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.

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!

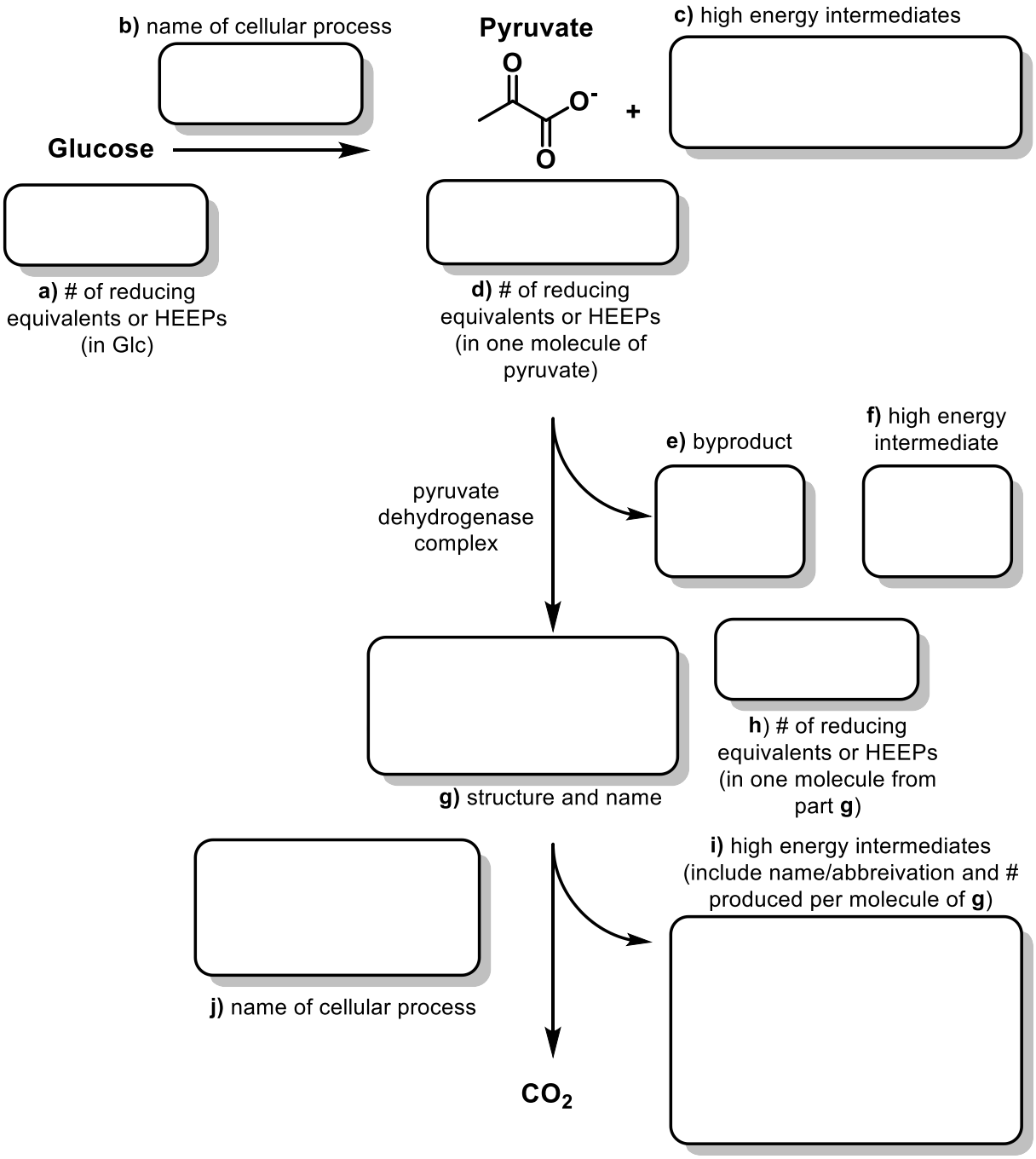
a. _____ In the process of glycolysis and citric acid cycle, HEEPs (highly exergonic epimer pairs), or reducing equivalents, are removed from glucose.

b. _____ The metabolic pathway of glycolysis is an example of an anabolic pathway, whereas gluconeogenesis is a catabolic pathway.

c. _____ 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.

