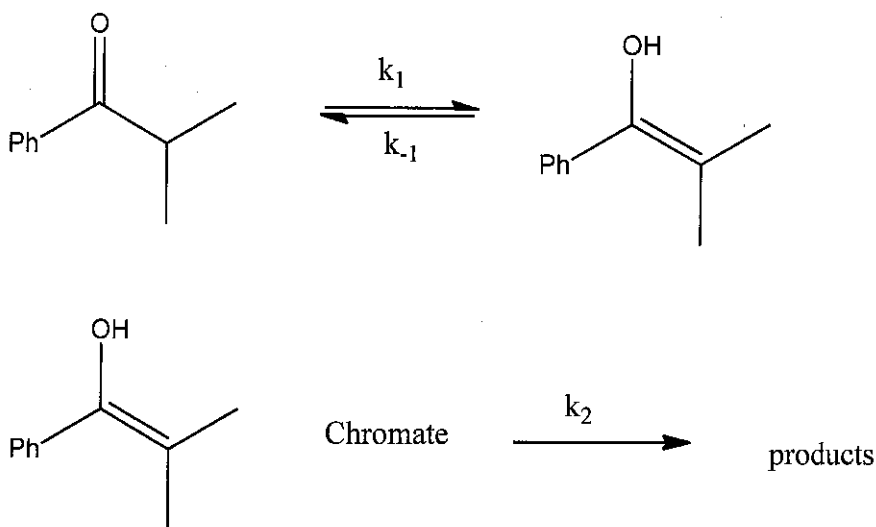


Mechanistic Investigation Exam
C344 Spring 2014

Name _____

1. (15pts) A. Given the following mechanism for this reaction, write a rate law for product formation using the steady state approximation. Make no assumptions concerning the relative rates of the steps.



+5 steady state

$$k_1 [\text{ketone}] = k_{-1} [\text{enol}] + k_2 [\text{enol}] [\text{chromate}]$$

+5 solving

$$[\text{enol}] = \frac{k_1 [\text{ketone}]}{k_{-1} + k_2 [\text{chromate}]}$$

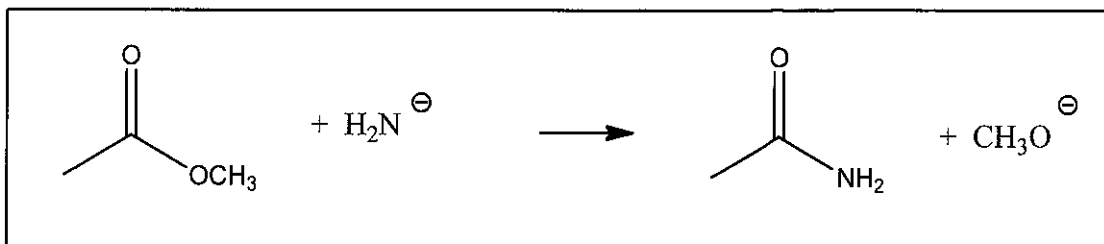
$$\text{rate} = \frac{k_1 k_2 [\text{ketone}] [\text{chromate}]}{k_{-1} + k_2 [\text{chromate}]}$$

B. Simplify this rate law assuming that the second step is rate limiting.

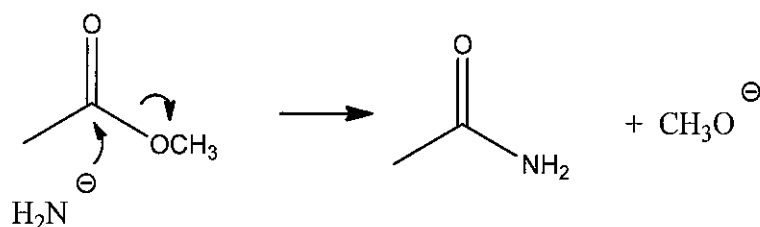
+5 k_2 is negligible

$$\text{rate} = \frac{k_1 k_2 [\text{ketone}] [\text{chromate}]}{k_{-1} + k_2 [\text{chromate}]} = \frac{k_1 k_2 [\text{ketone}] [\text{chromate}]}{k_{-1}}$$

