

Congratulations, you have been chosen to be part of a blue-ribbon panel of experts in order to design a new fragrance of air freshener. You will be designing a particular fragrance and comparing your compound with compounds synthesized by other members of your panel. The management is focusing on developing a new ester fragrance for their new line of celebrity fragrances scheduled to come out this summer. (The celebrity is yet unnamed.)

Esters are a class of compounds widely distributed in nature. The simpler esters tend to have pleasant odors. In many cases, although not exclusively so, the characteristic flavors and fragrances of flowers and fruits are due to compounds with the ester functional group. The organoleptic qualities (odors and flavors) of fruits and flowers may often be due to a single ester, but, more often, the flavor or the aroma is due to a complex mixture in which a single ester predominates. Some common flavor/aroma essences are given below:

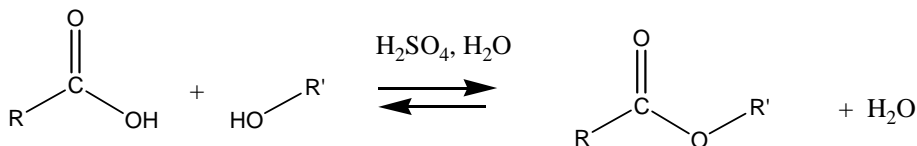
Acid	Alcohol	essence
Acetic (Ethanoic)	3-methyl-1-butanol	banana
Acetic (Ethanoic)	1-propanol	gummy worms
Acetic (Ethanoic)	1-octanol	orange
Formic (Methanoic)	Ethanol	rum
Butyric (Butanoic)	Ethanol	pineapple
Butyric (Butanoic)	Methanol	apple

Food and beverage manufacturers are thoroughly familiar with these esters and often use them as additives to enhance the flavor and odor of a dessert or beverage. Many times such flavors or odors are not even naturally occurring as in the case with the “juicy fruit” principle, 3-methyl-2-butenyl ethanoate. An instant pudding with has “rum” flavor may never have seen its alcoholic namesake – this flavor can be duplicated by the proper mixture, along with other minor components, of ethyl methanoate and 2-methylpropyl propanoate. The natural flavor and odor are not exactly duplicated, but most people can be fooled. Often only a trained person with a high degree of gustatory perception, a professional taster, can tell the difference.

A single compound is rarely used in good quality imitation flavoring agents. A formula for an imitation pineapple flavor, which might fool an expert is a combination of 7 esters, 3 carboxylic acids, and 7 essential oils!

Flavor is a combination of taste, sensation, and odor transmitted by receptors in the mouth (taste buds) and nose (olfactory receptors). The four basic tastes, sweet, salty, sour and bitter are perceived in specific areas of the tongue. However, the human actually possesses about 9000 taste buds that can sense and blend flavors. It is the combined response of these taste buds which allows us to perceive a particular flavor.

In this experiment, we will prepare an ester from a carboxylic acid and an alcohol under acidic conditions. This is an example of the Fischer esterification method. Esters can be prepared by the reaction of a carboxylic acid with an alcohol in the presence of a catalyst such as concentrated sulfuric acid.



The reaction reaches equilibrium after refluxing for a period of time. According to Le Châtelier's principle, the position of the equilibrium can be shifted by adding more of the carboxylic acid or alcohol, depending on cost or availability. The mechanism of the reaction involves initial protonation of the carboxyl group, attack by the nucleophilic hydroxyl, a proton transfer, and loss of water followed by loss of the catalyzing proton to give the ester. Each of these steps is completely reversible, so this process is also, in reverse, the mechanism for the hydrolysis of an ester.

Another way to upset the equilibrium is to remove water. This can be done by adding to the reaction mixture molecular sieves, which preferentially adsorb water. Water can also be removed as an azeotrope (a constant boiling mixture of water and an organic liquid).

In the isolation procedure for this experiment, much of the excess alcohol and the remaining sulfuric acid are removed by extraction with water. Any remaining carboxylic acid is removed by extraction with aqueous sodium bicarbonate.

This experiment is a variation of the “banana oil” Fischer Esterification that has been performed by Sophomore Organic Chemistry students for decades. However, in this experiment we are using an old reaction to make new (never been characterized) compounds! The discovery and characterization of new compounds is an important part of the chemistry enterprise. Not only does the discovery of new compounds increase the sum total of human knowledge, these compounds may also have useful properties that can be exploited to create a “more just and humane society”.