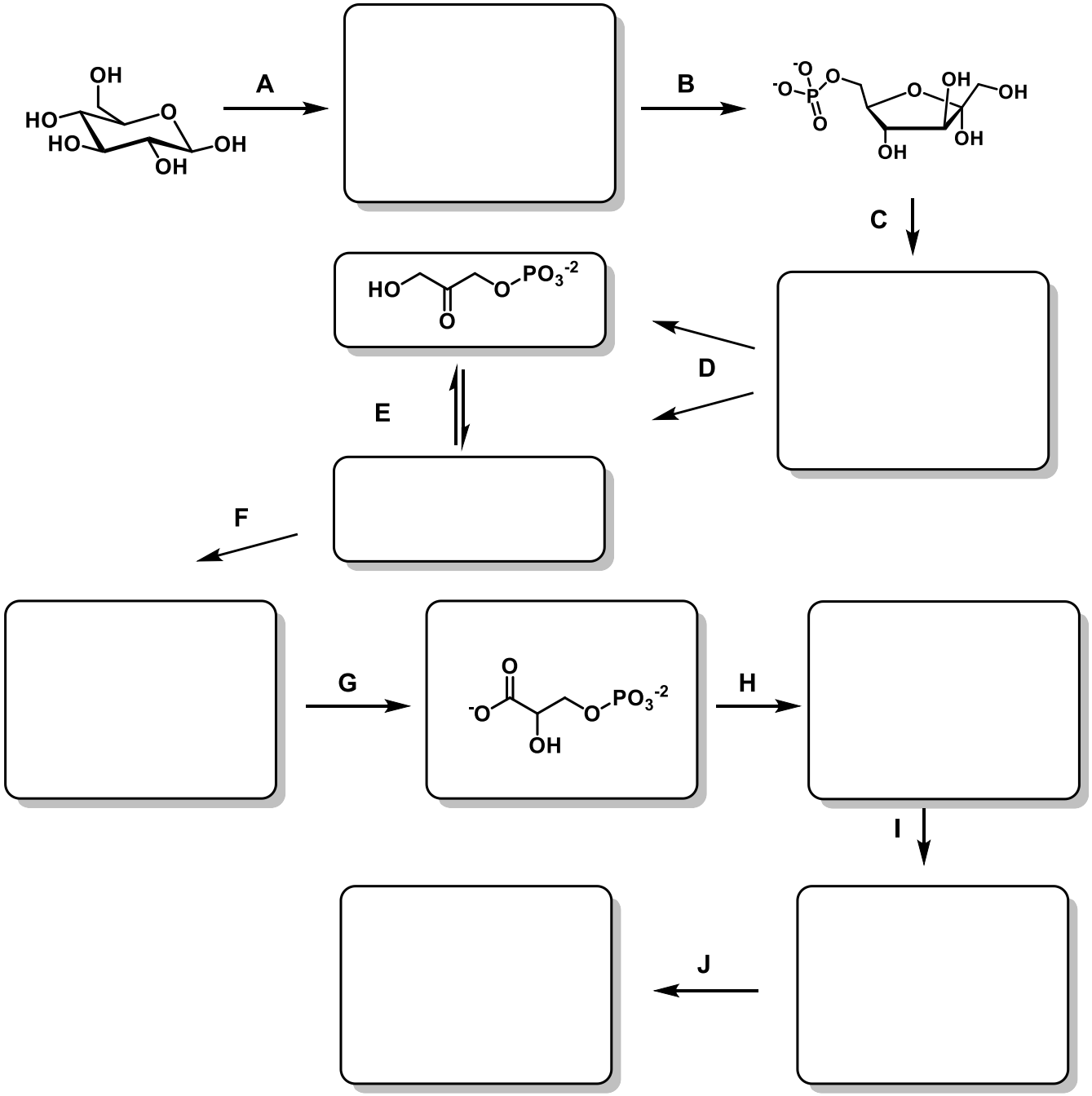
d. _____ ATP is an ideal candidate as a universal cellular energy carrier because it has a large, negative $\Delta G'^{\circ}$ of hydrolysis, it is kinetically unstable, and it possess diverse molecular recognition elements or "pizzazz".

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)



3.

