Department of Chemistry
Cumulative Examinations
April 26, 2008

You may choose to answer any exam from any area covered in the examination booklet. Each exam may contain multiple parts. You may answer more than one exam but each exam is scored separately and is treated as an individual examination result. Thus, answering parts of two exams with a score of 50% *would not* yield a 100% grade for this cumulative exam. Instead you would receive 50% on each examination attempted.

This booklet contains ***five*** examinations.

1) Analytical Cumulative Examination, Pages 1-2
2) Biochemistry Cumulative Examination, Page 3
3) Inorganic Cumulative Examination, Page 4
4) Organic Cumulative Examination, Pages 5-6
5) Physical Cumulative Examination, Pages 7-8

On your examination booklet:

1) Print your student ID number.
2) Print the Exam Booklet number.
3) Print the question number you are answering.
4) Print the Exam Date.

Do not write your name anywhere on the examination booklet. Each exam will be scored anonymously. If you attempt more than one exam, *you must use a separate examination booklet for each examination*.

When you complete the examination, return the examination and your answer booklet to the proctor. Exam results will be posted on bulletin board #2B on the north side of the hall near BRWN 2124.

PURDUE
UNIVERSITY

CUMULATIVE EXAMINATION IN ANALYTICAL CHEMISTRY

Apr 26, 2008

It is expected that the answer should contain several succinct straight-to-the-point sentences. If you feel like elaborating, please stay within an 8 sentence limit anyway. All questions carry the same weight. After each individual exam is graded, two questions with the lowest score will be dropped. In other words, you can completely miss two questions and still earn a perfect total score.

1. A (non-covalent) protein complex involving toxin A and antitoxin B is studied as a part of a drug development program. As a first step, the binding interface needs to be 'mapped out' (i.e. the portions of the polypeptide chain that form the binding interface need to be identified). For this purpose one can employ a mass spectrometry experiment which relies on H/D exchange of amide protons. Describe, in general terms, the concept of such an experiment.

2. A (non-covalent) protein complex involving toxin A and antitoxin B is studied as a part of a drug development program. As a first step, the binding interface needs to be 'mapped out'. For this purpose one can employ a popular NMR experiment, which relies on the chemical shift information (the so-called 'chemical shift mapping'). Describe, in general terms, the concept of such an experiment.

3. A (non-covalent) protein complex involving toxin A and antitoxin B is studied as a part of a drug development program. To determine the binding affinity, a titration is carried out and the inherent Trp fluorescence is measured through the course of the titration. How can these data be used to determine the binding affinity (i.e. the dissociation constant K_d)?

Footnote: for simplicity, assume that A contains a single Trp residue, while B contains none.

4. A (non-covalent) protein complex involving toxin A and antitoxin B is studied as a part of a drug development program. An ultimate characterization of the complex is offered by the X-ray crystallographic structure. As it turns out, all but a few crystallographic structures deposited in the Protein Data Bank do not contain proton coordinates (only heavy atom coordinates). What is the fundamental reason for this?

5. A (non-covalent) protein complex involving toxin A and antitoxin B is studied as a part of a drug development program. To confirm the purity of the sample, an SDS-PAGE gel has been used. What bands may one expect to see in this gel (monomers of A and B, complex A·B, dimers, trimers, higher-order oligomers of A, B, or A·B)?

6. Protein A has been extracted from a biological tissue and purified using liquid chromatography (LC). In operating an LC column it is important to maintain the optimal flow rate. If the flow is too slow or too fast, the outcome of the separation procedure can be unsatisfactory. Why it is not a good idea to run the column with an exceedingly low flow rate?

7. Protein A has been extracted from a biological tissue and purified using liquid chromatography (LC). In operating an LC column it is important to maintain the optimal flow rate. If the flow is too slow or too fast, the outcome of the separation procedure can be unsatisfactory. Why it is not a good idea to run the column with an exceedingly high flow rate?

8. The ^{1}H NMR spectrum of a certain protein sample recorded with 16 scans has a signal-to-noise ratio S/N=5.0. How many scans are needed to produce a spectrum with S/N=20.0?

9. Certain small protein contains a sole Glu residue. For this specific residue, the pK_a of the side-chain carboxylic acid is pK_a=4.3. Suppose that the protein is dissolved in a buffered solution, with pH carefully adjusted to pH=4.3 (pH=pK_a). Under these conditions, the Glu side chain appears as a mixture of protonated (glutamic acid, –COOH) and deprotonated (glutamate, $-COO^-$) species. What is the proportion of these two species?

