

Nitrogen Compounds

Amine (Derivative of NH_3)

Amines (Derivative of $-\text{COOH}$)

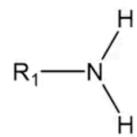
Amino Acids/ Proteins

Amine

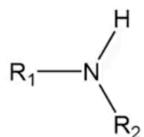
- Can be aliphatic/ aromatic
- Trigonal pyramidal around N⁺

Classification

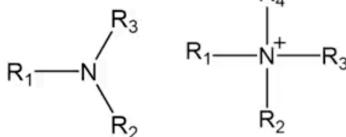
Primary amines



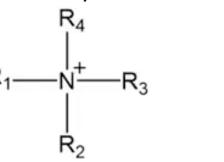
Secondary amines



Tertiary amines



Quaternary ammonium ion



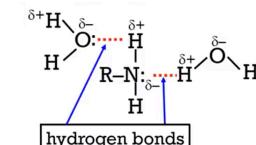
\neq ammonium ion! (NH_4^+)

Nomenclature

- ethyl (alkyl/ aryl group) amine ("amine")
- 2-propylamine (give position locant if ambiguous)
- 2-aminopropane (amide FG can be named as substituent)
- di-methylamine, tri-methylamine (symmetrical amines)
- N-methylethylamine (shorter alkyl group treated as substituent to N atom)
- 2-methylphenylamine (phenol group takes the highest priority)

Physical Properties

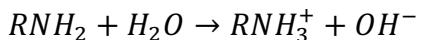
- Lower aliphatic amines are gases, 'ammonia' smell
- Amine with higher Mr are liquids, 'fishy' odour
- Amine with very high Mr are solid
- Boiling points of primary amine increase as no of C increase
→ increasing strength of id-id i
- For isomeric amine, boiling point $1^\circ & 2^\circ > 3^\circ$ amine
→ ability to form hb bet their molecules
- Lower members are very soluble in water
→ lone pair of e^- on N atom → able to form hb with water
- Solubility decreases as no of C atom increases
→ bulky, non polar aryl/ alkyl groups hinder formation of hb between amine and water molecules



Reactivity

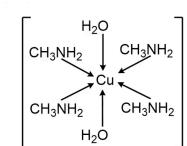
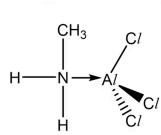
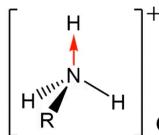
Availability of lone pair of electrons on N atoms allow amines to act as bases, nucleophiles and ligands.

Basicity



- Weak bases

| Bronsted-Lowry Base | Lewis Base |
|---|--|
| Availability of lone pair of electrons on N atoms for protonation → amine accepts proton by forming dative covalent bond with it | Amine act as base by donating electrons on N to chemical species with energetically accessible vacant orbitals → form dative covalent bond (e.g. Ligands) |



- Aliphatic amines are stronger bases than NH_3

- In (g), basicity $1^\circ < 2^\circ < 3^\circ$ amine

N.B. in (aq) state $2^\circ > 3^\circ$ amine (steric hindrance). Don't need know!

→ (more) electron donating alkyl group → lone pair of electrons on N atom of amine more available for protonation/donation

- Phenylamine weaker base than NH_3

→ p orbital of N atom overlaps with π electron cloud of BR → lone pair of e^- s on N atom of phenylamine delocalised into BR → less available for protonation/donation

| EDS | EWS |
|--|--|
| Make lone pair of e^- s on N atom more available for protonation → increase basicity | Make lone pair of e^- s on N atom less available for protonation → decrease basicity |

Preparation

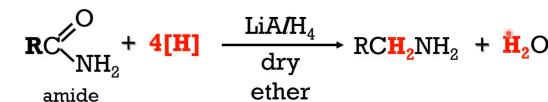
- Reduction of nitrile (Halogen Derivatives)

