Bromination of Alkenes

CHM226

Background

The carbon-carbon double bond, also known as an alkene, is a very important functional group in organic chemistry, and is often used as a precursor in the synthesis of complex molecules. One of the most common reactions that alkenes undergo is halogenation by an electrophilic addition mechanism. The general mechanism for this reaction is shown below (Scheme 1).

![Scheme 1: Electrophilic Addition Mechanism](image)

The \( \pi \)-electrons of the alkene attack the electrophile (\( E^+ \)) and generate a carbocation. The carbocation in turn is attacked by a nucleophile (\( Nu^- \)), and the result is a disubstituted alkane.

The two most common halogenation reactions are chlorination and bromination. The addition of these halogens to alkenes yields 1,2-dihalides. Chlorinations reactions are used to synthesize over 6 million tons per year of ethylene dichloride (1,2-dichloroethane) for use as a solvent and for subsequent polymerization to produce poly(vinylchloride) known more commonly as PVC which is used for plumbing and other commercial purposes.

The mechanism of this alkene halogenation is of importance because it explains the exclusive formation of the \( trans \)-product. This can be explained by further analysis of the intermediate formed in the mechanism. The following chlorination reaction involves a chloronium intermediate.

![Scheme 2: Formation of Di-Halide via Chloronium Intermediate](image)

In this case, the intermediate formed (indicated by brackets) plays a crucial role in the product’s stereochemistry. The incoming nucleophilic chloride ion is forced to attack the top side of the cyclohexane ring because the bottom side is shielded from attack by the positively charged chloronium species. The result of this anti-addition is always the \( trans \)-product. The same effects occur in the bromination of alkenes forming a bromonium ion intermediate and resulting in the \( trans \)-product.

Bromination of alkenes is widely applied in both the research laboratory and throughout industrial practices. The halogenated alkanes can be easily obtained using liquid bromine in inert or acidic solvents like dichlormethane (DCM) or glacial acetic acid (Scheme 3). Although these reactions are very robust and can be completed as quickly as ten minutes, handling liquid bromine can be dangerous and
presents a hazard in the teaching laboratory. Fortunately other methods of brominating alkenes exist that use milder reagents and provide similar yields and purity.

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\end{array}
\quad \xrightarrow{\text{Br}_2 \text{ solvent}}
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{Br} \\
\text{Br} \\
\end{array}
\]

Scheme 3: Bromination Using Liquid Molecular Bromine

Djerassi and Schloz\(^2\) have shown that a sufficient alternative to liquid bromine is the organic salt pyridinium tribromide (Scheme 4). This solid is significantly safer to handle, and the molecular bromine is generated \textit{in situ} (which means “in the reaction mixture”). Generation of the active reagent occurs due to a chemical equilibrium between the pyridinium tribromide and molecular bromine (Scheme 5). Recently Hutchison \textit{et al.} have shown that hydrobromic acid and hydrogen peroxide in ethanol provide another safe alternative with higher atom economy.\(^3\)

\[
\begin{array}{c}
\text{H}_3\text{C} \\
\text{H}_3\text{C} \\
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\quad \xrightarrow{1.) \text{pyridinium} \text{tribromide} \text{glacial acetic acid}}
\begin{array}{c}
\text{H}_3\text{C} \\
\text{H}_3\text{C} \\
\text{CH}_3 \\
\text{CH}_3 \\
\text{Br} \\
\end{array}
\]

Scheme 4: Bromination Using Safe Reagents

\[
\begin{array}{c}
\text{N}^+ \\
\text{H} \\
\end{array}
\quad \text{Br}_3^- 
\quad \rightleftharpoons 
\begin{array}{c}
\text{N}^+ \\
\text{H} \\
\end{array}
\quad \text{Br}^- 
\quad + 
\begin{array}{c}
\text{Br}_2 \\
\end{array}
\]

Scheme 5: Pyridinium Tribromide and Molecular Bromine Equilibrium

There are many prefixes to consider with stereochemistry. Configurations such as \textit{trans-}, \textit{cis-}, and \textit{meso-}, or \textit{R} and \textit{S} labeled chiral centers with the possibility of racemic mixtures indicated by (\textit{\pm}) are all necessary to differentiate between the three dimensional products that are actually formed. Stereochemistry can be very difficult to visualize. Working slowly and methodically will provide the correct and accurate results. Molecular model kits might also be helpful.
It is important to consider the stereochemistry of the products formed as a result of alkene bromination. The possibility to generate chiral centers exists and therefore multiple products can be formed from one reactant. Again, consider Scheme 4. Since each olefinic carbon in Scheme 4 has two methyl substituents, bromination does not generate any chiral center, and only one product is observed. However, if the substituents are changed, then chiral products may be formed. For example:

Unlike the first example, a chiral center is generated at only one of the carbons; therefore two enantiomeric products are observed. More complicated results can be seen when two chiral centers are generated and theoretically four products could potentially be observed. In actuality, only two of the possible compounds are observed, the (R, S) and the (S, R) diastereomers, because they are the resulting trans-products of the anti-addition mechanism.
Now let us look at the different possibilities for products resulting from the same substrate with different stereo-conformations. First we will consider the *cis*-configuration as a starting material.

\[ \text{cis-configuration} \]

(\(\pm\)-Racemic Mixture)

Two different products are observed. However, they are formed in a 1:1 ratio, so 50% of the products are of the (R,R) configuration and the other 50% are of the (S,S) configuration. In our experiment today we are unable to separate these, however they have the same melting point which we can use to differentiate between the *trans*-products shown below.

