ELSEVIER

Journal of Organometallic Chemistry 633 (2001) 131–136

Journal of Organometallic Chemistry

www.elsevier.com/locate/jorganchem

Reactions of lithium silenolates with benzophenone

Joji Ohshita [a],*, Hideaki Sakurai [a], Shin Masaoka [a], Mamiko Tamai [a],
Atsutaka Kunai [a],*, Mitsuo Ishikawa [b]

[a] *Department of Applied Chemistry, Graduate School of Engineering, Hiroshima University, Higashi-Hiroshima 739-8527, Japan*
[b] *Department of Chemical Technology, Kurashiki University of Science and Arts, 2640 Nishinoura, Tsurashima, Kurashiki 712-8505, Japan*

Received 18 April 2001; received in revised form 21 June 2001; accepted 25 June 2001

Abstract

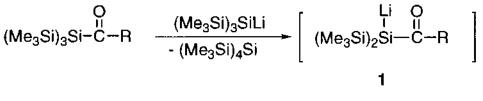
The reactions of lithium silenolates $(Me_3Si)_2LiSiCOR$ (R = OCy, OAd, Mes) with benzophenone afforded 1,3-dioxa-2-silacyclopentanes as the major products. The crystal structure of a 1,3-dioxa-2-silacyclopentane was determined by an X-ray diffraction study. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Enolate; Silyllithium; Carbonyl compounds

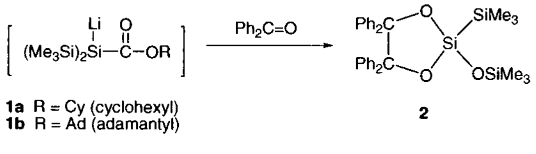
1. Introduction

There has been current interest in the chemistry of functionalized silyllithiums whose reactions with electrophiles would provide direct methods leading to functionalized organosilicon compounds [1]. Recently, we have demonstrated that interactions of acyltris(trimethylsilyl)silanes [2] and tris(trimethylsilyl)silanecarboxylates [3] with tris(trimethylsilyl)silyllithium give the corresponding lithium silenolates (**1**), by replacement of a trimethylsilyl group with lithium (Scheme 1). Silenolates **1** are silicon analogs of lithium enolates and allow numerous transformations. They react readily with electrophiles, such as water, chlorosilanes, and alkyl halides to give substitution products [2–4]. The reactions of **1** with dienes produced cyclic adducts, lithium 6,6-bis(trimethylsilyl)-6-silacyclohex-3-en-1-olate derivatives almost quantitatively at −40 °C, which undergo subsequent Peterson-type reaction producing the corresponding silacyclohexadienes at higher temperature [5]. Treatment of **1** with $PdCl_2$ produces oxidative coupling products as the first example of polysilanes with two Si–carbonyl groups linked by a silicon bridge [3,6].

We have also demonstrated that the reactions of **1** with aldehydes and acetophenone give products which can be explained by assuming the intermediates arising from the nucleophilic addition of **1** across the C=O bond [3,7]. In this paper, we report the reactions of lithium silenolates with benzophenone, which proceeded in a different fashion from those with aldehydes and acetophenone, to afford 1,3-dioxa-2-silacyclopentanes as the major products.



Scheme 1.



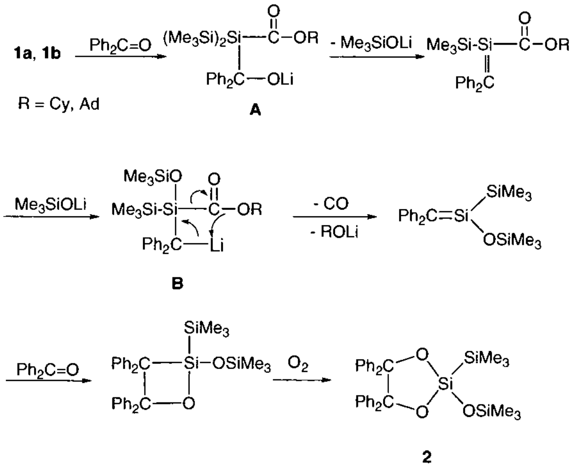
Scheme 2.

