Name: Answer Key

Chem 633: Advanced Organic Chemistry 2016 ··· Final Exam

This exam is ***closed note, closed book***.

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 16 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 16 pages before you begin.

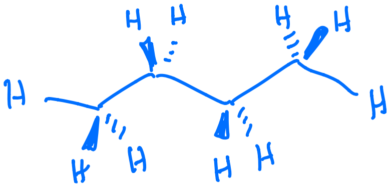
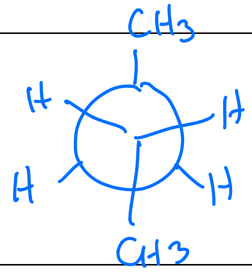
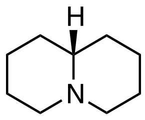
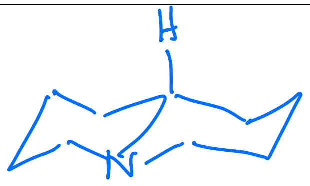
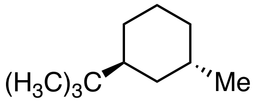
Molecular models are allowed.

Calculators are unnecessary and prohibited.

Problem	**Points**
1	______/15
2	______/15
3	______/4
4	______/10
5	______/36
6	______/20
TOTAL	______**/100**

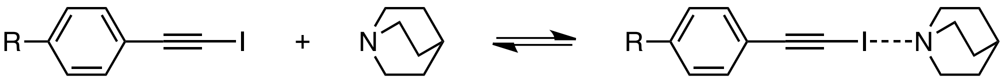
5 pts each

1. (15 points) Please clearly draw the lowest energy conformation of the following molecules.

(a) $H_3CCH_2CH_2CH_3$		
(b) 		
(c) 		2 pts for tBu eq. 4 for enantiomer

5 pts each

2. (15 points) Diederich's group studied the following equilibrium reaction (*Org. Lett.* **2014**, 4722).



1 **2** **3**

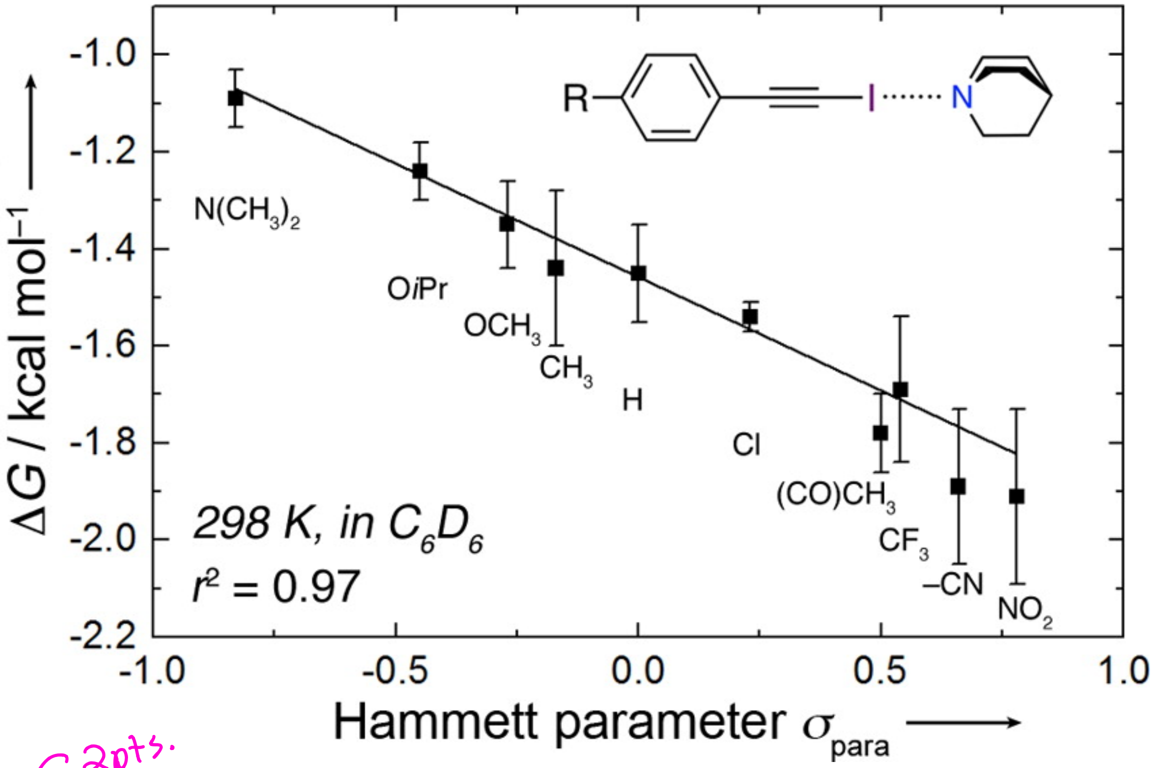
(a) For substrate **1** where R = Me, the equilibrium constant (K_{eq}) was determined to be 11 M^{-1}. Please give the equation that would allow you to convert this K_{eq} to ΔG. Also, please approximate ΔG for this K_{eq} = 11 M^{-1}.