R/C: $LiAlH_4$ in dry ether, or H_2 , Ni , heat

- Reduction of amide

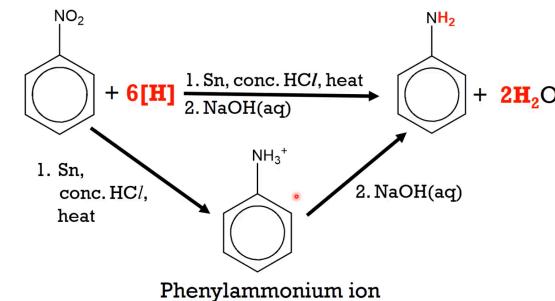
R/C: $LiAlH_4$ in dry ether

Cannot use H_2 , Ni , heat. Opportunity for selective pptn.



- Reduction of nitrobenzene

R/C: Tin, con HCl, heat, followed by NaOH (aq)



4. Nucleophilic substitution (Halogen Derivatives)

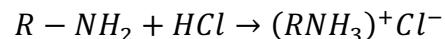
R/C: Excess ethanolic NH_3 , HIST

R/C: Alcoholic amine, HUR

N.B. Little practical use as mixture of amine is obtained that is difficult to separate

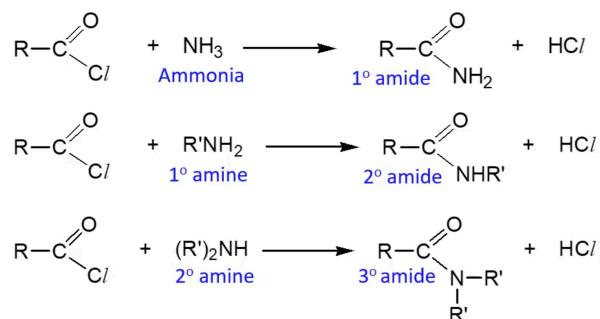
Reactions

1. Acid Base reaction



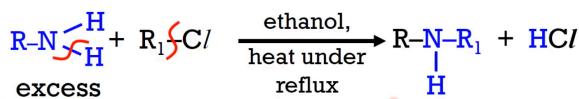
Phenylamine is insoluble in water (2 immiscible layers formed), but dissolves readily in HCl (homogenous soln formed).

2. Condensation (Carboxylic Acid Derivatives)

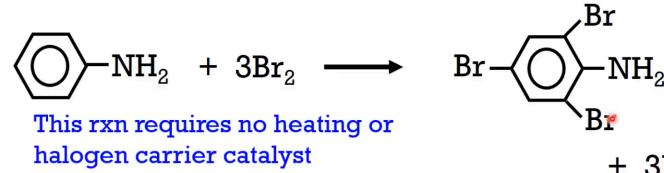


3. Nucleophilic Substitution

R/C: Ethanol, HUR



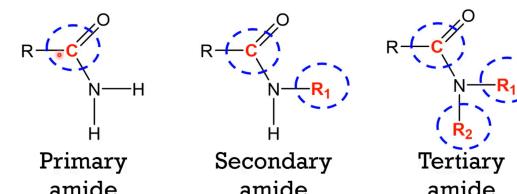
4. Electrophilic Substitution of Phenylmine



Observation: Orange Br_2 decolourises and white ppt of 2,4,6-tribromophenylamine is formed. White fumes of HBr may not be observed as HBr dissolves in (aq) medium.

Amides

Classification



Nomenclature

- ethanoic acidamide
- N-methylpropanamide

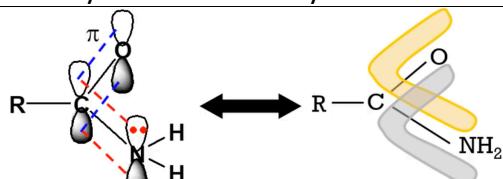
Physical Properties:

- Crystalline solids except methanamide, $HCONH_2$
 - Primary and secondary amides have relatively high bp and form dimers in liquid phase.
→ hb between molecules
- N.B. tertiary amides cannot form hb between itself

Remarks

Have to be careful when stating hybridisation states of organic compounds.

What do you think is the hybridisation of N in amide FG here?



