 Name Key

Biochemistry 5700
Fall, 1999
Exam 1

INSTRUCTIONS:

Do not begin until 10:30 AM. The in-class portion of the exam must be turned in by 11:20 AM. The in-class portion should have 8 questions and 5 pages. **ANSWER ANY 7 OF 8 OF THE QUESTIONS- Mark "DO NOT GRADE" on the one question you choose to skip. DO NOT answer all eight questions-if you do, cross the one out which you don't want graded.** Each graded question is worth 10 points. The take home portion contains two questions, worth a total of 30 points. The take home portion is due beginning of class Wednesday. Good Luck!!

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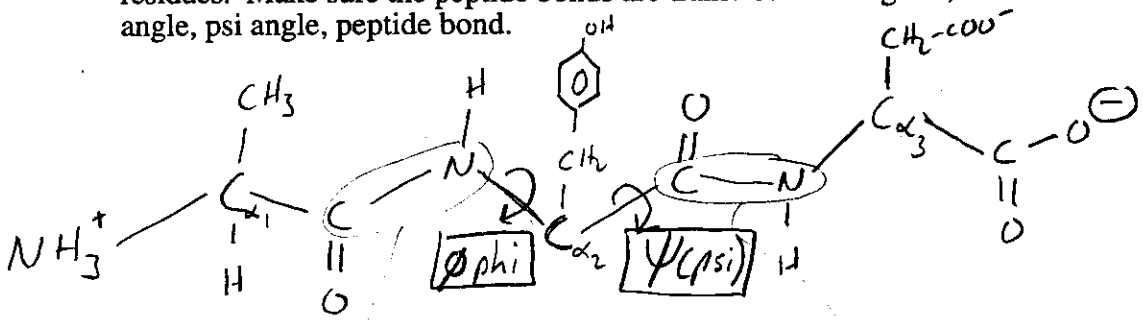
(1) Draw and name your favorite tripeptide at pH 7.0 consisting of three different amino acid residues. Make sure the peptide bonds are trans. On the diagram, label the bonds that define: phi angle, psi angle, peptide bond.



Ala - Tyr - asp

peptide

peptide

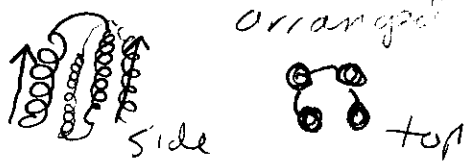
("Ala" & "gly" were the hands down class favorites. I wonder why...)

(2) Briefly explain the unique structural features of the following motifs. What are the orientations of adjacent elements (i.e. parallel and/or antiparallel). Feel free to use pictures to illust

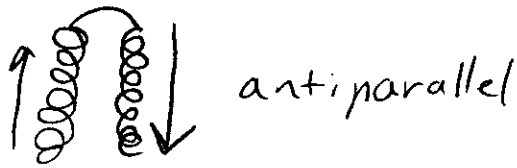
(a) four helix bundle

2 pts each

Four α-helices connected by 3 peptide loops. Adjacent α-helices are anti ||. 4 helices are arranged about a central core



(b) helix-turn-helix



antiparallel

(c) alpha-beta barrel

Core of 8 ~11 β strands arranged close together, like staves of a barrel. Connected by α-helice on outside of barrel:

etc.

(d) globin fold

a bundle of several α helices in anti || Orientation, giving a globular protein eg myoglob

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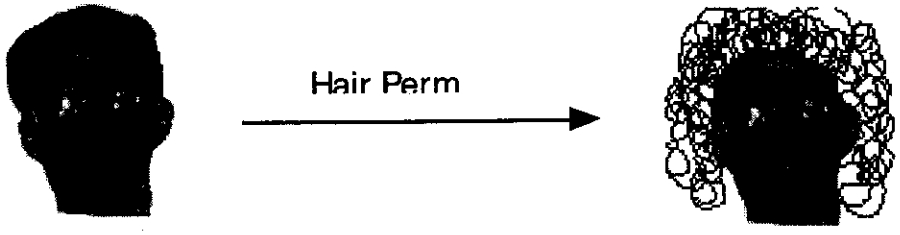
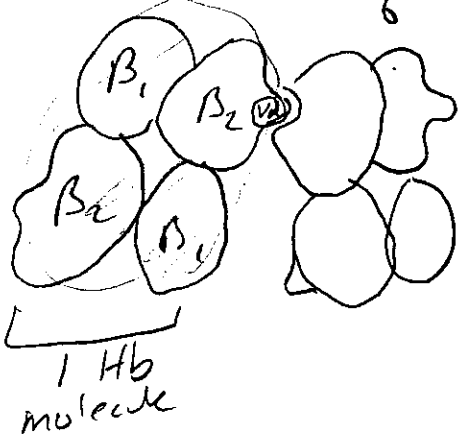
(3) The following pictures of Dr. Ensign are before and after he had his hair "permed". Explain the biochemical/molecular basis for this amazing transformation.



