34.4 AMINO ACIDS

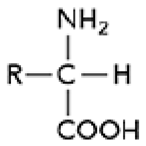
Learning outcomes

Candidates should be able to:

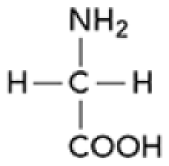
1. describe the acid/base properties of amino acids and the formation of zwitterions, to include the isoelectric point
2. describe the formation of amide (peptide) bonds between amino acids to give di- and tripeptides
3. interpret and predict the results of electrophoresis on mixtures of amino acids and dipeptides at varying pHs (the assembling of the apparatus will not be tested)

Introduction

- Amino acids are an important group of compounds that all contain:
  the basic amino group ($-NH_2$), and
  the acidic carboxylic acid group ($-COOH$).
- This makes the amino acids amphoteric, as they can behave as both an acid and a base.
- One type of amino acid has the $-NH_2$ group bonded to the carbon atom next to the $-COOH$ group. These 2 aminocarboxylic acids are the 'building blocks' that make up proteins. There are about 20 of these naturally occurring amino acids.
- The general structure of an amino acid (2-aminocarboxylic acid) molecule can be represented as:



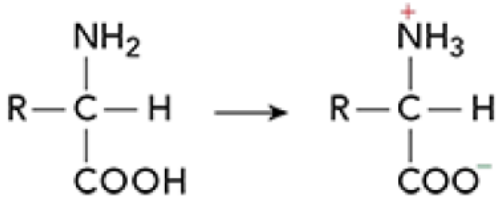
  - The general structural formula of an amino acid (2-aminocarboxylic acid) is $RCH(NH_2)COOH$.
  - The R group is the part of the amino acid that can vary in different amino acids. The simplest amino acid is glycine (systematic name aminoethanoic acid) in which R is an H atom:



glycine (aminoethanoic acid)

  - Alanine (systematic name 2-aminopropanoic acid) is an amino acid in which the R group is the methyl group, $-CH_3$.
  - The R group can be:
    - acidic (e.g., it contains another carboxylic acid group, $-COOH$ group),
    - basic (e.g., it contains another amine group, $-NH_2$ group), or
    - neutral (e.g., when R is an alkyl group).

  - Amino acids will undergo most reactions of amines and carboxylic acids. However, each molecule can interact with itself due to its basic $-NH_2$ group and its acidic $-COOH$ group:

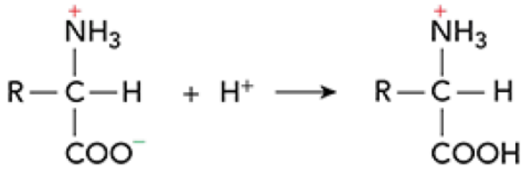


  - The ion is called a zwitterion (from the German 'zwei' meaning 'two') as it carries two charges: one positive ($-NH_3^+$) and one negative ($-COO^-$). The ionic nature of the zwitterions gives amino acids relatively strong intermolecular forces of attraction. They are crystalline solids that are soluble in water.

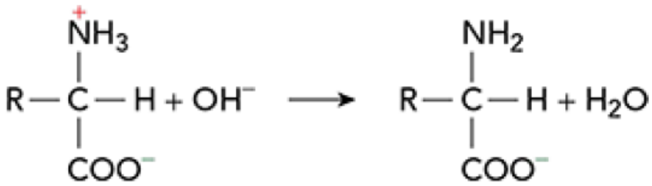
A zwitterion is a molecule that contains both a cationic group and an anionic group.

- A solution of amino acids in water contains zwitterions that have both acidic and basic properties (i.e. they are amphoteric). They will resist changes in pH when small amounts of acid or alkali are added to them. Solutions that do this are called buffer solutions

- If the pH is lowered by adding acid, the ─COO− part of the zwitterion will accept an H+ ion, re-forming the undissociated ─COOH group. This leaves a positively charged ion:



- If the pH is raised by adding a base, the ─NH_3^+ part of the zwitterion will donate an H^+ ion to the hydroxide ion (H+ + OH− → H_2O), re-forming the amine ─NH_2 group. This leaves a negatively charged ion:



- By adjusting the pH by small amounts, we can reach a point where neither the positive nor negative ions shown above dominate, so the amino acid has no charge overall. This pH is called the isoelectric point of an amino acid.
- The isoelectric point can be found by measuring the pH value of the amino acid solution when it is not attracted to either a positive electrode or a negative electrode

1. Define isoelectric point.

....

