Name: Answer Key

CHEM 633: Advanced Organic Chemistry: Physical
Final Exam

Please answer the following questions clearly and concisely.

You may write your answers in the space provided and/or on additional pages. If you write your answers on additional pages, please write "see attached" in the provided space.

Please write your initials on each page you wish to turn in.

There are 12 total pages to this exam. Please be sure your copy has 12 pages before you begin.

Molecular models and calculators are allowed.

Problem	Points
1	_____/16
2	_____/10
3	_____/10
4	_____/18
5	_____/10
6	_____/18
7	_____/8
8	_____/10
TOTAL	**_____/100**

Potentially Useful Constants

$k_B/h = 2.083 \times 10^{10}\ s^{-1}K^{-1}$

$\kappa = 1$ (kappa)

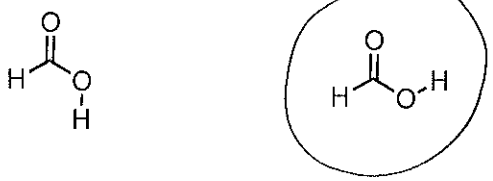
$R = 1.98$ cal/mol·K

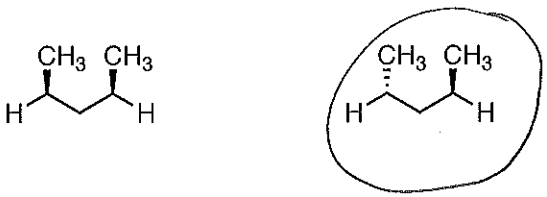
(2 pts each)

1. (16 points) Please circle the more stable conformation in each of the pairs below. No explanation is necessary.

(a) 

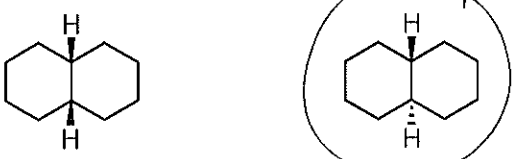
(b) 

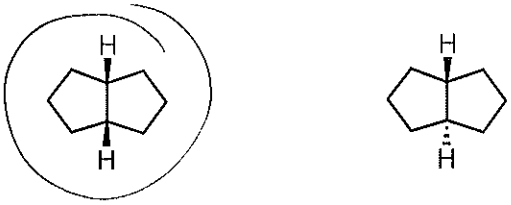
(c) 

(d) 

(e) 

(f) 

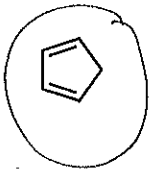
(g) 

(h) 

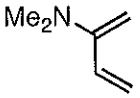
(2 points each)

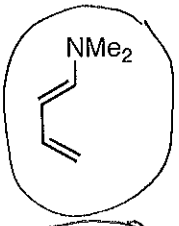
2. (10 points) In each of the following pairs, please circle the diene that will be more reactive in the Diels–Alder reaction with maleic anhydride. No explanation is necessary.

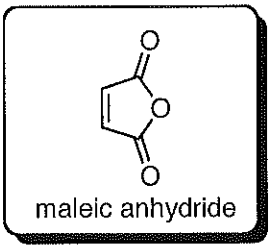
(a)



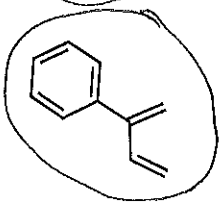
(b)



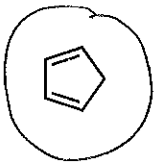


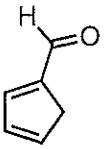


(c)

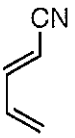


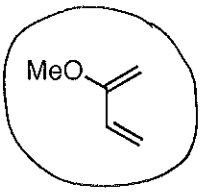
(d)





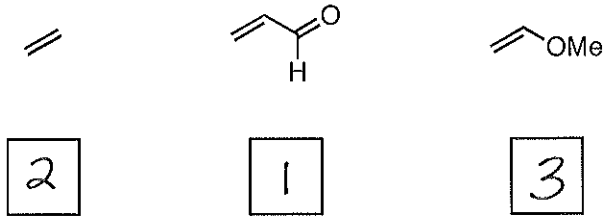
(e)



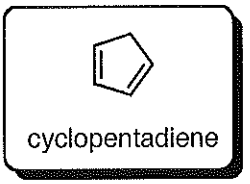


3. (10 points) (a) Rank the following dienophiles (**1**–**3**) in order or reactivity in the Diels–Alder reaction with cyclopentadiene with **1** being the more reactive and **3** being the least reactive.