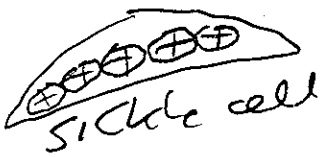
The α-keratin fibrous strands that are the main component of hair are cross-linked by disulfide bonds between adjacent cysteines on different strands. During a hair perm, these disulfides are reduced by a thiol-reducing agent to the free cysteines; then are then reoxidized to new disulfides which result in curly, wavy hair.

(4) Sickle cell anemia results from a change in a single amino acid residue in one of the polypeptide chains (glu to val). Explain the consequences of this change and how it gives rise to this disorder.

A surface glu → val change results in a hydrophobic exposed surface portion that can interact with a hydrophobic pocket on another subunit of a neighboring Hb molecule:



The Hb molecules then aggregate in chains within the cell, causing the cell to deform & not transport thru small blood vessels efficiently.



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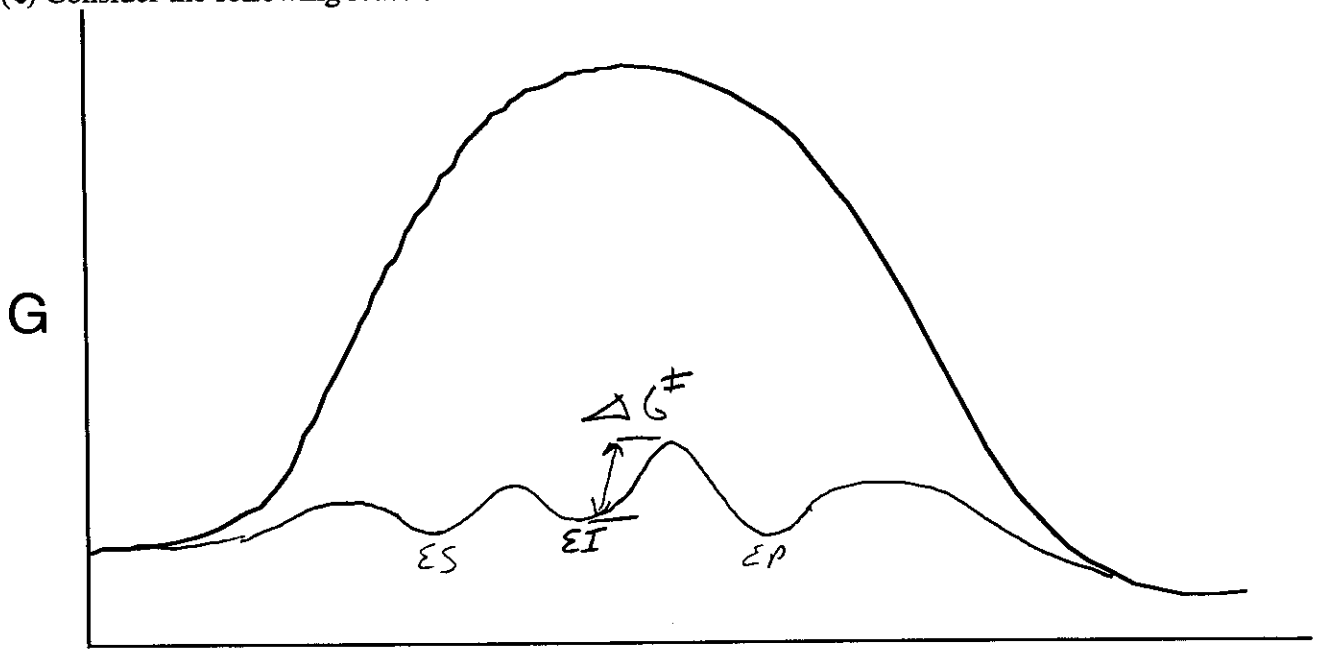
(4) Consider the following reaction coordinate:



(a) What is the sign of ΔG° for this reaction? negative

(b) Is K_{eq} for this reaction greater than one or less than one?

(c) Draw a new reaction pathway for this transformation on the above diagram that represents an enzyme-catalyzed reaction with the sequence: Label the positions of the intermediates

$$E + S \rightleftharpoons ES \rightleftharpoons EI \rightleftharpoons EP \rightleftharpoons E + P$$

(d) Indicate where $\Delta G^{\ddagger}$ is found on your new pathway Can differ - depends on which hump is biggest

6

(5) Explain the biochemical/molecular and physiological consequences of a diet deficient in vitamin C.

The three strands of the collagen triple helix are stabilized by H-bonding derived from a modified form of proline: 4-OH-Pro. The enzyme that makes OH-Proline uses Vitamin C as cofactor. When vitamin C is deficient, the triple helical strands do not form properly, resulting in skin lesions, poor wound healing, etc.

