

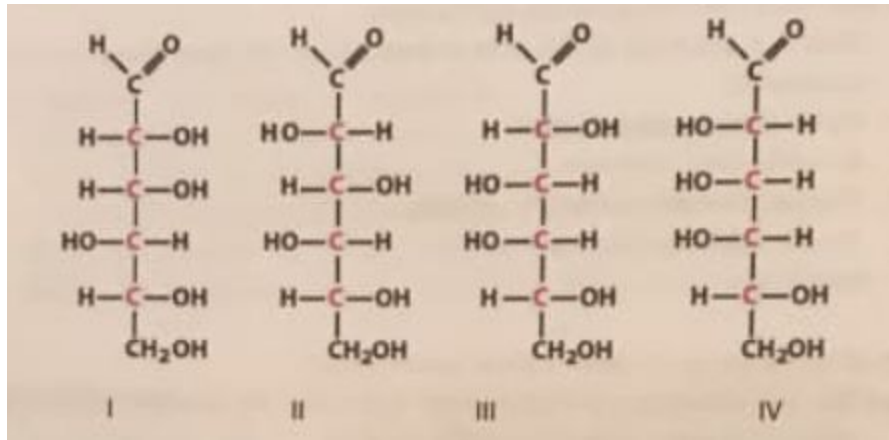
## Midterm 1

**Multiple Choice Questions. Once correct answer per question. (1 Mark each unless otherwise stated):**

- Which amino acid has three  $pK_a$ 's?
  - Leucine
  - Proline
  - Cysteine
  - Threonine
  - Glycine
- What is suggested in the "RNA world" hypothesis?
  - Arginine, asparagine, and alanine were the first three amino acids
  - Life was thought to evolve 6 billion years ago
  - DNA evolved later due to the instability of RNA
  - RNA was introduced to the early Earth from a meteorite
  - Chemical building blocks can be derived only from complex organic compounds
- At pH 2.2, the concentration of lactic acid is 0.60 M and the concentration of lactate is 0.01 M. What is the  $pK_a$  of lactic acid?
  - 0.4
  - 2.5
  - 3.1
  - 4.0
  - 4.8
- What is true for a spontaneous process?
  - $\Delta G > 0$
  - If  $\Delta S < 0$ ,  $\Delta H$  must be  $< 0$
  - It is called an endergonic process
  - It is always linked to an endergonic process
  - The reaction happens faster than an exergonic process
- Both D-ribose and D-glucose
  - Can form intramolecular hemiacetal bonds
  - Are hexoses
  - Lack functional groups that can form glycosidic linkages
  - Exist mainly in their pyranose form in biopolymers
  - Are crucial building blocks for nucleic acids

6. For which of the following pairs can the amino acid side chains interact via electrostatic interactions at neutral pH?
- Leu - Met
  - Cys - Val
  - Asp - Arg
  - Tyr - Gly
  - Glu - Ala
7. What statement concerning biopolymers is true?
- Their formation was shown to be thermodynamically spontaneous in the Miller-Urey experiment
  - RNA is more stable than DNA
  - $\Delta S > 0$  for their formation
  - They are thermodynamically unstable
  - Their breakdown releases water
8. Which of the following statements about water is false?
- The high dielectric constant of water means that electrostatic interactions are stronger in water than in non-polar solvents
  - The hydrophobic effect is driven by the entropy of the aqueous solvent
  - Water molecules form more hydrogen bonds in ice than in liquid form
  - Water is both an efficient hydrogen bond donor and hydrogen bond acceptor
  - The hydrogen bonding network among water molecules enables very fast movement of  $H^+$  and  $OH^-$
9. Identify the pair that shows the same monosaccharide in the linear (Fischer) and the cyclic form, respectively.
- I and IV
  - II and V
  - III and IV
  - III and VI
  - II and VI
10. If a polypeptide has 400 amino acid residues, what is the approximate molecular weight?
- 11,000
  - 22,000
  - 44,000
  - 88,000
  - 176,000

11. What is true for the illustrated monosaccharides?



- (I) is an aldopentose
  - (II) and (III) are enantiomers
  - (I) and (IV) are epimers
  - (III) and (IV) are epimers
  - They are all L-sugars
12. At pH 1, what is the net charge of WINTER? (2 marks)
- 2
  - 1
  - 0
  - +1
  - +2
13. What is true for peptide bonds?
- They hold the polypeptide chains of multisubunit proteins together
  - They are planar
  - They are formed by a hydrolysis reaction
  - Different types are found in different proteins
  - Both (b) and (c) are correct
14. What is true for nucleosides?
- They contain phosphates
  - They contain nitrogenous bases and monosaccharides
  - They can be linked together to form nucleic acids
  - They contain hexose sugars
  - All of the above

15. Which of the following pairs of amino acid residues are most likely to be found at the surface of a water-soluble protein?
- Thr and Asn
  - Thr and Ile
  - Val and Ile
  - Gln and Val
  - Val and Thr
16. At pH 10.5, what is the net charge of CINEMA? (2 marks)
- 4
  - 3
  - 1
  - 0
  - +3
17. Which bases pair together in DNA?
- Guanine and cysteine
  - Adenine and uracil
  - Guanine and adenine
  - Cysteine and thymine
  - Thymine and adenine

