Department of Chemistry
Cumulative Examinations
January 8, 2005

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, Pages 2-4
3) Inorganic Cumulative Examination, Page 5
   Organic Cumulative Examination, Pages 6-9
5) Physical Cumulative Examination, Page 10

On your examination booklet:

1) Print your student ID number.
2) Print this 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 January 8, 2005

1. Please briefly describe the principle, set-ups, and the primary function of gel electrophoresis (10 points).

2. For any given protein, please identify six factors that associate with the electrophoresis set-up and will affect the protein mobility (20 points).

3. For any particular electrophoresis set-up, please identify three molecular properties that will affect protein mobilities (15 points).

4. Why does 2D gel electrophoresis become a powerful tool in proteomics? Please briefly describe the principle and procedure of the protein 2D gel electrophoresis. To achieve a similar effect, please design a 2D gel system for RNA or DNA (30 points).

5. What are slab gel electrophoresis and capillary gel electrophoresis? Please compare them in terms of advantage/disadvantage and applications (15 points).

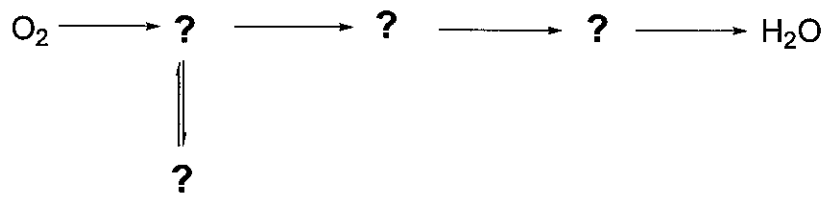
6. Commonly used gel matrixes are polyacrylamide and agarose. Why? Can you think about two other matrixes? (10 points)

Biochemistry Cumulative Examination
Department of Chemistry
Purdue University
Date: January 8, 2005
Title: Mechanisms of O_2-Activation in Metalloenzymes

(1). [30 points] (a) The major source of energy in aerobic organisms is the four-electron reduction of molecular oxygen (O_2) to water, eq 1, when coupled with the oxidation of organic materials (foods). Despite its thermodynamic oxidizing strength, oxygen does not react at any reasonable rate with most organic molecules. Explain why.

$$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O \qquad E^\circ = 0.815\ \text{V}$$

(b) The reduction of oxygen to water involves the transfer of four electrons, which does not occur in one concerted step. Complete the following reaction scheme showing all relevant reactive oxygen species (ROS). Remember to balance your chemical equations (add electrons etc. as needed).

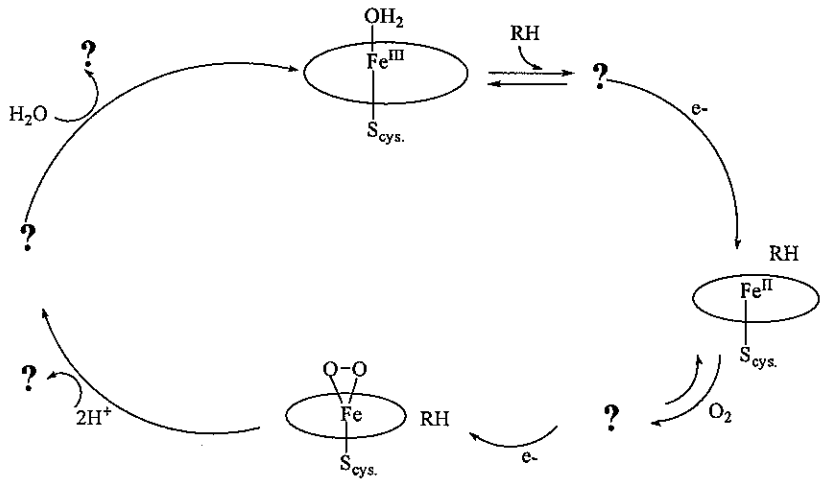


(c) Some of the ROS you outlined in (b) above are harmful in biology. Describe briefly biological defense mechanisms that protect against oxygen toxicity.