It is sp₂ hyb. It is **not** sp₃ hyb, because it has a p-orbital that can overlap sideways with the π electron cloud of carbonyl grp

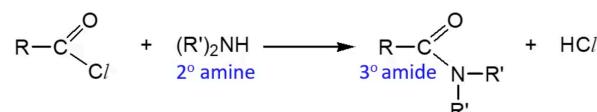
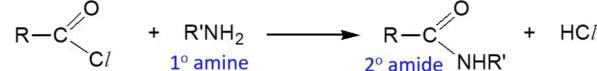
Basicity

Do not act as base and are neutral to litmus in aqueous solution.

The p-orbital of N atom overlaps with the π electron cloud of the neighbouring carbonyl group (C=O). The lone pair of electrons on N atom is delocalised into the C=O group and hence is not available for protonation.

Preparation:

1. Condensation (Carboxylic Acid Derivatives)

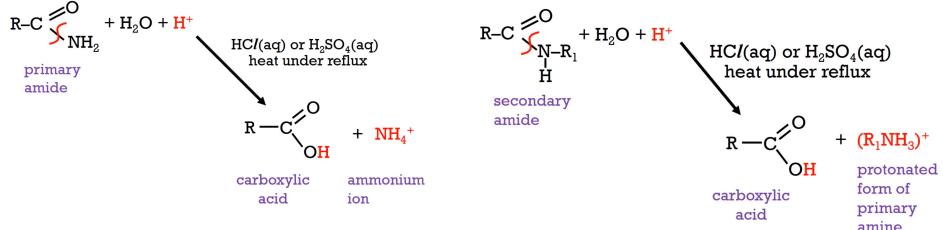


Carboxylic acid c/n be used, as it will undergo AB rxn with NH_3 and amines

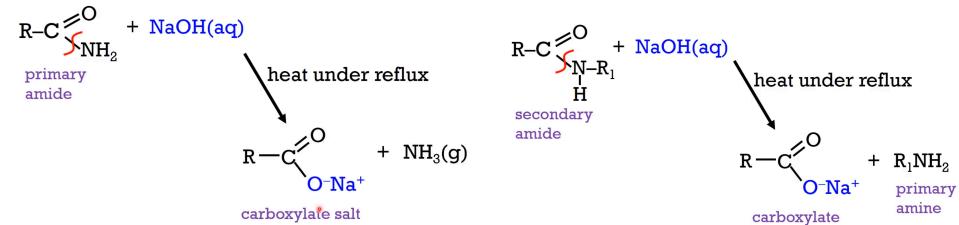
Reactions:

1. Hydrolysis

① Acidic: $\text{HCl}(\text{aq})$ or $\text{H}_2\text{SO}_4(\text{aq})$, HUR



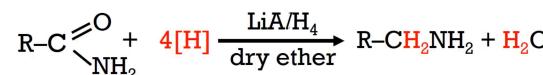
② Alkaline: NaOH , HUR



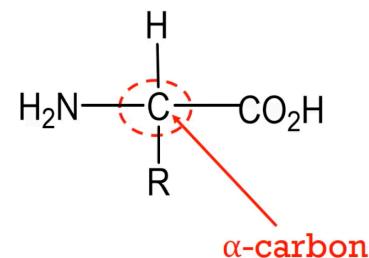
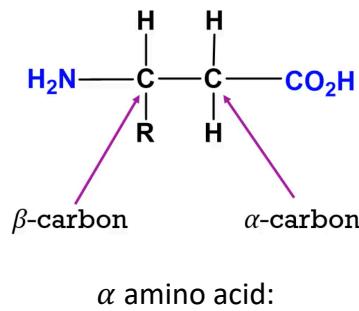
Identification Test for primary amide. Heat the compounds with NaOH (aq) and test the product with moist red litmus paper.
Observation: Colourless, pungent gas evolved turns moist red litmus blue

