12. The Williamson Ether Synthesis

A. Introduction

It would be beneficial if you review the chapter on substitution reactions in your textbook prior to lab. This is Ch. 11 in the 9th edition McMurry textbook. The Williamson Ether Synthesis can specifically be found in sections 17-2 and 18-2.

In the previous laboratory experiment a variety of substitution reactions (both S_N1 and S_N2) were carried out in order to qualitatively assess the rates of substitution with a variety of substrates. In this laboratory experiment, you will carry out a synthetically useful substitution reaction and isolate the organic product.

Previously, you should have found that S_N2 reactions work best with strong nucleophiles and primary or methyl halides. The S_N2 reaction is an important reaction for bond formation in both organic and biological chemistry. In this experiment, you will first generate a moderately strong nucleophile by deprotonation of 2-naphthol with sodium hydroxide to form a naphthoxide ion (figure 1a). The electrophile, 1-bromobutane, will then be added to the solution at which time the S_N2 reaction will take place to form 2-butoxynaphthalene (figure 1b). This product is commonly used in the food industry as a flavoring agent due to its fruity taste similar to raspberry or strawberry.

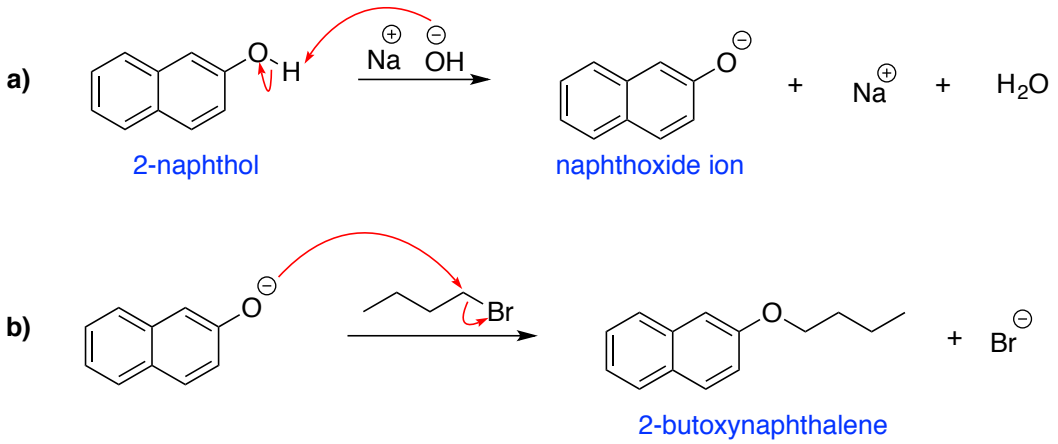


Figure 1. Generation of Nucleophile and Nucleophilic Substitution Reaction

A substitution reaction occurring between an oxygen nucleophile and an organohalide electrophile producing an ether product is known as a Williamson Ether Synthesis, named after Alexander William Williamson, Professor of Chemistry at University College, London from 1849-1887. Williamson is also known for his 1868 textbook *Chemistry for Students*. In this book, Williamson details both the theoretical and experimental details involving the reactions of several elements and the preparation of numerous inorganic and organic compounds. For his work on the synthesis of ethers, Williamson was awarded a Royal Medal 1862. Founded in 1825 by King George IV, this award is given annually by the Royal Society for the most important contributions in the physical, biological, and applied sciences.

B. Experimental Procedure

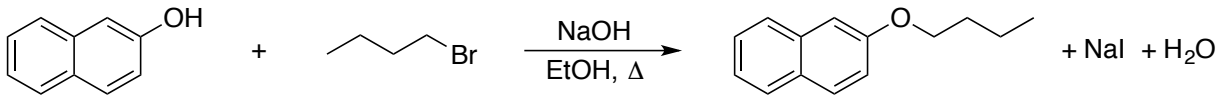


Table 1: Reagents

	Mol. Wt.	Density (g/mL)	Equiv.	Amount
2-naphthol	144.2	-	1	150 mg (1.04 mmol)
1-bromobutane	137.0	1.27	1.3	0.15 mL (1.35 mmol)
NaOH	40.0	-	2.1	87 mg (2.18 mmol)
EtOH	-	-	-	2.5 mL

