

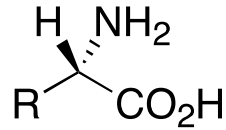
CYI101

Common CHEMISTRY(Organic)

Macromolecules: Introduction to peptides and proteins

Amino Acids: *Structure & Diversity*

20



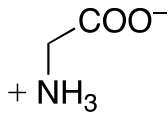
α - Amino Acid

R = sidechain

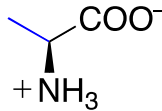
Peptides, and Proteins

monomer unit: α -amino acids

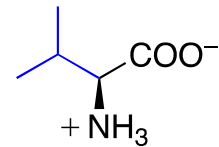
Nonpolar



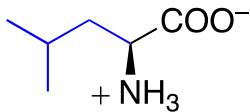
Glycine (Gly, G)



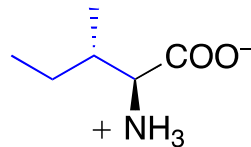
(S)-(+)-Alanine (Ala, A)



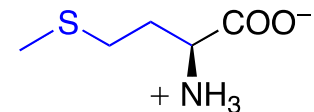
(S)-(+)-Valine (Val, V)



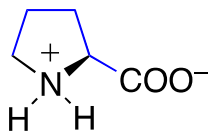
(S)-(-)-Leucine (Leu, L)



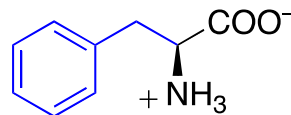
(2S,3S)-(+)-Isoleucine (Ile, I)



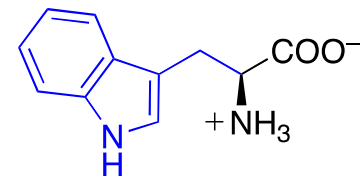
(S)-(-)-Methionine (Met, M)



(S)-(-)-Proline (Pro, P)

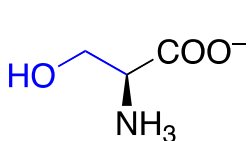


(S)-(-)-Phenylalanine (Phe, F)



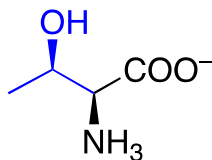
(S)-(-)-Tryptophan (Trp, W)

Polar



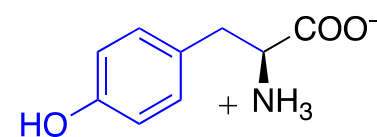
(S)-(-)-Serine (Ser, S)

pKa ~ 13



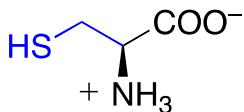
(2S,3R)-(-)-Threonine (Thr, T)

pKa ~ 13



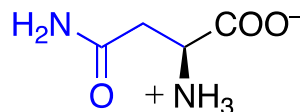
(S)-(-)-Tyrosine (Tyr, Y)

pKa ~ 10.1

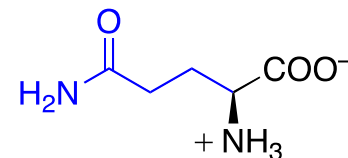


(R)-(-)-Cysteine (Cys, C)

pKa ~ 8.2

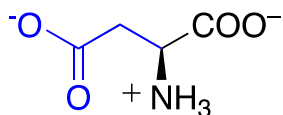


(S)-(-)-Asparagine (Asn, N)



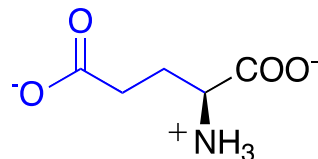
(S)-(+)-Glutamine (Gln, Q)

Acidic:



(S)-(+)-Aspartic Acid (Asp, D)

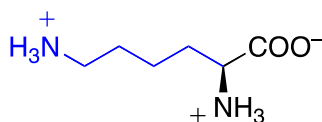
pKa ~ 3.6



(S)-(+)-Glutamic Acid (Glu, E)

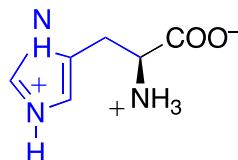
pKa ~ 4.2

Basic:



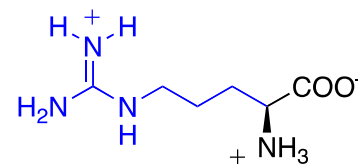
(S)-(+)-Lysine (Lys, K)

pKa ~ 10.5



(S)-(-)-Histidine (His, H)

pKa ~ 6.0

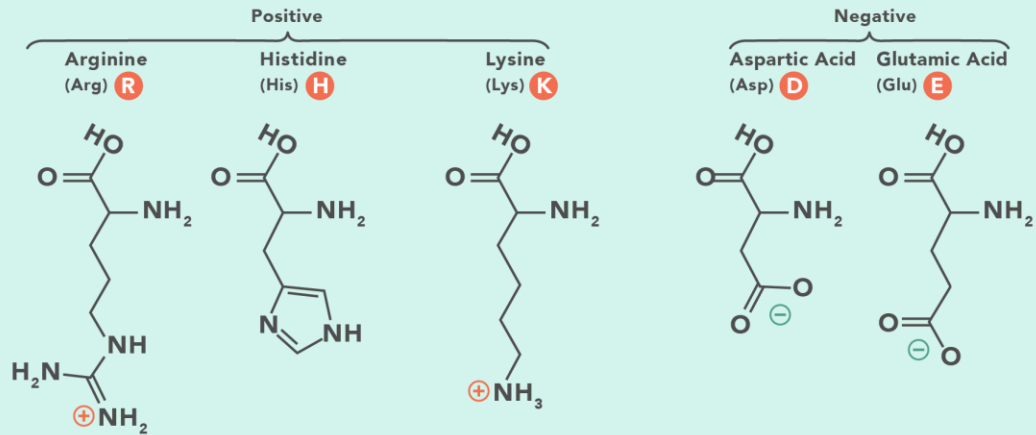


(S)-(+)-Arginine (Arg, R)

