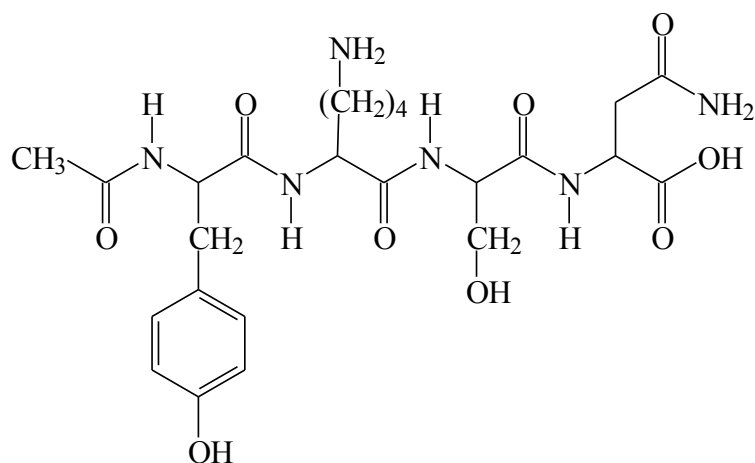
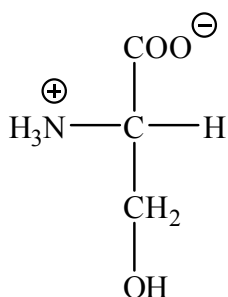


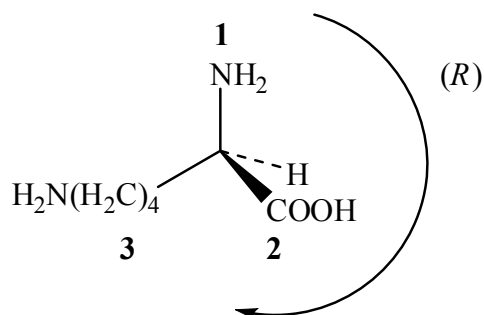
- The constitutional formula of a derivative of the naturally occurring tetrapeptide, Tyr-Lys-Ser-Asn is shown below.



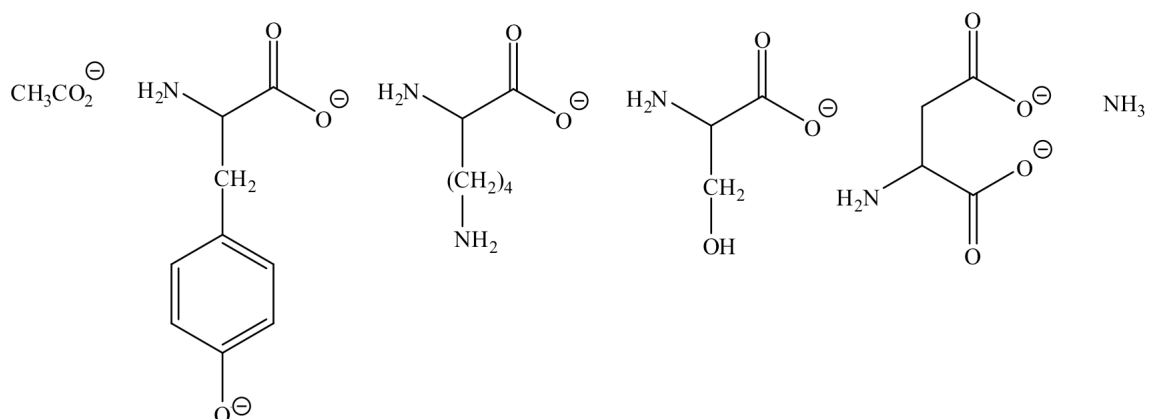
Give the Fischer projection of L-Ser as the zwitterion.



Complete the stereoformula of (R)-Lys.

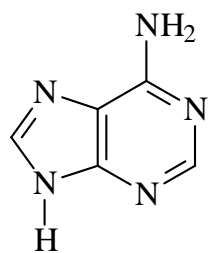


Give the constitutional formulas in the correct ionic states of the products obtained from the vigorous basic hydrolysis (5 M KOH) of the tetrapeptide.

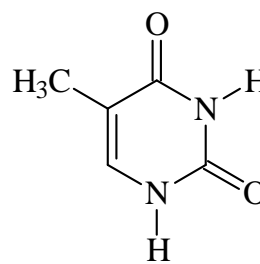


- Adenine and thymine have the structures shown below.

