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β-Carbonylsilanes with a silacyclohexane skeleton and additional *C*-functionalized organyl groups at the silicon atom: synthesis, reactivity, and NMR-spectroscopic characterization

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Abstract

A series of novel β-carbonylsilanes, with a silacyclohexane skeleton and additional *C*-functionalized organyl groups at the silicon atom, were synthesized, their reactivity was explored, and they were structurally characterized by multinuclear NMR spectroscopy. The aim of these investigations was to provide the basis for the development of novel silicon-based drugs containing a silacyclohexane skeleton, with a $CH_2C(O)R$ substituent and an additional *C*-functionalized organyl group at the silicon atom.

Keywords: β-Carbonylsilanes; Silicon; Silicon-based drugs

1. Introduction

β-Carbonylsilanes, $R_3SiCH_2C(O)R$, have attracted considerable interest for synthetic organic chemistry because they are useful reagents for the generation of enolate anions [1]. Their reactivity is mainly based on the weakness of the Si–$CH_2C(O)R$ bond, which is an intrinsic obstacle when tranformations of *C*-functionalized organyl groups at the silicon atom are intended. Therefore, most of the publications on the reactivity of β-carbonylsilanes report on reactions involving cleavage of the Si–$CH_2C(O)R$ bond [2]. A typical example of this is the use of $Me_3SiCH_2CO_2Et$ as a silylating agent. Thus, the development of convenient synthetic methods for functional group transformations in the very presence of an Si–$CH_2C(O)R$ group represents a challenging field in organosilicon chemistry to be explored.

In context with our research program dealing with the development of silicon-based drugs [3], we have been interested in (i) the synthesis of β-carbonylsilanes, with a silacyclohexane skeleton and an additional *C*-functionalized organyl group at the silicon atom, and in (ii) reactions of these compounds involving functional group transformations within the *C*-functionalized group without cleavage of the Si–$CH_2C(O)R$ bond. We report here on the synthesis and NMR-spectroscopic characterization of the β-carbonylsilanes **1**–**8** that show some structural analogies with sila-gabapentin (**9b**) [4], a silicon analogue of the antiepileptic gabapentin (**9a**).

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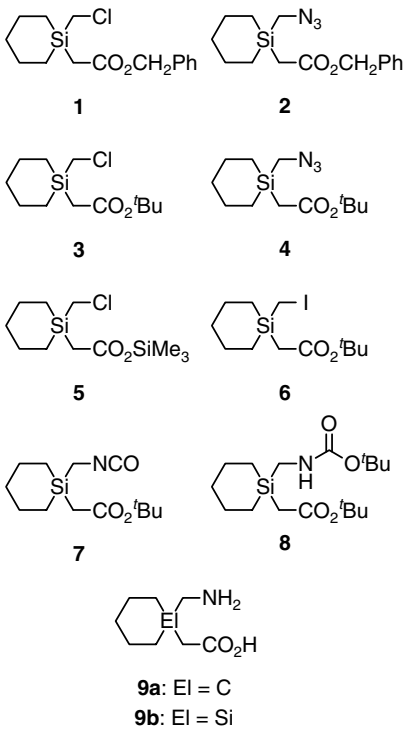
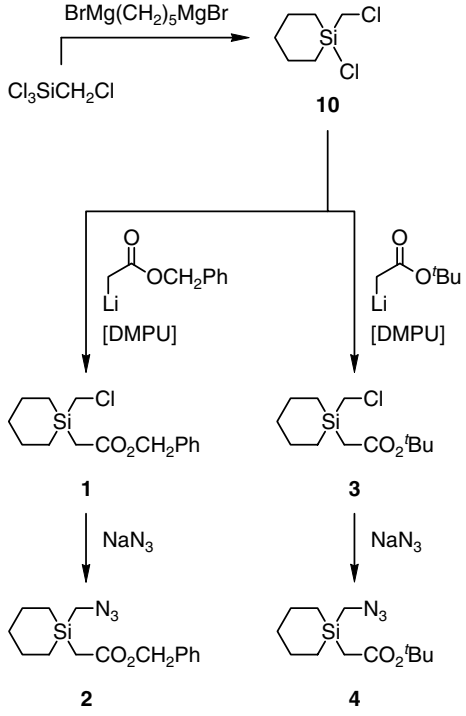
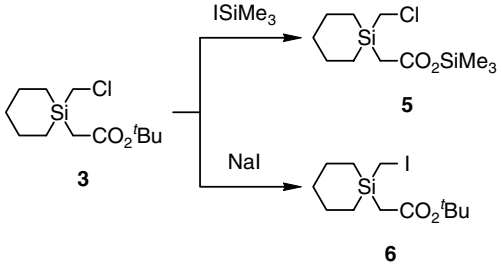


Formulas of **1**–**8**, **9a**, and **9b**



Scheme 1.



Scheme 2.

