Introduction to Alkyl Halides

- Organohalogens are compounds that contain halogens as their main functional group
- The three major classes of organohalogens
  - Alkyl halide: Halogen attached to sp³ hybridized carbon
  - Vinyl halide: Halogen attached to sp² hybridized carbon
  - Aryl halide: Halogen attached to sp² hybridized carbon on benzene ring
- Examples

Nomenclature

- The rules that apply to alkanes still apply to alkyl halides
  1. Find the longest continuous chain, this is the parent chain
  2. Locate all branch points
  3. Number the chain so that all substituents, alkyl or halide, get lowest possible location number
  4. If the parent chain can be numbered the same way from either end, begin at the end with the halogen
  5. Halogen substituents are named fluoro, chloro, bromo, or iodo
  6. If more than one halogen of the same type is present, use di, tri, tetra, etc.

Examples

- The longest continuous chain is 5, pentane
- Number from the end closest to the Br, this gives lowest set of location numbers
- Name substituents in alphabetical order
- The correct name is 2-Bromo-3-chloro-3-ethyl-2-methylpentane
Examples

• The longest continuous chain is 6, hexane is the parent chain
• The location numbers are the same from either end of the molecule, so start from the end nearest the Br
• Name the substituents in alphabetical order
• The correct name is 2-Bromo-5-methylhexane

![Chemical Structures]

Boiling Points of Alkyl Halides

• Alkyl halides have higher boiling points than the corresponding alkanes
• The major reason for this is the dipole moments due to C-X bond

\[ \text{δ⁺} \quad \text{δ⁻} \quad \text{δ⁺} \quad \text{δ⁻} \]

• Within the alkyl halide family, bp also depends on molecular weight and van der Waals forces
• As the halogen atoms get larger, the outer electrons are not held as tightly
• It becomes easier to polarize the atom
• The easier it is to polarize charge, the more effective van der Waals forces become
• This causes higher boiling points as you go from F to I

Boiling Points of Alkyl Halides

<table>
<thead>
<tr>
<th>R-X</th>
<th>X=H</th>
<th>X=F</th>
<th>X=Cl</th>
<th>X=Br</th>
<th>X=I</th>
</tr>
</thead>
<tbody>
<tr>
<td>-CH₃</td>
<td>-161.7°C</td>
<td>-78.4°C</td>
<td>-24.2°C</td>
<td>3.6°C</td>
<td>42.4°C</td>
</tr>
<tr>
<td>-CH₂CH₃</td>
<td>-88.6°C</td>
<td>-37.7°C</td>
<td>12.3°C</td>
<td>38.4°C</td>
<td>72.3°C</td>
</tr>
<tr>
<td>-CH₂CH₂CH₃</td>
<td>-42.1°C</td>
<td>-2.5°C</td>
<td>46.6°C</td>
<td>71.0°C</td>
<td>102.5°C</td>
</tr>
</tbody>
</table>
Bond Strength of Alkyl Halides

- The bond between C and X (halide) is made up of overlap between sp³ hybrid orbital and a p orbital
- As you go from F to I, the size of the p orbital increases, electron cloud becomes more diffuse
- Overlap in C-X bond diminishes
- Bond strength decreases

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>CH₃F</td>
<td>1.385Å</td>
<td>110 kcal/mol</td>
</tr>
<tr>
<td>CH₃Cl</td>
<td>1.784Å</td>
<td>85 kcal/mol</td>
</tr>
<tr>
<td>CH₃Br</td>
<td>1.929Å</td>
<td>71 kcal/mol</td>
</tr>
<tr>
<td>CH₃I</td>
<td>2.139Å</td>
<td>57 kcal/mol</td>
</tr>
</tbody>
</table>

Bond Polarity of Alkyl Halides

- Bond polarity depends on charge and distance
  \[ \mu = 4.8 \times \delta \times d \]
- Electronegativity decreases down the group
- Bond length increases down the group
- Dipole moment follows the trend shown
  - C-I, \( \mu = 1.29 \) D
  - C-Br, \( \mu = 1.48 \) D
  - C-F, \( \mu = 1.51 \) D
  - C-Cl, \( \mu = 1.56 \) D

