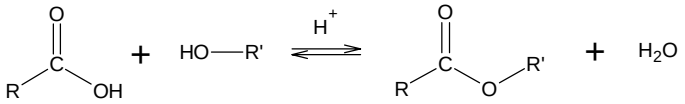
The Preparation and Identification of an Ester

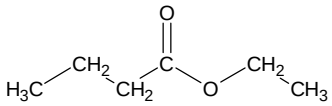
Background

Carboxylic acids react with alcohols to form compounds known as *esters* (**R** represents any hydrocarbon group):



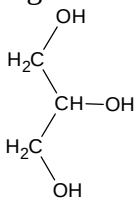
This acid-catalyzed equilibrium synthesis was developed by Emil Fischer (1852-1919). There are other pathways for making esters but this one is simple and interesting for reasons beyond the utility of making new compounds.

Esters are very common organic compounds. Typically we associate these substances with aromas and flavor essences. For example, ethyl butanoate:

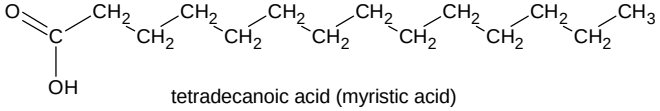


is one of the esters associated with the flavor and aroma of pineapples. The actual constituents of flavor and aroma in foods are many and not static. Over 50 esters have been identified among the volatile compounds found in Bartlett pears [a personal favorite]. As the chemical processes associated with ripening take place, the mix of chemicals also changes. This is one of the reasons why "artificial" flavorings never measure up to the real thing. It is neither cost effective nor entirely possible to recreate the subtle blend in natural foodstuffs.

The prevalence (and importance) of esters goes far beyond making things smell and taste good [and yes, some esters smell and taste *very* nasty]. Fats and oils are also esters. These are composed of the triol glycerol, and long-chain "fatty" acids:

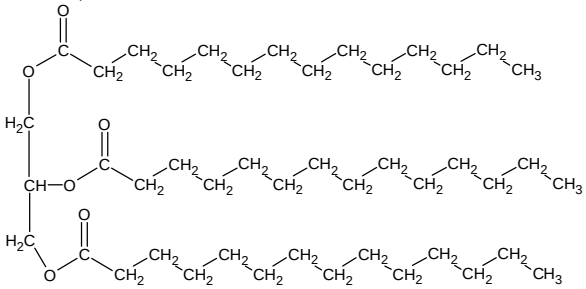


glycerol

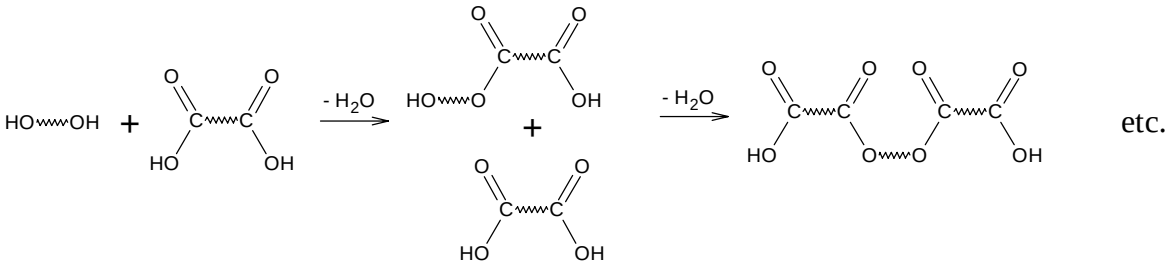


tetradecanoic acid (myristic acid)

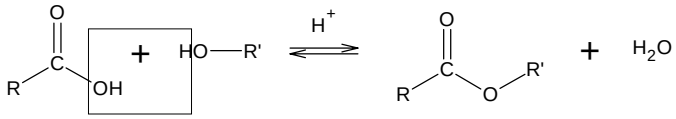
In these compounds the esterification reaction occurs at each alcohol site and thus involves three acids (which may or may not be the same):



Waxes likewise are esters of long-chain alcohols and long-chain acids and there are cyclic esters called *lactones* in which a molecule with both alcohol and carboxylic acid functional groups reacts with itself. Esters are also the units in some types of polymers (hence *polyester*):



Whatever the type of ester, the basics of the reaction involve a process called *condensation* in which a small molecule--in this case water--is split out between two compounds, leaving a linkage to form a larger molecule from the original units:

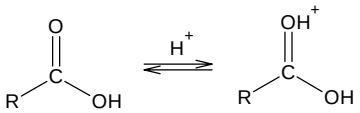


A moment of consideration will lead to the conclusion that this does not seem to make a lot of sense. Carboxylic *acids* should be proton donors, not acceptors. While the reaction might be boxed otherwise, studies with radioactive oxygen-tagged compounds indicate that this is the correct way in which the linkage forms in the ester.

