CHEM-643 Biochemistry Name _____
Final Examination
3:30 – 6:30 PM, Wednesday, 14 December 2005
Dr. H. White - Instructor

There are 11 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 is an **open-notes examination**. You may refer to your assignments and your lecture notes, but not textbooks. You may also refer to the metabolic pathway sheets available from the course website.

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 and is not in your text; however, the questions can be answered by applying basic principles 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. You may use the backs of pages, if you need more space.

The maximum possible score is 113. Graded Exams can be picked up Friday after 3 pm.

Exam Statistics: Class Range _37-101__ Class Mean _69.5__

Your Score _____ Your Rank in Class _____ out of 22

Course Grade _____

 Name _____

Part I - Short Answer Questions (1 point each)

_____ 1. Class of enzymes that use ATP to phosphorylate a substrate.

_____ 2. Class of enzymes that use NAD in redox reactions.

_____ 3. Class of enzymes associated with biotin as a cofactor.

_____ 4. Class of enzymes associated with S-adenosylmethionine as a cofactor.

_____ 5. Lipases, proteases, and nucleases involve reaction with ____?

_____ 6. Lysine is to Ornithine as Glutamine is to _____?

_____ 7. Tyrosine is to Phenylalanine as Serine is to _____?

_____ 8. PLP is to Vitamin B_6 as NAD is to _____?

_____ 9. Cellulose is to Glucose as Starch is to _____?

_____ 10. Creatine is to humans as Arginine is to _____?

_____ 11. Compound that reacts first with CO_2 in a C_4 plant.

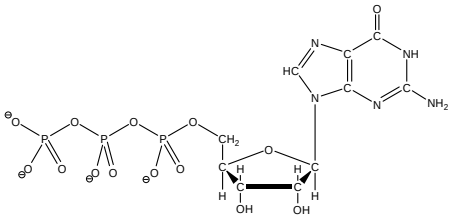
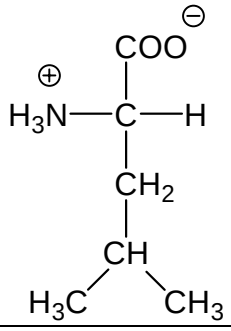
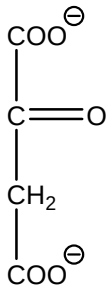
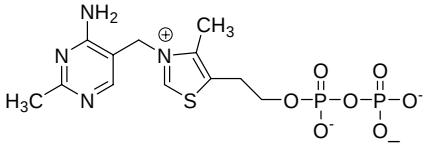
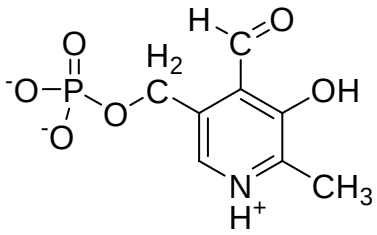
_____ 12. Primary source of ^{14}C in the atmosphere today.

_____ 13. Biological substance made out of hydroxyapatite, $Ca_5(PO_4)_3OH$.

 Name _____

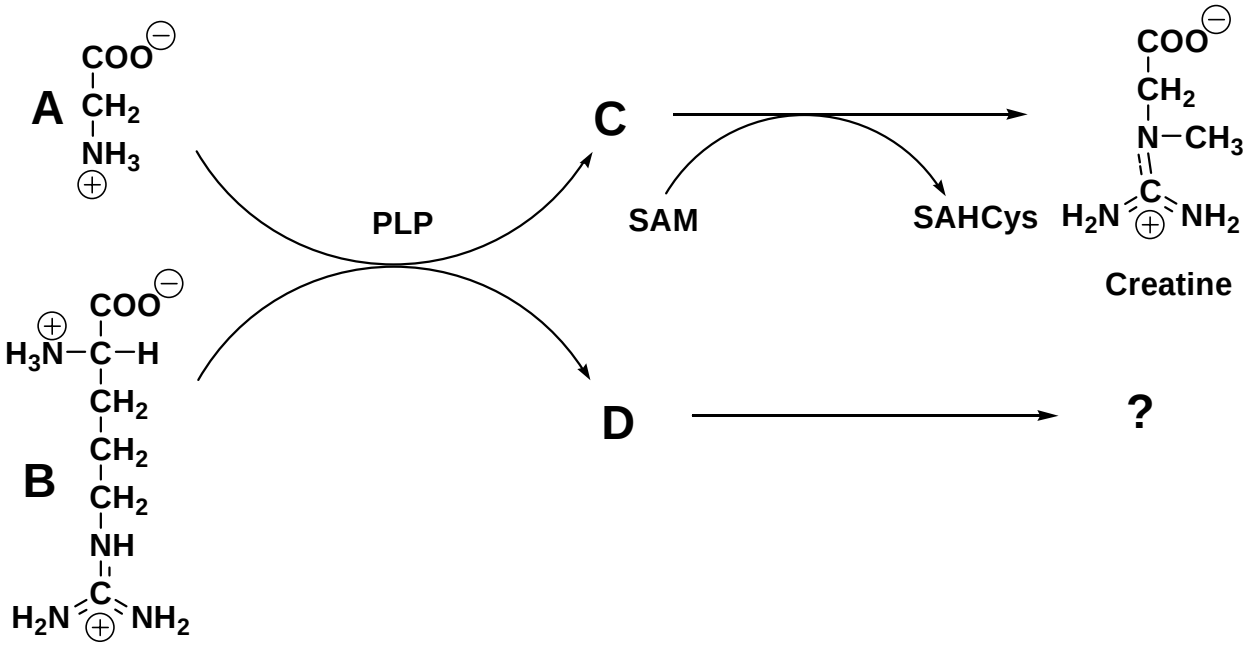
_____ 14. Expected $\delta^{13}C$ value for carbonate in Delaware's state fossil.

