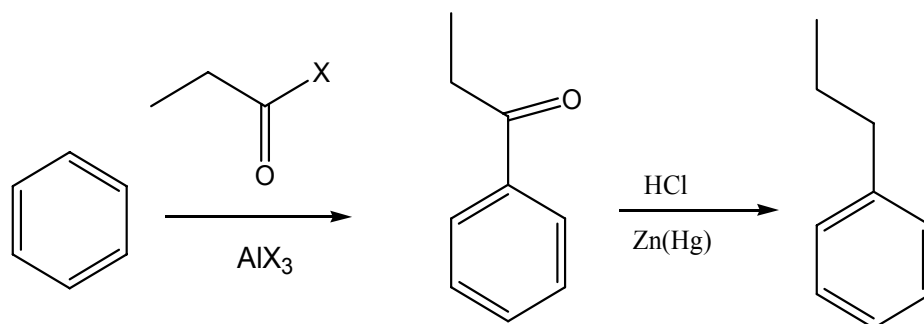


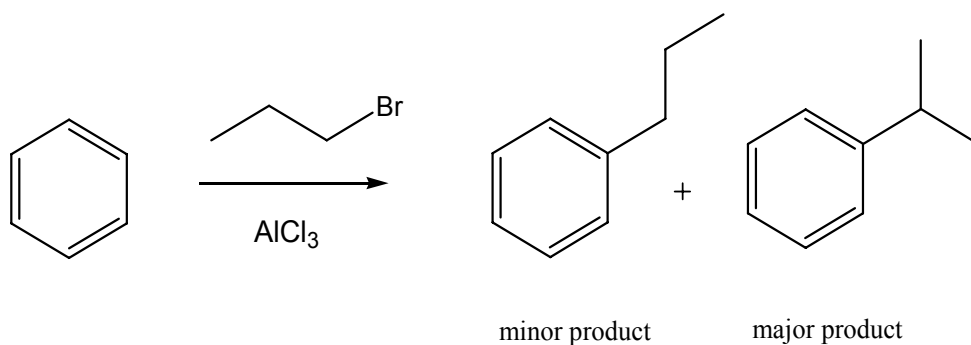
14 Friedel-Crafts Alkylation

14.1 Introduction

Friedel-Crafts alkylation and acylation reactions are a special class of electrophilic aromatic substitution (EAS) reactions in which the electrophile is a carbocation or acylium ion. These reactions are highly useful in that they involve carbon-carbon bond formation and allow alkyl and acyl groups to be substituted onto aromatic rings. If the objective is to introduce an *n*-alkyl group onto an aromatic ring, acylation followed by Clemmensen reduction is usually the preferred route:

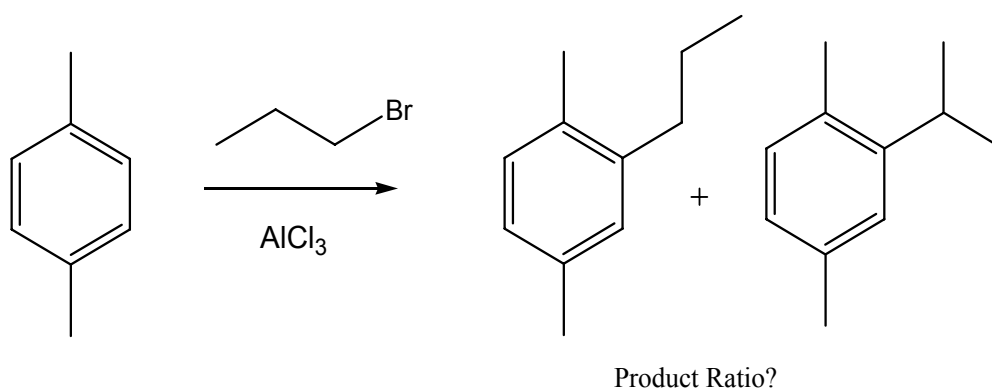


The acylation/Clemmensen reduction route prevents secondary alkyl substitution which results from carbocation rearrangement. However, in direct alkylation, the ratio of primary to secondary alkyl substitution can vary depending on aromatic substrate and reaction conditions. When benzene is alkylated using 1-bromopropane under conditions that favor monoalkylation, the result is a 1:2 ratio of *n*-propyl to isopropyl substitution:



In this experiment a Friedel-Crafts alkylation of *p*-xylene will be carried out using 1-bromopropane with aluminum chloride catalyst. To favor monoalkylation, the reaction will be run only part way to completion. The crude product will be contaminated with large amounts of the starting materials. Reduced pressure distillation (“vacuum distillation”) will be used to separate the monoalkylation products from unreacted starting materials.

