



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.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

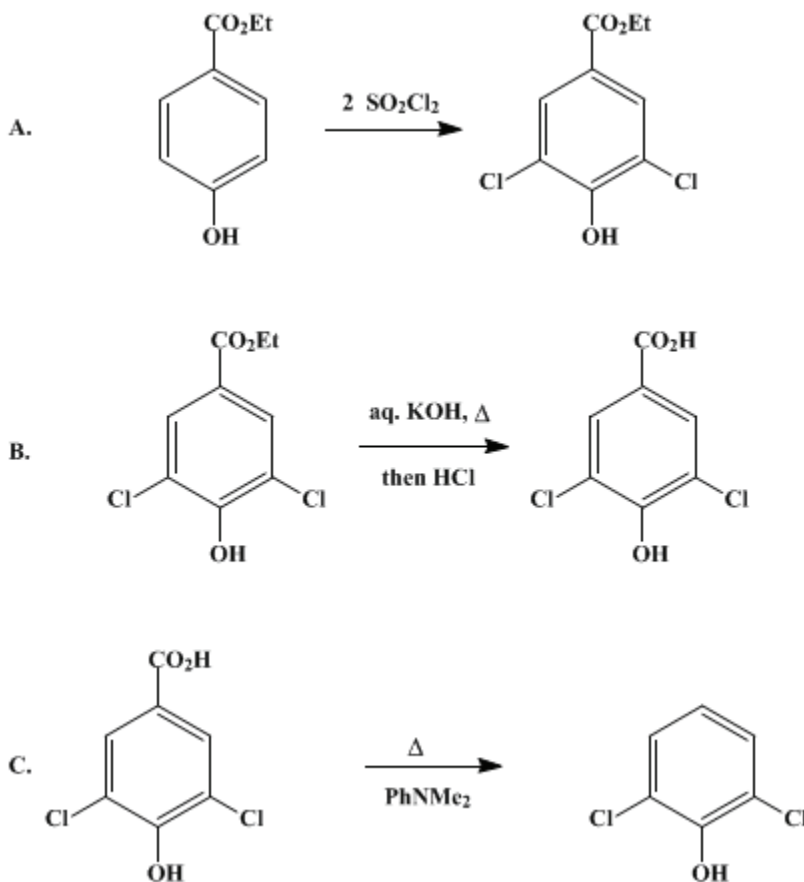
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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2,6-DICHLOROPHENOL

[Phenol, 2,6-dichloro-]



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Checked by R. L. Shriner and Arne Langsjoen.

1. Procedure

A. *Ethyl 3,5-dichloro-4-hydroxybenzoate*. A tared 2-l. round-bottomed flask is equipped with an efficient reflux condenser connected through a calcium chloride drying tube to a gas-absorption trap, and is set up on a steam bath in a hood. In the flask are placed 250 g. (1.5 moles) of ethyl 4-hydroxybenzoate (Note 1) and 444 g. (266 ml., 3.3 moles) of sulfuryl chloride. The mixture is warmed on the steam bath (gently at first) until gas is no longer evolved (about 1 hour). Then 50 ml. of sulfuryl chloride is added to the reaction flask, and the warming is continued until gas is no longer evolved. This entire chlorination procedure requires about 1.5 hours. The excess sulfuryl chloride is then removed by attaching a water pump through an empty safety flask to the reaction flask and warming on the steam bath until no evidence of vapor can be detected above the white solid in the reaction flask. The residue in the flask should weigh about 350 g. (Note 2). Recrystallization from a mixture of 600 ml. of ethanol and 140 ml. of water gives 315–334 g. (83–88%) of ethyl 3,5-dichloro-4-hydroxybenzoate hydrate (Note 3) melting at 110–114° with decomposition.

B. *3,5-Dichloro-4-hydroxybenzoic acid*. In a 2-l. round-bottomed flask equipped with a reflux condenser and set upon a steam bath are placed 315 g. (1.25 moles) of ethyl 3,5-dichloro-4-hydroxybenzoate hydrate and 600 ml. of Claisen's alkali (Note 4). Saponification is brought to completion by heating on the steam bath for 1 hour. A yellow homogeneous solution results which is diluted with 400 ml. of water and acidified to Congo red paper by pouring it into a rapidly stirred

solution of 320 ml. of concentrated [hydrochloric acid](#) and 380 ml. of water in a 4-l. beaker. The thick white slurry is then cooled to 0–10°; the acid is collected on a 20-cm. Büchner funnel and washed with two 250-ml. portions of cold water ([Note 5](#)). After being freed from as much water as possible by suction, the filter cake is broken up and dissolved in a boiling mixture of 1 l. of [ethanol](#) and 350 ml. of water. Cooling to 0° gives the first crop of crystals, weighing about 200 g. Concentration of the mother liquors to 750 ml. and cooling to 0° yields an additional 40–50 g. of product of equal purity. After drying in an oven at 85–95° for 8 hours, the white crystalline acid weighs 240–250 g. (93–97%) and melts at 266–268°.

