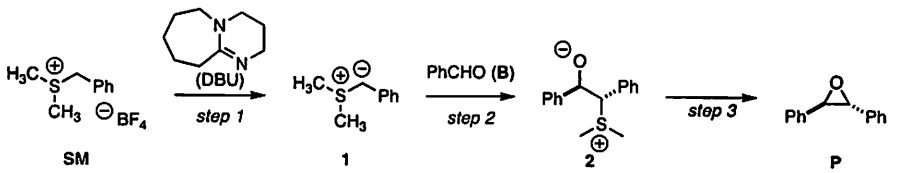
Name: Answer Key

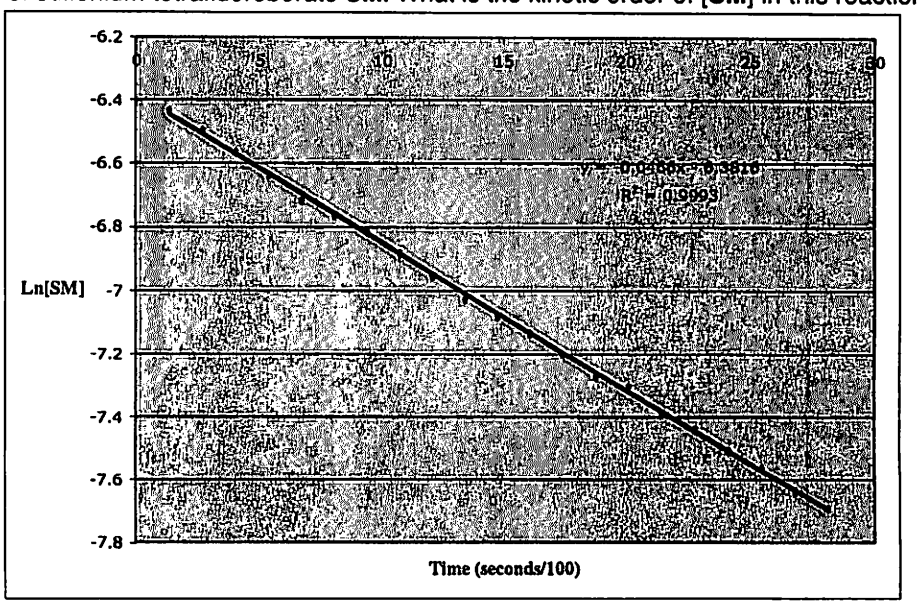
CHEM 633: Advanced Organic Chem: Physical
Problem Set 4
Due: Thurs, Nov 3, 2016

Please do not look up references until after you turn in the problem set unless otherwise noted.
For the following problems, please use Excel (or another graphing program), when necessary. ***Please submit your graphs with your problem set.***

1. Edwards, Montoya-Peleaz and Crudden have studied the mechanism of epoxidation of benzaldehyde (**B**) with sulfonium **SM** (*Org. Lett.* **2007**, *9*, 5481). The general mechanism for this transformation is believed to proceed via sulur ylide **1** and then intermediate **2**.



(a) Under pseudo-first-order conditions (large excess of benzaldehyde **B** and DBU), the authors monitored the disappearance of sulfonium tetrafluoroborate **SM**. What is the kinetic order of **[SM]** in this reaction?



1st order

* Graphs + excel data for (1) at the end of the answer key *

(1 – continued)

(b) Under pseudo-first-order conditions, the following data was obtained. In each of these reactions, **[B]** = 0.0174 M and temperature = 298 K. What is the kinetic order of **[DBU]**? $= -k_{obs}$

Entry	**[DBU]** (M)	Trendline from plot of ln**[SM]** vs. time (seconds/100)
1	0.0291	y = –0.0068x – 1.8296
2	0.0751	y = –0.0199x – 1.6405
3	0.113	y = –0.0329x – 1.6278
4	0.156	y = –0.0466x – 6.3816

slope of trendline $= -k_{obs} \Rightarrow k[DBU]^m[B]^n$ (plot k_{obs} vs. [DBU])

1st order rate dependence on [DBU]

(c) Under pseudo-first-order conditions, the following data was obtained. In each of these reactions, [DBU] = 0.156 M and temperature = 298 K. What is the kinetic order of **[B]**?

Entry	**[B]** (M)	Trendline from plot of ln**[SM]** vs. time (seconds/100)
1	0.0174	y = –0.0466x – 6.3816
2	0.0433	y = –0.1103x – 1.8947
3	0.0866	y = –0.1986x – 1.7842
4	0.130	y = –0.2474x – 1.7569
5	0.173	y = –0.3022x – 1.7994
6	0.260	y = –0.3192x – 1.7368

Saturation Kinetics: 1st order at low [B], going to zero-order at high [B]

(d) Based on the proposed mechanism and this data, derive a kinetic rate law for this transformation.