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



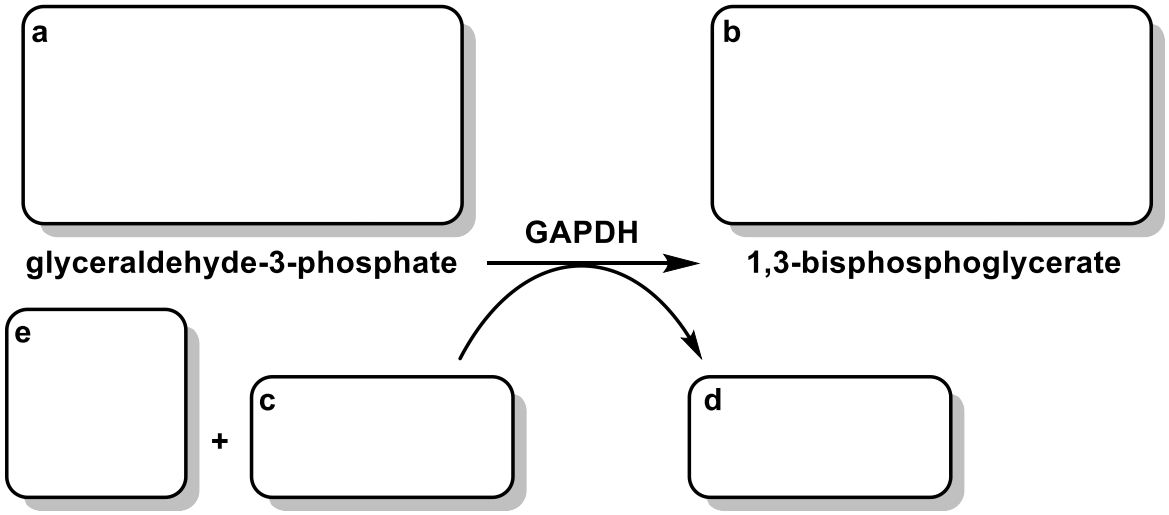
Several steps in glycolysis consume or produce high energy intermediates. Indicate which steps (A-J)

b. Produce NADH: (2 points)

c. Consume ATP: (2 points)

d. Produce ATP: (2 points)

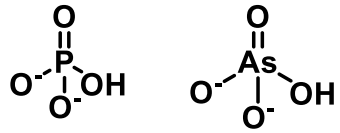
4. In glycolysis, the enzyme glyceraldehyde-3-phosphate dehydrogenase (GAPDH) catalyzes the oxidation of glyceraldehyde-3-phosphate to 1,3-bisphosphoglycerate, according to the equation below:



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)

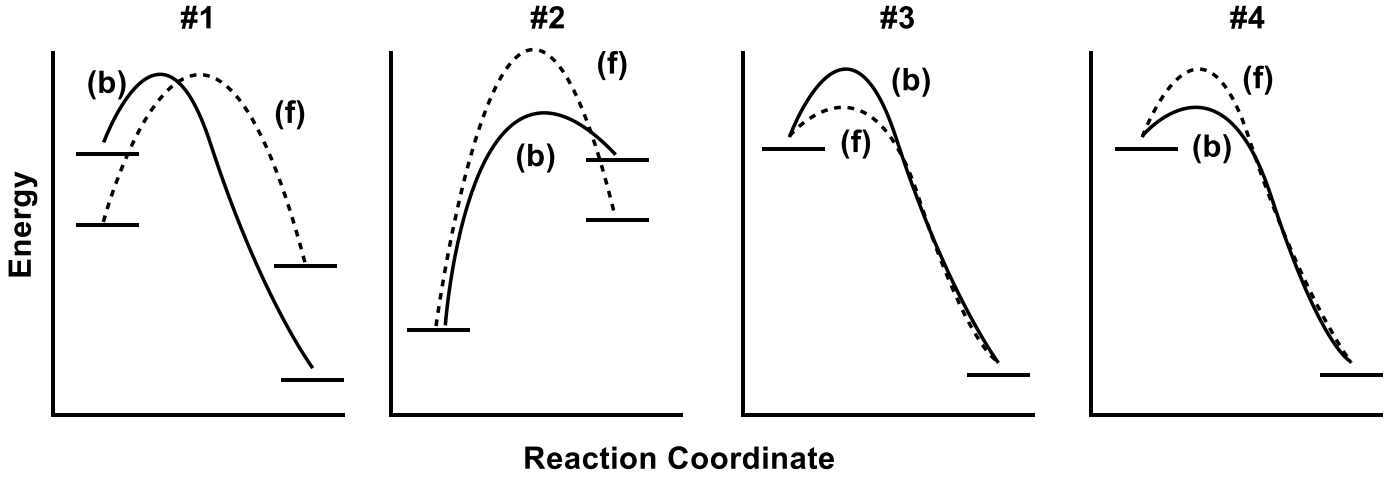
g. The hydrolysis of the products you identified in part (**b**) and (**f**) of this problem have nearly identical ΔG'° values. However, the arsenate-containing (**f**) is kinetically unstable in water. Select the reaction coordinate diagram below that most accurately describes the comparison between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

