

**Department of Chemistry
Cumulative Examinations
March 31, 2007**

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, Page 7

On your examination booklet:

- 1) Print your student ID number.
- 2) Print this Exam Booklet number: 59
- 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
U N I V E R S I T Y

Analytical Cume March 31, 2007

Metabolomics

1. (25 pts) Metabolomics involves the combination of high resolution spectroscopy and multivariate statistical analysis of complex biological samples. The most popular chemical analysis methods currently used in the field are ^1H NMR and LC-MS or GC-MS. Which of the following attributes are associated with each technique?

High reproducibility	Analysis time <10 min/sample
High sensitivity	Good selectivity
Excellent absolute quantitation	Excellent for structural identification
Excellent relative quantitation (diff. compounds)	Expensive on a per sample basis
Limited sample preparation	Requires lots of sample (>500 μL)
Spectral complexity (overlap)	Can suffer from ion suppression

2. (15 pts) Some of the more advanced methods currently being considered for metabolomics studies are the following. Briefly list 1 or 2 advantages and disadvantages of each advanced technique:

DESI MS

2D GCxGC/TOF MS

2D NMR

3. (10 pts) It is often better to combine NMR and MS to improve the separation (classification) of populations such as "sick" and "healthy." Give two reasons why this might be the case.

4. (10 pts) It has often been stated in the field of metabolomics that NMR is too insensitive for metabolomics studies, and yet NMR seems to classify sample populations at least as well as MS in a majority of studies. Why do you think this could be the case? (Hint: Think about the attributes of NMR you identified in problem 1 and the types of metabolites NMR can detect.)

5. (10 pts) The use of correlation in metabolomics is relatively new. Why do you think it could be advantageous to correlate the results of NMR and MS data in the same sample set?

6. (15 pts) In metabolomics, data scaling is often performed to improve the classification of samples and to help identify possible metabolite biomarkers. Two popular types of scaling are auto-scaling, in which the signal is divided by the standard deviation (SD), and Pareto scaling, in which the signal is divided by the square root of SD. A good biomarker has a high biological variation compared to the metabolite signal. Given the following data, which do you think would

be a more likely biomarker candidate, the one detected by NMR or MS? Show your work using both types of scaling for full credit.

	NMR	MS
Metabolite signal	150	80
Measurement variation	1.5	12
Biological variation	30	20

(The above variations are expressed as standard deviations).

7. (15 pts) Metabolomics is of course related biologically to proteomics and genomics. Suppose you could collect metabolomics data and at least one of the other two types of data on a sample set. Describe one way in which metabolomics data could be related to the other type of data.

1. The DNA double helix is stabilized by hydrogen bonds and base-stacking interactions. The structure is very stable and cannot be opened in a solution mimicking physiological conditions: i.e. at 37° C, in the presence of Mg⁺⁺. However, in order for replication to take place, in cells, the DNA must open up. Concisely describe how this is achieved by the cellular replication machinery.

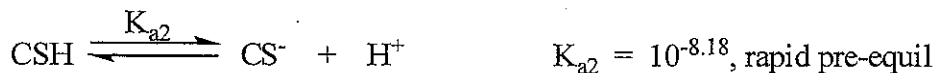
2. In the semicontinuous mode of DNA replication, relatively short RNA segments are synthesized by an RNA polymerase.
 - A. What is semicontinuous mode of DNA replication?
 - B. What is the function of the short RNA segments?
 - C. How are these RNA segments eliminated after DNA replication?
 - D. How does the cellular machinery create two continuous daughter DNA sequences from the parental DNA?

3. After completion of DNA replication, in cells, proper DNA segregation presents a major topological problem. Concisely describe how the prokaryotic and eukaryotic cells resolve this problem.

4. The pathways that work in conjunction with DNA replication are often targeted for creating anti-cancer agents.
 - A. Why these pathways are good targets for designing anti-cancer agents?
 - B. Thymidylate synthase is one of the favored targets for design of chemotherapeutic agents. Why Thymidylate synthase is a good target for specific anti-cancer agents?
 - C. 5-Fluorodeoxyuridylate is a potent antitumor agent. How does 5-Fluorodeoxyuridylate inhibit DNA replication?

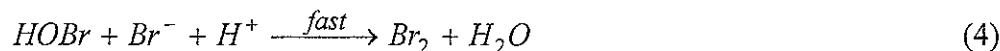
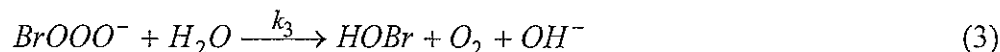
INORGANIC CHEMISTRY CUMULATIVE EXAM
March 31, 2007

1. Chlorine dioxide oxidation of cysteine (CSH) has been investigated under pseudo-first-order conditions (with excess CSH) in buffered solutions from pH 2.7 to 9.5. The reactions are observed spectrophotometrically by the rate of loss of ClO_2 . The proposed mechanism is:



- (a) If $[\text{CSH}]_T = [\text{CSH}] + [\text{CS}^-]$, derive the rate expression (in terms of $[\text{CSH}]_T$, $[\text{ClO}_2]$ and $[\text{H}^+]$) for the loss of ClO_2 .
- (b) Chlorine dioxide is an extremely reactive species. Sketch its electron-dot structure and explain why it is so reactive.

