

Electrophilic Aromatic Substitution using Green Chemistry: Iodination of Vanillin

Electrophilic aromatic substitution is useful for attaching functional groups to an aromatic ring. The functional group or groups already attached to the aromatic ring will determine the position of substitution. For an aromatic compound containing multiple groups, the groups that are more activating will determine the position of substitution.

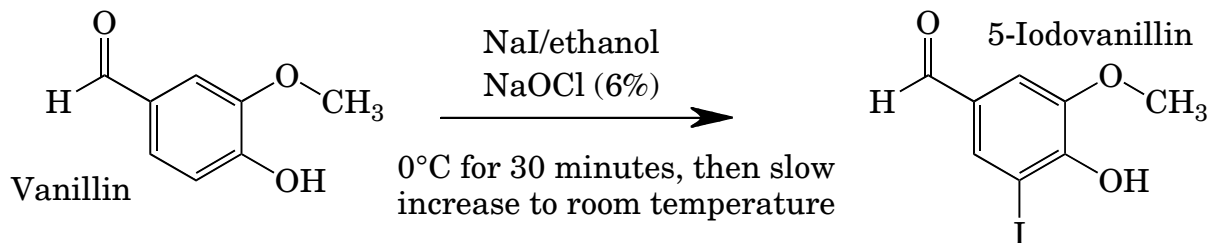


Figure 1. Electrophilic aromatic iodination of vanillin.

Halogenation of aromatic compounds traditionally involves treating the aromatic compound with Cl_2 , Br_2 or I_2 , in the presence of a catalyst. Iodination of an aromatic ring has traditionally involved adding iodine (a solid under standard conditions) and a strong mineral acid, such as nitric acid, to serve as a strong oxidizing agent. As you know, over the last few years, a movement known as **green chemistry** has been attempting to improve the safety and to reduce the environmental impact of chemical processes. In this reaction, we have replaced the strong mineral acid as an oxidizing agent with sodium hypochlorite, and we have chosen a compound that is modestly water-soluble so that minimal amounts of organic solvent are used in the procedure.

Procedure: Iodination of Vanillin¹

Place a stir bar in a 50 mL round-bottom flask², and dissolve 1 g of vanillin (3-methoxy-4-hydroxybenzaldehyde) in 20 mL of 90% ethanol. To this solution, add 1.2 equivalents of sodium iodide (1.2 g) and cool the reaction to 0°C with an ice-water bath on a stir plate. Using a buret (see Figure 2), slowly add 1.0 equivalent of aqueous sodium hypochlorite (12 mL ultra bleach that is 6% (w/w) in NaOCl), to the cooled flask over a 20 minute time period. Slow addition of bleach will result in a higher yield. Once the addition is complete, remove the ice bath, and allow the reaction to stir at room temperature for 30 minutes.

When the reaction is complete, add approximately 10 mL of a 10% (w/w) sodium thiosulfate solution to quench the reaction. Transfer the reaction mixture to a 250

¹ Procedure modified from: Edgar, K.J.; Falling, S.N. *J. Org. Chem.* **1990**, *55*, 5287-5291.

² As always, your glassware should be clean. Avoid having residual acetone on your glassware, as this will react with bleach.

ml round-bottomed flask, and then acidify the solution with about 3 ml 3 M hydrochloric acid. The aryl iodide should precipitate at this point.

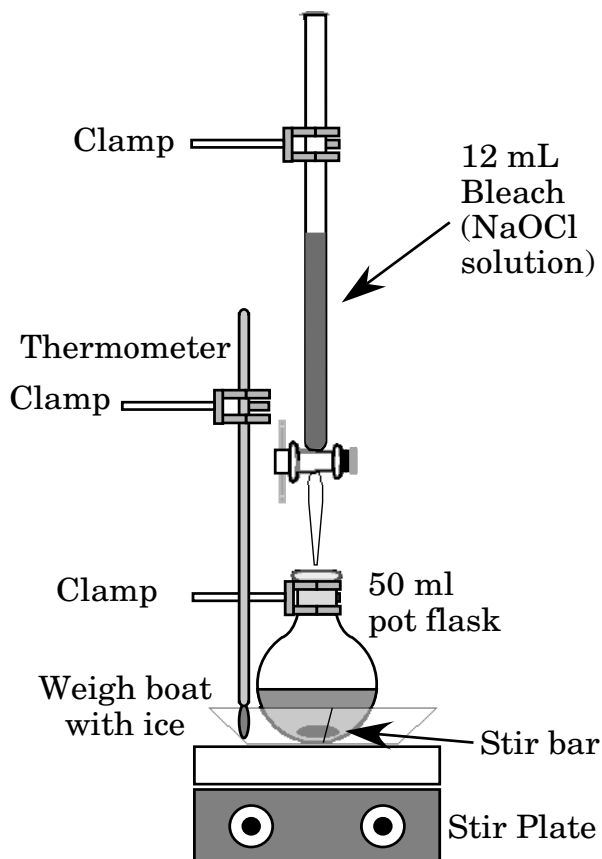


Figure 2. Iodination reaction apparatus.

Attach the flask to the rotary evaporator in order to remove ethanol from the suspension (with gentle heating, this should require no more than 15 minutes).

Cool the flask in ice for a few minutes, and collect the precipitate by vacuum filtration. Draw air over the product for a few minutes to facilitate drying. Place the product on a Petri dish, and weigh the product and determine a melting point for the crude product. Finally, cover the dish, and store the product overnight (or until the following week) to allow the water to evaporate.

Following overnight (or week-long) drying, weigh and determine the melting point and obtain IR and NMR spectra for the crude product.