**This exam consists of 4 pages and a total of 100 points. Allot 1 min per 2 points. Use the space provided or the back of the preceding page.**

1. (5 pts) Please do one of the following two choices

**Choice A**: A lithium atom has an electronic configuration of 1s2 and 2s1, i.e. two electrons in the 1s orbital and one in the 2s orbital, as shown on the right. What is the most likely ion that lithium will form? Why?

**Choice B:** What is the geometric difference between sp2 hybrid orbitals and sp3 hybrid orbitals?

2. (4 pts) Why is water a polar molecule?

3. (6 pts) The structure of a drug is shown on the right.

i) Add any missing hydrogen atoms to the carbon atom indicated by the box. *Justify your answer.*

ii) Does this drug have a chiral center? If so, where is it located? Why is it a chiral center?

4. (3 pts) In what way might a chiral center affect the activity of a drug?

5. (20 pts total, 12 this page) *(****Part iv of this question is on the next page****.)*

i) (6 pts) State the general rule for hydrogen bonds, that is, what are the properties of the three atoms involved in a hydrogen bond.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **H**2.1 |  |  |  |  |  |  |
| **Li**1.0 | **Be**1.5 | **B**2.0 | **C**2.5 | **N**3.0 | **O**3.5 | **F**4.0 |

ii) (4 pts) Identify all hydrogen bond donors (***d***) and acceptors (***a***) on the drug shown in question 3, add “a” or “d” to the above diagram, as appropriate. A table of electronegativities is on the right.

iii) (2 pt) Circle the ionizable group on the drug and state its name.

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iv) Please do choice A or B ( 8 pts)

**Choice A:** The ionizable group on this drug has a pKa of 3.0. Given that the pH of the small intestine is 8.0, how likely is it for this drug to be able to cross the cell membrane in this environment? *Justify your answer.*

**Choice B:** Compare the solubility of the drug at pH 1.0 and pH 5.0. At which pH would the solubility be higher? Why?

6. (10 pts) The drug in question 3 binds to its target protein with an enthalpy of -5 kJ/mol and an entropy of +5 J/mol-deg, giving an overall standard energy (ΔGo=ΔHo-TΔSo) change of -6.5 kJ/mol at 300K.

i) Based on the standard energy, what is favored – the unbound drug or the bound drug? Justify your answer. (4pts).

ii) Explain, with reference to functional groups on the drug, why the entropy change due to binding is positive. You may find it useful to look at the bonus question at the end of the exam to help you answer this one. (6 pts)

7. (12 pts) Pick any two amino acids that are **different** and:

i) Draw the resultant dipeptide that would be formed after the condensation reaction to form the peptide bond (4 pts).

ii) Identify the peptide bond (1 pt).

iii) Circle the mainchain atoms (1 pt).

iv) Identify all hydrogen bond donors and acceptors on the **mainchain** atoms (2 pts).

v) Write the sequence of your peptide (2 pts).

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8. (10 pts) Give **one** example of a secondary structure and:

i) State the force or interaction that stabilizes it (4 pts).

ii) Sketch the structure and indicate on your sketch the location of the stabilizing forces you stated in *part i*, and the location of the sidechains (6 pts).

9. (10 pts) Cartoon structures of four different proteins are shown below, the core, or interior of the protein is in the center in all four cases, but only labeled in the first case. In these diagrams:

 ⃝ = polar or charged amino acids • = non-polar amino acids

Given what you know about the location of amino acids in proteins, **and** the forces that stabilize proteins, explain why C is most likely to be a folded protein while the other three are unlikely. **Note**: The order of polar and non-polar amino acids in C and D are identical. *Justify your answer.*

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10. (4 pts) What are the properties of an active site of an enzyme?

11. (10 pts) Briefly describe why enzymes increase the rate of reaction.

12. (6 pts) Compare and contrast a competitive inhibitor to an allosteric inhibitor. Compare and contrast means to give similarities and differences between the two.

**Bonus (5 pts)**: A drug bound to its target protein is shown on the right. The drug is in bold. The ability of this drug to cross cell membranes depends on pH. How could you modify the drug to remove this dependence, but still allow binding to its target? [Hint: What functional group on the **drug** would you replace, and what would you replace it with?]

/20 + 5 (bonus)