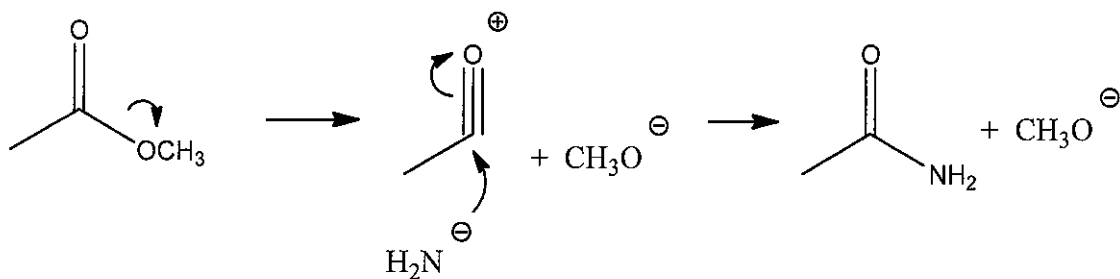
2. (20pts) Compared to nucleophilic substitution mechanism, the nucleophilic acyl substitution has more potentially acceptable mechanisms. Here are three:



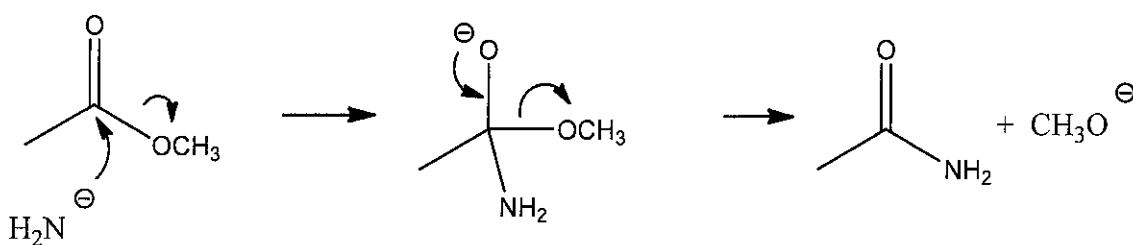
A.



B.



C.