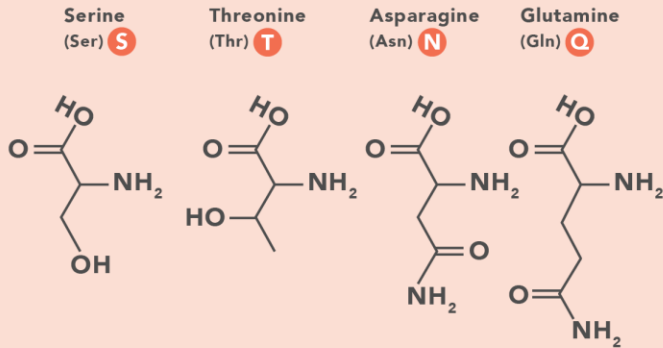
pKa ~ 12.5

Amino Acids: Structure & Diversity

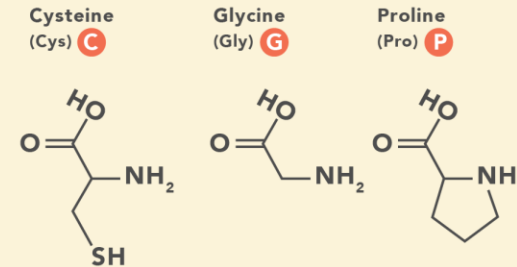
A. Amino Acids with Electrically Charged Side Chains



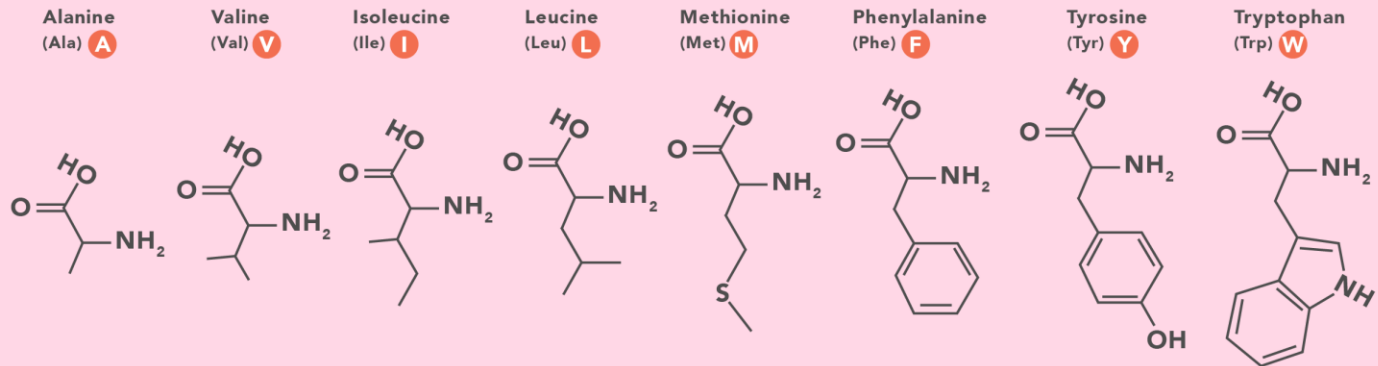
B. Amino Acids with Polar Uncharged Side Chains



