

Initials: _____

1

Name: ANSWER KEY

**Chem 633: Advanced Organic Chemistry
Final Exam**

Please answer the following questions *clearly and concisely*.

Write your answers in the space provided.

Write your initials on each page you want graded.

There are **17** total pages to this exam. Please be sure your copy has **17** pages before you begin.

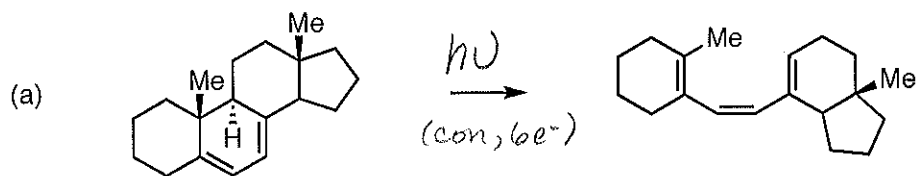
Molecular models are allowed.

Calculators are unnecessary and prohibited.

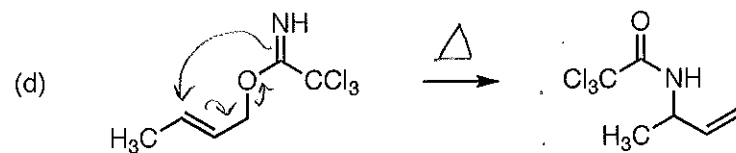
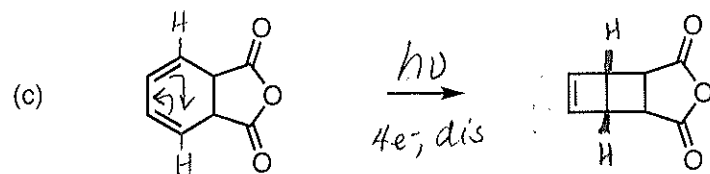
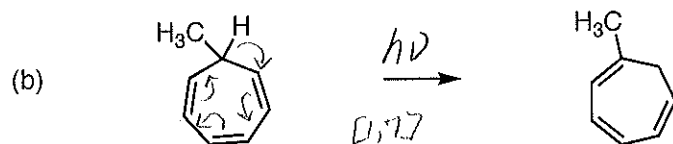
Problem	Points
1	<u>6</u> /8
2	<u>7</u> /8
3	<u>6</u> /8
4	<u>5</u> /8
5	<u>9</u> /12
6	<u>5</u> /8
7	<u>19</u> /30
8	<u>7</u> /9
9	<u>4</u> /9
TOTAL	<u>62</u> /100
	↑
	AVERAGES

2pts each

1. (8 points) For the following reactions, please state the conditions (thermal or photochemical) that must be used for these to be "allowed" transformations. No explanation is necessary.

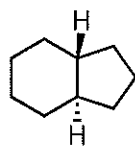
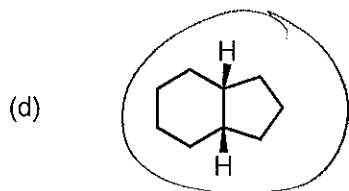
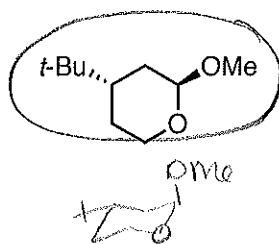
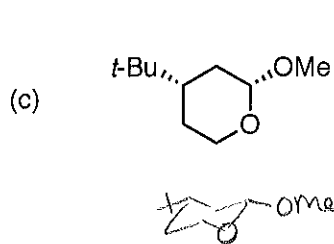
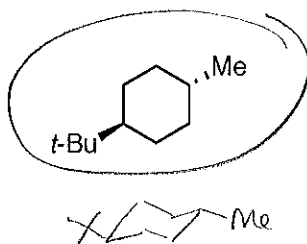
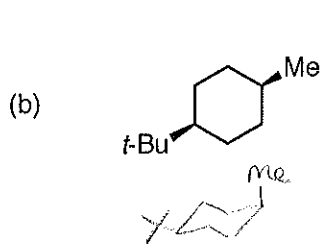
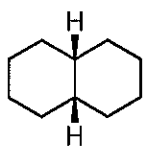
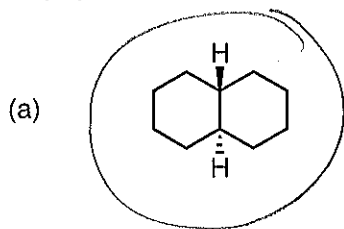


A&D, p. 969.



2pts each

2. (8 points) Please circle the lower energy isomer in each of the following pairs.

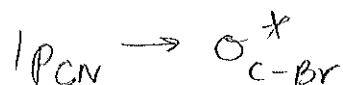
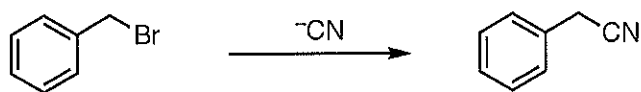


3. (8 points) For each of the transformations shown, please clearly identify the frontier molecular orbitals that interact. You do not need to draw the FMO's, just name them (lp_{Br} or n_{Br} , p_C , σ_{C-C} , etc.).

