Department of Chemistry
Cumulative Examinations
August 27, 2011

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, Pages 3-4
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 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.
Analytical Chemistry Cumulative Exam August 2011

Analytical chemistry is sometimes called the science of chemical measurement. Metrology is that branch of science and technology that is concerned with measurements and high quality values of physical, chemical, and biological properties. This suggests that there is much in common between the two subjects.

1. [20] The quality of particular analytical measurements can be quantitatively described by several different parameters. Give two of them and explain them or write appropriate equations that explain them.

2. [20] One of the best methods of quantitation is to make a measurement in which a ratio of taken of the intensities of signals for an analyte and an isotopic variant. This is called isotope dilution.
Think carefully about the sources of error in such a measurement and describe one non-trivial example (by non-trivial one means that all the usual sources of error are minimized, as would be done in any high quality analytical/metrology lab).

3. [10] Metrology involves measurements of fundamental constants like the charge on the electron. Name two areas of science in which a precise and accurate value of the charge on the electron is important and say WHY the value is important.

4. [10] Something like 20% of the non-biological papers in a typical issue of the journal Science depend on measurements of isotope ratios, usually made by mass spectrometry. Name four sub-fields of science in which such measurements are made and in each case give the element and isotopes involved.

5. [30] The mole is a fundamental unit in chemistry. Its exact value is important. What is the most straightforward way to determine the value of the mole? What errors are involved? As you think about this problem interrelationships with other physical properties and their values and how they are determined should occur to you. Write down your careful thoughts on these matters. Then consider if there might be an alternative path to the determination of the mole and describe the best alternative you can think of. [Credit in this question goes for logical thinking and assembling knowledge from a range of areas.]

6. {10} ANSWER EITHER QUESTION A OR B
   A. Several distributions commonly encountered in chemistry are Boltzmann, Gaussian and Lorentzian. Briefly explain each.
   B. The value of the proton affinity of ammonia is a standard value on the proton affinity scale. How might this value be determined?
Biochemistry Cumulative Exam

Title: Enzymes

August 27th, 2011

1. (a) (5 marks) Draw the catalytic triad of trypsin.
   (b) (15 marks) When Asp102 was replaced with Asn in trypsin, it reduced its activity by 10,000 fold. Based on this information, suggest a structure for the "uncatalytic triad" in this mutant enzyme. Why this mutant shows reduced activity?

2. (10 points) The $K_{cat}$ for alkaline phosphatase-catalyzed hydrolysis of methyl phosphate is approximately 14/sec at pH 8 and 25°C. The rate constant for the uncatalyzed hydrolysis of methyl phosphate is approximately $1 \times 10^{-15}$/sec. What is the difference in the free energy of activation of these two reactions?

3. (20 points). Define the following terms
   
   (a) Suicide inhibitors
   (b) Double reciprocal plot in enzyme kinetics
   (c) Hill plot
   (d) Isozymes

4. (10 points) Suggest a transition state analog for proline racemase.

5. (10 points) Design a chloromethyl ketone inhibitor for elastase.

6. (10 points) Estimate $K_i$ for a competitive inhibitor when $[I] = 5$ mM gives an apparent value of $K_M$ that is three times the $K_M$ for the uninhibited reaction.

7. (20 points) Based on some preliminary measurements, it appears that a sample of the enzyme contains an irreversible enzyme inhibitor. You decide to dilute the inhibitor 100-fold and re-measure the enzyme activity. What would your results show if the inhibitor in the sample is (a) irreversible or (b) reversible? Explain your reasoning.
Inorganic Cume

A. (40 points) A recent paper by Power and co-workers (JACS 2010, 132, 17399-17401) describes an unusual compound containing an Fe-Fe bond involving two iron centers with different spin states and different oxidation states. One can think of the compound (shown on the right) forming from a reaction between cationic and anionic precursors:

\[
\text{R} - \text{Fe}(\eta^2\text{-Cp})(\text{CO})_2^- + \text{Fe}(\eta^2\text{-Cp})(\text{CO})_2^- =
\]

The bulky R groups (tri-isopropyl phenyls) are present to stabilize the two-coordinate iron center, M(1) in the Figure. Cp = C₅H₅.

i. Power formulates the iron centers as Fe(0) and Fe(II). In that view, state the formal charge of each ligand involved, and give the electron count at each iron center.

ii. The Figure on the next page presents contour plots of the four singly-occupied molecular orbitals of the complex. Note the change to a side-view of the complex. Identify the most important atomic orbital of Fe(1) found in each MO depicted, under the assumption that the Fe(1)-Fe(2) vector defines the z-axis and the y-axis is perpendicular to the tetra-substituted phenyl ring bound to Fe(1).

iii. Why don't the four electrons involved in part (ii) fully occupy the two lower-energy MO's (at -9.82 and -9.93 eV, respectively)?

B. (30 points) Sketch the structure of a known compound with a non-transition metal, or d-10, center involved in the formation of a M-M single bond. Show the Cartesian axis system and briefly describe the atomic orbitals involved in the metal-metal bonding. (If no example comes to mind, for partial credit do the same for any X-X bond involving a main group element.)

