of nitroindole, 0.03 mol of RMgX is used.

Registry No. 1-Chloro-4-nitrobenzene, 100-00-5; 1-methoxy-4-nitrobenzene, 100-17-4; 6-nitrobenzothiazole, 2942-06-5; 2-methyl-6-nitrobenzothiazole, 2941-63-1; 6-nitrobenzoxazole, 17200-30-5; 5-nitro-1*H*-indole, 6146-52-7; 2-methoxy-1-nitronaphthalene, 4900-66-7; 1-methoxy-4-nitronaphthalene, 4900-63-4; 6-nitroquinoline, 613-50-3; 4-chloro-2-methyl-1-nitrobenzene, 5367-28-2; 4-chloro-2-(2-phenylethyl)-1-nitrobenzene, 72206-90-7; 4-methoxy-2-methyl-1-nitrobenzene, 5367-32-8; 4-methoxy-1-nitro-2-(2-phenylethyl)-benzene, 72206-91-8; 7-methyl-6-nitrobenzothiazole, 72206-92-9; 7-butyl-6-nitrobenzothiazole, 72206-93-0; 2,7-dimethyl-6-nitrobenzothiazole, 72206-94-1; 7-methyl-6-nitrobenzoxazole, 72206-95-2; 6-nitro-7-(2-phenylethyl)benzoxazole, 72206-96-3; 5-nitro-4-(2-phenylethyl)-1*H*-indole, 72206-97-4; 4-butyl-5-nitro-1*H*-indole, 72206-98-5; 2-methoxy-4-methyl-1-nitronaphthalene, 72206-99-6; 4-butyl-2-methoxy-1-nitronaphthalene, 69745-40-0; 4-methoxy-2-methyl-1-nitronaphthalene, 72207-00-2; 2-butyl-4-methoxy-1-nitronaphthalene, 72207-01-3.

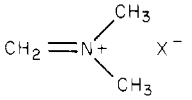
Preformed Mannich Salts: A Facile Preparation of Dimethyl(methylene)ammonium Iodide

Thomas A. Bryson,* Gordon H. Bonitz, Curtis J. Reichel, and Richard E. Dardis

Department of Chemistry, University of South Carolina, Columbia, South Carolina 29208

Received May 17, 1979

Preformed Mannich salts of the type **1a–c**, have recently

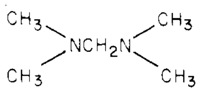


$$CH_2{=}\overset{+}{N}(CH_3)_2\ X^-$$

1a, X = I⁻
b, X = Cl⁻
c, X = ⁻OOCCF$_3$

found increased and varied usage[1] as electrophiles in a wide range of reactions, and dimethyl(methylene)ammonium iodide (**1a**) has been of particular interest due to its reactivity and stability. We have used the elegant but somewhat time-consuming procedure of Eschenmoser et al.[2] to prepare **1a**, but extensive use of this salt has required an alternate and more convenient source of this reagent which is disclosed herein.

We have found that **2** reacts cleanly and efficiently with

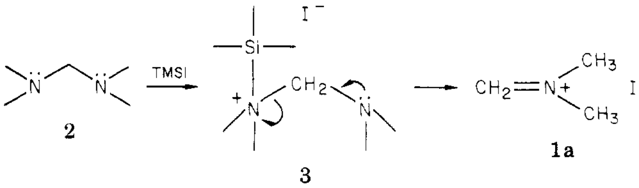


$$(CH_3)_2NCH_2N(CH_3)_2$$

2

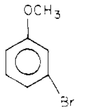
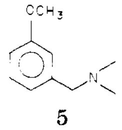
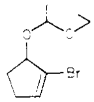
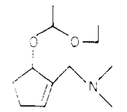
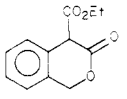
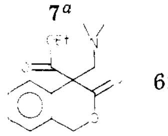
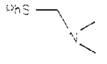
trimethylsilyl iodide[3] (TMSI) to form **1a** (96% yield) which is in all respects identical with **1a** formed by the Eschenmoser procedure.[2] The mechanism of this process can be rationalized by molding together the analogy of the Jung conversion of ketals to ketones using trimethylsilyl iodide[4] and the preparation of **1b** using acetyl chloride,[1e] leading to the assumption that **2** and TMSI form **3** which subsequently cleaves to give Mannich salt **1a** (Scheme I).[10]

Scheme I



2 **3** **1a**

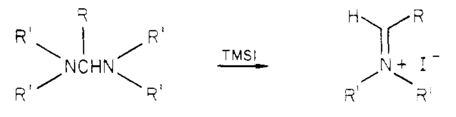
Table I

	sol- vent	base or metal	*t*, °C	product	% yield
 **4**	Et$_2$O	Mg	25 (2 h)	 **5**	86[1d]
 **6**	THF	*n*-BuLi	25	 **7**[a]	30[9]
 **8**	THF	NaH	25	 **9**	62
HSPh (**10**)	Et$_2$O	NaH	25	 **11**	80[8]

[a] Isolated as the methiodide salt.

