shown below. The system is quick and easy, and the two solutions are stable.

The Solutions

Solution A. 0.2 M anhydrous boric acid and 0.05 M citric acid monohydrate

Solution B. 0.1 M trisodium phosphate dodecahydate ($Na_3PO_4 \cdot 12H_2O$)

[1]Carmody, W. R. *J. Chem. Educ.* **1961**, *38*, 559.

Microscale Reactions of Vanillin

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Although many applications of organic chemistry are based on complex molecules, few traditional or microscale organic experiments use reactants with several functional groups. In this paper we present five microscale experiments which allow first-year organic students to study the properties and reactions of a multifunctional compound—vanillin, 4-hydroxy-3-methoxybenzaldehyde (*1*). These experiments incorporate common synthetic organic transformations involving aldehydes, phenols, and aromatics. They include

- reduction of the aldehyde group
- oxidation of the aldehyde group
- formation of a novel heterocyclic compound using a condensation reaction
- bromination of an aromatic ring
- esterification of a phenol

The five reactions occur quickly. Most are complete within 30 min. In each case, physical or chemical properties of the reactant or product make it possible for the student to follow the progress of the reaction. Although the methods and techniques presented in Mayo, Pike, and Butcher's laboratory text (*1*) are used, these experiments use simple glassware, common chemicals, and standard microscale procedures. Therefore, one or more of these experiments can be easily incorporated into a first-year organic laboratory program.

Since good yields are obtained for the five products, sufficient material is available for spectral analysis of each product. Comparison of the IR or ^1H NMR spectra of vanillin to that of the product establishes the formation or disappearance of the functional groups involved in the transformation. Students can readily compare the reactivity and selectivity of the four functional groups of vanillin toward several reagents. Procedures for the microscale preparation of five compounds (**2–6**) from vanillin (**1**) are described below.

Experimental

Reduction of Vanillin to Vanillyl Alcohol (2)

Dissolve 380 mg (2.5 mmol) of vanillin in 2.5 mL of 1 M NaOH solution in a 25-mL Erlenmeyer flask. Swirl the flask to obtain a yellow, homogeneous solution. Cool the contents of the flask to between 10–15 °C by swirling the flask in an ice–water bath. Add 75 mg (1.95 mmol) of $NaBH_4$ in three or four portions over a period of 3 min with

(*Continued on page A44*)

constant swirling. Allow the solution to stand at room temperature for 30 min.

Then put the solution back in the ice–water bath, and add 2.5 M HCl dropwise while swirling until the solution is distinctly acidic to litmus paper. Continue to cool the flask, and gently scratch the wall of the flask with a glass rod to induce crystallization. Filter the product using a Hirsch funnel, and wash the flask and filter cake with three 0.5-mL portions of cold water. Transfer the crude product to a watch glass to air-dry.

Students typically collect 263 mg (68.3% yield) of crude material with a melting point of 108–109 °C. Recrystallization from ethyl acetate yields fine, white crystals of vanillyl alcohol, 4-hydroxy-3-methoxybenzyl alcohol (**2**), with a melting point of 113–114 °C (lit. mp 113–114 °C) (*2*).

Oxidation of Vanillin to Vanillic Acid (3)

Preparation of Silver Oxide

In a 5-mL conical vial containing a magnetic-spin vane, dissolve 170 mg (1.0 mmol) of silver nitrate in 1.0 mL of distilled water. Add 0.5 mL of 2.5 M NaOH dropwise from a calibrated pipet to the stirred solution to precipitate silver oxide. Stir the mixture for 5 min using a small glass rod.

Allow the silver oxide to settle to the conical section of the vial. Then withdraw the aqueous layer with a Pasteur pipet. Next, wash the silver oxide free of nitrates with four 0.75-mL portions of water. Allow the silver oxide to settle, and withdraw the aqueous layer with a Pasteur pipet. Carefully withdraw the last traces of water from the silver oxide on the last wash.