(2). [20 points] The copper-zinc superoxide dismutase (SOD) is found in almost all eukaryotic cells and in a very few prokaryotes. What reaction does this enzyme catalyze? Describe how the enzyme's surface is adapted for this enzyme's function. Show in two steps the mechanism for this enzyme and propose a role for the zinc atom

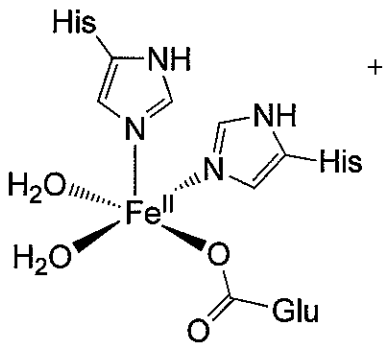
(3). [20 points] Cyctochrome P450 uses O_2 to catalyze synthesis of steroid hormones and bile salts. It is also an important enzyme in the detoxification of foreign substances (xenobiotic compounds). The general reaction catalyzed by P450 is given below. Fill in the missing species (designated with "**?**") in the accepted mechanism shown below.

$$RH + O_2 + NADPH + H^+ \rightarrow ROH + H_2O + NADP^+$$

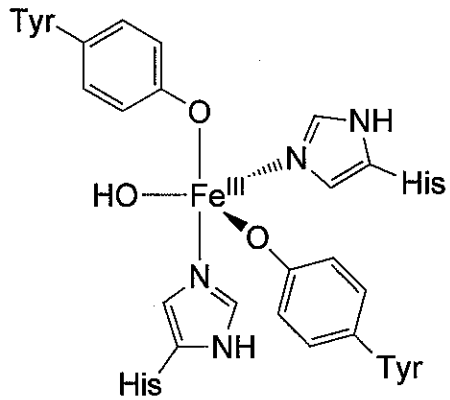


Give one difference between the active site iron in P450 and in peroxidases (enzymes that catalyze oxidation with H_2O_2 instead of O_2).

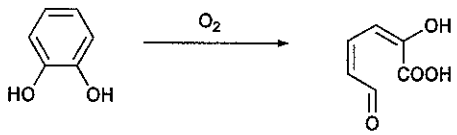
(4). [30 points] Non-heme iron oxygenases are very important in metabolic pathways of aromatic amino acids as well as in the oxidation of aromatic hydrocarbons. Catechol dioxygenases are ubiquitous to most soil bacteria. Two classes of catechol dioxygenases have been recognized (intradiol and extradiol, see the respective iron active sites below), and they are distinguished by their regioselectivity in effecting ring cleavage. Show the mechanism for each class and give a brief rationalization for how the ligands on the iron favor each mechanism.

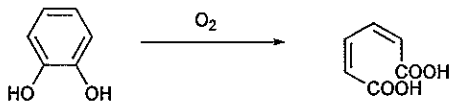


Extradiol catechol dioxygenase



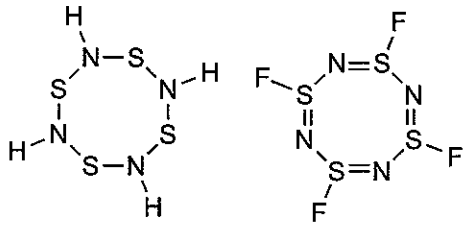
Intradiol catechol dioxygenase





Inorganic Cumulative Exam
January 8, 2005

(1). [15 points] The cage compounds $H_4N_4S_4$ and $N_4S_4F_4$ show contrasting structures. Give the reason(s) for the differences that exist between them.



(2). [30 points] The compounds MF_6 (M = Mo to Rh and W to Pt) are all regular octahedral molecules in the gas phase, although some of them are predicted to be distorted by Jahn-Teller effects. Show which of these transition metal hexafluorides you would predict to be "technically" subject to Jahn-Teller distortion. Explain your answer. [Hint: All complexes are low spin]

(3). [20 points] Rationalize the following observations:

(a) Reductive elimination of H_2 from the Pt dihydride shown below exhibits an inverse kinetic isotope effect, that is elimination of D_2 is faster than H_2.

$$L_2Pt(H)_2 \rightarrow [L_2Pt] + H_2$$

(b) Ligand substitution with $V(CO)_6$ proceeds 10^{10} faster than with $Cr(CO)_6$.

