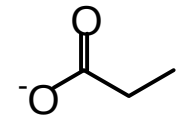
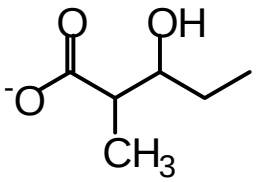
Chemistry 5.07
Problem Set 10 2013

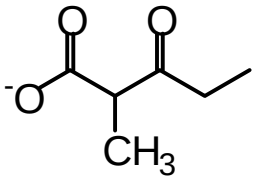
Problem 1. Many of our antibiotics are produced from soil microorganisms by a pathway called polyketide biosynthesis. A bacterium was isolated from the Thai rainforest that produces Compounds A, B and C, which are the precursors to important antibiotics. [This pathway is similar to one described on a PowerPoint presentation given in class.] The bacterium uses propionyl CoA (derived from propionate) instead of acetyl CoA. Instead of acetyl CoA carboxylase (which makes malonyl CoA), it uses propionyl CoA carboxylase to start its fatty acid biosynthesis pathway. Based upon what you know of the general principles of fatty acid biosynthesis, please show how compounds A, B and C are made. Start your synthesis with the formation of the appropriate –CoA ester. If cofactors are involved, please indicate which ones.



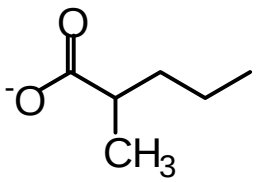
Propionate



Compound A



Compound B



Compound C

Problem 2. A well fed rat is given an injection of ^{14}C-acetate with the radiolabel in the -CH_3 group. Two hours later, the rat is sacrificed and triacylglycerides (TAGs) and glycogen are analyzed for the distribution of radioactivity in each.

- **a.** Would you expect the absolute levels of radioactivity in glycogen and TAGs to be similar or different? If different, which would have more? Explain.
- **b.** Draw the structure of a TAG and show which carbon(s) would be most heavily radiolabeled.
- **c.** You repeat the experiment with another well fed rat, but this time you inject ^{14}C-labeled glutamate with the label on the β-carbon. Show the label distribution in TAGs and glycogen and justify your answer.

Problem 3. Gluconeogenesis involves the synthesis of glucose from non-carbohydrate precursors. The organs most active from the perspective of gluconeogenesis are the liver and the kidney, which supply glucose to the organs that cannot synthesize it, yet have a strict need for glucose as an energy source.

- **a.** Gluconeogenesis requires several equilibrium steps of glycolysis to run in the reverse direction. Write out in detail the mechanism of the conversion of GAP and DHAP to F1,6BP. Is this reaction under standard conditions spontaneous in the direction of gluconeogenesis? [Look for free energy relationships in the book.]
- **b.** Similarly, write out the detailed mechanism of how GAPDH catalyzes the conversion of 1,3BPG to GAP. Show how its cofactor participates in the reaction. Is this reaction

spontaneous under standard conditions? [Again the book may contain some helpful information.]

c. Glycolysis as a ten-step pathway from glucose to pyruvate is spontaneous. Is gluconeogenesis spontaneous under standard conditions (i.e., is the $\Delta G^{o'}$ for the pathway negative)? Please explain.

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