Aminosilylation of aldehydes mediated by lithium perchlorate: novel method for synthesis of α-silylamines

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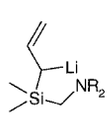
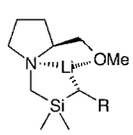
α-Silylated *N*,*N*-dialkylamines **7a**–**k** were easily synthesized in good to excellent yields from aldehydes **1**, (trimethylsilyl)dialkylamines **2**, and phenyldimethylsilyllithium **4**, diphenylmethylsilyllithium **5**, or triphenylsilyllithium **6**, in concentrated ethereal lithium perchlorate solution.

Introduction

Development of new synthetic methods for the preparation of organosilicon compounds continues to attract much attention. Organosilylmetallic compounds are useful reagents for constructing silicon–carbon bonds.[1,2] For many years alkylarylsilyllithium compounds have been used as nucleophiles for introducing a silyl group into a wide range of organic structures.[3] On the other hand, α-silylamines are important reagents in organic synthesis. For example, lithiated allylaminosilanes of the type A show high regioselectivity in addition reactions[4,5]



A



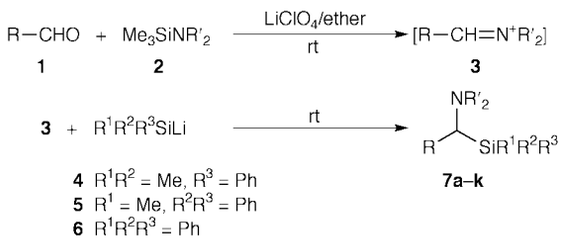
B

and chiral (lithiomethyl)aminosilanes of the type B induce high diastereoselectivity in these reactions.[6] α-Silylamines were also reacted with aldehydes in the synthesis of β-amino alcohols.[7] Despite these interesting and important applications, only a few methods are reported for preparing these compounds, such as, reaction of amides with lithiated silanes,[8–11] amination of α-bromoalkylsilanes,[7,12] reaction of Grignard reagents with α-amino-α-cyanoalkylsilanes,[13] reductive silylation of imines,[14] reaction of lithiosilanes with methyleneiminium salts,[15] and reaction of lithiomethylamines with chlorosilanes.[16] These methods suffer from the difficulty of preparing the starting materials, low yields, or are restricted to aminomethylation of silanes.

In this paper, we describe the one-pot three-component synthesis of a variety of α-silylated *N*,*N*-dialkylamines **7a**–**k** by the addition of phenyldimethylsilyllithium **4**, diphenylmethylsilyllithium **5**, or triphenylsilyllithium **6**, to aldehydes **1**, (enolizable and non-enolizable) and (trimethylsilyl)dialkylamines **2**, in a 5 M ethereal $LiClO_4$ solution.

Results

Aldehyde **1**, (trimethylsilyl)dialkylamines **2**, and organosilyllithium compounds in a 5 M ethereal $LiClO_4$ solution, followed by aqueous work-up, leads to the formation of α-silylated *N*,*N*-dialkylamines **7a**–**k**, within 30 min in good to excellent yields (Scheme 1). Therefore, reaction of dimethylphenylsilyl-, diphenylmethylsilyl-, or triphenylsilyllithium proceeds smoothly in the same manner, to give the corresponding α-silyl amines.



Scheme 1

Presumably due to the Lewis acidity of lithium ions and the high polarity of the medium, the reaction of **2** with aldehydes in a 5 M lithium perchlorate diethyl ether solution leads to the formation of an iminium salt **3** as the intermediate,[17,18] which is trapped *in situ* by the organosilyllithium nucleophiles. Due to the mild reaction conditions, no by-products are formed.

This protocol can also be applied to enolisable aldehydes such as isobutyraldehyde, but the yields are lower for these aldehydes. In these cases, the yield of the reaction is lowered by the formation of enamine as side-product in the iminium ion formation step. The results are summarized in Table 1.

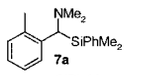
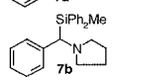
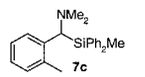
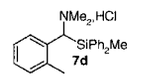
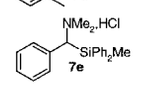
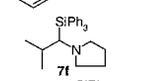
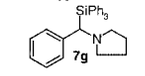
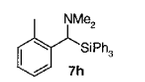
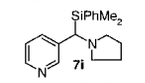
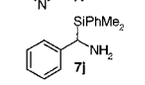
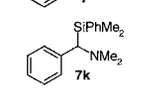
To extend this method for the preparation of α-trimethylsilylamines, hexamethyldisilane was treated with methyllithium solution in ether in HMPT, according to the procedure described in the literature.[19] The resulting red solution was added to the *in situ* preformed iminium salts **3**. After aqueous work-up, in contrast to the above results, no α-trimethylsilylamine could be detected as the product, but instead, compound **8** was isolated as the sole product in good yield. The reaction was carried out with benzaldehyde and (*o*-methyl)benzaldehyde several times, and the same results were obtained with 80 and 75% yields, respectively. Compound **8a** and **8b** were identified to be phosphonic diamide, by their ^{1}H-, ^{13}C-NMR, IR and MS spectra by comparison with those in the literature for **8a** (Scheme 2).[20]

