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 sulfonyl 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?

1\textsuperscript{st} 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, $[\text{B}] = 0.0174 \text{ M}$ and temperature $= 298 \text{ K}$. What is the kinetic order of [DBU]?

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<td>0.156</td>
<td>$y = -0.0466x - 6.3816$</td>
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Slope of trendline $= -k_{\text{obs}} = k [\text{DBU}]^n [\text{B}]^m$ (plot $k_{\text{obs}}$ vs. [DBU])

1st order rate dependence on [DBU]

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

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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.

\[
\begin{align*}
\text{rate} & = k_s [1][\text{B}] \\
\frac{d[1]}{dt} & \approx 0 = k_s [\text{SM}] [\text{DBU}] - k_1 [1][\text{DBU}^{\text{H}+}] - k_2 [1][\text{B}] \\
[S_\text{SA}]: \quad [1] & = \frac{k_s [\text{SM}] [\text{DBU}]}{k_s [\text{DBU}^{\text{H}+}] + k_1 [\text{B}]} \\
\text{rate} & = \frac{k_s k_c [\text{B}][\text{SM}][\text{DBU}]}{k_s [\text{DBU}^{\text{H}+}] + k_2 [\text{B}]} 
\end{align*}
\]
(1 – continued again)
(e) Assuming that step 3 is fast, what is the ratio of \( k_1 [DBU-H^+] / k_2 ? \)

\[
\frac{1}{k_{\text{obs}}} = \frac{1}{k_1[k_{\text{DBU-H^+}}] + \frac{k_2 \left[ DBU \right]}{k_{\text{DBU}}}}
\]

Use this to plot \( \frac{1}{k_{\text{obs}}} \) vs. \( \frac{1}{[B]} \)

(See Graph) \( y = \frac{1}{[B]} = 133.53 = \frac{k_2}{k_{\text{DBU}}} \)

\( k_1 = 4.8 \times 10^{-3} \text{M}^{-1} \text{s}^{-1} \)

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

(i) \[ H^+ + \text{MeH} \rightarrow \text{MeH}^+ \quad \text{and} \quad \text{MeH}^+ \rightarrow \text{MeH} + H^+ \]

(ii) \[ H^+ + \text{MeOH} \rightarrow \text{MeOH}^+ \quad \text{and} \quad \text{MeOH}^+ \rightarrow \text{MeOH} + H^+ \]

(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.

(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.
(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:

\[
\text{rate} = \frac{k_2 k_3 [H^+][A]^2}{k_{-2} + k_2 k_3 [CA]}
\]

\[k_1 k_3 [A] \ll k_{-2}, \text{ so cross out } k_1 k_3 [A]\]

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

\[k_{-2}[H^+] \gg k_3 [A], \text{ so cross out } k_3 [A] \text{ term!}
\]

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

Same as above, but:

\[k_1 k_3 [A] \gg k_{-2}, \text{ so}
\]

\[
\text{rate} = \frac{k_3 k_2 k_{-2} [H^+][A]^2}{k_{-2} k_3 [A]}
\]

\[= k_{\text{obs}} [H^+][A]
\]

\[k_{-2}[H^+] \ll k_3 [A]
\]

\[
\text{rate} = \frac{k_3 k_2 [H^+][A]^2}{k_{-2} k_3 [A]}
\]

\[= k_{\text{obs}} [H^+][A]
\]

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.

\[
\begin{array}{c}
\text{OMe} + \text{N} \xrightleftharpoons[k_{-1}]{k_1} \text{OMe} + \text{R} \xrightarrow[k_3]{\text{fast}} \text{R} \text{OMe} \\
\text{M} \quad \text{D (DABCO)} \quad \text{I} \quad \text{A}
\end{array}
\]

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

\[
\text{rate} = \frac{k_2[I][A]}{K_1 + K_2[A]}
\]

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

(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 not 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.

```
Ph —H —CuI
^     ^
1      1
Cu

Ph —H —CuI
^     ^
1      1
Cu

Me2Si — Ph — Me2Si
^    ^
1    1
Ph

Me2Si — Ph — Me2Si
^    ^
1    1
Ph
```

5.

**Mechanism for reduction of Pd**

```
Ph
^    ^
1    1
Ph

Pd
^    ^
1    1
Ph

Pd
^    ^
1    1
Ph
```

Elimination to form styrene possible; Pd**H** can re-insert into an alkene + β-hydride elimination.
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)

(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]?

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

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</tr>
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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]?

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<td>0.3192</td>
</tr>
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Saturation kinetics (first-order at low [B] going to zero-order at high [B])
Note the units are in S (not s/100).

<table>
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<tr>
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<th>kobs (s)</th>
<th>1/[B]</th>
<th>1/kobs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0174</td>
<td>0.000466</td>
<td>57.47126437</td>
<td>2145.922747</td>
</tr>
<tr>
<td>2</td>
<td>0.0433</td>
<td>0.001103</td>
<td>23.09468822</td>
<td>906.6183137</td>
</tr>
<tr>
<td>3</td>
<td>0.0866</td>
<td>0.001986</td>
<td>11.54734411</td>
<td>503.5246727</td>
</tr>
<tr>
<td>4</td>
<td>0.13</td>
<td>0.002474</td>
<td>7.692307692</td>
<td>404.2037187</td>
</tr>
<tr>
<td>5</td>
<td>0.173</td>
<td>0.003022</td>
<td>5.780346821</td>
<td>330.9066843</td>
</tr>
<tr>
<td>6</td>
<td>0.26</td>
<td>0.003192</td>
<td>3.846153846</td>
<td>313.283208</td>
</tr>
</tbody>
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\[
\text{y-intercept} = 133.53 = \frac{1}{k_{f(DBU)^{\text{L}}}} \\
[DBU] = 0.156 \text{ M}
\]

\[133.53 = \frac{1}{0.156 k_1} \Rightarrow k_1 = 4.8 \times 10^{-2} \text{ M}^{-1} \text{s}^{-1}\]

\[
\frac{\text{slope}}{\text{y-intercept}} = \frac{k_1 [DBU]^L}{k_{f(DBU)^{\text{L}}} \cdot \frac{k_1 k_2 [DBU]}{k_{-1}[DBU-H]^+}} = \frac{k_2}{k_{-1}[DBU-H]^+}
\]

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

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