A. Use these mechanisms to draw a MOFJ diagram on the next page.

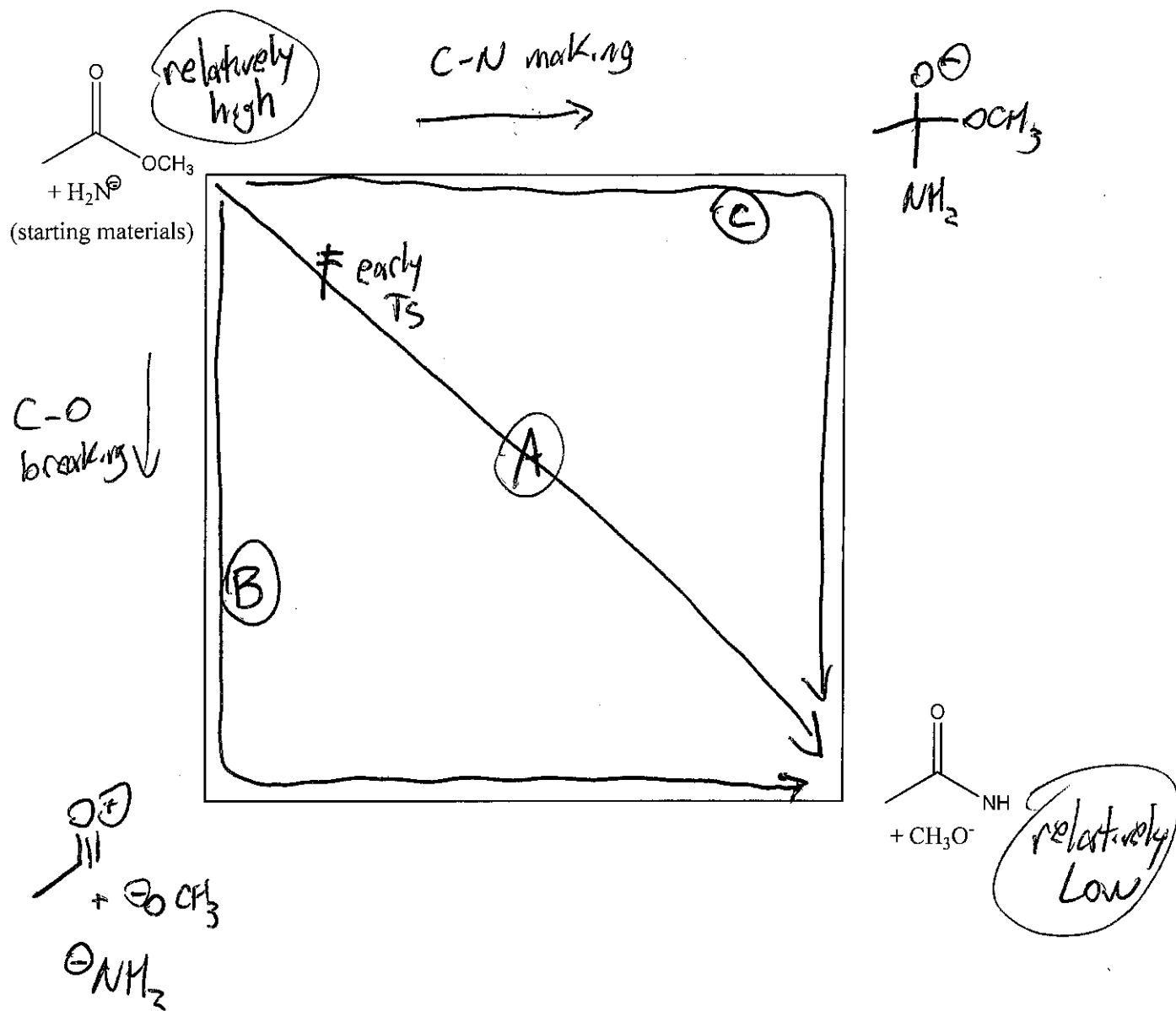
B. Referring to the mechanisms above, draw and label Path A, Path B, and Path C on your MOFJ diagram.

C. Mark the transition state of Path A with a double dagger (\ddagger), assuming that it is an early transition state.

D. If Path A has an early transition state, it tells you something about the relative energies of the corners of your plot. Indicate which corner(s) is/are relatively high, and which corner(s) is/are relatively low.