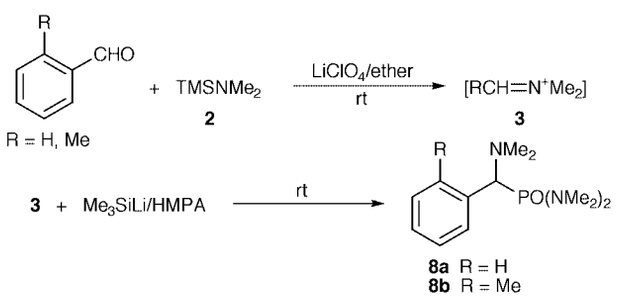
Therefore, this procedure can serve as a new method for the preparation of α-dialkylamino phosphonic diamides, **8**.

Experimental

Elemental Analysis: Carlo Erba Model 1104. IR spectra were

Table 1 α-Aminosilylation of aldehydes

Entry	Starting aldehyde	α-Silyl amine	Yield (%)
1		 **7a**	74
2		 **7b**	95
3		 **7c**	95
4		 **7d**	83
5		 **7e**	70
6		 **7f**	50
7		 **7g**	80
8		 **7h**	70
9		 **7i**	76
10		 **7j**	80[22]
11		 **7k**	85



Scheme 2

taken on Bruker IFS 25 and Matt Son 1000 Unicam FTIR spectrophotometers. ^{1}H and ^{13}C NMR were recorded on Bruker AM 400, AC 200 and AC 80 spectrometers in $CDCl_3$. Mass spectra were obtained on Varian MAT 311A, Varian MAT 111 or Fisson 800 Trio spectrometers. $LiClO_4$ (Fluka) was dried at 140 °C for 24 h at 10^{-2} Torr. The silyllithium nucleophiles were prepared according to the procedure reported in the literature.[2,21,22]

CAUTION: Although we did not have any accident using lithium perchlorate ($LiClO_4$), it is advisable to dry lithium perchlorate in a hood behind a lab-shield.

General procedure for the preparation of α-silylamines from aldehydes

The aldehyde (2 mmol) and 4 ml of 5 M $LiClO_4$ in diethyl ether were placed in a 50 ml flask under argon and stirred for 5 min. (Trimethylsilyl)dialkylamine (3 mmol) was then added *via* syringe. After 10 min the silyllithium nucleophile (3 mmol) was added and stirred for 15 min at room temperature. Then, water (about 30 ml) and diethyl ether (30 ml) were added. The organic phase was separated, dried with $MgSO_4$, and the solvent was removed by means of rotary evaporator. The crude material was further purified by chromatography on basic alumina or aqueous acid extraction, if needed.

(Dimethylphenylsilyl)(o-methylphenyl)-*N*,*N*-dimethylmethanamine 7a[23]

Oil; IR ν_{max} (film)/cm^{-1} 1248.4 (Si-Me), 1111.2 (Si-Ph). δ_H 0.01 (s, 3H), 0.47 (s, 3H), 2.19 (s, 9H, Ph*Me*, N*Me*$_2$), 3.27 (s, 1H), 7.00–7.51 (m, 9H). δ_C −4.57 (CH_3), −2.06 (CH_3), 20.38 (CH_3), 47.10 (CH_3), 61.56 (CH), 125.18 (CH), 125.95 (CH), 127.51 (CH), 128.11 (CH), 128.70 (CH), 130.06 (CH), 133.80 (CH), 135.00 (C), 139.08 (C), 140.93 (C). MS (70 eV) *m*/*z* (%) 283 (M^+, 1.8), 149 (12.5), 148 (100), 137 (5.4), 135 (3), 105 (6.6). $C_{18}H_{25}NSi$, *M* 283.

