



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.

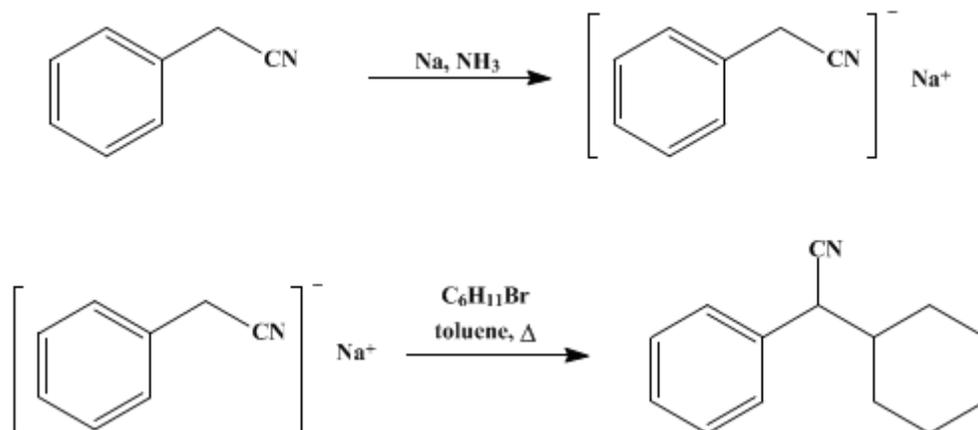
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.219 (1955); Vol. 25, p.25 (1945).

α -CYCLOHEXYLPHENYLACETONITRILE

[Cyclohexaneacetonitrile, α -phenyl-]



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1. Procedure

A 1-l. three-necked flask is equipped with a mercury-sealed stirrer, an inlet tube, and a reflux condenser which is connected through a sodalime tube to a gas-absorption trap. The apparatus is dried in an oven and assembled rapidly to exclude moisture; it is advisable to set up the apparatus in a hood to vent ammonia that may escape by accident. The flask is cooled in a Dry Ice-trichloroethylene bath, and 200 ml. of anhydrous (refrigeration grade) ammonia is introduced through the inlet tube from an ammonia cylinder which is either inverted or equipped with a siphon tube. Just before the apparatus is assembled, 8.1 g. (0.35 gram atom) of sodium is cut, weighed, and kept under kerosene in a small beaker. The Dry Ice bath is removed, the inlet tube is replaced by a rubber stopper, and a crystal of hydrated ferric nitrate (about 0.2 g.) is added. A small (about 5-mm.) cube of the sodium is cut, blotted rapidly with filter paper, and added quickly to the liquid ammonia. The solution is stirred until the blue color disappears, after which the remainder of the sodium is added in narrow, thin strips about as rapidly as it can be cut and blotted, while the solution is stirred vigorously (Note 1). After the solution has turned from blue to gray, the flask is swirled by hand until the blue flecks of sodium that have spattered onto the upper part of the flask are washed into the solution.

The flask is again cooled in the Dry Ice bath, and 41 g. (0.35 mole) of benzyl cyanide (Note 2) is added during about 10 minutes through a dry dropping funnel. The Dry Ice bath is removed, and the clear solution is stirred for about 15 minutes, after which 200 ml. of dry sulfur-free toluene (Note 3) and 25 ml. of anhydrous ether are added dropwise through the funnel while the ammonia evaporates. The solution is allowed to stand or is warmed in a water bath until it comes to room temperature; the ammonia may be vaporized at any rate that does not cause gas to escape through the mercury seal on the stirrer. The remainder of the ammonia is removed by turning off the water in the reflux condenser, warming the flask in a hot water bath, and distilling most of the ether (and ammonia) through the reflux condenser.

A fresh drying tube is attached to the reflux condenser, the cooling water is turned on, and to the warm solution is added 65.2 g. (0.4 mole) of bromocyclohexane (Note 4) during approximately 20 minutes. The reaction is vigorous and may require cooling. Refluxing is continued by heating the mixture in an oil bath for 2 hours. The reaction mixture is cooled and washed with 300 ml. of water. The aqueous layer is extracted with two 50-ml. portions of benzene, and the combined benzene and toluene solutions are washed with two 50-ml. portions of water and distilled from a 500-ml. modified Claisen

flask under reduced pressure. The yield of α -cyclohexylphenylacetonitrile boiling at 174–176°/13 mm. (Note 5) is 45–53 g. (65–77%); the distillate solidifies to a crystalline mass which has a melting point of 50–53.5°. The nitrile can be recrystallized from commercial pentane with approximately 15% loss; it then melts at 56–58°.

2. Notes

1. Vigorous stirring and addition of the sodium in small pieces decrease the time required for complete conversion of the sodium into sodamide.
2. Redistilled benzyl cyanide was used, b.p. 108–110°/13 mm.
3. The toluene (Merck reagent grade) was kept dry by storage over sodium wire. Dry thiophene-free benzene may be used instead but is less convenient because it freezes when added to the liquid ammonia solution.
4. Bromocyclohexane obtained from the Eastman Kodak Company was dried over calcium chloride and redistilled.
5. Another boiling point is 165–167°/9 mm.

3. Discussion

α -Cyclohexylphenylacetonitrile has been prepared by treating the sodium derivative obtained from benzyl cyanide and sodamide with bromocyclohexane in benzene,¹ in ether,² and in xylene.³

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 44
- Org. Syn. Coll. Vol. 4, 387
- Org. Syn. Coll. Vol. 4, 404
- Org. Syn. Coll. Vol. 4, 755

References and Notes

1. Venus-Danilova and Bol'shukon, *J. Gen. Chem. U.S.S.R.*, **7**, 2823 (1937) [*C. A.*, **32**, 2925 (1938)].
 2. Vasiliu, *Bul. Soc. Chim. România*, **19A**, 75 (1937) [*C. A.*, **33**, 4207 (1939)].
 3. Cheney and Bywater, *J. Am. Chem. Soc.*, **64**, 970 (1942).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sulfur-free toluene

calcium chloride (10043-52-4)

ammonia (7664-41-7)

Benzene (71-43-2)

ether (60-29-7)

toluene (108-88-3)

sodium,
sodium wire (13966-32-0)

Benzyl cyanide (140-29-4)

bromocyclohexane (108-85-0)

xylene (106-42-3)

Pentane (109-66-0)

sodamide (7782-92-5)

ferric nitrate

α -Cyclohexylphenylacetonitrile,
Cyclohexaneacetonitrile, α -phenyl- (3893-23-0)