CHEM-643 Biochemistry Name _____
Mid-term Examination
7:30 – 9:00 am, Friday, 3 November 2006

Dr. H. White - Instructor

There are 10 pages to this examination including this page. Write your name on each new page. Read every question so that you understand what is being asked. If you feel any question is unclear or ambiguous, clearly explain your answer or interpretation. Please call my attention to any errors you encounter.

This examination will assess your learning, problem-solving skills, and ability to communicate clearly. It is intended to be challenging even to the best students in the class. Some of the questions will deal with material you have not seen before; however, the questions can be answered by applying basic principles and patterns discussed in the course.

Do not expose your answers to the scrutiny of your neighbors. Please fold under each page before you go on to the next.

Breakdown of the examination by sections:

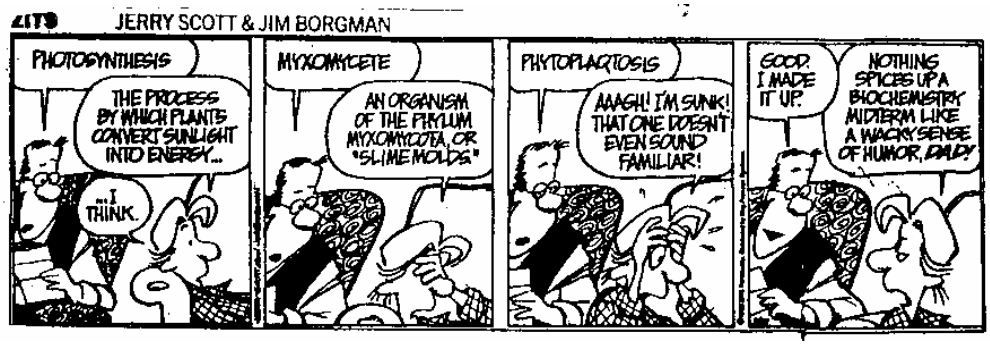
I. Short Answer	16 Points
II. Natural Product Synthesis	27 Points
III. Problems	47 Points
IV. Short Essay	10 Points
Total	100 Points

Exam Statistics

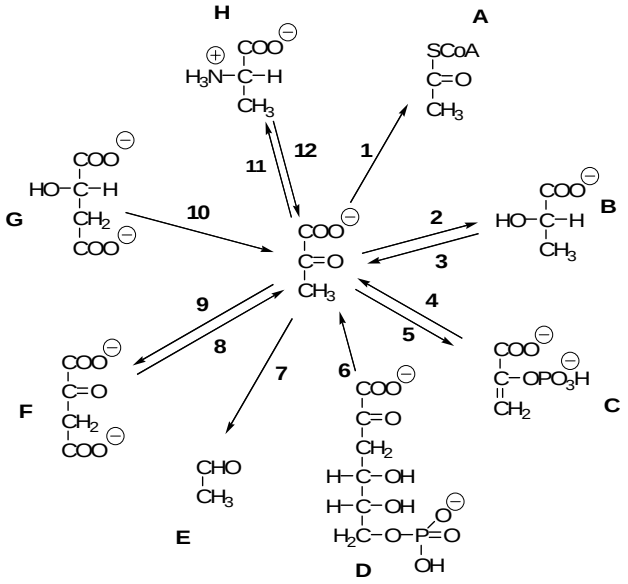
_____ Class Range

_____ Class Mean

_____ Your Rank in class



Part I - Short Answer Questions (1 point each, 16 Points Total)



The diagram at the left was used for an in-class assignment early in the semester. Since that time we have encountered every reaction displayed in a metabolic context. All of the questions in this section refer to this diagram.

1. Identify by name compounds:

   B. _____

   C. _____

   F. _____

   G. _____

   H. _____

2. Identify the (or a) pathway associated with the reactions indicated:

   1. _____

   4. _____

   5. _____

   7. _____

   10. _____

3. Identify a cofactor associated with each reaction, but don't use same one twice.

   1. _____

   2. _____

   7. _____

   9. _____

   10. _____

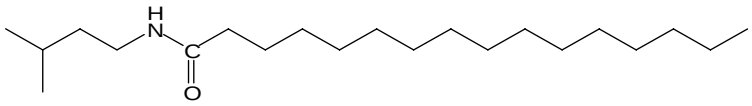
   12. _____

Part II Natural Product Biosynthesis:

