



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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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.*



sodium hydroxide solution (Note 6). The combined ethereal solutions are dried over anhydrous sodium sulfate and concentrated with a rotary evaporator. The residual crystalline solid is dried under reduced pressure (10–15 mm.) at room temperature, leaving 33.7–38.7 g. (65–75%) of the crude hydroxylamine product, m.p. 59–60°, which is sufficiently pure for use in the next step. The crude product may be recrystallized from pentane, yielding the pure *N-tert-butylhydroxylamine* as white plates, m.p. 64–65° (Note 7).

C. *2-Methyl-2-nitrosopropane*. A solution of sodium hypobromite is prepared by adding, dropwise and with stirring over a 5-minute period, 57.5 g. (18.5 ml., 0.360 mole) of bromine to a solution of 36.0 g. (0.900 mole) of sodium hydroxide in 225 ml. of water. The resulting yellow solution, contained in a 1-l., three-necked flask fitted with a mechanical stirrer, a thermometer, and an acetone–dry ice cooling bath, is cooled to –20°. A suspension of 26.7 g. (0.300 mole) of *N-tert-butylhydroxylamine* in 50 ml. of water is added to the reaction flask, with continuous stirring, as rapidly as possible without allowing the temperature of the reaction mixture to exceed 0°. The reaction solution is again cooled to –20° before the cooling bath is removed and the mixture is stirred for 4 hours while the reaction mixture warms to room temperature. The solid product, the nitroso dimer which has separated, is collected on a sintered glass funnel, pulverized, and washed with 1 l. of water (Note 8). The residual solid is dried at room temperature under reduced pressure (10–15 mm.), leaving 19.6–22.2 g. (75–85%) of the *2-methyl-2-nitrosopropane* dimer, m.p. 80–81° (Note 9). The product is sufficiently pure to be stored (Note 10) for use as a free radical trapping reagent.

## 2. Notes

1. *tert-Butylamine*, purchased from Aldrich Chemical Company, Inc., may be used without purification.
2. Approximately 1 l. of distillate needs to be collected to remove the product from the reaction mixture.
3. The principal contaminant is residual ether.
4. The purified product exhibits IR bands (CCl<sub>4</sub>) at 1545 cm<sup>-1</sup> (broad) and 1355 cm<sup>-1</sup> (NO<sub>2</sub>) with a UV maximum (95% C<sub>2</sub>H<sub>5</sub>OH) at 279 nm ( $\epsilon$  24) and a <sup>1</sup>H NMR (CCl<sub>4</sub>) singlet at  $\delta$  1.58 [(CH<sub>3</sub>)<sub>3</sub>C]. The mass spectrum has the following abundant fragment peaks: *m/e* (rel. int.), 57 (100), 41 (74), 39 (45), and 29 (57).
5. Since water is one of the reactants in this reduction, it is necessary that at least a stoichiometric quantity of water is present.
6. Since the hydroxylamine product is readily oxidized by air to the blue nitroso compound, these manipulations should be performed rapidly to minimize exposure of the product to atmospheric oxygen. Any nitroso compound formed at this stage will co-distil with the ether and is difficult to recover.
7. The product has IR absorption (CCl<sub>4</sub>) at 3600 cm<sup>-1</sup> and 3250 (broad) cm<sup>-1</sup> (OH and NH) with <sup>1</sup>H NMR (CCl<sub>4</sub>) singlets at  $\delta$  1.09 [9H, C(CH<sub>3</sub>)<sub>3</sub>] and 5.86 (2H, NH and OH). The mass spectrum has the following abundant peaks: *m/e* (rel. int.), 89 (M<sup>+</sup>, 11), 74 (96), 58 (41), 57 (100), 56 (52), 42 (41), 41 (74), 39 (34), 29 (54), and 28 (39).
8. Thorough washing to remove the last traces of alkali is essential, or the nitroso dimer will decompose to volatile products on standing.
9. When the colorless nitroso dimer is dissolved in various solvents, it partially dissociates, forming a blue solution which contains an equilibrium mixture of monomer and dimer. In C<sub>6</sub>D<sub>6</sub> and CCl<sub>4</sub>, the <sup>1</sup>H NMR spectrum of the initial solutions of dimer changes rapidly and equilibrium is established within 20–30 minutes. From <sup>1</sup>H NMR measurements at about 40° the equilibrium mixtures in CCl<sub>4</sub> and C<sub>6</sub>D<sub>6</sub> contain 80–81% of the monomer;<sup>2</sup> the <sup>1</sup>H NMR singlets attributable to *tert*-butyl groups are observed at  $\delta$  1.24 (monomer) and 1.57 (dimer) in CCl<sub>4</sub> and at  $\delta$  0.97 (monomer) and 1.49 (dimer) in C<sub>6</sub>D<sub>6</sub>. The IR spectrum of the equilibrated mixture (CCl<sub>4</sub>) exhibits absorption at 1565 cm<sup>-1</sup> attributable to the N=O group of the monomer; this peak is not observed in the IR spectrum (KBr) of the dimer. The mass spectrum of the product exhibits the following abundant fragment peaks: *m/e* (rel. int.), 72 (10), 57 (100), 56 (23), 55 (21), 42 (22), 41 (97), 39 (55), 30 (49), 29 (74), and 28 (53). A water solution of the dimer initially is colorless and exhibits a UV maximum at 287 nm ( $\epsilon$  8000). On standing, the solution slowly turns blue. A solution of the dimer in C<sub>2</sub>H<sub>5</sub>OH, after standing for 20–30 minutes, exhibits maxima at 292 nm ( $\epsilon$  682 dimer) and 686 nm ( $\epsilon$  14.5 monomer).
10. The submitters report that if the product is stored at 0° in the dark, it may be kept indefinitely.