$\text{rate} = k_2[1][B] \xrightarrow{\text{with SSA}} \text{rate} = \dfrac{k_2k_1[B][sm][DBU]}{k_{-1}[DBU^{\oplus}H] + k_2[B]}$

$\dfrac{d[1]}{d[t]} \approx 0 = k_1[sm][DBU] - k_{-1}[1][DBU^{\oplus}H] - k_2[1][B]$

SSA: $[1] = \dfrac{k_1[sm][DBU]}{k_{-1}[DBU^{\oplus}H] + k_2[B]}$

(1 – continued again)

(e) Assuming that step 3 is fast, what is the ratio of $k_{-1}[\text{DBU-H}^+]/k_2$?

START

$$K_{obs} = \frac{K_1K_2[B][DBU]}{K_{-1}[DBU^{\oplus}\text{-}H] + K_2[B]}$$

split the denominators + cancel things out

$$\frac{1}{K_{obs}} = \frac{K_{-1}[DBU^{\oplus}\text{-}H]}{K_1K_2[B][DBU]} + \frac{\cancel{K_2}[\cancel{B}]}{K_1\cancel{K_2}[\cancel{B}][DBU]}$$

$$\frac{1}{K_{obs}} = \frac{K_{-1}[DBU^{\oplus}\text{-}H]}{K_1K_2[B][DBU]} + \frac{1}{K_1[DBU]}$$

Use this to plot $\frac{1}{K_{obs}}$ vs. $\frac{1}{[B]}$

(See Graph) → y-int = 133.53 = $\frac{1}{K_1(0.156)}$

$K_1 = 4.8 \times 10^{-2}\ M^{-1}s^{-1}$

slope × $\frac{1}{\text{y-int}}$

$$\frac{1}{K_1[DBU]} \times \frac{K_1K_2[DBU]}{K_{-1}[DBU^{\oplus}\text{-}H]}$$

$$\frac{\text{slope}}{\text{y-int}} = \frac{K_2}{K_{-1}[DBU]} = \frac{34.755}{133.53} = 0.26$$

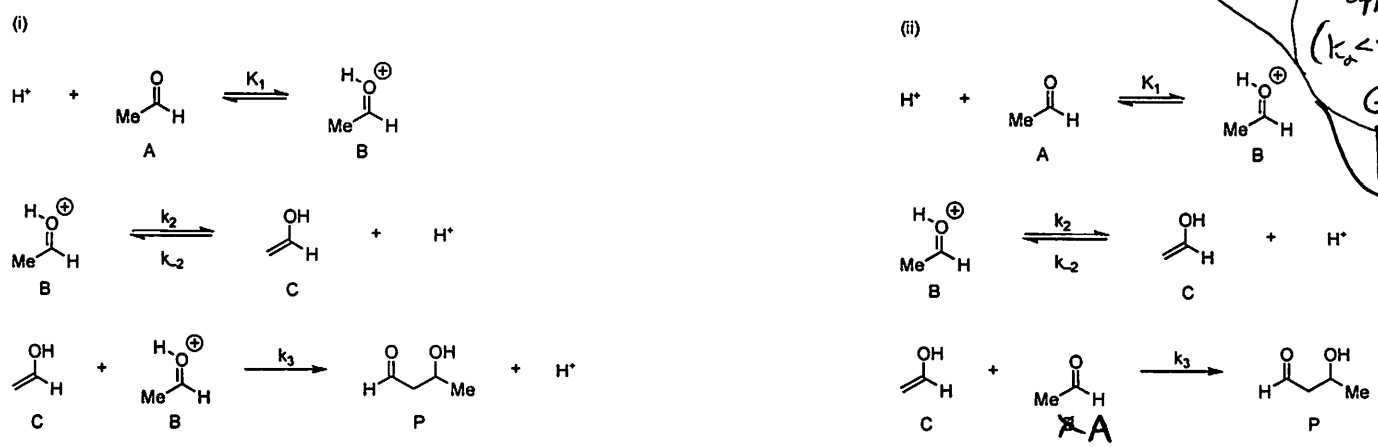
$[DBU] = 0.156\ M$

Pre-equilibrium approx. ($k_2 << k_{-1}[DBU^{\oplus}\text{-}H]$)

Good ✓

FINAL

2. Consider two possible mechanistic sequences for an acid-catalyzed aldol reaction, (i) and (ii).



(a) Derive a rate expression for sequence (i), using the steady state approximation where appropriate. Your final equation should only contain terms that are experimentally quantifiable (i.e., **A**, H^+). You may assume that the initial carbonyl protonation is a fast equilibrium and that the overall reaction is irreversible.

START

$$K_1 = \frac{[B]}{[H^+][A]} \longrightarrow [B] = K_1[H^+][A]$$

Apply to

$$[C] = \frac{K_2[B]}{K_3[B] + K_{-2}[H^+]} \longrightarrow [C] = \frac{K_2K_1[H^+][A]}{K_3K_1[H^+][A] + K_{-2}[H^+]}$$

now solve for [C]

$$\text{rate} = K_3[C][B]$$

Apply to rate

$$\text{rate} = K_3\left(\frac{K_2K_1[H^+][A]}{K_3K_1[H^+][A] + K_{-2}[H^+]}\right)(K_1[H^+][A])$$

SSA: $\frac{d[C]}{dt} = 0 = -K_3[C][B] + K_2[B] - K_{-2}[C][H^+]$

$$\text{rate} = \frac{K_3K_2K_1^2[H^+][A]^2}{K_{-2} + K_1K_3[A]}$$

FINISH

(b) Derive a rate expression for sequence (ii), using the steady state approximation where appropriate. Your final equation should only contain terms that are experimentally quantifiable. You may assume that the initial carbonyl protonation is a fast equilibrium and that the overall reaction is irreversible.