Marks  
4

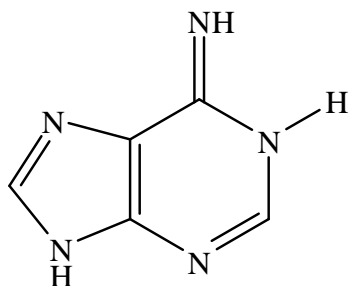


adenine



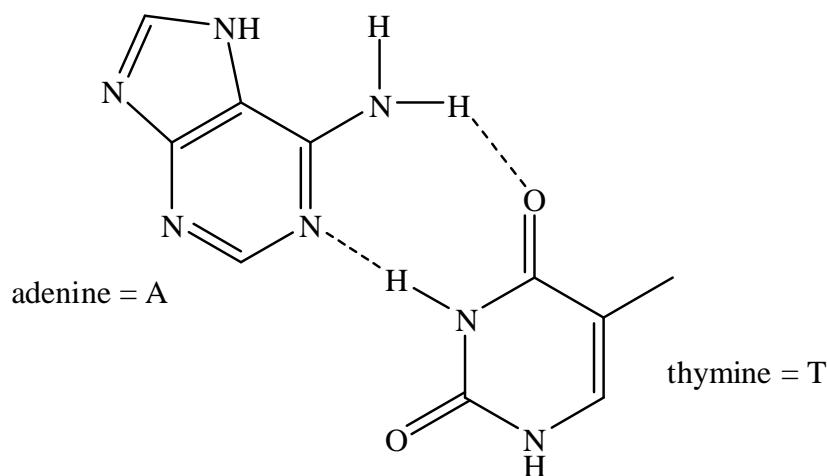
thymine

Draw a tautomer of the shown structure of adenine.

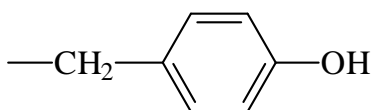


In DNA, adenine forms a “base pair” with thymine. Explain what is meant by “base pair” and indicate the point(s) of interaction between adenine and thymine.

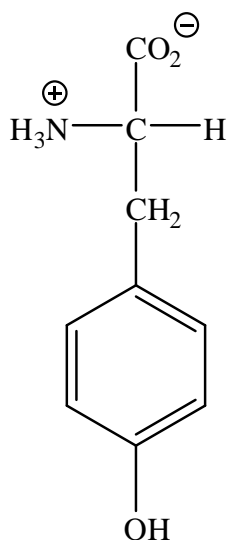
**Four different bases are found in DNA chains. The two strands in the double helix are held together by 3 hydrogen bonds between guanine (G) and cytosine (C), and by 2 hydrogen bonds between adenine (A) and thymine (T). The complementary bases C and G are called a “base pair”. A and T are another “base pair”.**



- L-Tyrosine is a naturally occurring amino acid with the following side-chain.



The  $pK_a$  values of tyrosine are 2.20 ( $\alpha$ -COOH), 9.19 ( $\alpha$ -NH<sub>3</sub><sup>⊕</sup>) and 10.47 (sidechain). Draw the Fischer projection of L-tyrosine indicating the correct charge state at physiological pH.



What is the absolute stereochemistry of L-tyrosine? Write (*R*) or (*S*).

**S**

What is the value of the pI of L-tyrosine?

$$pI = \frac{1}{2} (2.20 + 9.19) = 5.70$$

What does pI represent?

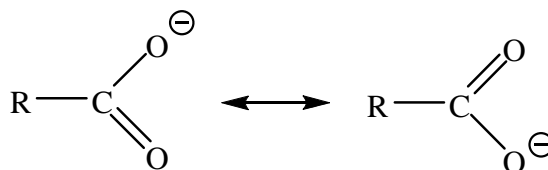
**pI represents the isoelectric point - the pH at which there is no net charge on the molecule.**

**Marks  
6**

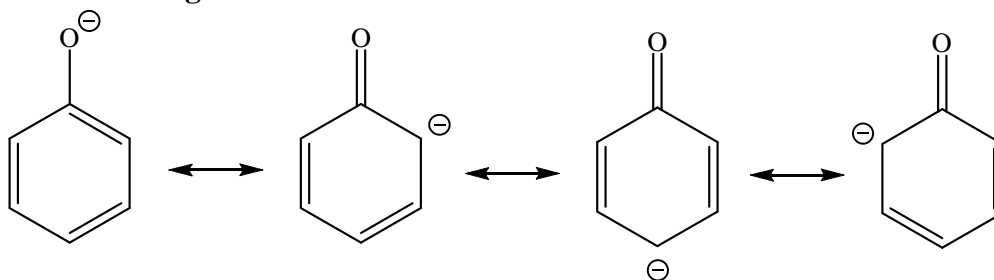
Account for the difference in acidity of the carboxylic acid group and the phenol.

**Acid strength is dependent on the stability of the conjugate base.**

**The carboxylate anion is resonance stabilised, with the charge being spread over the electronegative O atoms:**



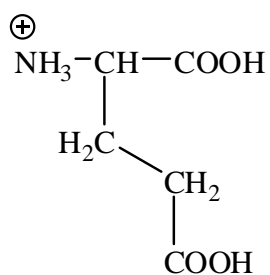
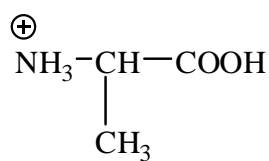
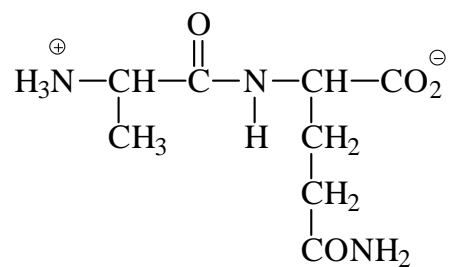
**The phenoxide anion is resonance stabilised also, but the charge in the resonance contributors is spread over the C atoms in the ring. C is not as electronegative as O, so these contributors are not as significant as that with the charge on the O.**



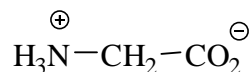
**Resonance stabilisation is not as great as for carboxylate and therefore phenol is weaker acid than carboxylic acid.**

- Draw the products of acid hydrolysis of the following peptide, indicating the correct charge state under these conditions.

