Expt 10: Friedel-Crafts Alkylation of p-Xylene

INTRODUCTION

The Friedel-Crafts alkylation reaction is one of the most useful methods for adding alkyl substituents to an aromatic ring. Mechanistically, this transformation is an electrophilic aromatic substitution reaction, with the electron-rich aromatic ring serving as the nucleophile. This electrophile is typically generated in situ from an alkyl halide and a strong Lewis acid such as aluminum chloride (AlCl$_3$).

However, the true nature of the electrophile depends on the structure of the alkyl halide substrate. For secondary and tertiary alkyl halides the electrophilic species is a free carbocation. Since secondary and tertiary carbocations are stabilized by hyperconjugation and inductive effects, the activation energy barrier for their formation is relatively low.

In contrast, primary and methyl halides are believed to react via a polarized complex since primary and methyl carbocations are typically too high in energy to be viable intermediates:

One complication that often arises in the Friedel-Crafts alkylation reaction is rearrangement of the electrophilic species to from a lower energy (i.e. more stable) intermediate. For example, in CHEM 331, you saw how a secondary carbocation could rearrange through hydride or methide shifts to form tertiary carbocations. A similar type of rearrangement can occur when certain primary alkyl halides are used in the Friedel-Crafts reaction, even though the reaction never proceeds through a free primary carbocation intermediate. In this case, the hydride shifts occur in the polarized complex, as shown below for 1-chloropropane:
In this case the aromatic ring would be able to react with either the polarized complex or the secondary carbocation. As a result, mixtures of alkylation products are often obtained under these conditions.

The general mechanism for the Friedel-Crafts reaction on benzene is shown below. In the first step of the mechanism, the alkyl halide forms an intimate ion pair (also known as the "activated electrophile") with a strong Lewis Acid catalyst. This ion pair then reacts with the aromatic ring forming a benzenonium carbocation. This carbocation is stabilized by resonance. The remaining tetrachloroaluminate anion liberates a chloride anion to act as a base, abstracting a proton from the aromatic ring, regenerating the aromaticity of the ring and reforming the initial Lewis acid.

### General Mechanism for Friedel-Crafts Alkylation

**Step 1: Fast**

\[
R^-X + \text{AlCl}_3 \rightleftharpoons R^+ (\text{AlCl}_4)^- 
\]

**Step 2: Slow, Rate-Determining Step**

\[
\text{R}^+ (\text{AlCl}_4)^- \rightarrow \text{R}^+ \text{H}^+ \text{Cl}^- \text{AlCl}_3 
\]

**Step 3: Fast**

\[
\text{R}^+ \text{H}^+ \text{Cl}^- \text{AlCl}_3 \rightarrow \text{R} \text{H} \text{Cl}^- \text{AlCl}_3 \rightarrow \text{R} \text{H} \text{Cl}^- \text{AlCl}_3
\]

In this experiment, p-xylene will be the aromatic substrate used for the Friedel-Crafts alkylation reaction. Because of the high symmetry of para-xylene, all the hydrogen atoms are equivalent. Substitution of any one of the four hydrogen atoms with one alkyl group will lead to the same alkylated product.
EXPERIMENTAL OVERVIEW:

In today’s reaction, you will carry out the Friedel-Crafts alkylation of p-xylene (1,4-dimethylbenzene) using 1-bromopropane and the Lewis acid aluminum chloride. Depending on the conditions used, the reaction could give the n-propyl substituted compound A, the isopropyl substituted compound B, or a mixture of the two. The overall reaction scheme is depicted below:

\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 & \text{Br} \\
\text{AlCl}_3 & \rightarrow \\
\text{CH}_3 \\
\text{CH}_3 & \text{A} \\
& \text{and/or} \\
\text{CH}_3 \\
\text{CH}_3 & \text{B}
\end{array}
\]

You will be assigned one of three possible sets of reaction conditions for this experiment in order to investigate the effect that temperature and order of addition of reagents has on the ratio of products. After reacting with the Lewis Acid catalyst, the reaction mixture will be neutralized, dried and analyzed by gas chromatography. Use of a short reaction time, limits the number of alkyl groups introduced onto the aromatic ring. A short reaction time is necessary - the aromatic ring is the nucleophile in the reaction and every time an alkyl group adds to the ring, it becomes even more reactive and thus ready to add another alkyl group. Every student will submit a sample of his or her product solution for analysis by gas chromatography. You will be given the GCs for the two known products themselves to help you identify the compounds. Once you have determined which is the major product, you are then going to be responsible for rationalizing the selectivity for formation of A and/or B in each case.

