

ELECTROPHILIC AROMATIC IODINATION

Iodination of *ortho*-vanillin (2-Hydroxy-3-methoxybenzaldehyde)

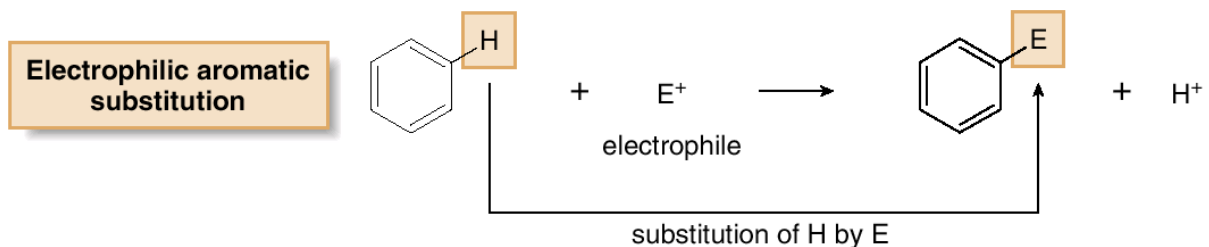
Reference: *Greener Approaches to Undergraduate Chemistry Experiments*; Published by the American Chemical Society

In this experiment you will:

1. Perform an electrophilic aromatic halogenation reaction.
2. Isolate, purify and characterize the product using melting point determination, TLC and spectral analysis.
3. Analyze the methodology using the 12 principles of green chemistry.

THEORY

Unlike alkenes that undergo electrophilic addition, aromatic compounds undergo electrophilic substitution reactions. Halogenation of aromatic compounds is an example of electrophilic aromatic substitution. In this reaction aromatic compounds are treated with halogens in the presence of a Lewis acid catalyst.



Scheme 1: Electrophilic Substitution Reaction of Aromatic Compounds

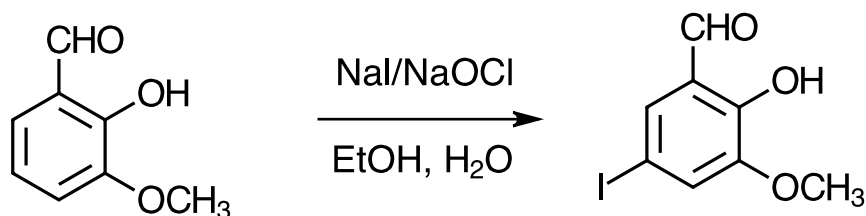
There are some problems associated with handling halogens. Cl₂ is a gas and can cause severe respiratory problems. Br₂ is a volatile liquid. It can cause serious burns to the skin and eyes, in addition to respiratory problems. However, aromatic halogenation is an important reaction and is of great synthetic utility. Iodine is relatively easy to work with. However, I₂ is very unreactive towards aromatic compounds. If I₂ is used in the presence of powerful oxidizing agents, iodination of the aromatic ring takes place. The oxidizing agent commonly used in iodination is nitric acid. If the aromatic ring has

activating groups, iodination occurs with relative ease but regiochemistry is difficult to control (polyiodination products are usually obtained). A clever way of introducing iodine in an aromatic ring is to block certain positions on the ring and thereby increase regioselectivity.

Greening the lab: In this lab, you will perform aromatic iodination of vanillin using 'greener' conditions. A convenient green alternative is using sodium or potassium iodide instead of iodine and common bleach in aqueous alcohol as the oxidizing agent.

The advantages of the modified reaction conditions are:

1. The reaction uses greener reagents, sodium iodide instead of I_2 .
2. The reaction uses benign solvents such as water and ethanol.
3. The reaction uses milder and safer oxidation conditions, household bleach instead of conc. HNO_3 .
4. The reaction is efficient and selective. Monoiodinated product is obtained as the major product.



Scheme 2: Electrophilic Iodination of *ortho*-Vanillin

PROCEDURE

In a 100-mL round-bottomed flask containing a magnetic stir bar, dissolve 1.0 g of *ortho*-vanillin in 20 mL of 90% ethanol. To this solution, add 1.17 grams of sodium iodide, then cool to 0 °C in an ice-water bath. Using a burette, **slowly** add 12 mL of aqueous sodium hypochlorite solution (6% w/w) drop wise to the stirred reaction mixture over a period of 30 minutes at 0 °C (See figure 1). **Slow addition of the hypochlorite solution at 0 °C will result in higher yield and easier purification.** During the

addition, the color will change from pale yellow to red-brown. Occasionally, the color may turn green. Once the addition is complete, stir the solution at 0 °C for an additional 10 minutes. Replace the ice bath with a room temperature water bath and allow the reaction mixture to stir for an additional 30 minutes.

