NAME:
SID:

Chemistry 135, Third Exam
November 7, 2018
Please only turn this page once instructed to do so by the instructor.

This exam will be worth 15% of your overall grade. Please read all of the instructions/questions carefully and answer the question in the space provided or indicated. There should **12** total pages containing **10** multi-part questions. Be sure to transfer any answers you wish to receive credit for to the space provided. No calculators, phones, electronic devices, etc. may be used during this exam. Good luck!

Questions

Question	Points	Question #	Points
1	16	6	24
2	17	7	16
3	20	8	15
4	33	9	22
5	21	10	14
	Total	198	

Remember that whenever you take an exam, you are really taking *two* tests. The first is a test of your knowledge from the class. The second, and more important, is a test of integrity: that the answers you put down represent your answers and not someone else's. Please make sure to pass the more important test!

You will not need any calculators, phones, electronic devices, headphones, etc. to complete this exam (indeed, they will slow you down), so please make sure these are put away.

Pre-Exam Survey: please help us understand the study habits of Chem 135 students and fill out this survey (3 questions) while you wait for the exam to start. There is no incorrect answer – I'm just trying to collect data on how to help students in Chem 135 succeed. ~Prof. Miller

1. I went to the following person's office hours: (circle the choice that most correctly describes you)

Prof. Miller Vanessa Dan Pavel More than one person None

2. I attended the review session held by Prof. Miller: YES NO

3. Did you use the textbook to aid your study preparations? YES NO

The following space is intentionally left blank and may be used as scratch paper, space for a poem, or even an illustration. If you do include work in this area, be sure to transfer any answers you want graded to the provided space in the exam.

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1. Please carefully evaluate the following statements. If the statement is correct, please mark it as "True." If the statement is false, please provide the correction(s) that renders the statement true. (4 points each)

For example:
The chemical biology program at Stanford is the best!
This would be marked as "FALSE" and could be corrected in the following way:

The chemical biology program at ~~Stanford~~ *Cal* is the best!

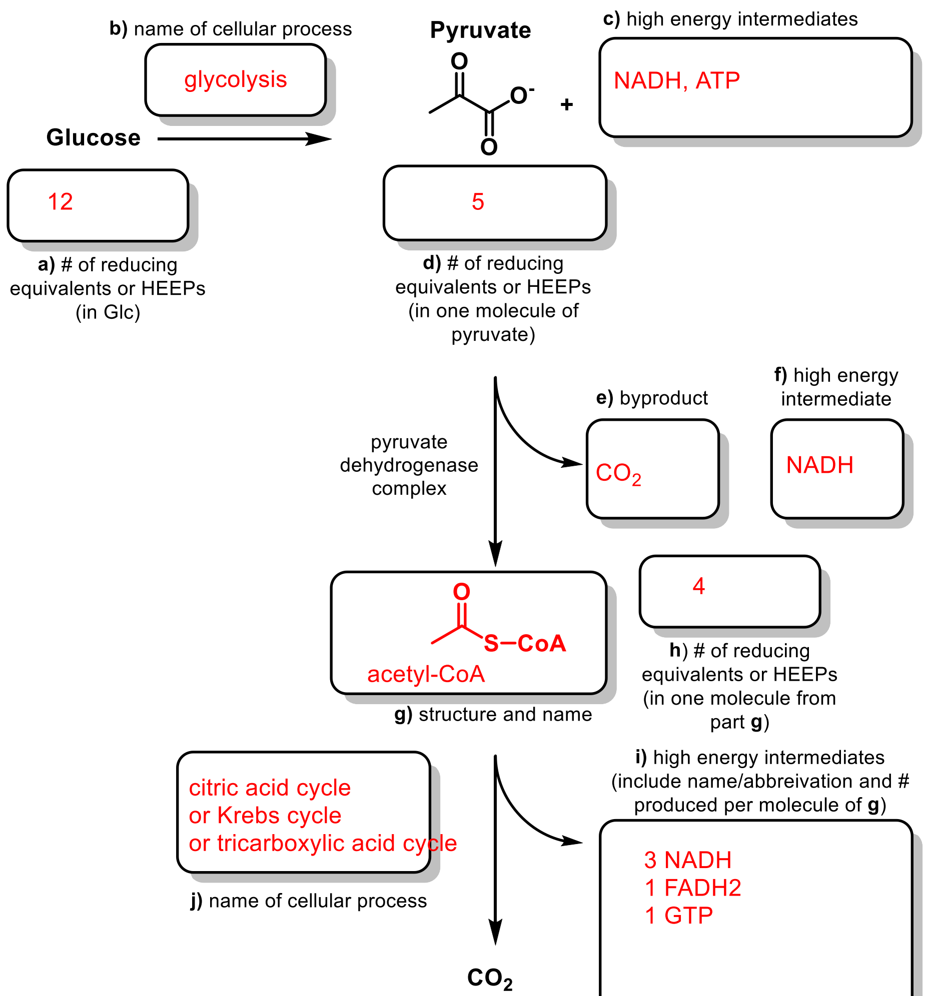
a. FALSE In the process of glycolysis and citric acid cycle, HEEPs (~~highly exergonic epimer pairs~~**high energy electron pairs**), or reducing equivalents, are removed from glucose.

