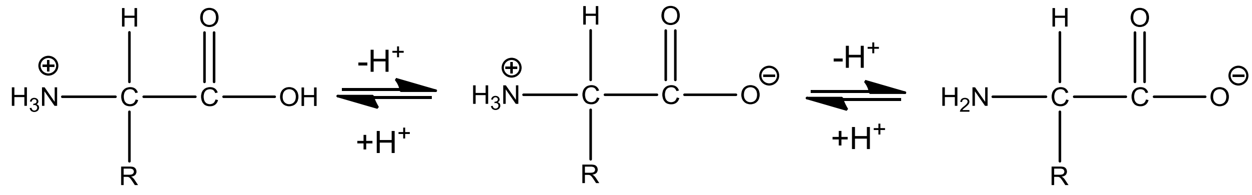
CHEM1611 Worksheet 13: Amino Acids and Polypeptides

Model 1: Amino Acids

There are 20 different amino acids in nature. These all contain a carboxylic acid group (α-COOH) and a basic amino group (α-NH_2). They differ in the nature of the side chain, labelled R in the scheme below. As shown in the scheme, the form in which they exist depends on the pH of the solution they are in. In solutions with a pH near neutral, the "zwitterionic" form in the middle dominates.



acidic **neutral** **basic**

When the solution pH equals the pK_a of a functional group, 50% of the molecules are protonated and 50% of the molecules are deprotonated. The deprotonated species predominates above the pK_a value, whilst below the pK_a value, the protonated form is the dominant species.

Critical thinking questions

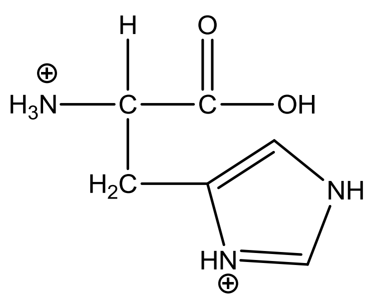
1. Write the overall charge of the ion underneath the 3 structures in the scheme above.
2. Draw the structure of the following amino acids as they would exist in the conditions stated.
   (a) Valine (R = -$CH(CH_3)_2$ in the stomach at pH 1.5.
   Data: pK_a (α-COOH) = 2.29 and pK_a (α-NH_3^+) = 9.72.

   (b) Serine (R = -CH_2OH) in the small intestine at pH 8.
   Data: pK_a (α-COOH) = 2.17 and pK_a (α-NH_3^+) = 9.15.

The zwitterion is the predominant species at or near the **isoelectric point, pI**. For amino acids such as those in Q2 which have neutral side chains, pI is equal to the average of pK_a (α-COOH) and pK_a (α-NH_3^+).

3. At what pH is the zwitterionic form of serine the predominant species?

Model 2: Amino Acids with Acidic and Basic Side Chains



Seven amino acids contain side-chains that can also be protonated or deprotonated depending on the pH of the solution. Three have side-chains that contain basic groups, two have side-chains that contain carboxylic acid groups and two (tyrosine and cysteine) contain functional groups that can be deprotonated at high pH.

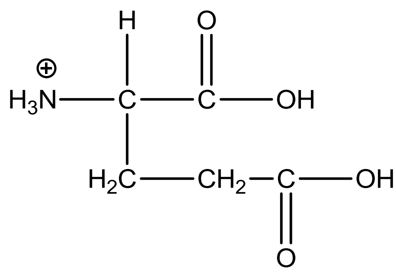
The structure of histidine in the stomach is shown to the right. The R group contains a basic imidazole ring and pK_a (α-COOH) = 1.77, pK_a (α-NH_3^+) = 9.18 and pK_a (side-chain) = 6.10. As stomach pH is lower than each of these values, each of these groups is protonated.

Critical thinking questions

1. Draw the structure of histidine that predominates at a pH of 7.64.

2. Is it possible to protonate the side chain and not protonate the α-NH_2 group? If your answer is yes, what pH value would achieve this? If your answer is no, briefly explain why not.

The structure of glutamic acid in the stomach is shown to the right. The R group contains a carboxylic acid group and pK_a (α-COOH) = 2.10, pK_a (α-NH_3^+) = 9.47 and pK_a (side-chain) = 4.07. As stomach pH is lower than each of these values, each of these groups is protonated.



