



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.

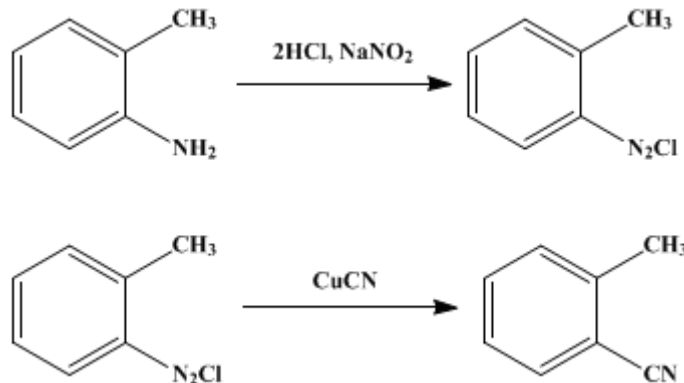
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

Organic Syntheses, Coll. Vol. 1, p.514 (1941); Vol. 4, p.69 (1925).

o-TOLUNITRILE AND *p*-TOLUNITRILE



Submitted by H. T. Clarke and R. R. Read.
Checked by C. S. Marvel and M. M. Brubaker.

1. Procedure

(A) *Preparation of Cuprous Cyanide Solution.*—Cuprous chloride prepared from 1250 g. (5 moles) of crystallized copper sulfate, according to the directions given on p. 170, is suspended in 2 l. of cold water in a 15-l. crock fitted with a mechanical stirrer. A solution of 650 g. (12.7–13 moles) of sodium cyanide (96–98 per cent) in 1 l. of water is added and the mixture stirred, whereupon the cuprous chloride enters into solution with considerable evolution of heat (Note 1). The mixture is then cooled by surrounding the crock with cold water (Note 2).

(B) *o-Tolunitrile.*—While the cuprous cyanide solution is cooling, 428 g. (427 cc., 4 moles) of *o*-toluidine is mixed in a 20-l. crock with 1 l. of commercial 28 per cent hydrochloric acid (sp. gr. 1.14) and enough cracked ice, about 4 kg., to bring the temperature of the mixture to 0°. A solution of 280 g. (4.06 moles) of sodium nitrite in 800 cc. of water is added, with stirring, to the resulting suspension of *o*-toluidine hydrochloride, the temperature being kept at 0–5° by the addition of cracked ice. The addition of the nitrite occupies about fifteen minutes; at the end of the operation, the mixture must show a distinct and permanent reaction for free nitrous acid on testing with starch-iodide paper (Note 3). The final volume of the solution is 5–6 l. The mixture is now cautiously neutralized by adding dry sodium carbonate with constant stirring, using litmus paper to determine the end-point; about 200 g. of the anhydrous carbonate is required (Note 4).

The cold cuprous cyanide solution is now chilled to 0–5° by the addition of ice, and 1 l. of benzene (Note 5) is poured on the surface. To this mixture is slowly added the cold neutralized diazonium solution. During the addition, which occupies about thirty minutes, such vigorous stirring is maintained that the benzene on the surface is constantly drawn to the stirrer, and the temperature is maintained at 0–5° by occasionally adding ice. As soon as the diazonium solution comes into contact with the cuprous cyanide, a dark yellow, oily precipitate is formed which at once begins to give off nitrogen; the resulting nitrile is taken up by the benzene as soon as it is formed (Note 6). When all has been added, the temperature is held at 0–5° for thirty minutes longer, and then is allowed to rise to that of the room (20–25°), which usually requires about three hours.

After stirring has been continued for two hours longer, the crock is surrounded by hot water or steam and warmed to 50° without stirring. The mixture is then allowed to stand until cool, when the aqueous layer is drawn off by means of a siphon. The upper oily layer is transferred to a 12-l. flask and distilled in a current of steam until no more oil passes over; about 10 l. of distillate is collected (Note 7). The water is drawn off and the benzene removed by distillation, by means of a 2-l. round-bottomed flask and a fractionating column about 90 cm. long. When benzene no longer distils over, the distillation is continued in the same apparatus under reduced pressure, and the fraction that boils at 94–96°/20 mm.

is collected. A small amount of dark-colored residue remains in the flask. The yield of almost colorless *o*-tolunitrile is 300–330 g. (64–70 per cent of the theoretical amount).

(C) *p*-Tolunitrile.—*p*-Tolunitrile can be prepared in exactly the same manner from *p*-toluidine; the product, which distils at 104–106°/20 mm., solidifies in the receiver to a mass of nearly colorless needles which melt at 25–27°. The yield is the same as with the ortho compound (Note 8).