can be opposite corners

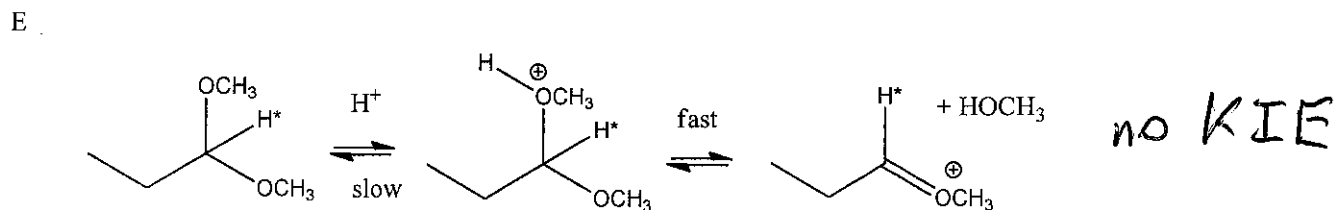
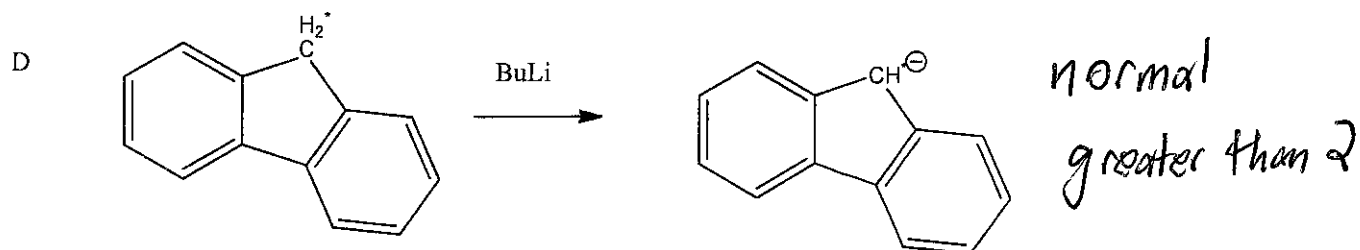
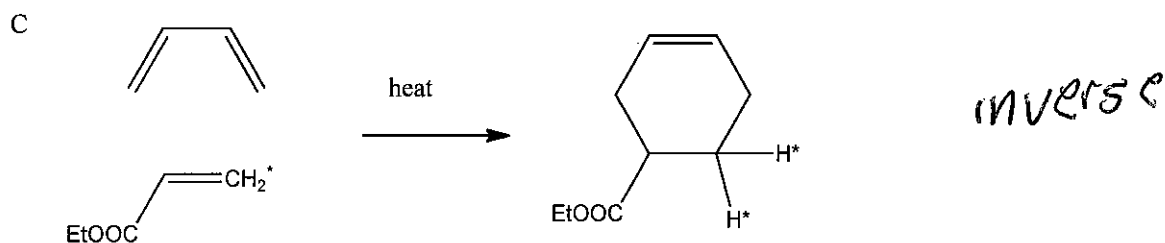
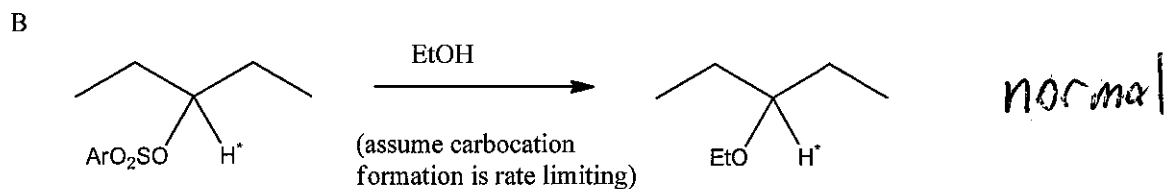
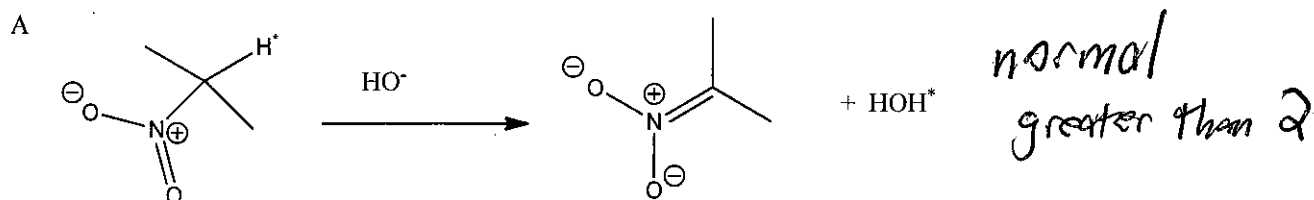
Problem 2 (continued)