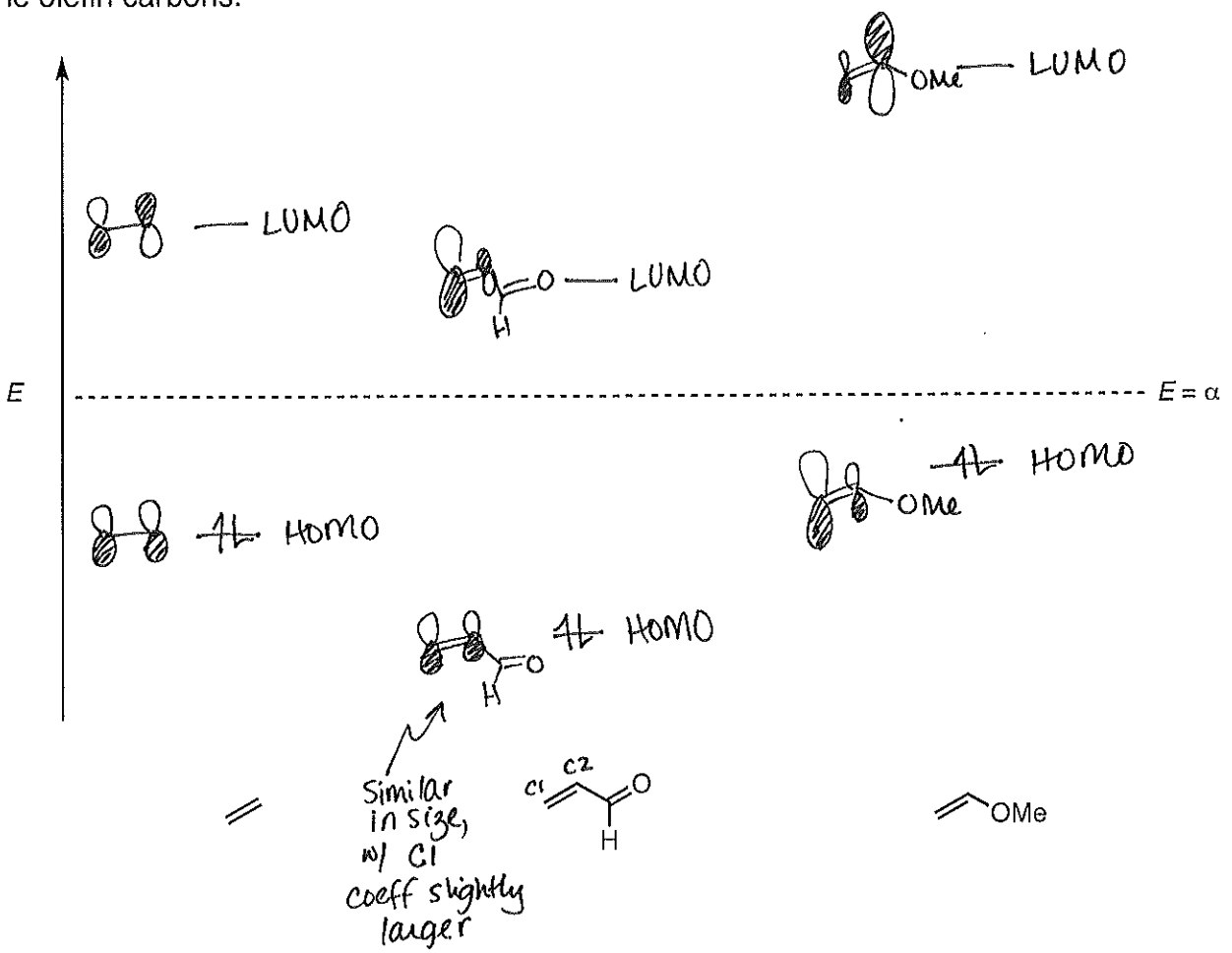
(2pts)



2	1	3



(b) Please place the HOMO and LUMO of the three dienophiles on the molecular orbital diagram below, clearly showing their relative energies and the relative size and shading of the p-orbitals on the olefin carbons.