Equation: $\Delta G^\circ = -RT \ln K_{eq}$ 3pts	ΔG ≈ −1.4 kcal/mol 2pts

1pt for ⊖ sign.

(2 – continued)

(b) What does the following graph tell you?



2pts.

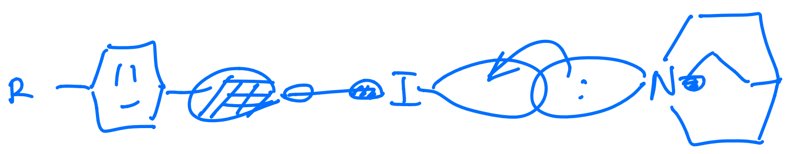
$\rho < 0$ ← True, but this is a funny Hammett plot (not $\log \left(\frac{K_x}{K_H}\right)$)

* Electron-withdrawing groups stabilize complex ③ → Bigger $-\Delta G$'s w/ EWG's.

5pts

(c) Based on your answer to part (b), please name and draw the major molecular orbital interaction responsible for the formation of complex **3**.

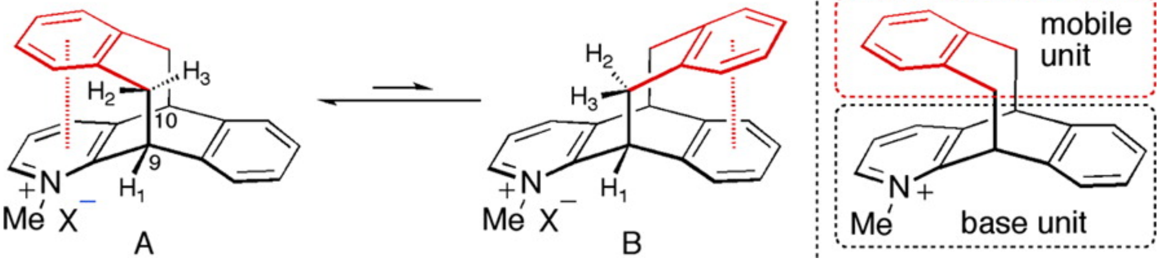
$lp_N \rightarrow \sigma^*_{I-C}$ 2pts

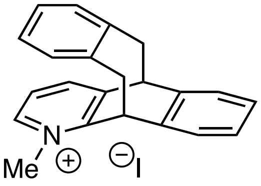


3 pts

2pts for "lp N" &, drawing

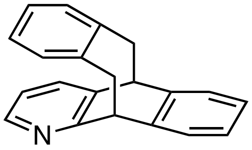
3. (4 points) Yamada et al studied the equilibrium of the following "molecular seesaw balance" (*Org. Lett.* **2015**, 4862). They found that conformation **A** is more strongly favored for pyridinium **1** than for neutral pyridine **2**. Please explain what interaction is responsible for this shift in equilibrium.





1

A:B = 92 : 8



2

A:B = 66 : 34

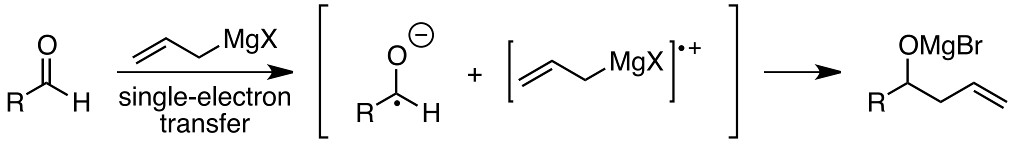
cation-π stabilizes A.

2pts for π-π

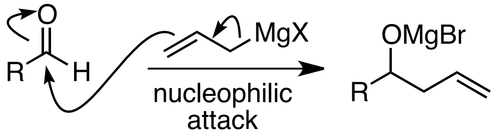
5pts each.

4. (10 points) The addition of allyl Grignard reagents to aldehydes has been proposed to occur either via Pathway A or B.

