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A Convenient Synthesis of Primary Amines by N-Alkylation of Cyclic Potassium Disilylamides

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Potassium 2,6-disilapiperidide, readily prepared from 2,2,6,6-tetramethyl-2,6-disilapiperidine and potassium hydride, can be smoothly *N*-alkylated with alkyl halides to give the corresponding primary amines after acid hydrolysis.

Keywords——potassium 2,6-disilapiperidide; potassium hydride; primary amine; *N*-alkylation; metal amide

Direct alkylation of ammonia with alkyl halides is the most straightforward method for preparing primary amines (**1**). However polyalkylations are inevitable[1)] and, therefore, reactions of metal amides of protected ammonia with alkyl halides are generally employed to obtain pure **1**.[2)] The best known method is the Gabriel synthesis.

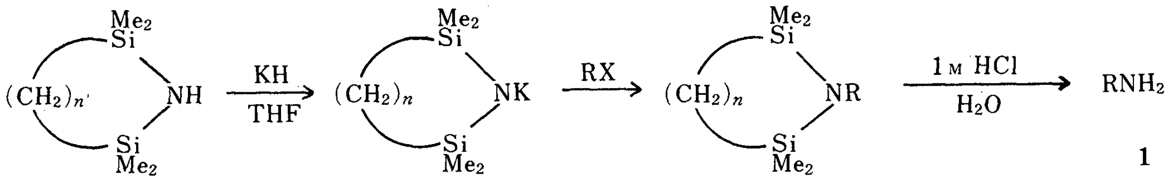
Recently silylamines have been widely utilized as potent silyl-transfer reagents in organic synthesis.[3)] In contrast, there are only a few reports on the fate of the nitrogen fragment of silylamines.[4)] Metal bis(trimethylsilyl)amides (**2**) are highly sterically hindered and non-nucleophilic bases, but their use as nitrogen sources does not necessarily give satisfactory results. Indeed, we could not always obtain satisfactory results in the *N*-alkylation of potassium amides (**2**).

We now report that potassium 2,2,6,6-tetramethyl-2,6-disilapiperidide (**5**) displays considerable nucleophilicity toward carbon nucleophiles such as alkyl bromides, probably due to smaller steric hindrance than **2**, and provides a convenient route to primary amines (**1**) by *N*-alkylation with alkyl halides (Chart 1).

The potassium amide (**5**), readily prepared from the reaction of the corresponding 2,6-disilapiperidine (**3**)[5)] with potassium hydride,[6)] is thermally stable in tetrahydrofuran (THF) and reacts with alkyl bromide very smoothly at reflux temperature to afford the corresponding *N*-alkylated 2,6-disilapiperidine (**7**) in high yields. The results are listed in Table I.

When ethyl bromide, propyl bromide and butyl bromide were employed as the alkylating reagents, the yield did not increase so much under the present reaction conditions, presumably because of the low boiling point of these bromides, although *n*-octyl bromide and benzyl chloride gave rather good results. Tetrahydrofuran gave the best results among various solvents examined. The alkylations of potassium bis(trimethylsilyl)amide (**2**) with alkyl bromide did not always proceed conveniently, resulting in 37%, 53%, and 60% yields with butyl bromide, octyl bromide and benzyl chloride, respectively.

The alkylation of other metal amides of **3**, such as lithium, sodium, copper, and magnesium, did not give satisfactory results, even when tetramethylethylenediamine or hexamethylphosphoric triamide was used as the activator of the metal amides. We had expected an improvement in the yield of the reaction by using 2,2,5,5-tetramethyl-2,5-



3 : $n=3$
4 : $n=2$

5 : $n=3$
6 : $n=2$

7a : $n=3$, R=Et
7b : $n=3$, R=n-Pr
7c : $n=3$, R=n-Bu
7d : $n=3$, R=n-Oct
7e : $n=3$, $R=PhCH_2$
7f : $n=3$, R=p-$CH_3C_6H_4CH_2$
8a : $n=2$, R=n-Bu
8b : $n=2$, R=n-Oct

Chart 1

TABLE I. Alkylations of Cyclic Potassium Disilylamides

Entry	Disilylamine	RX	Product	% Yield[a]
1	**3**	EtBr	**7a**	50 (59)[b]
2	**3**	n-PrBr	**7b**	61
3	**3**	n-BuBr	**7c**	72 (80)[b]
4	**3**	n-OctBr	**7d**	89
5	**3**	$PhCH_2Cl$	**7e**	85 (100)[b]
6	**3**	p-$CH_3C_6H_4CH_2Cl$	**7f**	85
7	**4**	n-BuBr	**8a**	29
8	**4**	n-OctBr	**8b**	47

a) Yield after isolation by distillation (Kugelrohr). *b*) Yield determined by GLC is shown in parentheses.

disilapyrrolidide (**6**), a lower homologue of **5**, but this was not the case. Thus, *N*-alkylations of **6** with butyl bromide and octyl bromide afforded the corresponding *N*-alkylated 2,5-disilapyrrolidines (**8a** and **8b**) in 29% and 47% yields, respectively.

