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.

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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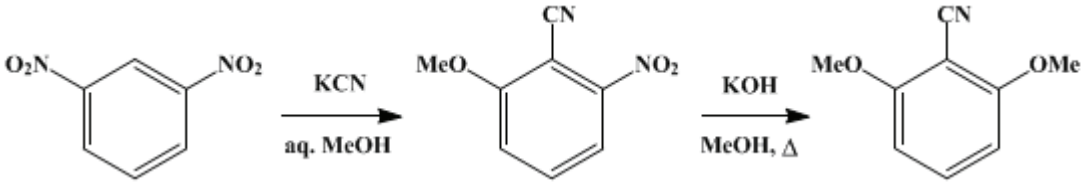
2,6-DIMETHOXYBENZONITRILE

[Benzonitrile, 2,6-dimethoxy-]



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1. Procedure

A. 2-*Nitro*-6-*methoxybenzonitrile*. Five hundred grams (2.97 moles) of technical *m*-dinitrobenzene (m.p. 88–89°) is dissolved in 7.5 l. of absolute methanol in a 12-l. round-bottomed flask fitted with an efficient mechanical stirrer. The temperature is raised to 40° by means of a water bath and maintained there while a solution of 230 g. of potassium cyanide in 400 ml. of water is added with stirring. The dark purple mixture is stirred for 2 hours and then is allowed to stand at room temperature for 2–3 days. The black precipitate is collected with suction on a Büchner funnel, pressed as dry as possible, and then spread out in the air to dry. It weighs about 185–188 g.

The filtrate is diluted with 60 l. of cold water (Note 1) and allowed to stand overnight. The brown sludge is filtered with suction (Note 2) and pressed as dry as possible on the funnel. After drying, it weighs about 164 g. The combined precipitates are refluxed for 30 minutes each with successive 650-, 500-, and 500-ml. portions of chloroform. The chloroform extracts are filtered while hot, and the bright red filtrates are combined and concentrated to a volume of 500 ml. by distillation. One liter of petroleum ether (b.p. 60–90°) is added, whereupon the crude 2-nitro-6-methoxybenzonitrile separates as a red powder. It is removed by filtration and air-dried. It weighs 120–125 g. (22–23%) and melts at 148–157° (Note 3). It is used without purification (Note 4).

B. 2,6-*Dimethoxybenzonitrile*. The crude nitrile is placed in a 3-l. flask and is refluxed for 2 hours with a solution of 75 g. of potassium hydroxide in 1.9 l. of methanol. The solution is concentrated by distillation to a volume of 400 ml. and then is poured into 4 l. of cold water. The brownish solid is filtered, washed thoroughly with cold water, and dried. The crude product (85–95 g.) is dissolved in 300 ml. of chloroform and refluxed with 8 g. of Darco for 30 minutes. The hot mixture is filtered, and 500 ml. of hot petroleum ether (b.p. 60–90°) is added to the filtrate. The solution is cooled, and the light-tan-colored needles of 2,6-dimethoxybenzonitrile are removed by filtration. The product weighs 75–86 g. (15–17%) and melts at 116–117° (Note 5).

2. Notes

1. The dilution is conveniently carried out by dividing the mixture among seven 3-gal. earthenware crocks.
2. The filtration can be performed by siphoning the mixture from the crocks through an 18.5 cm. Büchner funnel fitted to a 12-l. flask attached to a suction pump.
3. A fourth extraction with 500 ml. of chloroform gives only an additional 4 g. of product.
4. Dioxane is an excellent solvent for cleaning the flasks and crocks used in this first step.
5. This product is pure enough for most purposes. Pure white needles, melting at 117–118°, may be obtained by repeating the crystallization from the chloroform-petroleum ether mixture. The recovery is about 89–90%.

3. Discussion

The action of alcoholic potassium cyanide on *m*-dinitrobenzene was first studied by Lobry de Bruyn.[1] The present method is a modification of the procedure described by Mauthner.[2]

References and Notes

1. Lobry de Bruyn, *Rec. trav. chim.*, **2**, 205 (1883).
2. Mauthner, *J. prakt. Chem.*, (2) **121**, 259 (1929).

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

petroleum ether

chloroform-petroleum ether

alcoholic potassium cyanide

methanol (67-56-1)

chloroform (67-66-3)

potassium cyanide (151-50-8)

potassium hydroxide (1310-58-3)

dioxane (123-91-1)

2,6-Dimethoxybenzonitrile,
Benzonitrile, 2,6-dimethoxy- (16932-49-3)

2-Nitro-6-methoxybenzonitrile (38469-85-1)

m-dinitrobenzene (99-65-0)