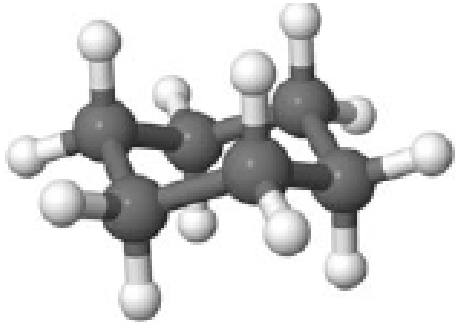
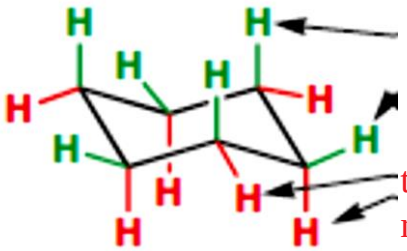
COURSE : SC202 (CHEMISTRY)

DR. SANGITA TALUKDAR

LECTURE-6

DATE: 19.1.2021



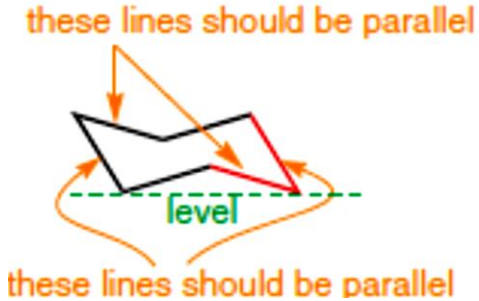


these hydrogen atoms are all 'up' relative to their partners on the same C carbon

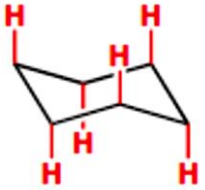
these hydrogens are all 'down' relative to their partners on the same C atom

All six carbon atoms are identical, but there are two types of protons—one type stick either vertically up or down and are called **axial** hydrogen atoms; the other sort stick out sideways and are called **equatorial** hydrogen atoms.

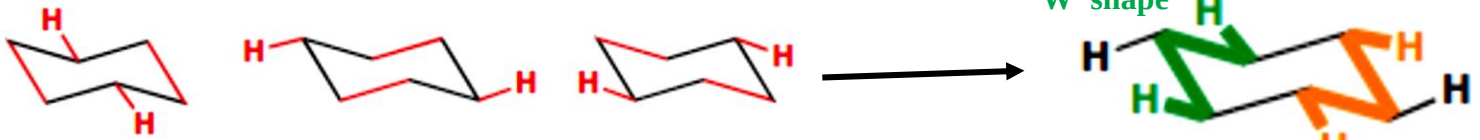
Guidelines for drawing cyclohexane



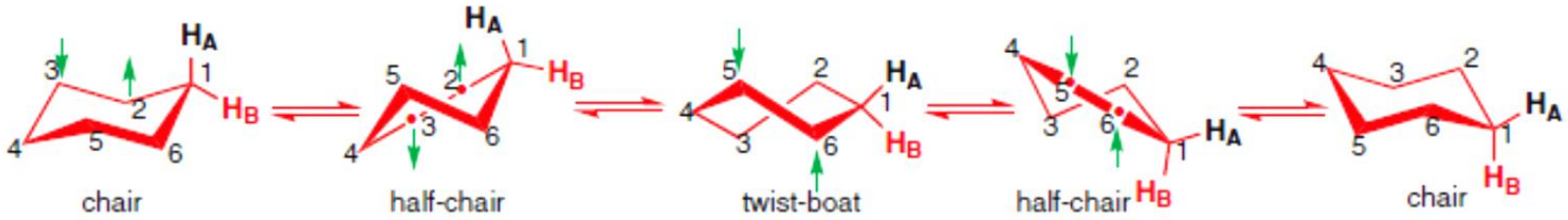
The axial bonds are relatively easy to draw in. They should all be vertically aligned and alternate up and down all round the ring.

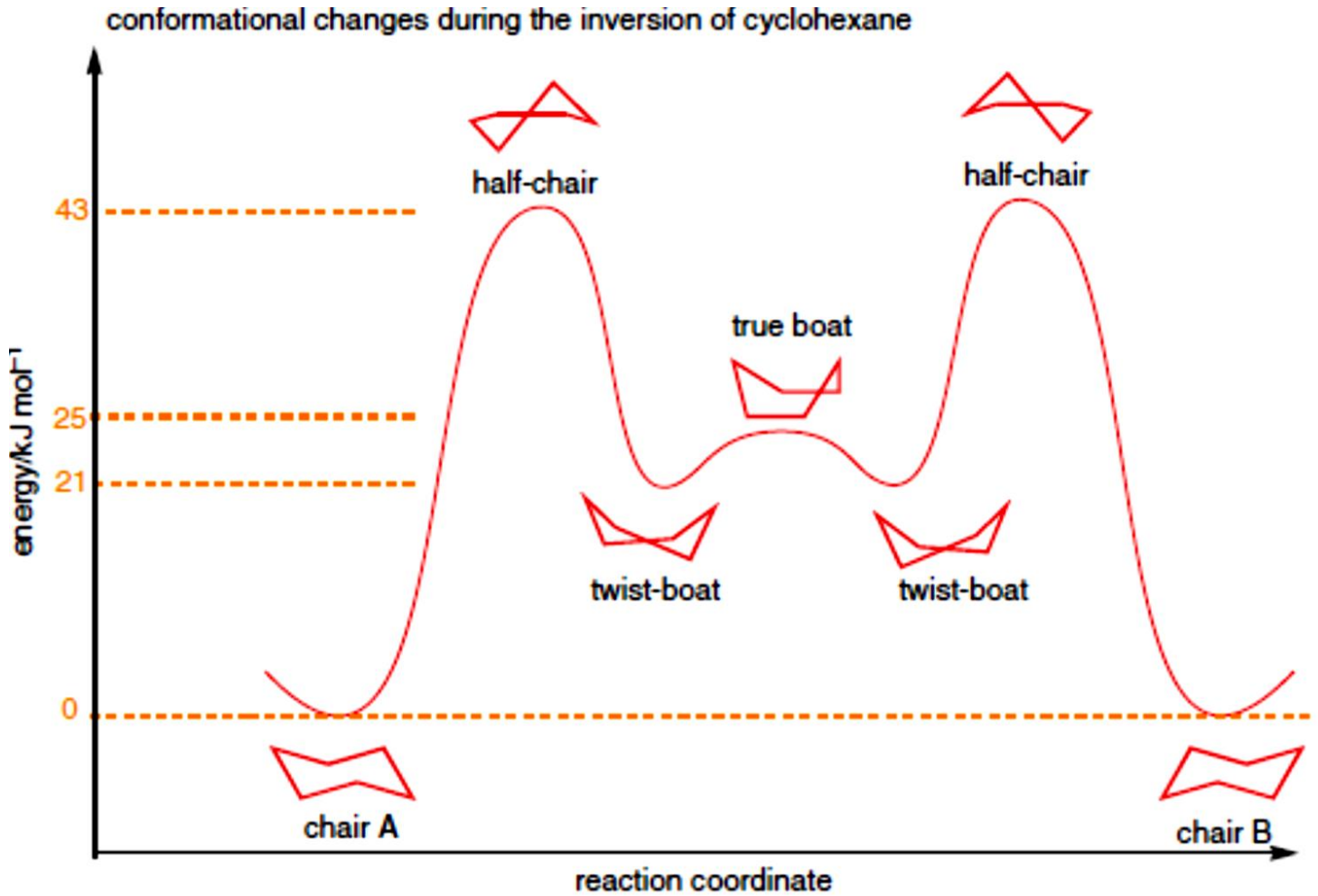


Each equatorial bond must be parallel to two C–C bonds.