START

same as above

$$[B] = K_1[H^+][A]$$

solve for C

$$\text{rate} = K_3[C][A]$$

$$[C] = \frac{K_2[B]}{K_{-2}[H^+] + K_3[A]}$$

Apply [B]

$$[C] = \frac{K_2K_1[H^+][A]}{K_{-2}[H^+] + K_3[A]}$$

Apply to rate

$$\text{rate} = \frac{K_1K_2K_3[H^+][A]^2}{K_{-2}[H^+] + K_3[A]}$$

SSA: $\frac{d[C]}{dt} = 0 = K_2[B] - K_{-2}[C][H^+] - K_3[C][A]$

FINISH

(2 – continued)

(c) Show that the two sequences are kinetically distinguishable when the final step (i.e., C–C bond formation) is rate-limiting.

If step 3 is rate-limiting:

a) $\text{rate} = \dfrac{k_3 k_2 k_1^2 [H^+][A]^2}{k_{-2} + \cancel{k_1 k_3 [A]}}$

$k_1 k_3 [A] << k_{-2}$, so cross out $k_1 k_3 [A]$

$\text{rate} = \dfrac{k_3 k_2 k_1^2 [H^+][A]^2}{k_{-2}} = k_{obs} [H^+][A]^2$

b) $\text{rate} = \dfrac{k_1 k_2 k_3 [H^+][A]^2}{k_{-2}[H^+] + \cancel{k_3 [A]}}$

$k_{-2}[H^+] >> k_3 [A]$, so cross out $k_3 [A]$ terms

$\text{rate} = \dfrac{k_1 k_2 k_3 \cancel{[H^+]} [A]^2}{k_{-2} \cancel{[H^+]}} = k_{obs} [A]^2$

different!

(d) Show that the two sequences are kinetically indistinguishable when the last step is rapid compared with the initial steps.

Same as above, but:

a) $k_1 k_3 [A] >> k_{-2}$, so

$\text{rate} = \dfrac{\cancel{k_3} k_2 k_1^{\cancel{2}} [H^+][A]^{\cancel{2}}}{\cancel{k_1 k_3 [A]}} = k_{obs} [H^+][A]$

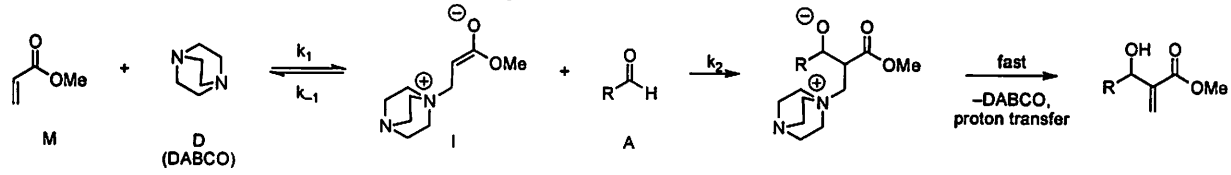
b) $k_{-2}[H^+] << k_3 [A]$

$\text{rate} = \dfrac{k_1 k_2 \cancel{k_3} [H^+][A]^{\cancel{2}}}{\cancel{k_3 [A]}}$

$\text{rate} = k_1 k_2 [H^+][A] = k_{obs} [H^+][A]$

identical

3. One proposed mechanistic sequence for the Baylis-Hillman reaction is shown below (e.g., *J. Org. Chem.* **2003**, *68*, 692). This reaction has recently been studied using the initial rates method (*Org. Lett*, **2005**, *7*, 147). You may assume that no observable intermediates accumulate during the course of the reaction.



(a) Derive a rate expression for this sequence, using the steady-state approximation where appropriate.

START

$\text{rate} = k_2[I][A]$ $\boxed{*\ [A] \text{ does } \underline{\text{not}} \text{ effect } k_{-1}\ *}$

SSA: $\frac{\partial[I]}{\partial t} \approx 0 = k_1[M][D] - k_{-1}[I] - k_2[I][A]$

$[I] = \frac{k_1[M][D]}{k_{-1} + k_2[A]}$

apply to rate

$\text{rate} = \frac{k_2 k_1[A][M][D]}{k_{-1} + k_2[A]}$ FINISH

(b) Show that the steady-state approximation and the pre-equilibrium approximation (for saturation kinetics) are equivalent when k_{-1} is large compared with k_2.