.... [1]

2. Amino acids can act as monomers.
State what is meant by the isoelectric point of an amino acid.

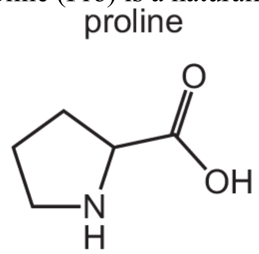
....

.... [1]

3. The isoelectric point of asparagine, asn, is at pH 5.4.
(i) Describe the meaning of the term isoelectric point. [1]

4. Phenylalanine, $C_6H_5CH_2CH(NH_2)COOH$, is an amino acid with an isoelectric point of 5.5.
(i) State what is meant by isoelectric point. [1]

5. Proline (Pro) is a naturally occurring amino acid.



At pH 6.5, proline exists in aqueous solution as a zwitterion.
Draw the structure of the zwitterion of proline.
Explain how the zwitterion of proline forms.

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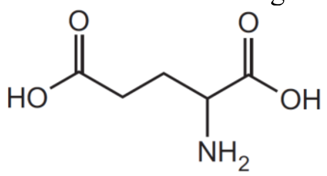
.... [2]

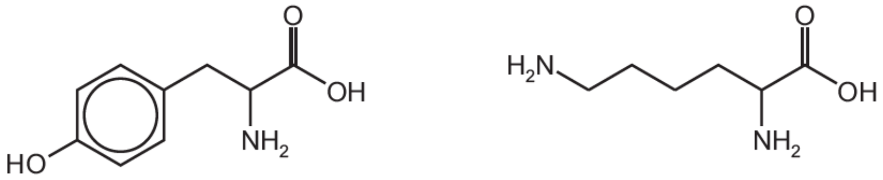
6. Glutamic acid is a naturally occurring amino acid.
The skeletal formula of glutamic acid is shown.



glutamic acid
The isoelectric point of glutamic acid is pH 3.
A sample of glutamic acid is dissolved in a solution of pH 1. A strong alkali is then added until the pH of the mixture reaches pH 14. During this process, all possible ionised forms of glutamic acid are present at different times, depending on the pH of the solution.
Complete the boxes below to show four different ionised forms of glutamic acid that are present at the stated pH values. [3]

at pH 1	at pH 3
at pH 9	at pH 14

7. Tyrosine and lysine, shown in Fig. 9.1, are naturally occurring amino acids found in proteins.



tyrosine lysine

Fig. 9.1

The isoelectric point of lysine is 9.47.
Draw the structure of lysine at the stated pH in the boxes below. [2]

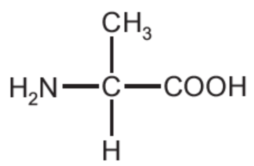
lysine at pH 7.00 lysine at pH 9.47 lysine at pH 12.00

8. Amino acids are molecules that contain —NH_2 and —COOH functional groups.
Glycine, H_2NCH_2COOH, is the simplest stable amino acid.
The isoelectric point of glycine is 6.2.
Draw the structure of glycine at pH 4. [1]

9. Phenylalanine, $C_6H_5CH_2CH(NH_2)COOH$, is an amino acid with an isoelectric point of 5.5.
Draw the structure of $C_6H_5CH_2CH(NH_2)COOH$ at pH 10. [1]

10. When $CH_3CHClCOOH$ reacts with aqueous NH_3, alanine forms.

alanine



Alanine is an amino acid. Its isoelectric point is 6.1.

(i) Give the structural formula of alanine at pH 2.

.... [1]

(ii) Write two equations to show how an aqueous solution of alanine can act as a buffer solution.

....

.... [2]

11. Asparagine and aspartic acid are two naturally occurring amino acids. Their structures and isoelectric points are shown in Table 8.1.

Table 8.1

amino acid	structure	isoelectric point
asparagine	$HOOCCH(NH_2)CH_2CONH_2$	5.41
aspartic acid	$HOOCCH(NH_2)CH_2COOH$	2.77

(i) Draw the structures of asparagine and aspartic acid at pH 2. [2]

(ii) Propanedioyl chloride reacts with an excess of asparagine to form compound G with molecular formula $C_{11}H_{16}N_4O_8$.