b. FALSE The metabolic pathway of glycolysis is an example of a~~n~~ **catabolic** ~~anabolic~~ pathway, whereas gluconeogenesis is a**n** ~~catabolic~~ **anabolic** pathway.

c. TRUE The enzyme phosphofructosekinase-1, or PFK-1, is sometimes referred to as the gatekeeper of glycolysis. PFK-1 is allosterically regulated by cellular metabolites. High concentrations of ATP lower the k_{cat}/K_m of PFK-1, while high concentrations of ADP raise the k_{cat}/K_m of PFK-1.

d. FALSE ATP is an ideal candidate as a universal cellular energy carrier because it has a large, negative $\Delta G'^\circ$ of hydrolysis, it is kinetically **stable** ~~unstable~~, and it possess diverse molecular recognition elements or "pizzazz".

2. The chart below represents many of the cellular metabolic processes we have encountered in the last section of class. In the boxes provided, fill in the missing components, as explicitly instructed above/below the box. (17 points)

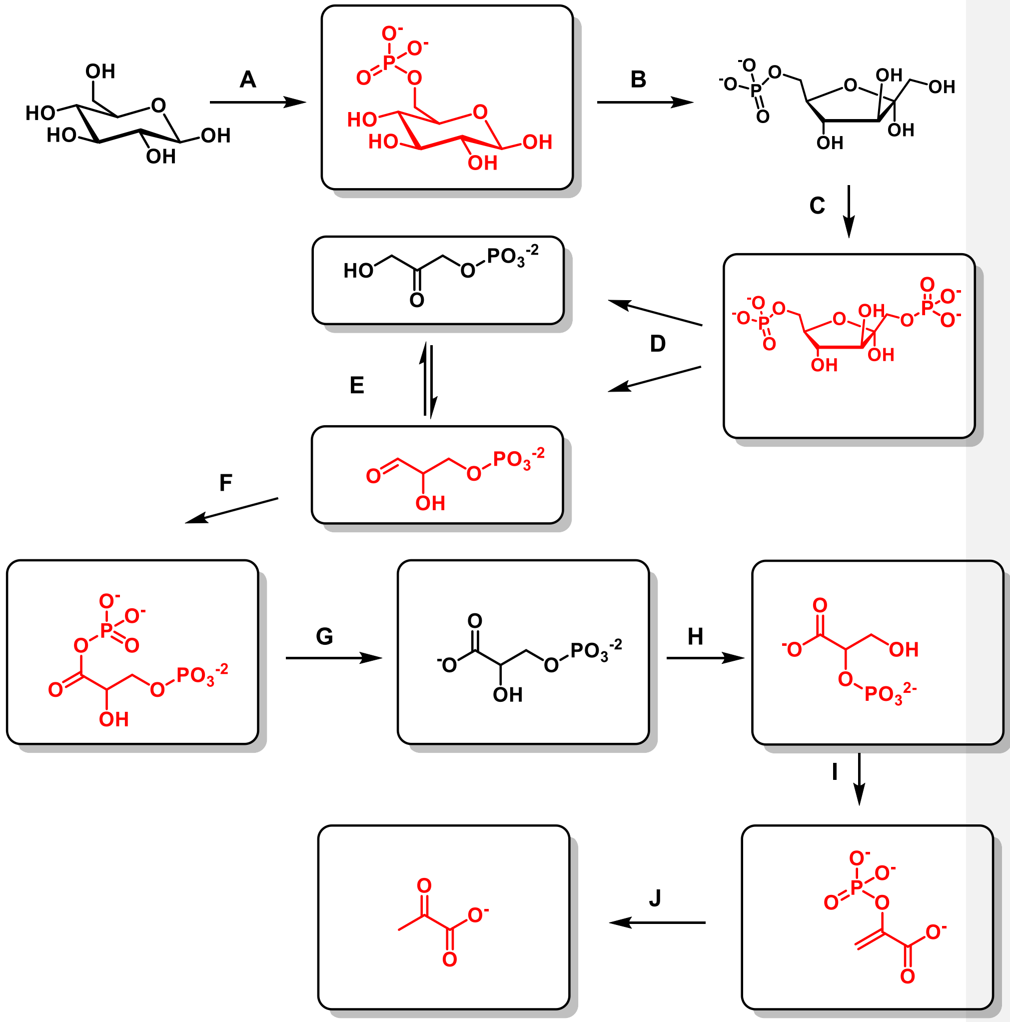


Commented [E1]: 1 pt per item/number in each box
a – 1
b – 1
c – 1 for nadh, 1 for atp (no numbers required)
d – 1
e – 1
f – 1
g) 1 for structure, 1 for name
h – 1
I – 1 each for nadh, fadh2, and GTP. 1 each for correct numbers (6 total)
j – 1 pt.

3.

