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.

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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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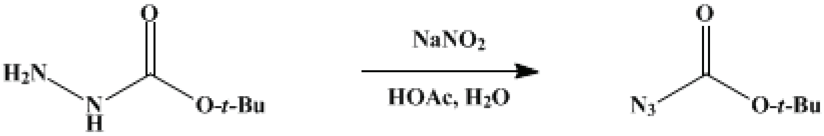
t-BUTYL AZIDOFORMATE

[Formic acid, azido-, *tert*-butyl ester]



Submitted by Louis A. Carpino, Barbara A. Carpino, Paul J. Crowley, Chester A. Giza, and Paul H. Terry[1].
Checked by Virgil Boekelheide and S. J. Cross.

1. Procedure

In a 1-l. round-bottomed flask fitted with a mechanical stirrer are placed 82 g. (0.62 mole) of *t*-butyl carbazate,[2] 72 g. of glacial acetic acid, and 100 ml. of water. The solution is cooled in an ice bath, and 47.0 g. (0.68 mole) of solid sodium nitrite is added over a period of 40–50 minutes, the temperature being kept at 10–15° (Note 1). The mixture is allowed to stand in the ice bath for 30 minutes, 100 ml. of water is added, and the floating oil is extracted into four 40-ml. portions of ether. The combined ether extracts are washed twice with 50-ml. portions of water and with 40-ml. portions of 1*M* sodium bicarbonate solution until no longer acidic (about three washings are required). The solution is dried over magnesium sulfate, and the ether is removed by distillation from a water bath maintained at 40–45°; water aspirator pressure of 140–150 mm. is used. The pressure is then lowered to 70 mm., and the water bath temperature is raised to 90–95°. The azide is distilled (*Caution! (Note 2)*) using a Claisen flask and is collected at 73–74° (70 mm.), $n^{24}D$ 1.4227, after a few drops of fore-run. The yield is 57–72.8 g. (64–82%) (Note 3) and (Note 4).

2. Notes

1. The sodium nitrite may be added as a concentrated aqueous solution.
2. It is recommended that the distillation be carried out behind a safety shield. The submitters have distilled this compound several hundred times without incident under the conditions given on a scale up to 300–400 g. per run. On the other hand, Prof. P. G. Katsoyannis (University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania) has reported that an explosion took place in the receiving flask while the compound was being distilled under conditions previously used without incident. The reason for the explosion could not be traced. According to Prof. R. Schwyzer (Ciba, Ltd., Basel, Switzerland) tests at a Swiss Federal Institute showed that the compound could not be exploded by mere heating: it simply decomposes. For explosion, one must apply a primary explosive such as lead azide or silver azide. An attempt by the submitters to distil the azide at atmospheric pressure resulted in vigorous carbonization, but no explosion occurred. In view of the potential hazard some investigators prefer not to distil the azide; they use the crude material after removal of solvent. High yields of carbo-*t*-butoxy derivatives may be obtained in this way.
3. When freshly distilled, the azide is water-white. When the azide is allowed to stand for several weeks, it slowly develops a light yellow color; however, this does not appear to affect its reactivity as an acylating agent.[3]
4. The azide should be handled with adequate ventilation. Careless inhalation of the substance was accompanied by development of a painful throbbing headache or a sensation of giddiness or both. These effects disappeared within several hours upon exposure to fresh air.

3. Discussion

t-Butyl azidoformate has been prepared by a variety of procedures,[3,4,5,6,7,8,9,10,11,12] of which the present procedure and that described elsewhere in this series[12] appear most satisfactory.

Because of the instability of *t*-butyl chloroformate a number of carbonic acid derivatives have been prepared and studied as reagents for the introduction of the carbo-*t*-butoxy group. A listing of these reagents and references to their preparation may be found in reference [13]. In spite of some disadvantages the most widely used reagent is still *t*-butyl azidoformate, although *t*-butyl 2,4,5-trichlorophenyl-carbonate appears to be another potentially useful reagent. *t*-Butyl azidoformate is a convenient reagent for the acylation of amines, hydrazines, and similar compounds.[3]

The acylation product of hydroxylamine, *t*-butyl N-hydroxycarbamate,[5] is a valuable intermediate in the synthesis of O-substituted hydroxylamines such as O-acyl- and O-sulfonylhydroxylamines, many of which are valuable aminating agents and have not be obtained in any other way.[14,15]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 160
- Org. Syn. Coll. Vol. 6, 199
- Org. Syn. Coll. Vol. 6, 203
- Org. Syn. Coll. Vol. 6, 207
- Org. Syn. Coll. Vol. 6, 418
- Org. Syn. Coll. Vol. 7, 70

References and Notes

1. Department of Chemistry, University of Massachusetts, Amherst, Massachusetts.
2. L. A. Carpino, D. Collins, and S. Göwecke, this volume, p. 166.
3. L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 4427 (1957).
4. L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 98 (1957).
5. L. A. Carpino, C. A. Giza, and B. A. Carpino, *J. Am. Chem. Soc.*, **81**, 955 (1959).
6. K. P. Polzhofer, *Chimia (Aarau)*, **23**, 298 (1969).
7. H. Yajima and H. Kawatani, *Chem. Pharm. Bull. (Tokyo)*, **16**, 182 (1968).
8. M. Itoh and D. Morino, *Experientia*, **24**, 101 (1968).
9. Y. A. Kiryushkin and A. I. Miroshnikov, *Experientia*, **21**, 418 (1965).
10. K. Inouye, M. Kanayama, and H. Otsuka, *Nippon Kagaku Zasshi*, **85**, 599 (1964).
11. D. S. Tarbell, *Accounts Chem. Res.*, **2**, 296 (1969).
12. M. A. Insalaco and D. S. Tarbell, *Org. Syntheses*, **50**, 9 (1970).
13. L. A. Carpino, K. N. Parameswaran, R. K. Kirkley, J. W. Spiewak, and E. Schmitz, *J. Org. Chem.*, **35**, 3291 (1970).
14. L. A. Carpino, *J. Am. Chem. Soc.*, **82**, 3133 (1960).
15. L. A. Carpino, *J. Am. Chem. Soc.*, **85**, 2144 (1963).

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

acetic acid (64-19-7)

ether (60-29-7)

sodium bicarbonate (144-55-8)

sodium nitrite (7632-00-0)

hydroxylamine (7803-49-8)

magnesium sulfate (7487-88-9)

silver azide

t-BUTYL AZIDOFORMATE,
Formic acid, azido-, tert-butyl ester (1070-19-5)

t-butyl carbazate (870-46-2)

t-butyl chloroformate

t-butyl 2,4,5-trichlorophenyl-carbonate (16965-08-5)

t-butyl N-hydroxycarbamate (36016-38-3)

lead azide