

Initials: _____

1

Name: Answer Key

Chem 633: Advanced Organic Chemistry 2016 ... Midterm 2

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 15 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 15 pages before you begin.

Molecular models are allowed.

Calculators are unnecessary and prohibited.

Problem	Points
1	_____/32
2	_____/20
3	_____/28
4	_____/20
TOTAL	_____/100

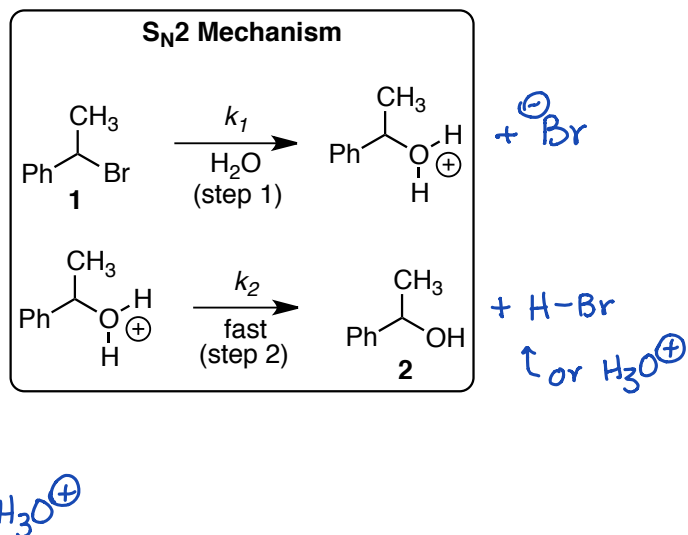
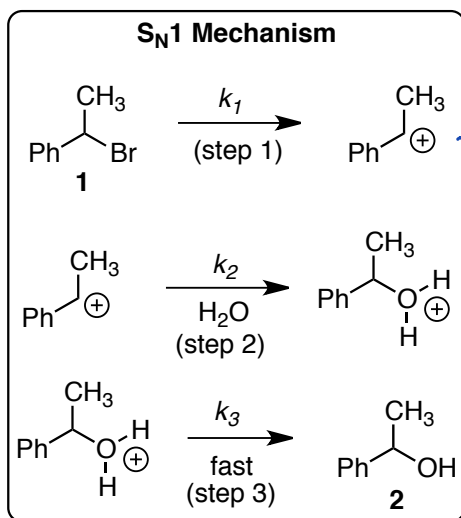
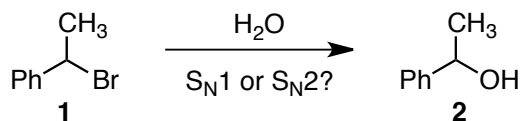
Initials: _____

2

4 pts each (7 parts total)

The reaction of bromide 1 and H₂O results in 2.

1. (32 points) ~~In water, bromide 1 slowly hydrolyzes to 2.~~ This reaction may proceed via either an S_N1 or S_N2 mechanism. For both mechanisms, you may assume that the final deprotonation to form 2 is fast.



(a) What is most likely rate-determining step for the S_N1 mechanism?

Step 1

(b) Based on your answer to (a), please write the expected rate law for the S_N1 mechanism.

$$\text{rate} = k_1 [1]$$

(c) What is most likely rate-determining step for the S_N2 mechanism?

