CHEMICAL REACTIVITY AND MECHANISMS, AND SUBSTITUTION REACTIONS

A STUDENT SHOULD BE ABLE TO:

1. Understand the concepts of: enthalpy, entropy, free energy, equilibrium, and kinetics. Given a reaction coordinate diagram, identify transition states and reactive intermediates, and calculate activation energies and enthalpies of reaction. Understand the Hammond Postulate as applied to exothermic and endothermic reactions.

2. Propose reaction mechanisms for simple transformations. A reaction mechanism will include a step-by-step explanation of bond-breaking and -making events that lead to product formation, intermediates (if any), and mechanistic arrows.

3. Define, recognize, and give examples of each of the following terms:
   - Nucleophile (electron pair donor) and electrophile (electron pair acceptor)
   - Substrate
   - Leaving group
   - Methyl halide, 1° RX, 2° RX, 3° RX, allylic RX, and benzylic RX
   - $S_N1$ and $S_N2$ reactions
   - Concerted versus stepwise reaction
   - Rate-determining step
   - Reaction stereochemistry: retention, inversion, racemization
   - Polar and nonpolar, protic and aprotic solvents

4. Predict the stability of carbocations, and predict when a carbocation will rearrange. Stability: $3° > 2° >> 1° > ^+\text{CH}_3 > ^+\text{vinyl} > ^+\text{phenyl}$. Also, delocalization stabilizes carbocations: allylic, benzylic, or carbocations adjacent to an atom with unshared pair of electrons.

5. Predict the product or products of nucleophilic substitution reactions, including the stereochemistry where appropriate. Note that the problem will usually not say which of the reaction types is occurring in any individual case.

6. From your knowledge of the mechanism, predict and interpret experimental results for $S_N1$ and $S_N2$ reactions. Be prepared to draw mechanisms with arrows that show electron movement. For a summary of important factors that influence reaction rates, see the study guide on the next page.

7. Propose syntheses using these reactions and those learned earlier. Use cyanide and acetylide anions in $S_N2$ reactions to make C-C bonds.
Factors Affecting The Rates Of Substitution Reactions:

Substrate:
- $S_N2$ reactions are fastest for methyl substrates; rates are: $\text{CH}_3 > 1^\circ > 2^\circ >> 3^\circ$ (this is a steric effect; larger groups interfere with the approaching nucleophile).
- $S_N1$ reactions are faster for $3^\circ$ substrates (because the more stable the carbocation, the faster the reaction; this means $3^\circ > 2^\circ >> 1^\circ > \text{CH}_3$).
- Vinylic ($R_2C=CR^-$) and aromatic substrates are unreactive in both reaction types.
- Allylic and benzylic substrates can react via either process.

Leaving group:
- Both reactions are faster when the leaving group is a weak base. For the alkyl halides as leaving groups, the resulting order is $\Gamma^- > Br^- > Cl^- >> F^-$. Other commonly used leaving groups are $\text{RSO}_3^-$ (such as tosyl or mesyl) and $\text{H}_2\text{O}$.

Nucleophile:
- $S_N2$ reactions are usually faster when a strong nucleophile is used (there are some solvent effects on this).
- Nucleophile identity and concentration have no effect on the rate of $S_N1$ reactions.

Solvent:
- Only polar protic solvents allow $S_N1$ reactions;
- $S_N2$ reactions can occur in any solvent but are fastest in polar aprotic solvents.

Temperature:
- High temperatures increase the rates of all reaction types by providing energy to the reaction, and increasing the collision frequency of the reactants.

Reactant concentration:
- The reaction rate is directly proportional to substrate concentration for all reaction types.
- For $S_N2$ reactions, the rate is also proportional to the nucleophile concentration.
- For $S_N1$ reactions, nucleophile concentration has no effect on the reaction rate at all.
To best prepare for this module, please work appropriate Skill Builder problems in the textbook.

