

Initials: _____

1

Name: Answer Key

Chem 633: Advanced Organic Chemistry 2013 ... Midterm

Please answer the following questions *clearly and concisely*. In general, use pictures and less than 10 words in your answers.

Write your answers in the space provided.


Write your initials on each page you want graded.

There are 12 total pages to this exam. The last 2 pages were intentionally left blank and may be used for scratch paper. Please be sure your copy has 12 pages before you begin.

Molecular models are allowed.

Calculators are unnecessary and prohibited.

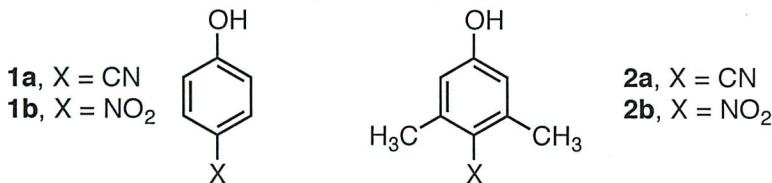
Problem	Points
1	<u>8</u> /20
2	<u>18</u> /30
3	<u>3</u> /15
4	<u>4</u> /20
5	<u>2</u> /15
TOTAL	<u>34</u> /100

Averages shown. 

(5 pts each.)

1. (20 points) Please explain the following observations. (Use pictures and few words.)

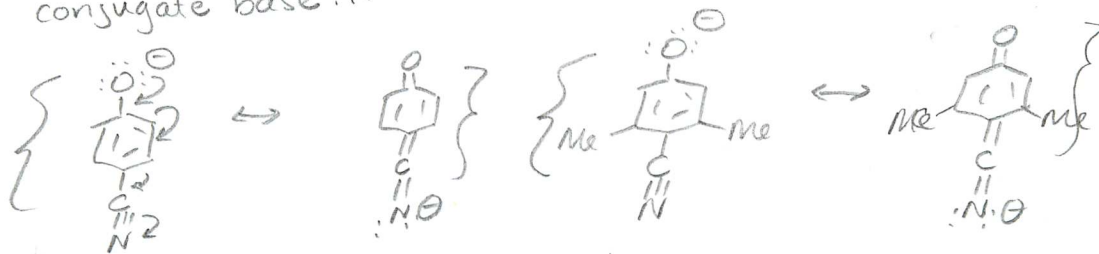
(a) The pK_a of **1a** and **2a** are the same, but the pK_a of **1b** is much lower than that of **2b**.



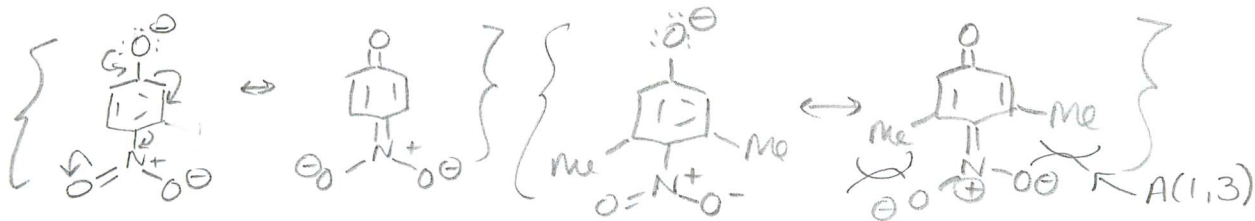
+2 for strain.
+1 for "cannot do resonance"

Consider conjugate base ...

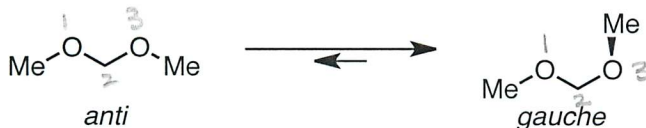
Me's do not affect stability of conj. base in 1a or 2a.