The ring inversion (flipping) of cyclohexane

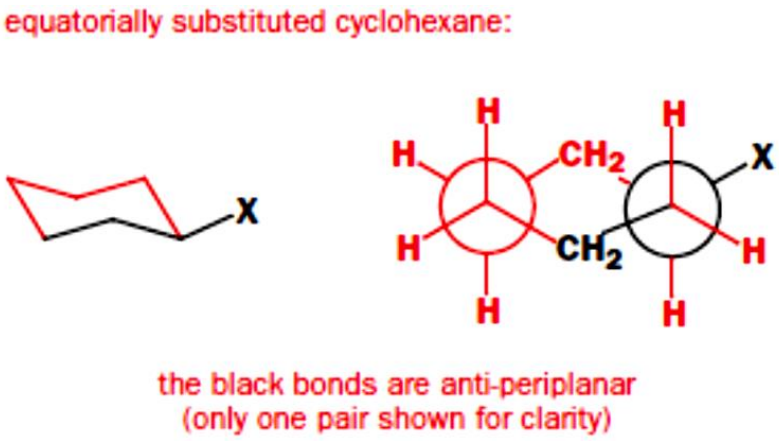


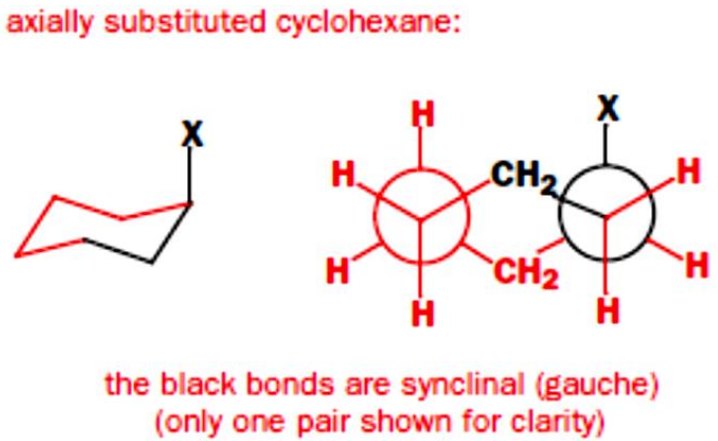


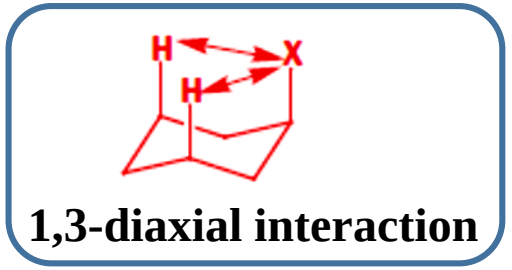
Substituted cyclohexanes

The conformer with the substituent axial is higher in energy, which means there will be less of this form present at equilibrium.

The first is that the axial conformer is destabilized by the repulsion between the axial group X and the two axial hydrogen atoms on the same side of the ring. This interaction is known as the **1,3-diaxial interaction**. As the group X gets larger, this interaction becomes more severe and there is less of the conformer with the group axial.





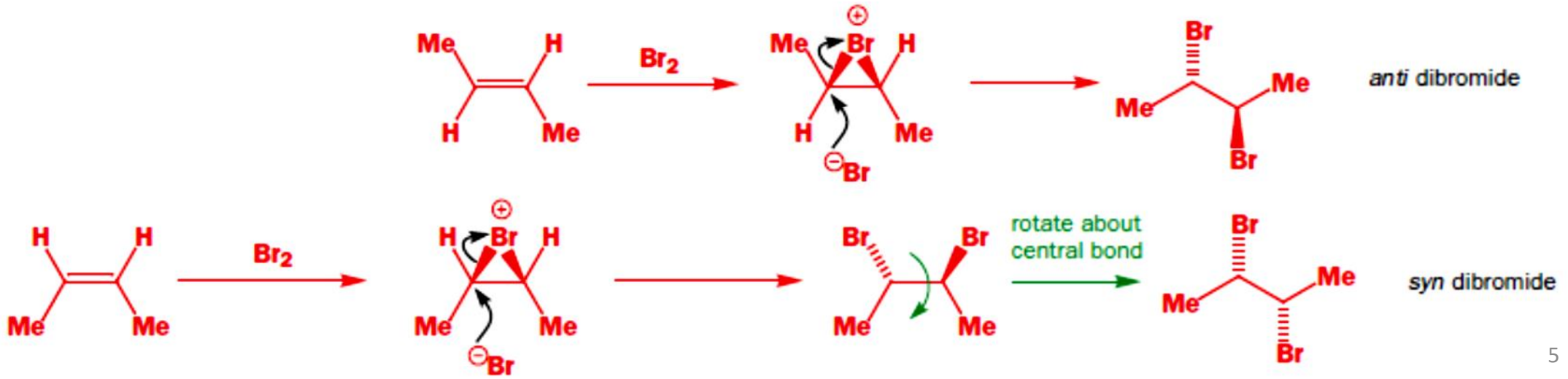


The second reason is that in the equatorial conformer the C–X bond is anti-periplanar to two C–C bonds, while, for the axial conformer, the C–X bond is synclinal (gauche) to two C–C bonds.

- **Stereospecific reactions**: reactions where the mechanism means that the stereochemistry of the starting material determines the stereochemistry of the product and there is no choice involved.

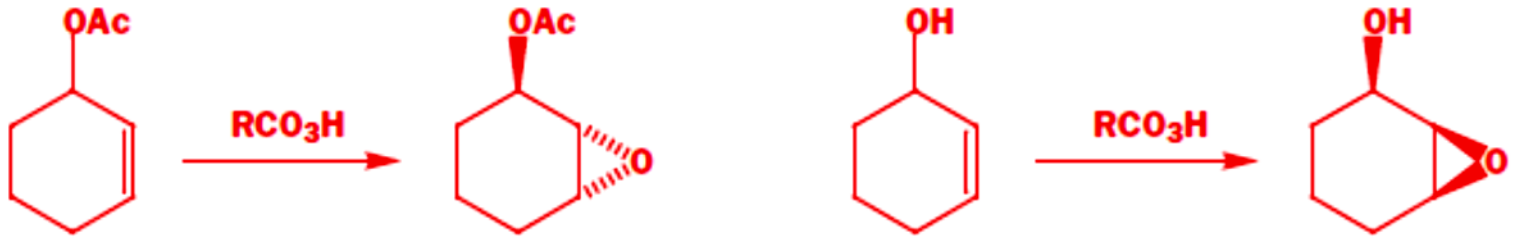
  1. S_N2 reactions are stereospecific: they proceed with inversion so that the absolute stereochemistry of the starting material determines the absolute stereochemistry of the product

  2. Electrophilic addition of bromine to alkenes is stereospecific and leads to *anti* addition across a double bond. So if we want the *anti* dibromide we choose to start with the *trans* double bond; if we want the *syn* dibromide we start with the *cis* double bond. The geometry of the starting material determines the relative stereochemistry of the product.

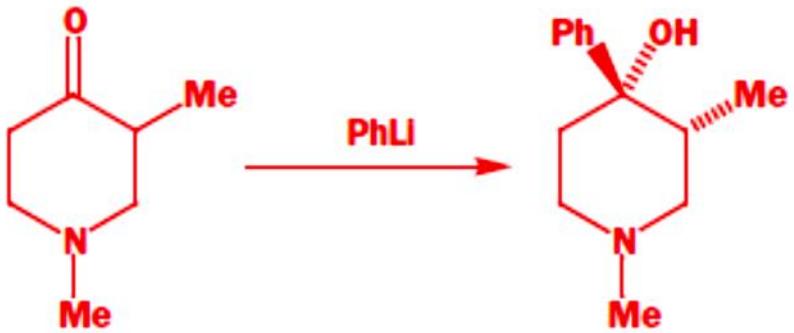


- **Stereoselective reactions:** reactions where one stereoisomer of product is formed predominantly because the reaction has a choice of pathways, and one pathway is more favourable than the other.

