CH386J

Dr. Eric Anslyn

Nov. 5, 2016

Exam 2

Name: KEY

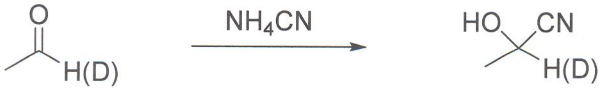
Problem	Earned Points	Total Points
1		8
2		13
3		8
4		6
5		9
6		8
7		10
8		8
9		3
10		16
11		12
12		14
13		7
Total		122
%		

1) Which type of kinetic isotope effect (primary, secondary, normal, inverse, or no effect) do you expect for each of the following reactions? Hint: Think about the mechanisms and the rate determining step. (2 pts each)

a)

no KIE

b)



2° inverse

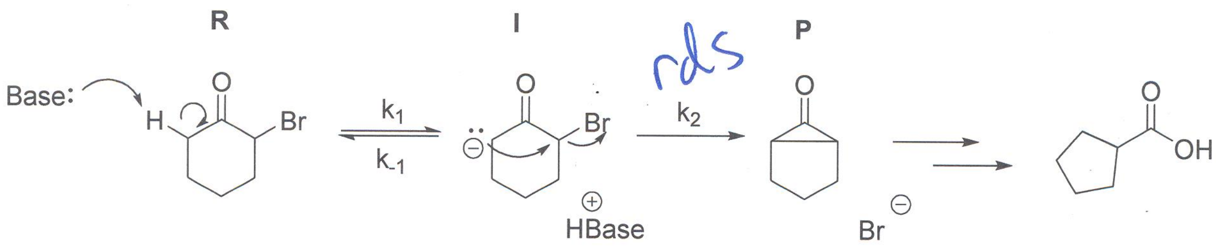
c)

2° normal

d)

1° normal

2) This is the Favorskii Rearrangement, which was one of the possible mechanisms for this exam. Instead, we're going to look at the kinetics of this reaction! The first steps are shown below.



(a) Using the Steady-State Approximation, write a rate law for the above reaction. You can use the abbreviations **R**, **I**, and **P** as necessary. (3 pts)

$$\frac{dP}{dt} = \frac{k_1 k_2 [R][Base]}{k_{-1}[\overset{\oplus}{H}Base] + k_2}$$

(b) In the above scheme, label the step you would expect to be rate-determining (rds). How does this simplify your rate law? (3 pts)

$k_{-1} >> k_2$

$$\frac{dP}{dt} = \frac{k_1 k_2 [R][Base]}{k_{-1}[\overset{\oplus}{H}Base]}$$

(c) Based on the rate law you wrote, what will happen to the rate if NaBr is added to the reaction? (2 pts)

no change

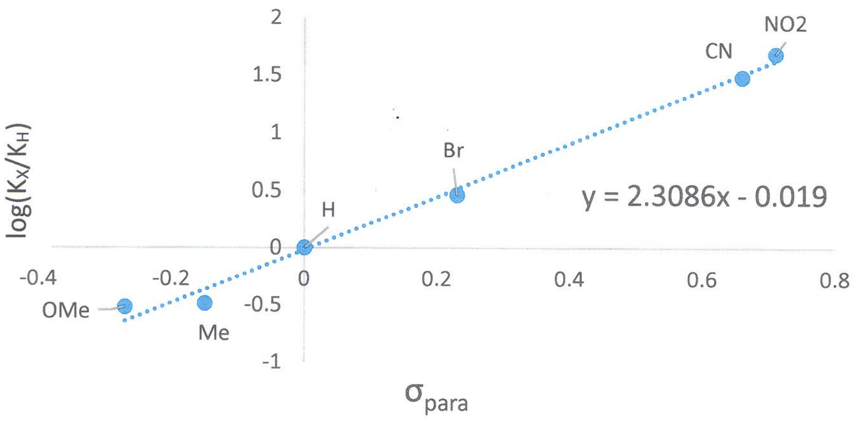
(d) Based on the rate law you wrote, what will happen to the rate if you raise the pH of the reaction? Explain. (3 pts)

increase. more $[\text{Base}]$ + less $[\text{HBase}^{\oplus}$

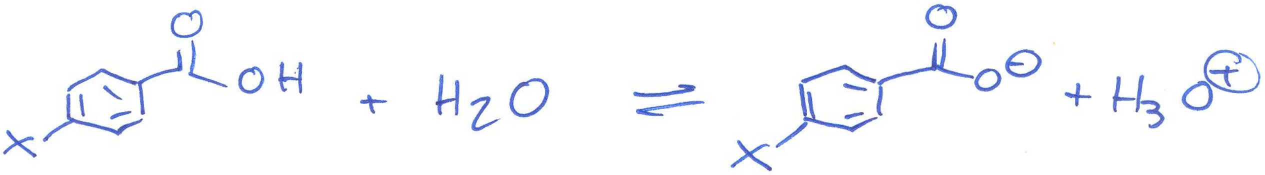
(e) What kind of base catalysis is involved in this reaction, specific or general? Explain. (2 pts)

Specific. rate depends on ratio of $\text{Base}/\text{HBase}^{\oplus}$ (i.e. pH). Also deprotonation prior to rds

3) Your TA Maggie has generated a Hammett Plot for her research. She measured the pK_a's of 6 different substrates and got the following plot.



(a) What is the reference reaction for a Hammett plot? (2 pts)



(b) Explain what a σ_{para} (sigma) value is. (1 pt)

substiuent parameter that describes the ratio of the log of rate or equilibrium constant vs. X = H. $\log\left(\frac{K_X}{K_H}\right) = \sigma$

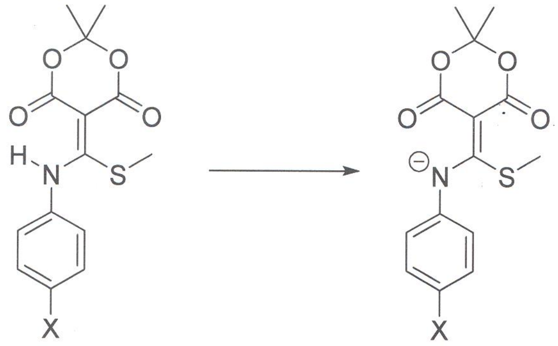
(c) In Maggie's Hammett plot, is positive or negative charge building? (1 pt)

negative

(d) Is the ~~deprotonation~~ reaction Maggie studied more or less sensitive to substituent changes than the reference reaction? Explain how you know this. (2 pts)

