Department of Chemistry
Cumulative Examinations
March 28, 2009

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

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

Analytical Cumulative Examination March 28, 2009

This question asks you to predict the limits of an analytical system and what one will see when analytical limits are exceeded.

It is becoming common in LC-MS analysis (i.e. in proteomics and metabolomics) of complex biological extracts to examine mixtures with thousands to millions of components. LC is required as a separation component instead of using MS^n alone because matrix effects preclude the simultaneous ionization of all components in a very complex mixture. Mixture fractionation greatly increases ionization efficiency.

The peak capacity of high resolution LC columns is in the range of 300 to 500. This means in the separation of very complex mixtures, a thousand or more peptides, metabolites, or natural products could be in some chromatographic peaks and will be entering the mass spectrometer simultaneously. Each compound will be seen by the mass spectrometer in multiple isotopic forms, probably in multiple charge states ranging from one to perhaps three or four, and across a mass range from 200 to 2,000. Also, when more that 1/3 of the separation space in any dimension is filled, peaks begin to over-lap. Although the mass range may be 1,800 and you have a 1,000 component mixture, probability says some components will over-lap.

1. What would the resolving power of a mass spectrometer have to be that precludes mass over-lap in a 1000 component mixture when the mass range of the components in the mixture varies between 200 to 2,000. Assume in addition to M^+ there are isotope peaks (deuterium and carbon-13 containing compounds) at M^{+1}, and M^{+2} and charge states of +1, +2, and +3 following electrospray ionization.
2. Compounds in complex mixtures do not ionize equally well. How does this impact what you are seeing in the spectra from chromatographic peaks?
3. Assume you have a mass spectrometer that gives unit resolution, i.e. one atomic mass unit across this mass range and a biological extract varying in component concentration by a million fold. Which components would be seen in the mass spectra of LC peaks from very complex mixtures?
4. Summarize your conclusions of what happens when the analytical limits of an LC-MS system and predict how they impact the data one obtains.

BIOCHEMISTRY CUMULATIVE EXAM

3/28/09
Enzymes

1. (35 points)

   A. An enzyme that follows Michaelis-Menten kinetics has a V_{max} of 450 μmol/min/mg and a K_m of 0.5mM. What concentration of substrate would be required to ensure that the initial velocity is at least 80% of V_{max}?

   B. Write the modified versions of the Michaelis-Menten equation to describe Michaelis-Menten kinetics in the presence of:
      1. A competitive inhibitor
      2. An uncompetitive inhibitor
      3. A mixed inhibitor (non-competitive)

   C. If a competitive inhibitor with a K_i of 50μM is added to the experiment described in 1A at a concentration of 100 μM, what will be the observed rate of the reaction? The substrate concentration is 0.8 mM in this experiment.

2. (35 points)

   A. Draw a Lineweaver-Burk double reciprocal plot for the kinetics in the presence and absence of each of the following types of inhibitors.
      1. A competitive inhibitor
      2. An uncompetitive inhibitor
      3. A mixed inhibitor (non-competitive)

      Be clear and show the effect of each type of inhibitor compared to the uninhibited enzyme. Label each line/curve and label the axes. You should have three plots with 2 lines/curves on each.

   B. What parameters can be determined from the plots you drew in 2A and how do you get this information.

   C. Why are uncompetitive and mixed inhibitors generally considered to be more effective *in vivo* than competitive inhibitors?

3. (30 points)

   Draw and briefly describe the general mechanism of the reaction catalyzed by a serine protease.

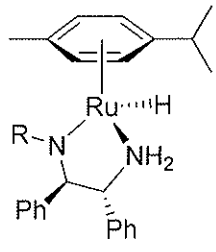
1. In the gas phase Me_3N is more basic than $MeNH_2$. However, in aqueous solution the trend is reversed. Explain. (20 points)

2. Explain why CO is a stronger field ligand than NH_3. (15 points)

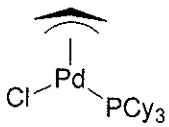
3. The vibration of free CO is at 2143 cm^{-1}. Would you expect ν_{CO} for $Ti(CO)_6^{2-}$ to be shifted to higher or lower energy? Explain your answer. (20 points)

4. Give electron count for the following compounds: (20 points)

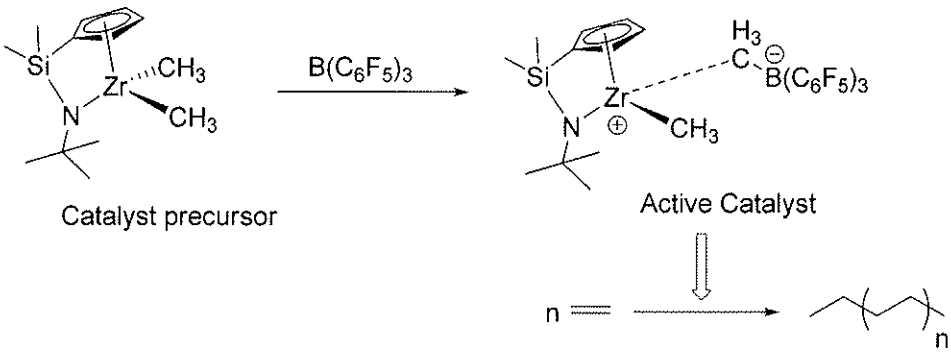
(a) $CH_3Re(O)_3$ (b) $CpRe(O)_3$ (c)



