Learning Guide for Chapter 8 - Organic Reactions II

I. Substitution, Addition, and Elimination Reactions
II. Oxidation and Reduction Reactions
III. Radical Reactions
IV. Reactive Intermediates
V. Stereochemistry of Reactions

I. Substitution, Addition, and Elimination Reactions

In the previous chapter, we learned to use association, dissociation, and displacement to describe Lewis acid/base reactions. Complete the following reactions.

association

\[ \text{where did the C}^+ \text{ come from?} \]

\[ \text{how will this compound become neutral?} \]

dissociation

\[ \text{how did the alcohol become protonated?} \]

\[ \text{what will happen to the C}^+? \]

displacement

\[ \text{how did the alcohol get deprotonated?} \]

Are these complete reactions?

- reactions usually start and end with neutral molecules
- these are steps in the mechanism of a reaction

What do the following terms mean?

substitution: a bond to one group is substituted for a bond to another group

addition: new atoms are added to a molecule, and a double bond is lost

elimination: atoms are lost from a molecule, and a double bond is gained

How are they different from the terms above?

- they refer to the end result of a reaction, not what happens to the electrons
Match the following reactions with one of the three descriptions on the previous page.

\[
\begin{align*}
\text{Br} & \quad \text{(CH}_3\text{)}_3\text{COK} & \quad \to & \quad \text{CH}_3\text{CH}=&\text{CH}_2 & + (\text{CH}_3\text{)}_3\text{COH} & + & \text{KBr} & \quad \text{elimination} \\
\text{Cl} & \quad \text{NaHN}_2 & \quad \text{NH}_3 & \quad \to & \quad \text{NH}_2 & + & \text{NaCl} & \quad \text{substitution} \\
\text{H}_2\text{SO}_4 & \quad \text{H}_2\text{O} & \quad \to & \quad \text{OH} & \quad \text{addition}
\end{align*}
\]

Which of these involve C=C?
- addition starts with a C=C
- elimination ends with a C=C

II. Oxidation and Reduction Reactions

How is oxidation defined in general chemistry?
- oxidation - loss of electrons (decrease in charge) \( \text{Ag} \to \text{AgO} \) (0 \to +2)
- reduction - gain of electrons (increase in charge) \( \text{KMnO}_4 \to \text{MnO}_2 \) (+7 \to +4)

Why won't this work in organic chemistry?
- compounds can be oxidized or reduced without changing charge
- oxidation states are more difficult to calculate

\[
\begin{align*}
\text{OH} & \quad \text{KMnO}_4 & \quad \to & \quad \text{O} & \quad + & \text{MnO}_2 & \quad \text{Mn was reduced, so the organic compound must have been oxidized}
\end{align*}
\]

How are oxidation and reduction defined in organic chemistry?
- oxidation: gaining bonds to O and/or losing bonds to H
- reduction: losing bonds to O and/or gaining bonds to H
Which of the following is occurring in each of these transformations?

- \( \text{C loses bonds to O and gains a bond to H reduction} \)

- \( \text{both C's lose a bond to H and gain a bond to O oxidation} \)

- \( \text{C gains 2 bonds to O oxidation} \)

- \( \text{both C's gain a bond to H reduction} \)

- \( \text{both C's gain a bond to O oxidation} \)

-called oxidative cleavage because a C-C was also broken

What are the highest and lowest oxidation states of carbon?

- \( \text{lowest - methane} \quad \text{highest - carbon dioxide} \)

Can atoms other than carbon be oxidized or reduced? \( \text{yes} \)

- \( \text{N loses 3 bonds to O, gains 2 bonds to H reduction} \)

Is only oxygen involved?

