Name: _____

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**

1. (32 points) The reaction of bromide **1** and H_2O results in **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.
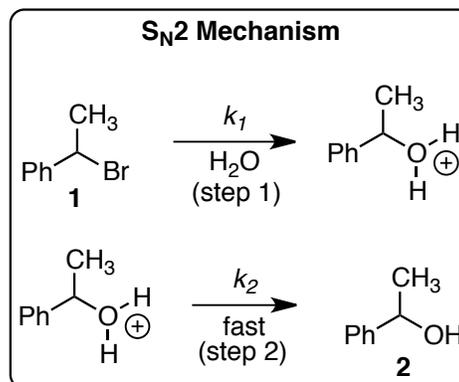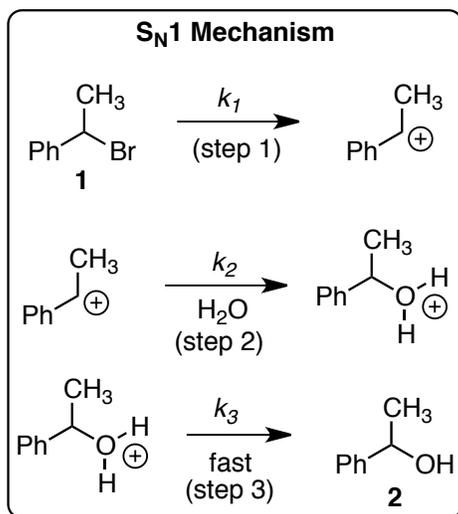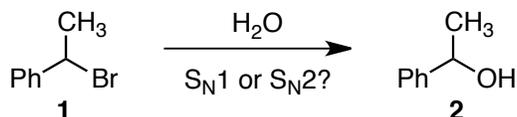
(a) What is most likely rate-determining step for the S_N1 mechanism?

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

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

(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 – continued)

(g) Determination of $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta G^{\ddagger}$ may also be helpful in determining the mechanism. Please describe the experiments and analysis you would do to determine these values.


(h) What do you expect $\Delta S^{\ddagger}$ to be for each mechanism?

S_N1 mechanism	S_N2 mechanism
$\Delta S^{\ddagger} =$ _____ eu	$\Delta S^{\ddagger} =$ _____ eu