Pre-equilibrium Approx: $K_1 = \frac{k_1}{k_{-1}} = \frac{[I]}{[M][D]} \rightarrow [I] = \frac{k_1[M][D]}{k_{-1}}$

$\text{rate} = \frac{k_1 k_2[M][D][A]}{k_{-1}}$

VS. w/SSA: $\text{rate} = \frac{k_1 k_2[M][D][A]}{k_{-1} + k_2[A]}$ if $k_{-1} >> k_2$

identical

$\text{rate} = \frac{k_1 k_2[M][D][A]}{k_{-1}}$

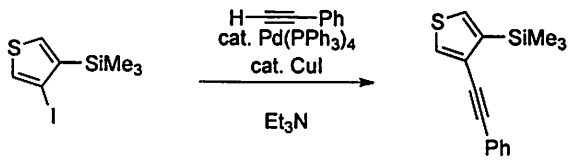
(c) Initial rate experiments showed that the initial rate is first order in [D], first order in [M], and second order in [A]. Evaluate the plausibility of the proposed mechanistic sequence on the basis of this initial rate data.

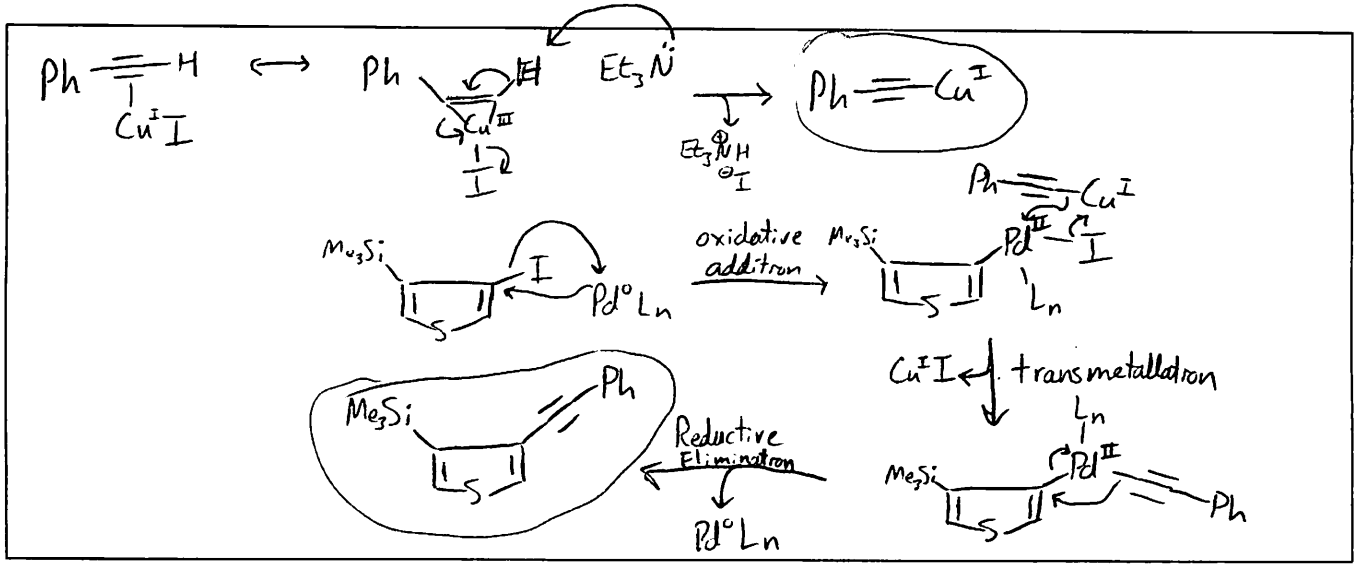
The proposed mechanism + the proposed rate expression from a) do not account for [A] being second order. Thus, the proposed mechanism is <u>not</u> correct.

Note: You will see kinetic isotope data for this reaction in the next problem set and be asked to propose an alternative mechanism then.

From* *The Art of Writing Reasonable Organic Reaction Mechanisms*, *Ch. 6: Please draw reasonable arrow-pushing mechanisms for the following transformations. If the metal reagent is used catalytically, be sure to regenerate the catalyst for the next catalytic cycle.

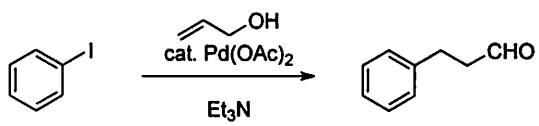
4.