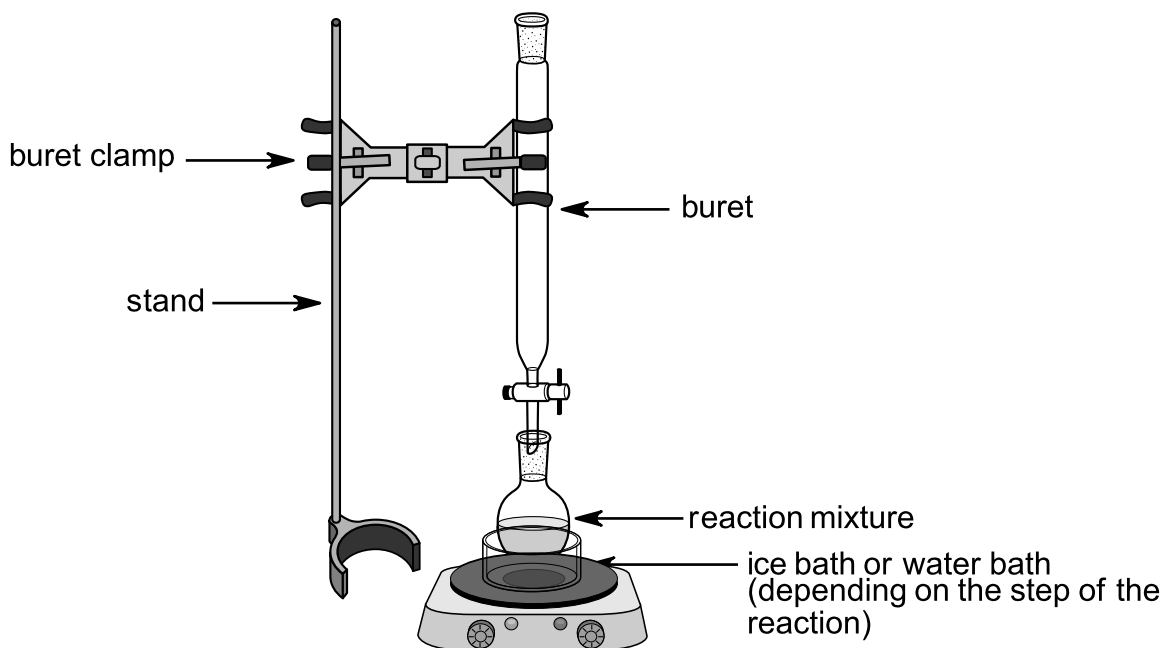


Figure 1: Reaction Set Up

Workup and Isolation

Remove the water bath but continue stirring the reaction mixture during the following work up.

Measure 10 mL of sodium thiosulfate (10% w/w) in a graduated cylinder and add drop wise to remove the excess unreacted iodine. Then using a pipet, acidify with HCl (10% w/w) dropwise. The product should precipitate at this point. Use pH paper to monitor the acidity. Continue adding HCl until pH is acidic.

Stop stirring and cool the flask in an ice bath for 10 minutes. Collect the product by suction filtration. Wash the product with 2 mL of **ice-cold** water.

Recrystallization

Transfer the product to a 125 mL Erlenmeyer flask and add some boiling stones.

Transfer 30 mL of 2-propanol to a 100 mL beaker and add some boiling stones. Bring the solvent to boiling. Add 10 mL of hot 2-propanol to the crude solid in the Erlenmeyer flask. Transfer the Erlenmeyer flask to the hot plate and heat the mixture. Add more 2-propanol if necessary to obtain a colored but clear solution. The challenge is to dissolve the product in as little 2-propanol as possible. Transfer the flask from the hot plate to the wire gauze and cover it with a small watch glass. Allow the solution to cool to room temperature and then place the flask in an ice bath for 5 minutes to ensure complete crystallization. Collect the product by suction filtration.

Drying of the Solid

Dry the product between folds of filter paper, followed by using a heat lamp to dry the product. Alternately, you may leave the product to air dry until the following week. Check with your instructor about which method is adopted for drying.

Product Characterization

Determine the yield and the melting point of the dry recrystallized product. The literature melting point of 5-Iodo-*o*-vanillin (FW = 278.04 g/mol) is 127 – 130 °C. Run an IR spectrum of the product and compare it to a standard sample if available. Run ¹H NMR spectra of both ortho-vanillin and the product obtained. Include both the spectra and the analyses in your lab report.

	Mass in grams or volume in mL	Molar Mass	Molarity	Density	Moles
Ortho-vanillin	1.0015 g		n/a	n/a	
Sodium iodide	1.1915 g		n/a	n/a	
Ethanol	20 mL		n/a		
Bleach	12 mL			n/a	
Product	1.393 g		n/a		