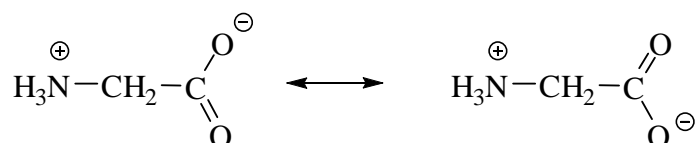
**Marks**  
**3**



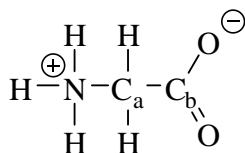
- Glycine,  $\text{NH}_2\text{CH}_2\text{COOH}$ , is the simplest of all naturally occurring amino acids. The  $\text{p}K_a$  of the acid group is 2.35 and the  $\text{p}K_a$  associated with the amino group is 9.78. Draw a structure that indicates the charges on the molecule at the physiological pH of 7.4.



Use your structure to illustrate the concept of resonance.



What are the hybridisation states and geometries of the two carbon atoms and the nitrogen atom in glycine?



**N has 4 bonds and no lone pairs:  $sp^3$  with a tetrahedral geometry.**

**$C_a$  has 4 bonds and no lone pairs:  $sp^3$  with a tetrahedral geometry.**

**$C_b$  has 3 bonds and no lone pairs:  $sp^2$  with a trigonal planar geometry.**

Propionic acid,  $\text{CH}_3\text{CH}_2\text{COOH}$ , has a melting point of  $-20.7\text{ }^\circ\text{C}$  while glycine has a melting point of  $292\text{ }^\circ\text{C}$ . Suggest a reason why these two molecules have such different melting points.

**The major intermolecular force in glycine is ionic bonding between the positively and negatively charged ends of the molecule. The major intermolecular force in propionic acid is hydrogen bonding between the carboxylic acid groups. Ionic bonding is much stronger than H-bonding so glycine has a much higher melting point.**

- Alanine ( $R = \text{CH}_3$ ) and lysine ( $R = \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ ) are two common amino acids. Using *ala* and *lys* to represent the two amino acids, represent all constitutional isomers of the tripeptide formed from one *ala* and two *lys* units.

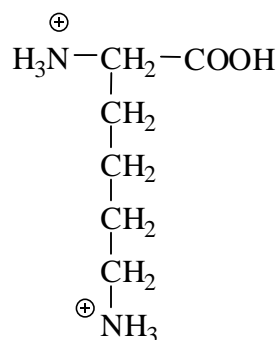
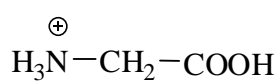
**Three tripeptides are possible: *ala-lys-lys*, *lys-ala-lys* and *lys-lys-ala***

Comment, giving your reason, on whether the tripeptide(s) will be acidic, neutral or basic in character.

**Lysine has a basic, amine sidechain ( $R = \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ ) whilst alanine has a neutral sidechain ( $R = \text{CH}_3$ ). The tripeptide(s) will thus be basic.**

Draw the constitutional formulas, indicating the correct ionic state, of the products formed from acid hydrolysis of one of your tripeptides.

**Each tripeptide will be hydrolysed to give alanine and lysine. In acid, these will be present with the basic amine groups (including the sidechain of lysine) and the carboxylic acid groups in the protonated forms:**



- In the spaces provided, explain the meanings of the following terms.

(a) enzyme

**A biological catalyst. Like any catalyst, it acts by providing an alternative reaction pathway with a lower activation energy. Enzymes are typically highly efficient and specific.**

(b) cofactor

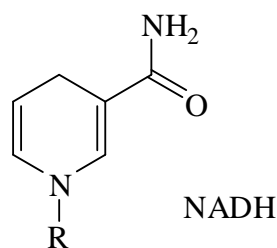
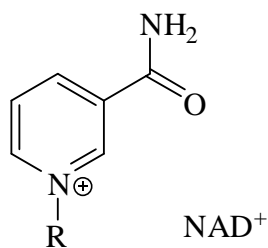
**The non-protein part of an enzyme, such as the haem group in haemoglobin, that is required for the enzymic activity.**

(c) peptide

**A sequence of amino acids linked by peptide bonds – a biological polymer formed by linking the carboxylic acid group of one amino acid and the amine group on another.**



- NAD<sup>+</sup>/NADH is a biological redox system. The two species may be represented by the structures below.



What are the requirements for a compound to be aromatic? Indicate which of NAD<sup>+</sup> and/or NADH fulfil these requirements.

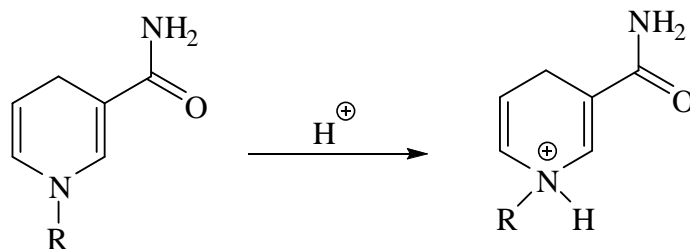
**An aromatic compound must be cyclic, planar, conjugated, and have  $4n+2$   $\pi$  electrons (with  $n$  being an integer).**

**NAD<sup>+</sup> is aromatic** – there are  $2 \times \text{C}=\text{C}$  and  $1 \times \text{C}=\text{N}$  bond each of which contributes  $2 \pi$  electrons, giving a total of 6. This is aromatic with  $n = 1$ .