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(7) Which state of hemoglobin, [R (oxy) or T(deoxy)] is most stabilized by the following:

(a) higher 2,3-BPG T

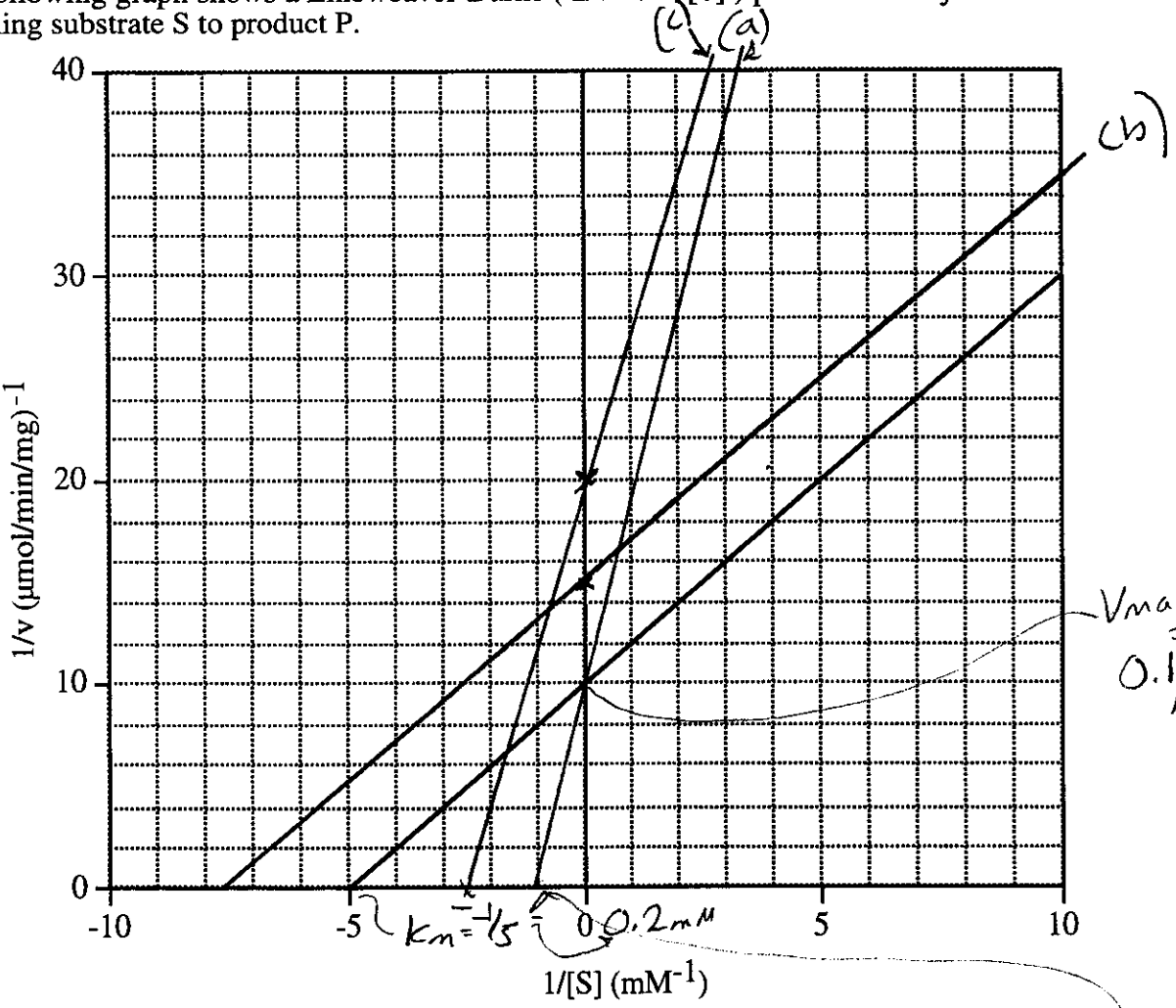
(b) lower $[CO_2]$ R

(c) lower $[H^+]$ R

(d) salt bridges T

(e) O_2 binding R
↳ to 1st of 4 subunits

8 (8) The following graph shows a Lineweaver-Burke (**1/v** vs. **1/[S]**) plot for an enzymatic reaction transforming substrate S to product P.



(a) Draw and label a line on the above graph representing the effect of a competitive inhibitor present at a concentration that would increase the apparent K_m by 5-fold. 0.2 → 1; $-1/1 = -1$

(b) Draw and label a line on the above graph representing the effect of an uncompetitive inhibitor present at a concentration that would decrease the apparent V_{max} by 1.5-fold. 0.1/1.5 = 0.67; 1/0.67 = 1.5

(c) Draw and label a line on the above graph representing the effect of a mixed (NC) inhibitor present at a concentration that would decrease the apparent V_{max} by 2-fold while increasing the apparent Km by 2-fold.