Preparation of Vanillic Acid

Add 2.5 mL of 2.5 M NaOH to the silver oxide precipitate. Stir with the magnetic-spin vane, and heat the reaction mixture to 55–60 °C (hot-water bath). Then add 152 mg (1 mmol) of vanillin in three or four small portions. Stir the reaction mixture at 55–60 °C for 15 min. During the course of the reaction, a silver mirror forms on the wall of the vial, and then falls off. Then particles of silver settle in the conical section of the vial.

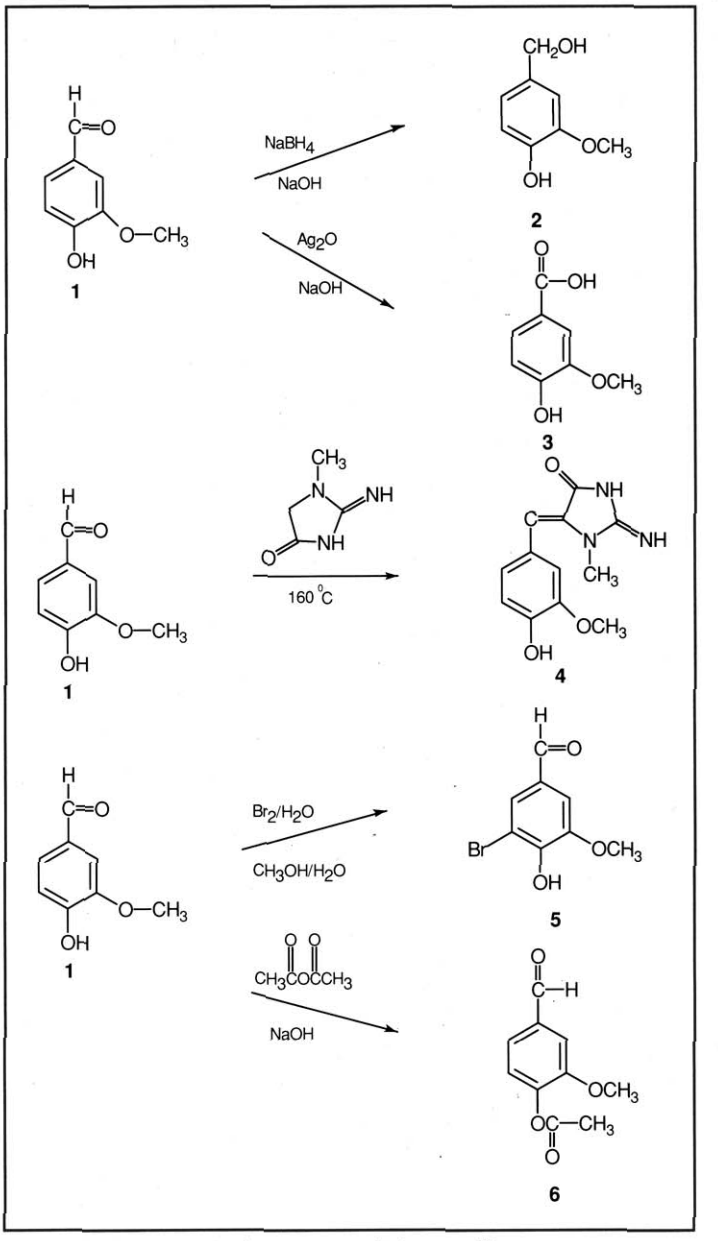
Next, use a Pasteur pipet to transfer the yellow reaction mixture to a 10-mL Erlenmeyer flask. Extract the metallic silver with four 0.75-mL portions of distilled water, and combine the extracts with the reaction mixture. If the reaction mixture contains any silver particles, use a Pasteur filter pipet to filter it. Isolate the product by adding 6 M HCl dropwise to the reaction mixture until the solution is acidic to litmus paper. Allow the reaction mixture to stand at room temperature for several min.

