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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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.

DOI:10.15227/orgsyn.003.0011

Organic Syntheses, Coll. Vol. 1, p.52 (1941); Vol. 3, p.11 (1923).

p-AMINOPHENYLACETIC ACID

[α-Toluic acid, *p*-amino-]

$$p\text{-}NO_2C_6H_4CH_2CO_2H + 3(NH_4)_2S + 3H_2O \longrightarrow p\text{-}NH_2C_6H_4CH_2CO_2NH_4 + 3S + 5NH_4OH$$

$$p\text{-}NH_2C_6H_4CH_2CO_2NH_4 + CH_3CO_2H \longrightarrow p\text{-}NH_2C_6H_4CH_2CO_2H + CH_3CO_2NH_4$$

Submitted by G. Ross Robertson
Checked by H. T. Clarke and J. H. Bishop.

1. Procedure

A 1500-cc. flask is fitted with a two-holed rubber stopper carrying a glass tube which ends below the middle of the flask. The second hole is fitted with a common glass stopcock (Note 1). To the flask is added 500 cc. of 6 *N* aqueous ammonia (sp. gr. about 0.95), and 100 g. (0.55 mole) of *p*-nitrophenylacetic acid (p. 406) is now slowly introduced, with shaking. The flask is then placed in an ice bath, and the mixture saturated with hydrogen sulfide, the temperature being held below 50°.

The stopper is removed from the reaction flask, and the solution of ammonium *p*-aminophenylacetate gently boiled under the hood until nearly all the excess hydrogen sulfide and ammonia have escaped. The solution changes from a dark orange-red to a pale yellow. The deposited sulfur is filtered off by suction, and 40 cc. of glacial acetic acid rapidly stirred into the hot filtrate. The *p*-aminophenylacetic acid which crystallizes out weighs 69–70 g., but it is contaminated with a small amount of free sulfur. On evaporating the mother liquor to a small volume, about 5 g. more can be obtained. The crude material is recrystallized from 4 l. of distilled water, 69–70 g. (83–84 per cent of the theoretical amount) of a product which melts at 199–200° being thus obtained (Note 2).

2. Notes

1. The use of a stopcock in the reaction flask during the saturation with hydrogen sulfide permits the occasional expulsion of hydrogen gas, which would otherwise accumulate. Apparently, commercial ferrous sulfide contains free iron as an impurity.
2. The procedure avoids the troubles of filtration incidental to the method of reduction with ferrous sulfate and ammonia, and the yield is better. Inasmuch as the only by-product is the very soluble ammonium acetate, a large yield can be secured by close evaporation.

3. Discussion

p-Aminophenylacetic acid can be prepared by the hydrolysis of *p*-aminobenzyl cyanide with concentrated hydrochloric acid,[1] and by the reduction of *p*-nitrophenylacetic acid with tin and hydrochloric acid[2] or with ferrous sulfate and ammonia.[3] Reduction of *p*-nitrophenylacetic acid with a platinum oxide catalyst is reported to furnish a quantitative yield of *p*-aminophenylacetic acid, but, because of more favorable solubilities, it is recommended that the ethyl ester be reduced and the reduction product then hydrolyzed to the acid.[4]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 63

References and Notes

1. Friedländer, Ber. **17**, 237 (1884); Gabriel, Ber. **15**, 835 (1882).

2. Radziszewski, Ber. **2**, 209 (1869); Bedson, J. Chem. Soc. **37**, 92 (1880).
3. Jacobs and Heidelberger, J. Am. Chem. Soc. **39**, 1437 (1917); Robertson and Stieglitz, ibid. **43**, 180 (1921).
4. Ferber and Bendix, Ber. **72**, 839 (1939).

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

ethyl ester

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ammonia (7664-41-7)

ammonium acetate (631-61-8)

hydrogen (1333-74-0)

iron (7439-89-6)

hydrogen sulfide (7783-06-4)

tin (7440-31-5)

α-Toluic acid (65-85-0)

sulfur (7704-34-9)

ferrous sulfide

ferrous sulfate (13463-43-9)

platinum oxide

p-AMINOPHENYLACETIC ACID (1197-55-3)

p-Nitrophenylacetic acid (104-03-0)

ammonium p-aminophenylacetate

p-aminobenzyl cyanide (3544-25-0)