10. A series of i=1, 2, ..., N samples with variable concentration of ferrocene were used to measure optical absorption. The resulting experimental data (concentrations X_i, absorbances Y_i) were fitted, in a least-square sense, with the equation $y = x + \alpha$. The procedure involved a single fitting parameter, α (intercept). Please, derive the analytical expression for α which ensures the best fit quality.

Biochemistry Cume Examination
April 26, 2008

Post-translational modifications are often involved in the mechanism of diseases.

1. Why would that be, i.e. how could post-translational modifications play a role in disease progression in general?

2. Describe two diseases (other than the example given below) in which a change in the degree of post-translational modification (PTM) plays a role and explain how the PTM contributes to disease mechanism.

3. How would you recognize a PTM in a protein? One example is sufficient.

4. PTM driven diseases involve changes in the concentration a PTM in a number of ways. One is with an increase in the relative amount of the PTM modified form of a protein while the total amount of all forms of the protein remains constant. In another, the ratio of the PTM and total amount of parent protein remain the same while the amount of both proteins increases. Describe a quantification procedure that would differentiate between these two cases.

5. Splice variant forms of proteins in which a PTM is part of the variable region often play a role in cancer. This is particularly true of glycoproteins on the outside of tumor cells. Explain how such splice variant glycoproteins might impact metastasis.

INORGANIC CHEMISTRY CUMULATIVE EXAM
April 26, 2008

1. (a) Is hexachloroiridate(III), $IrCl_6^{3-}$, slow or fast to undergo substitution reactions in aqueous solutions? Give reasons for the kinetic behavior that you have assigned.

(b) The outer-sphere oxidation of $IrCl_6^{3-}$ by ozone (O_3) has a second-order rate constant of $1.7 \times 10^4\ M^{-1}s^{-1}$ at 25.0 °C. What are the immediate products of the reaction?

(c) What experimental techniques are needed to study this reaction?

(d) The reduction potential for $[IrCl_6^{2-}]$ / $[IrCl_6^{3-}]$ is 0.867 V and its self-exchange rate constant is $2.3 \times 10^5\ M^{-1}s^{-1}$. Write the chemical equation for the self-exchange reaction.

(e) The one-electron reduction potential for O_3 is 1.02 V. Calculate a self-exchange rate constant for the O_3/O_3^- reaction (k_{22}) from its kinetic behavior with $IrCl_6^{2-}$. Assume the f_{12} term is unity. [Useful constants: log K = 16.9 E°.]

2. Values for water substitution rate constants of $Cr(H_2O)_6^{2+}$ and $Cr(H_2O)_6^{3+}$ differ by factor of 10^{15}. On the other hand the corresponding k^{M-H_2O} values for $V(H_2O)_6^{2+}$ and $V(H_2O)_6^{3+}$ differ by only a factor of 10.

(a) Give the relative substitution reactivity of these four aquo ions from the most labile to the most inert.

(b) For each of these four aquo ions, outline the various factors that affect their water substitution rate constants (k^{M-H_2O}).

(c) Explain <u>why</u> the factors in (b) cause the k^{M-H_2O} values to vary so greatly.

3. (a) What is the mathematical expression for the Boltzmann Distribution Law?

(b) The transition state theory makes use of the terms: $K^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$.

1. How are these terms related to each other?

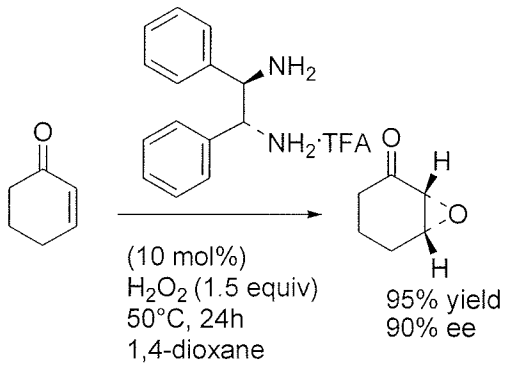
2. In what critical way do these terms differ from K, $\Delta G°$, and $\Delta S°$?