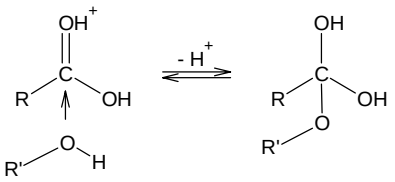
The proposed mechanism for Fischer esterification involves a process related to *nucleophilic substitution*. The word "substitution" is clear enough but a *nucleophile* needs some introduction. Organic chemists use the terms *nucleophile* and *electrophile* to describe certain electron-rich and electron-deficient species in a reaction. In terms that are familiar from the study of inorganic reactions, a nucleophile is a Lewis base or a structure with at least one lone pair of electrons. An electrophile, on the other hand, is a Lewis acid or a structure with an incomplete octet or perhaps a positive charge.

Because of their extra electron density, nucleophiles are attracted to parts of molecules with partial positive charges or electron deficiencies (such as sp^2 or sp carbons). Electrophiles are attracted to electron-rich sites such as lone pairs or partial negative charges.

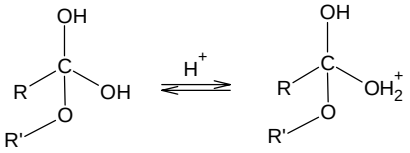
The mechanism of Fischer esterification is not thought to be a true nucleophilic substitution, but it involves a nucleophile (the alcohol) adding to the carboxylic acid and a subsequent elimination step. Initially the carboxylic acid is protonated by the stronger inorganic acid catalyst (typically sulfuric acid):



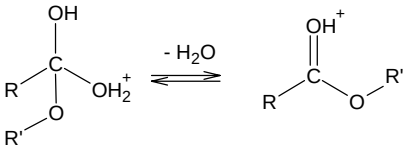
In the second step the alcohol nucleophile (two lone pairs on the oxygen) adds at the sp^2 carbon and the alcohol proton is lost:



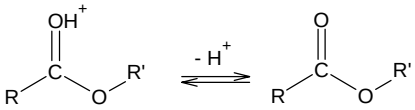
This is an important step in the mechanism because it is here that the new ester bond between the carboxyl group carbon and the alcohol oxygen forms. A series of fast equilibrium proton exchanges occur at either of the two acid -OH groups (which are equivalent):



Next, water is eliminated at one site or the other:



In the final step the excess proton leaves, regenerating the inorganic acid catalyst:



Although the uncatalyzed reaction is quite slow (several days at reflux temperatures), Fischer and Speier discovered in 1895 that the addition of only a small amount of mineral acid greatly accelerates the attainment of equilibrium.

Because each of these steps is an equilibrium and the equilibrium constant for many esterifications is less than 10, control of reaction conditions to maximize products is of some importance. Based on LeChâtelier's Principle, we know that increasing the amount of either of the reactants should help. If either the alcohol or acid is considerably less expensive this is one possible approach. Under the right experimental conditions it is also possible to remove water as refluxing is taking place. The disappearance of a product will tend to drive (or pull, if you like) the reaction to the right. However, in laboratory scale organic synthesis the usual aim is not so much getting a lot of product as it is determining how the product forms and how it can be isolated, purified and identified.

The Experiment

There are two parts to this experiment:

- synthesis and isolation of an ester
- analysis of the synthesis product by gas chromatography/mass spectrometry

The following non-locker materials will be provided:

- concentrated acetic, formic and propanoic acids [fume hood]
- concentrated sulfuric acid [fume hood]
- 1-propanol, 2-propanol, 2-methyl-1-propanol, 3-methyl-1-butanol, 1-pentanol
- micro sample vial with teflon seal
- saturated Na_2CO_3
- anhydrous $MgSO_4$
- 18 x 150 mm test tube
- beral pipets, pasteur pipet, cotton
- ice

The Chemicals

Formic acid (HCOOH) is a colorless liquid with a pungent odor. It is miscible with water and alcohol. *The concentrated liquid is dangerously caustic to skin!* It is used as a decalcifier, a reducing agent in dyeing wool fast colors, for tanning and in regenerating old rubber. **Persons with severe allergic reactions to bee stings should handle the liquid with extreme caution**.

Propanoic acid (C_2H_5COOH) or *propionic acid* is an oily liquid with a slightly pungent and rancid odor. It is used in textile dyeing and as a solvent for cellulose.

Acetic acid (or ethanoic acid) has a pungent odor and in concentrated form (17 M) produces painful burns on the skin. It is soluble in water and is itself an excellent solvent for many organic compounds. While it is a weak acid, concentrated solutions are extremely irritating to tissue, especially mucous membranes. It is used in the manufacture of various acetates including plastics and textiles, in dyeing, preserving foods and in many organic syntheses. Household vinegar is 5% acetic acid. Ingestion of more concentrated solutions may cause severe corrosion of the mouth with vomiting, circulatory collapse and eventual death.