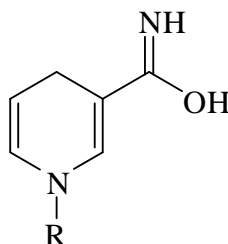
**NADH is not aromatic.** The presence of an  $sp^3$  carbon atom breaks the conjugation.

Which of NAD<sup>+</sup> and/or NADH will react with cold dilute H<sup>+</sup> in an acid/base reaction? Using the structures above, give the chemical equation for the reaction and a brief explanation for your choice.

**Only NADH will react.**



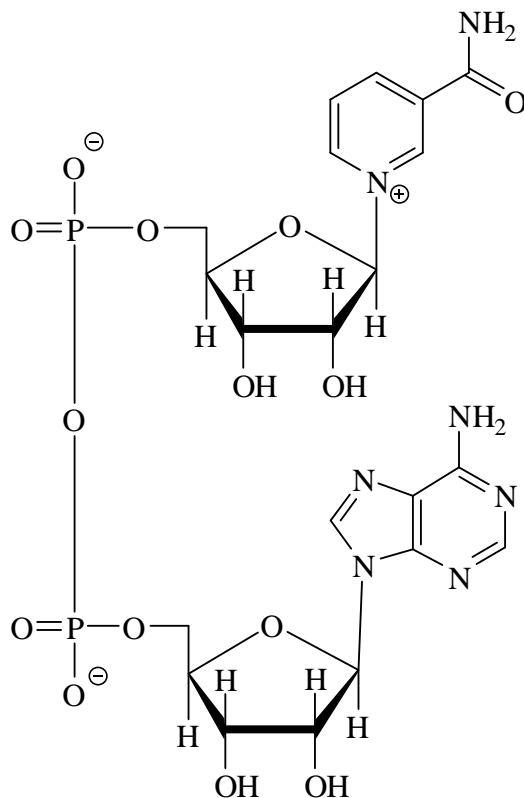
Draw the structure of a tautomer of NADH.



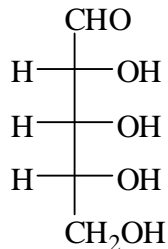
**THIS QUESTION CONTINUES ON THE NEXT PAGE**

The full structure of  $\text{NAD}^+$  contains ribose, two phosphate groups and adenine.

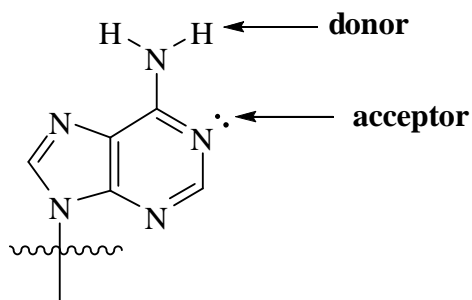
**Marks**  
**4**



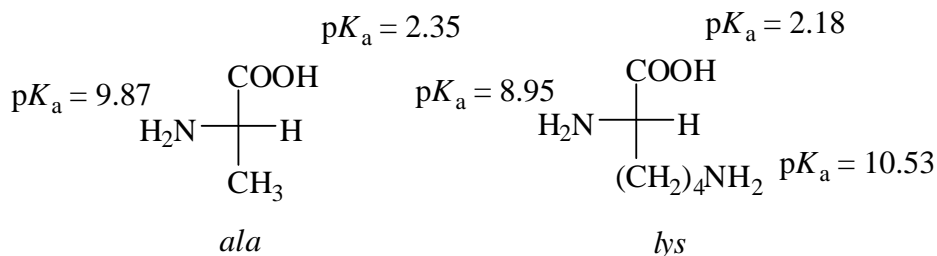
Draw ribose as a Fischer projection.



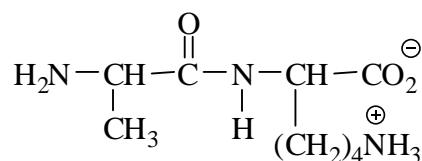
Adenine is also a component of DNA used in forming complementary strands by hydrogen bonding. Indicate the sites of hydrogen bonding on adenine that are used in forming complementary strands in DNA and differentiate between those sites that are hydrogen bond donors and those that are hydrogen bond acceptors.



- Alanine (*ala*) and lysine (*lys*) are two amino acids with the structures given below as Fischer projections. The  $pK_a$  values of the conjugate acid forms of the different functional groups are indicated.



Draw the structure of the dipeptide *ala-lys* in its zwitterionic form.



Would you expect the dipeptide to be soluble in water? Give a brief reason for your choice.

**The presence of oxygen and nitrogen atoms and O-H and N-H groups would lead to strong H-bonding and ion-dipole forces in water and so the dipeptide is likely to be water soluble.**

Would you expect the dipeptide to be acidic, neutral or basic? Give a brief reason for your choice.

**There is a basic  $-\text{NH}_2$  side chain on lysine. As there is a greater number of basic groups than acidic groups overall, it is likely to be basic.**

Estimate the isoelectric point of the dipeptide.