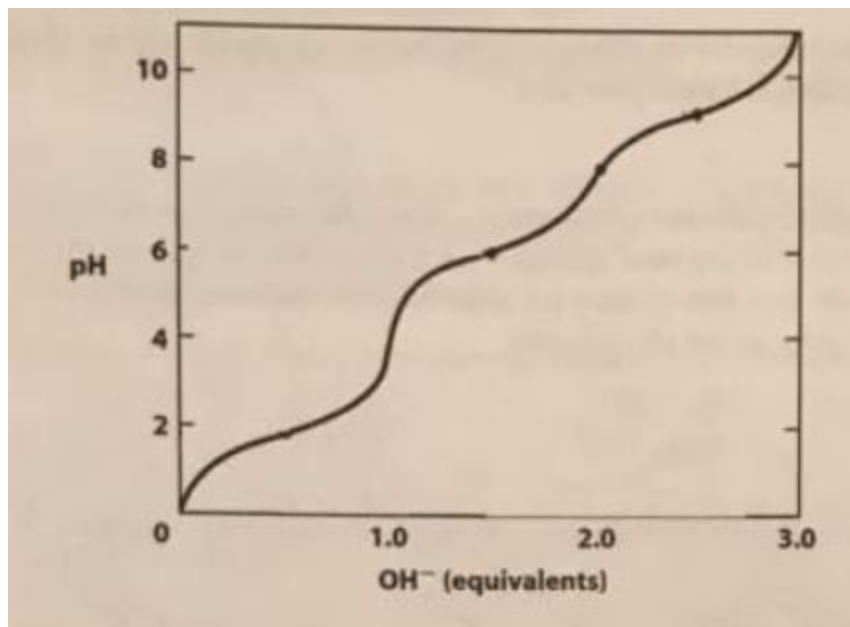
**True/False Questions (2 Marks Each):**

18. The isoelectric points for the free amino acids S and Ile will be approximately the same. T/F? Explain.
19. The bases A, G, and T were found in a nucleic acid. The nucleic acid was most likely RNA. T/F? Explain.
20. Considering only sidechain interactions between the pairs listed: Ser and Gly will interact stronger with each other than Leu and Phe. T/F? Explain.

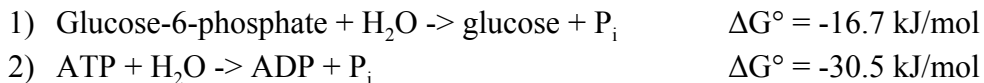
21. A mixture of the two compounds shown below would be ideal for making a buffer at pH 6. T/F? Explain.

**Short Answer Questions:**

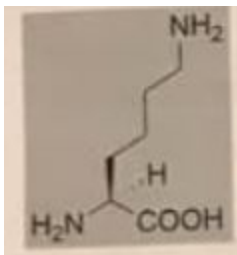
22. A titration curve for an amino acid is illustrated below. Which amino acid is it most likely to be (name, 3 letter code, & one letter code)? What is the side chain  $pK_a$  value for this amino acid? (4 marks)



23. The hexokinase enzyme catalyses the phosphorylation of glucose to glucose-6-phosphate. For the reaction between glucose and ATP, forming glucose-6-phosphate and ADP, calculate  $\Delta G^\circ$  and the equilibrium constant  $K_{eq}$  at 25°C based on the given values for the following reactions (4 marks):



24. The structure of an amino acid in its neutral state is given below.



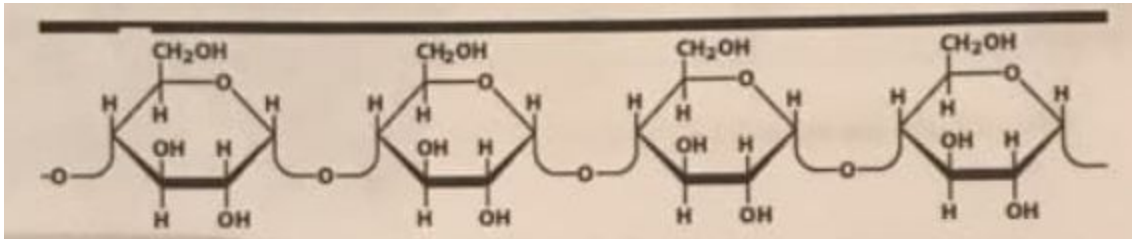
- Give the name, three letter code and one letter code for the amino acid. (2 marks)
- List the  $pK_a$  values for the different ionisable groups in the amino acid. (2 marks)
- Draw the different charged states of the amino acid that would be present during a complete titration with strong base, starting at pH 1 and continuing until the titration is complete. Order the ionization states in the order they would appear in the titration, starting at the lowest pH. (7 marks)

25. For the pentapeptide Glu-Met-Arg-Thr-Gly,

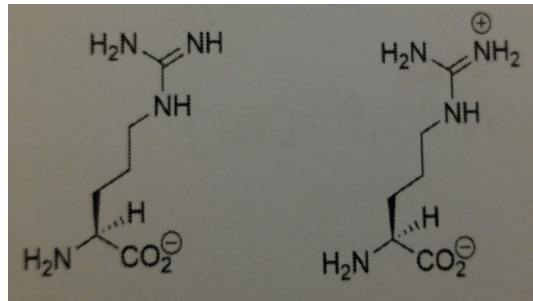
- Name the carboxyl terminal residue. (1 mark)
- Name the amino terminal residue. (1 mark)
- Which groups will be charged at pH 1 (including the termini if relevant)? (2 marks)

26. Part of a polysaccharide is shown below.

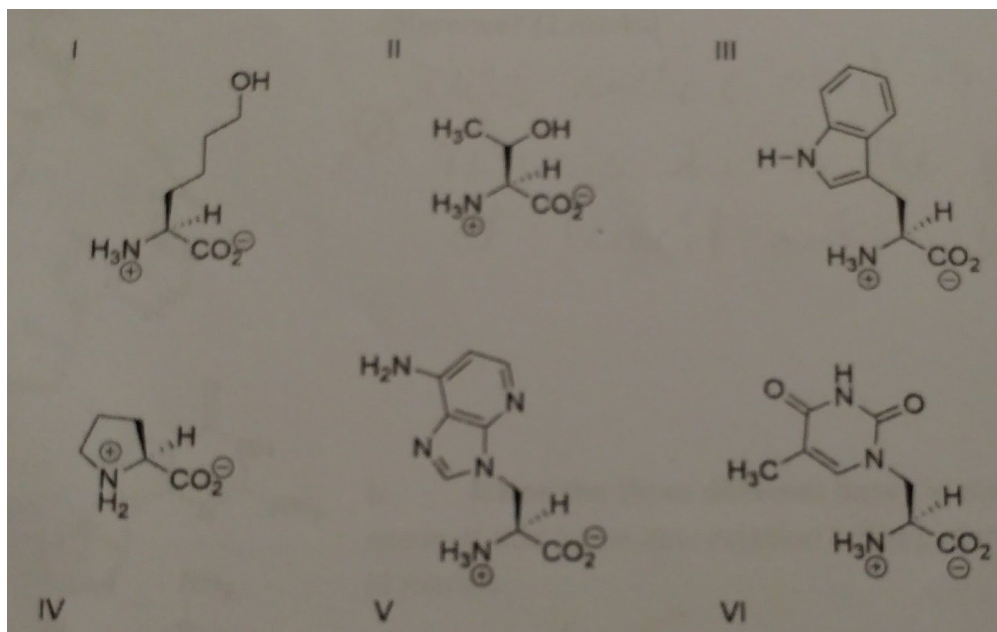
- What kind of bond is found between the monomers and what would you name it?
- Given the nature of the bond named in (a), is the polysaccharide likely to be digestible by humans? Why/Why not? (2 marks)



