Organic Syntheses

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.

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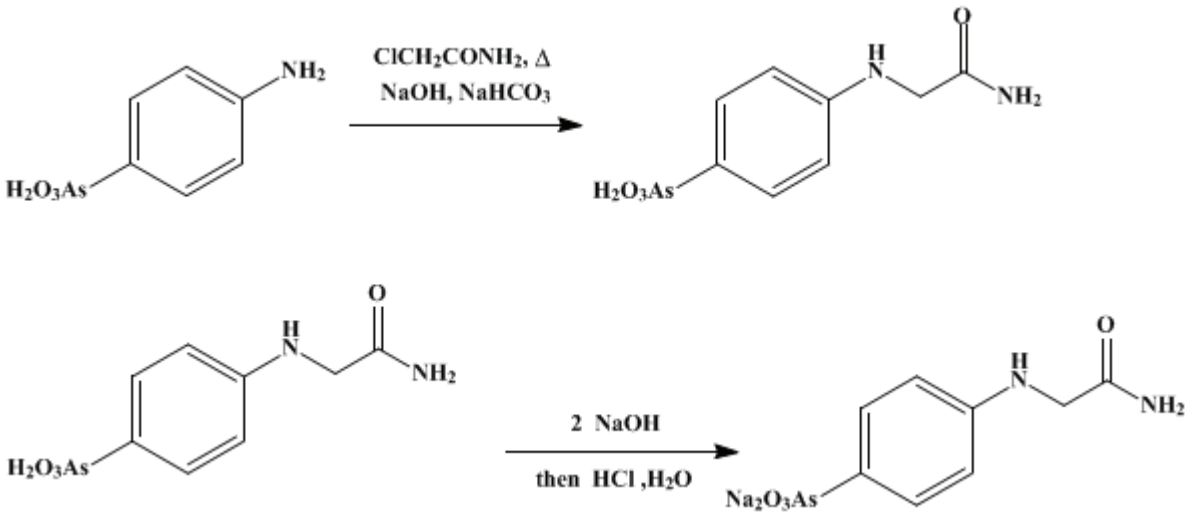
SODIUM *p*-ARSONO-*N*-PHENYLGLYCINAMIDE

[Tryparsamide]



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1. Procedure

To a solution of 130 g. (0.6 mole) of arsanilic acid (p. 70) in 600 cc. (0.6 mole) of normal sodium hydroxide are added 52 g. (0.62 mole) of sodium bicarbonate and 70 g. (0.75 mole) of chloroacetamide (p. 153). The mixture is heated on a water bath to 90–100°, and a steady evolution of carbon dioxide occurs. At the end of two hours, when gas evolution has practically ceased, the mixture is cooled to 40°, stirred vigorously, and 150 cc. of 20 per cent hydrochloric acid poured in rapidly. *p*-Arsonophenylglycinamide crystallizes at once and, after cooling to room temperature, is filtered by suction and washed once with 2 per cent hydrochloric acid (Note 1), then with cold water.

The crude product thus obtained is contaminated with some arsanilic acid and possibly other products. These are removed during purification. The crude product is suspended in about 400 cc. of water, and, with vigorous stirring, treated carefully with 25 per cent aqueous sodium hydroxide until solution is just complete. At this point the mixture is still acid to litmus, and an excess of sodium hydroxide is to be avoided to prevent decomposition of the product. About 15 g. of animal charcoal is added, the mixture stirred for five minutes without heating, and filtered. The filtrate is treated during vigorous stirring with 100 cc. of 20 per cent hydrochloric acid, and the pure acid at once separates. After cooling, it is filtered by suction and washed thoroughly with small portions of ice-cold water until the filtrate is practically halogen-free (Note 2).

The acid, without drying, is suspended in about 200 cc. of distilled water and, with vigorous stirring, cautiously (Note 3) treated with 25 per cent sodium hydroxide solution until dissolved and the solution reacts neutral to litmus. The solution is then filtered through folded filter paper which should be free from soluble calcium salts, otherwise the filtrate will remain clouded by a suspension of the calcium salt. The clear, faintly yellow or colorless filtrate is then vigorously stirred and treated with 1.5 volumes of 95 per cent alcohol. Crystallization is induced by rubbing with a rod, and then an additional volume of alcohol is added. The mixture should be allowed to cool to about 20° and stand for at least two hours to complete the precipitation of the salt, which is then filtered by suction and washed thoroughly with 85 per cent alcohol. The salt is then air-dried. The yield is 73–77 g. (38–40 per cent of the theoretical amount).

2. Notes

1. From this filtrate approximately 15–30 g. of arsanilic acid may be recovered by just neutralizing to Congo red with sodium hydroxide.
2. If the free acid is desired it may be obtained by drying the product at this stage. The yield of free acid is about 100 g. (60 per cent of the theoretical amount).
3. If sodium hydroxide is added too rapidly some solid precipitates which does not redissolve.

3. Discussion

This procedure described for the preparation of sodium *p*-arsono-*N*-phenylglycinamide has been reported in the literature.[1]

References and Notes

1. Jacobs and Heidelberger, J. Am. Chem. Soc. **41**, 1590 (1919); U. S. pat. 1,280,119 [C. A. **12**, 2658 (1918)].

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

alcohol (64-17-5)

hydrochloric acid (7647-01-0)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

carbon dioxide (124-38-9)

Arsanilic acid (98-50-0)

CHLOROACETAMIDE (79-07-2)

Sodium p-arsono-N-phenylglycinamide (834-03-7)

p-Arsonophenylglycinamide