



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. 2, p.363 (1943); Vol. 16, p.44 (1936).

ISONITROSOPROPIOPHENONE

[1,2-Propanedione, 1-phenyl-, 2-oxime]



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1. Procedure

A 3-l. three-necked, round-bottomed flask (A, Fig. 11) is provided with a reflux condenser, liquid-sealed mechanical stirrer, and two gas delivery tubes (T_1 and T_2) which extend as far as possible into the flask. Methyl nitrite is generated in a 2-l. Erlenmeyer flask B which is fitted with a 500-cc. dropping funnel C and connected to A by the tube T_1 . Dry hydrogen chloride is introduced through T_2 . The apparatus is assembled preferably in a hood with effective draft.

Fig. 11

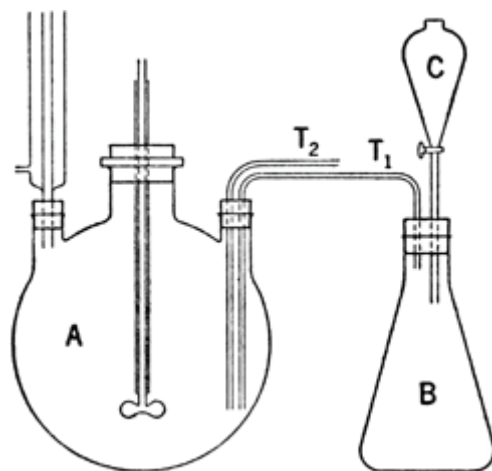


FIG. 11.

In A is placed a solution of 469 g. (3.5 moles) of propiophenone (Note 1) in 2.3 l. of ordinary ethyl ether, and in B a mixture of 290 g. (4 moles) of 95 per cent sodium nitrite, 180 cc. (142 g., 4.5 moles) of methyl alcohol, and 170 cc. of water. In the dropping funnel C is placed 455 cc. of cold dilute sulfuric acid (prepared by adding one volume of concentrated acid to two volumes of water).

The stirrer is started, and hydrogen chloride is introduced through T_2 at the rate of 6–10 bubbles a second. The acid in C is allowed to drop slowly into B, and the gaseous methyl nitrite (Note 2) is introduced through T_1 into the reaction mixture. The solution in A develops a brown-red color, and after about ten minutes the ether begins to reflux gently (Note 3). The rate of evolution of methyl nitrite is then adjusted so that the ether continues to reflux gently. About four hours is required for addition of the methyl nitrite. Stirring and addition of hydrogen chloride are continued for thirty minutes longer; at the end of this time the solution has ceased boiling and has assumed a clear yellow color.

The reaction mixture is allowed to stand for several hours (preferably overnight) and is then extracted repeatedly with 500-cc. portions of 10 per cent sodium hydroxide solution, until the alkaline extracting medium remains practically colorless when shaken with the ethereal solution (Note 4).

Usually five 500-cc. portions of the [sodium hydroxide](#) solution are required. The combined alkaline extracts are poured slowly, with stirring, into a mixture of 700–750 cc. of concentrated [hydrochloric acid](#) and about 1 kg. of ice. The crystals of [isonitrosopropiophenone](#) are filtered with suction and dried. The product weighs 370–390 g. (65–68 per cent of the theoretical amount) and melts at 111–113°. This material can be crystallized from about 550 cc. of [toluene](#) and yields 315–335 g. of snow-white crystals, m.p. 112–113° ([Note 5](#)).

2. Notes

1. [Propiophenone](#) may be prepared in 70–80 per cent yields from [benzene](#) and [propionyl chloride](#) or [propionic anhydride](#), in the presence of [aluminum chloride](#).
2. For the preparation of small amounts of the isonitrosoketone it is more convenient to employ a higher-boiling alkyl nitrite, such as [butyl nitrite](#) ([p. 108](#)), which can be added directly to the reaction mixture by substituting a dropping funnel for the tube T₁. [Butyl nitrite](#) must be freshly prepared or redistilled shortly before use.
3. The rate of stirring must be kept fairly constant since an abrupt increase in speed may cause the [ether](#) to boil at a dangerous rate.
4. The ethereal solution remaining from the alkaline extractions contains unreacted [propiophenone](#) which may be recovered by distilling the [ether](#) and fractionating the residue. The amount of recovered [propiophenone](#), collected at 210–216°, varies from 80 to 110 g.
5. About 25–30 g. of material may be recovered from the [toluene](#) mother liquor by extraction with alkali and reprecipitation with acid.

3. Discussion

[Isonitrosopropiophenone](#) has been prepared from esters of α -[benzoylpropionic acid](#) by a process involving saponification, nitrosation, and decarboxylation;¹ from [1-phenyl-1,2-propanedione](#) by the action of [hydroxylamine](#);² and from [propiophenone](#) by treatment with [amyl nitrite](#),³ [methyl nitrite](#),⁴ or [butyl nitrite](#).⁵

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 20](#)
- [Org. Syn. Coll. Vol. 3, 191](#)
- [Org. Syn. Coll. Vol. 3, 853](#)
- [Org. Syn. Coll. Vol. 6, 199](#)

References and Notes

1. v. Pechmann and Müller, *Ber.* **21**, 2119 (1888).
2. Kolb, *Ann.* **291**, 292 (1896).
3. Claisen and Manasse, *Ber.* **22**, 529 (1889).
4. Slater, *J. Chem. Soc.* **117**, 590 (1920).
5. Hartung and Munch, *J. Am. Chem. Soc.* **51**, 2264 (1929).

Appendix

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

[sulfuric acid](#) (7664-93-9)

[hydrogen chloride](#),

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methyl alcohol (67-56-1)

ether,
ethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium nitrite (7632-00-0)

aluminum chloride (3495-54-3)

toluene (108-88-3)

Butyl nitrite (544-16-1)

amyl nitrite (463-04-7)

hydroxylamine (7803-49-8)

methyl nitrite (624-91-9)

Propiophenone (93-55-0)

α -benzoylpropionic acid (2051-95-8)

ISONITROSOPROPIOPHENONE

1,2-Propanedione, 1-phenyl-, 2-oxime (119-51-7)

propionyl chloride (79-03-8)

propionic anhydride (123-62-6)

1-phenyl-1,2-propanedione (579-07-7)