

Experimental Procedure - Acylation of Anisole (updated)

1. Weigh 0.32 g of zinc oxide into a 25 mL round bottom flask equipped with a one inch stir bar. Place the flask into the correct hole of the aluminum heating block that is centered on the hotplate. Connect the Claisen adapter to the flask and the straight adapter onto the straight arm of the Claisen adapter.
2. Obtain 0.96 mL of benzoyl chloride and add it to the flask. Begin stirring the mixture by setting the stir plate to 4~5.
3. Obtain 0.88 mL of anisole with a one mL syringe and slowly add it dropwise to the flask through the straight adapter over a period of about 10 min (~1 drop every 20 seconds). (Caution: Reaction is very exothermic.) Continue stirring the mixture for 10 minutes after addition is complete.
4. Add 10 mL of ethyl acetate to the flask. If there is any solid sticking to the side of the flask, use a pipette to get it into solution.
5. Remove the stir bar from the round bottom flask and add the solution to a 15 mL centrifuge tube. Place the tube into the centrifuge and run for 5 minutes. Carefully decant the solution into the separatory funnel.
6. Wash the organic layer with a 20 mL portion of saturated sodium bicarbonate solution and let the layers separate. Drain off the bottom aqueous layer. Wash the organic layer with 15 mL of saturated sodium chloride. Let the layers separate and drain off the bottom aqueous layer.
7. Collect the organic layer into an Erlenmeyer flask and dry the solution over 1.0 g of anhydrous sodium sulfate. Decant the dried organic solution into another flask and add 1.0 g of potassium carbonate. Gently swirl the solution for one minute.
8. Filter the solution with a glass funnel and a small piece of cotton into a 150 mL beaker. Remove the ethyl acetate by air-drying it.
9. Add 4-5 mL of hexanes to the beaker and place into an ice-water bath for 10 minutes (If you see a layer of water at the bottom of the beaker, remove it with a pipette). If crystals have not formed, scratch the bottom of the flask with a spatula to induce crystallization and then place on ice for 10 minutes.
10. Collect the solid with a Büchner funnel set for vacuum filtration. Wash the solid with cold distilled water and then allow the solid to air dry over a week.
11. Weigh the product, determine its melting point, and obtain an IR spectrum.

Experimental Procedure – Relative Rates of Electrophilic Aromatic Bromination

Part 1. Relative Rates of Bromination of Oxygen-Substituted Arenes (work in pairs)

1. Obtain eight (8) disposable glass test tubes. Label four of the test tubes with bromine in acetic acid (Br_2/AcOH), and label each of the remaining four test tubes with either phenol, anisole, diphenyl ether or phenyl acetate.
2. Add 1.5 mL of a 0.2 M solution of each substrate (phenol, anisole, diphenyl ether and phenyl acetate) in acetic acid to the corresponding labeled test tubes.
3. Add 1.5 mL of a 0.05 M solution of bromine in acetic acid solution to each test tube labeled bromine.
4. Using four 250 mL-beakers prepare water baths with volumes of approximately 100 mL volume having the following approximate temperatures: two baths at 0 °C (ice-water bath), one bath at about 22 °C (room temperature), and one bath at 55 °C (hot water).

5. Place the four test tubes with the bromine solution in one ice-water bath for 5 min and the four test tubes labeled anisole, phenol, diphenyl ether and phenyl acetate in the other ice-water bath for 5 min.
6. For the remaining steps, it works best if one person mixes the solutions and one person records the times.
7. Using a Pasteur pipet, transfer the bromine solution from one of the test tubes to the test tube containing phenol. Mix the contents of the test tube by drawing the solution partially up into the pipet and then slowly expelling the solution from the pipet back into the test tube; repeat and record the time. The test tube containing the solution of phenol should remain in the ice-water bath during the addition and mixing steps. Record the time required for the solution to turn from orange-red to clear.
8. Repeat this process for each of the other test tubes containing solutions of anisole, diphenyl ether and phenyl acetate in acetic acid.
9. If the orange-red color does not turn clear after 10 min in any of the tubes in the ice-water bath, transfer the test tube(s) to the beaker that is maintained at room temperature. Record the time required for the solution to turn from orange-red to clear.
10. If the orange-red color does not turn clear after 10 min in any of the tubes at room temperature, transfer the test tube(s) to the beaker that is maintained at 55 °C. Record the time required for the solution to turn from orange-red to clear.

Part 2. Relative Rates of Bromination of Oxygen- vs Nitrogen-Substituted Arenes (work in pairs) (128L Only)

1. Obtain ten (10) disposable glass test tubes. Label three of the test tubes with bromine in acetic acid (Br_2/AcOH). Label 2 of the test tubes with bromine in dichloromethane ($\text{Br}_2/\text{CH}_2\text{Cl}_2$). Label each of the remaining 4 test tubes with either phenol, aniline, *N*-methylaniline, diphenyl aniline or acetanilide.
2. Add 1.5 mL of a 0.2 M solution of arene (*N*-methylaniline, diphenyl aniline or acetanilide) in acetic acid to the corresponding labeled test tubes.
3. Add 1.5 mL of a 0.2 M solution of phenol and aniline in dichloromethane to the corresponding labeled test tubes and pair them.
4. Add 1.5 mL of the solution of 0.05 M bromine in acetic acid to the 3 test tubes labeled bromine in acetic acid. Add 1.5 mL of the solution of 0.05 M bromine in dichloromethane to the 2 test tubes labeled bromine in dichloromethane.
5. For the remaining steps, it works best if one person mixes the solutions and one person records the times.
6. Reactions in acetic acid at room temperature
 - a. Using a Pasteur pipet, transfer the bromine solution from one of the test tubes to the test tube containing *N*-methylaniline. Mix the contents of the test tube by drawing the solution partially up into the pipet and then slowly expelling the solution from the pipet back into the test tube; repeat and record the time. Record the time required for the solution to turn from orange-red to clear.
 - b. Repeat this process for each of the other test tubes containing solutions of diphenyl aniline and acetanilide in acetic acid.
 - c. For each compound record the time it takes for the reaction to run to completion. Identify which was faster of each pair using the data from parts one and two. (diphenyl ether or diphenyl aniline, anisole or *N*-methylaniline, and phenyl acetate or acetanilide).

7. Reactions in dichloromethane at $-70\text{ }^{\circ}\text{C}$

- a. Add 100 mL of ethanol to a 250 mL beaker. Slowly add seven pieces of dry ice one at a time allowing for the bubbling to calm down before adding the next piece. Once all pieces are added, allow the mixture to stand for 5 min.
- b. Slowly place one of the test tubes containing bromine in dichloromethane and the test tube containing phenol into the cold bath, and allow them to sit in the bath for 5 min.
- c. Using a Pasteur pipet, transfer the bromine solution from the test tube to the test tube containing phenol. Mix the contents of the test tube by drawing the solution partially up into the pipet and then slowly expelling the solution from the pipet back into the test tube; repeat and record the time. Record the time required for the solution to turn from orange-red to clear.
- d. Remove the test tubes from the ethanol-dry ice bath, and carefully add 2 more pieces of dry ice one at a time. Allow the mixture to stand for 5 min
- e. Repeat the process from steps (b) and (c) above for aniline and record which one reacts faster.