a. Provide the structures of the missing glycolysis intermediates below (14 points)

Commented [E2]: 2 pt per structure.
minor errors in structure, -1 pt



Several steps in glycolysis consume or produce high energy intermediates. Indicate which steps (A-J)

b. Produce NADH: (2 points)

F

c. Consume ATP: (2 points)

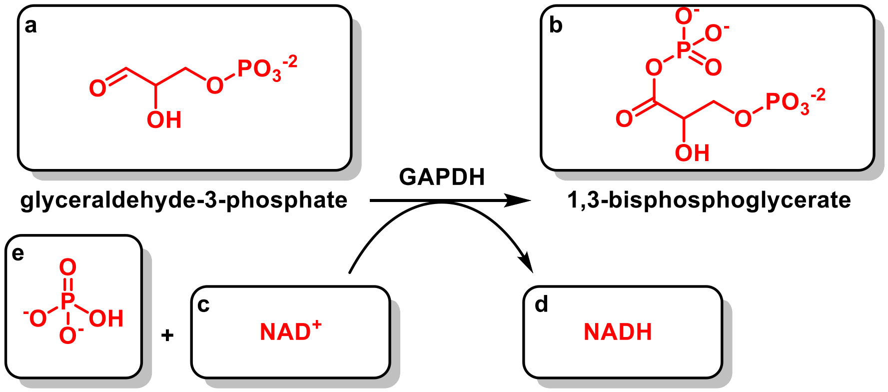
A, C

d. Produce ATP: (2 points) **G, J**

Commented [E3]: b) 2 pts
c) 1 pt for each
d) 1 pt for each

-1 pt for extra steps that are incorrect (i.e. if they have all of these steps, plus extra steps, remove points)

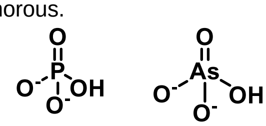
4. In glycolysis, the enzyme glyceraldehyde-3-phosphate dehydrogenase (GAPDH) catalyzes the oxidation of glyceraldehyde-3-phosphate to 1,3-bisphosphoglycerate, according to the equation below:



In the boxes provide above, indicate the following: (7 pts)

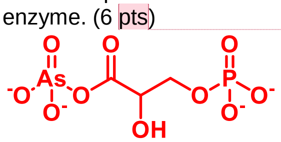
a. The structure for glyceraldehyde-3-phosphate.
b. The structure of 1,3-bisphosphoglycerate.
c. The cofactor (name or abbreviation) required by GAPDH to carry out this reaction.
d. The other product generated by the action of GAPDH on glyceraldehyde-3-phosphate.
e. The structure or name of the other reagent required by GAPDH to carry out this reaction.

