NAME ______________________________________

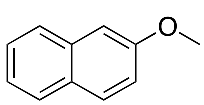
EXPERIMENT 9: PERFUMES-THE SYNTHESIS OF NEROLIN

NOTE: Assignments 1-4 **must** be completed before the start of the laboratory. Students will not be allowed into the laboratory to conduct the experiment until these assignments are completed. Extra laboratory time will not be provided for students who fail to complete these assignments.

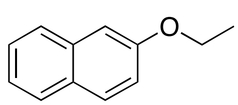
BACKGROUND

Certain aromatic ethers live up to their name by exuding, pleasant, distinctive odors, making them useful *aroma chemicals* for the formulation of perfumes. In the seventeenth century, Anna Maria de la Tremoille, the Italian princess of Neroli, introduced a perfume containing oil distilled from orange blossoms. A major constituent of her *neroli oil is* the aromatic ether nerolin (2-methoxynaphthalene), which is still used to impart its characteristic odor of orange blossoms to perfumes. 2-Ethoxynaphthalene, which has the same aromatic qualities as its methyl homolog, is sometimes called "new nerolin" because of its more recent discovery and use by the perfume industry.

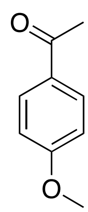
A number of anisole (methoxybenzene) derivatives are important aroma chemicals as well. *p*-Methoxyacetophenone is a natural component of hawthorn flowers and an ingredient of some perfumes. *p*-Methylanisole occurs in the oil of the Malayan ylang-ylang tree and also contributes a floral odor to perfumes. Anisole itself has an agreeable odor but is better known for its antioxidant properties, which make it a good preservative for beer and a stabilizer for vinyl polymers. A more widely used antioxidant is butylated hydroxyanisole (BHA), a mixture of *t*-butyl-*p*-hydroxyanisoles that is used to preserve butter, meat, cereals, baked goods, and candies. The phenolic OH group is the primary oxidation inhibitor in BHA, but the methoxy group has a synergistic effect.



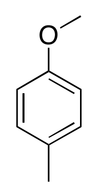
2-methoxynaphthalene
Nerolin



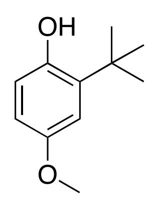
2-ethoxynaphthalene
New Nerolin



p-methoxyacetophenone



p-methylanisole



butylatedhydroxyanisole
BHA

The fragrances of perfumes have found their way into hundreds of products. Besides being used directly as perfumes, colognes, and lotions; perfumes are also found in soaps, shampoos, bath oils, deodorants, cosmetics, oils, creams, powders, and other household products.

Originally, all perfumes came from plant or animal sources. The tremendous demand for perfumes and the development of organic chemistry, have lead to synthetically derived perfumes from coal tar or petroleum products. The most expensive perfumes contain oils extracted or steam distilled from fresh flowers (the yield may be as little as a pound of oil from a ton of flowers).

Perfumes today consist of a blend of ingredients diluted in alcohol and water to a certain concentration. Perfumes may have as few as 10 ingredients or as many as 200; the exact composition is a closely guarded secret by the perfumers.

INTRODUCTION

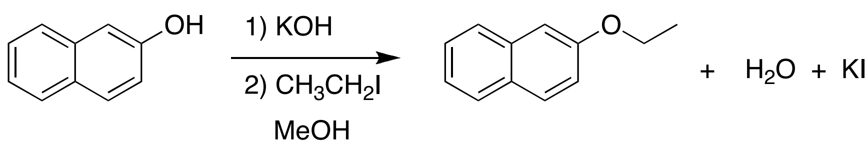
In the experiment you will prepare a derivative of nerolin (new nerolin), a synthetic perfume fixative. Nerolin is an important ingredient in many perfumes and as a fixative, which 'binds' the other ingredients. This diminishes the rate of evaporation of the more volatile components. If a fixative like nerolin were not present, the fragrance of a complex perfume would change with time as the more volatile oils evaporated and left behind the less volatile substances.

DESCRIPTION

Nerolin is chemically named 2-ethoxynaphthalene or β-naphthyl ethyl ether. Nerolin is prepared using a Williamson ether synthesis. This reaction utilizes an S_N2 mechanism. The reaction occurs between a nucleophillic alcohol and an electrophillic alkyl halide. The nucleophile, β-naphthol, is deprotonated by a methanolic solution of potassium hydroxide. The more nucleophillic β-naphthylolate anion substitutes for the excellent leaving group iodide, on the ethyl iodide.

In this synthesis potassium hydroxide is used rather than sodium hydroxide because of its greater solubility in the alcohol solvent (why is this?). After completion of the reaction to form Nerolin the reaction is cooled and the product is isolated by addition of ice-cold water. The crude product precipitates from solution. The crude product can be further purified through recrystallization. Due to Nerolin's favorable solubility in methanol a mixed solvent system, utilizing methanol and a small portion of water, is used for the recrystallization process.