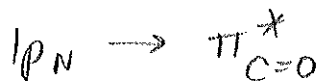
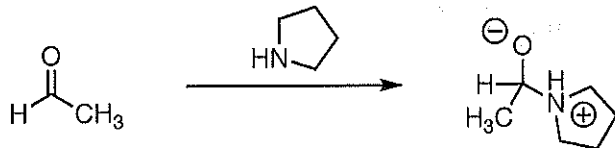
4 points



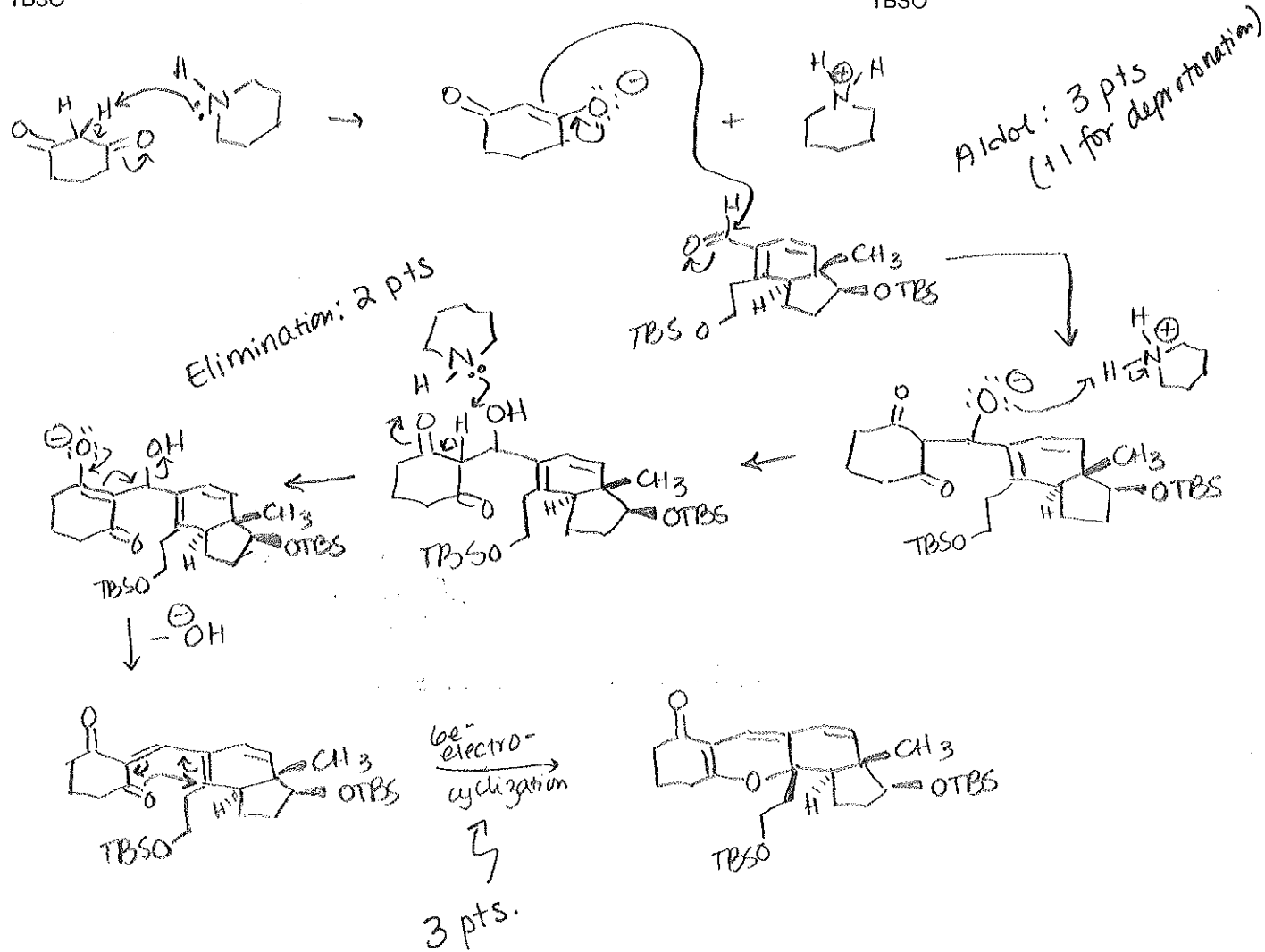
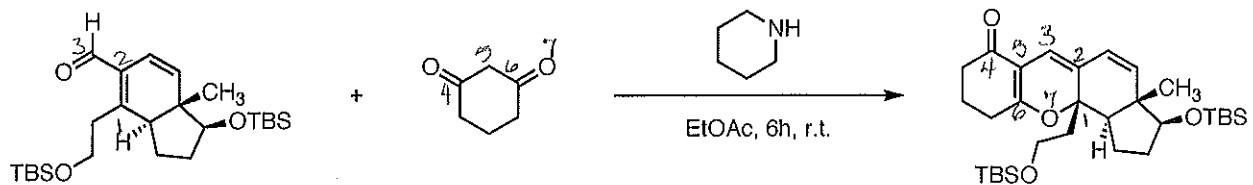
2 points



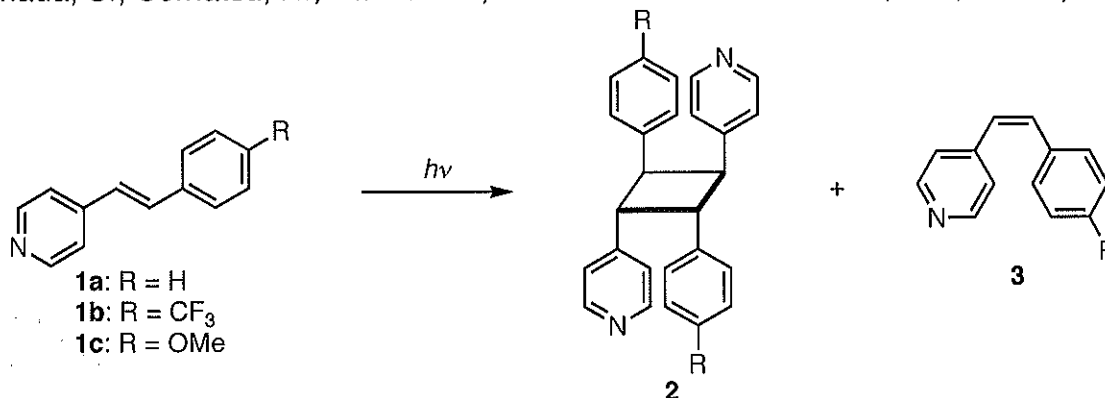
2 points



4. (8 points) Please propose a reasonable arrow-pushing mechanism for the following transformation (Yamashita, S.; Iso, K.; Hirma, M. *Org. Lett.* **2008**, *10*, 3413).