REAGENT TABLE:

<table>
<thead>
<tr>
<th>Reagents</th>
<th>MW (g/mol)</th>
<th>MP (°C)</th>
<th>BP (°C)</th>
<th>Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-xylene</td>
<td>106.17</td>
<td>13 (dec)</td>
<td>138</td>
<td>0.866</td>
</tr>
<tr>
<td>aluminum chloride</td>
<td>133.34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-bromopropane</td>
<td>122.99</td>
<td>-110</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>diethyl ether</td>
<td>74.12</td>
<td>-116</td>
<td>34.6</td>
<td>0.708</td>
</tr>
</tbody>
</table>
FOR YOUR SAFETY:
1. Aluminum chloride is highly corrosive and reacts with water vapor in the air to produce HCl gas. Keep this compound in the hood and wear gloves when handling it. If any of the compounds should come in contact with your skin, immediately rinse with cold running water.
2. Avoid skin contact and inhalation of the vapors of both p-xylene and 1-bromopropane. Both are somewhat volatile.

EXPERIMENTAL PROCEDURE 1: (Students on Front Bench, closest to clock)

1. Using a syringe, place 1.0 mL of dry p-xylene in a clean, dry 5 mL conical vial containing a spin vane. Then use a syringe to add 0.25 mL of dry pentane to the same conical vial.

2. In the hood, obtain one microspatula tip of aluminum chloride and add it to the conical vial as quickly as possible. Aluminum chloride is extremely hygroscopic, reacting readily with the water vapor in the air to produce HCl gas and aluminum hydroxide. Attach the Claisen adapter fitted with a drying tube, filled with calcium chloride pellets, and a cap with a rubber septum, as shown in Figure A.5A to the conical vial (the apparatus used in the Grignard experiment). Clamp the apparatus down in an ice-water bath that is cooled to approximately 5°C. Record the bath temperature of the cold bath using a thermometer. Begin magnetic stirring (setting of 5-6) and stir for at least 5 minutes to cool the vial contents to the temperature of the ice bath before adding the next solution.

3. In the hood, add 0.50 mL of 1-bromopropane in a clean dry small sample vial. To this small sample vial, add 0.5 mL dry p-xylene and stir with tip of microspatula to mix. Using the syringe from your kit, add the solution of 1-bromopropane in p-xylene, drop-wise, over a period of about two minutes to the conical reaction vial. The contents of the reaction vial will turn an orange/yellow color. Stir the reaction for 20 minutes on a magnetic stir plate. Be sure to maintain the cold temperature of your bath as your reaction proceeds.

4. After 20 minutes add 2 mL of diethyl ether to the 5 mL conical vial and transfer the total contents to a clean large sample vial.

5. Rinse the conical vial once more with an additional 2 mL of diethyl ether and add this to the large sample vial as well. Then add 4 mL of diethyl ether to the large sample vial (total volume of diethyl ether, 8 mL).
6. Add 4 mL of 5% sodium hydroxide solution to the vial containing the organic phase. Cap the vial and gently shake the contents, venting frequently to release any pressure build-up. Allow layers to separate then remove the lower aqueous layer with a pipette, transferring it to another vial labeled “aqueous waste”. Repeat this washing process two additional times, collecting the combined aqueous layers in the “aqueous waste” vial. Then was the organic layer twice with 2 mL of deionized water in order to remove traces of sodium hydroxide, again collecting the aqueous layers in the “aqueous waste” vial.

7. Dry the organic phase by adding small amounts of anhydrous magnesium sulfate to the organic layer in the vial. Gently swirl the contents of the vial and continue to add small amounts of magnesium sulfate until the organic layer is clear instead of cloudy and the drying agent is freely flowing. Do not add so much that you no longer have any visible liquid in your vial!

8. Remove the drying agent by gravity filtration, using a clean, dry glass funnel and fluted filter paper, collecting the dry filtrate in a clean, dry large sample vial. Label the new vial as “dried organic layer” along with your name and course section number.

9. **Place SIX drops** of the dried organic layer in a GC sample vial that will be provided by your instructor. Add enough diethyl ether (from hood, use brand new pipette) until the GC vial is at least 3/4 full and submit it to your instructor for GC or GC/MS analysis.