---

* Corresponding authors. Present address: Institute of Fundamental Research of Organic Chemistry, Kyushu University, Fukuoka 812-8581, Japan.

E-mail addresses: johshita@ms.ifoc.kyushu-u.ac.jp (J. Ohshita), akunai@hiroshima-u.ac.jp (A. Kunai).

0022-328X/01/$ - see front matter © 2001 Elsevier Science B.V. All rights reserved.
PII: S0022-328X(01)01071-3



Scheme 3.

2. Results and discussion

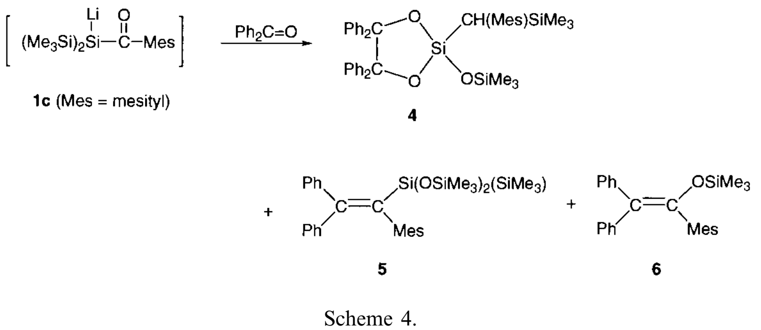
2.1. Reactions of lithium silenolates with benzophenone

Reactions of lithium ester silenolates **1a** and **1b** with 2.2 equivalents of benzophenone in THF at −80 °C gave 4,4,5,5-tetraphenyl-2-trimethylsiloxy-2-trimethylsilyl-1,3-dioxa-2-silacyclopentane (**2**) in 55 and 31% yields, respectively (Scheme 2). In addition, many unidentified minor products were detected in less than 10% each by GC–MS analysis of the reaction mixtures. The structure of **2** was confirmed by spectroscopic analysis and elemental analysis. The ^{1}H- and ^{13}C-NMR spectra indicated the presence of two kinds of phenyl groups and the ^{29}Si-NMR spectrum revealed three resonances including one at −34.0 ppm, which is slightly high field shifted from the standard values of trialkoxy-substituted silicons [8], due to the trimethylsilyl subsitution. The formation of product **2** may be best explained as shown in Scheme 3, involving the formation of lithium alkoxides **A** by addition of silenolates **1a** and **b** across the C=O bond of benzophenone as the initial step. Intermediates **A** undergo Peterson-type reaction producing silene intermediates [9], which react with Me_3SiOLi to give carbanions **B**. Simultaneous elimination of a lithium alkoxide and carbon monoxide from **B** gives a silene intermediate which adds to benzophenone producing a silaoxetane intermediate. Finally, the oxidation of the silaoxetane during work-up of the reaction mixtures would afford compound **2** In fact, AdOH was detected by GC–MS of the reaction mixture of **1b** with benzophenone, after hydrolysis. Formation of carbon monoxide in the present reactions was detected by the GC analysis of the reaction mixtures. Attempted detection of the silaoxetane intermediate by GC–MS was unsuccessful. Although some of silaoxetane derivatives have been isolated [10] or spectroscopically detected [11], it is true that they are unstable unless protected by sterically bulky substituents.

