Organic Chemical Reactions

Organic chemical reactions broadly organized in two ways:

1. What kinds of reactions occur

2. How those reactions occur

6.1 Kinds of Organic Reactions

Addition reactions
- Occur when two reactants add together to form a single product with no atoms “left over”
- Reaction of fumarate with water to yield malate (a step in the citric acid cycle of food metabolism)

These two reactants...

\[
\text{Fumarate} + \text{H}_2\text{O} \rightarrow \text{Malate}
\]
Kinds of Organic Reactions

Elimination reactions
- Occur when a single reactant splits into two products (usually with the formation of a small molecule such as water)
- Reaction of hydroxybutyryl ACP to yield trans-crotonyl ACP and water (a step in the biosynthesis of fat molecules)

Kinds of Organic Reactions

Substitution reactions
- Occur when two reactants exchange parts to give two new products
- Reaction of an ester such as methyl acetate with water to yield a carboxylic acid and an alcohol

Kinds of Organic Reactions

Rearrangement reactions
- Occur when a single reactant undergoes a reorganization of bonds and atoms to yield an isomeric product
- Rearrangement of dihydroxyacetone phosphate into its constitutional isomer glyceraldehyde 3-phosphate (a step in the metabolism of carbohydrates)
6.2 How Organic Reactions Occur: Mechanisms

Reaction Mechanism
• An overall description of how a reaction occurs at each stage of a chemical transformation
  • Which bonds are broken and in what order
  • Which bonds are formed and in what order
  • What is the relative rate of each step
• A complete mechanism accounts for all reactants consumed and all products formed

How Organic Reactions Occur: Mechanisms

All chemical reactions involve bond breaking and bond making

Two ways a covalent two-electron bond can **break**:
1. **Symmetrical**
   - One electron remains with each product fragment
   \[ \text{A} \text{B} \rightarrow \text{A}^+ \ + \text{B}^- \]
   - Half-headed arrow, “fishhook”, indicates movement of one electron
2. **Unsymmetrical**
   - Both bonding electrons remain with one product fragment, leaving the other with a vacant orbital
   \[ \text{A} \ + \text{B} \rightarrow \text{A}^+ \ + \text{B}^- \]
   - Full-headed arrow indicates movement of two electrons

How Organic Reactions Occur: Mechanisms

Two ways a covalent two-electron bond can **form**:
1. **Symmetrical**
   - One electron is donated to the new bond by each reactant (radical)
   \[ \text{A} + \text{B} \rightarrow \text{A} : \text{B} \]
2. **Unsymmetrical**
   - Both bonding electrons are donated by one reactant (polar)
   \[ \text{A}^+ + \text{B}^- \rightarrow \text{A} : \text{B} \]
Radical reaction
- Process that involves symmetrical bond breaking and bond making
  - Radical (free radical)
    - A neutral chemical species that contains an odd number of electrons and has a single, unpaired electron in one of its orbitals

Polar reactions
- Process that involves unsymmetrical bond breaking and bond making
  - Involves species that have an even number of electrons (have only electron pairs in their orbitals)
  - Common in both organic and biological chemistry

How Organic Reactions Occur: Mechanisms

6.3 Radical Reactions

Radical
- Highly reactive because it contains an atom with an odd number of electrons (usually seven) in a valence shell
- Can achieve a valence shell octet through:
  - Radical substitution reaction
    - Radical abstracts an atom and one bonding electron from another reactant

Radical Reactions
- Radical addition reaction
  - A reactant radical adds to a double bond, taking one electron from double bond and leaving one behind to form a new radical
Industrial radical reaction

- The chlorination of methane to yield chloromethane
- A substitution reaction
- First step in the preparation of the solvents dichloromethane (CH\textsubscript{2}Cl\textsubscript{2}) and chloroform (CHCl\textsubscript{3})

![Chemical equations and structures]

Radical Reactions: Radical chlorination of methane requires three kinds of steps: initiation, propagation, and termination

1. Initiation
   - Ultraviolet light breaks Cl-Cl bond to generate chlorine radicals

2. Propagation
   - Reaction with CH\textsubscript{4} to generate new radicals and propagate the chain reaction

(a) :Cl\cdot + H\cdot CH\textsubscript{3} \rightarrow H\cdot :Cl\cdot + :CH\textsubscript{3}

(b) :Cl\cdot :Cl\cdot + :CH\textsubscript{3} \rightarrow :Cl\cdot + :Cl\cdot :CH\textsubscript{3}
3. Termination
   - Two radicals combine to end the chain reaction
   - No new radical species is formed

Radical Reactions

Biological radical reaction
   - Prostaglandin synthesis initiated by abstraction of a hydrogen atom from arachidonic acid.