2. Reduction

R/C: LiAlH_4 in dry ether

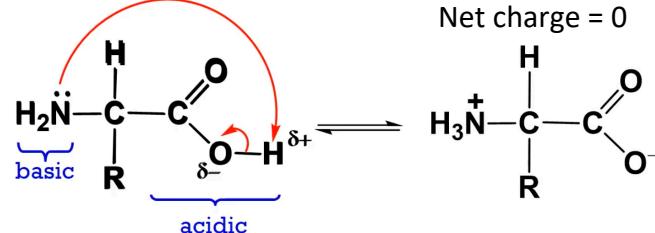


Amino Acids



Physical Properties

- Resemble that of ionic compounds as amino acid undergoes **intramolecular acid-base reaction**

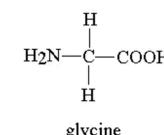


- R group determines if amino acid is **polar/ non-polar** (affect ability to form effective interaction with water molecules) and **acidic/ basic/ neutral**

| Polar | Non-Polar |
|--|--|
| $\text{H}_3\text{N}^+-\overset{\text{H}}{\underset{\text{CH}_2\text{OH}}{\text{C}}}-\text{COO}^-$ Serine (Ser) | $\text{H}_3\text{N}^+-\overset{\text{H}}{\underset{\text{CH}_3}{\text{C}}}-\text{COO}^-$ Alanine (Ala) |
| <ul style="list-style-type: none"> R group can form effective interaction with H_2O. hydrogen bonds | <ul style="list-style-type: none"> R group cannot form effective interaction with H_2O |

| Acidic | Basic | Neutral |
|---|---|--|
| $\text{H}_2\text{N}-\overset{\text{H}}{\underset{\text{CH}_2\text{COOH}}{\text{C}}}-\text{COOH}$ Aspartic acid (Asp) | $\text{H}_2\text{N}-\overset{\text{H}}{\underset{\text{NH}_2}{\text{C}}}-\text{COOH}$ Lysine (Lys) | $\text{H}_2\text{N}-\overset{\text{H}}{\underset{\text{C}(=\text{O})\text{NH}_2}{\text{C}}}-\text{COOH}$ Asparagine (Asn) |
| R group has an acidic group | R group has a basic group | R group has a neutral group |

- All amino acids except glycine are chiral, and are able to demonstrate **enantiomerism**.

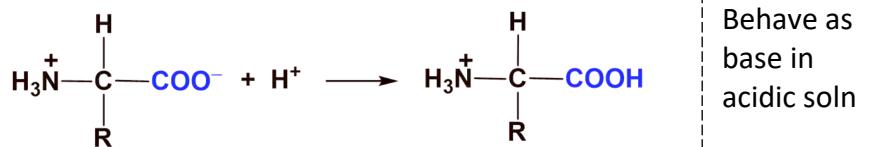


- Crystalline solids with **high mp**
→ strong electrostatic forces of attraction between opp charged groups of zwitterions
- Soluble in water, insoluble in non-polar solvents
→ effective ion-dipole interactions with water

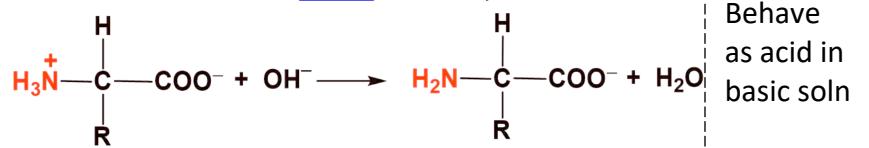
Acidic/ Basic Property

- Amino acids are **amphoteric**

When a *small amount* of **acid** is added,



When a *small amount* of **alkali** is added,



The cation/ anion will migrate to cathode/ anode in presence of electric field.

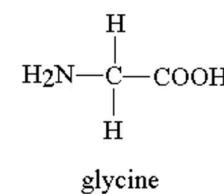
When small amount of acid/ base added, amino acids can act as buffers.