C. Special Cases

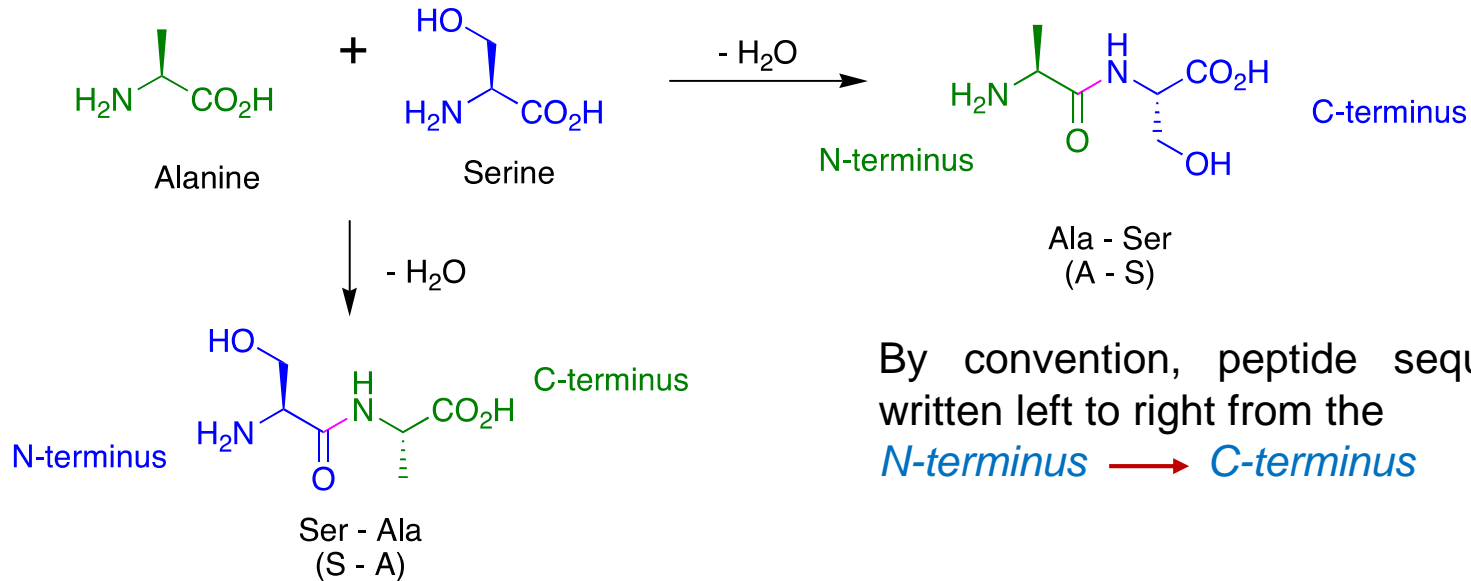


D. Amino Acids with Hydrophobic Side Chains



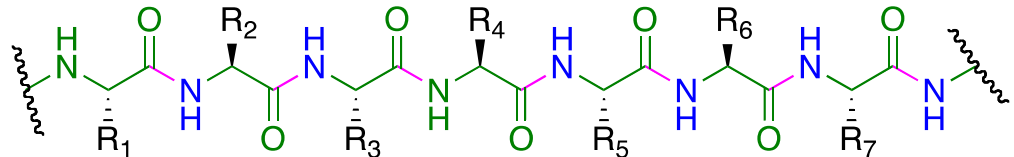
Peptide & Protein: *Sequences*

Proteins and peptides are **Biopolymers** made up of amino acid units (residues) that are linked together through the formation of amide bonds (**peptide bonds**) from the **aminogroup** of one residue and the **carboxylate** of a second residue



By convention, peptide sequences are written left to right from the *N-terminus* \rightarrow *C-terminus*

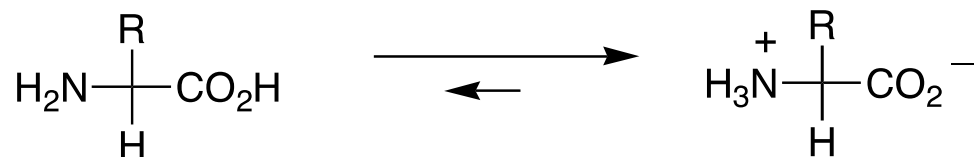
peptide (< 50 amino acids)
protein (> 50 amino acids)



Proteins are large, complex molecules that serve diverse functional and structural roles within cells.

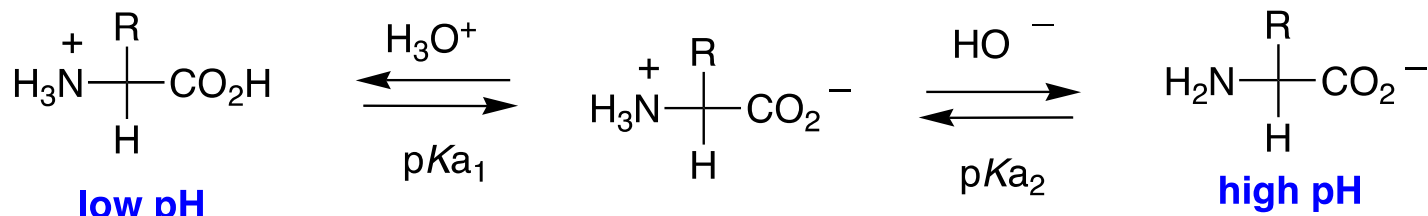
Amino Acids: Zwitterionic Behaviour

Acid-Base Behavior of Amino Acids: Amino acids exist as a **zwitterion**: a dipolar ion having both a formal positive and formal negative charge (overall charge neutral).

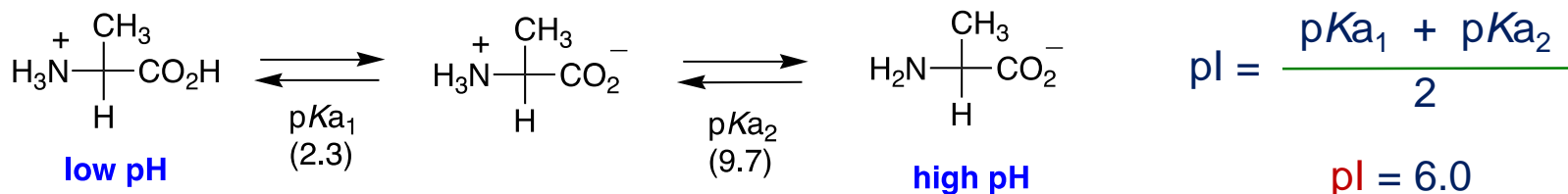


Amino acids are amphoteric: they can react as either an **acid** or a **base**. **Ammonium ion** acts as an **acid**, the **carboxylate** as a **base**.