REACTION



DESCRIPTION/TYPE OF REACTION TO BE PERFORMED

ASSIGNMENT 1. Provide a general description of the reaction to be performed including 1) the name of the synthesis, 2) the type of mechanism involved, and 3) the laboratory methods used.

ASSIGNMENT 2. Provide a mechanism for the reaction to be performed:

PROCEDURE

SAFETY NOTES

KOH is corrosive/caustic, and ethyl iodide is a skin irritant. Avoid skin exposure to these and all chemicals. In case of accidental contact, flood the affected area with copious amounts of water.

PREPARATION OF 2-ETHOXYNAPHTHALENE:

Place 20 ml of methanol, 0.020 mole of β-naphthol, and 0.026 mole of KOH into a 100 ml round bottom flask (***Caution***: *KOH is corrosive/caustic-Avoid skin contact*). Stir the mixture well. Allow a few minutes for the acid-base reaction to occur (why?). Add ethyl iodide in 10% excess (0.022 mole), attach a condenser and reflux the mixture for 2 hours. (You're boiling so don't forget the…)

After completion of refluxing allow the hot reaction mixture to cool. Add about 50 ml of ice-cold water. The nerolin may at this point appear as an oil, due to its low melting point and the impurities present, but eventually it will crystallize upon cooling. Collect the solid nerolin by suction filtration, and then further purify the compound by recrystallization. A mixed solvent system of methanol with a small amount of water can be used. (***Hint***: If you don't know what this means, find out beforehand!)

Place the solid sample in a 100 ml beaker and add enough ***hot methanol*** to just dissolve the solid (remember the solution needs to be kept hot also, why?). To encourage crystallization add a small amount of ***hot*** water until the solution turns turbid (look it up if you don't know what it means). Add a few drops of ***hot*** methanol to clear the solution. Allow the solution to cool undisturbed to room temperature, then place the solution in an ice-bath. Collect the crystals by suction filtration (remember the vacuum trap and its purpose), allowing air to be drawn through the sample by the vacuum to aid in drying of the sample.

Weigh the dry sample; determine the percent yield and melting point of the material. If the values are not satisfactory, the sample may be recrystallized again, or decolorizing carbon may be used followed by recrystallization to further purify the compound.

ASSIGNMENT 3. Fill in the chart below with appropriate *structures*, and *physical properties* of reagents needed to complete the reaction. In addition calculate the moles and mass or volume of the reagents. Experimental results are to be filled in during completion of the experiment.

NAME/STRUCTURE	FW	Circle correct		Circle correct	Moles	Equivalents
β-Naphthol		M.P./B.P. °C	Density (if needed)	Grams/Milliliter		
Ethyl iodide		M.P./B.P. °C	Density (if needed)	Grams/Milliliter		
Potassium hydroxide		M.P./B.P. °C	Density (if needed)	Grams/Milliliter		
Methanol		M.P./B.P. °C	Density (if needed)	Grams/Milliliter		
Nerolin		M.P. °C			Theoretical Moles	

Experimental Results			
Nerolin	Grams Recovered =	Theoretical Yield (g) =	Theoretical M.P. (°C) =
		Experimental % Yield =	Experimental M.P. (°C) =

SHOW ALL CALCULATIONS BELOW↓

ASSIGNMENT 4. Write a brief step-by-step procedure in your own words for the above reaction sequence. Number the steps 1, 2, 3, … Add observations as you perform these steps. Attach additional 8 ½ x 11 sheets if needed.

#	STEP	OBSERVATION

SUMMARY/ CORRECTIONS/DATA ANALYSIS

Provide a detailed summary of the experiment including observations, analysis of all data, and methods to correct errors or optimize the experiment. Describe new knowledge obtained from the laboratory. Use complete sentences and math as necessary. Use additional Summary sheets if needed. If an IR spectrum is taken, attach the annotated spectra to the report.

QUESTIONS:

1. If you suspect that the product nerolin contained unreacted β-naphthol (Hint: acid/base), *describe* another method (purification technique) to purify the product and remove the contaminant.

2. If nerolin is a solid, why are you able to smell it?

3. Why should perfume bottles be stored tightly capped and away from heat and direct sunlight?

4. Describe how the order of reagent addition avoided a possible side reaction in this synthesis. (Hint: This means why did we do what we did. There are reasons we didn't just throw everything in the flask and let it cook) Show a mechanism for this side reaction below.

5. Why do we react β-naphthol with ethyl iodide rather than react ethyl alcohol with 2-iodonaphthalene? Draw out a putative mechanism for ethyl alcohol reacting with 2-iodonaphthalene and explain why this method wouldn't work.