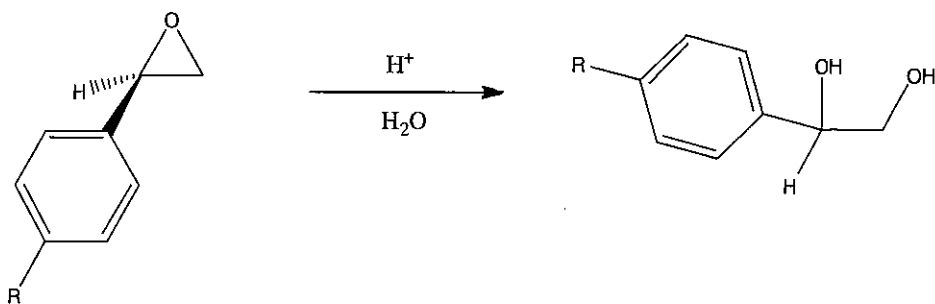
- (+6) MOFJ (+3 for each corner, or designating rxn coordinate)
- (+2) for each path
- (+4) mark ‡
- (+4) high/low corners (+0 for totally wrong, +2 for backwards)

+3 each

3. (15pts) Predict whether you would see normal or inverse kinetic isotope effects (KIE) for each reaction below. Also indicate which reactions would have KIEs > 2. (The isotopic substituted hydrogens are marked with asterisks.)



4. (25 pts) The following data was used to investigate the reaction below. On the following page, draw a mechanism consistent with the data, then explain how each piece of data is consistent with the proposed mechanism.



Experiment A. The rate of the reaction is measured in a series of buffers at different concentrations but the same pH. The rates of reaction do not change across the series of buffers.

Experiment B. The effect of changing substituents on rate is as follows.

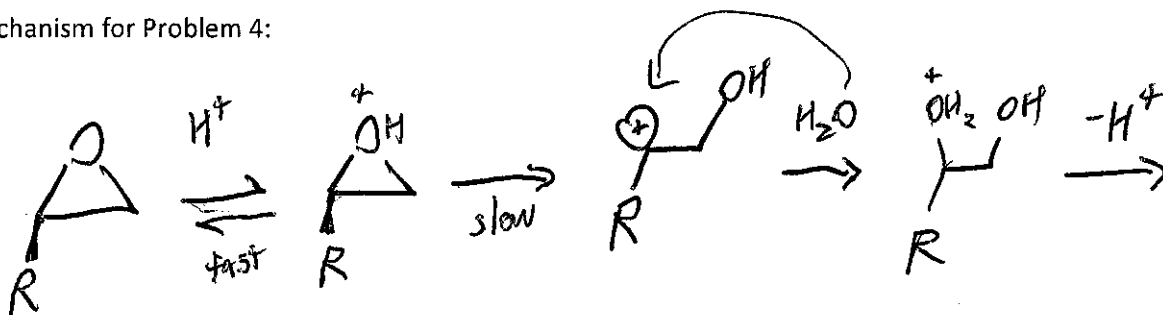
R =	Rate constant ($\text{M}^{-1}\text{s}^{-1}$)	σ_p
methoxy	11000	-.78
H	5.8	0
chloro	2.0	.11
methyl	116	-.31

Experiment C. If the reaction is run in $^{18}\text{OH}_2$, the isotope label ends up only in the benzylic position (closer to the aryl group.)

Experiment D. Starting with the optically active substrate above, the hydrolysis leads to an optically inactive product (a racemic mixture.)

Mechanism for Problem 4:

+5 total



+3 for anything with rate determining carbocation formation

How is Experiment A consistent? Be specific.

Because the pH, but not [HA] affects rate, the protonation is pre-equilibrium, specific acid catalysis
(+2) (+3)

How is Experiment B consistent? Be specific.

+2 { EDG speed the rxn, while EWG slow the rxn, making the LFER have a negative ρ value.
+3 { This suggests significant δ^+ buildup in the TS of the RDS, consistent with carbocation formation in RDS.

