

# Literature Exam

## Analytical

Dr. Boris Mizaikoff

03/26/2007

Only a clean copy of the paper by Do-Kyun Kim et al. (Anal. Chem.) is allowed at the exam!

Exam grading key: 100 pt total, 50 pt per question; Lit. exam points: 0-20: 0; 21-40: 1; 41-60: 2; 61-80: 3; 81-100: 4

1. The paper by Do-Kyun Kim and co-workers reports on a concept for an optical biosensor using gold-deposited porous anodic alumina layers resembling gold-capped oxide nanostructures utilized for surface plasmon resonance and simultaneous interferometric sensing.
  - (a) Explain the fundamental principle of surface plasmon resonance (for a planar SPR surface), how it works, what we measure, and provide a schematic to explain the principle.
  - (b) SPR at colloidal particles is different from SPR at solid noble metal surfaces giving rise to localized surface plasmon resonance (LSPR). Explain why and how! Which particle parameters will affect the LSPR and how?
  - (c) Explain the main limitations of SPR (if any) in detecting biomolecular interactions. Are there limitations? Where would you see difficulties?



2. Next to SPR, Do-Kyun Kim and co-workers use an interferometric readout and the relative reflected intensity (RRI) for enhancing the signal
  - (a) Explain how the fundamental measurement works and why/how the thickness of the PAA layer affects the RRI and the number of apparent interference fringes.
  - (b) The authors claim an enhancement of the red-shift of  $\lambda_{\max}$  and the interferometric characteristic due to the presence of uniformly fabricated nanopores. On the other hand, it is discussed that the Au overlayer is responsible for the enhancement of the red shift and the RRI signal. Explain why nanopores should enhance these signals and what the contribution of gold is to elevating these signals, i.e., try to deconvolute these effects and explain which is more/less likely to have a significant impact and why.
  - (c) Nanopores require the analyte to diffuse to the receptor immobilized within that porous structure. Discuss this sensing concept in terms of sensitivity vs. response time. Do you expect any trade-offs here? If yes/no, explain why! Also, the authors claim that each nanopore could be modified with a different receptor – do you see any problems with that? Discuss the feasibility of this approach!



Biochemistry Cum Questions (March 26, 2007)

Answers to the questions can contain no more than 100 words. Any number of figures/schematics are OK.

1. (8 points) In the study of proteomics, activity-based probes have several specific advantages when compared to other methods for studying the proteome such as the use of antibodies, transcriptional profiling, etc. Cite some of the specific advantages for the use of activity-based probes for proteomic profiling.

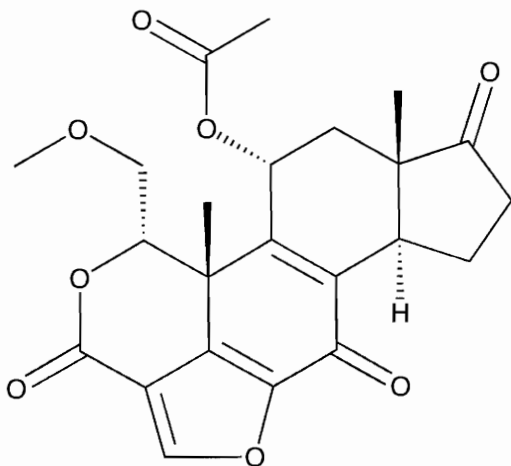
2. (24 points) In each of the following, draw the mechanism for the inhibition of the targeted enzyme by the listed class of inhibitor. A detailed mechanism including active site residues is required.

