



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.

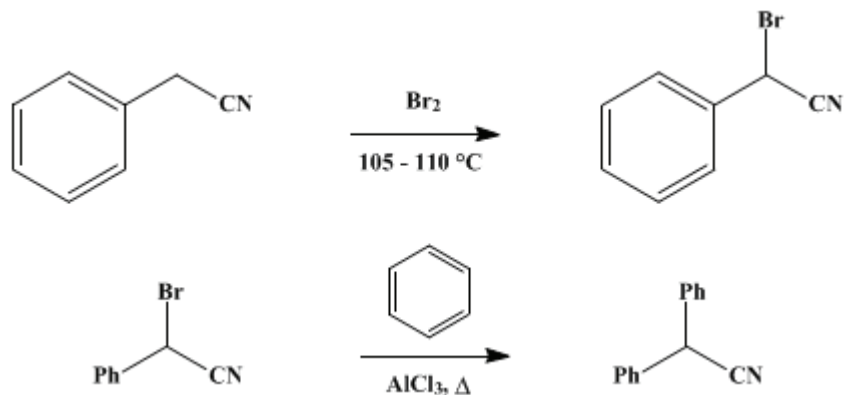
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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DIPHENYLACETONITRILE

[Acetonitrile, diphenyl-]



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1. Procedure

A. *α-Bromo-α-phenylacetone nitrile*. In a well-ventilated hood (Note 1), a dry 500-ml. round-bottomed three-necked flask is equipped with a sealed stirrer, an air condenser (Note 2), and a cork carrying a dropping funnel and a thermometer. In the flask is placed 117 g. (1 mole) of benzyl cyanide (Note 3). The thermometer is adjusted so that the bulb is immersed in the benzyl cyanide. The flask is placed in a bath and heated to 105–110° (inside temperature). With good stirring, 176 g. (1.1 moles) of bromine (Note 4) is added over a period of 1 hour; during the addition and for 15 minutes thereafter the temperature of the liquid is maintained at 105–110°. At the end of the heating period the evolution of hydrogen bromide gas has practically ceased. The dropping funnel is replaced by a cork carrying a glass tube reaching to within 2–3 cm. of the surface of the reaction mixture. Dry nitrogen is then led through the apparatus for 30 minutes. The hot mixture is poured into the 500-ml. addition funnel fitted to the apparatus to be used in the next step (see part B). The reaction flask is rinsed with 100 g. (1.3 moles) of dry benzene (Note 5), and this is added to the bromonitrile. The benzene solution thus obtained is used immediately in the next step (Note 6).

B. *Diphenylacetone nitrile*. A dry 2-l. round-bottomed three-necked flask, equipped with a sealed stirrer, a 500-ml. dropping funnel, and a dry reflux condenser (Note 2), is mounted on a steam bath. In the flask are placed 368 g. (4.7 moles) of dry benzene (Note 5) and 133.5 g. (1 mole) of powdered anhydrous aluminum chloride. The stirrer is started, and the benzene is heated to vigorous refluxing. The α-bromo-α-phenylacetone nitrile solution is added to the boiling mixture over a period of 2 hours in small portions (Note 7). After the addition is complete, the reaction mixture is refluxed for an additional hour. The flask is cooled, and the mixture is poured into a stirred mixture of 1 kg. of crushed ice and 100 ml. of concentrated hydrochloric acid in a 3-l. beaker.

The benzene layer is separated. The aqueous layer is extracted with 500 ml. of ether in two equal portions. The ether and benzene solutions are combined and washed successively with 500 ml. of water, 250 ml. of saturated sodium bicarbonate solution, and 500 ml. of water. The organic layer is dried over 100 g. of anhydrous sodium sulfate. The drying agent is separated from the solution, and the solvents are removed by heating on a steam bath. The last traces of benzene are removed by vacuum distillation from a 250-ml. Claisen flask heated on a steam bath. The residue weighs about 190 g. A receiver is connected directly to the side arm (Note 8) of the Claisen flask, and the product is distilled under reduced pressure. It boils at 122–125°/1–2 mm. and crystallizes to a yellow solid which melts at 68–70°. The solid is recrystallized from isopropyl alcohol (1 ml. per g.); the flask containing the filtered hot solution is placed on an asbestos mat, and the solution is allowed to cool only to room temperature

without shaking or stirring. The crystals are then collected and washed on the funnel with chilled [isopropyl alcohol](#) (one-fifth the volume used in the recrystallization). The product is dried in a vacuum desiccator over concentrated [sulfuric acid](#) or [phosphorus pentoxide](#). The yield of pure white product, melting at 74–75°, is 97–116 g. (50–60% based on [benzyl cyanide](#)) (Note 9).

2. Notes

1. [α-Bromo-α-phenylacetonitrile](#) is a lachrymator.
2. The mouth of the condenser is fitted with a cork carrying a short U-tube, to prevent condensed moisture from running back into the flask.
3. The [benzyl cyanide](#) used was a redistilled grade obtained from the Benzol Products Company.
4. Reagent grade [bromine](#) was used.
5. Reagent grade [benzene](#) was subjected to distillation until no droplets of water formed in the distillate. The residual [benzene](#) was used directly without further distillation or drying.
6. The checkers found that the work could be interrupted for as much as 1 day after the preparation of [α-bromo-α-phenylacetonitrile](#) without appreciable effect on the yield.
7. The reaction is vigorous, but it can be readily controlled by adding the [bromonitrile](#) frequently in small portions.
8. The flask must be of such a type that the side arm can be heated to prevent plugging by the solidified distillate.
9. A second crop, amounting to 10–15 g. and melting at 68–70°, can be obtained by chilling the mother liquor, but recrystallization of this fraction from [isopropyl alcohol](#) does not raise the melting point.

3. Discussion

[Diphenylacetonitrile](#) has been prepared by the dehydration of [diphenylacetamide](#),^{1,2,3,4,5,6,7,8,9} by the reaction of [diphenylbromomethane](#) and [mercuric cyanide](#),¹⁰ by the reaction of diphenylacetic acid and [lead thiocyanate](#),¹¹ by the removal of [ammonia](#) from [diphenylacetamide](#),¹² by phenylation of [potassium acetonitrile](#) with [chlorobenzene](#) in liquid [ammonia](#),¹³ by the action of [benzene](#) on [benzaldehyde cyanohydrin](#) in the presence of [aluminum chloride](#),¹⁴ and from [diphenylmethane](#) and [cyanogen chloride](#).¹⁵ The present method is a modification of that of Hoch.^{16,17}

References and Notes

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

isopropyl alcohol

diphenylacetic acid

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

ether (60-29-7)

sodium bicarbonate (144-55-8)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

chlorobenzene (108-90-7)

aluminum chloride (3495-54-3)

isopropyl alcohol (67-63-0)

Diphenylmethane (101-81-5)

Benzyl cyanide (140-29-4)

benzaldehyde cyanohydrin (532-28-5)

mercuric cyanide (592-04-1)

cyanogen chloride (506-77-4)

Diphenylacetonitrile,
Acetonitrile, diphenyl- (86-29-3)

bromonitrile

α -bromo- α -phenylacetonitrile (5798-79-8)

diphenylacetamide (519-87-9)

diphenylbromomethane (776-74-9)

diphenylacetamide

potassium acetonitrile

phosphorus pentoxide (1314-56-3)

lead thiocyanate