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The Preparation of Alkyl Halides through $S_{N1}$ and $S_{N2}$ Reactions

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Organic Chemistry I

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**Introduction:**

The preparation of alkyl halides is done mainly through substitution reactions, specifically, $S_N1$ and $S_N2$ reactions. These two reactions were discovered by Edward Hughes and Christopher Ingold in 1935. Hughes and Ingold discovered that both reactions have different processes and limitations. $S_N2$ reactions occur in one step, and is dependent on two molecules coming together. The nucleophile – an electron heavy element that easily reacts with a partial positive charge – forms a bond to the substrate at the same time the leaving group – an element of substrate that leaves the reaction – leaves (Hughes and Ingold, 1935). $S_N2$ occurs in one step, and both the nucleophile and substrate are involved in the rate determining step; therefore, the rate is dependent on both the concentration of substrate and that of the nucleophile (Phan, Nolte, Kobayashi, Ofial, & Mayr, 2009). The process of $S_N2$ reactions is shown in Figure 1, and the rate equation is shown by Equation 1.

![Figure 1](image)

Figure 1 depicts the nucleophilic attack, along with the leaving group exiting

\[
\text{Rate} = k[\text{Substrate}][\text{Nucleophile}] \quad \text{Equation 1}
\]

In an $S_N2$ reaction, the nucleophile attacks the backside of the substrate due to the alpha carbon’s chiral center. As shown in Figure 1, an inversion occurs due to the method of attack. Furthermore, there are limitations to when an $S_N2$ reaction is able to occur. Since the $S_N2$ reaction proceeds through a backside attack, the reaction will only proceed if the empty orbital is
accessible. Thus, the more groups that are present around the vicinity of the leaving group, the slower the reaction will be. This is why the rate of reaction proceeds from primary (fastest) to secondary to tertiary (slowest) (Phan et al., 2009) This barrier is called steric hindrance.

S\textsubscript{N}1 reactions differ from S\textsubscript{N}2 in a few ways. Although, they both have a nucleophile and substrate, S\textsubscript{N}1 reactions proceed stepwise. The leaving group first leaves, whereupon a carbocation – positively charged carbon – forms that is attacked by the nucleophile (Hughes and Ingold, 1935). S\textsubscript{N}1 reactions also differ, in that, the concentration of the nucleophile has no effect on the rate of reaction. This is the result of the S\textsubscript{N}1 process having an intermediate with the nucleophile rather than a transition state. The S\textsubscript{N}1 reaction is multistep because of the formation of the carbocation. The process is shown below in Figure 2, and the rate equation is shown in Equation 2.

Figure 2 depicts the multistep process of an S\textsubscript{N}1 reaction

\[ \text{Rate} = k[\text{Substrate}] \quad \text{Equation 2} \]

Since the first step of the S\textsubscript{N}1 reaction is loss of a leaving group to give a carbocation, the rate of the reaction will be proportional to the stability of the carbocation. Carbocation stability increases with increasing substitution of the carbon (meaning tertiary is the fastest and primary is the slowest) as well as with resonance.
There are certain factors that decide whether or not the reaction will be $S_N1$ or $S_N2$. The $S_N2$ reactions tend to proceed with strong nucleophiles, meaning negatively charged nucleophiles such as $\text{CH}_3\text{O}^-$, $\text{CN}^-$, $\text{RS}^-$, $\text{N}_3^-$, $\text{HO}^-$, etc. (Garst, 1971) $S_N1$ reactions tend to proceed with weak nucleophiles – generally neutral compounds such as solvents like $\text{CH}_3\text{OH}$, $\text{H}_2\text{O}$, $\text{CH}_3\text{CH}_2\text{OH}$, and so on (Garst, 1971). The $S_N2$ reaction is favored by polar aprotic solvents – such as acetone, acetonitrile, etc. – that are polar enough to dissolve the substrate and nucleophile, but do not participate in hydrogen bonding with the nucleophile; however, the $S_N1$ reaction tends to proceed in polar protic solvents such as water, alcohols, and carboxylic acids. They also tend to be the nucleophiles for these reactions as well (Phan et al., 2009)

The lab performed an experiment which converted t-butanol into t-butyl chlorine to observe an $S_N1$ reaction. This mechanism is depicted in Figure 3.

![Figure 3](image.png)

Figure 3 depicts the $S_N1$ conversion of t-butanol into t-butyl chlorine

A separatory funnel was filled with tert-butanol along with hydrochloric acid mixed with tert-butanol. Once the aqueous and organic layers separated, the aqueous layer was drained; the product was washed with sodium bicarbonate and sodium chloride. The product was then analyzed using gas chromatography.
Gas chromatography is comprised of a mobile and a stationary phase. The mobile phase is comprised of an inert gas. The stationary phase consists of a packed column where the packing or solid support itself acts as stationary phase, or is coated with the liquid stationary phase. The separation of compounds is based on the different strengths of interaction of the compounds with the stationary phase. The stronger the interaction is, the longer the compound interacts with the stationary phase, and the more time it takes to migrate through the column (Grob and Barry, 2004).

The lab converted 1-butanol into 1-bromobutane to observe an $S_N2$ reaction. Sulfuric acid, sodium bromide and 1-butanol were boiled in a round bottom flask. Reflux – the process of vaporizing a liquid, only for it to be collected again – occurred within a long glass tube. The mixture went under reflux for distillation purposes. Once the organic layer was collected, the product was washed in sodium bicarbonate, sodium chloride. Finally, anhydrous sodium sulfate was added. The product was then left at room temperature. Figure 4 displays the $S_N2$ process.