**EXPERIMENTAL PROCEDURE 2: (Students on Center Bench)**

If not already done, set up a 40 mL hot water bath in a 50 mL beaker and begin to heat to boiling.

1. Using a syringe, place 1.0 mL of dry p-xylene in a clean, dry 5 mL conical vial containing a spin vane.

2. **In the hood**, obtain one microspatula tip of aluminum chloride and add it to the conical vial as quickly as possible. Aluminum chloride is extremely hygroscopic, reacting readily with the water vapor in the air to produce HCl gas and aluminum hydroxide. Attach the conical vial to a Claisen adapter fitted with a cap and rubber septum (directly above the vial) and a water-cooled condenser with a drying tube, filled with calcium chloride pellets, attached to top of the condenser, as shown in Figure A.5D (similar to esterification apparatus). Make sure the water is running through the condenser and carefully clamp the apparatus so the reaction vial is immersed about halfway in the hot water bath. Begin magnetic stirring, and stir for at least five minutes in order to warm the contents of the reaction vial to the
temperature of the hot water bath (record the actual temperature of the hot water bath using a thermometer). Then place a mini-hood above the reaction apparatus before proceeding to the next step.

3. **In the hood**, add 0.50 mL of 1-bromopropane in a clean dry small sample vial. Add 0.5 mL p-xylene and stir with tip of a microspatula to thoroughly mix the contents of the vial. Using the syringe from your kit, add the solution of 1-bromopropane in p-xylene, drop-wise, over a period of approximately two minutes to the conical reaction vial. The contents of the reaction vial may turn an orange/yellow color. Stir the reaction for 20 minutes on a magnetic stir plate. At the end of 20 minutes, cool the vial back to room temperature by removing from the hot water bath and lowering the apparatus into a cool water bath. Watch for further color changes.

4. Steps 4-9 are the same as for Procedure 1. However, when preparing your sample for GC analysis, **only use THREE drops** of your dried organic layer and fill the rest of the GC vial at least 3/4 full with diethyl ether (as described in earlier procedure, Step 9).

**EXPERIMENTAL PROCEDURE 3: (Students on Back Bench, next to IR room)**

If not already done, set up a 40 mL hot water bath in a 50 mL beaker and begin to heat to boiling.

1. Using a syringe, place 0.50 mL of 1-bromopropane in a clean, dry 5 mL conical vial containing a spin vane.

2. **In the hood**, measure one microspatula tip of aluminum chloride and add it to the conical vial as quickly as possible. Aluminum chloride is extremely hygroscopic, reacting readily with the water vapor in the air to produce HCl gas and aluminum hydroxide. Attach the conical vial to a Claisen adapter fitted with a cap and rubber septum (directly above the vial) and a water-cooled condenser with a drying tube, filled with calcium chloride pellets, attached to top of the condenser, as shown in Figure A.5D (similar to esterification apparatus). Make sure the water is running through the condenser and carefully clamp the apparatus so the reaction vial is immersed about halfway in the hot water bath. Begin magnetic stirring, and stir for **at least five minutes** in order to warm the contents of the reaction vial to the temperature of the hot water bath (record the actual temperature of the hot water bath using a thermometer). Then place a mini-hood above the reaction apparatus before proceeding to the next step. Watch for color changes.
3. **In the hood**, add 1.5 mL of dry p-xylene in a clean dry small sample vial. Using the syringe from your kit, add the p-xylene, drop-wise over a period of about two minutes to the conical reaction vial. Stir the reaction for 20 minutes on a magnetic stir plate. At the end of 20 minutes, cool the vial back to room temperature by removing from the hot water bath and lowering the apparatus into a cool water bath.

4. Steps 4-9 are the same as for Procedure 1. However, when preparing your sample for GC analysis, **only use THREE drops** of your dried organic layer and fill the rest of the GC vial at least 3/4 full with diethyl ether (as described in earlier procedure, Step 9).

**WASTE DISPOSAL**

Place all of the basic aqueous layers in the vial labeled “aqueous waste” in the waste bottle located in the hood labeled “basic aqueous waste”. Carefully wash all of the remaining equipment used in this experiment, and return it to your locker station.

**CALCULATIONS**

Any necessary calculations will be discussed in the prelab for the next lab period.