

**WORKSHOP, Chapter 25**  
*Amino Acids, Peptides, and Proteins*

1. Identify the expected state of ionization of the following in aqueous solutions of pH 4, 7, and 10.

a) amino acids - threonine, asparagine, tyrosine, histidine, and proline

b) peptides - isoleucylarginine, AlaTrpGluLeu, polyglycine

2. The name for the amino acid threonine comes from its similarity in structure to the sugar D-threose.

Write the structure for threonine in a Fischer projection that clearly shows its similarity to D-threose. Identify each stereocenter in threonine as R or S.

Only one other amino acid (of the 20 common ones in your table) has two stereocenters. Which one? Write its structure with both stereocenters in the S configuration.

3. Consider an unknown heptapeptide consisting of the following amino acids:

Arg, Asp, His, Ile, Phe, Tyr, Val

Deduce its primary structure from the following data:

Edman degradation releases Asp

carboxypeptidase releases Phe

chymotrypsin cleaves it to a tripeptide and a tetrapeptide, A and B

A has Ile at its N-terminus and Phe at its C-terminus

B can be partially hydrolyzed to give dipeptides Arg Val, AspArg and ValTyr

- Use the amino acids in this peptide to illustrate the following aspects of tertiary structure. Draw just the specific side chain structures involved.

- a) electrostatic attraction
- b) H-bonding
- c) hydrophobic interactions

4. Illustrate the steps in the synthesis of the tripeptide AlaGlnLeu.

Predict the isoelectric point for this tripeptide.

5. Recreate the chymotrypsin template on the board and trace the steps in peptide hydrolysis.

- 1) A polypeptide enters the active site and the aromatic amino acid side chain nestles into the hydrophobic pocket.
- 2) Ser-195 acts as a nucleophile to add to the carbonyl group of the peptide, while His-57 removes a proton from Ser-195 to make it a better nucleophile.
- 3) The tetrahedral intermediate splits out an amino group, while His-57 donates a proton to the amino group to make it a better leaving group.
- 4) The broken peptide fragment (the N-part) leaves the active site and is replaced by water.
- 5) Water acts as a nucleophile to add to the carbonyl group of the intermediate (which is now an ester), while His-57 removes a proton from water to make it a better nucleophile.
- 6) The tetrahedral intermediate splits out the Ser-195 group, while His-57 donates a proton to Ser-195 to make it a better leaving group.
- 7) The other part of the broken peptide (the C-part) leaves the active site and is replaced by another polypeptide (same as step 1 above).

## The Chymotrypsin Active Site