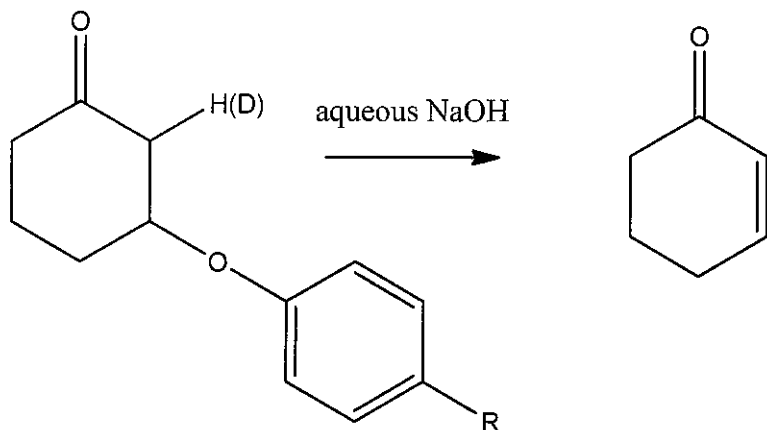
How is Experiment C consistent? Be specific.

+5 { The Nucleophile only attacks the benzylic position, so this is the electrophilic center. It is not S_N2-like, with attack on less substituted side of epoxide.

How is Experiment D consistent? Be specific.

+5 { Racemization is consistent with S_N1-like (carbocation formation) rather than inversion (S_N2-like)

5. (25pts) The following data was used to investigate the reaction below. On the following page, draw a mechanism consistent with the data, and indicate the rate determining step. Then write a paragraph to support your answer, referring to the data.



Experiment A. The rate was determined to be first order in respect to base, and first order in respect to ketone.

Experiment B. When a series of Electron Withdrawing R-groups were tested, the ρ value was close to zero.

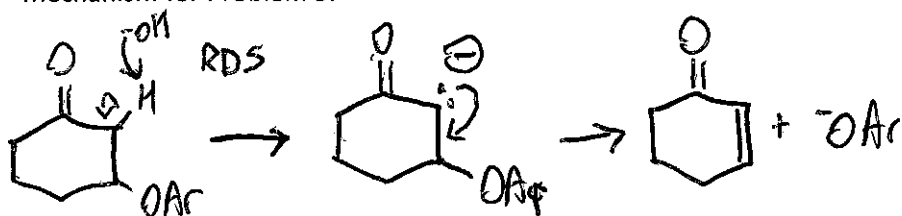
Experiment C. The KIE for the reaction with the deuterated α -carbon was found to be about $k_{\text{H}}/k_{\text{D}} = 6.2$.

Experiment D. If the reaction is run in deuterated water, no starting material was ever recovered that had incorporated deuterium.

* Scores around +20 for E2

* Significant partial credit for answers in which mechanism matches data interpretation below.

Mechanism for Problem 5:

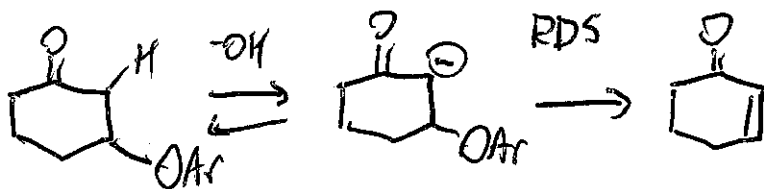


Justification for the proposed mechanism:

The rate data is inconsistent with E1 formation because base is first order. The LFER suggests very little charge buildup on LG, so the LG must leave after the RDS. The KIE suggests that deprotonation occurs in the RDS. The fact that no D is reincorporated means that once the anion forms, it partitions irreversibly forward, not in a pre-equilibrium.

Bonus: When a LFER experiment was run with a series of Electron Donating R-groups, a ρ value of 2.5 was obtained. How can you explain this?

EDG slow the second step so that it becomes RDS



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