

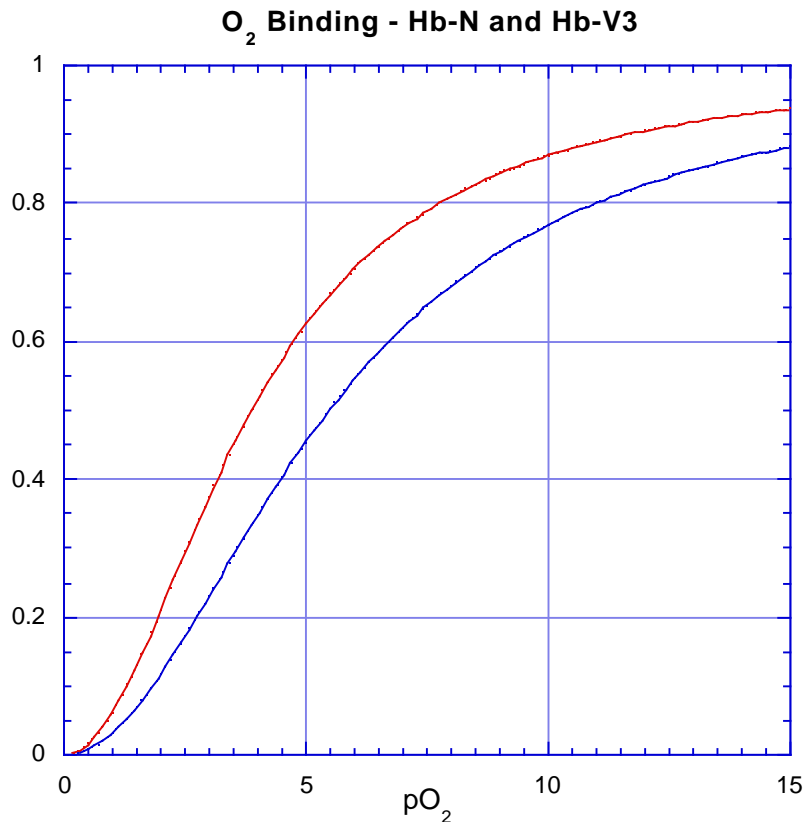
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Exam II - Chemistry 341 - November 10 2000 - 100 points total - 20 bonus points

**Look over the whole exam and work on what you feel more comfortable FIRST!
Show all your calculations if you want to receive partial credit.**

Be clear and concise.

- 1) (20 points) As part of your continuing studies of hemoglobin, you found a new variant, Hb-V3. After you performed BPG affinity studies, you found that variant Hb-V3 binds BPG better than native hemoglobin (Hb-N).
- Based on the structure of BPG and its binding site in Hb-N, what type of amino acid residues may be present in Hb-V3 in larger numbers, and what will be their most likely location in the hemoglobin tetramer? You don't need to pinpoint exactly their location in the chains, just their relative position in the tetramer.
 - You have gathered oxygen binding data for Hb-N and Hb-V3, shown in the plots presented below. In what is now becoming a very disturbing habit of yours, you lost the labels for the graphs again. Which plot corresponds to Hb-N, and which one to Hb-V3? Justify your answer clearly.



Use the space on the following page to write your answers

Name: _____

Answer page - Question (1)

Name: _____

- 2) (20 points) Keep thinking about hemoglobin for now. The affinity for O_2 of hemoglobin in the R-state is different to the affinity for O_2 of T-state.
- i) Which state has higher affinity for O_2 , and what intra-molecular forces are responsible for this difference in affinity?
 - ii) Considering what you just wrote, explain what will happen to the O_2 affinity of hemoglobin if the polarity of the solution was lowered by addition of a non-polar organic solvent? Do not consider denaturation of hemoglobin by addition of the organic solvent.