As with the alkylation of benzene shown on the previous page, the reaction with *p*-xylene can result in *n*-propyl as well as isopropyl substitution, but not necessarily in the same ratio. The objective of this experiment is to determine the product ratio obtained for alkylation of *p*-xylene and provide a mechanistic rationale for the observed ratio in comparison with that reported for alkylation of benzene.



Pre-lab Questions:

1. Write a step-wise mechanism for alkylation of *p*-xylene as shown in the reaction above. Show the separate pathways leading to each product using curved arrows to show the movement of all electron pairs. Show the structure of the electrophile that leads to each product and how the electrophile is formed.
2. Compared to alkylation of benzene, what do you expect for the ratio of *n*-propyl to isopropyl substitution for *p*-xylene? Explain your reasoning.

14.2 Experimental Techniques

Some important new experimental techniques are demonstrated here: 1) manipulation of a highly reactive chemical, aluminum chloride, 2) control of a noxious gases formed in the reaction, hydrogen bromide and hydrogen chloride, and 3) purification of product by distillation at reduced pressure.

Highly Reactive Chemical:

Aluminum chloride is a strong Lewis acid. It reacts vigorously and exothermically with water forming hydrogen chloride, which is both corrosive and poisonous. Any spills are cleaned up immediately. The cover on the container of aluminum chloride is replaced immediately after the desired amount has been weighed out.

Gas Trap

During the reaction, hydrogen bromide and hydrogen chloride are formed and some provision has to be made to prevent them from being released into the laboratory. Figure 14.1 shows a setup for a small scale Friedel-Crafts reaction. A vacuum adapter is placed on top of the reaction apparatus and a hose to a water aspirator is connected to it (NOTE: The system is left open to the atmosphere). Air is drawn through the apparatus and sweeps the hydrogen chloride gas out with it. The hydrogen chloride dissolves in the water at the water aspirator.

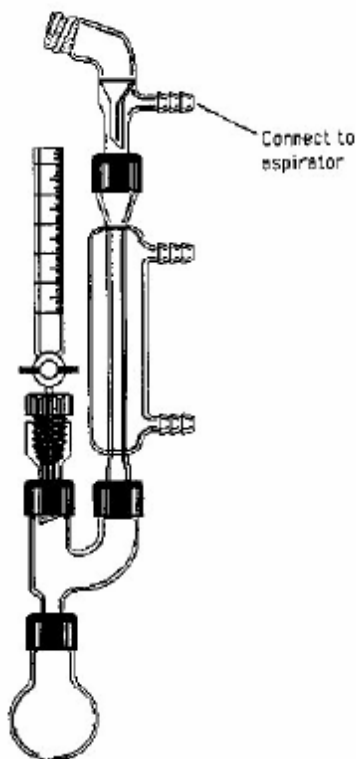


Figure 14.1: Reaction vessel with dropping funnel and gas trap

Reduced Pressure Distillation

Considering the physical description of boiling point as discussed in Chapter 5 and Appendix A5 of this lab manual, it should be apparent that the boiling point of a liquid is dependent on the air pressure above the liquid. At reduced pressures, liquids boil at lower temperatures. Organic chemists often take advantage of this fact when they purify high boiling compounds by distillation. Many high boiling compounds will partially or completely decompose if distillation is attempted at normal atmospheric pressure, but the same compounds can be easily distilled at lower temperatures by carrying out the distillation at reduced pressure. This technique is also commonly referred to as “vacuum distillation”.

The apparatus for a simple vacuum distillation is shown in Figure 14.2. The vacuum adapter tube is connected by **heavy wall rubber tubing** to a safety trap. This trap is to protect the system from a backup of water due to a sudden drop in water pressure. The trap is in turn connected by heavy wall rubber tubing to a water aspirator.

The contents of the distillation flask should be at or below room temperature when the system is first evacuated. A hot liquid will often begin to distill (sometimes violently) before the system is fully evacuated.