A(1,3) strain prevents NO₂ from being in conju

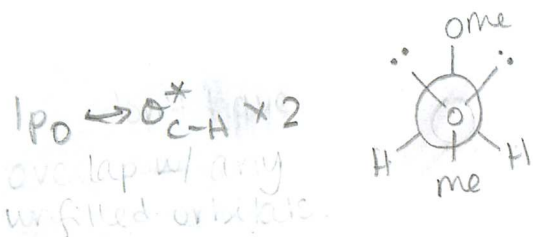


(b) The gauche conformation of the following molecule is favored over the anti conformation.

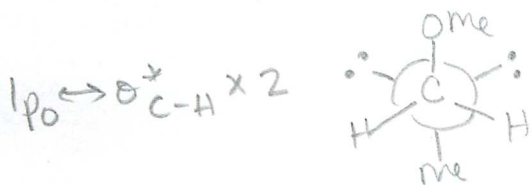


ANTI

Looking down O1-C2 bond:

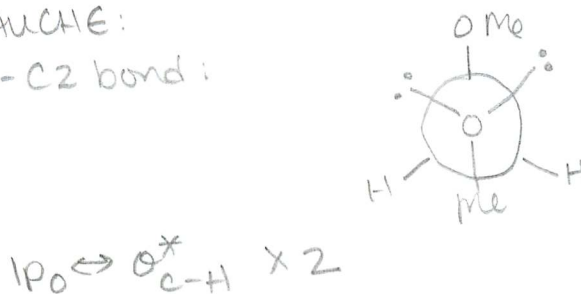


Looking down C2-O3 bond:

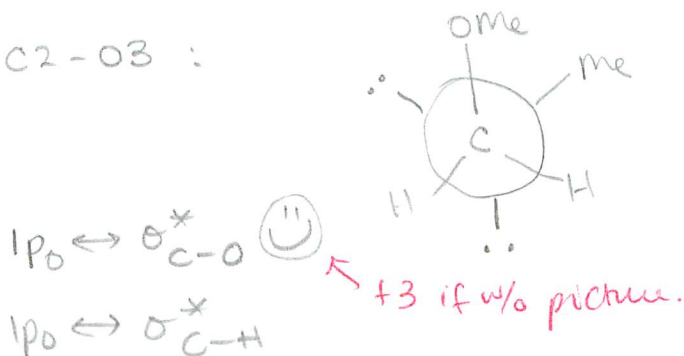


GAUCHE:

O1-C2 bond:

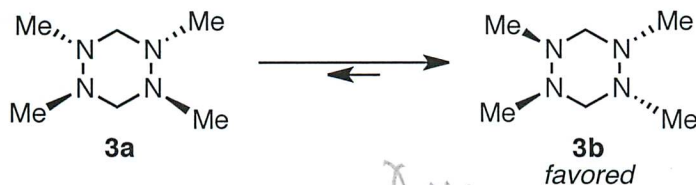


C2-O3 :

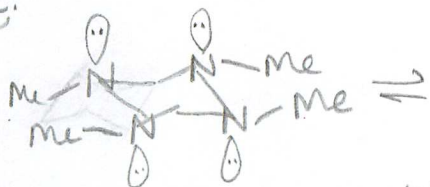


(1 - continued)

(c) The more stable conformation of this tetraaza-cyclohexane has the methyls arranged as shown in **3b**.



3a:



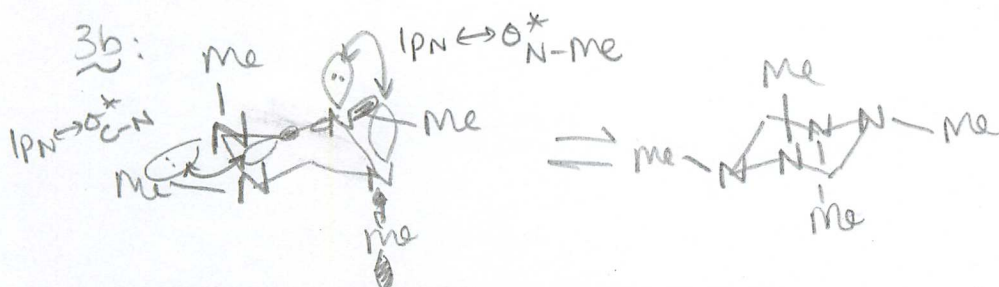
Me's are all equatorial, but lp_N 's are not able to overlap w/ any unfilled orbitals.