Sulfuric acid is a clear, colorless, oily liquid in concentrated form (98%). It is highly corrosive and has a high affinity for water, abstracting it from wood, paper, sugar, etc., leaving a carbon residue behind. Dilution of concentrated sulfuric acid generates a tremendous amount of heat. Here in the lab your instructor prepares the dilute sulfuric acid you use by pouring the concentrated acid slowly over ICE while stirring! Even so, the resulting solution is very warm. As with all acid dilutions, acid is added to water, not the reverse, since the heat generated can boil the water at the point of contact and cause spattering.

Sulfuric acid is used to make fertilizers, explosives, dyes, parchment paper, and glue. It is used, in concentrated form, in automobile batteries as the electrolyte. It is corrosive to all body tissues and contact with eyes may result in total blindness. Ingestion may cause death. Frequent skin contact with dilute solutions may cause dermatitis.

1-propanol (C_3H_7OH) or *n*-propyl alcohol is a liquid with an alcoholic, slightly stupefying odor. It is miscible with water, ethanol and ether. The compound is used as a solvent for resins and cellulose esters. It may be mildly irritating to the eyes and mucous membranes and have a depressant action similar to ethanol.

2-propanol or isopropyl alcohol is a flammable liquid, miscible with water and common organic solvents. It forms a low-boiling azeotrope with water and can also be used to make low-freezing mixtures (i.e., as an antifreeze). It is a solvent in many quick-drying commercial preparations (inks, shellacs, oils, etc.) and is used as a topical antiseptic in a 70% solution (*rubbing alcohol*). Ingestion of as little as 100 mL can be fatal.

2-methyl-1-propanol or isobutyl alcohol is a colorless, flammable liquid with an odor similar to 1-pentanol, but weaker. It is soluble in about 20 parts water. The compound is used in the manufacture of esters for fruit flavoring essences and as a solvent in paint and varnish removers. Its toxicity is similar to 1-propanol.

3-methyl-1-butanol or isopentyl alcohol (*or* isoamyl alcohol) has a characteristic disagreeable odor and a repulsive taste. Vapors are poisonous. It is used as a solvent for fats, resins, etc., in the manufacture of mercury fulminate, artificial silk, lacquers and smokeless powders. Its initial topical toxicity is similar to 1-propanol but higher vapor or liquid concentrations may cause depression and narcosis.

1-pentanol or *n*-amyl alcohol has a mild, characteristic odor and is only slightly soluble in water. It is used as a solvent in organic syntheses. Irritating to the eyes and respiratory passages, prolonged exposure to the compound can cause giddiness, headache and even delirium.

Sodium carbonate occurs in nature in various mineral forms but much is manufactured by the Solvay process or from brines and alkali lake beds. The dry powder is slightly hygroscopic. Aqueous solutions are strongly basic. It is used in the manufacture of other sodium salts, in glass, soap, as a general cleanser ("washing soda") and in photography.

Magnesium sulfate occurs in nature as the mineral kieserite. The anhydrous compound is a white powder. The heptahydrate (commonly known as *Epsom salts*) is slightly efflorescent. It is used in bleaching, the manufacture of mother-of-pearl and frosted papers, for fireproofing and in mineral waters. It has relatively low toxicity. Oral doses as high as 15 grams have been prescribed as a cathartic.

Technique Discussion

You will be assigned an acid/alcohol pair from which to synthesize an ester.

Reactions of this sort are often quite slow, even with a catalyst. They are therefore generally *refluxed*. This means that the vapor is trapped and allowed to condense and drip back into the mixture during a heating period. Generally this is done with a water-jacketed condenser. However, in this experiment since the refluxing temperature is fairly low and the amounts--and therefore the time--are fairly small, a microscale method utilizing a small, sealed vial will be adequate as long as there is no leakage of material during the heating process.

A 250 mL beaker of boiling water [hotplate] should be prepared while the sample is being mixed. About 1 g of the assigned alcohol is placed in the vial and 2.5 mL of the assigned organic acid is added. About 5 drops of concentrated sulfuric acid should be added last (this functions as the catalyst). The vial must then be tightly sealed. Leakage will result in loss of reactants and products and will invalidate yield calculations [not to mention spoiling results]. Masses of the reactants should be recorded [rough balance].

The vial is placed carefully into the boiling water bath and heated for about 25 minutes. A constant tiny stream of bubbles issuing from around the cap is a sign of a leak. If this is caught early the vial can be removed from the bath and the cap tightened. After heating the vial should be placed on the bench to cool to touch. Cooling in an ice/water bath for 3 minutes should reduce any possible pressure buildup and also limit the solubility of the ester in the mixture.