3. Draw the structure of glutamic acid that predominates at a pH of 3.10.

4. Is it possible to deprotonate the side chain and *not* deprotonate the α-COOH group? If your answer is yes, what pH value would achieve this? If your answer is no, briefly explain why not.

The isoelectric point for amino acids with basic side chains, such as histidine, is the average of the two *highest* pK_a values. The isoelectric point for amino acids with acidic side chains, such as glutamic acid, is the average of the two *lowest* pK_a values.

5. What are the values of the isoelectric point for each of the two amino acids above?

   (a) histidine; pI =   (b) glutamic acid; pI =

6. Calculate the pI value for the two amino acids below and draw the structure of their zwitterions.

   (a) Aspartic acid (R = -CH_2COOH)

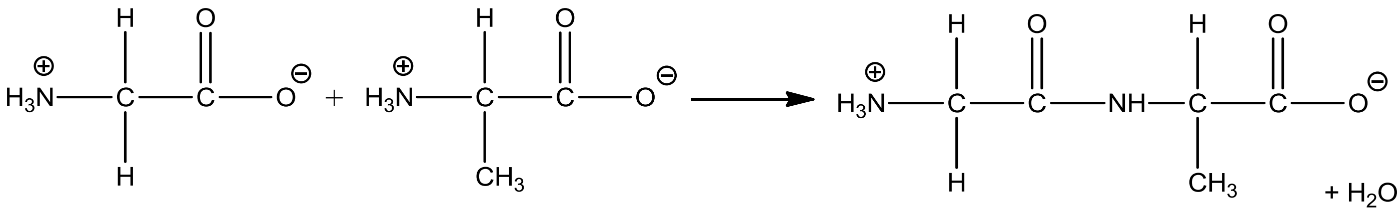
   Data: pK_a (α-COOH) = 2.10, pK_a (α-NH_3^+) = 9.82 and pK_a (side chain) = 3.86

(b) Lysine (R = $-CH_2CH_2CH_2CH_2NH_2$).

Data: pK_a (α-COOH) = 2.18, pK_a (α-NH_3^+) = 8.95 and pK_a (side chain) = 10.53

Model 3: Formation of Peptides

The amino group of one amino acid and the acid group of another can undergo a condensation reaction to form a **dipeptide** containing the amide functional group. Further condensations can lead to tripeptides, tetrapeptides, etc and ultimately to polypeptides. The new bond that is formed is called a **peptide bond** or **amide bond**. The scheme below shows the condensation of glycine and alanine to make the dipeptide glycylalanine.

