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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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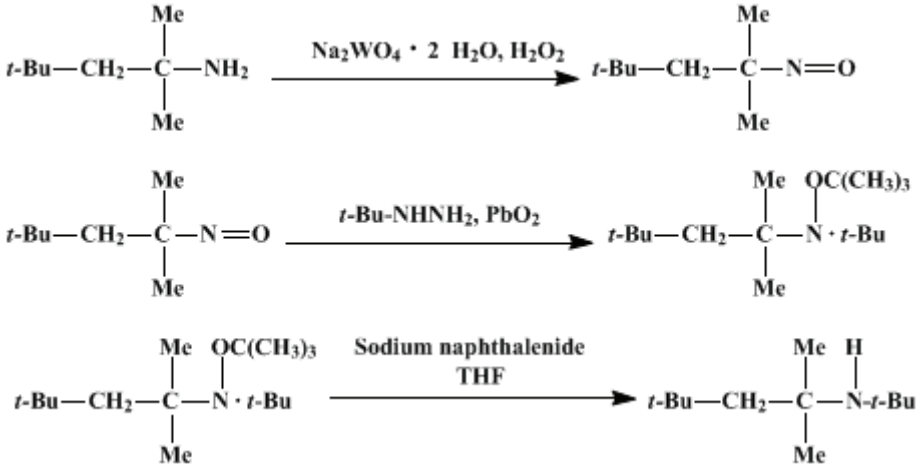
tert-BUTYL-*tert*-OCTYLAMINE

[2-Pentanamine, *N*-(1,1-dimethylethyl)-2,4,4-trimethyl-]



Submitted by E. J. Corey and Andrew W. Gross[1].
Checked by Axel H. K. Paul and Clayton H. Heathcock.

1. Procedure

A. *Nitroso-tert-octane*.[2] To a 1-L, three-necked flask equipped with an addition funnel, a mechanical stirrer, and a thermometer are added 120 mL of methanol, 51.7 g of *tert*-octylamine (0.4 mol), and 90 mL of water containing 1.2 g (0.0028 mol) of the tetrasodium salt of ethylenediaminetetraacetic acid and 2.52 g (0.0076 mol) of sodium tungstate dihydrate. The solution is cooled to 15°C in an ice bath and hydrogen peroxide (361 mL of a 16% solution, 1.7 mol) (Note 1) and (Note 2) is added over 5 hr. The blue reaction mixture is stirred for an additional 16 hr and the product is extracted with petroleum ether (3 × 50 mL). Unreacted amine is removed by washing twice with 2 *N* hydrochloric acid. After the blue organic layer is washed with brine, it is dried over $MgSO_4$. Petroleum ether is removed by distillation at atmospheric pressure. Continued distillation of the product affords 29.7 g of nitroso-*tert*-octane (52%), bp 45–55°C, 18 mm. On standing, the product crystallizes as the colorless dimer, mp 63–65°C. For use in the subsequent reaction the required amount of the dimer is stirred for 1 hr in hexane to establish monomer–dimer equilibrium (Note 3) and (Note 4).

B. *N-tert-Butyl-N-tert-octyl-O-tert-butylhydroxylamine.* Into a 1-L, three-necked flask equipped with a dropping funnel, a mechanical stirrer, and a gas inlet tube is placed a solution of 22.8 g (0.16 mol of monomer) of nitroso-*tert*-octane in 500 mL of hexane. After the mixture is stirred for 1 hr, lead dioxide (132 g, 0.55 mol) (Note 5) is added. To the rapidly stirring mixture is added 48.8 g (0.55 mol) of *tert*-butylhydrazine (Note 6) dropwise at such a rate as to give brisk but controlled nitrogen evolution (approximately 30 min). Cooling is provided by an ice bath so as to maintain the reaction temperature between 15 and 25°C. Progress of the reaction is monitored visually by the disappearance of the blue nitroso monomer color (Note 7). After the blue color has disappeared (about 1.5 hr), the lead oxides are removed by filtration through a pad of Celite and the residue is washed with ether/hexane (1 : 1). The filtrate and washes are combined and the solvents are removed at reduced pressure with a rotary evaporator to give a 6 : 1 mixture of *N*-*tert*-butyl-*N*-*tert*-octyl-*O*-*tert*-butylhydroxylamine and *N*-*tert*-octyl-*O*-*tert*-butylhydroxylamine (Note 8) and (Note 9).

