

22. The Fischer Esterification

A. Background

Esters are an incredibly important functional group in organic chemistry. Esters are typically very pleasant smelling molecules and are therefore frequently used in the fragrance industry and as flavoring ingredients. Some representative esters are shown in figure 1 below. Additionally, esters are found in biological systems in the form of triacylglycerols (triglycerides), which are derived from glycerol and three fatty acid units. Triglycerides make up both fats and oils. A representative triglyceride along with its glycerol and fatty acid constituents are shown in figure 2. The ester units contained within the structures in figures 1 & 2 are highlighted in red.

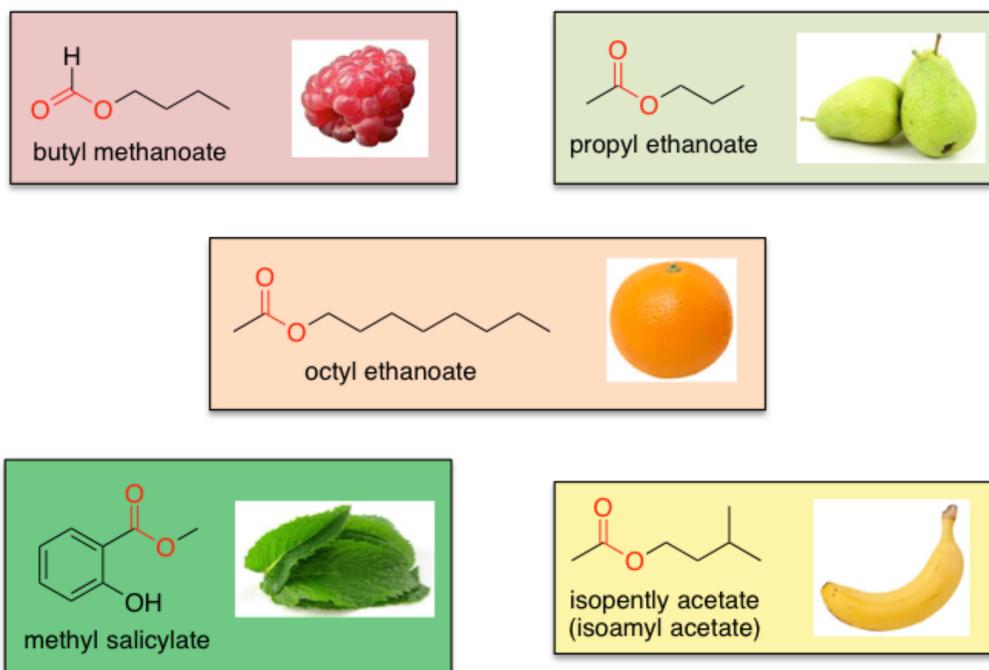


Figure 1. Some Representative Esters and their Fragrances

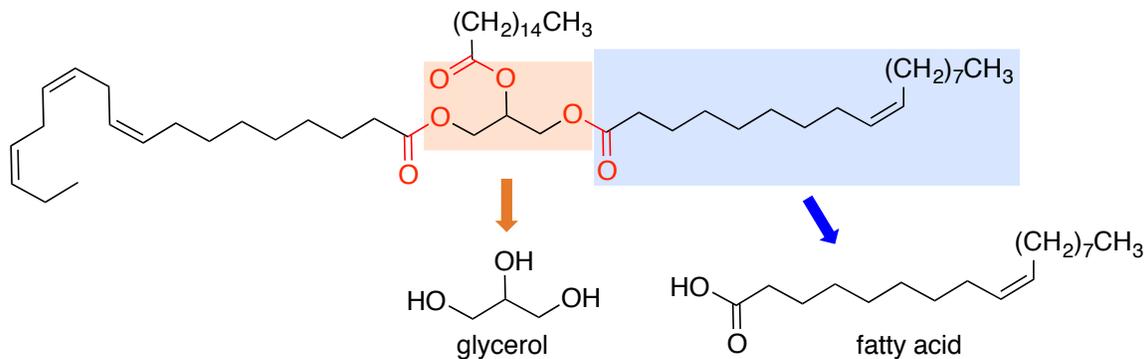


Figure 2. A Triglyceride Containing Three Ester Units

There are a number of different reactions that allow for the preparation of esters. In the previous laboratory experiment, you prepared aspirin by acylating salicylic acid, forming the molecule's ester bond. Another frequently used reaction to form esters is the Fischer esterification, which was first reported by Emil Fischer in the late 1800s. The Fischer esterification involves reaction of a carboxylic acid with an alcohol. The products of the reaction are an ester and water. The reaction is catalyzed by addition of an acid such as sulfuric acid or phosphoric acid.