i.e. 1,3-bisphosphoglycerate + H_2O → 3-phosphoglycerate + P_i

vs

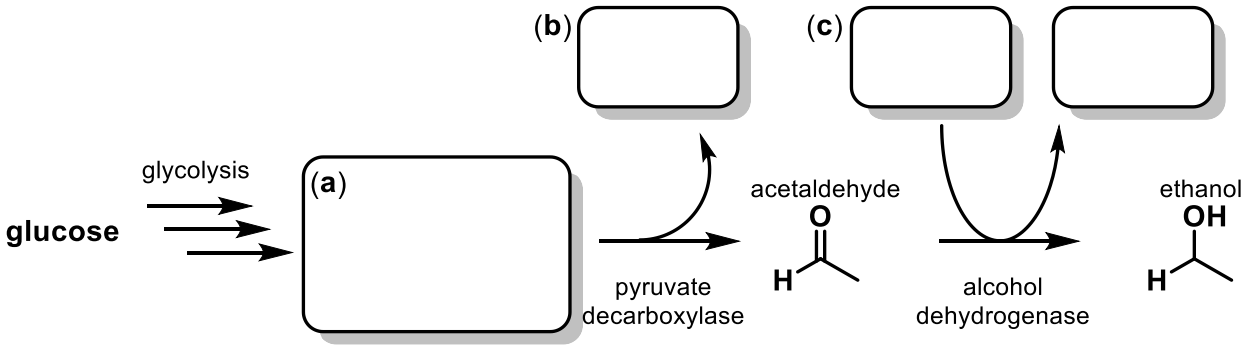
(f) + H_2O → 3-phosphoglycerate + arsenate

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



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)

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)

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

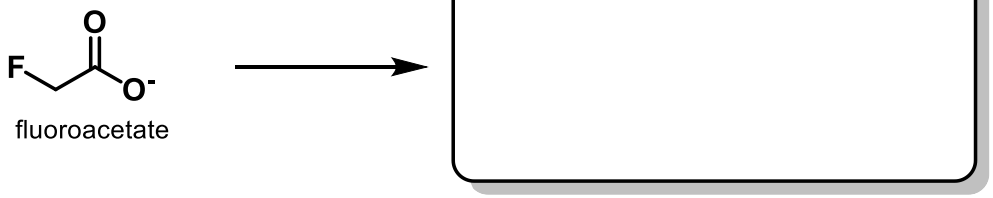
a. First, inorganic phosphate is essential for fermentation. When inorganic phosphate runs out, fermentation stops, even if glucose is still present. Why does fermentation stop in the absence of inorganic phosphate? Explain your reasoning by describing which biochemical step requires phosphate. (8 points)

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)

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)

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)



fluoroacetate

fluoroacetyl CoA (provide structure)