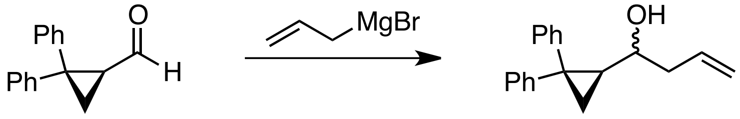
Pathway A



Pathway B

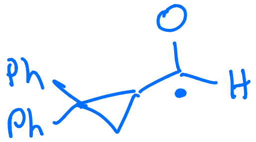


(a) Woerpel et al performed the allylation of aldehyde **1** and observed **2** as the only product. What does this result tell you about the mechanism?



1 **2**

Radical does not form (or is very short lived).



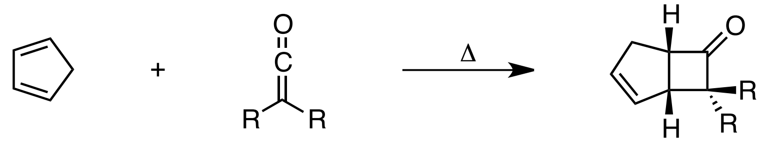
(b) Can you rule out Pathway A or B based on this data? If yes, which Pathway is ruled out?

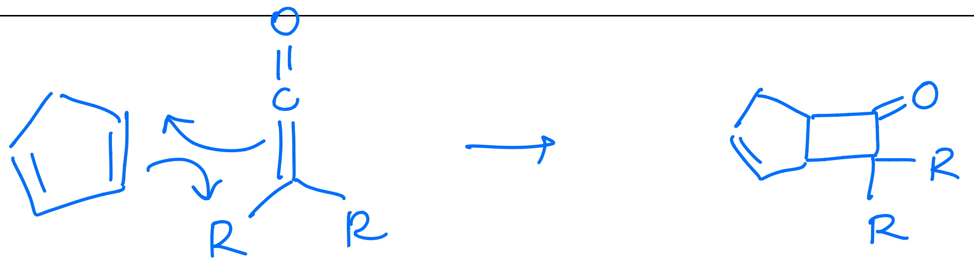
Yes. Rules out Pathway A.

4 pts each.

5. (36 points) (Parts of this problem are from Grossman, Chapter 4.)

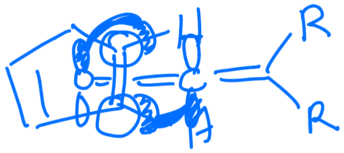
(a) A [2+2] cycloaddition is the generally accepted mechanism for the following reaction. Please draw the arrows for this arrow-pushing mechanism.





(b) Using any of the three theories discussed in class, please explain the stereochemical requirements of the [2+2] mechanism for the reaction in part (a). Be sure to include a clearly drawn picture in your answer.

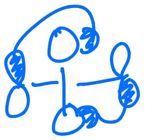
FMO: $[2\pi_s + 2\pi_a]$



Homo of  } suprafacial

LUMO of $O{=}C{=}C\langle^{R}_{R}$ } antarafacial

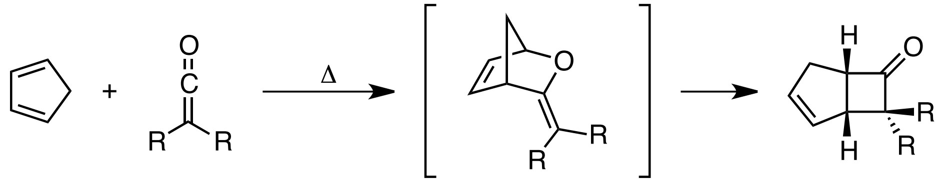
2 pts for correct picture but wrong pericyclic rxn / description.

 } antara

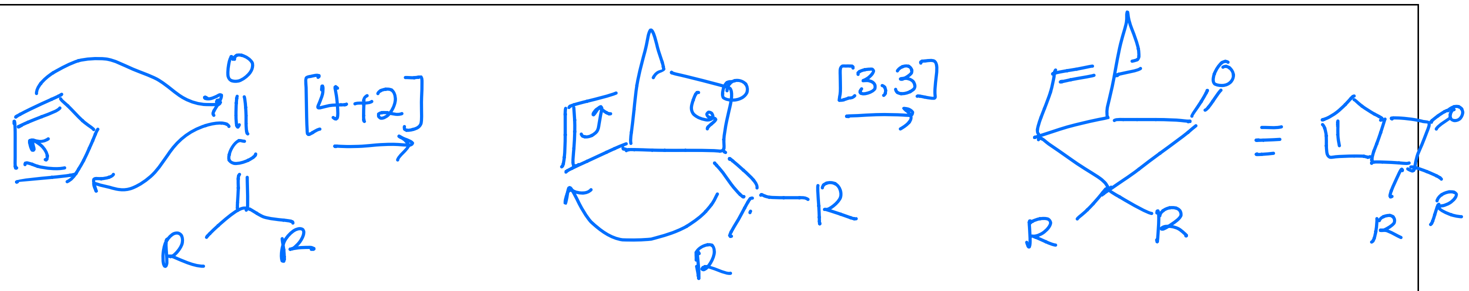
↑ supra

(5 – continued)

