Chemistry 310
Spring 2009
Prof. B. Hanson

Name: KEY

Exam #3

1. _____ 20 points

2. _____ 20 points

3. _____ 20 points

4. _____ 20 points

5. _____ 20 points

100 points

"The study of chemistry is the most important as it is the most difficult of all the collateral branches of a pharmaceutist's education; the one that gives him the most power when applied in his professional pursuits, and the most reputation among the scientific. Chemistry is indeed the groundwork of every important process, and none can expect to excel who do not make it their study. The student of chemistry should, as early as practicable, get a mental outline grasp (if we may so speak) of the leading principles of the science."

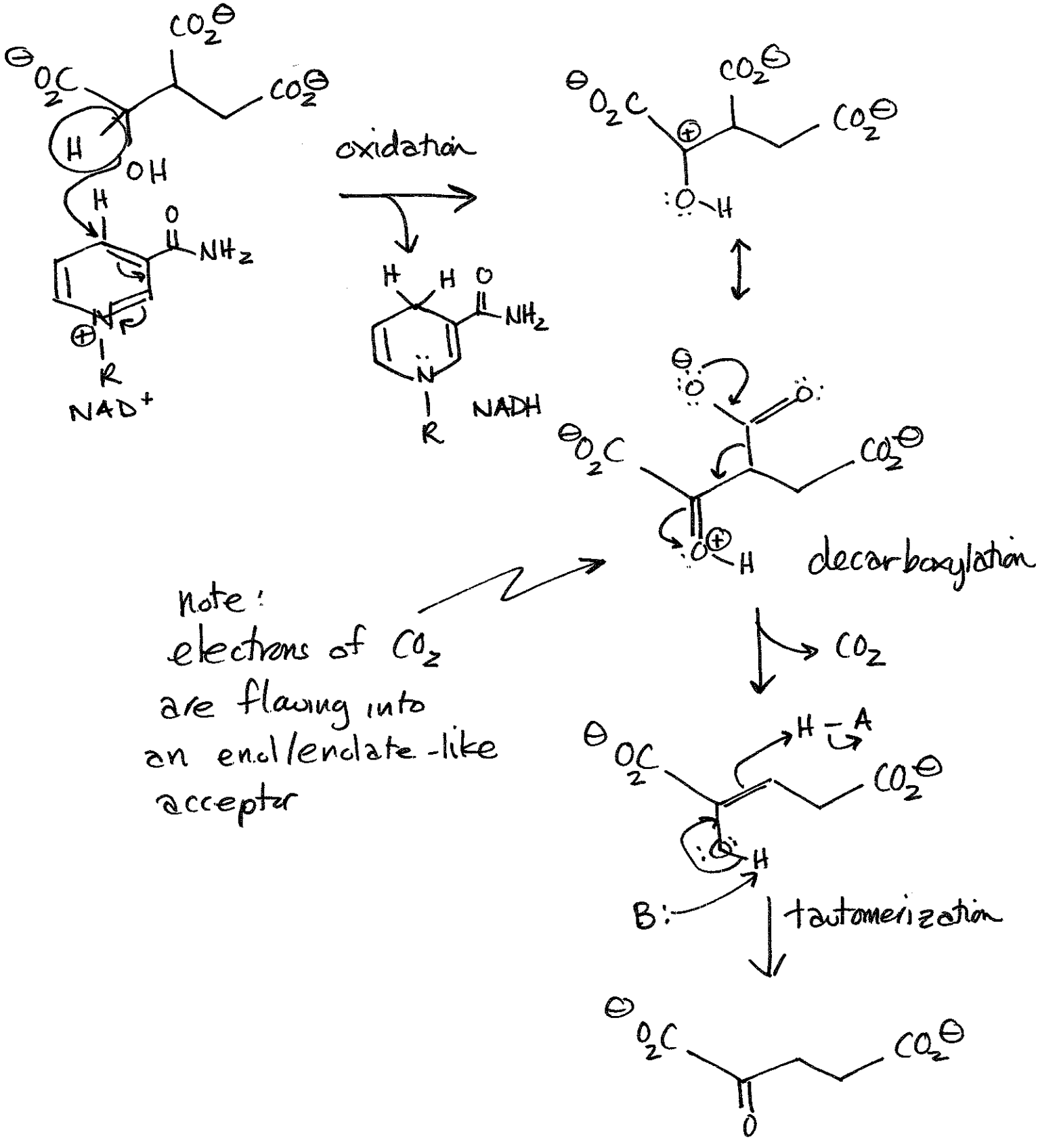
Proctor, Ellis & Sharp
American Journal of Pharmacy 28 (1856): 490-493.