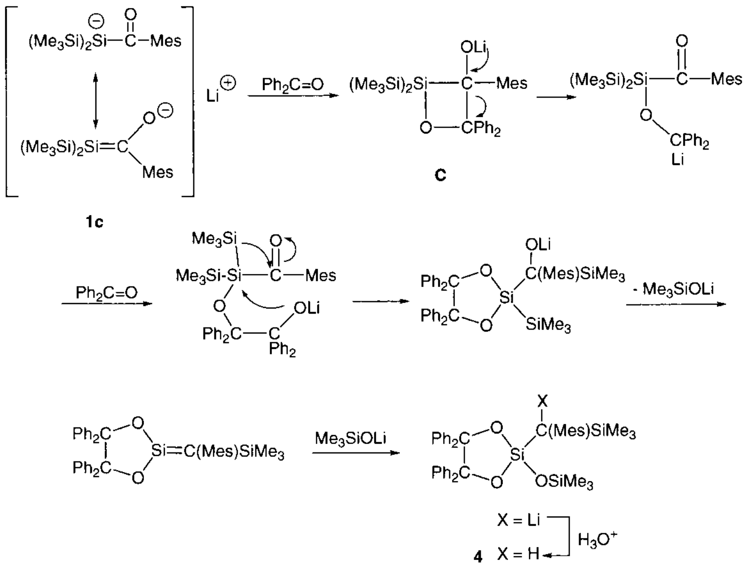
In a previous paper, we have reported that **1a** reacts with mesitaldehyde giving a carbanion intermediate analogous to **B** which is trapped by methyl iodide [3]. However, in the present reactions, no 1:1 adducts of silenolates and benzophenone were separated from the reaction mixture even when quenched by methyl iodide at low temperature. The reaction of **1b** with 1.5 equivalents of benzophenone under the same conditions, again gave **2** in 36% yield, together with a 30% of diphenylmethoxytris(trimethylsilyl)silane ($Ph_2CHOSi(SiMe_3)_3$, **3**). However, to date, there have been no data obtained to propose the reaction pathway leading to **3**.

The reaction of lithium silenolate **1c** with benzophenone in excess afforded 4,4,5,5-tetraphenyl-2-trimethylsiloxy-2-mesityl(trimethylsilyl)methyl-1,3-dioxa-2-silacyclopentane (**4**) in 33% yield (Scheme 4). In this reaction, compounds **5** and **6** were also obtained in 12 and 8% yields, respectively. Again, many unidentified products, including one in 7% yield whose mass spectrum showed the parent signal at *m*/*z* 386, identical with that of compound **6**, were detected by GC–MS analysis of the reaction mixture.

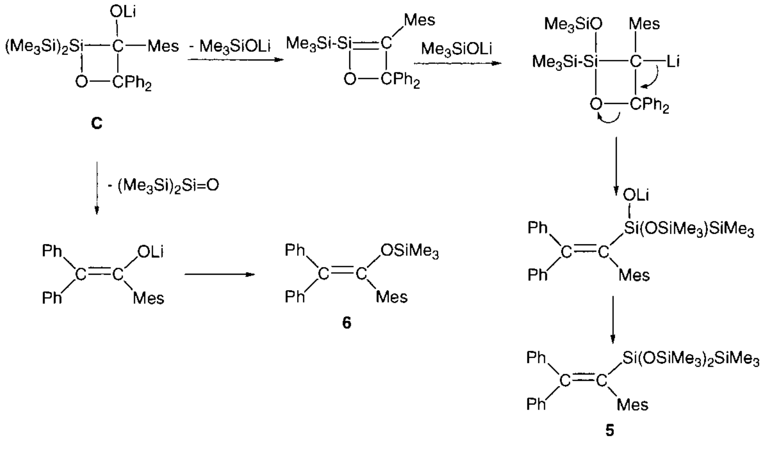
Scheme 5 represents a possible mechanistic interpretation for the formation of **4**, involving cycloaddition of **1c** with benzophenone producing a silaoxetane intermediate **C** as the initial step. Siloxetane **C** undergoes ring opening giving a carbanion, whose reaction with benzophenone, followed by ring closure accompanied with a 1,2-silyl shift, would form a siladioxacyclopentane system. Peterson-type silene formation and addition of Me_3SiOLi to the silene produces a carbanion which is



Scheme 4.