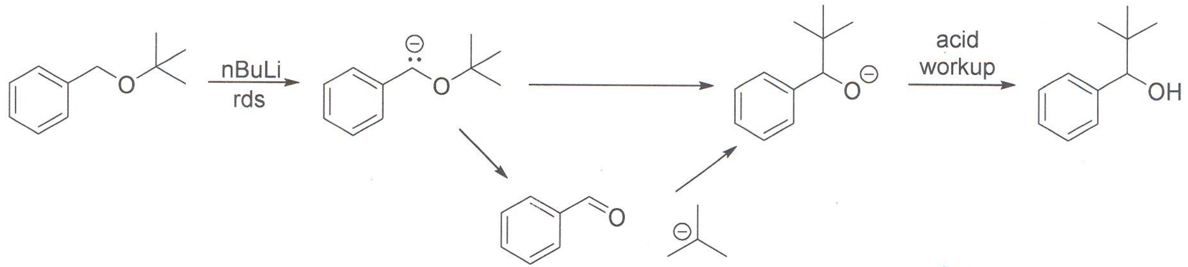
more slope > 1

(e) Here are the substrates Maggie looked at. Based off these structures, explain why this is more or less sensitive to the reference reaction. (2 pts)



negative charge can delocalize into aryl ring.

4) The following transformation could occur through either a dissociative mechanism or a concerted mechanism. Propose two experiments to distinguish between these two mechanisms. (6 pts)

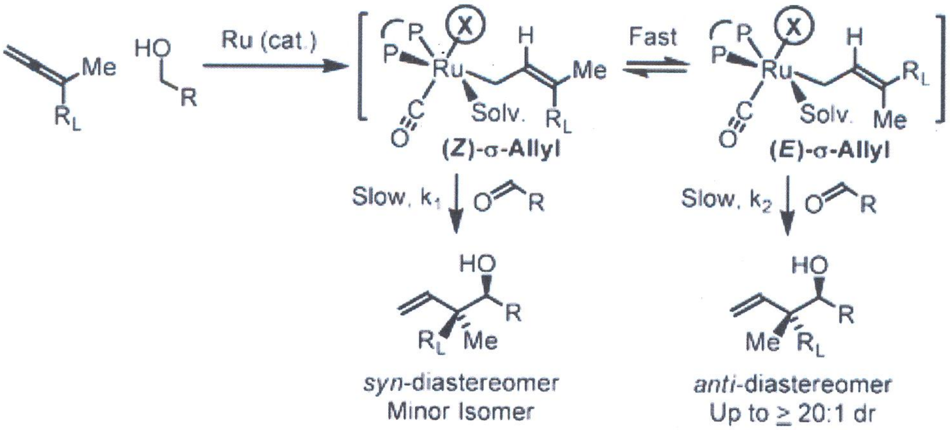


① cross-over

② include stereochem for t-butyl group

~~③ KIE at benzyl position~~

5) The following study on ruthenium catalyzed hydrohydroxyalkylation of allenes was published by Dr. Krische in 2011. It was proposed that the intermediate (Z)- and (E)-σ-allylruthenium isomers are in rapid equilibrium, with each of the intermediates giving rise to a distinct diastereomer of the product.



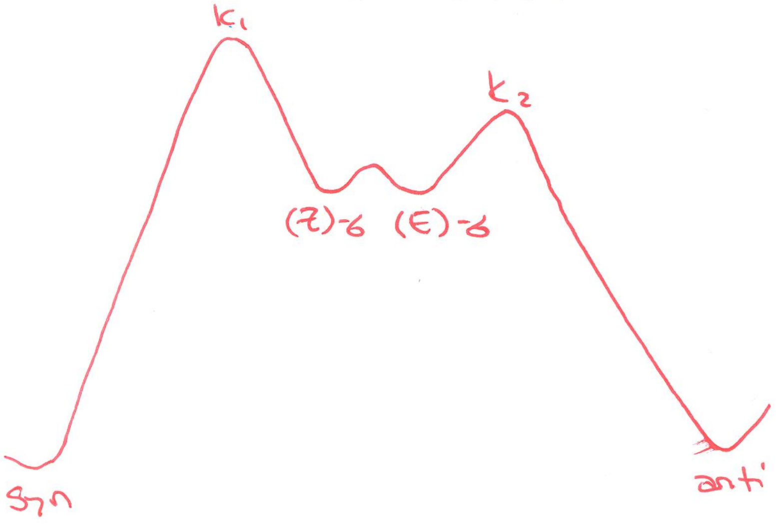
a) Assuming that equilibration of the intermediates is fast relative to k_1 and k_2, what determines the observed product ratio? (2 pts)

Relative barrier heights to product formation.

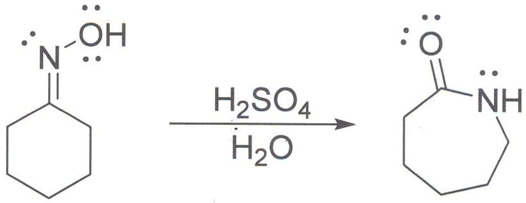
b) What is this effect called? (1 pts)