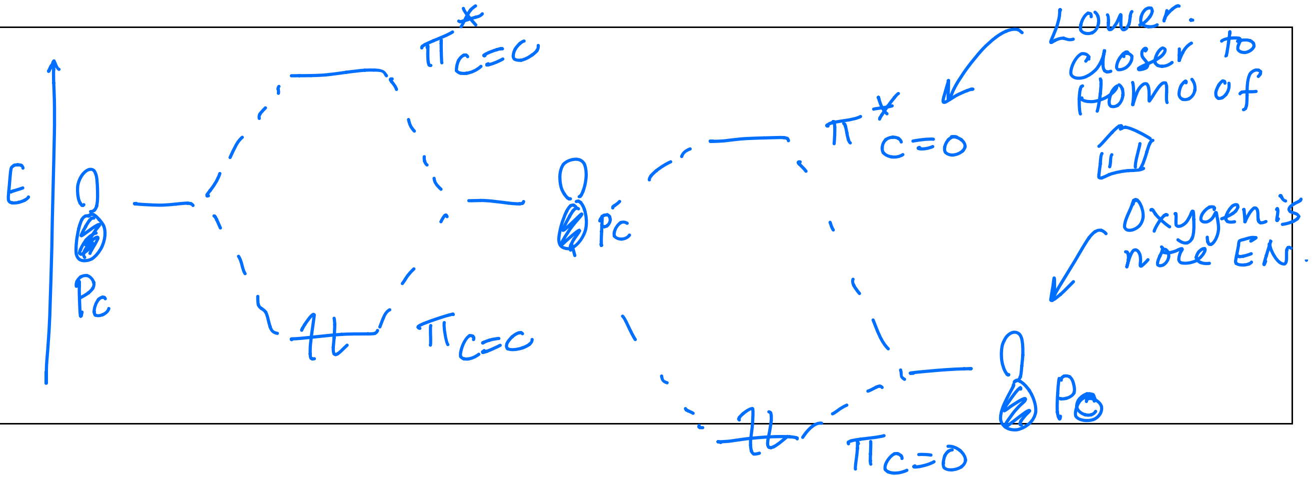
(c) The following two-step mechanism was recently proposed as an alternative mechanism.



Please draw the arrows for this mechanism.



(d) Explain why the C=O and not the C=C bond of the ketene reacts with the 1,3-diene in the first step of the mechanism proposed in part (c).

