Glycolysis worksheet

Overview

This worksheet has three parts. Although they are intended to be done in sequence, you could reasonably jump around and do the parts in any order. What is important is that you gain practice in analyzing both the organic and biochemical ideas. I do not expect you to know the pathway; it is the practice working with the ideas that is important.

Part 1 asks you to draw out the compounds in the glycolysis pathway, given their names. This is introduced below.

Parts 2-3, p 3, both ask you questions about the glycolysis pathway.

Part 1

The worksheet on p 2 outlines the pathway of glycolysis, giving the names of the chemicals. It also includes the conversion of the final product of glycolysis to the entry compound of the citric acid cycle. For reference, each reaction is numbered, with a superscript just after the reaction arrow.

To do:

- Draw the structure of each compound shown.
- Notes:
  - All chiral compounds are of the D-series.
  - For the hexoses and their derivatives (i.e., the C_6 compounds), show them in the linear (open chain) form, using Fischer projections.
  - The names shown are "common" names, but you should be able to figure out most of the structures, by making sense of the changes from one compound to the next. Of course, you can look up some of the names in the book.
  - The names shown for organic acids reflect that the cellular pH is near neutral, so carboxylic acids are ionized; the names are given as the anions.
  - You can show phosphate groups as a circled P, a common biochemical shorthand. But I would encourage you to show one phosphate group in detail, for practice.
  - "Glyceric acid" is the acid made by oxidizing one end of glycerol.
  - For coenzyme A carrying an acyl group, you can show it as -SCoA. This is a common shorthand; it avoids the complexity of the coenzyme, which is largely irrelevant to our story, but shows the thioester linkage. (Ouellette, p 348)

When you are done, check yourself. A good source of the complete glycolysis pathway is at http://www.bio.davidson.edu/Courses/Molbio/MolStudents/spring2005/Gemberling/protein.html

D-glucose →[1] glucose 6-phosphate →[2] fructose 6-phosphate

→[3] fructose 1,6-bisphosphate →[4] dihydroxyacetone phosphate
+ D-glyceraldehyde 3-phosphate
(see Ouellette, p 289 & p 291)

The two C_3 compounds created in step 4 are interconvertible; it is the glyceraldehyde 3-phosphate that continues. That is, both C_3 halves from step 4 continue as glyceraldehyde 3-phosphate. →[5]

1,3-bisphosphoglycerate →[6] 3-phosphoglycerate →[7] 2-phosphoglycerate
(see note)

→[8] phosphoenolpyruvate →[9] pyruvate →[10] acetyl CoA
(see note)

Parts 2-3, on this page, both ask you questions about the glycolysis pathway. They do this in different forms. They assume that you have a complete version of the pathway. Answers for these two sections are on p 4.

Part 2. For each step, describe the chemical change. If possible, describe it in terms of organic chemical reactions that you have encountered. In any case, describe what is different. For this part, don't worry about biochemical issues, such as cofactors involved.

Part 3. Each question asks you about some feature of the pathway, either in organic chemistry or biochemistry terms. Many questions can be answered by giving a reaction number, from the pathway (p 2).

1. Three reactions involve adding a phosphate group to something. They are:

2. Two of those are simple additions of a phosphate group. They are:

3. For those simple additions of a phosphate group, what biochemical would you expect to donate the phosphate group?

4. Some reactions involve removing a phosphate group. They are:

5. In each case of phosphate removal, the phosphate is "captured", by combining with the common biochemical phosphate carrier ______ to make ______.

6. Considering all of the above questions, the net production of ______ (captured phosphates) as one glucose molecule is metabolized through this pathway is ______ (how many, per glucose).

(The third phosphate addition is a more complex reaction. In terms of phosphate, it actually uses simple phosphate ions, and so does not affect this calculation.)

7. Which reaction(s) involve an oxidation or reduction? (Careful, there are not many!)

8. For each reaction that you listed in #7, above: is it an oxidation or a reduction? _______ And the likely biochemical cofactor would be ______, which would be _______ (oxidized or reduced) to ______.

9. Which reaction involves a decarboxylation?

10. In 1,3-bisphosphoglycerate, the two phosphates are in different functional groups. What is the functional group for each phosphate?

Answer key

Part 2

1. Phosphorylate glucose at the 6-position, making an ester. (Ouellette, pp 354-5.)
2. Isomerize glucose to fructose. This reverses the position of the alcohol and carbonyl groups. This proceeds through an enediol intermediate (Ouellette, p 313).
3. Phosphorylate the sugar at the 1-position, making another ester.
4. Split the molecule in half, breaking a C-C bond. You can think of this as the reverse of an aldol condensation, involving a C-H bond adding across a carbonyl group. The interconversion between the two chemicals shown is via an enediol intermediate (as for reaction 2).
5. Oxidize the aldehyde to an acid, and then phosphorylate, creating an anhydride linkage.
6. Hydrolyze the anhydride.
7. Isomerize. Move the phosphate group to position 2. (No change in basic functionalities.)
8. Eliminate water.
9. Hydrolyze the phosphate ester. This creates an enol, which tautomerizes to form the more stable keto form.
10. Decarboxylate (remove CO_2), and attach the remaining part to CoA, as a thioester.

Part 3

1. 1, 3, 5
2. 1, 3
3. ATP.
4. 6, 9
5. ADP, ATP (That is, ADP + $P_i \rightarrow$ ATP, where P_i refers to a phosphate group.)

   These reactions are substrate-level phosphorylations. That is, ATP is produced directly from the substrate, rather than through the more indirect process of oxidative phosphorylation.
6. ATP, 2. (Remember… the reactions of C_3 compounds have to be counted double.)
7. #5
8. oxidation (aldehyde $\rightarrow$ acid), NAD^+, reduced, NADH (or FAD, $FADH_2$; you have no way to predict which cofactor would be used.)

   Why do we refer to it as an oxidation when, like any redox reaction, it has both an oxidation component and a reduction component? Good point. But our main interest is in what happens to the glucose. From that perspective, it is an oxidation.
9. #10 (Note that, strictly speaking, this is not part of glycolysis per se.)
10. The phosphate at position 1 is part of an acid anhydride; the phosphate at position 3 is part of an ester.