diaxial interactions disfavor this conformation

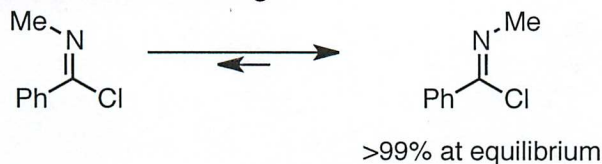
+2 if w/o picture

3b:

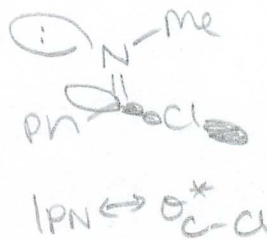


Me, Me
* NO 1,3-diaxial interactions in either chair conformation (only Me, H)
* Equatorial + axial lp_N 's overlap w/ σ_{C-N}^* ($\times 4$).

(d) The following equilibrium lies to the right.

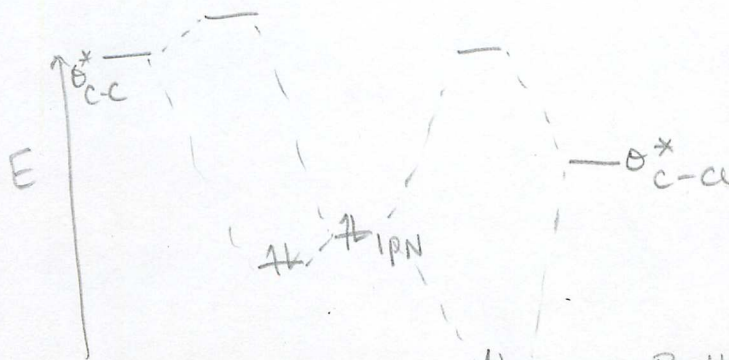


vs.



+1 for steric hindrance

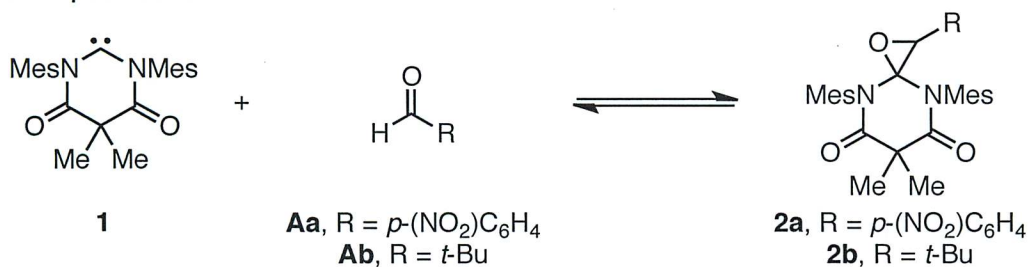
$lp_N \leftrightarrow \sigma_{C-C}^*$



Better energetic overlap \rightarrow more stabilization

(5 points each)

2. (30 points) The reaction of carbene **1** and aldehyde **A** leads to epoxide **2**. This reaction is rapid and reversible.



(a) The reaction of aldehyde **Aa** leads to quantitative conversion of the starting materials to the product. Estimate K_{eq} and ΔG° for this reaction.

Quantitative conversion... $K_{eq} \geq \frac{100}{1} \left(= \frac{[2]}{[1][A]} \right)$

$$\Delta G^\circ \geq -2.8 \text{ kcal/mol}$$

(Recall: 1 order of magnitude in $K_{eq} \Rightarrow 1.4 \text{ kcal/mol}$ in ΔG°)

+4 if sign is wrong, but clear that pdt is favored.

