	_	5.68	

The structures, pK_a and pI values of the 20 naturally occurring amino acids are shown below.

Name	Abbrevi	ations	MW	Structure	p <i>K</i> ₄ α-CO₂H	p <i>K</i> ₄ α-NH₃⁺	p <i>K</i> ₄ side chain	p <i>I</i>
Threonine	Thr	Т	119	HO H O H ₃ C C O^{Θ} H ₃ N H	2.09	9.10	_	5.60
Tryptophan	Тгр	W	204	$ \begin{array}{c} $	2.83	9.39	_	5.89
Tyrosine	Tyr	Y	181		2.20	9.11	10.07	5.66
Valine	Val	V	117	$\begin{array}{c} CH_3 & O \\ H_3C & U \\ H_3N & H \end{array} \\ \end{array} \\ \begin{array}{c} CH_3 & O \\ H_3N & H \end{array} \\ \end{array}$	2.32	9.62	_	5.96
Acidic Amino Ac	ids					-		
Aspartic acid	Asp	D	133		1.88	9.60	3.65	2.77
Glutamic acid	Glu	E	147		2.19	9.67	4.25	3.22
Basic Amino Aci	ds	•	•					
Arginine	Arg	R	174	$\begin{array}{c} {}^{\circledast} NH_2 & O \\ II & II \\ H_2 N & & \\ & H \\ H_3 N & H \end{array}$	2.17	9.04	12.48	10.76
Histidine	His	Н	155		1.82	9.17	6.00	7.59
Lysine	Lys	К	146	H ₃ N H ₃ N H ₃ N H	2.18	8.95	10.53	9.74

Source: Organic Chemistry by John McMurry, 7th Edition