Preparation of Alkyl Halides

- We have discussed several ways to synthesize alkyl halides
  - Addition of HX to alkenes
  - Addition of X₂ to alkenes
  - Radical halogenation of alkanes
- While the degree of selectivity is large for the first two methods, selectivity is poor in radical halogenation
- Alkyl halides can also be prepared from alcohols
Free-Radical Preparation of Alkyl Halides

- Not a good way to prepare alkyl halides in the lab
  - Too many different sites for monohalogenation
  - High probability of multiple halogenation in one molecule
- Example
  \[
  \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 + \text{Cl}_2 \xrightarrow{hv} 2 \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}
  \]
  - Mainly used for industrial preparation of alkyl halides
  - Bromination much more selective than chlorination

Chlorination of Propane

- Why so many monochlorinated products?
  - This occurs because the 8 hydrogens in propane fall into two groups
  - 6 hydrogens are primary (1°) and 2 hydrogens are (2°)
  \[
  \text{CH}_3\text{CH}_2\text{CH}_3 \xrightarrow{\text{Cl}_2} \text{1°} \quad \text{2°} \quad \text{1°}
  \]
  - The statistical product distribution should be 6:2 or 3:1
  - 75% should be 1-chloropropane and 25% should be 2-chloropropane
  - The actual product distribution is 40% 1-chloropropane and 60% 2-chloropropane
  - This says that 2° hydrogens react 4.5 x faster than 1° hydrogens

Chlorination of 2-methylpropane

- Like propane, 2-methylpropane yields two monochlorinated products
- Again, there are two types of hydrogens, primary (1°) and tertiary (3°)
  \[
  \text{CH}_3\text{C(CH}_3\text{)}\text{CH}_3 \xrightarrow{\text{Cl}_2} 3° \quad 1°
  \]
  - 9 hydrogens are 1° and 1 hydrogen is 3°
  - The statistical product distribution should be 90% 1-chloro-2-methylpropane and 10% 2-chloro-2-methylpropane
  - Actual is 68% 1-chloro-2-methylpropane and 32% 2-chloro-2-methylpropane
  - This means that 3° hydrogens react 5.1 x faster than 1° hydrogens
Free Radical Stability

- From the experimental data, 3°>2°>1°=methyl
- Why should this be?
- The energy necessary to break the C-H bond must decrease from 3° to methyl.

<table>
<thead>
<tr>
<th>Type of Bond</th>
<th>RPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃-H</td>
<td>104 kcal/mol</td>
</tr>
<tr>
<td>CH₃CH₂H</td>
<td>98 kcal/mol</td>
</tr>
<tr>
<td>CH₃CH₂CH₂-H</td>
<td>95 kcal/mol</td>
</tr>
<tr>
<td>CH₃CH₂CH₂H</td>
<td>91 kcal/mol</td>
</tr>
</tbody>
</table>

- The major reason is due to the fact that more substitution, more electron density around radical, higher stability of radical.

Problem

- Given the fact that the relative reactivities of 3°:2°:1° are 5.1:4:5.1, predict the % of each monochlorinated product for 2-methylbutane.

Bromination of Propane

- Is the energy diagram and product distribution identical for the reaction of Br₂ or Cl₂ with propane?
- NO! When Br₂ reacts with propane, two monobrominated products are formed.
- But, 97% of the product is 2-bromopropane and 1% is 1-bromopropane.
- The chlorination yields 40% of 1-chloropropane and 60% of 2-chloropropane.
- The data from bromination says that 2° hydrogens react 97x faster than 1° hydrogens.
- This means that bromination of propane is more selective than chlorination.
- Why?
Comparison of Br₂ vs Cl₂

- In both cases, the first propagation step is rate determining.
- But, the first step for Cl₂ has a smaller $E_a$ and is exothermic.
- The first propagation step for Br₂ has a larger $E_a$ and is endothermic.
- In the case of Cl₂, the energy of the starting materials are closer in energy to the transition state than products.
- In the case of Br₂, the opposite is true, the energy difference between starting materials and the transition state is great, the transition state is closer in energy to the products.