+2 for K_{eq} only.

(2 – continued)

(b) The reaction of aldehyde **Ab** proceeds to less than 85% conversion. To study this reaction, researchers performed experiments and obtained the following data. Please show how you would determine ΔG° from this data. (Note: You do not need to calculate ΔG° . Just show the equations and how you would plug in the numbers.)

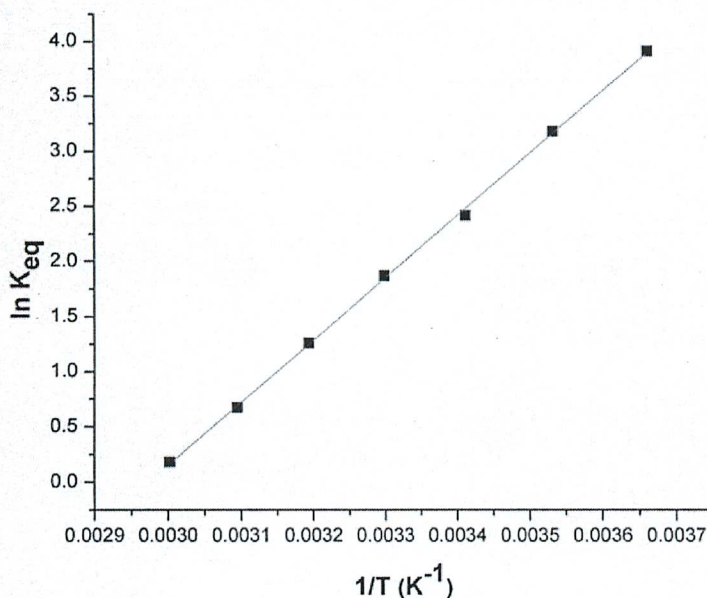


Figure S1. Plot of $\ln K_{eq}$ vs $1/T$ for the reaction **1** + pivaldehyde \rightarrow **2h**. The equation for the best fit line shown in red is as follows: $y = mx + b$, where $m = 5650 \pm 60 \text{ K}$ and $b = -16.8 \pm 0.2$.

$$\ln K_{eq} = -\frac{\Delta H^\circ}{RT} + \frac{\Delta S^\circ}{R}$$

$$m = \text{slope of the line} = \frac{-\Delta H^\circ}{R} \quad R = 1.984 \frac{\text{cal}}{\text{K}\cdot\text{mol}} = 8.31 \frac{\text{J}}{\text{K}\cdot\text{mol}}$$

$$\Delta H^\circ = -mR = -(5650 \text{ K}) \left(1.984 \frac{\text{cal}}{\text{K}\cdot\text{mol}} \right) \left(\frac{\text{kcal}}{1000 \text{ cal}} \right) = -11.2 \text{ kcal/mol}$$

