Organic Chem
Chapter 7:
Alkyl Halides: Nucleophilic Substitution & Elimination Reactions
What is chemotherapy…

Let’s read p. 271

Did you ever Wonder....
Ch 7.1
Topic: Introduction to Substitution and Elimination Reactions
EQ: How do halogens affect hydrocarbon reactions?

READ pg. 272 - 273 then take notes
• **Alkyl halides** — compounds in which a halogen (F, Cl, Br, or I) is connected to an $sp^3$ hybridized carbon atom.

- Undergo 2 types of reactions - **substitution** and elimination rxns
• Alkyl Halides can undergo a substitution reaction when reacted with a nucleophile.
• When treated with a nucleophile, an alkyl halide can undergo a substitution reaction, in which the nucleophile replaces the halogen.
• Alkyl Halides can undergo an **elimination reaction** when reacted with a **base**.
• When treated with a base, an alkyl halide can undergo an **elimination reaction**, in which a $\pi$ bond (an alkene) is formed:
• When the reagent can act as a nucleophile or a base, (such as −OH) elimination and substitution will be competing reaction pathways (seen below).

• For the remainder of the chapter we will use the term **substrate** to refer to the alkyl halide.
Two main reasons why alkyl halides undergo substitution and elimination reactions:

1. The halogen withdraws electron density via dipole moment, rendering the adjacent carbon atom electrophilic, and therefore subject to attack by a nucleophile.

![Diagram showing the withdrawal of electron density by a halogen atom, making the carbon atom electrophilic.](image)
2. The halogen can serve as a **leaving group**, and substitution/elimination processes can only occur when a leaving group is present. **Good leaving groups are the conjugate bases of strong acids.**

- For example, iodide (I\(^-\)) is the conjugate base of a very strong acid (HI).

  ![Chemical Reaction Diagram](image)

- Iodide is a very weak base, which makes it an excellent leaving group.
In contrast, hydroxide is a bad leaving group, because it is not a stabilized base.

In fact, hydroxide is a relatively strong base, and therefore, it rarely functions as a leaving group.

Table 7.1 shows a list of good leaving groups, all of which are the conjugate bases of strong acids.
### Table 7.1 The Acidity of Several Compounds and the Stability of Their Conjugate Bases

<table>
<thead>
<tr>
<th>Acid</th>
<th>pKₐ</th>
<th>Conjugate base</th>
</tr>
</thead>
<tbody>
<tr>
<td>I⁻H</td>
<td>-11</td>
<td>Most stable base</td>
</tr>
<tr>
<td>Br⁻H</td>
<td>-9</td>
<td>Br⁻</td>
</tr>
<tr>
<td>Cl⁻H</td>
<td>-7</td>
<td>Cl⁻</td>
</tr>
<tr>
<td>H₃C-[(\text{Ph}-\text{SO}-\text{SO}-\text{H})]⁻</td>
<td>-3</td>
<td><img src="image" alt="Ph-SO-SO-" /></td>
</tr>
<tr>
<td>F⁻H</td>
<td>3</td>
<td><img src="image" alt="F⁻" /></td>
</tr>
<tr>
<td>H₂O⁻H</td>
<td>15.7</td>
<td><img src="image" alt="H₂O⁻" /></td>
</tr>
<tr>
<td>CH₃O⁻H</td>
<td>16</td>
<td><img src="image" alt="CH₃O⁻" /></td>
</tr>
<tr>
<td>CH₂O⁻H</td>
<td>18</td>
<td><img src="image" alt="CH₂O⁻" /></td>
</tr>
</tbody>
</table>

**Strongest acid**

**Weakest acid**

**Best leaving group**

**Good leaving groups**

**Least stable base**

**Bad leaving groups**

**Worst leaving group**
Ch 7.2
Topic: Nomenclature and Uses of Alkyl Halide
EQ: How are alkyl halides named?
READ pg. 273-276 then take notes
In an alkyl halide, each carbon atom can be described in terms of its proximity to the halogen, using letters of the Greek alphabet.

