Exp’t 83

Everything’s Peachy Keen Synthesizing Benzyl Acetate

from K. L. Williamson, Macroscale and Microscale Organic Experiments, 2nd Ed. 1994, Houghton Mifflin, Boston p385; revised 6/27/06

Prelab Exercise:

Give the detailed mechanism for the synthesis of isobutyl formate by Fischer esterification.

Introduction:

The ester group is an important functional group that can be synthesized in a number of different ways. The low-molecular-weight esters have very pleasant odors and indeed are the major components of the flavor and odor aspects of a number of fruits. Although the natural flavor may contain nearly a hundred different compounds, single esters approximate the natural odors and are often used in the food industry for artificial flavors and fragrances. For example, benzyl acetate has the characteristic fragrance of peach. In this experiment, you will synthesize this fruity ester.

<table>
<thead>
<tr>
<th>Ester</th>
<th>Formula</th>
<th>Boiling Point (°C)</th>
<th>Fragrance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isobutyl formate</td>
<td>HCOCH₂CH₂CH₃</td>
<td>98.4</td>
<td>Raspberry</td>
</tr>
<tr>
<td>n-Propyl acetate</td>
<td>CH₃COCH₂CH₂CH₃</td>
<td>101.7</td>
<td>Pear</td>
</tr>
<tr>
<td>Methyl butyrate</td>
<td>CH₃CH₂CH₂COCH₃</td>
<td>102.3</td>
<td>Apple</td>
</tr>
<tr>
<td>Ethyl butyrate</td>
<td>CH₃CH₂CH₂COCH₂CH₃</td>
<td>121</td>
<td>Pineapple</td>
</tr>
<tr>
<td>Isobutyl propionate</td>
<td>CH₃CH₂COCH₂CHCH₃</td>
<td>136.8</td>
<td>Rum</td>
</tr>
<tr>
<td>Isoamyl acetate</td>
<td>CH₃COCH₂CH₂CHCH₃</td>
<td>142</td>
<td>Banana</td>
</tr>
<tr>
<td>Benzyl acetate</td>
<td>CH₂COCH₂苯环</td>
<td>206</td>
<td>Peach</td>
</tr>
<tr>
<td>Octyl acetate</td>
<td>CH₃COCH₃(CH₂)₆CH₃</td>
<td>210</td>
<td>Orange</td>
</tr>
<tr>
<td>Methyl salicylate</td>
<td>苯环 COCH₃</td>
<td>222</td>
<td>Wintergreen</td>
</tr>
</tbody>
</table>
Esters can be prepared in a variety of ways. One method includes reacting alcohols with acid anhydrides to form esters, and this is the method used in this experiment:

\[
\text{Ethanol} + \text{Acetic anhydride} \rightarrow \text{Ethyl acetate} + \text{Acetic acid}
\]

Esters can also be prepared by the reaction of a carboxylic acid with an alcohol in the presence of a catalyst such as concentrated sulfuric acid, hydrogen chloride, \( p \)-toluenesulfonic acid, or the acid form of an ion exchange resin. This type of esterification is known as a Fischer esterification; an example is shown below. The Fischer esterification reaction reaches equilibrium after a few hours of refluxing. The position of the equilibrium can be shifted by adding more of the acid or of the alcohol, depending on cost or availability.

\[
\text{Acetic acid} + \text{Ethanol} \rightarrow \text{Ethyl acetate} + \text{H}_2\text{O}
\]

Acid chlorides form esters by reaction with alcohols. An organic base such as pyridine is added to react with the HCl by-product.

\[
\text{1-Propanol} + \text{Acetyl chloride} \rightarrow \text{n-Propyl acetate + HCl}
\]

A number of other methods can be used to synthesize the ester group. Among these are the addition of 2-methylpropene to an acid to form t-butyl esters, the addition of ketene to make acetates, and the reaction of a silver salt with an alkyl halide. See below.
Synthesis of Benzyl Acetate:

\[
\text{H}_3\text{C}-\text{O} \quad \text{O} \quad \text{CH}_3 + \text{C}_6\text{H}_5\text{CH}_2\text{OH} \xrightarrow{\text{H}^+} \text{C}_6\text{H}_5\text{CH}_2\text{OCOCH}_3 + \text{H}_3\text{C-OH}
\]