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- 3) (20 points) You have found a peptide related to Alzheimer disease, and started work on the elucidation of its primary structure. The complete peptide was too long for a single round of Edman degradation, so you had to chop it up in pieces first. For such purpose, you used an enzymatic degradation with chymotrypsin and a cyanogen bromide digestion. These are the fragments you obtained from the two digestions:

Chymotrypsin digestion

H₂N-PLSATWQI-COOH
H₂N-HEQADMCVIAGF-COOH
H₂N-ASDTLIPF-COOH
H₂N-GQKTKEMPLIAGAQF-COOH

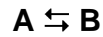
CNBr digestion

H₂N-PLIAGAQFHEQADM-COOH
H₂N-ASDTLIPFGQKTKEM-COOH
H₂N-CVIAGFPLSATWQI-COOH

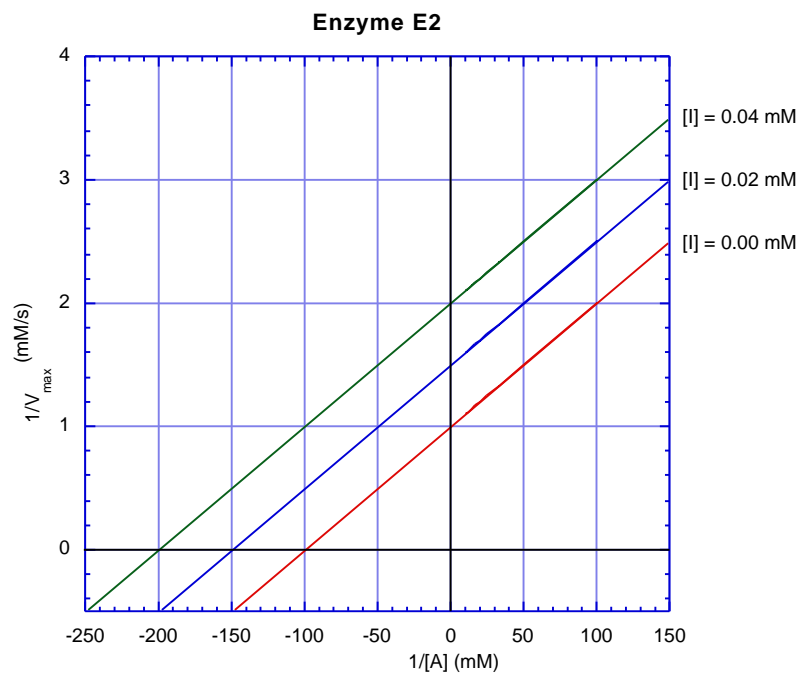
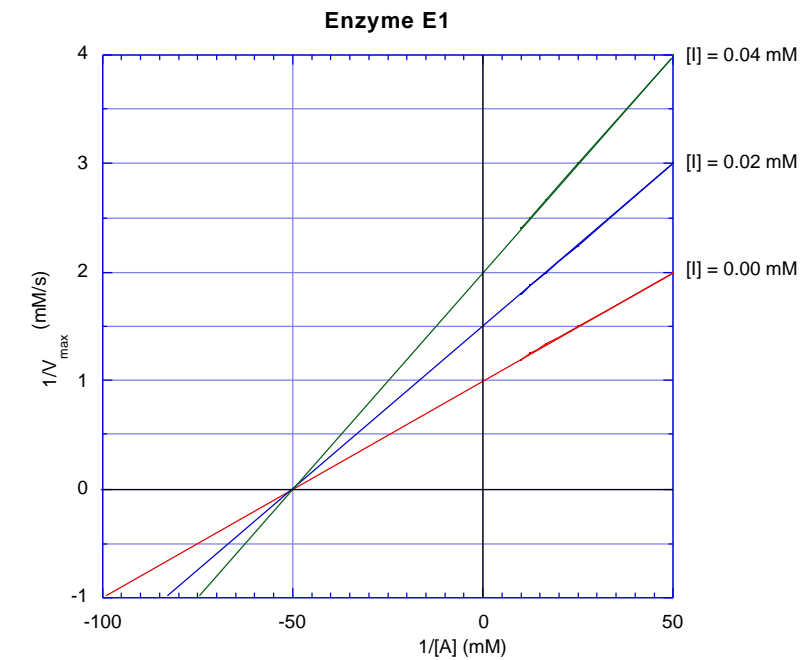
You also know that **Alanine** is the N-terminal amino acid and **Isoleucine** the C-terminal amino acid. Using these data, determine the primary structure of the peptide. Explain your reasoning clearly.