C. *tert-Butyl-tert-octylamine.* In a dry, 500-mL, three-necked flask equipped with a mechanical stirrer, an addition funnel, and a nitrogen inlet are placed 25.6 g (0.20 mol) of naphthalene, 250 mL of dry tetrahydrofuran (THF), and 10.8 g (0.47 mol) of sodium pieces. The mixture is stirred at room temperature for 30 min. To the blue-green sodium naphthalenide solution is added the hydroxylamine mixture (Note 10) in 50 mL of THF over 20 min. *(Caution! Exothermic reaction.)* The mixture is stirred

for 2.5 hr at room temperature (Note 11). The reaction mixture is carefully decanted from excess sodium and the excess reducing agent is cautiously quenched with isopropyl alcohol. After dilution with 150 mL of hexane, the mixture is acidified with 300 mL of ice-cold 2 *N* hydrochloric acid, the aqueous layer is separated, and the organic layer extracted twice more with 100-mL portions of 2 *N* hydrochloric acid. The combined acidic extracts are washed with 80 mL of petroleum ether (Note 12), neutralized with 4 *N* sodium hydroxide, and extracted with ether (3 × 100 mL). The ether extract is dried over $MgSO_4$ and the solvent is removed with a rotary evaporator. Distillation of the residue gives a small forerun, followed by 18–19 g of *tert*-butyl-*tert*-octylamine, bp 79°C (17 mm). The yield is 60–64% based on nitroso-*tert*-octane (Note 13).

2. Notes

1. Mallinckrodt 30% H_2O_2 was diluted with water to give a solution of 16% H_2O_2 in water.
2. Although it is used in excess, the amount of H_2O_2 used seems to be critical. The checkers found that the use of 2.1 mol of H_2O_2 results in considerable overoxidation to nitro-*tert*-octane, resulting in a yield of nitroso-*tert*-octane of only 40%.
3. Nitroso-*tert*-octane may also be prepared by oxidation of *tert*-octylamine with peracetic acid in ethyl acetate, obtained by the submitters from the Union Carbide Corporation.[3] To a 1-L, three-necked flask equipped with a mechanical stirrer and an addition funnel are added 51.7 g of *tert*-octylamine (0.4 mol), 50 mL of water, and 50 mL of ethyl acetate. The flask is placed in an ice bath and the contents are stirred until the temperature reaches 0–5°C. A solution of peracetic acid in ethyl acetate (3.15 *M* solution, 51 mL, 0.16 mol) is added dropwise over a 30-min period. The blue reaction mixture is stirred at 0°C until the absence of peroxy acid is indicated by starch–iodide test paper. The reaction mixture is transferred to a separatory funnel and diluted with 200 mL of hexane. Unreacted *tert*-octylamine is removed by washing with 4 *N* hydrochloric acid. The aqueous washes are backwashed until colorless with 50-mL portions of hexane. The combined, blue organic fractions are dried over sodium sulfate and used directly in the next step. When the nitroso compound is prepared in this manner, isolation is unnecessary. The checkers did not employ this procedure because the peracetic acid/ethyl acetate solution is not commercially available.
4. Care should be taken in distilling the nitroso compound because it is thermally unstable; its half-life is less than 5 min at 150°C.[2]
5. If technical-grade lead dioxide (Fisher Scientific Company) is used, a somewhat greater amount must be added to compensate for the decreased Pb(IV) content.
6. *tert*-Butylhydrazine is conveniently liberated from its hydrochloride (Aldrich Chemical Company, Inc.) by distillation from 40% KOH (bp 104–107°C). The distillate consists of a mixture of *tert*-butylhydrazine and water. On addition of several grams of KOH pellets, the distillate separates into two layers. The upper layer, consisting of slightly wet *tert*-butylhydrazine, is dried over KOH pellets.
7. Additional lead dioxide and/or *tert*-butylhydrazine may be necessary to complete the reaction.
8. The spectral properties are as follows. *N*-*tert*-Butyl-*N*-*tert*-octyl-*O*-*tert*-butylhydroxylamine ^{1}H NMR ($CDCl_3$) δ: 1.00 (s, 9 H), 1.26 (s, 12 H), 1.30 (s, 3 H), 1.31 (s, 9 H), 1.76 (s, 2 H); *N*-*tert*-octyl-*O*-*tert*-butylhydroxylamine ^{1}H NMR ($CDCl_3$) δ: 1.01 (s, 9 H), 1.12 (s, 6 H), 1.15 (s, 9 H), 1.40 (s, 2 H), 4.44 (s, 1 H).
9. The trisubstituted hydroxylamine is sensitive to both acid and heat.
10. The yield of product is greatly reduced if the hydroxylamine mixture is not rigorously freed of solvent from the previous reaction.
11. The submitters report that the sodium naphthalenide color is discharged on addition of the hydroxylamine mixture, and that completion of the reduction is indicated by reappearance of the characteristic blue-green color of the reagent. The checkers did not observe disappearance of the reagent color.
12. If the acidic solution is not extracted at this point, the final product will be contaminated with 2–3% naphthalene.
13. The ^{1}H NMR spectrum of *tert*-butyl-*tert*-octylamine is as follows ($CDCl_3$) δ: 1.02 (s, 9 H, CH_3), 1.19 (s, 9 H, CH_3), 1.24 (s, 6 H, CH_3), 1.44 (s, 2 H, CH_2).