27. During a titration with strong base, at which pH would the concentration of the two compounds shown below be equal? (1 mark)

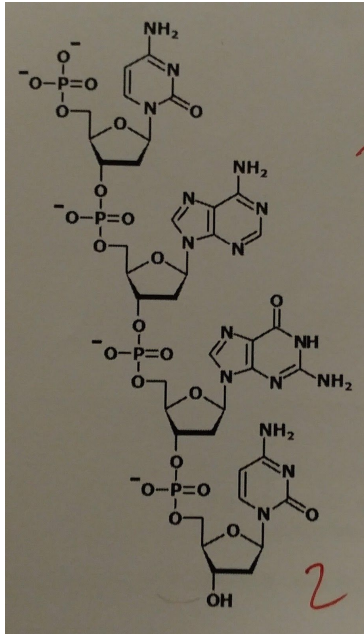


28. Among the six structures shown below, three are proteogenic amino acids. Fill in the table with their names, three letter codes, and one letter codes. (6 marks)



<b>Compound number</b>			
<b>Name</b>			
<b>3-letter code</b>			
<b>1-letter code</b>			

29. The charged form of the imidazole ring on the side chain of histidine is believed to participate in a reaction catalyzed by an enzyme. At pH 7, what (approximate) proportion of the imidazole ring will be charged? (2 marks)
30. The structure below shows parts of a nucleic acid.



a. Is the nucleic acid DNA or RNA? How can one tell the difference? (2 marks)

b. Name the three different bases in the structure (full name or one letter abbreviation is fine), starting from the top. (3 marks)

c. Where in the figure in the 3' end? And the 5' end?

## Midterm 2

If you need the gas constant, the following value can be used:  $R = 8.316 \text{ J}/(\text{mol} \cdot \text{K})$

### Multiple Choice Questions. One correct answer per question. (1 mark each)

1. What is true for DNA?
  - a. DNA in the B-DNA form is rarely observed in cells
  - b. The two chains in the DNA double helix are identical, wherefore each can serve as a template in replication.
  - c. Due to the double helical structure, DNA is generally a very rigid molecule
  - d. Hairpin structures can form upon intrastrand base pairing
  - e. All of the above are true
2. Fatty acids
  - a. Are found in all lipid molecules
  - b. Are classified as omega-3 fatty acids if they have three double bonds
  - c. Generally only have trans double bonds
  - d. Have higher melting points the more carbon atoms they have
  - e. Most often have more than 28 carbon atoms
3. Which three amino acids all have hydrogen bond donors in their side chains at pH 7.4?
  - a. TND
  - b. RGS
  - c. WTF
  - d. YES
  - e. HKQ
4. RNA
  - a. Can have enzymatic activity
  - b. Can form complex structures even when single stranded
  - c. Of the messenger class (mRNA) can be seen as an intermediate between DNA and protein
  - d. Undergoes hydrolysis at high pH
  - e. All of the above are true
5. Which of the following statements about lipids is true?
  - a. Storage lipids are only used for energy storage
  - b. Diversity in structural lipids are caused only by the variation in head group
  - c. One of the most important types of structural lipids are made from glycerol, fatty acids and phosphate
  - d. A triacylglycerol made from three trans monounsaturated fatty acids with 18 carbon atoms will have the same melting point as the triacylglycerol made from the same fatty acids in the cis configuration
  - e. All lipids in membranes have only one polar end (the head) and one apolar end (the tail)

6. Which of the following statements about fibrous proteins is true?
- Fibrous proteins are always helical
  - Fibrous proteins tend to be water soluble due to the high occurrence of charged residues
  - Fibrous proteins sometimes form left-handed helices
  - Fibrous proteins are only synthesized by mammals
  - Serine is crucial for the correct structure of collagen to allow for tight junctions in the coiled coil
7. Which of the following statements about protein folding and denaturation is false?
- Denaturation causes irreversible loss of function for any protein with defined structure
  - The native state is constantly in equilibrium with partially folded states
  - Protein aggregates can be broken up into the individual proteins by chaperones
  - Organic solvents can denature proteins by disturbing the packing of hydrophobic core
  - The formation of hydrogen bonds is important for secondary structure formation

**“Fill in the Blank” Questions (1 mark each)**

8. How many full turns does an  $\alpha$ -helix of 23 residues make? \_\_\_\_\_
9. How many residues does it take to form an  $\alpha$ -helix which is 18 Å long? \_\_\_\_\_
10. How long is a  $\beta$ -strand made from 7 residues in a antiparallel  $\beta$ -sheet? \_\_\_\_\_
11. The helix dipole moment causes one end of an  $\alpha$ -helix to be slightly positive and the other end to be slightly negative. Which end is positive? \_\_\_\_\_
12. Name the given fatty acid using standard nomenclature ( $\Delta$ ). \_\_\_\_\_



13. Is the fatty acid shown in question 12 an  $\omega$ -3 fatty acid? \_\_\_\_\_
14. For a newly identified protein, each chain was found to have 479 residues. The molecular weight of the protein was around 53000. What is the highest level of protein structure for this protein? \_\_\_\_\_

**True/False Questions. Briefly explain your choice. (2 marks each)**

15. Having a K in position 4 in an  $\alpha$ -helix and an R in position 7 can stabilise the helix. T/F? Explain.
16. X binds to Y with an association constant of  $0.7 \mu\text{M}^{-1}$ . We would hence characterize X as a strong binder. T/F? Explain.