15-20 Identify the structures shown.

15 	16 	17 
18 	19 	20 $CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^-$

Part II Problems:

1. (10 Points) Our bodies are perfectly capable of synthesizing creatine from compounds you know.



On the diagram above:
a. (2 points) Provide the names for A and B.
b. (2 points) Provide the structure of C
c. (3 point) Provide the name and structure for D.
d. (3 points) What would be the fate of D?

2. (10 Points) Steele (1952) fed a mouse almost 0.5 mCi of ^{14}C-sugar for a short time and then "sacrificed" it three days later (Table 1). Proteins from the mouse were isolated and hydrolyzed into constituent amino acids. After separation by chromatography, the amino acids were quantified and their radioactivity measured. Eagle (1955) studied the amino acid requirements of mouse fibroblast cells in tissue culture by comparing cell growth when one amino acid was missing to growth with all other amino acids present (Table 2). When there was no cell growth, the ratio of cells at the beginning and the end of the experiment would be 1.0. Thus, if cells were dying, the values would be less than 1.0.

Table 1. Specific radioactivity of amino acids biosynthesized from ^{14}C sucrose in three days by a mouse.

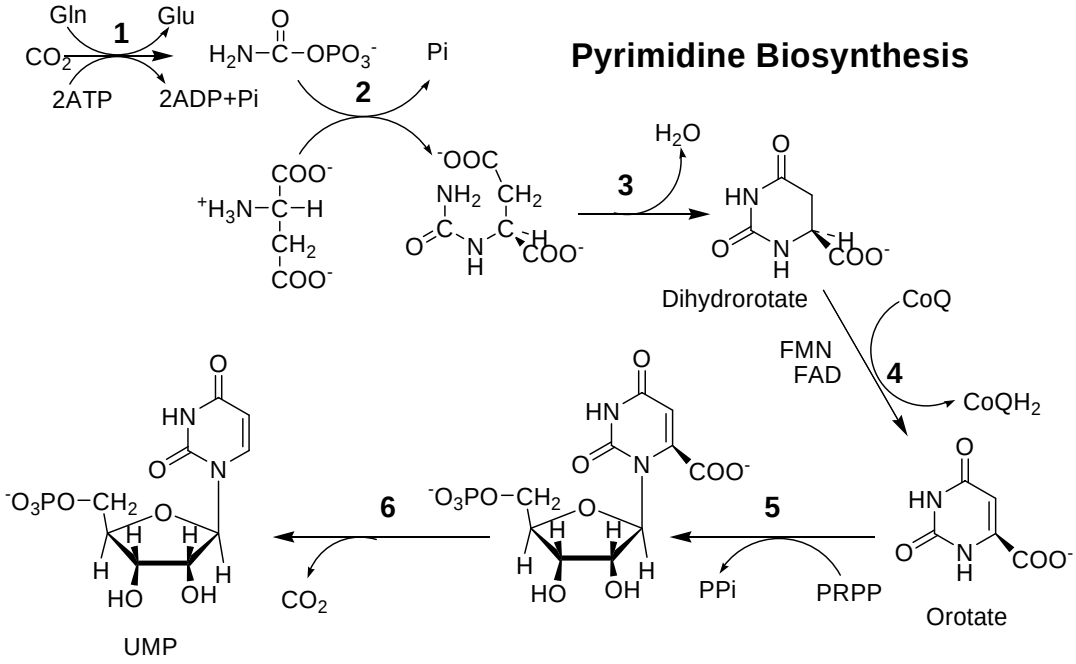
Amino Acid	nCi/mgC	Amino Acid	nCi/mgC	Amino Acid	nCi/mgC	Amino Acid	nCi/mgC
Glu	19.0 ± 1.9	Thr	0.09 ± 0.02	Val	0.02 ± 0.01	Lys	0.0 ± 0.02
Asp	15.8 ± 0.9	Ser	8.4 ± 0.1	Phe	0.02 ± 0.07	His	0.07 ± 0.08
Ala	26.5 ± 3.3	Gly	5.1 ± 0.2	Tyr	0.0 ± 0.07	Cys	3.3 ± 0.3
Pro	3.1 ± 0.1	Ile	0.06 ± 0.05	Arg	3.0 ± 0.2	Met	1.03 ± 0.06