Then place the reaction mixture in an ice–water bath, and scratch the wall of the flask to induce crystallization. Filter the product using a Hirsch funnel, and wash the flask and filter cake with three 0.5-mL portions of cold water. Transfer the crude product to a watch glass to air-dry.

Students typically collect 104 mg (61.9% yield) of crude material with a melting point of 198–204 °C. Recrystallization from boiling water (0.1 g/1.2 mL) yields 4-hydroxy-3-methoxybenzoic acid (**3**), with a melting point of 210–211 °C (lit. mp 210–211 °C) (*3*).

Condensation Reaction of Vanillin and Creatinine (4)

Place 240 mg (1.6 mmol) of vanillin and 113 mg (1.0 mmol) of creatinine in a 12 × 75-mm test tube, and mix the two compounds intimately with a microspatula. Heat the mixture while stirring in a sand bath maintained at 165–170 °C for about 5–10 min. During this time, the mixture melts, a vigorous reaction occurs, water is released, and the orange–red condensation product solidifies.



Reactions to produce the five compounds from vanillin

Heat the contents for an additional 3 min to complete the reaction. Next, allow the tube and contents to cool to room temperature, and add 1.0 mL of ethanol. Warm and stir the mixture to break up the solid and to form a suspension. Wash any remaining product from the test tube onto the filter with several 0.5-mL portions of ethanol. Wash the solid on the filter with three 0.5-mL portions of hot water, and transfer the solid to a watch glass to air-dry.

Students typically collect 200 mg (81% yield) of the orange–red condensation product with a melting point of 263–268 °C. Recrystallization from glacial acetic acid yields 5-(4-hydroxy-3-methoxybenzal)creatinine (**4**) with a melting point of 271–273 °C (lit. mp 273 °C) (*4*).

(*Continued on page A46*)

Bromination of Vanillin to 5-Bromovanillin (5)

Dissolve 228 mg (1.50 mmol) of vanillin in 3 mL of methanol and 3 mL of water in a 50-mL Erlenmeyer flask. Under a fume hood, add several drops of bromine–water reagent slowly with swirling until the reddish brown color of bromine remains in the solution and no more product forms. Cork the flask, and allow the reddish brown mixture to stand at room temperature for at least 10 min with intermittent swirling to complete the reaction.

To isolate the product, add 15 mL of water to the reaction mixture. Stir and cool the reaction mixture in an ice–water bath for 15 min to maximize the product yield. Filter the product using a Hirsch funnel, and wash it with three 1.0-mL portions of sodium thiosulfate to remove any unreacted bromine. Next, wash the crude product with three 0.5-mL portions of cold water. Dry the product partially by drawing air through the crystals for several minutes. Then transfer the product to a watch glass to air-dry.

Students typically collect 150 mg (43% yield) of the crude 5-bromovanillin, with a melting point of 163–164 °C. Recrystallization from methanol–water yields 120 mg (35% yield) of 5-bromo-4-hydroxy-3-methoxybenzaldehyde (**5**) with a melting point of 163–164 °C (lit. mp 164 °C) (*6*).

Instructor Preparation of Aqueous Brominating Reagent

Under a fume hood, dissolve 8 g of KBr in 50 mL of water. Add 6 g (2 mL) of bromine.

Esterification of Vanillin to Vanillyl Acetate (7)

Dissolve 304 mg (2.0 mmol) of vanillin in 5 mL of 10% NaOH solution in a 50-mL Erlenmeyer flask. Add 6 g of crushed ice and 0.866 g (0.8 mL) of acetic anhydride. Cork the flask and shake the reaction mixture several times for 15 min. Filter the product using a Hirsch funnel, and wash it with three 1-mL portions of cold water.

Students typically collect 129 mg (33% yield) of crude material with a melting point of 75–76 °C. Recrystallization from ethanol–water (1:4) yields white crystals of vanillyl acetate, 4-formyl-3-methoxyphenyl acetate (**6**) with a melting point of 78–78.5 °C (lit. mp 77–79 °C) (*6*).

Acknowledgment

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