



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](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.

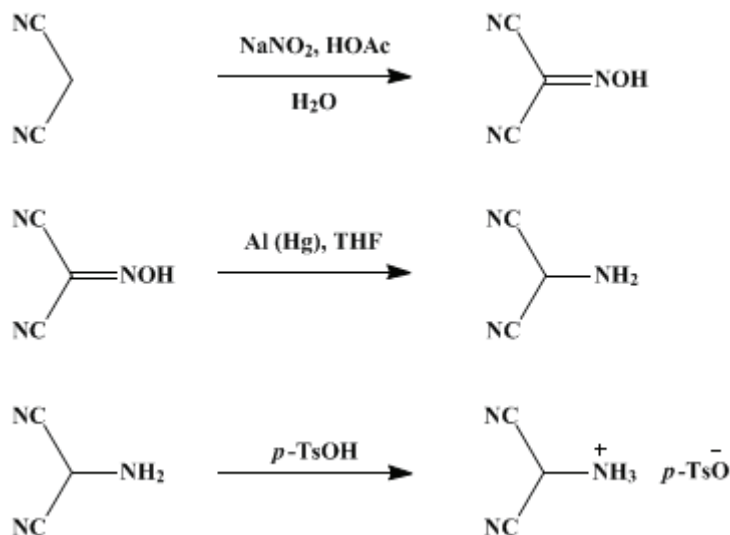
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 5, p.32 (1973); Vol. 48, p.1 (1968).*

## AMINOMALONONITRILE *p*-TOLUENESULFONATE

### [Malononitrile, amino-, *p*-toluenesulfonate]



Submitted by J. P. Ferris, R. A. Sanchez, and R. W. Mancuso<sup>1</sup>.

Checked by O. W. Webster and R. E. Benson.

### 1. Procedure

A. *Oximinomalononitrile*. Malononitrile (Note 1) (25 g., 0.38 mole) is dissolved in a mixture of 20 ml. of water and 100 ml. of acetic acid in a 1-l. round-bottomed flask equipped with a stirrer, a thermometer, and a powder funnel. The solution is cooled to  $-10^\circ$  with a dry ice-acetone bath, and 50 g. (0.72 mole) of granulated sodium nitrite is added in approximately 2-g. portions over a 30-minute period while the temperature is maintained at  $0^\circ$  to  $-10^\circ$ . After the addition is complete a wet ice bath is used to maintain the temperature below  $5^\circ$  while the mixture is stirred for 4 hours. Four hundred milliliters of tetrahydrofuran (Note 2) and 400 ml. of ether are added in separate portions, and the mixture is stored at  $-40^\circ$  overnight. The mixture is filtered rapidly, and the solid is washed with a mixture of 200 ml. of tetrahydrofuran (Note 2) and 200 ml. of ether. The filtrate and washings are combined and concentrated by distillation to a volume of 250 ml. by the use of a water aspirator and a bath at  $40^\circ$  (Note 3). This solution of oximinomalononitrile is used directly in the next step.

B. *Aminomalononitrile p-toluenesulfonate*. Aluminum foil (13.7 g., 0.51 g. atom) is cut into half-inch squares and is covered with a 5% aqueous solution of mercuric chloride until a mercury coating is visible on the aluminum (ca. 30 seconds). The mercuric chloride solution is decanted, and the amalgamated aluminum is washed twice with water, once with ethanol, and twice with tetrahydrofuran (Note 2). The amalgamated aluminum is transferred to a 2-l. round-bottomed flask fitted with a condenser, a stirrer, and a 250-ml. addition funnel and is covered immediately with 300 ml. of tetrahydrofuran (Note 2). The mixture is cooled in a dry ice-acetone bath, and the solution of oximinomalononitrile from procedure A is added with stirring over a 15-minute period while the temperature is maintained at  $-15^\circ$  to  $-30^\circ$ . Stirring is continued for an additional 5 minutes. The dry-ice acetone bath is then removed, and the mixture is allowed to warm to room temperature. (*Caution! Cooling with a dry ice-acetone bath is usually needed to control the reaction.*) After the spontaneous reaction subsides, the mixture is warmed to reflux until most of the aluminum is consumed (45 minutes). The reaction mixture is cooled to room temperature, 200 ml. of ether is added with stirring, and the aluminum salts are removed by vacuum filtration through Celite filter aid. The solid is washed with 250 ml. of tetrahydrofuran (Note 2) followed by 500 ml. of ether (Note 3) and (Note 4). The original filtrate and washings are combined and concentrated to about 250 ml. by the use of a water