Addition of salt **1a** (formed by this procedure) to nucleophiles such as Grignard reagents, vinyllithium reagents, sodium thiophenoxide, and stabilized carbanions gives the expected results, some of which are summarized in Table I.

Further studies show that cleavage of tetraalkyl aminals (i.e., **12**) with TMSI gives the desired Mannich salts cleanly and efficiently. These salts (**13a,b**) were further characterized by addition of organolithium reagents generating amines (**14**).



12a, R = Et; R′,R′ = (CH$_2$)$_5$
b, R = CH(CH$_3$)$_2$; R′ = *n*-Bu

13a, R = Et; R′ = (CH$_2$)$_5$
b, R = CH(CH$_3$)$_2$; R′ = *n*-Bu

These studies indicate that TMSI cleavage of tertiary geminal diamines is generally applicable to afford preformed Mannich salts and perhaps the corresponding neutral enamine structures. We are currently investigating other aspects of the TMSI cleavage of symmetrical and unsymmetrical aminals.

Experimental Section

Preparation of Dimethyl(methylene)ammonium Iodide (1a). A 250-mL three-necked, round-bottomed flask, equipped with a magnetic stirring bar, rubber septum, and N$_2$ inlet, was

---

(1) (a) S. Danishefsky, T. Kitahara, R. McKee, and P. F. Schuda, *J. Am. Chem. Soc.*, **98**, 6715 (1976); (b) S. Danishefsky, P. F. Schuda, T. Kitahara, and S. J. Etheredge, *ibid.*, **99**, 6066 (1977); (c) J. Hooz and J. N. Bridson, *ibid.*, **95**, 602 (1973); (d) C. D. Poulter, J. L. Roberts, and P. S. Borromeo, *Tetrahedron Lett.*, 1299 (1977); J. L. Roberts and C. D. Poulter, *ibid.*, 1621 (1977); (e) G. Kunst and L.-F. Tietze, *Angew. Chem., Int. Ed. Engl.*, **15**, 239 (1976); (f) N. L. Holy and Y. F. Wang, *J. Am. Chem. Soc.*, **99**, 944 (1977).

(2) J. Schreiber, H. Maag, N. Hashimoto, and A. Eschenemoser, *Angew. Chem., Int. Ed. Engl.*, **10**, 330 (1971).

(3) We realized optimum yields when the TMSI was prepared fresh according to Jung's procedure [M. E. Jung and M. A. Lyster, *J. Org. Chem.*, **42**, 3761 (1977)]; however, salt 1a was produced in 94% yield when commercially available TMSI was used.

(4) M. E. Jung, W. A. Andrus, and P. L. Ordstein, *Tetrahedron Lett.*, 4175 (1977).

0022-3263/80/1945-0524$01.00/0

flame-dried and charged with freshly prepared trimethylsilyl iodide[3] (32.8 g, 0.164 mol) dissolved in anhydrous ether (20 mL). At 0 °C 2-methyl-2-butene[5] (1 mL) was added followed by a dropwise addition of *N,N,N′,N′*-tetramethylmethylenediamine[6] (16.8 g, 0.164 mol) in anhydrous ether (20 mL). A white precipitate formed immediately and this mixture was allowed to stir for 20 min. The precipitate was collected by vacuum filtration and washed with anhydrous ether (3 × 75 mL), air-dried, and rapidly[7] transferred to a vacuum desiccator for storage affording **1a**: yield 29.1 g, 96%; sublimed [140 °C (0.25 torr)] or recrystallized from sulfolane;[2] ^{1}H NMR (Me_4Si, Me_2SO-d_6) δ 3.6 (s, 6 H), 8.2 (s, 2 H); IR (Nujol) ν_{max} 3115, 1682 cm^{-1}.

3-[(Dimethylamino)methyl]anisole (5). Compound **5** was prepared from *m*-bromoanisole by the procedure of Poulter et al.[1d] in 86% yield: IR (neat film) ν_{max} 2780, 1600, 1145, 775 cm^{-1}; ^{1}H NMR (Me_4Si, CCl_4) δ 2.10 (s, 6 H), 3.25 (s, 2 H), 3.60 (s, 3 H), 6.50–7.20 (m, 4 H); mass spectrum *m/e* 165 (M^+).