The monoalkylated disilylamines (**7d** and **7e**), thus obtained, which are temporarily protected by silyl groups,[7] can be converted readily to primary amines (**1**) by hydrolysis with aqueous 1 M hydrochloric acid to give *n*-octylamine and benzylamine in 84% and 94% yields, respectively.

The present method appears to provide a useful and convenient synthesis of primary amines from readily accessible starting materials[5] under moderate conditions.

Experimental

^{1}H-NMR spectra were recorded in CCl_4 or $CDCl_3$ on Varian T-60, JEOL JNM-PMX-60, and FX-90Q spectrometers. Chemical shifts are given as δ in ppm. Infrared (IR) spectra were taken in Hitachi EPI and JASCO IRA-2 spectrometers. Mass spectra (MS) were recorded on JEOL JMS-300D and JMS-DX303 GC-MS spectrometers. Analytical gas liquid chromatography (GLC) was performed on a Hitachi 163 or Shimadzu 8A gas chromatograph equipped with a thermal conductivity detector using a 1 m × 3 mm column packed with 15% Silicone SE 30 on Celite 545 (60—80 mesh).

Preparation of 2,2,6,6-Tetramethyl-2,6-disilapiperidine (3)——1,2-Bis(trimethylsilyl)propane was prepared first by hydrosilylation of allyltrimethylsilane with methyldichlorosilane catalyzed by chloroplatinic acid (71%),[8] followed by methylation with methylmagnesium bromide (87%). Chlorodemethylation with chlorotrimethylsilane–aluminum chloride (87%)[5] gave 1,3-bis(chlorodimethylsilyl)propane,[5] which was treated with ammonia in ether to give **3** (67%), according to a procedure similar to that described in the literature.[9] bp 55—56 °C (21 Torr, 1 Torr = 133.322 Pa). Similarly, **4** was prepared from 1,2-bis(chlorodimethylsilyl)ethane[10] in 57% yield. bp 61—65 °C

(60 Torr) (lit.[10]) bp 141 °C). All other materials are commercially available and were used after drying. 2,2,5,5-Tetramethyl-2,5-disilapyrrolidine (**4**) was also prepared according to methods similar to those described in the literature.[11])

Alkylation of Disilylamines (3): General Procedure——Disilylamide (**3**) (2.0 mmol) in THF (5 ml) was added to a suspension of potassium hydride (2.3 mmol) in THF (7 ml) under an argon atmosphere, with stirring at room temperature. After 30 min, an alkyl halide (2.3 mmol) was added and the mixture was heated at reflux for 3—5 h. The solvent was removed under reduced pressure, and the alkylated disilylamine (**7**) was obtained by distillation (Kugelrohr). After hydrolysis of **7** with 1 M HCl at reflux for 8 h followed by ether extraction of organic materials, the solution was made alkaline with aqueous NaOH and the product was extracted with ether. The solvent was removed by evaporation and pure **1** was obtained by distillation (Kugelrohr) of the residue.

^{1}H-NMR δ (CCl_4), ^{13}C-NMR δ ($CDCl_3$), IR ν_{max} (liquid film) cm^{-1} and low (LRMS) or high (HRMS) resolution mass (*m/z*) spectral data are given below.

2,2,6,6-Tetramethyl-2,6-disilapiperidine (**3**): ^{1}H-NMR δ: 0.09 (12H, s, CH_3), 0.60 (4H, t, $J=7$ Hz, C–CH_2–N), 1.65—2.15 (2H, m, C–CH_2–C). IR: 3390, 2960, 2860, 1420, 1260, 1170, 1040, 955, 925, 860, 810, 700, 670, 630 cm^{-1}. LRMS *m/z*: 173 (M^+, 21), 158 (100), 130 (38), 100 (27), 86 (10).

2,2,5,5-Tetramethyl-2,6-disilapyrrolidine (**4**): ^{1}H-NMR δ: 0.07 (12H, s, CH_3), 0.73 (4H, s, CH_2). IR: 3420, 2950, 1420, 1250, 1100, 870, 780 cm^{-1}. LRMS *m/z*: 159 (M^+, 6), 146 (10), 145 (27), 144 (100), 117 (13), 116 (27), 100 (10), 73 (13), 64 (7), 59 (7).