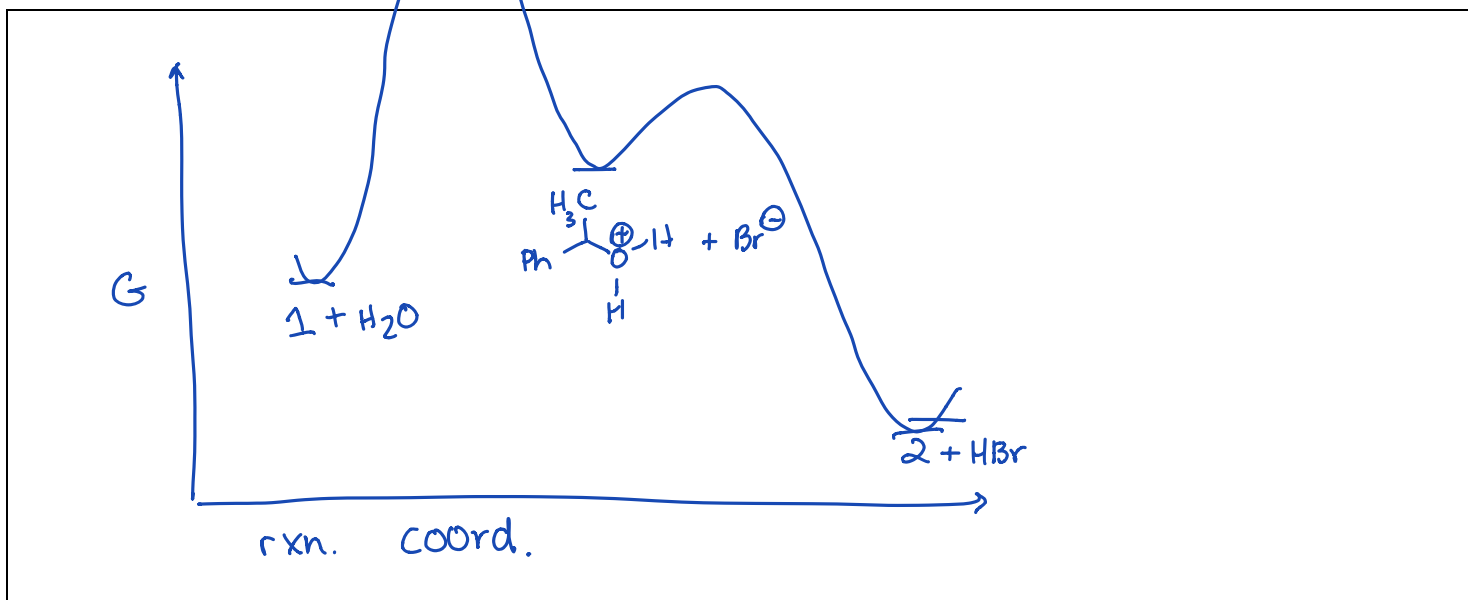
Step 1

(1 – continued)

(d) Based on your answer to (c), please write the expected rate law for the S_N2 mechanism.



(e) Please draw a reaction coordinate diagram for the S_N2 mechanism.



(f) Please describe the experiments and analysis you would do to show that the reaction kinetics are consistent with either the S_N1 or S_N2 mechanism.

- 1) Pseudo-first order Conditions: Run rxn w/ 10, 20, 30, 40, etc. equiv H₂O. *measure [1] vs time.*
- 2) Show that $\ln[1]$ vs. time is linear \rightarrow confirms 1st order rate dependence on 1 (expected for both mechanisms).
- 3) Extract k_{obs} from each plot (slope = $-k_{\text{obs}}$)
- 4) Plot k_{obs} vs. $[\text{H}_2\text{O}]_0$. Should either see horizontal line \rightarrow 0th order in $[\text{H}_2\text{O}]$ or sloped line \rightarrow 1st order in $[\text{H}_2\text{O}]$.

0th order in $[\text{H}_2\text{O}]$
 \downarrow
S_N1 mech

1st order in $[\text{H}_2\text{O}]$
 \downarrow
S_N2 mech.

slope = $-k_{\text{obs}}$

(1 – continued)

(g) Determination of ΔH^\ddagger , ΔS^\ddagger , and ΔG^\ddagger may also be helpful in determining the mechanism. Please describe the experiments and analysis you would do to determine these values.

1) Pseudo-first order conditions: Run rxn w/ 10 equiv H_2O at various temperatures. Measure $[I]$ vs. time.

2) Extract k_{obs} for each temp from plot of $\ln[I]$ vs. time

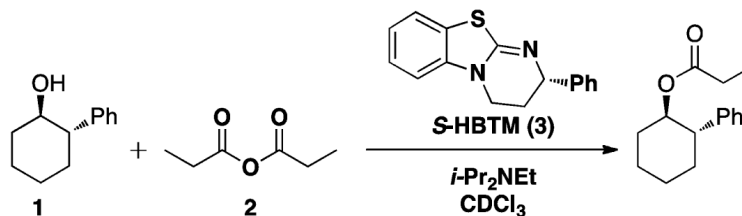
3) Plot $R \ln\left(\frac{kh}{k_B T}\right)$ vs. $\frac{1}{T}$

$$R \ln\left(\frac{kh}{k_B T}\right) = -\Delta H^\ddagger \left(\frac{1}{T}\right) + \Delta S^\ddagger$$