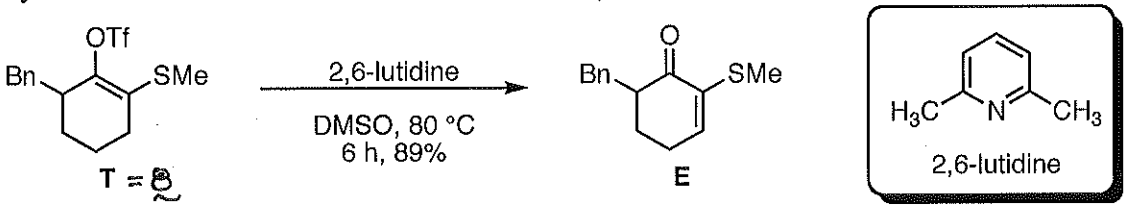


2 pts : Correct relative energies

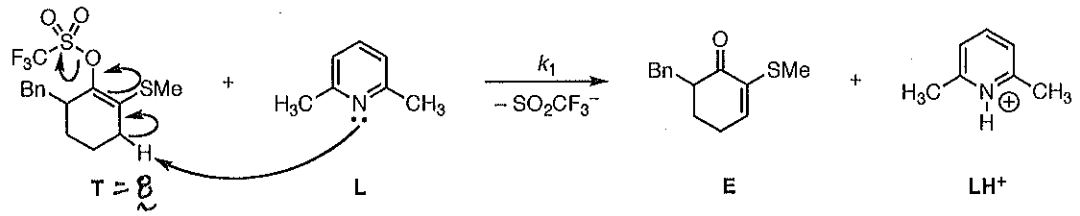
2 pts / dienophile : Correct coefficients (+1 for HOMO, +1 for LUMO)

(2 pts each)

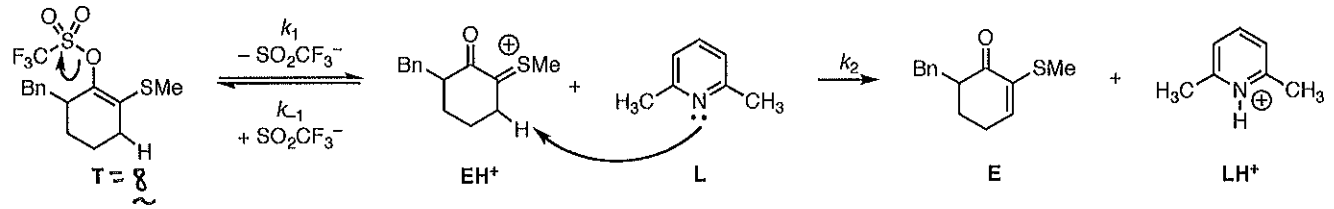
4. (18 points) The Overman group discovered the unique transformation of β-sulfenyl enol triflate 8 to sulfenyl enones **E** (Hynes, J.; Nasser, T.; Overman, L. E.; Watson, D. A. *Org. Lett.* **2002**, *4*, 929). They envisioned that two mechanisms were possible, Mechanism A and Mechanism B.



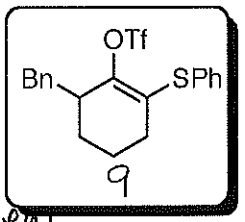
Mechanism A



Mechanism B



(a) The transformation of 8 to **E** is more rapid with methyl-substituted substrate 8 than with phenyl-substituted substrate 9. What does this tell you about the mechanism of this reaction? Does this support Mechanism A, Mechanism B, both or neither?



R	σ_p^+
–SMe	–0.60
–SPh	–0.55

Faster w/ more electron-donating substituent.
⇓ ← +1 for just this.
Build-up of ⊕ charge on carbon sulfur is attached to.
⇓
Supports Mechanism B. ← +1 for just this.

(b) Derive a rate expression for Mechanism A, using the steady-state approximation where appropriate. You may assume that no observable intermediates accumulate during the reaction. Your rate expression should only contain terms that are experimentally quantifiable.

rate = $k_1[8][L]$ −1 per mistake

4 – continued.

(c) Derive a rate expression for Mechanism B, assuming that step 2 is rate-determining. Use the steady-state approximation where appropriate. You may assume that no observable intermediates accumulate during the reaction. Your rate expression should only contain terms that are experimentally quantifiable.

