



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.

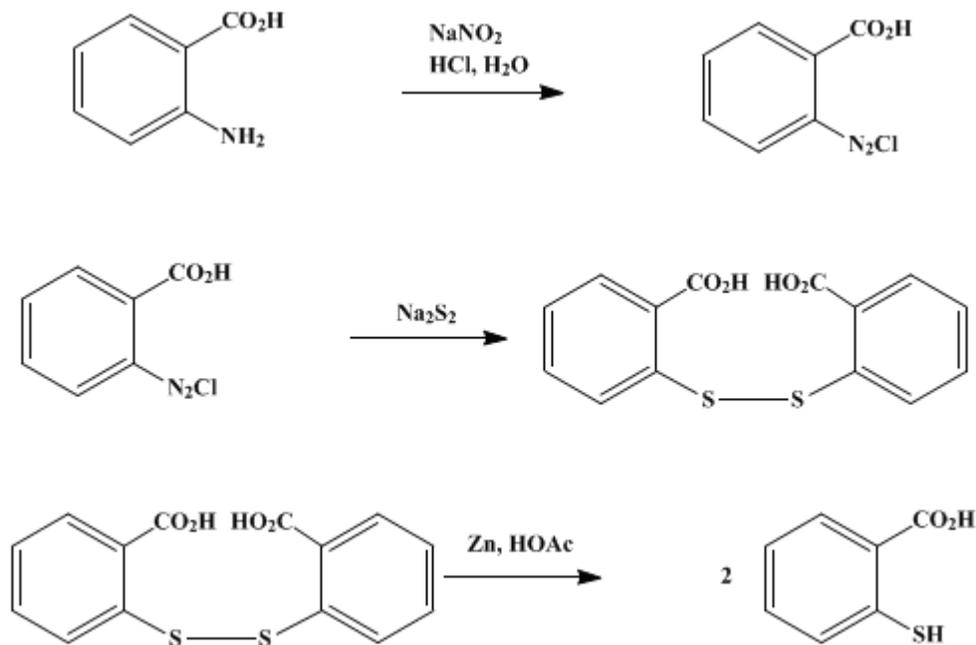
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.580 (1943); Vol. 12, p.76 (1932).

THIOSALICYLIC ACID

[Benzoic acid, *o*-mercapto-]



Submitted by C. F. H. Allen and D. D. MacKay.

Checked by Roger Adams and A. E. Knauf.

1. Procedure

Caution! Recently it was reported to us that workers, following the procedure in *Coll. Vol. II*, pg 580 (diazotization of anthranilic acid and its reaction with sodium disulfide) but substituting 2,3-dimethylaniline for anthranilic acid, experienced a serious explosion upon addition of the diazonium salt solution to the disulfide solution. We urge that extreme caution should always be exercised in the handling of diazonium salts even when they are in solution.

In a 4-l. beaker, 290 cc. of water is heated to boiling, and 260 g. (1.1 moles) of crystallized sodium sulfide ($\text{Na}_2\text{S}\cdot 9\text{H}_2\text{O}$) and 34 g. of powdered sulfur are dissolved by heating and stirring. A solution of 40 g. of sodium hydroxide in 100 cc. of water is then added and the mixture cooled, first in cold water, and finally by a freezing mixture of ice and salt.

In a 2-l. beaker, set in a freezing mixture and provided with a stirrer and a thermometer for reading temperatures to 0° , are placed 500 cc. of water, 137 g. (1 mole) of anthranilic acid, and 200 cc. of concentrated hydrochloric acid; the stirrer is started and the mixture cooled to about 6° . Meanwhile 69 g. (1 mole) of sodium nitrite is dissolved in 280 cc. of hot water and the solution cooled in ice; portions are then placed in a separatory funnel of convenient size, supported in such a way that the lower end of the stem extends beneath the surface of the anthranilic acid solution. When the temperature has fallen to 5° , the nitrite solution is run in; about 500 g. of cracked ice is added at such a rate as to keep the temperature below 5° . This takes about ten minutes (Note 1). A drop of the solution should give an immediate blue color with starch-iodide paper.

The stirrer and thermometer are now transferred to the alkaline sulfide solution, the temperature of which must be below 5° . The diazo solution is added over a period of twenty to thirty minutes along with 950 g. of ice to prevent the temperature from rising above 5° . When addition is complete, the water

bath is removed and the mixture allowed to warm up to room temperature; after two hours the evolution of **nitrogen** ceases (Note 2). About 180 cc. of concentrated **hydrochloric acid** is added until the solution is acid to Congo red paper, and the precipitate of dithiosalicylic acid is filtered and washed with water.

To remove the excess **sulfur**, the precipitate is dissolved by boiling with a solution of 60 g. of anhydrous sodium carbonate (soda ash) in 2 l. of water, and the mixture is filtered while hot. It is divided into five equal parts (Note 3), and the dithiosalicylic acid is reprecipitated as before with concentrated **hydrochloric acid**. The solid is filtered, the cake being sucked as dry as possible.