Comparison of Energy Diagrams
Hammond Postulate

- When a reaction is endothermic, the products are higher in energy than the reactants, transition state looks more like products.
- When reaction is exothermic, products are lower in energy than reactants, transition state looks more like reactants.
- Reactions with late transition states tend to be more selective.

Comparison of Transition States

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<table>
<thead>
<tr>
<th>Reaction</th>
<th>Products</th>
<th>Transition State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl₂ → Br₂ (hv)</td>
<td>92.2% Cl₂, 7.38% Br₂, 0.28% Cl₂, 0.14% Br₂</td>
<td>Close in structure, close in energy.</td>
</tr>
<tr>
<td>Cl₂ → Cl₂ (hv)</td>
<td>22% Cl₂, 33% Cl₂, 30% Cl₂, 15% Cl₂</td>
<td>Close in structure, close in energy.</td>
</tr>
</tbody>
</table>
```

Compare Br vs Cl Reaction with Isopentane
Preparing Alkyl Halides from Alcohols

- The most common laboratory method for preparing alkyl halides is from alcohols
- Alkyl halides may be prepared from 1°, 2°, and 3° alcohols
- However, different methods are needed for preparing each type of alcohol

\[
\begin{align*}
RCH_2OH & \rightarrow R\text{CH}_2\text{Br} \\
RCH_2OH & \rightarrow R\text{CH}_2\text{Cl} \\
R\text{COH} & \rightarrow R\text{COCl}
\end{align*}
\]

Alkyl Halides from 3° Alcohols

- 3° alkyl halides can be made readily from 3° alcohols by reaction with HBr or HCl
- The reaction proceeds through a cation intermediate

\[
\begin{align*}
\text{H}_3\text{C} & \text{OH} \overset{\text{HCl (g)}, \text{Ether}, \text{0°C}}{\rightarrow} \text{H}_3\text{C} \text{Cl} + \text{H}_2\text{C} \\
1\text{-Methylcyclohexanol} & \rightarrow 1\text{-Chloro}-1\text{-methylcyclohexane (80%)}
\end{align*}
\]

Alkyl Halides from 1° and 2° Alcohols

- Addition of HBr and HCl to 1° and 2° alcohols is slow and yields are generally poor
- For this reason, these alcohols are treated with either SOCl₂ or PBr₃

\[
\begin{align*}
\text{Benzoin} & \overset{\text{SOCl}_2, \text{Pyridine}}{\rightarrow} \text{2-Benzoyl chloride (80%)} \\
3\text{CH}_2\text{CH}_2\text{CH}_3 & \overset{\text{PBr}_3, \text{Ether}, \text{85°C}}{\rightarrow} 3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{H}_3\text{PO}_4 \\
2\text{-Butanol} & \overset{\text{PBr}_3, \text{Ether}, \text{85°C}}{\rightarrow} 2\text{-Bromobutane (80%)}
\end{align*}
\]
Allylic Free-Radical Preparation of Alkyl Halides

- More selective than halogenation of an alkane
- Mechanism is the same as normal halogenation

Initiation step

\[ \text{Br}_2 \xrightarrow{hv} 2 \text{Br}^- \]

Propagation step 1

\[ \text{CH}_2=\text{CHCH}_2^- + \text{Br}^- \rightarrow \text{CH}_2\text{CH}^-\text{CH}_2 + \text{HBr} \]

Propagation step 2

\[ \text{BrCH}_2\text{CH}^-\text{CH}_2 + \text{Br}^- \rightarrow \text{BrCH}_2\text{CH}^-\text{CH}_2 + \text{Br}^- \]

Allylic radical more stable than 3o radical

Reactivity of Allylic Radicals

Allylic radical very stable due to resonance

Resonance Stability of Allylic Radical
Allylic Bromination with NBS

- While Br₂ can be used in the presence of light to generate Br radicals, it is hard to handle
- Br₂ is rarely used for allylic bromination since the C=C can also be attacked
- N-Bromosuccinimide or NBS is more commonly used in allylic brominations