The **alpha (α) position** is the carbon atom connected directly to the halogen, while the **beta (β) positions** are the carbon atoms connected to the α position.
An alkyl halide will have only one α position, but there can be as many as three β positions. Alkyl halides are classified as primary (1°), secondary (2°), or tertiary (3°) based on the number of alkyl groups connected to the α position.
Naming Alkyl Halides

- Alkyl halides are compounds where a carbon group (alkyl) is bonded to a halide (F, Cl, Br, or I)
- Recall from section 4.2 the (IUPAC) steps we use to name a molecule
  1. Identify and name the parent chain
  2. Identify the name of the substituents
  3. Assign a locant (number) to each substituents
  4. Assemble the name alphabetically
- The halide group is the key substituent we will name and locate
The same exact four-step procedure is used to name compounds that contain halogens, and all of the rules discussed in Chapter 4 apply here as well.

Halogens are simply treated as substituents and receive the following names: fluoro-, chloro-, bromo-, and iodo-.

2-Chloropropane  2-Bromo-2-methylpentane
When a chiral center is present in the compound, the configuration must be indicated at the beginning of the name: 

(R)-5-Bromo-2,3,3-trimethylheptane
Some simple molecules are also recognized by their common names.

- the alkyl group is named as the substituent, and the halide is treated as the parent name

Methylene chloride is a commonly used organic solvent
• The **systematic name** treats the halogen as a substituent, calling the compound a **haloalkane**.

• The **common name** treats the compound as an alkyl substituent connected to a halide, and the compound is called an **alkyl halide**, or more generally, an **organohalide**.
Uses of Organohalides

- Many organohalides are toxic and have been used as insecticides:
- Halides appear in a wide variety of natural products and synthetic compounds
- The structure of the molecule determines its function, and functions include…
  - Insecticides (DDT, etc.)
  - Dyes (tyrian purple, etc.)
  - Drugs (anticancer, antidepressants, antimicrobial, etc.)
  - Food additives (Splenda, etc.)
  - Many more
- Let's Read p. 275-276!!!
Ch 7.3

Topic: $S_N^2$ Reactions

EQ: What is the difference between a concerted and stepwise mechanism?

READ pg. 276-282 then take notes
In the 1930s, Christopher Ingold & Edward D. Hughes investigated substitution reactions to elucidate their mechanisms.

They proposed...

1) Two different mechanisms for nucleophilic substitution reactions: **concerted and stepwise**.

2) Each mechanism operates under specific set if conditions.
1. The **concerted mechanism** involves breaking of the bond to the leaving group and making of the bond to the nucleophile at the same time.
2. The **stepwise mechanism** the leaving groups leaves first, to give a carbocation intermediate, followed by nucleophilic attack.
• Both mechanisms involved *Nucleophilic attack* and *Loss of a leaving group* (focus on the timing though)

<table>
<thead>
<tr>
<th>Concerted mechanism</th>
<th>Stepwise mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both events happen simultaneously (they occurred in a <em>Concerted Fashion</em>)</td>
<td>Events occurs separately (they occurred in a <em>Stepwise Fashion</em>)</td>
</tr>
</tbody>
</table>

1) Leaving group gives an intermediate carbocation
2) Nucleophile attacks the carbocation in a separate step

(Covered in Ch 7.10)
Ingold and Hughes found that the rate of the reaction depends on the concentration of both the alkyl halide and the nucleophile. Doubling the concentration of alkyl halide causes the reaction rate to double. Doubling the concentration of nucleophile causes the reaction rate to double. These observations are consistent with a second order process that has the following equation:

\[
\text{Rate} = k \ [\text{alkyl halide}] \ [\text{nucleophile}]
\]
Ingold and Hughes concluded that the mechanism must exhibit a step in which the alkyl halide and nucleophile collide with each other.

Because the step involves two chemical entities, it is said to be bimolecular.

They came up with the term **$\text{S}_\text{n}2$** to refer to biomolecular nucleophilic substitution reaction:
• The experimental observations for $S_N^2$ reactions are consistent with a concerted process, involving both the nucleophile and the alkyl halide in a single step.
When the α position is a chiral center, a change in configuration is generally observed as illustrated in the following example:

- Reactants exhibits the R configuration ➔
- Products exhibit S configuration
Stereospecificity of $S_N2$ Reactions

- Reaction is said to proceed with **inversion of configuration**.
- This means that the **nucleophile can only attack from the back side** (side opposite of leaving group) and never from the front.

![Diagram of SN2 reaction showing back-side and front-side attack](image_url)
There are two ways to explain why the rxn proceeds through back-side attack:

1) Lone pairs of leaving group create regions of high e- density that block the front side of the substrate, forcing the nucleophile to only approach from the back.

