9. a. On page 8983 the authors report several substituent effect values. For example, the substituent effect on K_E is reported as $\Delta_R\Delta G^o = 4.1$ kcal mol^{-1}. Show how this number is calculated.

b. Rank the following compounds in order of increasing acidity: **1**, **2**, **9**, **10**, **14**, **15**, and **16** (the pK_a of **16** is 22). Briefly give your reasoning using data from the paper to support it.

6. Sketch the NMR spectrum of *N*-acetylamino-*p*-methylacetophenone in the keto form. Be sure to show the splitting and relative shift down field of each peak (you will have to estimate some shifts). Also show the relative areas. Which peak(s) in your spectrum would change, and how would they change, as the compound switches from the keto to the enol conformation? Superimpose these changes on your first sketch (overlay only the peaks that change substantially).

7. The authors argue that Newman Projection **13** is less stable than **12** for several reasons. However, they have neglected a major phenomenon in their analysis. What is it, and how does it affect their results? Illustrate your answer.

8. In their discussion of the equilibrium results (pg 8983), the authors use resonance to explain the effect of the N-acetyl group on K_E (equation 14). What would be the effect on K_E if the N-acetyl group were replaced by a fluorine atom (i.e. X = F)? Would K_E^F be larger or smaller than K_E^H? Briefly give your reasoning.

4. In the experimental section where the authors describe their ketonization rate measurements they state that "The data obtained conformed to the first-order rate law, and observed first-order rate constants were obtained by least-squares fitting of an exponential function." Sketch and fully label a diagram showing conceptually how the raw data for this experiment would have looked. Then explain how they processed it so that they had data which could fitted to a linear function.

5. In equation 9 the authors show a mechanism for general base catalysis. Starting with the following relationship

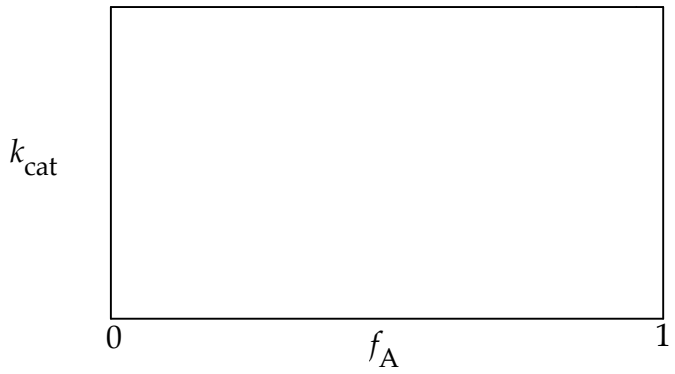
$$k_B[\text{enol}][B] = k'_{HA}[\text{enolate}][HA]$$

show that equation 10 is correct.

3. a. In evaluating the catalytic effect of buffers on the reaction's rate, k_{cat}, the authors make use of the following equation

$$k_{cat} = k_B + (k_{HA} - k_B)f_A$$

where k_B is the rate constant for general base catalysis, k_{HA} is the rate constant for general acid catalysis, and f_A is the fraction of the buffer in its conjugate base form. By plotting k_{cat} as a function of f_A they conclude that only general base catalysis is present. On the axes below, sketch a graph showing the sort of data the authors must have obtained and clearly explain why your graph is consistent with the buffers exhibiting only general base catalysis.



b. Explain how Figure 3 can have more than two data points even though only two values of the $[DCO_3^{-3}]/[CO_3^{2-}]$, which determines the pH, are employed.

2. a. Which of the buffer compounds used in the ketonization rate studies (see the left column of Table 1) would be appropriate for preparing a buffer of pH 4? Briefly describe your reasoning. Write the equation which approximately describes buffer pH as a function of buffer salt concentrations.

b. Explain how the ketonization buffers can be made so that they have a constant ionic strength, constant buffer ratio, but varying buffer concentrations.

c. Figure 1 is constructed using "zero-buffer-concentration intercepts" (k_o) according to equation 5. Why did the authors do this?

d. What is meant by the terms "specific acid catalysis" and "general acid catalysis"?

e. What is the significance of the slope ( ) of a Bronsted plot like Figure 2?

c. Using the data in Table 2, sketch and clearly label a reaction coordinate diagram for your mechanism. Make the activation energy barriers between the various species and the relative energy of the species reasonably accurate from a quantitative perspective. Label each energy barrier with both the rate constant symbol the authors use and its numerical value.

d. The authors claim this work is of relevance to biological systems. Draw the structure of **1** and then immediately below it, a piece of a peptide in such a way that the structures correspond. Then write a mechanism for the racemization of a peptide consistent with the findings in this paper (you can choose the pH conditions for your mechanism).

1. The authors describe several alternative mechanisms for the ketonization process on page 8981, in the first column (these mechanisms are coordinated with Figure 1 in the paper, and are extrapolated to *exclude* buffer species from the mechanism, other than the effect the buffer species have on the concentration of H^+ and HO^-).

a. Based upon the authors' descriptions and Figure 1, write a complete mechanism for the ketonization of compound **2** at pH 7. Use mechanistic arrows and show all reaction intermediates. Label the rate determining step with the rate constant symbol used by the authors. Use equilibrium reaction arrows or single reaction arrows to correspond with the authors' verbal description.

b. This particular mechanism is described by the authors as "... a process whose rate is inversely proportional to $[H^+]$, giving an apparent hydroxide ion catalysis." Derive a rate law for the mechanism you drew above. Use the same rate constant and equilibrium constant symbols as the authors use. Be sure your rate law is expressed in terms of observable (or knowable) concentrations (i.e. it should not contain intermediates).

DePauw University, Department of Chemistry
Comprehensive Exam
Fall 2002, Exam #2

Wednesday November 13th, 2002 7-10 pm

Name _____

The following exam is based upon the article:

Chiang et al "Keto-Enol/Enolate Equilibria in the *N*-Acetyl-*p*-methylacetophenone System. Effect of a □-Nitrogen Substituent" *J. Am. Chem. Soc.* **2001** *123* 8979-8984.

- You will be given a new copy of the article to use as a reference during the exam. No other materials except a calculator are allowed in the exam room.
- You will have three hours in which to answer the questions. Be sure that you use your time wisely.
- Do not write your name or initials anywhere on this exam except on this cover sheet.
- Answer the questions in the spaces provided. Do not write parts of your answers on another page or on the back of a page unless you clearly note both the exam number and the problem number (no names or initials please).
- Please write legibly.
- Because we copy the exams for grading, please be certain that your writing is dark enough to show on a copy.
- Ask the proctor if you have any questions.