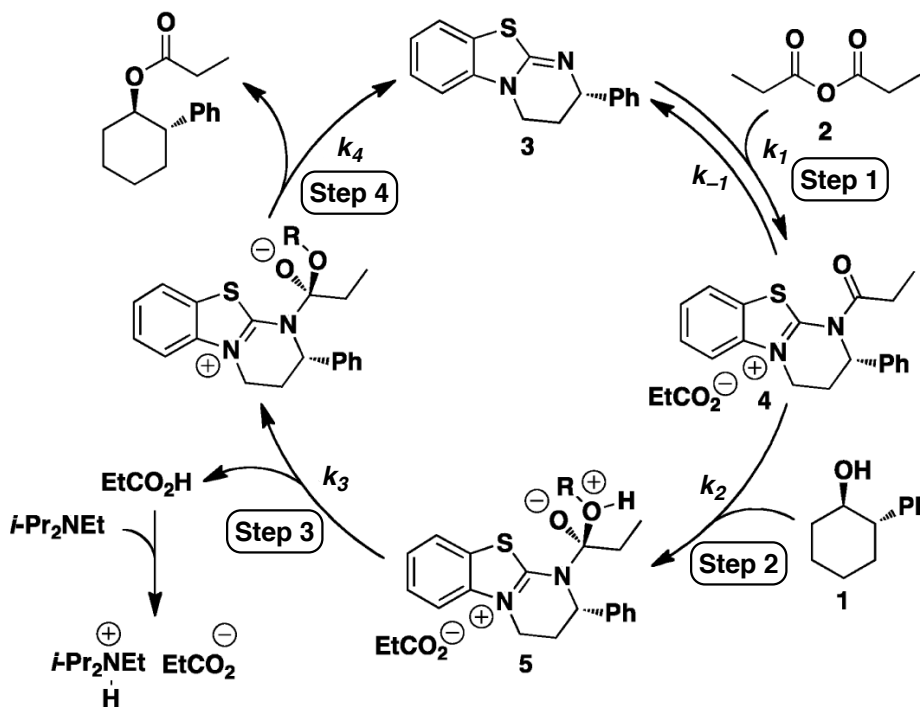
(h) What do you expect ΔS^\ddagger to be for each mechanism?

S _N 1 mechanism	S _N 2 mechanism
$\Delta S^\ddagger = \underline{+10}$ eu	$\Delta S^\ddagger = \underline{-30}$ eu
↑ highly disordered TS	↑ highly ordered TS

2. (20 points) The Rychnovsky group has developed a method for determination of the absolute configuration of an alcohol stereocenter using the *S*-HBTM catalyst (**3**). This acylation catalyst reacts more quickly with one enantiomer of alcohol than the other. To validate this method, they studied the mechanism of the acylation of alcohol **1**.



They proposed the following catalytic cycle.



(a) Assuming Step 2 is rate-limiting and all subsequent steps to regenerate **3** 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 [4]. Express your rate law in terms of **1**, **2**, and [catalyst]_{total}.

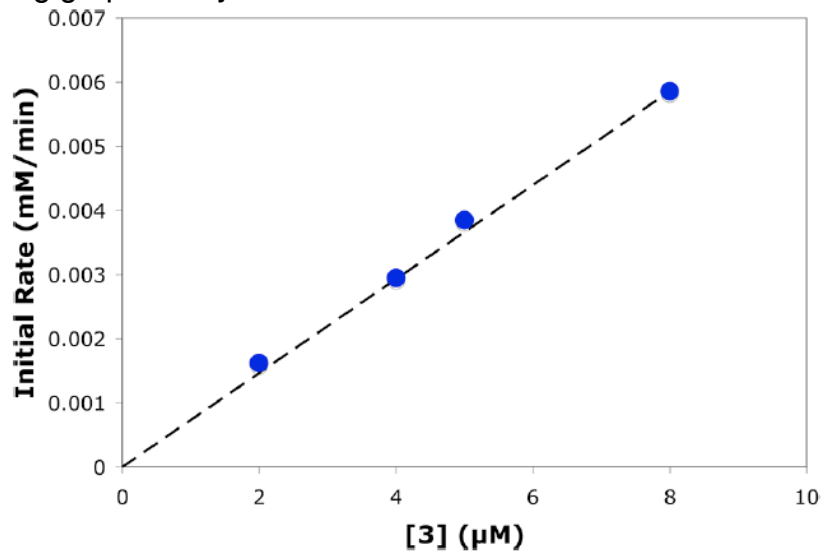
Note that **4** is a tight ion pair and can be treated as a single species.

$$\text{rate} = \frac{k_1 k_2 [\text{catalyst}]_{\text{total}} [1][2]}{k_{-1} + k_2 [1] + \frac{k_1 [2]}{k_{-1} + k_2 [1]}}$$

