Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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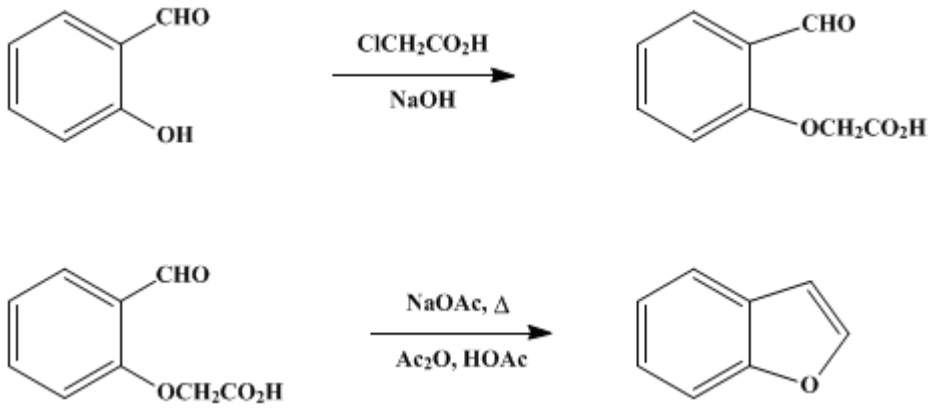
COUMARONE

[Benzofuran]



Submitted by Albert W. Burgstahler and Leonard R. Worden[1].
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1. Procedure

A. *o-Formylphenoxyacetic acid*. A solution of 80.0 g. (2 moles) of sodium hydroxide pellets in 200 ml. of distilled water is added to a mixture of 106 ml. (122 g., 1 mole) of salicylaldehyde (Note 1), 94.5 g. (1 mole) of chloroacetic acid (Note 1) and (Note 2), and 800 ml. of water. The mixture is stirred slowly and heated to boiling. The resulting black solution (Note 3) is heated under reflux for 3 hours (Note 4). The solution is acidified with 190 ml. of concentrated hydrochloric acid (sp. gr. 1.19) and is steam-distilled to remove unchanged salicylaldehyde (40.0–40.5 g.) (Note 5). The residual acidic mixture is cooled to 20°, and the precipitated product is collected on a Büchner funnel and rinsed with water. The light tan solid when dry weighs 99–100 g. (82–83% based on recovered salicylaldehyde), m.p. 130.5–133.0° (Note 6).

B. *Coumarone*. A mixture of 90.0 g. (0.5 mole) of crude (Note 7), dry *o*-formylphenoxyacetic acid, 180 g. of anhydrous, powdered sodium acetate, 450 ml. of acetic anhydride, and 450 ml. of glacial acetic acid (Note 8) in a 2-l. flask is heated under gentle reflux with stirring for 8 hours. The hot black solution (total volume *ca.* 1.2 l.) (Note 3) is poured into 2.5 l. of ice water and extracted with one 600-ml. portion of ether (Note 9). The ether layer is washed with one 600-ml. portion of water and then with several portions of cold dilute 5% sodium hydroxide solution (Note 10) until the aqueous layer is basic. The ether layer is washed successively with water and saturated sodium chloride solution and is partially dried over anhydrous granular sodium sulfate. The ether is removed at water-bath temperature and the product is distilled, b.p. 166.5–168.0° (735 mm.) or 97.5–99.0° (80 mm.). The water-white benzofuran weighs 37.5–40.0 g. (63.5–67.8%, 52–56% overall from salicylaldehyde), n^{20}D 1.5672; λ_{max} 245 (log ε 4.08), 275 (3.45), and 282 mμ (3.48).

2. Notes

1. Matheson, Coleman and Bell practical grade material was used.
2. The yield is not increased by use of bromoacetic acid or 2 moles of chloroacetic acid and an additional mole of sodium hydroxide.
3. At no time did the checkers observe a black solution. The color of the solution changed from yellow to red-brown.
4. The yield is not increased by longer reflux periods.
5. Removal of unchanged salicylaldehyde by steam distillation (followed conveniently by testing the distillate with 2,4-dinitrophenylhydrazine reagent) provides a product sufficiently pure for use in the

next step. Also, the recovered salicylaldehyde can be used again without further purification.
6. Three crystallizations of 36 g. of the crude *o*-formylphenoxyacetic acid from 360 ml. of water with 10 g. of activated carbon give 18 g. of glistening colorless plates, m.p. 133.0°–133.5°.
7. Use of purified *o*-formylphenoxyacetic acid increases the yield in this step by only 11%.
8. If no acetic acid is used, benzofuran is formed in only 30–31% yield, and coumarilic acid, m.p. 194–196°, is isolated in about 45% yield.
9. An additional extraction does not increase the yield appreciably.
10. About 250 ml. of this solution is required.