3. Discussion

In addition to the procedure given here for the oxidation of *tert*-octylamine to nitroso-*tert*-octane,[2]

the oxidation may be carried out with *m*-chloroperoxybenzoic acid[4] or with a solution of peroxyacetic acid in ethyl acetate.[3] The lead dioxide oxidation of alkylhydrazines to alkyl radicals appears to have general application. In addition to *tert*-butylhydrazine, various secondary alkylhydrazines (e.g., bornylhydrazine and menthylhydrazine) have been used to good effect. The reduction of tri-*tert*-alkylhydroxylamine to the di-*tert*-alkylamine has also been achieved with sodium in ammonia, but the insolubility of the hydrophobic substrate makes this procedure difficult. The use of sodium naphthalenide[5] gives higher yields and is more reproducible.

In addition to the commercially available 2,2,6,6-tetramethylpiperidine,[6] di-*tert*-alkylamines have been prepared by Rathke[7] by the copper-catalyzed coupling of acetylenic amines with acetylenic chlorides in an improvement of the procedure of Hennion.[8] Di-*tert*-butylamine has been synthesized by the reaction of 2-methyl-2-nitropropane with sodium, followed by reduction.[9]

The three-step procedure described here illustrates a convenient, general route to di-*tert*-alkylamines. Extensive purification or isolation of intermediates is not required. The reactions are easily monitored. Only in the final step is the exclusion of air and moisture necessary. It should be noted that *tert*-butyl-*tert*-octylamine is considerably more hindered than 2,2,6,6-tetramethylpiperidine. *tert*-Butyl-*tert*-octylamine is inert to methyl iodide, while 2,2,6,6-tetramethylpiperidine gives a white precipitate of the pentamethylammonium iodide within minutes on treatment with methyl iodide at room temperature. The extreme hindrance of this amine has been exploited in the selective deprotonation of carbon acids and in other reactions.[10]

References and Notes

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

petroleum ether

amine

brine

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ethyl acetate (141-78-6)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

sodium (13966-32-0)

isopropyl alcohol (67-63-0)

Naphthalene (91-20-3)

hydrogen peroxide (7722-84-1)

Methyl iodide (74-88-4)

Tetrahydrofuran (109-99-9)

peracetic acid,
peroxyacetic acid (79-21-0)

hexane (110-54-3)

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

2,2,6,6-tetramethylpiperidine (768-66-1)

ethylenediaminetetraacetic acid (60-00-4)

Nitroso-tert-octane (31044-98-1)

sodium tungstate dihydrate (10213-10-2)

sodium naphthalenide

bornylhydrazine

menthylhydrazine

pentamethylammonium iodide

m-chloroperoxybenzoic acid (937-14-4)

lead dioxide

tert-octylamine

tert-Butyl-tert-octylamine

2-Pentanamine, N-(1,1-dimethylethyl)-2,4,4-trimethyl- (90545-94-1)

tert-butylhydrazine (32064-67-8)

N-tert-Butyl-N-tert-octyl-O-tert-butylhydroxylamine (90545-93-0)

N-tert-octyl-O-tert-butylhydroxylamine

nitro-tert-octane

Di-tert-butylamine (21981-37-3)