$$y\text{-int} = \frac{\Delta S^\circ}{R}$$

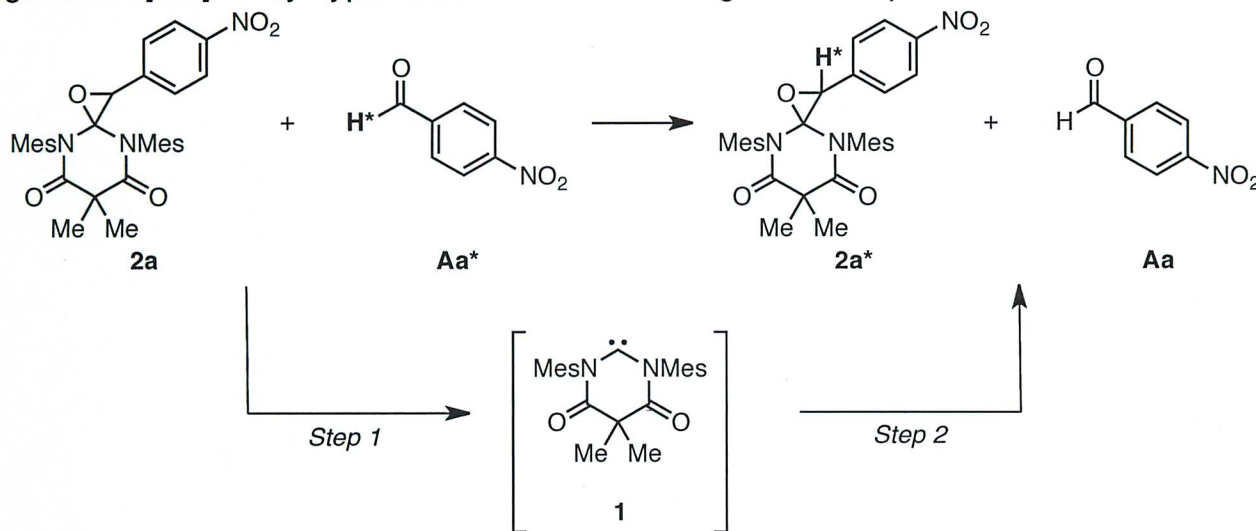
$$\Delta S^\circ = (R) \times (y\text{-int}) = \left(1.984 \frac{\text{cal}}{\text{K}\cdot\text{mol}} \right) (-16.8) = -33.3 \text{ cal/mol}\cdot\text{K}$$

+3 if doesn't use plot given \rightarrow Divide by R.

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

(2 – continued)

(c) Researchers also wanted to determine ΔG^\ddagger , but the reaction was too fast. Instead, they studied the rate of exchange of aldehyde with epoxide **2a**. For these experiments, they used a labeled aldehyde **Aa*** (labeled at **H***) and observed the decay of **[Aa*]** and growth of **[2a*]**. They hypothesize that this exchange reaction proceeds via **1**.



What do the following data tell you?

Entry	Equiv of Aa*	k_{obs} (s^{-1})
1	4	4.0 ± 0.6
2	2	4.4 ± 0.5
3	1	4.3 ± 0.4

\emptyset order in $[\text{Aa}^*]$

(d) What do the following data tell you?

$$\Delta H^\ddagger = 23.9 \pm 1.9 \text{ kcal/mol}$$

$$\Delta S^\ddagger = 8 \pm 5 \text{ cal/mol}\cdot\text{K}$$

$\Delta S^\ddagger > 0 \rightarrow$ Transition state is more disordered than starting material (ground state).

~~3~~

Initials: _____

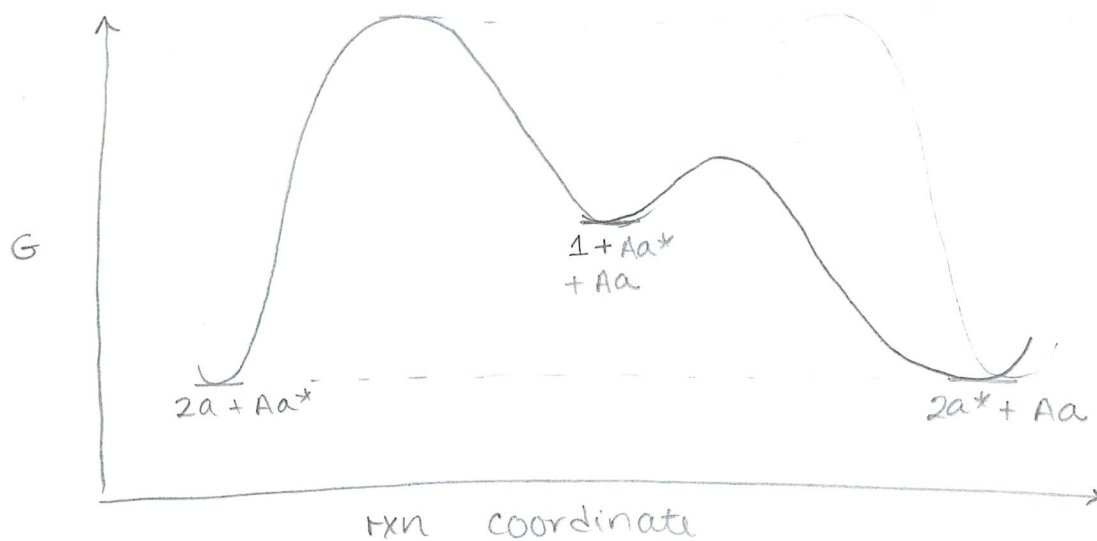
7

(2 – continued)

(e) Based on the above data, which step is rate determining (Step 1 or Step 2)?