(d)

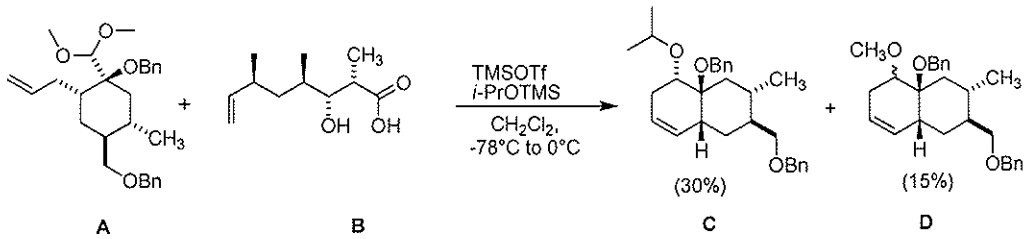


5. The zirconium complex shown below is a constrained geometry olefin polymerization catalyst precursor. It has been used industrially for making polyethylene. It can be activated with a Lewis acid such as $B(C_6F_5)_3$ to generate an ion pair. Show a mechanism for how this active ion pair produces polyethylene and suggest one possible reaction in which polymer growth is terminated. (25 points)

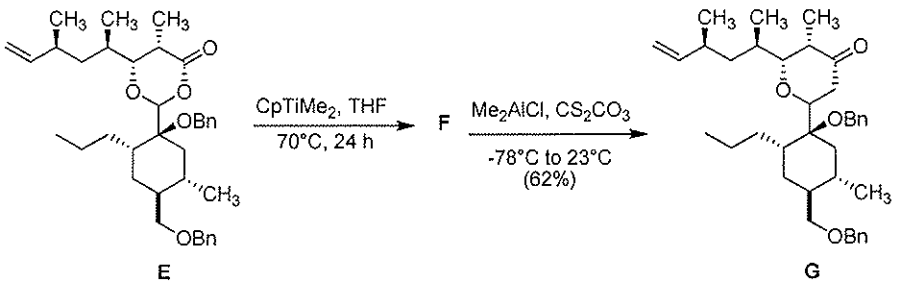


Organic Division Exam
March 28, 2009

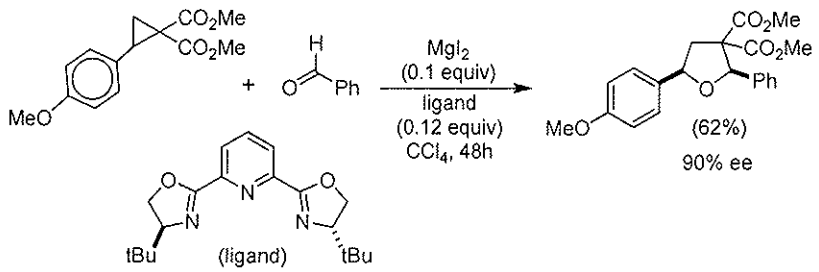
1. During the synthesis of (-)-okilactomycin (*JACS* **2009**, *131*, 2348), Smith and Co-workers reacted acetal **A** with β-hydroxy acid **B** under the reaction conditions shown below. The expected product, a dioxanone derivative was not formed. Instead, product **C** and **D** were formed. Write the structure of the expected product. Show how products **C** and **D** were formed.



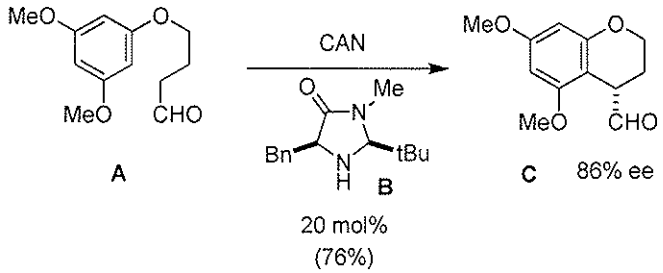
2. Treatment of compound **E** with Cp_2TiMe_2 under the specified conditions provided an intermediate product **F** (*JACS* **2009**, *131*, 2348). Treatment of **F** with Me_2AlCl provided the Petasis-Ferrier rearrangement product **G** in 62% yield. Write the structure of product **F**. Show the mechanism of formation of product **G** from **F**.



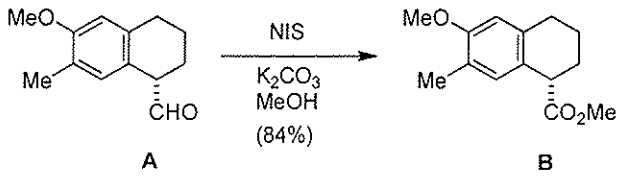
3. Recently, Johnson and Parsons (*JACS*, **2009**, *131*, 3122) reported the enantioselective synthesis of tetrahydrofurans using a dynamic kinetic asymmetric [3+2] cycloaddition process. Show the cycloadduct intermediate for the formation of the THF product and rationalize the stereochemical outcome.