3. Give the mathematical expression for the rate constant in terms of the activation enthalpy and activation entropy.

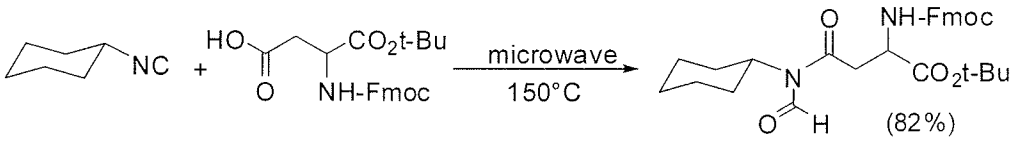
Organic Division Exam
April 2008

JACS **2008** (ASAP)

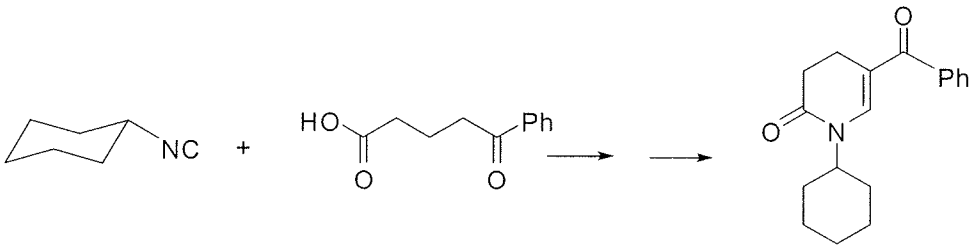
1. List and co-workers developed a catalytic asymmetric epoxidation of cyclic enone to provide the following epoxy ketone in excellent enantioselectivity. Propose a plausible mechanism for this enantioselective reaction.



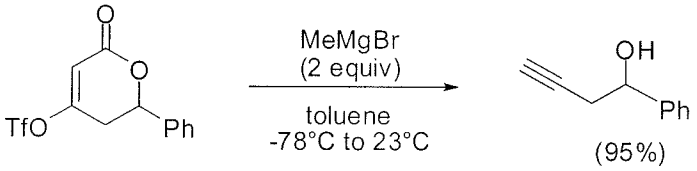
2. *JACS* (**2008**) *130*, 5446
   Describe Passerini reaction with an example. Recently, Danishefsky and Li described a variant of Passerini chemistry to form an asparagine derivative show below. Propose a mechanism for this transformation.



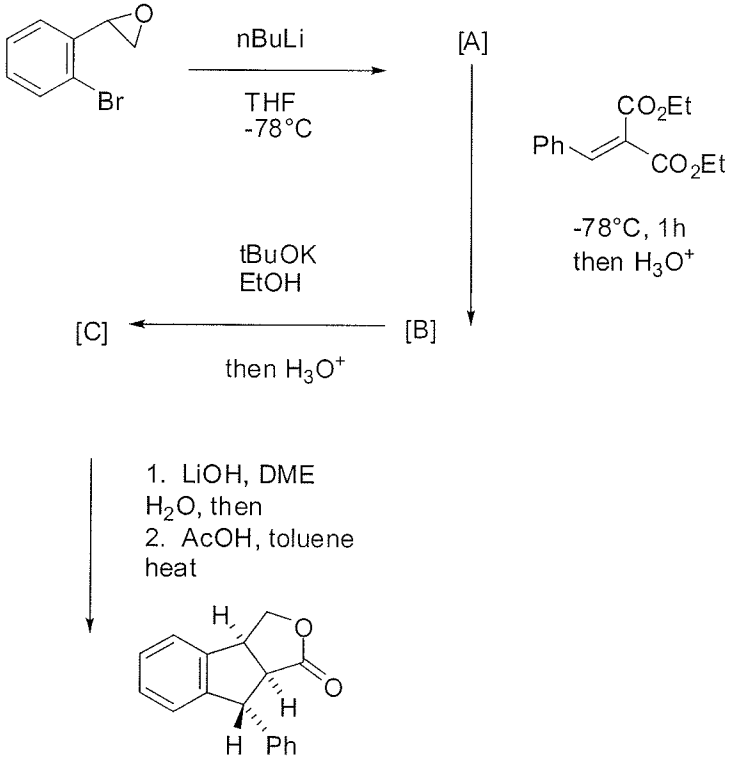
3. *JACS* (**2008**), *130*, 5447
   Based upon above chemistry, how would you carry out the synthesis of dihydropyridone derivative using the keto acid and isonitrile show below?



4. *JACS* (**2008**), 130, 5050
In an alternative pathway, Dudley and Tummatorn have demonstrated a tandem nucleophilic addition/C—C bond cleavage reaction of a cyclic vinylogous acyl triflate to provide the following homopropargyl alcohol. Show a stepwise mechanism of this transformation.



5. *Org. Lett.* (**2008**), ASAP
Write down structures for A-C with appropriate stereochemistry.