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**.
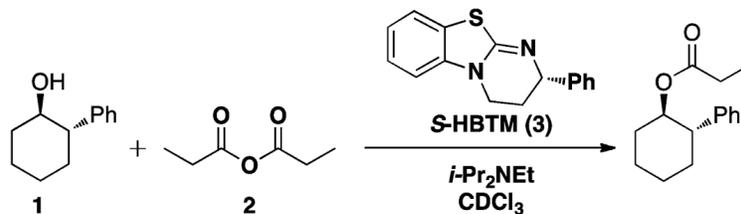
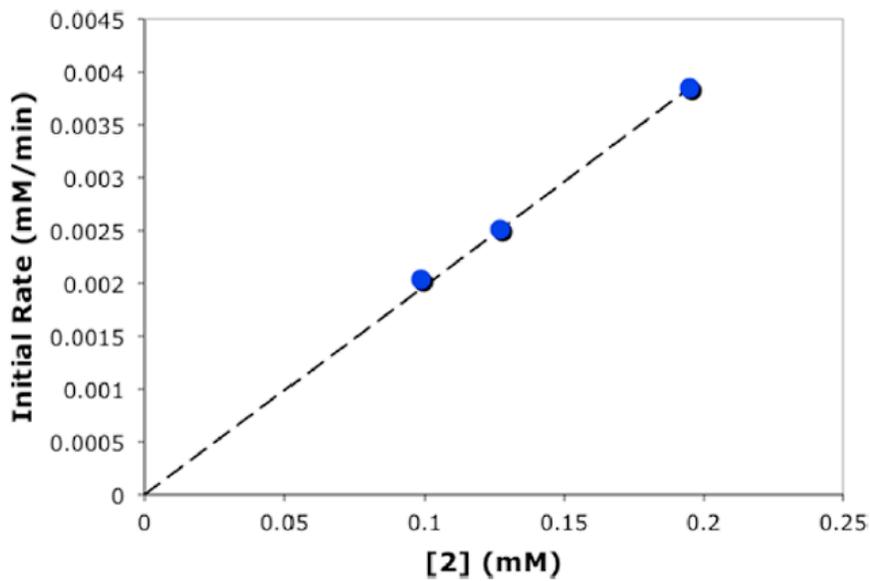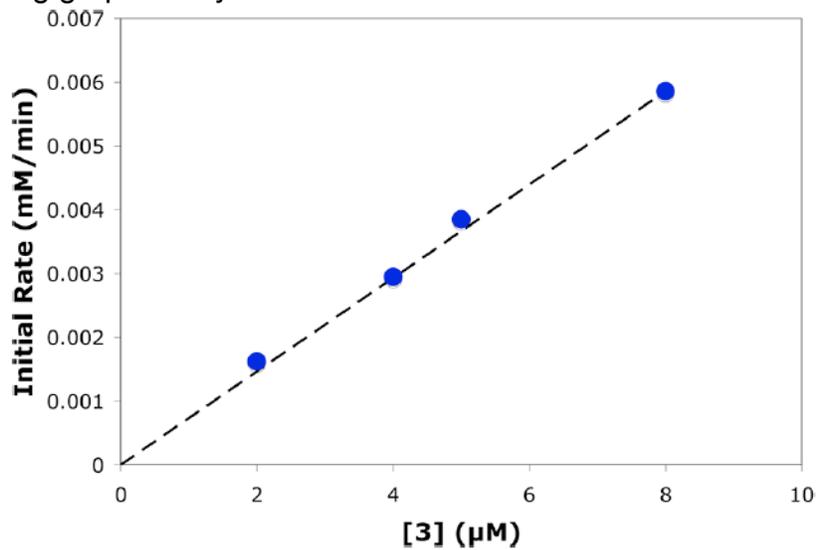
They proposed the following catalytic cycle.
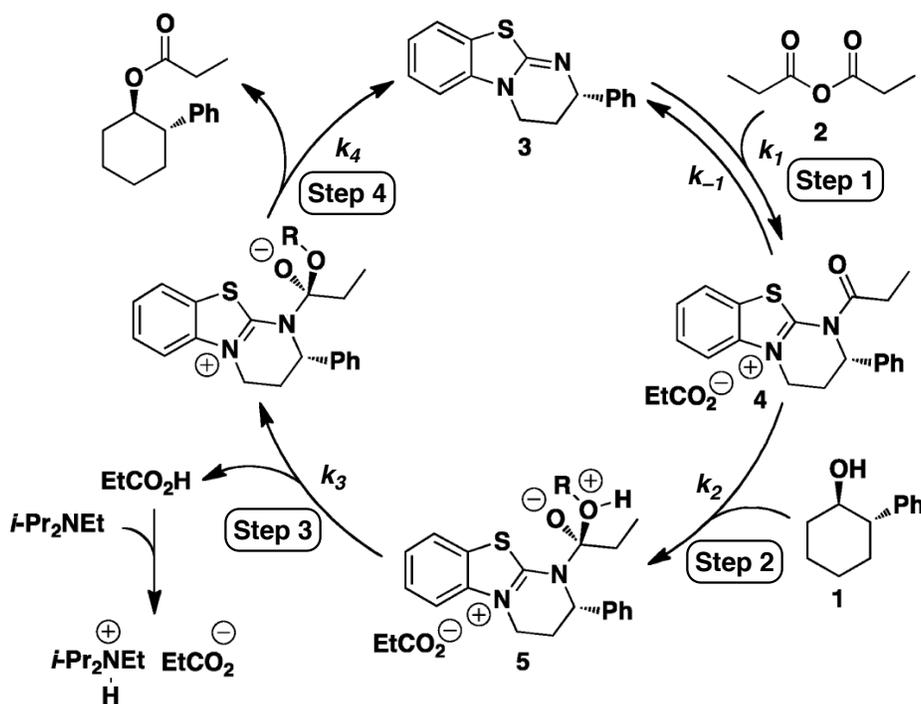
(a) Assuming Step 2 is rate-limiting and all subsequent steps to regenerate **3** are rapid and irreversible, please write a "one plus" catalytic rate expression for this catalytic cycle. Use the rate constants depicted in the catalytic cycle above, and apply the steady-state approximation to [**4**]. 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.
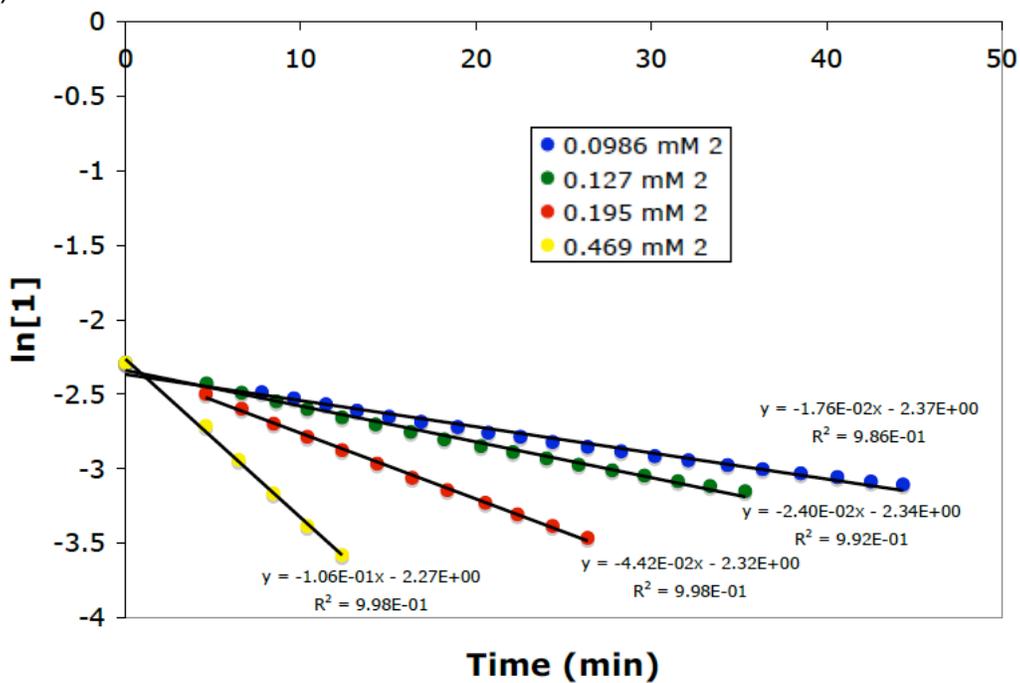
(2 – continued)
(b) What do the following graphs tell you?

