Exp’t 61

1,4-Di-t-butylbenzene via Friedel-Crafts Alkylation

from K. L. Williamson, Macroscale and Microscale Organic Experiments, 2nd Ed. 1994, Houghton Mifflin, Boston. p435; revised2/28/02

Prelab Exercise

How would you synthesize acetophenone from benzene using Friedel-Crafts acylation?

Introduction

\[
\text{Friedel-Crafts alkylation of aromatic rings most often employs an alkyl halide and a strong Lewis acid catalyst. Some of the catalysts that can be used, in order of decreasing activity, are the halides of Al, Sb, Fe, Ti, Sn, Bi, and Zn. Although useful, the reaction has several limitations. The aromatic ring must be unsubstituted or bear activating groups. Because the product, an alkylated aromatic molecule, is more reactive than the starting material, multiple substitutions usually occur. Furthermore, primary halides will rearrange under the reaction conditions.}
\]

In the present reaction, a tertiary halide and the most powerful Friedel-Crafts catalyst, AlCl₃, are allowed to react with benzene. The initially formed t-butylbenzene is a liquid, while the product, 1,4-di-t-butylbenzene, which has a symmetrical structure, is a beautifully crystalline solid. The alkylation reaction probably proceeds through the carbocation under the conditions of the present experiment. The reaction is reversible. If 1,4-di-t-butylbenzene is allowed to react with t-butyl chloride and aluminum chloride (1.3 mol) at 0 to 5 °C, 1,3-di-t-butyl-benzene, 1,3,5-tri-t-t-butylbenzene, and unchanged starting material are found in the reaction mixture. Thus the mother liquor from crystallization of 1,4-di-t-butylbenzene in the present experiment probably contains t-butylbenzene, the desired 1,4-di-product, the 1,3-di-isomer, and 1,3,5-tri-t-t-butylbenzene. Even though the mother liquor probably contains a mixture of several components, the 1,4-di-t-butylbenzene can be isolated as crystals.

TLC

You are required to run a TLC to monitor the progress of the reaction. Plates should have three spots (or lanes) on the origin: one for the main organic starting material that is being transformed, one for a cospot (starting material and the reaction mixture), and one for the reaction mixture.

Procedure: 1,4-Di-t-butylbenzene

Measure, using a 1.0 mL plastic syringe, 0.40 mL of dry 2-chloro-2-methyl-propane (t-butyl chloride) and 0.20 mL of dry benzene into a dry 10 x 100 mm reaction tube equipped with a septum and tubing. The benzene and the alkyl chloride will usually be found in septum-stoppered containers. Cool the tube in ice, and then add to it 20 mg of aluminum chloride*. Weighing and transferring this small quantity are difficult because aluminum chloride reacts very rapidly with moist air.

*Note: Aluminum chloride is a strong Lewis acid that acts as a catalyst in the Friedel-Crafts alkylation reaction.
Keep the reagent bottle closed as much of the time as possible while weighing the reagent into a very small, dry, capped vial. Since the aluminum chloride is a catalyst, the amount need not be exactly 20 mg. Weigh AlCl₃ in the hood. Cap the bottle immediately. Keep the bottle in a dessicator jar.

*Before adding the aluminum chloride to your mixture of t-butyl chloride and dry benzene, make sure your apparatus is set up correctly. See Figure 1. Aluminum chloride is the catalyst most often used for the Friedel-Crafts reaction, but it is difficult to store and to weigh out because it reacts very rapidly with moisture in the air. Weigh it very quickly under inert atmosphere in the hood.*

Mix the contents of the reaction tube by flicking the tube with a finger. A vigorous reaction sets in, with bubbling and liberation of hydrogen chloride. The hydrogen chloride is trapped using the apparatus by the wet cotton in the empty reaction tube, which will dissolve the hydrogen chloride. To thread a Teflon tube through a septum, make a hole through the septum with a needle, and then push a toothpick through the hole. Push the Teflon tube firmly onto the toothpick, and then pull and push on the toothpick. The tube will slide through the septum. Finally, pull the tube from the toothpick.