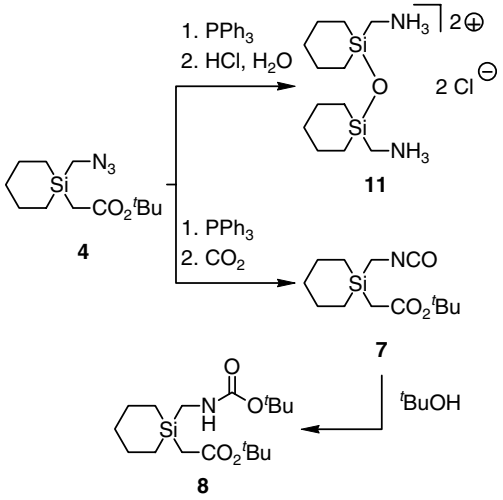
2. Results and discussion

The β-carbonylsilanes benzyl 2-(1-(chloromethyl)-1-sila-1-cyclohexyl)acetate (**1**) and *tert*-butyl 2-(1-(chloromethyl)-1-sila-1-cyclohexyl)acetate (**3**) were synthesized according to Scheme 1 by reaction of 1-chloro-1-(chloromethyl)-1-silacyclohexane (**10**) (prepared from trichloro(chloromethyl)silane in 52% yield by reaction with 1,5-bis(bromomagnesio)pentane [5]) with the lithium reagents $LiCH_2CO_2CH_2Ph$ (→ **1**, yield 43%) or $LiCH_2$- $CO_2{}^tBu$ (→ **3**, yield 79%) in the presence of 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one (DMPU). Treatment of **1** and **3** with sodium azide gave benzyl 2-(1-(azidomethyl)-1-sila-1-cyclohexyl)acetate (**2**, yield 86%) and *tert*-butyl 2-(1-(azidomethyl)-1-sila-1-cyclohexyl)acetate (**4**, yield 89%), respectively (Scheme 1).

Further transformations of **3** (see Scheme 2) include: (i) the displacement of the *tert*-butyl group by a trimethylsilyl moiety by reaction with iodotrimethylsilane to give trimethylsilyl 2-(1-(chloromethyl)-1-sila-1-cyclohexyl)acetate (**5**, yield 85%) and (ii) a chlorine/iodine exchange by reaction with sodium iodide to give *tert*-butyl 2-(1-(iodomethyl)-1-sila-1-cyclohexyl)acetate (**6**, yield 88%).

Reaction of **4** with triphenylphosphine, followed by treatment with carbon dioxide, gave *tert*-butyl 2-(1-(isocyanatomethyl)-1-sila-1-cyclohexyl)acetate (**7**, yield 34%), which upon reaction with *tert*-butanol afforded *tert*-butyl 2-(1-(((*tert*-butoxycarbonyl)amino)methyl)-1-sila-1-cyclohexyl)acetate (**8**, yield 44%) (Scheme 3). In addition, compound **4** was reacted with triphenylphosphine according to Scheme 3, followed by treatment with hydrochloric acid, to give 1,1′-oxybis(((1-sila-1-cyclohexyl)methyl)ammonium) dichloride (**11**, yield 38%). Thus, the attempted transformation of the $SiCH_2N_3$ group into the $SiCH_2NH_2$ moiety and the transformation of the $SiCH_2CO_2{}^tBu$ group into the $SiCH_2COOH$ moiety in a one-pot synthesis (→ formation of **9b**) resulted in an Si–C bond cleavage.

The identities of compounds **1**–**8**, **10**, and **11** were established by elemental analyses and multinuclear NMR experiments (^1H, ^{13}C, ^{15}N (**2**, **4**, **7**, and **8** only), ^{29}Si). In addition, compound **11** · $2H_2O$ was structurally characterized by single-crystal X-ray diffraction. The crystal data and the experimental parameters used for



Scheme 3.

this crystal structure analysis are summarized in Table 1. The structure of the cation of **11** · $2H_2O$ is depicted in Fig. 1; selected bond lengths and angles (which do not need any further discussion) are given in the figure legend.

Table 1
Crystal data and experimental parameters for the crystal structure analysis of **11** · $2H_2O$

Empirical formula	$C_{12}H_{34}Cl_2N_2O_3Si_2$
Formula mass (g mol^{-1})	381.49
Collection T (K)	173(2)
λ (Mo Kα) (Å)	0.71073
Crystal system	Monoclinic
Space group (no.)	$P2_1/c$ (14)
a (Å)	16.5887(19)
b (Å)	6.6154(6)
c (Å)	19.072(2)
β (°)	103.955(14)
V (Å^3)	2031.2(4)
Z	4
D_{calc} (g cm^{-3})	1.248
μ (mm^{-1})	0.447
$F(000)$	824
Crystal dimensions (mm)	$0.5 \times 0.2 \times 0.2$
2θ range (°)	4.52–55.96
Index ranges	$-21 \leqslant h \leqslant 21$, $-8 \leqslant k \leqslant 8$, $-25 \leqslant l \leqslant 25$
Number of collected reflections	17341
Number of independent reflections	4847
R_{int}	0.0379
Number of reflections used	4847
Number of parameters	220
S[a]	0.974
Weight parameters a/b[b]	0.0537/0.0000
R_1[c] [$I > 2\sigma(I)$]	0.0287
wR_2[d] (all data)	0.0757
Maximum/minimum residual electron density (e Å^{-3})	+0.408/−0.415

[a] $S = \{\sum[w(F_o^2 - F_c^2)^2]/(n-p)\}^{0.5}$ where n is number of reflections and p is number of parameters.
[b] $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$, with $P = [\max(F_o^2,0) + 2F_c^2]/3$.
[c] $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$.
[d] $wR_2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{0.5}$.