↳ new V_{max} = 0.05; 1/0.05 = 20

new K_m = 0.4 mM; $-1/0.4 = 2.5$

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Take home portion of Exam 1: You may consult any reference texts you like when working this portion. You are to work the problems individually- do not discuss with fellow students, faculty, etc. Turn in your solutions to me at beginning of class Wednesday.

(1) An enzyme-catalyzed reaction produces 0.04 mol H^+ / L in 10 min.

(a) 5 pts. If the reaction is carried out in pure water in the absence of a buffer, what would be the pH of the reaction mixture after 5 min, assuming the reaction is linear with time?

(b) 10 pts. If the reaction is carried out in 0.100 M Tris buffer ($pK_a = 8.1$) starting at pH 8.3, what would be the pH after 5 minutes?

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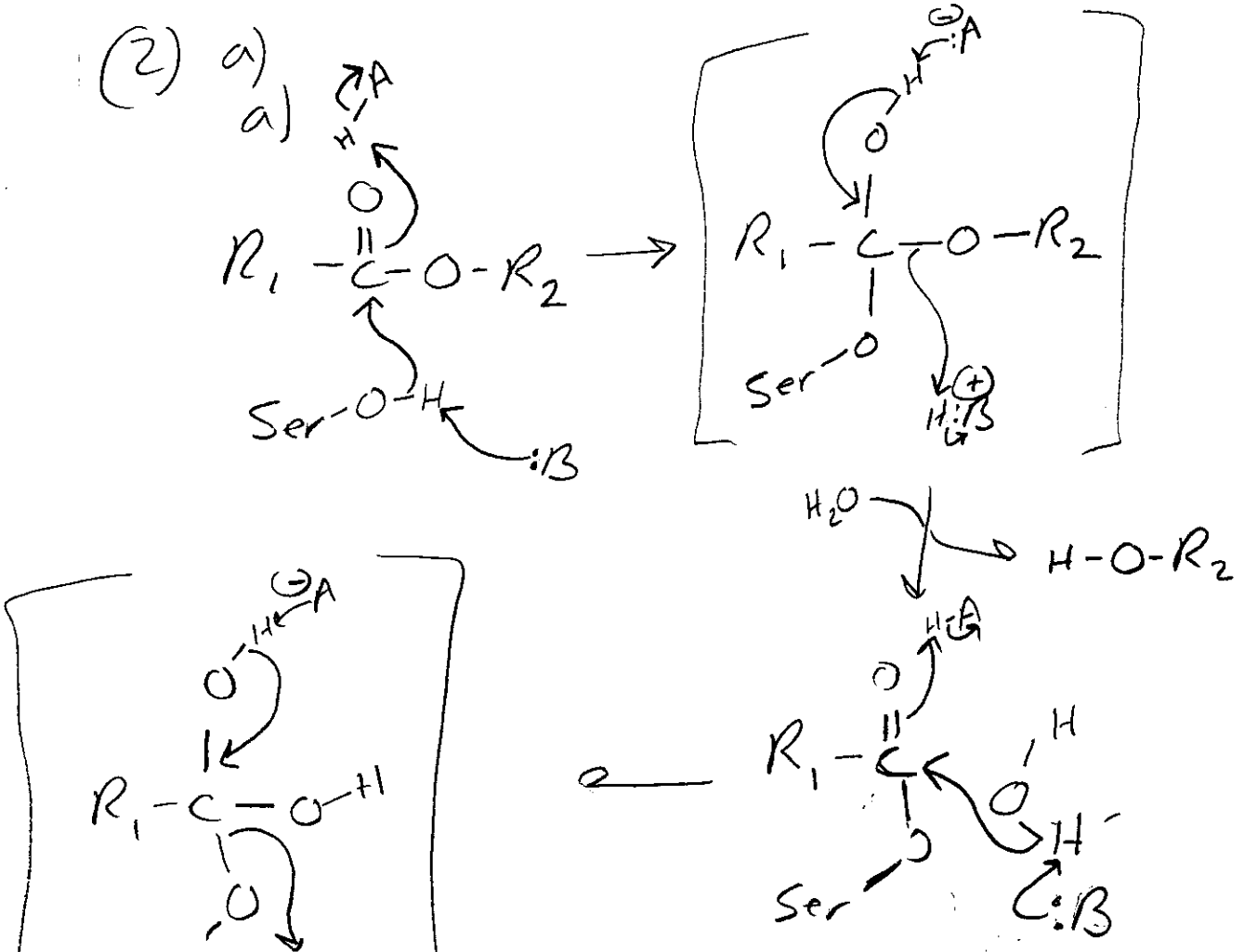
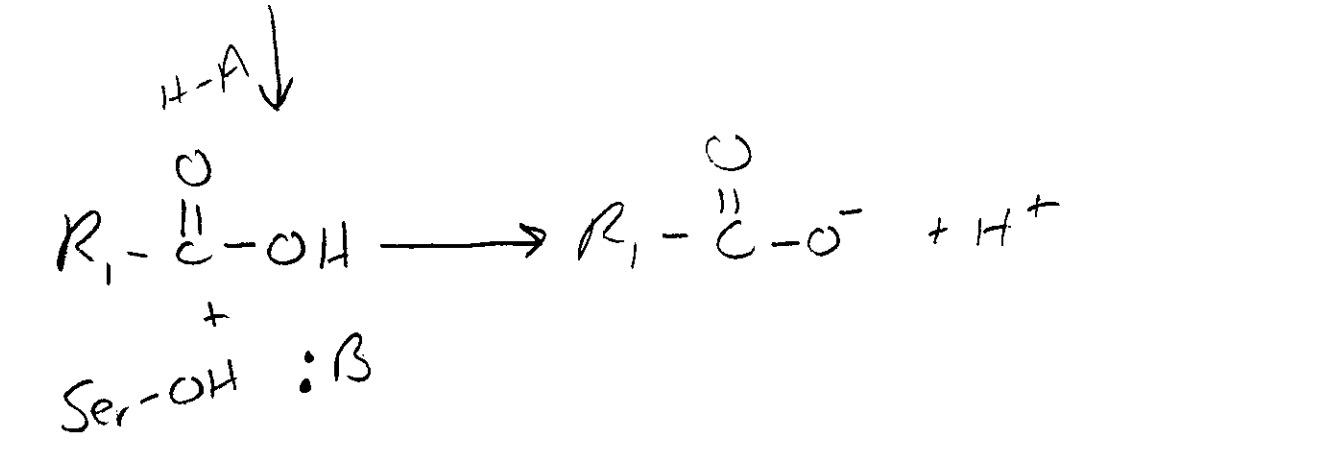
(2) 15 points. Draw two different mechanisms for ester hydrolysis that involve:
(a) covalent catalysis
(b) metal ion catalysis.

