Fall 00
Exam 3
Key

Name Key

(1) For each of the terms below, write a complete reaction (structures not necessary) from central metabolism that is relevant to the term.

(a) cis-enediolate reaction intermediate

glc-6-P → frc-6-P

(b) Schiff base reaction intermediate

Frc 1,6-di P → DHAP + Glyceraldehyde-3-P

(c) discrimination of prochiral substrate groups

citrate → isocitrate

(d) homolytic bond cleavage

Methyl-malonyl CoA → succinyl-CoA

(e) phosphorylated enzyme intermediate

2-P-glycerate → 3-P-glycerate

(2) Match the enzyme with the appropriate cofactor(s). Note: cofactors may be used more than once, or not at all. Some enzymes may have more than one type of cofactor or none of the listed cofactors.

(a) Biotin
(b) Thiamine pyrophosphate
(c) NAD+
(d) NADP+
(e) Cobalamin
(f) Lipoic acid
(g) FAD
(h) Zinc

Enzyme	Cofactor(s)
alpha-ketoglutarate dehydrogenase	c f b g
Alcohol dehydrogenase	h (c)
aldolase	
Glucose-6-phosphate dehydrogenase	d
~~Pyruvate carboxylase~~	
Acyl-CoA dehydrogenase	g
Propionyl-CoA carboxylase	a
Methylmalonyl-CoA mutase	e

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(4) 2 points each.
(a) The first reaction in glycolysis that results in the formation of an energy-rich compound (i.e., a compound whose hydrolysis has a highly negative $\Delta G^{\circ\prime}$) is catalyzed by what enzyme?

glyceraldehyde-3-phosphate DH

(b) Which enzyme catalyzes the committed step of glycolysis ?

phosphofructokinase

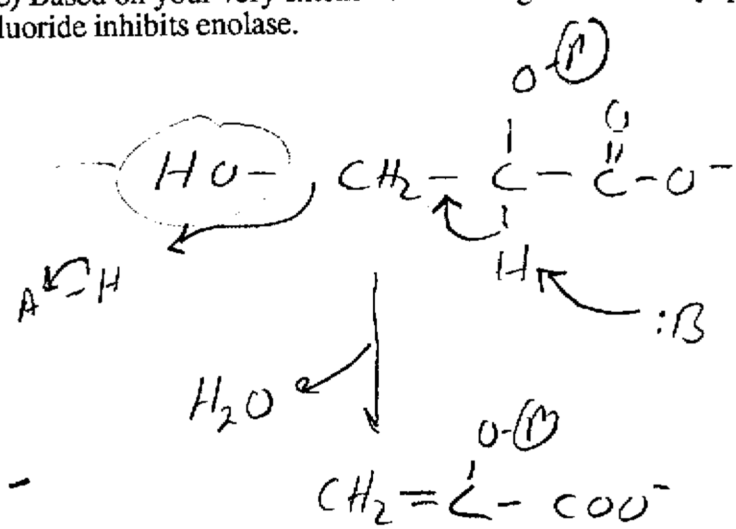
(c) Which enzyme of the citric acid cycle catalyzes substrate level phosphoylation?

succinyl-CoA synthetase

(d) Inorganic fluoride inhibits enolase (AAAAAAAUUUUGH- STOP WATER FLUORIDATION!!). In an anaerobic system that is metabolizing glucose as a substrate, which one compound would you expect to increase in concentration following the addition of fluoride?

2-(P)-glycerate

(e) Based on your very extensive knowledge of chemistry, provide a plausible explanation for why fluoride inhibits enolase.



looks like F⁻ in size charge

I'm guessing F⁻ behaves as an analog of OH⁻; ie it is a product-like inhibitor of the reaction

<u>Note</u> - any reasonable answer is OK!

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(5)
(a) (2 pts) What is the name given collectively to the compounds acetoacetate, ß-hydroxybutyrate and acetone?

Ketone bodies

(b) (2 pts) Name two specific conditions where these compounds might accumulate in the blood stream to higher than normal levels.

1) starvation

2) diabetes

(c)(2 pts) Under the conditions of (b), in which organ are the compounds produced in greatest amount?

liver

(d) (4 pts) Outline the reactions that lead to the production of these compounds. Use either names or structures for the metabolites.

AcCoA + AcCoA

↓ → HSCoA

AcAc-CoA

↓ Ac-CoA → HSCoA

HMG-CoA

↓ → AcCoA

acetoacetate → CO_2 → acetone

↓ NADH → NAD^+

ß-HB

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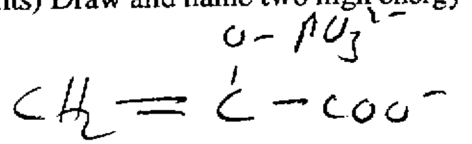
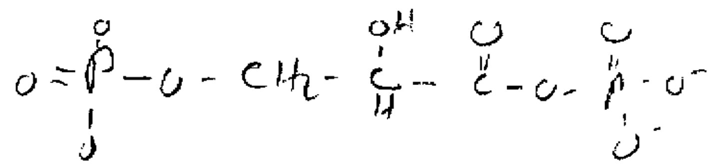
(6)
(a) (2 points) In one sentence, define "high energy compound".

A cmpd whose hydrolysis releases a large amt. of free Σ

(b) (4 points) Draw and name two high energy compounds from central metabolism other than ATP.