C. (30 points) Sketch the structure of a transition metal compound with a M≡M triple bond. Again, show the Cartesian axes and briefly describe the atomic orbitals involved in metal-metal bonding.
1) (40 points) Schreiner and co-workers have recently been investigating the occurrence of tunneling in organic reactions. In an article in *Org. Lett.*, 2011, 13 (13), pp 3526–3529, they examined the competition between H and C tunneling in cyclopropyl carbenes.

a) Borden and co-workers have recently shown that the ring opening of cyclopropylmethyl radical can occur by tunneling. As Schreiner and co-workers describe, the evidence that tunneling occurs is succinctly summarized by this scheme.

```
  H  \-\  C-tunneling
   \-\                        \-\      2
  methylcyclohexane, -100 °C  k = 10^8 s^-1, KIE (/2C/13C) = 1.163
```

Explain how the information shown in this scheme indicates that the reaction occurs by tunneling.

b) A common indication that tunneling is occurring is the lack of temperature dependence in an Arrhenius plot. Schreiner and co-workers based their assessments on the predicted Arrhenius plots for H and C tunneling reactions.

```
  3             8 R = H
    \-\      \-\      \-\      \-\      4
  13
```

Provide a qualitative sketch of an Arrhenius plot that shows the expected appearance for i) thermal reaction and ii) tunneling reaction. Indicate the plot for the thermal reaction with a solid line, and that for the tunneling reaction with a dashed line. Label the axes of the plot properly, including units.

c) Why does the Arrhenius plot for a tunneling reaction have the shape it does?

d) What are the three critical features that affect the rate at which tunneling can occur? (HINT: it might help you to draw a potential energy diagram)

2) (24 pts) Dułach and co-workers have described the bismuth catalyzed tandem-cyclization reaction shown below. Bismuth triflate is commercially available as the hydrated salt.


```
  EIOOC    \-\    EIOOC
  EIOOC      \-\    EIOOC
```

a) Provide a mechanism for the reaction

b) Bismuth is an unusual choice for a Lewis acid catalyst. The Aldrich catalog says that Bi(OTf)_3 "catalyzes direct substitution of allylic, propargylic, and benzylic alcohols with sulfonamides, carbamates, and carboxamides" which has nothing to do with this application. Similarly, the authors themselves state "It is unusual to observe Bi^{III} compounds exhibiting a π-Lewis character, while they are commonly used as π-Lewis acids." Yet, Bi(OTf)_3 was found to be the best catalyst for the reaction. Provide an explanation why?
3) (36 points) The reactions below are taken from the abstracts in the July issues of Org. Lett. Provide “arrow pushing” mechanisms for THREE (and only three) of them (only your first three answers will be graded). Account for why all the reagents were involved, and stereochemistry, where appropriate.

a) HINT: TMEDA = tetramethylethylenediamine

\[
\begin{align*}
\text{H} & + \text{H}_2\text{N}-\text{R}^2 + \text{NaN}_3 & \text{cat. Cul/TMEDA} & \text{DMSO, 120 °C} & \text{R}^1 & \text{N-}\text{R}^2 \\
\text{R}^1 &= \text{H, 5-F, 4,5-OCH}_2\text{O, 4-Me} \\
\text{R}^2 &= \text{aryl, alkyl} \\
\text{30-96% yields} & \text{25 examples}
\end{align*}
\]

b)

\[
\begin{align*}
\text{BF}_2\text{OEt}_2, \text{CH}_2\text{Cl}_2, 15 \text{ min} & \text{59-97%} \\
\text{(R}^1-R^4 = \text{Me, Ph, H, (CH}_3\text{)}_3 \text{)} & \text{(R}^7 = \text{OMe, Ph, H, SI-Bu)} & \text{(2 new C-C bonds; up to 5 new stereocenters)}
\end{align*}
\]

c)

d) HINT: assume MX = Me$_3$SiCl in CH$_2$Cl$_2$ solvent

\[
\begin{align*}
\text{Lewis acid (MX)} & \text{2 equiv H}_2\text{O} \\
\text{23 °C}
\end{align*}
\]

e) HINT: TBHP = tBuOOH

\[
\begin{align*}
\text{up to 93% yield}
\end{align*}
\]

f)

\[
\begin{align*}
\text{Up to 88% yield}
\end{align*}
\]

6
Consider a chemical reaction in which the system is transformed from a lower energy \((\varepsilon_o)\) reactant which has a single conformation state (with a degeneracy of \(g_o=1\)) to a higher energy \((\varepsilon_i)\) product which has three conformational states of approximately the same energy (and thus a degeneracy of \(g_i=3\)). In answering the following question you may neglect the additional internal degrees of freedom of the reactant and product species, by treating this as a two-energy-level system.

a) (20 points) At what value of \(\beta \Delta \varepsilon = (\varepsilon_i - \varepsilon_o)/RT\) will the product and reactant populations be equal to each other?

b) (20 points) Predict the value of the equilibrium constant for such a reaction at 298 K, if the energy difference between the reactants and products is 5 kJ/mol.

c) (20 points) How is the above equilibrium constant related to the Gibbs free energy \(\Delta G\) for this reaction?

d) (20 points) Use the Gibbs-Helmholtz relation \(\Delta H = \left[ \frac{\partial (\Delta G)}{\partial (1/T)} \right]_{\mu}\) to determine the reaction enthalpy.

e) (20 points) Combine your results in (c) and (d) to obtain an expression for reaction entropy \(\Delta S\), and show that it is consistent with the results obtained using the thermodynamics identity \(\Delta S = -\left(\frac{\partial \Delta G}{\partial T}\right)_\mu\).
# Periodic Classification of the Elements

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<th>I A</th>
<th>II A</th>
<th>III A</th>
<th>IVA</th>
<th>VA</th>
<th>VIA</th>
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<td>Cm  247</td>
<td>Bk  247</td>
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</table>

*Lanthanides

†Actinides

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