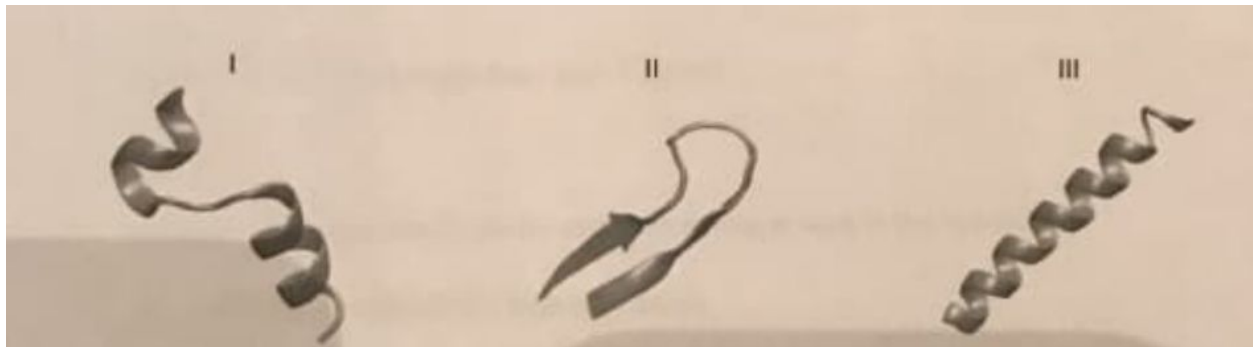
17. For a  $\beta$ -sheet to have a hydrophilic side and a hydrophobic side, every second amino acid sidechain has to be hydrophilic and the other ones hydrophobic. T/F? Explain.

**Short Answer Questions**

18. Three sections of protein structures are illustrated below (I, II, and III). For each structure, the matching sequence is found among the five sequences given (a-e). Which sequence gives rise to each of the three sections of protein structure? Fill in the label.

(6 marks)

- a. QMGLFIGASILTVLELFDY
- b. FFTLIHSSYTANLAAFLTVERM
- c. SYYHNCYVTCSSNTN
- d. AIYHFGTPGVGLRPYVS
- e. REGGHDKVLKEKRNHPE



Protein	Sequence
I	
II	
III	

19. Energy required for biochemical reactions is often acquired from hydrolysis of a particular nucleotide. Draw this nucleotide as it appears before hydrolysis. (2 marks)

20. Draw the structure of the tripeptide WAQ at neutral pH, using correct stereochemistry. For the central residue, show on your drawing where the phi and psi angles are. (6 marks)

21. (9 marks)      DNA has two base pairs - which?

How many hydrogen bonds are formed upon pairing in each of the two pairs?

Draw the base pairing for the pair that forms the most hydrogen bonds. Use nucleotide structures for your illustration

22. Two amino acid residues are rarely found in  $\alpha$  helices. One of them is known as a “helix-breaker”, the other one is highly flexible. Give the one letter code for these two residues and draw their structures with correct stereochemistry and protonation states at neutral pH. (3 marks)

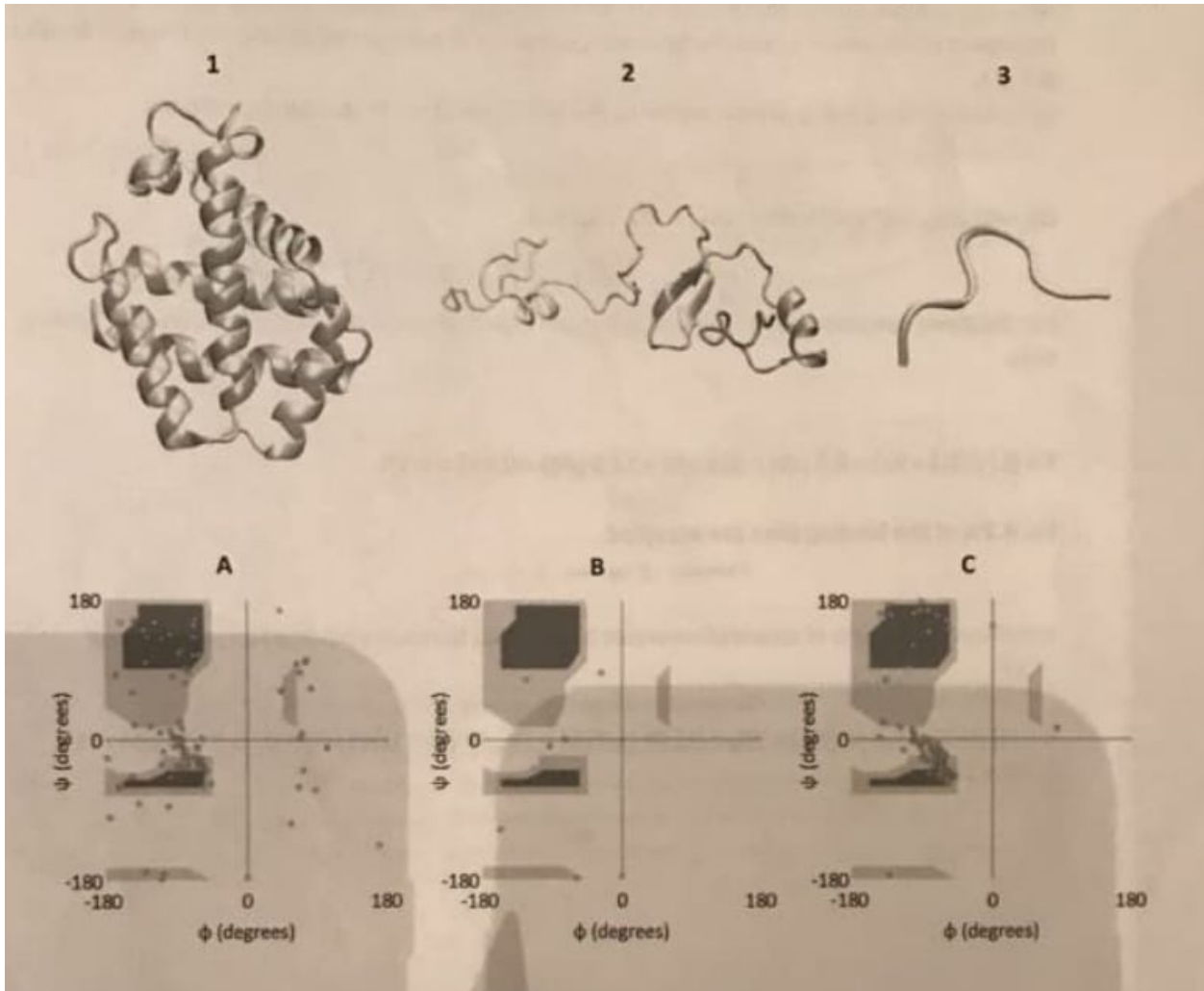
23. Enkephalins are pentapeptides which interact with opioid receptors. An enkephalin was digested with chymotrypsin, which gave three fragments for which the amino acid composition was as follows