Several useful charts are on the back of this exam. You may wish to tear them off.
Do not put any answers on them!

When a mechanism is requested, include appropriate arrows, lone pairs on Ns and Os, formal charges etc. You can use B: as a general purpose base and H–A as a general purpose acid.
Show intermediates!
Don't pile a bunch of arrows on a poor helpless structure!
Draw carefully and neatly!

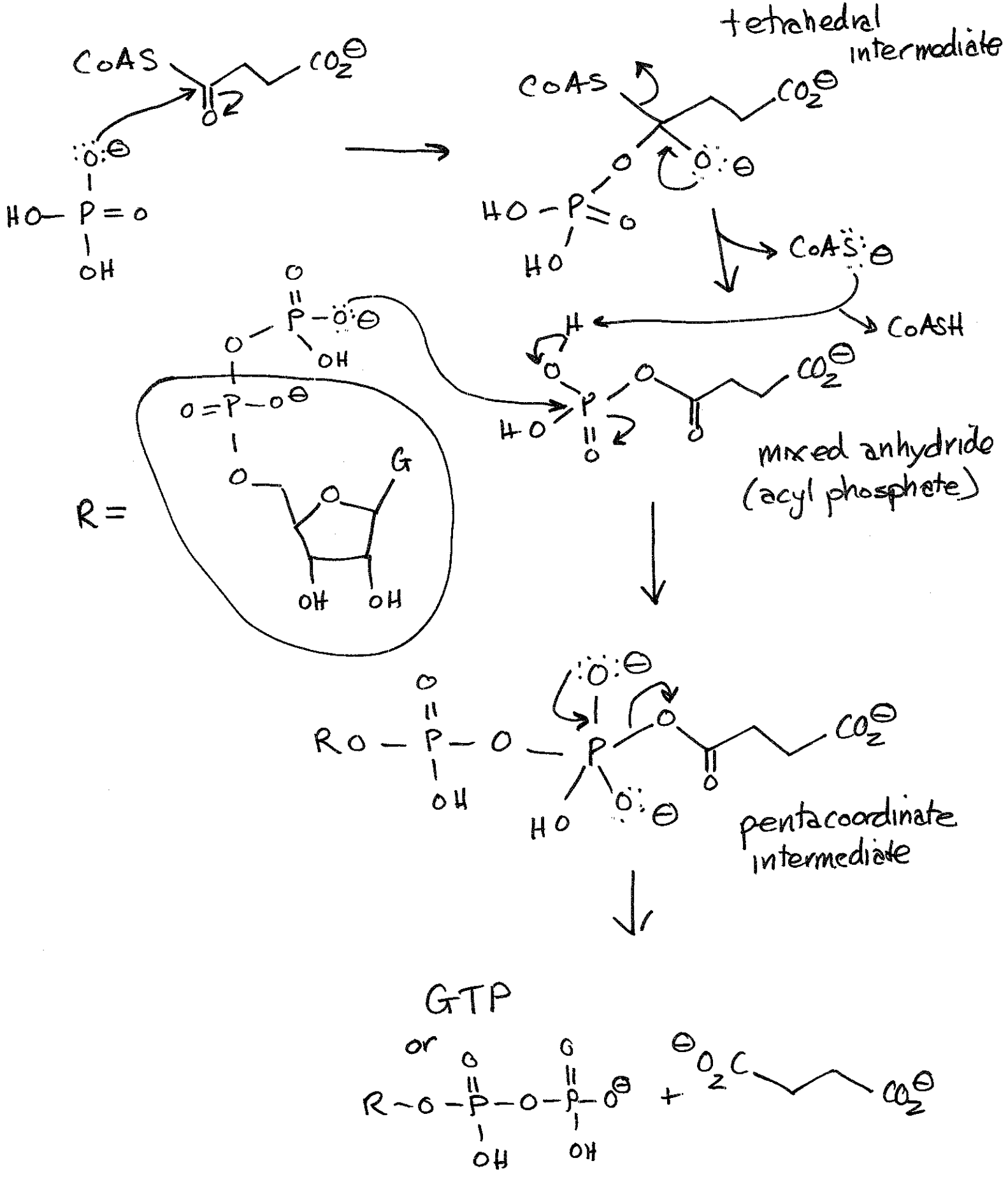
Variations are possible for proton transfers

1. (20 points). Draw a mechanism for step 3 of the citric acid cycle. You may limit the structure of NADH/NAD$^+$ to just the ring that is doing the work.