1. Epoxidation of cyclic alkenes is stereoselective, with reaction taking place on the less hindered face, or directed by hydrogen bonding to a hydroxyl group



2. Nucleophilic attack on six-membered ring ketones is stereoselective: small nucleophiles attack axially and large ones equatorially

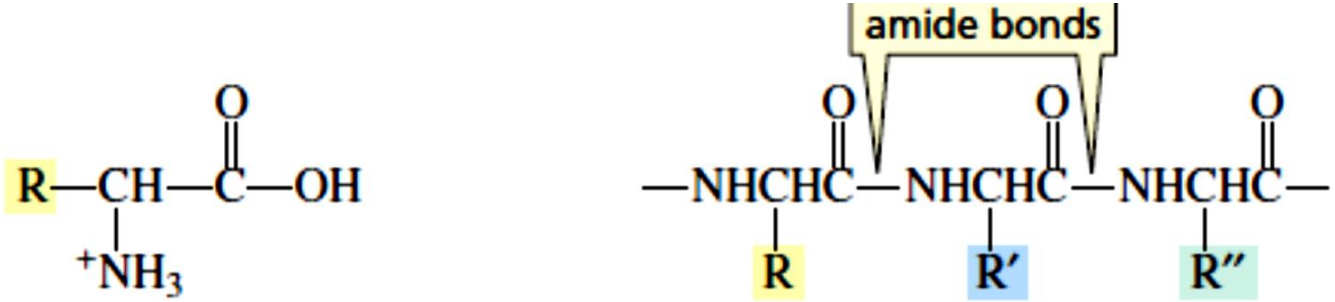


- **Regiochemistry:** If a reaction takes place on an unsymmetrical compound, different pathways are possible. This is known as regiochemistry.
- If a **reaction** takes place that produces two or more products and one of the products predominates, the **reaction** is said to be **regioselective**. On the other hand, if one of the products completely predominates (or nearly so), then the **reaction** is said to be **regiospecific**.

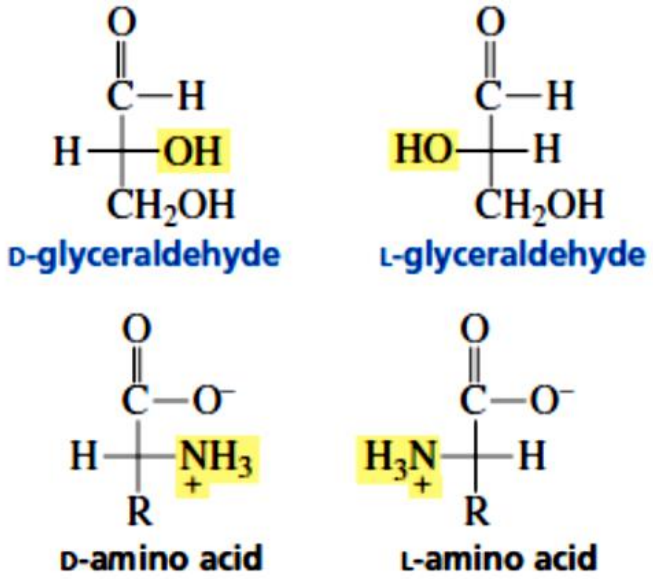
Amino Acids, Peptides and Proteins

Peptides and **proteins** are polymers of **amino acids** linked together by amide bonds. The repeating units are called **amino acid residues**.

Amino acid polymers can be composed of any number of monomers. A **dipeptide** contains two amino acid residues, a **tripeptide** contains three, an **oligopeptide** contains three to 10, and a **polypeptide** contains many amino acid residues

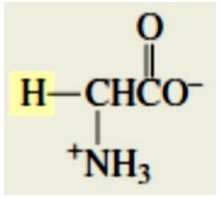


An amino acid drawn in a Fischer projection with the carboxyl group on the top and the R group on the bottom of the vertical axis is a **D-amino acid** if the amino group is on the right and an **L-amino acid** if the amino group is on the left.