Use acid-base catalysis as needed in each mechanism to facilitate catalysis. Indicate what "intermediates" in your three mechanisms represent transition states, and briefly discuss how the catalytic group(s) stabilize these states.

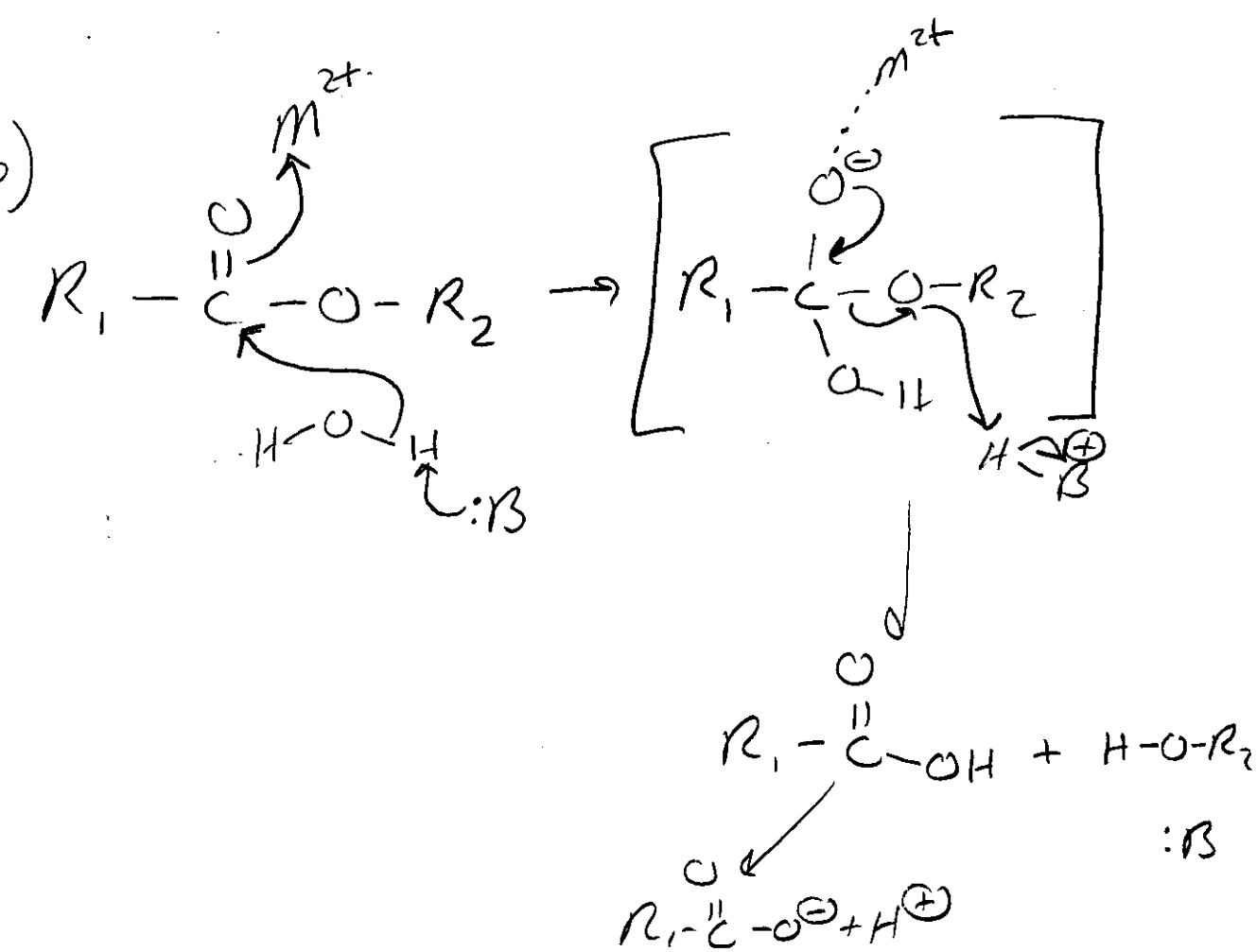
(2) a)