rate = $k_2[EH^+][L]$

SSA: $\frac{d[EH^+]}{dt} = 0 = k_1[8] - k_{-1}[EH^+][SO_2CF_3^-] - k_2[EH^+][L]$

$[EH^+] = \frac{k_1[8]}{k_{-1}[SO_2CF_3^-] + k_2[L]}$

rate = $\frac{k_1 k_2 [8][L]}{k_{-1}[SO_2CF_3^-] + k_2[L]}$

-1/mistake

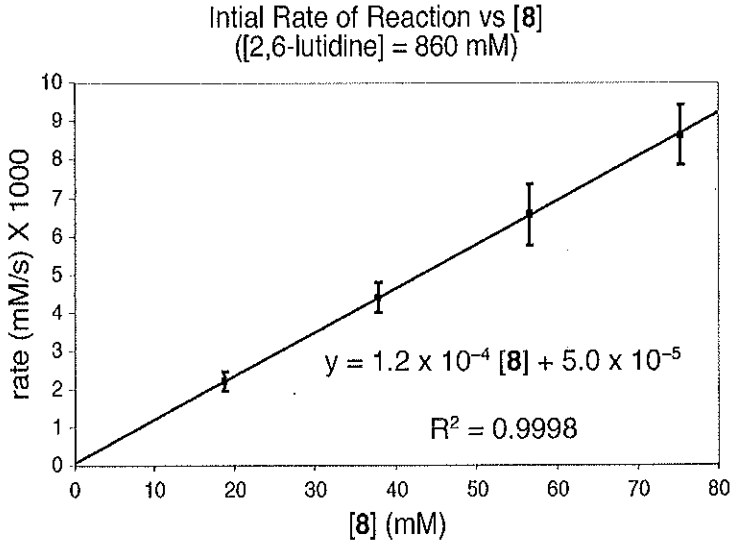
(d) Provide a simplified rate expression for Mechanism B, assuming that step 1 is rate-determining.

$k_2[L] >> k_{-1}[SO_2CF_3^-]$

rate = $\frac{k_1 k_2 [8][L]}{k_2[L]}$

rate = $k_1[8]$

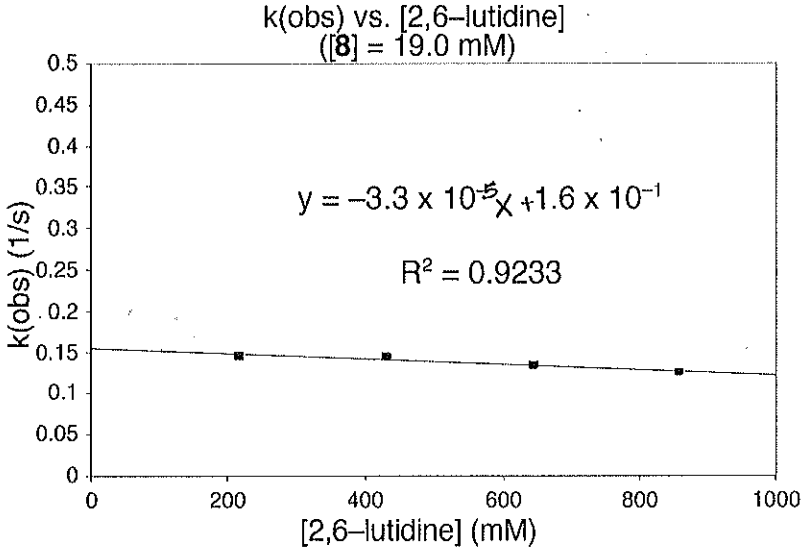
(e) What can be concluded from the following data?



First-order rate dependence on [8]

4 – continued.

(f) What can be concluded from the following data?



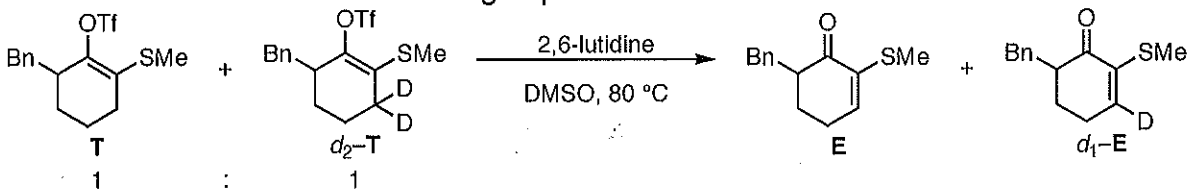
Zero order dependence on [2,6-lutidine]

t½ for not 1st order

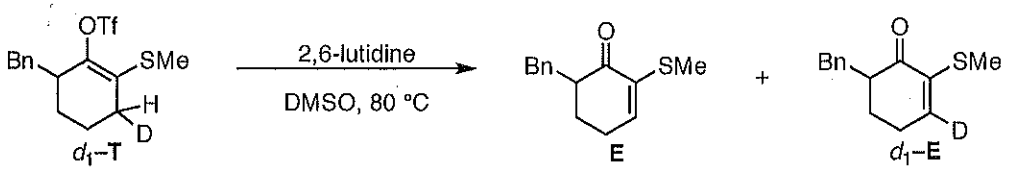
(g) Does the data in (e) and (f) allow you to rule out either Mechanism A or Mechanism B? If so, which one? (No explanation is necessary.)

Yes. Rules out Mech A.

(h) Based on your favored mechanism, please predict the kinetic isotope effect (or range of the KIE) that will be observed in the following experiments.