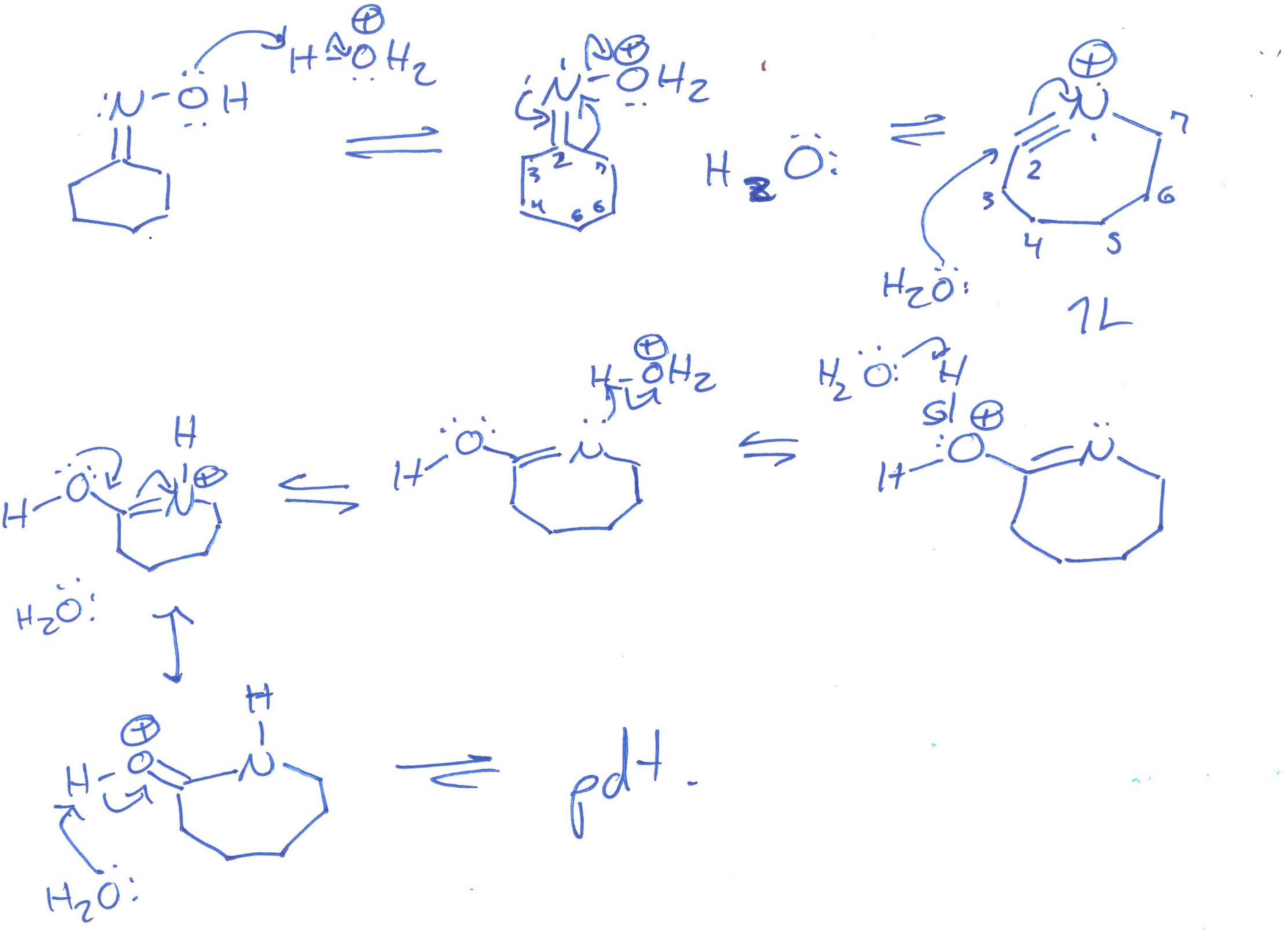
Curtin-Hammett

c) Draw a diagram of the second part of the reaction (intermediates and products), including relative energies of all stable species and transition states. Label all stable species and which energy barrier corresponds to k_1 and k_2, respectively. (6 pts)

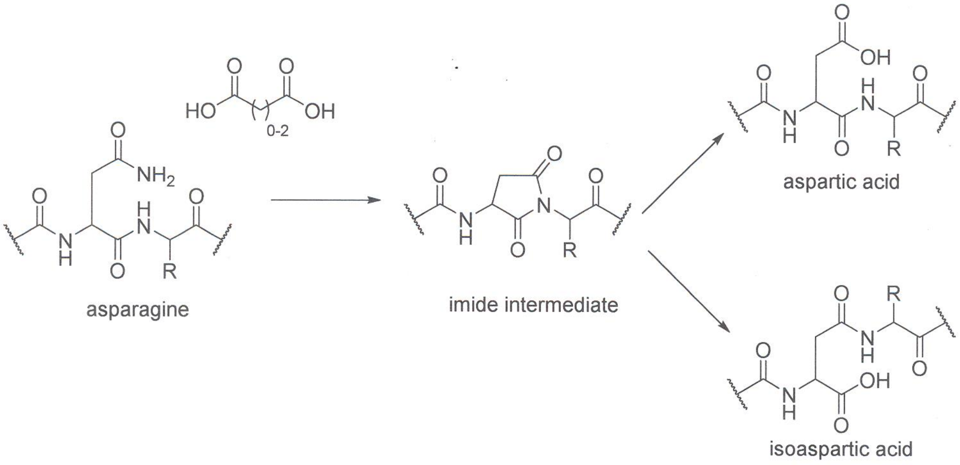


6) Please provide an arrow-pushing mechanism for the following Beckmann rearrangement. Be sure to show all steps, electrons, and side products. (8 pts)

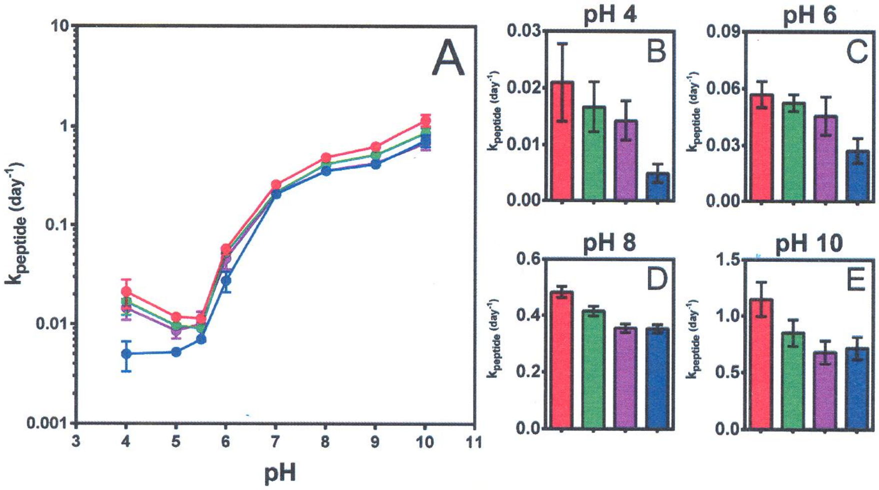




7) The amino acid aspargine is known to deamidate to form the imide intermediate below, which is hydrolyzed into either aspartic acid or isoaspartic acid. This reaction is thought to be one of the factors that limits the useful lifetime for proteins. The mechanism of this was studied at various pH and with various carboxylic acids which help facilitate the reaction.