References:

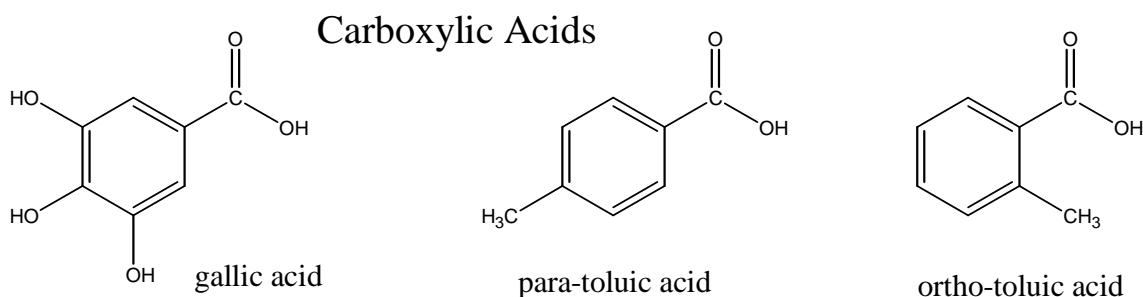
Pavia D. L.; Lampman G. M.; Kriz G. S. “Introduction to Organic Laboratory Techniques: a contemporary approach” 1st edition 1976 W. B. Saunders Company.

Wade P.A.; Rutkowsky S.A.; King D.B. A simple combinatorial experiment based on Fischer esterification - An experiment suitable for the first-semester organic chemistry lab. *J Chemical Education* **2006**, 83(6), 927-928.

The “banana oil” lab 2001 may be found at

<http://domin.dom.edu/faculty/jbfriesen/chem254/banana.ppt>

Here are the acids and alcohols you will be combining in search of an exquisite fragrance:



Assignments:

	gallic acid	p-toluic acid	o-toluic acid
1-propanol	1R, 4R, 7R	2R, 5R, 8R	3R, 6R, 9
2-propanol	1L, 4L, 7L	2L, 5L, 8L	3L, 6L, 10

Procedure:

Obtain a round 250mL bottom flask supported with a cork ring. Add 0.02 moles of your carboxylic acid into the round bottom flask. Add 20 mL of alcohol to the flask.

Carefully add 5 mL of concentrated sulfuric acid (DANGER: CORROSIVE) to the contents of the flask, with swirling. Add three boiling stones to the mixture.

Assemble a reflux apparatus. Make sure the water is running through the condenser. Bring the mixture to a boil with a suitable heating source (thermwell). Allow the mixture to reflux for 30 minutes.

After 30 minutes: remove the heating source pour the contents of the round bottom into a beaker as soon as you are able to handle it. You may rinse the flask with ether. Allow the mixture to cool to room temperature. The mixture may solidify when cooled. Add at least 40 ml of MTBE (methyltert-butylether). More ether may be needed to completely dissolve a solid product. Pour the ether mixture into a separatory funnel and carefully add 25 mL of water.

Stopper the separatory funnel and shake it several times. Separate the lower aqueous layer from the upper organic layer. You may perform a second extraction of the lower aqueous layer if you deem it necessary. You may discard the aqueous layer after making certain that the correct layer has been saved.

The crude ester in the organic layer may contain some unreacted carboxylic acid, which can be removed by extraction with 5% aqueous sodium bicarbonate solution. Carefully add 30 mL of the 5% aqueous sodium bicarbonate solution to the organic layer contained in the separatory funnel. Swirl the separatory funnel gently until carbon dioxide gas is no longer evolved. Stopper and gently shake the funnel once or twice, and then vent the vapors. Shake the funnel until no vapors are evolved with the separatory funnel is vented.

Remove the lower aqueous layer. Check the pH of the aqueous layer. If it is no longer basic, repeat the extraction with fresh 5% NaHCO_3 solution.

Discard the aqueous layers and extract the organic layer with one 30 mL portion of saturated aqueous NaCl . Carefully separate the lower aqueous layer and discard it.

When the water has been removed, drain the contents of the separatory funnel into a beaker. Add a teaspoon of anhydrous sodium sulfate (Na_2SO_4) to dry the solution. Swirl the beaker gently. Allow the crude ester solution to stand until the liquid is clear.

Weigh a new beaker. Decant or gravity filter the solution to separate out the hydrated magnesium sulfate.

Evaporate the ether in a hot water bath or by the forced air method.

Obtain the mass of the product.

Testing your Ester:

These are novel (new) compounds they have not been previously characterized!