Isoelectric point (pI): The pH at which the amino acid exists largely in a neutral, zwitterionic form (influenced by the nature of the side chain)

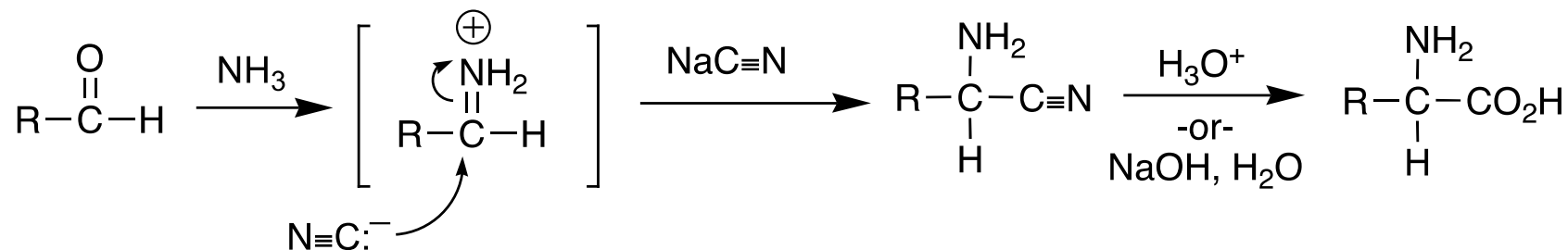


Calculating the Isoelectric Point of Alanine:

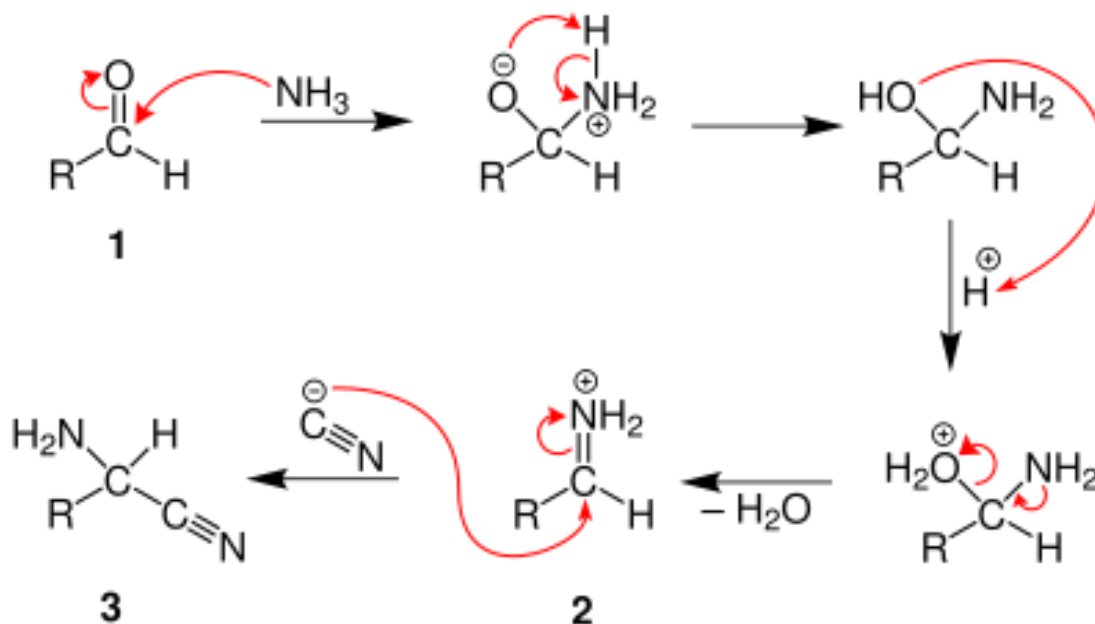


Amino Acids: *Synthesis*

Strecker Synthesis: The Strecker amino acid synthesis, is a method for the synthesis of amino acids by the reaction of an **aldehyde** with **ammonium chloride** in the presence of **Sodium cyanide**.

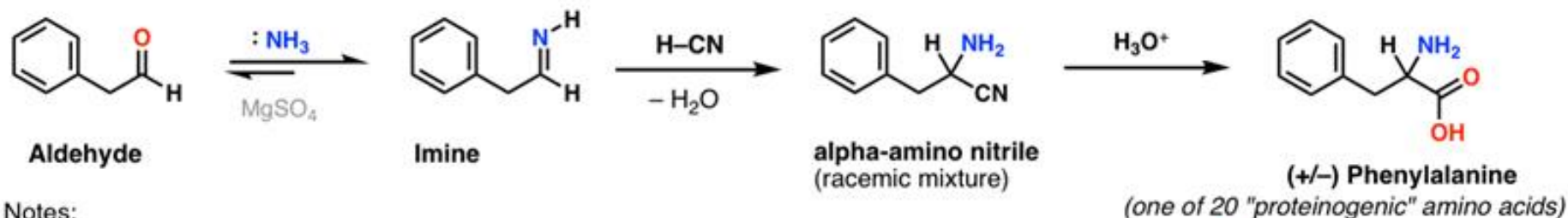


Mechanism



Amino Acids: *Synthesis*

The Strecker Synthesis of Amino Acids From Aldehydes



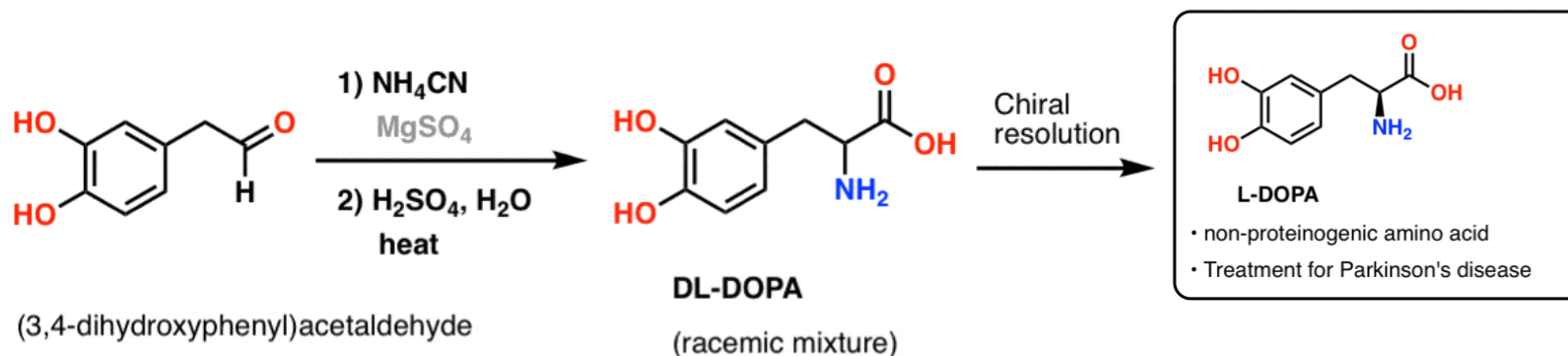
Notes:

