



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](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.

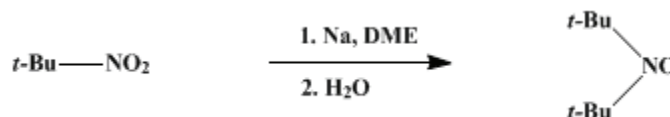
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 5, p.355 (1973); Vol. 48, p.62 (1968).*

## DI-*t*-BUTYL NITROXIDE

[Nitroxide, di-*tert*-butyl]



Submitted by A. K. Hoffmann, A. M. Feldman, E. Gelblum, and A. Henderson<sup>1</sup>.

Checked by R. A. Haggard and William D. Emmons.

### 1. Procedure

(Note 1)

Thirteen hundred milliliters of 1,2-dimethoxyethane (glyme) is distilled from lithium aluminum hydride (*Caution! Under no circumstances should distillation be carried to dryness since explosive decomposition of the residual hydride may occur.*) (Note 2) directly into a 2-l., nitrogen-flushed, three-necked, Morton flask equipped with a nitrogen inlet, an outlet, and a high-speed stirrer with a stainless steel propeller-type blade. The flask is charged with 89.7 g. (0.87 mole) of *t*-nitrobutane (Note 3) and 19.9 g. (0.87 g. atom) of sodium cut into pea-sized pieces (Note 4). The stirrer is started and initially operated at a speed just adequate to draw some of the sodium through the blade. The onset of reaction is signaled when the solution is pale lavender and the sodium surface is clearly etched and colored bright gold (Note 5). The temperature of the reaction mixture is maintained at 25–30° (Note 6) by directing an air blast at the sides of the flask and by controlling the rate at which sodium is drawn through the blades of the stirrer. As the reaction progresses, colorless solid is formed, and at the end of the reaction (*ca.* 24 hours) the reaction mixture consists of solid and a colorless glyme solution. Most of the glyme is removed by evaporation under reduced pressure at room temperature with a water bath at 20–25° to leave a thick, colorless slurry. To the slurry under nitrogen (Note 7) is added 270 ml. of water, and the reddish brown organic layer is separated. The aqueous layer (Note 8) is extracted with several portions of pentane until the extract is colorless. The organic layer and pentane extracts are combined, cooled to 0°, and washed rapidly and thoroughly with two 70-ml. portions of ice-cold 0.25*N* hydrochloric acid to remove hydroxylamine impurities (Note 9). The pentane solution of the product is washed immediately with 70 ml. of cold water followed by 70 ml. of cold, aqueous 0.2*N* sodium hydroxide. The combined, cold, aqueous acidic washings are extracted with small portions of pentane until colorless. This pentane extract is used to extract the aqueous sodium hydroxide layer and is then washed with water and combined with the initial pentane extract.

The pentane solution is dried over anhydrous magnesium sulfate and fractionated with an efficient spinning-band column (Note 10). After foreruns of pentane and glyme containing *t*-nitrosobutane are removed (Note 11), 26–27 g. (42–43%) of red di-*t*-butyl nitroxide, b.p. 59–60° (11 mm.), is obtained.

### 2. Notes

1. The submitters obtained similar results using a preparative scale 7.5 times that described here; yield 36%.
2. The 1,2-dimethoxyethane (Ansul Chemical Co.) was predried for several days over calcium hydride, filtered, and stored over lithium aluminum hydride prior to its distillation at atmospheric pressure immediately before use. For a larger-scale preparation it is expeditious to distil simultaneously from two 5-l. flasks rather than from a single large one. Under these conditions, distillation of the glyme can be completed in 8–10 hours.
3. The *t*-nitrobutane employed was prepared by the procedure of Kornblum, Clutter, and Jones.<sup>2</sup> This method is essentially the same as that previously reported in *Organic Syntheses*.<sup>3</sup>
4. Throughout all transfers, air must be rigorously excluded from the flask by the nitrogen blanket.
5. When great care has not been taken to ensure the absence of moisture, induction times as long as

several minutes are observed before the onset of reaction.

6. The temperature of the reaction mixture must never be allowed to exceed 30°; above this temperature drastic diminution of yield occurs.

7. A nitrogen blanket is used here to prevent ignition of [hydrogen](#) resulting from traces of unreacted [sodium](#).

8. At this point during one run the checkers obtained a considerable amount of water-insoluble, colorless solid; however, the product yield was not changed.

9. It is essential to keep the reaction mixture and acid cold since otherwise substantial decomposition of product results.

10. The pot temperature should not exceed 100° until the [di-\*t\*-butyl nitroxide](#) fraction is collected.

11. In several runs it was noted that, despite the acid extraction, small amounts of [N,N-di-\*t\*-butylhydroxylamine](#) crystallized in the cooler parts of the fractionating column head. In such cases, repetition of the acid extraction procedure is required before fractionation.

### 3. Discussion

The procedure described is that of Hoffmann, Feldman, Gelblum, and Hodgson<sup>4</sup> and is the only one known at this time for the preparation of substantial amounts of [di-\*t\*-butyl nitroxide](#).

### 4. Merits of the Preparation

The method is specific for the preparation of [di-\*t\*-butyl nitroxide](#), a liquid member of a group of stable free radicals useful for the inhibition of a variety of reactions proceeding by radical chain mechanisms as well as for providing standards for e.s.r. measurements.

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### References and Notes

1. American Cyanamid Company, Stamford Research Laboratories, 1937 West Main Street, Stamford, Connecticut 06904.
  2. N. Kornblum, R. J. Clutter, and W. J. Jones, *J. Am. Chem. Soc.*, **78**, 4003 (1956).
  3. [N. Kornblum and W. J. Jones, this volume, p. 845](#).
  4. A. K. Hoffmann, A. M. Feldman, E. Gelblum, and W. G. Hodgson, *J. Am. Chem. Soc.*, **86**, 639 (1964).
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### Appendix

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

*t*-nitrobutane

glyme

*t*-nitrosobutane

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

[hydrogen](#) (1333-74-0)

[sodium hydroxide](#) (1310-73-2)

[nitrogen](#) (7727-37-9)

sodium (13966-32-0)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

lithium aluminum hydride (16853-85-3)

calcium hydride (7789-78-8)

1,2-dimethoxyethane (110-71-4)

DI-t-BUTYL NITROXIDE,  
Nitroxide, di-tert-butyl (2406-25-9)

N,N-di-t-butylhydroxylamine