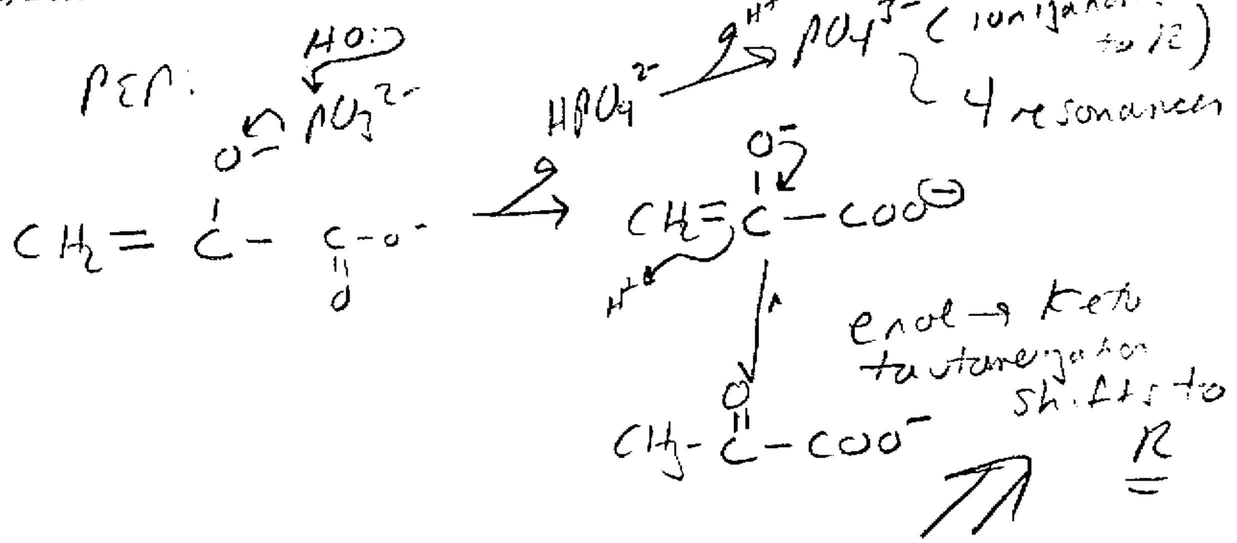
Phosphoenolpyruvate



1,3-DPG

etc, etc

(c) (4 points) Describe the features of one of the molecules from (b) that makes it a high energy compound.



major factor

Common themes-
charge separation
→ ionization of products
⇒ tautomerization
→ resonance stab.

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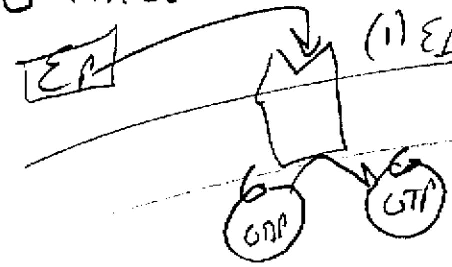
(7) Describe the series of events involved in the allosteric and hormonally-controlled mobilization of stored glycogen for use as an energy source (i.e. describe what happens from the time of hormone production and release from the adrenal gland). either muscle or liver

Muscle Allosteric regulation - AMP binds to an allosteric site on phosphorylase b, the dephosphorylated "inactive" form of glycogen phosphorylase. This causes partial activation of phosphorylase b, resulting in some glycogen breakdown

- For hormonal control, G.P.b gets phosphorylated to G.P.a - which is the most active form this occurs by an amplification cascade as outlined below:



(1) Epinephrine binds to extracellular domain of receptor protein

(2) Ep. binding causes conf. change in G protein that causes GDP dissociation & GTP binding

(3) Activated G protein activates adenylate cyclase

(4) adenylate cyclase makes cAMP

ATP → cAMP + PPi

(5) cAMP activates protein kinase

$PK_i + cAMP \rightarrow PK_a \cdot cAMP$

(6) PKa phosphorylates phosphorylase kinase, turning it on

(7) phosphorylase kinase phosphorylates glycogen phosphorylase, thereby activating it.

8) glycogen phosphorylase breaks down glycogen

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(8) Alcohol dehydrogenase catalyzes the following reversible reaction:

Acetaldehyde + NADH + H^+ → Ethanol + NAD^+

Use the following information to answer the questions below:

Acetaldehyde + $2H^+$ + $2e^-$ → ethanol	$E'^\circ = -0.20$ V
NAD^+ + H^+ + $2e^-$ → NADH	$E'^\circ = -0.32$ V

For thermodynamic and electrochemical equations and constants see Page 1.

+4 (a) Calculate $\Delta G'^\circ$ for the reaction as written. Show your work.
+2 (b) Given your answer to (a), what is the $\Delta G'^\circ$ for the reaction occurring in the reverse direction?
+2 (c) Which reaction (forward or reverse) will tend to occur spontaneously under standard conditions?
+2 (d) In the cell, the reaction actually proceeds in the direction that has a positive $\Delta G'^\circ$. Explain how this could be possible.

a)
$$Ac + \cancel{2e} \rightarrow EtOH \quad -0.2$$
$$NADH \rightarrow NAD^+ + \cancel{2e} \quad +0.32$$
$$+0.12\text{ V}$$

$$\Delta G^{\circ\prime} = \cancel{-RT\ln K = -(8.314\,\tfrac{J}{mol\,K})(298K)}$$
$$= -nF\mathcal{E}^\circ = -(2)\left(96.5\,\tfrac{kJ}{\cancel{V\,mol}}\right)(0.12\text{ V})$$
$$= -23.2\text{ kJ/mol}$$

b) +23.2 kJ/mol

c) Forward

d) concentrations of substrates & reactants are maintained at non-standard concentrations, such that $\Delta G'$ is (−), i.e., [P]<[S]