(2 – continued)

Time (min)

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

y = -1.76E-02x - 2.37E+00
R² = 9.86E-01

y = -2.40E-02x - 2.34E+00
R² = 9.92E-01

y = -4.42E-02x - 2.32E+00
R² = 9.98E-01

y = -1.06E-01x - 2.27E+00
R² = 9.98E-01

Legend:
- 0.0986 mM 2
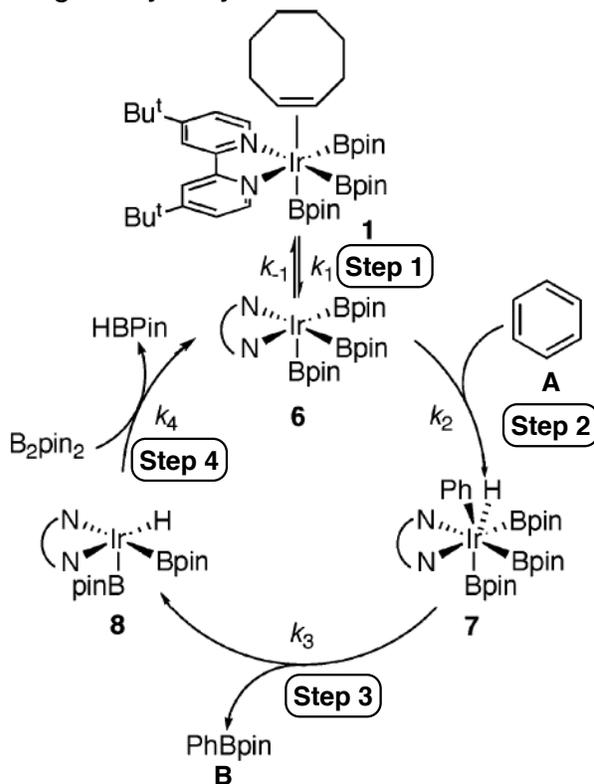- 0.127 mM 2
- 0.195 mM 2
- 0.469 mM 2

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

(d) What is the primary catalyst resting state?