Here is the correlation between pH and the observed rate constant. Look at the y-axis – note that they have included a logarithmic scale instead of plotting log(k). This means that you can treat the data between pH 6 and pH 11 as linear even though it doesn't look it. The different colored lines are the rates with different carboxylic acids. The difference found between rates with different acids is **not** due to differences in acid/base catalysis but instead something that will be discussed in part (d).



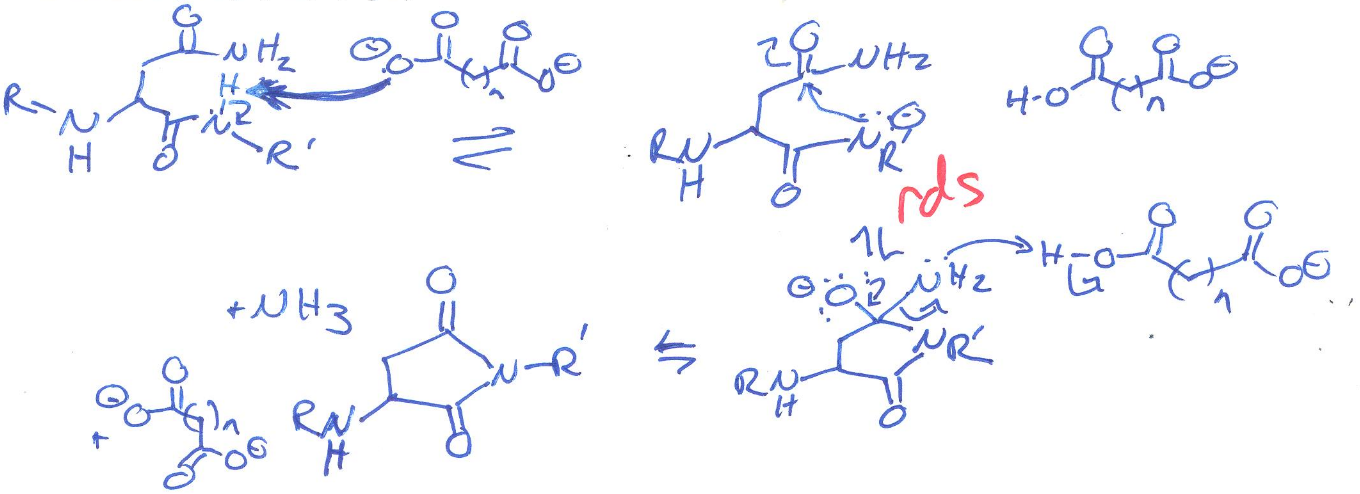
(a) What type of catalysis is happening between pH 4 and pH 5? (Ignore the blue line for this part) (2 pts)

specific acid

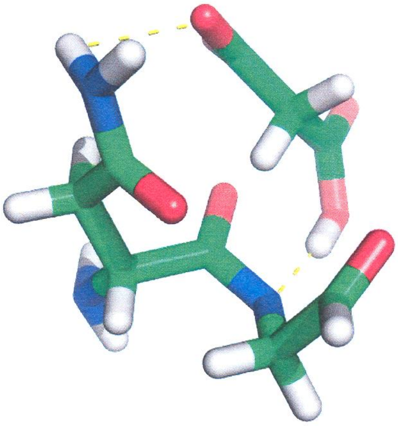
(b) What type of catalysis is happening between pH 5 and pH 10? (2 pts)

specific base

(c) Write a mechanism for imide formation based on your answer in (b). Label the rate-determining step (rds). (4 pts)

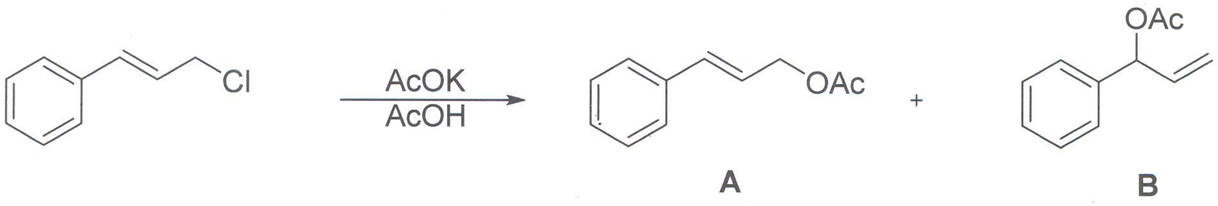


(d) Thermodynamic analysis shows that the carboxylate helps stabilize the transition state of the cyclization step. (Model shown) How does this help explain the small changes in rates between acids? (2 pts)



different lengths of carboxylates will stabilize the TS of the cyclization more or less

8) The following reaction initially gives mixtures of isomers **A** and **B**. After stirring for longer, **A** is the predominate product.



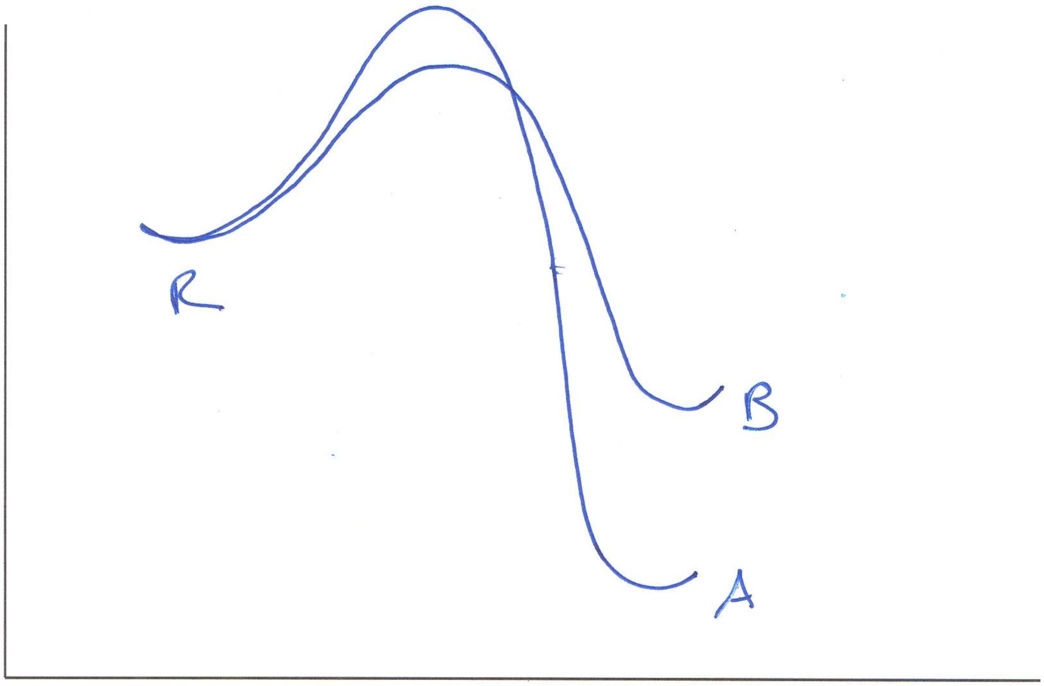
(a) Which is the thermodynamic product? (2 pts)