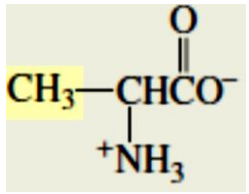


Classification of Amino Acids

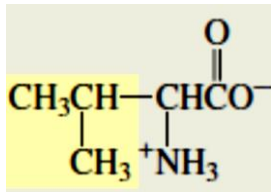
Achiral amino acid



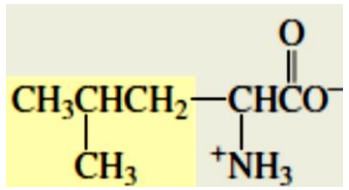
Glycine



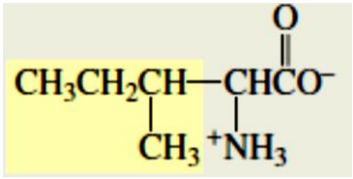
Alanine



Valine

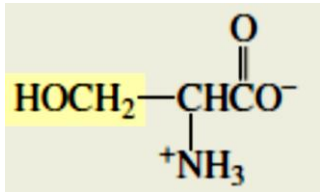


Leucine

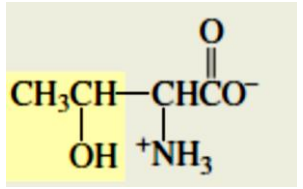


Isoleucine

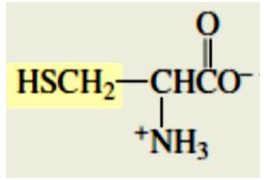
Aliphatic side chain amino acids



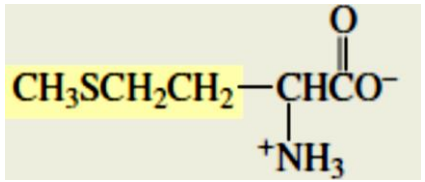
Serine



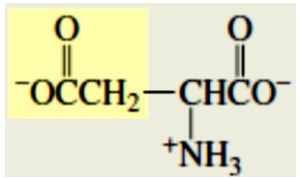
Threonine



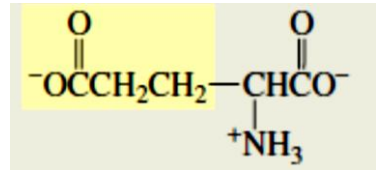
Cysteine



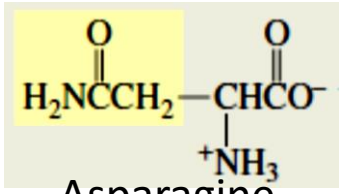
Methionine



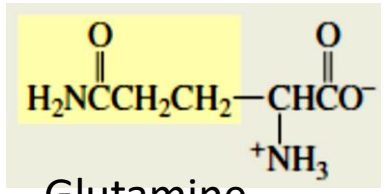
Aspartic acid



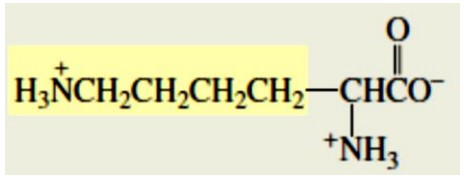
Glutamic acid



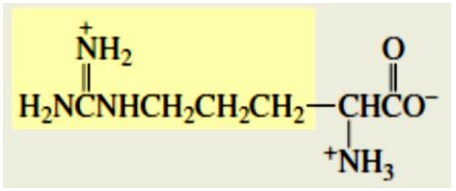
Asparagine



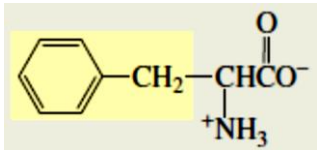
Glutamine



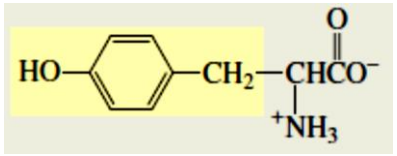
Lysine



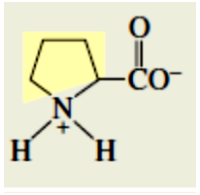
Arginine



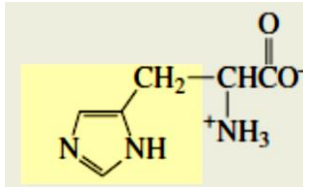
Phenyl alanine



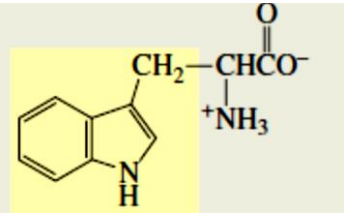
Tyrosine



Proline



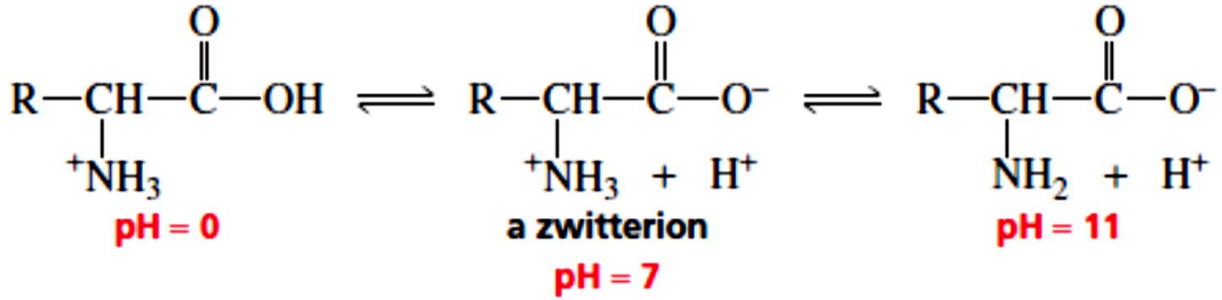
Histidine



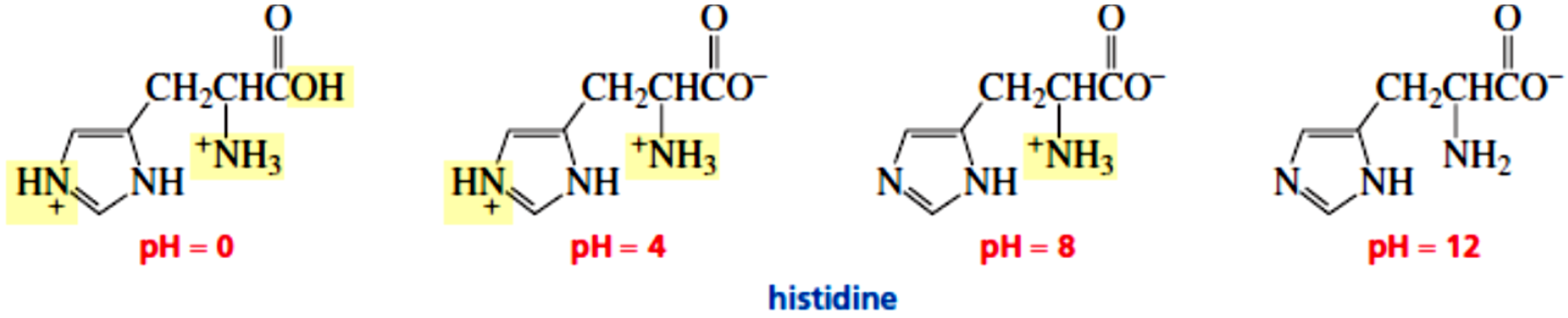
Trytophan

Acid–Base Properties of Amino Acids

A **zwitterion** is a compound that has a negative charge on one atom and a positive charge on a nonadjacent atom. (The name comes from *zwitter*, German for "hermaphrodite" or "hybrid.")

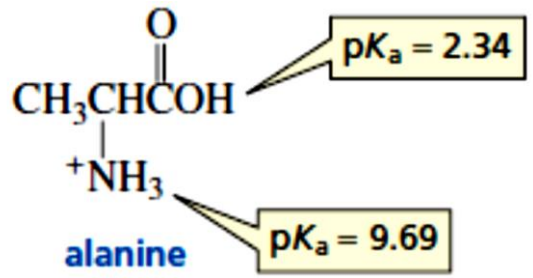


A few amino acids have side chains with ionizable hydrogens. The protonated imidazole side chain of histidine, for example, has a pKa of 6.04. Histidine, therefore, can exist in four different forms, and the form that predominates depends on the pH of the solution



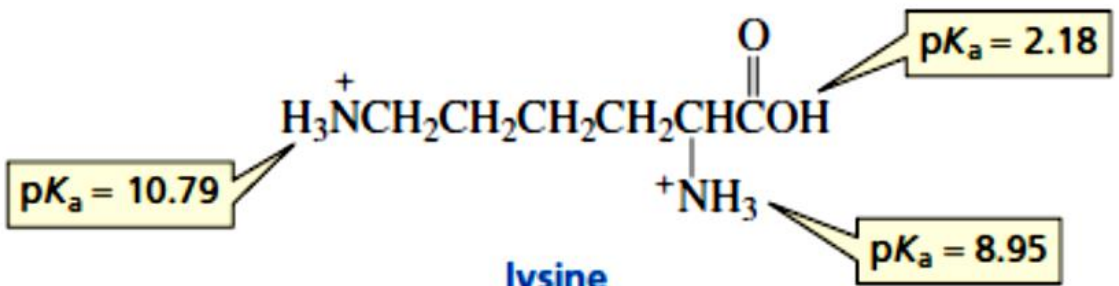
The **isoelectric point** (pI) of an amino acid is the pH at which it has no net charge. In other words, it is the pH at which the amount of positive charge on an amino acid exactly balances the amount of negative charge:

pI (isoelectric point) = pH at which there is no net charge

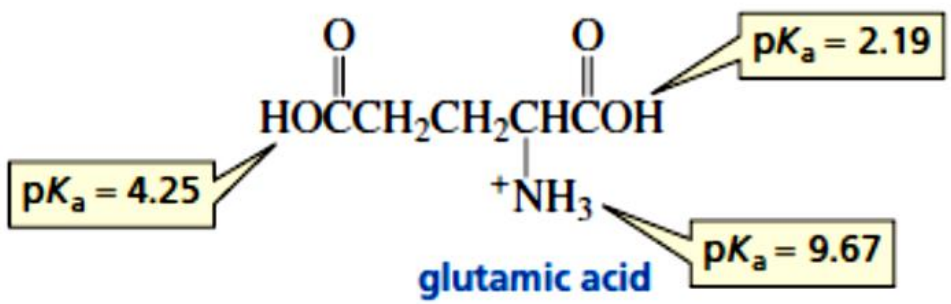


$$pI = \frac{2.34 + 9.69}{2} = \frac{12.03}{2} = 6.02$$

The pI of an amino acid that *has* an ionizable side chain is the average of the pKa values of the similarly ionizing groups.



