



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.

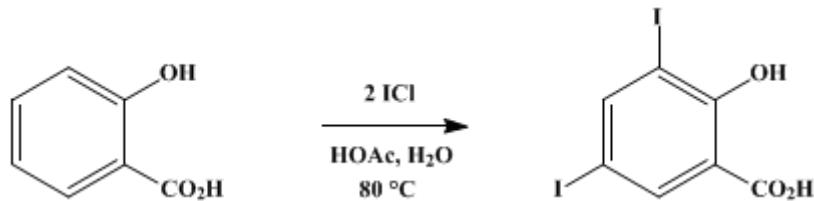
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.343 (1943); Vol. 14, p.52 (1934).

2-HYDROXY-3,5-DIIODOBENZOIC ACID

[Salicylic acid, 3,5-diido-]



Submitted by G. H. Woollett and W. W. Johnson.

Checked by W. W. Hartman and E. J. Rahrs.

1. Procedure

Twenty-five grams (0.18 mole) of **salicylic acid** (m.p. 159–160°) is dissolved in 225 cc. of glacial **acetic acid** in a 2-l. beaker provided with a mechanical stirrer (Note 1). To this is added with stirring a solution of 62 g. (0.38 mole) of **iodine monochloride** (Note 2) in 165 cc. of glacial **acetic acid**; then 725 cc. of water is added. A yellow precipitate of **diiodosalicylic acid** appears. The reaction mixture is gradually heated with stirring on a hot plate to 80° and kept at approximately that temperature for twenty minutes. The entire period of heating should be about forty minutes. Toward the end of the reaction the mixture becomes rather difficult to stir because of the voluminous precipitate. After cooling to room temperature (Note 3), the precipitate is filtered on a Büchner funnel and washed with **acetic acid** and then with water. When no more water is removed by suction, the solid (75 g.) is dissolved in 100 cc. of warm **acetone** and filtered by gravity. To the filtrate 400 cc. of water is slowly added with shaking. The fine, flocculent precipitate is filtered by suction, washed with water, and dried. The yield of **diiodosalicylic acid** melting at 235–236° is 64–64.5 g. (91–92 per cent of the theoretical amount) (Note 4).

2. Notes

1. The amount of glacial **acetic acid** used may not be sufficient to dissolve the **salicylic acid** completely. Solution will be completed upon the addition of the **iodine chloride** solution.
2. **Iodine monochloride** of sufficient purity for this preparation may be made as follows: Dry **chlorine** is led in at, or below, the surface of 127 g. (1 mole) of **iodine** in a 125-cc. distilling flask while the flask is gently shaken. When 34.5 g. (0.97 mole) of **chlorine** has been introduced, the **iodine chloride** is distilled in an ordinary distilling apparatus with a filter flask, protected from atmospheric moisture by a calcium chloride tube, as a receiver. The yield of **iodine chloride**, boiling between 97° and 105°, is 142 g. (87 per cent of the theoretical amount). The product can be preserved in a dry, glass-stoppered bottle. An excess of **iodine** is essential in this preparation.
3. Free **iodine**, if present, is removed by the addition of 5 per cent **sodium sulfite** solution.
4. The checkers found that **4-hydroxy-3,5-diiodobenzoic acid** can be made from **4-hydroxybenzoic acid** using the above directions with the exception that the product is not recrystallized from **acetone**, in which it is only slightly soluble. The yield of **4-hydroxy-3,5-diiodobenzoic acid**, melting at 278–279° with decomposition, is 59 g. (84 per cent of the theoretical amount).

3. Discussion

The method given is based on that of Cofman.¹ **Diiodosalicylic acid** has been prepared by heating **salicylic acid** with **iodine** in alcohol;² by using the same reagents with the addition of **mercuric oxide**;³ by treating **salicylic acid** with **iodine** in the presence of alkali;^{3, 4} and by treating **salicylic acid** with **iodine** and **iodic acid**.⁵ None of these methods, however, appears to give a good yield or a pure product.

This preparation is referenced from:

References and Notes

1. Cofman, Gazz. chim. ital. **50** (II) 297 (1920).
2. Lautemann, Ann. **120**, 300 (1861).
3. Weselsky, ibid. **174**, 103 (1874).
4. Kekulé, ibid. **131**, 226 (1864).
5. Liechti, ibid. Spl. 7, 133, 141 (1870).

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

acetic acid (64-19-7)

sodium sulfite (7757-83-7)

salicylic acid

mercuric oxide (21908-53-2)

iodine (7553-56-2)

acetone (67-64-1)

chlorine (7782-50-5)

iodic acid (7782-68-5)

iodine monochloride,
iodine chloride (7790-99-0)

2-Hydroxy-3,5-diiodobenzoic acid,
Salicylic acid, 3,5-diido- (133-91-5)

diiodosalicylic acid

4-Hydroxy-3,5-diiodobenzoic acid (618-76-8)

4-hydroxybenzoic acid (99-96-7)