3. AN INTRODUCTION TO ORGANIC REACTIONS

OBJECTIVES

1. Classify types of reaction
   Addition, Substitution, Elimination, Rearrangement
2. Define the concept of “Mechanism”
3. Describe acid-base reactions
4. Develop relationships between structure and acidity/basicity
Reactions are conveniently classified as substitutions, additions, eliminations and rearrangements. These terms describe the overall process, simply comparing the structure of starting materials and products. They do not indicate anything about the pathway ("mechanism") by which the reaction proceeds.

Substitutions

Additions

Eliminations

Rearrangements
(often in combination with another type of reaction)

e.g., Substitution
e.g., Addition

\[ \text{H}_3\text{C} - \text{C} = \text{CH}_2 \xrightarrow{\text{H}_2\text{O}, \text{H}_2\text{SO}_4} \]

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e.g., Elimination

\[ \text{H}_3\text{C} - \text{C} - \text{OH} \xrightarrow{\text{H}_2\text{SO}_4} \]

\[ \text{H}_3\text{C} - \text{CH}_3 \]
WHAT IS A MECHANISM?

A mechanism is a proposal for a step-by-step pathway by which a reaction proceeds. Each step involves bond making and/or breaking. The mechanism takes into account all currently available evidence (kinetics, formation of byproducts, effect of structure on reactivity). Any new data collected must be consistent with the proposed mechanism, or the mechanism itself must be modified to account for the new finding.

An understanding of common mechanistic steps can be applied to new combinations of reagents to predict the outcome of a new reaction. As such, development of an understanding of mechanisms will save you from memorizing a huge amount of material.

Do not try to pass this course by just memorizing the outcome of reactions!
What is a Mechanism?

A chemical reaction mechanism is a description of the process by which reactant(s) are converted to product(s). The mechanism describes when and how new bonds are broken and formed. Often mechanisms are divided into discrete steps in which intermediates are generated. The relative rates of these steps and the stability of the proposed intermediates are a part of the mechanism. The proposed mechanism for a given reaction is the best description of the above events, that is consistent with all of the experimental evidence, which is currently available. Thus, proposed mechanisms may change with time as new experimental evidence is accumulated.

The principal types of experimental evidence that are used to determine a mechanism are:

**Structure** - determination of the structure (including stereochemistry) and amounts of all products.

**Kinetics** - how the reaction rate depends on the concentration of the various reactants under different conditions.

**Intermediates** - evidence for the presence and structure of all intermediates.

**Structure-Activity** - how changing the structure of the reactant(s) affects the reaction.

The general idea of a "mechanism" is to show the movement of electrons within and between reactant(s) to form new bonds and break existing bonds in such a way as to form intermediates and/or products. Most reactions proceed in discrete steps. Sometimes these steps lead to intermediates that are quite stable and can be isolated, or to very reactive intermediates whose existence can only be inferred. Intermediates, whether stable or reactive, lie on an energy minimum along the reaction coordinate. The high energy point is the transition state which has no appreciable lifetime. Reactions that occur in a single step often do not have intermediates to describe; in these cases (and others) it is often necessary to attempt to look at the transition state to understand the reaction.

The formalism of writing mechanisms shows the reactant(s) (in close proximity to each other when more than one is involved) and curved DOUBLE HEADED arrows indicating the movement of PAIRS of electrons to form or break bonds. In radical reactions, in which single UNPAIRED electrons are involved, the movement of an electron is shown with curved arrows with SINGLE HEADS.
BOND MAKING AND BOND BREAKING

Heterolytic bond cleavage

\[ \text{A—B} \quad \rightarrow \]

Homolytic bond cleavage

\[ \text{A—B} \quad \rightarrow \]
Concerted Bond Making and Bond Breaking

A—B

Defining Electrophiles and Nucleophiles

Nucleophile

Electrophile
e.g., Problem 3.20(c). Show the non-bonding electrons and curved arrows to account for the following reaction step.

\[
\begin{align*}
\text{H} & \quad \text{H} \quad \text{F} \\
\text{H} & \quad \text{C} \quad \text{C} \quad \text{H} \\
\text{H} & \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{F} & \quad \text{H} \\
\text{C} & \quad \text{C} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]

\[\rightarrow\]

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{C} \quad \text{C} \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{F} & \quad \text{H} \\
\end{align*}
\]

\[\text{C} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{F}^{-}\]

e.g., Problem 3.31(d). Show the curved arrows to account for the following reaction step.

