Lab 7 Nucleophilic Substitution Preparation of Nerolin

Objectives

- Synthesize nerolin by nucleophilic substitution
- Understand mechanism of nucleophilic substitution

Background

Nucleophilic Substitution Reactions

Substitution reactions are a general class of organic reactions in which one atom or group is replaced with another. A very common pathway for substitution is nucleophilic, in which a nucleophile is added to the molecule as a leaving group leaves. If the attack of the nucleophile occurs at the same time as the leaving leaves, as seen in Figure 1, the mechanism is classified as S_N2, with the 2 referring to the bimolecular rate law. An S_N1 mechanism involves the leaving group leaving first, creating a carbocation intermediate, before the nucleophile attacks.

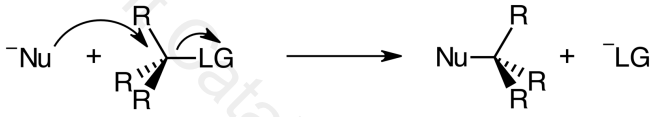

Figure 1 General scheme of a S_N2 reaction of a nucleophile (Nu) attacking as a leaving group (LG) leaves

Preparation of Nerolin

Nerolin, a common name for 2-ethoxynaphthalene, is an important perfume fixative that can be synthesized by an S_N2 substitution reaction, as shown in Figure 2. As a fixative, nerolin "binds" the other ingredients together to diminish the rate of evaporation of the more volatile compounds. If a fixative like nerolin were not present in a perfume, the fragrance of the complex mixture would change with time as the more volatile oils evaporated and left behind the less volatile substances.

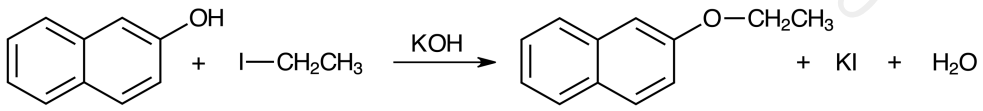

Figure 2 Overall preparation of nerolin by nucleophilic substitution of 2-naphthol

In the synthesis of nerolin, potassium hydroxide acts as a base and deprotonates the slightly acidic phenolic proton of the 2-naphthol. The resulting 2-naphthoxide acts as the nucleophile to attack iodoethane and displace the iodide ion, as shown in Figure 3. This substitution occurs by an S_N2 bimolecular mechanism. The bimolecular reaction means that the rate of reaction depends on the concentration of both the 2-naphthol and the iodoethane.

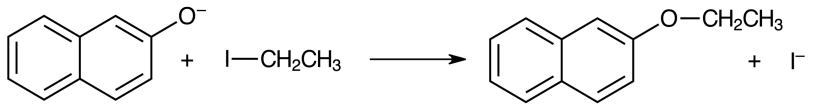

Figure 3 Nucleophilic substitution step of 2-naphthoxide with iodoethane

An additional consideration of the reaction is solubility. Strong bases generally have low solubility in the organic solvents needed for the organic compounds. The nerolin synthsis reaction uses potassium hydroxide rather than sodium hydroxide as the potassium compound has a higher solubility in ethanol, which is a suitable solvent for the reactants. The nerolin product is less soluble in ethanol, so the product is will precipitate with the addition of ice-cold water and can be recrystallized from alcohol and water.

Materials

- 2-Naphthol
- Ethanol
- Potassium hydroxide
- Iodoethane
- Microscale glassware kit
- Boiling chips
- Ice bath
- Vacuum filtration set-up
- Melting point apparatus
- FTIR

Safety goggles are required!

All work should be performed in the hood.

2-naphthol is a toxic irritant. Ethanol is a flammable irritant. Potassium hydroxide is corrosive and toxic; wash thoroughly if skin contact is made.

Procedure

Nucleophilic Substitution Preparation of Nerolin

1. Place 2.0 mL of ethanol, approximately 0.29 g of 2-naphthol, and 0.17 g of potassium hydroxide into the long neck round bottom flask.
2. Swirl the mixture gently for 5 minutes to allow dissolution and the acid-base reaction to occur.
3. Add 0.20 mL of iodoethane to the flask.
4. Add a couple of boiling chips to the flask.
5. Set up for reflux using the elastomeric connector and the tube on top of the flask, wrapped in a wet paper towel.
6. Reflux the mixture at a gentle boil for 2 hours.
7. Set up an ice bath toward the end of the reflux time.
8. Allow the mixture to cool to room temperature once the reflux is done.
9. Transfer the contents of the round bottom flask to an Erlenmeyer flask.
10. Add 5.0 mL of ice-cold water.
11. Place the reaction mixture in the ice bath.
12. Stir as well as gently scratch the bottom and sides with a stir rod to induce crystallization.
13. Collect the crystals using vacuum filtration with a Hirsch funnel.
14. Move the crystals from the Hirsch funnel to a watch glass for drying and place the watch glass in the oven for about 5 minutes.
15. Measure and record the mass of the crystals.
16. Measure the melting point of the crystals.

17. Obtain an IR spectrum using an FTIR instrument.
18. All solvents are to go into the **halogenated** waste container. Crystals can be dissolved in ethanol and go into the non-halogenated container. Wash glassware with soap and water.

Pre-Lab Questions

Prepare for lab by completing and understanding the answers to these questions. Refer to the Background or another resource, such as your textbook, if necessary.

1. What precautions should one use when working with potassium hydroxide?

2. Why is it important that the number of moles of 2-naphthoxide ion be the same as the number of moles of iodoethane used for the synthesis of nerolin?

3. What effect would not properly drying the filtered nerolin have on your results?

4. Identify the nucleophile and leaving group for the reaction.

Lab 7: Nucleophilic Substitution Preparation of Nerolin Report Sheet

Name _____ Section _____

Date _____ Instructor _____

Nucleophilic Substitution Preparation of Nerolin

Amount of reactant used (grams) _____

Amount of reactant used (moles) _____

Space for calculations:

Product obtained (grams) _____

Product obtained (moles) _____

Space for calculations:

Product theoretical yield _____

Space for calculations:

Product percent yield _____

Space for calculations:

Product melting point _____

Write the equation for the reaction.

Major IR peaks in cm^{-1}

Post-lab Questions

1. Is your percent yield within reason of what you would expect? Explain your answer.

2. Does your product melting point indicate that your sample is indeed nerolin? Cite additional evidence that your product is nerolin.

3. If there were multiple products, comment on finding the mixture melting point of the products. Does your sample appear to be a mixture or pure?