4. What is CAN? Treatment of aldehyde **A** with CAN in the presence of 20 mol% organo catalyst **B** afforded 76% yield of product **C** in 86% ee. Show the intermediate for the formation of product **C** (*JACS* **2009**, *131*, 2086).



5. Treatment of **A** with NIS, K_2CO_3, and methanol in acetonitrile provided methyl ester **B** in 84% yield. Write the structure of NIS (*JACS* **2009**, *131*, 2086). Show the mechanism of this transformation.



Physical Cumulative Examination
March 28, 2009

P-Chem Cume on an announced topic: Molecular orbital theory and spectroscopy.

Part I.

Let's consider the π-bonding molecular electronic orbitals in (cis)-butadiene (shown below), which can be considered as arising from linear combinations of the four out-of-plane atomic one-electron 2*p*-orbitals.

1. (15) Draw the four low-lying π-bonding electronic molecular orbitals in butadiene and rank their relative energies. Please note, many of the subsequent questions hinge on getting these right, so double-check your predictions. Which are occupied and which are unoccupied in the ground electronic state?

2. (20) There are 4 possible one-electron $\pi \rightarrow \pi^*$ transitions present in butadiene. Based on your inspection of the orbitals, which are optically allowed and which are not? Rank their relative oscillator strengths. **Explain your reasoning**.

3. (20) Of those that are optically allowed, how are they polarized (i.e., in which direction within the molecular frame does the transition moment point, connecting the two states by an oscillating electric dipole)? **Explain your reasoning.**

4. (30) The relative energies of the different π electronic states of butadiene can be approximated by Hückl theory. Each of the wavefunctions from part 1 can be generated from linear combinations of atomic orbitals, ϕ:

$$\psi = c_1\phi_1^{2p} + c_2\phi_2^{2p} + c_3\phi_3^{2p} + c_4\phi_4^{2p}$$

The subscript refers to each p-type orbital down the conjugated chain. According to Hückl theory, only the interactions between adjacent atomic p-orbitals are considered, with the interaction energy given by $H_{ij} = \int \phi_i^{2p} \hat{H} \phi_j^{2p} d\tau \equiv \beta$. In the case of butadiene, the coefficients on the atomic orbitals used to generate the molecular orbitals via the above expression can be generated from a matrix incorporating those energies.

$$\begin{pmatrix} \alpha - E & \beta & 0 & 0 \\ \beta & \alpha - E & \beta & 0 \\ 0 & \beta & \alpha - E & \beta \\ 0 & 0 & \beta & \alpha - E \end{pmatrix} \cdot \begin{pmatrix} c_1 \\ c_2 \\ c_3 \\ c_4 \end{pmatrix} = \vec{0}$$

The values for α refer to the energies of the p-orbitals prior to "turning on" mixing by considering β (note: β will be negative-valued for a stabilizing energy). Rewrite the above expression in an eigenvalue/eigenfunction equation and solve for the four sets of coefficients for the molecular wavefunctions. (hint#1 – if we define the energy of the unperturbed system as zero, α=0. This is ok, since we only probe energy differences spectroscopically. Hint #2 – the following matrix has the following eigenfunctions:)

Matrix

$$\begin{pmatrix} 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 \end{pmatrix}$$

Eigenvectors

$$\begin{pmatrix} 0.372 \\ -0.602 \\ 0.602 \\ -0.372 \end{pmatrix}, \quad \begin{pmatrix} -0.602 \\ 0.372 \\ 0.372 \\ -0.602 \end{pmatrix}, \quad \begin{pmatrix} 0.372 \\ 0.602 \\ 0.602 \\ 0.372 \end{pmatrix}, \quad \begin{pmatrix} -0.602 \\ -0.372 \\ 0.372 \\ 0.602 \end{pmatrix}$$

Corresponding eigenvalues: -1.618 -0.618 1.618 0.618

a) Which eigenvectors correspond to which states from question 1? **Explain your reasoning.**
b) Confirm the eigenvalue/eigenvector relationship for one of the eigenvector/eigenvetor pairs.
c) From the above relationships, estimate the energies of each allowed spectroscopic transition from question 2, expressed as factors of β. **Explain your reasoning.**

5. (15) Cis-butadiene has C_{2v} symmetry. Using the character table provided below, what is the symmetry of each of the four molecular orbital wavefunctions generated in part 2? **Explain your reasoning.**

Character table for C_{2v} point group

	E	C_2 (z)	σ_v(xz)	σ_v(yz)	linear, rotations	quadratic
A_1	1	1	1	1	z	x^2, y^2, z^2
A_2	1	1	-1	-1	R_z	xy
B_1	1	-1	1	-1	x, R_y	xz
B_2	1	-1	-1	1	y, R_x	yz

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.)