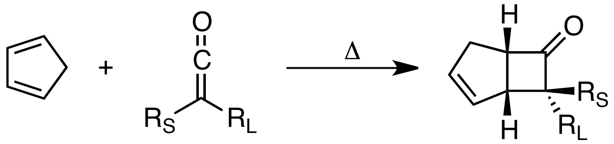


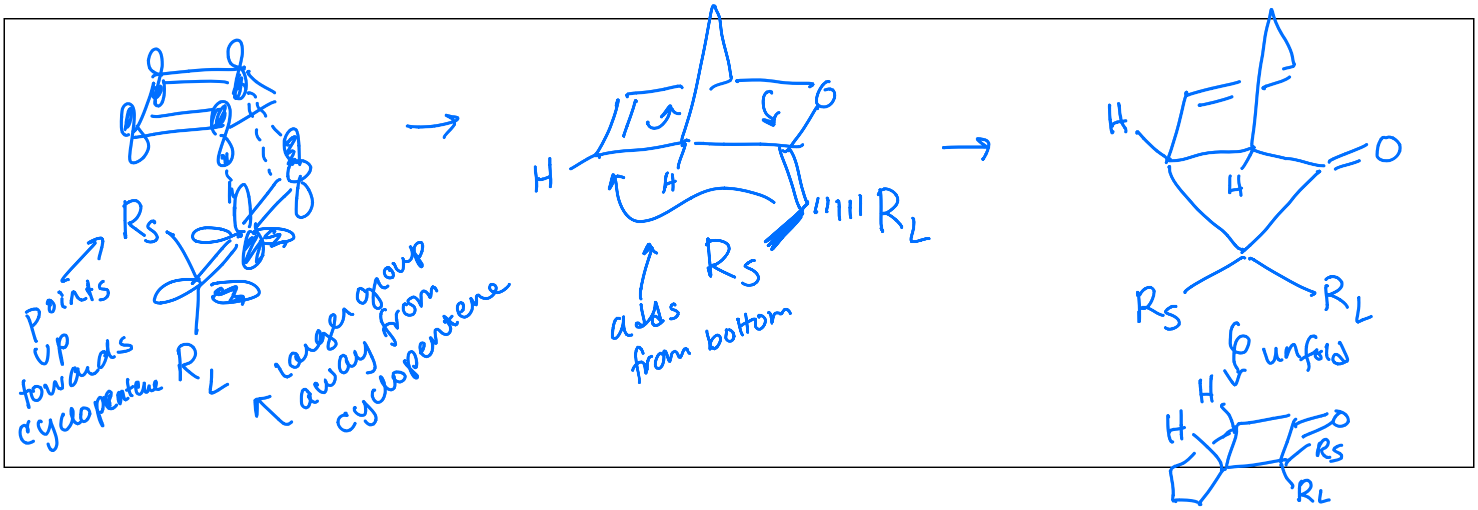
Lower. closer to Homo of

Oxygen is more EN.

(5 – continued again)

(e) When an unsymmetrically substituted ketene **2** is used in this reaction, the larger group (R_L) is found in the more sterically hindered endo position in the ultimate product ("chemical masochism"), as shown below. Use the mechanism from part (c) to explain (in words and pictures) this phenomenon. You will need to look at the stereochemical result of both steps of the mechanism.

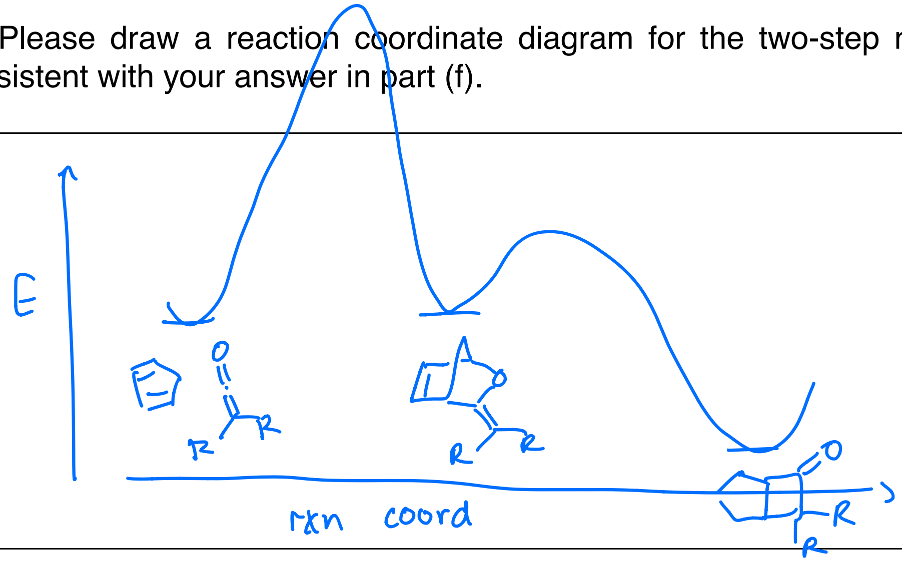




(f) Based on the information in part (e), which step of the mechanism in part (c) is likely the rate-determining step?

Step 1 = [4+2]

(g) Please draw a reaction coordinate diagram for the two-step mechanism (from part (c)) that is consistent with your answer in part (f).



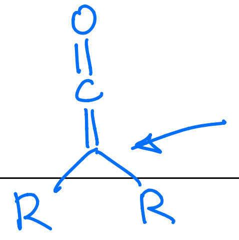
(5 – continued yet again)

(h) Given all the information above, are the two mechanisms kinetically distinguishable? Please provide rate laws for both mechanisms to explain your answer.

Kinetically distinguishable (circle one): YES or [✓ NO] 2pts.	
Rate law for 1-step mechanism in part (a): Rate = k_1[cyclopentene][ketene] 1pt	Rate law for 1-step mechanism in part (c): Rate = k_1[cyclopentene][ketene] 1pt.

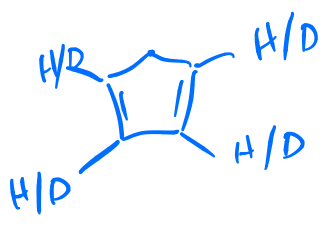
(i) Please propose one additional experiment that will allow you to distinguish between the two mechanisms.

Kinetic isotope effect.



If step 1 of 2nd mech is rds, no KIE ($^{13}C/^{12}C$) here. Could also look for rehybridization if R=H.