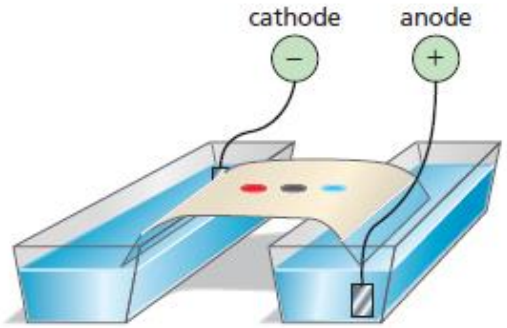
$$pI = \frac{8.95 + 10.79}{2} = \frac{19.74}{2} = 9.87$$

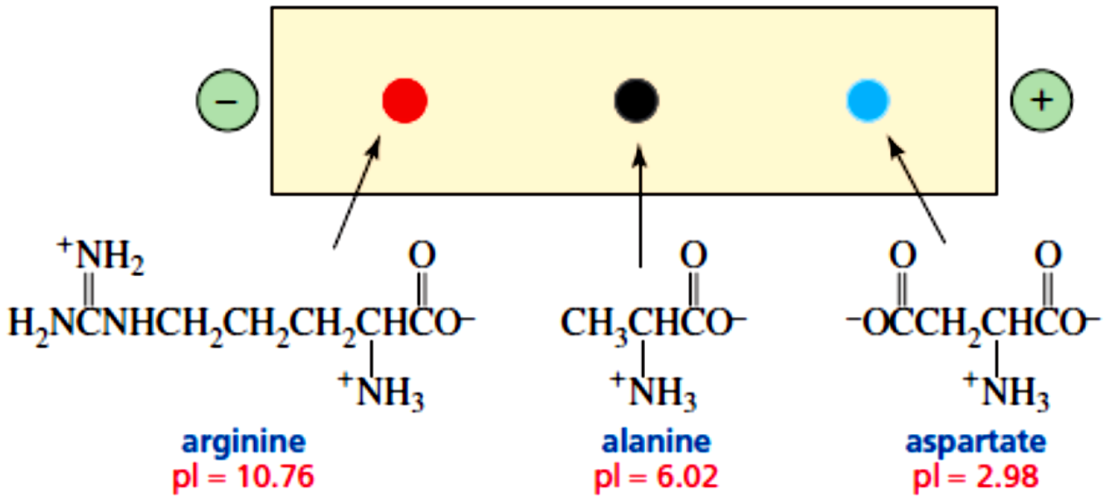


$$pI = \frac{2.19 + 4.25}{2} = \frac{6.44}{2} = 3.22$$

Separation of Amino Acids

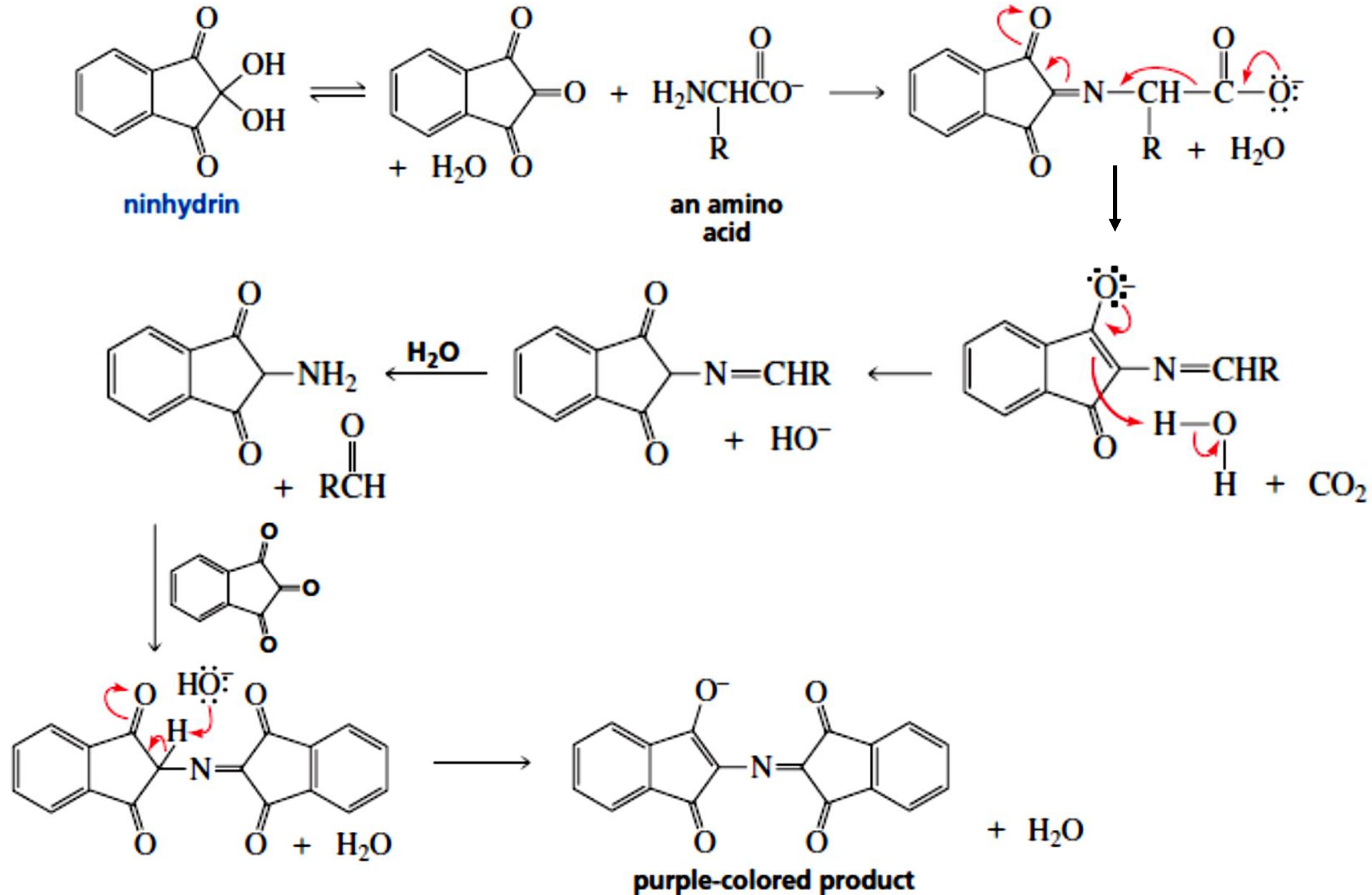
Electrophoresis





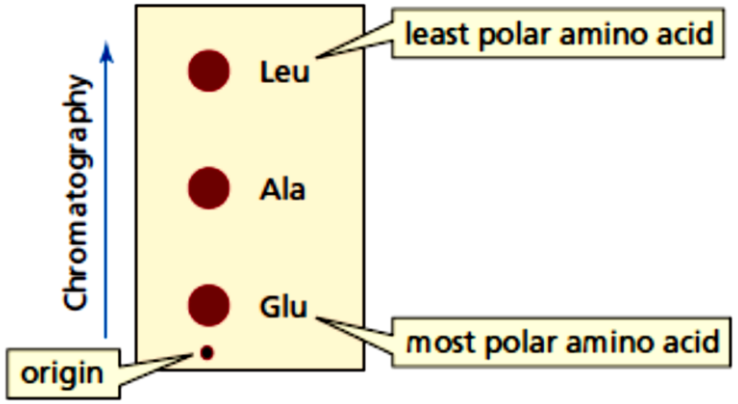
Electrophoresis separates amino acids on the basis of their pI values. A few drops of a solution of an amino acid mixture are applied to the middle of a piece of filter paper or to a gel. When the paper or the gel is placed in a buffered solution between two electrodes and an electric field is applied, an amino acid with a pI greater than the pH of the solution will have an overall positive charge and will migrate toward the cathode. An amino acid with a pI less than the pH of the buffer will have an overall negative charge and will migrate toward the anode (the positive electrode). If two molecules have the same charge, the larger one will move more slowly during electrophoresis because the same charge has to move a greater mass.

