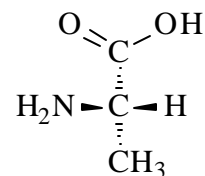


Chapter 15

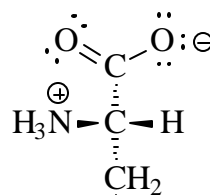
2. Eighteen of the 19 L-amino acids have the S configuration at the α -carbon. Cysteine is the only L-amino acid that has an R configuration. Explain.

All of the 19 L-amino acids have four different groups attached to the α -carbon. The 20th amino acid – glycine – has two hydrogens attached to the α -carbon and is achiral. The four groups attached to the α -carbon in the L-amino acids are the amino group, the carboxyl group, a hydrogen, and the R group. The R group is, of course, different for each amino acid – it is what makes them different. For all of the L-amino acids the amino group has the highest priority and the hydrogen has the lowest priority when specifying R or S configuration. In 18 of the 19 L-amino acids the carboxyl group has the second priority and the R groups have third priority. In the case of cysteine, however, this is reversed because the R group is $-\text{CH}_2\text{SH}$ and sulfur has a larger atomic number than the oxygens in the $-\text{COOH}$ group. The bottom line is that eighteen of the L-amino acids are S, but cysteine is R.

3. Draw L-alanine in the standard three-dimensional format using solid, wedged, and dashed lines.

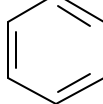


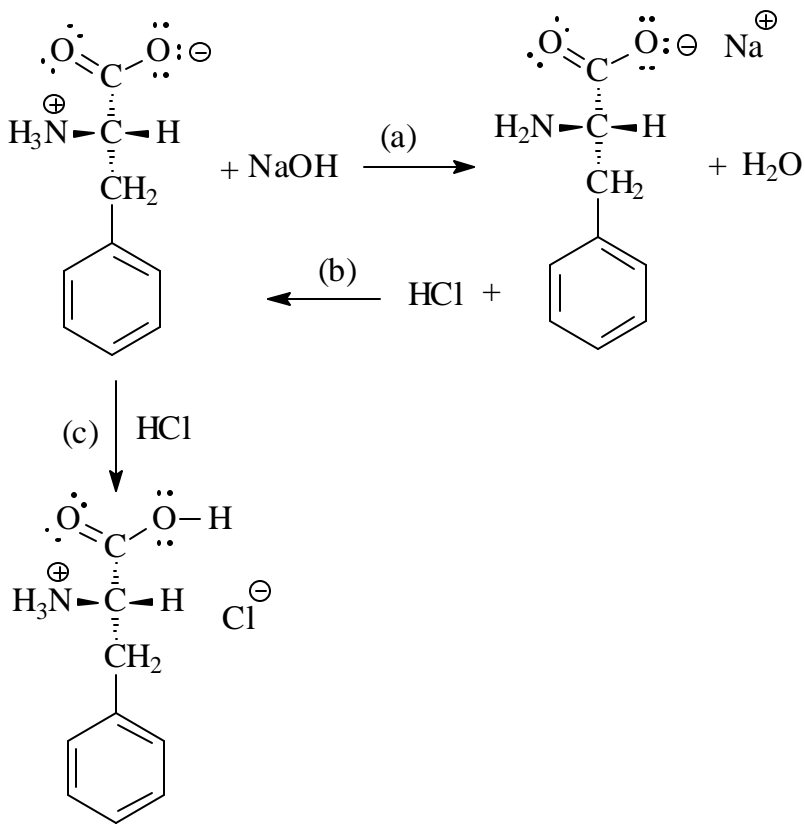
4. Draw phenylalanine in its zwitterionic form.



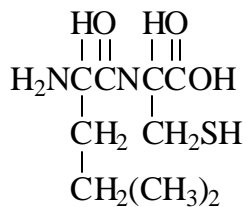
5. Write structural formulas for the following equations.

- (a) phenylalanine + 1 equiv NaOH \longrightarrow
 (b) product of (a) + 1 equiv HCl \longrightarrow
 (c) product of (a) + 2 equiv HCl \longrightarrow

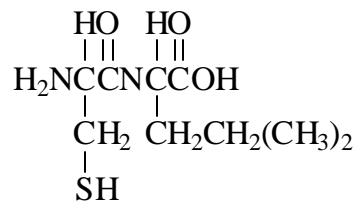




8. Draw the two dipeptides made from leucine and cysteine.



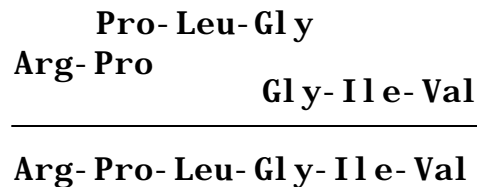
Leu-Cys



Cys-Leu

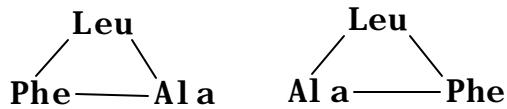
13. Give the amino acid sequence of a hexapeptide containing Arg, Gly, Ile, Leu, Pro, and Val that produces the following fragments on partial acid hydrolysis: Pro-Leu-Gly, Arg-Pro, Gly-Ile-Val.