A

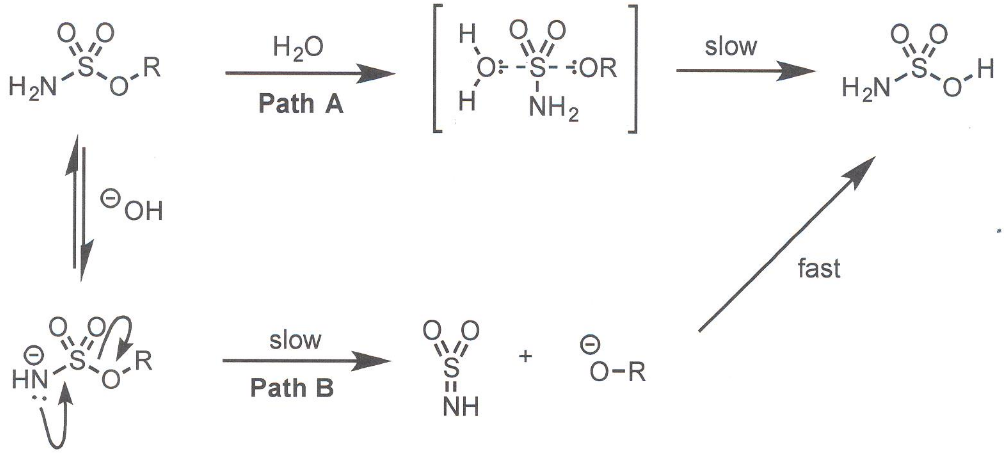
(b) Which is the kinetic product? (2 pts)

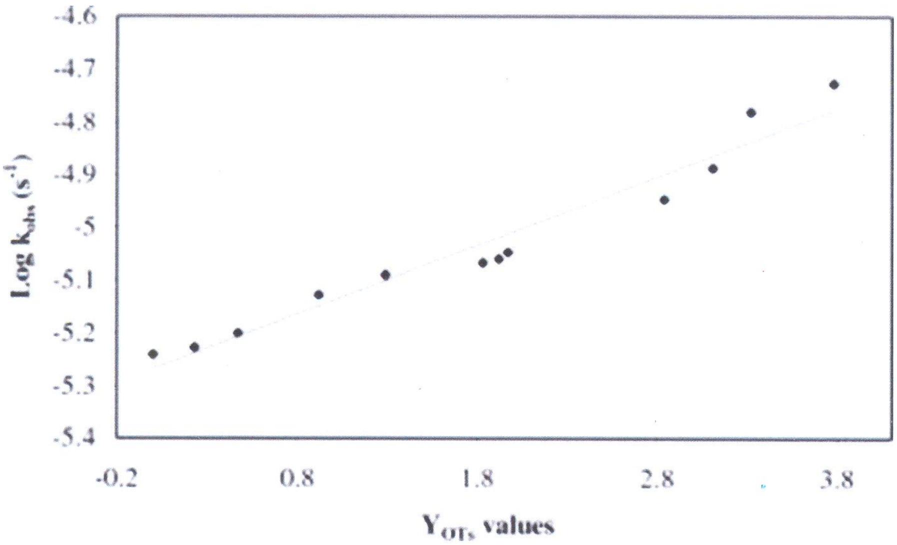
B

(c) Draw the reaction coordinate diagrams for the formation of both products. Label which is **A** and which is **B**. Be sure to show the relative energies of the transition states and products. (4 pts)



9) Two possible mechanism are shown for the hydrolysis reaction of medicinally important sulfamate esters. To distinguish between the two mechanisms, the authors generated a Grunwald-Winstein plot (shown below) by measuring the rate constants in varying ratios of ethanol and water. The slope of the plot was found to be m = 0.13.



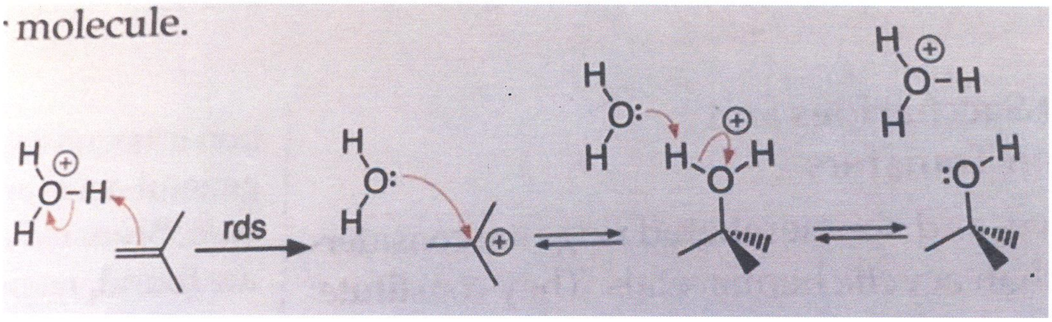


Which of the two mechanisms (path A or B) is supported best by the data presented? Explain your reasoning. (~~5~~ 3 pts)

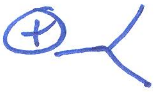
Path A : No charges are generated in path A

→ not very sensitive to solvent polarity.