**The dipeptide has three ionizable groups – the amine function on the alanine ( $pK_a$  9.87), the carboxylic acid group on the lysine ( $pK_a$  2.18) and the amine group on the lysine side chain ( $pK_a$  10.53).**

**The fully protonated form of the dipeptide has the two  $-\text{NH}_2$  and the  $-\text{COOH}$  groups protonated and has a +2 charge. This form will exist at low pH. The fully deprotonated form, the amine functions are not protonated and the carboxylic acid is deprotonated ( $-\text{COO}^-$ ) giving the molecule a -1 charge.**

ANSWER CONTINUES ON THE NEXT PAGE

At low pH, the protonated (+2) form dominates. As the pH is raised the group with the lowest  $pK_a$  (the carboxylic acid group) will become steadily deprotonated. At a  $pK_a$  of 2.18, there is a 50:50 mixture of the +2 and +1 forms. The latter having the carboxylic acid group deprotonated.

As the pH is raised further, the group with the next lowest  $pK_a$  (the alanine amine group) becomes steadily deprotonated. At a  $pK_a$  of 9.87, there is a 50:50 mixture of the +1 and neutral forms. The latter having the alanine amine group deprotonated.

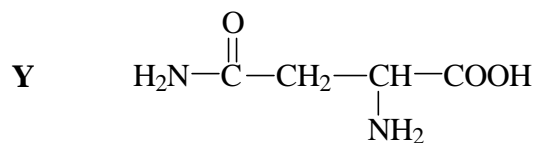
As the pH is raised even more, the final group (lysine side-chain amine) becomes deprotonated. At a  $pK_a$  of 10.53, there is a 50:50 mixture of the neutral and -1 forms.

A pH of 9.87 gives a 50:50 mixture of +1 and neutral. A pH of 10.53 gives a 50:50 mixture of -1 and neutral. Hence, a pH intermediate between these values will give a solution predominately containing the neutral form. This is the isoelectric point:

$$pI = \frac{pK_{a1} + pK_{a2}}{2} = \frac{(10.53 + 9.87)}{2} = 10.2$$

**Marks**  
**4**

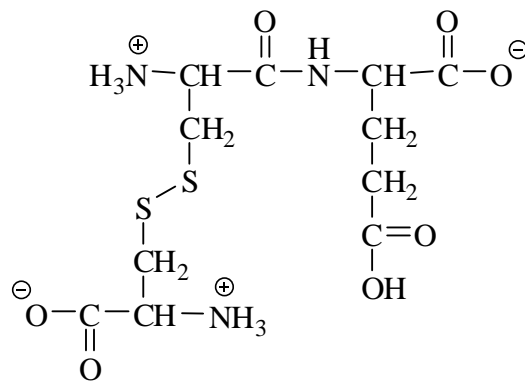
- The amino acid, asparagine, was isolated from asparagus juice in 1806. The uncharged form, **Y**, is given below.



Draw the constitutional formula of the product(s) formed in the reaction of **Y** with the following reagents.

Cold, dilute hydrochloric acid  $\text{H}_2\text{N}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\underset{\oplus\text{NH}_3}{\text{CH}}-\text{COOH}$	Cold, dilute sodium hydroxide  $\text{H}_2\text{N}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\underset{\text{NH}_2}{\text{CH}}-\text{CO}_2^\ominus$
Hot, 6 M hydrochloric acid  $\overset{\ominus}{\text{NH}}_4^+ + \text{HO}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\underset{\oplus\text{NH}_3}{\text{CH}}-\text{COOH}$	Hot, 6 M sodium hydroxide  $\text{NH}_3 + \overset{\ominus}{\text{O}}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\underset{\text{NH}_2}{\text{CH}}-\text{CO}_2^\ominus$

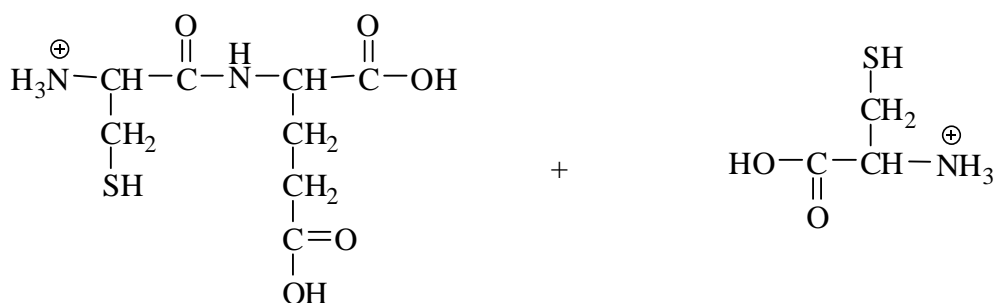
- A peptide has the following structure.



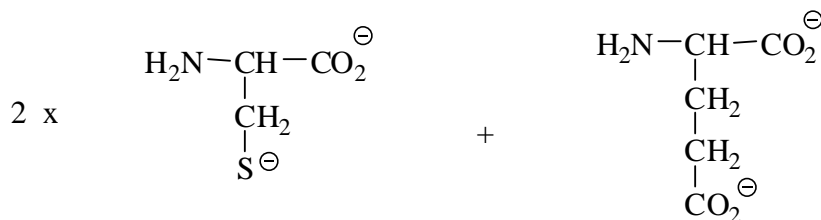
Would you expect this peptide to be soluble in water? Explain your answer.