Table 2. Growth of mouse fibroblasts (L-cells) in media lacking the indicated amino acid.

Amino Acid	Cell Growth	Amino Acid	Cell Growth	Amino Acid	Cell Growth	Amino Acid	Cell Growth
Glu	3.6 - 4.5	Thr	0.2	Val	0.06 - 0.2	Lys	0.2 - 0.5
Asp	3.6 - 6.1	Ser	2.5 - 2.8	Phe	0.3 - 0.4	His	0.3 - 0.4
Ala	2.2 - 2.6	Gly	3.6 - 3.7	Tyr	0.06 - 0.2	Cys	0.1 - 0.3
Pro	2.4 - 6.8	Ile	0.1 - 0.4	Arg	0.4 - 0.9	Met	0.3 - 0.4

Neither Arginine nor Methionine support mouse fibroblast growth, yet both incorporate some radioactivity from labeled sugar. Select ***either*** Arginine or Methionine and explain how labeling occurs in each case. Provide diagrams for support. Provide quantitative justification as appropriate.

3. (13 Points) Arginine is a non-essential amino acid for adults but not for children. The pattern appears to be true for rats as well. Milner and Visek [Nature 245, 211 (1973)] observed that rats fed a diet balanced in amino acids excreted very small amounts of orotate, an intermediate in the pyrimidine biosynthetic pathway. However, orotate excretion increased over 200-fold in young rats deprived of arginine The pyrimidine biosynthetic pathway is shown below.



A. (3 points) Reaction 3 involves a dehydration but does not use ATP. Explain.

B. (3 points) In bacteria, reaction 4 is specific for NAD, not NADP. Explain.

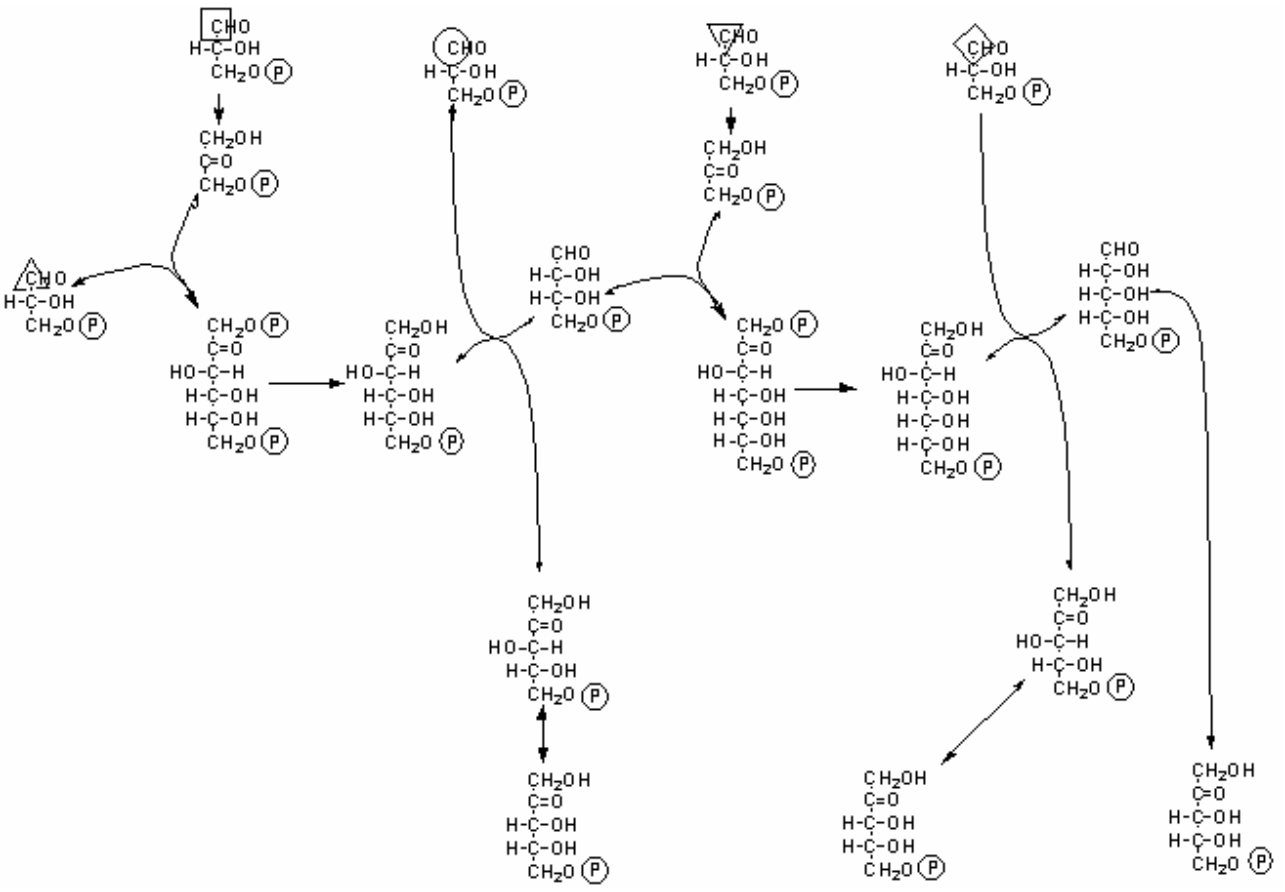
C. (3 points) Which enzyme reaction would you predict to regulate the flux in this pathway? Why?