Near the end of the reaction, the product separates as a white solid. When this occurs, remove the tube from the ice and let it stand at room temperature for 5 min.

Add about 1.0 mL of ice water to the reaction mixture, mix the contents thoroughly, and extract the product with three 0.8-mL portions of ether (use the wet ether found in a supply bottle in each hood).

Wash the combined ether extracts with about 1.5 mL of saturated sodium chloride solution, and dry the ether over anhydrous calcium chloride pellets. Add sufficient drying agent so that it does not clump together.

After 5 min., transfer the ether solution to a dry, tared reaction tube, using more ether to wash the drying agent, and evaporate the ether under a stream of air in the hood. Remove the last traces of ether under house vacuum. The oily product should solidify on cooling and weigh about 300 mg.

For crystallization, dissolve the product in 0.40 mL of methanol, and let the solution cool to room temperature without disturbance. After thorough cooling at 0 °C, remove the methanol with a Pasteur pipette, and rinse the crystals with a drop of ice-cold methanol while keeping the

Figure 1. Reaction apparatus for the Friedel-Crafts alkylation of benzene.
reaction tube in ice. Save this methanol solution for analysis by thin-layer chromatography. The yield of recrystallized material after drying under aspirator vacuum should be about 160 mg. After weighing your product, perform a thin-layer chromatography. Using thin-layer chromatography, compare the pure crystalline product with the residue left after evaporation of the methanol. Attach all TLCs to report.

Cleaning Up
Place any unused t-butyl chloride in the halogenated organic waste container and any unused benzene in the hazardous waste container for benzene. Any unused aluminum chloride should be mixed thoroughly with a large excess of sodium carbonate and the solid mixture added to a large volume of water before being flushed down the drain. The combined aqueous layers from the reaction should be neutralized with sodium carbonate and then flushed down the drain. Methanol from the crystallization is to be placed in the organic solvents container.

Analysis
In addition to TLC analysis, you may be instructed to analyze your final product by IR or NMR. Analyze your sample according to your assignment sheet and the instructions on Sample Preparation in Lab Guide.

C-H Out-of-Plane Bending Vibrations of Substituted Benzenes

<table>
<thead>
<tr>
<th>Substituted Benzene</th>
<th>Peak 1 (cm⁻¹)</th>
<th>Peak 2 (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>671</td>
<td></td>
</tr>
<tr>
<td>Monosubstituted benzenes</td>
<td>770-730</td>
<td>710-690</td>
</tr>
<tr>
<td>1,2-Disubstituted</td>
<td>770-735</td>
<td></td>
</tr>
<tr>
<td>1,3-Disubstituted</td>
<td>810-750</td>
<td>710-690</td>
</tr>
<tr>
<td>1,4-Disubstituted</td>
<td>835-810</td>
<td></td>
</tr>
<tr>
<td>1,2,3-Tri substituted</td>
<td>780-760</td>
<td>745-705</td>
</tr>
<tr>
<td>1,2,4-Trisubstituted</td>
<td>825-805</td>
<td>885-870</td>
</tr>
<tr>
<td>1,3,5-Trisubstituted</td>
<td>865-810</td>
<td>730-75</td>
</tr>
<tr>
<td>1,2,3,4-Tetrasubstituted</td>
<td>810-800</td>
<td></td>
</tr>
<tr>
<td>1,2,3,5-Tetrasubstituted</td>
<td>850-840</td>
<td></td>
</tr>
<tr>
<td>1,2,4,5-Tetrasubstituted</td>
<td>870-855</td>
<td></td>
</tr>
<tr>
<td>Pentasubstituted</td>
<td>870</td>
<td></td>
</tr>
</tbody>
</table>

\[ ^1H \text{ NMR spectrum of 1,4-di-t-butylbenzene (90) } \]
Post Lab Questions

1. Explain why the reaction of 1,4-di-t-butylbenzene with t-butyl chloride and aluminum chloride gives 1,3,5-tri-t-butylbenzene.
2. Why must aluminum chloride be protected from exposure to the air?
3. Draw a detailed mechanism for the formation of 1,4-di-t-butyl-benzene.