Mechanism for the reaction of an amino acid with ninhydrin to form a colored product



Paper Chromatography and Thin-Layer Chromatography

The technique of paper chromatography separates amino acids on the basis of polarity. A few drops of a solution of an amino acid mixture are applied to the bottom of a strip of filter paper. The edge of the paper is then placed in a solvent (typically a mixture of water, acetic acid, and butanol). The solvent moves up the paper by capillary action, carrying the amino acids with it. Depending on their polarities, the amino acids have different affinities for the mobile (solvent) and stationary (paper) phases and therefore travel up the paper at different rates. The more polar the amino acid, the more strongly it is adsorbed onto the relatively polar paper. The less polar amino acids travel up the paper more rapidly, since they have a greater affinity for the mobile phase. Therefore, when the paper is developed with ninhydrin, the colored spot closest to the origin is the most polar amino acid and the spot farthest away from the origin is the least polar amino acid



Paper chromatography has largely been replaced by **thin-layer chromatography** (TLC). Similar to paper hromatography, TLC differs from it in that TLC uses a plate with a coating of solid material instead of filter paper.

Ion-Exchange Chromatography

Preparative separation, in which larger amounts of amino acids are separated for use in subsequent processes, can be achieved using **ion-exchange chromatography**.

This technique employs a column packed with an insoluble resin. A solution of a mixture of amino acids is loaded onto the top of the column and eluted with a buffer. The amino acids separate because they flow through the column at different rates, as explained below.

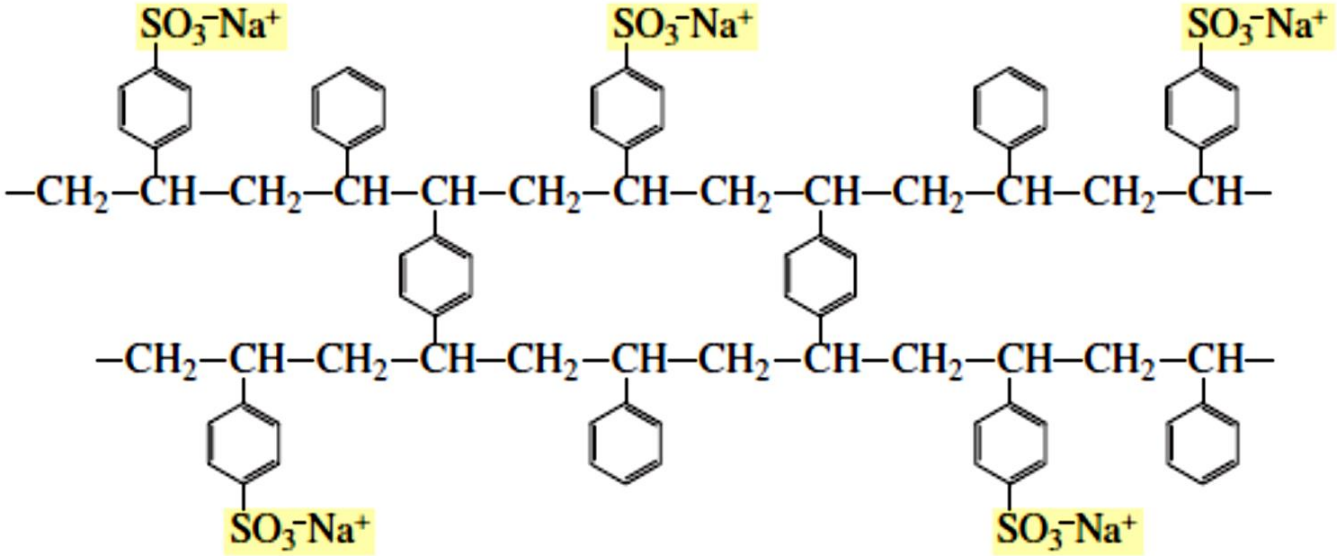


Figure A section of a cation-exchange resin. This particular resin is called Dowex® 50.

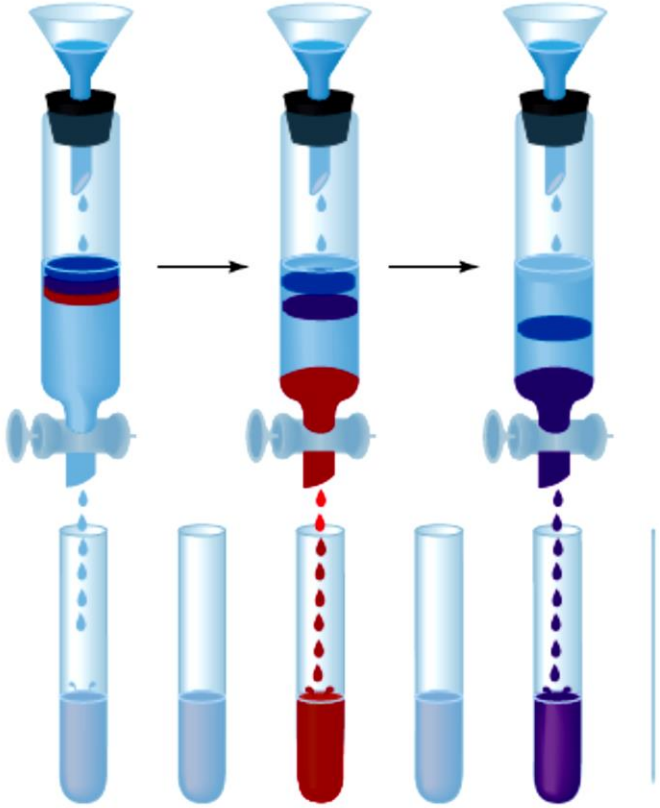
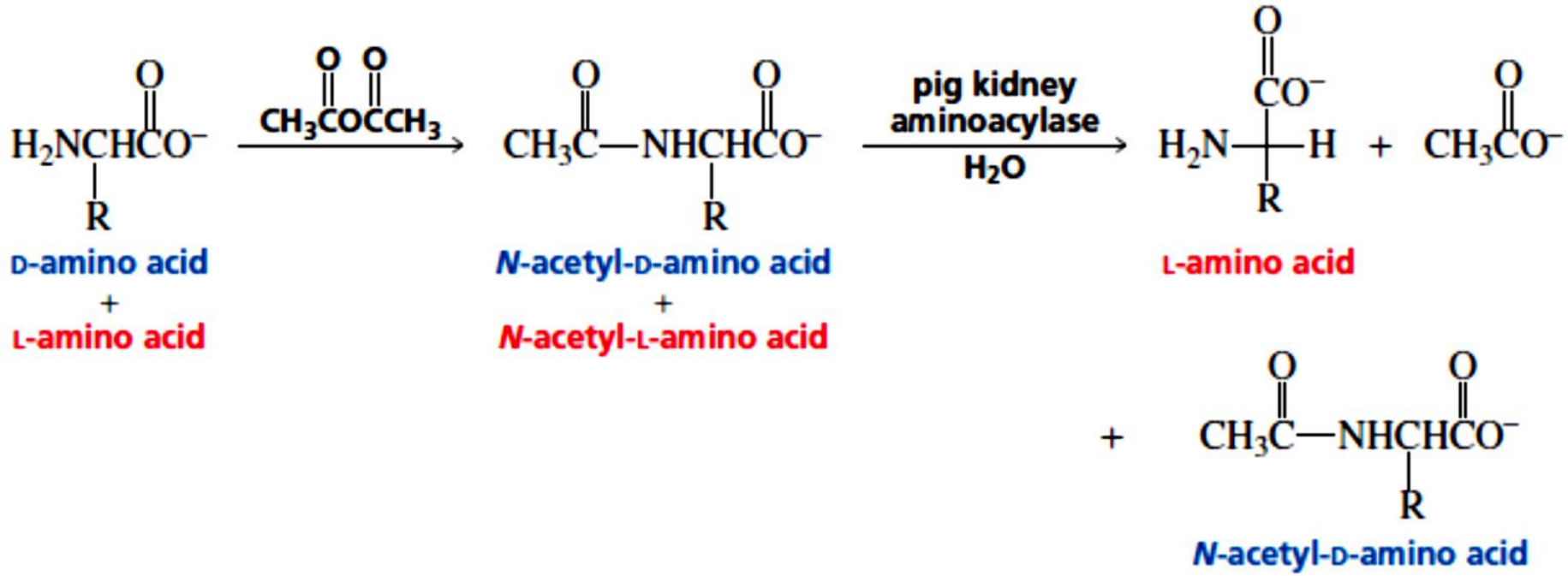


Figure : Separation of amino acids by ion-exchange chromatography.

