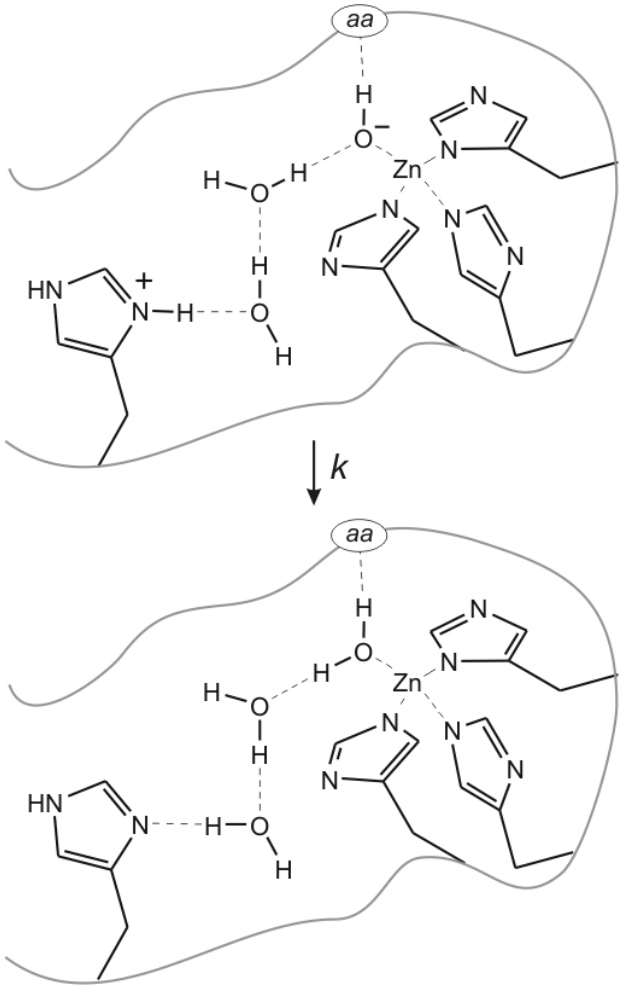
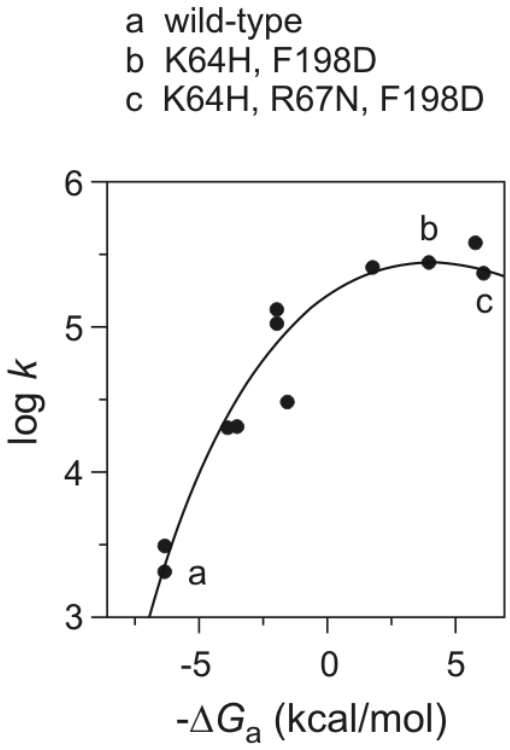
Chemistry 4011/8011 Monday, November 6

Workshop 8

Our bodies' respiration cycle produces carbon dioxide, but most of that CO_2 is actually transported by blood as bicarbonate (HCO_3^-). An enzyme in red blood cells, carbonic anhydrase, catalyzes the rapid conversion of CO_2 generated by cells to HCO_3^-, and then catalyzes the reverse reaction in the lungs where CO_2 is released.[1] One interesting feature of carbonic anhydrase is that protons are shuttled extremely quickly from a histidine near the enzyme surface to the catalytic ZnOH center of the enzyme through a chain of coordinated water molecules in one, concerted step. Silverman and coworkers argue that the rate constant *k* for this step is modeled well by Marcus Theory.[2]





A diagram for the proton transfer in the active site is shown above. Silverman and coworkers were able to vary the exothermicity of this step by engineering different

[1] See http://www.rcsb.org/pdb/molecules/pdb49_1.html for more background.
[2] Silverman, D. N. *Biochim. Biophys. Acta* **2000**, *1458*, 88-103.

H-bonding amino acids ("*aa*") into the active site which affected the basicity of the ZnOH species. They also ran the reaction under conditions that made this step rate-limiting. Data from these experiments, as well as a putative curve fit to the Marcus equation, is shown on the right.

a. We'll assume for now that Silverman is correct, and that point "*b*" represents the maximum rate on the Marcus curve. For each of the labeled points (*a*, *b*, and *c*) draw a potential energy diagram that illustrates how the reaction coordinate can be modeled in terms of simple, intersecting parabolae.

b. On the diagrams, what is the physical meaning of each parabola? What aspects of the reaction coordinate does each parabola model? What is the physical meaning of the intercept?

c. Silverman argues that Marcus theory applies to this reaction because the intrinsic barrier to hydrogen-bond exchange is so low. Based on the curve fit, what is $\Delta G^{\ddagger}_{int}$?

d. Using Eyring's equation, what would you calculate for the maximum reaction rate (k_{max}) at the top of the Marcus curve? Does this correlate with the rate constants measured by Silverman's group?