- NBS provides a low, steady amount of Br₂
- Typically a nonpolar solvent such as CCl₄ is used
- It also uses up the HBr which is generated during the course of the reaction

Reactions of Alkyl Halides

- Alkyl halides undergo substitution reactions with nucleophiles (Chapter 11)
- Alkyl halides undergo elimination reactions with base to form alkenes (Chapter 11)
- Alkyl halides can form a variety of organometallic reagents
  - Grignard reagents
  - Lithium dialkylcopper reagents
Grignard Reagents

- Preparation
  \[ R-X + Mg \rightarrow \text{Anhydrous conditions} \]
  \[ \delta^- \rightarrow \delta^2 \rightarrow \delta^- \]
  \[ R-Mg \rightarrow X \]
  \[ X = \text{Cl, Br, I} \]

- The use of a Lewis base for the solvent such as diethyl ether both stabilizes and solubilizes the Grignard Reagent

\[
\begin{align*}
\text{H}_3\text{C}_{\text{CH}} & \text{CH}_2 \quad \text{H}_3\text{C}_{\text{CH}} \\
\delta^- & \delta^2 \delta^- \\
\text{R} & \text{Mg} \rightarrow \text{X} \\
\text{H}_3\text{C}_{\text{CH}} & \text{CH}_2
\end{align*}
\]

Grignard Reagents as Nucleophiles and Bases

- The alkyl metal bond is very polar
- The C-Mg bond has 35% ionic character
- This makes the Grignard Reagent a very good nucleophile
- However, it is also extremely basic

\[
\begin{align*}
\delta^- & \delta^2 \delta^- \\
\text{R} & \text{Mg} \rightarrow \text{X} + \text{H-DH} \\
\text{R-H} & \rightarrow \text{MgOHX}
\end{align*}
\]

- For this reason, Grignard reactions must be carried out in the absence of water or acidic hydrogens
- Groups such as RC=CH, RNH2, RCOOH, RSH, or ROH contain acidic hydrogens

Lithium Dialkylcopper Reagents

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} & \rightarrow \text{Li} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{Li} + \text{LiBr} \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{Li} & \rightarrow \text{Li} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{Cu} + \text{Li} \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{Li} & + \text{CH}_3\text{CH}_2\text{CH}_2\text{Cu} \rightarrow \text{Li} \rightarrow \text{1,1,1,1-Tetralkyl-2,2'-} & \text{L}_2 \\
\left[ \text{CH}_3\text{CH}_2\text{CH}_2\text{Cu} \right] \text{L}_2 & + \text{CH}_3\text{CH}_2\text{Li} \rightarrow \text{Li} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{Cu} + \text{Li}
\end{align*}
\]
Lithium Dialkylcopper Reagents

- Methyl and primary alkyl halides work best when preparing the lithium dialkyl cuprate
- Steric hinderance can cause cuprates formed from secondary and tertiary alkyl halides to react slowly and decompose
- The dialkyl cuprate reacts best with methyl or primary alkyl halides
- The dialkyl cuprate react fastest with iodides and slowest with fluorides
- Dialkyl cuprates will react with aromatic and vinyl halides

Examples

```
\[ \text{n-C}_3\text{H}_7\text{H} + \text{n-C}_3\text{H}_7\text{CuLi} \rightarrow \text{n-C}_3\text{H}_7\text{H} + \text{n-C}_3\text{H}_7\text{Cu} + \text{LiI} \]
```

```
\text{trans-1-Iodo-1-methene} + \text{CH}_2\text{CuLi} \rightarrow \text{trans-5-Tridecene (T1\%)}
```

```
\text{Indanene} + \text{CH}_2\text{CuLi} \rightarrow \text{Toluene (91\%)}
```

Synthesis

Complete the following syntheses:

```
\[ \text{\_} \rightarrow \text{\_} \]
```

```
\[ \text{\_} \rightarrow \text{\_} \]
```

```
\[ \text{\_} \rightarrow \text{\_} \]
```