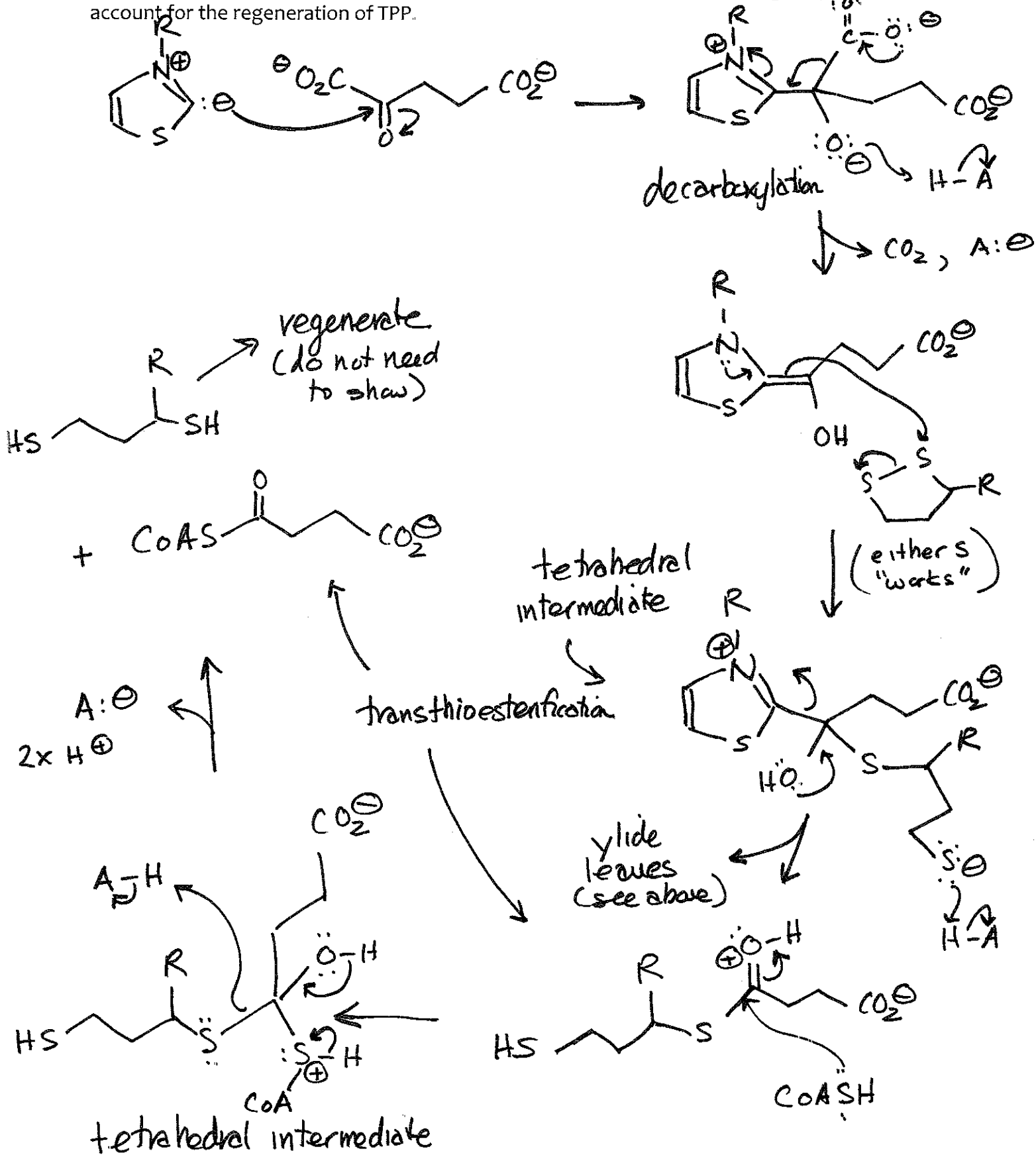


Variations are possible w/ regard to proton transfers

2. (20 points). Draw a mechanism for step 5 of the citric acid cycle. You may use G to represent the guanine base in GTP.