- i. L
- ii. Y
- iii. F, G, G

The order of the fragments, as well as the order of the individual amino acids, is unknown. However, the sidechain of the N-terminal residue is known to be relatively large. Determine the sequence of the given enkephalin, and note down the sequence with the full names for the amino acids. Determine the charge of this enkephalin at pH 1. (6 marks)

24. One amino acid sidechain is capable of forming covalent bonds which are important for the stability of the tertiary and quaternary structure of some proteins. Give the name and one letter code for this amino acid and draw the structure with correct stereochemistry at neutral pH. Then, draw two such residues, showing the covalent bond. (3 marks)

25. Match the structures given below with their Ramachandran plots by filling in the table.  
(6 marks)



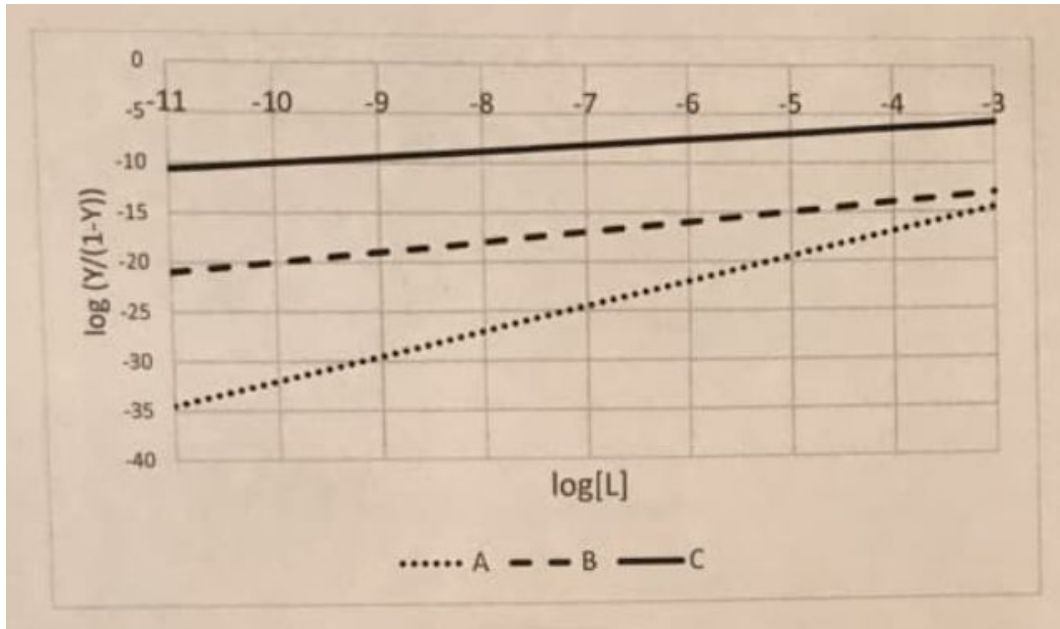
Protein	Ramachandran Plot
1	
2	
3	

26. (6 marks) The NMDA receptor in the brain can be blocked by e.g. memantine and amantadine with dissociation constants of  $17.9 \mu\text{M}$  and  $694 \mu\text{M}$ , respectively. Memantine is used in the treatment of Alzheimer's, and the brain concentration of memantine during treatment is around  $0.8 \mu\text{M}$ . Calculate  $\Delta G$  for binding of memantine to the NMDA receptor at standard concentrations.

For the given concentration memantine in the brain, calculate the fraction of occupied binding sites.

Which concentration of amantadine would be required to reach a binding site saturation of 75%?

