Friedel-Crafts Alkylation of m-Xylene

Adapted by R. Minard and D. Dorisio (Penn State Univ.) from a microscale procedure used by the University of California, Irvine, in its undergraduate labs. The procedure is based on an experiment introduced to the UCI Organic Chemistry Laboratory Program in the early 1970's by Marjorie C. Caserio, Professor of Chemistry. Revised 10/9/00.

Introduction:

Friedel-Crafts alkylation is an example of electrophilic aromatic substitution. The electrophile is a carbocation which displaces a proton on the aromatic ring; the carbocation is generated from a haloalkane in the presence of a Lewis acid catalyst, AlCl₃.

![Chemical structure](image)

In the method used in this experiment, instead of handling the very air-sensitive AlCl₃, you will make it by direct reaction of activated (mercury amalgamated) aluminum metal with excess t-butyl chloride.

![Chemical reaction](image)

Although Friedel-Crafts alkylation is a general method for introducing alkyl groups into the benzene ring, there are practical limitations which prohibit the use of Friedel-Crafts alkylations in synthetic organic chemistry. Since the reaction involves the development of a positive charge on the alkyl carbon atom, rearrangement of the alkyl group may occur. Moreover, polyalkylated by-products may be formed because the alkylated product is even more susceptible to electrophilic substitution than the starting material. Steric effects are important as well as "scrambling" of alkyl groups when a thermodynamically more stable product can arise from one that is formed initially in a faster reaction. FOR A MORE THOROUGH DISCUSSION OF FRIEDEL-CRAFTS ALKYLATION, REFER TO YOUR ORGANIC CHEMISTRY TEXTBOOK.

The objectives of this experiment are: 1) to prepare aluminum chloride in-situ by the reaction of aluminum metal and an alkyl chloride. 2) to alkylate m-xylene with t-butyl chloride in the presence of a mercury-aluminum catalyst; 3) to determine the structure of the product by analysis with infrared spectroscopy; and 4) to discuss the product formation in terms of orientation effects on the benzene ring, steric factors, and thermodynamic versus kinetic control.

The following table, taken from J. A. Landgrebe, *Theory and Practice in the Organic Laboratory* (D. C. Heath, 1982), will be useful for interpreting your experimental results.

<table>
<thead>
<tr>
<th>Compound</th>
<th>cm⁻¹</th>
<th>cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>671</td>
<td>-</td>
</tr>
<tr>
<td>Monosubstituted benzene</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>833-810</td>
<td>-</td>
</tr>
<tr>
<td>1,2,3-Trisubstituted</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>730-675</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>

Table I: C-H Out-of-Plane Bending Vibrations of Substituted Benzenes
Prelaboratory Exercises:

(1) Write a balanced equation for the reaction between m-xylene and t-butyl chloride in the presence of Lewis acid catalyst giving the expected substitution pattern using your knowledge regarding electrophilic substitution on substituted benzenes.
(2) Why is removal of unreacted xylene important for determining the major isomer present in the product? What could you do during the instant microscale distillation to be sure that the vapors forming inside the tube truly are just unreacted m-xylene?

Cautions:
Mercury and all its compounds are highly toxic; wash your hands after handling mercuric chloride and do not pour any mercury salts down the drain.

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.

Synthesis:

\[
\text{CH}_3\text{C}_6\text{H}_4\text{CH}_3 + \text{CH}_3\text{C}_6\text{H}_4\text{Cl} + \text{Al}^+(\text{Hg})_{\text{(AlCl)}_3} \rightarrow \text{CH}_3\text{C}_6\text{H}_4\text{C}-(\text{CH}_3)_{1 \text{ or } 2?}
\]

Use a toothpick to insert polyethylene tubing through a septum. Place 0.5 mL m-xylene and 0.5 mL t-butylchloride (2-chloro-2-methylpropane) in a thoroughly dry reaction tube and seal the tube with the septum. To prepare the catalyst, cut a 3-inch length of aluminum wire and coil one end using approximately one third of the wire. The coil should be narrow enough so that it will fit easily into your reaction tube. Immerse the coiled end of the wire for a minute in 1M (5%) NaOH solution; this will remove any surface oxide coating from the wire. Wash the coiled end with water and dip the cleaned coil directly into the bottle containing 0.2M mercuric chloride (HgCl₂) solution until the coil is coated with a thin layer of mercury. Remove the coiled wire from the bottle and place it directly in a reaction or test tube containing enough methanol to cover the coiled piece and take this to the hood in which you are going to run the reaction. MERCURY IS A LIQUID AT ROOM TEMPERATURE AND WILL DRIP FROM THE WIRE IF TOO MUCH MERCURY HAS BEEN FORMED BECAUSE THE ALUMINUM WIRE WAS ALLOWED TO SIT IN THE MERCURIC CHLORIDE SOLUTION FOR TOO LONG. Remove the coiled wire from the methanol and dip it directly into another tube containing dichloromethane.

Transfer the amalgamated aluminum wire directly from the dichloromethane to the m-xylene/t-butylchloride mixture to start the Friedel-Crafts reaction. As soon as the amalgamated aluminum has been added to the reaction mixture, cap the reaction tube with the septum/gas trap tube connection. Evolution of HCl should begin within a minute or two. You can check this by holding the end of the polyethylene tube close to a wet piece of pH paper. If the reaction gets too vigorous, cool the reaction tube and its contents in an ice-water bath. Swirl the reaction tube occasionally and wait for the reaction to subside.

Isolation and Purification:

Unstopper the reaction tube and add 0.5-1.0 mL of ice-cold water. Add the water slowly with agitation and observe which layer is the organic layer. After the layers have separated, use a Pasteur pipet to transfer most of the organic layer to a clean reaction tube. The leftover Al wire, the aqueous layer, and any residual droplets of Hg should be placed immediately in the Heavy Metals Waste Container. Wash the organic layer with water, remove the water with a Pasteur pipet, and dry the organic layer with anhydrous Na₂SO₄. Decant the dried crude product to a clean dry reaction tube and use the instant microscale distillation method (see Lab Guide Ch 1) to remove a major portion of the unreacted m-xylene which boils at 139°C. The product boils over 200°C. This step is extremely important since the presence of m-xylene prevents correct interpretation of your results. (Why?) It is better to suffer the loss of some product in order to make sure that all of the m-xylene is removed.

Cleaning-up:
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.

Infrared Spectral Analysis:
Take the infrared spectrum of your crude product using the salt-plate method for liquids. Annotate the three or four right-most absorption peaks in the spectrum.

Final Report:
By referring to Table I, which lists the absorption frequencies of the aromatic C-H out-of-plane bending modes, deduce the structure of your product. Answer these questions:

1. Write a complete mechanism for the Friedel-Crafts reaction of t-butyl/chloride with m-xylene, including formation of the electrophile, arenium ion, and the expected major product.
2. Give a brief explanation of the product obtained in terms of orientation effects of alkyl groups on the benzene ring, steric hindrance and any other important factors.