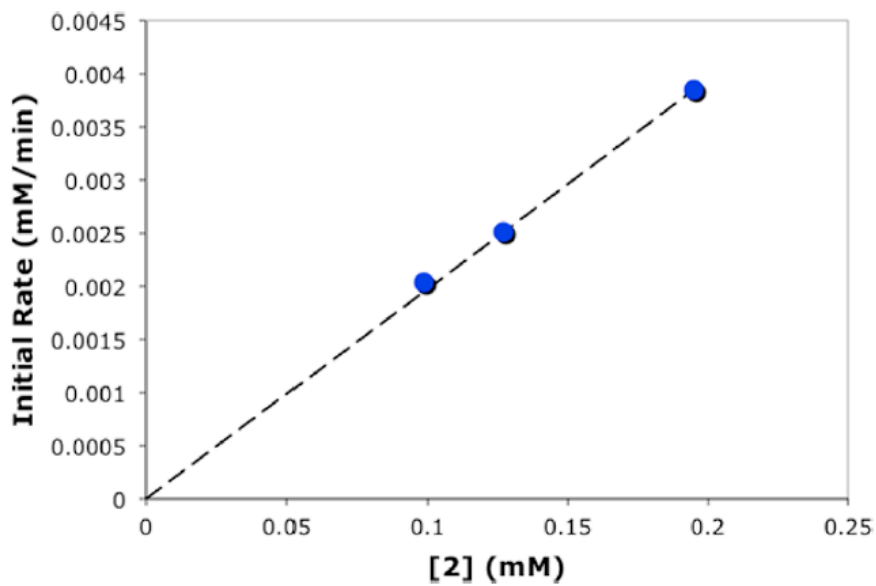
Initials: _____

(2 – continued)

(b) What do the following graphs tell you?

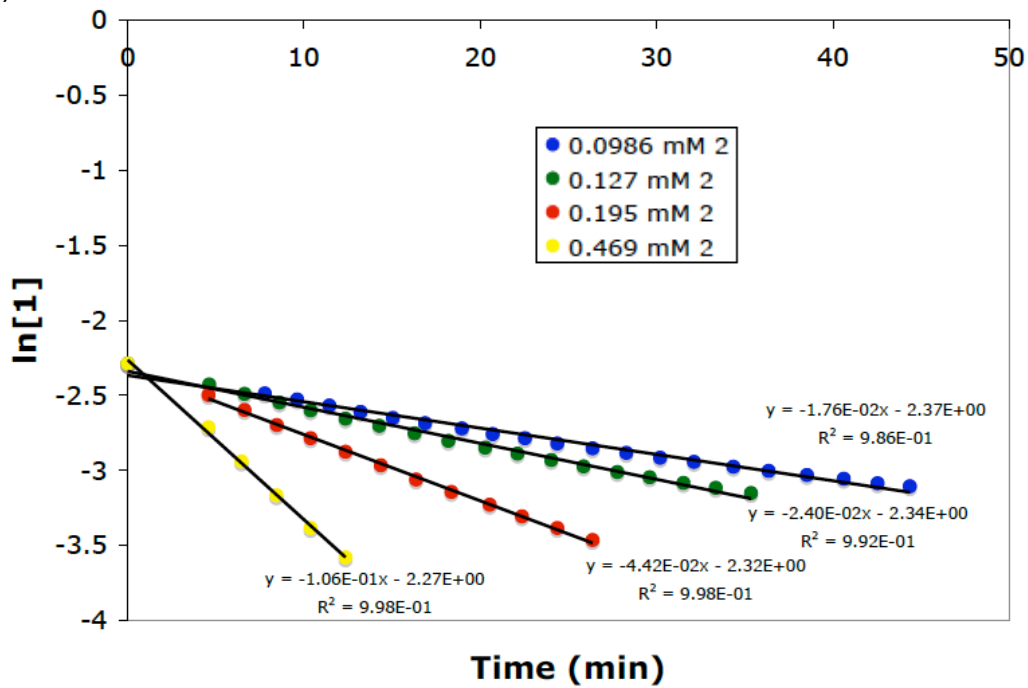


1st order in [3]



1st order in [2]

(2 – continued)



(For this graph, you may just focus on one of the trend lines.)

1st order in [1]

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

If $k_{-1} \gg k_2 [1]$, then

$$\text{rate} = \frac{k_1 k_2 [\text{catalyst}]_{\text{total}} [1][2]}{k_{-1} + k_2 [1]} \left(1 + \frac{k_1 [2]}{k_{-1} + k_2 [1]} \right)$$

To be 1st order in [2], $\frac{k_1 [2]}{k_{-1} + k_2 [1]}$ must be only catalyst resting state, or $1 \gg \frac{k_1 [2]}{k_{-1}}$

$$= \frac{k_1 k_2 [\text{catalyst}]_{\text{total}} [1][2]}{k_{-1}} \left(1 + \frac{k_1 [2]}{k_{-1}} \right)$$