(Aminomethyl)cyclopentene 7. The metalation of **7** was accomplished by the procedure of Smith.[9] The amine salt **1a** was added as a solid at −78 °C, and the solution was allowed to warm to room temperature and stirred for 2 h. Water was added and the solution was extracted with ether. The combined organic extracts were washed with water and brine, dried over magnesium sulfate, filtered, and concentrated in vacuo, leaving a dark brown oil. To the crude oil stirred at room temperature was added excess methyl iodide. The solid produced was filtered by suction and washed with hexane: ^{1}H NMR (Me_4Si, $CDCl_3$) δ 5.7 (m, 1 H), 4.7 (m, 2 H), 3.7 (m, 2 H), 3.3 (s, 9 H), 2.3 (m, 2 H), 1.2 (m, 6 H).

4-(Carboethoxy)-4-[(dimethylamino)methyl]-3-isochromanone (9). A solution of 4-(carboethoxy)-3-isochromanone (**8**) (1.00 g, 4.55 mmol) in dry THF (4 mL) was added dropwise to a suspension of NaH dispersion (50%, 0.23 g, and the mixture was washed with hexane (3 × 10 mL)) at 0 °C under N_2 and stirred at 25 °C for 10 min. To this solution was added salt **1a** (930 mg, 5.00 mmol) as a solid in one portion, and the mixture was allowed to stir at 25 °C for 2 h. Following addition of water (20 mL), the reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined CH_2Cl_2 extracts were washed with water (2 × 20 mL) and 10% HCl (4 × 10 mL). The acid washes were combined and extracted with Et_2O (20 mL), made basic to litmus with 10% K_2CO_3, and extracted with CH_2Cl_2 (3 × 20 mL). The CH_2Cl_2 extracts were combined, washed with water (2 × 20 mL) and brine (20 mL), dried with $MgSO_4$, and evaporated to dryness to give 0.781 g (62%) of a clear colorless viscous oil: IR (neat film) ν_{max} 2780, 1740, 1725 cm^{-1}; ^{1}H NMR (Me_4Si, $CDCl_3$) δ 1.29 (t, 3 H, J = 8 Hz), 2.00 (s, 6 H), 3.25 (AB q, 2 H, J_1 = 38 Hz, J_2 = 14 Hz), 4.18 (q, 2 H, J = 8 Hz), 5.35 (AB q, 2 H, J_1 = 30 Hz, J_2 = 16 Hz), 7.1–7.5 (m, 4 H); mass spectrum *m/e* 277 (M^+).

(Dimethylamino)methyl Phenyl Sulfide (11). To a stirred suspension of NaH (50%, 0.48 g, 9.99 mmol) in THF (20 mL) was slowly added thiophenol (1.00 g, 9.09 mmol) at room temperature under N_2. After 0.5 h, the salt **1a** was added as a solid and the resulting solution stirred overnight. Following addition of water (20 mL), the resulting mixture was extracted with ether (3 × 20 mL), and the combined organic extracts were washed successively with a saturated aqueous $NaHCO_3$ solution, water, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo, leaving a yellow oil. Bulb-to-bulb distillation at 80 °C (5 mm) yielded a clear oil (1.21 g, 80%): IR (neat film) 3030, 2940, 2860, 1580, 1440, 745, 690, 620 cm^{-1}.

1,1-Dipiperidinopropane (12a). This compound was prepared by the general method of Mannich and Davidson[11] in 85% yield: IR (neat film) ν_{max} 2935, 2860, 2800 cm^{-1}; ^{1}H NMR (Me_4Si, $CDCl_3$) δ 2.50–2.97 (m, 9 H), 1.32–1.80 (m, 17 H); mass spectrum *m/e* 210 (M^+).

1,1-Bis(di-*n*-butylamino)-2-methylpropane (12b). This compound was prepared in a 64% distilled[11] [bp 63 °C (1.5 torr)] yield: IR (neat film) ν_{max} 2955, 2920, 2860, 2795 cm^{-1}; ^{1}H NMR (Me_4Si, $CDCl_3$) δ 0.78–1.10 (m, 18 H), 1.10–1.65 (m, 6 H), 2.25–2.63 (m, 9 H); ^{13}C NMR (Me_4Si, $CDCl_3$) δ 14.16, 20.91, 29.17, 54.16; mass spectrum *m/e* 312 (M^+).