2. Notes

1. If desired, the cuprous chloride may be suspended in 3 l. of water and the sodium cyanide added in the solid form.
2. If several runs are to be made it may be more convenient to prepare a large quantity of cuprous cyanide solution, since this appears to be stable for several days.
3. If the sodium nitrite is not of the highest technical purity it may be necessary to employ more than the indicated quantity. It is essential that the test for nitrous acid be permanent; if any unchanged amine remains, a precipitate of the diazoamino compound is formed on neutralization. A moderate excess of nitrite does not appear to interfere with the reaction, especially since the greater portion of the free nitrous acid is removed by the carbon dioxide liberated on neutralization.
4. Sodium carbonate is preferable to sodium hydroxide because very little heat is evolved on neutralization. A slight excess of carbonate does not appear to be harmful.
5. It is suggested that 1 l. of toluene be used instead of benzene. Since the benzene freezes at 0° to 4° it does not extract the nitrile until it melts much later in the procedure. (R. L. Shriner, private communication.)
6. It is essential that the stirring be very vigorous. If the intermediate addition compound is allowed to collect on the surface of the liquid, it decomposes spontaneously with the evolution of much heat; this decomposition may take place with almost explosive violence. The presence of the benzene tends to diminish the viscosity of the intermediate product and permit it to be readily distributed throughout the mixture. Decomposition is quite rapid at 0° and is practically complete when room temperature is reached; it appears, however, to be advisable to warm the mixture to 50°, since if this is omitted the yield is slightly decreased.
7. The apparatus described on p. 479 is suitable for the steam distillation.
8. The product, as obtained in the above procedure, is of high purity; cresols do not appear to be formed under the conditions specified. The process has the advantage over that described in the literature¹ of giving rise to no poisonous fumes during the formation of the cuprous cyanide and during the interaction of this with the diazonium salt. The yield is practically the same as in the older method.

3. Discussion

o- and *p*-Tolunitriles can be prepared by the interaction of the corresponding diazonium solutions with cuprous cyanide,² or alkali cupric diammino-cyanide.³ Nickel cyanide is said to be better than copper cyanide in the preparation of nitriles by the Sandmeyer reaction.⁴ A mixture of *o*- and, predominantly, *p*-tolunitrile is obtained by treating toluene with trichloroacetonitrile and aluminum chloride, then cleaving the resulting ketimines with alkali.⁵ *p*-Tolunitrile can be prepared from the corresponding amide by heating it with the double salt of aluminum chloride and sodium chloride.⁶

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 586
- Org. Syn. Coll. Vol. 2, 588
- Org. Syn. Coll. Vol. 3, 626
- Org. Syn. Coll. Vol. 5, 480

References and Notes

1. Sandmeyer, Ber. **17**, 2653 (1884); **18**, 1492, 1496 (1885).

2. Sandmeyer, Ber. **17**, 2653 (1884); Ber. **18**, 1492, 1496 (1885); Cahn, Ber. **19**, 756 (1886); Kröber, Ber. **23**, 1026 (1890); Clarke and Read, J. Am. Chem. Soc. **46**, 1001 (1924).
 3. I. G. Farbenind. A.-G., Brit. pat. 326,149 [C. A. **24**, 4055 (1930)].
 4. Korczynski and Fandrich, Compt. rend. **183**, 421 (1926).
 5. Houben and Fischer, Ber. **66**, 339 (1933).
 6. Norris and Klemka, J. Am. Chem. Soc. **62**, 1433 (1940).
-

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

cresols

alkali cupric diammino-cyanide

double salt of aluminum chloride

o- and p-Tolunitriles

o- and, predominantly, p-tolunitrile

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

sodium hydroxide (1310-73-2)

sodium cyanide (143-33-9)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

carbonate (3812-32-6)

nitrogen (7727-37-9)

Cuprous Cyanide (544-92-3)

copper sulfate (7758-98-7)

sodium nitrite (7632-00-0)

nitrous acid (7782-77-6)

carbon dioxide (124-38-9)

aluminum chloride (3495-54-3)

toluene (108-88-3)

cuprous chloride (7758-89-6)

o-Tolunitrile (529-19-1)

p-Tolunitrile (104-85-8)

Nickel cyanide (557-19-7)

copper cyanide (544-92-3)

trichloroacetonitrile (545-06-2)

p-toluidine (106-49-0)

o-toluidine (95-53-4)

o-toluidine hydrochloride (636-21-5)