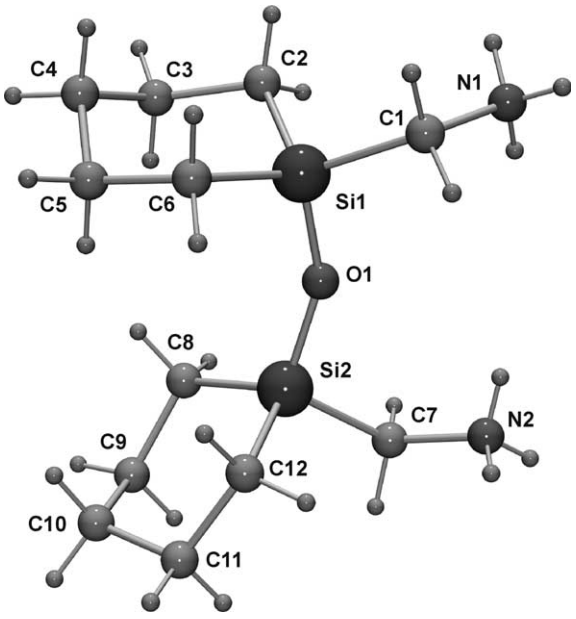


Fig. 1. Structure of the dication in the crystal of **11** · $2H_2O$. Selected bond distances (Å) and angles (°): Si1–O1 1.6317(9), Si2–O1 1.6360(9), Si1–C1 1.8826(12), Si1–C2 1.8574(14), Si1–C6 1.8677(12), Si2–C7 1.8859(12), Si2–C8 1.8589(13), Si2–C12 1.8584(13), Si1–O1–Si2 152.05(6), O1–Si1–C1 107.67(5), O1–Si1–C2 110.54(6), O1–Si1–C6 111.88(6), O1–Si2–C7 106.47(5), O1–Si2–C8 112.94(6), O1–Si2–C12 111.04(6), C1–Si1–C2 112.33(6), C1–Si1–C6 109.22(6), C2–Si1–C6 105.25(6), C7–Si2–C8 108.66(6), C7–Si2–C12 111.11(6), C8–Si2–C12 106.67(6).

The crystal structure of **11** · $2H_2O$ is governed by hydrogen bonds [6], leading to an infinite two-dimensional network along the base vectors [0 1 0] and [0 0 1]. All six NH groups of the dication and all OH groups of the two crystallographically independent water molecules act as proton donors, whereas both chloride anions and the oxygen atoms of both water molecules act as proton acceptors.

3. Conclusions

In this study, a series of β-carbonylsilanes, with a silacyclohexane skeleton and an additional *C*-functionalized organyl group at the silicon atom, were synthesized and structurally characterized by multinuclear NMR spectroscopy. Multistep transformations were carried out successfully in the *C*-functionalized periphery of this type of molecules, without cleavage (in most cases) of the labile Si–CH_2C(O)R bond. These results may be helpful for the development of silicon-based drugs of the β-carbonylsilane type containing a silacyclohexane framework and an additional *C*-functionalized organyl group bound to the silicon atom.

4. Experimental

4.1. Syntheses

4.1.1. General procedures

All syntheses were carried out under dry nitrogen. The organic solvents used were dried and purified according to standard procedures and stored under dry nitrogen. A Büchi GKR 50 apparatus was used for the bulb-to-bulb distillations. Melting points were determined with a Büchi Melting Point B-540 apparatus using open glass capillaries. The ^{1}H, ^{13}C, ^{15}N, and ^{29}Si NMR spectra were recorded on a Bruker DRX-300 NMR spectrometer (^{1}H, 300.1 MHz; ^{13}C, 75.5 MHz; ^{15}N, 30.4 MHz; ^{29}Si, 59.6 MHz). $CDCl_3$, CD_2Cl_2, [D$_6$]DMSO, or C_6D_6 were used as the solvent. All spectra were recorded at 22 °C. Chemical shifts (ppm) were determined relative to internal $CHCl_3$ (^{1}H, δ 7.24; $CDCl_3$), internal $CDCl_3$ (^{13}C, δ 77.0; $CDCl_3$), internal $CHDCl_2$ (^{1}H, δ 5.32; CD_2Cl_2), internal CD_2Cl_2 (^{13}C, δ 53.8; CD_2Cl_2), internal [D$_5$]DMSO (^{1}H, δ 2.49; [D$_6$]DMSO), internal [D$_6$]DMSO (^{13}C, δ 39.5; [D$_6$]DMSO), internal C_6HD_5 (^{1}H, δ 7.28; C_6D_6), internal C_6D_6 (^{13}C, δ 128.0; C_6D_6), external formamide (^{15}N, δ −268.0; CD_2Cl_2, C_6D_6), or external TMS (^{29}Si, δ 0; $CDCl_3$, CD_2Cl_2, [D$_6$]DMSO, C_6D_6). Analysis and assignment of the ^{1}H NMR data was supported by ^{1}H,^{1}H and ^{13}C,^{1}H correlation experiments. Assignment of the ^{13}C NMR data was supported by DEPT 135 and ^{13}C,^{1}H correlation experiments.