10) The following is the standard arrow pushing for the mechanism of Markovnikov hydration of isobutylene (ignore the word “molecule” in the upper left corner, Dr. Anslyn took this photo on his phone).



a) The arrow pushing shown could indicate the formation of two possible carbocations, albeit only one is drawn. Draw the other possible carbocation and explain why only the one drawn above is shown. (2 pts)

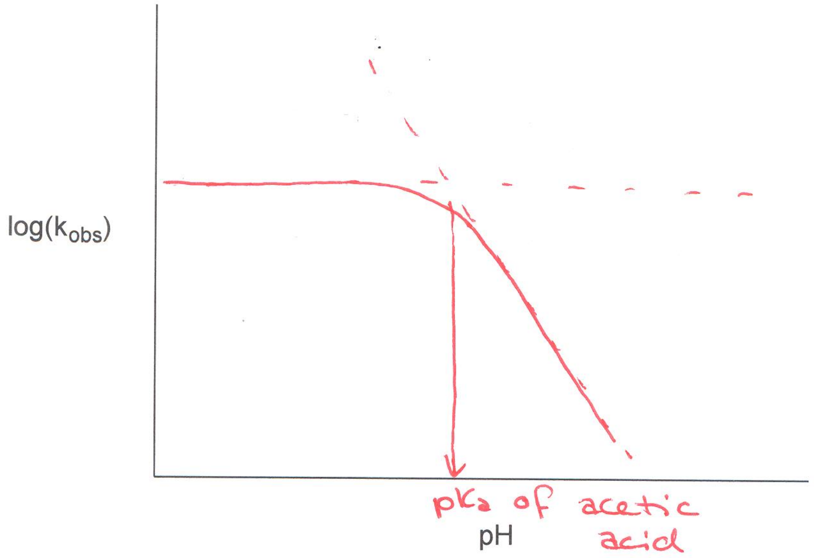


3° carbocation is stabilized more by hyperconjugation

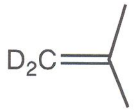
b) What is the name of the kind of acid catalysis found in the first step (specific or general)? Briefly explain your answer. (2 pts)

general. catalysis is in rds

d) This time we add acetic acid to the solution of isobutylene and water. Based on your answers to part (b) and (c), draw the kind of kinetic plot you would expect for your predicted form of catalysis using acetic acid. (3 pts)



e) If dideuterio isobutylene, as shown, is used as the reactant, what kind of a kinetic isotope effect would you expect for this reaction? (2 pts)

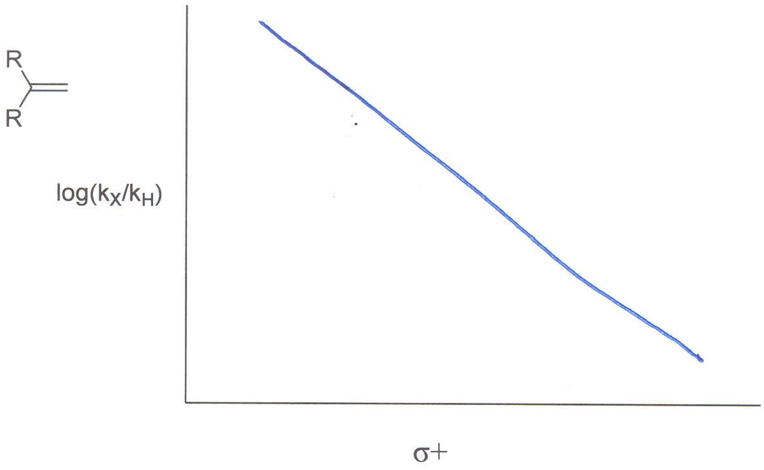


2° inverse

f) None of the deuteriums in the reactant of part (e) are lost to the solvent during the reaction; they are all incorporated into the product. What does this tell you about the first step of the mechanism? (2 pts)

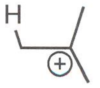
It is irreversible

g) The R groups on the alkene can be varied and from this, a Hammett plot can be drawn. The axes have been labeled for you. Draw the line you would expect from this reaction. (2 pts)



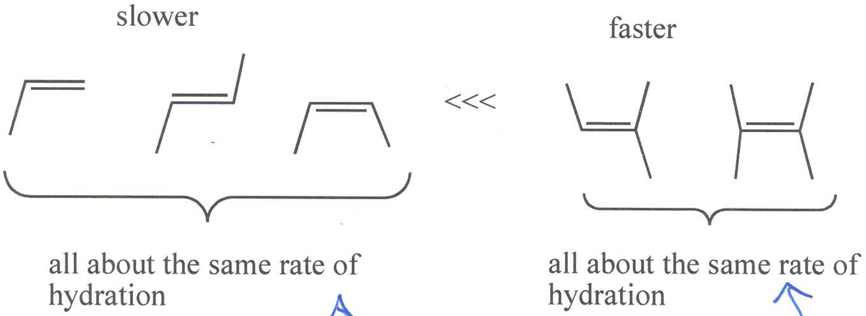
h) Let's go a bit deeper, there are two kinds of carbocations: carbenium ions and carbonium ions. The first has a localized positive charge, while the second is delocalized, respectively. It has been postulated that a discrete carbenium ion is not formed in the hydration of an alkene, but that instead the proton bridges the pi-system of an alkene to give a carbonium ion, analogous to a bromonium ion.

Carbenium ion



Carbonium ion

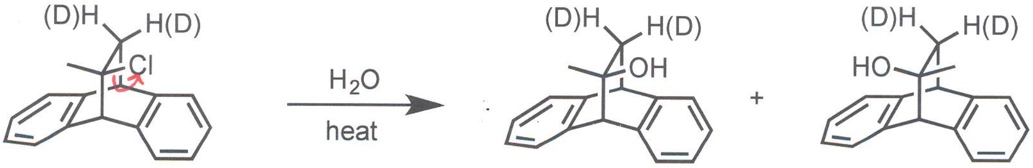
To distinguish these two possibilities, the rate of hydration of the following olefins were compared, and the first three are about the same, while the second two are about the same. Which kind of a carbocation does this data support, the carbenium ion or carbonium ion? Explain your answer. (3 pts)