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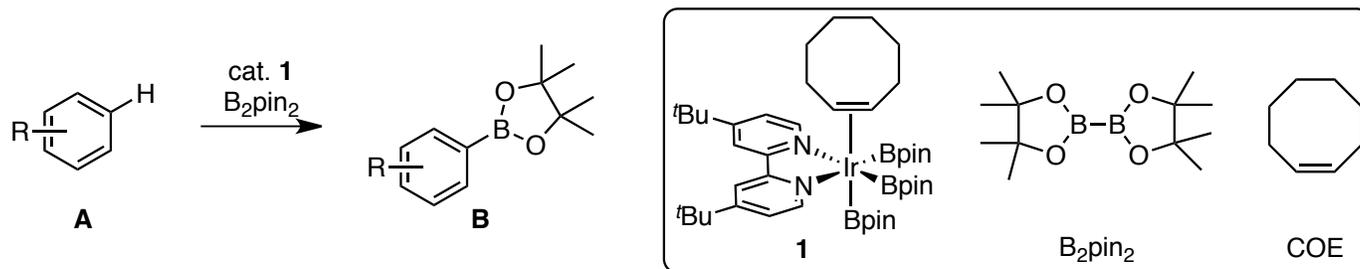

They proposed the following catalytic cycle.

(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, COE, and $[Ir]_{total}$.
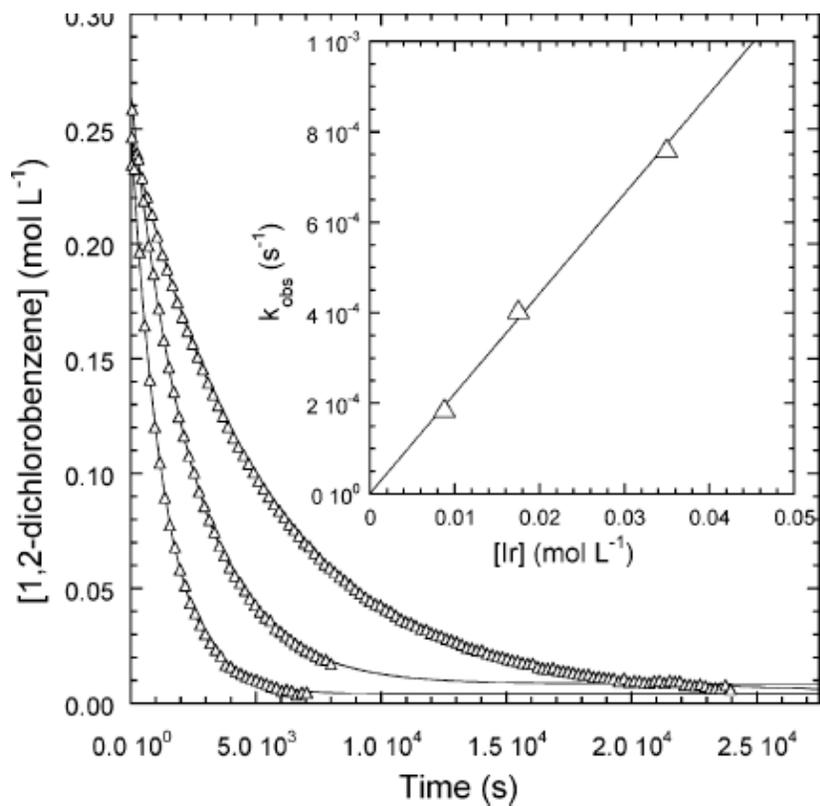
(3 – continued)

(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."