![Figure 4](image)

Figure 4 depicts the $S_N2$ conversion of 1-butanol into 1-bromobutane

After the reactions were completed, the percentage yield was calculated for each. The percentage yield represents how efficient the reaction was done. The equation for overall percentage yield is
shown by Equation 3. The determination of the limiting reactant is used to calculate percentage yield.

\[
\frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100 = \text{Percentage yield}
\]  \hspace{1cm} \text{Equation 3}

The theoretical yield is the value of the limiting reagent, while the actual yield is what was observed. Equation 4 shows the calculation of the limiting reagent given the mass of reactant.

\[
\text{Mass of Reactant} \times \frac{1 \text{ mole of reactant}}{\text{mole of reactant}} \times \frac{1 \text{ mole of product}}{1 \text{ mole of reactant}} = \text{mol of product}
\]  \hspace{1cm} \text{Equation 4}

Equation 5 shows the calculation of the limiting reagent given the volume of the reagent.

\[
\text{Volume of Reactant} \times \frac{1 \text{ mol of reactant}}{1 \text{ mL of reactant}} \times \frac{1 \text{ mol of product}}{\text{mole of reactant}} = \text{mol of product}
\]  \hspace{1cm} \text{Equation 5}

Equation 6 shows the conversion of the calculated limiting reactant back into its mass, in order to be used in Equation 3 as the theoretical yield.
Results:

$\text{S}_\text{N1 GC Results:}$

Figure 5 shows the results from the GC after the t-butanol product was inserted into the machine. Tert-butanol retention time is shown in red, Tertbutyl chloride is shown in blue, and the product is shown in green.

Table 1

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Mass of Tert-but</td>
<td>4.012g</td>
</tr>
<tr>
<td>Mass of Tert-but Vial</td>
<td>8.36g</td>
</tr>
<tr>
<td>Mass of vial + product</td>
<td>10.11g</td>
</tr>
<tr>
<td>Mass of product</td>
<td>1.75g</td>
</tr>
</tbody>
</table>

Table 1 shows the measured mass of the final product of Tert-butanol.

Table 2

<table>
<thead>
<tr>
<th>Compound</th>
<th>Retention Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tert-butanol</td>
<td>1.8</td>
</tr>
<tr>
<td>Tertbutyl chloride</td>
<td>1</td>
</tr>
<tr>
<td>Product</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2 shows the relative retention times for the vaporized compounds.
$\text{SN}_2$ GC Results:

Table 3

<p>| | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Mass of Sodium Bromide</td>
<td>1.995 g</td>
</tr>
<tr>
<td>Volume of 1-butanol used</td>
<td>2 mL</td>
</tr>
<tr>
<td>Mass of Product</td>
<td>0.483 g</td>
</tr>
</tbody>
</table>

Table 3 shows the initial mass of sodium bromide along with the volume of 1-butanol used.

Table 4

<table>
<thead>
<tr>
<th>Compound</th>
<th>Observations at Room Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Nothing</td>
</tr>
<tr>
<td>1-bromobutane</td>
<td>Precipitate</td>
</tr>
</tbody>
</table>

Table 4 compares the observations of a water sample versus the 1-bromobutane sample.

Figure 6

Figure 6 displays the precipitate that was formed from the 1-bromobutane sample.
**Percentage Yield Results:**

Figure 7 is the calculated percentage yield for the $\text{S}_\text{N}1$ reaction. Equations 3-5 were used. The same calculations were used for the $\text{S}_\text{N}2$ reaction, which had a 25.43% percentage yield.

**Discussion:**

Both the $\text{S}_\text{N}1$ and $\text{S}_\text{N}2$ reactions were successful. Because –OH was the leaving group in both reactions, using $\text{H}_2\text{SO}_4$ and $\text{HCl}$ was required for the $\text{S}_\text{N}2$ and $\text{S}_\text{N}1$ reactions, respectively, since –OH groups are relatively unstable. Furthermore, each reaction had products that were solubility sensitive. The organic layers of both experiments were washed in sodium bicarbonate, because it is a strong base that neutralized the excess acid produced along with the product. Saturated sodium chloride was also added to salt out the solution. Salting out is a purification method that uses the reduced solubility of certain molecules in a solution of very high ionic strength. Salting out is typically, but not limited to, the precipitation of large biomolecules such as proteins. In the lab, salting out was used to separate the aqueous and organic layers even further. The precipitate that formed suggests primary halide formation. Figure 4 displays the halide product of the $\text{S}_\text{N}2$
reaction, bromobutane. Because a precipitate formed in the $S_N2$ reaction, the lab concludes that experiment was a success.

The results from Figure 5 and Table 2 suggest that tert-butanol had the latest retention time while its product had the earliest retention time. Because of vaporation, boiling point factors into the retention time; thus, tert-butanol has a higher boiling point in comparison to the product and t-butyl chloride. These results make sense, because GC functions by vaporizing the solution.

The percentage yield values of both the $S_N1$ and $S_N2$ reactions – 34.93% and 25.43%, respectively – were poor at best. The abysmal percentage yield can be attributed to experimental errors. For example, while separating the aqueous and organic layer for the $S_N2$ reaction, the organic layer was emptied into the waste beaker rather than a clean beaker to be put back and mixed in the separatory funnel. This put the waste product along with the organic layer back into the funnel, skewing results.

The lab can conclude that, for the $S_N1$ reaction, the hydrogen from HCl is donated to the $–OH$; then a methyl shift results in rearrangement before the leaving group exits; finally, a tertiary carbocation is formed and the nucleophile attacks the chlorine. For the $S_N2$ reaction, a proton transfers from $H_2SO_4$ to $–OH$ group, simultaneously, the leaving group exits and the nucleophile attack from the bromide.
References

Garst, John F. "Electron Transfer, Naphthalene Radical Anion, and Alkyl Halides."