4.1.2. Benzyl 2-(1-(chloromethyl)-1-sila-1-cyclohexyl)acetate (*1*)

A 2.5 M solution of *n*-butyllithium in *n*-hexane (45.6 ml, 114 mmol of *n*-BuLi) was added dropwise [7] at 0 °C within 10 min to a stirred (mechanical stirrer) solution of diisopropylamine (12.5 g, 124 mmol) in tetrahydrofuran (THF) (100 ml), and the mixture was stirred at the same temperature for another 15 min and then cooled to −80 °C, followed by dropwise addition of benzyl acetate (17.2 g, 115 mmol) within 15 min while the reaction temperature was kept at −75 °C (±5 °C). The mixture was stirred at this temperature for another 15 min, followed by dropwise addition of 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one (DMPU) (58.5 g, 456 mmol) at −75 °C (±5 °C) within 30 min (formation of a slurry), and the mixture was then cooled to −100 °C, followed by dropwise addition of **10** (20.8 g, 114 mmol) within 75 min while the temperature was kept at −95 °C (±5 °C) (formation of a highly viscous slurry). The mixture was warmed to −30 °C within 4 h (formation of a clear solution), and the cold solution was poured into a stirred two-phase mixture of a saturated aqueous sodium hydrogen carbonate solution (300 ml, solution A) and diethyl ether (200 ml) (formation of a precipitate which remained in the aqueous phase). The organic phase was separated and washed with a saturated aqueous sodium hydrogen carbonate solution (300 ml, solution B), the organic phase was separated, the first aqueous wash solution A was extracted with diethyl ether (200 ml), the resulting ethereal extract was used to extract the second aqueous wash solution B, and the organic extract was separated, followed by a second extraction of the wash solutions A and B with a fresh portion of diethyl ether (200 ml), using the same protocol as described for the first extraction sequence. The combined organic solutions were dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the oily residue was purified by rapid bulb-to-bulb distillation in vacuo (Kugelrohr apparatus). The distillate (33 g, 140–155 °C/0.001 mbar) was redistilled in vacuo (Vigreux column, 10 cm) to give **1** in 43% yield as a colorless liquid (14.4 g, 48.5 mmol); b.p.: 137–138 °C/0.001 mbar. ^{1}H NMR ($CDCl_3$): δ 0.65–0.87 (m, 4H, SiCH_2C), 1.32–1.43 (m, 2H, Si(CH$_2$)$_2$CH$_2$C), 1.56–1.74 (m, 4H, SiCH$_2$CH$_2$C), 2.10 (s, 2H, SiCH$_2$C(O)), 2.86 (s, 2H, SiCH$_2$Cl), 5.07 (s, 2H, OCH$_2$Ph), 7.26–7.38 (m, 5H, C$_6$H$_5$). ^{13}C NMR ($CDCl_3$): δ 9.7 (SiCH$_2$C), 21.7 (SiCH$_2$C(O)), 23.8 (SiCH$_2$CH$_2$C), 27.4 (SiCH$_2$Cl), 29.2 (Si(CH$_2$)$_2$CH$_2$C), 66.2 (OCH$_2$Ph), 128.2 (*C*-4, Ph), 128.4 (*C*-2/*C*-6 or *C*-3/*C*-5, Ph), 128.5 (*C*-2/*C*-6 or *C*-3/*C*-5, Ph), 136.0 (*C*-1, Ph), 171.9 (*C*=O). ^{29}Si NMR ($CDCl_3$): δ −0.8. Anal. Found: C, 60.7; H, 7.0. Calc. for $C_{15}H_{21}ClO_2Si$: C, 60.69; H, 7.13%.