Arsenate (AsO_4H^{2-}) (below) is a toxic analog of inorganic phosphate (PO_4H^{2-}) in which the element arsenic replaces phosphorous.



phosphate **arsenate**

f. Arsenate is structurally and chemically analogous to inorganic phosphate and can often "trick" enzymes into using it instead of phosphate. However, organic compounds containing arsenate are less kinetically stable than their corresponding phosphate compounds. For example, like inorganic phosphate, arsenate can form acyl anhydrides with carboxylic acids. Draw the product of the reaction catalyzed by GAPDH if arsenate is instead used by the enzyme. (6 pts)



Commented [E4]: a) 1 pt
b) 1 pt
c) 2 pts (must be NAD+ here…no credit for NADH here)
d) 2 pts (must be NADH here…no credit for NAD+)
e) 1 pt

Commented [E5]: we can assign some partial credit – depends on what answers look like

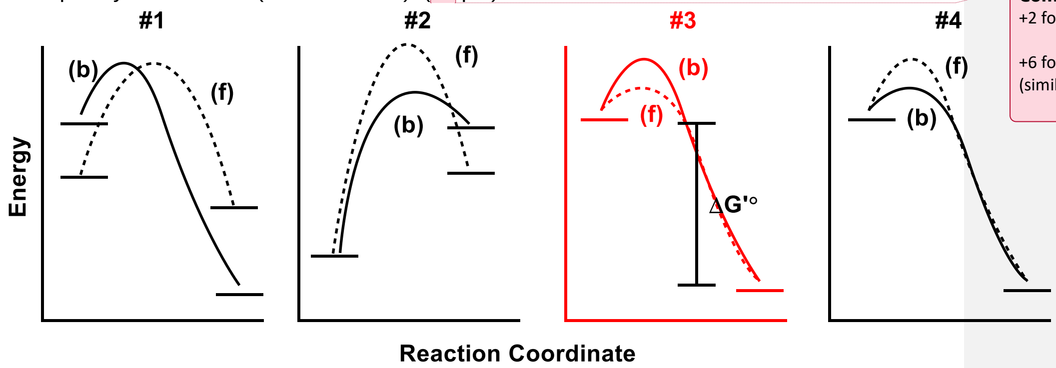
g. The hydrolysis of the products you identified in part (**b**) and (**f**) of this problem have nearly identical ΔG'° values. However, the arsenate-containing (**f**) is kinetically unstable in water. Select the reaction coordinate diagram below that most accurately describes the comparison between the hydrolysis of the products in **(b)** and **(f)**.

i.e. 1,3-bisphosphoglycerate + H_2O → 3-phosphoglycerate + P_i
vs
(f) + H_2O → 3-phosphoglycerate + arsenate

Identify the correct reaction coordinate and label the feature that corresponds to ΔG'°. Briefly explain your selection (2-3 sentences). (10 pts)

Commented [E6]: +2 for #3 graph
+2 for correct delta G indication

+6 for explanation
(similar delta G, but lower barrier for F)

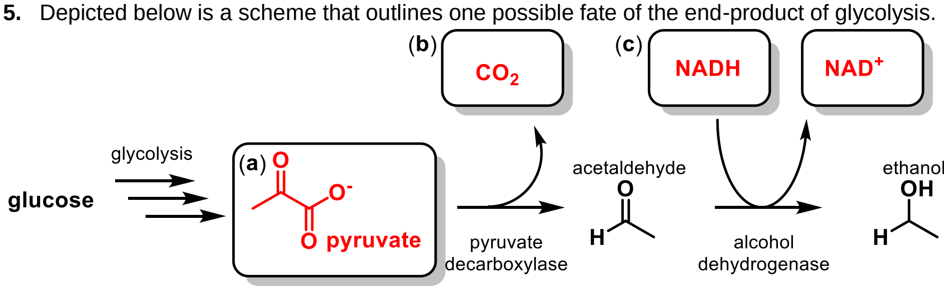


#3 is the correct choice, because the hydrolysis reactions have the same/similar ΔG'°. However, the kinetically unstable (**f**) has a lower activation energy barrier than the kinetically more stable (**b**).

h. Arsenate is generally *very* toxic to organisms. Provide a probable explanation for this observation by discussing the consequences to metabolism if arsenate is used by GAPDH (3-4 sentences). (10 pts)

Because the arsenate analog of 1,3-bisphosphoglycerate is kinetically unstable, in hydrolyzes before it can transfer the arsenate group to ATP. Therefore, the subsequent step in glycolysis proceeds without making ATP. This results in <u>no net synthesis</u> of ATP in glycolysis, because the only other place to make ATP is at the hydrolysis of PEP.

