

Experiment 8	Synthesis of Isopentyl Acetate
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Objectives

To prepare isopentyl acetate from isopentyl alcohol and acetic acid by the Fischer esterification reaction.

Introduction

Esters are derivatives of carboxylic acids in which the acyl carbon bears an alkoxy substituent (-OR) rather than the hydroxyl substituent (-OH) of the acid. Simple esters tend to have pleasant, fruity odors and are widely used as flavors and fragrances. Table 1 below shows the flavors or fragrances associated with some esters.

Ester	Scent
Isopentyl acetate	Banana
Isobutyl formate	Raspberry
Isobutyl propionate	Rum
<i>n</i> -propyl acetate	Pear
Methyl butyrate	Apple
Methyl anthranilate	Grape
Methyl salicylate	Wintergreen
Ethyl butyrate	Pineapple
Ethyl phenyl acetate	Honey
Benzyl acetate	Peach
Benzyl butyrate	Cherry
Octyl acetate	Orange

Table 1 Esters and their corresponding scents

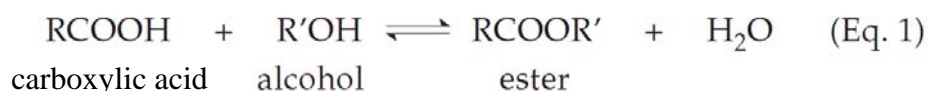
The volatile compounds in natural fruits and flowers are usually complex mixtures of compounds, where esters frequently predominate. Many artificial flavorings contain esters or mixtures of esters. For example, the volatile oil of ripe pineapple contains several esters, as shown in Table 2.

<i>constituent</i>	<i>percent, %</i>
total volatile oil	0.1900
ethyl acetate	0.1196
ethyl alcohol	0.0605
acetaldehyde	0.0014
ethyl acrylate	0.0008
ethyl <i>i</i> -valerate	0.0004
ethyl <i>n</i> -caproate	0.0008

Table 2 Composition of the volatile oil of ripe pineapple

Isopentyl acetate is known as banana oil because of its characteristic odor. This ester has also been shown to be one of the active substances in the alarm pheromone of the honeybee. When a honeybee worker stings an intruder, an alarm pheromone is secreted along with the venom. The pheromone causes other bees to become aggressive and attack the intruder.

Esterification generally refers to the formation of esters from alcohol and carboxylic acids, as shown in Equation 1.

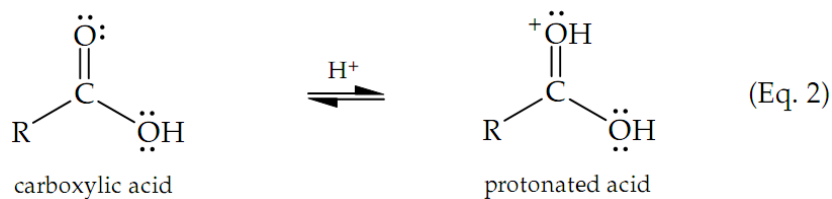


The reaction proceeds by way of a nucleophilic substitution at the acyl carbon of the carboxylic acid. When catalyzed by a strong acid, usually sulfuric acid or *p*-toluenesulfonic acid, the reaction is called the Fischer esterification.

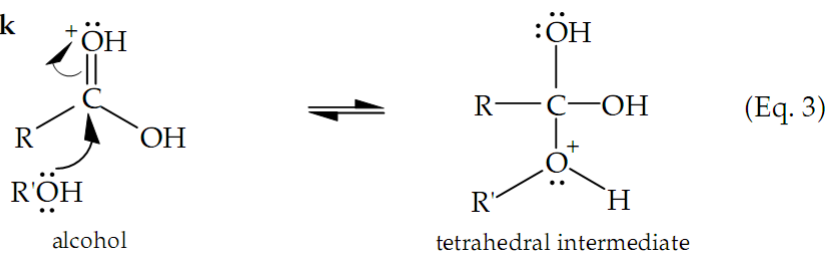
The reaction mechanism is shown in Equations 2-6. Equation 2 shows the protonation of the acyl oxygen of the carboxylic acid. The protonation activates the acyl carbon toward nucleophilic attack. Equation 3 shows the nucleophilic attack at the acyl carbon by the oxygen atom of the alcohol to form a tetrahedral intermediate. Equation 4 shows a proton transfer to the hydroxyl oxygen of the carboxyl group. This protonation converts the hydroxyl group into the good leaving group, water. Equation 5 shows the loss of water forming the protonated

ester. Finally, Equation 6 shows the proton transfer to a base, resulting in the formation of the ester.

