14.15: Amino Acids and Peptides

Knowing something about proton transfer changes how we look at some important biomolecules. Amino acids are the fundamental building blocks of peptides and proteins. Peptides, which are chains of amino acids, are frequently used as signaling molecules within the body (some hormones are peptides). Proteins, which are very large peptides, have a variety of uses. They form the key components of muscles, for instance, and they also form enzymes that carry out a multitude of chemical reactions necessary for life.

Amino acids are so called because they all contain two common components. One is an amine, or a tetrahedral nitrogen attached to a carbon. The other is a carboxylic acid, which is a carbon that is double bonded to an oxygen and also attached to an OH or hydroxyl group.

We have seen that carboxylic acids are moderately acidic. Most of them have pKa's of 3 to 5. That means a small fraction of the OH groups are ionized in a large group of carboxylic acids.

Figure 14.15.1: A carboxylic acid in water.

We have also seen that tetrahedral nitrogens are somewhat Lewis basic. The nitrogen can donate its lone pair to Lewis acidic atoms. Protons are good Lewis acids. Amines are easily protonated if protons are available.

Figure 14.15.2: An amine in a proton-rich environment.

Because the carboxylic acid is a pretty good source of protons and because protons bind to amines pretty well, it seems reasonable that a proton transfer may occur from one site to the other.

Figure 14.15.3: Two forms of an amino acid, related by proton transfer.

Does one of these forms dominate the equilibrium? Compare the pKa's. The pKa of the acid is near 5, and the pKa of the ammonium is near 9. The ammonium holds the proton more tightly than does the acid. The proton stays on the nitrogen.

Amino acids are zwitterionic. A zwitterion is a compound that has no overall charge but that has charge separation within it. The zwitterionic nature of amino acids has an effect on their properties. For example, they are usually pretty soluble in water and other polar solvents.

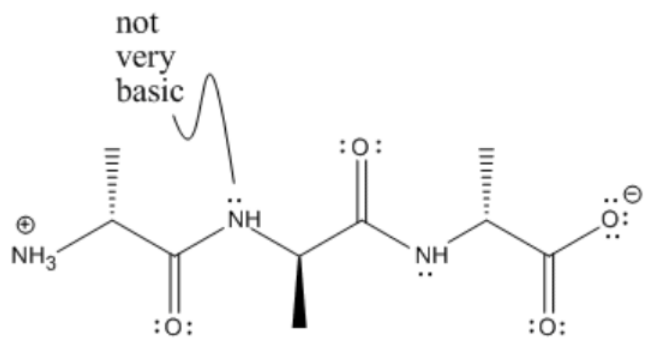


Figure 14.15.4: A peptide.

Amino acids are joined together via "amide linkages" to form peptides and proteins. In these structures, the individual amino acids no longer have the same acidic carboxylic acid group; the carbonyl (or C=O) no longer has a hydroxyl group attached. The amino acids no longer contain amines, either; a nitrogen attached to a C=O has very different properties than a regular nitrogen attached to carbon. Only the "N-terminus" and "C-terminus" are ionic. The nitrogens along the chain are not very basic and are not protonated.

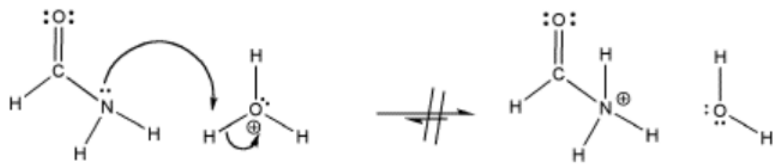
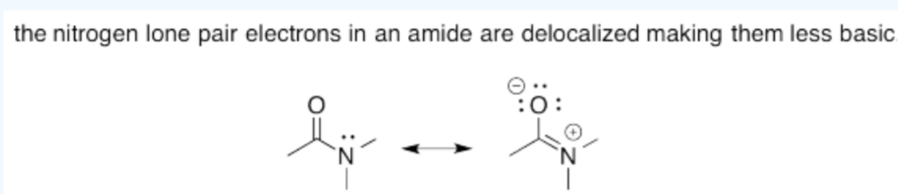


Figure 14.15.5: An amide, and the unfavorable protonation of an amide

Exercise 14.15.1

Explain why an amide nitrogen is not very basic.