The moist cake is mixed with 27 g. of **zinc** dust and 300 cc. of glacial **acetic acid** in a 1-l. round-bottomed flask, and the mixture is refluxed vigorously for about four hours (Note 4). When the reduction is complete, the mixture is cooled and filtered with suction. The filter cake is washed once with water and then transferred to a 1-l. beaker. The cake is suspended in 200 cc. of water, and the suspension is heated to boiling. The hot solution is made strongly alkaline by the addition of about 40 cc. of 33 per cent aqueous **sodium hydroxide** solution. The alkaline solution is boiled for about twenty minutes to ensure complete extraction of the product from the filter cake, filtered from the insoluble material (Note 5), and the **thiosalicylic acid** is then precipitated by the addition of sufficient concentrated **hydrochloric acid** to make the solution acid to Congo red paper. The product is filtered with suction, washed once with water, and dried in an oven at 100–110°. The yield of a product which melts at 162–163° is 110–130 g. (71–84 per cent of the theoretical amount based on the **anthranilic acid**).

This product is sufficiently pure for most purposes (Note 6).

For recrystallization 5 g. of this material is dissolved in 20 cc. of hot 95 per cent **alcohol**, and 40 cc. of water is added. The solution is boiled with a little **decolorizing carbon**, filtered hot, and then allowed to cool. The product crystallizes in yellow flakes. The yield of recrystallized material is 4.7 g.; the melting point of the material is 163–164°.

2. Notes

1. This method is much more rapid than when external cooling alone is used (*Org. Syn. Coll. Vol. I, 1941, 374*). The total volume of the solution is not important since the insoluble dithiosalicylic acid is readily filtered.

2. Foaming sometimes becomes very during the evolution of **nitrogen**. The addition of a few cubic centimeters of **ether** from time to time helps to keep this foaming under control.

3. The dithiosalicylic acid may be precipitated all at once if desired and the entire amount reduced in one operation. If this is done, the reduction must be carried out in a 5-l. flask fitted with a good stirrer. The mixture needs to be refluxed about ten hours over a ring burner. In the laboratory, this is much less convenient than it is to divide the material and reduce in smaller amounts. The yield is not materially lowered by making the reduction in one portion.

4. The reduction does not always run smoothly. If the **zinc** lumps and becomes inactive more must be added. To determine whether reduction is complete, a sample is removed, cooled, and filtered. The precipitate is boiled with strong **sodium hydroxide** solution, filtered, and then acidified with **hydrochloric acid**. If the reduction is complete, the precipitated material will melt at 164° or lower. If the reduction is not complete, the precipitated material will melt above 164°. If the reduction is not complete, the refluxing of the main portion must be continued (and perhaps more **zinc** must be added) until a test portion shows that the reaction is complete.

In determining the melting point of the material, the capillary tube containing the test sample should be inserted in a bath previously heated to 163–164°.

5. When the reduction is carried out in five portions, one extraction with **sodium hydroxide** is usually sufficient for each portion. If the reduction is carried out in one operation, several extractions are usually required. When the material is to be extracted more than once, it is best to boil the residue from the first alkaline treatment with **hydrochloric acid**, filter, and then treat again with the alkali.

6. **Thiosalicylic acid** is used for the preparation of **oxythionaphthene** and many thioindigoid dyes.

3. Discussion

Of the several methods described for the production of [thiosalicylic acid](#), only the following are of preparative interest: heating *o*-halogenated benzoic acids with an alkaline [hydrosulfide](#) at 150–200° in the presence of copper or copper salts,^{1, 2} or with [sodium sulfide](#) at 200°;³ and reduction of dithiosalicylic acid with [glucose](#),⁴ or metals^{5, 2} in alkaline solution. The dithiosalicylic acid is prepared by treating diazotized [anthranilic acid](#) with [sodium disulfide](#) in alkaline solution.⁵

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 809](#)

References and Notes

1. (a) Cassella and Company, Ger. pat. 189,200 [C. A. 2, 607 (1908)]; (b) Cain, "Intermediate Products for Dyes," p. 151.
 2. Chem. Age 21, Dyestuffs Suppl. p. 11 (1929).
 3. Cassella and Company, Ger. pat. 193,290 [C. A. 2, 1514 (1908)]; Ref. 1(b).
 4. Claasz, Ber. 45, 2427 (1912).
 5. Kalle and Company, Ger. pat. 204,450 [C. A. 3, 1695 (1909)]; Ref. 1(b).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

[sodium sulfide](#) (Na₂S·9H₂O)

[dithiosalicylic acid](#)

[sodium carbonate](#) (soda ash)

[copper](#) or [copper salts](#)

[o-halogenated benzoic acids](#)

[alcohol](#) (64-17-5)

[hydrochloric acid](#) (7647-01-0)

[acetic acid](#) (64-19-7)

[ether](#) (60-29-7)

[sodium hydroxide](#) (1310-73-2)

[nitrogen](#) (7727-37-9)

[sodium nitrite](#) (7632-00-0)

sulfur (7704-34-9)

decolorizing carbon (7782-42-5)

zinc (7440-66-6)

sodium sulfide (1313-82-2)

sodium disulfide

Anthranilic Acid (118-92-3)

glucose (492-62-6)

hydrosulfide

Thiosalicylic acid,
Benzoic acid, o-mercapto- (147-93-3)

oxythionaphthene