(Diphenylmethylsilyl)phenyl(pyrrolidino)methane 7b

Oil; IR ν_{max} (film)/cm^{-1} 1426.9 (s), 1248.6 (Si-Me), 1110.8 (Si-Ph). δ_H 0.41 (s, 3H), 1.57–1.67 (m, 4H), 2.32–2.45 (m, 4H), 3.44 (s, 1H), 7.00–7.80 (m, 15H). δ_C −4.38 (CH_3), 23.46 (CH_2), 55.49 (CH_2), 63.98 (CH), 125.43 (CH), 127.36 (CH), 127.68 (CH), 127.72 (CH), 128.50 (CH), 128.72 (CH), 129.24 (CH), 134.72 (CH), 135.35 (C), 135.41 (CH), 137.63 (C), 142.26 (C). MS (70 eV) *m*/*z* (%) 357 (M^+, 1.3), 199 (2.3), 197 (2.9), 161 (13.0), 160 (100), 91 (10.7). $C_{24}H_{27}NSi$, calcd. 357.1913; found 357.1907 (HRMS). $C_{24}H_{27}NSi$ (357.2): calcd. C 80.66, H 7.56, N 3.92; found C 80.65, H 7.68, N 4.11%.

(Diphenylmethylsilyl)(o-methylphenyl)-*N*,*N*-dimethylmethanamine 7c[23]

Mp 84–85 °C. IR ν_{max} (KBr)/cm^{-1} 1250.7 (s, Si-Me), 1067.9 (s, Si-Ph). δ_H 0.50 (s, 3H), 1.90 (s, 3H), 2.20 (s, 6H), 3.60 (s, 1H), 6.8–7.8 (m, 14H). δ_C −5.17 (CH_3), 20.16 (CH_3), 47.42 (CH_3), 60.42 (CH), 125.33 (CH), 125.87 (CH), 127.10 (CH), 127.79 (CH), 128.55 (CH), 128.67 (CH), 129.24 (CH), 130.05 (CH), 134.95 (CH), 135.11 (CH), 135.56 (C), 136.16 (C), 136.99 (C), 140.17 (C). MS (70 eV) *m*/*z* (%) 345 (M^+, 1.4), 197 (2.2), 149 (11.5), 148 (100), 132 (2.7), 118 (1.5). $C_{23}H_{27}NSi$, *M* 345.

(Diphenylmethylsilyl)(o-methylphenyl)-*N*,*N*-dimethylmethanamine, hydrochloride 7d[23]

Mp 189 °C (decomposed). IR ν_{max} (KBr)/cm^{-1} 1428 (s), 1265 (s, Si-Me), 1106 (s, Si-Ph), 792 (s), 736 (s), 700 (s). δ_H 1.20 (s, 3H), 0.47 (s, 3H), 1.82 (s, 3H), 2.66 (dd, 6H, *J* 4.3, 15.5 Hz), 4.38 (d, 1H, *J* 9.8 Hz), 6.7–8.3 (m, 14H), 12.1–12.4 (br, 1H, N^+H). δ_C −6.30 (CH_3), 19.85 (CH_3), 44.88 (CH_3), 46.22 (CH_3), 61.05 (CH), 127.36 (CH), 127.70 (CH), 128.24 (CH), 128.67 (CH), 128.90 (CH), 129.80 (CH), 130.67 (CH), 130.93 (CH), 131.83 (C), 132.29 (C), 133.56 (C), 134.66 (CH), 135.07 (CH), 135.76 (C).

(Diphenylmethylsilyl)phenyl-*N*,*N*-dimethylmethanamine, hydrochloride 7e

Mp 188 °C. δ_H 1.00 (s, 3H), 2.55 (d, 3H), 2.65 (d, 3H), 4.90 (d, 1H), 7.0–7.6 (m, 13H), 7.0 (m, 2H), 12.35 (br, 1H). δ_C −6.18 (CH_3), 45.14 (CH_3), 46.16 (CH_3), 66.47 (CH), 127.74 (CH), 128.28 (CH), 128.83 (CH), 129.16 (CH), 129.31 (CH), 129.84 (CH), 130.66 (CH), 132.42 (CH), 133.23 (C), 133.36 (C), 134.71 (C), 134.73 (CH). $C_{22}H_{26}ClNSi$, calcd. C 71.79, H 7.13; found C 71.70, H 7.13%.

1-(Triphenylsilyl)-2-methyl-1-(pyrrolidino)propane 7f

Oil; IR ν_{max} (film)/cm^{-1} 1106.9 (Si-Ph). δ_H 0.91 (d, 6H, *J* 6.4 Hz), 1.58 (m, 4H), 2.36 (m, 1H), 2.70 (m, 4H), 3.05 (d, 1H, *J* 6.8 Hz) 7.20–7.70 (m, 15H). δ_C 22.38 (CH_3), 23.94 (CH_3), 24.68 (CH_2), 30.30 (CH), 52.45 (CH_2), 57.57 (CH), 127.49 (CH), 128.92 (C), 136.43 (CH). MS (70 eV) *m*/*z* (%) 385 (M^+), 342 (1.4), 276

(33.1), 259 (16.5), 199 (65.8), 181 (8.1), 126 (100), 77 (10.4). $C_{26}H_{31}NSi$, *M* 385.

