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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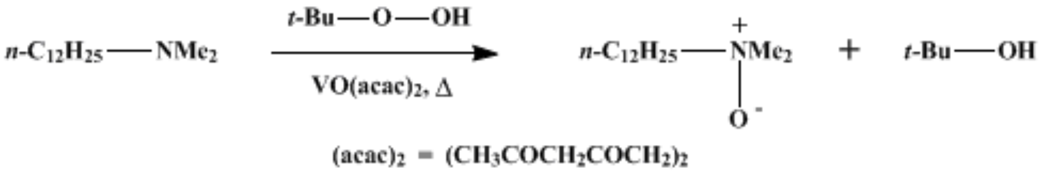
N,N-DIMETHYLDODECYLAMINE OXIDE

[Dodecanamine, *N,N*-dimethyl-, *N*-oxide]



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1. Procedure

Caution! Reactions and subsequent operations involving peracids and peroxy compounds should be run behind a safety shield. Peroxy compounds should be added to the organic material, never the reverse. For relatively fast reactions, the rate of addition of the peroxy compound should be slow enough so that it reacts rapidly and no significant unreacted excess is allowed to build up. The reaction mixture should be stirred efficiently while the peroxy compound is being added, and cooling should generally be provided since many reactions of peroxy compounds are exothermic. New or unfamiliar reactions, particularly those run at elevated temperatures, should be run first on a small scale. Reaction products should never be recovered from the final reaction mixture by distillation until all residual active oxygen compounds (including unreacted peroxy compounds) have been destroyed. Decomposition of active oxygen compounds may be accomplished by the procedure described in Korach, M.; Nielsen, D. R.; Rideout, W. H. Org. Synth. 1962, 42, 50 (Org. Synth. 1973, Coll. Vol. 5, 414). [Note added January 2011].

Caution! Methyl iodide, in high concentrations for short periods or in low concentrations for long periods, can cause serious toxic effects in the central nervous system. Accordingly, the American Conference of Governmental Industrial Hygienists[2] has set 5 p.p.m., a level which cannot be detected by smell, as the highest average concentration in air to which workers should be exposed for long periods. The preparation and use of methyl iodide should always be performed in a well-ventilated fume hood. Since the liquid can be absorbed through the skin, care should be taken to prevent contact.

A solution of 21.3 g. (0.100 mole) of freshly distilled *N,N*-dimethyldodecylamine (Note 1), 9.6 g. (0.10 mole) of 94% *tert*-butyl hydroperoxide (Note 2), and 0.050 g. of vanadium oxyacetylacetonate (Note 3) in 27 g. (34 ml.) of *tert*-butyl alcohol is placed in a 250-ml., round-bottomed flask fitted with a thermometer, a reflux condenser, and a heating mantle. The reaction mixture is heated to approximately 65–70°, at which point an exothermic reaction begins. The heating is discontinued until the vigorous exothermic reaction subsides (about 5 minutes); the reaction mixture is then heated at reflux (the reaction mixture boils at 90°) for 25 minutes. After the resulting mixture has been cooled to room temperature, *it is analyzed* (Note 4) *to establish the absence of tert-butyl hydroperoxide*, then concentrated with a rotary evaporator (30–35° bath with 30–40 mm. pressure). The crude solid residue is triturated with 50 ml. of cold (0–5°), anhydrous diethyl ether and filtered under conditions which prevent exposure of the residual amine oxide to atmospheric moisture (Note 5). The solid is washed with 50 ml. of cold (0–5°) anhydrous ether and dried under reduced pressure, leaving 12.9–15.5 g. of the crystalline amine oxide, m.p. 131–131.5°. Concentration of the mother liquors and trituration of the residual paste with 25 ml. of cold (0–5°) anhydrous ether separates another 4.9–3.4 g. of the amine oxide, m.p. 130–131°. The total yield of the crystalline amine oxide (Note 6) is 17.4–18.9 g. (76–83%).