Each molecule of compound G has four amide groups.

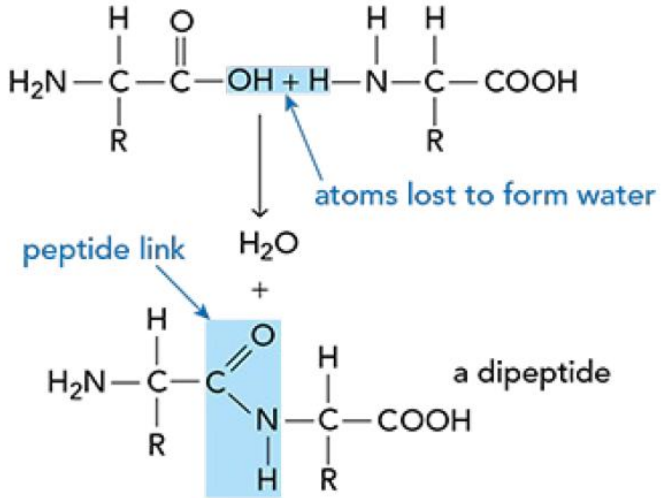
Draw the structure of compound G. [2]

Compound **G**, $C_{11}H_{16}N_4O_8$

(d) Asparagine is hydrolysed with an excess of hot NaOH(aq).
Draw the structure of the organic product of this reaction. [2]

Formation of amide (peptide) bonds

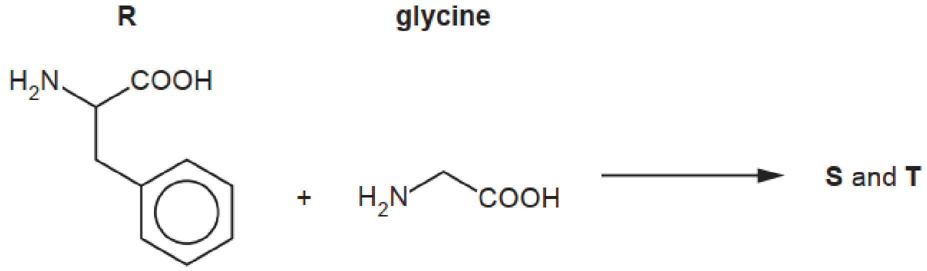
Amino acid molecules can also react with each other. The acidic —COOH group in one animo acid molecule reacts with the basic $-NH_2$ group in another molecule. When two amino acids react together, the resulting molecule is called a **dipeptide**.



Note that the shaded area is the **amide bond** between the two amino acids. An amide bond between two amino acid molecules is also called a peptide bond or peptide link. The reaction is a condensation reaction, as a small molecule, in this case water, is eliminated when the reactant molecules join together.
You can see that the dipeptide product still has an amine group, $-NH_2$, at one end and a carboxylic acid group, —COOH, at the other end. Therefore, the reaction can continue, to form a **tripeptide** initially, and then ever-longer chains of amino acids. The longer molecules are known as polypeptides, and then proteins , as they become even longer sequences of amino acids.

Peptide bond: the -CONH- link (amide link) between amino acid residues in a peptide or protein

12. A molecule of phenylalanine, R, can react with a molecule of glycine to form two dipeptides, S and T. S and T are structural isomers.



Draw the structures of these dipeptides. The peptide bond formed should be shown fully displayed

S

T

13. The structures of the amino acids serine and lysine are shown in Fig. 9.1.

serine lysine

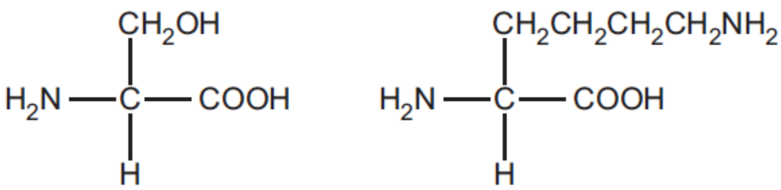


Fig. 9.1

Draw the structure for the dipeptide, ser–lys, with molecular formula $C_9H_{19}N_3O_4$.
The peptide functional group formed should be displayed.