Reaction	$k_{rel.}$
$Cr(CO)_6 + L \rightarrow Cr(CO)_5L + CO$	1
$V(CO)_6 + L \rightarrow V(CO)_5L + CO$	10^{10}

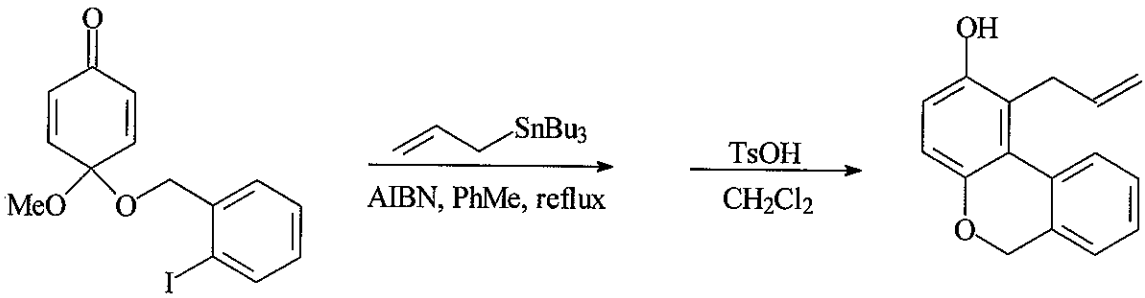
(4). [30 points] Consider the "brown ring" reaction given below. How would you go about measuring k_{on} & k_{off}? What is the dissociation constant for the brown $Fe(OH_2)_5(NO)^{2+}$ complex? The nitric oxide ligand could be linear or bent. Describe the bonding interaction for each scenario and rationalize which one would be favored in this case.

$$Fe(OH_2)_6^{2+} + NO \underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}} Fe(OH_2)_5(NO)^{2+}$$

$k_{on} = 1.42 \times 10^6\ M^{-1}\ s^{-1}$ $\qquad$ $k_{off} = 3240\ s^{-1}$

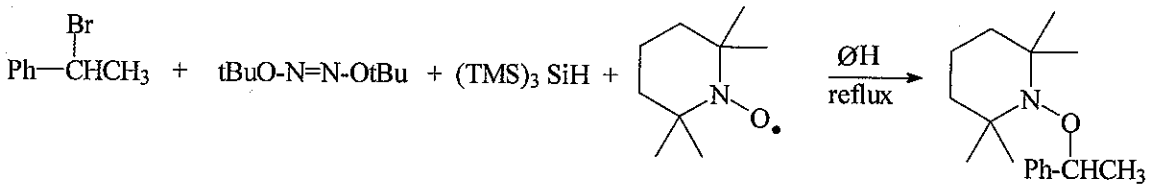
Organic Cumulative Examination
January, 2005

1. **(10 pts)** Provide a mechanism for the following reaction.



See J. Org. Chem., *69*, 3282 (2004)

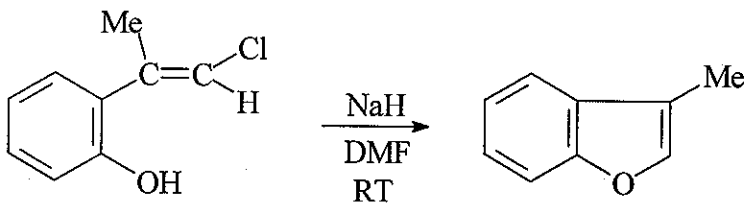
2. **(10 pts)** Provide a mechanism for the following reaction.



See Org. Lett. *6*, 2233 (2004)

3. **(15 pts)**

   a. Draw a mechanism for the following reaction.



b. The Z isomer of the vinyl chloride is totally unreactive under these reaction conditions. Can your answer in "a" explain this result? If not, provide a new mechanism that accommodates this fact. (Hint: be prepared to think "outside of the box").