Pentamethylene(ethylidene)ammonium Iodide (13a). This compound was prepared as described above for formation of salt **1a**, in 80% yield: IR (Nujol) ν_{max} 3075, 1660 cm^{-1}; ^{1}H NMR (Me_4Si, Me_2SO-d_6) δ 1.40–2.00 (m, 13 H), 2.60–2.85 (m, 4 H), 8.6 (m, 1 H); mass spectrum *m/e* 263 (M^+).

Di-*n*-butyl(2-methylpropylidene)ammonium Iodide (13b). This compound was prepared as described above for formation of salt **12**, in 76% yield: IR (Nujol) ν_{max} 3070, 1655 cm^{-1}; ^{1}H NMR (Me_4Si, Me_2SO-d_6) δ 0.95 (t, 6 H), 1.20–1.90 (m, 15 H), 2.90–3.20 (m, 4 H), 8.85 (m, 1 H); mass spectrum *m/e* 311 (M^+).

3-Piperidinoheptane (14a). *n*-Butyllithium was added to ammonium salt **13a**, according to the procedure of Poulter et al.[1d] Chromatography of the crude adduct on silica (4:1, cyclohexane–ethyl acetate) afforded **14a** (40%): IR ($CHCl_3$) ν_{max} 2930, 2850 cm^{-1}; NMR (Me_4Si, $CDCl_3$) δ 2.5–2.9 (m, 5 H), 1.3–1.75 (m, 12 H), 0.95 (t, 6 H, J = 6 Hz); mass spectrum *m/e* 183 (M^+).

1-(Di-*n*-butylamino)-1-phenyl-2-methylpropane (14b). Phenyllithium was added to ammonium salt **13b**, according to the procedure of Poulter et al.[1d] Chromatography of crude adduct on silica (4:1, cyclohexane–ethyl acetate) afforded **14b** (38%): IR ($CHCl_3$) ν_{max} 2920, 2840, 1590 cm^{-1}; NMR (Me_4Si, $CDCl_3$) δ 0.95 (t, 12 H, J = 7 Hz), 1.4 (m, 9 H), 2.4 (t, 5 H, J = 16 Hz), 2.1–2.7 (m, 5 H); mass spectrum *m/e* 237 (M^+).

Acknowledgment. Support for this study was provided by the National Institutes of Health (Grant No. AM-18802) and the A. P. Sloan Foundation.

---

[5] The 2-methyl-2-butene was used to react with any HI that may be present from the hydrolysis of TMSI.

[6] The *N,N,N′,N′*-tetramethylmethylenediamine was purchased from Aldrich and used without further purification.

[7] We found the iodide salt to be considerably less hygroscopic than the chloride salt **1b**.

[8] D. Michelot, R. Lorne, C. Hyunh, and S. Julia, *Bull. Chim. Soc. Fr.*, 1482 (1976).

[9] M. A. Guaciaro, P. M. Wovkulich, and A. B. Smith, III, *Tetrahydron Lett.*, 4661 (1978).

[10] Carbon and hydrogen elemental analyses for **1a** agreed, within experimental error, with calculated values.

[11] C. Mannich and H. Davidson, *Ber. Dtsch. Chem. Ges. B*, **69**, 2106 (1939).

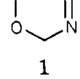
Stereospecific Bromohydroperoxylation of 4,4-Dimethyl-3,5-diphenyl-4*H*-pyrazole. Synthesis and Crystal Structure of 3-Bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole

Michael E. Landis,* Ronald L. Lindsey, William H. Watson,* and Volker Zabel

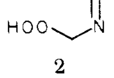
Departments of Chemistry, Southern Illinois University, Edwardsville, Illinois 62026, and Texas Christian University, Fort Worth, Texas 76129

Received August 7, 1979

The importance of halo hydroperoxides as precursors for four[1]- and five[2]-membered-ring peroxides is well established. These hydroperoxides are conviently synthesized by the addition of electrophilic halogen to alkenes[1] or strained σ bonds[2] in the presence of concentrated (90% or greater) hydrogen peroxide. Dehydrohalogenation[1,2] to a cyclic peroxide is generally realized with base or silver salts. Our interest in the synthesis of cyclic azo peroxides[3,4] such as **1**, a model compound for an elusive intermediate postulated in the chemiluminescent oxidation of luminol,[4] has led to the development of a synthetic method for bromo hydroperoxy azo compounds (e.g., **2**) that might be



1



2

---

* Address correspondence to M.E.L. at Southern Illinois University and W.H.W. at Texas Christian University.