- although "NH₄CN" may sometimes be written, NH₄CN itself is not a stable solid. However NH₄CN is made in solution by combining NH₄Cl and KCN, with KCl as a byproduct
- MgSO₄ is sometimes used to assist in imine formation, as it absorbs H₂O and drives the equilibrium towards the imine

• (greatly preferred to using HCN gas!)

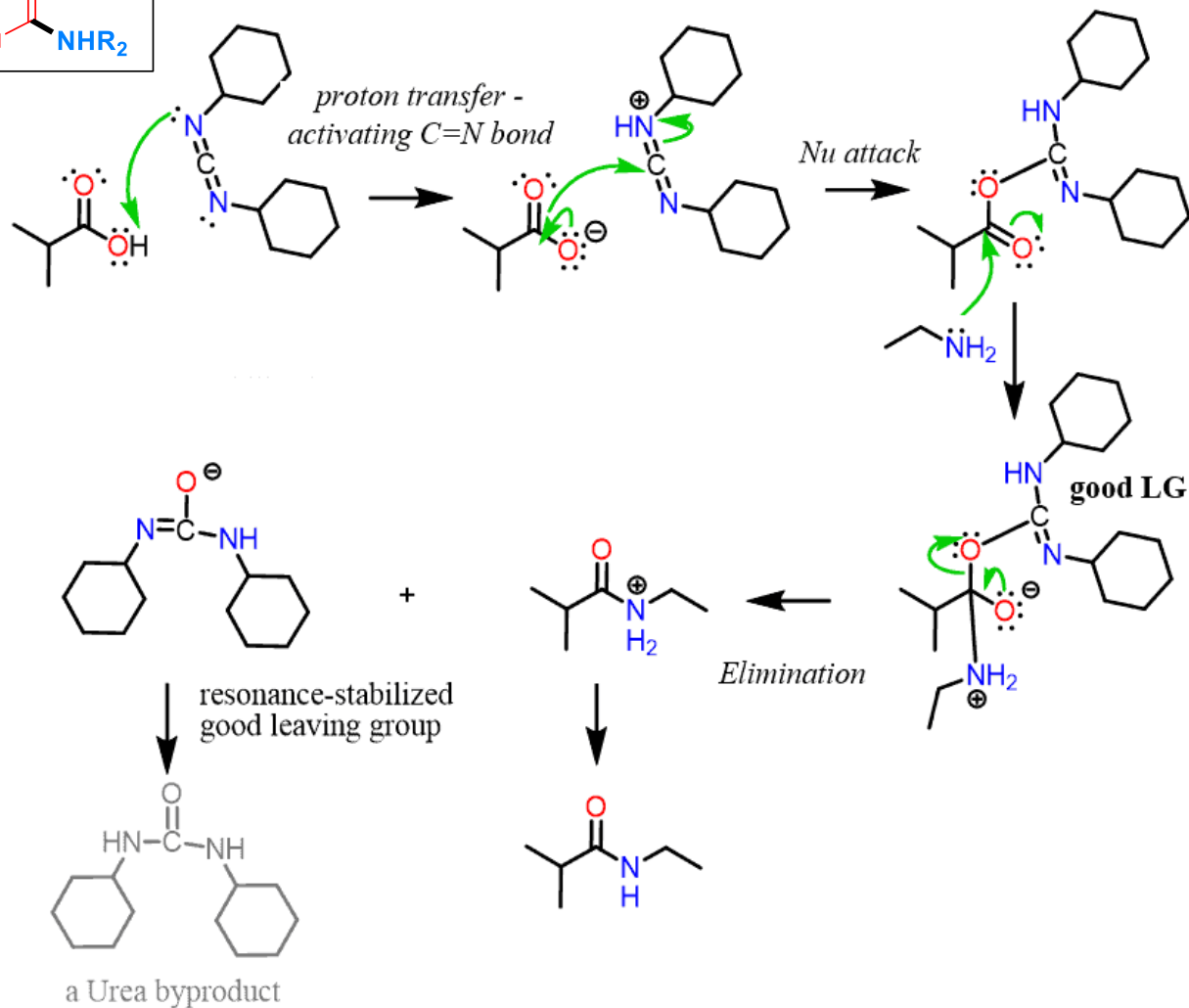
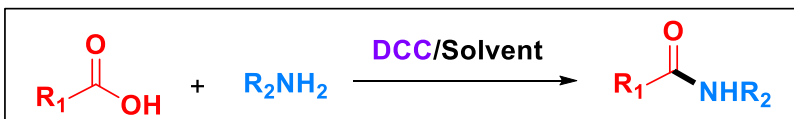


An application of the Strecker: synthesis of important non-proteinogenic amino acids