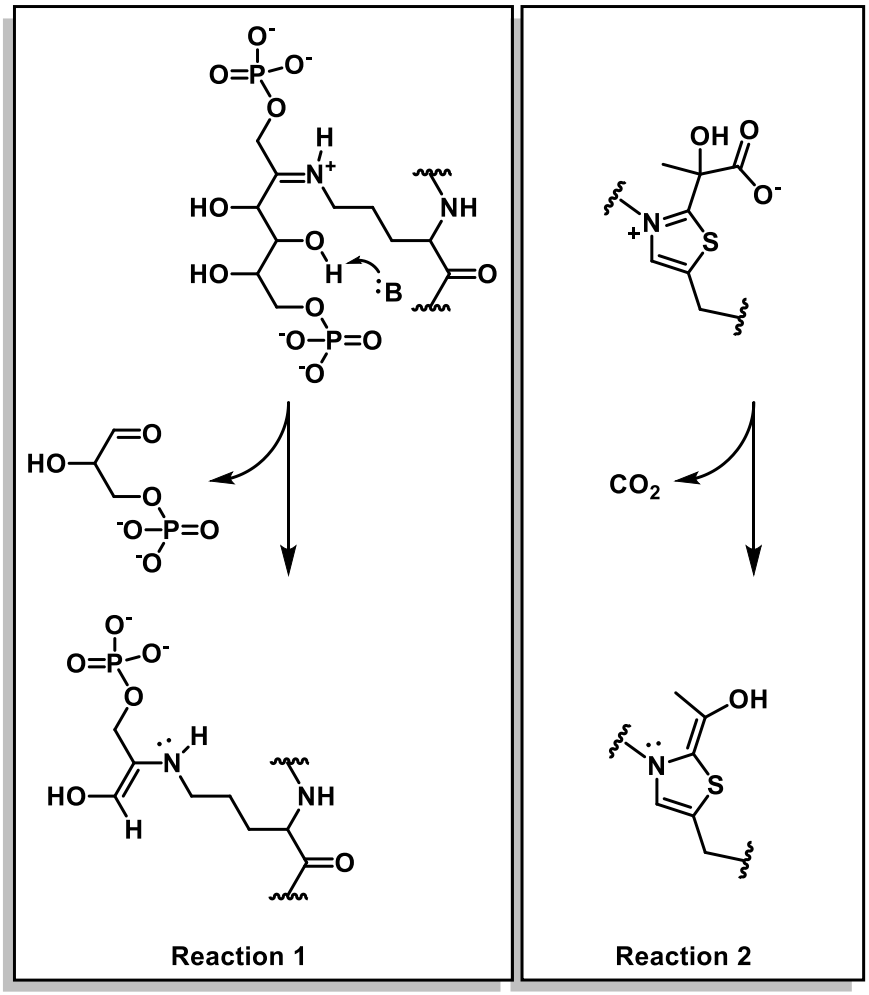
b. Provide an estimate of the ΔG'° of formation of fluoroacetyl-CoA from fluoroacetate and coenzyme A. Briefly explain why you chose this value (1-2 sentences). (2 points)

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)

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)

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)



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

b. Reaction 1: Reaction 2:

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)

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)

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

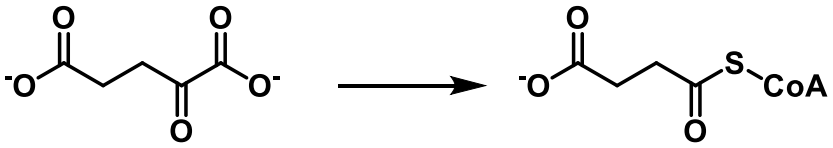
(**1**) 1,3-bisphosphoglycerate + ADP → 3-phosphoglycerate + ATP; ΔG'° = -4.4 kcal/mol

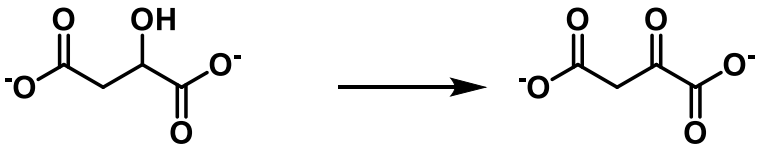
(**2**) phosphoenolpyruvate + ADP → pyruvate + ATP; ΔG'° = -7.5 kcal/mol

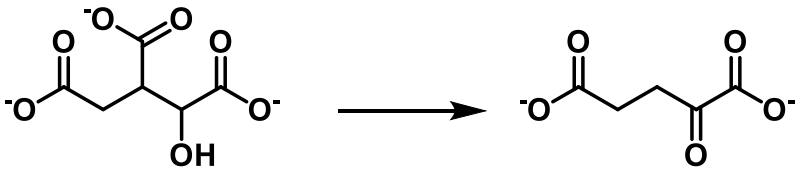
Under cellular conditions, one of these reactions has an actual free energy that is very close to zero. Please identify which reaction and explain your reasoning 2-3 sentences. (8 points)

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 (**f**), which one uses the same enzyme in both glycolysis and gluconeogenesis? Please explain your choice in light of your answer to part (**f**). (8 points)

10. Shown below are three reactions.

(**1**) 

(**2**) 

(**3**) 

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

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

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

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

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)