Scheme 5.



Scheme 6.

hydrolyzed to give **4**. Products **5** and **6** can be understood also by assuming silaoxetane intermediate **C** as shown in Scheme 6. Peterson-type silene formation from **C**, followed by the addition of Me_3SiOLi to the silene gives a carbanion. The carbanion would undergo ring opening leading to a lithium silanolate which may abstract trimethylsilyl group from any of the trimethylsilyl sources, giving compound **5**. Product **6** may be explained by [2 + 2] cycloreversion of **C** giving lithium diphenylmesitylenolate. To know more about the reaction mechanism, we attempted to trap any of the intermediates. However, even when **1c** was treated with a mixture of benzophenone and chlorotriethylsilane at − 80 °C, compound **4** was obtained as the major product.

Nucleophilic addition, giving key intermediates analogous to **A**, is generally the initial step for the reactions of lithium silenolates with carbonyl compounds [3,7]. In marked contrast to this, the reaction of **1c** with benzophenone gave products, all of which can be explained by assuming intermediate **C** arising from [2 + 2] cycloaddition of the reactants. Similar reaction has been reported for the reaction of **1c** with mesitaldehyde, which gives a 14% of a product via an intermediate analogous to **C**. In this reaction, the nucleophilic addition of **1c** to the C=O bond of mesitaldehyde proceeds as the major route and a 61% combined yield of products probably arising from an intermediate analogous to **A** are also obtained. Presumably, less hindered mesitaldehyde would tend to undergo nucleophilic addition, rather than cycloaddition. In fact, the reaction of even less hindered benzaldehyde gives only the products which may be best explained by assuming the intermediate analogous to **C** [7].

That the nature of the substituent on the carbonyl carbon of silenolates significantly affects the chemical behavior of silenolates, has been often observed [2,3,5,7]. This is due to the difference of the electronic states of the lithium silenolates depending on the substituent. Higher sp^2 character of the center Si–C bond and lower degree of localization of anionic charge on the center silicon atom in **1c** relative to **1a** and **b** have been demonstrated on the basis of their NMR spectral data [2,3], which seem to facilitate the [2 + 2] cycloaddition reaction.

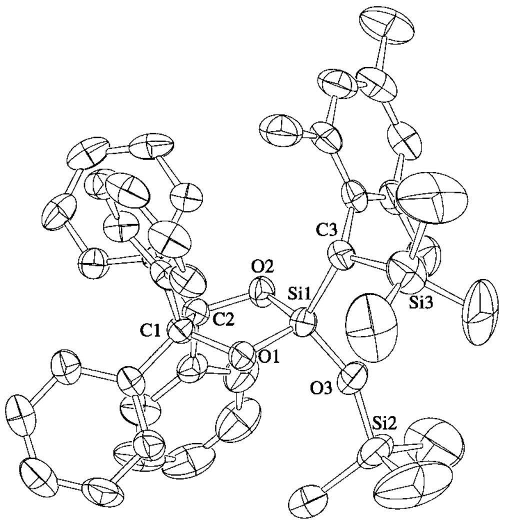


Fig. 1. ORTEP drawing of compound **4**. Protons are omitted for clarity. Thermal ellipsoids are drawn at 50% probability.