4.1.3. Benzyl 2-(1-(azidomethyl)-1-sila-1-cyclohexyl)acetate (*2*)

A stirred mixture of **1** (10.8 g, 36.4 mmol), sulfolane (25 ml), and sodium azide (4.94 g, 76.0 mmol) was heated at 55 °C for 3 days and was then cooled to 20 °C and poured into a stirred two-phase mixture of diethyl ether (100 ml) and water (200 ml) containing 500 mg of sodium carbonate. The organic layer was separated, the aqueous phase was extracted with diethyl ether (2 × 100 ml), all organic extracts were combined and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (column dimensions, 60 × 5.5 cm; silica gel (15–40 μm, Merck 1.15111), 590 g; eluent, *n*-hexane/diethyl ether 86:14 (v/v)). The relevant fractions (TLC control) were combined, and the solvent was completely removed under reduced pressure to give **2** in 86% yield as a colorless oily liquid (9.50 g, 31.3 mmol). ^{1}H NMR (CD_2Cl_2): δ 0.67–0.85 (m, 4H, SiCH_2C), 1.36–1.46 (m, 2H, Si(CH$_2$)$_2$CH$_2$C), 1.63–1.75 (m, 4H, SiCH$_2$CH$_2$C), 2.07 (s, 2H, SiCH$_2$C(O)), 2.92 (s, 2H, SiCH$_2$N$_3$), 5.08 (s, 2H, OCH$_2$Ph), 7.29–7.40 (m, 5H, C$_6$H$_5$). ^{13}C NMR (CD_2Cl_2): δ 10.3 (SiCH$_2$C), 22.3 (SiCH$_2$C(O)), 24.2 (SiCH$_2$CH$_2$C), 29.6 (Si(CH$_2$)$_2$CH$_2$C), 39.0 (SiCH$_2$N$_3$), 66.5 (OCH$_2$Ph), 128.5 (*C*-4, Ph), 128.78 (*C*-2/*C*-6 or

C-3/*C*-5, Ph), 128.81 (*C*-2/*C*-6 or *C*-3/*C*-5, Ph), 136.8 (*C*-1, Ph), 171.9 (*C*=O). ^{15}N NMR (CD_2Cl_2): δ −319.8 ($CH_2\mathit{N}NN$), −172.7 ($CH_2N\mathit{N}N$), −130.0 ($CH_2N\mathit{N}N$). ^{29}Si NMR (CD_2Cl_2): δ −1.3. Anal. Found: C, 59.7; H, 6.9; N, 13.6. Calc. for $C_{15}H_{21}N_3O_2Si$: C, 59.37; H, 6.98; N, 13.85%.

4.1.4. tert-Butyl 2-(1-(chloromethyl)-1-sila-1-cyclohexyl)acetate (3)

Compound **3** was prepared analogous to the preparation of **1** (see above): THF, 100 ml; 2.7 M solution of *n*-butyllithium in *n*-hexane, 41.4 ml (112 mmol of *n*-BuLi); diisopropylamine, 12.5 g (124 mmol); *tert*-butyl acetate, 13.0 g (112 mmol); DMPU, 57.4 g (448 mmol); **10**, 20.9 g (114 mmol); distillate after bulb-to-bulb distillation, 28 g (100–130 °C/0.001 mbar). The product was redistilled in vacuo (Vigreux column, 20 cm) to give **3** in 79% yield (related to **10**) as a colorless liquid (23.8 g, 90.5 mmol); b.p.: 70 °C/0.001 mbar. ^{1}H NMR ($CDCl_3$): δ 0.68–0.91 (m, 4H, SiCH_2C), 1.34–1.46 (m, 2H, Si(CH$_2$)$_2$CH_2C), 1.41 (s, 9H, CCH_3), 1.60–1.76 (m, 4H, SiCH$_2$CH_2C), 1.94 (s, 2H, SiCH_2C(O)), 2.90 (s, 2H, SiCH_2Cl). ^{13}C NMR ($CDCl_3$): δ 9.7 (Si*C*H$_2$C), 23.0 (Si*C*H$_2$C(O)), 23.9 (SiCH$_2$*C*H$_2$C), 27.5 (Si*C*H$_2$Cl), 28.2 (C*C*H$_3$), 29.3 (Si(CH$_2$)$_2$*C*H$_2$C), 80.1 (*C*CH$_3$), 171.4 (*C*=O). ^{29}Si NMR ($CDCl_3$): δ −1.2. Anal. Found: C, 54.5; H, 8.5. Calc. for $C_{12}H_{23}ClO_2Si$: C, 54.83; H, 8.82%.

4.1.5. tert-Butyl 2-(1-(azidomethyl)-1-sila-1-cyclohexyl)acetate (4)

