



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.

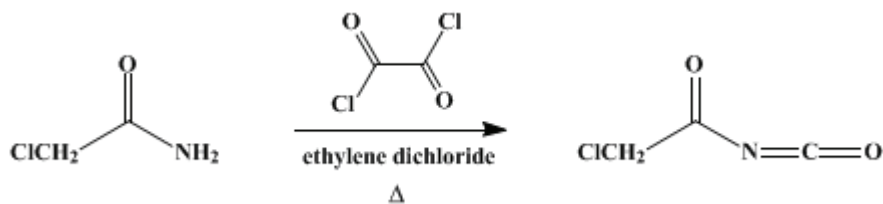
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## **$\alpha$ -CHLOROACETYL ISOCYANATE**

[Isocyanic acid, anhydride with chloroacetic acid]



Submitted by A. John Speziale and Lowell R. Smith<sup>1</sup>.

Checked by Leif A. Hoffmann and V. Boekelheide.

### 1. Procedure

In a 250-ml. round-bottomed flask fitted with a magnetic stirrer (Note 1), a thermometer, and a condenser carrying a calcium chloride tube (Note 2) are placed 46.7 g. (0.5 mole) of  $\alpha$ -chloroacetamide (Note 3) and 100 ml. of ethylene dichloride. The mixture is chilled in an ice bath to about 2° and stirred while 76.2 g. (0.6 mole) of oxalyl chloride (Note 4) is added all at once. The mixture is removed from the ice bath, stirred for 1 hour, and then heated to reflux at 83° with stirring for 5 hours (Note 5). The solution is chilled in an ice bath to 0–10°, the condenser is replaced by a 120-mm. distillation column packed with glass helices, and the solvent is removed at 70 mm. pressure with stirring. The ice bath is removed after the solvent boils without foaming and is replaced by a heating mantle or oil bath. Distillation gives 39 g. (65%) of  $\alpha$ -chloroacetyl isocyanate, b.p. 68–70° (70 mm.), as a colorless oil,  $n_D^{25}$  1.4565.

### 2. Notes

1. For larger-scale preparations mechanical stirring is recommended.
2. Moisture must be rigorously excluded from the reaction mixture and the product.
3. The  $\alpha$ -chloroacetamide was obtained from Eastman Kodak Co. and used without purification.
4. The oxalyl chloride was obtained from Aldrich Chemical Co. and used without purification. Oxalyl chloride vapor is irritating and toxic, and therefore manipulations must be carried out in a hood.
5. Because a large amount of hydrogen chloride is evolved, the reaction must be carried out in a hood.

### 3. Discussion

The only preparation reported for  $\alpha$ -chloroacetyl isocyanate is that described by the submitters.<sup>2</sup>

### 4. Merits of the Preparation

The procedure may be adapted for the preparation of other acyl isocyanates (*i.e.*, dichloroacetyl, trichloroacetyl, phenylacetyl, diphenylacetyl, benzoyl, etc.) and is generally more convenient than the reaction of acid chlorides with silver cyanate.<sup>3 4</sup> Acyl isocyanates react with amines, alcohols, and mercaptans to yield acyl ureas, carbamates, and thiocarbamates, and have been shown to undergo a variety of interesting reactions.<sup>5</sup>

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### References and Notes

1. Research Department, Agricultural Division, Monsanto Company, St. Louis 66, Missouri.
2. A. J. Speziale and L. R. Smith, *J. Org. Chem.*, **27**, 3742 (1962); **28**, 1805 (1963).
3. O. C. Billeter, *Ber.*, **36**, 3213 (1903).

4. A. J. Hill and W. M. Degnan, *J. Am. Chem. Soc.*, **62**, 1595 (1940).
  5. L. R. Smith, A. J. Speziale, and J. E. Fedder, *J. Org. Chem.*, **34**, 633 (1969).
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

Isocyanic acid, anhydride with chloroacetic acid

hydrogen chloride (7647-01-0)

ethylene dichloride (107-06-2)

$\alpha$ -chloroacetamide (79-07-2)

oxalyl chloride (79-37-8)

$\alpha$ -Chloroacetyl isocyanate (4461-30-7)

silver cyanate (3315-16-0)

dichloroacetyl isocyanate

trichloroacetyl isocyanate

phenylacetyl isocyanate

diphenylacetyl isocyanate

benzoyl isocyanate