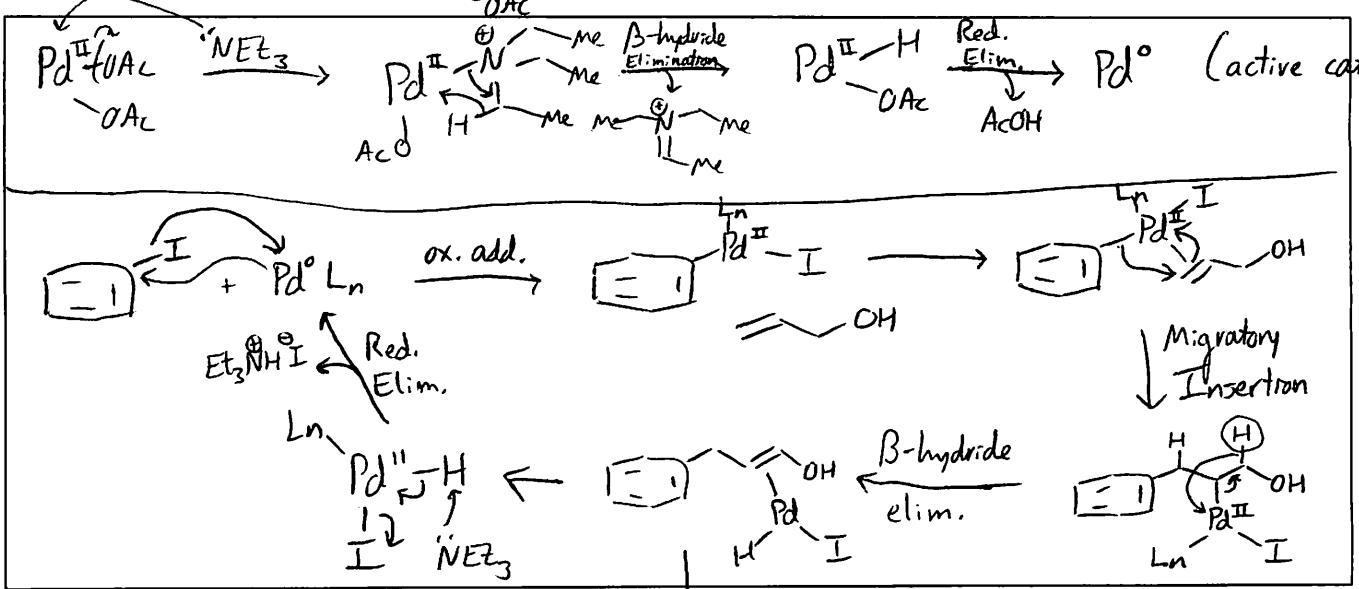


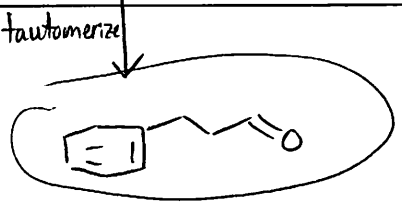


5.

Mechanism for reduction of Pd^{II} to Pd^{0}

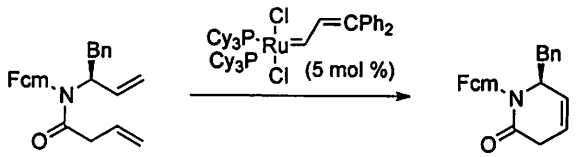






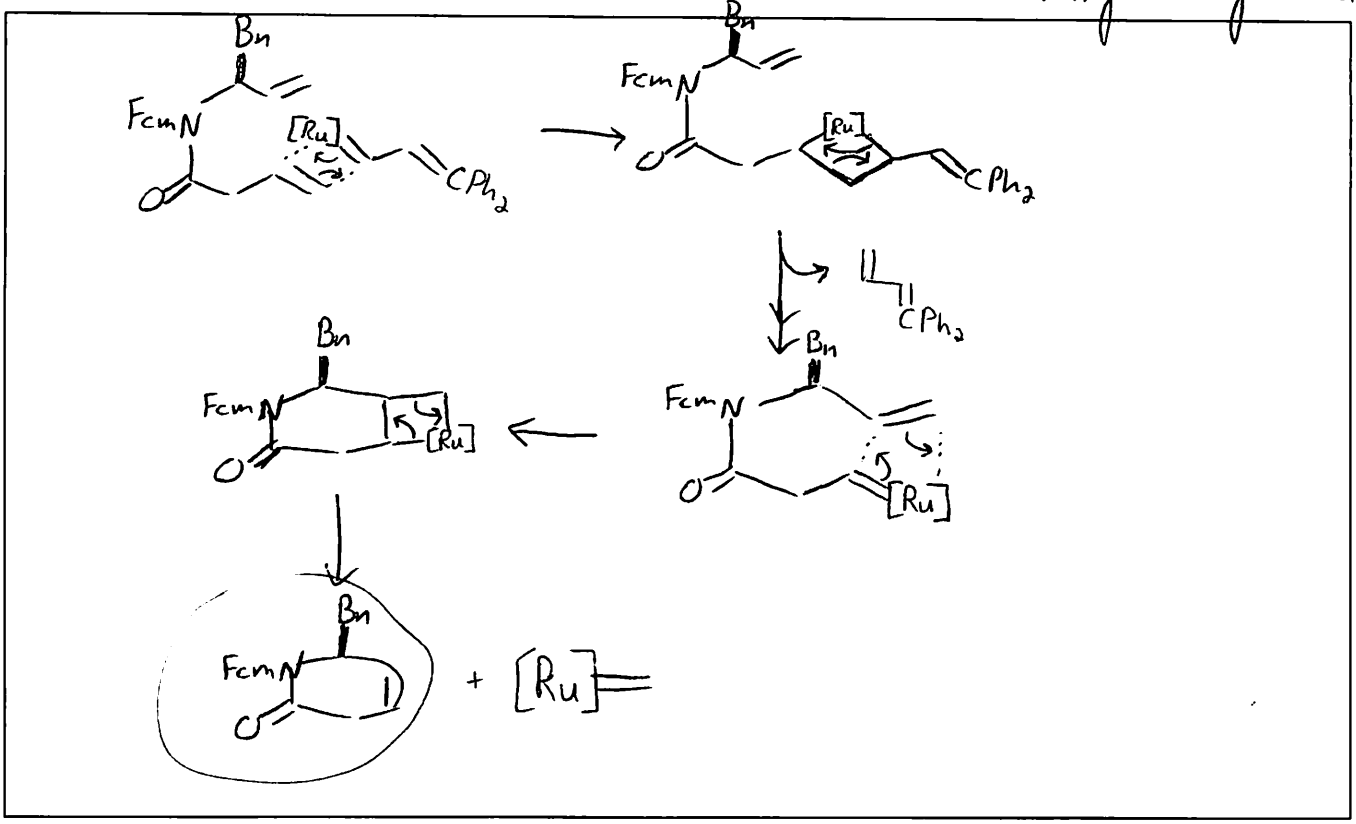
*β-hydride elimination to form styrene possible; Pd^{II}-H can re-insert into an alkene + β-hydride elim. to other position