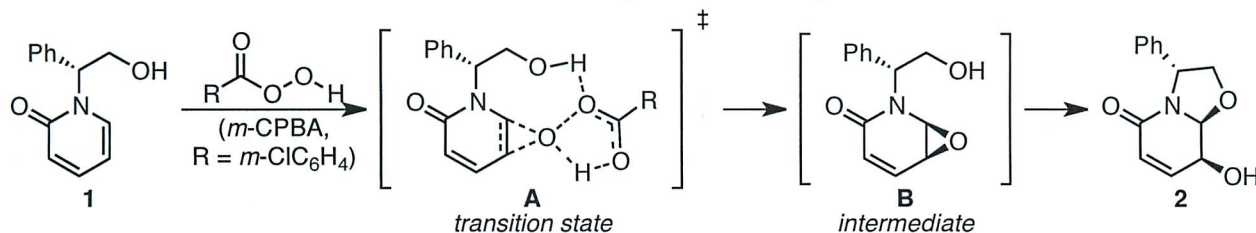
Step 1

(f) Please draw a reaction coordinate diagram for the exchange reaction.



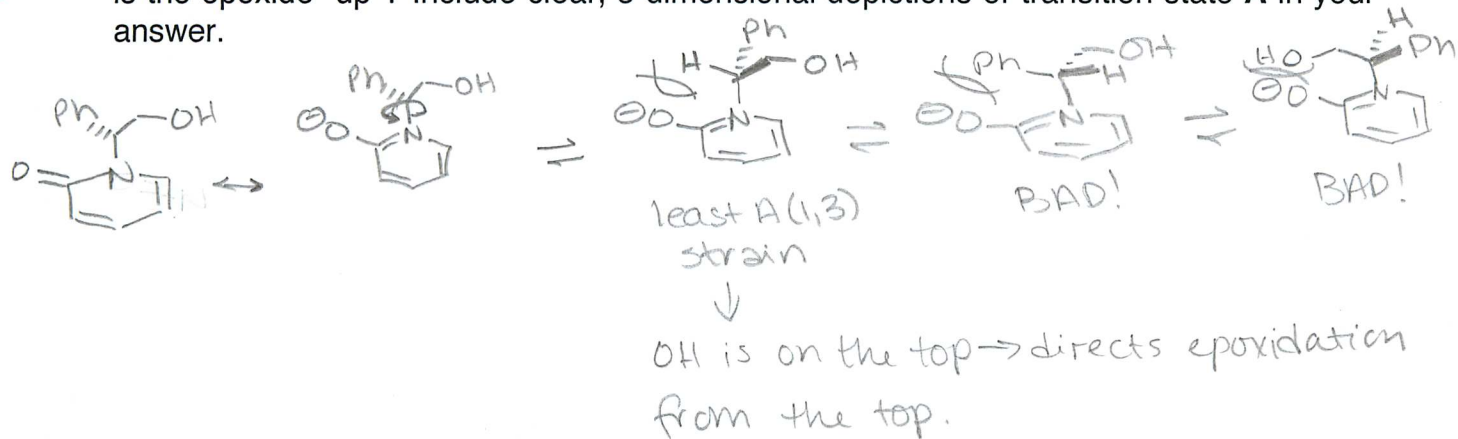
(Also ok to draw barriers the same height)

3. (15 points) Hydroxyl groups (OH) can be used to direct epoxidations with *m*-CPBA, as shown in transition state **A** below. The epoxidation step is irreversible.



