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.

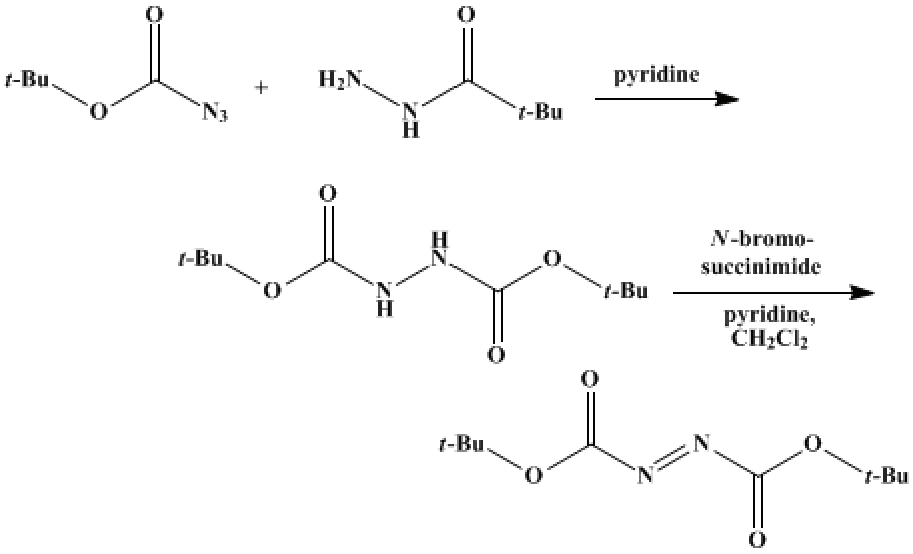
*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

DOI:10.15227/orgsyn.044.0018

*Organic Syntheses, Coll. Vol. 5, p.160 (1973); Vol. 44, p.18 (1964).*

# *t*-BUTYL AZODIFORMATE

## [Formic acid, azodi-, di-*tert*-butyl ester]



Submitted by Louis A. Carpino and Paul J. Crowley[1].
Checked by Virgil Boekelheide and S. J. Cross.

## 1. Procedure

A. *t-Butyl hydrazodiformate*. A solution of 28.6 g. (0.2 mole) of *t*-butyl azidoformate[2] and 26.4 g. (0.2 mole) of *t*-butyl carbazate[3] in 60 ml. of pyridine (Note 1) is allowed to stand at room temperature for 1 week and is then diluted with 500 ml. of water. The snow-white microcrystalline powder that separates is removed by filtration and is washed with two 50-ml. portions of water. The yield of air-dried hydrazide, m.p. 124–126°, is 35.5–37 g. (77–80%). The product is pure enough for most applications but may be purified by recrystallization from a 1:1 mixture of benzene and ligroin (60–90°) from which it separates as small white needles, m.p. 124–125.5°. The recovery is 92%.

B. *t-Butyl azodiformate*. In a 500-ml. Erlenmeyer flask is placed a solution of 23.2 g. (0.1 mole) of crude *t*-butyl hydrazodiformate (m.p. 124–126°) in 175 ml. of methylene chloride and 7.9 g. (0.1 mole) of pyridine (Note 1). The solution is cooled by a stream of running tap water while 18.2 g. (0.102 mole) (Note 2) of N-bromosuccinimide (Note 1) is added during 6–7 minutes with swirling. The resulting solution is allowed to stand at room temperature for 5 minutes and is washed with two 100-ml. portions of water followed by one 100-ml. portion of 10% sodium hydroxide. The solution is dried for 30 minutes over magnesium sulfate, filtered into a large evaporating dish, and allowed to evaporate. The yellow-orange crystalline residue, m.p. 90–91.5°, which amounts to 20.7–21.8 g. (90–94.5%), is recrystallized by covering the dry solid with 35–40 ml. of petroleum ether (b.p. 30–60°) and adding ligroin (b.p. 60–90°) to the boiling solution until the solid dissolves. *t*-Butyl azodiformate, 19.8–20.0 g., m.p. 90.7–92°, separates from the cooled solution as large lemon-yellow crystals. Evaporation of the filtrate gives an additional amount of yellow solid which is recrystallized as before, yielding 0.4–0.7 g. of pure material, m.p. 90–92°. The total yield is 20.2–20.7 g. (88–90%).

## 2. Notes

1. The pyridine was a pure product, b.p. 113–115°, obtained from Mallinckrodt Chemical Company and used as supplied. The methylene chloride (technical grade) and N-bromosuccinimide (practical grade) were obtained from the Matheson Company and used as received.
2. Unless a 2% excess of N-bromosuccinimide is used, the azo compound is contaminated by an

impurity, possibly the original hydrazo compound, which separates along with the desired product in the form of long, easily distinguished needles. The two substances cannot be separated by crystallization from ligroin.

## 3. Discussion

*t*-Butyl hydrazodiformate has been prepared by acylation of *t*-butyl carbazate by means of *t*-butyl azidoformate[4] or *t*-butyl cyanoformate.[5] *t*-Butyl azodiformate has been prepared only by oxidation of the hydrazo compound.[6]

## 4. Merits of the Preparation

The potassium salt of *t*-butyl hydrazodiformate can be easily alkylated and thus used in the synthesis of acyclic and cyclic 1,2-disubstituted hydrazines.[7]

Ethyl azodiformate is a well-known and useful dienophile in the Diels-Alder reaction.[8] *t*-Butyl azodiformate behaves similarly, although it is somewhat less reactive.[6] *t*-Butyl azodiformate does, however, provide products with ester groups that are easily cleaved. Monosubstituted hydrazines may be prepared by the addition of Grignard reagents to azoformates followed by cleavage.[6]

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## References and Notes

1. Department of Chemistry, University of Massachusetts, Amherst, Massachusetts.
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3. L. A. Carpino, D. Collins, S. Göwecke, J. Mayo, S. D. Thatte, and F. Tibbetts, this volume, p. 166.
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## Appendix
## Chemical Abstracts Nomenclature (Collective Index Number);
## (Registry Number)

ligroin

petroleum ether

Benzene (71-43-2)

sodium hydroxide (1310-73-2)

pyridine (110-86-1)

methylene chloride (75-09-2)

magnesium sulfate (7487-88-9)

N-bromosuccinimide (128-08-5)

Ethyl azodiformate

t-BUTYL AZIDOFORMATE (1070-19-5)

t-butyl carbazate (870-46-2)

t-BUTYL AZODIFORMATE (870-50-8)

Formic acid, azodi-, di-tert-butyl ester

t-butyl hydrazodiformate

t-butyl cyanoformate

potassium salt of t-butyl hydrazodiformate