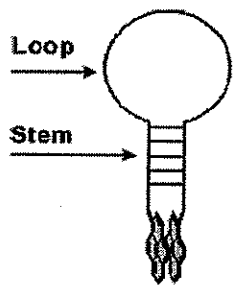
c. Your answer to "b" should surprise you. Why?

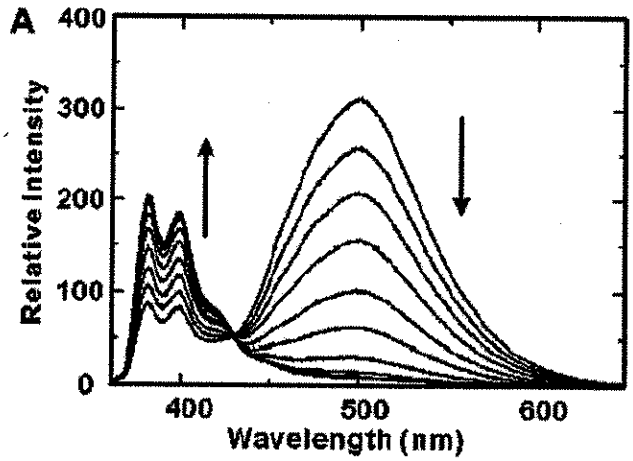
See Org. Lett. *6*, 2461 (2004)

4. (10 pts)

The preparation of "molecular beacons" was recently described in which pyrene units were attached to the 3' and 5' ends of a single-stranded oligo which have a stem-and-loop structure (see diagram). The pyrene units fluoresce with a λ_{max} at 500 nm (pale blue). When this oligo is placed in the presence of a complementary "target" 19-mer DNA (i.e. to which it hybridizes) the pyrene fluorescence changes to a λ_{max} of ca. 400 nm (yellow-green). The emission curves are shown below.

Explain why these changes occur.

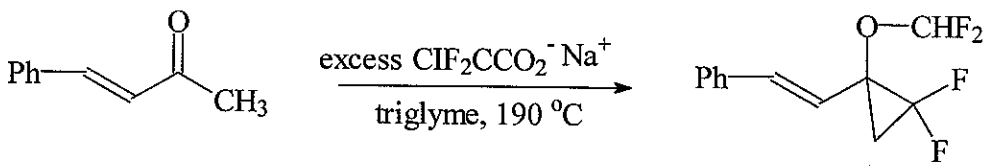




See J. Org. Chem. *69*, 3271 (2004)

5. (10 pts)

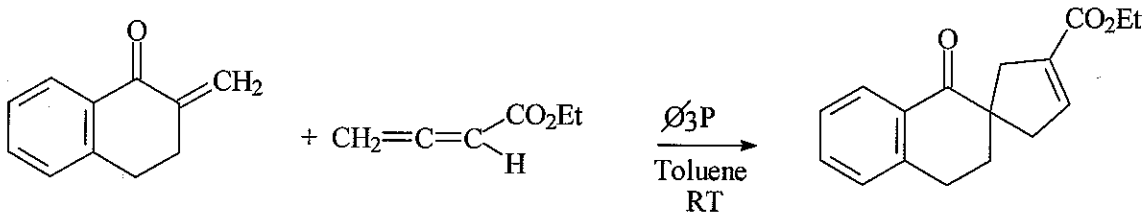
Consider the reaction shown below. When the phenyl group is substituted with a 4-MeO substituent, the reaction is appreciably faster than when a 4-NO_2 group is present. Provide a mechanism for this reaction.