- The resin is a chemically inert material with charged side chains. One commonly used resin is a copolymer of styrene and divinylbenzene with negatively charged sulfonic acid groups on some of the benzene rings. This kind of resin is called a **cation-exchange resin** because it exchanges the counterions of the groups for the positively charged species that are added to the column.
- Resins with positively charged groups are called **anion-exchange resins** because they impede the flow of anions by exchanging their negatively charged counterions for negatively charged species that are added to the column.
- Cations bind most strongly to cation-exchange resins.
- Anions bind most strongly to anion-exchange resins.

Resolution of Racemic Mixtures of Amino Acids

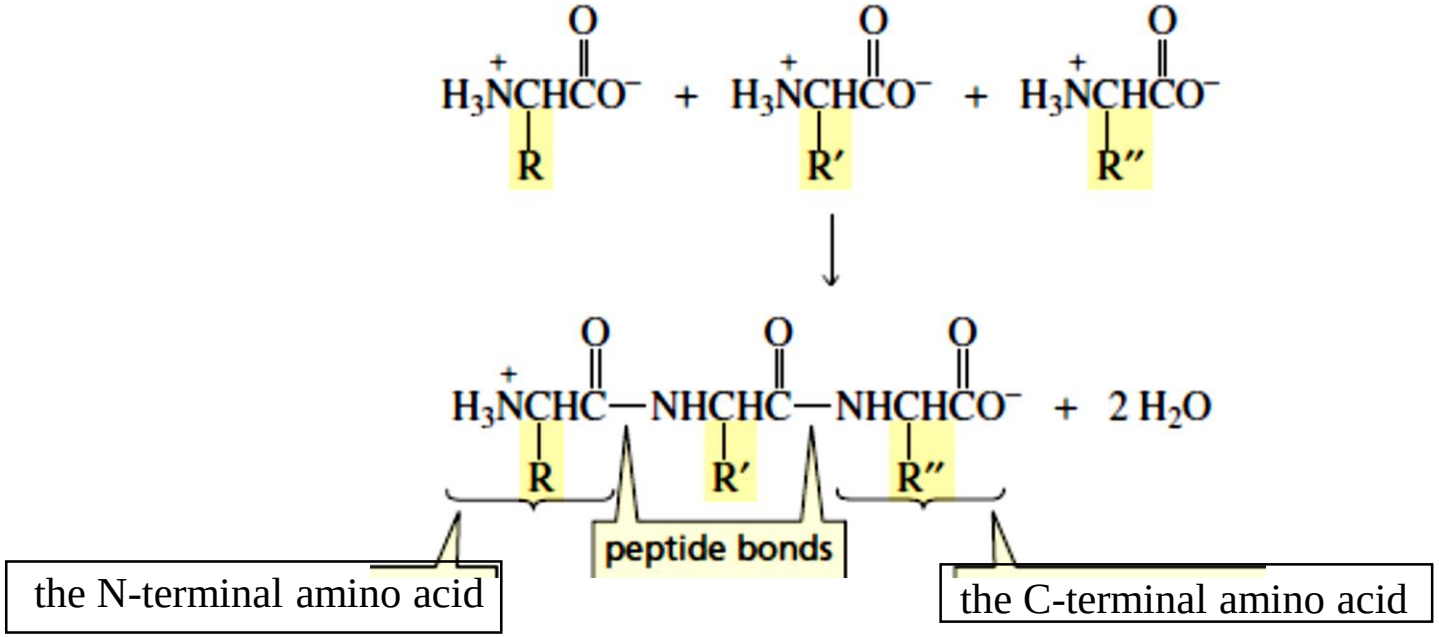
- When amino acids are synthesized in the laboratory, the product is usually a racemic mixture of D and L enantiomers
- They can be separated by means of an **enzyme- catalyzed reaction**. Because an enzyme is chiral, it will react at a different rate with each of the enantiomers



Because the resolution (separation) of the enantiomers depends on the difference in the rates of reaction of the enzyme with the two *N*-acetylated compounds, this technique is known as a **kinetic resolution**

Peptide Bonds

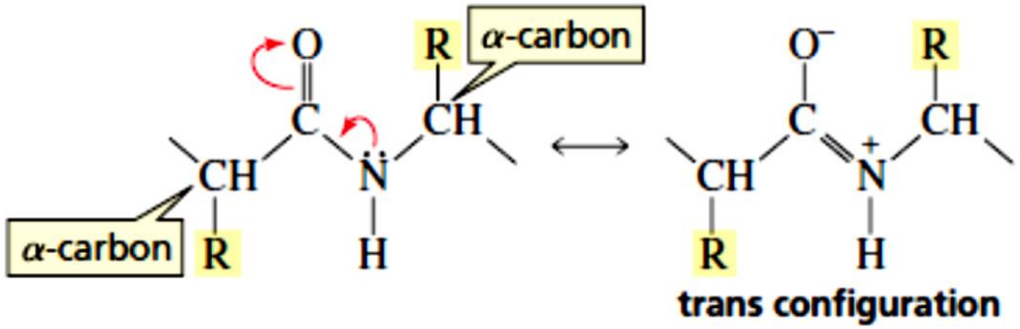
The amide bonds that link amino acid residues are called **peptide bonds**. By convention, peptides and proteins are written with the free amino group (the **N-terminal amino acid**) on the left and the free carboxyl group (the **C-terminal amino acid**) on the right.



Glu, Cys, His, Val, Ala
the pentapeptide contains the indicated amino acids, but their sequence is not known

Val-Cys-Ala-Glu-His
the amino acids in the pentapeptide have the indicated sequence

- The amino acids are numbered starting with the N-terminal end. The glutamate residue is referred to as Glu 4 because it is the fourth amino acid from the N-terminal end.
- In naming the peptide, adjective names (ending in "yl") are used for all the amino acids except the C-terminal amino acid. Thus, this pentapeptide is named valylcysteylalanylglutamylhistidine.



- A peptide bond has about 40% double-bond character because of electron delocalization.
- Free rotation about the peptide bond is not possible because of its partial double-bond character.

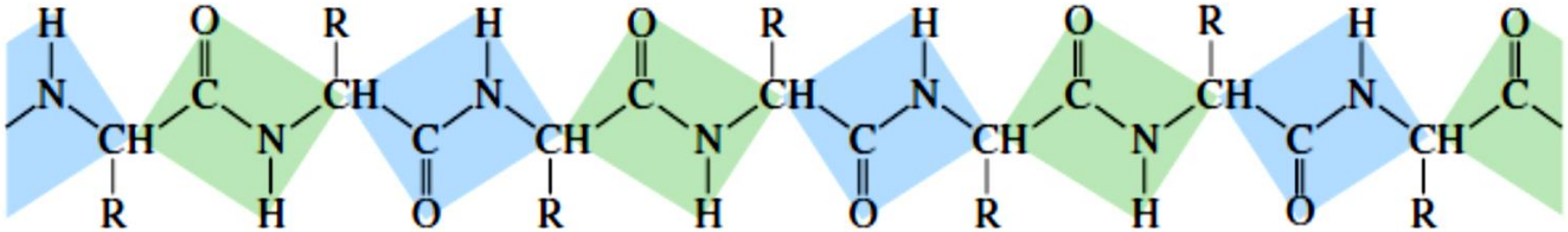
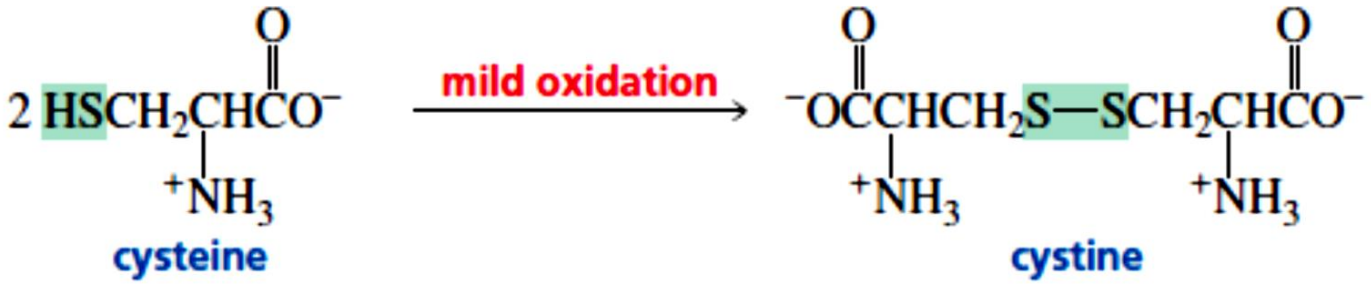