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- 5) (20 points) You found two enzymes, **E1** and **E2**, that catalyze the by now infamous reaction:



As usual, both enzymes are inhibited by the same inhibitor, **I**. You gathered kinetic data for the two enzymes in the presence and in the absence of inhibitor, and plotted the results as the double-reciprocal plots shown below:

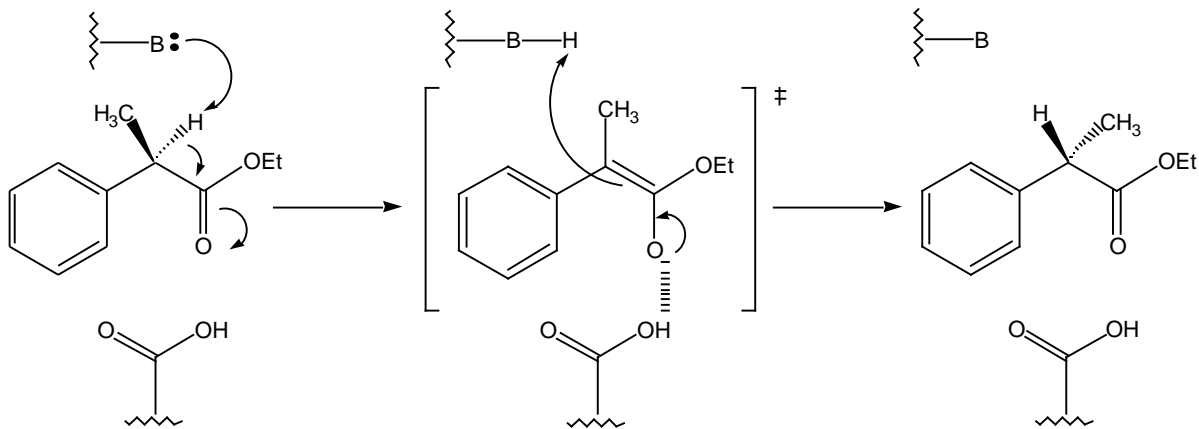


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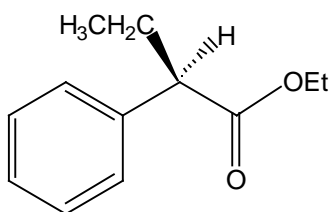
- i) What type of inhibition does inhibitor **I** has on **E1** and **E2**? Justify your answer.
- ii) Calculate the values of V_{\max} and K_M for both enzymes in the absence of inhibitor. Which enzyme is faster? Which enzyme has higher affinity for substrate **A**?
- iii) Will one enzyme be faster than the other at a certain concentration of inhibitor **I**, or will their V_{\max} be affected equally? Hint: Calculate the V_{\max} for each enzyme at different $[I]$ and compare the values obtained.

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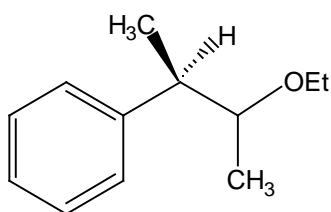
6) Bonus question (20 points). A certain racemase (i.e., an enzyme that converts R-stereocenter into an S-stereocenter) has the following reaction mechanism:



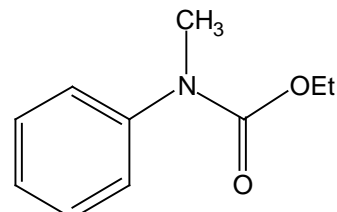
Which of the following molecules will be the transition state analog? Justify your answer in terms of interactions between the enzyme and the inhibitor.



A



B



C

Hint: Try to recognize if the electronic configuration of the transition state is mimicked by any of the molecules...