**Yes. It has a number of charged groups that will be solvated by water molecules due to ion-dipole interactions.**

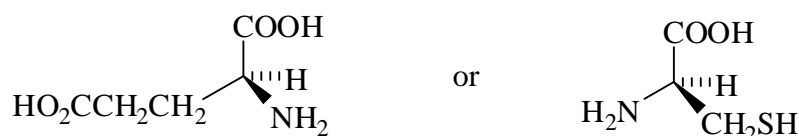
Give the products formed after treatment of the peptide with  $\text{Zn}/\text{H}^+$ .



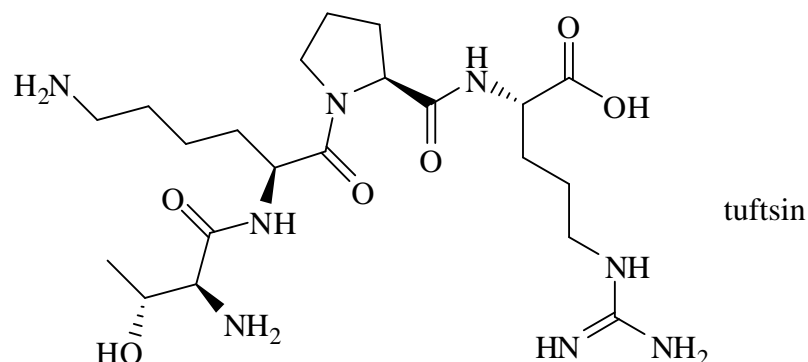
These products are then heated with excess aqueous  $\text{OH}^-$ . Draw the constitutional formulas of the different amino acids formed. Ensure you represent the amino acids in the correct charge state for the conditions.



Choose one of the amino acids produced on hydrolysis and draw the (*S*) configuration.



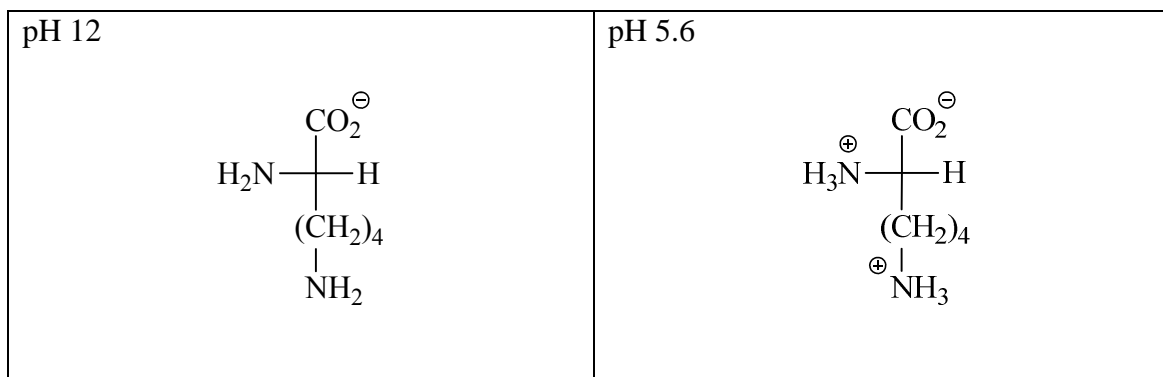
- Tuftsins is a tetrapeptide (Thr-Lys-Pro-Arg) produced by enzymatic cleavage of the Fc-domain of the heavy chain of immunoglobulin G. It is mainly produced in the spleen and its activity is related primarily to immune system function.



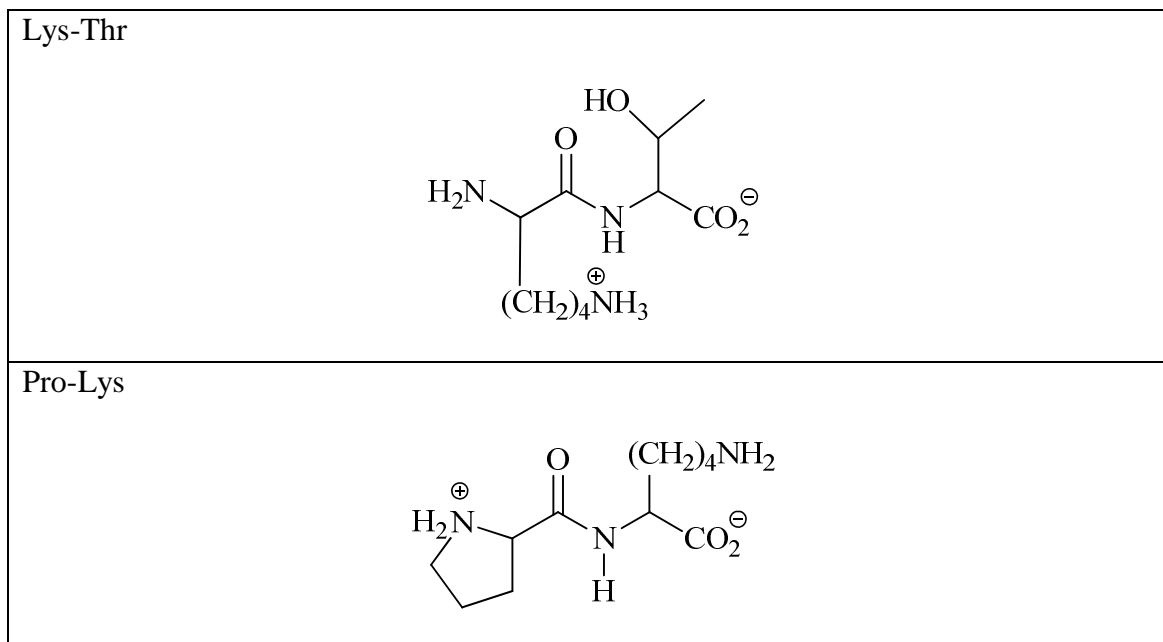
Draw the Fischer projections of the four L-amino acids that result from the acid hydrolysis of tuftsins.