14. $C_6H_5CH_2CH(NH_2)COOH$ and alanine, $CH_3CH(NH_2)COOH$, react to form a dipeptide containing both amino acid residues.
Draw the structure of this dipeptide.
The peptide functional group formed should be displayed. [2]

15. Glutamic acid is another amino acid that acts as a buffer.

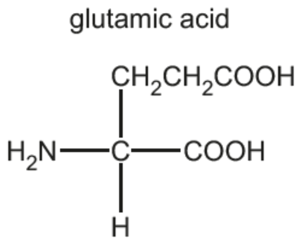
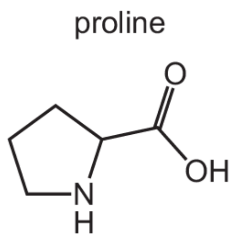


Fig. 7.1

(i) Draw the skeletal formula for glutamic acid. [1]

(ii) Draw the structure for the dipeptide, ala-glu, formed from one molecule of alanine and one molecule of glutamic acid.
The peptide bond formed should be displayed. [2]

16. Proline (Pro) is a naturally occurring amino acid.



Proline is often found bonded to glycine (Gly) in a protein.
(i) Draw the dipeptide Pro-Gly.
The peptide bond must be shown fully displayed. [2]

(ii) Name the type of reaction that forms a dipeptide from two amino acids.

.... [1]

17. A mixture of serine, $HOCH_2CH(NH_2)CO_2H$, and lysine, $H_2N(CH_2)_4CH(NH_2)CO_2H$, reacts to form several different products.
(i) Draw the structures of the two structural isomers with the molecular formula $C_6H12N_2O_5$ that could be present in the product mixture.
The functional group formed in each case should be displayed.

[3]

(ii) Predict the number of different structural isomers with the molecular formula $C_9H_{19}N_3O_4$ that could be present in the product mixture.

molecular formula	number of structural isomers formed
$C_9H_{19}N_3O_4$	

[1]

18. Amino acids can act as monomers.
Electrophoresis can be used to separate and identify amino acids.
Table 4.3 shows information about the three amino acids glycine, lysine and glutamic acid.
Table 4.3

amino acid	structural formula of amino acid	isoelectric point
glycine (gly)	H_2NCH_2COOH	6.0
lysine (lys)	$H_2NCH(CH_2CH_2CH_2CH_2NH_2)COOH$	9.7
glutamic acid (glu)	$H_2NCH(CH_2CH_2COOH)COOH$	3.2

(i) A mixture containing these three amino acids is analysed in a buffer solution of pH 6.0.
Draw and label three spots on Fig. 4.1 to indicate the predicted position of each of these amino acids, gly, lys and glu, after electrophoresis. [2]

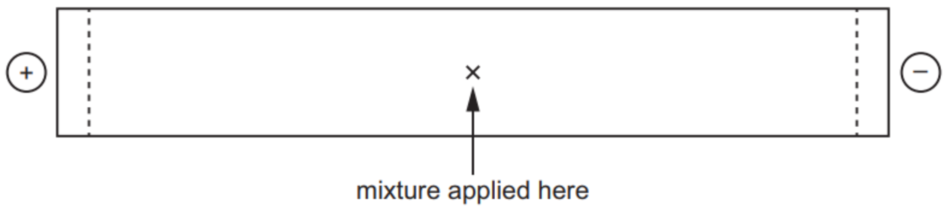


Fig. 4.1

(ii) Electrophoresis is repeated using a buffer solution of pH 11.
Predict how the position of glycine will change, if at all, after electrophoresis.

....

.... [1]

19. The isoelectric point of serine is 5.7 and of lysine is 9.7.

A mixture of serine, lysine and ser–lys is analysed by electrophoresis using a buffer at pH 5.7.

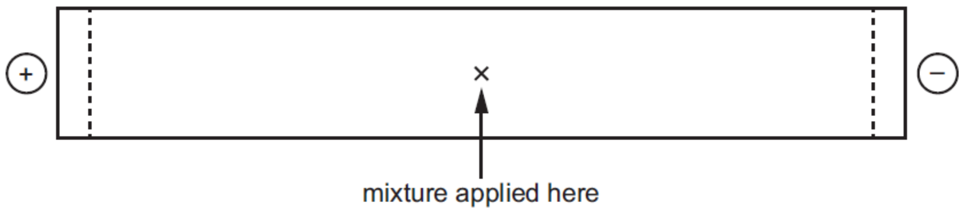


Fig. 9.2

Draw and label three spots on Fig. 9.2 to indicate the predicted position of each of these three species, serine, lysine and ser–lys, after electrophoresis.
Explain your answer.