N-Ethyl-2,2,6,6-tetramethyl-2,6-disilapiperidine (**7a**): bp 90—150 °C (30 Torr, Kugelrohr). ^{1}H-NMR δ: 0.13 (12H, s, Si–CH_3), 0.70 (4H, t, $J=7$ Hz, Si–CH_2), 1.13 (3H, t, $J=7$ Hz, C–CH_3), 1.73—2.06 (2H, m, C–CH_2–C), 2.90 (2H, q, $J=7$ Hz, C–CH_2–N). IR: 2960, 2900, 1440, 1410, 1370, 1310, 1260, 1160, 1100, 1070, 1030, 930, 840, 780, 680 cm^{-1}. LRMS *m/z*: 202 (2), 201 (M^+, 9), 188 (9), 187 (20), 186 (100), 158 (11), 100 (6), 73 (9), 59 (15). HRMS *m/z* Calcd for $C_9H_{23}NSi_2$: 201.1367. Found: 201.1349.

N-Propyl-2,2,6,6-tetramethyl-2,6-disilapiperidine (**7b**): bp 120—140 °C (24 Torr, Kugelrohr). ^{1}H-NMR δ: 0.10 (12H, s, Si–CH_3), 0.67 (4H, t, $J=7$ Hz, Si–CH_2), 0.90 (3H, t, $J=7$ Hz, C–CH_3), 1.48 (2H, qt, $J=7$, 7 Hz, C–CH_2–C), 1.67—2.00 (2H, m, Si–C–CH_2–C), 2.70 (2H, t, $J=7$ Hz, C–CH_2–N). IR: 2960, 2900, 2860, 1460, 1410, 1250, 1170, 1090, 1030, 1000, 950, 910, 860, 840, 800, 780, 680 cm^{-1}. LRMS *m/z*: 215 (M^+, 3), 200 (15), 188 (9), 187 (20), 186 (100), 73 (7), 59 (11). HRMS *m/z* Calcd for $C_{10}H_{25}NSi_2$: 215.1526. Found: 215.1532.

N-Butyl-2,2,6,6-tetramethyl-2,6-disilapiperidine (**7c**): bp 80—140 °C (3 Torr, Kugelrohr). ^{1}H-NMR δ: 0.04 (12H, s, Si–CH_3), 0.60 (4H, t, $J=7$ Hz, Si–CH_2), 0.93 (3H, t, $J=7$ Hz, C–CH_3), 1.11—1.61 (4H, m, C–$(CH_2)_2$–C), 1.62—1.96 (2H, m, Si–C–CH_2–C), 2.70 (2H, t, $J=8$ Hz, C–CH_2–N). IR: 2930, 2870, 2850, 1250, 1080, 900 cm^{-1}. LRMS *m/z*: 229 (M^+, 5), 214 (9), 186 (100), 73 (86), 59 (10). HRMS *m/z* Calcd for $C_{11}H_{27}NSi_2$: 229.1680. Found: 229.1167.

N-Octyl-2,2,6,6-tetramethyl-2,6-disilapiperidine (**7d**): bp 100—180 °C (1 Torr, Kuelrohr). ^{1}H-NMR δ: 0.04 (12H, s, Si–CH_3), 0.65 (4H, t, $J=7$ Hz, Si–CH_2), 0.96 (3H, t, $J=7$ Hz, C–CH_3), 1.10—1.60 (12H, m, C–$(CH_2)_6$–C), 1.63—1.95 (2H, m, Si–C–CH_2–C), 2.74 (2H, t, $J=8$ Hz, C–CH_2–N). ^{13}C-NMR δ: 0.07 (q), 14.03 (q), 17.75 (t), 22.65 (t), 27.48 (t), 29.51 (t), 31.86 (t), 17.75 (t), 22.65 (t), 27.48 (t), 29.51 (t), 31.86 (t), 44.32 (t). IR: 2940, 2860, 1470, 1260, 1100, 930 cm^{-1}. LRMS *m/z*: 285 (M^+, 3), 270 (5), 186 (100), 73 (4), 59 (6). HRMS *m/z* Calcd for $C_{15}H_{35}NSi_2$: 285.2306. Found: 285.2298.