a) proteasome by a peptidyl vinyl sulfone

b) serine hydrolase with a fluorphosphate

c) cysteine protease by an peptidyl acyloxymethyl ketone

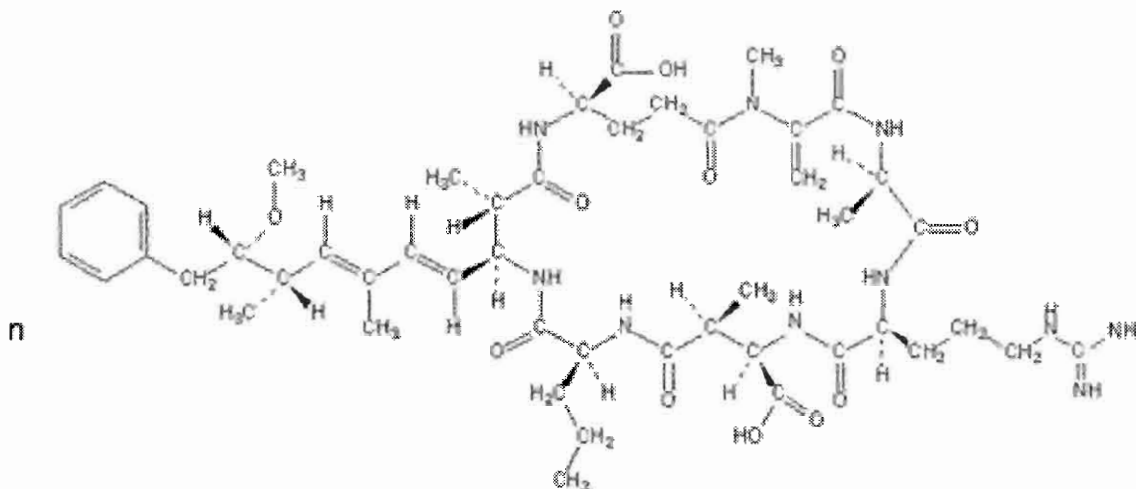
3. (10 points). Wortmannin is a fungal metabolite that covalently labels kinases of the phosphoinositide-3 kinase (PI3K) family by targeting a conserved residue in the nucleotide binding site. Draw a mechanism for the inhibition of the enzyme by Wortmannin.



b) Show chemically how a biotin or fluorophore could be attached to Wortmannin to make a kinase probe.

4. (10 points) Microcystin RR is a mechanism-based inactivator for serine/threonine phosphatases.

a) Draw a mechanism for the inactivation of a phosphatase by microcystin RR.



b) SAR studies showed that the Arg residue of microcystin was not essential for activity and this Arg residue was used as the point of attachment for a linker containing a fluorophore. Show the chemistry involved in attaching this fluorophore linker to the arginine residue.

5. (10 points). Cravatt and his coworkers have used reversible inhibitors to label the active sites of metalloproteases.

a) Show the structure of this class of inhibitor and show the active site of a metalloprotease bound to one of these reversible inhibitors.

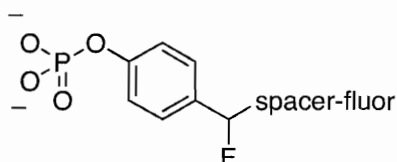
b) Cravatt et al. also prepared probes using these reversible inhibitors to covalent link to the active sites of metalloproteases. Show the chemistry of bond formation between the metalloprotease probe and the active site of the enzyme.

c) Show the structure of a probe containing a reversible inhibitor, a moiety to covalent link to the enzyme, and a reporter group. Outline how such a molecule could be constructed.

6. (6 points) "Tag-Free" strategies for ABPP (activity-based protein profiling) involve first labeling proteins with an activity-based probe containing only a small additional functional group. After labeling the targeted proteins, this functional group is then used to attach a reporter tag using either "Click chemistry" or the Staudinger ligation. Describe the chemical reactions involved in either one of these methods.

7. (6 points) Biotin is frequently part of activity-based probes. Draw the structure of biotin and outline the chemistry necessary to attach biotin to an activity-based probe. Describe the advantages of having a biotin moiety attached to your probe.