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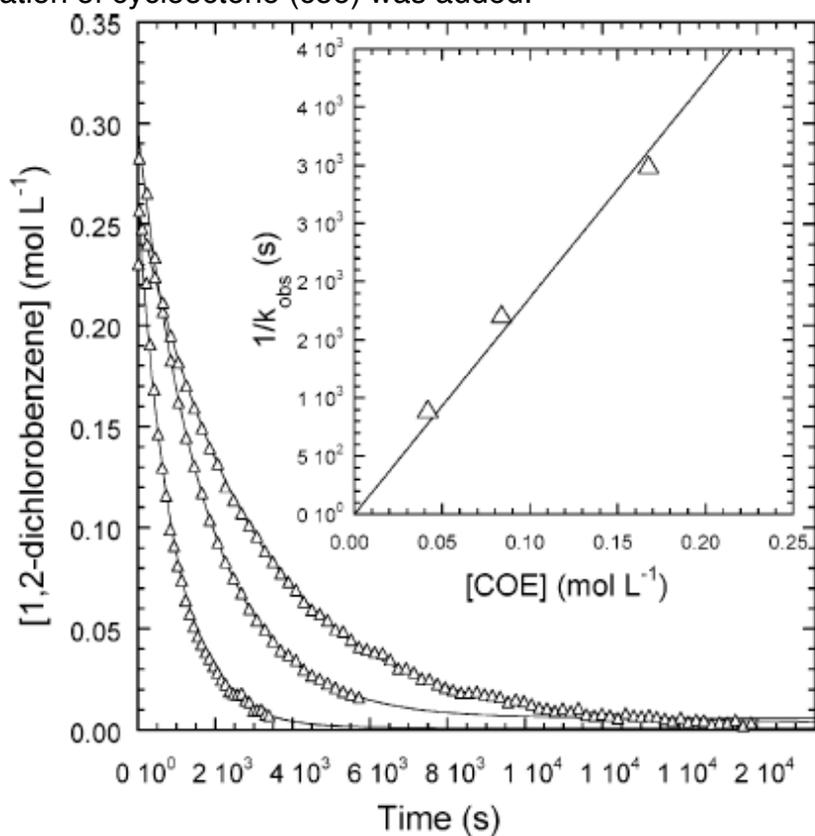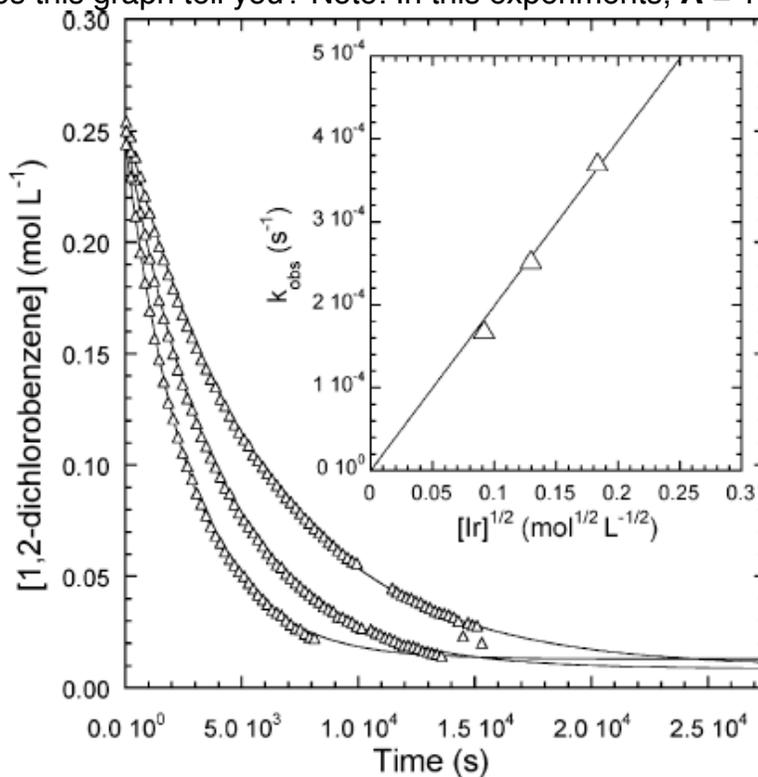
(3 – continued)

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

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

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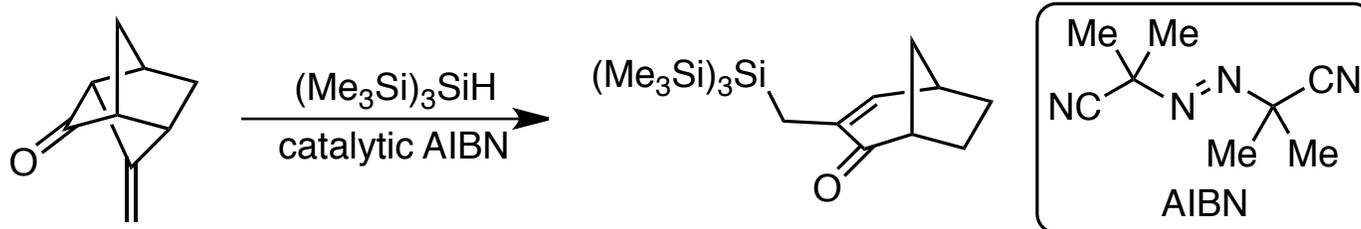
(3 – continued)

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

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*.

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