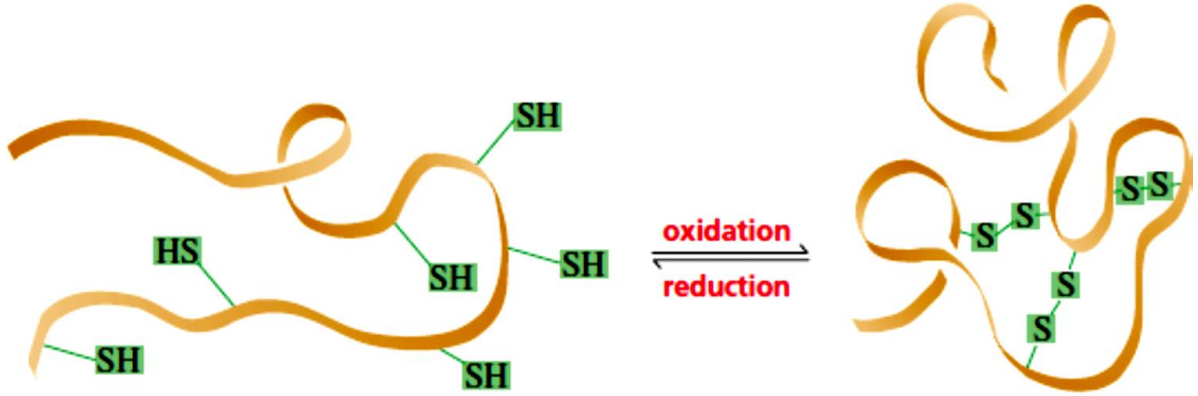
Figure: A segment of a polypeptide chain. The plane defined by each peptide bond is indicated. The R groups bonded to the α carbons are on alternate sides of the peptide backbone

Disulfide Bonds

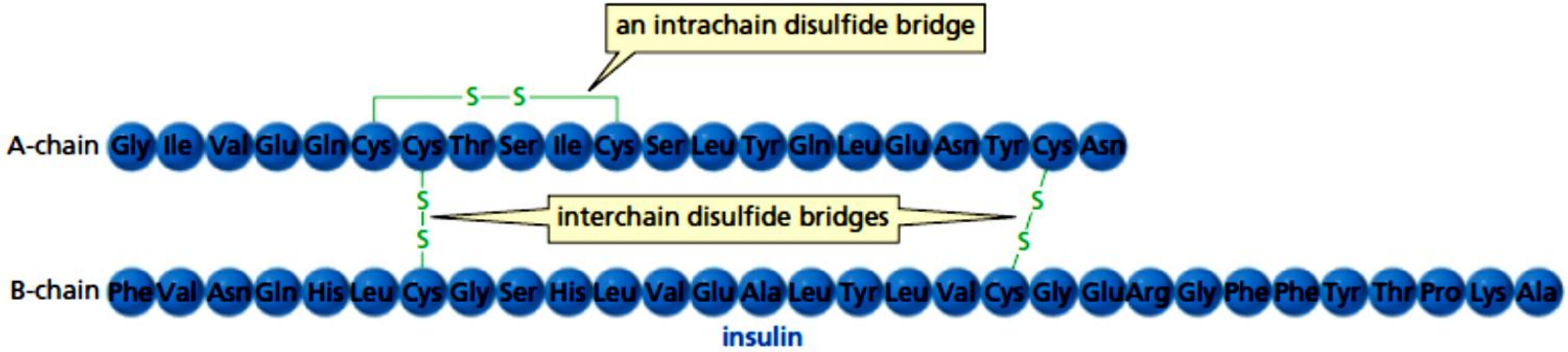
- When thiols are oxidized under mild conditions, they form disulfides. A **disulfide** is a compound with an S-S bond.
- Cysteine is an amino acid that contains a thiol group. Two cysteine molecules therefore can be oxidized to a disulfide. This disulfide is called cystine. This S-S bond is known as a **disulfide bridge**.



- Disulfide bridges are the only covalent bonds that can form between nonadjacent amino acids. They contribute to the overall shape of a protein by holding the cysteine residues in close proximity.

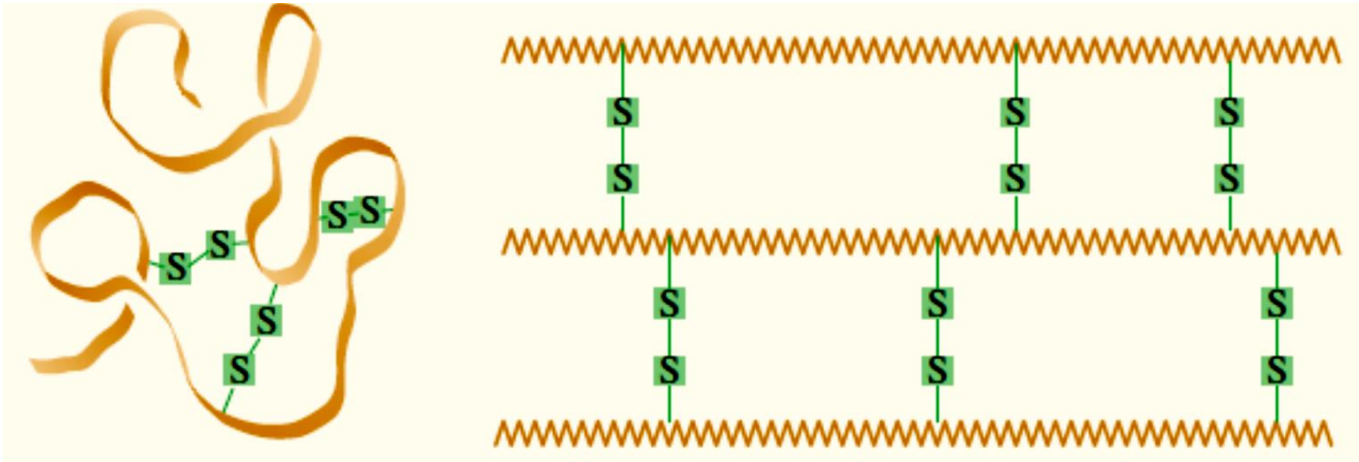


disulfide bridges cross-linking portions of a polypeptide



Insulin is a polypeptide with two peptide chains. The short chain (the A-chain) contains 21 amino acids and the long chain (the B-chain) contains 30 amino acids. The two chains are held together by two disulfide bridges. These are **interchain disulfide bridges** (between the A- and B-chains). Insulin also has an **intrachain disulfide bridge** (within the A-chain).

Hair is made up of a protein known as keratin. Keratin contains an unusually large number of cysteine residues (about 8% of the amino acids), which give it many disulfide bridges to maintain its three-dimensional structure.



Curly hair Straight hair