## UCI DEPARTMENT OF ORGANIC CHEMISTRY PEER TUTORING REVIEW SESSION FEEDBACK EVALUATION

<table>
<thead>
<tr>
<th>Quarter:</th>
<th>Date:</th>
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<tbody>
<tr>
<td>Class:</td>
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<tr>
<td>Tutors’ Names: Clever Chiu, Jason Lo, Jacqueline Nguyen</td>
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### COMMENTS/FEEDBACK

(VERY IMPORTANT!)

Name: Clever Chiu
Name: Jason Lo
Name: Jaqueline Nguyen

What worked best?
What could be improved?
What would you like to see next time?

<table>
<thead>
<tr>
<th>This review was interactive and engaging.</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Neither Agree or Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
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<tr>
<td>Comments</td>
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<td>The presentation volume was acceptable.</td>
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<td>The presentation was visually clear and logically organized.</td>
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<td>The review improved/reinforced your understanding of the material.</td>
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<td>The quality of the review packet was</td>
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<td>Comments</td>
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Please fill out this evaluation, even if you plan to leave early. Thank you very much.
Chem 51B Midterm 1 Review

1) Rank the species in each group in order of increasing nucleophilicity. (7.50, 5th)
   a. CH₃CH₂S⁻, CH₃CH₂O⁻, CH₃CO₂⁻ in CH₃OH
   b. CH₃NH₂, CH₃SH, CH₃OH in acetone

2) For each reaction, determine if the mechanism is E2, E1, Sₙ2, or Sₙ1. (7.34, 5th)
   a. \[
   \text{CH}_3\text{CH}_2\text{Cl} + \text{CH}_3\text{OH} \xrightarrow{\text{CH}_3\text{OH} \text{ or DMSO}} \text{CH}_3\text{CH}_2\text{OH} + \text{HCl}
   \]
   b. \[
   \text{CH}_3\text{CH}_2\text{Br} + \text{OH} \xrightarrow{\text{H}_2\text{O} \text{ or DMF}} \text{CH}_3\text{CH}_2\text{OH} + \text{Br}^-
   \]

3) What is the structure of diphenhydramine? **Only draw the products in the box.** (7.66, 5th)
4) **In the box below**, draw the major product for the following reaction. (8.54, 5th)

![Reaction Diagram](image)

5) **Fill in the box** with the correct reagent needed to obtain the products below. (8.63, 5th)

![Reagents and Products](image)

6) Determine the mechanism of nucleophilic substitution of each reaction and draw the products, including stereochemistry.

a. ![Reaction a](image)

b. ![Reaction b](image)

c. ![Reaction c](image)
7) Fill in the appropriate reagent or starting material in each of the following reactions.

8) Taking into account anti periplanar geometry, predict the major E2 product formed from each starting material.
9) Sometimes carbocation rearrangements can change the size of a ring. Draw a stepwise, detailed mechanism for the following reaction.

\[ \text{cyclopentanol} + \text{H}_2\text{SO}_4 \rightarrow \text{product} + \text{H}_2\text{O} \]

10) Prepare each compound from cyclopentanol. More than one step may be needed.

a. [Chemical Structure Image]

b. [Chemical Structure Image]
11) Draw a stepwise mechanism for the reaction. Draw all products and label the major product.

```
OH

CH₃

H₂SO₄

H

H

H
```

12) Draw the products of each reaction and indicate stereochemistry around stereogenic centers.

```

CH₃

H

H

H

H

H

H

H

```

```
a.

H

H

H
```

```

H

H

H
```
13) Draw two different routes for the following ether using a Williamson ether synthesis. Indicate the preferred route.
14) Draw the products and a stepwise mechanism for the reaction.

\[
\text{HI} \quad (2 \text{ equiv})
\]

15) Draw the products of each reaction.

a.

b. [1] \( \text{CH}_3\text{CH}_2\text{O}^- \text{ Na}^+ \)
   [2] \( \text{H}_2\text{O} \)
Study Guide

- Leaving Groups
  - More stable leaving groups are better able to accept the electron pairs, so weaker bases are better leaving groups.
  - Periodic trend: better leaving groups going towards the right and going down.
  - Good Leaving Group Examples: Cl-, Br-, I-, H₂O.
  - Poor Leaving Group Examples: F-, OH-.