2. Notes

1. *N,N*-Dimethyldodecylamine purchased from Eastman Organic Chemicals is approximately 90% pure. This material should be fractionally distilled with a spinning band column to obtain the pure amine, b.p. 116–117° (4 mm.).
2. *tert*-Butyl hydroperoxide purchased from the Lucidol Division, Wallace and Tiernan, Inc., is approximately 92% pure. A portion of the major impurity, water, can be removed by drying the commercial material over anhydrous magnesium sulfate for 2 days, leaving material that is 94–97% pure.
3. Vanadium oxyacetylacetonate may be purchased from Alfa Inorganics, Inc., Beverly, Massachusetts.
4. Although consumption of the hydroperoxide is normally complete, the absence of this peroxide in the reaction mixture should be established by testing with moist starchiodide paper or by iodometric titration.[3] The amine oxide content may be determined by titration with standard hydrochloric acid after any amine present has reacted with methyl iodide for 1 hour at room temperature.[4] From this volumetric analysis the submitters determined the yield of amine oxide to be 86%. The checkers found that the reaction could be followed by measuring the ^{1}H NMR spectra in *tert*-butyl alcohol solution where the *N*-methyl signals of the amine (δ 2.03) and the amine oxide (δ 2.98) are readily observed.
5. The amine oxide is exceedingly hygroscopic and must be protected from atmospheric moisture during filtration. The submitters found it convenient to use a Büchner funnel covered with a large, inverted rubber stopper. After the mixture of amine oxide and ether is added to the funnel, the mouth of the funnel is covered with the inverted rubber stopper, and suction is applied. The flat surface of the inverted rubber stopper forms a seal against the mouth of the funnel, preventing the entrance of moist air while the last traces of ether are removed. The checkers employed a sintered-glass funnel fitted to maintain a nitrogen atmosphere above the crystalline product.
6. The hygroscopic amine oxide should be protected from moisture during storage. The checkers found that the initial product could be recrystallized from toluene under anhydrous conditions to yield the amine oxide as white needles, m.p. 130–131°.

3. Discussion

Aqueous or alcoholic solutions of amine oxides are normally obtained by oxidizing tertiary amines with either hydrogen peroxide or a peracid.[5] For example, *N,N*-dimethyldodecylamine oxide has been prepared by treating *N,N*-dimethyldodecylamine with aqueous hydrogen peroxide.[6] The procedure illustrated in this preparation permits the oxidation of tertiary amines with *tert*-butyl hydroperoxide in organic solvents under relatively anhydrous conditions.[7] In this procedure the reaction time is short, and the method is as convenient as that with aqueous hydrogen peroxide or a peracid as the oxidant. Furthermore, isolation of the anhydrous amine oxide is often relatively simple.

References and Notes

1. The Research and Development Department, ARCO Chemical Company, A Division of Atlantic Richfield Company, Glenolden, Pennsylvania. [Present address: The Research and Development Department, ARCO Chemical Company, A Division of Atlantic Richfield Company, Newtown Square, Pennsylvania 19073.]
2. American Conference of Governmental Industrial Hygienists (ACGIH), “Documentation of Threshold Limit Values,” 3rd ed., Cincinnati, Ohio, 1971, p. 166.
3. D. H. Wheeler, *Oil Soap (Chicago)*, **9**, 89 (1932) [*Chem. Abstr.*, **26**, 3128 (1932)].
4. L. D. Metcalfe, *Anal. Chem.*, **34**, 1849 (1962).
5. A. C. Cope and E. R. Trumbull, *Org. React.*, **11**, 378 (1960).
6. G. L. K. Hoh, D. O. Barlow, A. F. Chadwick, D. B. Lake, and S. R. Sheeran, *J. Am. Oil Chem. Soc.*, **40**, 268 (1963).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

peracid

vanadium oxyacetylacetonate

hydrochloric acid (7647-01-0)

ether,
diethyl ether (60-29-7)

nitrogen (7727-37-9)

toluene (108-88-3)

hydrogen peroxide (7722-84-1)

Methyl iodide (74-88-4)

magnesium sulfate (7487-88-9)

tert-butyl alcohol (75-65-0)

tert-butyl hydroperoxide (75-91-2)

N,N-dimethyldodecylamine (112-18-5)

N,N-Dimethyldodecylamine oxide,
Dodecanamine, N,N-dimethyl-, N-oxide (1643-20-5)