2) According to MO theory, e- density flows from the HOMO of the nucleophile to the LUMO of the electrophile.
   - Lets look at the LUMO of methyl bromide (figure 7.3) to get a greater understanding.
The nucleophile attacks from the back-side

- Electron density repels the attacking nucleophile from the front-side
- Proper orbital overlap cannot occur with front-side attack because there is a node on the front-side of the LUMO
• The observed stereochemical outcome for an $S_{N2}$ process (inversion of configuration) is consistent with a concerted mechanism.

• The nucleophile attacks with simultaneous loss of the leaving group.

• This causes the chiral center to behave like an umbrella flipping in the wind:

• This reaction is said to be **stereospecific**, because the configuration of the product is dependent on the configuration of the starting material.
When \((R)-2\)-bromobutane is treated with sodium hydroxide (NaOH), a mixture of products is obtained. An \(S_N2\) process is responsible for generating one of the minor products, while the major product is generated via an elimination process, as will be discussed later in this chapter. Draw the \(S_N2\) product that is obtained when \((R)-2\)-bromobutane reacts with a hydroxide ion.

**SOLUTION**

First draw the reagents described in the problem statement:

\[
\begin{align*}
\text{(R)-2-Bromobutane} & \quad + \quad \text{Hydroxide} \\
\end{align*}
\]

Now identify the nucleophile and the substrate. \((R)-2\)-Bromobutane is the substrate, and hydroxide is the nucleophile. When hydroxide attacks, it will eject the bromide ion as a leaving group. The net result is that Br will be replaced with OH. In this case, the \(\alpha\) position is a chiral center, so we expect inversion of configuration:
Effect of Substrate Structure on the Rate of an S\textsubscript{N}2 Process

- Rate of S\textsubscript{N}2 process is extremely sensitive to the nature of the starting alkyl halide.
- Alkyl groups branching from the \(\alpha\) and \(\beta\) carbons hinder the backside attack of the nucleophile, resulting in a slower rate of reaction.
- When comparing the relative rates in Table 7.2 (which compares the relative rates of reaction for a series of alkyl bromides) the following tend to emerge:

\begin{table}[h]
\centering
\begin{tabular}{|c|c|}
\hline
\textbf{Effect of }\(\alpha\)-\textbf{Substituents} & \textbf{Effect of }\(\beta\)-\textbf{Substituents} \\
\hline
\textbf{Structure} & \textbf{Relative rate}\textsuperscript{*} & \textbf{Structure} & \textbf{Relative rate}\textsuperscript{*} \\
\hline
\(\text{H}_3\text{C}\text{Br}\) & 145 & \(\text{Br}\) & 1 \\
\hline
\(\text{Br}\) & 1 & \(\text{Br}\) & 0.8 \\
\hline
\(\text{Br}\) & 0.008 & \(\text{Br}\) & 0.04 \\
\hline
\(\text{Negligible}\) & & \(\text{Negligible}\) & 0.00001 \\
\hline
\end{tabular}
\caption{Effect of Substituents on the Rates of S\textsubscript{N}2 Reactions}
\end{table}

*All rates are relative to the rate of reaction between ethyl bromide and iodide in acetone at 25\textdegree C.
1. Rate of $S_N2$ is most sensitive to the number of substituents at the $\alpha$ position.

Look at table for trends (Read only)

- Methyl bromide is one hundred times more reactive than ethyl bromide (a primary alkyl halide)
- Ethyl bromide is one hundred times more reactive isopropyl bromide (a secondary alkyl halide)
- $t$-butyl bromide (a tertiary alkyl halide) is unreactive towards $S_N2$
• These observations indicate that $S_{N2}$ reactions are most effective for methyl halides and primary alkyl halides (not with tertiary alkyl halides)

![Diagram showing reactivity of alkyl halides](attachment:image.png)

- Methyl
- $1^\circ$ halide
- $2^\circ$ halide
- $3^\circ$ halide

$H_3C - X$
2. Rate of $\text{SN}_2$ reaction is sensitive to substituents at the $\beta$ position, but not as sensitive as the $\alpha$ position

- Three substituents in the $\beta$ position causes the $\text{SN}_2$ reaction to significantly reduce that it is too slow for any practical use (two substituents at the $\beta$ position would cause the rate to moderately reduce)

- $\text{SN}_2$ reaction WILL NOT occur if there are three substituents at either $\alpha$ or $\beta$
To understand the nature of the steric effects that govern $S_N2$ reactions, we must explore the transition state for a typical $S_N2$ reaction, shown here in general form.

