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.

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.

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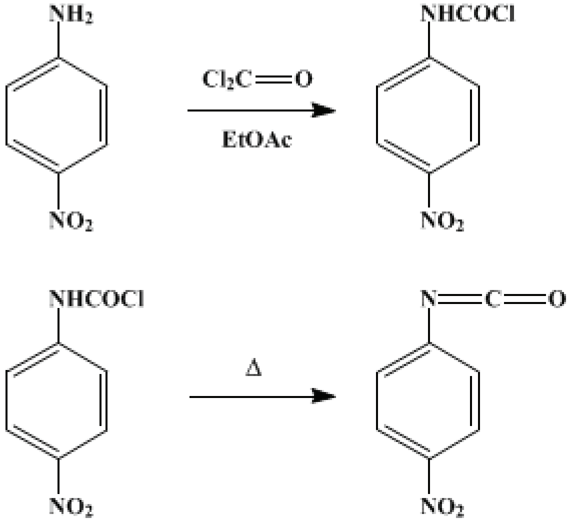
p-NITROPHENYL ISOCYANATE

[Isocyanic acid, *p*-nitrophenyl ester]



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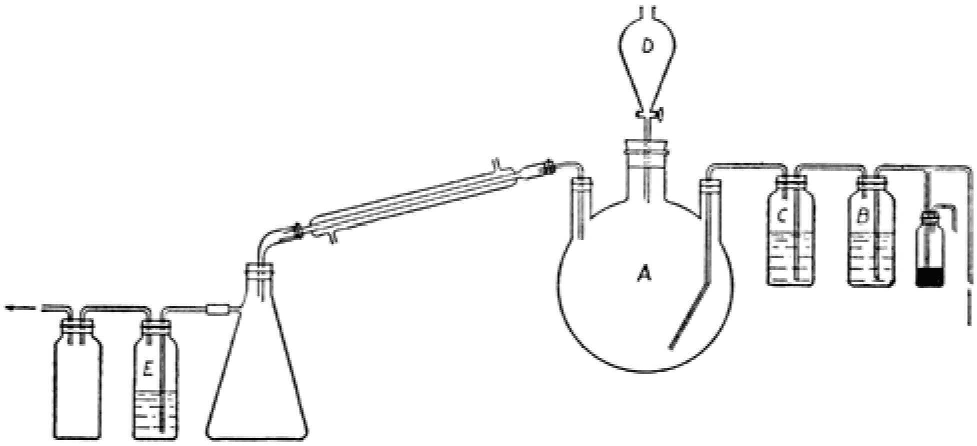
1. Procedure

The apparatus is shown in Fig. 16. Phosgene is introduced at one end of the apparatus, and gentle suction is applied at the other. In the 5-l. flask, A, 500 cc. of dry ethyl acetate (Note 1) is saturated with phosgene at room temperature. The phosgene is purified by bubbling it through cottonseed oil, B, to remove chlorine, and then through concentrated sulfuric acid, C, as shown in the figure (Note 2). A solution of 150 g. (1.09 moles) of *p*-nitroaniline in 1.5 l. of dry ethyl acetate is run in slowly from the separatory funnel, D, over a period of three to four hours. The addition of the *p*-nitroaniline solution must be at such a rate that the precipitate of *p*-nitroaniline hydrochloride that is formed at first is allowed to dissolve and not accumulate (Note 3). During this time a steady stream of phosgene is passed through the solution to ensure an excess (Note 4). Towards the end of the reaction, the solution must be boiled gently with a Bunsen flame to break up the lumps of *p*-nitroaniline hydrochloride which otherwise dissolve very slowly.

Fig. 16



After the addition of the last of the *p*-nitroaniline, the stream of phosgene is continued for five minutes and then shut off. The flame under the flask is then turned up and the ethyl acetate distilled. Care must be taken at the end not to overheat the residue. The brown residue (Note 5) is treated with 800 cc. of hot dry carbon tetrachloride, and the insoluble residue (the disubstituted urea) is removed by filtration.