Radical Reactions

- The carbon radical reacts with $O_2$ to give an oxygen radical
- Oxygen radical reacts with C=C bond (several steps)
- Prostaglandin $H_2$ produced
6.4 Polar Reactions

Polar reactions
• Occur because of electrical attraction between positive and negative centers on functional groups in molecules
• Most organic compounds are electrically neutral, they have no net charge

Bond polarity
• Certain bonds within a molecule are polar
  • Consequence of an unsymmetrical electron distribution in a bond
  • Due to the difference in electronegativity of the bonded atoms.

Polar Reactions

Certain bonds within molecules, particularly those in functional groups, are polar
• Oxygen, nitrogen, fluorine, and chlorine are more electronegative than carbon
• Carbon is always positively polarized (\(\delta^+\)) when bonded to more electronegative elements
• Carbon is negatively polarized (\(\delta^-\)) when bonded to metals

<table>
<thead>
<tr>
<th>Compound type</th>
<th>Functional group structure</th>
<th>Compound type</th>
<th>Functional group structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td></td>
<td>Carbonate</td>
<td></td>
</tr>
<tr>
<td>Alkene</td>
<td>Symmetrical, nonpolar</td>
<td>Carboxylic acid</td>
<td></td>
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<tr>
<td>Alkyl halide</td>
<td></td>
<td>Carboxylic acid chloride</td>
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</tr>
<tr>
<td>Alkene</td>
<td></td>
<td>Thioether</td>
<td></td>
</tr>
</tbody>
</table>

Chloromethane
Methyl lithium
Polar Reactions

Polar bonds
- Can also result from interactions of functional groups with acids or bases
- Methanol
  - In neutral methanol the carbon atom is somewhat electron-poor
  - Protonation of the methanol oxygen by an acid makes carbon much more electron-poor

Polarizability of the atom
- The measure of change in electron distribution around the atom to an external electrical influence
- Larger atoms (more, loosely held electrons) – more polarizable
  - Smaller atoms (fewer, tightly held electrons) – less polarizable

Effects of polarizability on bonds
- Although carbon-sulfur and carbon-iodine bonds are nonpolar according to electronegativity values, they usually react as if they are polar because sulfur and iodine are highly polarizable
Electron-rich sites react with electron-poor sites

- Bonds made when electron-rich atom donates a pair of electrons to an electron-poor atom
- Bonds broken when one atom leaves with both electrons from the former bond

A curved arrow shows electron movement

- Electron pair moves from the atom (or bond) at tail of arrow to atom at head of arrow during reaction

Electrophile (electron-poor) + Nucleophile (electron-rich) → A⁻ + B⁺

This curved arrow shows that electrons move from B⁻ to A⁺.

The electrons that moved from B⁻ to A⁺ end up here in this new covalent bond.

Polar Reactions

Nucleophile

- Substance that is "nucleus-loving"
- Has a negatively polarized electron-rich atom
- Can form a bond by donating a pair of electrons to a positively polarized, electron-poor atom
- May be either neutral or negatively charged

Electrophile

- Substance that is "electron-loving"
- Has a positively polarized, electron-poor atom
- Can form a bond by accepting a pair of electrons from a nucleophile
- May be either neutral or positively charged

Polar Reactions

Electrostatic potential maps identify:

- Nucleophilic atoms (red; negative)
- Electrophilic atoms (blue; positive)
Neutral Compounds

- React either as nucleophiles or electrophiles (depending on circumstances)
- Water
  - Nucleophile when it donates a nonbonding pair of electrons
  - Electrophile when it donates H^+
- Carbonyl compound
  - Nucleophile when it reacts at its negatively polarized oxygen atom
  - Electrophile when it reacts at its positively polarized carbon atom
- A compound that is neutral but has an electron-rich nucleophilic site must also have a corresponding electron-poor electrophilic site

Polar Reactions

Nucleophiles and Electrophiles

- Similar to Lewis acids and Lewis bases
- Lewis bases
  - Electron donor
  - Behave as nucleophiles
- Lewis acids
  - Electron acceptors
  - Behave as electrophiles
- Terms nucleophile and electrophile used primarily when bonds to carbon are involved

Worked Example 6.1

Identifying Electrophiles and Nucleophiles

Which of the following species is likely to behave as a nucleophile and which as an electrophile?

(a) \((\text{CH}_3)_2\text{S}^+\)

(b) \(^{-}\text{CN}\)

(c) \(\text{CH}_3\text{NH}_2\)