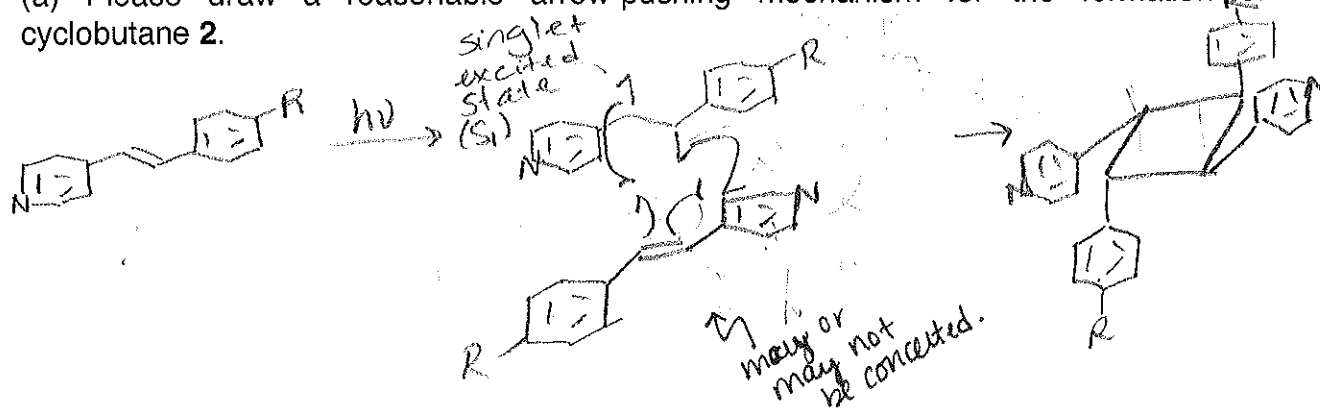


5. (12 points) The Yamada group recently studied the effect of hydrochloric acid (HCl) and aromatic substitution on the following photodimerization of *trans*-styrylpyridines (Yamada, S.; Uematsu, N.; Yamashita, K. *J. Am. Chem. Soc.* **2007**, *129*, 12100).



(a) Please draw a reasonable arrow-pushing mechanism for the formation of cyclobutane **2**.

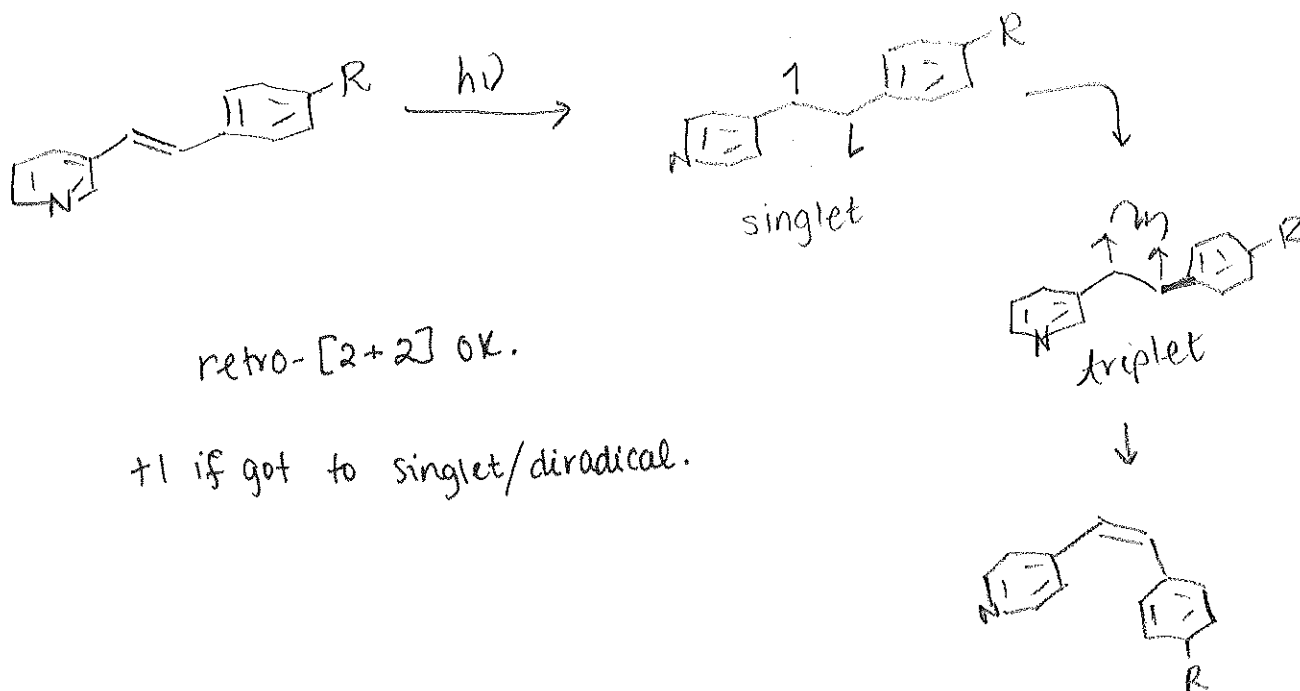
3pts



+2 if combined 2 excited states.

(b) Please draw a reasonable mechanism for the formation of *cis*-olefin **3**.

3pts

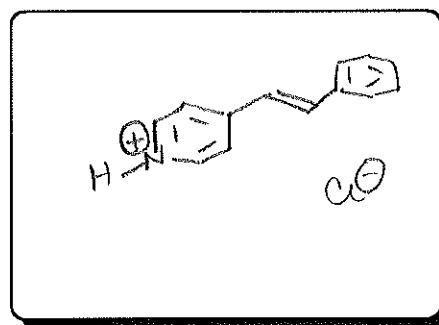
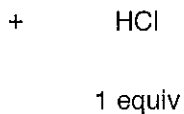
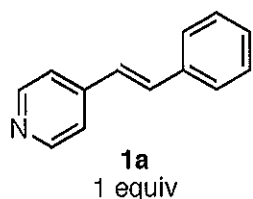


(5 – continued)

(c) Without HCl, olefin **3** is the major product observed (entry 1). With added HCl, product **2** becomes the major product with the ratio of **2:3** increasing with increasing equivalents of HCl (entries 2-6).