- Dotted lines represent bonds in the process of breaking/forming
- The double-dagger symbol (outside the brackets) indicates that the drawing is a transition state (not an intermediate)
  - Recall that a transition state is the peak (maximum) of an energy diagram
AP Review

• Highest point on the curve represents transition state

• If transition state is high in energy → activation energy \((E_a)\) will be large and rate will be slow

• If transition state is low in energy → activation energy \((E_a)\) will be small and rate will be fast
• Take a close look at the transition state. The nucleophile is in the process of forming a bond with the alkyl halide, and the leaving group is in the process of breaking its bond. Notice that there is a partial negative charge on either side of the transition state.

• Nucleophile is in the process of forming a bond (with the alkyl halide) and breaking a bond
If the hydrogen atoms are replaced with alkyl groups, steric interactions cause the transition state to be even higher in energy, raising $E_a$ for the reaction.

Compare the relative energy diagrams for reactions involving methyl, primary, and secondary alkyl halides.

Which reaction will have the fastest rate of reaction?
• For a methyl halide, $E_a$ is relatively small, and the reaction is **rapid**.
• In contrast, $E_a$ for the reaction of a secondary alkyl halide is relatively high, and the reaction is slower.
• With a tertiary alkyl halide, there are three substituents connected to the $\alpha$ position, and the $S_{N2}$ transition state is so high in energy that the reaction occurs **too slowly** to be observed.
7.2 Drawing the transition state of an S_n2 process

LEARN the skill

Draw the transition state of the following reaction:

\[ \text{Cl} \xrightarrow{\text{NaSH}} \text{SH} + \text{NaCl} \]

SOLUTION

First identify the nucleophile and the leaving group. These are the two groups that will be on either side of the transition state:

STEP 1
Identify the nucleophile and the leaving group.

Nucleophile: \( \text{SH} \)
Leaving group: \( \text{Cl} \)
The transition state will need to show a bond forming with the nucleophile and a bond breaking with the leaving group. Dotted lines are used to show the bonds that are breaking or forming:

**STEP 2**

Draw the carbon atom with the Nuc and LG on either side.

Notice that a $\delta^-$ symbol is placed on both the incoming nucleophile and the outgoing leaving group to indicate that the negative charge is spread out over both locations. Now we must draw all of the alkyl groups connected to the $\alpha$ position. In our example, the $\alpha$ position has one CH$_3$ group and two H's:
So we draw these groups in the transition state connected to the \( \alpha \) position. One group is placed on a straight line, and the other two groups are placed on a wedge and on a dash. It does not matter whether the CH\(_3\) group is placed on the line, wedge, or dash. But don't forget to indicate that the drawing is a transition state by surrounding it with brackets and using the double-dagger symbol that indicates a transition state.

**STEP 3**

Draw the three groups attached to the carbon atom, draw brackets around the structure, and draw the double-dagger symbol indicating a transition state.
Ch 7.4
Topic: Nucleophilic Strength & Solvent Effects in S\textsubscript{N}2 Reactions?

EQ: Can nucleophiles affect the rate of reaction?

READ pg. 285-287 then take notes
Nucleophilicity

- **Nucleophilicity** – refers to the rate at which a nucleophile will attack a suitable electrophile.
- A **strong** nucleophile will give a relatively **fast** $S_N$2 reaction, while a **weak** nucleophile will give a relatively **slow** reaction.
- For this reason, a **strong nucleophile** is generally required in order for an $S_N$2 reaction to be efficient and practical.
- FYI - Be able to recognize a given nucleophile as being strong or weak.
There are many factors that contribute to nucleophilicity, as first described in Section 6.7. One such factor is the presence of a charge, which can be illustrated by comparing hydroxide ($OH^-$) and water ($H_2O$).

- Hydroxide has a negative charge, and is therefore a strong nucleophile.
- In contrast, water lacks a charge and is a weak nucleophile.
- Indeed, hydroxide is over a million times more reactive than water toward an $S_N2$ reaction with methyl iodide:

```
\[ \text{Strong nucleophile} \quad \text{Fast} \quad \text{Weak nucleophile} \]
```

```
\[ \text{Strong nucleophile} \quad \text{Very slow} \quad \text{Weak nucleophile} \]
```
Another factor that impacts nucleophilicity is **polarizability**, which is often even **more** important than charge.