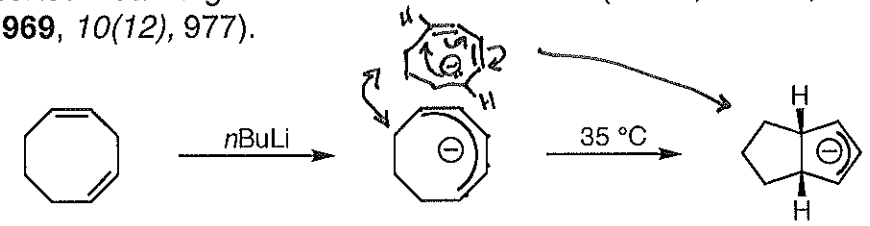
$k_H / k_D =$ 1.0 – 2 pts



$k_H / k_D =$ 1-7 – 2 pts

8 total

5. (10 points) 1,4-Cyclooctadiene can be deprotonated with *n*-BuLi to form anion **1**. Anion **1** undergoes a concerted rearrangement to form anion **2** (Bates, R. B.; McCombs, D. A. *Tetrahedron Lett.* **1969**, *10(12)*, 977).



1,4-cyclooctadiene **1** **2**

(a) What type of pericyclic reaction is the rearrangement of **1** to **2**?

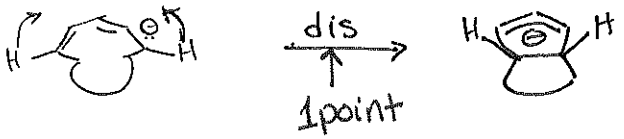
2 points electrocyclization or electrocyclic ring closure

+1 for "ring closure"

(b) Please characterize the rearrangement of **1** to **2**, as is appropriate for this type of pericyclic reaction.

2 points 6electron

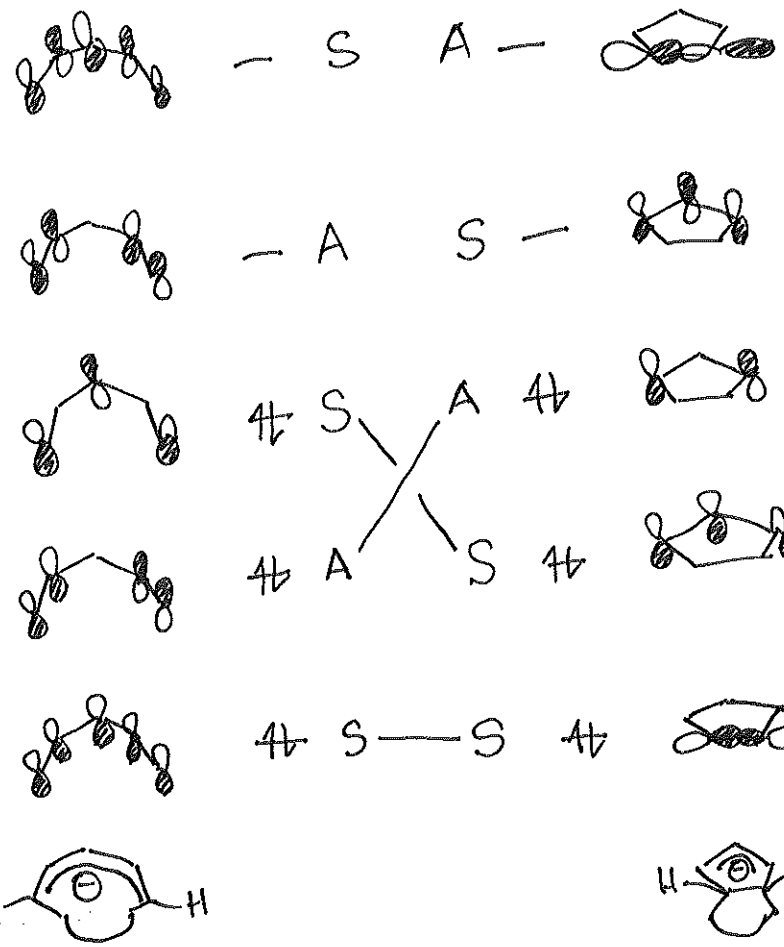
(c) Draw a Woodward–Hoffmann correlation diagram to show that the thermally allowed rearrangement of **1** to **2** gives the observed stereochemistry of **2**.



1point

Symmetry Element Conserved ⇒ σ-plane

1 point



Ground state → Ground state ALLOWED

4 points for correlation diagram.

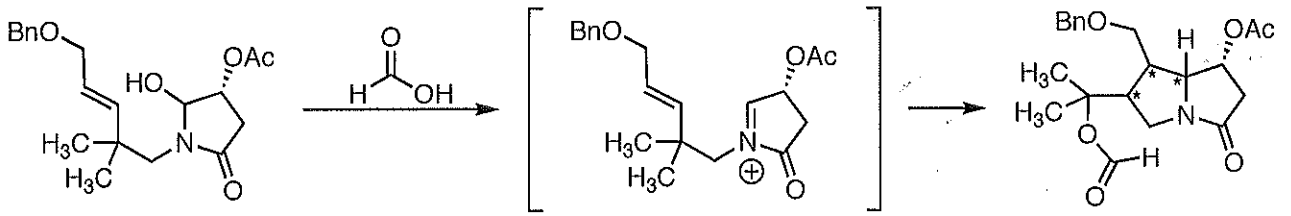
+3 if almost right

OK

-1 for wrong MO's but 1st mistake is free.