Measure out 150 mg of 2-naphthol and add the solid to a 5 mL conical reaction vial equipped with a spin vane. Add 2.5 mL of ethanol and commence stirring. Next add 87 mg of crushed[1] solid sodium hydroxide. Once the sodium hydroxide has been added, equip the vial with an air condenser (a water condenser without running water can also be used) and heat the solution to reflux for 10 min. The boiling point of ethanol is 78 °C. Your aluminum block temperature should be a bit above this temperature to achieve a good reflux. Be sure to secure your reaction apparatus using by placing the vial in the aluminum block and by using a clamp if possible. After 10 min of reflux, allow the solution to cool to at least 60 °C and then temporarily remove the air condenser and add 0.15 mL of 1-bromobutane via syringe. Reattach the air condenser and reheat the reaction to reflux for 50 min at which time the reaction should complete. Remove the vial from heat and allow it to cool to at least 50 °C. Remove the air condenser and add ice to the reaction vial to bring the total volume to ~5 mL. Next, place the reaction vial in an ice bath for 10 min to precipitate as much product as possible. The solid can then be collected using a Hirsch funnel and vacuum flask. Rinse the reaction vial with 1-2 mL of ice-cold water and empty this wash portion into the Hirsch funnel along with the rest of your product. Draw air through the solid for 5-10 min. Scrape the solid product onto a weighed watch glass. If solid precipitated out in the filtrate, you should do a second filtration to collect additional product. Determine the percent yield and melting point of your product. Heat the melting point sample slowly as the melting point of the product is below 50 °C. You should also obtain an IR spectrum of the product. *If necessary, the solid can be left to dry in your drawer until the next lab period at which time data can be collected.*

C. Pre-Lab Questions

1. Draw the complete electron pushing mechanism for reaction that you are performing. For the substitution step, identify the nucleophile, electrophile, and leaving group.

2. Why is it important to mix the 2-naphthol and sodium hydroxide prior to adding 1-bromobutane? What might happen is you were to mix 2-naphthol, NaOH, and bromobutane all simultaneously?

3. Compare the acidity of 2-naphthol and ethanol. Which is more acidic? Why?

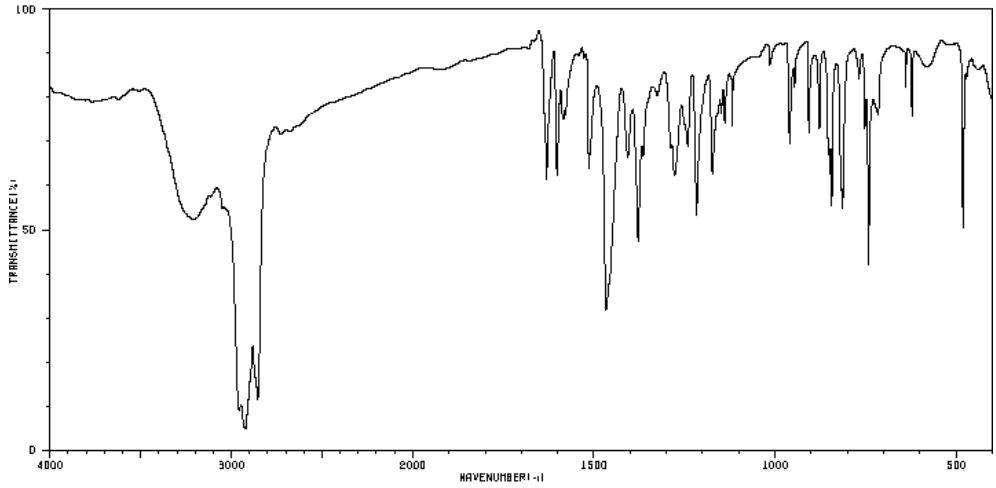
[1] Crushed NaOH can be obtained by wrapping 2-3 NaOH pellets inside a piece of filter paper and subsequently pounding the wrapped solid with the aluminum block. NaOH is hydroscopic and will pick up moisture quickly. You should work quickly to crush and measure out the solid NaOH.

D. Post-Lab Questions

1. Do you have to worry about NaOH deprotonating ethanol to any appreciable extent? Explain.

2. How do the think the reaction would have been affected if 1-iodobutane were used as the electrophile instead of 1-bromobutane?

3. The IR spectrum of 2-naphthol is shown below. Based on the IR spectrum of your product, how can you confirm that the starting material was converted to the desired product?



E. Acknowledgements

This procedure was adapted from:
A Simple S_N2 Reaction for the Undergraduate Laboratory, J.J. Esteb, J.R. Magers, L. McNulty, P. Morgan, A.M. Wilson, *J. Chem. Ed.* **2009**, *86*, 850.