



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.

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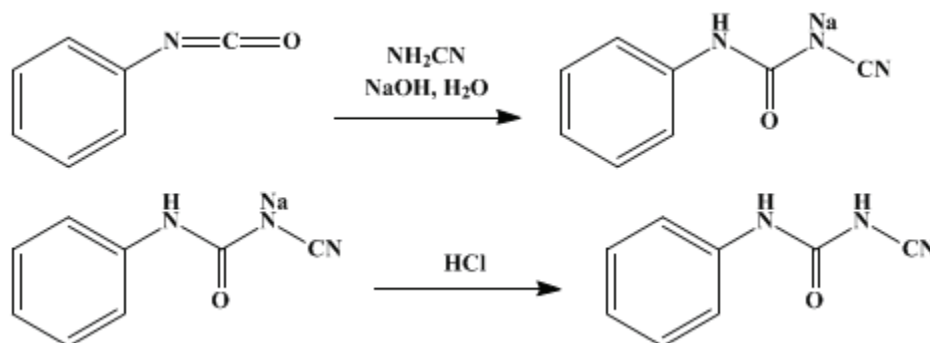
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.213 (1963); Vol. 36, p.8 (1956).

1-CYANO-3-PHENYLUREA

[Urea, 1-cyano-3-phenyl-]



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Checked by John C. Sheehan and Ernest R. Gilmont.

1. Procedure

To a solution of 16.8 g. (0.40 mole) of [cyanamide](#) in 50 ml. of water ([Note 1](#)) contained in a 400-ml. flask or beaker is added 50 ml. of aqueous 3*N* [sodium hydroxide](#) (0.15 mole). To the resulting solution, cooled to 15–18°, is added, in 2-ml. portions with shaking over a 15–18 minute period, 23.8 g. (22.0 ml., 0.2 mole) of [phenyl isocyanate](#). The isocyanate dissolves rapidly, while the temperature rises slightly. The mixture is maintained at 20–25° by occasional external cooling in ice water. When half the [phenyl isocyanate](#) has been introduced, a second portion of 50 ml. (0.15 mole) of 3*N* [sodium hydroxide](#) is added to keep the reaction mixture strongly alkaline throughout the experiment. When addition is complete ([Note 2](#)), the slightly turbid liquid is diluted with 40 ml. of water and is filtered immediately under reduced pressure ([Note 3](#)) to remove undissolved impurities and traces of separated [diphenylurea](#) ([Note 4](#)). The cyanourea is precipitated from the clear colorless filtrate by the slow addition of concentrated [hydrochloric acid](#) with stirring until a permanent turbidity just appears ([Note 3](#)). Cracked ice (30–40 g.) is added to lower the temperature to 18–20°. Precipitation is then completed in this temperature range by the alternate addition of concentrated [hydrochloric acid](#) (total volume required, approximately 30 ml.) and cracked ice until the suspension is acid to Congo red. The crude cyanourea forms a microcrystalline, white precipitate, which, after storage at 0° for 3 hours, is collected by filtration under reduced pressure ([Note 5](#)) and is washed with two portions of cold water (20–25 ml.) ([Note 6](#)). The crude product is drained thoroughly, air-dried at room temperature, and finally dried to constant weight in a desiccator over [phosphorus pentoxide](#). The yield of crude [1-cyano-3-phenylurea](#) ([Note 7](#)), m.p. 122–126° with decomposition ([Note 8](#)), varies between 29 and 30.5 g. (90–95%). The dried material is purified as follows. A solution of the crude product in 100 ml. of boiling [acetone](#) is diluted slowly with gentle swirling with 30–40 ml. of petroleum ether (boiling range 40–60°). As crystallization proceeds, an additional 20–30 ml. of petroleum ether is added carefully at such a rate that the supernatant liquid does not become turbid. After 15 minutes at room temperature, the mixture is set aside at 0°. The product is collected by filtration under reduced pressure and washed successively with 50 ml. of an acetone-petroleum ether mixture (1:3) and 50 ml. of petroleum ether. [1-Cyano-3-phenylurea](#) thus obtained forms colorless lustrous needles, m.p. 127–128° with decomposition ([Note 8](#)), yield 20–21.5 g. (62–67%). Slow dilution of the filtrates with petroleum ether to a total volume of 350–400 ml. and storage at 0° affords a second crop, m.p. 123–126° (dec.), of satisfactory purity; yield 4–5 g. (12–16%). The synthesis is generally applicable to the preparation of 1-cyano-3-arylureas ([Note 9](#)).