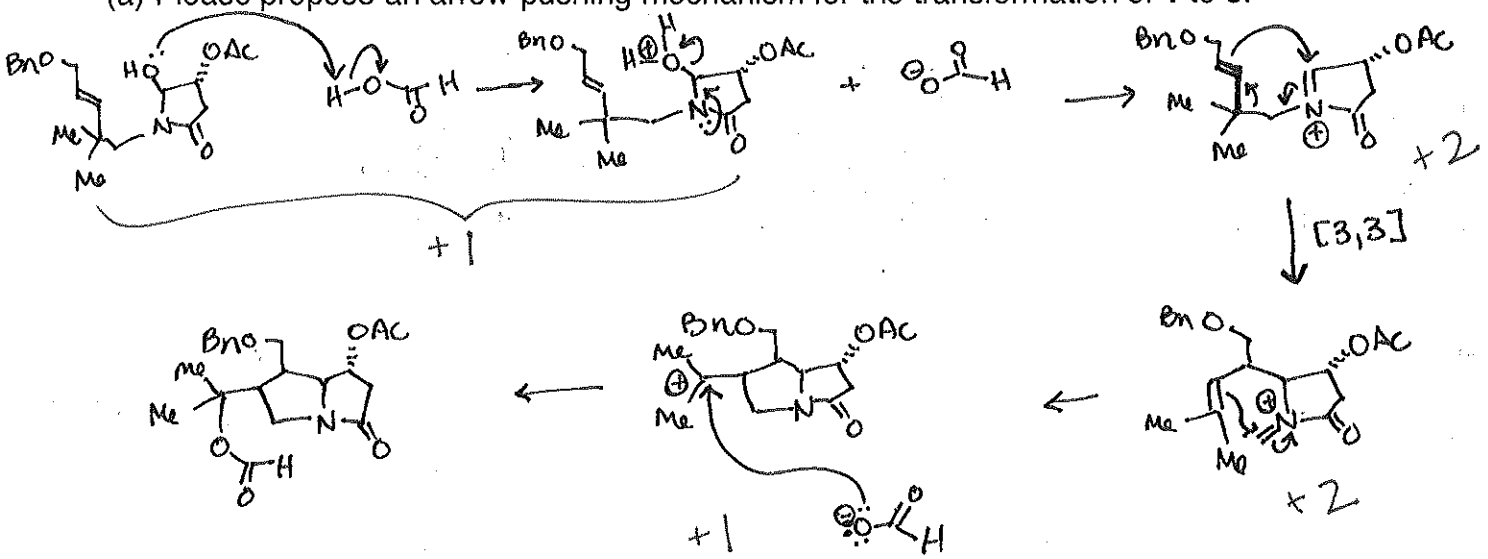
+1 for trying/knowing what c.d. is.

6. (18 points) Hart and coworkers found that treatment of substrate **1** with formic acid resulted in the formation of pyrrolizidinone **3**, presumably via iminium **2** (Hart, D. J.; Yang, T.–K. *J. Org. Chem.* **1985**, *50*, 235).



1 **2** **3** (60%)

6 pts (a) Please propose an arrow-pushing mechanism for the transformation of **1** to **3**.

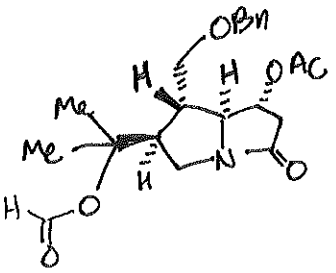


(or H-O attacks & then is deprotonated)