27. Using the plot illustrated below, determine whether the three proteins (A, B, and C) show cooperativity when binding with ligand L. (3 marks)



Protein	Positive cooperativity	Negative cooperativity	No cooperativity
A			
B			
C			

### Midterm 3

If you need to use the gas constant, the following value can be used:  $R = 8.314 \text{ J}/(\text{mol} \cdot \text{K})$

#### Multiple Choice Questions. One correct answer per question. (1 mark each)

- Which of the following statements are true for enzyme catalysis?
  - Enzymes increase reaction rates by binding the product very tightly, favouring the product state over the reactants.
  - Enzymes increase reaction rates by lowering the activation barrier through stabilizing the transition state
  - Negatively charged metal ions can be crucial for metal ion catalysis
  - Enzymes can change an overall reaction from being nonspontaneous to being spontaneous
  - Enzymes are catalysts and hence never form covalent bonds to the reactants
- The entropy of a reaction refers to
  - The energy of the transition state
  - The effect of temperature on the rate of the reaction
  - The tendency of the system to move towards maximal randomness
  - The difference in energy between reactants and products
  - The heat given off by the reaction
- Hemoglobin transports both  $\text{O}_2$ ,  $\text{H}^+$ , and  $\text{CO}_2$ . Which of the following statements regarding hemoglobin transport function is false?
  - Upon reaction between  $\text{CO}_2$  and water,  $\text{H}^+$  is released. The increase in  $[\text{H}^+]$  contributes to a reduction in  $\text{O}_2$  affinity
  - $\text{O}_2$  binding causes a flattening of the heme group which is converted to larger conformational changes at the subunit interfaces
  - $\text{H}^+$  binding to ionisable sidechains can stabilize hemoglobin in the T-state
  - $\text{CO}_2$  binds covalently to the N-terminal and stabilizes the T-state by causing a change in electrostatic interactions
  - $\text{O}_2$  binds cooperatively; i.e. binding of  $\text{O}_2$  to one subunit increases  $K_D$  for  $\text{O}_2$  binding to the other subunits
- Which statement concerning irreversible inhibition is false?
  - Irreversible inhibition is a mix between competitive and uncompetitive inhibition
  - Transition state analogs sometimes bind tightly enough to be considered irreversible inhibitors
  - Suicide inhibitors react with the enzyme and form a covalent bond to the enzyme
  - Penicillin is an example of an irreversible inhibitor
  - Irreversible inhibition can destroy catalytically important functional groups

5. Myoglobin is great for storing oxygen, and the  $p_{50}$  is 0.26 kPa. The minimal partial pressure required for maintaining consciousness is around 2.65 kPa. What is the fractional occupancy of  $O_2$  sites in myoglobin under these conditions?
  - a. 0.23
  - b. 0.41
  - c. 0.58
  - d. 0.74
  - e. 0.91
6. What is  $[S]/K_m$  when the initial velocity of an enzyme-catalyzed reaction is 80% of  $V_{max}$ ?
  - a. 0.25
  - b. 0.8
  - c. 2.5
  - d. 4.0
  - e. 5.2
7. 2,3-bisphosphoglycerate (BPG) is an allosteric modulator for hemoglobin. Changes in the BPG concentration contributes to altitude adaption (where  $pO_2$  is reduced). What is true for this modulation?
  - a. BPG stabilizes the R state, increasing the  $O_2$  affinity, hence enabling better transport of  $O_2$  to tissue at high altitude
  - b. BPG binds to the heme group and reduced  $O_2$  binding by competing for the binding site
  - c. BPG stabilizes the low-affinity T state and enables a more efficient  $O_2$  transport to tissue
  - d. The Bohr Effect explains why  $O_2$  release in tissue is more efficient at higher [BPG]
  - e. At higher [BPG], more  $O_2$  binds to heme in the lungs and more  $O_2$  is released in tissue, which increases the amount of  $O_2$  delivered to tissue

**True/False Questions. Give a brief explanation. (2 marks each)**

8. For a standard enzyme reaction scheme,  $K_m$  equals the dissociation constant for the ES complex when  $k_{-1}$  is approximately equal to  $k_2$ . True/False? Briefly explain why/why not.
  
9. In the sequential model for cooperativity, all subunits undergo a conformational change simultaneously. True/False? Briefly explain why/why not.

10. The Fab fragments of immunoglobulins recognize antigens, and the binding affinity is strengthened through induced fit. True/False? Briefly explain why/why not
  
11. In uncompetitive inhibition,  $K_m$  increases as an inhibitor is added. True/False? Briefly explain why/why not
  
12. The HIV protease is used by the virus to form the carbohydrate molecules to be displayed at the surface of the virus. True/False? Briefly explain why/why not.
  
13. A stimulatory allosteric enzyme modulator can cause the sigmoidal dependence of  $V_0$  on  $[S]$  to become almost hyperbolic. True/False? Briefly explain why/why not
  
14. The majority of enzyme-catalyzed reactions involves two substrates. For an enzyme to catalyze a reaction involving two molecules, the two molecules must be bound to the enzyme at the same time. True/False? Briefly explain why/why not.
  
15. Enzymes can be covalently modified by being linked to other proteins for regulatory purposes. True/False? Briefly explain why/why not.

### Short Answer Questions

16. For enzyme regulation, what is the most common type of reversible covalent modification? (1 mark)
17. Molecular recognition is dependent on the so-called weak interactions. For each of the mentioned types of interactions in the table below, indicate all the characteristics (a-h) that apply to that interaction (you can list a given characteristic for several interaction types). (3 marks)
- Require nonpolar species
  - Involve charged species only
  - Require polar or charged species
  - Involve either O and H or N and H atoms
  - Involve nonspecific atoms
  - Are also called electrostatic interactions
  - Only exist in water
  - Are weakened in water

Interaction	Characteristics
Salt bridges	
Hydrophobic interactions	
Van der Waal's interactions	
Hydrogen bonds	

18. Sometimes it is said for protein-ligand interactions that some types of interactions are mostly important for specificity, while other types of interactions are those which provide the “glue”, i.e. increase the binding affinity. (4 marks)
- Based on the table in question 17, which types of interactions would be most important for specificity?

And which would be most important for ensuring a strong binding?

19. Acetylcholinesterase, which cleaves acetylcholine, has a turnover number of  $1.4 \times 10^4 \text{ s}^{-1}$ . (3 marks)  
What does this number tell us?

Suppose the concentration of acetylcholinesterase is 0.3 nM. What would  $V_{\text{max}}$  be in the given situation?