Entry	Substrate	Equiv HCl	Yield of 2 (%)	Yield of 3 (%)
1	1a	0	20	52
2	1a	1	50	26
3	1a	2	58	22
4	1a	3	64	10
5	1a	5	67	9
6	1a	10	71	8

What intermediate forms when you combine 1 equivalent of **1a** and 1 equivalent of HCl?



(5 – continued)

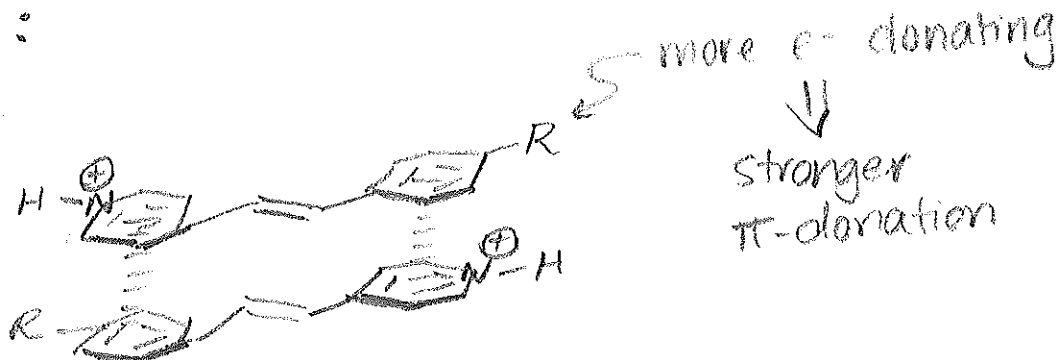
(d) With 3 equivalents of HCl, there was a substantial substituent (R) effect on the ratio of 2:3, as shown in the table below.

Entry	Substrate	Equiv HCl	Yield of 2 (%)	Yield of 3 (%)
1	1a	3	64	10
2	1b	3	27	43
3	1c	3	95	3

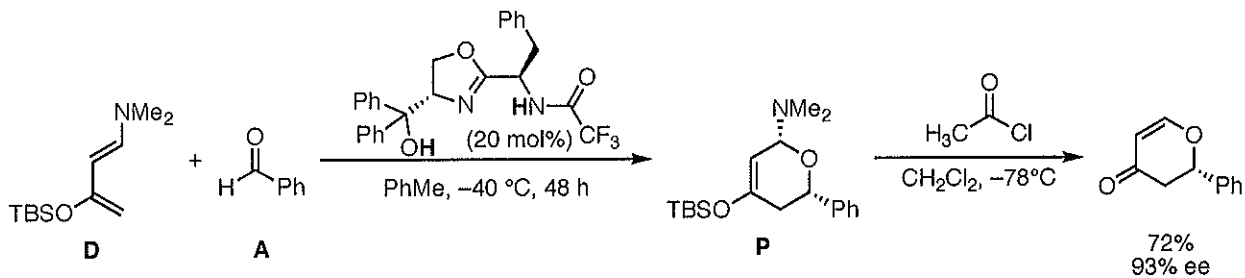
Please provide a rationale for how the addition of HCl and the use of more electron-rich aromatic groups favor formation of 2 over 3. Please illustrate your answer and use less than 10 words.

cation- π interaction ⁺¹ favors/accelerates formation of 2:

3 pts.



7. (30 points) The Sigman group has recently published a careful mechanistic study of their dual hydrogen-bond donor catalyst in the following hetero-Diels–Alder reaction (Jensen, K. H.; Sigman, M. S. *J. Org. Chem.* **2010**, *75*, 7194). Please note that the catalyst's hydrogens that participate in hydrogen bonding are in bold.

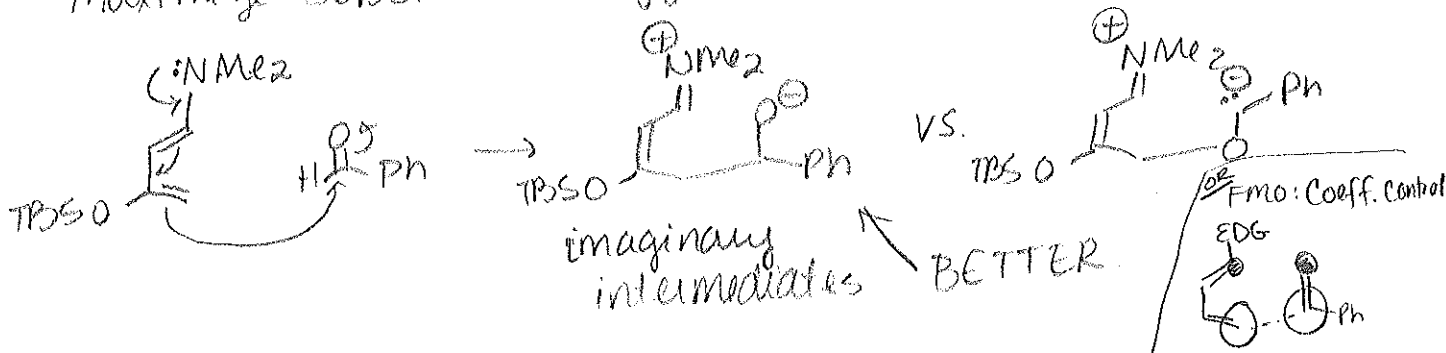


(a) Is product **P** the endo or exo hetero-Diels–Alder adduct? (No explanation necessary)

3 points
endo

(b) Please rationalize the regiochemistry of the hetero-Diels–Alder reaction. Illustrate your answer and use less than 10 words.