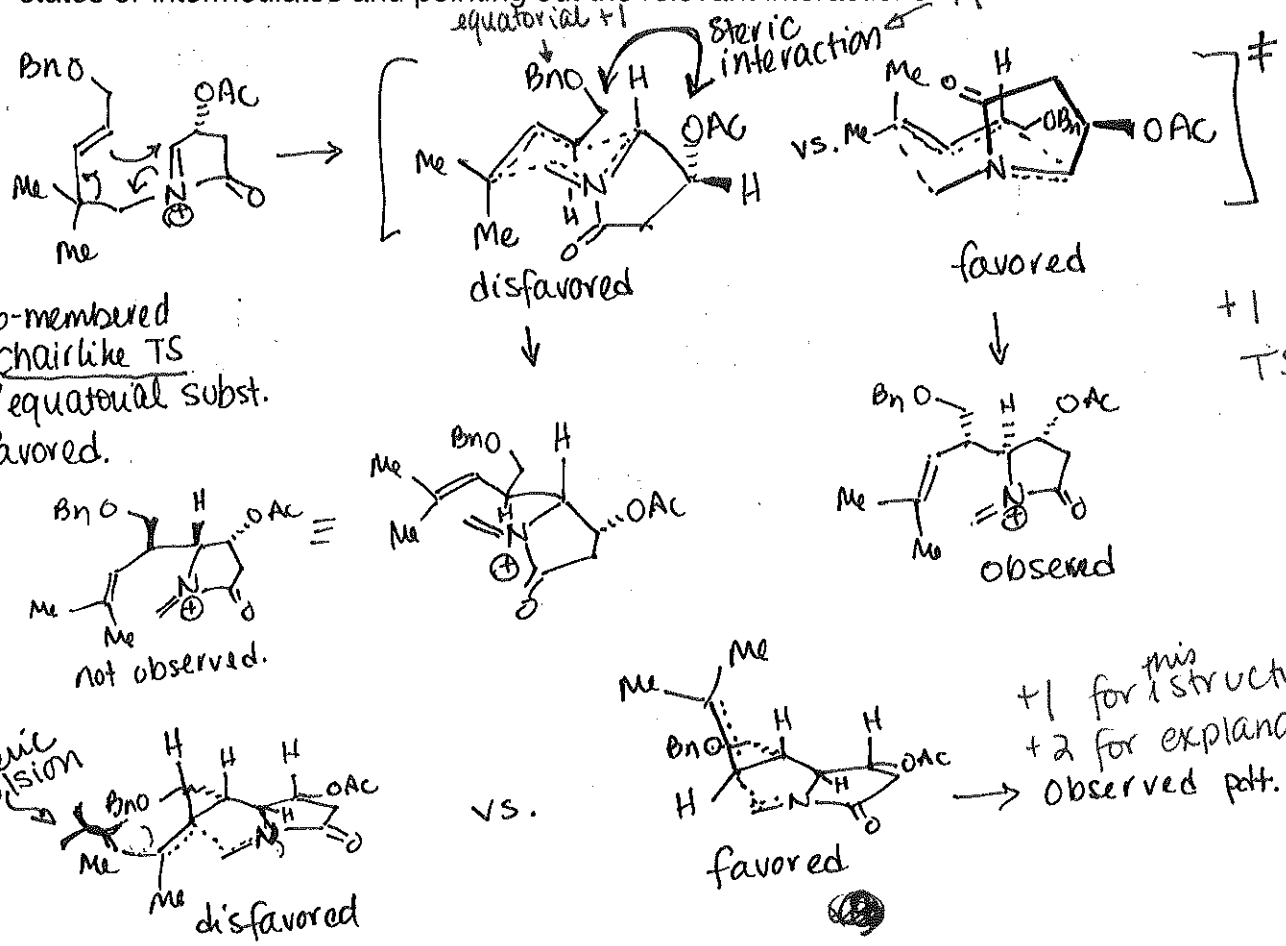
6 – continued.

(b) Predict the stereochemistry of at each of the starred carbons in product **3**.

3points (1 pt/center)



6 points (c) Rationalize your stereochemical prediction in (b) by clearly illustrating the relevant transition states or intermediates and pointing out the relevant interactions. +1



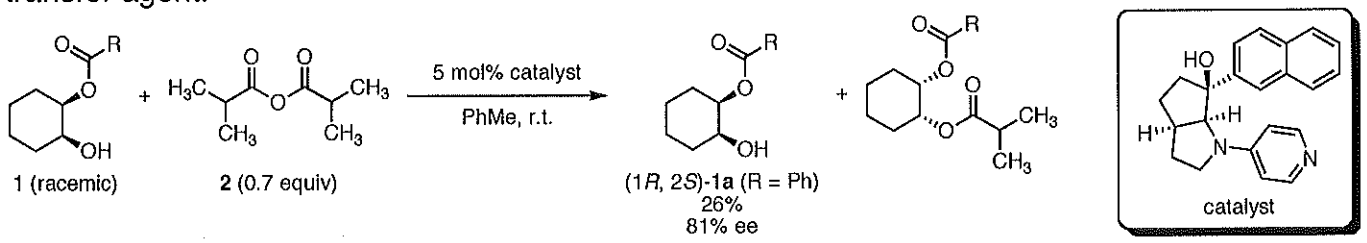
(d) Is the transformation of **1** to **3** enantioselective? (No explanation is necessary.)