- \( \text{no - any other atom which is more electronegative than C counts (N, halogens)} \)

- \( \text{not as common to use these terms} \)

- \( \text{C lost a bond to Cl, gained a bond to H reduction} \)
Are all reactions oxidation and reductions?

no - sometimes the starting material and product are in the same oxidation state

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

1st C stays at 3 bonds to O 
2nd C stays at 1 bond to O
no change

1 C gained a bond to O, 
1 C gained a bond to H
no net change

C lost a bond to Br, gained a bond to O
both are more EN than C
no change

loss of H and change of charge means
no change in oxidation state

acid/base reactions are not redox reactions

What is an oxidizing agent?

a compound which is easily reduced, oxidizes other compounds

What are some common oxidizing agents, and how can you recognize them?

\[
\begin{align*}
\text{Na}_2\text{CrO}_4 & \quad \text{sodium chromate} \\
\text{KMnO}_4 & \quad \text{potassium permangante} \\
\text{H}_2\text{O}_2 & \quad \text{hydrogen peroxide} \\
\text{O}_3 & \quad \text{ozone}
\end{align*}
\]
metal atom in a high oxidation state, lots of O's
O bonded to itself

What is a reducing agent, and how can you recognize them?

a compound which is easily oxidized, reduces other compounds

\[
\begin{align*}
\text{H}_2 & \quad \text{hydrogen gas} \\
\text{NaBH}_4 & \quad \text{sodium borohydride} \\
\text{LiAlH}_4 & \quad \text{lithium aluminum hydride (LAH)} \\
\text{Na} & \quad \text{sodium metal} \\
\text{Sn} & \quad \text{tin metal}
\end{align*}
\]
hydride reagents (H bonded to group III atoms)
metals in elemental state
III. Radical reactions

What is a radical? 
\[
\begin{align*}
\text{H} & \rightarrow \cdot \text{O} \\
\text{: Br} & \rightarrow \cdot \text{Br} \\
\text{carbon radical} & \text{hydroxyl radical bromine radical}
\end{align*}
\]

an atom (or molecule) with an unpaired electron

Are radicals very reactive?

yes! they have an incomplete octet

Are radicals dangerous?

yes - when they are formed inside the body, they can react with proteins and DNA and cause damage to cells; they are thought to play a part in aging

How are radicals formed?

\[
\begin{align*}
\text{: Br} & \rightarrow \cdot \text{Br} \quad \text{hv or light} \quad \cdot \text{Br} + \cdot \text{Br} \\
\text{: O} & \rightarrow \cdot \text{O} \quad \text{hv or light} \quad \text{H}_3\text{C} - \cdot \text{O} + \cdot \text{O} - \text{CH}_3
\end{align*}
\]

a molecule with a weak bond absorbs energy from heat or light and breaks homolytically

What kinds of molecules form radicals in this way?

molecules with two highly EN and/or large atoms bonded to each other

What are reactions like this called?

initiation steps - bonds break to form radicals

How are carbon radicals formed?

they react with radicals formed by initiation steps

What is this type of reaction called?

propogation - one radical creates another
How do carbon radicals become stable again?

2 ways:

1) they take atoms from stable molecules, forming new radicals
   another propagation step

2) two radicals come together

What are these kinds of reactions called?
   termination - two radicals come together

Which of these two is more likely?
   a radicals are very reactive, very short lived, radical reactions are very fast
   so a radical is more likely to collide with a stable molecule than a radical

The halogenation of alkanes is a radical reaction. What does its mechanism look like?

\[
\text{CH}_4 + \text{Cl}_2 \overset{\text{hv or heat}}{\longrightarrow} \text{CH}_3\text{Cl} + \text{HCl}
\]

Initiation step:

\[
\begin{align*}
\text{hv or light} & \quad \text{hv or light} \\
\text{hv or light} & \quad \text{hv or light}
\end{align*}
\]

Propagation steps:

Termination steps:
What role does the initiation step play?

- gets the reaction started - no light or heat, nothing happens
- Why are many chemicals stored in dark bottles in cool places?
  - to prevent radicals from forming

What role do the propagation steps play?

- organic compound reacts and forms the product - main steps

What role do termination steps play?

- they are side reactions
- they slow the reaction down
- one recreates SM, one creates product, one creates a side product
- they occur mostly at the end when no reagents are left
- we don't always worry about these

Does the reaction stop at the product shown? What other products would be formed?

- nope - the product could react with another Cl radical
  - CH₂Cl, CHCl₃, CCl₄

Many radical reactions are also chain reactions. Is this one? How can you tell?