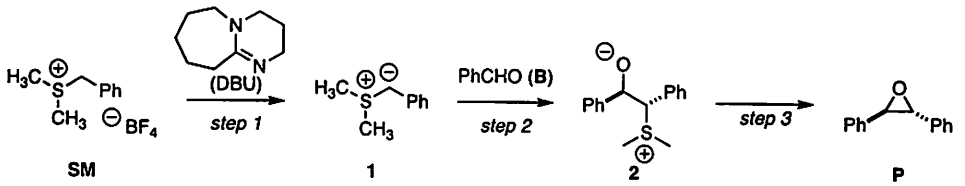
6.



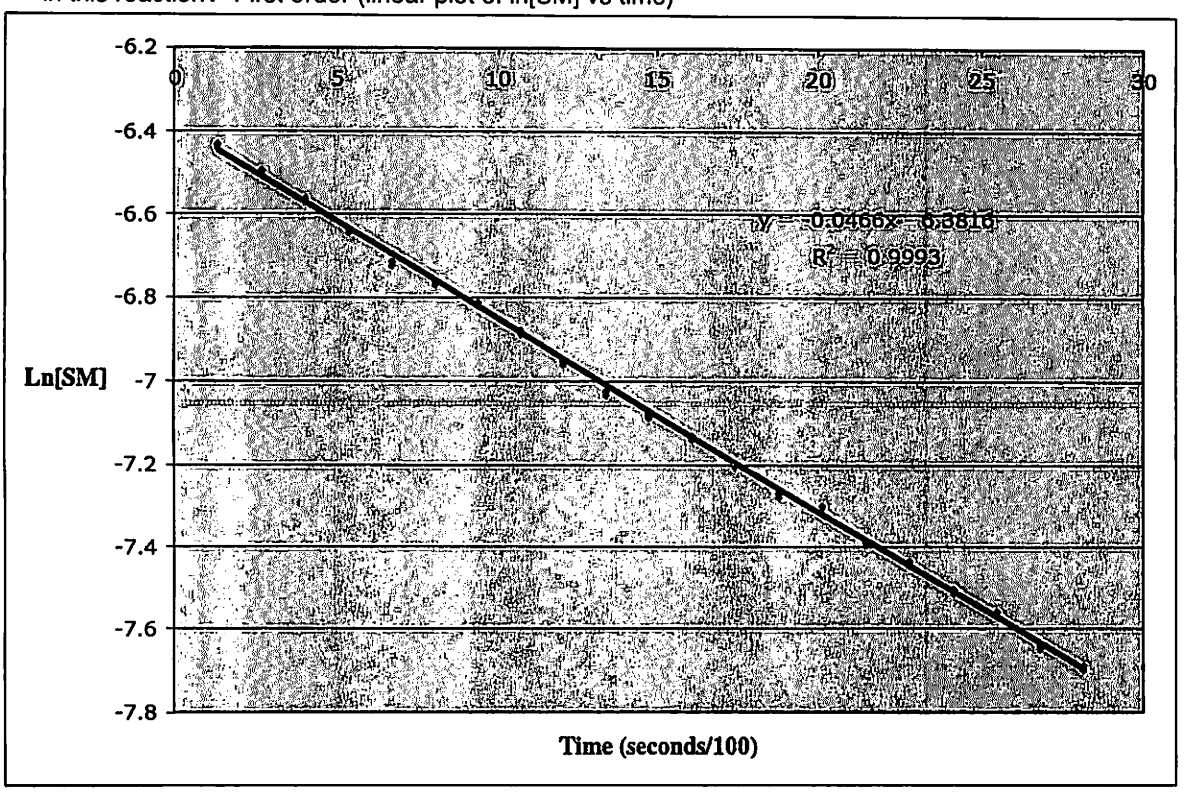
(RCM)

Ring-closing metathesis





(a) Under pseudo-first-order conditions (large excess of benzaldehyde **B** and DBU), the authors monitored the disappearance of sulfonium tetrafluoroborate **SM**. What is the kinetic order of **[SM]** in this reaction? First order (linear plot of ln[SM] vs time)



