



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](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.

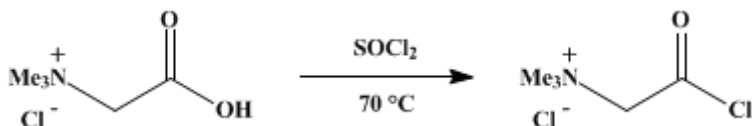
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 4, p.154 (1963); Vol. 35, p.28 (1955).*

## N-CHLOROBETAINYL CHLORIDE

[Ammonium chloride, [(chloroformyl)methyl]trimethyl-]



Submitted by B. Vassel and W. G. Skelly<sup>1</sup>.

Checked by John C. Sheehan and J. Iannicelli.

### 1. Procedure

*Caution! This preparation should be conducted in a good hood.*

A 1-l. round-bottomed flask is equipped with an internal thermometer, a sealed stirrer, and a reflux condenser, the upper end of which is protected with a calcium chloride drying tube. In this flask are placed 307 g. (2 moles) of dry, pulverized [betaine hydrochloride](#) ([Note 1](#)) and 285 g. (174 ml., 2.4 moles) of [thionyl chloride](#). The mixture is stirred and heated slowly. When the internal temperature reaches 68° copious evolution of [sulfur dioxide](#) and [hydrogen chloride](#) occurs, and the mass becomes pasty. The temperature is maintained with stirring at 68–70° for 1.5 hours ([Note 2](#)).

Warm (80°) dry [toluene](#) (150 ml.) is added to the melt, and stirring is continued for 5 minutes. The entire mass is quickly poured into a dry beaker ([Note 3](#)) and slowly stirred, manually, until the entire mass has crystallized ([Note 4](#)). The cool [toluene](#) is decanted rapidly, and 150 ml. of warm [toluene](#) is added. The mixture is heated sufficiently to melt the crystals (about 68°), then allowed to cool again with stirring. The [toluene](#) is decanted once more, and 150 ml. of hot (60°) dry [benzene](#) is added. The mass is melted once more and cooled with stirring. The crystalline mass, with the [benzene](#) layer still covering it, is transferred rapidly to a Büchner funnel sufficiently large to hold all the contents of the beaker. The funnel is immediately covered with a rubber diaphragm, and suction is applied ([Note 5](#)). The crystals are quickly covered with 150 ml. of dry [methylene chloride](#), dried with suction, and quickly transferred into a glass vacuum oven at 50° ([Note 6](#)). The yield of N-chlorobetainyl chloride is 337–344 g. (98–100%) of 98–100% purity if moisture was rigorously excluded ([Note 7](#)).

### 2. Notes

1. The [betaine hydrochloride](#) was obtained from International Minerals and Chemical Corporation. It was pulverized, dried at 105° for 3 hours, ground again, and dried once more at 105° for 3 hours.
2. The mixture should be fluid after about the first 20 minutes of heating. If at this stage the [betaine hydrochloride](#) has not completely lost its granular appearance it is probable that it had not been adequately dried or that the reaction temperature had been below 68°. If it is considered that the [betaine hydrochloride](#) had not been dry enough the reaction may be completed by adding an additional 41 g. (25 ml., 0.34 mole) of [thionyl chloride](#) and continuing the stirring and heating for 1.25 hours.
3. Success in the isolation of the pure acid chloride depends upon the rigorous exclusion of moisture. The acid chloride hydrolyzes to the hydrochloride with great rapidity when exposed to even traces of moist air. During the stirring of the warm melt, care must be exercised that a layer of [toluene](#) covers the melt at all times.
4. If the melt is permitted to crystallize without stirring, a hard glasslike layer forms which cannot be broken up without exposure to air.
5. The rubber diaphragm is sold by Fisher Scientific Company as dental dam. It is held in place by two strong rubber bands. The suction flask is protected from moisture by attachment of a calcium chloride drying tube to the vacuum line if a water aspirator is used.
6. The dried acid chloride is conveniently stored in about 25 bottles with tightly fitting plastic screw

caps which are kept in a desiccator over [phosphorus pentoxide](#). In this manner the acid chloride is exposed to a minimum of atmospheric moisture when reactions are run which require only part of the preparation.

7. The same yield and purity were obtained when 1229 g. (8 moles) of [betaine hydrochloride](#) was used. In this case the volumes of [toluene](#), [benzene](#), and [methylene chloride](#) do not have to be increased proportionally if narrow, tall beakers are used. About 300 ml. of each is sufficient.

### 3. Discussion

N-Chlorobetainyl chloride has been prepared by treating [betaine hydrochloride](#) with either [thionyl chloride](#),<sup>2</sup> [phosphorus pentachloride](#) in [acetyl chloride](#),<sup>3,4</sup> or [phosphorus pentachloride](#) in [phosphorus oxychloride](#).<sup>5</sup> None of the patents mentions the instability of the acid chloride towards moisture or describes a method for the isolation of the pure product.

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### References and Notes

1. Central Research Laboratories, International Minerals and Chemical Corporation, Skokie, Illinois.
  2. Linch, U. S. pats. 2,359,862; 2,359,863 [*C. A.*, **39**, 2076, 2077 (1945)]; Byrne, U. S. pat. 2,888,383 [*C. A.*, **53**, 15492 (1959)].
  3. Society of Chemical Industry of Basel, Brit. pats. 589,232; 590,727 [*C. A.*, **42**, 230, 210 (1948)].
  4. Ruzicka and Plattner, U. S. pat. 2,429,171 [*C. A.*, **42**, 930 (1948)].
  5. Plattner and Geiger, *Helv. Chim. Acta*, **28**, 1362 (1945).
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### Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

N-Chlorobetainyl chloride

[hydrogen chloride](#) (7647-01-0)

[Benzene](#) (71-43-2)

[phosphorus pentachloride](#) (10026-13-8)

[acetyl chloride](#) (75-36-5)

[thionyl chloride](#) (7719-09-7)

[sulfur dioxide](#) (7446-09-5)

[Phosphorus Oxychloride](#) (21295-50-1)

[toluene](#) (108-88-3)

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

[Ammonium chloride, \[\(chloroformyl\)methyl\]trimethyl-](#) (53684-57-4)

betaine hydrochloride

phosphorus pentoxide (1314-56-3)

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