- yes! the radical needed to react with the alkane is regenerated by the propagation steps; initiation only has to happen once
  - (this is referred to as high quantum yield - lots of product for less light)

How are reactions involving radicals different from reactions of acids and bases or nucleophiles and electrophiles?

- electrons don't move in pairs

How are the arrows different?

- they are single-headed; they flow in opposite directions

Which is more common in organic chemistry?

- only a few reactions in this course have a radical mechanism
- they seem to be common as unwanted reactions
### IV. Reactive Intermediates

What is a reactive intermediate?

*a high energy molecule which is formed and then quickly reacts*

Why are they important?

*anything which affects their stability will have a big impact on the reaction*

Fill in the chart below.

<table>
<thead>
<tr>
<th>description</th>
<th>example</th>
<th>charge</th>
<th>hybridization</th>
<th>why reactive?</th>
</tr>
</thead>
<tbody>
<tr>
<td>stable carbon</td>
<td>four bonds</td>
<td>0</td>
<td>sp&lt;sup&gt;3&lt;/sup&gt;, sp&lt;sup&gt;2&lt;/sup&gt;, sp</td>
<td></td>
</tr>
<tr>
<td>carbocations</td>
<td>3 bonds empty orbital</td>
<td>+</td>
<td>sp&lt;sup&gt;2&lt;/sup&gt;</td>
<td>no octet</td>
</tr>
<tr>
<td>carbanions</td>
<td>3 bonds e- pair</td>
<td>-</td>
<td>sp&lt;sup&gt;2&lt;/sup&gt;</td>
<td>low EN</td>
</tr>
<tr>
<td>carbon radicals</td>
<td>3 bonds unpaired e-</td>
<td>0</td>
<td>sp&lt;sup&gt;2&lt;/sup&gt;</td>
<td>no octet</td>
</tr>
<tr>
<td>carbenes</td>
<td>2 bonds e- pair empty orbital</td>
<td>0</td>
<td>sp&lt;sup&gt;2&lt;/sup&gt;</td>
<td>no octet</td>
</tr>
</tbody>
</table>

What do their molecular orbitals look like? What is the geometry of the substituents?

<table>
<thead>
<tr>
<th>carbocation</th>
<th>carbanion</th>
<th>carbon radical</th>
<th>carbene</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="trig planar" /></td>
<td><img src="image2.png" alt="trig pyramid" /> or <img src="image3.png" alt="trig planar" /> (resonance)</td>
<td><img src="image4.png" alt="trig planar" /></td>
<td><img src="image5.png" alt="bent" /></td>
</tr>
</tbody>
</table>

1. ![image1.png](image1.png)
2. ![image2.png](image2.png)
3. ![image3.png](image3.png)
4. ![image4.png](image4.png)
5. ![image5.png](image5.png)
Stabilization

How does resonance stabilize carbocations, carbanions, and radicals?

the positive charge, negative charge, or unpaired electron are spread over more than one atom

\[
\text{more stable}
\]

pi bond overlaps with the other orbital

molecular orbital models

What does the molecule have to have in order for resonance to occur?

a double bond one atom away from the unstable atom

How does having alkyl substituents stabilize carbocations and radicals?

the sigma bonds overlap with the electron-deficient orbital and donate some electron density to it - called hyperconjugation

In which direction does stability increase?

more stable

+ CH₃

methyl doesn't form

1° doesn't form

2° less stable but can form

3° most stable
Does hyperconjugation stabilize carbanions?

no - that orbital is not electron-deficient, so sharing e- density doesn't help

How can electronegative atoms stabilize carbanions?

they draw e-density away from the C

Why aren't carbenes stabilized by either resonance or alkyl substitution?

they usually don't have any other groups attached

Formation

How are carbocations formed?