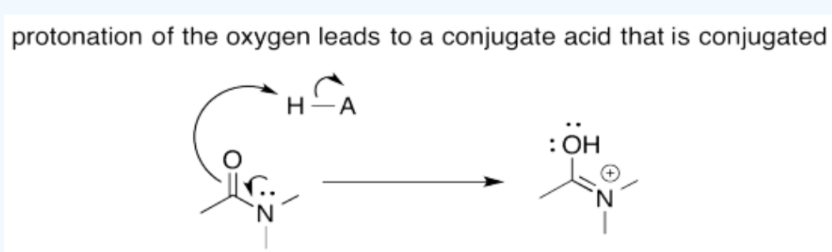
Answer



Exercise 14.15.2

The favored site of protonation in an amide is the carbonyl oxygen. Show why.

Answer



The acidic and basic groups found in individual amino acids are masked in peptides and proteins. However, peptides and proteins do have basic and acidic sites. These sites are found on the side chains of the amino acids, the part that varies from one amino acid to another. In some cases, the side chain contains an acidic group. Examples are aspartic acid and glutamic acid.

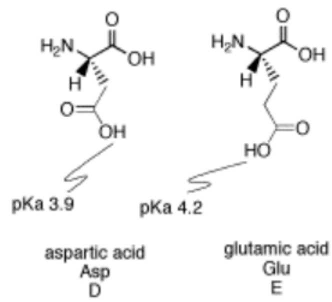


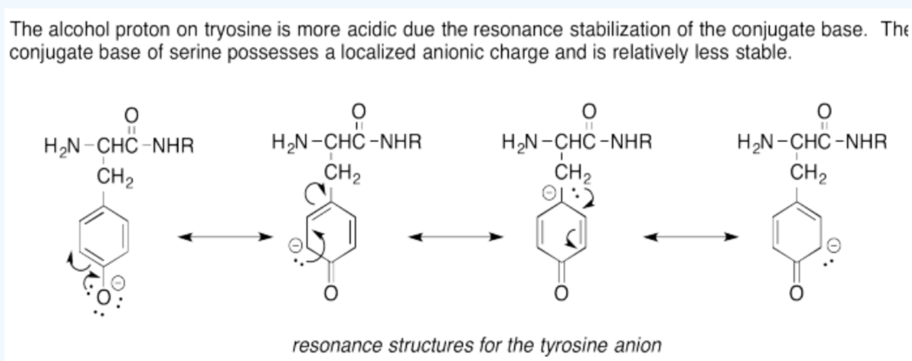
Figure 14.15.6: Acidic amino acids.

There are other side chains that are weakly acidic. For example, tyrosine is sometimes able to supply protons, and so is cysteine. The proton comes from the OH and SH groups, respectively, on these two compounds. However, neither of these compounds can supply protons as easily as aspartic acid or glutamic acid. Furthermore, serine, which also has an OH group, is not really able to supply protons that easily.

Exercise 14.15.3

Explain the difference in acidity between serine and tyrosine, which both contain OH groups.

Answer



Exercise 14.15.4

Explain the difference in acidity between serine and cysteine, which have very similar structures but with a sulfur atom in place of an oxygen.

Answer

The thiol proton on cystine is more acidic due to the polarizability of the sulfur anion stabilizing the conjugate base's anionic charge. The oxygen anion is less polarizable and therefore less stable rendering the alcohol proton less acidic.

Sometimes the amino acid side chain contains a basic group. Examples are histidine, lysine and arginine. There is a big difference in basicity between these three compounds. The difference can be seen by looking at the pKa's of the conjugate acids in each case. The higher the pKa of the conjugate acid, the more tightly the proton is held, and so the more basic the nitrogen atom. Arginine is by far the most basic and histidine is the least basic.