A STUDENT WHO HAS MASTERED THE OBJECTIVES FOR THIS UNIT SHOULD BE ABLE TO SOLVE THE FOLLOWING PROBLEMS AND RELATED ONES:

1.1 Use the Bond Dissociation Energies (BDE, kJ/mol) in your book to calculate the $\Delta H_{\text{rxn}}$. Then, state whether the reaction is exothermic or endothermic, and state if the enthalpy is favorable or unfavorable.

a) $(\text{CH}_3)_2\text{CHBr} + \text{H}_2\text{O} \rightarrow (\text{CH}_3)_2\text{CHOH} + \text{HBr}$

b) $\text{CH}_3\text{OH} + \text{HCl} \rightarrow \text{CH}_3\text{Cl} + \text{H}_2\text{O}$

1.2 Predict whether the $\Delta S_{\text{rxn}}$ will be positive (favorable), negative (unfavorable), or about zero, and explain why.

a)

\[\begin{array}{c}
\text{O} \\
\text{H}
\end{array} + \text{H}_3\text{O}^+ \rightarrow
\begin{array}{c}
\text{O} \\
\text{H}
\end{array} + \text{H}_2\text{O} \]

b)

\[\begin{array}{c}
\text{H} \\
\text{O} \text{CH}_3
\end{array} + \begin{array}{c}
\text{H} \\
\text{O} \text{CH}_3
\end{array} \rightarrow
\begin{array}{c}
\text{H} \\
\text{O} \text{CH}_3
\end{array} \]

c)

\[\begin{array}{c}
\text{Br}
\end{array} \rightarrow
\begin{array}{c}
\text{Br}
\end{array} \]

1.3 In the reaction coordinate diagram shown: a) What point(s) represent(s) transition state(s)? b) What point(s) is (are) reactive intermediate(s)?
1.4 Answer the following questions using the reaction coordinate diagram shown.

a) What is $E_{act}$ of $A \rightarrow B$?

b) What is $E_{act}$ for $B \rightarrow A$?

c) What is $\Delta H$ for $A \rightarrow B$?

d) What is $\Delta H$ for $B \rightarrow A$?

e) For the reaction $A \rightarrow B$, the transition state comes _________ along the reaction coordinate, and is structurally similar to the ________.

A. early, reactant  
B. early, product  
C. late, reactant  
D. late, product

2.1 Draw mechanistic arrows. HINT: include lone pairs and implied H as necessary.

a) 

\[
\begin{align*}
\text{O} & \quad + \quad \text{H} & \quad \text{O} & \quad \text{H} & \quad \rightarrow & \quad \text{O} & \quad + \quad \text{H}_2\text{O} \\
\text{CH}_3 & & & & & & & \text{CH}_3
\end{align*}
\]

b) 

\[
\begin{align*}
\text{O} & \quad + \quad \text{H} & \quad \text{O} & \quad \text{CH}_3 & \quad \rightarrow & \quad \text{H} & \quad \text{O} & \quad \text{CH}_3 \\
\text{CH}_3 & & & & & & & \text{CH}_3
\end{align*}
\]

c) 

\[
\begin{align*}
\text{Br} & \quad \rightarrow & \quad \text{Br} & \quad + & \quad \text{Br} \\
\text{Br} & & & & & & & \text{Br}
\end{align*}
\]

d) 

\[
\begin{align*}
\text{CH}_3 & \quad \rightarrow & \quad \text{CH}_3 & \quad + & \quad \text{CH}_3 \\
\text{CH}_3 & & & & & & & \text{CH}_3
\end{align*}
\]
2.2. Draw the appropriate mechanistic arrows for each reaction. Draw the product that results from your arrows. HINT: include lone pairs and implied H as necessary.

a) Rearrangement.

b) Loss of Leaving Group

![Diagram]

c) Proton Transfer

![Diagram]

d) Nucleophilic Attack

![Diagram]

3.1 Identify the substrate, the nucleophile, and the leaving group in the following reactions. Classify the substrate as methyl, primary, secondary or tertiary.