Table 1
Crystal data, experimental conditions, and summary of structural refinement for compound **4**

Compound	**4**
Molecular formula	$C_{42}H_{50}O_3Si_3$
Molecular weight	687.11
Temperature (K)	296
Wavelength (Å)	1.5418 (Cu–K_α)
Space group	$P2_1/c$
Unit cell dimensions	
a (Å)	18.244(1)
b (Å)	13.092(2)
c (Å)	18.327(2)
β (°)	114.643(5)
V (Å^3)	3978.9(6)
Z	4
D_{calc} (Mg m^{-3})	1.147
$F(000)$	1472.00
Crystal size (mm^3)	$0.5 \times 0.3 \times 0.1$
Crystal color	colorless
μ (mm^{-1})	1.371
Diffractometer	Rigaku AFC-6S
Monochromator	Graphite crystal
Scan type	ω–2θ
Scan speed (° min^{-1})	4
Scan width (°)	$6 \leq 2\theta \leq 126.0$
Number of unique reflections	5790
Number of observed reflections ($I \geq 3\sigma(I)$)	3750
Corrections	Lorentz–polarization absorption
Transmission factors	0.8377–0.9992
R	0.069
R_w [a]	0.078

[a] Weighting scheme is $(\sigma(F_o)^2+0.0004|F_o|^2)^{-1}$.

2.2. Crystal structure of 4

We determined the crystal structures of **3** and **4** by X-ray diffraction studies. Fig. 1 shows the ORTEP drawing and Tables 1 and 2 summarize the cell dimensions, data collections and refinement parameters, and selected bond lengths and bond angles of **4**.

As shown in Fig. 1, all bond lengths and angles of **4** are in the normal range, except for the narrow O1–Si1–O2 angle (96.2(2)°). The structure possesses a siladioxacyclopentane ring with an envelope-type conformation as shown in Fig. 1. Thus, Si1, O1, O2, and C2 lie almost on the same plane with the maximum deviation of 0.072(6) Å for C2 from the least-square-plane defined by these atoms, and C1 atom is located at 0.485 Å away from the plane.

3. Experimental

3.1. General

All reactions were carried out under an atmosphere of purified Ar. Mass spectra were measured on a Hitachi M-80B spectrometer. NMR spectra were recorded on JEOL EX-270 and Lambda-400 spectrometers using Me_4Si as an internal standard. IR spectra were measured on a Perkin–Elmer FT1600 spectrophotometer. UV spectra were measured with a Hitachi U-3210 spectrophotometer.

3.2. Materials

Tetrahydrofuran was dried over Na–K alloy and distilled just before use. Lithium silenolates were prepared as reported in the literature and used without purification [2,3].

3.3. Reactions of lithium silenolates with benzophenone

An illustrative procedure for the reactions of **1a**–**c** with benzophenone is as follows. To a solution of 185 mg (1.02 mmol) of benzophenone in 2 ml of THF was added a solution of **1a**, prepared from 152 mg (0.47 mmol) of cyclohexyl tris(trimethylsilyl)silanecarboxylate and an equimolar amount of tris(trimethylsilyl)silyllithium in 1 ml of THF, at − 80 °C. The resulting mixture was allowed to warm to room temperature, and then hydrolyzed with water. The organic layer was separated and the aqueous layer was extracted with

Table 2
Selected bond distances (Å) and bond angles (°) for **4** with their estimated S.D.s in parentheses

Si1–O1	1.641(4)	Si1–O2	1.639(4)	Si1–O3	1.598(4)
Si1–C3	1.853(6)	O1–C1	1.459(6)	O2–C2	1.442(7)
C1–C2	1.641(8)				
O1–Si1–O2	96.2(2)	O1–Si1–O3	106.6(2)		
O1–Si1–C3	116.6(3)	O2–Si3–O3	117.3(2)		
O2–Si1–C3	106.5(3)	O3–Si1–C3	112.9(3)		
Si1–O1–C1	112.1(3)	Si1–O2–C2	113.3(3)		
O1–C1–C2	102.2(4)	O2–C2–C1	103.6(4)		