- Transition states are in brackets
- " " " are stabilized in this mechanism by a general acid that donates a proton to the oxyanion.

2 b)



Transition state is stabilized by charge stabilization of oxyanion by metal ion.

Take Home portion Exam 1 KEY

(1) a) $\left(\frac{0.04 \text{ mol } H^+}{10 \text{ min} \cdot \ell}\right)(5 \text{ min}) = 0.02 \frac{\text{mol } H^+}{\ell}$

$pH = -\log[H^+] = -\log(0.02)$

$= 1.70$

b) $pH = pKa + \log \frac{[A^-]}{[HA]}$

Initially, $pH = 8.1 + \log \frac{A^-}{HA} = 8.3$

$\frac{[A^-]}{[HA]} = 10^{0.2} = 1.585$; $[A^-] = 1.585[HA]$

$[A^-] + [HA] = 0.1$; $1.585[HA] + [HA] = 0.1$

$[HA]_{init} = 0.0387$, $[A^-]_{init} = 0.0613$

During the reaction, 0.02 M H^+ are made. These will react with $A^- \rightarrow HA$ as follows:

$A^- + H^+ \longrightarrow HA$.

So $[HA]$ increases by 0.02 M & $[A^-]$ decreases by 0.02 M:

$[HA]_{new} = 0.0387 + 0.02 = 0.0587$ M

$[A^-]_{new} = 0.0613 - 0.02 = 0.0413$ M

now, $pH = 8.1 + \log \frac{0.0413}{0.0587} = 7.95$

Note- the ΔpH in presence of buffer was only 0.35 units, while without buffer it was 5.3 units!