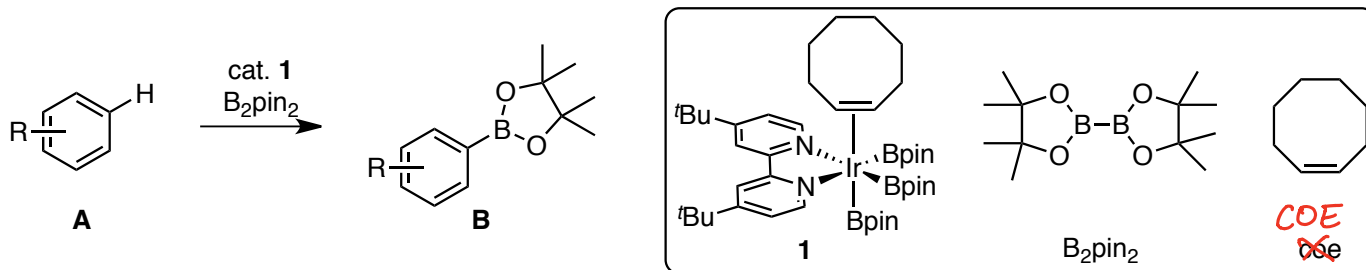
$$\text{rate} = \frac{k_1 k_2 [\text{catalyst}]_{\text{total}} [1][2]}{k_{-1}}$$

$$\text{rate} = \frac{k_1 k_2}{k_{-1}} [\text{catalyst}]_{\text{total}} [1][2]$$

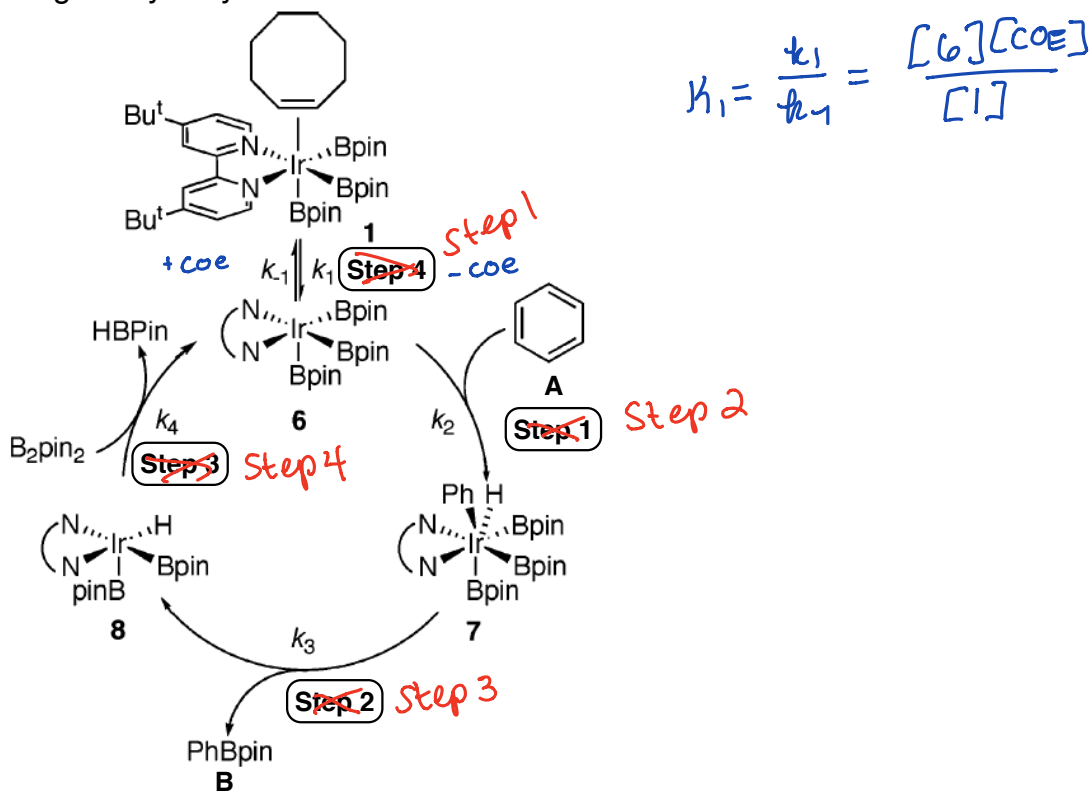
(d) What is the primary catalyst resting state?

3

3. (28 points) The Hartwig group studied the iridium-catalyzed borylation of arenes via C–H bond activation.