- Nucleophiles
  - Generally, a strong base will indicate a strong nucleophile.
    - A negative charge is a good indicator of a strong nucleophile.
    - **Exception**: Big bulky bases (ie. tert-butoxide, DBU, DBN) are strong bases but bad nucleophiles.
      - Therefore, if the nucleophile is not bulky and has a negative charge, it will most likely be a good nucleophile.
      - Bad nucleophiles and bad bases are neutrally or positively charged.
        - They will usually have another H added to their conjugate base (ie. H₂O, H₃O⁺, CH₃OH).
  - Steric Hindrance: a decrease in reactivity when bulky groups are present at the site of the reaction. It decreases nucleophilicity but not basicity.
  - Periodic trend:

- Polar Protic Solvent
○ Contains OH or NH bond so is capable of hydrogen bonding and solvating nucleophile (wraps around Nu and prevents reactivity)
○ Examples: H₂O, CH₃OH, CH₃CH₂OH

- Polar Aprotic Solvent
  ○ No OH or NH bonds so it cannot H bond, only solvates cations well
  ○ Examples: Acetone, THF, DMSO, DMF, acetonitrile

- Sₙ₁ vs Sₙ₂
  ○ 4 factors to consider: 1) Alkyl Halide; 2) Nucleophile; 3) Leaving Group; 4) Solvent

<table>
<thead>
<tr>
<th>Alkyl Halide</th>
<th>Mechanism</th>
<th>Other Factors</th>
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<tbody>
<tr>
<td>CH₃X; RCH₂X (primary)</td>
<td>Sₙ₂</td>
<td>Favored by:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Strong Nu (usually negatively charged)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Polar aprotic solvent (avoids H-bonding w/ Nu)</td>
</tr>
<tr>
<td>R₃CX (tertiary)</td>
<td>Sₙ₁</td>
<td>Favored by:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Weak Nu (usually neutral)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Polar protic solvent (H-bonds w/ Nu; enabling C+ formation)</td>
</tr>
<tr>
<td>R₂CHX (secondary)</td>
<td>Sₙ₁ or Sₙ₂</td>
<td>● Strong Nu: favors Sₙ₂&gt;Sₙ₁</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Polar protic solvent favors Sₙ₁&gt;Sₙ₂</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Polar aprotic solvent favors Sₙ₂</td>
</tr>
</tbody>
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- Important Notes:
  ○ Sₙ₂ involves backside attack which causes an inversion of stereochemistry
  ○ Sₙ₁ has a trigonal planar carbocation so there is equal attack from the top and bottom face, leading to a racemic mixture
- Steps of Dehydrohalogenation
  1) Find alpha sp³ Carbon bonded to leaving group
  2) Identify all beta carbons that have H atoms
  3) Remove H&X from beta and alpha carbons and form a pi bond
Common bases for dehydrohalogenation: NaOH, NaOCH₃, tert-butoxide, non-nucleophilic base, KOH, NaOCH₂CH₃

- E1 vs E2

<table>
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<tr>
<th>E1</th>
<th>E2</th>
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| • Secondary<Tertiary in terms of reaction rate  
  ○ Primary carbons will NEVER react in E1  
  • Base: Weaker bases favors E1 (ex: H₂O, ROH)  
  • Regioselectivity: E1 reactions favor more substituted products | • Stronger bases increase E2 rate  
  ○ Examples: OH-, OR-, DBN, DBU  
  • Better leaving groups (weaker bases), faster reaction rate  
  • Primary<Secondary<Tertiary in terms of reaction rate (opposite of Sₙ₂)  
  • Solvent effects: Polar aprotic solvent increase reaction rate  
  • Only occurs in anti-periplana geometry  
  ○ Staggered conformation (lower energy)  
  ○ Incoming negatively charged base and leaving group are most separated |

