



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.

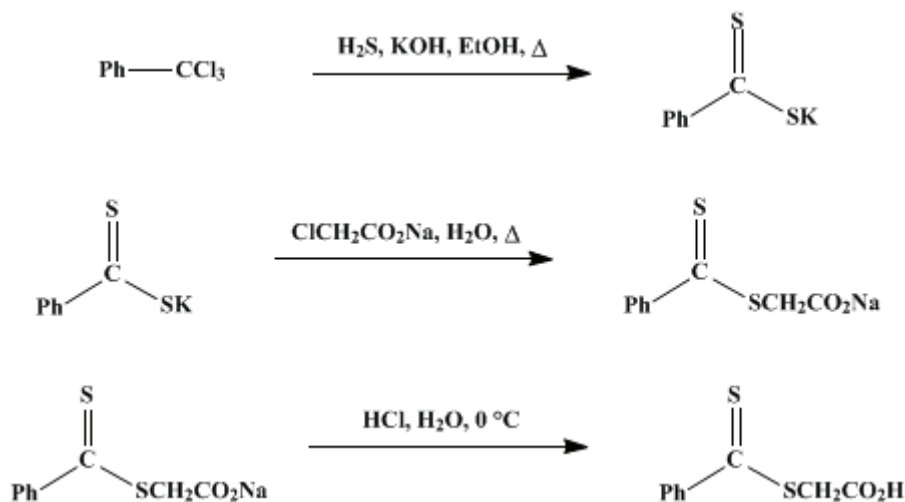
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.1046 (1973); Vol. 42, p.100 (1962).

THIOBENZOYLTHIOGLYCOLIC ACID

[Benzoic acid, dithio-, carboxymethyl ester]



Submitted by Frederick Kurzer and Alexander Lawson¹.

Checked by Max Tishler, G. A. Stein, and W. F. Jankowski.

1. Procedure

A solution of alcoholic caustic potash, prepared by dissolving 59.3 g. of 85% potassium hydroxide (0.90 mole) in 400 ml. of absolute ethanol with warming, is divided into two equal portions, one of which is saturated with hydrogen sulfide at room temperature (Note 1). The recombined solutions are placed in a 1-l. three-necked flask fitted with a Hershberg stirrer (Note 2), a gas delivery tube (Note 3), and a reflux condenser carrying a dropping funnel (Note 4). The air is displaced from the apparatus by passing a stream of nitrogen through the stirred liquid (Note 5). The solution is warmed to approximately 45–50°, and 49 g. (35 ml., 0.25 mole) of benzotrichloride is added dropwise through the condenser from a dropping funnel at a rate to maintain the temperature of the reaction mixture at approximately 60°; this requires 1–1.5 hours (Note 6). The reaction mixture turns deep red soon after the addition is started. When all the benzotrichloride has been added, the stirred deep-red suspension is refluxed gently for 30 minutes. A solution of 33.1 g. (0.35 mole) of chloroacetic acid in 200 ml. of water, neutralized with 29.4 g. (0.35 mole) of solid sodium bicarbonate, is next rapidly added through the condenser, the stirred mixture heated to boiling as rapidly as possible and refluxed (Note 5) for 5 minutes.

The resulting brownish red suspension is added to 750–1000 g. of ice contained in a 2-l. beaker (Note 7) and the turbid orange solution slowly acidified (to Congo red) with good stirring (Note 8) by the addition of approximately 50 ml. (Note 9) of concentrated hydrochloric acid. The deep-scarlet crystalline precipitate is collected at the pump after 30 minutes at 0° and rinsed with small quantities of water.

The air-dried product is crystallized by dissolving it in chloroform (approximately 120 ml.), followed by dilution of the filtered boiling liquid (Note 10) with hot petroleum ether (boiling range 60–80°, 60–80 ml.). The crystalline product, which separates rapidly, is collected at 0°, rinsed on the filter with a mixture of chloroform and petroleum ether (1:3), and dried. The yield of magnificent deep-scarlet lustrous prisms, m.p. 127–128°, varies between 28.9 and 30.4 g. (54–57% of the theoretical). Concentration of the combined filtrates and wash liquids under reduced pressure to a small volume (50–80 ml.) yields an additional small quantity (1.5–3.0 g., 3–6%) of material of satisfactory purity, m.p. 121–124°.