Et_2O. The organic layer and the extracts were combined and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was analyzed by GLC as being product **2** (55% yield). Compound **2** was separated from the residue by chromatography on a silica gel column followed by preparative GPC. Data for **2**. Colorless oil; MS; *m*/*z*: 554 [M^+]; ^{1}H-NMR (C_6D_6): δ 0.22 (s, 9H, Me_3Si), 0.13 (s, 9H, Me_3SiO), 6.96–7.05 (m, 12H, *m*- and *p*-Ph), 7.59 (dd, 4H, *o*-Ph, $J = 8.5$, 1.5 Hz), 7.66 (dd, 4H, *o*-Ph, $J = 8.5$, 1.5 Hz); ^{13}C-NMR ($CDCl_3$): δ −1.6, 2.0, 91.7, 126.4, 126.5, 126.7, 127.1, 128.8, 129.1, 144.7, 145.6; ^{29}Si-NMR (C_6D_6): δ −34.0, −22.7, 9.3; Anal. Found: C, 68.90; H, 7.07. Calc. for $C_{32}H_{38}O_3Si_3$: C, 69.26; H, 6.90%.

The other reactions of **1b** and **c** with benzophenone were carried out in a similar fashion to above.

Data for **3**. Colorless crystals; m.p. 75 °C; MS; *m*/*z*: 415 [$M^+ - Me$]; ^{1}H-NMR (C_6D_6): δ 0.25 (s, 27H, Me_3Si), 5.58 (s, 1H, HCO), 7.03 (t, 2H, *p*-Ph, $J = 7.7$ Hz), 7.16 (t, 4H, *m*-Ph, $J = 7.7$ Hz), 7.45 (d, 4H, *o*-Ph, $J = 7.7$ Hz); ^{13}C-NMR (C_6D_6): δ 0.5, 81.6, 126.3, 127.4, 128.3, 145.8; ^{29}Si-NMR (C_6D_6) δ −15.3, 3.8; Exact MS: Found, 263.1144. Calc. for $C_9H_{27}OSi_4$ [$OSi(SiMe_3)_3^+$]: 263.1139; Found, 167.0859. Calc. for $C_{13}H_{11}$ [Ph_2CH^+]: 167.0861.

Data for **4**. Colorless crystals; m.p. 204–207 °C; MS; *m*/*z*: 671 [$M^+ - Me$]; ^{1}H-NMR (C_6D_6) δ 0.04 (s, 9H, Me_3Si), 0.31 (s, 9H, Me_3SiO), 1.82 (s, 3H, Mes), 2.21 (s, 3H, Mes), 2.65 (s, 3H, Mes), 2.52 (s, 1H, methyne), 6.82 (s, 1H, Mes), 6.87 (s, 1H, Mes), 6.95–7.07 (m, 12H, Ph), 7.38 (br dd, 2H, *o*-Ph, $J = 7.9$, 2.7 Hz), 7.50 (br d, 2H, *o*-Ph, $J = 7.9$ Hz,), 7.62 (br d, 2H, *o*-Ph, $J = 7.6$ Hz), 7.72 (br d, 2H, *o*-Ph, $J = 7.9$ Hz); ^{13}C-NMR (C_6D_6) δ 1.4, 1.8, 20.7, 21.1, 22.1, 23.7, 91.5, 92.0, 126.7, 126.9, 127.07, 127.14, 127.4, 127.5, 127.6, 127.9, 128.3, 128.9, 129.5, 129.6, 129.8, 130.3, 133.2, 134.4, 136.2, 136.6, 145.6 (2C), 146.1, 146.6; ^{29}Si-NMR (C_6D_6) δ −39.0, 2.8, 11.1. Anal. Found: C, 73.36; H, 7.36. Calc. for $C_{42}H_{50}O_3Si_3$: C, 73.42; H, 7.33%.

