



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.

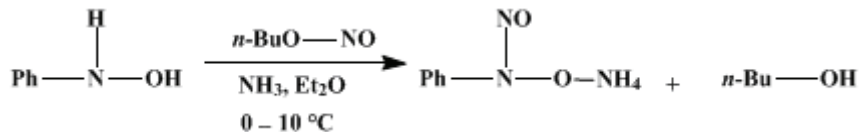
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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. 1, p.177 (1941); Vol. 4, p.19 (1925).

CUPFERRON



Submitted by C. S. Marvel
Checked by Oliver Kamm

1. Procedure

The moist [phenylhydroxylamine](#) obtained from 1 kg. (8.1 moles) of [nitrobenzene](#), by the procedure described on [p. 445](#), is weighed and dissolved in 4.5 l. of ordinary [ether](#) ([Note 1](#)). The ether-insoluble material ([sodium chloride](#) and water) is also weighed, the difference between the two weighings being a fairly accurate measure of the amount of [phenylhydroxylamine](#) in solution.

The [ether](#) solution is filtered through a dry filter paper into a 5-l. round-bottomed flask which is fitted with an efficient mechanical stirrer and immersed in an ice-salt bath. When the temperature of the solution has fallen to 0° ([Note 2](#)), a rapid stream of dry [ammonia](#), from a cylinder of the compressed gas, is passed into the solution.

After about fifteen minutes, the theoretical amount of freshly distilled [n-butyl nitrite](#) (95 g. for every 100 g. of [phenylhydroxylamine](#)) is added slowly through a dropping funnel ([Note 3](#)) and ([Note 4](#)). The addition of [butyl nitrite](#) usually requires about one hour ([Note 5](#)), during which time the stream of [ammonia](#) gas is continued in order that [ammonia](#) may always be in excess. If this precaution is not observed, a colored product will result. The temperature of the reaction mixture should be maintained below 10° and this may be done best by controlling the rate at which the [butyl nitrite](#) is added ([Note 6](#)). An appreciable rise in temperature will cause the volatilization of considerable quantities of [ether](#) and of [ammonia](#) ([Note 7](#)).

After the [butyl nitrite](#) has been added, the reaction mixture is stirred for about ten minutes longer in order to insure completion of the reaction, after which the [cupferron](#) is filtered off and washed several times with small portions of fresh [ether](#). The product is spread on sheets of paper until all traces of [ether](#) have been lost, and is then stored in bottles where it is exposed to the vapors of [ammonium carbonate](#). This may be done by protecting each cork with a double sheet of filter paper and placing a lump of [ammonium carbonate](#) between the cork and the filter paper ([Note 8](#)).

The yield of [cupferron](#) based on a given weight of [phenylhydroxylamine](#) averages 85–90 per cent of the theoretical amount.

2. Notes

1. The solvent [ether](#) may be replaced by [benzene](#), but this modification offers no advantages for the preparation of [cupferron](#) on a laboratory scale.
2. The temperature must be kept low. If it is not, the material is generally colored brown and the reaction does not run smoothly. Probably the most important factor in securing successful results is always to have an excess of [ammonia](#) present.
3. The [butyl nitrite](#) is freshly distilled as a general precaution, because a product which has stood for some time is often partially decomposed.
4. It is suggested that gaseous [ethyl nitrite](#) be passed in until the precipitate ceases to increase (W. W. Hartman, private communication). However, it is probable that [butyl nitrite](#) is more convenient for a laboratory method. A method for the preparation of [ethyl nitrite](#) is described in *Org. Syn.* **10**, 22.
5. In the preparation of [cupferron](#), it has been recommended that the [butyl nitrite](#) be added all at one time. This procedure is satisfactory only when the amount of [phenylhydroxylamine](#) used is less than 200 g.; otherwise the reaction becomes extremely vigorous and an excessive proportion of [ether](#) is lost. The

directions given above, on the other hand, are adaptable for the preparation of large quantities of [cupferron](#). For the rapid preparation of small quantities of material, the [butyl nitrite](#) may be added all at one time, provided sufficient excess of [ammonia](#) is present.

6. If [ammonia](#) is kept in a definite excess at all times, a rise of temperature to the boiling point of [ether](#) appears to do no harm. The lower temperature was used because it makes possible a more rapid addition of the [nitrite](#).

7. It is found that 75 per cent of the [ether](#) and 95 per cent of the [butyl alcohol](#) used may be recovered, and that one person, working six to seven hours, is able to prepare 800 g. of [cupferron](#). The recovered ether may be used over again, provided the following procedure is observed: The [phenylhydroxylamine](#) is dissolved in a little fresh ether, the solution cooled and treated with [ammonia](#), then the recovered ether added. This precaution is necessary owing to the presence of some [butyl nitrite](#) in the recovered ether.

8. The addition of a small quantity of [acetophenetidide](#) to a solution of [cupferron](#) reagent tends to prevent its decomposition.¹

[Cupferron](#) has been kept in dark bottles sealed with viscose caps for a year without decomposition.

3. Discussion

Nitroso- β -phenylhydroxylamine, of which [cupferron](#) is the ammonium salt, can be prepared by the action of [sodium nitrite](#) and [hydrochloric acid](#) on β -phenylhydroxylamine,² from a mixture of alkyl nitrite and β -phenylhydroxylamine in the presence of [ammonia](#) in [ether](#) or [benzene](#) solution,³ and by the zinc dust reduction of [nitrobenzene](#) in the presence of [amyl nitrite](#) and [ammonium hydroxide](#) solution.⁴

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 445](#)

References and Notes

1. Germuth, *Chemist-Analyst*, **17**, No. 3, 3; 15 (1928) [*C. A.* **22**, 3372 (1928)].
2. Wohl, *Ber.* **27**, 1435, 1554 (1894); Bamberger and Landau, *Ber.* **52**, 1839 (1919); Marvel and Kamm, *J. Am. Chem. Soc.* **41**, 280 (1919).
3. Baudisch, *Chem. Ztg.* **35**, 913 (1911); Baudisch and King, *J. Ind. Eng. Chem.* **3**, 629 (1911); Kasanof, *ibid.* **12**, 799 (1920); Marvel and Kamm, *J. Am. Chem. Soc.* **41**, 280 (1919); Slotta and Jacobi, *Z. anal. Chem.* **80**, 97 (1930); This last method, using ethyl nitrite, is promising but has not been checked completely.
4. Baudisch, *Ger. pat.* 227, 659 [*Frdl.* **10**, 126 (1910–12)].

Appendix

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

Nitroso- β -phenylhydroxylamine

ammonium salt

β -Phenylhydroxylamine

[hydrochloric acid](#) (7647-01-0)

[ammonium carbonate](#) (506-87-6)

ammonia (7664-41-7)
Benzene (71-43-2)
ether (60-29-7)
sodium chloride (7647-14-5)
sodium nitrite (7632-00-0)
nitrite (14797-65-0)
butyl alcohol (71-36-3)
Nitrobenzene (98-95-3)
Cupferron (135-20-6)
Phenylhydroxylamine (100-65-2)
Butyl nitrite,
n-butyl nitrite (544-16-1)
ethyl nitrite (109-95-5)
acetophenetidide (62-44-2)
amyl nitrite (463-04-7)
ammonium hydroxide (1336-21-6)