Synthesis of 1-(Trimethylsilyl)alkylamines

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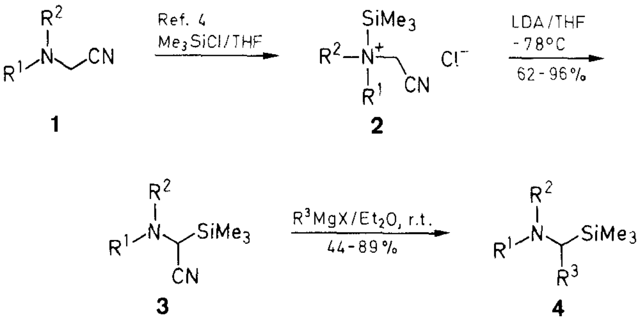
Several *N*,*N*-dialkyl[1-(trimethylsilyl)alkyl]amines **4** were synthesized by the reaction of a Grignard reagent with 2-dialkylamino-2-(trimethylsilyl)acetonitriles **3** prepared by silylation of (dialkylamino)acetonitriles **1**.

No general synthetic method for 1-(trimethylsilyl)alkylamines has yet been reported, whereas (trimethylsilyl) methylamines are conveniently prepared by the reaction of amines with (chloromethyl)trimethylsilane.[1,2] Although *N*,*N*-dialkyl[1-(trichlorosilyl)alkyl]amines obtainable by the reductive silylation of *N*,*N*-dialkylamides with trichlorosilane can be converted to *N*,*N*-dialkyl[1-(trialkylsilyl)alkyl]amines,[3] the trichlorosilyl analogues are tricky compounds to handle in the laboratory. In this paper we report a convenient new method of synthesizing N,N-dialkyl[1-(trimethylsilyl)alkyl]amines **4** from 2-dialkylamino-2-(trimethylsilyl)acetonitriles **3** with Grignard reagents.

Padwa and coworkers[4] reported that the addition of chlorotrimethylsilane to (benzylmethylamino)acetonitrile (**1k**) resulted in the formation of silylammonium salt **2k**. Treatment of a suspension of **2k** in tetrahydrofuran with lithium diisopropylamide (LDA) gave 2-benzylmethylamino-2-(trimethylsilyl)acetonitrile (**3k**) in high yield. Their attempt to extend the silylation reaction to other (dialkylamino)acetonitriles containing simple alkyl groups, however, failed to produce the expected 2-dialkylamino-2-(trimethylsilyl)acetonitriles.



1-4	R¹	R²	R³
a	Me	Me	CH_3
b	Et	Me	–[a]
c	Et	Et	n-C_4H_9
d	Et	Et	n-C_6H_{11}
e	Et	Et	$PhCH_2$
f	Et	Et	Ph
g	$-(CH_2)_4-$		$PhCH_2$
h	$-(CH_2)_5-$		C_2H_5
i	$-(CH_2)_5-$		n-C_4H_9
j	$-(CH_2)_5-$		Ph
k	$PhCH_2$	Me	CH_3
l	$PhCH_2$	Me	C_2H_5
m	$PhCH_2$	Me	n-C_4H_9
n	$PhCH_2$	Et	CH_3
o	4-$MeOC_6H_4CH_2$	Me	CH_3

[a] Compound **4b** was not prepared.

We re-examined the application of this silylation reaction on seven (dialkylamino)acetonitriles **1a–1c**, **1g**, **1h**, **1n**, and **1o**. When the reaction was carried out in a manner similar to that described by Padwa et al.[4] and worked-up with a saturated ammonium chloride solution,[5] high yields of 2-dialkylamino-2-(trimethylsilyl)acetonitriles **3a–3c**, **3g**, **3h**, **3n**, and **3o** were obtained (Table 1).

Reaction of **3a**, **3c**, **3g**, **3h**, **3k**, **3n**, **3o** with various Grignard reagents afforded **4a**, **4c–o** at room temperature in good yields, except for **4a** (Table 2). The low yield of N,N-dimethyl[1-(trimethylsilyl)ethyl]amine (**4a**) is due to the loss of the volatile product in small-scale distillation. In the preparation of **4f** and **4j** by the reaction with phenylmagnesium bromide, consumption of the starting nitrile required considerable time.

All reactions were carried out in a N_2 or Ar atmosphere. Et_2O and THF were dried by distillation from sodium benzophenone ketyl prior to use. ^1H-NMR spectra were obtained using a JEOL JNM-PMX 60, JEOL JNM-MH-100, JEOL JNM-FX-100, or JEOL JNM-GSX-400 spectrometer. IR spectra were obtained using a JASCO IRA-2-spectrophotometer. All boiling points are uncorrected. BuLi was purchased from Nakarai Chemicals, Ltd., Kyoto.