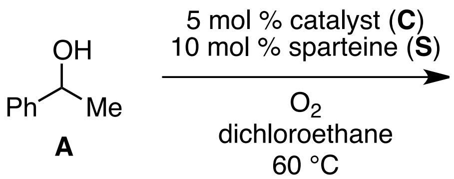
If 1st mech is right, should see KIE at this C.

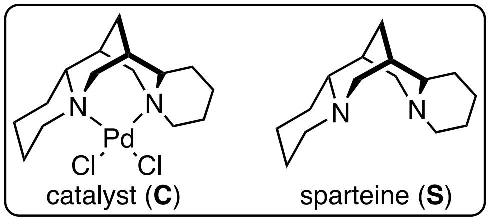


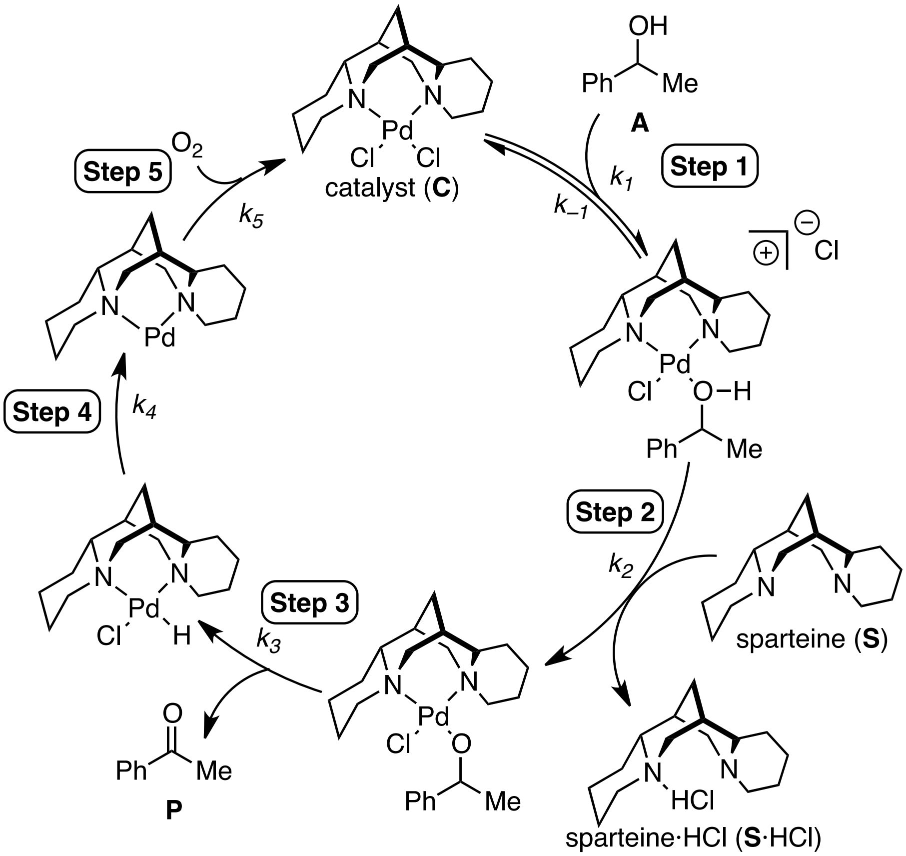
} would also work.

4 pts each.

6. (20 points) The Sigman group developed and studied the mechanism of the palladium-catalyzed oxidation of benzylic alcohols, such as **A** (*JACS* **2002**, 8202). The proposed mechanism is shown below.