Now we will consider the *trans*-configuration as a starting material. We can draw two possible products for this reaction.

\[ \text{trans-configuration} \]

Initially it might appear as if two different products are formed. However upon careful examination of the stereochemistry, we can prove otherwise. Let us focus on the stereochemistry of one of our above products. If we rotate the molecule of product 2 so that carbon 2 is now on top and carbon 1 is on the bottom the new stereochemical configuration is shown below.
Furthermore, if we take that configuration and rotate it so the methyl groups are in the same position as our original products from the bromination reaction, we can make a stunning conclusion.

After all of those fun twists and turns we can conclude that we have in fact only made one product. A final concept to consider is that of meso-compounds. In order to do this, we must look at the Fisher projection of the above compound.

Fisher Projection

The stereochemistry does not change when converting to a Fisher Projection. The important thing to notice is that a plane of symmetry can be drawn through the molecule. Whenever this is possible, the compound is considered to be in a meso-configuration, and is not considered a chiral compound. In the experiment you are about to perform, you will be given an unknown stilbene (trans-stilbene or cis-stilbene) to perform the bromination reaction on. Each reactant will result in a different configuration similar to the examples above. Fortunately, the resulting melting points (m.p.) are drastically different and these can be used to identify the true configuration of your product.
**Toxicity of Reagents**

Acetic acid: Corrosive
Cinnamic acid: Irritant
Ethanol: Flammable, Irritant
Pyridinium tribromide: Corrosive, Lachrymator
Silver Nitrate: Toxic, Oxidizer, stains skin black

**Procedure**

**Notes:**

1.) The reaction will be performed using a technique called **reflux**. To understand this concept, consider a boiling pot of water. If you were to leave this liquid boiling for too long it would all evaporate. Now, if a cooling condenser is fixed to the top of the pot of water, then the hot vapors will condense and drip back into the original pot. This cycle will continue as long as the vapors don’t get too hot, and the cold temperature of the condenser is maintained. This system is referred to as refluxing.

<table>
<thead>
<tr>
<th>Table 1: Table of Reagents:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compound</strong></td>
</tr>
<tr>
<td>Unknown A</td>
</tr>
<tr>
<td>Unknown B</td>
</tr>
<tr>
<td>Glacial Acetic Acid</td>
</tr>
<tr>
<td>Pyridinium Tribromide</td>
</tr>
</tbody>
</table>

Add the spin vane to the 5 mL conical vial. Make sure the vane is pointing straight down. You will be assigned an unknown alkene by your TA. Either unknown A or unknown B. Add the alkene followed by 2.00 mL of acetic acid and pyridinium tribromide successively. Record the exact masses/volumes of these reactants. To assemble the reflux apparatus, attach the conical vial to the condenser using the plastic adapter (Figure 1). Submerge the vial in the sand bath on the hot/stir plate and begin stirring. Apply heat to the apparatus by slowly increasing the temperature of the hot/stir plate. Reflux the mixture for 15 minutes, making sure all reactants have dissolved. Remove the apparatus from the sand bath and allow it to cool to room temperature. Remove the stir bar with a magnetic wand and then add 2.5 mL of deionized or distilled water. Place the vial in an ice/water bath for 15 minutes. Carefully filter the reaction mixture through a Hirsch funnel. If some precipitate goes through, filter the filtrate again to maximize yield. Let the product dry by scraping it from the funnel and apply the vacuum for 15 minutes. Transfer the product to a piece of pre-weighed wax weighing paper and determine the experimental yield. Calculate the percent yield of your crude product.
Identification of Product

Product of trans-stilbene = M.P. = 238 °C

Product of cis-stilbene = M.P. = 110 °C

Melting Point Determination: Prepare a melting point capillary as demonstrated by your TA. Obtain the melting point range of your product. Use this melting point to identify your product.

Silver Nitrate Test: Vicinal dihalides react with alcoholic silver nitrate to form a precipitate of the corresponding silver halide. Dissolve approximately 10 mg of your product in 0.5 mL of 95 % ethanol using a small test tube. Add 0.5 mL of 2% ethanolic silver nitrate. Allow the test tube to stand for at least 5 minutes. Record the presence or absence of a precipitate. What does this indicate?

Figure 1- Microscale Reflux Apparatus