**Polarizability is directly related to the size of the atom** and, more specifically, to the **number of electrons** that are distant from the nucleus.

The following is a list of some commonly encountered nucleophiles:

<table>
<thead>
<tr>
<th>Strong nucleophiles</th>
<th>Weak nucleophiles</th>
</tr>
</thead>
<tbody>
<tr>
<td>I⁻, Br⁻, Cl⁻, HS⁻, HO⁻, N≡C⁻</td>
<td>H₂O, ROH</td>
</tr>
</tbody>
</table>
• In general, anions are strong nucleophiles
• *Polarizable* atoms are good nucleophiles
• Notice that many of the halides are present on the list, but fluoride is absent. Why?
  • Fluoride can behave as a weak nucleophile or as a strong nucleophile, *depending on the identity of the solvent*
• The nucleophilicity of fluoride is an excellent illustration of the *impact that the solvent can have on a rate of an* $S_N 2$ *process*
Solvent Effects in $S_N2$ Reactions

- For $S_N2$ reactions, the nucleophile is generally ionic, as is the leaving group, so a polar solvent is required in order to solvate these ionic species.
- The transition state also has ionic character, so a polar solvent helps stabilize the transition state as well.
- Polar solvents are broadly classified into two categories: protic and aprotic.
  - **Protic solvents** – contain a hydrogen atom connected directly to an electronegative atom (engage in H-bonding).
  - **Polar aprotic solvents** – lack such a hydrogen atom.
Need a **polar aprotic** solvent for $S_N2$ rxns

<table>
<thead>
<tr>
<th>Protic solvents</th>
<th>Polar aprotic solvents</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-O-H</td>
<td>O</td>
</tr>
<tr>
<td>Water</td>
<td>Acetone</td>
</tr>
<tr>
<td>CH₃O─H</td>
<td>H─N─O</td>
</tr>
<tr>
<td>Methanol</td>
<td>Dimethylformamide (DMF)</td>
</tr>
<tr>
<td>O─H</td>
<td>N─P</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Hexamethylphosphoramide (HMPA)</td>
</tr>
<tr>
<td>H─N─H</td>
<td>O─C─N</td>
</tr>
<tr>
<td>Ammonia</td>
<td>Acetonitrile</td>
</tr>
<tr>
<td>H─C─O</td>
<td>H₃C─C≡N</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>Acetone</td>
</tr>
</tbody>
</table>

- Aprotic solvents also have hydrogen atoms, but none of those hydrogen atoms are connected to an electronegative atom
- $S_N2$ reactions are generally **much faster** when performed in **polar aprotic solvents**, rather than protic solvents
• When NaCl is dissolved in a protic solvent, such as water, both the $Na^+$ and the $Cl^-$ ions are well solvated.

• Protic solvents have electronegative atoms with lone pairs (in this case oxygen) that can stabilize $Na^+$ ions, and protic solvents also have the ability to form hydrogen bonds with $Cl^-$ ions, thereby stabilizing them as well.

• In contrast, a polar aprotic solvent can only stabilize the cations, not the anions.
For example, dimethylsulfoxide (DMSO) can stabilize the $Na^+$ ions, but it lacks the ability to stabilize the $Cl^-$ ions via hydrogen bonds. DMSO is not a protic solvent, and the region of $\delta^+$ is sterically inaccessible, so anions are not stabilized.

In DMSO, the electron-poor region is located at the center of the compound, surrounded by lone pairs and methyl groups.

For steric reasons, this electron-poor region is relatively inaccessible to an anion dissolved in the solvent, so anions are not stabilized by the solvent.
In conclusion:

- The result is that nucleophiles are less stabilized (higher in energy) when placed in a polar aprotic solvent.
- Polar aprotic solvents enhance the rate of an $S_N 2$ process by raising the energy of the nucleophile, giving a smaller $E_a$ (faster rxn).

Aprotic solvents are best for $S_N 2$ reactions.
Ch 7.5
Topic: \( \text{S}_2 \text{N} \) Reactions in Biological System: Methylation

EQ: How can methyl groups be transferred in \( \text{S}_{\text{N}2} \) rxns?

READ pg. 287-288 then take notes
In the laboratory, the transfer of a methyl group can be accomplished via an \( S_N2 \) process using methyl iodide:

This process is called **alkylation**, because an alkyl group has been transferred to the nucleophile.