2. Notes

1. Saturation is complete when a slow stream of gas is passed through the solution during 2.5–3 hours. The initially turbid liquid generally clears and remains nearly colorless during this process. The checkers on several occasions obtained a small amount of a flocculent precipitate that most probably was [potassium carbonate](#).
2. The checkers used a Trubore stirrer with a Teflon paddle.
3. The delivery tube is fitted to allow the stream of [nitrogen](#) to enter as far under the surface of the liquid as possible without obstructing the operation of the stirring device.
4. The checkers used a pressure-equalizing dropping funnel.
5. The passage of [nitrogen](#) is continued throughout the experiment.
6. The exothermic nature of the reaction maintains the temperature of the mixture between 50° and 60°, depending upon the rate of the addition of the [benzotrichloride](#).
7. The checkers used a 3-l., wide-necked, round-bottomed flask equipped with a mechanical stirrer.
8. Some unmelted ice should remain during the acidification, which is carried out slowly at 0°, to prevent the separation of the crude material in the form of an oil.
9. The checkers found that 25–30 ml. of concentrated [hydrochloric acid](#) was sufficient.
10. The submitters filtered the solution rapidly with suction through a preheated Büchner funnel. The checkers found that the product often crystallized too rapidly and plugged the filter. As a result, the crude product was dissolved in an excess of [chloroform](#) (160–175 ml.), then filtered, and the excess solvent evaporated before dilution with light petroleum ether. In some cases, no filtration was necessary because the [chloroform](#) solution was clear.

3. Discussion

[Thiobenzoylthioglycolic acid](#) has been prepared by the interaction of [potassium dithiobenzoate](#) and alkali [chloroacetate](#).^{2,3,4} The required intermediate, [dithiobenzoic acid](#), has been obtained from [phenylmagnesium bromide](#) and [carbon disulfide](#),^{2,3,5} or by the condensation of [benzaldehyde](#) and hydrogen polysulfides,^{2,6} or most conveniently by treatment of [benzotrichloride](#) with [potassium hydrogen sulfide](#).^{2,4,7} The last procedure has been adapted here to afford improved yields.

4. Merits of Preparation

[Thiobenzoylthioglycolic acid](#) is a useful thiobenzoylating agent,^{2,3,4,8,9,10,11,12} and the resulting products find application for the synthesis of various heterocycles. These applications of [thiobenzoylthioglycolic acid](#) have recently been reviewed.¹³

References and Notes

1. Royal Free Hospital School of Medicine, University of London, 8 Hunter Street, London W. C. 1, England.
 2. B. Holmberg, *Arkiv Kemi, Mineral., Geol.*, **17A**, No. 23 (1944).
 3. A. Kjaer, *Acta Chem. Scand.*, **4**, 1347 (1950).
 4. J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 2071 (1951).
 5. J. Houben, *Ber.*, **39**, 3224 (1906).
 6. I. Bloch and F. Höhn, *J. Prakt. Chem.*, **82**, 486 (1910).
 7. A. Engelhardt and P. Latschinoff, *Z. Chem.*, **11**, 455 (1868).
 8. B. Holmberg, "Svedberg Memorial Volume," Uppsala, 1944, p. 299.
 9. A. Kjaer, *Acta Chem. Scand.*, **6**, 1374 (1952).
 10. B. Holmberg, *Arkiv Kemi*, **9**, 47 (1955).
 11. J. B. Jepson, A. Lawson, and V. D. Lawton, *J. Chem. Soc.*, 1791 (1955).
 12. A. Lawson and C. E. Searle, *J. Chem. Soc.*, 1556 (1957).
 13. F. Kurzer, *Chem. & Ind. (London)*, 1333 (1961).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

petroleum ether

ethanol (64-17-5)

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

hydrogen sulfide (7783-06-4)

nitrogen (7727-37-9)

benzaldehyde (100-52-7)

chloroacetic acid,
chloroacetate (79-11-8)

potassium hydroxide (1310-58-3)

benzotrichloride (98-07-7)

carbon disulfide (75-15-0)

potassium hydrogen sulfide (1310-61-8)

Phenylmagnesium bromide (100-58-3)

Thiobenzoylthioglycolic acid

Benzoic acid, dithio-, carboxymethyl ester (942-91-6)

potassium dithiobenzoate

dithiobenzoic acid