5. Depicted below is a scheme that outlines one possible fate of the end-product of glycolysis.

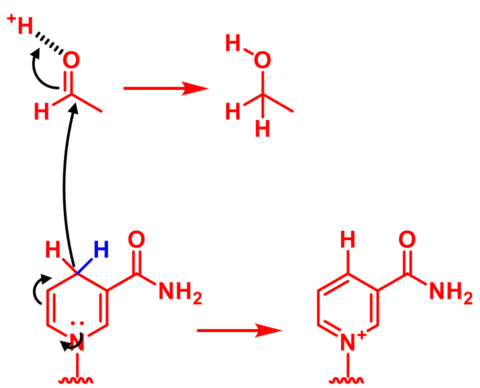


a. In the box above, provide the name or structure of the endproduct of glycolysis. (1 pt)

b. In the box above, provide the name or structure of the byproduct of the reaction catalyzed by pyruvate decarboxylase. (2 pts)

c. In the two boxes provided above, indicate the additional cofactor required for the reaction catalyzed by alcohol dehydrogenase (abbreviation is fine). (2 pts)

d. Provide a reasonable arrow-pushing mechanism for the reaction catalyzed by alcohol dehydrogenase. Be sure to indicate how the co-factor you identified in part (**c**) is involved. (12 pts)



e. Alcohol dehydrogenase uses metal ion catalysis as a strategy for catalysis. What metal ion does alcohol dehydrogenase use to catalyze the conversion of acetaldehyde to ethanol? (2 pts)

zinc, or Zn^{2+}

Commented [E7]: 2 pts for Zn2+ or zinc

6. Scientists examining the conversion of glucose to ethanol and CO_2 by yeast made the following observations.

a. First, inorganic phosphate is essential for fermentation. When inorganic phosphate runs out, fermentation stops, even if glucose is still present. Why does fermentation stop in the absence of inorganic phosphate? Explain your reasoning by describing which biochemical step requires phosphate. (8 points)

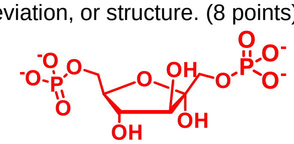
Commented [E8]: +4 for identifiying the correct step

+4 for conveying the idea that glycolysis stops there and pyruvate can't be made so fermentation stops
(maybe break it into +2 for glycolysis stops and +2 for no pyruvate therefore no fermentation)

Conversion of glyceraldehyde-3-phosphate (GA3P) to 1,3-bisphosphoglycerate (13BPG) requires Pi. So, glycolysis stops at GA3P, pyruvate cannot form, and fermentation cannot take place.

b. Second, the researchers noticed that when inorganic phosphate runs out, as described above, a hexose bisphosphate accumulates. What is the likely identity of the hexose bisphosphate. You may provide a name, abbreviation, or structure. (8 points)

1,6-bisphosphofructose.

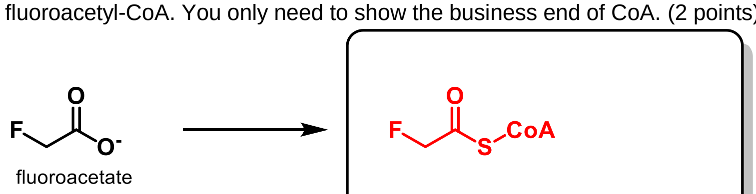


c. Finally, the scientists conducting this study found that when arsenate replaced phosphate in the sample, the hexose bisphosphate did not accumulate, but that glucose was completely converted to ethanol and CO_2. Why did arsenate prevent the accumulation of hexose bisphosphate, and allow fermentation to proceed? Explain in 1-2 sentences. (8 points)

Arsenate replaces Pi, allowing oxidation of GA3P, relieving blockage of glycolysis and the production of pyruvate and conversion to CO2 and ethanol.