aspirator and a bath at 40°. To the resulting brown solution is slowly added with stirring a mixture of 60 g. (0.32 mole) of *p*-toluenesulfonic acid monohydrate as a slurry in 250 ml. of ether (Note 5). The total volume is brought to 1 l. with ether, the mixture is cooled to 0°, and the crystalline solid is collected by vacuum filtration. The product is washed successively with 200 ml. of ether, 200 ml. of cold (0°) acetonitrile, and 200 ml. of ether and dried at 25° (1 mm.) to give light tan crystals, m.p. 169–171° (dec.); yield, 75–79 g. (78–82%).

This product is suitable for most synthetic purposes. An almost colorless product may be obtained by recrystallization from boiling acetonitrile (100 ml. dissolves 1.8 g. of product) with treatment with activated carbon. The recovery of aminomalononitrile *p*-toluenesulfonate, m.p. 172° (dec.), is ca. 80%.

## 2. Notes

1. Commercial malononitrile is purified by dissolving 260 g. in 1 l. of ether, refluxing the solution with 5 g. of activated carbon for 10 minutes, and filtering through Celite under vacuum. The malononitrile crystallizes from the filtrate as a result of the cooling and concentration during the filtration. It is collected by filtration and washed with 350 ml. of cold (–20°) ether to give 214 g. of white crystals.
2. Tetrahydrofuran from Fisher Scientific Co. was used by the checkers. [*Caution! See page 976 for a warning regarding the purification of tetrahydrofuran.*]
3. Occasionally a precipitate may form in the filtrate. It is removed by filtration before proceeding to the next step.
4. Additional washing is necessary if the washings are not colorless at this point.
5. One can check for complete precipitation of the aminomalononitrile by adding *p*-toluenesulfonic acid to the clear supernatant liquid.

## 3. Discussion

The present procedure is a modification of the original synthesis.<sup>2</sup> Previous reports of the synthesis of aminomalononitrile are in error.<sup>2</sup> Oximinomalononitrile was prepared by a modification of the procedure of Ponzio.<sup>3</sup>

## 4. Merits of the Preparation

This procedure provides a convenient synthesis of aminomalononitrile, which has been demonstrated to be a useful intermediate for the preparation of substituted imidazoles, thiazoles, oxazoles, purines, and purine-related heterocycles.<sup>2</sup> It is also a convenient starting material for the preparation of diaminomaleonitrile.<sup>2,4</sup>

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 344

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## References and Notes

1. The Salk Institute for Biological Studies, San Diego, California [Present address (J.P.F.): Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181].
  2. J. P. Ferris and L. E. Orgel, *J. Am. Chem. Soc.*, 88, 3829 (1966); 87, 4976 (1965).
  3. G. Ponzio, *Gazz. Chim. Ital.*, 61, 561 (1931).
  4. J. P. Ferris and R. A. Sanchez, *this volume*, p. 344.
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## Appendix Chemical Abstracts Nomenclature (Collective Index Number);

## (Registry Number)

Amalgamated aluminum

ethanol (64-17-5)

acetic acid (64-19-7)

ether (60-29-7)

acetonitrile (75-05-8)

sodium nitrite (7632-00-0)

aluminum,  
Aluminum foil (7429-90-5)

mercury (7439-97-6)

carbon (7782-42-5)

mercuric chloride (7487-94-7)

Malononitrile (109-77-3)

Tetrahydrofuran (109-99-9)

Oximinomalononitrile (36568-05-5)

aminomalononitrile

Diaminomaleonitrile (1187-42-4)

p-toluenesulfonic acid (104-15-4)

p-toluenesulfonic acid monohydrate (6192-52-5)

Aminomalononitrile p-toluenesulfonate,  
Malononitrile, amino-, p-toluenesulfonate (5098-14-6)