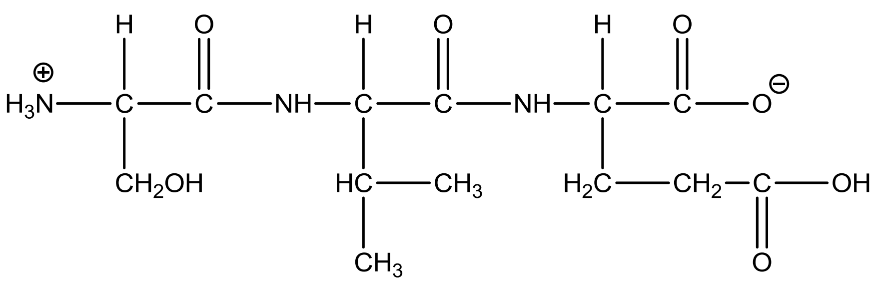


glycine or gly **alanine or ala** **glycylalanine or gly-ala**

Critical thinking questions

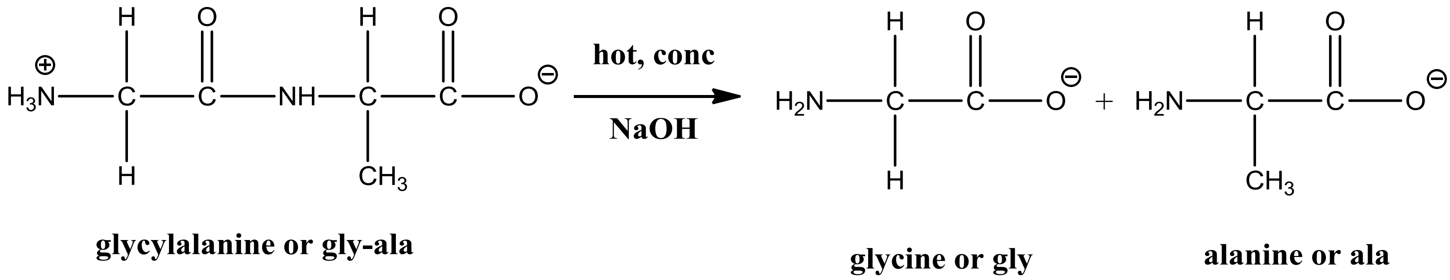
1. Draw a box around the part of glycylalanine that originated in glycine.
2. Draw a box around the part of glycylalanine that originated in alanine.
3. Draw an arrow to the peptide bond and label it.
4. Would the dipeptide alanylglycine (ala-gly) be same molecule? If not, draw its structure.

5. A tripeptide is shown below. Label the two peptide bonds and draw a circle around the side chains (R groups). What three amino acids condensed to make this tripeptide?



Model 4: Reactions of Amino Acids and Peptides

All amino acids and peptides contain a weakly basic amine group and a weakly acidic carboxylic acid group. These groups are protonated or deprotonated according to the pH as discussed in Model 1. The peptide bond is extremely stable and can only be broken by using hot, concentrated acid or hot, concentrated base. Under these conditions, the condensation reaction is reversed and the peptide is hydrolysed back to the amino acids from which it was made. The scheme below shows this for gylcylalanine.

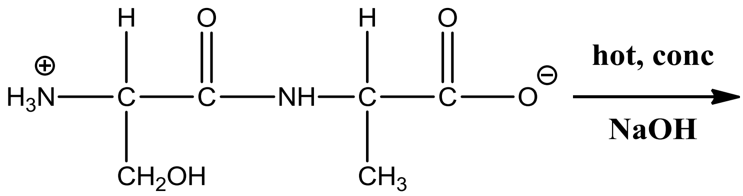


Critical thinking questions

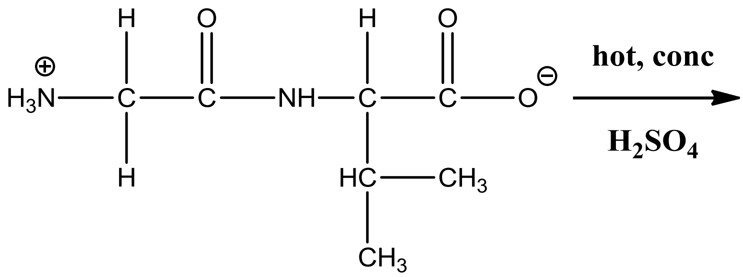
1. Draw an arrow to the peptide bond in glycylalanine and label it.
2. Why are the amine groups in the products not protonated?

3. Draw the products of the hydrolysis reactions below.

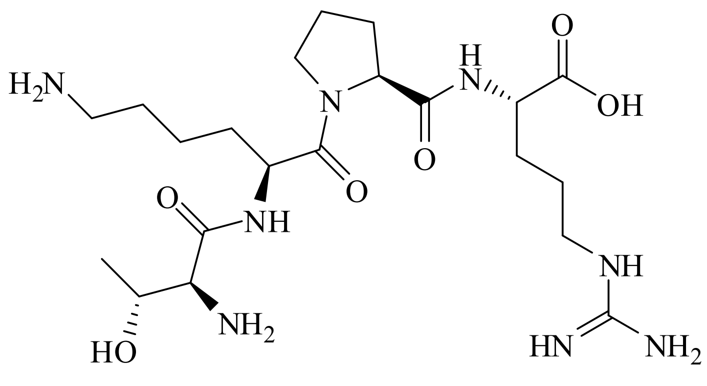
(a)



(b)



4. Tuftsin is a tetrapeptide (Thr-Lys-Pro-Arg) produced by enzymatic cleavage of the Fc-domain of the heavy chain of immunoglobulin G. It is mainly produced in the spleen and its activity is related primarily to immune system function.



Draw the Fischer projections of the four L-amino acids that result from the acid hydrolysis of tuftsin.