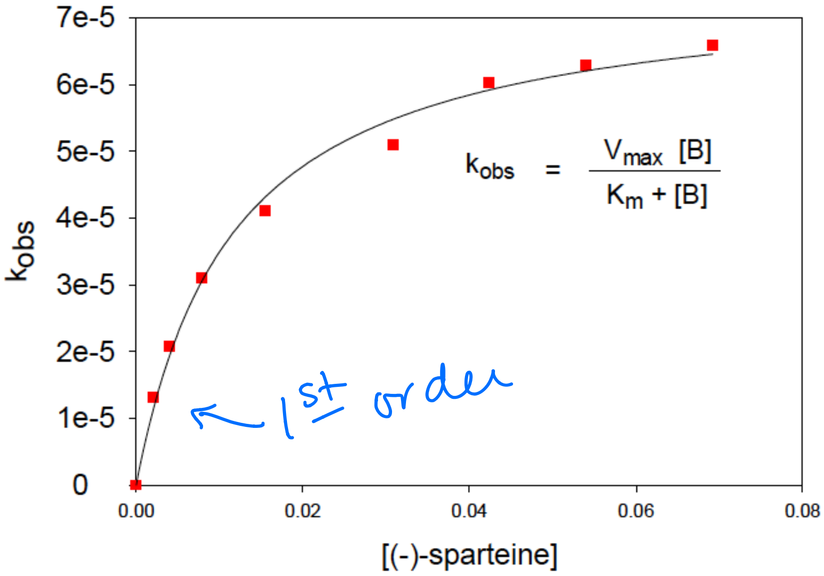


(a) Assuming Step 2 is rate-limiting and all subsequent steps to regenerate **C** are rapid and irreversible, please write a "one plus" catalytic rate expression for this catalytic cycle. Use the rate constants depicted in the catalytic cycle above, and apply the steady-state approximation to the concentration of any relevant intermediates. Express your rate law in terms of **A**, **S**, and [catalyst]$_{\text{total}}$.

$$\text{rate} = \frac{\dfrac{k_1 k_2 [\text{catalyst}]_{\text{total}}[A][S]}{k_{-1} + k_2[S]}}{1 + \dfrac{k_1[A]}{k_{-1} + k_2[S]}}$$

(6 – continued)

(b) What do the following graphs tell you?

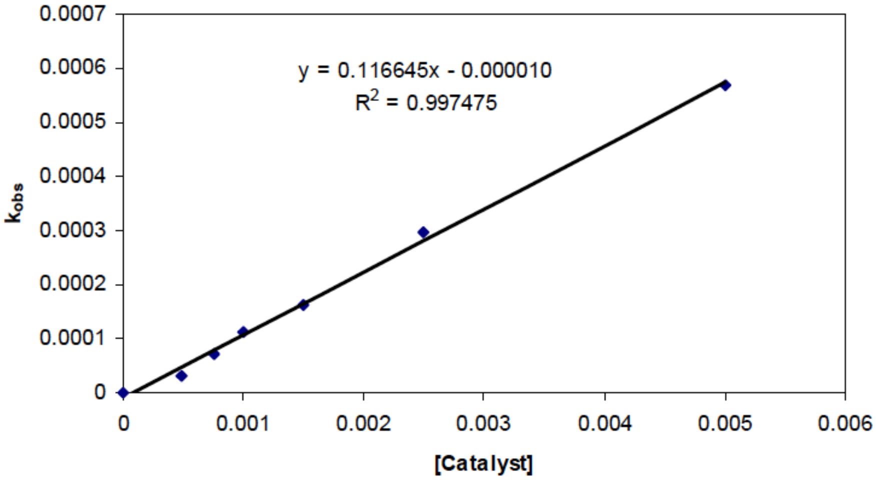


0 order

1st order

Saturation in [sparteine]

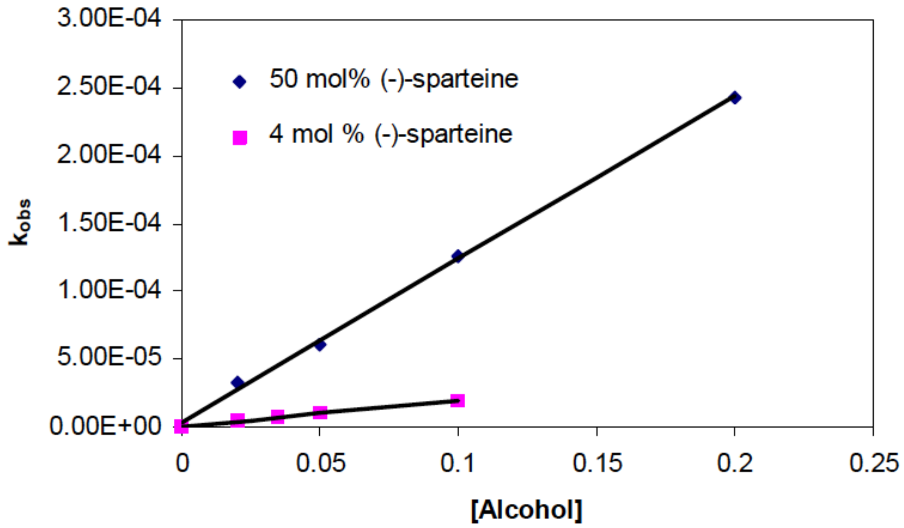
2pts



1st order in [catalyst]

1pt

(6 – continued)



1st order in [alcohol] at both high + low [sparteine]

1pt

(c) Please show that your catalytic rate expression from (a) is consistent with this data.

