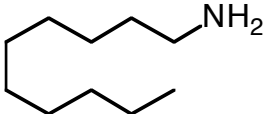
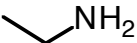
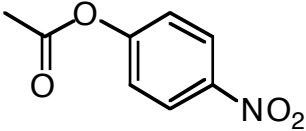
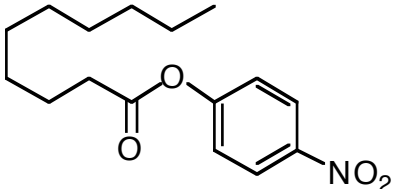


Biochemistry 704  
 Problem Set 5  
 Due 03/11/2008

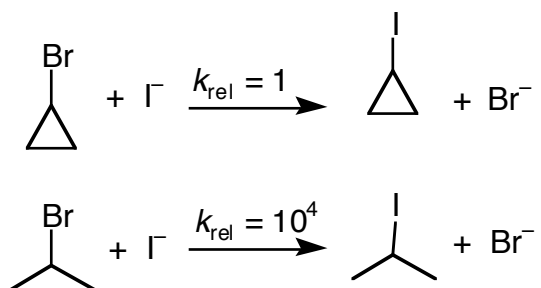
1. In water at 35 °C, the rate constants for the aminolysis (by ethylamine and decylamine) and hydrolysis (by hydroxide ion) of an acetate and decanoate ester are as follows.

Rate Constant for Aminolysis or Hydrolysis ( $k$ ; $M^{-1}s^{-1}$ )			
	 <chem>CCCCCCCCCNH2</chem>	 <chem>CCNH2</chem>	$^-OH$
 <chem>CC(=O)Oc1ccc([N+](=O)[O-])cc1</chem>	39	5.7	9.4
 <chem>CCCCCCCCC(=O)Oc1ccc([N+](=O)[O-])cc1</chem>	130	0.42	1.2

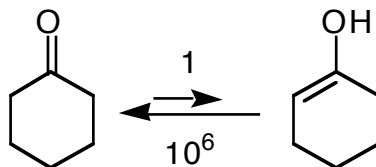
- a. Why is the ratio  $k_{\text{decylamine}}/k_{\text{ethylamine}}$  for attack on the decanoate ester  $\gg 1$ ?
- b. If the environment were altered by decreasing the dielectric constant of the medium, would this ratio increase or decrease? Explain briefly.

c. Why is the ratio  $k_{\text{decanoate ester}}/k_{\text{acetate ester}}$  for attack by hydroxide ion  $<1$ ?

2. The relief of strain in the transition state can accelerate a chemical reaction. Cyclopropyl bromide has a large amount (25–30 kcal/mol) of ring strain energy. Yet, cyclopropyl bromide undergoes nucleophilic attack by  $\text{I}^-$  in acetone (to form cyclopropyl iodide)  $10^4$  times more slowly than does isopropyl bromide. Explain. What lesson can be learned from this example about the role of strain in reaction kinetics?



3. Understanding energetic relationships is essential to understanding catalysis. In water at 25 °C, cyclohexanone is in equilibrium with  $10^{-6}$  parts of a tautomer. Which of the two species is a stronger acid (has a lower  $pK_a$ )? Explain by using a diagram that shows the relative free energies (in kcal/mol) of the relevant species. If the  $pK_a$  of the tautomer is 12, what is the calculated  $pK_a$  of cyclohexanone? Show your reasoning.





c. In 1948, Linus Pauling wrote:

“An enzyme has a structure closely similar to that found for antibodies, but with one important difference, namely, that the surface configuration of the enzyme is not so closely [complementary] to its specific substrate as is that of an antibody to its homologous antigen, but is instead complementary to an unstable molecule with only transient existence—namely, the ‘activated complex’ for the reaction that is catalyzed by enzyme.”

Would Pauling’s enzyme catalyze a chemical reaction? Explain using a free energy profile.

d. Describe briefly how, given a team of synthetic chemists and immunologists, you could use Pauling’s notion to generate novel catalysts.