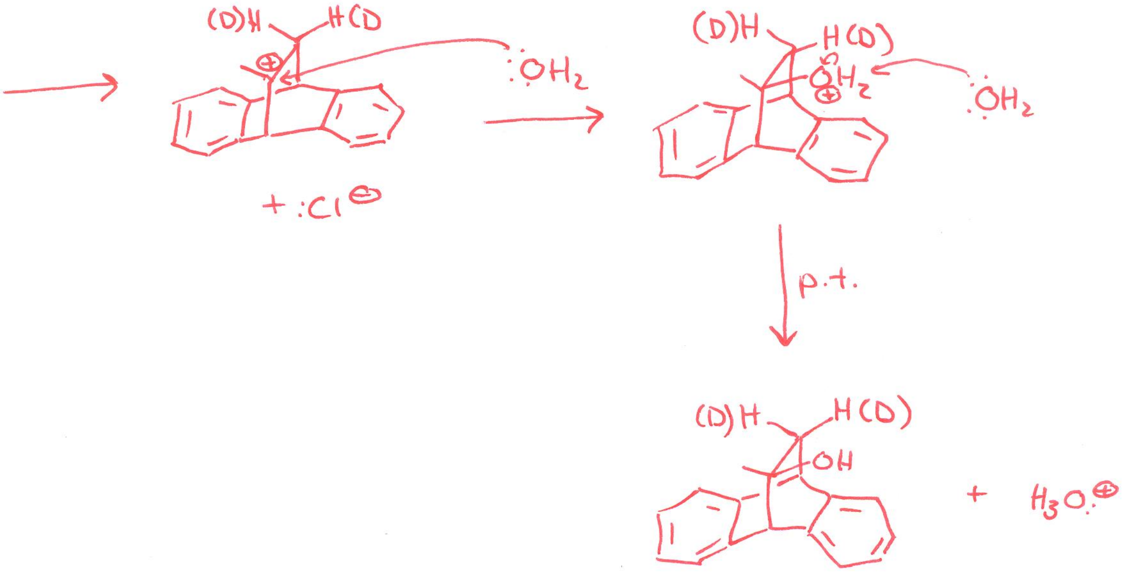
Carbenium

all 2° + all 3° are same rates

11) For the following solvolysis reaction, a kinetic isotope effect of **k_H/k_D = 1.14** is observed.



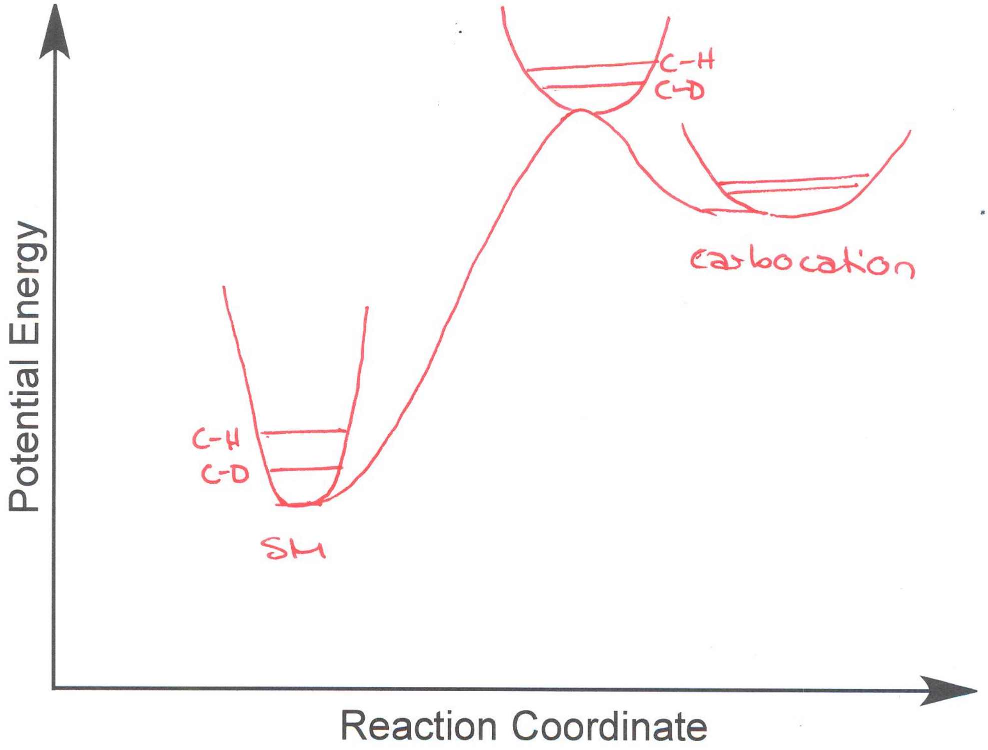
a) Provide a reasonable mechanism for the transformation. (4 pts)



b) What type of KIE does a value of 1.14 most likely correspond to (primary, secondary, normal, inverse)? (2 pts)

2° normal

c) Draw the reaction coordinate diagram for the rate determining step. Show the relative energy wells of the starting material, transition state and product (of the rds) that would give rise to the observed kinetic isotope effect value. Draw and label the ZPEs of H and D in each well. (4 pts)