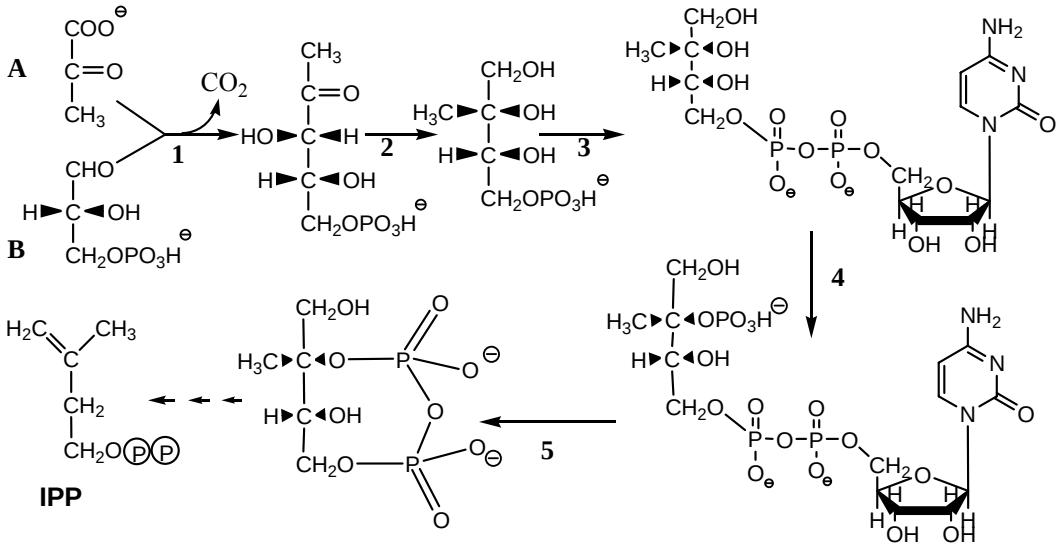
1. (13 Points Total) A strain of alfalfa is resistant to feeding damage by the potato leafhopper due to a homologous series of N-(3-methylbutyl) amides of normal saturated fatty acids it produces [Ranger et al. (2005) *Phytochemistry* **66**, 529-541]. The structure of one of these compounds is given below:
   A. (2 Points) What fatty acid (give the common name) is a precursor to this compound?

   B. (2 Points) What amino acid is a precursor to this compound?

   C. (9 Points) Starting with the compounds you have identified, propose a biochemically reasonable biosynthetic pathway that includes all intermediates and necessary cofactors. A retrobiosynthetic approach may help.



2. (14 Points Total) Only relatively recently did researchers discover that plants have a different pathways to generate isopentenylpyrophospate (IPP) than do animals. The plant pathway, which was not discussed in class, is shown below [Modified from Fellermeier et al. (2001) *Eur. J. Biochem* **268**, 6302]. The questions that follow refer to the plant pathway and its comparison to the pathway in us.



A. (2 Points) Name compounds A and B.

B. (2 Points) What coenzyme would you expect to be involved in step 1?

C. (2 Points) What nucleotide triphosphate is a substrate in step 3?

D. (4 Points) If Compound A were labeled at its carbonyl carbon, where would that label appear in the product IPP? (Draw a circle around the carbon in IPP.)

E. (4 Points) If carbonyl-labeled Compound A were used as a precursor in the mammalian synthesis of IPP, where would the label appear in IPP? (Put a box around the carbon(s) in IPP above.)

Part III Problems

3. (10 Points Total) The US Army Cold Weather Research Laboratory in Natick, Massachusetts is interested in the well being of American troops in cold climates. Among other things, they study the responses of small experimental mammals under environmental stress. The data in the following table report the amount of carnitine in two groups of four rats; one group kept at 25°C and the other at 5°C for six weeks. The half-life of carnitine in these animals was also determined. The rats were fed identical standard diets ad libitum (they ate as much as they wanted whenever they wanted). The diet contained no carnitine.

Environmental Temp	Carnitine (mg/100g body wt)	Carnitine half-life (days)
25°C	22.5	9.7
5°C	172	4.8