The ester can be roughly separated from the mixture by pouring the contents of the vial into a test tube containing about 8 mL of the ice/water mixture from the cooling bath. *The vial should be opened cautiously since there may be residual pressure inside which could cause the contents to spurt out*. A small additional rinse of the vial with ice water is advisable. The ester should be more or less water-insoluble while the acid and perhaps the alcohol are more water-soluble. After gentle stirring the ester forms a layer on top of the water and can be carefully removed with a beral pipet.

Depending on the amount of product it may be advisable to use a smaller test tube for the extraction and removal process. A narrower tube will make the ester layer easier to see and separate from the aqueous layer.

Residual alcohol dissolved in the ester may be removed by the cautious addition of about 2 mL of saturated Na_2CO_3. The ester is insoluble in this solution while the alcohol is very soluble. The sodium carbonate should also destroy any acid residue that remains in the sample. The ester phase should again be removed with a clean beral pipet. A small amount of solid $MgSO_4$ is then added to the ester to dry it. Complete drying may take 3-5 minutes. When drying is complete the liquid should show no sign of cloudiness. Fine suspended crystals of the drying agent may not be visible but they will jam (and ruin) the chromatography syringes if there are not removed. The dried ester should therefore be filtered through cotton packed into the end of a pasteur pipet. The final product should be massed and stored in a tightly capped vial for subsequent GC analysis.

Your instructor has written data acquisition programs for the esters in this experiment so that no additional instrument set-up is required on your part. The detector for the GC is the *HP 5790* Mass Spectrometer. As each substance emerges from the column it is not only quantified but also analyzed and the mass spectrum for the substance (which is stored with the data output) can be subsequently compared with a library of standard spectra for identification. You will be furnished with a computer-generated report on your sample on the day following injection.

Everyone will use the same acquisition routine but **you must be sure to enter a unique file name for your data** since it will be processed after class hours. Be sure to follow the instructions below carefully.

---

1. Press F2 to begin **Data Acquisition**.
2. Press F5 to **Load Parameters**. Type in place of the parameter file shown:
   PARAM:ESTER.A
3. Press F5 again to **Load** the actual parameter file. This is *very important*. If you simply press <Return> instead, the parameter file will not be loaded.
4. Press F1 to **Prepare to Inject**.
5. Type in the data file space:
   DATA:1.D (substitute your locker number for the 1)
   Follow by <Return>. Please do not use any other kind of file names. These are the only kinds of files the instructor will look for when processing the data.
6. Use TAB to move to the operator name field and type in your name.
7. Wait for temperature equilibration and the message **Ready to Inject**.
8. Use the "empty syringe" method to inject your mixture and start the run. Wait for run completion.
9. Press F8 (Exit, Quit) twice. This should leave the instrument as you found it, ready for the next student.

After you have run your sample through the instrument, turn in your ester (labeled) to the instructor.

The Report

Your initial calculations should include:

1. The theoretical yield from the esterification based on the masses of the acid and alcohol

2. The "actual" yield as determined from the mass of the collected and dried product

3. The probable identity of components in your mixture based on Mass Spectra library database match

4. The actual yield as determined from the chromatogram peaks [see conversion calculations on next page]

5. The % purity of the final sample (as mass % of the "actual" yield from #2)

Your conclusion to this experiment should include a reaction for the production of your ester. Use structural formulas. Give the correct name of the ester and its handbook boiling point along with a 3D molecular diagram.

Why would concentrated hydrochloric acid NOT be a good choice for a catalyst in the esterification reaction? [hint: how much water is present in each concentrated acid?]

Converting mole fraction data to mass fractions

The general solution:

$$\text{mole fraction of a component} = \chi_i = \frac{\text{moles i}}{\text{total moles}} = \frac{n_i}{n_T} = \frac{\frac{g_i}{MM_i}}{n_T}$$

- χ_i is discovered from the chromatogram peak ratios and the MM of the component is known
- thus g_i [the mass of the component in the sample] and n_T remain unknown

rearranging the final expression above to solve for g_i you have:

$$g_i = \chi_i \, MM_i \, n_T$$

- here, both g_i and n_T are still unknown

However, by summing all of the g_i values, you obtain the measured mass of the sample in the vial:

$$\sum_{i=1}^{c} g_i = \text{sample mass in vial} \quad \text{(where c = total number of components)}$$

This expression is equivalent to:

$$\sum_{i=1}^{c} \chi_i \, MM_i \, n_T \quad \text{which is equal to the sample mass in the vial}$$

- **YOU CAN NOW SOLVE FOR n_T**

Once you know n_T you can find the masses of individual components since:

$$\chi_i \, n_T = n_i \quad \text{and} \quad n_i = g_i/MM_i$$

- Thus $g_i = n_i MM_i$ (but then we knew that!)