• Zaitsev Rule: the major product in beta-elimination has a more substituted double bond  
  ○ FYI: trans alkenes are more stable than cis alkenes  

• Sₙ₁ vs Sₙ₂ vs E₁ vs E₂  
  ○ To determine which reaction will proceed…  
  1) Classify alkyl halide as primary, secondary, or tertiary  
  2) Classify Nu or base as strong, weak, or bulky

<table>
<thead>
<tr>
<th>Alkyl Halide</th>
<th>Reaction With</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary RCH₂X</td>
<td>Strong Nu</td>
<td>Sn₂</td>
</tr>
<tr>
<td>Primary RCH₃X</td>
<td>Strong, bulky base</td>
<td>E₂</td>
</tr>
<tr>
<td>Secondary R₂CHX</td>
<td>Strong base &amp; Nu</td>
<td>Sn₂ &amp; E₂</td>
</tr>
<tr>
<td>Secondary R₂CHX</td>
<td>Strong, bulky base</td>
<td>E₂</td>
</tr>
<tr>
<td>Secondary R₂CHX</td>
<td>Weak base &amp; Nu</td>
<td>Sn₁ &amp; E₁</td>
</tr>
</tbody>
</table>
Tertiary R₃CX | Weak base & Nu | Sn1 & E1
---|---|---
Tertiary R₃CX | Strong base | E2

- Sodium Hydride
  - Use to make an alkoxide salt
  - *Useful in Williamson Ether Synthesis* (formation of an ether, just add an alkyl halide!)

- Epoxide Synthesis: Intramolecular S_N₂

- Dehydrations of Alcohols to Alkenes
  - X must be a good base/good leaving group
  - Acid-catalyzed dehydration: converting an alcohol from being a poor leaving group to being a good leaving group
    - Examples: H₂SO₄, TsOH
  - Secondary & Tertiary ROH Dehydration: E1 Mechanism
  - Primary ROH Dehydration: E2 Mechanism
  - Rate of Dehydration: Tertiary > Secondary > Primary

- Carbocation Rearrangements
  - 1,2-alkyl shift or 1,2-hydride shift
  - Forms more stable carbocation

- Conversion of ROH to R-X

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<thead>
<tr>
<th>Reaction</th>
<th>Reagent</th>
<th>Note</th>
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<tbody>
<tr>
<td>ROH → RCl</td>
<td>HCl</td>
<td>• Useful for all ROH</td>
</tr>
<tr>
<td>ROH → RBr</td>
<td>HBr</td>
<td>• Secondary &amp; Tertiary ROH → S_N1</td>
</tr>
<tr>
<td>ROH → RI</td>
<td>HI</td>
<td>• Primary, methyl ROH → S_N2</td>
</tr>
</tbody>
</table>
ROH $\rightarrow$ RCl

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<thead>
<tr>
<th>SOCl$_2$</th>
<th>● Use for methyl, primary, and secondary ROH $\rightarrow$ S$_N^2$</th>
</tr>
</thead>
</table>

ROH $\rightarrow$ RBr

<table>
<thead>
<tr>
<th>PBr$_3$</th>
<th>● Use for methyl, primary, and secondary ROH $\rightarrow$ S$_N^2$</th>
</tr>
</thead>
</table>

● SOCl$_2$/pyridine and PBr$_3$ proceed through S$_N^2$ mechanisms (backside attack -> invert stereochemistry)

● Epoxide Opening
  ○ With a strong nucleophile (i.e. -OH, -OR, -CN, -SR); S$_N^2$ mechanism, Nu attacks at least substituted carbon
  ○ Acid-catalyzed
    ■ Examples of acids used: H$_2$SO$_4$, HI, HBr, HCl
    ■ Nucleophile attacks most substituted carbon