20. For two substrates of the enzyme fumarase, the turnover numbers and the Michaelis constants differ as listed: fumarate (turnover number:  $8 \times 10^2 \text{ s}^{-1}$ ; Michaelis constant:  $5 \times 10^{-6} \text{ M}$ ) and malate (turnover number:  $9 \times 10^2 \text{ s}^{-1}$ ; Michaelis constant:  $2.5 \times 10^{-5} \text{ M}$ ). For which substrate does the enzyme display the highest catalytic efficiency? (2 marks)

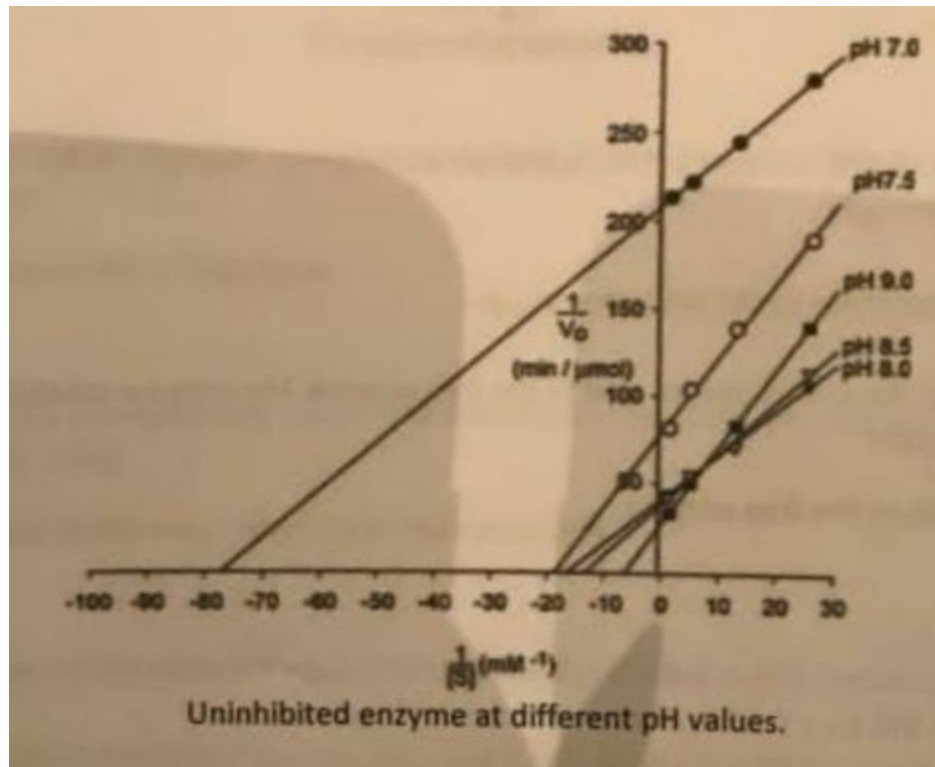
21. (10 marks) Cysteine proteases catalyze the cleavage of peptide bonds. Three residues form the catalytic triad in the active site of the enzyme. Draw these three residues (using correct stereochemistry and the standard protonation state at pH 7).

Briefly state the main role of each of these residues for the catalysis reaction.

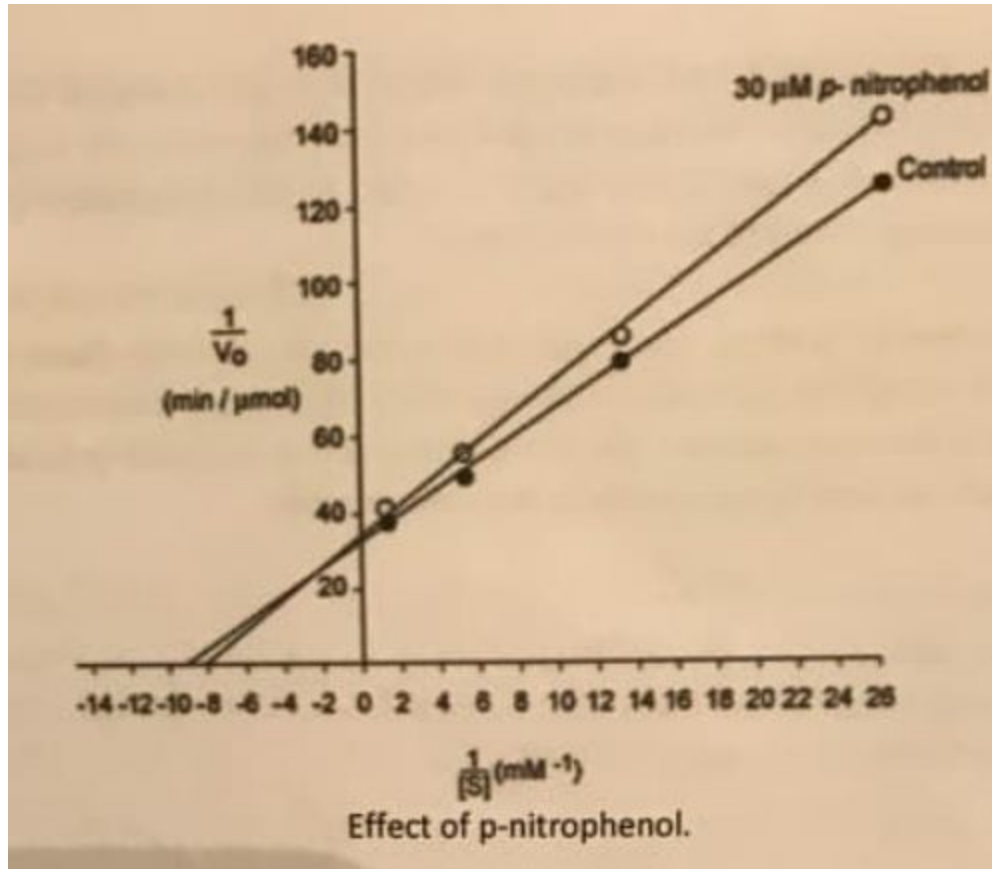
List the two most important mechanisms of catalysis expected for a cysteine protease.

22. (2 marks) For a given protein, tests suggest a molecular weight of around 67,000. However, after treatment with a chemical that cleaves disulfide bonds, the molecular weight is a bit less than 34,000. The protein is known to bind to ligand L. Based on the information given above, could L possibly bind cooperatively to the native protein?