3 pts
Maximize substituent effect:

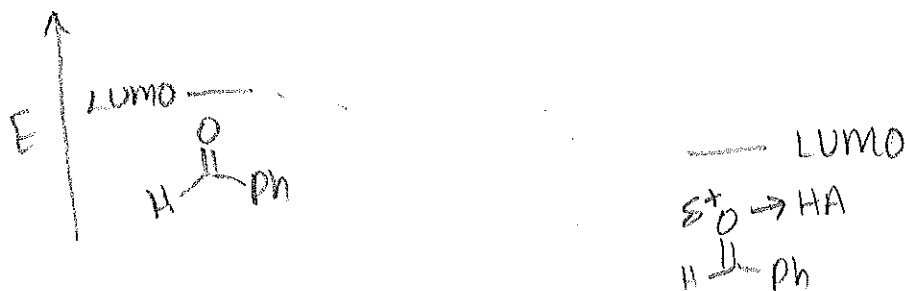


(c) Please explain why the catalyst accelerates the hetero-Diels–Alder reaction. Illustrate your answer and use less than 10 words.

3 pts
Lowers LUMO of dienophile: ← +2 (+1 for "perturbs MO's")



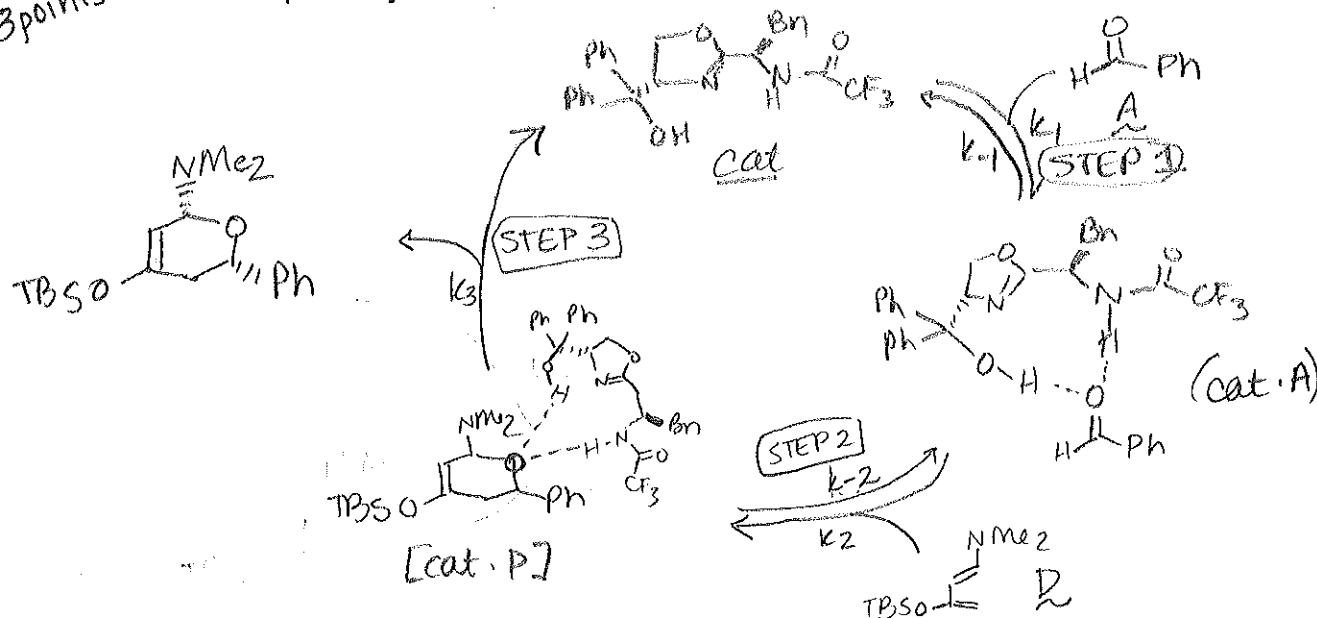
+1 for showing H-bonding



(7 - continued)

(d) Please draw a catalytic cycle for the formation of product **P** (you do not need to consider pathways to the minor diastereomers or enantiomer).

3 points



+2 if left out cat. P

(e) Please write "one plus" catalytic rate expression for this catalytic cycle. Use the rate constants depicted in your catalytic cycle in (d).

3 points

$$\text{rate} = \frac{k_1 k_2 k_3}{k_{-1} k_{-2}} \frac{[\text{cat}]_{\text{tot}} [\text{A}][\text{D}]}{1 + \frac{k_1}{k_{-1}} [\text{A}] + \frac{k_1 k_2}{k_{-1} k_{-2}} [\text{A}][\text{D}]}$$

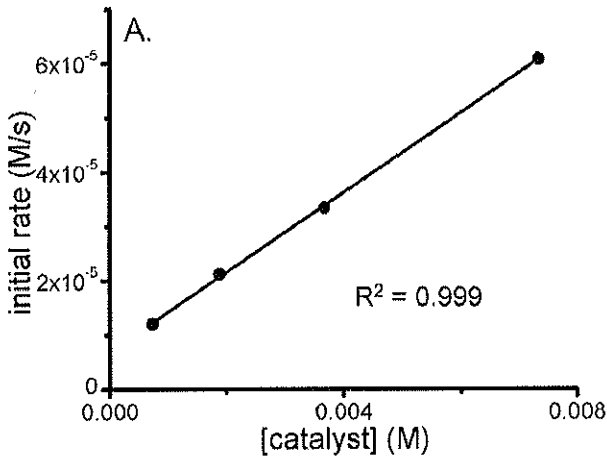
This solution was found by assuming $k_3 \ll k_2$ or k_{-2} (Pre-equilibrium Approximation for $[\text{cat}\cdot\text{P}]$), and SSA for $[\text{cat}\cdot\text{A}]$.