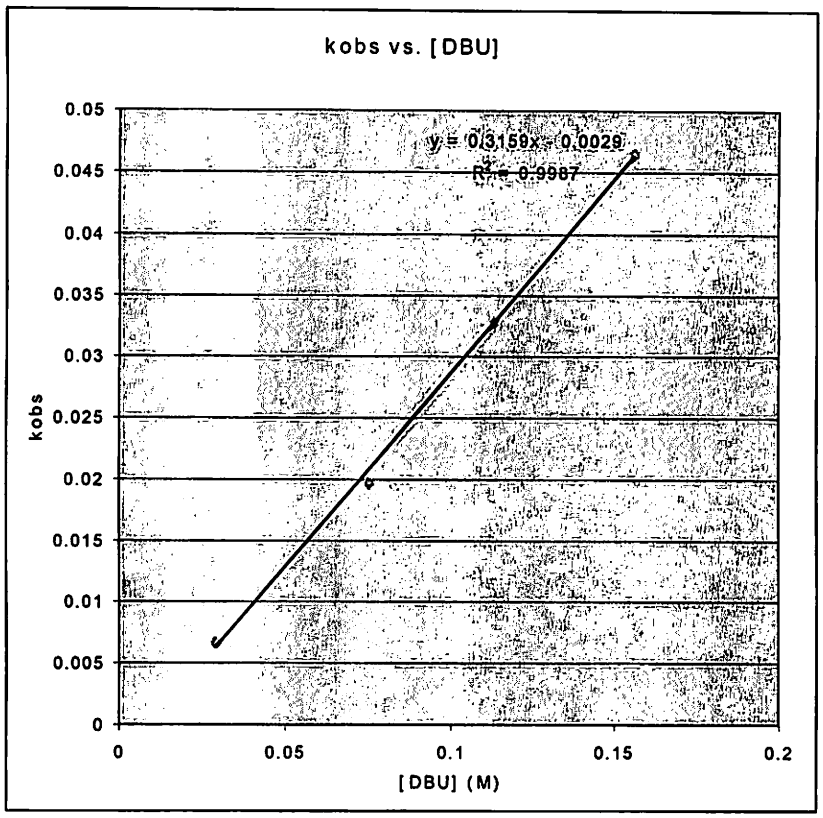
1b

(b) Under pseudo-first-order conditions, the following data was obtained. In each of these reactions, **[B]** = 0.0174 M and temperature = 298 K. What is the kinetic order of **[DBU]**?

Entry	**[DBU]** (M)	Trendline from plot of ln**[SM]** vs. time (seconds/100)
1	0.0291	y = –0.0068x – 1.8296
2	0.0751	y = –0.0199x – 1.6405
3	0.113	y = –0.0329x – 1.6278
4	0.156	y = –0.0466x – 6.3816

Slope of the trendline = $-k_{obs} = k\,[DBU]^m\,[B]^n$

entry	[DBU] (M)	kobs
1	0.0291	0.0068
2	0.0751	0.0199
3	0.113	0.0329
4	0.156	0.0466



1b

Linear relationship between k_{obs} & [DBU], so m = 1... **first-order rate dependence on [DBU]**.

(c) Under pseudo-first-order conditions, the following data was obtained. In each of these reactions, [DBU] = 0.156 M and temperature = 298 K. What is the kinetic order of [B]?

Entry	[B] (M)	Trendline from plot of ln[SM] vs. time (seconds/100)
1	0.0174	y = –0.0466x – 6.3816
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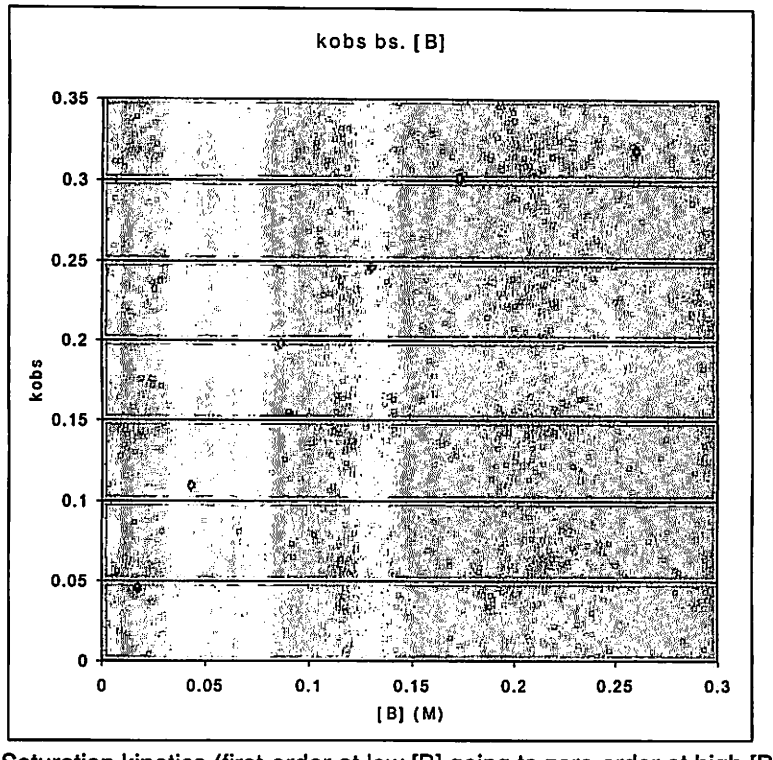
5	0.173	y = –0.3022x – 1.7994
6	0.260	y = –0.3192x – 1.7368

entry	[B] (M)	kobs
1	0.0174	0.0466
2	0.0433	0.1103
3	0.0866	0.1986
4	0.13	0.2474
5	0.173	0.3022
6	0.26	0.3192

