18a. Nitrogen Compounds I

Isoelectronic point: Can be defined as the pH at which the amino acid exists predominantly as zwitterions and does not migrate under the effect of an electric field.

- AMINES DO NOT FORM AMIDES WITH COOH, they will react acid-base style. To form amide, use acid chloride!!!
- Secondary amines have lower boiling points than primary amines as H is less electronegative than C and thus primary amines are more polar, thus stronger pd-pd attractive forces.
- Borderline solubility of amines in water is reached at about 6 carbon atoms.
- **CN (triple bond) is neutral as the lone pair is in the sp orbital and given its greater s-character, is held more strongly to the nucleus. Hence making it neutral.**
- **Amides** are effectively **neutral** as the lone pair of electrons on the N atom delocalises into the CO double bond/involved in the stabilisation of the amide by resonance and is hence not available for co-ordination with a proton. (therefore, lacks basicity)
- Hydrolysis of amides (using HCl or NaOH with heat) can be used to distinguish amides with 5 carbons or less as it produces amines, and only amines with 5 carbons or less are volatile enough (low enough bp) to be vapourised by the surrounding heat. **Pungent gas evolves that turns moist red litmus paper blue.**
- Note that **H2/Ni** cannot be used to reduce an amide
- Note that if NH3 is produced through heating with NaOH, other than the reactant being an amide, it could be a nitrile too…
- Note that for an amino acid, solubility is lowest at the isoelectric point as the closeness of charged ends of the zwitterion results in intramolecular ionic bonding, thus hindering the formation of ion-dipole interactions with water molecules.

Questions

1. Why can't Zn and HCl be used to convert a nitrile into an amine if we are trying to obtain an amine?

Ans: Zn and HCl will react to form H2 gas, which will reduce nitrile to form an amine. However, the HCl will react with the amine to form an amine salt.

18b. Nitrogen Compounds II

Denaturation: The disruption of secondary, tertiary and quaternary structure of proteins by breaking their non-covalent interactions (but including disulfide links) that holds these structures in their native conformation, resulting in the loss of biological function.

- **Increase in temperature** results in strong molecular vibrations which agitate the polypeptide chains enough to overcome the interactions that stabilise the protein conformation → Protein structure becomes disorganized and the protein unfolds → **coagulation** can occur as the unfolded protein molecules can get entangled and aggregate to form a solid → Irreversible denaturation.
-

Primary structure: **The sequence of amino acids in the polypeptide chain(s)**

- The peptide bond has partial double bond character due to delocalisation of electrons from the CO double bond and the lone pair on the N atom.
- The C and N of the peptide bond and the two attached atoms lie in the same plane with 120 degrees between them. This results in restricted bond rotation and hence reduces backbone flexibility since the 6 atoms in the peptide unit are forced to lie in a single plane.
- Complete hydrolysis gives the number and relative amounts of amino acids but not the order.
- Partial hydrolysis gives smaller polypeptide fragments, thus retaining sequence information.
- Peptide bond cleaved upon heating in the presence of acid or alkali. Cleavage is not very selective. For **complete** hydrolysis, heating with conc. HCl at 100-120 degrees for 10-36 hours in an evacuated tube is required.

Secondary structure: **Refers to the way in which segments of the polypeptide backbone orientate into a regular pattern through hydrogen bonding between the N-H and C=O groups of the peptide linkages in the polypeptide backbone.**

- In the alpha helix, the coil is stabilised by the formation of H bonds between the C=O group of one amino acid residue and the N-H group of the amino acid four residues away.
- H bonds are linear and thus maximally stable.
- R groups pointed outside of the helix and are perpendicular to the main axis of the helix.
- Beta pleated sheets are connected by H bonds between all the peptide linkages.
- Antiparallel beta sheets are more stable than parallel beta sheets as the N-H --- O atoms in antiparallel sheets lie in a straight line while those in parallel sheets lie at an angle.
- R groups project above or below the sheet perpendicularly.
- Alpha-helix: A coiled arrangement in which the long chain of the primary structure formed a right handed screw with 3.6 amino acid residues per turn.
- Beta-sheet: Segments of a polypeptide chain which fold back on themselves such that adjacent strands are arranged in rows and connected by…

Tertiary structure: **Refers to the 3D arrangement of the protein due to the folding of the secondary structural elements together with the spatial disposition of the side-chains.** Folding is due to R-group interactions.

- If the folding of a protein brings 2 cysteine residue together, the two -SH chains can be oxidised to form a strong covalent disulfide bond.
- These disulfide bonds cross-link the polypeptide chain in the tertiary structure, usually locking the protein structure in place after other forms of stabilising interactions are in place.
- Folding gives rise to 2 groups of proteins, fibrous and globular.
- Fibrous R groups directed outwards, generally insoluble.
- Globular hydrophobic directed inwards while hydrophilic directed outwards, thus soluble in water.

Quaternary structure: **Refers to the spatial arrangement and association of polypeptide subunits to form proteins.** It is the combination of several protein chains into a larger 3-dimensional structure held together by side chain/R group interactions.

- HAEMOGLOBIN
    - ➢ Two alpha subunits and two beta subunits
    - ➢ Although there is little contact between similar subunits, there are considerable side chain R group interactions to stabilise the quaternary structure, namely VDW interactions, ionic attractions, hydrogen bonds and disulfide linkages.
    - ➢ Each subunit is **dative covalently bonded** to a haem residue. The iron in the haem group then binds to oxygen.
    - ➢ Hence each haemoglobin molecule can bind to four oxygen.

<u>Questions</u>

1. Question on transporting long chain fatty acids.
Ans: Choose the non-polar amino acids.

2. Explain why glycine-rich regions of the protein structure give rise to its flexibility.
Ans: Only van der Waals' forces of attraction present between the side chains of glycine which can be easily overcome allowing that region of the protein structure to be more flexible.