About two-thirds of the carbon tetrachloride is distilled. The solution is cooled, and the crystals of *p*-nitrophenyl isocyanate are filtered as quickly as possible in order to avoid prolonged exposure of the compound to the moisture of the air. By concentration of the mother liquor a further crop is obtained. The product is recrystallized from dry carbon tetrachloride and is obtained in the form of light yellow needles melting at 56–57° (Note 6). The yield after one recrystallization is 152–170 g. (85–95 per cent of the theoretical amount) (Note 7).

2. Notes

1. The ethyl acetate, free from ethyl alcohol, is dried with anhydrous magnesium sulfate.
2. This arrangement permits the phosgene reaction to be carried out conveniently and without danger, provided that a good hood and an exhaust fan are available. A slight vacuum is maintained in the system. The excess phosgene is absorbed in 20 per cent sodium hydroxide solution, E.
Although phosgene can be shipped only in steel cylinders in the United States, in some other countries it is available in glass ampoules. If an ampoule of phosgene is used in this preparation, only one-third the weight of *p*-nitroaniline necessary to react with the phosgene should be taken. In this way an excess of phosgene is assured; compare (Note 4). Because of the danger involved, the use of glass ampoules of phosgene is not recommended.
3. The mixture may be warmed if necessary to dissolve the *p*-nitroaniline hydrochloride.
4. The excess of phosgene retards the following reaction: $p\text{-}NO_2C_6H_4NHCOCl + p\text{-}NO_2C_6H_4NH_2 \rightarrow p\text{-}NO_2C_6H_4NHCONHC_6H_4NO_2\text{-}p + HCl$
5. The crude residue is a mixture of *p*-nitroaniline hydrochloride, *p*-nitrophenyl carbamyl chloride, *p*-nitrophenyl isocyanate, and *p,p′*-dinitrodiphenylurea. The *p*-nitrophenyl carbamyl chloride is converted to *p*-nitrophenyl isocyanate during recrystallization from the hot carbon tetrachloride.
6. The freshly prepared material melts at 56–57° but after storage soon starts to melt at 54°, particularly if the bottle in which it is stored is opened occasionally. In contact with the moisture of the air, *p,p′*-dinitrodiphenylurea is formed (m.p. 360°). This reaction with water is avoided if the material is sealed in a glass container.
7. *p*-Nitrophenyl isocyanate distils undecomposed at 160–162°/18 mm.

3. Discussion

p-Nitrophenyl isocyanate has been prepared by heating *p*-nitrophenyl carbamyl chloride. The latter has been obtained by the action of phosgene on *p*-nitroaniline in benzene-toluene solutions,[1] and by the action of phosphorus pentachloride on methyl *p*-nitrophenylcarbamate.[2] The preparation given above is based upon directions published by the submitters.[3]

References and Notes

1. Vittenet, Bull. soc. chim. (3) **21**, 586 (1899); Van Hoogstraten, Rec. trav. chim. **51**, 418 (1932).
2. Swartz, Am. Chem. J. **19**, 318 (1897).
3. Shriner and Cox, J. Am. Chem. Soc. **53**, 1603 (1931); Horne and Shriner, ibid **53**, 3186 (1931).

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

ethyl alcohol (64-17-5)

sulfuric acid (7664-93-9)

Benzene (71-43-2)

ethyl acetate (141-78-6)

sodium hydroxide (1310-73-2)

phosphorus pentachloride (10026-13-8)

carbon tetrachloride (56-23-5)

chlorine (7782-50-5)

toluene (108-88-3)

phosgene (75-44-5)

magnesium sulfate (7487-88-9)

p-NITROPHENYL ISOCYANATE,
Isocyanic acid, p-nitrophenyl ester (100-28-7)

p-nitroaniline (100-01-6)

p-nitroaniline hydrochloride (15873-51-5)

p-nitrophenyl carbamyl chloride

p,p'-dinitrodiphenylurea

methyl p-nitrophenylcarbamate (1943-87-9)