a) \( \text{CH}_3\text{CH}_2\text{Br} + \text{CH}_3\text{S}^- \rightarrow \text{CH}_3\text{CH}_2\text{SCH}_3 + \text{Br}^- \)

b) \( (\text{CH}_3)_2\text{CHO}_{\text{SO}_2}\text{F} + \Gamma \rightarrow (\text{CH}_3)_2\text{CH} + \text{FSO}_3^- \)
3.2 Characterize each of the following reactions as proceeding with retention, inversion, or racemization. Classify the substrate as methyl, primary, etc. What is the reaction type (SN1, SN2)?

a) 
\[ \text{H} \quad \text{H} + \text{N}_3^- \rightarrow \text{Br}^- + \text{H} \quad \text{N}_3^- \]

b) 
\[ (\text{CH}_3)_2\text{HC} \quad \text{C} \quad \text{CH}_3 \quad \text{I} \quad \text{CH}_3 \quad \text{+ H}_2\text{O} \rightarrow \text{HI} \quad + \quad (\text{CH}_3)_2\text{HC} \quad \text{C} \quad \text{CH}_3 \quad \text{OH} \quad + \quad (\text{CH}_3)_2\text{HC} \quad \text{C} \quad \text{CH}_3 \quad \text{OH} \quad \text{CH}_2\text{CH}_3 \]

c) 
\[ \text{H} \quad \text{H} + \text{OH}^{-} \rightarrow \text{Cl}^- + \text{H} \quad \text{H} \quad \text{CH}_3 \quad \text{CH}_2\text{CH}_2\text{CH}_2\text{Cl} \quad \text{CH}_3 \quad \text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \]

3.3 Which of the following solvents is/are protic? Which is/are polar, aprotic?

a) CH₃CH₂CH₂CH₂CH₃  b) CH₃SCH₃  c) CH₃CH₂OH  d) HCN(CH₃)₂

4.1 Arrange these carbocations based on stability, #1 = most stable.

4.2 Which of these carbocations is likely to rearrange? Draw the expected product.
5. Predict the major organic product of each of the following reactions.

a) \( \text{CH}_3\text{CH}_2\text{CH}_2\text{Br} + \text{CH}_3\text{CO}_2\text{Na} \)

b) \( \text{CH}_3\text{I} + (\text{C}_6\text{H}_5)_3\text{P} \)

c) \( \text{OSO}_2\text{CF}_3 \xrightarrow{\text{NaCN}} \text{(CH}_3)_2\text{C}=\text{O} \) (acetone)

d) \( \text{OSO}_2\text{CF}_3 \xrightarrow{\text{CH}_3\text{OH}} \)

e) \( \text{OTs} \xrightarrow{\text{CH}_3\text{OH}} \)

f) \( \text{OH} \xrightarrow{\text{HBr}} \)

6.1 Provide curved mechanistic arrows for each of the following reactions. Add in missing lone pairs where necessary.

a) \( \text{H}_3\text{C} \xrightarrow{\Theta \text{OH}} \text{S}_\text{N}2 \xrightarrow{\Theta \text{Br}} \text{H}_3\text{C} \)
6.1 Consider the reaction CH₃CHBrCH₃ + SH₂ → CH₃CH(CH₃)SH₂⁺ + Br⁻

What is the effect on the rate of the reaction if each of the following changes is made? Possible answers: increases, decreases, remains the same.

<table>
<thead>
<tr>
<th>CHANGE</th>
<th>IF THE RXN.</th>
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</thead>
<tbody>
<tr>
<td>Use CH₃CH₂Br instead of CH₃CHBrCH₃</td>
<td>IS S₁</td>
<td>IS S₂</td>
</tr>
<tr>
<td>Use CH₃CHICH₃ instead of CH₃CHBrCH₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use SH⁻ instead of SH₂</td>
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<td></td>
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<tr>
<td>Increase the concentration of CH₃CHBrCH₃</td>
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<td></td>
</tr>
<tr>
<td>Decrease the concentration of SH₂</td>
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<td></td>
</tr>
<tr>
<td>Use DMSO as solvent rather than water</td>
<td></td>
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</tr>
</tbody>
</table>

6.2 What is the effect on the rate of the reaction if each of the following changes is made? Possible answers: increases, decreases, remains the same.