In this laboratory experiment, you will prepare banana oil (isopentyl acetate) by the Fischer esterification of acetic acid and isopentyl alcohol (figure 3). The reaction will be catalyzed by the addition of sulfuric acid. Once the reaction is complete, a distillation will be performed to isolate the pure organic ester, which will be a liquid.

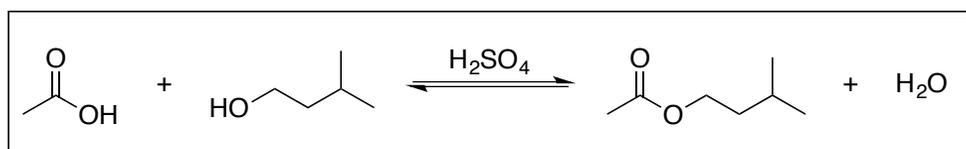


Figure 3. Fischer Esterification to Prepare Isopentyl Acetate

Figure 4 shows the mechanism for the acid catalyzed Fischer esterification. First, the carbonyl oxygen of acetic acid is protonated by the acid catalyst. This generates a highly activated form of the carbonyl electrophile. Next, the alcohol adds to the activated carbonyl carbon. Through proton transfer, the proton is removed from the ether oxygen and subsequently added to the alcohol oxygen to give a tetrahedral intermediate containing $-\text{OH}_2^+$, which is a great leaving group. Water then is lost from the molecule along with formation of the $\text{C}=\text{O}$ double bond. Finally, the proton is removed from the carbonyl oxygen providing the ester product and regenerating the acid catalyst.

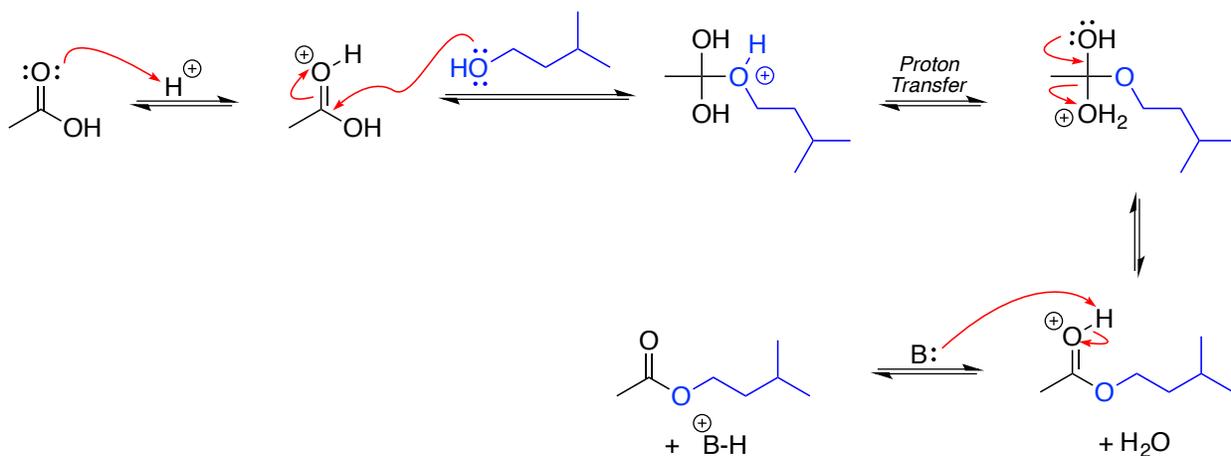


Figure 4. Mechanism of the Acid Catalyzed Fischer Esterification

The Fischer esterification is an equilibrium process. Energetically, the products have nearly identical stability to the starting materials and there is no significant driving force for the reaction. We must take advantage of Le Châtelier's principle to generate and isolate a usable quantity of product. There are a few methods by which one can take advantage of Le Châtelier's principle in order to shift the reaction equilibrium to the right. The first method involves removing one of the products from the reaction mixture as it is formed. Water is one of the reaction products and there are straightforward methods that will allow one to remove water from a reaction as it is

formed. Typically, a special piece of glassware known as a Dean-Stark apparatus is used for this process. Another method that can sometimes be employed is to selectively distill away the desired product as it is formed. This method is only successful when the product has a lower boiling point than the reactants. One final method involves adding a large excess of **one** reactant, which then creates a disturbance in the equilibrium, shifting it towards products. This method is most desirable when one of the reactants is very cheap. In this laboratory experiment, we will take advantage of the last method. One of the starting materials, acetic acid, is available in large quantities for a very low cost. You will use nearly a four-fold excess of acetic acid to drive the reaction toward products.