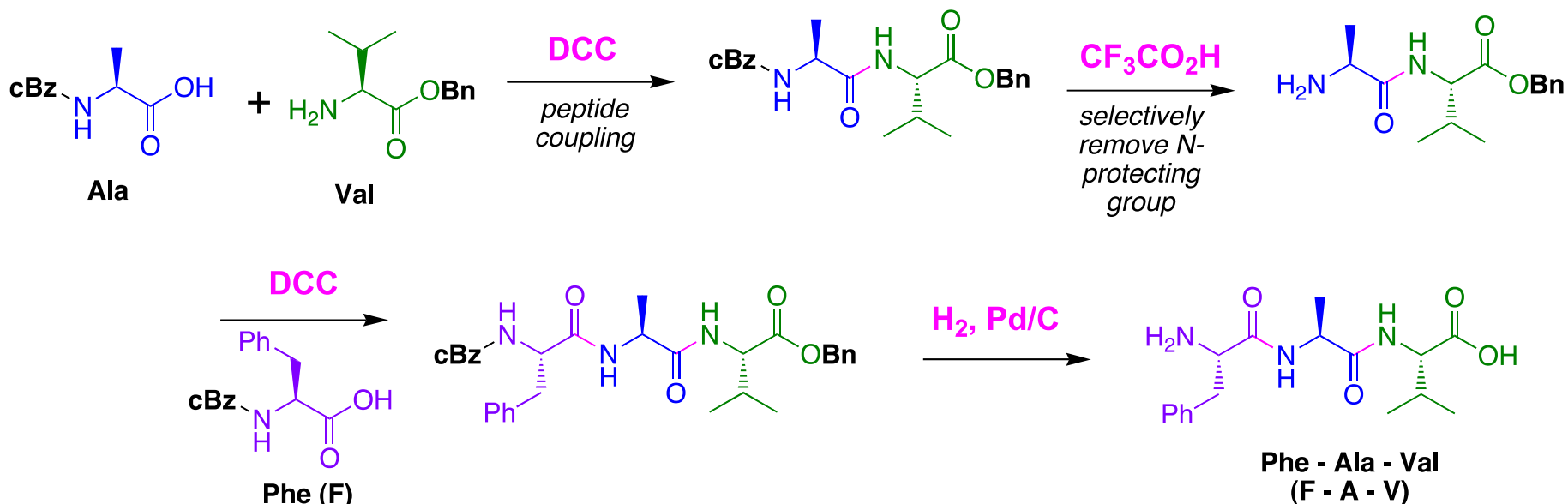


Peptide Synthesis: *Amide Bond*

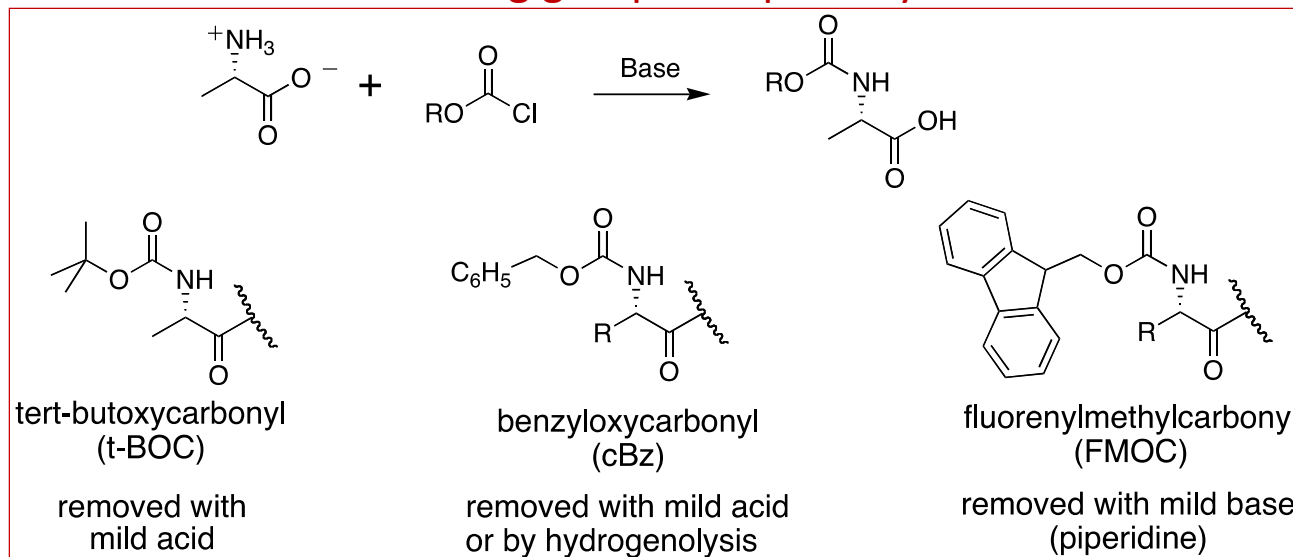
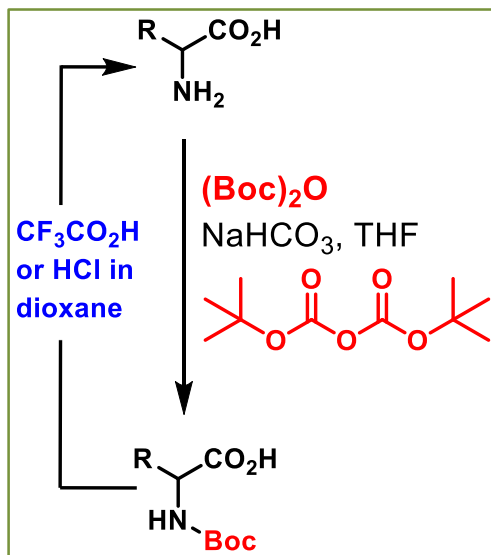
Peptide Bond Formation. Amide formation from the reaction of an amine with a carboxylic acid is slow. Amide bond formation (peptide coupling) can be accelerated if the carboxylic acid is activated. *Reagent: dicyclohexylcarbodiimide (DCC)*