- Acetic anhydride
  - MW 102.09, bp 139°C
  - density 1.082
  - \(n_\text{D}^0 = 1.3900\)
- Benzyl alcohol
  - MW 108.14, bp 205°C
  - density 1.045
  - \(n_\text{D}^0 = 1.5400\)
- Benzyl acetate
  - MW 150.18
  - bp 206°C, density 1.040
  - \(n_\text{D}^0 = 1.5020\)
- Acetic acid

To a reaction tube add 540 mg of benzyl alcohol and 510 mg of acetic anhydride and a boiling chip. Attach the empty distilling column as an air condenser. Reflux the resulting mixture for 1 h or more, then cool it to room temperature. Add 1 mL of ether (use the wet ether found in a supply bottle in each hood) and take a drop out of the flask to run a TLC analysis. TLC plates should have three spots (or lanes) on the origin: one for the main organic starting material that is being transformed (the benzyl alcohol), one for a cospot (starting material and the reaction mixture), and one for the reaction mixture. You will need to find the appropriate mobile phase; start by using 30% EtOAc in hexanes.

Once the TLC analysis is complete, add 1 mL of water, separate the organic layer. Wash the aqueous layer with 1 mL of ether. Combine the ether layers, wash with sodium bicarbonate (2 X 1 mL), water (2 X 1 mL), and saturated sodium chloride solution (1 mL). Dry the ether layer with anhydrous sodium sulfate, remove the organic layer into a vial and evaporate the ether by blowing it off in a stream of \(\text{N}_2\).

Isolation and Purification:
On a larger scale, the product would probably be isolated and purified by vacuum distillation, but this is difficult to do on a microscale without severe losses of material and thus poor yields. Therefore, chromatography is used here for purification.

Prepare the Column:
Assemble a microscale chromatography column (see Lab Guide for review), being sure it is clamped in a vertical position. Close the valve, and fill the column with dichloromethane to the bottom of the funnel. Prepare a slurry of 1 g of silica gel in 4 mL of dichloromethane in a small beaker; be sure the slurry is fluid and easy to pour (add more dichloromethane if necessary). Stir the slurry gently to get rid of air bubbles, and gently swirl, pour, and scrape the slurry into the funnel, which has a capacity of 10 mL. After some of the silica gel has been added to the column, open the stopcock and allow solvent to drain slowly into an 25 mL Erlenmeyer flask. Use this dichloromethane to rinse the beaker containing the silica gel. As the silica gel is being added, tap the column with a pencil so the adsorbent will pack tightly into the column. Continue to tap the column while cycling the dichloromethane through the column once more. Once the column is packed, allow the level of the dichloromethane reach the very top of the silica gel column. Add sand (not the sand used for heating mantles!) to the top of the silica gel so that
you have about 1/2” to 1” of sand.

Next, drain the solvent to the top surface of the silica. Add 10 drops of CH₂Cl₂ to the product mixture and using a Pasteur pipet, add this solution to the column by carefully squirting the liquid down the sides of the column; allow the liquid to settle to the top of the column. As you do this, keep the stopcock of the column open so that you’re draining the solvent and allow the sample to adsorb completely onto the top of the column. The product vial is rinsed twice with 0.5-mL portions of dichloromethane that are run into the column, with the eluent being collected in a tared reaction tube. Once all of the sample has been transferred to the column, wash the walls of the column twice with 0.5 mL portions of fresh solvent to ensure that none of your sample remains on the walls of the column; remember to keep the stopcock open during this time; close the stopcock once the solvent reaches just above the top of the sand. Add fresh solvent and open the stopcock to collect the fractions; use small test tubes. The elution is completed with a few more mLs of fresh dichloromethane. You will need to collect several 1 mL fractions. Analyze these by TLC using 50:50 hexane:CH₂Cl₂ spotting starting benzyl alcohol as a standard.

Evaporate the dichloromethane under a stream of nitrogen in the hood, and remove the last traces by connecting the reaction tube to the vacuum. Since the dichloromethane boils at 40°C and the product at 206°C, separation of the two is easily accomplished. Determine the weight of the product, and calculate the yield. The ester should be a perfectly clear, homogeneous liquid. Analyze your product by the method listed on your assignment slip, preparing the sample according to the instructions in the Lab Guide.

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 prepare it as per the instructions on Sample Preparation in the Lab Guide.

Cleaning Up:
After drying, place the used silica gel in the solid waste bin. Any dichloromethane should be placed in the halogenated organic waste container.

Post Lab Questions:

1. Write the reaction for the synthesis of benzyl acetate from a silver salt and a bromo compound.
2. Write the reaction for the synthesis of benzyl acetate from an alcohol and an acid chloride.