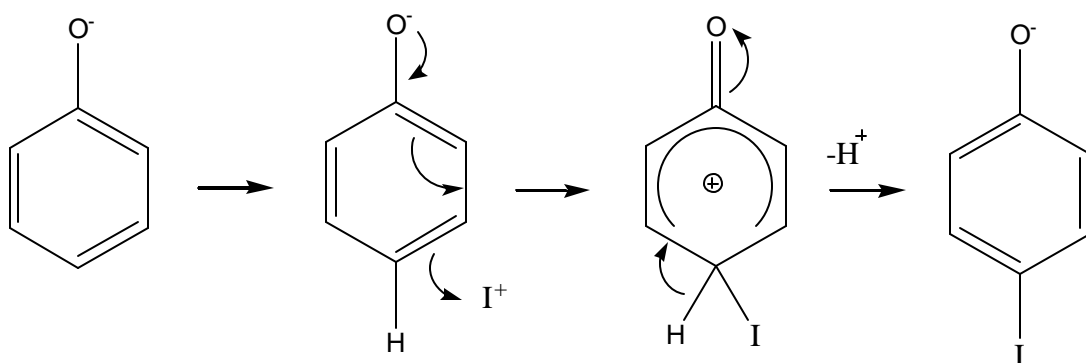


## Iodination of Phenols

### Aromatic Substitution Crystallization

The iodination of a phenol is an example of an electrophilic aromatic substitution reaction in which a proton of the aromatic ring is replaced by an iodo anion. Many such aromatic substitution reactions are known to occur when an aromatic substrate is allowed to react with a suitable electrophilic reagent, and many other groups besides iodine may be introduced to the ring.

Because addition to an aromatic ring means a loss of the stabilization that resonance provides, reactions of this type normally require powerful electrophilic reagents at elevated temperatures. In this case, however, the hydroxy group is a strong electron withdrawing group. Under basic conditions the iodine ion is sufficiently electrophilic to add to the benzene ring, temporarily interrupting ring resonance.



The intermediate formed is somewhat stabilized by resonance, and does not readily undergo reaction with the nucleophile. Aromaticity can be restored to the ring if elimination occurs instead, and yields a net substitution in which a hydrogen has been replaced by an iodine.

The hydroxy group is an *ortho/para* director, and in this reaction, the aromatic substitution occurs preferentially to those positions *para* to it. When the phenol has a group already *para* to the hydroxy, the substitution will occur in the *ortho* position. Also, it is possible for the iodination to occur more than once on the ring, and the extent of iodination can be controlled by stoichiometry. A small amount of iodinated and triiodinated impurities may form, but these side products can be removed when the desired product is washed and purified by crystallization.

### Required Reading

Review:           Technique 5 (Crystallization)  
                      Technique 9 (The Melting Point)

### Special Instructions

Care must be taken in the addition of NaOCl drop-wise to the solution in the round bottom flask because the too rapid addition of this reagent will result in more di/triiodinated impurities.

### Notes to the Instructor

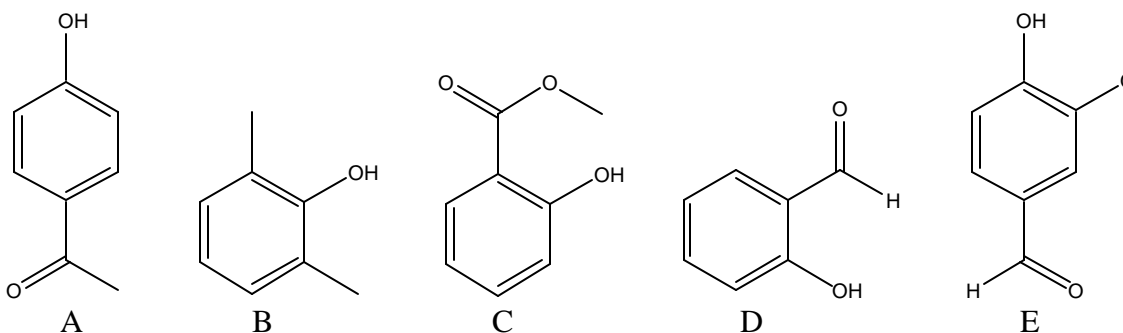
A 6% NaOCl solution produces a cleaner product in higher yields, and this lab has been adapted for it. However, common household bleach can be used. Also, it is recommended to assign phenols to students the week prior to lab, and require they perform the calculations in a pre-lab.