Marks  
4

What is the major species present when lysine (Lys) is dissolved in water at pH 12 and pH 5.6. The  $pK_a$  values of lysine are 1.82 ( $\alpha$ -COOH), 8.95 ( $\alpha$ -NH<sub>3</sub><sup>+</sup>) and 10.53 (side chain).



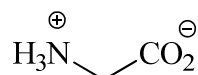
Give the constitutional formulas for the following dipeptides in their zwitterionic states. The  $pK_a$  values of proline are 1.95 and 10.64.



2

- Glycine, NH<sub>2</sub>CH<sub>2</sub>COOH, is the simplest of the naturally occurring amino acids. It has a melting point of 238 °C, while CH<sub>3</sub>CH<sub>2</sub>COOH has a melting point of -21 °C. Give one reason for this difference.

**Glycine is an amino acid and has the following zwitterionic structure.**



**Propionic acid has strong hydrogen bonds, giving it a relatively high m.p. However, glycine has very strong ionic bonds between the NH<sub>3</sub><sup>+</sup> and CO<sub>2</sub><sup>-</sup> groups giving it very high melting point.**

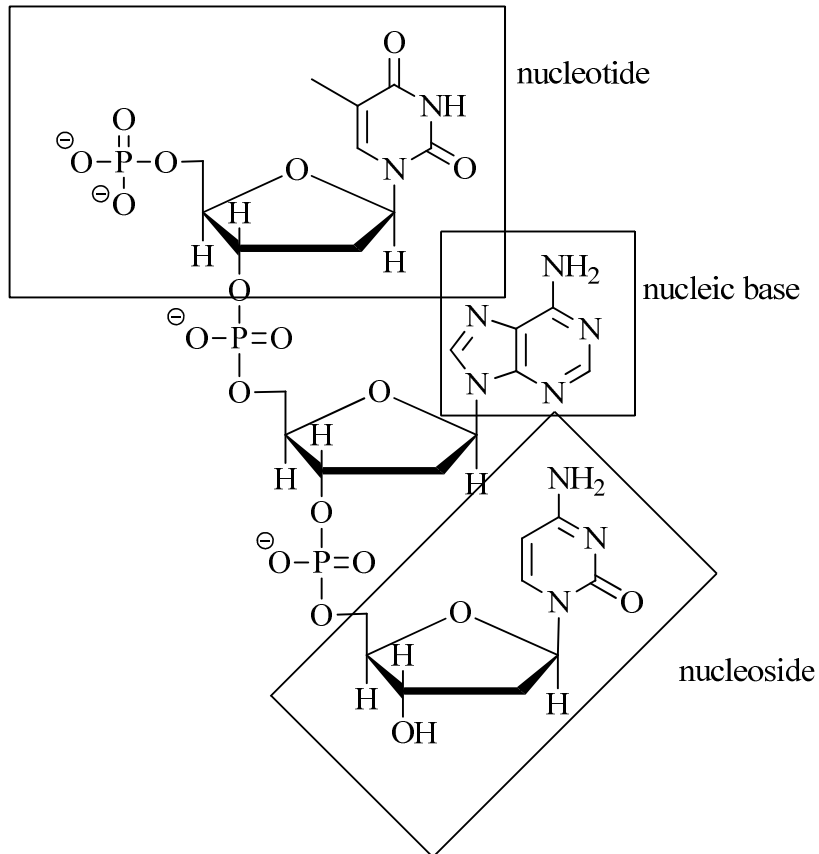


- Is the following structure a fragment of DNA or RNA? Give two reasons.

**Marks**  
**5**

**It is a DNA fragment:**

- The sugar is deoxyribose (RNA has ribose as the sugar).**
- The topmost nucleic base is thymine (RNA utilises uracil instead of thymine).**



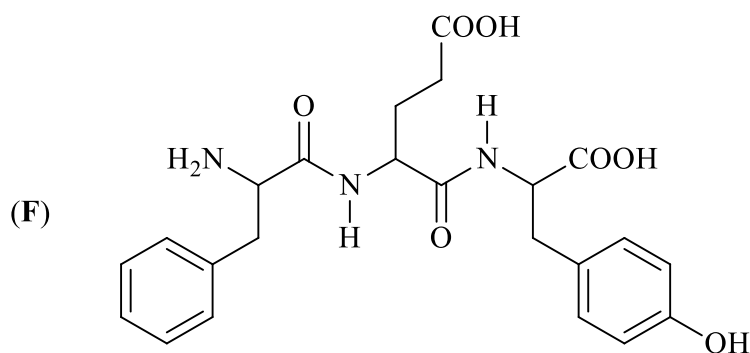
Clearly identify on the above structure one example of each of the following subunits.