1c



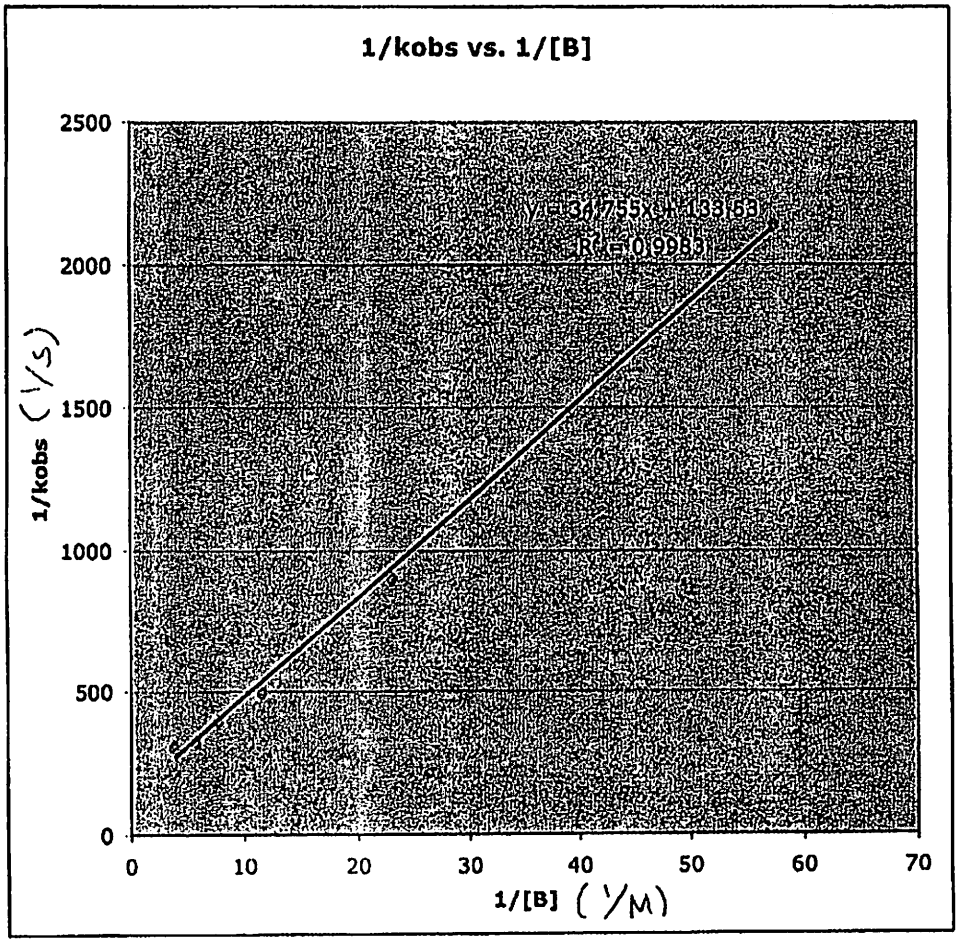
1c

Saturation kinetics (first-order at low [B] going to zero-order at high [B])

Note the units are in s (not s/100)

entry	[B] (M)	kobs (s)	1/[B]	1/kobs
1	0.0174	0.000466	57.47126437	2145.922747
2	0.0433	0.001103	23.09468822	906.6183137
3	0.0866	0.001986	11.54734411	503.5246727
4	0.13	0.002474	7.692307692	404.2037187
5	0.173	0.003022	5.780346821	330.9066843
6	0.26	0.003192	3.846153846	313.283208

1e



y-intercept = 133.53 = $\frac{1}{k_1[DBU]}$ [DBU] = 0.156 M

133.53 = $\frac{1}{0.156\, k_1}$ ⇒ $k_1 = 4.8 \times 10^{-2}\ M^{-1} s^{-1}$

$$\frac{\text{slope}}{\text{y-intercept}} = \frac{\frac{1/k_1[DBU]}{k_{-1}[DBU\text{-}H^+]}}{k_1 k_2 [DBU]} = \frac{1}{k_1[DBU]} \cdot \frac{k_1 k_2 [DBU]}{k_{-1}[DBU\text{-}H^+]} = \frac{k_2}{k_{-1}[DBU\text{-}H^+]}$$

$$\frac{\text{slope}}{\text{y-intercept}} \approx \frac{k_2}{k_{-1}[DBU\text{-}H^+]} = \frac{34.755}{133.53} = 0.26$$

Pre-equilibrium approximation ($k_2 \ll k_{-1}[DBU\text{-}H^+]$) OK ☺