2. Notes

1. The checkers used 16.8 g. of Eastman Kodak Company [cyanamide](#) (P1995) without further purification. A convenient method of preparing [cyanamide](#) from commercial calcium cyanamide has

been described (p.645). According to the submitters, an aqueous solution of crude cyanamide is satisfactory in the present synthesis and is obtained by adapting this published procedure (p.645) as follows.

The residual crude cyanamide remaining after evaporation of the ethereal extracts (which need not be dried previously) is dissolved readily in the appropriate volume of cold water. A small quantity of water-insoluble oily or semisolid by-products is removed by shaking the solution with carbon and filtering the liquid through a small ordinary filter, followed by rinsing with a few milliliters of water. The clear filtrate is suitable for the subsequent operation.

In order to allow for small losses in the filtration and for the presence of impurities (such as solvent and oily by-products) an excess of approximately 10–15% by weight of crude cyanamide is allowed.

2. The reaction is completed when the liquid no longer has the odor of phenyl isocyanate; shaking is continued until this stage is reached.

3. The reaction mixture is not cooled during the addition of the last two or three portions of phenyl isocyanate, so that the final temperature is near 25°; this procedure prevents separation of the sodium salt of cyanophenylurea, which crystallizes readily at low temperatures. For the same reason, the filtered solution of the salt is not precooled, but rather is cooled during the precipitation of the free cyanourea.

4. The residue on the filter is rinsed with 5–10 ml. of water, in order to redissolve any small quantities of the sodium salt of cyanophenylurea that may have been collected.

5. The aqueous filtrate does not deposit any further material on storage at 0° and is discarded.

6. For the purpose of washing, the filter cake on the funnel is covered with ice water. After being allowed to remain in contact for a few seconds, the liquid is quickly drained under reduced pressure. The second portion of washing water should no longer be acid to Congo red.

7. According to the submitters the crude material may turn very pale pink on drying, but the product is again colorless after recrystallization. The checkers found that the crude product could be dried to less than 0.2% moisture by drawing air through the filter cake for 3 hours.

8. The decomposition temperature is somewhat influenced by the rate of heating. The material does not form a clear melt during the decomposition.

9. According to the submitters 1-cyano-3- α -naphthylurea² is obtained similarly from α -naphthyl isocyanate in 85–90% yields. Crystallization from acetone-petroleum ether (12 and 6 ml., respectively, per gram of crude product; recovery approximately 60% per crystallization) yields lustrous prisms, m.p. 148–149° with decomposition.

3. Discussion

1-Cyano-3-phenylurea, first obtained by the alkaline hydrolysis of 5-anilino-3-*p*-toluyl-1,2,4-oxadiazole,³ has been prepared by the condensation of phenyl isocyanate and the sodium salt of cyanamide.⁴ However, in these publications an incorrect structural assignment for the product was made. 1-Cyano-3-phenylurea is obtained also, together with other products, by warming gently 1-cyano-3-phenylthiourea with caustic soda in the presence of ethylene chlorohydrin,⁵ or by gradually adding caustic potash to a boiling solution of 1-phenyldithiobiuret and ethylene chlorohydrin in ethanol.⁵

References and Notes

1. Royal Free Hospital School of Medicine, University of London, London, England.
 2. Kurzer and Powell, *J. Chem. Soc.*, **1955**, 1500.
 3. Böseken, *Rec. trav. chim.*, **16**, 350 (1897).
 4. Böseken, *Rec. trav. chim.*, **29**, 279 (1910).
 5. Fromm and Wenzl, *Ber.*, **55B**, 809 (1922).
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Appendix

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

caustic soda

petroleum ether

calcium cyanamide

sodium salt of cyanophenylurea

caustic potash

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

sodium hydroxide (1310-73-2)

acetone (67-64-1)

carbon (7782-42-5)

ethylene chlorohydrin (107-07-3)

diphenylurea (603-54-3)

phenyl isocyanate (103-71-9)

cyanamide (420-04-2)

1-phenyldithiobiuret

1-Cyano-3-phenylurea,
Urea, 1-cyano-3-phenyl- (41834-91-7)

1-cyano-3- α -naphthylurea

α -naphthyl isocyanate (86-84-0)

1-cyano-3-phenylthiourea

phosphorus pentoxide (1314-56-3)

5-anilino-3-p-toluy-1,2,4-oxadiazole

sodium salt of cyanamide