Compound **4** was prepared analogous to the preparation of **2** (see above): **3**, 11.5 g (43.8 mmol); sulfolane, 25 ml; sodium azide, 5.74 g (88.3 mmol). The product was isolated in 89% yield as a colorless oily liquid (10.5 g, 39.0 mmol). ^{1}H NMR (CD_2Cl_2): δ 0.70–0.87 (m, 4H, SiCH_2C), 1.35–1.51 (m, 2H, Si(CH$_2$)$_2$CH_2C), 1.43 (s, 9H, CCH_3), 1.65–1.80 (m, 4H, SiCH$_2$CH_2C), 1.92 (s, 2H, SiCH_2C(O)), 2.97 (s, 2H, SiCH_2N$_3$). ^{13}C NMR (CD_2Cl_2): δ 10.4 (Si*C*H$_2$C), 23.6 (Si*C*H$_2$C(O)), 24.3 (SiCH$_2$*C*H$_2$C), 28.3 (C*C*H$_3$), 29.7 (Si(CH$_2$)$_2$*C*H$_2$C), 39.3 (Si*C*H$_2$N$_3$), 80.3 (*C*CH$_3$), 171.4 (*C*=O). ^{15}N NMR (CD_2Cl_2): δ −319.5 ($CH_2\mathit{N}NN$), −172.0 ($CH_2NN\mathit{N}$), −129.5 ($CH_2N\mathit{N}N$). ^{29}Si NMR (CD_2Cl_2): δ −1.6. Anal. Found: C, 53.6; H, 8.4; N, 15.8. Calc. for $C_{12}H_{23}N_3O_2Si$: C, 53.50; H, 8.60; N, 15.60%.

4.1.6. Trimethylsilyl 2-(1-(chloromethyl)-1-sila-1-cyclohexyl)acetate (5)

Iodotrimethylsilane (5.15 g, 25.7 mmol) was added in one portion at 20 °C to a stirred solution of **3** (6.00 g, 22.8 mmol) in dichloromethane (20 ml). The mixture was heated under reflux for 30 min (quantitative conversion (GC control)), the solvent was removed under reduced pressure, and the residue was distilled in vacuo (Vigreux column, 5 cm) from copper powder (116 mg, 1.83 mmol) to give **5** in 85% yield (5.44 g, 19.5 mmol) as a colorless liquid; b.p.: 73–74 °C/0.001 mbar. ^{1}H NMR ($CDCl_3$): δ 0.25 (s, 9H, SiCH_3), 0.69–0.91 (m, 4H, SiCH_2C), 1.35–1.46 (m, 2H, Si(CH$_2$)$_2$CH_2C), 1.61–1.76 (m, 4H, SiCH$_2$CH_2C), 2.05 (s, 2H, SiCH_2C(O)), 2.89 (s, 2H, SiCH_2Cl). ^{13}C NMR ($CDCl_3$): δ −0.2 (Si*C*H$_3$), 9.7 (Si*C*H$_2$C), 23.8 (Si*C*H$_2$C(O)), 23.9 (SiCH$_2$*C*H$_2$C), 27.5 (Si*C*H$_2$Cl), 29.3 (Si(CH$_2$)$_2$*C*H$_2$C), 172.6 (*C*=O). ^{29}Si NMR ($CDCl_3$): δ −1.2 (*Si*C$_4$), 23.0 (O*Si*C$_3$). Anal. Found: C, 47.1; H, 8.1. Calc. for $C_{11}H_{23}ClO_2Si_2$: C, 47.37; H, 8.31%.

4.1.7. tert-Butyl 2-(1-(iodomethyl)-1-sila-1-cyclohexyl)acetate (6)

A stirred mixture of **3** (6.11 g, 23.2 mmol), sodium iodide (4.30 g, 28.7 mmol), and acetone (40 ml) was heated under reflux for 2 h (quantitative conversion (GC control)). The solids were removed by filtration and washed with *n*-heptane (2 × 50 ml), the filtrate and the wash solutions were combined, and the solvent was removed under reduced pressure until a residual volume of ca. 100 ml was obtained (postprecipitation), followed by addition of water (100 ml). The organic phase was separated, the aqueous layer was extracted with diethyl ether (2 × 50 ml), all organic extracts were combined and dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the residue was distilled in vacuo (Vigreux column, 5 cm) from copper powder (122 mg, 1.92 mmol) to give **6** in 88% yield as a colorless liquid (7.24 g, 20.4 mmol); b.p.: 87 °C/0.002 mbar. ^{1}H NMR ($CDCl_3$): δ 0.71–0.90 (m, 4H, SiCH_2C), 1.32–1.46 (m, 2H, Si(CH$_2$)$_2$CH_2C), 1.41 (s, 9H, CCH_3), 1.61–1.72 (m, 4H, SiCH$_2$CH_2C), 1.96 (s, 2H, SiCH_2C(O)), 2.11 (s, 2H, SiCH_2I). ^{13}C NMR ($CDCl_3$): δ −17.2 (Si*C*H$_2$I), 11.4 (Si*C*H$_2$C), 23.9 (Si*C*H$_2$C(O)), 24.0 (SiCH$_2$*C*H$_2$C), 28.2 (C*C*H$_3$), 29.4 (Si(CH$_2$)$_2$*C*H$_2$C), 80.0 (*C*CH$_3$), 171.4 (*C*=O). ^{29}Si NMR ($CDCl_3$): δ 0.3. Anal. Found: C, 40.9; H, 6.3. Calc. for $C_{12}H_{23}IO_2Si$: C, 40.68; H, 6.54%.