7.1 What substrate reacts with the alkynide anion shown to make the product?

a) CH₃CH₂C≡C⁻ + ??? → CH₃CH₂C≡CCH₂CH₃

b) (CH₃)₂CHC≡C⁻ + ??? → (CH₃)₂CHC≡CCH₂CH₂OCH₃

c) CH₃(CH₂)₃C≡C⁻ + ??? → CH₃(CH₂)₃C≡CCH₂CH₂CH(CH₃)₂

d) CH₂=CHC≡C⁻ + ??? → CH₂=CHC≡CCH₂C₆H₅
7.2 What alkyne anion reacts with the substrate shown to make the product?

a) ??? + CH₃CH₂CH₂Br $\rightarrow$ CH₃C≡CCH₂CH₂CH₃

b) ??? + ICH₂CH₃ $\rightarrow$ (CH₃)₃CC≡CCH₂CH₃

c) ??? + CH₂=CHCH₂Cl $\rightarrow$ CH₂=CHCH₂C≡CCH(CH₃)₂

7.3 Propose syntheses of each of the compounds shown, from the given starting materials and any other needed reagents.

a) CH₃CH₂C≡N from ethyl bromide

b) OCH₂CH₃ from CH₃CH₂Br

c) racemic CH₃CH(OH)CH₂CH₂CH₃ from (R)-2-bromopentane

d) 2-hexyne from 1-chloropropane

e) CH₃CH₂OSO₂Ph from CH₃CH₂OH

f) 2-octyne from CH₃C≡CH (Hint: this takes two steps)

g) (CH₃)₃CCH₂CH₂C≡CCH₂CH₃ from 1-butyne
7.3  h) \( C_6H_5CH_2C=CH(CH_3)_2 \) from \( C_6H_5CH_2Cl \)

i) \( CH_2=CHCH_2OCH_3 \) from \( NaOCH_3 \)

SOLUTIONS TO SAMPLE PROBLEMS:

1.1  a) \((CH_3)_2CHBr + H_2O \rightarrow (CH_3)_2COH + HBr\)

\[
\begin{array}{c|c|c}
\text{break:} & \text{form:} & \Delta H_{\text{rxn}} \\hline
2^\circ \text{C-Br} & 2^\circ \text{C-OH} & +34 \text{kJ/mol} \end{array}
\]

endothermic, unfavorable

b) \( CH_3OH + HCl \rightarrow CH_3Cl + H_2O \)

\[
\begin{array}{c|c|c}
\text{break:} & \text{form:} & \Delta H_{\text{rxn}} \\hline
CH_3-OH & CH_3-Cl & -37 \text{kJ/mol} \end{array}
\]

exothermic, favorable

1.2  a) \( \Delta S_{\text{rxn}} \sim 0 \): no great change in order/disorder. Same number of molecules/moles.

b) \( \Delta S_{\text{rxn}} < 0 \): large decrease in disorder (2 reactants make 1 product); unfavorable entropy

c) \( \Delta S_{\text{rxn}} > 0 \): large increase in disorder (1 reactant makes 2 products); favorable entropy

1.3  a) B and D are transition states.

b) C is a reactive intermediate.