## 3. Discussion

The oxidation of *tert*-butylamine to 2-methyl-2-nitropropane is an example of a procedure previously illustrated in *Org. Synth.*<sup>3</sup> *N-tert*-Butylhydroxylamine has previously been prepared by acid-catalyzed hydrolysis of 2-*tert*-butyl-3-phenyloxazirane<sup>4</sup> and by oxidation of *tert*-butylamine.<sup>5</sup> The procedure described here is based on a method mentioned briefly by Smith and co-workers.<sup>6</sup> 2-Methyl-2-nitrosopropane has been prepared directly by oxidation of *tert*-butylamine,<sup>2,5</sup> but is usually obtained by oxidation of the hydroxylamine.<sup>7</sup> 2-Methyl-2-nitrosopropane has also been prepared by electrolytic reduction<sup>8</sup> or by zinc dust reduction<sup>9</sup> of 2-methyl-2-nitropropane.

2-Methyl-2-nitrosopropane is an excellent scavenger of free radicals and is now widely used in "spin trapping" experiments<sup>10,11</sup> (although it has certain disadvantages).<sup>12</sup> In this technique, a reactive radical is trapped by the nitroso compound and identified by analysis of the e.s.r. spectrum of the so-formed stable nitroxide radical. The perdeuterated derivative of 2-methyl-2-nitrosopropane has also been recommended for this purpose.<sup>13</sup> *tert*-Butylhydroxylamine, an intermediate in the present procedure, may also be used to synthesize *tert*-butylphenylnitron which has been used as a "spin-trapping" reagent.<sup>11</sup> The reaction of 2-methyl-2-nitrosopropane with aryl Grignard reagents has been used to prepare *N*-aryl-*N-tert*-butylhydroxylamines.<sup>14</sup>

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## References and Notes

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## Appendix

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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ether,  
diethyl ether (60-29-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

potassium permanganate (7722-64-7)

bromine (7726-95-6)

sodium sulfate (7757-82-6)

oxygen (7782-44-7)

aluminum (7429-90-5)

zinc (7440-66-6)

mercury(II) chloride (7487-94-7)

Pentane (109-66-0)

sodium hypobromite

magnesium sulfate (7487-88-9)

2-Methyl-2-nitropropane (594-70-7)

2-Methyl-2-nitrosopropane,  
Propane, 2-methyl 2-nitroso- (6841-96-9)

N-tert-Butylhydroxylamine,  
tert-Butylhydroxylamine (16649-50-6)

2-tert-Butyl-3-phenyloxazirane (7731-34-2)

tert-Butylamine (75-64-9)

tert-butylphenylnitrene