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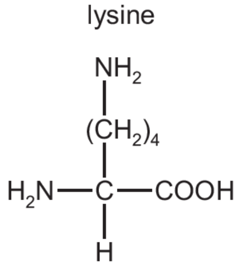
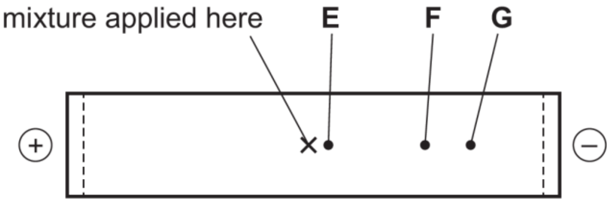
.... [3]

20. The isoelectric point of lysine, lys, is at pH 9.8.



The isoelectric point of asparagine, asn, is at pH 5.4.

A mixture of the dipeptide lys-asn and its two constituent amino acids, asparagine and lysine, is analysed by electrophoresis using a buffer at pH 5.0. The results obtained are shown in



Suggest identities for the species responsible for spots E, F, and G. Explain your answers.

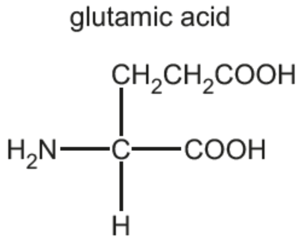
spot	Identity
E	
F	
G	

....

....

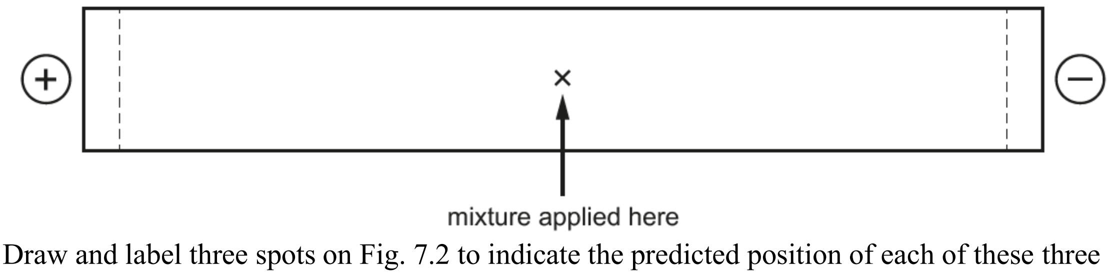
.... [3]

21. Glutamic acid is another amino acid that acts as a buffer.



(d) The isoelectric point of alanine is 6.0 and of glutamic acid is 3.2.

A mixture of the dipeptide, ala-glu, and its two constituent amino acids, alanine and glutamic acid, is analysed by electrophoresis using a buffer at pH 6.0.



Draw and label three spots on Fig. 7.2 to indicate the predicted position of each of these three species after electrophoresis.

Explain your answer.

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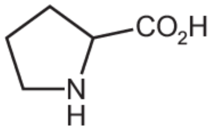
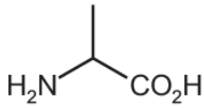
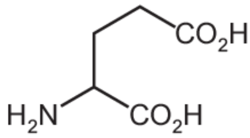
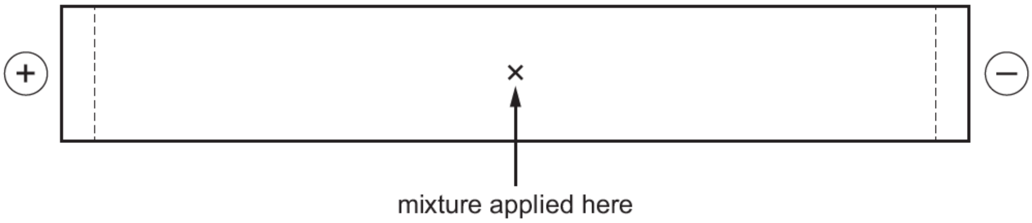
.... [3]

22. The isoelectric point of an amino acid is the pH at which it exists as a zwitterion.
Three of the amino acids in gelatin are proline, alanine and glutamic acid. Their isoelectric points are shown.

	proline	alanine	glutamic acid
amino acid			
isoelectric point	6.5	6.0	3.1

A mixture of these amino acids was analysed by electrophoresis using a buffer solution at pH 4.0.
Draw and label three spots on the diagram of the electropherogram to indicate the likely position of each of these three species after electrophoresis.
Explain your answer.