Take Home portion Exam 1 KEY

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Lecture 3

b) $pH = pKa + \log\frac{[A^-]}{[HA]}$

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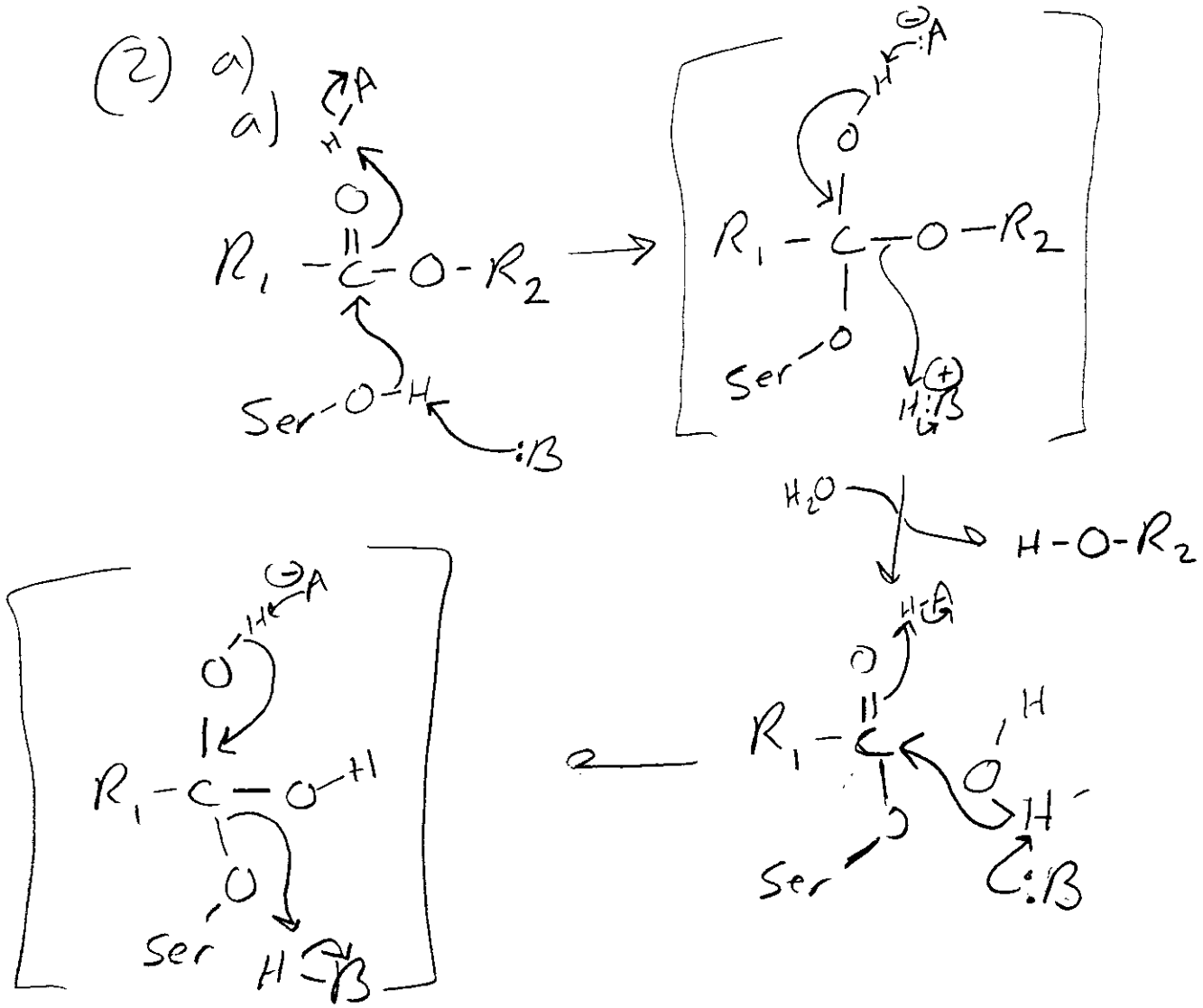