4.1.8. tert-Butyl 2-(1-(isocyanatomethyl)-1-sila-1-cyclohexyl)acetate (7)

Compound **4** (9.26 g, 34.4 mmol) was added in one single portion to a solution of triphenylphosphine (9.30 g, 35.5 mmol) in toluene (300 ml), and the mixture was stirred at 20 °C for 1 day. Subsequently, a gas stream of carbon dioxide (ca. 100 g; prepared from dry ice and dried by passing the gas stream through a column packed with anhydrous calcium chloride) was passed through the stirred solution over a period of 3 h. The solvent was removed under reduced pressure, the residue was purified by bulb-to-bulb distillation in vacuo (Kugelrohr apparatus), and the distillate (4.4 g, 100–175 °C/0.001 mbar) was redistilled in vacuo (Vigreux column, 5 cm) to give **7** in 34% yield as a colorless liquid (3.16 g, 11.7 mmol); b.p.: 98–99 °C/0.002 mbar. ^{1}H NMR (CD_2Cl_2): δ 0.75–0.85 (m, 4H, SiCH_2C),

1.38–1.49 (m, 2H, $Si(CH_2)_2CH_2C$), 1.43 (s, 9H, CCH_3), 1.62–1.82 (m, 4H, $SiCH_2CH_2C$), 1.93 (s, 2H, $SiCH_2C(O)$), 2.93 (s, 2H, $SiCH_2N$). ^{13}C NMR (CD_2Cl_2): δ 10.0 ($SiCH_2C$), 23.3 ($SiCH_2C(O)$), 24.3 ($SiCH_2CH_2C$), 28.3 (CCH_3), 29.0 ($SiCH_2N$), 29.7 ($Si(CH_2)_2CH_2C$), 80.4 (CCH_3), 120.5 (NCO), 171.2 (C*C*(=O)O). ^{15}N NMR (CD_2Cl_2): δ −361.3. ^{29}Si NMR (CD_2Cl_2): δ −0.8. Anal. Found: C, 57.9; H, 8.5; N, 5.4. Calc. for $C_{13}H_{23}NO_3Si$: C, 57.96; H, 8.60; N, 5.20%.

4.1.9. tert-Butyl 2-(1-(((tert-butoxycarbonyl)amino)methyl)-1-sila-1-cyclohexyl)acetate (**8**)

A solution of **7** (802 mg, 2.98 mmol) in *tert*-butanol (5 ml) was heated under reflux for 1 day. The solvent was removed under reduced pressure, and the residue was purified by bulb-to-bulb distillation in vacuo (Kugelrohr apparatus). The fraction collected at 110–130 °C/0.001 mbar (717 mg) was crystallized from diethyl ether (25 ml) at −27 °C over a period of 3 days. The product was isolated by filtration, washed with cold (–27 °C) *n*-pentane (5 ml), and dried in vacuo (0.001 mbar, 20 °C, 4 h) to give **8** in 44% yield as a colorless crystalline solid (450 mg, 1.31 mmol); m.p.: 84–85 °C. ^1H NMR (C_6D_6): δ 0.64–0.74 (m, 4H, $SiCH_2C$), 1.27–1.39 (m, 2H, $Si(CH_2)_2CH_2C$), 1.50 (s, 9H, CCH_3), 1.59 (s, 9H, CCH_3), 1.61–1.73 (m, 4H, $SiCH_2CH_2C$), 1.90 (s, 2H, $SiCH_2C(O)$), 2.96 (d, $^3J_{HH}$ = 5.4 Hz, 2H, $SiCH_2N$), 5.1 (br s, 1H, NH). ^{13}C NMR (C_6D_6): δ 10.5 ($SiCH_2C$), 23.7 ($SiCH_2C(O)$), 24.2 ($SiCH_2CH_2C$), 27.9 ($SiCH_2N$), 28.2 (CCH_3), 28.5 (CCH_3), 29.7 ($Si(CH_2)_2CH_2C$), 78.4 (CCH_3), 79.9 (CCH_3), 156.8 (NC(=O)O), 171.9 (C*C*(=O)O). ^{15}N NMR (C_6D_6): δ −310.4. ^{29}Si NMR (C_6D_6): δ −3.0. Anal. Found: C, 59.5; H, 9.5; N, 4.1. Calc. for $C_{17}H_{33}NO_4Si$: C, 59.44; H, 9.68; N, 4.08%.