-1 for not defining C's w/ small k's.
~~for assuming step 2 is rds.~~

(7 – continued)

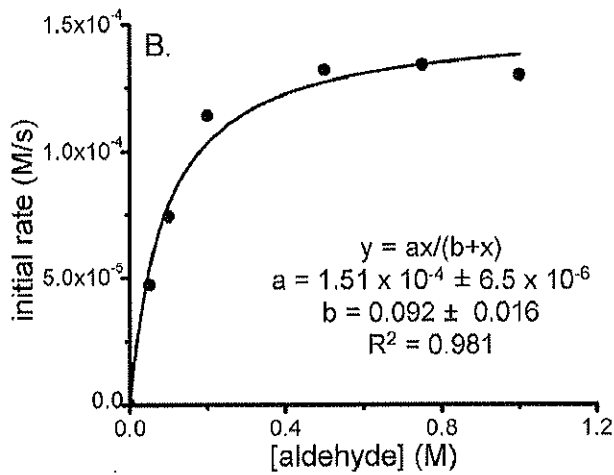
(f) What do the following graphs tell you?

3 points
(1 pt each)

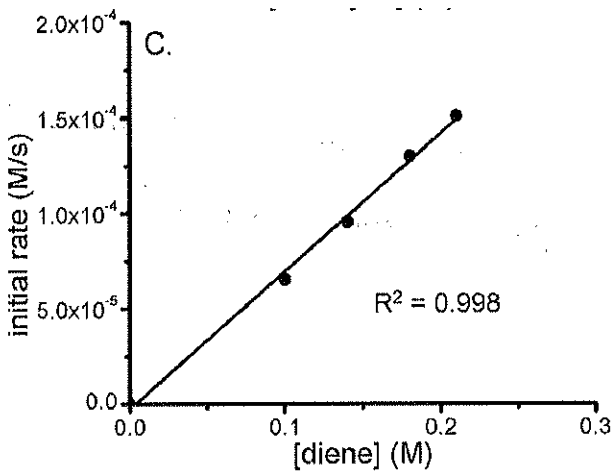


1st order in [cat]

(Please note: The non-zero y-intercept above is attributed to a non-catalyzed background reaction due to these reactions being run at room temperature instead of -40 °C. Other reactions were run at colder temperatures.)



Saturation behavior
w/ [A]



1st order in [D]

(7 - continued)

3 points

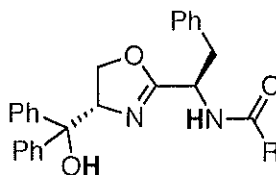
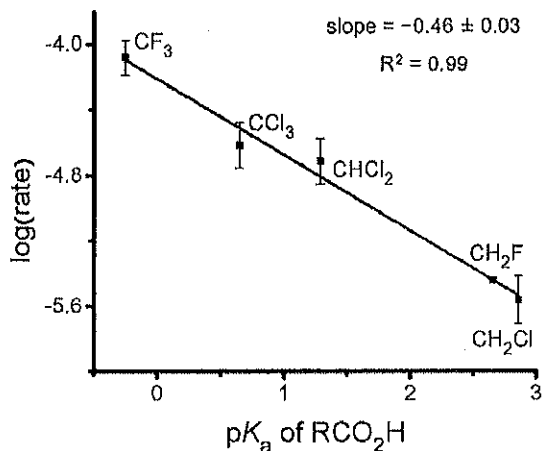
(g) Show that the data in part (f) is consistent with your proposed catalytic cycle and rate expression.

+1 → If step 2 = rds, rate = $\frac{k_1 k_2 k_3}{k_{-1} k_{-2}} \frac{[cat]_{tot} [A][D]}{1 + \frac{k_1}{k_{-1}} [A]}$ b/c $\frac{k_1 k_2}{k_{-1} k_{-2}} [A][D]$ is small.
(step 3 is fast)

+2 { @ low [A]: rate = $\frac{k_1 k_2 k_3}{k_{-1} k_{-2}} [cat]_{tot} [A][D] \rightarrow 1^{st}$ order in $[cat]_{tot}, [A]$ & $[D]$
@ high [A]: rate = $\frac{k_2 k_3}{k_{-2}} [cat]_{tot} [D] \rightarrow 0^{th}$ order in $[A]$. 1^{st} order in $[cat]_{tot}$ & $[D]$.

3 points

(h) Sigman studied the effect of catalyst acidity by analyzing the activity of catalysts with varying R substituents.



Conditions:
[A] = 0.78 M
[D] = 0.18 M
[catalyst] = 0.036 M

Which step of the catalytic cycle is being studied under these conditions?

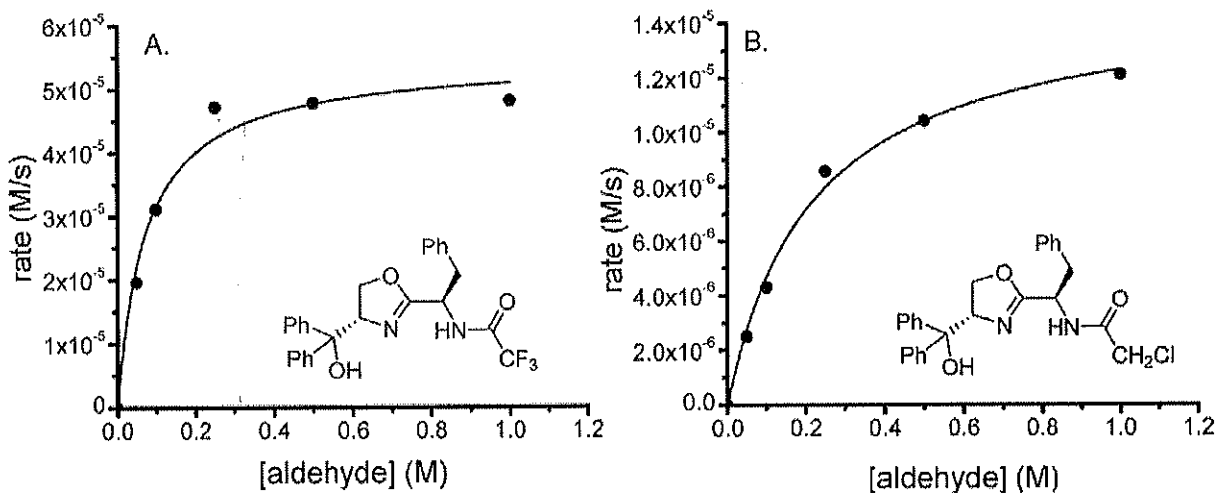
+1 → Step 2

How does the catalyst acidity affect the rate of that step?