It is an \( S_N2 \) process, which means there are limitations on the type of alkyl group that can be used.
• Tertiary alkyl groups cannot be transferred.
• Secondary alkyl groups can be transferred, but slowly.
• Primary alkyl groups and methyl groups are transferred most readily.
• The alkylation process shown above is the transfer of a methyl group and is therefore called **methylation**.
• Halides are common leaving groups for laboratory use, but are not common substrates in biological $S_N2$ reactions.

• Both of these compounds are good *methylating* reagents: a good nucleophile will attack the CH$_3$ via an $S_N2$ mechanism.
Ch 7.6
Topic: Introduction to E2 Reactions
EQ: How does E2 rxns differ from $\text{S}_{\text{N}}\text{2}$ rxns?

READ pg. 289-290 then take notes
At the beginning of this chapter, we noted that alkyl halides can undergo substitution as well as elimination reactions.

- **Elimination reactions** involve the use of bases, rather than nucleophiles, so we must quickly review some differences between strong bases and weak bases.

- For **anionic bases** (bearing a negative charge), a weak base is a stabilized base, and a strong base is an unstable base.

- In **Chapter 3**, we saw several factors (**ARIO**) that can stabilize an anionic base.

- We also saw an inverse relationship between the strength of a base and the strength of its conjugate acid.

- For example, iodide ($I^-$) is a very weak base, and its conjugate acid (HI) is a very strong acid.

- Another example, hydroxide ($\text{HO}^-$) is a strong base, and its conjugate acid ($\text{H}_2\text{O}$) is a weak acid.
When treated with a strong base, an alkyl halide can undergo a type of elimination process, called **beta elimination**, also known as **1,2-elimination**

- A proton is removed from the β position
- The halide is ejected as a leaving group ($X^-$) from the α position
- A double bond is formed between the α and β positions:
When an alkyl halide undergoes a beta elimination reaction, the process is also called a dehydrohalogenation, because H and X are removed from the substrate.

- In this chapter, we will explore two different mechanisms for beta elimination reactions, and we will see that each mechanism operates under a specific set of conditions.
These two mechanisms are shown here.

- Both mechanisms involve **proton transfer and loss of a leaving group**, but consider the **timing** of these events

1. **Concerted Mechanism** - both events occur **simultaneously**

- A **strong base** will react in a concerted mechanism, called an **E2 elimination**.

A concerted mechanism
2. **Stepwise Mechanism** - they occur *separately*

- First the leaving group leaves to give an intermediate carbocation, and then a proton is transferred in a separate step (more to come in 7.10 for stepwise process)
• When an alkyl halide is treated with a strong base, the rate of reaction is generally found to be dependent on the concentrations of both the alkyl halide and the base.

• Specifically, doubling the concentration of the alkyl halide causes the reaction rate to double, and similarly, doubling the concentrations of the base also causes the rate to double.

• These observations are consistent with a second-order process that has the following rate equation:

\[ \text{Rate} = k[\text{alkyl halide}][\text{base}] \]
Based on these observations, we conclude that the mechanism must exhibit a step in which the alkyl halide and the base collide with each other.

Because that step involves two chemical entities, it is said to be bimolecular.

Bimolecular reactions are called E2 reactions:

The experimental observations for E2 reactions are consistent with a concerted process, involving both the base and the alkyl halide in a single step (Mechanism 7.2).

If the observations had been otherwise, a concerted mechanism could not have been proposed.
Effect of Substrate Structure on the Rate of a E2 Process

- In Section 7.4, we saw that the rate of an $S_N2$ process with a tertiary alkyl halide is generally so slow that it can be assumed that the alkyl halide is inert under such reaction conditions.
- It might therefore come as a surprise that tertiary alkyl halides undergo E2 reactions quite rapidly.
- This is due to the difference in role played by the reagent in both substitution and elimination.
- A substitution reaction occurs when the reagent functions as a nucleophile and attacks the α position, while an elimination reaction occurs when the reagent functions as a base and abstracts a proton from a β position.
• With a tertiary substrate, steric hindrance prevents the reagent from functioning as a nucleophile at an appreciable rate, but the reagent can still function as a base without encountering much steric hindrance.

• Consider a reagent such as NaOH, which is a strong nucleophile ($S_{N2}$) and a strong base ($E2$)…

when the **substrate is sterically hindered, E2 elimination will occur.**
Ch 7.7
Topic: Nomenclature and Stability of Alkenes

EQ: What are the rules for naming alkenes?