7. The active ingredient of a widely-used pesticide sold under the trade-name "Compound 1080" is fluoroacetate. Fluoroacetate is highly toxic, and its use in the United States was severely curtailed in the 1970s. In the lab, rat hearts treated with fluoroacetate exhibit several drastic physiological changes. We'll discuss some of these changes, below.

a. First, however, fluoroacetate is converted to fluoroacetyl-CoA. Please provide the structure of fluoroacetyl-CoA. You only need to show the business end of CoA. (2 points)



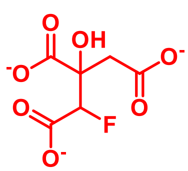
fluoroacetyl CoA (provide structure)

b. Provide an estimate of the ΔG'° of formation of fluoroacetyl-CoA from fluoroacetate and coenzyme A. Briefly explain why you chose this value (1-2 sentences). (2 points)

Commented [E9]: +1 for +7 kcal.
+1 for comparison to acetyl CoA

+7.5 kcal/mol. This is similar to the ΔG'° of formation of acetyl-CoA from acetate and Coenzyme A.

c. If fluoroacetyl-CoA behaves similarly to acetyl-CoA, what would you predict is the compound formed when fluoroacetate is incorporated into the Citric Acid cycle? Please provide a structure *or* name. (4 points)



fluorocitrate

d. After treatment of the rat hearts with fluoroacetate, researchers measured the concentration of all intermediates of the Citric Acid Cycle. They found that all *decrease*, except for citrate, which was elevated. Based on this observation, which step (chemical transformation) or enzyme in the Citric Acid cycle is blocked by the metabolite of fluoroacetate? (8 points)

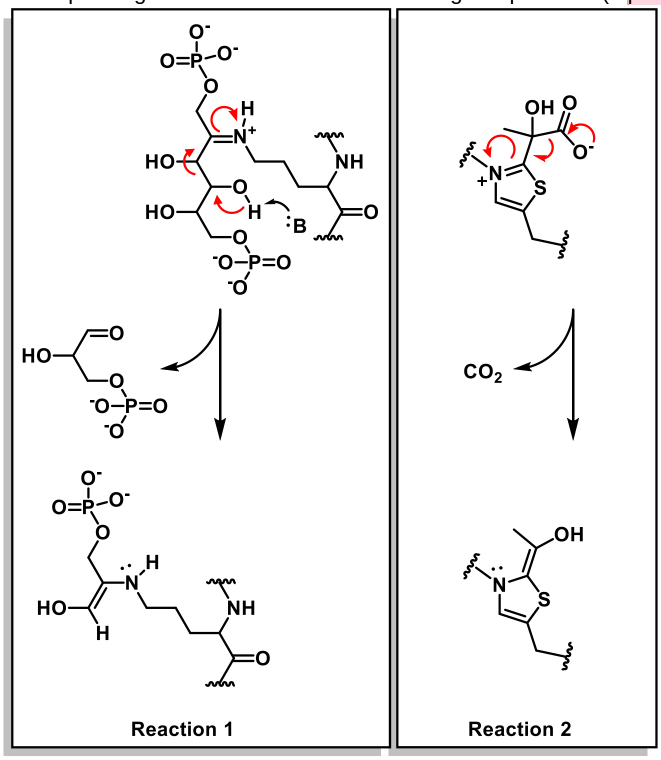
Commented [E10]: can state either citrate to isocitrate – or- indicate aconitase.

fluorocitrate inhibits the conversion of citrate to isocitrate (aconitase is the enzyme)

8. Shown below are two structures from two separate arrow pushing mechanisms we have reviewed during this section.

a. Provide an arrow-pushing mechanism to account for the given products (3 points each)

Commented [E11]: 1 pt for each arrow



For each reaction, provide the metabolic process or pathway associated with each. (3 points each)

b. Reaction 1:
glycolysis

Reaction 2:
pyruvate dehydrogenase complex
-or- pyruvate to acetyl CoA
-or- ethanolic fermentation

c. Although the two mechanisms incorporate structurally diverse elements, there is a common theme or purpose of the positively-charged nitrogen in each of these cases. Briefly discuss the role of the positively charged nitrogen atom. (1-2 sentences) (6 points)

The positively charged nitrogen acts as an electron sink to facilitate the loss of a leaving group: CO_2 in the case of reaction 2, and an enolate equivalent in the case of Reaction 1.