8 pts.

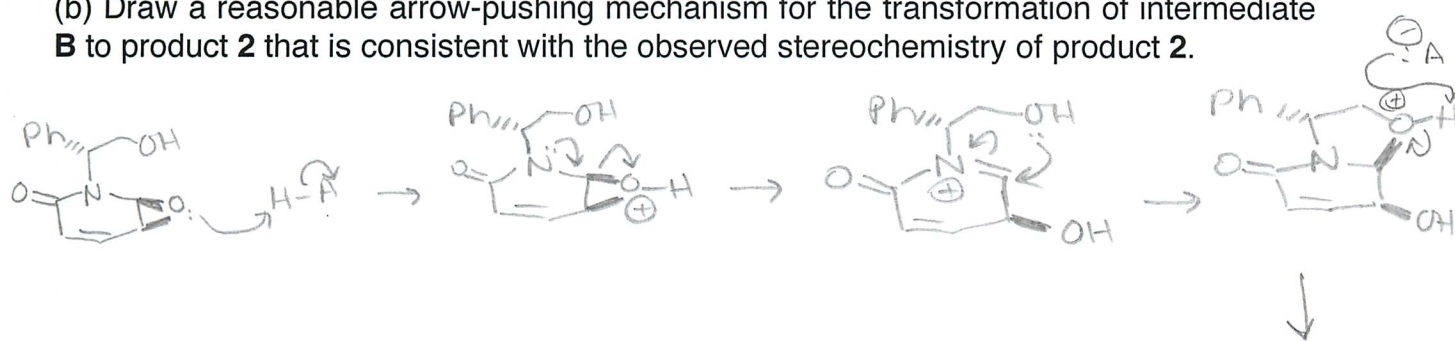
(a) Please explain the observed stereochemistry of intermediate **B**. In other words, why is the epoxide "up"? Include clear, 3-dimensional depictions of transition state **A** in your answer.



+1 for $N = sp^2$

7 pts.

(b) Draw a reasonable arrow-pushing mechanism for the transformation of intermediate **B** to product **2** that is consistent with the observed stereochemistry of product **2**.

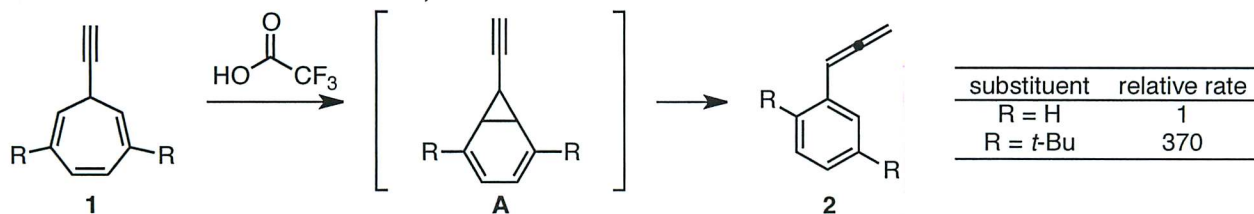


(cannot be $S_N2 \rightarrow$ Retention of Stereochem)

Pdt.

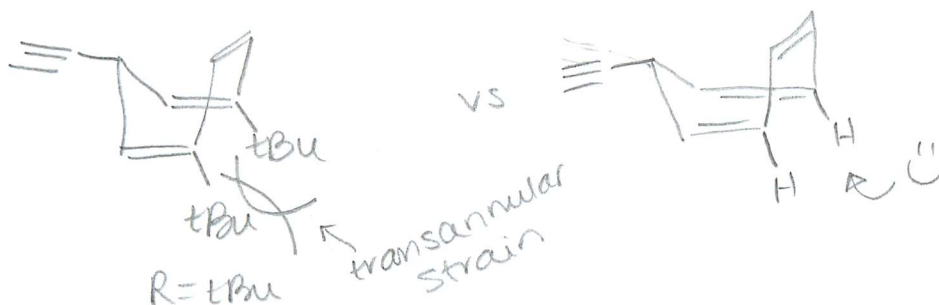
~~8~~

4. (20 points) The identity of R has a large effect on the rate of the rearrangement shown below. When R = *t*-Bu, the reaction is 370 times faster than when R = H.