(Triphenylsilyl)phenyl(pyrrolidino)methane 7g

Mp 142–144 °C. IR ν_{max} (KBr)/cm^{-1} 1428 (m), 1101.5 (m, Si-Ph), 697 (s), 525 (s). δ_H 1.71–1.61 (m, 4H), 2.30–2.48 (m, 4H), 3.71 (s, 1H), 6.97–7.44 (m, 20H). δ_C 23.50 (CH_2), 55.80 (CH_2), 63.90 (CH), 125.56 (CH), 127.45 (CH), 127.74 (CH), 129.15 (CH), 129.21 (CH), 134.59 (CH), 136.53 (C), 141.91 (C). MS (70 eV) *m*/*z* (%) 419 (M^+), 259 (3), 181 (2), 160 (100), 91 (6). $C_{29}H_{29}NSi$ (419.2) calcd. C 83.05, H 6.91, N 3.34; found C 83.13, H 7.01, N 3.54%.

(Triphenylsilyl)(*o*-methylphenyl)-*N*,*N*-dimethylmethanamine 7h[23]

Mp 148–150 °C. IR ν_{max} (KBr)/cm^{-1} 1484.9 (m), 1427.3 (s), 1105.9 (s, Si-Ph), 745.6 (s), 700.8 (s). δ_H 1.73 (s, 3H), 2.25 (s, 6H), 3.87 (s, 1H), 6.75–7.77 (m, 19H). δ_C 19.98 (CH_3), 48.14 (CH_3), 61.05 (CH), 125.43 (CH), 125.97 (C), 127.43 (CH), 129.22 (CH), 129.90 (CH), 134.57 (C), 136.25 (C), 136.50 (CH), 139.93 (C). MS (70 eV) *m*/*z* (%) 407 (M^+), 259 (3), 181 (2), 148 (100), 132 (3), 105(4). $C_{28}H_{29}NSi$ (407).

(Dimethylphenylsilyl)(pyridin-3-yl)(pyrrolidino)methane 7i[11]

Oil; δ_H 0.23 (s, 6H), 1.53 (m, 4H), 2.36 (m, 4H), 3.86 (s, 1H), 7.00–9.35 (m, 9H). MS (70 eV) *m*/*z* (%) 332 (M^+, hydrochlorate salt), 161 (100), 135 (80).

(Dimethylphenylsilyl)phenylmethanamine 7j[11]

Oil; δ_H 0.21 (s, 6H), 1.35 (br s, 2H), 2.36 (s, 3H), 4.70 (s, 1H), 7.00–7.83 (m, 9H). δ_C −1.52 (CH_3), 21.18 (CH_3), 64.68 (CH), 126.76 (CH), 127.14 (CH), 128.77 (CH), 129.51 (CH), 133.14 (C), 133.57 (C), 134.23 (C).

(Dimethylphenylsilyl)phenyl-*N*,*N*-dimethylmethanamine 7k[11]

Oil; δ_H 0.31 (s, 6H), 2.16 (s, 6H), 4.63 (s, 1H), 7.28–8.00 (m, 10H).

[Bis(dimethylamino)phosphoryl](*o*-methylphenyl)-*N*,*N*-dimethylmethanamine 8b

Mp 79–81 °C. IR ν_{max} (KBr)/cm^{-1} 1204.1 (P=O), 978.5. δ_H 2.17 (d, 3H, $J_{P\text{-}H}$ 8.5 Hz), 2.29 (s, 6H), 2.31 (s, 3H), 2.66 (d, 6H, $J_{P\text{-}H}$ 9.09 Hz), 4.21 (d, 1H, $J_{P\text{-}H}$ 18.4 Hz), 7.81–7.08 (m, 4H). δ_C 20.28 (CH_3), 36.09 (CH_3), 36.13 (CH_3), 36.63 (CH_3), 36.65 (CH_3), 43.13 (CH_3), 43.22 (CH_3), 59.68 (CH), 60.99 (CH), 125.25 (CH), 127.38 (CH), 130.49 (CH), 130.87 (CH), 130.90 (CH), 131.77 (CH), 131.81 (CH), 136.88 (CH), 136.98 (C). MS (70 eV) *m*/*z* (%) 283 (M^+), 198 (100), 132 (2.9), 105 (3.3), 91 (1.5), 44 (4.2), 126 (100), 77 (10.4). $C_{14}H_{26}N_3OP$, *M* 283.

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