H-base

dissocation or reaction of alkenes with acid

How are carbanions formed?

by removing a H from a C
How are carbon radicals formed?

\[
\begin{align*}
\text{H} & \text{C} = \text{H} \\
\text{H} & \text{C} = \text{H} \\
\end{align*}
\xrightarrow{\text{Cl}^*} \\
\xrightarrow{\text{Cl}^*}
\]

by reacting with existing radicals in propagation steps

How are carbenes formed?

\[
\begin{align*}
\text{H} & \text{C} = \text{N} \equiv \text{N} : \\
\text{H} & \text{C} = \text{N} \equiv \text{N} : \\
\end{align*}
\xrightarrow{\text{base}} \\
\xrightarrow{\text{heat or light}}
\]

base takes a H, then dissociation

Reactivity

How do carbocations react?

\[
\begin{align*}
\text{H} & \text{C}^+ \\
\text{H} & \text{C}^+ \\
\end{align*}
\xrightarrow{\text{Nu}} \\
\xrightarrow{\text{base}}
\]

as electrophiles or acids

How do carbanions react?

\[
\begin{align*}
\text{O}^- & \\
\text{O}^- \\
\end{align*}
\xrightarrow{\text{H-base}}
\]

as nucleophiles or bases
How do carbon radicals react?

\[ \cdot \text{CH}_3 + \cdot \text{CH}_3 \rightarrow \text{H}_3\text{C-} + :\text{H} \cdot \]

- take atoms from other molecules (propagation)
- combine with other radicals (termination)

How do carbenes react?

\[ \text{C} = \text{C} + \text{e}^- \rightarrow \cdot \text{CH}_2 \rightarrow \cdot \text{CH}_2 \]

- electrocyclic reactions (both give and receive e-)

### Summary

<table>
<thead>
<tr>
<th></th>
<th>Stabilization</th>
<th>Formation</th>
<th>Reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbocations</td>
<td>resonance hyperconjugation</td>
<td>dissociation or C= C + acid</td>
<td>E or acid</td>
</tr>
<tr>
<td>carbanions</td>
<td>resonance induction</td>
<td>base takes a H</td>
<td>Nu or base</td>
</tr>
<tr>
<td>carbon radicals</td>
<td>resonance hyperconjugation</td>
<td>react with another radical</td>
<td>propagation, termination</td>
</tr>
<tr>
<td>carbenes</td>
<td>N/A</td>
<td>lose an H, then dissociate</td>
<td>electrocyclic reactions</td>
</tr>
</tbody>
</table>
Rearrangements of Carbocations

What happens to a carbocation when it undergoes rearrangement?

  a bond moves into the empty orbital, leaving the positive charge on another atom

\[
\begin{array}{c}
\begin{array}{c}
+ \\
\text{C} \\
\text{C}
\end{array}
\end{array} 
\quad \rightarrow 
\begin{array}{c}
\begin{array}{c}
+ \\
\text{C} \\
\text{C}
\end{array}
\end{array}
\]

Is this resonance, or a chemical reaction? a reaction - atoms moved!

Why do rearrangements occur?

  so that the C+ can become more stable

Which of the carbocations commonly undergoes rearrangements?

  * 1° - doesn't form
  * 2° - wants to become 3°
  * 3° - already stable

What are the two ways in which a carbocation can rearrange?

  hydride shift, alkyl shift

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

  hydride shift
  H moves with its e-

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

  alkyl shift
  carbon moves with its e-

Why can't the following carbocation rearrange?

\[
\begin{array}{c}
\begin{array}{c}
+ \\
\text{C} \\
\text{C}
\end{array}
\end{array} 
\quad \text{equally stable}
\quad \begin{array}{c}
\begin{array}{c}
+ \\
\text{C} \\
\text{C}
\end{array}
\end{array} 
\quad \text{less stable}
\quad \begin{array}{c}
\begin{array}{c}
+ \\
\text{C} \\
\text{C}
\end{array}
\end{array} 
\quad \text{too far away can't happen}
\]

What is the most likely rearrangement of the following carbocation?

smallest group is most likely to move
methyl shifts are most common

Why don't radicals, carbanions, or carbenes rearrange?