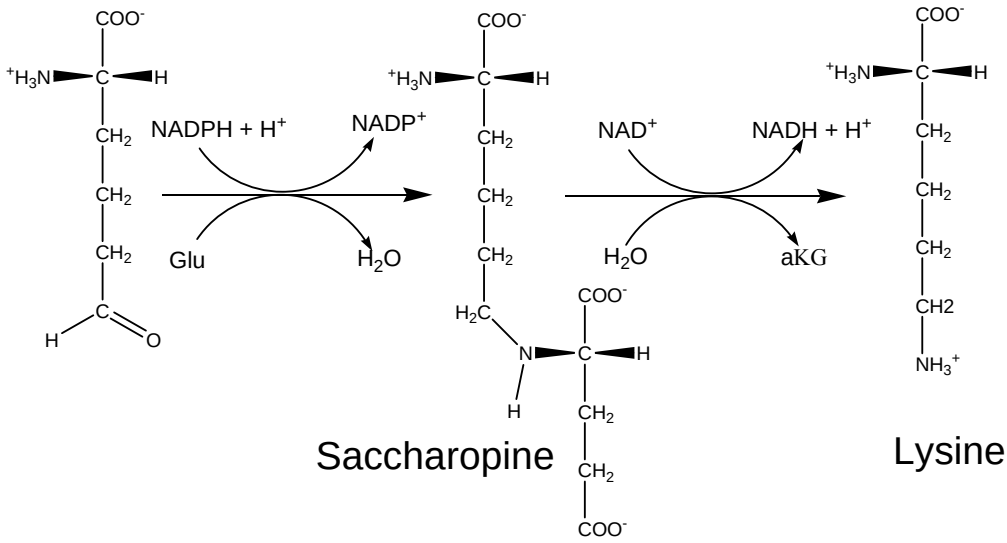
Data derived from: Therriault & Mehlman (1965) *Can. J. Biochem*. **43**, 1437-1443.

In a separate and unpublished experiment, two groups of rats raised at warm temperatures were transferred to a frigid environment. Shortly before the transfer, one group was fed carnitine. All of the carnitine-fed rats survived the transfer while none of the unsupplemented rats survived.

A. (6 Points) What are the major implications of these experiments? (Implications are different than results.) Explain.

B. (4 Points) Generate two substantive questions relating to these experiments, the results, or the implications.

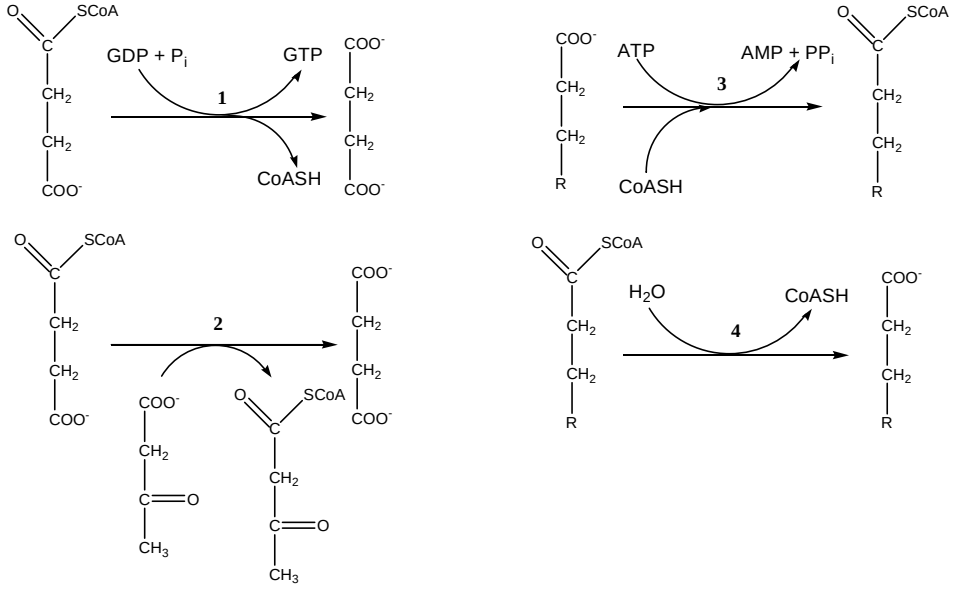
4. (10 Points Total) The formation of saccharopine and its conversion to lysine in fungi is shown below. Both reactions involve oxidation-reduction with pyridine nucleotide coenzymes.



A. (5 Points) Explain the metabolic logic that rationalizes the use of NADP in the first step and NAD in the second.

B. (5 Points) Pick the first **or** second reaction and show with chemical structures what is being oxidized or reduced and how it is formed or broken down.

5. (12 Points Total) Below are four reactions involving thioesters and their corresponding carboxylic acids. Reaction 1 is found in the TCA cycle and is an example of a substrate-level phosphorylation. Reaction 2 occurs in mitochondria and shows how acetoacetate, a ketone body, is converted to acetoacetyl CoA in tissues where ketone bodies are "burned". Reaction 3 is the reaction that converts fatty acids to their corresponding thioesters. Reaction 4 shows the hydrolysis of a thioester to its acid and free CoASH. All reactions are shown in the direction that carbon would flow metabolically.