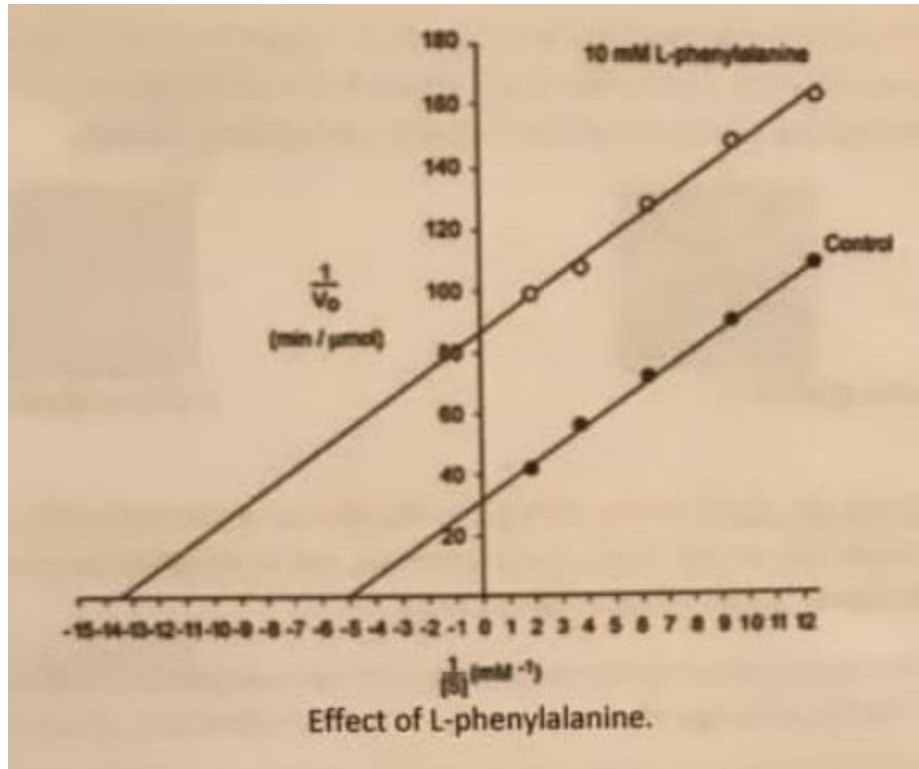
23. The following questions (a-k) concern the hydrolysis of p-nitrophenyl phosphate, catalyzed by the enzyme alkaline phosphatase. (Data from Dean, *Biochem. Mol. Biol. Edu.* (2002)). Use the plots provided to answer the questions. (14 marks)



- At which pH value is the highest possible reaction rate observed?
- What is the approximate  $V_{\max}$  at this pH value?
- What is the approximate  $K_m$  value?



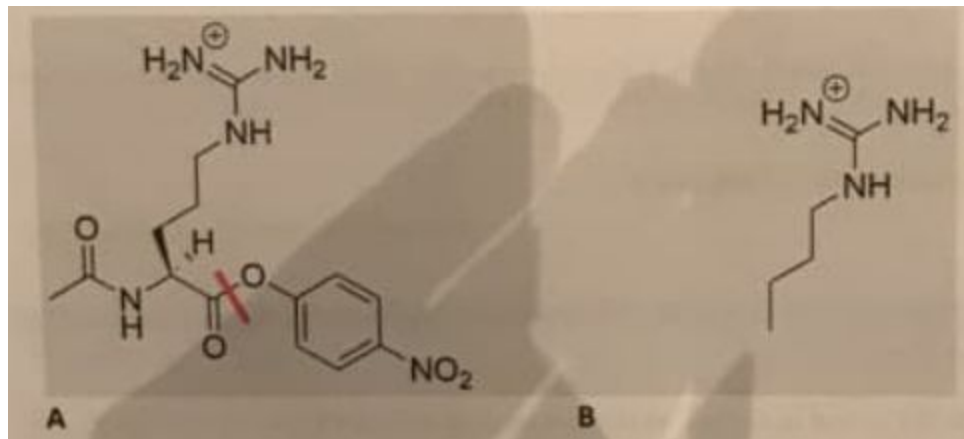
- d. One of the products, p-nitrophenol, inhibits the reaction. What type of inhibition is occurring?
- e. Does the p-nitrophenol bind to the free enzyme, the enzyme-substrate complex only, or to both?
- f. Can this type of inhibition be overcome? If yes, then how?



- g. L-phenylalanine also inhibits the reaction. What type of inhibition does L-phenylalanine cause?
- h. Does L-phenylalanine bind to the free enzyme only, the enzyme-substrate complex only, or to both?
- i. How are the apparent values for  $V_{\max}$  and  $K_m$  affected by the addition of L-phenylalanine?
- j. Given that 10 mM L-phenylalanine was used for the experiments, calculate the approximate inhibition constant ( $K_i$  or  $K_i'$ ).

- k. The D-isomer of phenylalanine is, however, not an inhibitor. Draw the D- and L-isomers of phenylalanine (remember to state which is D and which is L). Briefly explain how L-phenylalanine can be an inhibitor when D-phenylalanine is not.

24. Compound **A** is a good substrate for the trypsin protease. Compound **B** is an effective inhibitor of trypsin.  $\Delta G^\circ$  for the cleavage of compound **A** is  $-20.92$  kJ/mol at  $25^\circ\text{C}$ . (8 marks)



- Which amino acid forms part of compound **A**? Illustrate clearly on the drawing above where trypsin would cleave. From which other amino acid can one design a similar substrate for trypsin?
- Explain briefly why compound **B** is an inhibitor for trypsin, and whether the inhibition will be competitive or uncompetitive.
- Calculate the equilibrium constant,  $K_{\text{eq}}$ , for the cleavage of **A** at  $25^\circ\text{C}$ . Once at equilibrium, will there be more reactant or more product?