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.... [4]

23. At pH 11 alanine exists as $H_2NCH(CH_3)CO_2^-$ ions and glutamic acid exists as $H_2NCH(CH_2CH_2CO_2^-)CO_2^-$ ions.
A mixture of alanine and glutamic acid at pH 11 is subjected to electrophoresis.
(i) State how the mixture can be maintained at pH 11 during electrophoresis.

.... [1]

(ii) Draw a fully labelled diagram for the apparatus that would be used to carry out this electrophoresis. Your diagram should include the position of the mixture of alanine and glutamic acid at the start of the electrophoresis experiment. [2]

(iii) Identify the electrode that each amino acid travels towards during electrophoresis at pH 11.

alanine ....

glutamic acid .... [1]

(iv) In a particular electrophoresis experiment at pH 11, the glutamic acid travels 3.4 cm.
Alanine travels a shorter distance.
Explain the factors that account for the difference in the distances travelled.

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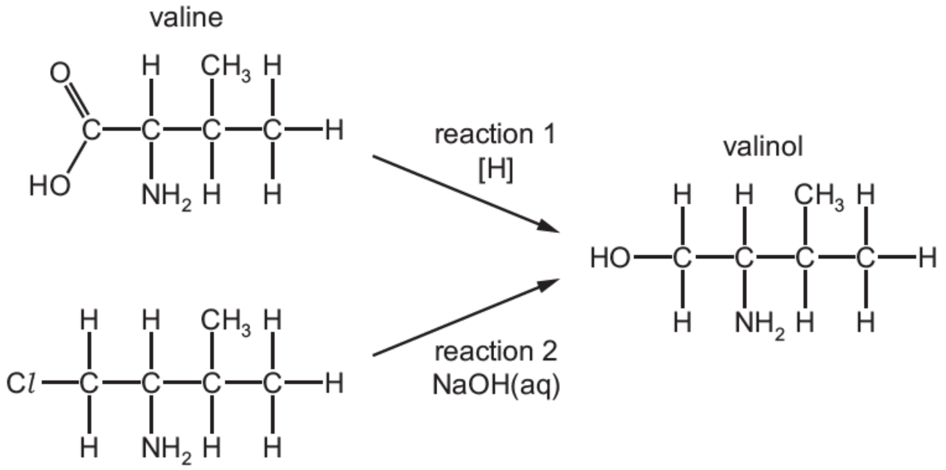
.... [2]

Conversions

24. Valinol can be synthesised by the following reactions. Reaction 1 uses valine as the starting material.



(a) (i) Write an equation for reaction 1, using [H] to represent the reducing agent.

.... [1]

(ii) Suggest a suitable reagent for reaction 1.

.... [1]

(iii) Name the mechanism for reaction 2.

.... [1]

(b) Valine and glycine, H_2NCH_2COOH, form the tripeptide Gly–Val–Gly.
Draw the structure of this tripeptide. Show the peptide bonds fully displayed. [2]

(c) (i) Valine exists as two stereoisomers.
Draw three-dimensional diagrams to show the two stereoisomers of valine. In your diagrams, the –CH(CH3)$_2$ group can be represented by –R.
State the type of stereoisomerism shown.

type of stereoisomerism .... [2]

(ii) Valine is an amino acid.
Draw the zwitterion of valine. [1]

(iii) Valinate, Val^-, is the anion of valine. It takes part in a ligand substitution reaction with hexaaquanickel(II) ions. Complex **Z** is formed.
Z
$[Ni(H_2O)_6]^{2+}(aq) + 2Val^-(aq) \rightleftharpoons [Ni(H_2O)_2(Val)_2](aq) + 4H_2O(l)$

Write an expression for *K*stab for this equilibrium.

*K*stab = [1]

(iv) At room temperature, the numerical value of *K*stab is 2.34×10^5.
Explain what this value indicates about the equilibrium and the stability of complex **Z**.

....

....

.... [1]

(v) **Z** is an octahedral complex with formula $[Ni(H_2O)_2(Val)_2]$.
Use this information to state the type of ligand that the valinate ion is acting as in this complex.

.... [1]

*****This is not a complete note. It is just to guide you. It is recommended to study the prescribed textbooks along with this material. *****