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.

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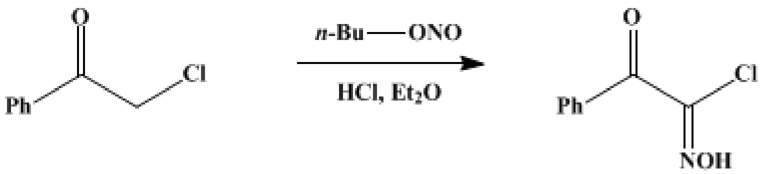
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.024.0025

Organic Syntheses, Coll. Vol. 3, p.191 (1955); Vol. 24, p.25 (1944).

ω-CHLOROISONITROSOACETOPHENONE

[Glyoxylyl chloride, phenyl-, oxime]



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1. Procedure

A 500-ml. three-necked round-bottomed flask is provided with a small dropping funnel, a sealed mechanical stirrer, a reflux condenser connected to a gas-absorption trap, and a hydrogen chloride delivery tube which extends to the bottom of the flask.

In the reaction flask are placed 15.4 g. (0.1 mole) of phenacyl chloride (Note 1) and 100 ml. of dry ether. The stirrer is started, and, after the solid has dissolved, anhydrous hydrogen chloride (Note 2) is introduced at the rate of 2–3 bubbles per second. Ten and three-tenths grams (11.8 ml., 0.1 mole) of freshly distilled *n*-butyl nitrite[1] (Note 3) is then admitted from the dropping funnel in 0.5- to 1-ml. portions. After addition of the first portion of nitrite the reaction mixture becomes orange-brown, and after several minutes, light yellow; at this point a second portion of nitrite is added and a similar color change takes place, whereupon a third portion is added; further additions are made until all the butyl nitrite has been added. The reaction mixture warms up, and the ether begins to reflux gently (Note 4). After all the nitrite has been added (about 30 minutes is required), stirring and addition of hydrogen chloride are continued an additional 15 minutes. At this point, the solution will have practically ceased boiling and will have assumed an orange color.

The reaction mixture is allowed to stand for 1–2 hours (or overnight, if more convenient); after this interval the solution will have assumed a clear, pale yellow color. The condenser is then set for downward distillation, stirring is resumed, and the solvent is removed by distillation from a steam bath (Note 5). After nearly all the ether has been removed, the distillation is continued under reduced pressure (40–50 mm.) until no further appearance of crystals is noted. The residue, which consists of yellow crystals of the crude product, is then allowed to stand until dry in a vacuum desiccator which contains concentrated sulfuric acid, soda lime, and anhydrous calcium chloride (Note 6).

The dried product is then recrystallized from 30–35 ml. of a 1:3 mixture of boiling benzene and carbon tetrachloride (Note 7). The yield of snow-white crystals is 15–15.7 g. (82–86%); the recrystallized product melts at 131–132° and is sufficiently pure for synthetic purposes. A second recrystallization gives a product which melts at 132–133° (Note 8) and (Note 9).

2. Notes

1. Commercial phenacyl chloride may be used; if unavailable the chloride may be prepared in 85–88% yield by a Friedel-Crafts reaction, using 234 g. (265 ml., 3 moles) of dry benzene and 79.5 g. (53 ml., 0.70 mole) of chloroacetyl chloride, in the presence of 103 g. (0.77 mole) of powdered anhydrous aluminum chloride; the product distils at 120–125°/4 mm. and melts at 56–57°. *Phenacyl chloride is a strong lachrymator and vesicant; it should be handled with care.*
2. Hydrogen chloride is now available in cylinders.
3. Any alkyl nitrite may be employed. The submitters preferred the use of isopropyl nitrite, since the low boiling point of the isopropyl alcohol formed facilitates its removal.
Isopropyl nitrite may be prepared according to the procedure given for *n*-butyl nitrite.[1]

A mixture of 147 g. (80 ml., 1.5 moles) of concentrated sulfuric acid (sp. gr. 1.84), 60 ml. of water, and 180 g. (230 ml., 3 moles) of 97% isopropyl alcohol, previously cooled to 0°, is added to a solution of 227.7 g. (3.3 moles) of 97% sodium nitrite in 1 l. of water, cooled to −5°. About 2 hours is required for the addition of the alcohol solution, during which time the temperature of the reaction mixture is maintained at −2° to 0°. The product may be isolated and purified as described under butyl nitrite. After drying over 15–20 g. of anhydrous sodium sulfate, the nitrite is distilled from a steam bath using a 20-cm. column. Practically all the isopropyl nitrite distils at 39–40°/745 mm. as a pale yellow oil; the yield of product is 191 g. (71.4%). Isopropyl nitrite, when stored in a refrigerator, has been found to be much more stable than butyl nitrite.

The checkers used commercially available *n*-butyl nitrite and experienced no difficulty in removing the *n*-butyl alcohol.

4. The rate of stirring must be kept fairly constant since an abrupt increase in speed may cause the ether to reflux at an undesirably rapid rate. The rate of addition of the nitrite is also governed by the rate of the refluxing.
5. The recovered ether may be employed without purification as the solvent in a subsequent run.
6. ω-Chloroisonitrosoacetophenone is extremely soluble in butanol, hence the alcohol should be removed as completely as possible before the crude product is recrystallized.
7. This is most conveniently done by dissolving the chloride in the benzene and then diluting.
8. This procedure works equally well in 0.5-mole runs.
9. This procedure, with minor changes, may be applied to various nuclear-substituted phenacyl chlorides. The yields vary from 74% to 92%.[2,3]

3. Discussion

The above procedure[2] is modeled after that described for the nitrosation of arylethyl ketones.[4,5] ω-Chloroisonitrosoacetophenone has been prepared by the chlorination of isonitrosoacetophenone;[6,7,8] by treating the ammonium salt of ω-nitroacetophenone with anhydrous hydrogen chloride,[9] or by refluxing ω-nitroacetophenone with dilute alcoholic hydrogen chloride;[10] and by the nitrosochlorination of acetophenone with nitrosyl chloride.[11] The isolation of small quantities of ω-chloroisonitrosoacetophenone from the reaction product obtained by nitrosating acetophenone in the presence of hydrogen chloride has been reported.[12,13]

References and Notes

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

soda lime

ammonium salt of ω-nitroacetophenone

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

sodium nitrite (7632-00-0)

butanol,
n-butyl alcohol (71-36-3)

Acetophenone (98-86-2)

aluminum chloride (3495-54-3)

isopropyl alcohol (67-63-0)

chloroacetyl chloride (79-04-9)

Butyl nitrite,
n-butyl nitrite (544-16-1)

nitrosyl chloride (2696-92-6)

isonitrosoacetophenone

ω-Chloroisonitrosoacetophenone (4937-87-5)

Glyoxylyl chloride, phenyl-, oxime

phenacyl chloride (532-27-4)

isopropyl nitrite (541-42-4)

ω-nitroacetophenone (614-21-1)