8. (10 points) Two recent reports describe the preparation of fluorescently labeled derivatives of 4-(fluoromethyl)phenyl phosphate (example shown below) and 2-(difluoromethyl)phenyl phosphate as electrophilic probes for tyrosine phosphatases. Outline a mechanism for the inhibition of a tyrosine kinase by these new inhibitors.



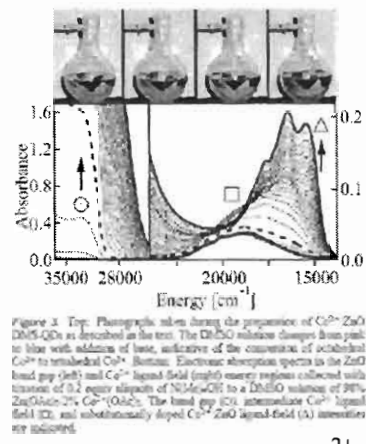
9. (8 points) Several enzyme probes have been described which label enzymes of several mechanistic classes. Draw the structure of one such probe, list several mechanistically different enzymes that would be labeled, and show the mechanism of inhibition.

10. (8 points) Draw the mechanism of a  $\beta$ -retaining glycosidase and show the structure of a specific inhibitor for these enzymes.

### Dilute Magnetic semiconductor quantum dots (DMS-QDs): work from the lab of Daniel Gamelin

- 1) JACS, 125, 13205-13218 (2003)
- 2) Advanced Materials, 16, 2115-2119 (2004)
- 3) JACS 127, 5292-5293 (2005).
- 4) JACS 128, 3910-3911 (2006).

Q1



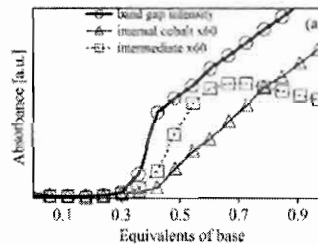
The above graphs show optical absorption spectra as Co<sup>2+</sup>:ZnO DMS DQ are prepared from solution. As the nanoparticles form, the absorption maximum at ~19,000 cm<sup>-1</sup> is ultimately replaced by much stronger absorption centered at ~17,000 cm<sup>-1</sup>. This gives rise to the observed pink to blue color change.

a) Explain why the ligand field absorption maximum for the cobalt moves to lower energy as the nanoparticles form. Use your general knowledge of transition metal optical spectroscopy to help you with this.

b) Explain why the ligand field absorption for the cobalt in the nanoparticles is stronger than that observed for the starting cobalt. Use your general knowledge of transition metal optical spectroscopy to help you with this.

Q2) In Gamelin's papers, average QD size estimates from TEM photographs, x-ray diffraction and optical spectroscopy are reported. Comment briefly on why we do not necessarily expect these numbers to be identical, particularly if there is a distribution of particle sizes.

Q3)



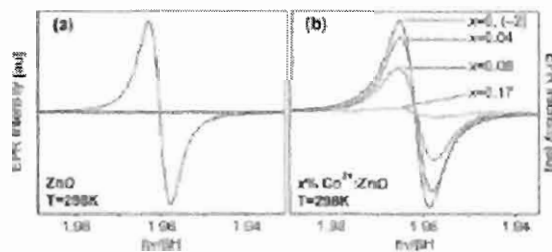
The above graph shows absorbance for the band gap transition (open circles) and ligand field transitions of included cobalt (open triangles) as a function of total added base during a synthesis of  $\text{Co}^{2+}:\text{ZnO}$  DMS QD.

What features of this data lead the authors to conclude that cobalt is not incorporated in the QDs during nucleation?

Q4) Two of the papers that you were asked to examine include data showing that doping (n or p-type) of the DMS QD based on ZnO plays a very important role in determining if long range magnetic ordering will occur at or above room temperature. Briefly explain, in simple terms, why doping plays a role in determining the magnetic ordering temperature.

Q5) What does the notation  $Zn_i$  mean?