- Structure and net charge of amino acid changes in aq soln depends on the **pH of the solution**
 pK_a values of $\text{COOH}/ \text{NH}_3^+$ (there could be a separate value for $pK_a \text{NH}_3^+$ in R group of will be provided, and you'll have to decipher if the groups will exist in protonated or

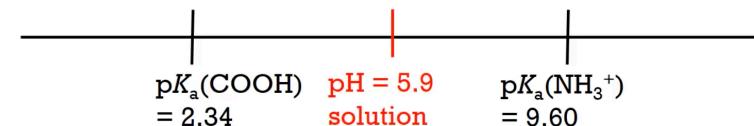
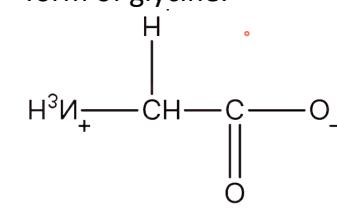
deprotonated form which affect the net charge of amino acids

| Protonated Form (Bronsted Lowry Acid) | Deprotonated Form (Bronsted Lowry Base) |
|--|--|
| -COOH | -COO ⁻ |
| -NH ₃ ⁺ | -NH ₂ |

- Example:



At pH=5.9, predominate form of glycine:



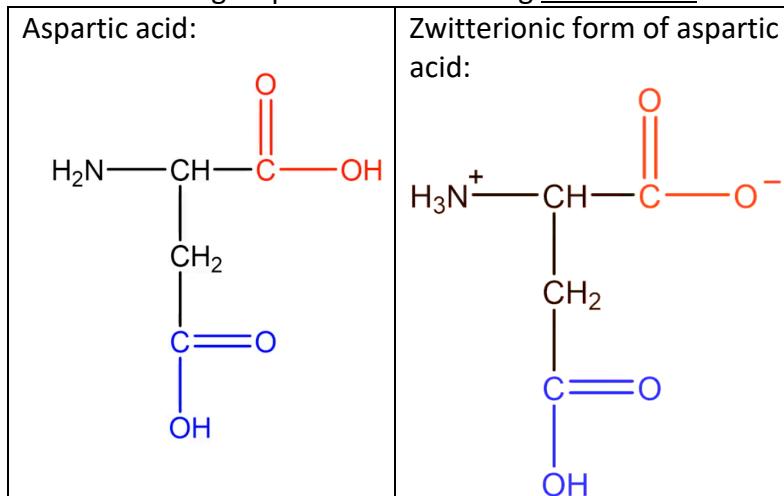
$\text{pH } 5.9 > pK_a(\text{COOH})$
✓ $-\text{COOH} \rightarrow -\text{COO}^-$
✓ **deprotonated**

Behave as acid in relatively more basic soln

$\text{pH } 5.9 < pK_a(\text{NH}_3^+)$
✓ $-\text{NH}_3^+$ (unchanged)
✓ **protonated**

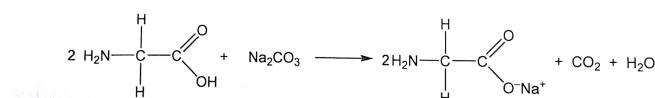
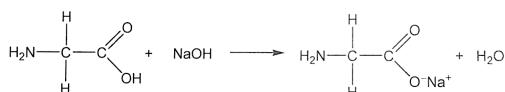
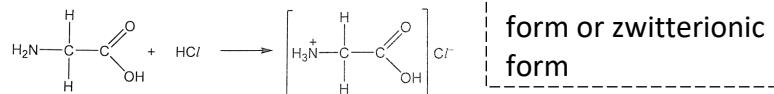
Behave as base in relatively more acidic soln

- Take note that the more acidic $-COOH$ on α carbon will deprotonate first to give a stable ion. This is because the electron withdrawing N atom is nearer, helping to disperse the -ve charge on $-COO^-$ group more effectively, leading to the on $-COO^-$ group on α carbon being more stable.