4.1.10. 1-Chloro-1-(chloromethyl)-1-silacyclohexane (**10**)

50 ml of a solution of 1,5-dibromopentane (161 g, 700 mmol) in diethyl ether (500 ml) were added to a stirred suspension of magnesium turnings (37.4 g, 1.54 mol) in diethyl ether (200 ml), and the reaction was started by gentle heating. Subsequently, the remaining ethereal 1,5-dibromopentane solution was added within 90 min, causing the mixture to boil under reflux. After the addition was complete, the mixture was heated under reflux for a further 90 min and then cooled to 20 °C within 1 h. The resulting two-phase Grignard reagent (which was separated from residual magnesium turnings by decantation, followed by washing of the magnesium with diethyl ether (2 × 50 ml)) was added dropwise within 90 min to a solution of trichloro(chloromethyl)silane (129 g, 701 mmol) in diethyl ether (300 ml), causing the mixture to boil under reflux. During the addition, the mixture was stirred vigorously with a mechanical stirrer (formation of a precipitate). After the addition was complete, the mixture was stirred at 20 °C for 16 h, the precipitate was separated by filtration and washed with diethyl ether (2 × 200 ml), the filtrate and the wash solutions were combined, and the solvent was removed by distillation under atmospheric pressure, causing a postprecipitation. The precipitate was separated by decantation and washed with *n*-pentane (2 × 50 ml), and all organic solutions were combined. The solvent was removed as described above, and the crude product (79 g) was isolated by distillation in vacuo (Vigreux column, 30 cm; b.p.: 80–95 °C/18 mbar) and then further purified by redistillation to afford **10** in 52% yield (related to 1,5-dibromopentane) as a colorless liquid (67.4 g, 368 mmol); b.p.: 88–90 °C/18 mbar. ^1H NMR ($CDCl_3$): δ 0.92–1.12 (m, 4H, $SiCH_2C$), 1.21–1.37, 1.56–1.79, and 1.81–1.95 (m, 6H, $SiCH_2(CH_2)_2C$), 2.98 (s, 2H, $SiCH_2Cl$). ^{13}C NMR ($CDCl_3$): δ 13.4 ($SiCH_2C$), 23.3 ($SiCH_2CH_2C$), 28.9 ($Si(CH_2)_2CH_2C$), 29.0 ($SiCH_2Cl$). ^{29}Si NMR ($CDCl_3$): δ 20.8. Anal. Found: C, 39.0; H, 6.3. Calc. for $C_6H_{12}Cl_2Si$: C, 39.35; H, 6.60%.

4.1.11. 1,1'-Oxybis(((1-sila-1-cyclohexyl)methyl)-ammonium) dichloride (**11**)

A solution of **4** (720 mg, 2.67 mmol) in toluene (5 ml) was added at 20 °C in one single portion to a solution of triphenylphosphine (722 mg, 2.75 mmol) in toluene (5 ml), and the mixture was stirred at 20 °C for 1 day. The solvent was removed under reduced pressure, 6 M hydrochloric acid (20 ml) was added to the residue, and the mixture was then heated under reflux for 2 h [8], cooled to 20 °C, and washed with dichloromethane (2 × 10 ml) to remove any triphenylphosphine oxide formed. The aqueous phase was kept undisturbed at −20 °C for 2 days, and the resulting precipitate was isolated by filtration and recrystallized from 6 M hydrochloric acid at −20 °C over a period of 2 days. The product was isolated by filtration and dried in vacuo (0.001 mbar, 20 °C, 8 h) to give **11** in 38% yield (including workup of the mother liquor) as a colorless crystalline solid (177 mg, 512 μmol); m.p.: 256–257 °C (dec.) ^1H NMR ([D$_6$]DMSO): δ 0.62–0.78 and 0.82–0.96 (m, 8H, $SiCH_2C$), 1.25–1.46 (m, 4H, $Si(CH_2)_2CH_2C$), 1.49–1.76 (m, 8H, $SiCH_2CH_2C$), 2.29 (q, $^3J_{HH}$ = 5.9 Hz, 4H, $SiCH_2N$), 8.1 (br s, 6H, NH_3). ^{13}C NMR ([D$_6$]DMSO): δ 13.7 ($SiCH_2C$), 23.7 ($SiCH_2CH_2C$), 25.5 ($SiCH_2N$), 28.8 ($Si(CH_2)_2CH_2C$). ^{29}Si NMR ([D$_6$]DMSO): δ 0.7. Anal. Found: C, 41.4; H, 8.3; N, 8.0. Calc. for $C_{12}H_{30}Cl_2N_2OSi_2$: C, 41.72; H, 8.75; N, 8.11%.

4.2. Crystal structure analysis

A suitable single crystal of **11** · $2H_2O$ was obtained directly from the preparation of this compound (see above; crystallization from 6 M hydrochloric acid at

−20 °C; no subsequent drying to avoid loss of the water of crystallization). The crystal was mounted in inert oil (perfluoroalkyl ether, ABCR) on a glass fiber and then transferred to the cold nitrogen gas stream of the diffractometer (Stoe IPDS; graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å)). The structure was solved by direct methods [9]. All non-hydrogen atoms were refined anisotropically [10]. The N*H* and O*H* hydrogen atoms were localized in difference Fourier syntheses and refined freely. A riding model was employed in the refinement of the C*H* hydrogen atoms. In addition, crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-247202. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

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[8] Under milder reaction conditions (20 °C), the same product was obtained, but it was formed at a much slower rate.

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