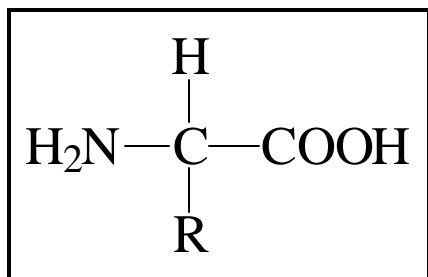


## *Amino Acids, Polypeptides and Proteins*

An  $\alpha$ -amino acid is a carboxylic acid which has an amino group attached to the carbon  $\alpha$  to the COOH.

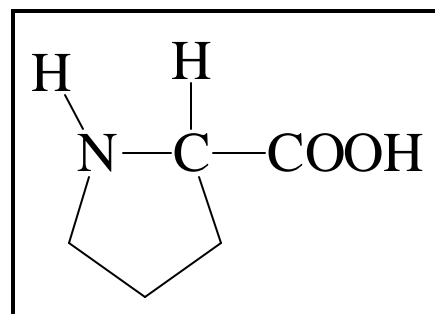
Polypeptides and proteins are composed, either completely or partially, of  $\alpha$ -amino acid fragments, called *residues*, which are joined to each other to form chains.

Twenty different amino acids are commonly found in proteins. Nineteen of them are 1° amino acids having this structure:



where the R group is alkyl or substituted alkyl.

The 20th, proline, has a 2° amino group.



## Properties of Amino Acids

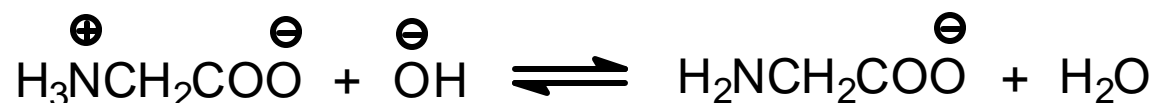
- ☞ Non-volatile, high mp. (glycine, 262°C.)
- ☞ Insoluble in non-polar solvents; somewhat soluble in water.
- ☞ Large dipole moments. Glycine: 14D, *cf.* propylamine, 1.4D; propanoic acid, 1.7D
- ☞  $K_a$  and  $K_b$  are much smaller than expected — *eg.* for glycine,  $\text{H}_2\text{NCH}_2\text{COOH}$ ,

$$K_a = 1.6 \times 10^{-10}, \quad K_b = 2.5 \times 10^{-12}$$

*cf.*  $K_a \sim 10^{-5}$  for typical  $\text{COOH}$ ,  
 $K_b \sim 10^{-4}$  for typical  $\text{NH}_2$

All of this suggests the existence of a *zwitterion*, *eg.* for glycine:  $\text{H}_3\text{N}^+\text{CH}_2\text{COO}^-$ . In this zwitterionic form the acid is the  $\text{H}_3\text{N}^+$  (which can donate a proton to become  $\text{H}_2\text{N}$ ), not the  $\text{COOH}$ . Also, the base is the  $\text{COO}^-$  (which can accept a proton to become  $\text{COOH}$ ), not the  $\text{NH}_2$ .

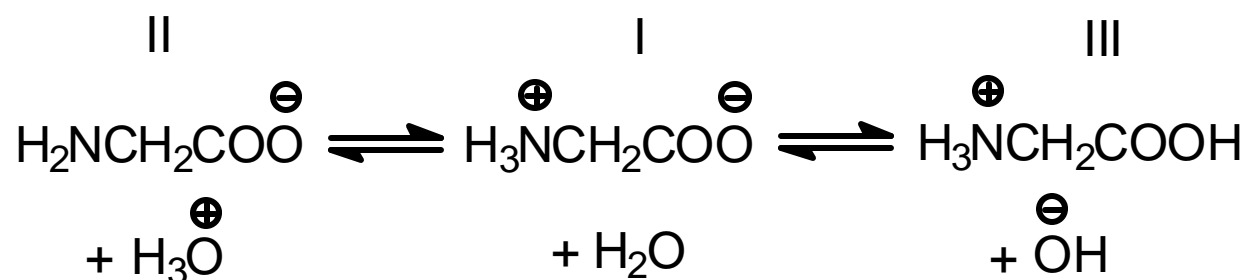
In base:



In acid:



$\overset{\oplus}{\text{H}_3\text{N}}\text{CH}_2\overset{\ominus}{\text{COO}}$  may react as if it were  $\text{H}_2\text{NCH}_2\text{COOH}$  because of the equilibria which exist:



In other words, in solution, there are glycine molecules that have a COOH group and others that have an NH<sub>2</sub>. [There are even a very few that are completely unionized.]

The hydrogen ion concentration at which [II] = [III] is known as the *isoelectric point* of the amino acid. If the amino acid is placed in an electric field at this pH, it will show no *net* migration toward anode (+) or cathode (-).