The play here is to place the fragments in successive rows and align the amino acid residues so that the same residue is in each column, as shown to the right.



14. Propose two structures for a tripeptide that gives Leu, Ala, and Phe on hydrolysis but doesn't react with phenyl isothiocyanate.

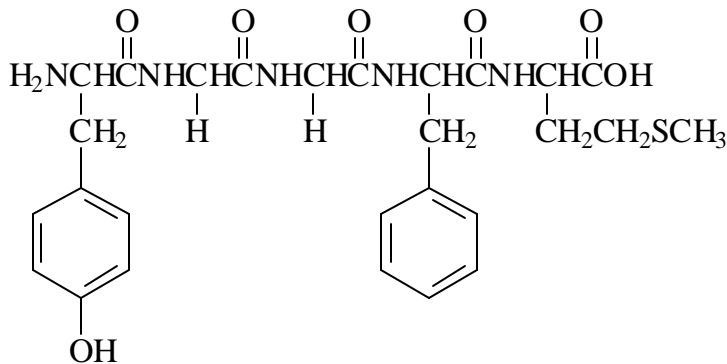
If the tripeptide does not react with phenyl isothiocyanate we might infer that it does not have an N-terminus. A straight-chain polypeptide would have to have an N-terminus, but a cyclic polypeptide would not have one. [We are talking about a polypeptide that is cyclic by virtue of the peptide bonds, not possible disulfide bridges, which would allow for an N-terminus.]



21. Why is cysteine such an important amino acid for determining the tertiary structure of a protein?

Because the disulfide bridges that this amino acid makes possible will play a major role in how the protein backbone (helix, pleated sheet, whatever) twists and turns in space.

22. The endorphins are a group of naturally occurring compounds in the brain that act to control pain. The active part of an endorphin is a pentapeptide called an enkephalin, which has the structure Tyr-Gly-Gly-Phe-Met. Draw the structure of this enkephalin.



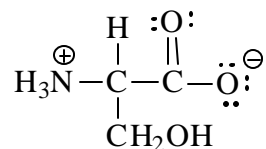
27. Define the following terms.
 (a) amphoteric, (b) isoelectric point, (c) peptide, (d) N terminus, (e) C terminus, (f) zwitterion

- (a) amphoteric - a compound that can act as both an acid and a base.
 (b) isoelectric point - this is the pH at which the concentration of the anionic (deprotonated) and cationic (protonated) forms of an amino acid or polypeptide are of equal concentration.
 (c) peptide - A peptide bond is an amide bond: the bond between the carbonyl carbon and nitrogen in an amide. Polypeptides are sometimes called peptides.
 (d) N terminus - The end of a polypeptide or protein chain that has the free amino group.
 (e) C terminus - The end of a polypeptide or protein chain that has the free carboxyl group.

(f) zwitterion - a molecule (not an ion!) in which one part has a full positive charge and another part has a full negative charge.

29. Draw the following amino acids in their zwitterionic forms.

(a) serine



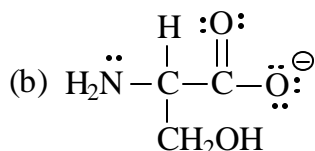
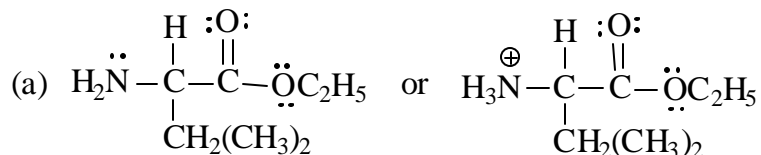
32. Which of the following amino acids are more likely to be found on the outside of a globular protein, and which of the inside? Explain.

(a) valine, (b) aspartic acid, (c) isoleucine, (d) lysine

The inside of globular proteins is likely to be somewhat hydrophobic, while the outside is in contact with water and should, therefore, be somewhat hydrophilic. Alkyl groups are hydrophobic because they are nonpolar. On the other hand, a polar R-group would be hydrophilic. Consequently, we would expect valine and isoleucine (R group = alkyl) to be inside. Aspartic acid has a -COOH group in the R-group and lysine has an -NH₂. These groups can hydrogen bond with water and should be hydrophilic and are, therefore, more likely to be outside.