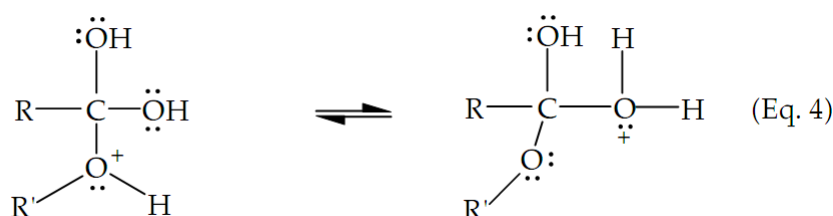
Protonation



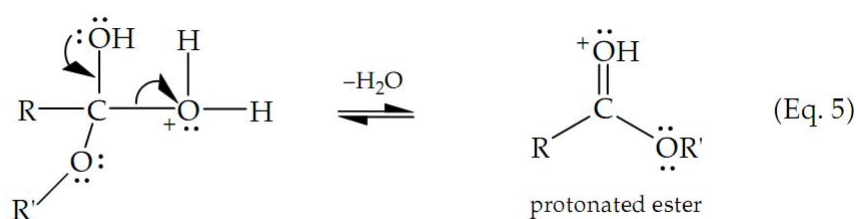
Nucleophilic Attack



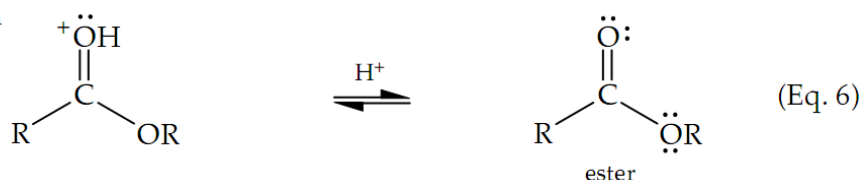
Proton Transfer



Dehydration



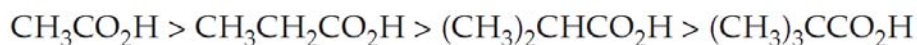
Dehydrogenation



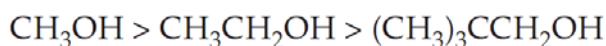
Each step of the reaction mechanism is reversible and, therefore, the reaction reaches equilibrium. **Le Chatelier's principle** suggests that the amount of ester produced in an equilibrium reaction might be increased either by using an excess of one of the reactants or by removing one of the products. In practice, an excess of carboxylic acid or alcohol, whichever is more readily available, is added, and/or water is removed as the reaction proceeds. A water-absorbing substance such as molecular sieves might be included in the reaction mixture, or the water might be removed as part of an azeotrope with benzene or toluene.

The mechanism suggests that steric effects might be important in Equation 3, the step involving the attack by the alcohol at the acyl carbon of the carboxylic acid. Indeed, alkyl-group

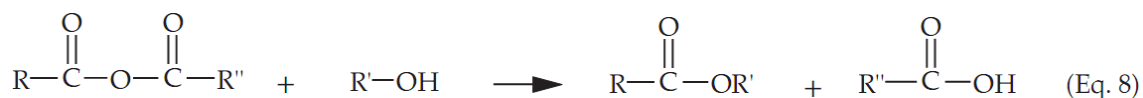
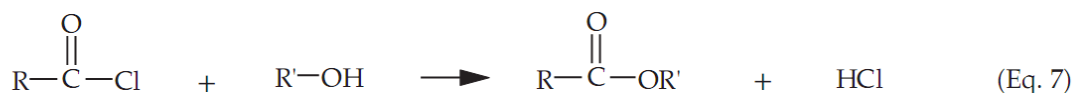
branching at the α - or β -carbon of the acid slows the rate of esterification. For example, the relative rates of esterification with methanol follow the order:



Sterically hindered alcohols also react more slowly in the esterification reaction. The relative rates for esterification of alcohols with acetic acid follow the order:



Fischer esterification is an example of an acyl transfer reaction. The acyl group from the acid is transferred to the alcohol. Acid chlorides and anhydrides also serve as acylating agents. Because acid chlorides and anhydrides contain good leaving groups, these compounds are very reactive toward nucleophilic substitution by an alcohol, as shown in Equations 7-8.