3points

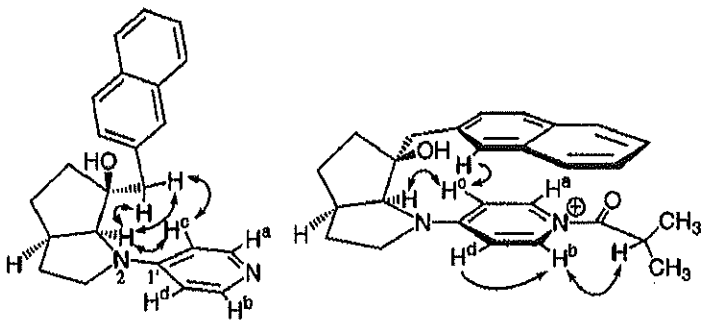
NO (diastereoselective)

12 total

7. (8 points) Fuji and co-workers designed a novel catalyst for the kinetic resolution of alcohols via selective acylation of one alcohol enantiomer over the other (Kawabata, T.; Nagato, M.; Takasu, K.; Fuki, K. *J. Am. Chem. Soc.* **1997**, *119*, 3169). This chiral catalyst acts as an acyl transfer agent.



1 (racemic) 2 (0.7 equiv) (1*R*, 2*S*)-1a (R = Ph) 26% 81% ee



A (open conformation) **B** (closed conformation)

(a) By NMR analysis, the catalyst exists in an open conformation (**A**) in solution, but folds into a closed conformation (**B**) when acylated. Why does the acylated catalyst exist in the closed conformation?

2pts cation-π

π-charge: +1

(b) Why is the open conformation the most stable for the "naked" catalyst?

2pts steric hindrance (probably)

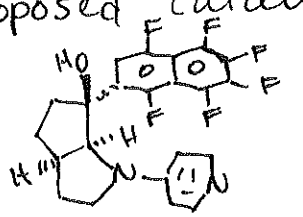
+1 for destabilizing stacked benzene!

(c) Fuji also proposed that the closed conformation is necessary to achieve selectivity in the acylation step. Please propose *two* ways to probe the plausibility of the closed conformation during the acylation step.

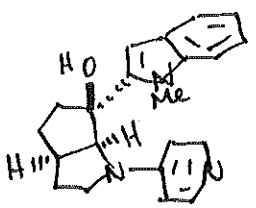
2pts 1) Computationally study transition state structures

2pts 2) Examine how changing napthyl ring on catalyst changes selectivity of acylation rxn.

Proposed catalysts:

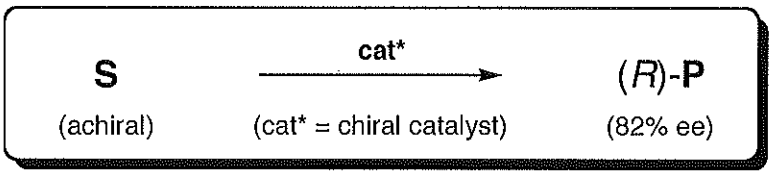


(worse π-donor)

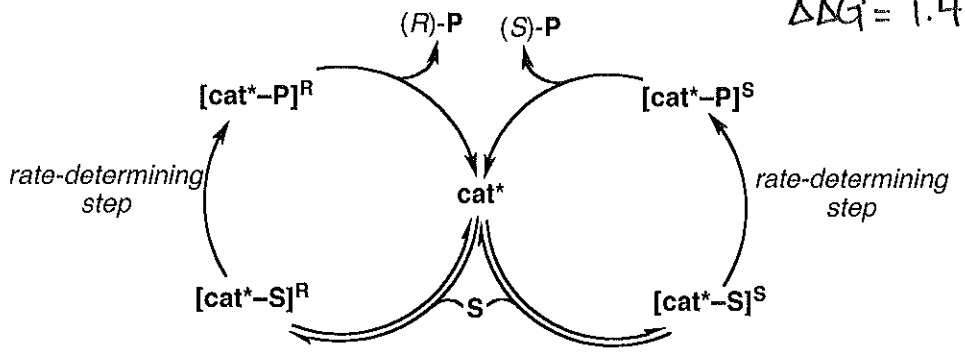


(better π-donor)

8. (10 points) Please consider the following generic reaction, in which a enantiopure chiral catalyst (**cat***) transforms an achiral substrate (**S**) into product (**P**) in 82% ee, favoring the *R* enantiomer of product. **Cat*** is the catalyst resting state.



82% ee
⇓
10 : 1 e.r.
⇓
$\Delta\Delta G^{\ddagger}$ = 1.4 kcal/mol



Draw a reaction coordinate diagram consistent with this reaction, clearly showing the relative energies of the ground , and transition states. On your reaction coordinate diagram, please clearly label the energy difference responsible for the observed enantioselectivity and give the numerical value of this difference in kcal/mol.