### Suggested Waste Disposal

Dispose of all waste in a container labeled for aqueous waste.

### Procedure

At the instructor's option, a number of phenols can be used as starting material for this reaction: A) 4-hydroxyacetophenone; B) 2,6-dimethylphenol; C) methyl salicylate; D) salicylaldehyde; or E) vanillin.



Reaction: To a 100-mL round bottom flask, add 1 g of your assigned phenol and 20-mL of methanol. Using a magnetic stir bar, stir until dissolved. Add 1 mol equivalent of potassium iodide, and continue to stir. After the potassium iodide has dissolved into solution, put the round bottom flask on an ice/water bath, positioned over the magnetic stirrer so that the solution is still stirring. Using a 10 mL graduated cylinder, measure 1 mol equivalent of a 6% solution of sodium hypochlorite and transfer to a 60-mL separatory funnel. Carefully add the sodium hypochlorite solution dropwise to the round bottomed flask over a period of 30 minutes. During this time, add ice to the ice bath as necessary to maintain a mixture with enough water that the surface area of the round bottomed flask is covered and enough ice that the bath is still 0 °C. Also, check occasionally that the solution is still stirring, as some will thicken as the reaction progresses. After the addition of the sodium hypochlorite solution is complete, continue to stir the solution at 0 °C for 60 minutes.

Isolation: Remove the ice/water bath, and add 10-mL of a 10% (w/w) solution of sodium thiosulfate. Allow the solution to stir for 5 minutes. With continued stirring, acidify with a 2 M solution of hydrochloric acid in 2-mL portions. Track the acidity of the solution using pH paper, and do not overacidify; pH 3 or 4 is fine. The iodophenol will have precipitated out by this point. Take the round bottomed flask off of the magnetic stirrer, and remove the stir bar before placing the round bottomed flask in an ice

bath to cool for 10 minutes. Isolate the product by vacuum filtration through a Büchner funnel and wash with two 2-mL portions of ice-cold water. Transfer the product to a watch glass and allow to it dry. Cover the watch glass with an inverted beaker.

#### Crystallization.

Weigh the product and transfer the crystals to a 10-mL Erlenmeyer flask.

Recrystallize the dry iodophenol product in the following solvents based on your assigned phenol.

- A) 4-hydroxyacetophenone—recrystallize in boiling water, decanting off the liquid from any diiodinated impurities.
- B) 2,6-dimethylphenol—recrystallize in boiling acetone/hot water with the mixed solvent method.
- C) methyl salicylate—recrystallize in boiling 2-propanol/hot water with the mixed solvent method.
- D) salicylaldehyde—recrystallize in boiling ethanol/hot water with the mixed solvent method.
- E) vanillin—recrystallize in boiling 2-propanol/hot water with the mixed solvent method.

Any solid impurities for B-E can be removed using the fluted filter method described in technique 5.3B. Refer to techniques 5.7 and 5.9 for further assistance on recrystallization techniques.

Determine the melting point of the purified iodophenol. (Technique 9)

#### Spectroscopy.

Infrared. Obtain the infrared spectrum of the iodophenol as a dry film by dissolving a sample in 1 mL *dry* acetone (Technique 25, Section 25.4). Alternatively, a KBr pellet of the iodophenol can be prepared to obtain the spectrum (Technique 25, Section 25.5). Include the infrared spectrum in your laboratory report, along with an interpretation of the principal peaks, with emphasis on the out-of-plane bending region and substitution patterns.

#### Report

Attach your infrared spectra to your report and label the major peaks with the type of bond or group of atoms that is responsible for the absorption. Be sure to also include your weight percentage recovery calculation. Submit your sample in an appropriately labeled vial.