9.

a. Under cellular conditions, the ratio of ATP is approximately 10,000 times that of ADP and inorganic phosphate. In the space below, estimate the actual free energy of ATP hydrolysis under cellular conditions. (6 points)

ΔG = ΔG'° + 1.4 $\log_{10}$ (Q) **Q = 10^{-4}**

one order of magnitude = 1.4 kcal/mol. 10,000 = 10^4, so 1.4 x 4 = 5.4 kcal/mol more negative.

ΔG = -7.3 kcal/mol + -5.4 kcal/mol = -12.7 kcal/mol

Commented [E12]: +2 for ATP hydrolysis of about -7 kcal
+2 for additional -5 kcal mol
+2 for proper signs to get to a more negative value of about -12 kcal.

b. The following reactions in glycolysis are highly exergonic, with the following ΔG'° values:

(**1**) 1,3-bisphosphoglycerate + ADP → 3-phosphoglycerate + ATP; ΔG'° = -4.4 kcal/mol

(**2**) phosphoenolpyruvate + ADP → pyruvate + ATP; ΔG'° = -7.5 kcal/mol

Under cellular conditions, one of these reactions has an actual free energy that is very close to zero. Please identify which reaction and explain your reasoning 2-3 sentences. (8 points)

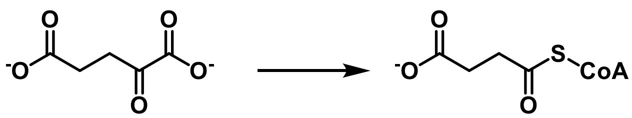
(1) has actual free energy close to zero. ATP formation is approximately +5 kcal more difficult under cellular conditions, which makes reaction 1 close to zero (-4.4 + 5)

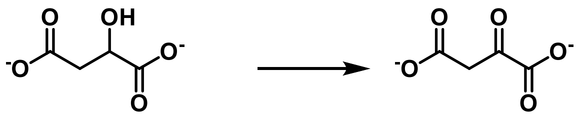
Commented [E13]: +4 ID that (1) is the right choice
+3 explaining that actual free energy associated with ATP formation makes the reaction less negative and closer to zero
+1 for linking the value they found in (a) to this answer (in some way)

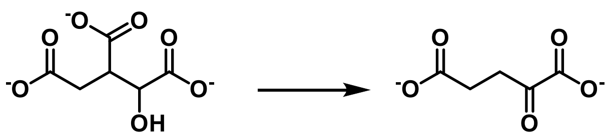
c. The process of gluconeogenesis generates glucose from pyruvate. Both the process of glycolysis and gluconeogenesis take place in the cytosol and share many of the same enzymes for key chemical transformations. Of the two steps described in part (**b**), which one uses the same enzyme in both glycolysis and gluconeogenesis? Please explain your choice in light of your answer to part (**b**). (8 points)

(1) is used in both. The actual free energy for this transformation is close to zero, so the reaction is reversible under cellular conditions. Reaction 2 will be irreversible.

10. Shown below are three reactions.

(**1**) 

(**2**) 

(**3**) 

a. Which metabolic pathway is most closely associated with these three transformations? (2 points)

TCA/Krebs cycle/citric acid cycle/tri carboxylic acid cycle (not Calvin cycle)

b. Of the three reactions, which one(s) employ(s) TPP as a co-factor? (3 points)

1

c. Of the three reactions, which one(s) is/are accompanied by a loss of CO_2? (3 points)

1 and 3

d. Of the three reactions, which one(s) is/are reduction/oxidation (redox) reaction? (3 points)

all of them

e. For the reaction(s) you identified in part (**d**), list the redox active cofactor used for that particular transformation (if you identified multiple reactions in part **d**, they may all use different cofactors). (3 points)

They all use NAD^+ and generate NADH.
(students may also indicate use of FAD and additional co-factors for reaction 1, which is fine)