D. (4 point) Suggest a reasonable explanation for the overproduction of orotate in young rats deprived of arginine.

4. (10 pts) Consider an algal suspension exposed to $^{14}CO_2$. The first labeled compound formed in the Calvin Cycle is [1-^{14}C]-3-phosphoglyceric acid. This goes on to form carbonyl-labeled glyceraldehyde-3-phosphate. Below is a diagram of the "carbon scramble" of the Calvin Cycle, with the carbonyl carbon of each of five GAPs identified distinctively with a geometric shape.

   a. (8 points) Using the same labels, trace the path of each carbon through the pathway to ribulose-5-phosphate.

   b. (2 Points) If a sample of ribulose-5-phosphate were isolated at this point, what proportion of the ^{14}C would be on each carbon?



C-1 _____% C-2 _____% C-3 _____% C-4 _____% C-5 _____%

5. (15 points) On the last day of class you and your group were asked to diagnose the metabolic defect in a six-year old child who became severely hypoglycemic and comatose upon fasting for 22 hours. Analysis of his blood after ingestion of medium-chain triglycerides showed large increases in the plasma levels of C_{10}, C_8, and C_6, but ***not*** C_4, 3-hydroxy fatty acids. HMGCoA Synthase, HMGCoA Lyase, and β-Hydroxybutyrate Dehydrogenase were considered as possibly defective. Based on the identified defect [NEJM 337:1203-7 (1997)], one could predict that leucine catabolism would be normal in this boy.
    a. (10 points) Which enzyme is defective? How does the information about leucine catabolism eliminate the other possibilities? Your answer must include an informative metabolic diagram that supports your argument.

    b. (5 points) Given the accumulation of C_{10}, C_8, and C_6 3-hydroxy fatty acids, one might expect that the C_4 3-hydroxy fatty acid (β-hydroxybutyrate) was also being produced but not in the usual way. What is this alternate way to form β-hydroxybutyrate? Why wasn't it detected?

6. (10 Points) Intermediary metabolism deals primarily on the flow of carbon-containing compounds through various enzyme-catalyzed pathways in a living organism. However, one can also think of the flow of other elements through these pathways. Imagine a phosphorus atom in a phosphate ion just consumed in a soft drink. Describe clearly a path that phosphorus could take to end up in DNA. Feel free to draw a diagram to support your narrative.

7. (10 pts) A forensic chemist consults with you about a potential criminal case in which a health food chain had been selling vitamin C advertised as "100% natural", "from strawberries". The criminal authorities suspected that the vitamin C being sold was in fact inexpensive vitamin C synthesized chemically in several steps from abundant corn sugar. A pure sample of the vitamin C is available.
    a. (6 points) Suggest a way to determine the source of the vitamin C and indicate the result you would expect if the sample were not from strawberries.
    b. (4 points) Would there be any difference in the way vitamin C would be metabolized by your body if its source were strawberries versus chemically synthesized from corn sugar? Explain.

8. (15 Points) Polly Glew was pterin her hair out. She had been assigned the job of converting her group's roughed out folate concept map into a colorful computerized document. Unfortunately, as she was walking back from the group's late-night session, a gust of wind blew off most of the Post It® notes into the darkness so that all she had was a poster sheet with words and arrows connecting mostly blank spaces. Please help Polly by filling in the terms and concepts that she needs to complete her folate concept map on the following page.

Overview of Folate Metabolism in Sickness and Health