2-Dialkylamino-2-(trimethylsilyl)acetonitrile (3); General Procedure: BuLi (15% in hexane, 4.2 mL, 6.5 mmol) is added to a stirred solution of diisopropylamine (658 mg, 6.5 mmol) in THF (5 mL) and stirring is continued at – 78 °C for 0.5 h. The resulting LDA solution is added to a suspension of the silylammonium salt **2** derived from aminoacetonitrile **1** (5 mmol) and chlorotrimethylsilane (815 mg, 7.5 mmol) in THF (5 mL) at – 78 °C. The mixture

Table 1. 2-Dialkylamino-2-[(trimethylsilyl)methyl]acetonitriles **3** Prepared

Product	Yield[a] (%)	bp[b] (°C)/mbar	Molecular Formula[c] or Lit. bp (°C)/mbar	IR (film) ν (cm^{-1})	^1H-NMR ($CDCl_3$/TMS) δ, J (Hz)
3a	62	105–107/71	$C_7H_{16}N_2Si$ (156.3)	2225, 1260, 860, 762	0.25 (s, 9H), 2.33 (s, 6H), 3.02 (s, 1H)
3b	95	126/80	$C_8H_{18}N_2Si$ (170.3)	2200, 1255, 850, 755	0.23 (s, 9H), 1.06 (t, 3H, J = 7), 2.28 (s, 3H), 2.46 (q, 2H, J = 7), 3.11 (s, 1H)
3c	86	95/16	$C_9H_{20}N_2Si$ (184.4)	2200, 1255, 850	0.23 (s, 9H), 1.06 (t, 6H, J = 7), 2.51 (q, 4H, J = 7), 3.22 (s, 1H)
3g	93	115/16	$C_9H_{18}N_2Si$ (182.3)	2220, 1275, 870, 770	0.27 (s, 9H), 1.63–1.97 (m, 4H), 2.50–2.80 (m, 4H), 3.25 (s, 1H)
3h	92	140/23	$C_{10}H_{20}N_2Si$ (196.4)	2185, 1250, 845, 750	0.23 (s, 9H), 1.23–1.82 (m, 6H), 2.38–2.63 (m, 4H), 2.98 (s, 1H)
3k	96[d]	123/0.7	135–140/0.7[4]	2220, 1255, 850, 740	0.20 (s, 9H), 2.18 (s, 3H), 3.03 (s, 1H), 3.45, 3.77 (ABq, 2H, J = 13), 7.28 (s, 5H)
3n	91	130/0.5	$C_{14}H_{22}N_2Si$ (246.4)	2200, 1255, 850, 755	0.20 (s, 9H), 1.10 (t, 3H, J = 7), 2.38–2.90 (m, 2H), 3.14 (s, 1H), 3.38, 3.94 (ABq, 2H, J = 14), 7.31 (s, 5H)
3o	83	140–142/0.5	$C_{14}H_{22}N_2OSi$ (262.4)	2185, 1240, 845, 755	0.61 (s, 9H), 2.31 (s, 3H), 3.04 (s, 1H), 3.33, 3.67 (ABq, 2H, J = 13), 3.77 (s, 3H), 6.55 (d, 2H, J = 9), 6.96 (d, 2H, J = 9)

[a] Yield of isolated product **3** base on **1**.

[b] Oven temperature of Buchi Kugelrohr distillation apparatus.

[c] Satisfactory microanalyses obtained: C ±0.27, H ±0.12, N ±0.21.

[d] Reference 4, yield 96%.