Physical Chemistry

April 26, 2008

- (40) Consider the one-dimensional problem of a particle of mass m in a potential

$$V(x) = \infty \;\; for \;\; x < 0, \;\; V(x) = 0 \;\; for \;\; 0 \leq x \leq \alpha, \;\; and \;\; V(x) = V_0 \;\; for \;\; x > \alpha \quad (1)$$

The bound state energies are given by the equation

$$tan\frac{\sqrt{2mE\alpha}}{\hbar} = -\sqrt{\frac{E}{V_0 - E}} \quad (2)$$

Without solving the Schrodinger equation:

Sketch the lowest two eigenfunctions Ψ_0 and Ψ_1 and explain their behavior as a function of the variables α and V_0

1. (5) $\alpha = 0$
2. (20) $\alpha = 2a.u.$ $V_0 = 100a.u.$ (a.u.=atomic units)
3. (5) $\alpha = \infty$
4. (10) What happens to the eigenvalues if you add the momentum operator, $p = -i\hbar\frac{d}{dx}$, as perturbation (the new Hamiltonian is $H = H_0 + \lambda p$, where H_0 is the original Hamiltonian with the above potential and λ is the strength of the perturbation)

- (20) Write down the Hamiltonian for the H^- anion, explain the physical meaning of each term. Can you suggest a good variational wave function for the ground state $1s^2$, explain your results.

- (40) Consider the following crude one-dimensional model for chemical bonding in H_2^+. Initially, the electron is placed in either potential box, each having infinite walls and the width $L/2$. These represent two protons. Then, the boxes are united to form a single box of width L with an electron, which represent the molecule H_2^+.

  1. (10) Define chemical bonding and calculate the energy for the reaction using this crude model. Can you suggest a better model for this reaction, explain.
     For a particle in a box of length L, the energy levels are given by $E = \frac{n^2h^2}{8mL^2}$, n=1,2,3...
  2. (10) Sketch the potential energy of the electron along an axis passing through the protons.
  3. (5) Sketch the electron ground state wave function at equilibrium
  4. (5) What happens to the two lowest energy levels in the limit that the protons are moved far apart
  5. (10) Explain the Born-Oppenheimer approximation for molecular systems, when do you think this approximation will break down, give an example

Periodic Classification of the Elements

I A	II A	III B	IV B	V B	VI B	VII B	VIII			I B	II B	III A	IV A	V A	VI A	VII A	O
1 H 1.00797																	2 He 4.0026
3 Li 6.939	4 Be 9.0122											5 B 10.811	6 C 12.01115	7 N 14.0067	8 O 15.9994	9 F 18.9984	10 Ne 20.183
11 Na 22.9898	12 Mg 24.312											13 Al 26.9815	14 Si 28.086	15 P 30.9738	16 S 32.064	17 Cl 35.453	18 Ar 39.948
19 K 39.102	20 Ca 40.08	21 Sc 44.956	22 Ti 47.90	23 V 50.942	24 Cr 51.996	25 Mn 54.9380	26 Fe 55.847	27 Co 58.9332	28 Ni 58.71	29 Cu 63.54	30 Zn 65.37	31 Ga 69.72	32 Ge 72.59	33 As 74.9216	34 Se 78.96	35 Br 79.909	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.905	40 Zr 91.22	41 Nb 92.906	42 Mo 95.94	43 Tc (99)	44 Ru 101.07	45 Rh 102.903	46 Pd 106.4	47 Ag 107.870	48 Cd 112.40	49 In 114.82	50 Sn 118.69	51 Sb 121.75	52 Te 127.60	53 I 126.9044	54 Xe 131.30
55 Cs 132.905	56 Ba 137.34	57 La* 138.91	72 Hf 178.49	73 Ta 180.948	74 W 183.85	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.09	79 Au 196.967	80 Hg 200.59	81 Tl 204.37	82 Pb 207.19	83 Bi 208.980	84 Po (210)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	89 Ac† (227)															

*Lanthanides	58 Ce 140.12	59 Pr 140.907	60 Nd 144.24	61 Pm (147)	62 Sm 150.35	63 Eu 151.96	64 Gd 157.25	65 Tb 158.924	66 Dy 162.50	67 Ho 164.930	68 Er 167.26	69 Tm 168.934	70 Yb 173.04	71 Lu 174.97
†Actinides	90 Th 232.038	91 Pa (231)	92 U 238.03	93 Np (237)	94 Pu (242)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (249)	99 Es (254)	100 Fm (253)	101 Md (256)	102 No (256)	103 Lw (257)

(Numbers in parentheses are the mass numbers of the most stable isotopes.)