nucleic base – **see above**

nucleoside – **see above**

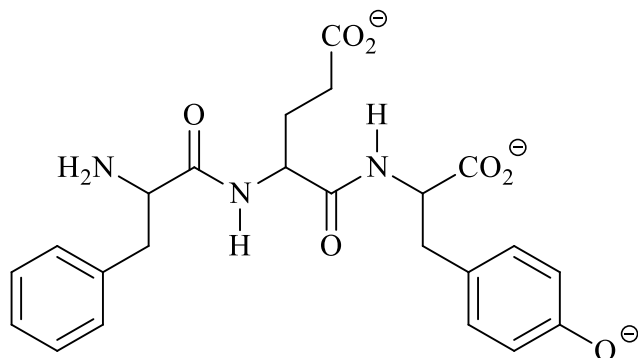
nucleotide - **see above**

- Consider the tripeptide phenylalanylglutamyltyrosine (Phe-Glu-Tyr) (**F**), whose constitutional formula is shown below.

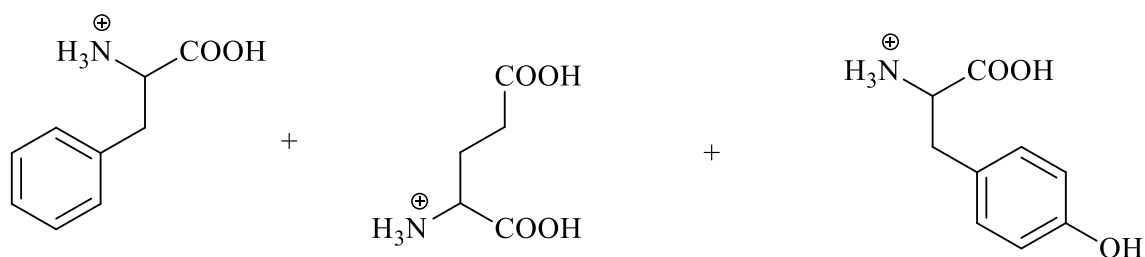


Draw the constitutional formula(s) of the product(s) obtained when the tripeptide (**F**) is subjected to the following conditions. Make sure you show the products in the appropriate ionic states.

cold 2 M NaOH

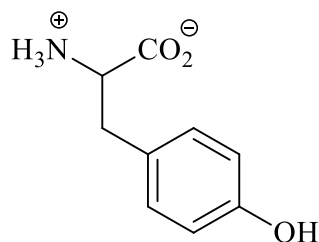


5 M HCl / heat



The  $pK_a$  values of tyrosine are  $pK_{a1} = 2.20$  ( $\alpha$ -COOH),  $pK_{a2} = 9.11$  ( $\alpha$ -NH<sub>3</sub><sup>⊕</sup>) and  $pK_{a3} = 10.07$  (-CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OH). Draw the structure of the zwitterionic form of tyrosine.

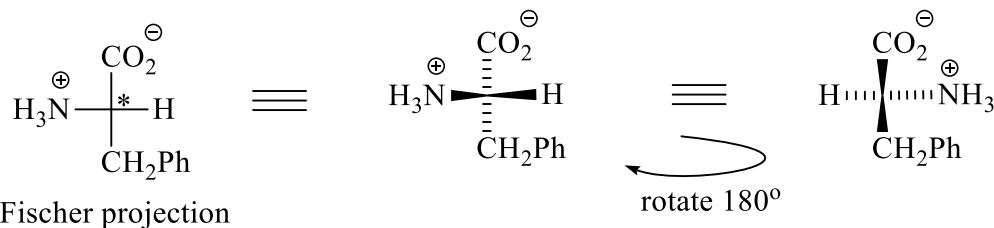
**Marks**  
**4**



At what pH will this be the predominant species in aqueous solution?

**5.66**  
**(halfway**  
**between  $pK_{a1}$**   
**and  $pK_{a2}$ )**

The naturally occurring isomer of phenylalanine is (L)-phenylalanine. Draw the zwitterionic structure of (L)-phenylalanine and indicate the stereogenic centre with an asterisk (\*). Determine whether this amino acid has the (*R*) or (*S*) configuration. Show your working.



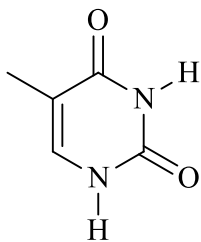
**Horizontal bonds in Fischer projections are out of the paper, vertical bonds are into the paper. Order of priority of substituents is  $NH_3^+ > CO_2^- > CH_2Ph > H$ . Reorient the molecule so that the lowest priority group (H) is at the back. Viewing down the C-H bond, the orientation of  $NH_3^+ \rightarrow CO_2^- \rightarrow CH_2Ph$  is anticlockwise. Therefore (L)-phenylalanine has (*S*) configuration.**

**THE REMAINDER OF THIS PAGE IS FOR ROUGH WORKING ONLY.**

- Draw a tautomer of the structure of thymine, shown below.

**Marks**  
**1**

thymine



tautomer of thymine