Table 2. *N,N*-Dialkyl[1-(trimethylsilyl)alkyl]amines **4** Prepared

Product	Reaction Time (h)	Yield[a] (%)	bp (°C)/mbar	Molecular Formula[c] or Lit. bp (°C)/mbar	IR (film) ν(cm^{-1})	^{1}H-NMR (CDCl$_3$/TMS) δ, *J*(Hz)
4a	0.5	48	135–136/1013	30/11[3]	1267, 855, 765	0.05 (s, 9H), 1.02 (d, 3H, *J* = 6), 2.05 (q, 1H, *J* = 6), 2.26 (s, 6H)
4c	0.5	86	120/48	$C_{12}H_{29}NSi$ (215.5)	1253, 840	0.03 (s, 9H), 0.97 (t, 9H, *J* = 7), 1.16 (m, 6H), 2.13 (t, 1H, *J* = 6), 2.43 (q, 4H, *J* = 7)
4d	4	72	115/40	$C_{14}H_{33}NSi$ (243.5)	1250, 840	0.04 (s, 9H), 0.89 (t, 3H, *J* = 7), 1.00 (t, 6H, *J* = 7), 1.27 (br s, 10H), 2.15 (t, 1H, *J* = 7), 2.53 (q, 4H, *J* = 7)
4e	3	82	120/11	$C_{15}H_{27}NSi$ (249.5)	1250, 840, 750, 700	−0.06 (s, 9H), 0.97 (dd, 6H, *J* = 7.0, 7.2), 2.45–2.61 (m, 6H), 2.95 (dd, *J* = 6.6, 13.1), 7.12–7.25 (m, 5H)
4f	20	82	100/16	$C_{14}H_{25}NSi$ (235.4)	1250, 840, 742, 700	−0.03 (s, 9H), 0.98 (t, 6H, *J* = 7), 2.65 (q, 2H, *J* = 7), 2.67 (t, 2H, *J* = 7), 3.37 (s, 1H), 7.20 (br s, 5H)
4g	0.5	77	120–125/5	$C_{15}H_{25}NSi$ (247.5)	1240, 840, 740, 695	−0.03 (s, 9H), 1.50–1.82 (m, 4H), 2.33–3.00 (m, 7H), 7.12 (s, 5H)
4h	0.5	75	130/53	$C_{11}H_{25}NSi$ (199.4)	1250, 860, 745	0.04 (s, 9H), 0.94 (t, 3H, *J* = 7), 1.37–1.52 (m, 7H), 1.59–1.69 (m, 1H), 1.81 (t, 1H, *J* = 7), 2.46–2.59 (m, 4H)
4i	0.5	75	120/27	$C_{13}H_{29}NSi$ (227.5)	1255, 845, 760	0.03 (s, 9H), 0.90 (t, 3H, *J* = 7), 1.10–1.80 (m, 12H), 2.40–2.60 (m, 5H)
4j	14.5	89	160/20	$C_{15}H_{25}NSi$ (247.5)	1250, 840, 750, 745	−0.05 (s, 9H), 1.41–1.70 (m, 6H), 2.30–2.56 (m, 4H), 2.79 (s, 1H), 7.32 (s, 5H)
4k	0.5	85	140–145/36	$C_{13}H_{23}NSi$ (221.4)	1250, 850, 740, 695	0.10 (s, 9H), 1.10 (d, 3H, *J* = 8), 2.24 (s, 3H), 2.32 (q, 1H, *J* = 8), 2.57, 3.69 (ABq, 2H, *J* = 13), 7.20–7.50 (m, 5H)
4l	1	87	150/35	$C_{14}H_{25}NSi$ (235.4)	1250, 840, 750, 740	0.09 (s, 9H), 1.00 (t, 3H, *J* = 7.4), 1.43–1.55 (m, 1H), 1.69–1.80 (m, 1H), 2.12 (dd, 1H, *J* = 6.4, 7.5), 2.23 (s, 3H), 3.68 (s, 2H), 7.19–7.34 (m, 5H)
4m	1	73	163–164/17	$C_{16}H_{29}NSi$ (263.5)	1250, 835, 735, 750	0.09 (s, 9H), 0.91 (t, 3H, *J* = 7), 1.29–1.42 (m, 5H), 1.67–1.75 (m, 1H), 2.11 (dd, 1H, *J* = 5.3, 7.9), 2.23 (s, 3H), 3.66 (s, 2H), 7.19–7.33 (m, 5H)
4n	0.5	86	93–94/3.3	$C_{14}H_{25}NSi$ (235.4)	1250, 840, 755, 740	0.02 (s, 9H), 0.98 (t, 3H, *J* = 7), 1.02 (d, 3H, *J* = 7), 2.33 (q, 1H, *J* = 7), 2.37–2.49 (m, 2H), 3.46, 3.72 (ABq, 2H, *J* = 14), 7.18–7.36 (m, 5H)
4o	0.5	89	111–114/2	$C_{14}H_{25}NOSi$ (251.4)	1250, 1040, 1260, 855	0.04 (s, 9H), 1.02 (d, 3H, *J* = 7), 2.15 (s, 3H), 2.24 (q, 1H, *J* = 7), 3.48 (s, 2H), 3.74 (s, 3H), 6.63 (d, 2H, *J* = 8), 7.06 (d, 2H, *J* = 8)

[a] Yield of isolated product **4** base on **3**.

[b] Oven temperature of Buchi Kugelrohr distillation apparatus.

[c] Satisfactory microanalyses obtained: C ±0.27, H ±0.29, N ±0.25.

is stirred at the same temperature for 3 h and is then allowed to warm to r.t. The mixture is poured into a sat. NH_4Cl solution (20 mL) and extracted with Et_2O (3 x 20 mL). The ethereal extract is washed with water (4 x 30 mL), dried ($MgSO_4$) and concentrated at reduced pressure. The resulting oil is distilled at reduced pressure, and the major fraction corresponding to **3** is collected (Table 1).

N,N-Dialkyl[1-(trimethylsilyl)alkyl]amine (4); General Procedure: Grignard reagent, prepared from alkyl halide (5 mmol) and Mg turnings (267 mg, 5.5 mmol) in Et_2O (6 mL), is added to a solution of **3** (2.5 mmol) in Et_2O (5 mL). The mixture is stirred at r.t. (the reaction time is listed in Table 2), then quenched with 10% HCl (10 mL). Et_2O (20 mL) is added to the mixture and the layer separated. The organic layer is extracted with 10% HCl (3 x 10 mL). The HCl extract is made alkaline with conc. NH_4OH, and extracted with Et_2O (3 x 20 mL). The ethereal extract is washed with water (3 x 30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue is distilled at reduced pressure, and the major fraction corresponding to **4** is collected (Table 2).

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(5) Padwa et al.[4] workes up the reaction mixture with water. Dialkylamino(trimethylsilyl)acetonitriles **3** are easily hydrolyzed in an alkaline medium at r.t.