



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.

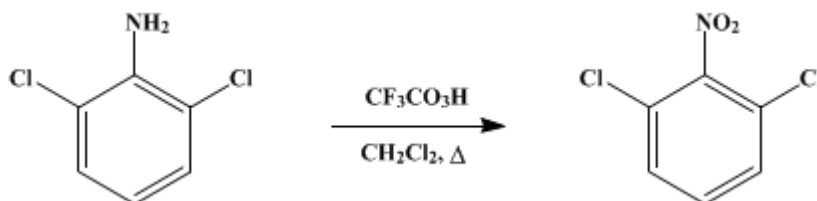
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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2,6-DICHLORONITROBENZENE

[Benzene, 1,3-dichloro-2-nitro-]



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1. Procedure

Caution! The preparation and handling of peroxytrifluoroacetic acid should be carried out behind a safety screen. Precautions to be observed with 90% hydrogen peroxide are described in (Note 3) and should be carefully followed.

A 300-ml. three-necked flask equipped with a Trubore stirrer, dropping funnel, and reflux condenser protected with a calcium chloride drying tube is charged with 100 ml. of methylene chloride (Note 1). To this solvent is added without stirring 5.4 ml. (0.20 mole) of 90% hydrogen peroxide (Note 2), (Note 3), (Note 4), (Note 5). The hydrogen peroxide is not miscible with the solvent and separates as the lower layer at the bottom of the flask. The flask is then cooled in an ice bath, and the stirrer is started. To this cold solution over a 20-minute period is added 34.0 ml. (0.24 mole) of trifluoroacetic anhydride. After addition is complete, the ice bath is removed and the solution is stirred at room temperature for 30 minutes.

A solution is then prepared from 8.1 g. (0.05 mole) of 2,6-dichloroaniline (Note 6) and 80 ml. of methylene chloride. This solution is added dropwise over a 30-minute period to the previously prepared peroxytrifluoroacetic acid reagent (Note 7). During this addition the exothermic reaction causes the mixture to reflux. After addition is complete, the mixture is heated under reflux for 1 hour. It is then cooled and poured into 150 ml. of cold water. The organic layer is separated, washed with 100 ml. of water, with two 100-ml. portions of 10% sodium carbonate solution (Note 8), and finally with 50 ml. of water. The organic extract is treated with activated charcoal and anhydrous magnesium sulfate. After standing overnight, the volatile solvent is removed at aspirator pressure with the aid of a warm water bath. There is obtained 8.6–8.8 g. (89–92%) of yellow 2,6-dichloronitrobenzene, m.p. 63–68°. The product is recrystallized from a minimum volume (12–15 ml.) of ethanol and washed on the filter with 10 ml. of cold ethanol to give 5.7–7.0 g. (59–73%) of a slightly off-white product, m.p. 69–70° (reported,² 70.5°).

2. Notes

1. Reagent grade methylene chloride was used without further purification.
2. Available from Becco Chemical Division, Food, Machinery and Chemical Co., Buffalo, New York.
3. The precautions to be observed with 90% hydrogen peroxide have been described in detail.³ In essence, it is important to prevent contact of this reagent with any easily oxidizable substrate such as wood, alcohols, and sugars and with heavy metal salts since these substances catalyze its decomposition. Storage of hydrogen peroxide in the laboratory should be arranged in such a way that, even if the bottle containing the reagent breaks, the hydrogen peroxide will not come into contact with any material of this kind. Small samples of 90% hydrogen peroxide are regularly shipped in vented glass bottles provided with a protective outside metal container, and it is desirable to use this container while storing the reagent in the laboratory. In the event that spillage of the reagent occurs, dilution with

at least several volumes of water is recommended. In weighing out 90% [hydrogen peroxide](#) it is good practice never to return excess reagent to the stock bottle; rather, it should be diluted with water and discarded to avoid any possibility that the stock bottle will be contaminated.

4. It is convenient to measure out the [hydrogen peroxide](#) by a 10-ml. graduate or by a 10-ml. pipet actuated by a glass syringe connected via a ground-glass joint.

5. The procedure described here for the preparation of [peroxytrifluoroacetic acid](#) in [methylene chloride](#) has been carried out by the submitters several hundred times without incident and is believed to be the best available. However, it has been pointed out that suspensions of 90% [hydrogen peroxide](#) in [methylene chloride](#) can be detonated by impact under certain conditions.⁴ Accordingly, the use of the recommended safety screen is imperative, and the preparation should not be scaled up without special precautions. The homogeneous solution of [peroxytrifluoroacetic acid](#), once obtained, is undoubtedly much safer to handle than the suspension of [hydrogen peroxide](#) in [methylene chloride](#). The latter suspension is not transferred, however, and exists for only a brief time period during the preparation.

6. Available from Aldrich Chemical Company, Inc.

7. Addition of the peracid solution to the aniline invariably resulted in a poor-quality product in low yield.

8. The [sodium carbonate](#) extracts are quite dark.

3. Discussion

[2,6-Dichloronitrobenzene](#) has been prepared by deamination of [3,5-dichloro-4-nitroaniline](#)² and of [2,4-dichloro-3-nitroaniline](#).⁵ This procedure is an example of the rather general oxidation of anilines to nitrobenzenes with [peroxytrifluoroacetic acid](#).^{6,7} Use of this reagent is frequently the method of choice for carrying out this transformation, and it is particularly suitable for oxidation of negatively substituted aromatic amines. Conversely, those aromatic amines, such as [p-anisidine](#) and [β-naphthylamine](#), whose aromatic nuclei are unusually sensitive to electrophilic attack give intractable mixtures with this reagent.⁶ This is not a serious limitation, however, and many of the nitrobenzenes which are available from this procedure have in the past required tedious multistep syntheses.

References and Notes

1. Rohm and Haas Company, Spring House, Pennsylvania.
2. C. B. Kremer and A. Bendich, *J. Am. Chem. Soc.*, **61**, 2658 (1939).
3. E. S. Shanley and F. P. Greenspan, *Ind. Eng. Chem.*, **39**, 1536 (1947).
4. J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 627 (1962).
5. G. Körner and A. Contardi, *Atti Accad. Nazl. Lincei*, **18**, **I**, 100 (1909).
6. W. D. Emmons, *J. Am. Chem. Soc.*, **76**, 3470 (1954).
7. L. I. Klmel'nitskii, T. S. Novikova, and S. S. Novikov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 516 (1962) [*Chem. Abstr.* **57**, 14979 (1962)].

Appendix

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

[ethanol](#) (64-17-5)

[sodium carbonate](#) (497-19-8)

[hydrogen peroxide](#) (7722-84-1)

[methylene chloride](#) (75-09-2)

magnesium sulfate (7487-88-9)

2,6-Dichloroaniline (608-31-1)

2,6-Dichloronitrobenzene,
Benzene, 1,3-dichloro-2-nitro- (601-88-7)

peroxytrifluoroacetic acid,
peroxytrifluoroacetic acid

β -naphthylamine (91-59-8)

trifluoroacetic anhydride (407-25-0)

3,5-dichloro-4-nitroaniline

2,4-dichloro-3-nitroaniline

p-anisidine (104-94-9)