READ pg. 291-294 then take notes
Nonnomenclature of Alkenes

Alkenes are given IUPAC names using the same procedure to name alkanes, with minor modifications

1. Identify the parent chain, which includes the C=C double bond
2. Identify and Name the substituents
3. Assign a locant (and prefix if necessary) to each substituent. Give the C=C double bond the lowest number possible
4. List the numbered substituents before the parent name in alphabetical order. Ignore prefixes (except iso) when ordering alphabetically
5. The C=C double bond locant is placed either just before the parent name or just before the -ene suffix
1. Identify the parent chain, which should include the C=C double bond
   - The name of the parent chain should end in -ene rather than -ane

   - The parent chain should include the C=C double bond

   ![Diagram](image1.png)
   - Parent = octane
   - Parent = heptene
2. Identify and Name the substituents
3. Assign a locant (and prefix if necessary) to each substituent. **Give the C=C double bond the lowest number possible**

- The locant of the double bond is a single number, and is the number indicating where the double bond **starts**. The alkene above is located at the “2” carbon (not 3).
4. List the numbered substituents before the parent name in alphabetical order. Ignore prefixes (except iso) when ordering alphabetically.

5. The C=C double bond locant is placed either just before the parent name or just before the -ene suffix.

Note: This alkene has the E configuration, which must be indicated in the name, in parentheses: \((E)-5,5,6\text{-trimethylhept-2-ene}\)
Recall how to assign $E$ or $Z$ to alkene stereoisomers…

- First, prioritize the groups attached to the C=C double bond *based on atomic number*.
• If the top priority groups are cis to each other, it is the \textit{Z} isomer
• If the top priority groups are trans to each other, it is the \textit{E} isomer

IUPAC nomenclature recognizes \underline{common names} for the \underline{following groups} when they appear as substituents in a compound:
Stability of Alkenes

- Because of steric strain, \textit{cis} isomers are generally less stable than \textit{trans}

- The difference in stability can be quantified by comparing the heats of combustion (small difference but it is different)

\[
\begin{align*}
\text{cis-2-Butene} & \quad + \quad 6 \text{ O}_2 & \quad \rightarrow & \quad 4 \text{ CO}_2 & \quad + & \quad 4 \text{ H}_2\text{O} & \quad \Delta H^\circ = -2682 \text{ kJ/mol} \\
\text{trans-2-Butene} & \quad + \quad 6 \text{ O}_2 & \quad \rightarrow & \quad 4 \text{ CO}_2 & \quad + & \quad 4 \text{ H}_2\text{O} & \quad \Delta H^\circ = -2686 \text{ kJ/mol}
\end{align*}
\]
- Alkyl groups stabilize the C=C pi bond via hyperconjugation (donating electron density to neighboring sp\(^2\)-hybridized carbon atoms).

More alkyl groups = more highly substituted = more stable alkene
Stability of Cycloalkenes

- Cycloalkenes comprised of fewer than seven carbon atoms cannot accommodate a *trans* π bond. These rings can only accommodate a π bond in a *cis* configuration:

![Cycloalkenes](image)

- So we do not need to indicate if the alkene is *cis* or *trans* unless the ring contains 8 carbons or more
- An eight-membered ring is the smallest ring that can accommodate a *trans* double bond and be stable at room temperature
• This rule also applies to bridged bicyclic compounds and is called **Bredt’s rule**.
  
  • Bredt’s rule states that it is not possible for a bridgehead carbon of a bicyclic system to possess a C=C double bond if it involves a *trans* $\pi$ bond being incorporated in a small ring.
  
  • For example, the following compound is too unstable to form:
• This compound would require a *trans* double bond in a six-membered ring, highlighted in red.
• The compound is not stable because the geometry of the bridgehead prevents it from maintaining the parallel overlap of *p* orbitals necessary to keep the *π* bonding intact.
• As a result, this type of compound is extremely high in energy, and its existence is fleeting.
• Bridged bicyclic compounds can only exhibit a double bond at a bridgehead position if one of the rings has at least eight carbon atoms.

This compound is stable.
• DON’T GO ON…Im not finished 😞
Ch 7.8
Topic: Regiochemical & Stereochemical Outcomes for E2 Reactions

EQ:
READ pg. 295-303 then take notes
Ch 7.9
Topic: EQ:
READ pg. 305-314 then take notes