Data for **5**. Colorless oil; MS; *m*/*z*: 576 [M^+]; ^{1}H-NMR (C_6D_6) δ 0.05 (s, 18H, Me_3Si), 0.23 (s, 9H, Me_3SiO), 2.08 (s, 3H, Mes), 2.44 (s, 6H, Mes), 6.67 (br s, 2H, Mes), 6.81–6.87 (m, 1H, *p*-Ph), 6.93 (br t, 2H, *m*-Ph, $J = 7.6$ Hz), 7.07 (br dd, 2H, *o*-Ph, $J = 8.5$, 1.3 Hz), 7.15–7.20 (m, 1H, *p*-Ph), 7.34 (br t, 2H, *m*-Ph, $J = 6.3$ Hz), 7.66 (br dd, 2H, *o*-Ph, $J = 8.3$, 1.3 Hz); ^{13}C-NMR ($CDCl_3$): δ −1.5, 2.4, 20.6, 21.0, 124.8, 125.9, 126.3, 127.7, 128.3, 128.8, 129.8, 130.9, 134.9, 137.2, 137.8, 141.5, 141.9, 146.3; ^{29}Si-NMR (C_6D_6)δ −21.9, −6.8, 7.6. Anal. Found: C, 66.53; H, 8.13. Calc. for $C_{32}H_{48}O_2Si_4$: C, 66.60; H, 8.38%.

Data for **6**. Colorless oil; MS; *m*/*z*: 386 [M^+]; ^{1}H-NMR (C_6D_6) δ −0.03 (s, 9H, Me_3Si), 2.07 (s, 3H, Mes), 2.36 (s, 6H, Mes), 6.68 (br s, 2H, Mes), 6.86–6.89 (m, 1H, *p*-Ph), 6.95 (br t, 2H, *m*-Ph, $J = 7.9$ Hz), 7.12–7.17 (m, 3H, *o*- and *p*-Ph), 7.30 (br t, 2H, *m*-Ph, $J = 7.9$ Hz), 7.58 (br d, 2H, *o*-Ph, $J = 7.6$ Hz); ^{13}C-NMR (C_6D_6) δ 0.8, 20.5, 21.1, 124.8, 126.0, 126.4, 127.7, 128.0, 128.7, 130.2, 131.0, 135.0, 136.9, 137.8, 141.5, 141.8, 146.0. Anal. Found: C, 80.68; H, 7.79. Calc. for $C_{26}H_{30}OSi$: C, 80.78; H, 7.82%.

3.4. X-ray crystallographic analysis of **3** *and* **4**

The structures were solved by heavy-atom Patterson methods [12] for **3** and by SIR92 direct methods [13] for **4**, and were expanded using DIRDIF94 Fourier techniques [12]. The non-hydrogen atoms were refined anisotropically. Neutral atom scattering factors were taken from Cromer and Waber [14]. Anomalous dispersion effects were included in F_{calc} [15]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley [16]. The values for the mass attenuation coefficients are those of Creagh and Hubbel [17]. All calculations were performed using the TEXSAN [18] crystallographic software package of Molecular Structure Corporation.

4. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos. 161837 and 161838 for compounds **3** and **4**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: de-posit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

This work was supported by the Ministry of Education, Culture, Sports, Science, and Technology (Grant-in-Aid for Scientific Research, No. 13650922). We thank Sankyo Kasei Co. Ltd and Sumitomo Electric Industry for financial support. We also thank Shin-Etsu Chemical Co. Ltd for gifts of chlorosilanes.

References

[1] For reviews, see: (a) K. Tamao, A. Kawachi, Bull. Chem. Soc. Jpn. 70 (1997) 945;
(b) K. Tamao, A. Kawachi, Adv. Organomet. Chem. 38 (1995) 1.

[2] (a) J. Ohshita, Y. Masaoka, S. Masaoka, M. Ishikawa, A. Tachibana, T. Yano, T. Yamabe, J. Organomet. Chem. 473 (1994) 15;
(b) J. Ohshita, Y. Masaoka, S. Masaoka, H. Hasebe, M. Ishikawa, A. Tachibana, T. Yano, T. Yamabe, Organometallics 15 (1996) 3136.

