Organic Syntheses

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.

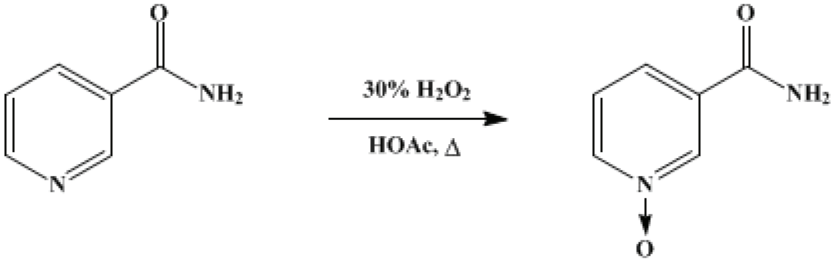
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries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

DOI:10.15227/orgsyn.037.0063

*Organic Syntheses, Coll. Vol. 4, p.704 (1963); Vol. 37, p.63 (1957).*

# NICOTINAMIDE-1-OXIDE



Submitted by E. C. Taylor, Jr.[1] and Aldo J. Crovetti[2].
Checked by Charles C. Price and Walter A. Schroeder.

## 1. Procedure

In a 2-l. round-bottomed flask with ground-glass joint (Note 1) are placed 100 g. (0.82 mole) of powdered nicotinamide (Note 2) and 1 l. of C.P. glacial acetic acid, and the mixture is warmed with occasional shaking on a steam bath until a clear solution is obtained. To this mixture is added 160 ml. (1.39 moles) of cold 30% hydrogen peroxide. An air condenser is attached to the reaction flask, and the mixture is heated on a steam bath for 3.5 hours.

The reaction mixture is then distilled under reduced pressure (80–100 mm.) (Note 3). After 600–700 ml. has distilled, the mixture is diluted with 150–200 ml. of distilled water and the distillation is continued. The product separates near the end of the distillation, causing somewhat vigorous bumping for a short period. When the bumping has almost ceased, the pressure is reduced to 20 mm. and the distillation continued almost to dryness (Note 4).

The major portion of wet solid is removed from the flask and transferred to a 1-l. Erlenmeyer flask. The remaining solid is washed out with a little distilled water, and the washings are transferred to the flask. The solid is dissolved in the smallest amount of boiling water required, the flask removed from the heat source, and 50 ml. of ethyl alcohol added (Note 5). The flask is allowed to cool slowly, and, after the major portion of the product has separated, the flask is cooled to 5° overnight. The solid is removed by filtration and washed with cold alcohol, then acetone, and finally ether. The white, crystalline, air-dried product weighs 82–93 g. (73–82%), m.p. 291–293° dec. (rapid heating); the compound starts to turn brown at about 280–285° (Note 6).

## 2. Notes

1. Since hydrogen peroxide attacks rubber stoppers, glass-jointed equipment is recommended.
2. U.S.P. Niacinamide (Mallinckrodt) was used.
3. For the distillation, the still head consisted of a Claisen-type adapter with a parallel side arm (24/40 standard taper joints), 21 cm. high and 10.5 cm. wide. An ordinary straight still head is attached to the parallel side arm. This large still head prevents any bumping solid from entering the condenser.
4. Distilling to complete dryness exposes the solid to prolonged heating and causes oxidation of the product, which is obtained colored and in lower yield.
5. The alcohol serves to retain the brown color upon recrystallization and to decompose any excess hydrogen peroxide.
6. Because of the questionable value of the melting point as a criterion of purity, the checkers analyzed two samples of the product: Calcd. for $C_6H_6N_2O$: C, 52.17; H, 4.34. Found (Sample 1): C, 52.34; H, 4.44. Found (Sample 2): C, 52.61, 52.63; H, 4.46, 4.53.

## 3. Discussion

The procedure given is essentially that described by Taylor and Crovetti.[3] Nicotinamide-1-oxide (m.p. 275–276° dec.) has also been prepared by the alkaline hydrolysis of nicotinonitrile-1-oxide[4] and by the action of ammonium hydroxide on methyl nicotinate-1-oxide.[5] The melting point of the product prepared by the latter synthesis is reported to be 282–284° dec.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 166

## References and Notes

1. Princeton University, Princeton, New Jersey.
2. University of Illinois, Urbana, Illinois.
3. Taylor and Crovetti, *J. Org. Chem.*, **19**, 1633 (1954).
4. Jujo, *J. Pharm. Soc. Japan*, **66**, 21 (1946) [*C. A.*, **45**, 6200 (1951)].
5. Shimizu, Naito, Ohta, Yoshikawa, and Dohmori, *J. Pharm. Soc. Japan*, **72**, 1474 (1952) [*C. A.*, **47**, 8077 (1953)].

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

Niacinamide

ethyl alcohol (64-17-5)

acetic acid (64-19-7)

ether (60-29-7)

acetone (67-64-1)

hydrogen peroxide (7722-84-1)

ammonium hydroxide (1336-21-6)

nicotinamide (98-92-0)

nicotinamide-1-oxide (1986-81-8)

nicotinonitrile-1-oxide (14906-64-0)

methyl nicotinate-1-oxide