To break the vacuum, after distillation is complete, or to trouble shoot the vacuum system, keep the aspirator running, and carefully ease off the vacuum hose connected to the distillation apparatus (see Figure 14.2.) **Do not break the vacuum by removing a hose fitting from the trap or from the aspirator as this may result in back-up of water or other contaminants into the distillation apparatus.**

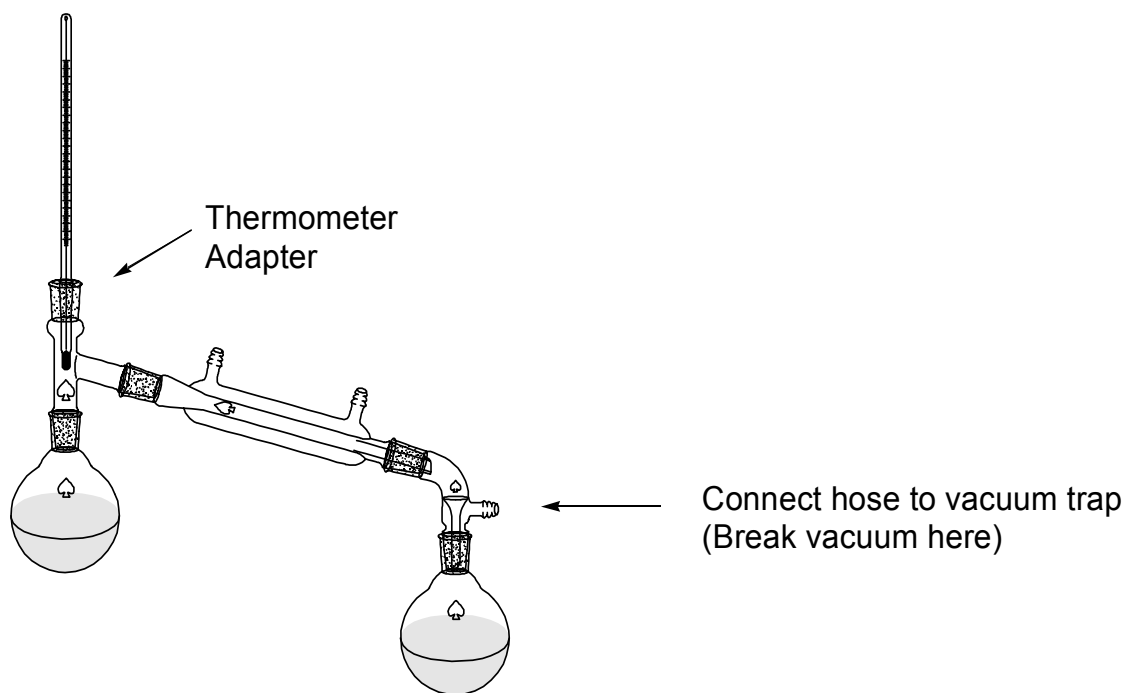


Figure 14.2: Reduced Pressure Distillation Apparatus

With a water aspirator, a pressure of 15 to 25 mm of mercury can normally be obtained. When troubleshooting a system, check the vacuum of the aspirator first. Then check the vacuum with the safety trap connected to the aspirator, and finally check the vacuum with the system connected to the trap.

The vacuum gauges used to measure the the pressure of the system are checked out at the stockroom. They should be handled very carefully to prevent jarring or breakage. These gauges measure vacuum or negative pressure relative to ambient atmospheric pressure in inches of Hg. However, vacuum distillation data is always reported using absolute residual pressure expressed as mm Hg. To convert the vacuum gauge reading to absolute residual pressure in mm Hg, the reading must be subtracted from the “perfect” vacuum reading and multiplied by 25.4 to convert from inches to mm. The vacuum gauges have been calibrated to determine the “perfect” vacuum reading for each gauge which is recorded on the tag attached to the gauge.

Here are a few additional suggestions that should help when setting up a vacuum distillation. To promote even boiling, a magnetic stirrer is used to agitate the contents of the distillation pot. When the apparatus is set up, the ground glass joints are lightly greased and the system should fit together easily. The clamps supporting the apparatus should not pull any joints apart or add any extra stresses to the glass. For small distillation apparatus of the type in this experiment, using only one clamp attached securely to the middle of the condenser is sufficient as long as good-fitting keck clips are used to secure all joints. This allows for easy repositioning of the apparatus as needed.

Heavy wall rubber tubing is used for all vacuum connections. Thin wall tubing will collapse under the vacuum. The water valve at the aspirator should be turned on full; this will minimize the effect of any sudden changes in the water pressure.