+2 → more acidic ⇒ faster cycloaddition step.

(7 – continued)

(i) Sigman also studied the rate dependence on [aldehyde] with different catalysts.

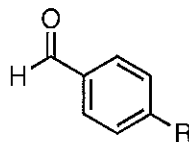
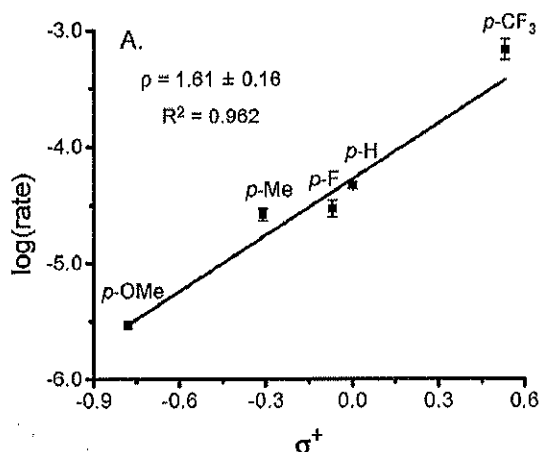
What do these graphs tell you? *Be brief!*

Stronger binding of A w/ more acidic catalyst.

Saturation @ lower $[A]$.

(7 - continued)

(j) Finally, Sigman studied the effect of benzaldehyde substituents with his original catalyst and obtained the following data.



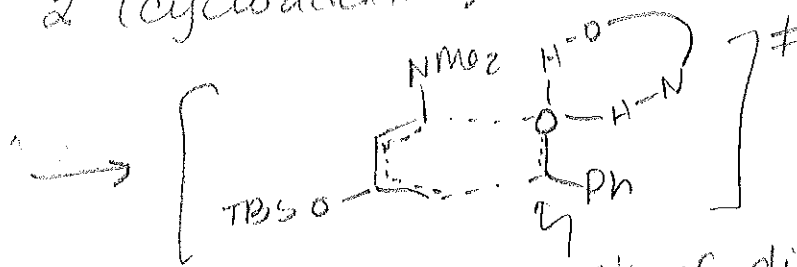
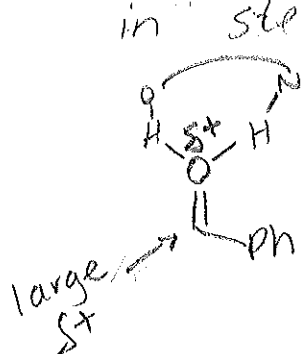
Conditions:
 [A] = 1.0 M
 [D] = 0.16 M
 [catalyst] = 0.016 M

high [A],
 saturation
 conditions,
 studying
 step 2.

What does this data tell you about the mechanism of the reaction? Is it consistent with your proposed catalytic cycle?

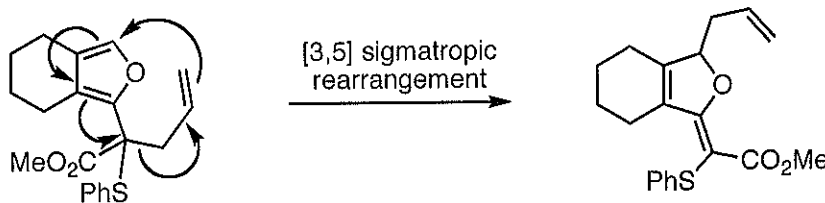
Positive slope \Rightarrow Positive $\rho \Rightarrow$ Build-up of \ominus charge
 -OR-
 Decrease in amount of \oplus charge.

+1 Consistent: \oplus charge on carbonyl C decreases in step 2 (cycloaddition):

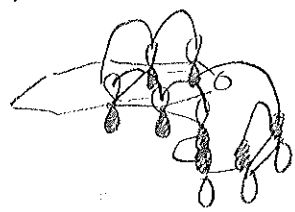


attack of diene
 decreases \oplus charge.

8. (9 points) A [3,5] sigmatropic rearrangement has been proposed to explain the following isomerization reaction, which proceeds upon standing at room temperature and is not a photochemically induced transformation (Kato, Y.; Miki, K.; Nishino, F.; Ohe, K.; Uemura, S. *Org. Lett.* **2003**, *5*, 2619).

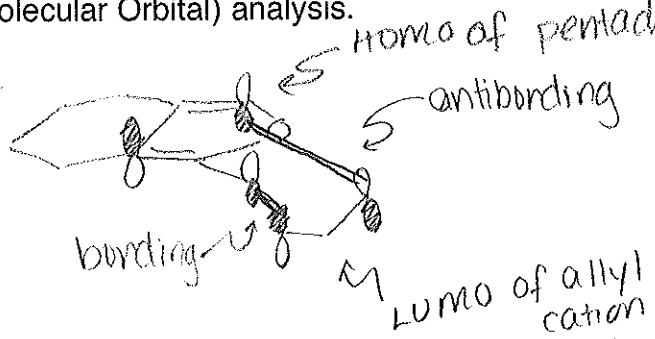


3pts (a) Please illustrate why this mechanism is forbidden using Dewar-Zimmerman analysis.



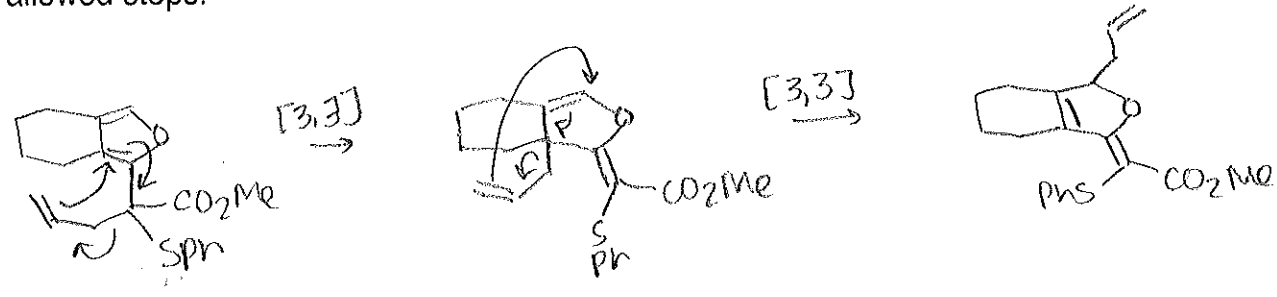
0 phase inversions
 Hückel topology
 $8e = 4n \Rightarrow$ Antiaromatic
 FORBIDDEN
 -1 w/o #e's.

