



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.

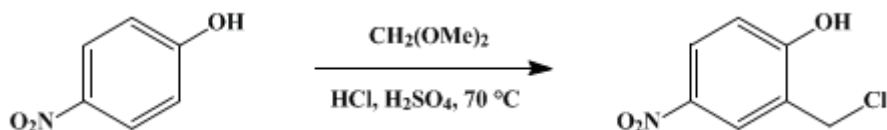
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.468 (1955); Vol. 20, p.59 (1940).

2-HYDROXY-5-NITROBENZYL CHLORIDE

[Toluene, α -chloro-2-hydroxy-5-nitro-]



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1. Procedure

In a 1-l. three-necked round-bottomed flask equipped with a mechanical stirrer, short reflux condenser, and bent glass tube reaching below the surface of the liquid for the introduction of hydrogen chloride, are placed 50 g. (0.36 mole) of *p*-nitrophenol (Note 1), 650 ml. of concentrated hydrochloric acid, 5 ml. of concentrated sulfuric acid (Note 2), and 76 g. (1 mole) of methylal (Note 3). The mixture is stirred while the temperature is maintained at $70 \pm 2^\circ$ for 4–5 hours by means of a water bath (Note 4). During this time hydrogen chloride is bubbled into the reaction mixture through the bent glass tube, and the excess gas is carried away through the reflux condenser to a hood or gas-absorption trap (Note 5).

The 2-hydroxy-5-nitrobenzyl chloride begins to separate as a solid about 1 hour after the beginning of the reaction. At the end the mixture is cooled in ice for 1 hour whereby more crystals separate, after which the acid liquors are either filtered or decanted from the crystals (Note 6). The 2-hydroxy-5-nitrobenzyl chloride is purified by recrystallization from 125 ml. of hot benzene (Note 7). The yield is 46 g. (69% based on *p*-nitrophenol) of a white product melting at $129\text{--}130^\circ$.

2. Notes

- Best results are obtained by using *p*-nitrophenol of a grade melting above 112° .
- The reaction will proceed in the absence of sulfuric acid, but in its presence a greater reaction velocity results.
- Methylal, used in excess, is prepared according to the method given by Houben.¹ Twelve hundred grams of methanol is added to 800 g. of anhydrous calcium chloride in a 5-l. round-bottomed flask equipped with a reflux condenser. Twenty-four grams of concentrated hydrochloric acid is added, and then, with cooling, 800 g. of technical 35–40% formaldehyde is slowly dropped in through a dropping funnel. The reaction is strongly exothermic, requiring about 2 hours for complete addition of the formaldehyde. When all the formaldehyde has been added, the mixture is heated with a Bunsen flame for a few minutes until the liquid boils vigorously. The methylal forms quickly as an upper layer and, after 6 hours' standing, is fractionally distilled, preferably using a Clarke and Rahrs column.² The $42\text{--}46^\circ$ fraction is sufficiently pure for use.
- Temperatures higher than 72° may result in the formation of oily-resinous material with a corresponding decrease in chloride. The reaction is nearly complete at the end of 4 hours, but additional time will result in a slightly increased yield.
- Rubber joints should be used sparingly as the hydrogen chloride causes an internal swelling of the rubber with subsequent blocking of the lines.
- The high acid concentration makes ordinary filtration difficult. By allowing the reaction mixture to stand in an ice bath for 1 hour, the solid clings together, and filtration with gentle suction or decantation can be used with ease.
- The solid material should be air-dried for several hours or, better, overnight to remove all water before recrystallizing from hot benzene. The chlorine atom is very labile and hydrolyzes easily to form 2-hydroxy-5-nitrobenzyl alcohol.

3. Discussion

2-Hydroxy-5-nitrobenzyl chloride can also be prepared from 2-hydroxy-5-nitrobenzyl alcohol by passing hydrogen chloride into an ethanolic solution at $70 \pm 2^\circ$ for 2 hours. In this case the yield of chloride is almost quantitative. The foregoing detailed procedure has been arrived at from that given in German Patent 132,475.³

References and Notes

1. Houben, *Die Methoden der organischen Chemie*, 3rd Ed., Vol. III, p. 193, Verlag Georg Thieme, Leipzig, 1930.
 2. Clarke and Rahrs, *Ind. Eng. Chem.*, **18**, 1092 (1926).
 3. *Frdl.*, **6**, 142 (1904).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrogen chloride,
hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methanol (67-56-1)

formaldehyde (50-00-0)

chlorine (7782-50-5)

methylal (109-87-5)

2-Hydroxy-5-nitrobenzyl chloride,
Toluene, α -chloro-2-hydroxy-5-nitro- (2973-19-5)

2-hydroxy-5-nitrobenzyl alcohol

p-nitrophenol (100-02-7)