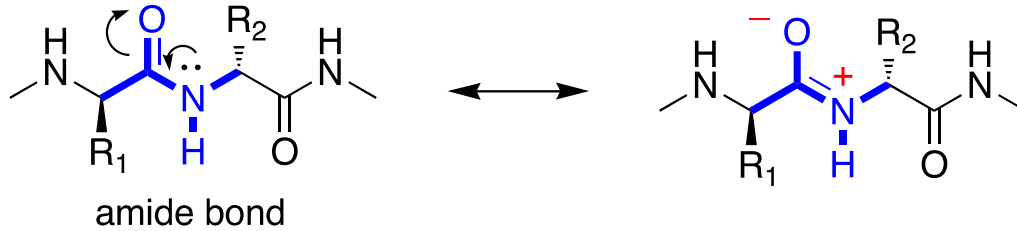
Peptide Synthesis: *Phe-Ala-Val*



Common Protecting group in Peptide Synthesis

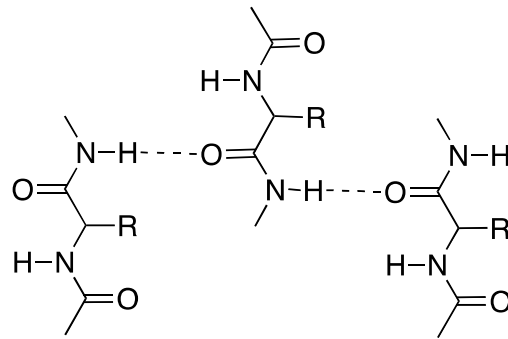


The *amide (peptide) bond* has $C=N$ double bond character due to resonance resulting in a planar geometry

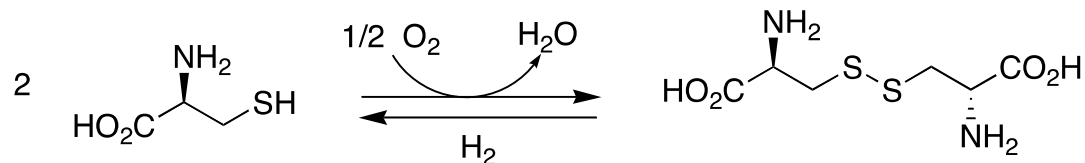


- *restricts rotations*
- *resistant to hydrolysis*

The $N-H$ bond of one amide linkage can form a hydrogen bond with the $C=O$ of another.



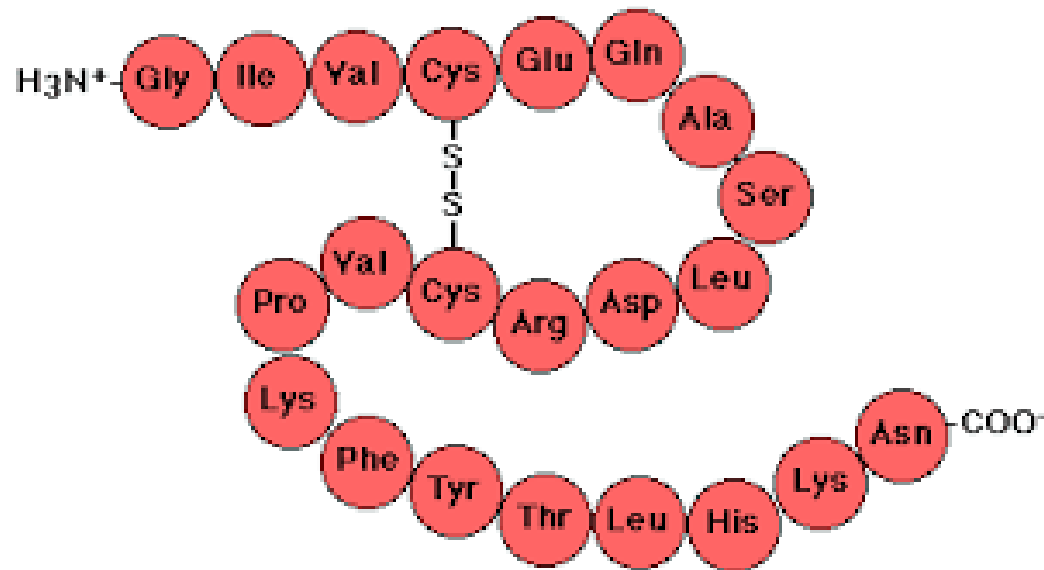
Disulfide bonds: the thiol groups of cysteine can be oxidized to form disulfides (Cys S-S-Cys)



Protein: *Primary structure*

The primary structure is the sequence of amino acids.

Protein primary structure is the linear sequence of *amino acids in a peptide* or protein. By convention, the primary structure of a protein is reported starting from the *amino-terminal (N)* end to the *carboxyl-terminal (C)* end. The amino acids in the primary structure are held together by *covalent bonds*, which are made during the process of protein synthesis.