Q6)



Explain why the EPR signal from electrons in the conduction band of phototreated  $Co^{2+}$ :ZnO decreases as the average amount of cobalt in the nanocrystals increases.

# Organic Literature Exam March 2007

## **You must sign the Honor Code Agreement**

Having read the Georgia Institute of Technology Academic Honor Code, I understand and accept my responsibility as a member of the Georgia Tech Community to uphold the Honor Code at all times. In addition, I understand my options for reporting honor violations as detailed in the code.

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Signature

## **Grading Scale**

The exam is worth 100 points (percent).

85-100%	4 points
70-85%	3 points
60-70%	2 points
50-60%	1 point
0-50%	0 points

Question	Points possible	Your Score
1	20	
2	20	
3	30	
4	30	
Total:	100	

### **Question #1 (20 points)**

Provide five (5) classes of catalytic reactions that are catalyzed by metallated salen catalysts. These classes have to be DISTINCT, i.e. using for examples different nucleophile for the same class of reaction is NOT acceptable. Make sure you provide for each reaction:

- a) a reaction scheme
- b) the metallated salen catalyst
- c) ANY by- or side-products

## **Question #2 (20 points)**

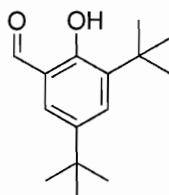
The review describes in detail the differences between heterogeneous and homogeneous catalysis.

- a) Provide an example of YOUR CHOICE of a metallated salen catalyst that has been supported and utilized on a homogeneous and on a heterogeneous support.
- b) What are the supports? Describe them in detail.
- c) What are the advantages and disadvantages of each support?
- d) How would YOU optimize both supports for the catalysts you chose? You are NOT allowed to use optimization strategies for the support/catalyst system that are reported in the literature.

### Question #3 (30 points)

Now some basic organic chemistry. The compound below is a key intermediate for the synthesis of the salen ligand.

- Provide a detailed reaction sequence for the synthesis of this compound starting from benzene.
- Provide a **step-by-step** (curved arrow) reaction mechanism for EACH step of your synthesis.



### **Question #4 (30 points)**

Imagine you are working for Salenisis, a company that works on supported salen complexes for catalysis. You are charged with developing the next generation of supported metallated salen catalysts for an organic transformation of YOUR choice.

- a) Describe YOUR choice of organic transformation in detail. Why did you choose this transformation? What are the shortcomings of current catalysts for this transformation?
- b) Describe your new and improved catalyst in detail. Pay particular attention to the metal, the ligand and the support. Explain your choice of all these variables.
- c) Suggest a catalytic cycle for your choice of catalyst and transformation.

## PHYSICAL CHEMISTRY LITERATURE EXAM

March 2007

**Topic:** Chemistry and Physics of/at Gas-Liquid Interfaces

**Literature:**

Spectroscopy of Growing and Evaporating Water Droplets: Exploring the Variation in Equilibrium Droplet Size with Relative Humidity, L. Mitchem, J. Buajarearn, R.J. Hopkins, A.D. Ward, R.J.J. Gilham, R.L. Johnson, and J.P. Reid, *J. Phys. Chem. A* **2006**, *110*, 8116-8125.

New Experimental and Theoretical Approach to the Heterogeneous Hydrolysis of NO<sub>2</sub>: Key Role of Molecular Nitric Acid and its Complexes, K.A. Ramazan, L.M. Wingen, Y. Miller, G.M. Chaban, R.B. Gerber, S.S. Xantheas, and B.J. Finlayson-Pitts, *J. Phys. Chem. A* **2006**, *110*, 6886-6897.

Mass Accomodation and Chemical Reactions at Gas-Liquid Interfaces, P. Davidovits, C.E. Kolb, L.R. Williams, J.T. Jayne, and D.R. Worsnop, *Chem. Rev.* **2006**, *106*, 1323-1354.