14.3 Procedure

(Safety Note; **CAUTION:** Anhydrous aluminum chloride **reacts vigorously with water** forming corrosive and noxious hydrogen chloride. The work up of this reaction **MUST BE CARRIED OUT IN A FUME HOOD.**)

Anhydrous aluminum chloride (0.40 g, 3.0 mmol) is weighed into an aluminum weighing boat in the fume hood and quickly transferred to a clean dry 25 ml round bottom flask containing a magnetic stir bar. The flask is stoppered and brought to the bench where it is fitted with a Claisen adaptor, a dropping funnel, and a condenser vented to a gas trap as shown in Figure 14.1. Dry *p*-xylene (6.0 mL, 49 mmol) is added to the round bottom flask, and 1-bromopropane (4.5 mL, 49 mmol) is added to the dropping funnel. The water aspirator is turned on to provide the vapor sweep and an ice bath is prepared in case it is needed to cool the reaction.

While rapidly stirring the *p*-xylene/aluminum chloride mixture, 1-bromopropane is added *slowly* dropwise over a period of about 10 minutes. ***The reaction can become very vigorous if the 1-bromopropane is added too rapidly. Do this addition carefully. If the reaction solution starts bubbling too vigorously, use the ice bath to cool it down before continuing the addition.*** After the addition is complete, continue stirring the reaction mixture at room temperature for an additional 30 min.

The reaction flask is removed from the apparatus and taken to a fume hood where the mixture is **cautiously and slowly** poured into a 50 mL beaker containing about 5 g of ice. The resulting mixture is stirred in the hood until all fuming ceases, then taken to the bench. The two phase aqueous/organic mixture is rapidly stirred using a magnetic stirrer while solid sodium chloride is added until the aqueous phase is saturated as evidenced by undissolved sodium chloride. The mixture is decanted to a separatory funnel (leaving behind undissolved sodium chloride). The organic layer is separated, transferred to a 50 mL Erlenmeyer flask and dried over anhydrous sodium sulfate. If the organic liquid appears cloudy after swirling over the sodium sulfate for about 1 minute, additional amounts of sodium sulfate are added until the solution becomes clear. The dried organic layer is decanted into a clean 25 mL round bottom flask which is sealed and stored until the next lab period.

The 25 mL round bottom flask containing the crude product is fitted for simple distillation, and the unreacted 1-bromopropane (bp=71°C) is distilled off at atmospheric pressure. After all of the bromopropane has been collected, heating is discontinued and the distillation flask is allowed to cool to room temperature. The bromopropane is disposed of in halogenated solvent waste, and the apparatus is fitted for reduced pressure distillation as shown in Figure 14.2 and described on pages 114-115. With the remaining contents of the distillation flask at room temperature and rapidly stirred, the pressure is reduced. Heating is then resumed to distill off *p*-xylene. Depending on the reduced pressure, the *p*-xylene should distill in the temperature range 30-60 °C. When removal of *p*-xylene is complete there should be a small amount (< 1 mL) of higher boiling liquid remaining in the distillation flask. Be careful not to distill the final fraction over with the *p*-xylene. At this point, remove the heating mantle, break the vacuum where the hose connects to the distillation adaptor, and replace the receiver flask with a clean, dry flask to collect the final high boiling fraction. Then reduce the pressure again and resume heating to collect the final fraction which, depending on the pressure, should distill in the range 70-90 °C. The distillation flask should be taken nearly to dryness in collecting the final fraction.

Analysis

The ¹H NMR spectrum of the starting material is shown at the end of this chapter (page 118). A ¹H NMR spectrum, gas chromatogram and IR spectrum are obtained on the product mixture (final high boiling fraction). The relative amounts of n-propyl versus isopropyl substitution can be determined by interpreting the spectral data.

Although excess unreacted 1-bromopropane and *p*-xylene are removed from the product during the reduced pressure distillation, the final product is likely to still have a significant amount of *p*-xylene and possibly some 1-bromopropane contamination. Although the ¹H NMR spectrum is likely to be complex and not completely assignable, careful examination of the alkyl region should reveal the compounds present and the relative amounts. The gas chromatogram provides an independent check on the number of compounds present and their relative amounts. It should be possible to assign all peaks in the gas chromatogram.

Post - Lab Questions (to be included in lab report):

1. How does the ratio of *n*-propyl to isopropyl substitution in your experiment compare to that reported for alkylation of benzene? Is the result consistent with your original prediction?
2. Provide a detailed mechanistic rationale for your results compared to those reported for alkylation of benzene.