B. Experimental Procedure

Reagent	Mol. Wt.	Density	BP (°C)	Mass	Mmol	Equiv.
Isopentyl Alcohol	88.2	0.809 g/mL	130	1 mL (0.809 g)	9.17	1
Acetic Acid	60.1	1.05 g/mL	117-118	2.05 mL (2.15 g)	35.8	3.9
H ₂ SO ₄	98.1	-	-	5 drops	-	Cat.
Product						
Isopentyl Acetate	130.2	0.876	142			

Table 1. Reagents and Physical Properties

Equip a 5 mL conical reaction vial with a spin vane. Add the isopentyl alcohol followed by the acetic acid. Next, add 5 drops of concentrated sulfuric acid. Attach an air condenser to the vial using a lock nut. With stirring, heat the reaction mixture to reflux. Bring the temperature of the aluminum block to ~160 °C. Allow the reaction mixture to reflux for 45 min. Remove the vial from heat and allow it to cool at room temperature for 5 min then transfer the vial to cool water bath for an additional 5 min. Finally, cool the vial in an ice bath. Remove the air condenser and add water to bring the volume of the solution to ~4 mL. Stir the solution rapidly for 1-2 min. Stop stirring and allow the layers to separate. Carefully remove the lower aqueous layer by pipet and discard it.

Add 2 mL of ether to the vial to dissolve all organics then add 2 mL of cold water. Stir the solution rapidly for 1-2 min. Stop stirring, allow the layers to separate, then remove and discard the lower aqueous layer. Next, add 1 mL of 5% aqueous NaHCO₃ and stir the two-phase mixture rapidly once again. Stop stirring, allow the layers to separate, then remove and discard the lower aqueous layer. Finally, wash the organic layer by adding 1 mL of brine (saturated aqueous sodium chloride). Stir rapidly, allow the layers to separate, then remove and discard the lower aqueous layer. Pass the organic solution through a sodium sulfate drying column prepared from a pipet plugged with cotton containing 3-4 cm of anhydrous Na₂SO₄. Collect the solution in a conical vial. Be careful not to transfer any residual aqueous layer to the drying column. Use 1 mL of ether to wash any residual product from the drying column and collect this wash in the vial with the rest of your organic solution.

The next part of the procedure involves a distillation to isolate the pure ester product. First, add a spin vane to the vial and evaporate the ether with heating and rapid stirring. With the vial in the aluminum block, bring the block temperature up to 50 °C and then gradually raise the temperature to 100 °C. After 2-3 min at 100 °C all of the ether will have evaporated. Attach a Hickman still to the conical vial using a screw connector as shown in figure 5. At the top of the

Hickman still, suspend a thermometer into the very top of the vial using a septum containing a hole (do not use a screw cap). Continue heating until the aluminum block reaches a temperature of $\sim 210\text{ }^{\circ}\text{C}$. You should observe the ester product collecting in the Hickman still. Be sure to record the temperature range at which the product collects in the still. Discontinue heating when the distillation temperature begins to drop off due to the fact that ester is no longer being collected. Transfer the distilled ester to a pre-weighed vial. Determine the yield and record an IR spectrum of the product. If time permits, determine the refractive index of your product. Using the wafting technique, observe the odors of acetic acid, isopentyl alcohol, and the isopentyl acetate product. Record these observations in your notebook.

Note: During heating, be sure to remove the thermometer from the heating block well before the temperature limit of the thermometer is reached.