[3] J. Ohshita, H. Sakurai, Y. Tokunaga, A. Kunai, Organometallics 18 (1999) 4545.

[4] J. Ohshita, Y. Tokunaga, H. Sakurai, A. Kunai, J. Am. Chem. Soc. 121 (1999) 6080.

[5] J. Ohshita, S. Masaoka, Y. Morimoto, M. Sano, M. Ishikawa, Organometallics 16 (1997) 1123.

[6] J. Ohshita, S. Masaoka, M. Ishikawa, Organometallics 15 (1996) 2198.

[7] J. Ohshita, S. Masaoka, Y. Morimoto, M. Ishikawa, Organometallics 16 (1997) 906.

[8] E.A. Williams, in: S. Patai, Z. Rappoport (Eds.), The Chemistry of Organic Silicon Compounds, vol. 1, Wiley, New York, 1989 (chap. 8).

[9] Peterson-type reactions leading to the formation of silenes have been reported previously. For example, see: (a) A.G. Brook, P. Chiu, J. McClenaghnan, A.J. Lough, Organometallics 10 (1991) 3292;
(b) J. Ohshita, Y. Masaoka, M. Ishikawa, Organometallics 10 (1991) 3775;
(c) J. Ohshita, Y. Masaoka, M. Ishikawa, T. Takeuchi, Organometallics 12 (1993) 876;
(d) Y. Apeloig, M. Bendikov, M. Yuzefovich, M. Nakash, D. Bravo-Zhivotovskii, J. Am. Chem. Soc. 118 (1996) 12228;
(e) F. Luderer, H. Reinke, H. Oehme, J. Organomet. Chem. 510 (1996) 181;
(f) C. Krempner, D. Hoffmann, H. Oehme, R. Kempe, Organometallics 16 (1997) 1828;
(g) K. Sakamoto, J. Ogasawara, H. Sakurai, M. Kira, J. Am. Chem. Soc. 119 (1997) 3405.

[10] (a) A.G. Brook, W.J. Chatterton, J.F. Sawyer, G.W. Hughes, K. Vorspohl, Organometallics 6 (1987) 1246;
(b) A.G. Brook, R. Kumarathasan, W. Chatertton, Organometallics 12 (1993) 4085.

[11] (a) W.J. Leigh, G.W. Sluggett, J. Am. Chem. Soc. 115 (1993) 7531;
(b) W.J. Leigh, G.W. Sluggett, Organometallics 13 (1994) 269;
(c) N.P. Toltl, W.J. Leigh, Organometallics 15 (1996) 2554;
(d) M. Trommer, W. Sander, Organometallics 15 (1996) 736.

[12] P.T. Beurskens, G. Admiraal, G. Beurskens, W.P. Bosman, R. de Gelder, R. Israel, J.M.M. Smits, The DIRDIF-94 Program System, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands, 1994.

[13] A. Altomare, M.C. Burla, M. Camalli, M. Cascarano, C. Giacovazzo, A. Guagliardi, G. Polidori, J. Appl. Crystallogr. 27 (1994) 435.

[14] D.T. Cromer, J.T. Waber, International Tables for X-ray Crystallography, vol. IV, The Kynoch Press, Birmingham, England, 1974 (Table 2.2 A).

[15] J.A. Ibers, W.C. Hamilton, Acta Crystallogr. 17 (1964) 781.

[16] D.C. Creagh, W.J. McAuley, in: A.J.C. Wilson (Ed.), International Tables for Crystallography, Kluwer Academic, Boston, 1992, pp. 219–222 (Table 4.2.6.8).

[17] D.C. Creagh, J.H. Hubbell, in: A.J.C. Wilson (Ed.), International Tables for Crystallography, Kluwer Academic, Boston, 1992, pp. 200–206 (Table 4.2.4.3).

[18] TEXSAN: Crystal Structure Analysis Package, Molecular Structure Corporation, 1985 and 1992.