1.4  a) \( E_{\text{act}} \) for \( A \rightarrow B = 20 \text{ kJ/mole} \)

b) \( E_{\text{act}} \) for \( B \rightarrow A = 30 \text{ kJ/mole} \)

c) \( \Delta H \) for \( A \rightarrow B = -10 \text{ kJ/mole} \)

d) \( \Delta H \) for \( B \rightarrow A = +10 \text{ kJ/mole} \)

e) A (based on Hammond Postulate)

2.1  a) proton transfer: 2 arrows
2.1 b) nucleophilic attack: 1 arrow

\[ \text{H} + \text{OCH}_3^- \rightarrow \text{H}^+ + \text{CH}_3 \text{O}^- \]

c) loss of leaving group: 1 arrow

\[ \text{Br^-} \rightarrow \text{Br}^- + \text{Br}^- \]

d) carbocation rearrangement (1,2-hydride shift): 1 arrow

\[ \text{H} \rightarrow \text{H} \]

2.2 a). Rearrangement. The rearranged 3° carbocation is more stable because it is resonance delocalized.

\[ \text{H} \rightarrow \text{H} \]

b) Loss of Leaving Group. Leaving group leaves, taking electrons with it. The substrate is left with a positive charge.

\[ \text{H} \rightarrow \text{H} \]

c) Proton Transfer. Needs two arrows.

\[ \text{OH}^- + \text{OH}^- \rightarrow \text{OH}^- + \text{OH}^- \]
2.2  d) Nucleophilic Attack

\[
\begin{array}{ccc}
\text{CH}_3 & \text{CH}_2 & \text{ Br} \\
\text{CH}_3 & \text{C} & \text{N} \\
& & \text{C} \\
\end{array}
\]

3.1  a) CH\textsubscript{3}CH\textsubscript{2}Br is a primary substrate; CH\textsubscript{3}S\textsuperscript{-} is the nucleophile; Br\textsuperscript{-} is the leaving group. SN\textsubscript{2} reaction will happen here.

b) (CH\textsubscript{3})\textsubscript{2}CH-OSO\textsubscript{2}F is a secondary substrate; I\textsuperscript{-} is the nucleophile; FSO\textsubscript{3}\textsuperscript{-} is the leaving group. SN\textsubscript{2} reaction will happen here.

3.2  a) Inversion at the reacting C, retention at the other chirality center; 2\textdegree\ RX; SN\textsubscript{2}

b) Racemization; 3\textdegree\ RX; SN\textsubscript{1}

c) Retention at the chirality centers (reaction does not take place at a chirality center); 1\textdegree\ RX; SN\textsubscript{2}

3.3  Compound (c) is a protic solvent: has OH. The rest only have CH, are aprotic. Compounds (b) and (d) are polar, aprotic.

4.1  \#2, secondary \#4, vinylic \#1, tertiary and allylic \#3, primary

4.2  CH\textsubscript{3}: migration; 2\textdegree\ to 3\textdegree\ H: migration; 2\textdegree\ to 2\textdegree/benzyl (delocalized)

5.  a) CH\textsubscript{3}CH\textsubscript{2}CH\textsubscript{2}Br + CH\textsubscript{3}CO\textsubscript{2}Na \rightarrow CH\textsubscript{3}CH\textsubscript{2}CH\textsubscript{2}OC(O)CH\textsubscript{3} + Br\textsuperscript{-} (SN\textsubscript{2})

   primary RX, good nucleophile

b) CH\textsubscript{3}I + (C\textsubscript{6}H\textsubscript{5})\textsubscript{3}P: \rightarrow (C\textsubscript{6}H\textsubscript{5})\textsubscript{3}P\textsuperscript{+}CH\textsubscript{3} + I\textsuperscript{-} (SN\textsubscript{2})

   methyl RX, good nucleophile

c) secondary substrate \rightarrow \text{SN}_{2}, with inversion
5. 