**Allowed Materials:** None other than writing implements and a calculator (which shouldn't be needed).

**This exam has a total of 100 points.**

1. (20 points) In the space provided describe or define each of the following (use words, not mathematical equations):

(a) The mass accommodation coefficient ( $\alpha$ )

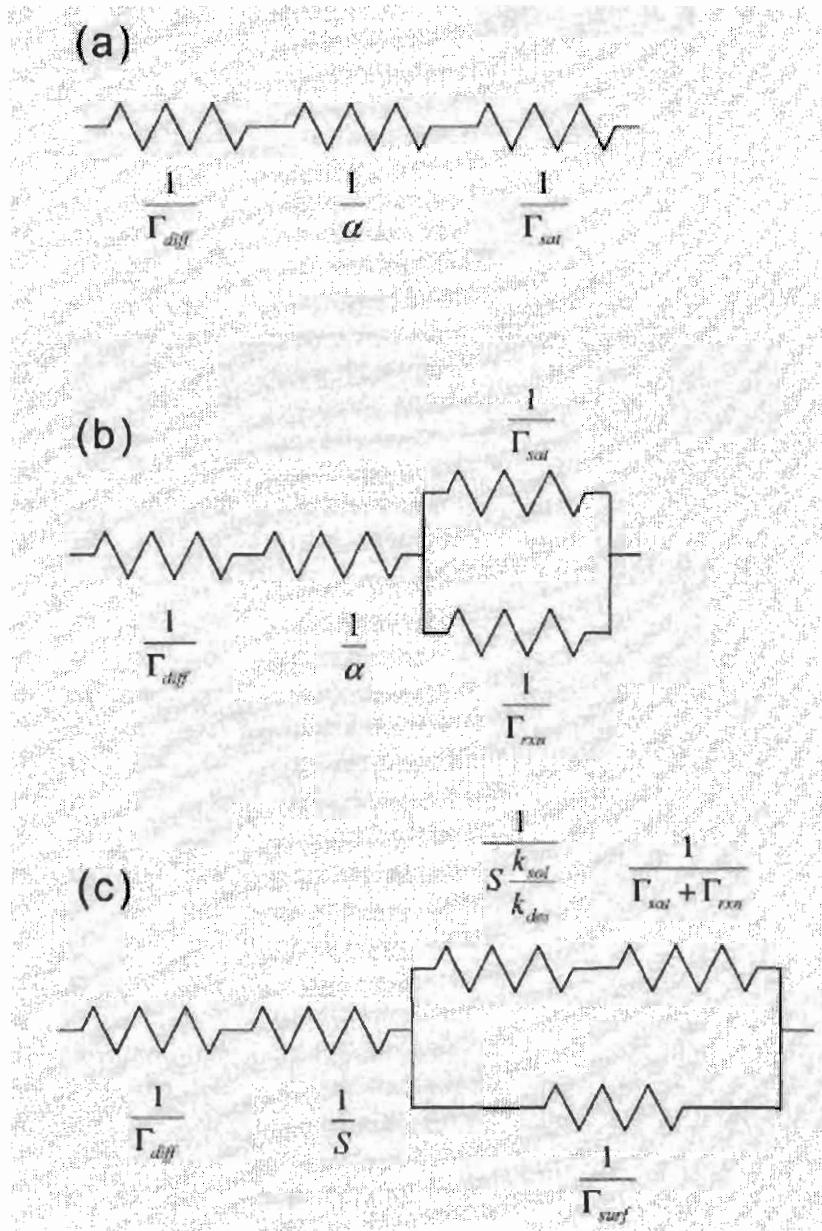
(b) The net uptake coefficient ( $\gamma$ )

(c) Raman spectroscopy

(d) Attenuated total reflection infrared spectroscopy

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2. (15 points) Discuss the physico-chemical factors that control the *equilibrium* size of an aqueous atmospheric aerosol droplet.