\[
\begin{align*}
\text{H} & \quad \text{O}^{-} \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{C} & \quad \text{I} \\
\text{H} & \quad \text{O} \quad \text{CH}_{3}
\end{align*}
\]

\[\rightarrow\]

\[
\begin{align*}
\text{H} & \quad \text{O}^{-} \quad \text{H} \\
\text{H} & \quad \text{C} \quad \text{H} \quad \text{H} \quad \text{I}^{-} \\
\end{align*}
\]

\[\text{H} \quad \text{CH}_{3} \quad \text{I}^{-}\]
Energy-reaction coordinate diagram for one-step reaction

\[ \Delta H^o = H^o_{\text{products}} - H^o_{\text{reactants}} \]

\[ \Delta G^o = G^o_{\text{products}} - G^o_{\text{reactants}} \]

\[ K = \frac{[\text{products}]}{[\text{reactants}]} \]

\[ \Delta G^o = -2.303 \, RT \log K_{eq} = -RT \ln K_{eq} \quad R = \text{gas constant} \]

\[ T = \text{temperature} / K \]

\[ \Delta G^o = \Delta H^o - T \Delta S^o \]
Question 1. Arrange the reactions (A B C D), by their classification, in the following order: (i) Substitution; (ii) Addition; (iii) Elimination; (iv) Rearrangement.

1. B C D A
2. C D A B
3. C B D A
4. D A B C

Question 2. Which of the following statement is true?

1. The heterolysis of a bond always produces a carbocation.
2. Carbanions are Lewis acids
3. Carbocations are electrophiles
4. Nucleophiles seek centers of high electron density (e.g., a negative charge).
ACID-BASE REACTIONS

A–H + OH\textsubscript{2} $\rightleftharpoons$ A + H–OH\textsubscript{2}

$K_{eq} =$

$K_a =$

$pK_a =$

p\textsubscript{K}_a and Acid Strength

“Acidity”: ability to donate a proton

Strong acids have weak conjugate bases

Anions which are better able to accommodate negative charge are weaker bases.
Predicting Equilibrium Constants

\[ A^- + B^- \rightleftharpoons A^- + B^- \]

HWeb10

Question 1. Which of the following statement is not true?

1. Acid-base reactions are under equilibrium control.
2. Organic amines generally dissolve in aqueous hydrochloric acid.
3. Usually the weaker acid and base are favored at equilibrium.
4. Organic acids generally dissolve in aqueous hydrochloric acid.
Question 2. What is the approximate equilibrium constant \( (K_{eq}) \) at 25 °C for a reaction with a \( \Delta G^\circ \) value of –5.7 KJ/mole (1.4 Kcal/mole).

1. 1
2. 10
3. 10000
4. 1E24
We have ways to assess the ability of ions (anions and cations) to accommodate charge based on:

- Inductive effects (substituents donate or withdraw electron density via sigma bonds)
- Resonance effects (electron donation or withdrawal by pi-bonds)

In order to assess the relative strengths of acids, consider the ability of the conjugate base to accommodate negative charge. Stronger acids have weaker conjugate bases...

\[ \text{A}^-+\text{H}^+ + \text{B} \rightarrow \text{A}^- + \text{H}\text{B} \]

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Observation 1: Down a column of the periodic table

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>pK\text{a}</td>
<td>H–F</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>H–Cl</td>
<td>-7</td>
</tr>
<tr>
<td></td>
<td>H–Br</td>
<td>-9</td>
</tr>
<tr>
<td></td>
<td>H–I</td>
<td>-10</td>
</tr>
<tr>
<td></td>
<td>F\text{–}</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cl\text{–}</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Br\text{–}</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I\text{–}</td>
<td></td>
</tr>
</tbody>
</table>
Observation 2: Across of the periodic table

<table>
<thead>
<tr>
<th></th>
<th>H–CH₃</th>
<th>H–NH₂</th>
<th>H–OH</th>
<th>H–F</th>
</tr>
</thead>
<tbody>
<tr>
<td>$pK_a$</td>
<td>48</td>
<td>38</td>
<td>15.7</td>
<td>3.2</td>
</tr>
</tbody>
</table>

\[ -\text{CH}_3, -\text{NH}_2, -\text{OH}, -\text{F} \]

Observation 3: Hybridization

<table>
<thead>
<tr>
<th></th>
<th>H–CH₂CH₃</th>
<th>H–CH=CH₂</th>
<th>H–C≡CH</th>
</tr>
</thead>
<tbody>
<tr>
<td>$pK_a$</td>
<td>50</td>
<td>44</td>
<td>25</td>
</tr>
</tbody>
</table>

\[ -\text{CH}_2\text{CH}_3, -\text{CH}≡\text{CH}, -\text{C≡CH} \]
Observation 4: Resonance

\[
\begin{array}{l}
pK_a \\
\text{CH}_3\text{CH}_2\text{OH} & 16 \\
\text{CH}_3\text{CO}_2\text{H} & 4.75
\end{array}
\]