3. (20 points) Draw a mechanism for step 4 in the citric acid cycle. This reaction also requires TPP and lipoamide, but they are regenerated and hence catalytic and not shown in the net reaction on the chart (but they *must* be part of your mechanism). Your mechanism does not need to show the regeneration of dihydrolipoamide (which is shown on one of the attached Figures), but it should account for the regeneration of TPP.

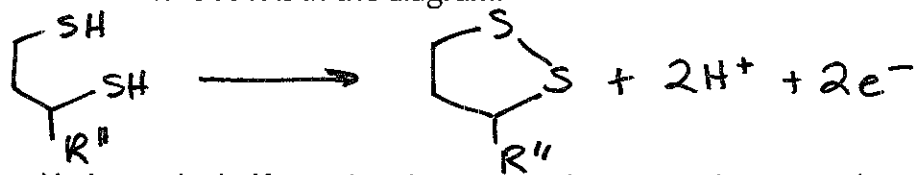


For (d) take answer to (a) and add to it

$NAD^+ + H^+ + 2e^- \rightarrow NADH$, then cancel

4. (20 points). One of the attached Figures describes how lipoamide can be regenerated, with FAD and NAD+ powering the process.

a. Write and balance the half reaction that dihydrolipoamide undergoes in this Figure. You may abbreviate the structure as it is in the diagram.

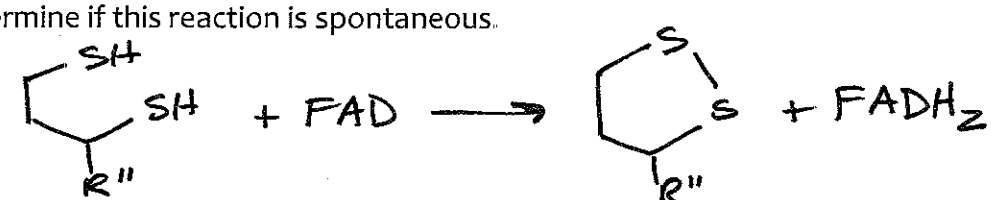


$E^\circ \sim 0.29V$ using lipoic acid as an analog

b. Write and balance the half reaction that FAD undergoes in this Figure (you may abbreviate it with FAD etc).

$FAD + 2H^+ + 2e^- \rightarrow FADH_2$ $\quad E^\circ \sim 0$

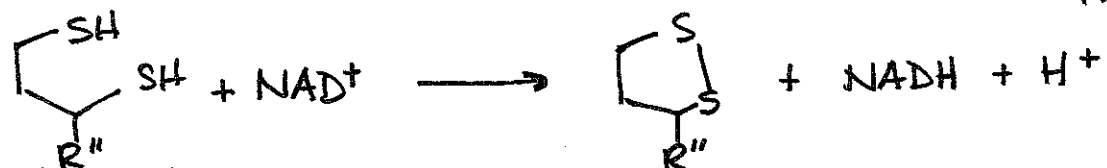
c. Add together and balance the two reactions above, and show the calculation necessary to determine if this reaction is spontaneous.



$E^\circ \sim 0.29$ since $\Delta G^\circ = -n\mathcal{F}\Delta E^\circ$ rxn is spontaneous

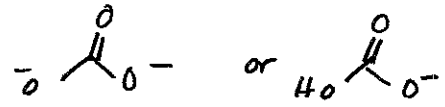
see above ↑

d. Write and balance the net reaction that occurs in this scheme.



5. (20 points) Answer the following question using Chimera and the file I will send you electronically. This question concerns the formation of N-carboxybiotin as shown in one of the attached Figures by the enzyme biotin carboxylase.

a. In this structure, in what chemical form does the CO2 make an appearance? Draw its structure here:



are reasonable answers

b. What **two** residues appear to stabilize the structure in (a)? Give the name, ID # and state what kind of intermolecular force is involved.

arg 292.B electrostatic forces glu 296.B – probably a hydrogen bond to OH of bicarb

c. What residue is interacting with the carbonyl oxygen of the biotin ring? Give the name & ID #.

gln 237.B

d. Which atom of the molecule in (a) is closest to the nucleophilic atom of biotin? Give the full ID information, including the particular atom. Give the distance of this closest atom.

BCT 1007.B O2 2.70 Å