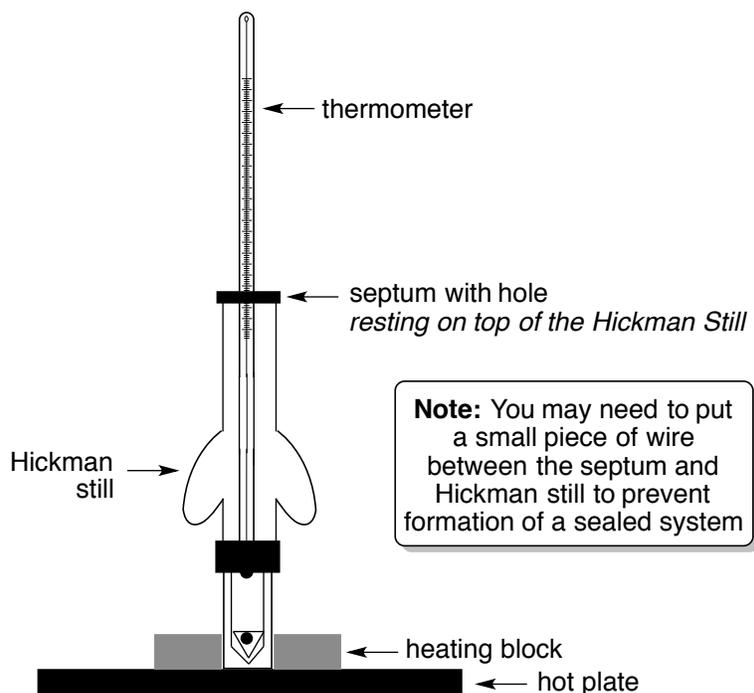
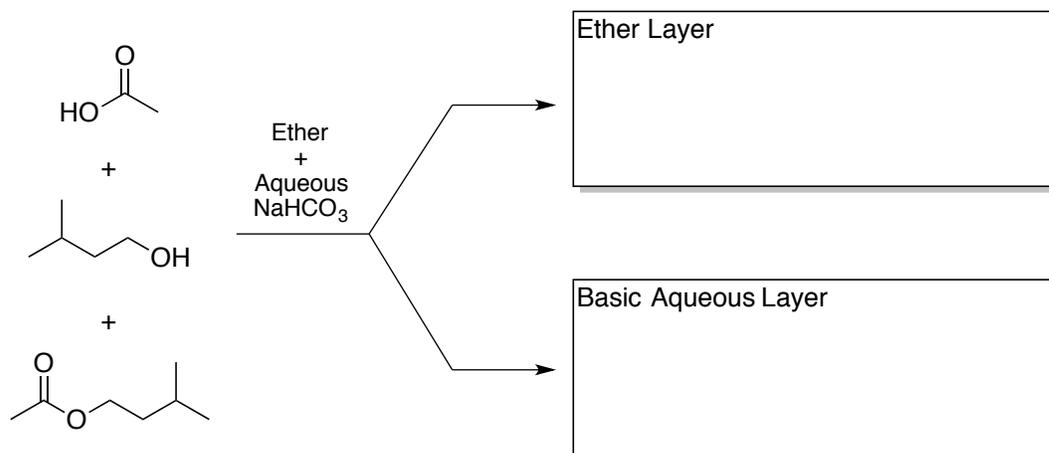


Figure 5. Distillation Apparatus

C. Prelab Questions

- 1) When the reaction is complete and you cease heating, your reaction mixture contains mostly acetic acid, and the isopentyl acetate product. There may also be a small amount of isopentyl alcohol remaining, which is more soluble in ether than in water. Complete the extraction scheme below to show how the product is isolated during the extraction. *You may want to take a look at post-lab question 1 to help you answer this question.*



- 2) Explain why it is necessary to distill your organic product?
- 3) When setting up the distillation apparatus, you are instructed **not** to use a lock nut to tighten down the septum. This prevents the possibility of heating a closed system. Why should you avoid heating a closed system?
- 4) Do you expect the ester that you form in the reaction (isopentyl acetate) to be water-soluble? Explain.

D. Postlab Questions

- 1) During the workup, you added NaHCO3 to the reaction mixture. This base reacts with the leftover acetic acid. This reaction is the vinegar and baking soda reaction that you may have performed as a child. The final products of the neutralization reaction are CO2 and water.
 - a. Write a balanced equation for this neutralization reaction.
 - b. What product is initially formed? *This product decomposes to give CO2 + H2O.*
- 2) What change, if any, would be observed if you increased the amount of sulfuric acid added to the reaction mixture?
- 3) Considering the reversibility of the Fischer esterification, what would the reaction product be if isopentyl acetate were reacted with a large quantity of water in the presence of an acid catalyst?
- 4) Describe the odor of your ester product (isopentyl acetate) compared to the odor of the reactants (acetic acid and isopentyl alcohol).
- 5) Considering the boiling points listed in table 1, would it be reasonable to attempt collecting your ester product as it is formed by a continuous distillation during the reaction?
- 6) How does your experimental boiling point range compare to the literature boiling point value listed in table 1?