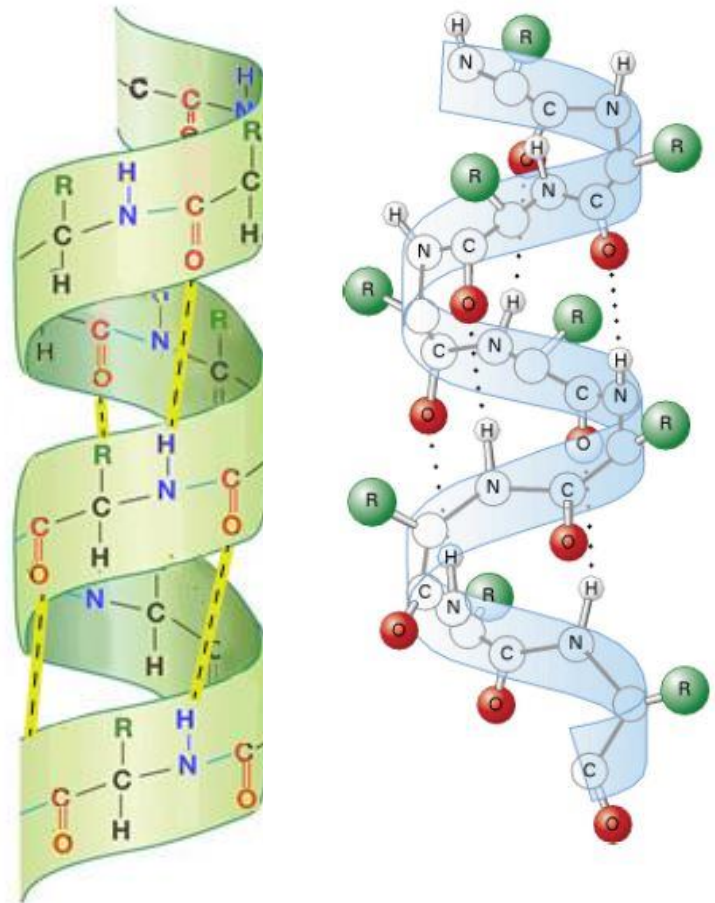
The secondary structure is primarily composed of **alpha helices** and **beta-sheets**.

Protein: *Secondary structure*

Secondary structure of proteins is formally defined by the *pattern of hydrogen bonds* between the *amino hydrogen* and *carboxyl oxygen* atoms in the peptide backbone. The most common secondary structures are *alpha helices* and *beta sheets*.

The *alpha helix* (α -helix) is a common motif in the secondary structure of proteins and is a right hand-helix conformation in which every *backbone N-H group* hydrogen bonds to the *backbone C=O group* of the *amino acid located three or four residues earlier along the protein sequence*.

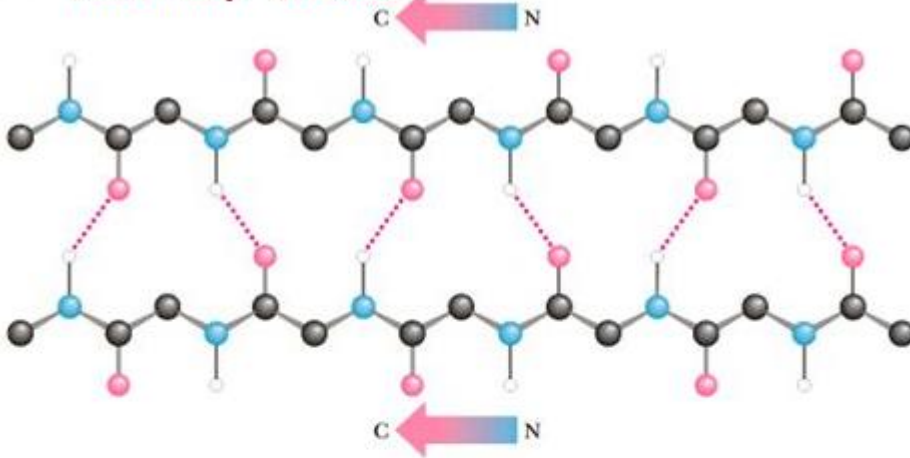
Alpha helix (α -helix)



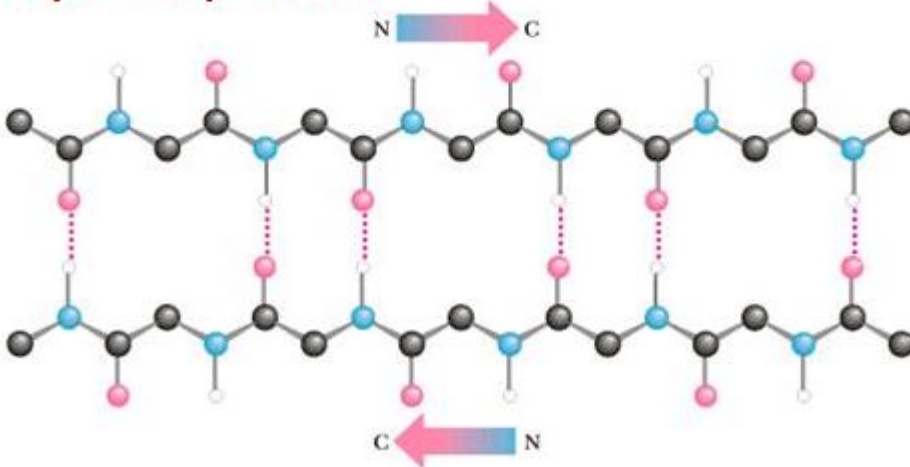
Protein: *Secondary structure*

The β -sheet is a common motif of regular secondary structure in proteins. Beta sheets consist of so β -strand connected laterally by at least two or three backbone hydrogen bonds, forming a generally twisted, pleated sheet.

Parallel β -sheets



Anti-parallel β -sheets



- β -sheets formed from multiple side-by-side beta-strands.
- Can be parallel or anti-parallel configuration.
- Anti-parallel beta-sheets are more stable.

The supramolecular association of β -sheets has been implicated in formation of the protein aggregates and fibrils observed in many human diseases, notably the amyloidosis such as Alzheimer's disease.