They proposed the following catalytic cycle.



$$k_1 = \frac{k_1}{k_{-1}} = \frac{[6][COE]}{[1]}$$

(a) Assuming Step ² is rate-limiting and all subsequent steps to regenerate **6** 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. Express your rate law in terms of **A**, B_2pin_2 , and $[Ir]_{total}$, and $[COE]$.

$$rate = \frac{k_2 [Ir]_{total} [A]}{1 + \frac{k_{-1} [COE]}{k_1}}$$

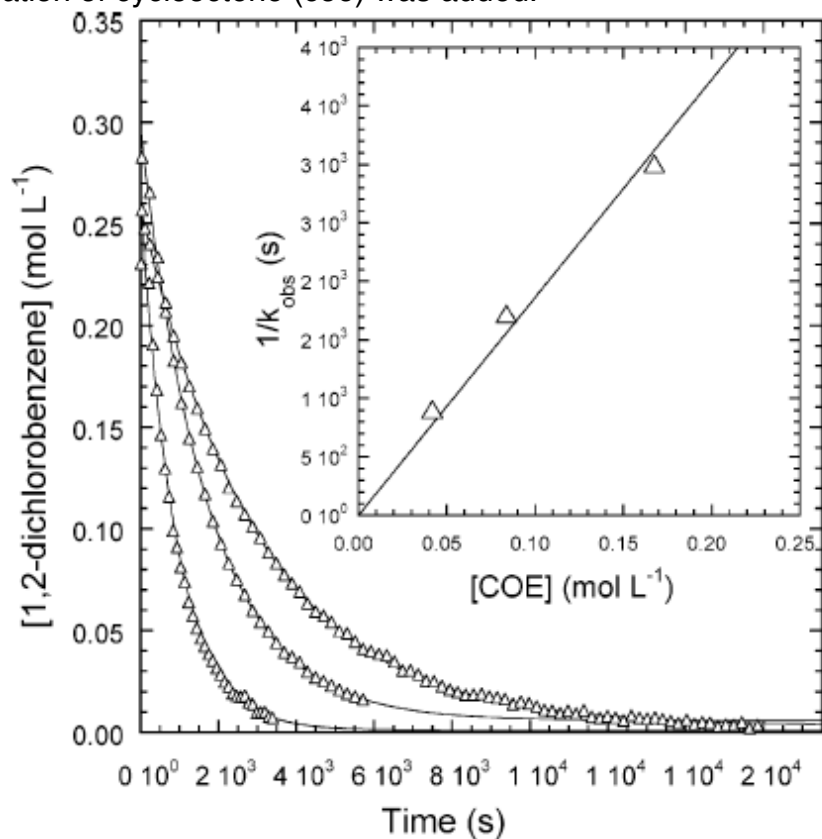
(3 – continued)

(b) What does the following excerpt from the paper tell you?

“The concentration of arene (**A**) decayed exponentially during all reactions with an excess of B_2pin_2 . Plots of $\ln[A]$ vs time were linear over 3–4 half-lives.”

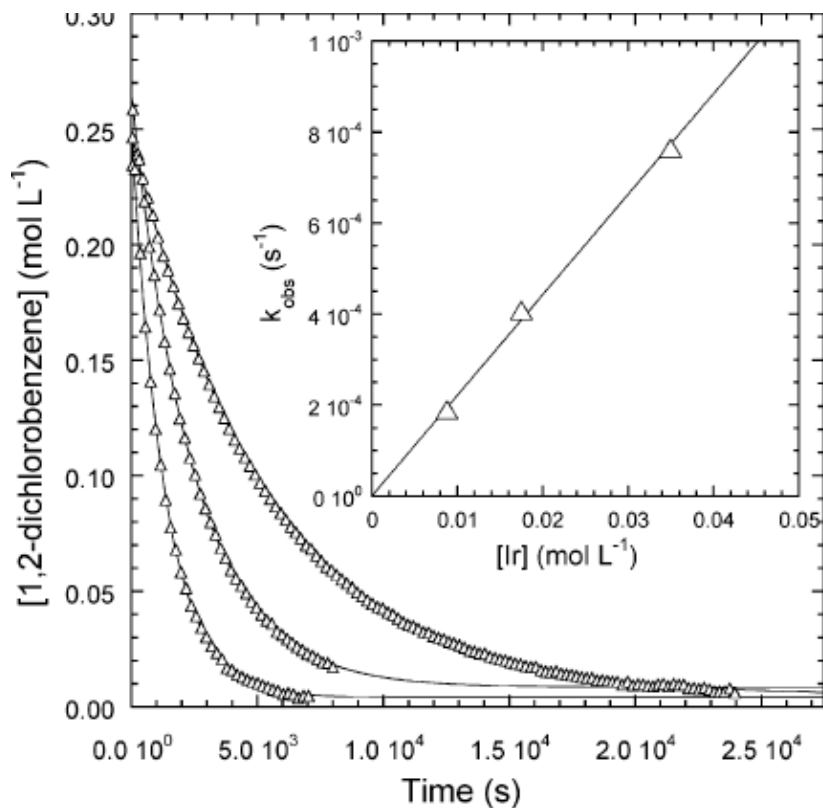
1st order in A

(c) What do the following graphs tell you? Note: In these experiments, **A** = 1,2-dichlorobenzene, and a constant concentration of cyclooctene (coe) was added.



inverse 1st order in [COE]