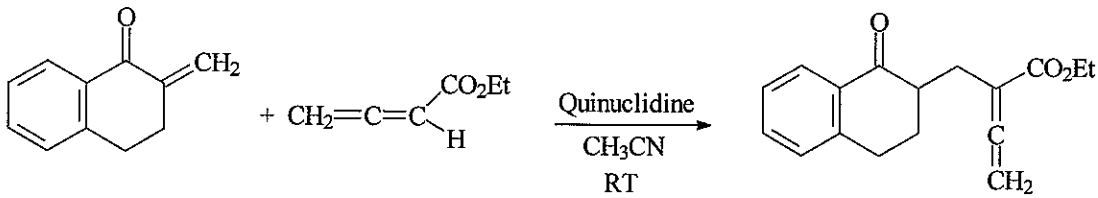
See J. Org. Chem. *69*, 4210 (2004)

6. (15 points)

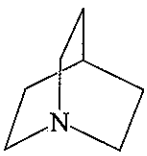
a. Provide a mechanism for the reaction shown below.



b. When quinuclidine is substituted for the the triphenyl phosphine, a different reaction course is followed. Provide a mechanism for this reaction.



<u>Note</u> Quinuclidine =

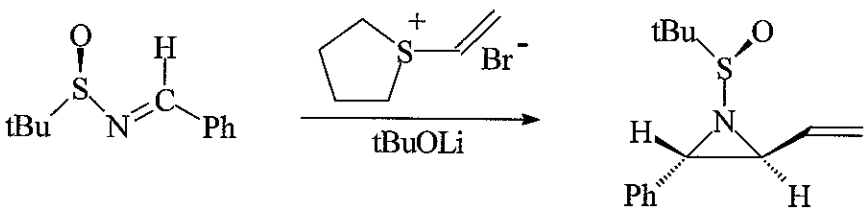


c. Explain why the two reactions diverge.

See J. Am. Chem.. Soc. *125*, 12395 (2003)

7. (15 pts)

a. Provide a mechanism for the following reaction.

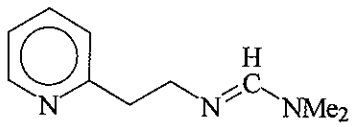


b. In addition to the product shown above, a diastereomer is formed in which the phenyl ring and vinyl groups are *cis* to one another. However, the *trans* isomer dominates (71:29). Explain the preference for the *trans* isomer by analyzing the stereochemistry of the relevant transition states.

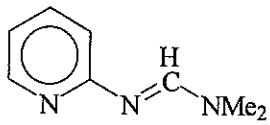
See Org. Lett. *6*, 2377 (2004)

8. (15 pts)

Gas phase basicities have been obtained for the following molecules:



1



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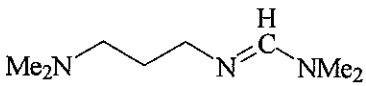

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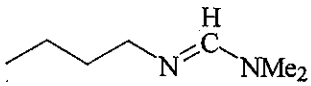

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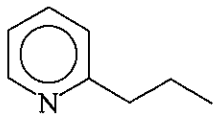

5

Gas Phase Basicities (GB)[a]

Compound	GB[b]
1	241.1
2	232.9
3	241.7
4	234.5
5	220.8

[a]Higher GB = more basic compound

[b]kcal/mole

a. For compound **1**, which N atom do you predict to be the most basic? Explain why this is the case.

b. Explain why compounds **1** and **3** are more basic than compound **4**.

c. What site do you predict to be most basic in compound **2**? Explain your choice.

See J. Org. Chem. *69*, 4023 (2004)

January 8, 2005

1. A piston weighted by a mass *m* descends a distance *h* in a cylinder of diameter *d*. As a result, the cylinder walls become warmer than the surrounding air. What has happened? Describe physically why this temperature rise occurs. Next, make reference to laws of thermodynamics and characterize the process formally (by means of equations). Clearly state your assumptions and define the variables that you introduce.

2. A firefighter discharges a CO_2 fire extinguisher. The expanding gas cools sufficiently to form an aerosol of solid CO_2. State what causes the gas to cool physically. Next, describe this process in formal terms using thermodynamic laws and equations of state.

3. Removing a partition causes reagents to mix and, as the system inside proceeds to chemical equilibrium, a reaction vessel becomes cooler than the surrounding air. How can such a thing happen spontaneously? For any such process, one can assess the comparative disorder created in the system and in the surroundings. How do these quantities compare under the present conditions. How can you account for such a process in terms of thermodynamic equations of state?

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.)