2. The following mechanism is proposed for the reaction of ozone with excess bromide ion in acidic solutions, where BrOOO^- is a steady-state intermediate:



- (a) Give the equation of the overall reaction. Is this reaction (1) acid catalyzed or (2) acid assisted, or (3) neither?
- (b) Derive the rate expression for the rate of O_3 loss and rate of Br_2 formation.
- (c) What is meant by a "steady-state intermediate"? How does this differ from transition states? What is the composition of the transition state(s) for this mechanism?

Organic Chemistry

March 31, 2007

Prof. David Liu at Harvard is a pioneer in DNA-templated organic synthesis (DTS). He uses DNA strands to bring chemical reagents together and promote chemical reactions between these reagents. One example is shown below.

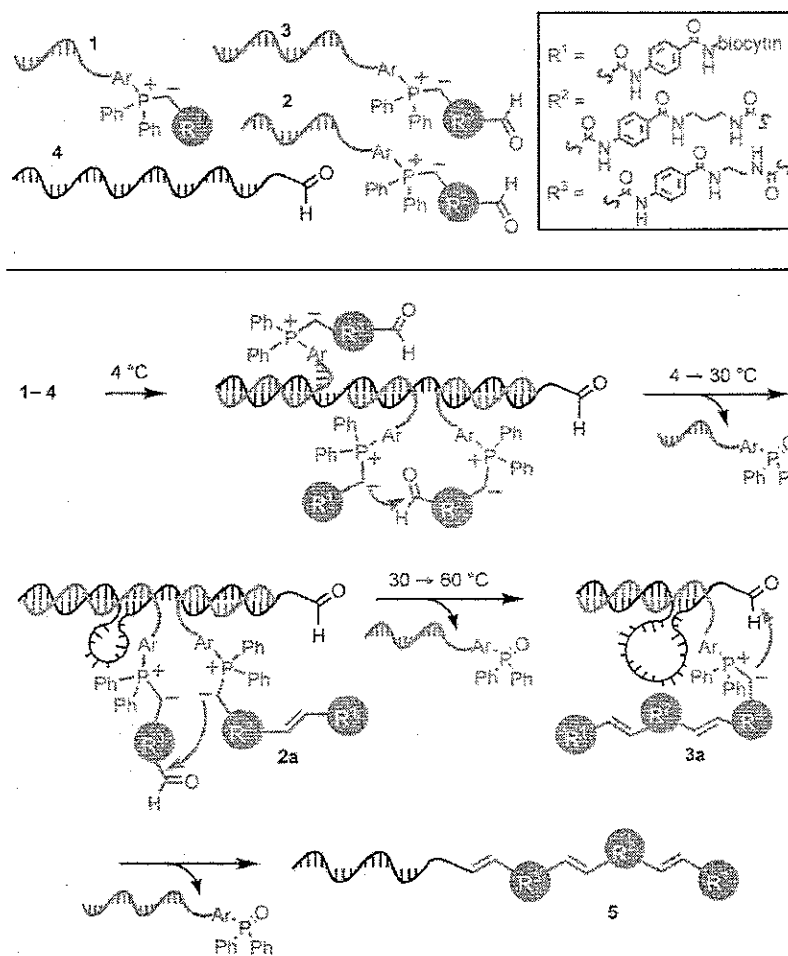


Figure 1. Strategy for the single-solution synthesis of an ordered triolefin. Building blocks are transferred sequentially among phosphorane reagents 1-3 before addition to an aldehyde-linked template 4. The rigidity of double-stranded DNA enforces Wittig olefination regioselectivity. As the reaction temperature is elevated, the DNA secondary structure undergoes sequence-programmed changes that enables the desired Wittig olefination to take place selectively. [Snyder, T. M. & Liu, D. R. Ordered Multistep Synthesis in a Single Solution Directed by DNA Templates. *Angew. Chem. Int. Ed.* **44**, 7379-7382 (2005)].

- (1) Briefly discuss the advantages of DTS. (20 points)
- (2) For the reactions that can be done through DTS, what are their common features? And then give two specific examples of the applicable chemical reactions besides those in the above example. (20 points)
- (3) Briefly discuss the potential disadvantages/limitations of DTS. (10 points)
- (4) Could you design a strategy to overcome these limitations? If yes, briefly describe how. (10 points)
- (5) Identify one specific application of DTS and discuss it in detail. (20 points)
- (6) Could you generalize DTS to other biomacromolecules? How? Please discuss with specifics. (20 points)

- 1) (25 points) Explain the relationship between Helmholtz free energy and the chemical potential.
- 2) (25 points) How are the chemical potentials of water molecules in the vapor, liquid and solid phase related to each other at the following three temperatures (at ambient pressure): 0°C, 50°C, and 100°C.
- 3) (25 points) What constraint does the Gibbs-Duhem equation place on chemical potentials in a mixture at constant temperature and pressure?
- 4) (25 points) What is the Legendre Transformation that converts Gibbs free energy to a potentially energy function which determines the direction of spontaneous transformations in system held at constant P , T and μ_1 (where μ_1 is the chemical potential of one of the components in the system, and you may assume that the system is enclosed by a container that is impermeable to all the other components).

Periodic Classification of the Elements

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I A		II A		III A		IV A		V A		VI A		VII A		VIII		IX A		X A																																																																																				
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 Act† (227)	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	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)

*Lanthanides

†Actinides

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