**d)**

\[
\text{secondary substrate} \quad \text{OSO}_2\text{CF}_3 \quad \xrightarrow{\text{CH}_3\text{OH}} \quad + \quad \text{OCH}_3 \\
\text{weak nucleophile} \quad \text{polar, protic solvent} \\
S_N^1, \text{racemic}
\]

**e)**

\[
\text{allyl substrate} \quad \text{OTs} \quad \xrightarrow{\text{CH}_3\text{OH}} \quad + \quad \text{OCH}_3 \\
\text{weak nucleophile} \quad \text{polar, protic solvent} \\
S_N^1 \text{ OK for allyl substrate due to resonance stabilized carbocation}
\]

**f)**

\[
\begin{align*}
\text{3° substrate, but poor LG} & \quad \xrightarrow{\text{HBr}} \quad \text{good LG now} \\
\text{weak base} & \quad \xrightarrow{S_N^1} \quad + \quad \text{H}_2\text{O}
\end{align*}
\]

6.1 Curved mechanistic arrows:

**a)**

\[
\text{H}_3\text{C} \quad \xrightarrow{S_N^2} \quad \text{H}_3\text{C} \\
\]

**b)**

\[
\begin{align*}
\text{H}_3\text{CH}_2\text{C} & \quad \xrightarrow{S_N^1} \quad \text{H}_3\text{CH}_2\text{C} \\
\text{note: the enantiomer will also form}
\end{align*}
\]
### 6.2

<table>
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<tr>
<th>CHANGE</th>
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<th>IF THE RXN. IS $S_{N2}$</th>
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<tbody>
<tr>
<td>Use $\text{CH}_3\text{CH}_2\text{Br}$ instead of $\text{CH}_3\text{CHBrCH}_3$</td>
<td>decreases</td>
<td>increases</td>
</tr>
<tr>
<td>Use $\text{CH}_3\text{CHICH}_3$ instead of $\text{CH}_3\text{CHBrCH}_3$</td>
<td>increases</td>
<td>increases</td>
</tr>
<tr>
<td>Use $\text{SH}$ instead of $\text{SH}_2$</td>
<td>remains the same</td>
<td>increases</td>
</tr>
<tr>
<td>Increase the concentration of $\text{CH}_3\text{CHBrCH}_3$</td>
<td>increases</td>
<td>increases</td>
</tr>
<tr>
<td>Decrease the concentration of $\text{SH}_2$</td>
<td>remains the same</td>
<td>decreases</td>
</tr>
<tr>
<td>Use DMSO as solvent rather than water</td>
<td>decreases</td>
<td>increases</td>
</tr>
</tbody>
</table>

### 7.1

- a) $\text{BrCH}_2\text{CH}_3$
- b) $\text{ClCH}_2\text{CH}_2\text{CH}_2\text{OCH}_3$
- c) $\text{ICH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$
- d) $\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$

### 7.2

- a) $\text{CH}_3\text{C}≡\text{C}^-$
- b) $(\text{CH}_3)_3\text{C}≡\text{C}^-$
- c) $(\text{CH}_3)_2\text{CHC}≡\text{C}^-$

### 7.3

- a) $\text{CH}_3\text{CH}_2\text{C}≡\text{N}$ from $\text{CH}_3\text{CH}_2\text{Br}$

\[
\text{CH}_3\text{CH}_2\text{Br} + \text{Na}^+ \text{CN} \rightarrow \text{CH}_3\text{CH}_2\text{C}≡\text{N} + \text{Br}^- (S_{N2})
\]

- b) $\text{OCH}_2\text{CH}_3$ from $\text{CH}_3\text{CH}_2\text{Br}$

\[
\text{CH}_3\text{CH}_2\text{Br} + \bigcirc\text{O}^\ominus \rightarrow \bigcirc\text{OCH}_2\text{CH}_3 + \text{Br}^\ominus
\]

will have counter ion, such as $\text{Na}^+$, $\text{K}^+$ etc.