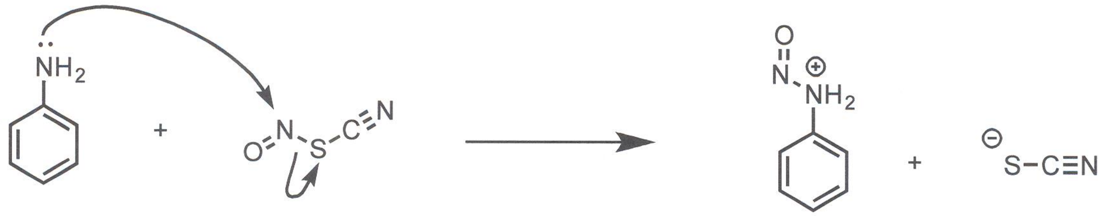


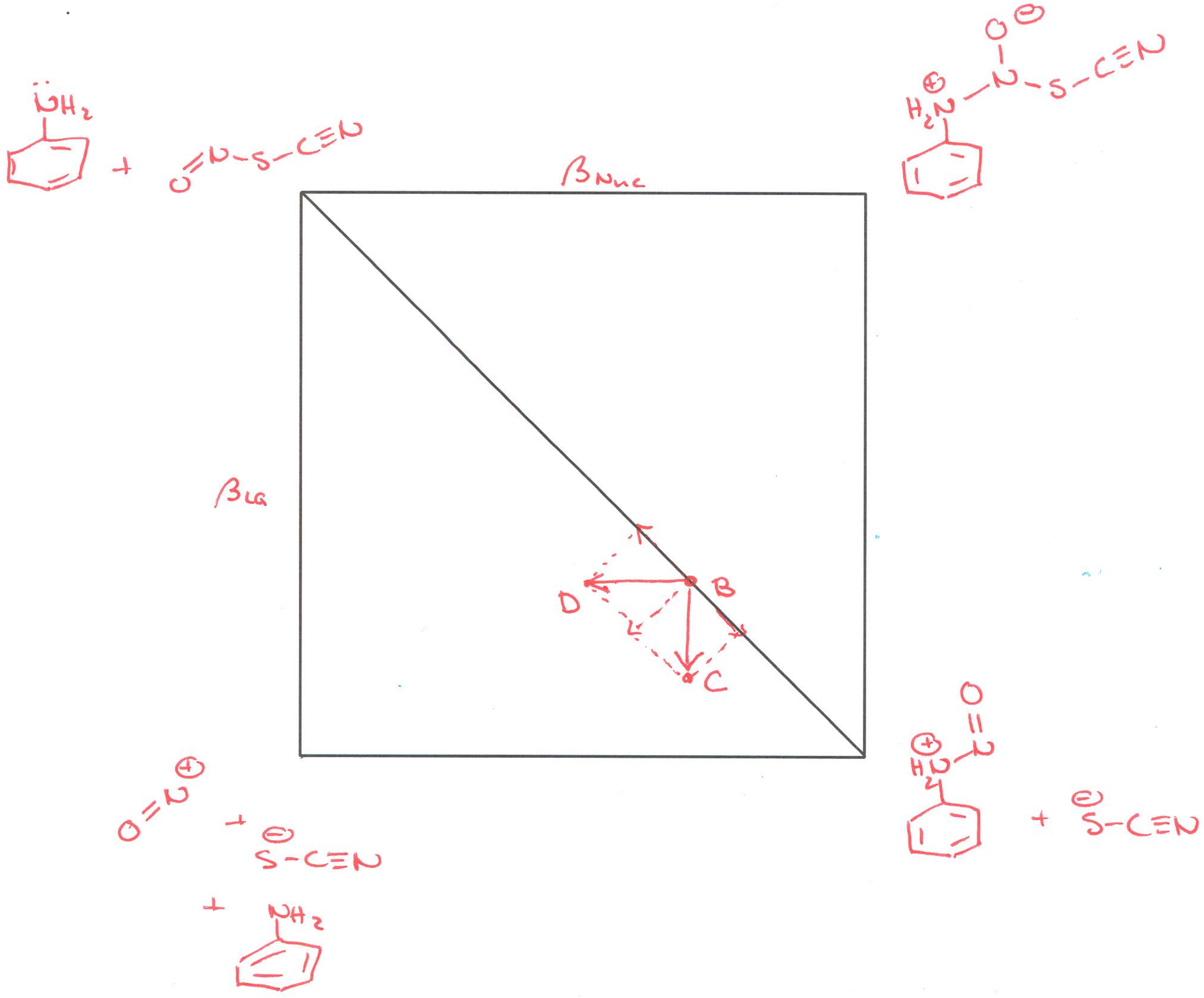
d) Explain how the changes that the C-H(D) bonds experience in the rate determining step could lead to the observed isotope effect. (2 pts)

Hyperconjugation weakens the C-H(D) bond.

12) a) Draw a More O'Ferrall-Jencks plot for the nitrosylation reaction shown below. The concerted mechanism is shown, but there are also two possible stepwise mechanisms: associative and dissociative. (6 pts)

i. Draw the reactants and products corresponding to each of the possible mechanism in the corners of the plot below, with the bottom left corner corresponding to the dissociative mechanism, and top right to the associative mechanism.
ii. Label the axes of the plot with the corresponding LFER parameter (α, β, β_{Nuc}, β_{LG}).

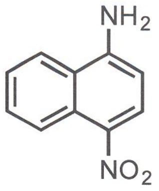




b) It was found that the reaction proceeds via a well balanced, concerted mechanism with similar extents of leaving group departure and nucleophilic attack at the transition state. Taking into account that the reaction is endergonic by 6 kcal/mol, put a dot on the More O'Ferrall-Jencks plot corresponding to the transition state of the reaction and label it as "B". (~~1~~2 pt)

c) How would the transition state of the concerted reaction change, if the substrate is changed to the following molecule? Show the transition state on the More O'Ferrall-Jencks plot and label it as "C". What changes in the transition state, and why does this make sense? (2 pts)

less nucleophilic
→ raise right
corners



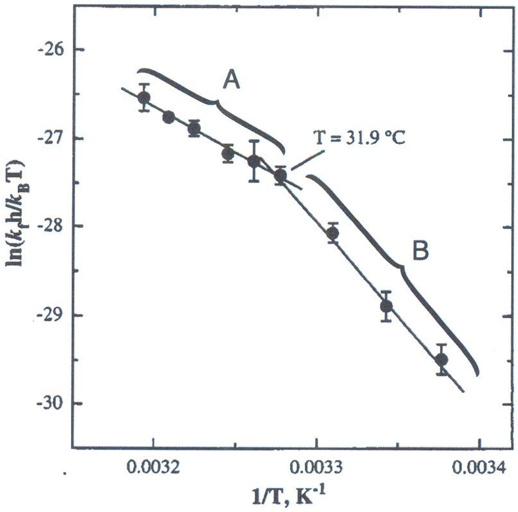
⇒ Extent of nuc. attack stays the same, larger extent of LG departure required to get nuc. to attack.

d) How would the transition state of the concerted reaction change, if a nitrosylating agent with a better leaving group is used? Show the transition state on the More O'Ferrall-Jencks plot and label it as "D". What changes in the transition state, and why does this make sense? (2 pts)

→ lower bottom corners

⇒ less nuc. attack at T.S.; same extent of LG departure

13) The following Eyring plot was obtained for a bond cleavage reaction of the overall formula S → $P_1 + P_2$. The two distinct linear regions A and B were interpreted as a change in mechanism.



$$\ln\left(\frac{kh}{\kappa k_B T}\right) = -\left(\frac{\Delta H^{\neq}}{R}\right)\left(\frac{1}{T}\right) + \frac{\Delta S^{\neq}}{R}$$

a) Circle the correct answer:

i. Which mechanism is preferred at high temperature? (1 pts)

[✓ A] B

ii. Which mechanism has the more favorable $\Delta H^{\neq}$? (1 pts)

[✓ A] B

iii. Which mechanism has the more favorable $\Delta S^{\neq}$? (1 pts)

A [✓ B]

b) Considering your answers to a) ii. and iii., does your answer to a) i. make sense? Why? Why not? (2 pts)

No, B has larger $\Delta S^{\neq}$, so it should be preferred at high T

c) The reaction discussed herein is catalyzed by an enzyme. What could happen to an enzyme as a function of temperature that would influence which mechanism is used? (2 pts)

Conformational change (not denaturation at high T, as rate at high T is still faster)