(3 – continued)



1st order in [Ir]

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

If $\frac{1}{k_1}$ = primary catalyst resting state, then $1 \ll \frac{k_1}{k_{-1}[\text{COE}]}$

$$\text{rate} = \frac{k_2 [\text{Ir}]_{\text{total}} [\text{A}]}{\frac{k_{-1} [\text{COE}]}{k_1}} = \frac{k_1 k_2 [\text{Ir}]_{\text{total}} [\text{A}]}{k_{-1} [\text{COE}]}$$

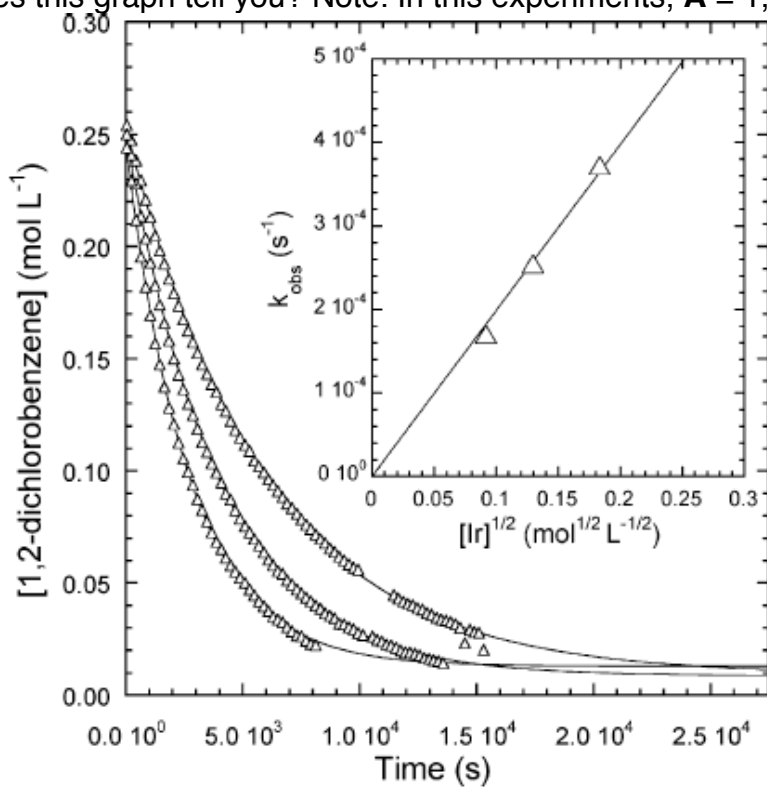
1st order in $[\text{Ir}]_{\text{total}}$
 1st order in $[\text{A}]$
 Inverse 1st order in $[\text{COE}]$

(3 – continued)

(e) What is the primary catalyst resting state under these conditions?

①

(f) When the kinetic experiments were performed in the absence of added ~~CO~~^{COE}, the following graph was obtained. What does this graph tell you? Note: In this experiments, **A** = 1,2-dichlorobenzene.



$\frac{1}{2}$ order in $[Ir]$

(3 – continued)

(g) Please show that the data in (f) ^{are} also consistent with ~~your proposed rate law.~~ ^{the proposed mechanism,} ^{rate-determining} ^{step, and} ^{catalyst resting} ^{state.}

When no COE is added, $[COE] = [G]$

$$\text{rate} = k_2 [G][A]$$

$$K_1 = \frac{k_1}{k_{-1}} = \frac{[G][COE]}{[I]} = \frac{[G]^2}{[I]} \quad \text{when } [G] = [COE]$$

