



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.

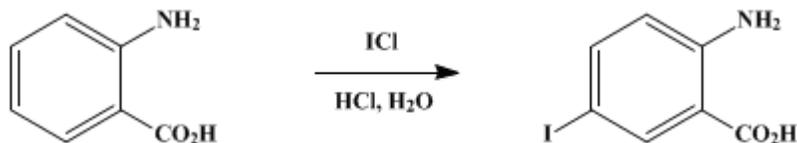
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.349 (1943); Vol. 19, p.52 (1939).

5-IODOANTHRANILIC ACID

[Anthranilic acid, 5-iodo-]



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1. Procedure

In a 3-l. beaker, 110 g. (0.8 mole) of [anthranilic acid](#) ([Note 1](#)) is dissolved in 1 l. of water and 80 cc. of c.p. concentrated [hydrochloric acid](#) (sp. gr. 1.19); the solution is cooled to 20°. In a 2-l. beaker a solution of [iodine monochloride](#) in [hydrochloric acid](#) is prepared by diluting 140 cc. of c.p. concentrated [hydrochloric acid](#) with 500 cc. of cold water, adding just sufficient crushed ice to bring the temperature to 5°, and, during about two minutes, stirring in 131 g. (0.8 mole) of [iodine monochloride](#) ([p. 197](#)).

The [iodine monochloride](#) solution at 5° is stirred rapidly into the [anthranilic acid](#) solution at 20°. [5-Iodoanthranilic acid](#) separates almost immediately as a granular, tan to violet precipitate, and the reaction temperature rises to 18–22°. The mixture is stirred for an hour, while warming to room temperature, then filtered on a 13-cm. Büchner funnel. The acid is pressed as dry as possible, washed with three 100-cc. portions of cold water, and then dried at 90–100°. There is obtained 185–189 g. (88–90 per cent of the theoretical amount) of brown to purple acid which melts at 185–190°, with decomposition ([Note 2](#)).

[5-Iodoanthranilic acid](#) is best purified by recrystallization of its ammonium salt, as follows: To 100 g. of the acid in a 400-cc. beaker is added 200 cc. of hot water, and the acid is dissolved by stirring in concentrated [ammonia](#) (sp. gr. 0.9) until solution is complete at 60° and there is a slight excess of [ammonia](#). About 40 cc. of concentrated [ammonia](#) is required. [Sodium hydrosulfite](#) is added in about 1-g. portions until no further bleaching action is observed, about 5 g. of decolorizing charcoal is added, and, after stirring three minutes, the mixture is filtered with suction on a preheated Büchner funnel into a preheated flask. The filter is washed with 10 cc. of boiling water.

The combined filtrate and washings are transferred to a 400-cc. beaker, allowed to cool slowly without agitation until crystal formation appears complete, then cooled to 5°. The crystalline ammonium salt is then removed by suction filtration on a large Büchner funnel, washed with 15 cc. of ice water, sucked as dry as possible, and spread in a thin layer on an enameled or glass tray and allowed to dry in air at 35–50°. The yield of yellow to violet ammonium salt is 80–89 g., representing a recovery of 76–84 per cent ([Note 3](#)) and ([Note 4](#)).

The ammonium salt is dissolved in three parts of hot water, [ammonia](#) is added if necessary to effect complete solution at 60°, the solution is again treated with [sodium hydrosulfite](#) and 3–4 g. of decolorizing charcoal, filtered hot, and the [5-iodoanthranilic acid](#) is precipitated by adding c.p. [hydrochloric acid](#) in 3- to 5-cc. portions, stirring thoroughly after each addition, until the reaction mixture is just faintly acid to Congo red. Ice is then added until the temperature is reduced to 20°, and the precipitated acid is removed by suction filtration, washed freely with cold water, and dried at 100–110° ([Note 5](#)). [5-Iodoanthranilic acid](#) is almost quantitatively precipitated from its ammonium salt solution and is obtained as a yellow powder, m.p. 190–195° (decomp.) ([Note 6](#)).

2. Notes

1. Commercial "Acid Anthranilic Sublimed" is satisfactory.

2. The decomposition point varies with the method of determination. The values given herein were determined by placing the sample in a capillary tube, inserting the tube in the bath at a temperature 25° below the decomposition point, and heating at the rate of 2–3° per minute.
3. The ammonium salt is not stable under the drying conditions. The dry product is a mixture of [5-iodoanthranilic acid](#) and its ammonium salt. Contact with air may change its color from yellow to violet.
4. Crude [5-iodoanthranilic acid](#) is recovered from the mother liquor by carefully making it just acid to Congo red, using a spot plate, with concentrated [hydrochloric acid](#), cooling to 20°, filtering, washing freely with cold water, and drying at 90–110°. This acid can be added to crude acid in further crystallizations or worked up alone.
5. The drying oven must have good air circulation and uniform temperature control; drying at 120° causes the evolution of considerable amounts of free [iodine](#).
6. This product is sufficiently pure for conversion to [m-iodobenzoic acid](#) (p. 353). If greater purity is desired the ammonium salt can be recrystallized from twice its weight of water, between 45° and 5°, with 85–90 per cent recovery. When the salt remains nearly white after drying, the acid precipitated from it melts with decomposition at a temperature above 210°. Four or five recrystallizations may be required.

3. Discussion

[5-Iodoanthranilic acid](#) has been prepared by the reduction of [2-nitro-5-iodobenzoic acid](#);¹ by treatment of [anthranilic acid](#) with [iodine](#) in [potassium hydroxide](#) solution;² by treatment of the anhydride of 5-hydroxymercurianthranilic acid with [iodine](#) in aqueous [potassium iodide](#) solution;³ and by iodination of [anthranilic acid](#) in glacial [acetic acid](#) solution with [iodine monochloride](#),⁴ or in dilute [acetic acid](#) solution with [iodine](#).⁵

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 2, 353](#)

References and Notes

1. Grothe, J. prakt. Chem. (2) **18**, 326 (1878).
2. Wheeler and Johns, Am. Chem. J. **43**, 403 (1910); Klemme and Hunter, J. Org Chem. **5**, 230 (1940).
3. Schoeller and Hueter, Ber. **47**, 1938 (1914).
4. Borsche, Weusmann, and Fritzsche, *ibid.* **57**, 1774 (1924).
5. Miltzer, Smith, and Evans, J. Am. Chem. Soc. **63**, 436 (1941).

Appendix

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

anhydride of 5-hydroxymercurianthranilic acid

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

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

[ammonia](#) (7664-41-7)

[potassium iodide](#) (7681-11-0)

sodium hydrosulfite (7775-14-6)

iodine (7553-56-2)

potassium hydroxide (1310-58-3)

Anthranilic Acid (118-92-3)

iodine monochloride (7790-99-0)

5-IODOANTHRANILIC ACID,
Anthranilic acid, 5-iodo- (5326-47-6)

2-nitro-5-iodobenzoic acid

m-iodobenzoic acid (618-51-9)