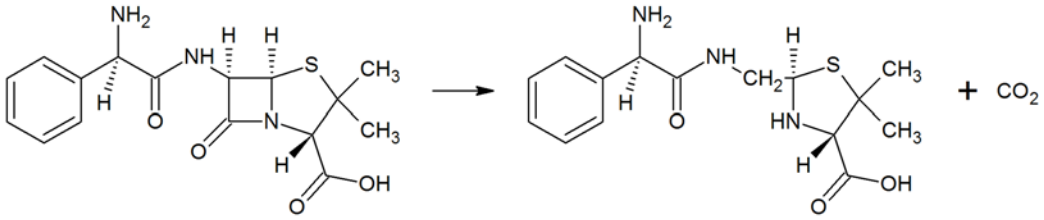
Biophysical Chemistry – CH 4403 01
Assignment 9 (60 points)

Due Friday, November 14 at 4:30 pm

Please complete the answers to this assignment on a separate page (or pages), showing your work and sources (if you referred elsewhere for constants, enthalpies, etc.).

1. Under basic conditions, ampicillin decomposes through hydrolysis of its β-lactam ring. For a discussion of the reaction mechanism, see Hou, J. P., and Poole, J. W. "Kinetics and Mechanism of Degradation of Ampicillin in Solution." *J. Pharm. Sci.* (1969) 58(4): 447. The net reaction appears below. Under conditions of fixed pH and ionic strength, ampicillin decomposes by a first-order rate law.



At pH 7.2, the kinetic rate constants for the decomposition of ampicillin were measured over several temperatures:

Temperature (°C)	k (hr^{-1})
30	19.1×10^{-3}
35	31.3×10^{-3}
40	50.7×10^{-3}
50.5	132.4×10^{-3}

   a. Determine the activation energy for this reaction. (*Hint:* Make a plot.) (5 points)

   b. Calculate the entropy and enthalpy of activation for the reaction. For equation 9.52, use an average temperature of 39 °C. (4 points)

   c. Predict the half-life of ampicillin in refrigerated solution (at 4 °C). (3 points)

2. The reaction mechanism for dimer formation is shown below:

$$2A \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} A_2$$

   Using the procedure outlined in class (and on p. 349-54 in your book), show that for relaxation dynamics, the time constant for a small perturbation from equilibrium is $\tau = \frac{1}{4k_1[\bar{A}]+k_{-1}}$. Assume that $[\bar{A}]$ and $[\bar{A}_2]$ are the final equilibrium concentrations of monomer and dimer after

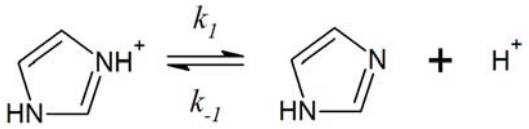
the perturbation. *Hint:* In your original expressions for $[\bar{A}]$ and $[\bar{A}_2]$ make sure that for every x dimer formed that you use up $2x$ monomers. (5 points)

3. Tinoco Chapter 9, question #31. *Hint:* For part (a), start with an expression for $[P_{tot}]$ in terms of free [P] and rate constants (eliminate $[P_2]$). Then, work with your expression for $1/\tau^2$ to write it in terms of $[P_{tot}]$. (10 points)

4. A reaction rate is measured at 25^0C for a reaction where two monovalent ions of opposite charges react to form a product. When the ionic strength is 0.050 M, k is found to be 2.71 L^2 mol^{-2} min^{-1}. Estimate the rate constant of this reaction at zero ionic strength. (3 points)

5. Tinoco, Chapter 9, question #33. Note that, for gaseous reactions such as this one, the pressure is used in rate laws instead of concentrations. *Hint:* For part (a), mechanism I, note that two 3 moles of O_2 are formed; therefore the "normal" rate law would produce 3 moles of O_2 for every collision. For part (b), you will have to normalize your enthalpy scheme to the consumption of one mole of O_3. (7 points)

6. Histidine is an important amino acid because its side chain ionizes near neutral pH. The side chain of histidine is an imidazole group (Im). Imidazole dissociates reversibly according to the mechanism below:



In this reaction, k_1 is 1.5×10^3 s^{-1} and k_{-1} is 1.5×10^{10} $M^{-1}s^{-1}$.

a. A temperature jump from 20 °C from 25 °C is made on a 0.1 M imidazole solution at pH 6. Calculate the relaxation time for the following reaction, assuming the complete mechanism is shown.

$$Im + H^+ \rightleftarrows ImH^+$$

Strictly speaking, an $[OH^-]$-catalyzed ionization pathway is also possible, but we assume this is slow at pH 6 (see question 9.36 for more information). (5 points)

b. The relaxation time is a function of pH. At what pH will the relaxation time have its largest value? In this problem, you will derive an expression similar to

$$\tau([H^+]) = \frac{1}{C + f([H^+])}$$

where C is some constant. In this situation, τ as a function of $[H^+]$ will be maximized when $f([H^+])$ is minimized. Recall from calculus that $f(x)$ is maximized/minimized when $\frac{df(x)}{dx} = 0$. (13 points)

c. How could you measure the activation energy of k_{-1} at pH 6? Given that this reaction appears to be very nearly diffusion-limited ($A \approx 10^{10}\ s^{-1}$, see p. 354-356), estimate a value for the activation energy of this reaction. (3 points)

d. According to Debye-Hückel theory, would you expect the relaxation time to increase, decrease, or stay the same if 0.1 M NaCl is added to the solution? Why? (2 points)