- c) $\text{OH}$ from $\text{H}_2\text{O}$; $S_{N1}$
d) 6C from CH₃C≡CH (Hint: this takes two steps)

\[
\begin{align*}
\text{CHCl}_3 + ? & \rightarrow \text{CHCl}_3 + \text{NaC≡C-CH}_3 & \text{NaCl} \\
\end{align*}
\]

e) \(\text{OSO}_2\text{Ph}\) from \(\text{OH}\)

\[
\begin{align*}
\text{PhSO}_2\text{Cl} + \text{pyridine} & \rightarrow \text{OSO}_2\text{Ph} \\
\end{align*}
\]

f) 2-octyne from CH₃C≡CH (Hint: this takes two steps)

\[
\begin{align*}
\text{H} & \rightarrow \text{NaNH}_2 & \rightarrow \text{Br} & \rightarrow \text{CH}_3(\text{CH}_2)_4\text{C≡CCH}_3 \\
\end{align*}
\]

g) \((\text{CH}_3)_3\text{CCH}_2\text{CH}_2\text{C≡CCH}_2\text{CH}_3\) from 1-butynel

\[
\begin{align*}
\text{H} & \rightarrow \text{NaNH}_2 & \rightarrow \text{Br} & \rightarrow (\text{CH}_3)_3\text{CCH}_2\text{CH}_2\text{C≡CCH}_2\text{CH}_3 \\
\end{align*}
\]

h) \(\text{C}_6\text{H}_5\text{CH}_2\text{C≡CH(CH}_3)_2\) from \(\text{C}_6\text{H}_5\text{CH}_2\text{Cl}\)

\[
\begin{align*}
\text{Cl} + \text{NaC≡C} & \rightarrow \text{C}_6\text{H}_5\text{CH} & \rightarrow \text{C}_6\text{H}_5\text{C≡CHCH}_2\text{CH}_3 \\
\end{align*}
\]

i) \(\text{CH}_2\text{CHCH}_2\text{OCH}_3\) from \(\text{NaOCH}_3\)

\[
\begin{align*}
\text{Br} + \text{NaOCH}_3 & \rightarrow \text{CHCH}_2\text{OCH}_3 \\
\end{align*}
\]
1. Consider the reaction \((\text{CH}_3\text{CH}_2)_2\text{CHCl} + \text{CH}_3\text{OH} \rightarrow (\text{CH}_3\text{CH}_2)_2\text{CHOCH}_3 + \text{Cl}^-\)
   What is the effect of each of the given changes on the rate of the reaction?
   Possible answers: increases, decreases, remains the same.
   Change
   | Effect if rxn is S$_\text{N}2$ | Effect if rxn is S$_\text{N}1$
   |-----------------------------|-----------------------------
   Use CH$_3$O$^-$, not CH$_3$OH
   Use (CH$_3$CH$_2$)$_2$CHOH, not (CH$_3$CH$_2$)$_2$CHCl
   Increase the concentration of CH$_3$OH
   Use (CH$_3$CH$_2$)$_3$CCl, not (CH$_3$CH$_2$)$_2$CHCl

2. Consider the reaction shown.
   What is the mechanism of this reaction? Use the data provided.
   \[
   \begin{array}{ccc}
   \text{Br} & + & \text{NaSCH}_3 \\
   \text{SCH}_3 & + & \text{NaBr}
   \end{array}
   \]
   
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<thead>
<tr>
<th>[RBr]</th>
<th>[NaSCH$_3$]</th>
<th>relative rate</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0.01</td>
<td>1</td>
</tr>
<tr>
<td>0.02</td>
<td>0.01</td>
<td>2</td>
</tr>
<tr>
<td>0.01</td>
<td>0.02</td>
<td>2</td>
</tr>
</tbody>
</table>

3. What are the values of a) $\Delta H$ and b) $E_{\text{act}}$ for A $\rightarrow$ B? Use the reaction diagram shown.
   a) 
   b) 

4. Predict the major organic product or products of each of the following reactions.
   a) \(\text{CH}_3\text{CH}_2\text{CH}_2\text{Br} + \text{H}_2\text{O} \rightarrow \)
   b) 

5. Propose a synthesis of (CH$_3$)$_2$CHOCH$_2$CH$_3$ from CH$_3$CH$_2$Br and any other needed reagents.

6. Propose a mechanism for the reaction of (CH$_3$)$_3$CCl + H$_2$O $\rightarrow$ (CH$_3$)$_3$COH + HCl
1. Draw the structure of the product or products of each of the following reactions. You must show the three-dimensional structure where appropriate.