33. Predict the product of the reaction of valine with the following reagents.

(a) CH₃CH₂OH, H⁺, (b) NaOH, H₂O



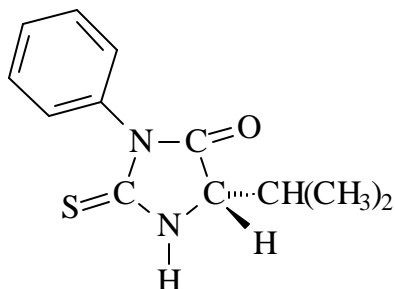
(a) The conditions of the Fischer esterification are acidic, so, as long as the acid catalyst is present, we would expect some of the amino acid ester to be protonated on the amine.

(b) The base deprotonates the amino acid. The counterion, Na⁺, is not shown.

39. Draw the structure of the phenylthiohydantoin product you would expect to obtain from Edman degradation of the following peptides.

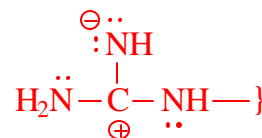
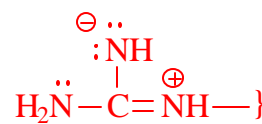
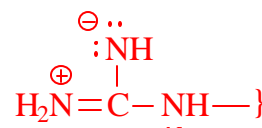
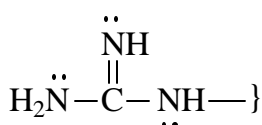
(a) Val-Leu-Gly

Well, it is the N-terminal amino acid that will show up in the phenylthiohydantoin, in this case it is valine.

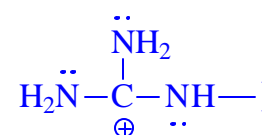
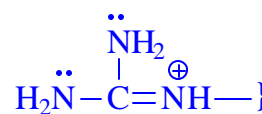
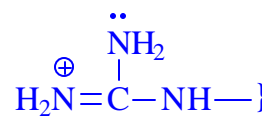
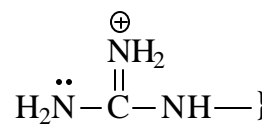


40. Arginine, which contains a guanidino group in its side chain, is the most basic of the 20 common amino acids. How can you account for this basicity?

It is possible to draw four resonance structures for both the guanidino group (left side of figure) and its protonated form (right side). However, the structures in red (guanidino) are not as favorable as the corresponding structures in blue (protonated guanidino) owing to the charge separation in the red structures. So the conjugate acid (protonated guanidino) is favored by resonance. The guanidino group “wants” to get protonated; therefore it is a strong base.



Three of the guanidino resonance structures above suffer from charge separation.

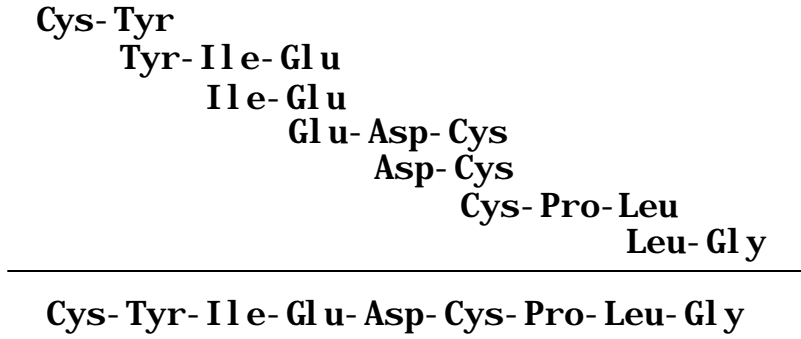


None of the protonated guanidino resonance structures above suffers from charge separation.

50. Sorry, I'm tired of typing, so I'm not going to retype this question.

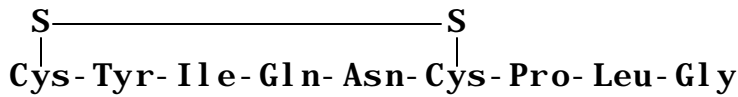
The disulfide bridge is obviously between the two cysteines. The problem states this.

The partial hydrolysis information will give us the sequence of the amino acid residues. This is shown to the right.



The problem indicates that the side chain carboxyl groups of Glu and Asp are in amide form (the OH of the carboxylic acid has been replaced by an NH₂). So, we need to replace Glu by Gln and Asp by Asn.

Consequently, oxytocin should have the structure shown below.



Actually, oxytocin has the structure shown below. McMurry neglected to mention that the C-terminal glycine is actually present as its amide (the OH is replaced by an NH₂).