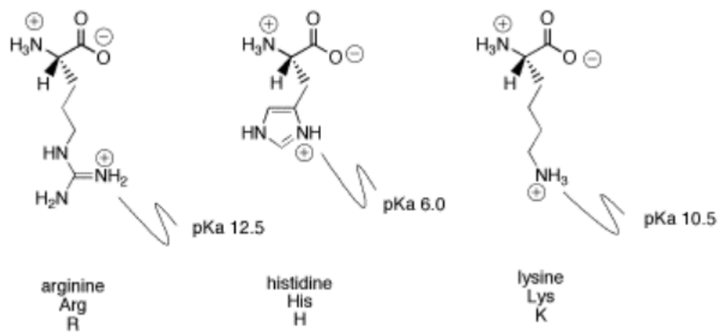
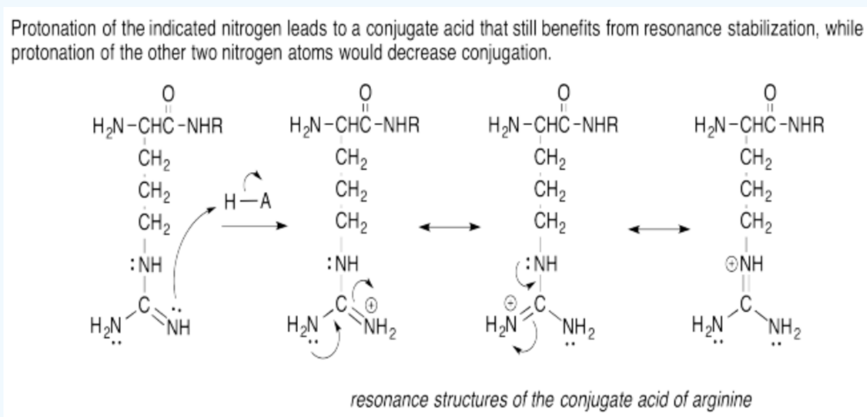


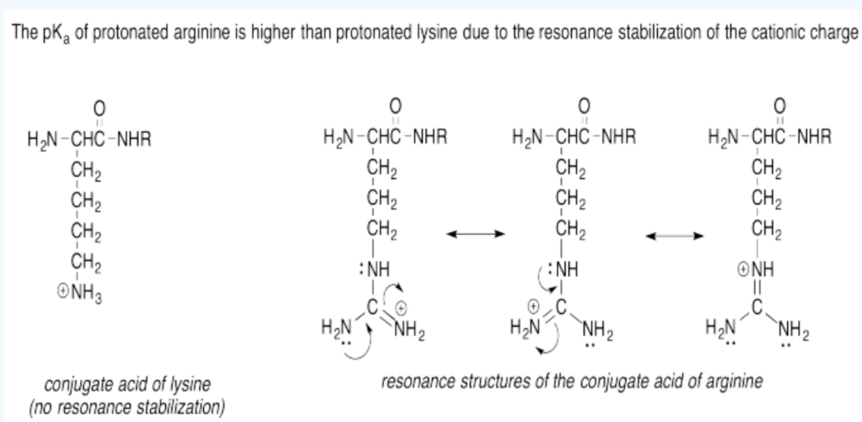
Figure 14.15.7: Basic amino acids

Exercise 14.15.5

Show why the indicated nitrogen in arginine's side chain is protonated, and not the others. Also, explain the difference in basicity between arginine and lysine.

Answer



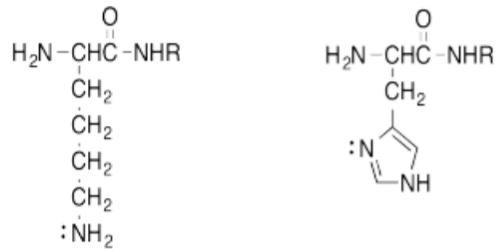


Exercise 14.15.6

Explain the difference in basicity between histidine and lysine.

Answer

Lysine is a stronger amine base than histidine due to the difference in hybridization (sp^3 vs. sp^2)



In contrast to the basic amino acids shown above, other amino acids with nitrogen in their side chains are not considered basic. These compounds are not protonated easily on their side chains.

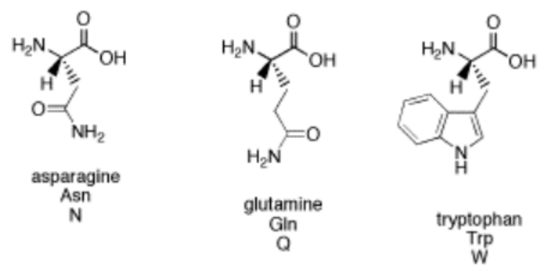


Figure 14.15.8: Some un-basic, nitrogen-containing amino acids.

Exercise 14.15.7

Explain why the three un-basic amino acids are not easily protonated on their side chain nitrogen atoms.

Answer

The lone pair electrons on the un-basic are resonance delocalized and not avaliable for protonation. The side chain nitrogens on asparagine and glutamine are found in amide groups and the nitrogen on tryptophan is part of an aromatic ring. Protonation of any of these nitrogens would break up a conjugated system.