[Remember: Chemical equilibrium is a dynamic process and Lowry-Bronsted acid/base equilibria involving nitrogens and oxygens are usually fast. So, a given amino acid molecule will move toward the anode when it is in anionic (II) form, but a moment later it will be in zwitterionic form (I) and will not move, and a moment later it will be in cationic form (III) and move *back* toward the cathode. So, the molecule does a little dance in place – back and forth – but there is no *net* motion toward either electrode.]

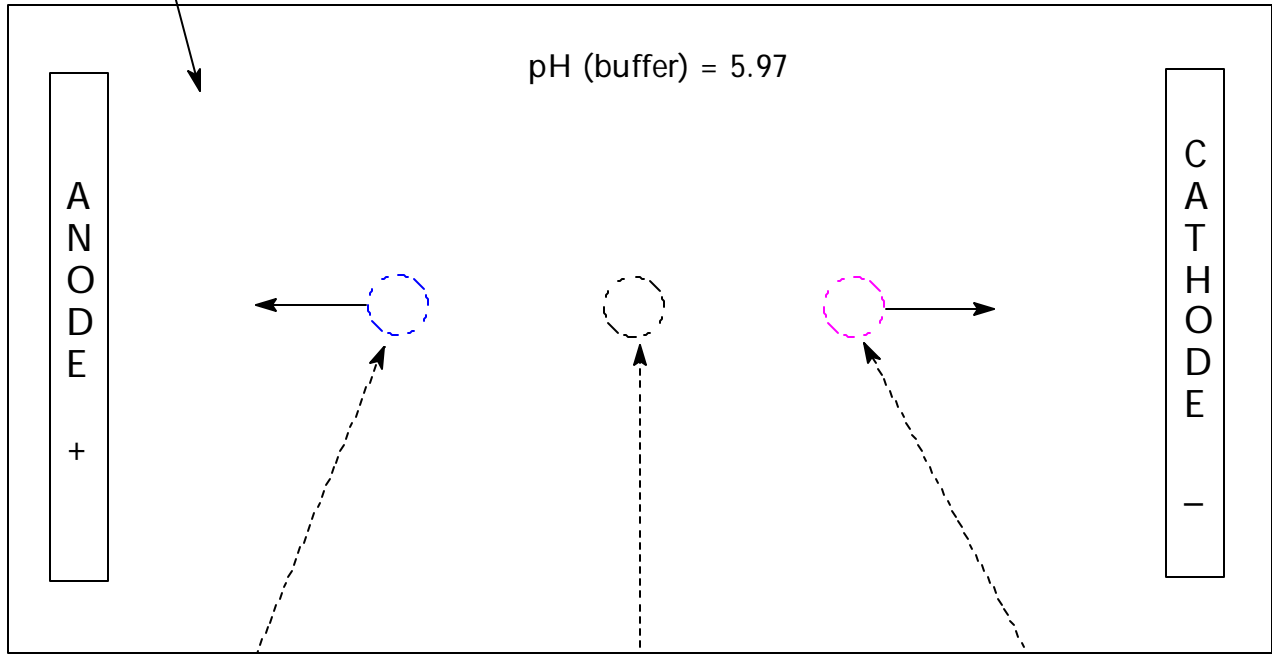
If the pH is increased,  $[II] > [III]$  (and a given amino acid molecule spends more time in state II than in state III) so there will be net migration toward the anode.

If the pH is decreased,  $[III] > [II]$  and there will be net migration toward the cathode.

Amino acids with neutral R-groups are more acidic than basic. Therefore, the isoelectric point is acidic, *ie*  $pI < 7$ , for these compounds. For amino acids with a basic R,  $pI > 7$ . For amino acids with an acidic R,  $pI \ll 7$ .

Different amino acids have different isoelectric points. Consequently, they can be separated from each other by *electrophoresis*:

Gel or paper



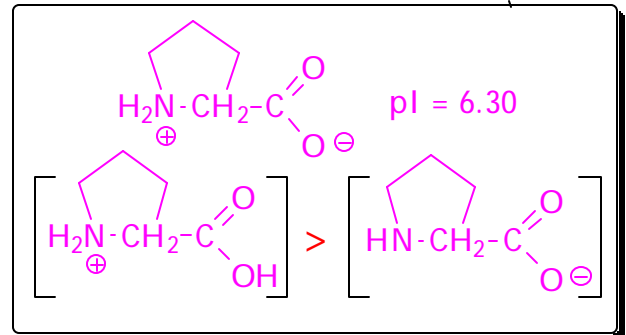
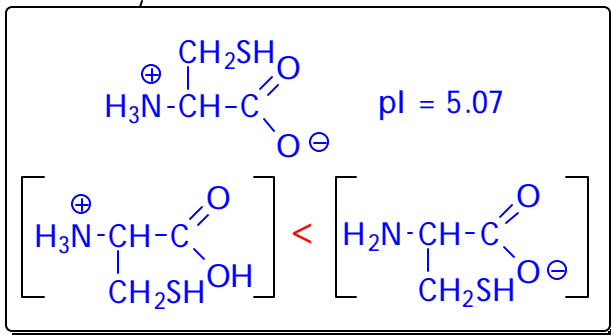
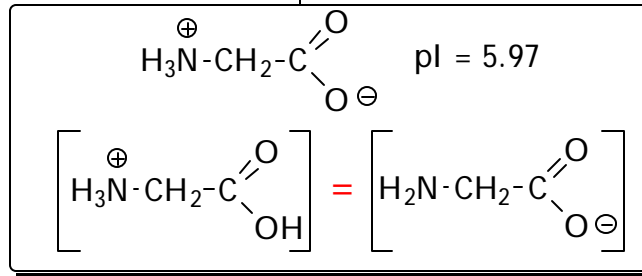
pH (buffer) = 5.97