Question 1. Arrange the following ions in order of increasing basicity.

\[
\begin{array}{cccc}
\text{F}^- & \text{HO}^- & \text{H}_2\text{N}^- & \text{H}_3\text{C}^- \\
\text{A} & \text{B} & \text{C} & \text{D}
\end{array}
\]

1. C<D<A<B
2. C<D<B<A
3. A<B<C<D
4. B<A<D<C
Question 2. Based on the resonance structures of the acetate anion shown below, which of the following statements are true.

A. Both carbon-oxygen bond lengths are the same.
B. The negative charge is shared equally at both oxygens.
C. The structures are of equal energy.
D. The acetate anion is a very strong base.

1. Only A, B, C
2. Only A, B
3. Only C, D
4. A, B, C, D

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**ORGANIC BASES**

\[ \text{R-NH}_2 + \text{HCl} \rightarrow \text{R-NH}_3^+ + \text{Cl}^- \]

\[ \text{H}_2\text{C=CH}_2 + \text{HCl} \rightarrow \text{H}_2\text{C=CH}_2\text{Cl} \]

\[ \text{R-OH} + \text{HCl} \rightarrow \text{R-OH}_2^- + \text{H}^+ \]
Explaining Trends in Basicity

Using electronegativity, hybridization, resonance and hybridization to account for trends in basicity... assess the electron donating ability of the base.

\[ \text{RO}^- > \text{ROH} \]

\[ \text{R}_{\text{N}}\text{H}_2 > \text{ROH} \quad \text{R}_2\text{N}^- > \text{RO}^- \]

\[ \text{R}_3\text{N} > \text{R}_2\text{C}=\text{NR} > \text{RC}≡\text{N} \]

\[ \text{HO}^- > \text{CH}_3\text{CO}_2^- \]

\[ \text{R}_3\text{N} > \text{R}_2\text{NH} > \text{RNH}_2 > \text{NH}_3 \quad \text{(gas phase basicity)} \]
ACID-BASE REACTIONS IN NON-AQUEOUS MEDIA

“Protic Solvent”:

H$_3$O$^+$ is the strongest acid which can be present in water, HO$^-$ is the strongest base which can be formed. In any solvent, the strongest acid which can be present is the conjugate acid of the solvent.

TWO MULTISTEP MECHANISMS IN WHICH THE FIRST STEP IS AN ACID-BASE REACTION

Addition of HBr to an Alkene

Overall Reaction

Observations of kinetics, regiochemistry and the effects of structure on reactivity will be discussed later in the course….
Mechanism
  – Protonation

– Nucleophilic Addition

Energy-reaction co-ordinate diagram for a two-step reaction
2. Substitution of tert-Butanol

Overall Reaction

Observations of kinetics, regiochemistry and the effects of structure on reactivity will be discussed later in the course.

Mechanism

– Protonation

– Heterolytic Cleavage

– Nucleophilic Addition
Question 1. Arrange the following molecules in order of increasing acidity.

FCH₂CO₂H  CH₃CO₂H  ClCH₂CO₂H  BrCH₂CO₂H

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C &lt; B &lt; D &lt; A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>A &lt; D &lt; C &lt; B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>D &lt; C &lt; A &lt; B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>B &lt; D &lt; C &lt; A</td>
<td></td>
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</tbody>
</table>

Question 2. Which statement is true concerning the reaction of tert-butyl alcohol with conc. HCl to give tert-butyl chloride?

\[
\text{CH}_3\text{CH}
\text{CH}_3
\text{OH} \xrightarrow{\text{HCl}} \text{CH}_3\text{CH}
\text{CH}_3\text{Cl} + \text{H}_2\text{O}
\]

1. This is a substitution reaction
2. The reaction has a reactive intermediate called a carbanion.
3. The reaction proceeds in one step from reactant to product.
4. The reaction has a large positive ΔG°.
CHAPTER 3 FOR EXAM 2

Types of Questions
- Classify organic reactions
- Compare acid (or base) strength
- Show movement of electrons

*The problems in the book are good examples of the types of problems on the exam!*

Preparing for Exam 2:
- Get up to date *now!*
- Work as many problems as possible
- Work in groups
- Do the “Learning Group Problem” at the end of the chapter