- Observe the physical properties of your ester.
- Characterize the odor of your ester.¹
- You may obtain an
 - IR spectrum,
 - UV spectrum, or
 - TLC (at least one of the three.)
- Submit a sample for GC testing



Disposal:

Dispose of aqueous solutions in the liquid waste container.

Dispose of non-aqueous materials that have come in contact with laboratory chemicals in the solid waste container.

¹ Image → http://phudson.com/uploaded_images/Nose%202-793768.jpg

PRELAB

Title:

Purpose:

Physical constants

Name	Formula	M.W. g/mole	m.p. °C	b.p. °C	Density g/mL
gallic acid	C ₇ H ₆ O ₅	170.12	250		solid
p-toluic acid	C ₈ H ₈ O ₂	136.15	177-180	274-275	solid
o-toluic acid	C ₈ H ₈ O ₂	136.15	102-104	258-259	solid
1-propanol	C ₃ H ₈ O	60.10	-127	97	0.804
2-propanol	C ₃ H ₈ O	60.10	-89	82.3	0.786
Aqueous concentrated Sulfuric Acid	H ₂ SO ₄	98.078		~ 290	1.840
Aqueous Sodium Bicarbonate	NaHCO ₃	84.007	~0	~100	~1
water	H ₂ O	18.01	0	100	0.995
Aqueous Sodium chloride	NaCl	58.442	~0	~100	~1

Safety/solubility information

Name	Solubility	Safety Information
Aromatic carboxylic acids	Soluble in basic aqueous solutions. Somewhat soluble in alcohol and nonpolar solvents	Flammable, irritant to skin, eyes, and especially the respiratory system.
1-propanol	Miscible with water and alcohols. Somewhat Miscible with non-polar solvents	Flammable, irritant to skin, eyes, and especially the respiratory system.
2-propanol	Miscible with water and alcohols. Somewhat Miscible with non-polar solvents	Flammable, irritant to skin, eyes, and especially the respiratory system.
Sulfuric acid	Soluble in water and alcohols. Insoluble in non-polar solvents	Corrosive material, will cause burns, harmful to skin
Aqueous Sodium Bicarbonate	Soluble in water (10g/100mL)	irritant to skin and eyes.
Water	Miscible in alcohol, immiscible with nonpolar solvents	Safe
Sodium chloride	Soluble in water	Irritant to skin

Sources: Aldrich Catalog, Chemfinder.com, Wikipedia.com

Flowchart

Calculations and Questions:

- 1) Determine the mass of the carboxylic acid you must use.
- 2) Determine the number of moles of alcohol you are adding.
- 3) Draw the structure of your product.
- 4) Calculate molecular weight and the theoretical yield of your ester.
- 5) Search the data for your carboxylic acid at “<http://www.chemspider.com>” record the ACD/LogP for your carboxylic acid. What does the LogP represent?
- 6) At “chemspider” record the # of Rule of 5 Violations for your carboxylic acid. What is the role of “The Rule of 5” also called “Lipinski's Rule of Five” in drug discovery?

Safety Question: For 2-propanol, record the “SAF-T-DATA Ratings” (on a scale of 0-4) for Health, Flammability, Reactivity, and Contact. What is the Storage Color Code?

Experimental Observations and Data:

Hand in a copy of your experimental observations and data before you leave lab.

Experimental Observations: Refer to Laboratory Syllabus for guidelines.

Raw Data: Refer to Laboratory Syllabus for guidelines.

Lab report:*Results.*

- ___ % yield of your ester. Show your calculations please.
- ___ Interpret the UV spectrum of your ester if you performed this in lab.
- ___ Interpret the IR spectrum of your ester if you performed this in lab.
- ___ Interpret the TLC of your ester if you performed this in lab.
- ___ Interpret the GC-FID chromatogram of your ester.
- ___ Interpret the ^1H and ^{13}C NMR of your ester as posted on the CHEM254lab website.

Discussion and Conclusion

- ___ One method for favoring the formation of the ester is to add an excess of alcohol. Suggest another method, involving the right-hand side of the Fischer esterification equation, which will favor the formation of the ester.
- ___ Why are primary or secondary alcohols typically used for Fischer esterification syntheses and not tertiary alcohols?
- ___ Green Question: What is the worst violation of Green Chemistry principles in this lab? Propose at least one alternative to make it more “green.”
- ___ What celebrity would you like to develop a fragrance for?

<p>We are living in a world today where lemonade is made from artificial flavours and furniture polish is made from real lemons... Alfred E. Newman</p>
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