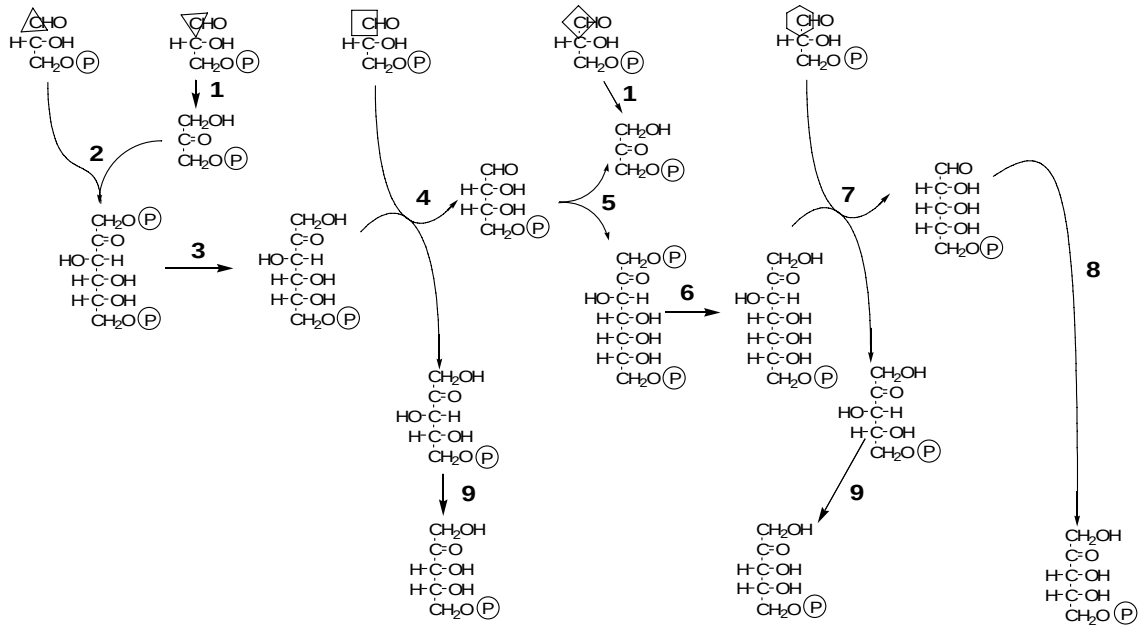
A. (2 Points) Which reaction above has an equilibrium constant closest to 1?

B. (2 Points) Which reaction above would be metabolically wasteful?

C. (4 Points) From a chemical perspective, the energetics of the isolated Reactions 1 and 3 are not very different other than their directions are reversed. From a metabolic perspective, explain circumstances where reactions like Reaction 3 that produce PP_i would be preferred over reactions like Reaction 1 (in reverse) that would produce P_i.

D. (4 Points) In ketone body metabolism, what would be a reasonable explanation for why reaction 2 is used rather than the type in reaction 3?

6. (15 Points) The figure below depicts the conversion of five molecules of glyceraldehyde-3-P into three molecules of ribulose-5-P.



a. (5 Points) Starting with [1-^{14}C] glyceraldehyde-3-P, trace the five ^{14}C-labeled carbon atoms through part of one turn of the cycle into the five carbons of ribulose-5-P. Maintain the identifying shapes associated with each of the five carbon atoms.

b. (3 Points) Although the diagram does not indicate easily reversible reactions, most of the reactions are reversible. Mark with an "X" through the number of the reaction or reactions that would have the largest -ΔG°′?

c. (2 Points) Aside from enzyme reactions 1 and 9, which are represented twice, all of the other reactions represent distinct enzymes. What other reaction is chemically most similar to reaction 1?

d. (5 Points) It takes 6 turns of the Calvin Cycle to fix six carbon atoms—enough to make one glucose unit in a starch molecule. On the diagram above, indicate with a dashed arrow where carbon would be removed from the cycle on its way to starch synthesis. At the end of your dashed arrow, draw the structure of the first intermediate on the way to starch.

Part IV Essay Questions-<u>Answer *only one* of the two Questions</u>

Writing reflects how you think. Among the "right answers" I will read for the following questions, some will be better than others because they show greater depth of understanding, avoid extraneous or inaccurate information, provide a more logical structure, use appropriate examples, and choose words with precision. Better quality answers will receive higher marks. Therefore organize your thoughts before you write. Strive to write not that you may be understood, but rather that you cannot possibly be misunderstood. Stream of consciousness answers are rarely well organized or clearly presented.

7. (10 Points) There are a large number of inherited metabolic diseases, none of which are particularly common. What are the various analytical strategies for detecting and identifying metabolic diseases? If you were in charge of laboratory screening newborn children for metabolic diseases, what strategy or strategies would most effective in identifying the metabolic block?

8. (10 Points) (Do not answer if you have answered question 7 for credit.) Parents of children with metabolic disease are heterozygous carriers of the disease and yet are phenotypically normal. In terms of flux analysis, explain the lack of parental symptoms.