The Fischer esterification is conducted at reflux. The purpose of reflux is to heat a reaction mixture at its boiling temperature to form products, without losing any of the compounds in the reaction flask.

In practice, a condenser is set vertically into the top of the reaction flask. Any compound that vaporizes will condense when it enters the cool environment of the reflux condenser and will then drain back into the reaction flask. Reflux apparatus using glassware for a semi-microscale technique is used in the procedure.

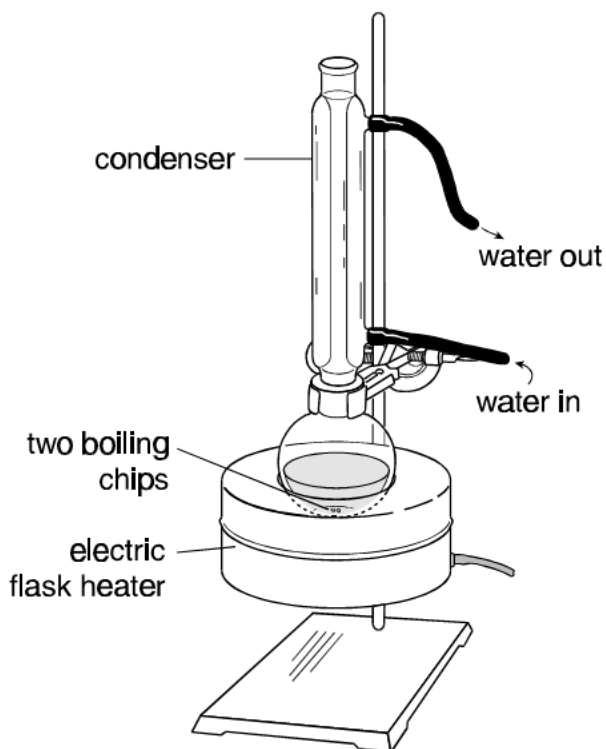
In this experiment, you will prepare isopentyl acetate by reacting an excess of acetic acid with isopentyl alcohol. You will use sulfuric acid to catalyze the reaction.

After the reaction is complete, you will remove the excess acetic acid and sulfuric acid from the reaction mixture by extraction with sodium hydrogen carbonate.

Experimental Procedure

- 1) Mix isopentyl alcohol (5.4 mL, via burette) and glacial acetic acid (8.5 mL, via graduated cylinder) in a round-bottom flask. Carefully add 20 drops of conc. H_2SO_4 to the mixture.
- 2) Put in a few boiling chips and assemble the reflux apparatus (Figure 1).

Figure 1
Reflux apparatus



- 3) After having your set-up checked by the instructor, heat the reaction mixture under reflux conditions for 1 hour.
- 4) Cool the reaction mixture to room temperature. Transfer the mixture into a 125 mL separatory funnel and add cold water (25 mL). Extract and separate the aqueous layer.
- 5) Wash the organic layer twice with 5% NaHCO_3 (25 mL each time).
- 6) Wash the organic layer with saturated NaCl solution (25 mL).
- 7) Dry the organic layer with anhydrous Na_2SO_4 . Decant the crude ester into a clean 25 mL round-bottom flask. Add a boiling chip.
- 8) Assemble a simple distillation apparatus. Distill the product and collect the 134-143°C fraction into a pre-weighed test tube.
- 9) Weigh the product and calculate the yield. Submit the product to your instructor.

Laboratory Safety Precaution

- 1) Wear safety goggles and lab coat at all times while working in the laboratory.

- 2) Isopentyl alcohol (3-methyl-1-butanol) is irritating. Glacial acetic acid is corrosive. Concentrated sulfuric acid is corrosive and oxidizing. Prevent eye, skin, and clothing contact. Avoid inhaling vapors and ingesting these compounds.
- 3) Neutralizing acids with sodium hydrogen carbonate generates CO₂ gas. Vent the separatory funnel frequently to avoid pressure build-up.
- 4) Wash your hands thoroughly with soap or detergent before leaving the laboratory.