3. Discussion

o-Formylphenoxyacetic acid has been prepared previously in 46% yield by alkylation of salicylaldehyde with chloroacetic acid[2,3] and in unspecified yield by alkylation with ethyl bromoacetate followed by hydrolysis.[4]

Benzofuran is found in coal tar.[5] It has been prepared in 40–46% overall yield from coumarin by bromination, conversion of the resulting 3,4-dibromocoumarin to coumarilic acid, and then decarboxylation,[6] and also by passage of coumarin vapor through an iron tube at 860°.[7] The method given here is a variation of that described by Rössing,[2] who omitted the addition of acetic acid (see (Note 8) above). Benzofuran also has been prepared by the cyclization of ω-chloro-*o*-hydroxystyrene[8] or phenoxyacetaldehyde[9] in unspecified low yields and by the cyclization of phenoxyacetaldehyde diethyl acetal in 9% yield.[10] High-temperature catalytic dehydrocyclization of *o*-ethylphenol affords benzofuran in as much as 59% yield after recycling unchanged *o*-ethylphenol.[11]

4. Merits of the Preparation

Although the high-temperature catalytic dehydrocyclization of *o*-ethylphenol[11] gives benzofuran in fair yield, these conditions are not convenient in the laboratory and cannot be applied easily to functionally substituted *o*-formylphenoxyacetic acids. The other methods of preparation give unsatisfactory yields, are unnecessarily lengthy, or require expensive starting materials. The method of Rössing,[2] on which the present procedure is based, gives good yields in its original form only in the case of *o*-acylphenoxyacetic acids; *o*-formylphenoxyacetic acids give principally the corresponding coumarilic acids. Often these can be decarboxylated only in very poor yield.[12] In the preparation described here, benzofuran is obtained directly in fair overall yield from readily available and inexpensive starting materials without the necessity of a separate decarboxylation step.

References and Notes

1. Department of Chemistry, University of Kansas, Lawrence, Kansas. This investigation was supported in part by a Public Health Service Fellowship, GPM-13, 681-03, from the Division of General Medical Sciences, U.S. Public Health Service.
2. A. Rössing, *Ber.*, **17**, 2988 (1884).
3. H. Cajar, *Ber.*, **31**, 2803 (1898); A. Zubrys and C. O. Siebenmann, *Can. J. Chem.*, **33**, 11 (1955).
4. H. Dumont and St. v. Kostanecki, *Ber.*, **42**, 911 (1909).
5. G. Kraemer and A. Spilker, *Ber.*, **23**, 78 (1890).
6. R. Fittig and G. Ebert, *Ann.*, **216**, 162 (1883); A. L. Mndzhoian, A. A. Aroian, and N. Kh. Khachatrian, "Synthesis of Heterocyclic Compounds," Vols. 3 and 4, Consultants Bureau, New York, 1960, p. 83.
7. N. A. Orlow and W. W. Tistschenko, *Ber.*, **63**, 2948 (1930).
8. G. Komppa, *Ber.*, **26**, 2968 (1893).
9. R. Stoermer, *Ber.*, **30**, 1700 (1897).
10. R. Stoermer, *Ann.*, **312**, 237 (1900).
11. C. Hansch and G. Helmkamp, *J. Am. Chem. Soc.*, **73**, 3080 (1951), and earlier papers cited therein; B. B. Corson, H. E. Tiefenthal, J. E. Nickels, and W. J. Heintzelman, *J. Am. Chem. Soc.*, **77**, 5428 (1955).

12. R. Aneja, S. K. Mukerjee, and T. R. Seshadri, *Tetrahedron*, **2**, 203 (1958).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

o-acylphenoxyacetic acids

o-formylphenoxyacetic acids

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

acetic anhydride (108-24-7)

sodium acetate (127-09-3)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

chloroacetic acid (79-11-8)

carbon (7782-42-5)

Salicylaldehyde (90-02-8)

2,4-Dinitrophenylhydrazine (119-26-6)

Bromoacetic acid (79-08-3)

Ethyl bromoacetate (105-36-2)

coumarin

3,4-dibromocoumarin (55077-11-7)

Coumarone,
Benzofuran (271-89-6)

phenoxyacetaldehyde (2120-70-9)

phenoxyacetaldehyde diethyl acetal

o-Formylphenoxyacetic acid (6280-80-4)

ω-chloro-o-hydroxystyrene

o-ethylphenol (90-00-6)

Coumarilic acid (496-41-3)