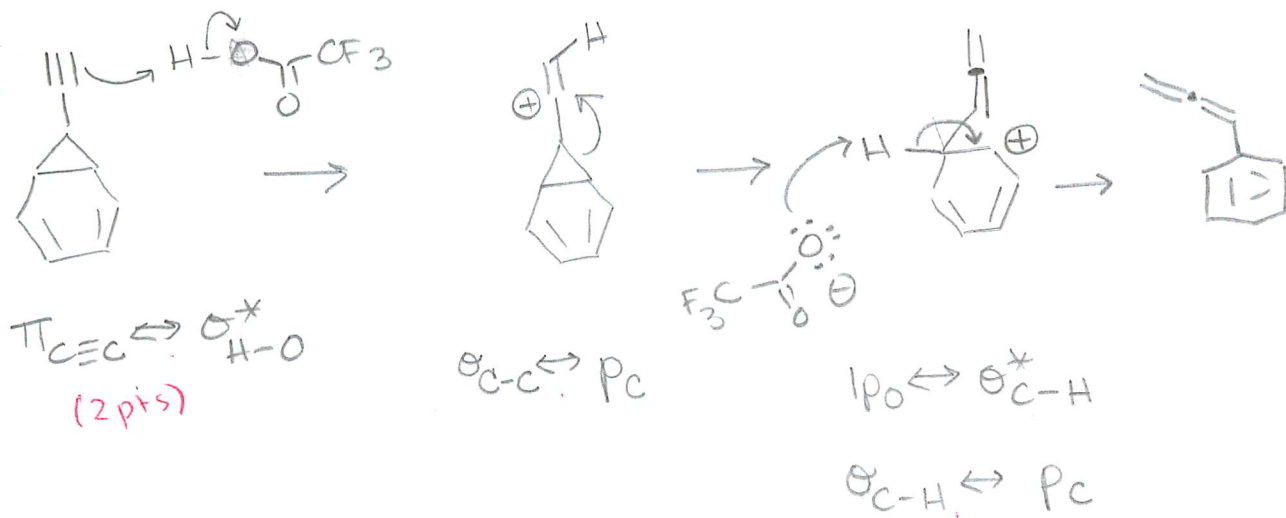
(a) Please explain this rate difference.

5pts If R = *t*Bu \rightarrow transannular strain in Δ .



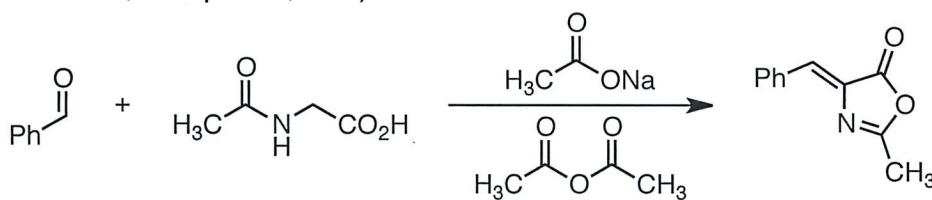
(b) Please draw a reasonable arrow-pushing mechanism for the conversion of intermediate **A** to **2**. For each step, please name the HOMO-LUMO interaction(s). You do not need to draw the HOMO or LUMO.

5pts for arrow-pushing.
5pts for HOMO/LUMO's



Mech:
+4 if draw ~~multiple steps~~ multiple steps as concerted.

5. (15 points) Please draw a reasonable arrow-pushing mechanism for the following reaction (Grossman, Chapter 2, #2h).



Note: $\ominus\text{OAc}$ is not a great base... you can only deprotonate fairly acidic H's.