3pts (b) Please illustrate why this mechanism is forbidden using Fukui FMO (Frontier Molecular Orbital) analysis.

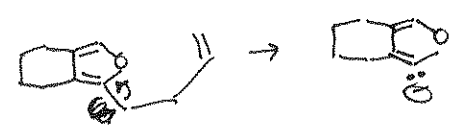


No net bonding.
 -1 for wrong MO depiction.

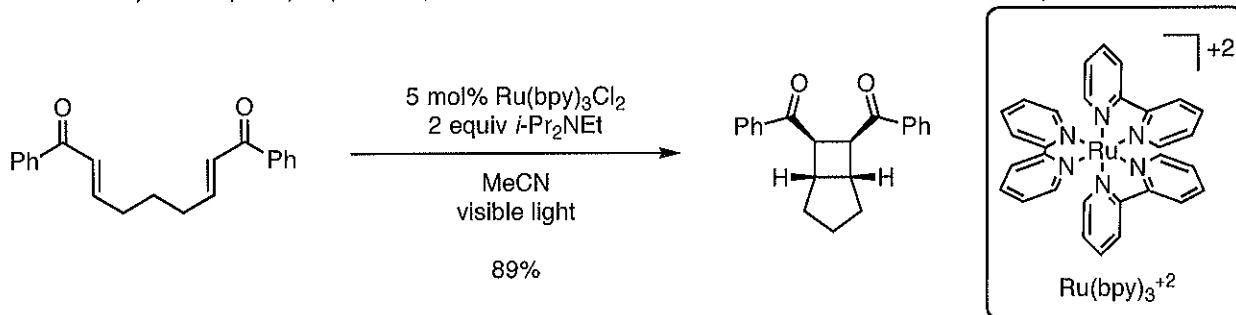
3pts (c) Please propose an alternative arrow-pushing mechanism that proceeds via thermally allowed steps.



+2 for crazy DA.
 +3 for [1,5]



9. (9 points) In his recent seminar, Professor Dave MacMillan discussed related work from Prof Teshik Yoon's group, specifically the following reaction (Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 12886).

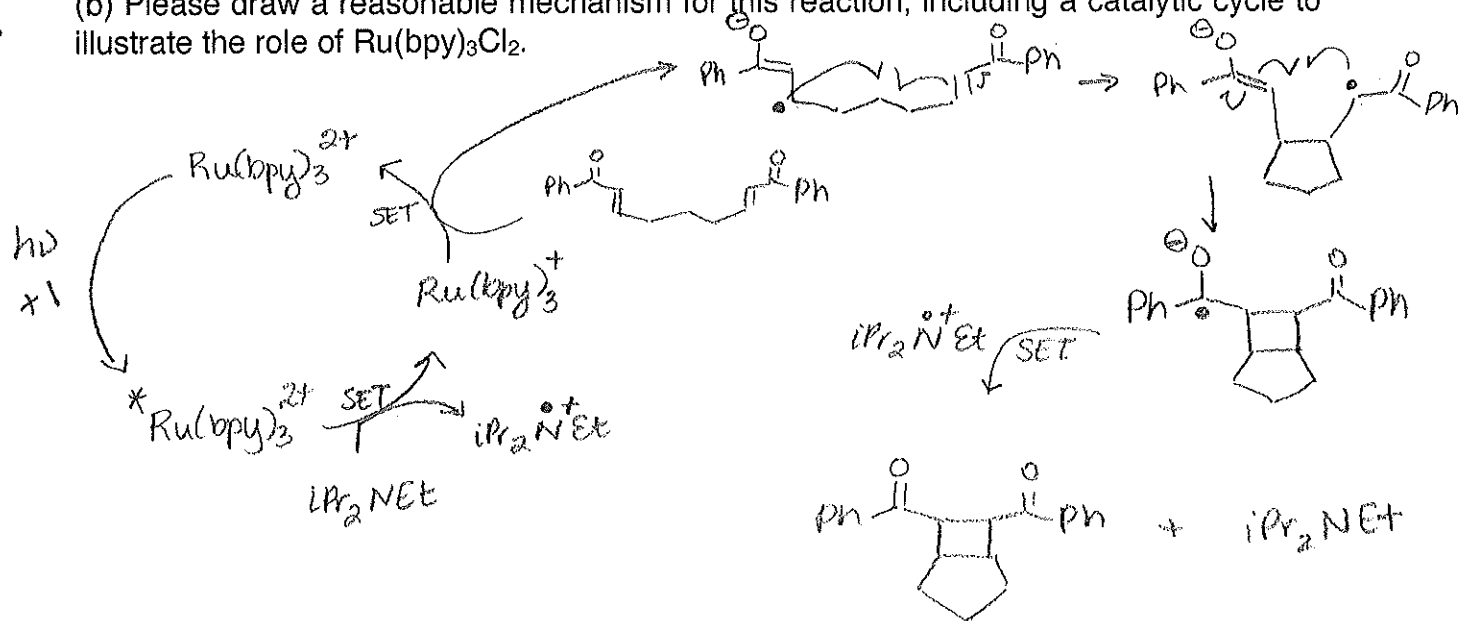


(a) What is the role of $\text{Ru}(\text{bpy})_3\text{Cl}_2$ in this reaction?

Photoredox catalyst

+1 for "catalyst"
or +1 for SET...

(b) Please draw a reasonable mechanism for this reaction, including a catalytic cycle to illustrate the role of $\text{Ru}(\text{bpy})_3\text{Cl}_2$.



(c) Is this reaction enantioselective?

NO