$$[G] = K_1^{1/2} [I]^{1/2}$$

$$\text{rate} = K_1^{1/2} k_2 [I]^{1/2} [A]$$

If primary catalyst resting state is 1, then

$$\text{rate} = K_1^{1/2} k_2 [Ir]_{\text{total}}^{1/2} [A]$$

↑ 1/2 order rate dependence
on $[Ir]_{\text{total}}$

Initials: _____

Break

C1-C7

π C8=C9

C8-C3

Make

C9-Si

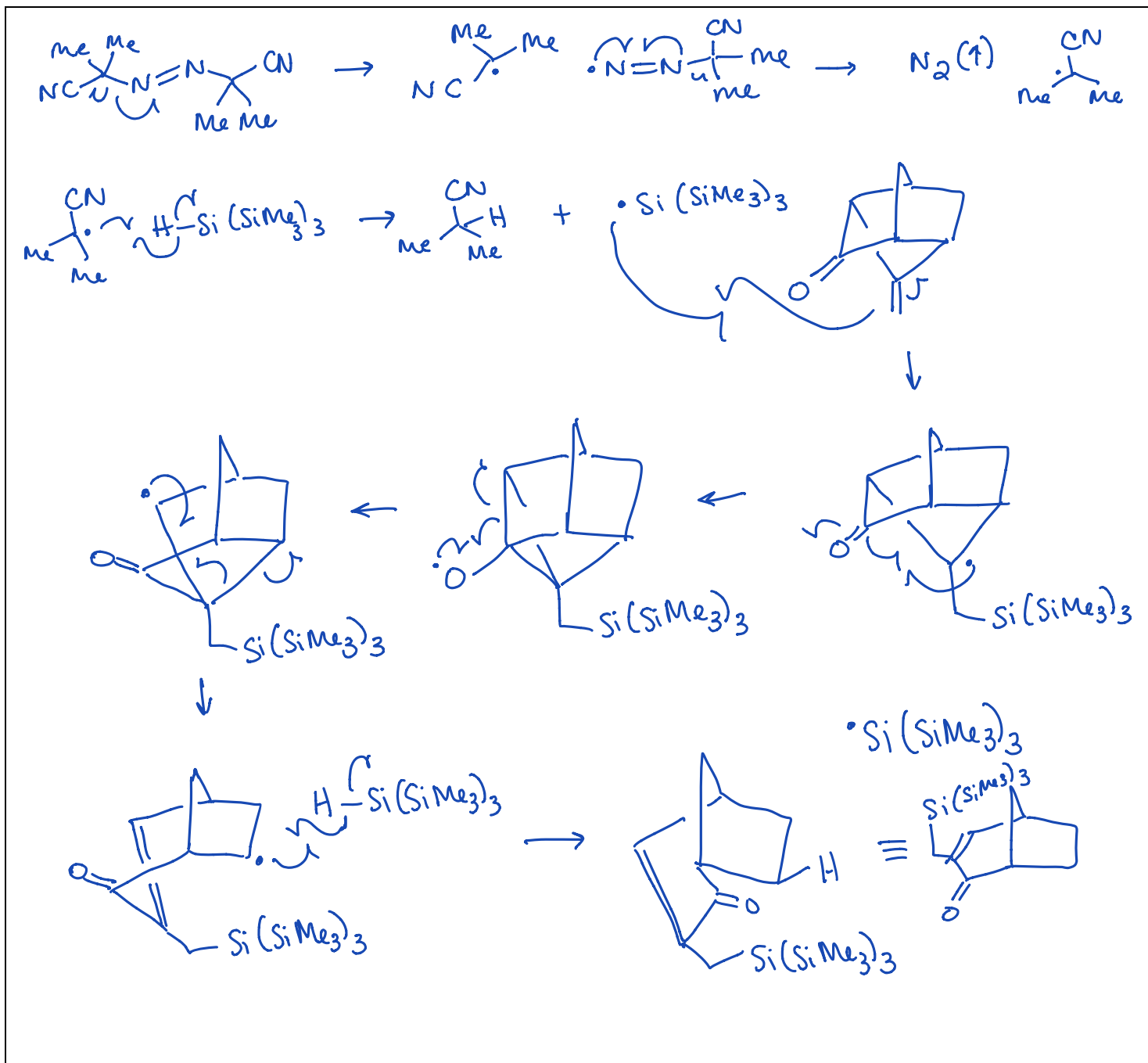
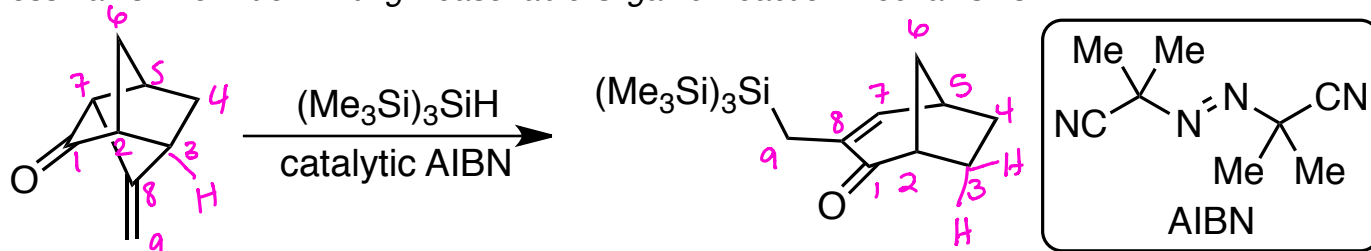
π C7=C8

C1-C8

C3-H

13

4. (20 points) Please draw a reasonable arrow-pushing mechanism for the following reaction from Grossman's *The Art of Writing Reasonable Organic Reaction Mechanisms*.



Initials: _____

This page has intentionally been left blank, so that you may use it for scratch paper.

Initials: _____

This page has intentionally been left blank, so that you may use it for scratch paper.