3. (24 points) Shown below is Figure 2 from the paper by Davidovits et al. which gives a schematic of the resistor model for (a) non-reactive uptake of gaseous species X into the liquid phase, (b) part a plus a bulk liquid phase reaction that destroys X, and (c) part b plus a surface reaction that destroys X.



- (a) What is the most significant approximation involved in the formulation of the resistor model?

(b) Define each of the parameters  $(\Gamma_{\text{diff}})^{-1}$ ,  $\alpha$ ,  $(\Gamma_{\text{sat}})^{-1}$ ,  $(\Gamma_{\text{rxn}})^{-1}$ ,  $S$ ,  $k_{\text{sol}}$ ,  $k_{\text{des}}$ , and  $(\Gamma_{\text{surf}})^{-1}$  (see above figure).

(c) Write down mathematical expressions that can be used to evaluate the net uptake coefficient ( $\gamma$ ) for cases (a), (b) and (c) shown schematically in the above figure.

(d) What experimental data could be used to differentiate between a bulk liquid-phase reaction and a surface reaction as a pathway for destroying species X?

4. (21 points) Shown below is Figure 5 from the paper by Ramazan et al. (typical concentration-time profiles of *gas phase* species observed in a  $\text{NO}_2$  heterogeneous hydrolysis experiment). Also shown below is Figure 2 from reference 26 in the Ramazan et al. paper, which shows a proposed mechanism for the heterogeneous hydrolysis of  $\text{NO}_2$ . Use the proposed mechanism as a guide to answer the questions that appear below the figures.

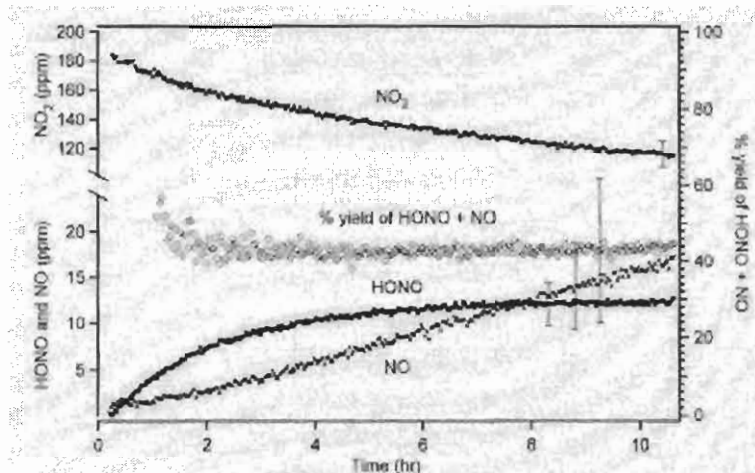


Figure 5. Concentration-time profiles for a typical  $\text{NO}_2$  hydrolysis experiment with 184 ppm  $\text{NO}_2$  in 1 atm of  $\text{N}_2$  at 51% RH. Error bars are  $\pm 2\sigma$ .

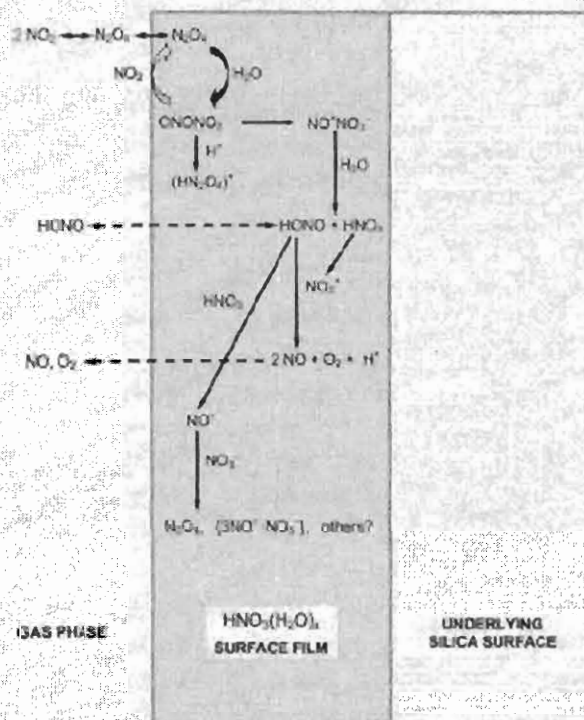


Fig. 2. Schematic diagram of proposed mechanism of heterogeneous hydrolysis of  $\text{NO}_2$ .