A  
N  
O  
D  
E

+

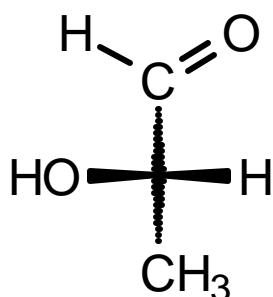
C  
A  
T  
H  
O  
D  
E

-



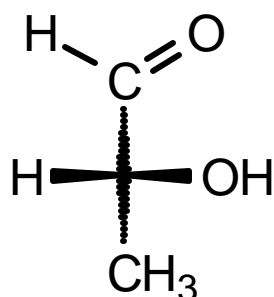
Amino acids usually are least soluble in water at their isoelectric point.

*Configuration of amino acids* —  
Specification of configuration of stereocenter based on D- and L-glyceraldehyde.



(S)-glyceraldehyde

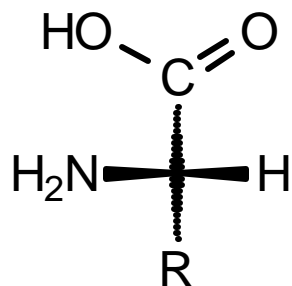
L-glyceraldehyde



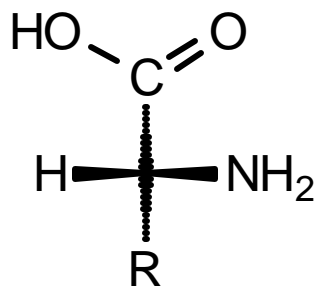
(R)-glyceraldehyde

D-glyceraldehyde

Amino Acids:



L-amino acid



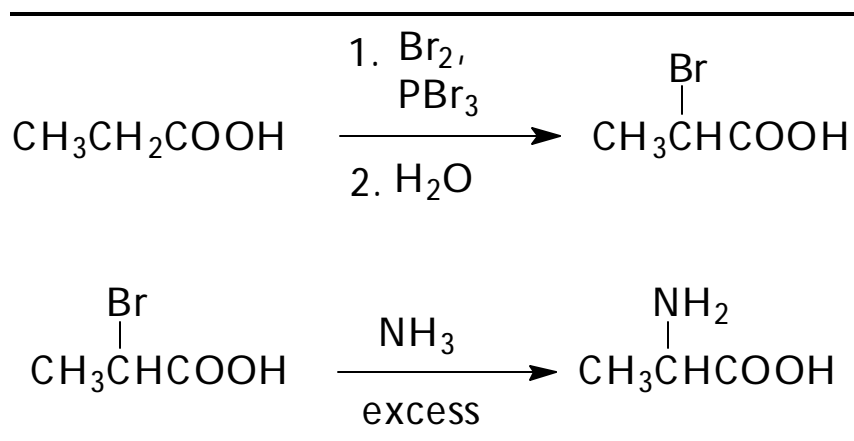
D-amino acid

Almost all naturally occurring amino acids, except glycine (no stereocenter), have the L-configuration.

### Synthesis of Amino Acids in the Laboratory

There are several ways to synthesize amino acids. One of these ways is shown here. Note that this synthesis will lead to racemic mixtures (except for glycine).

Hell-Volhard-Zelinskii method —



Since it is usually the L-amino acids that are of interest, the racemic amino acids synthesized above would have to be resolved. The classic method is to form diastereomeric salts. One could form the carboxylate salts of the racemic amino acids using enantiomerically pure alkaloids, eg (-)-brucine or (-)-strychnine, or one could form the ammonium salts using (+)-tartaric acid. In any case the salts are diastereomeric and can be separated by ordinary means. Once separated, the amino acids can be

regenerated from the salts as enantiomerically pure compounds.

An alternative method of resolution is to acetylate the amino group of the racemic mixture using acetic anhydride. The acetylated racemic mixture is then hydrolyzed using an enzyme (carboxypeptidase, hog kidney acylase) that will hydrolyze only one of the enantiomers (actually the L-isomer). [This is OK because the enzyme is chiral and enantiomerically pure.] The hydrolyzed amino acid can then be separated from the unhydrolyzed material by ordinary means. A generic example follows —