Ea too high? rate too slow compared to reaction with another molecule?
not stabilized by alkyl substitution can only be formed on a C stabilized by resonance or induction by EN atoms

:CH₂ nowhere to go can't shift e- pair and empty orbital at the same time anyway

V. Stereochemistry of Reactions

What are the two conditions under which the stereochemistry of the reaction is important?

stereocenter is involved in a reaction
stereocenter(s) created

Existing stereocenter undergoes a reaction

What three things can happen to a stereocenter involved in a reaction?

conserved: :OH \xrightarrow{SOCl_2} :Cl same orientation
inverted: :Br \xrightarrow{NaOH} :OH opposite orientation
racemized: :OH \xrightarrow{HCl} :Cl + :Cl both orientations are formed
What determines which of these occurs?

the mechanism of the reaction

What happens if the compound isn't enantiomerically pure?

\[
\begin{align*}
\text{racemic mixture} & \quad \text{NaOH} \\
\begin{array}{c}
\text{Br} \quad \text{Br} \\
\text{50%} \quad \text{50%}
\end{array} & \quad \rightarrow \quad \begin{array}{c}
\text{Br} \quad \text{Br} \\
\text{50%} \quad \text{50%}
\end{array} \\
\text{no effect}
\end{align*}
\]

\[
\begin{align*}
\text{80% o.p.} & \quad \text{NaOH} \\
\begin{array}{c}
\text{Br} \quad \text{Br} \\
\text{90%} \quad \text{10%}
\end{array} & \quad \rightarrow \quad \begin{array}{c}
\text{OH} \quad \text{OH} \\
\text{90%} \quad \text{10%}
\end{array} \\
\text{opposite preference}
\end{align*}
\]

\[
\begin{align*}
\text{enantiomerically pure} & \quad \text{NaOH} \\
\begin{array}{c}
\text{Br} \quad \text{Br} \\
\text{100%} \quad \text{100%}
\end{array} & \quad \rightarrow \quad \begin{array}{c}
\text{OH} \\
\text{100%}
\end{array} \\
\text{totally switched}
\end{align*}
\]

What if the stereocenter isn't involved in the reaction?

\[
\begin{align*}
\text{Br} & \quad \text{NaOH} \\
\rightarrow \quad & \text{OH} \\
\text{it doesn't change!}
\end{align*}
\]

One new asymmetric carbon

When only one new stereocenter is formed, how many stereoisomers can result?

\[
\begin{align*}
\text{NaBH}_4 & \\
\rightarrow & \begin{array}{c}
\text{OH} \\
\text{50%}
\end{array} \quad \begin{array}{c}
\text{OH} \\
\text{50%}
\end{array} \\
\text{2}
\end{align*}
\]

What mixture will you usually get, and why? racemic

reactions have the same Ea
same $\Delta H$
formed at the same rate
What could we do to favor one enantiomer over the other?

1) use an enantiomerically pure reagent

(hard to tell which way will be favored just by looking)

2) use an enantiomerically pure starting material with the stereocenter nearby

(less crowded one is favored)

What is this kind of reaction called, and why is it useful?

stereoselective reactions - useful for making enantiomerically pure compounds like pharmaceuticals!
Two new asymmetric carbons

When two new stereocenters are formed, how many stereoisomers can result?

4 are possible, but some reactions give only 2 (depends on the mechanism)

- **syn addition**
  
  \[ \text{syn addition} \quad \text{KMnO}_4 \quad \rightarrow \quad \text{H}_2\text{O} \quad \begin{array}{c}
  \text{new substituents on the same side} \\
  \text{1 pair of enantiomers} \\
  \text{or a meso compound}
  \end{array} \]

- **anti addition**
  
  \[ \text{anti addition} \quad \text{Br}_2 \quad \rightarrow \quad \begin{array}{c}
  \text{new substituents on opposite sides} \\
  \text{1 pair of enantiomers}
  \end{array} \]

- **nonselective**
  
  \[ \text{nonselective} \quad \text{HCl} \quad \rightarrow \quad \begin{array}{c}
  \text{all possible stereoisomers} \\
  \text{(2 pairs of enantiomers)}
  \end{array} \]

Can these reactions be stereoselective? yes!

use a chiral reagent or a chiral starting material

\[ \text{chiral reagent} \quad 98\% \quad 2\% \]