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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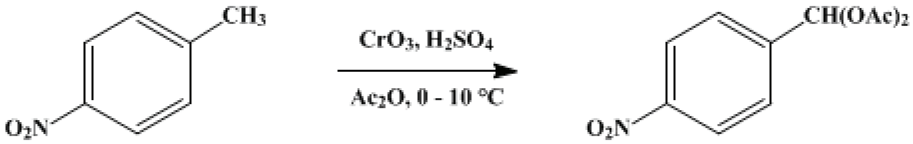
o- AND *p*-NITROBENZALDIACETATE

[Toluene-α,α-diol, *o*-nitro-, diacetate]

[Toluene-α,α-diol, *p*-nitro-, diacetate]



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1. Procedure

A. *p-Nitrobenzaldiacetate.* In a 2-l., three-necked flask provided with a mechanical stirrer, dropping funnel, and thermometer, surrounded by an ice-salt bath, are placed 400 ml. of acetic anhydride (Note 1) and 50 g. (0.36 mole) of *p*-nitrotoluene (Note 2). To this solution is added slowly, with stirring, 80 ml. of concentrated sulfuric acid. When the mixture has cooled to 0°, a solution of 100 g. (1.0 mole) of chromium trioxide (Note 3) in 450 ml. of acetic anhydride is added slowly, with stirring, at such a rate that the temperature does not exceed 10° (Note 4), and stirring is continued for 2 hours at 5–10° in an ice-water bath after the addition is complete. The contents of the flask are poured into two 3-l. beakers one-third filled with chipped ice, and water is added until the total volume is 5–6 l. The solid is separated by suction filtration and washed with water until the washings are colorless. The product is suspended in 300 ml. of 2% aqueous sodium carbonate solution and stirred. After thorough mixing, the solid is collected on a filter (Note 5), washed with water and finally with 20 ml. of ethanol. The product, after drying in a vacuum desiccator, weighs 60–61 g. (65–66% of the theoretical amount), m.p. 121–124° (Note 6).

B. *o-Nitrobenzaldiacetate*. *o*-Nitrotoluene (the fraction boiling at 217–219° of commercial product) is treated in a manner exactly similar to that for *p*-isomer, except that the reaction mixture is stirred mechanically for 3 hours at 5–10° after the addition of chromium trioxide is complete. Washing of the crude product with ethanol is omitted; instead, the crude product is heated under reflux with petroleum ether for 30 minutes. The product melts at 82–84° with preliminary softening. The yield is 33.6–34.5 g. (36–37%).

2. Notes

1. The industrial grade of acetic anhydride was used without further purification.
2. Commercial *p*-nitrotoluene (m.p. 53–54°) was used.
3. The chromium trioxide was of 97% purity. Cooling is necessary on dissolving chromium trioxide in acetic anhydride. *Caution! Addition of acetic anhydride to solid chromium trioxide has resulted in explosive decompositions. The trioxide should be added in small portions to the cooled anhydride.*
4. With a good ice-salt bath, the time required for the addition is 1.5–2.0 hours.
5. By acidification of the sodium carbonate washings, 2–4 g. of *p*-nitrobenzoic acid, m.p. 235–237°, is obtained.
6. A similar procedure may be used for the preparation of *p*-cyanobenzaldiacetate from *p*-tolunitrile. Information submitted by Rorig and Nicholson, of G. D. Searle and Company, indicates that the critical step in this preparation is to maintain the reaction temperature below 10° throughout the process. Exposure of *p*-cyanobenzaldiacetate to excess chromic, acetic, and sulfuric acids causes a reduction in yield. During the oxidation care should be taken to prevent chromium trioxide from adhering to the walls of the flask above the reaction mixture and then dropping in large amounts into the solution.

3. Discussion

These have been reviewed in an earlier volume.[2] *p*-Nitrobenzaldehyde has also been prepared in 32% yield by heating *p*-nitrobenzyl chloride with potassium *tert*-butylperoxide.[3] The preparation of *o*-nitrobenzaldiacetate has been described in an earlier volume.[4]

o- and *p*-Nitrobenzaldiacetate also have been obtained from the corresponding aldehydes by reaction with acetic anhydride in the presence of phosphoric acid.[5]

References and Notes

1. Kitasato Institute for Infectious Diseases, 138, Shiba-Shirokane-Sanko-cho, Minato-ku, Tokyo, Japan.
2. *Org. Syntheses Coll. Vol.* **2**, 441 (1943).
3. Campbell and Coppinger, *J. Am.. Chem. Soc.*, **73**, 1788 (1951); U. S. pat. 2,628,256 [*C. A.*, **48**, 724 (1954)].
4. *Org. Syntheses Coll. Vol.* **3**, 641 (1955).
5. Davey and Gwilt, *J. Chem. Soc.*, **1955**, 1384.

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

petroleum ether

o- and p-Nitrobenzaldiacetate

potassium tert-butylperoxide

ethanol (64-17-5)

sulfuric acid (7664-93-9)

acetic anhydride (108-24-7)

sodium carbonate (497-19-8)

phosphoric acid (7664-38-2)

o-nitrotoluene (88-72-2)

p-Tolunitrile (104-85-8)

chromium trioxide (1333-82-0)

p-Nitrobenzaldiacetate,
Toluene-α,α-diol, p-nitro-, diacetate (2929-91-1)

p-Nitrobenzaldehyde (555-16-8)

o-Nitrobenzaldiacetate,
Toluene-α,α-diol, o-nitro-, diacetate (6345-63-7)

p-NITROBENZOIC ACID (62-23-7)

p-nitrotoluene (99-99-0)

p-nitrobenzyl chloride (100-14-1)

p-cyanobenzaldiacetate