a) 
\[
\begin{array}{c}
\text{CH}_3 \\
\text{H} \\
\text{CH}_2\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_2\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_2\text{CH}_3 \\
\end{array} 
\xrightarrow{\text{NaN}_3} 
\xrightarrow{\text{DMSO}} 
\]

\[
\begin{array}{c}
\text{CH}_3 \\
\text{H} \\
\text{CH}_2\text{CH}_3 \\
\end{array} 
\]

b) 
\[
\begin{array}{c}
\text{(CH}_3\text{)}_3\text{Cl} \\
\text{CH}_3 \\
\text{CH}_2\text{CH}_3 \\
\end{array} 
\xrightarrow{(\text{CH}_3\text{)}_2\text{CHOH}} 
\]

\[
\begin{array}{c}
\text{(CH}_3\text{)}_3\text{Cl} \\
\text{CH}_3 \\
\text{CH}_2\text{CH}_3 \\
\end{array} 
\]

c) 
\[
\begin{array}{c}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{I} \\
\end{array} 
\xrightarrow{\text{CH}_3\text{CH}_2\text{O}^\ominus} 
\]

2. For each of the following sets, predict which reaction will be faster.

Set 1 _____

a) (CH\text{3CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{)}_3\text{CCl} + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COH} + \text{HCl}

b) (CH\text{3CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{)}_3\text{CBr} + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COH} + \text{HBr}

Set 2 _____

a) CH\text{3CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{H}_2\text{S} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{SH} + \text{HBr}

b) CH\text{3CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{HS}^- \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{SH} + \text{Br}^-

Set 3 _____

a) CH\text{3CH}_2\text{CH}_2\text{CH}_2\text{OSO}_2\text{Ph} + \text{OH} \xrightarrow{\text{DMSO}} \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} + \text{PhSO}_3^- 

b) CH\text{3CH}_2\text{CH}_2\text{CH}_2\text{OSO}_2\text{Ph} + \text{OH} \xrightarrow{\text{CH}_3\text{OH}} \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} + \text{PhSO}_3^-
3. The reaction shown below was run several times using different concentrations of reagents and the rate of the reaction was determined each time. The results are shown. From this information, deduce the mechanism of the reaction. Note: OTs is shorthand for \(-\text{OSO}_2\text{C}_\text{6}\text{H}_4\text{CH}_3\), the \(p\)-toluenesulfonate or tosylate group, a strong leaving group.

\[
(\text{CH}_3\text{CH}_2\text{CH}_2)\text{CHOTs} + \text{Br}^- \rightarrow (\text{CH}_3\text{CH}_2\text{CH}_2)\text{CHBr} + \text{TsO}^-
\]

<table>
<thead>
<tr>
<th>[ROTs]</th>
<th>[Br(^-)]</th>
<th>Relative Rate</th>
<th>Circle the correct mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.02</td>
<td>0.02</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.04</td>
<td>0.02</td>
<td>2</td>
<td>(\text{S}<em>\text{N}1) (\text{S}</em>\text{N}2)</td>
</tr>
<tr>
<td>0.04</td>
<td>0.04</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

4. Sketch a reaction coordinate diagram for an \(\text{S}_\text{N}2\) reaction. Label the positions for the reactants, the products, and the transition state, and indicate where the energy of activation would be measured.

5. Label each solvent as polar aprotic, polar protic, or nonpolar.

a) \(\text{CCl}_4\)  b) \(\text{HOCH}_2\text{CH}_2\text{OH}\)  c) \(\text{HC}^-\text{N(CH}_3\text{)}_2\)  d) \(\text{H}_2\text{O}\)

6. Characterize both the stereochemistry and the mechanism of the following reaction.

Stereochemistry at chirality centers (circle one): retention  inversion  racemization

Mechanism (circle one): \(\text{S}_\text{N}1\) \(\text{S}_\text{N}2\)