(a) Why does the concentration of HONO become independent of time during the time period 7-10 hours after the reaction is initiated?

(b) Why does the slope of the plot of NO concentration versus time increase with increasing time during the first few hours of reaction?

(c) Explain why the concentration versus time behavior of NO during the time period 7-10 hours (after the reaction is initiated) is very different from that of HONO, i.e., why does NO increase linearly as a function of time while HONO is independent of time?

5. (20 points) Discuss a topic that you became acquainted with during preparation for this literature exam that *is not* addressed in questions 1 – 4 above. Pose a potential exam question that your discussion addresses. Note that this problem will be scored like Olympic diving, i.e., your score will be based on both the quality of the discussion and the “degree of difficulty” of the question.

# Polymer Literature Exam March 2007

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3	20	
4	30	

Total: 100

## Question #1 (20 points)

A) Describe IN DETAIL the formation of:

- a) block copolymers
- b) macrocycles
- c) graft copolymers
- d) tetra-arm copolymers

using 1,3 dipolar cycloadditions as the key step.

B) Provide examples from the literature for parts a-d.

## Question #2 (30 points)

Barry Sharpless coined the name 'click chemistry' for 1,3 dipolar cycloadditions (he actually named a whole class of reactions 'click' chemistry. See his famous review of 2001 in *Angewandte*).

- 1) Provide a detailed mechanism of 1,3 dipolar cycloadditions using a Cu catalyst.
- 2) What is the more general definition of Sharpless' 'click' chemistry?
- 3) Has the Sharpless group 'invented or found' this reaction (1,3 dipolar cycloadditions)? If not, when and by whom was this type of reaction first explored in detail? What is the contribution (besides the name) of the Sharpless group to this class of reactions? What are the advantages of the Sharpless group contributions?

### Question #3 (20 points)

1,3 Dipolar cycloadditions belong to the large class of pericyclic reactions.

A) Are 1,3 dipolar cycloadditions thermally allowed or forbidden?

B) What is the closest related pericyclic reaction (a very famous one)?

C) Provide the molecular orbital of each component that are involved in 1,3 dipolar cycloadditions.

D) Provide a correlation diagram for either the 1,3 dipolar cycloaddition OR for the reaction you identified in part B (this one is easier).

To: J Cameron Tyson <cam.tyson@chemistry.gatech.edu>  
From: Marcus Weck <marcus.weck@chemistry.gatech.edu>  
Subject: lit exam

Cam,

Question 3 part D is a bonus question on the polymer lit exam.

Marcus

#### Question #4 (30 points)

A) One of the faculty at GeorgiaTech used click chemistry to synthesize poly(fluorenylene-triazolene).

Provide a reaction sequence from commercially available starting material for the synthesis of poly(fluorenylene-triazolene) using click chemistry as key step.

B) 1,3 Dipolar cycloadditions are ideal for bioconjugation. Why is this the case? Based on your answer, suggest two other covalent transformations (some perhaps that are described in the literature) that fulfill the criteria you outlined in the first part of B.

C) Imagine you are working for Techo-click a company that commercializes biomaterials using 'click' chemistry. You are in charge of product development. Suggest a new biomaterial that is polymer based and uses 'click' chemistry. Your polymer must be NEW and should not be in the literature. Describe your selection IN DETAIL. Pay attention to the reasoning (why is your polymer the best on the market) and compare your system to other biomaterials out there.