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.

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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.

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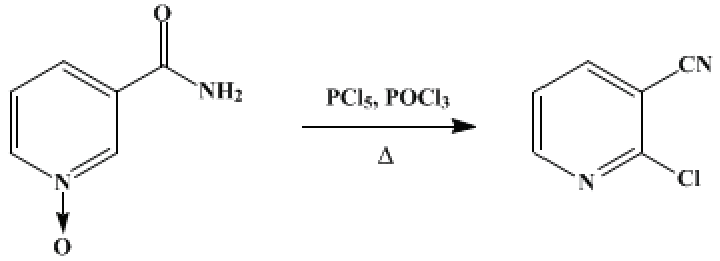
2-CHLORONICOTINONITRILE

[Nicotinonitrile, 2-chloro-]



Submitted by E. C. Taylor, Jr.[1] and Aldo J. Crovetti[2].
Checked by Charles C. Price and Walter A. Schroeder.

1. Procedure

This preparation should be conducted in a good hood.

In a 1-l. round-bottomed flask are placed 85.0 g. (0.62 mole) of nicotinamide-1-oxide (p. 704) and 180.0 g. (0.86 mole) of phosphorus pentachloride (Note 1), and the solids are thoroughly mixed. Two hundred and forty-three milliliters of phosphorus oxychloride is added slowly with shaking. A spiral condenser provided with a drying tube is attached to the flask which is then placed in an oil bath preheated to 60–70°. The temperature is slowly (20–25 minutes) raised to 100°, during which time the reaction mixture is occasionally shaken. In the range 100–105° the evolution of hydrogen chloride gas increases, and a spontaneous, vigorous refluxing of the phosphorus oxychloride begins. The reaction flask is removed from the oil bath, and the rate of refluxing is controlled by the application of an ice-water bath (Note 2). After the vigorous reaction has subsided (about 5 minutes) the oil bath is replaced, and heating under reflux is continued at 115–120° for 1.5 hours.

After the reaction mixture has been cooled, the excess phosphorus oxychloride is distilled under reduced pressure (80–100 mm.) (0.5–1.0 hour). Near the end of the distillation the product begins to sublime into the still head. The residual dark-brown oil is poured with stirring into an 800-ml. beaker containing 280–300 g. of crushed ice (Note 3) and (Note 4). The volume of the ice-water mixture is brought to 600 ml. and allowed to stand at 5° overnight. The crude light-brown product is filtered by suction and washed with water.

The solid is suspended in 300 ml. of 5% sodium hydroxide at 15° (Note 5). The mixture is stirred for 30 minutes, and the solid is filtered by suction and washed with water until the filtrates are no longer alkaline. The procedure is repeated, but stirring is continued for 0.75–1.0 hour. After the solid has been filtered by suction, washed, and pressed as dry as possible, it is dried under reduced pressure over phosphorus pentoxide for 12–16 hours.

The solid is transferred to a Soxhlet thimble (45 × 125 cm.) containing a 5-cm. layer of anhydrous sodium carbonate on the bottom (Note 6), and the solid is extracted for 2 to 3 hours with anhydrous ether (700–800 ml.). The total volume of ether is brought to 800–900 ml. The ethereal solution is treated with charcoal and boiled for 10–15 minutes under reflux; then the solution is filtered by suction (Note 7). After evaporation of solvent, 30–33 g. (35–39%) of white 2-chloronicotinonitrile is obtained, m.p. 105–106° (Note 8).

2. Notes

1. *To avoid exposure to irritating fumes, the phosphorus pentachloride and oxychloride are handled in*

the hood. The heating under reflux is also carried out in the hood.

2. The reaction becomes very exothermic and if uncontrolled there is serious flooding of the condenser. The reaction mixture also becomes dark red to black when the reaction temperature is not controlled.
3. It is difficult to transfer all the oil before solidification starts in the flask. The residual solid is removed by melting on the steam bath and pouring on ice. By repeating this procedure several times, almost all the product can be removed from the flask. Any remaining solid is removed by adding cold water to the flask, breaking the solid with a spatula, and swirling the mixture out of the flask.
4. It is important to stir as rapidly as possible to break the product into small pieces. The beaker should be secured by a large clamp. If the stirring is too slow or the oil is poured too fast, large clumps result which do not solidify completely.
5. Most of the acidic impurities are removed in this step.
6. The sodium carbonate retains any residual moisture and acidic impurities. After the extraction, a brown, gummy, hygroscopic mass remains in the thimble.
7. The checkers found a sintered-glass filter funnel suitable.
8. This product may be recrystallized from ligroin-acetone with 80–85% recovery. Analysis of the product after such recrystallization gave the following analytical results: Calcd. for $C_6H_3ClN_2$: C, 51.98; H, 2.16; Cl, 25.63; N, 20.21. Found: C, 52.41; H, 2.39; Cl, 25.43; N, 19.60.

3. Discussion

The preparation described here is a modification of that reported by Taylor and Crovetti.[3] 2-Chloronicotinonitrile has also been prepared by the dehydration of 2-chloronicotinamide[4] and by the Sandmeyer reaction on 3-amino-2-chloropyridine.[5]

References and Notes

1. Princeton University, Princeton, New Jersey.
2. University of Illinois, Urbana, Illinois.
3. Taylor and Crovetti, *J. Org. Chem.*, **19**, 1633 (1954).
4. Späth and Koller, *Ber.*, **56**, 880 (1923).
5. von Schickh, Binz, and Schulz, *Ber.*, **69**, 2593 (1936).

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

phosphorus pentachloride and oxychloride

hydrogen chloride (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

phosphorus pentachloride (10026-13-8)

sodium carbonate (497-19-8)

Phosphorus Oxychloride (21295-50-1)

2-Chloronicotinonitrile,

Nicotinonitrile, 2-chloro- (6602-54-6)

nicotinamide-1-oxide (1986-81-8)

2-chloronicotinamide (10366-35-5)

3-amino-2-chloropyridine (6298-19-7)

phosphorus pentoxide (1314-56-3)