From before:

$$\text{rate} = \frac{\dfrac{k_1 k_2 [\text{catalyst}]_{\text{total}} [A][S]}{k_{-1} + k_2[S]}}{1 + \dfrac{k_1[A]}{k_{-1} + k_2[S]}}$$

If Ⓒ is primary catalyst resting state,

$$\text{rate} = \frac{\dfrac{k_1 k_2 [\text{cat}]_T [A][S]}{k_{-1} + k_2[S]}}{1 + \cancel{\dfrac{k_1[A]}{k_{-1} + k_2[S]}}}$$

2pts

At low [S], $k_{-1} >> k_2[S]$:

1st order in $[\text{cat}]_T$, [A], [S] @ low [S]

$$\text{rate} = \frac{k_1 k_2 [\text{cat}]_T [A][S]}{k_{-1}}$$

At high [S], $k_2[S] >> k_{-1}$:

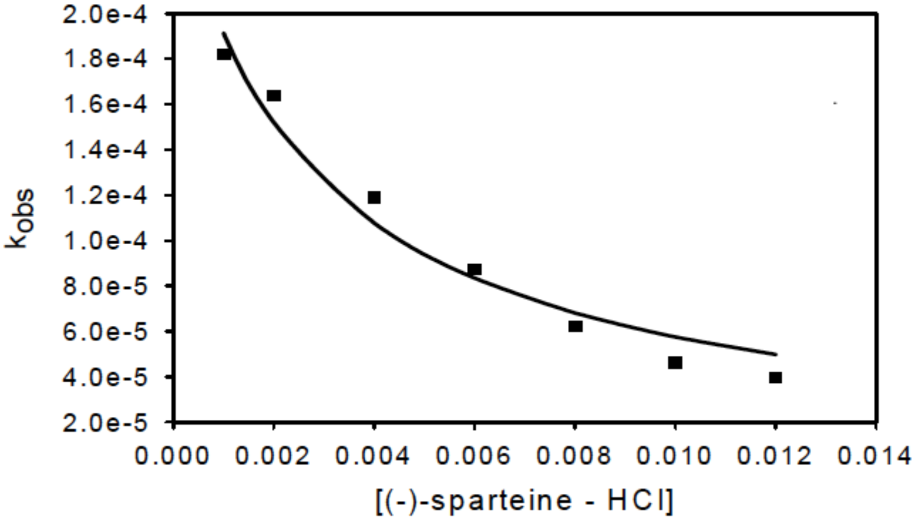
2pts.

1st order in $[\text{cat}]_T$, [A]; 0 order in [S] @ high [S].

$$\text{rate} = \frac{k_1 \cancel{k_2} [\text{cat}]_T [A] \cancel{[S]}}{\cancel{k_2 [S]}}$$

(6 – continued)

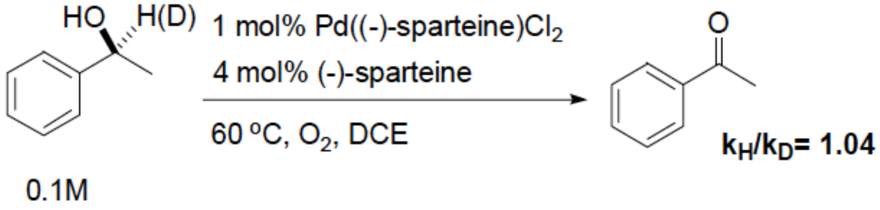
(d) The researchers then ran an additional experiment, using 50 mol % **S** (high [**S**]). What does the following graph tell you? Is this data consistent with step 2 being the rate-determining step?



- inverse dependence on [S·HCl] 2pts
- NO ; inconsistent w/ step 2 as rds. 2pts

(e) They also performed two kinetic isotope effect experiments, at different concentrations of sparteine. Given this data, and all data above, what is the rate-determining step under each of these conditions (low and high [**S**])?

Low [S]:

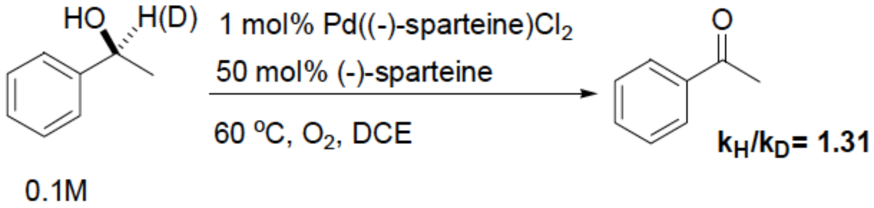


No KIE → step 2 = rds

2pts

(6 – continued)

High [S]:



Primary KIE : C-H bond breaking in rds

↓

Step 3 = rds.

2pts.

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