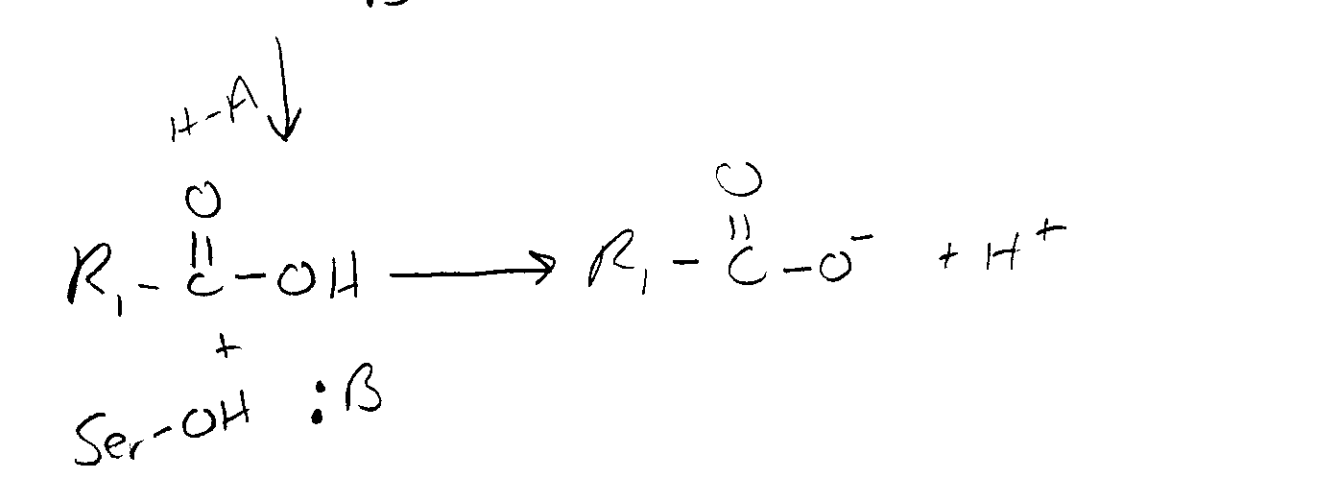

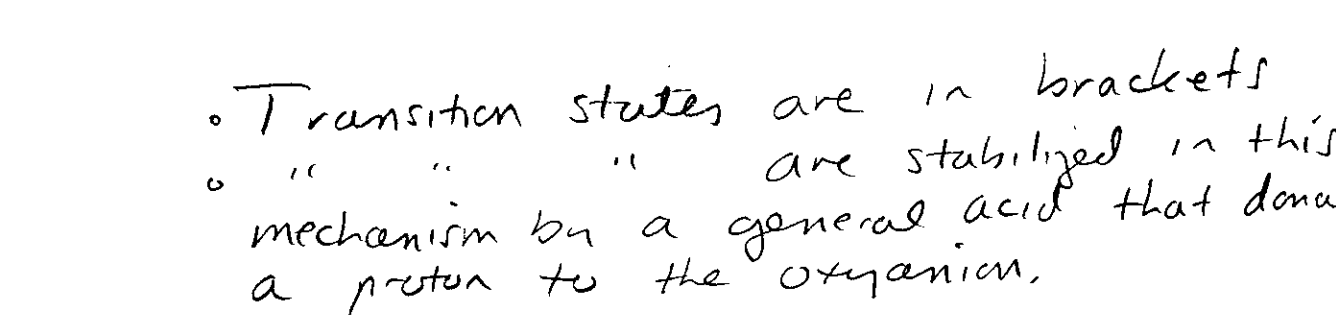

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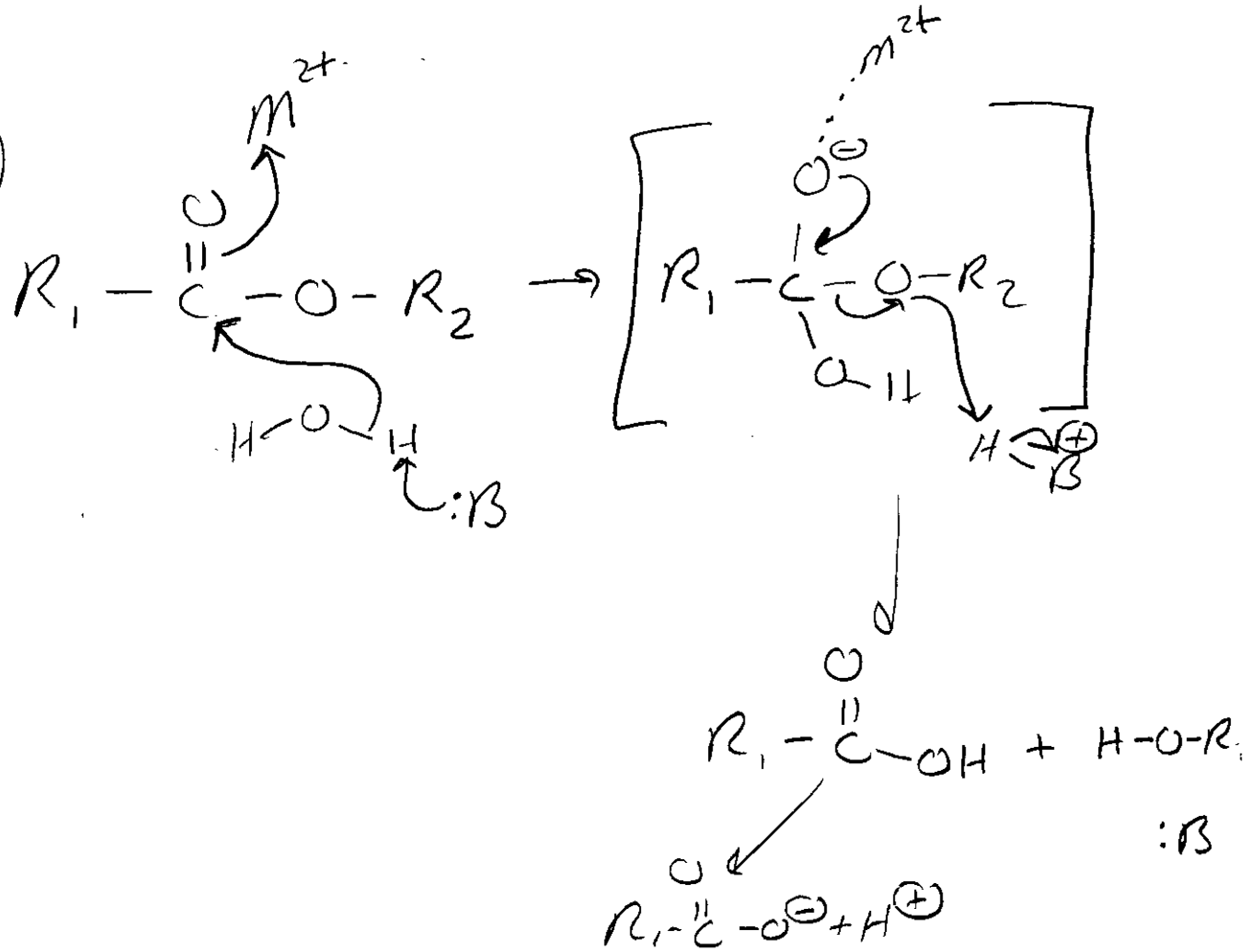

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