N-Benzyl-2,2,6,6-tetramethyl-2,6-disilapiperidine (**7e**): bp 100—190 °C (1 Torr, Kugelrohr). ^{1}H-NMR δ: 0.00 (12H, s, Si–CH_3), 0.70 (4H, t, $J=7$ Hz, Si–CH_2), 1.70—2.05 (2H, m, Si-C–CH_2), 3.99 (2H, s, N–CH_2), 7.17 (5H, s, Ph). IR: 3020, 2920, 2900, 2850, 1450, 1250, 695 cm^{-1}. LRMS *m/z*: 263 (M^+, 20), 248 (100), 186 (8), 73 (7), 59 (12). HRMS *m/z* Calcd for $C_{14}H_{25}NSi_2$: 263.1523. Found: 263.1528.

N-*p*-Methylbenzyl-2,2,6,6-tetramethyl-2,6-disilapiperidine (**7f**): bp 100—200 °C (0.7 Torr, Kugelrohr). ^{1}H-NMR δ: 0.07 (12H, s, Si–CH_3), 0.80 (4H, t, $J=7$ Hz, Si–CH_2), 1.80—2.13 (2H, m, Si–C–CH_2–C), 2.43 (3H, s, *p*-CH_3), 4.05 (2H, s, N–CH_2), 7.00—7.27 (4H, m, Ar-H). IR 3020, 2900, 2850, 1450, 1250, 695 cm^{-1}. LRMS *m/z*: 263 (M^+, 20), 248 (100), 186 (8), 73 (7), 59 (12). HRMS *m/z* Calcd for $C_{15}H_{27}NSi_2$: 277.1681. Found: 277.1674.

N-Butyl-2,2,5,5-tetramethyl-2,5-disilapyrrolidine (**8a**): bp 120—190 °C (23 Torr, Kugelrohr). ^{1}H-NMR δ: 0.06 (12H, s, Si–CH_3), 0.70 (4H, s, Si–CH_2), 0.94 (3H, t, $J=7$ Hz, C–CH_3), 1.10—1.90 (4H, m, $(CH_2)_2$), 2.79 (2H, $J=7$ Hz, N–CH_2). IR: 2960, 2930, 2860, 1470, 1380, 1260, 1160, 1040, 970, 900, 800 cm^{-1}. LRMS *m/z*: 215 (M^+, 3), 200 (11), 174 (8), 173 (19), 172 (100), 145 (8), 117 (9), 72 (12), 59 (14). HRMS *m/z* Calcd for $C_{10}H_{25}NSi_2$: 215.1526. Found: 215.1526.

N-Octyl-2,2,5,5-tetramethyl-2,5-disilapyrrolidine (**8b**): bp 90—150 °C (1 Torr, Kugelrohr). ^{1}H-NMR δ: 0.07 (12H, s, Si–CH_3), 0.73 (4H, s, Si–CH_2), 0.94 (3H, t, $J=7$ Hz, C–CH_3), 1.10—1.70 (12H, m, $(CH_2)_6$), 2.79 (2H, t, $J=7$ Hz, N–CH_2). IR: 2920, 2850, 1460, 1250, 1140, 1040 cm^{-1}. LRMS *m/z*: 21 (M^+, 1), 256 (5), 198 (3), 174 (8), 173 (18), 172 (100), 117 (2), 73 (9), 59 (9). HRMS *m/z* Calcd for $C_{14}H_{33}NSi_2$: 271.2150. Found: 271.2150.

Hydrolysis of 7d——A mixture of **7d** (1.08 g, 3.8 mmol) and 1 M HCl (10 ml) was heated in a 50 ml flask at reflux temperature for 8 h with stirring. Hydrochloric acid and ether (20 ml) were added, and the organic layer was removed. The aqueous layer was made alkaline with 25% sodium hydroxide and extracted with ether. After drying of the extract over sodium sulfate, the solvent was evaporated off and the residue was distilled in a Kugelrohr apparatus. *n*-

Octylamine (0.410 g, 3.2 mmol) was obtained in 84% yield. bp 80—120 °C (78 Torr). ^{1}H-NMR (CCl_4) δ: 0.90 (3H, t, J=7 Hz, CH_3), 1.10—1.60 (12H, m, $-(CH_2)_6-$), 2.45—2.80 (2H, m, N-CH_2). Similarly *N*-benzyl-*N′*-phenylurea (0.153 g, 0.68 mmol) was obtained from **3e** (0.189 g, 0.72 mmol) in 94% yield, after hydrolysis and successive treatment with phenylisocyanate (0.119 g, 1.0 mmol). mp 166—167 °C. *Anal.* calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; H, 12.38. Found: C, 74.29; H, 6.23; N, 12.27.

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