C. [2,6-Dichlorophenol](#). A mixture of 250 g. (1.2 moles) of dry [3,5-dichloro-4-hydroxybenzoic acid](#) and 575 g. (600 ml., 4.8 moles) of redistilled [dimethylaniline](#) is placed in a 2-l. round-bottomed flask provided with a thermometer and a short air-cooled condenser and is heated slowly in an oil bath. Evolution of gas commences at 130° and is vigorous at 150°. The solution is heated at 190–200° for 2 hours or until the evolution of gas has ceased. After cooling, the solution is poured by portions into 600 ml. of concentrated [hydrochloric acid](#) in a 3-l. separatory funnel, with cooling from time to time by holding the funnel under a stream of cold water. When the solution is thoroughly cooled and acid to Congo red paper, the [phenol](#) is extracted with three 250-ml. portions and three 100-ml. portions of [ether](#) ([Note 6](#)). The combined [ether](#) extracts are washed with 15 ml. of 6 N [hydrochloric acid](#), dried overnight over 20 g. of anhydrous [sodium sulfate](#), and filtered into a 2-l. Claisen flask, and the [ether](#) is removed by distillation. After cooling, the residue begins to solidify, and 500 ml. of petroleum ether (40–60°) is added. After the [phenol](#) has been brought into solution by refluxing gently on the steam bath it is poured into a 1-l. beaker and cooled to 0°. A crop of white crystals (130–140 g.) is collected, having a melting point of 64.5–65.5°. By concentration of the mother liquor to 200 ml., a second crop (25–40 g.) melting at 64–65° can be collected. The total yield amounts to 157–180 g. (80–91%) ([Note 7](#)).

2. Notes

1. The [ethyl 4-hydroxybenzoate](#) was obtained from the Eastman Kodak Company and melted at 115.5–116°.
2. If the product weighs much less than 350 g. at this point, an additional 50 ml. of [sulfuryl chloride](#) should be added and the heating continued until gas is no longer evolved.
3. The ester crystallizes from dilute [ethanol](#) as the monohydrate; after long drying in a vacuum desiccator over [phosphorus pentoxide](#), it melts at 111–112°.
4. Claisen's alkali is prepared by dissolving 350 g. of [potassium hydroxide](#) in 250 ml. of water, cooling, and diluting to 1 l. with [methanol](#).
5. If the acid is dried completely at this point it contains about 5% [potassium chloride](#). The submitters state that recrystallization is unnecessary if the acid is to be used in Part C.
6. The aqueous layer should be saved. Low yields are due to incomplete extraction of the [2,6-dichlorophenol](#). If the final yield is low, the aqueous layer should be extracted with three 100-ml. portions of [ether](#) and the product recovered by following the procedure outlined.
7. If the product is colored or low melting it may be purified further by recrystallization from 600 ml. of petroleum ether (40–60°) containing about 4 g. of [Norit](#). By cooling and concentrating, 170–175 g. may be recovered (m.p. 65–66°) from 180 g. of crude product.

3. Discussion

[2,6-Dichlorophenol](#) has been prepared by the chlorination of [phenol](#) with [chlorine](#) gas in the presence of [nitrobenzene](#) and fuming [sulfuric acid](#),¹ by the decomposition of the diazotate of [2,6-dichloro-4-aminophenol](#),² and by the decarboxylation of [3,5-dichloro-4-hydroxybenzoic acid](#) in [quinoline](#)³ or [dimethylaniline](#).⁴

References and Notes

1. Huston and Neeley, *J. Am. Chem. Soc.*, **57**, 2177 (1935).
2. Seifart, *Ann., Spl.*, **7**, 203 (1870).
3. Blicke, Smith, and Powers, *J. Am. Chem. Soc.*, **54**, 1467 (1932).

4. Tarbell and Wilson, *J. Am. Chem. Soc.*, **64**, 1066 (1942).

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

petroleum ether

Claisen's alkali

diazotate of 2,6-dichloro-4-aminophenol

ethanol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

phenol (108-95-2)

sodium sulfate (7757-82-6)

Norit (7782-42-5)

sulfuryl chloride (7791-25-5)

chlorine (7782-50-5)

potassium hydroxide (1310-58-3)

Nitrobenzene (98-95-3)

dimethylaniline (121-69-7)

Quinoline (91-22-5)

potassium chloride (7447-40-7)

2,6-Dichlorophenol,
Phenol, 2,6-dichloro- (87-65-0)

ethyl 4-hydroxybenzoate (120-47-8)

ethyl 3,5-dichloro-4-hydroxybenzoate hydrate

3,5-dichloro-4-hydroxybenzoic acid (3336-41-2)

phosphorus pentoxide (1314-56-3)

Ethyl 3,5-dichloro-4-hydroxybenzoate (17302-82-8)