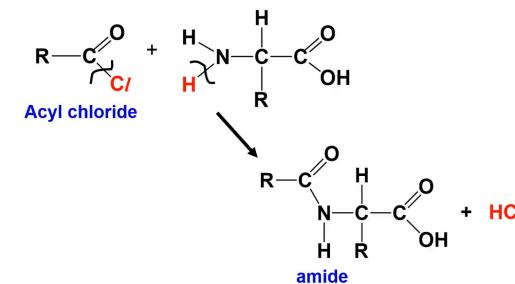


Reactions:

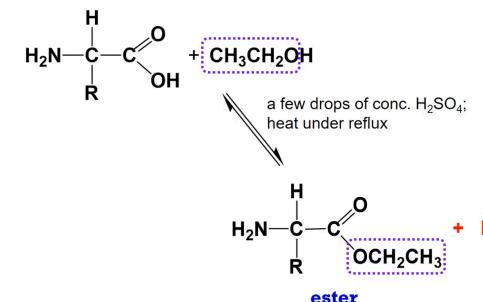
1. Acid Base Reaction



2. Condensation Reaction (form amide)



3. Condensation Reaction (form ester)

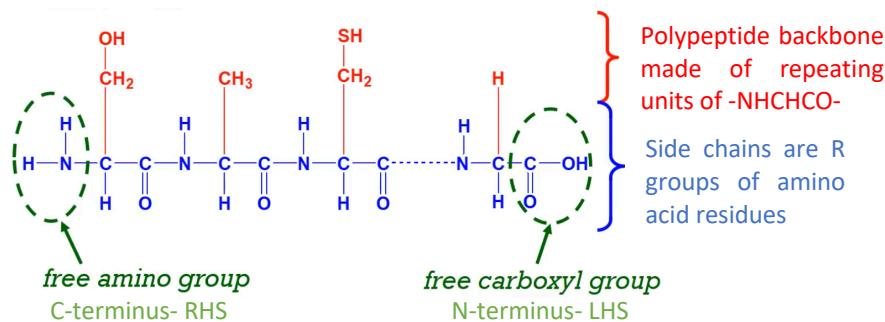


Proteins

Amino acids can be joined by **peptide bond/ linkage** through **condensation reaction** ($-CONH-$) to form dipeptide, tripeptide, tetrapeptide

N.B. di, tri, tetra refers to the number of amino acids

N.B. To draw structural formula of peptides: ① Orientate the constituent amino acids $-NH_2$ on LHS, $-COOH$ on RHS (convention) ② Depending on medium, there may be protonated/ deprotonated groups



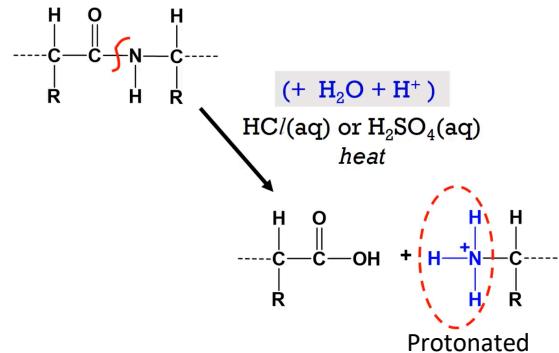
Acidity/ Basicity

- All peptides and/or their side chains exhibit **acid/ base characteristics**

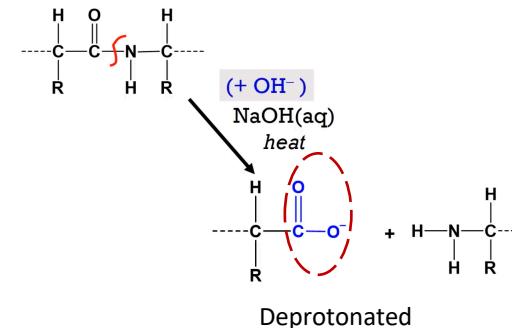
Reaction:

1. (Complete) Hydrolysis

① Acidic: $\text{HCl} \text{ (aq)}$ or $\text{H}_2\text{SO}_4 \text{ (aq)}$, heat for several hours



② Alkaline: $\text{NaOH} \text{ (aq)}$, heat for several hours



③ Enzymatic

Not to be used as chemical method

