Syntheses, Characterization, and Molecular Mechanics Calculations of Optically Active Silatrane Derivatives

Motoyuki Tasaka, Masakazu Hirotsu, and Masaaki Kojima

Department of Chemistry, Faculty of Science, Okayama University, Tsushima, Okayama 700, Japan

Shunji Utsuno

Department of Chemistry, Faculty of Science, Shizuoka University, Oya, Shizuoka 422, Japan

Yuzo Yoshikawa*

Coordination Chemistry Laboratories, Institute for Molecular Science, Myodaiji, Okazaki 444, Japan

Received March 29, 1996[⊗]

A series of optically active silatrane derivatives, [Si{N(CHRCH$_2$O)(CH$_2$CH$_2$O)$_2$}X] (R = Me, *i*-Pr; X = Ph, OMe) has been synthesized by the reaction of optically active triethanolamine derivatives with XSi(OMe)$_3$, and characterized by ^{1}H NMR, ^{13}C NMR, ^{29}Si NMR, and mass spectroscopy, and the structures of six compounds have been determined by X-ray analysis. Molecular mechanics methods have also been employed to obtain the energy-minimized structures. The ^{29}Si NMR chemical shifts and the lengths of Si−N determined by X-ray analysis are sensitive to the bulkiness of the substituent (R). The Si−X bond lengths (X: trans position to nitrogen) do not appreciably differ from one another. The MM2 calculations indicated that the substituent exists in the equatorial position, and the results are in agreement with those of X-ray analysis and ^{1}H NMR spectroscopy. Crystallographic data: [R = H; X = OMe], $C_7H_{15}NO_4Si$, orthorhombic, $Pna2_1$, a = 13.407(1) Å, b = 8.761(2) Å, c = 8.191(1) Å, Z = 4; [R = Me; X = OMe], $C_8H_{17}NO_4Si$, orthorhombic, $P2_12_12_1$, a = 10.110(3) Å, b = 11.083(2) Å, c = 9.474(2) Å, Z = 4; [R = *i*-Pr; X = OMe], $C_{10}H_{21}NO_4Si$, monoclinic, $P2_1$, a = 8.481(1) Å, b = 7.805(1) Å, c = 10.218(2) Å, β = 111.31(1)°, Z = 2; [R = Me; X = Ph], $C_{13}H_{19}NO_3Si$, orthorhombic, $P2_12_12_1$, a = 8.813(1) Å, b = 11.137(2) Å, c = 13.757(1) Å, Z = 4; [R = *i*-Pr; X = Ph], $C_{15}H_{23}NO_3Si$, orthorhombic, $P2_12_12_1$, a = 8.365(1) Å, b = 13.538(2) Å, c = 13.841(2) Å, Z = 4.

Introduction

The five-coordinated silicon compounds silatranes (1-substituted-2,8,9-trioxa-5-aza-1-silabicyclo[3.3.3]undecanes) shown in Figure 1 (R = H) are a class of organosilicon compounds that have pentacoordinated trigonal bipyramidal structures. Much attention is being paid to the unique molecular structure, biological activity, and chemical reactivity by biologists and pharmacologists, etc.[1−14] Silatranes show a variety of biological activities. 1-Phenylsilatrane (R = H; X = C_6H_5) is especially toxic; the LD_{50} value in rats (0.3−0.5 mg kg^{-1}) is six times as small as that for KCN.[15] It is interesting to note that among 13 nitrilotriethoxy silanes tested for biological activity, only the phenyl derivatives showed high activity with respect to the central nervous system.[1]

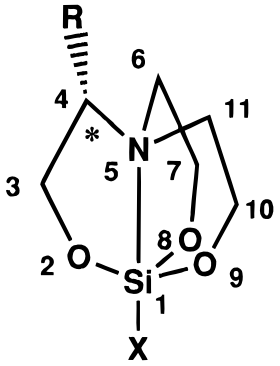


Figure 1. General formula of silatrane derivatives.

Another intriguing aspect of this structure is the existence of and influence of a "transannular bond" between the silicon and nitrogen atoms. The fact that this transannular bond exists in silatranes was demonstrated by Turley and Boer through a single-crystal X-ray study.[16] The silicon−nitrogen internuclear

[⊗] Abstract published in *Advance ACS Abstracts,* October 15, 1996.

(1) Voronkov, M. G. *Pure Appl. Chem.* **1966**, *13*, 35.
(2) Tandura, S. N.; Voronkov, M. G.; Alekseev, N. V. *Top. Curr. Chem.* **1986**, *131*, 99.
(3) Voronkov, M. G.; Dyakov, V. M.; Kirpichenko, S. V. *J. Organomet. Chem.* **1982**, *233*, 1.
(4) Hencsei, P.; Parkanyl, V.; Fulop, V.; Baryshok, V. P.; Voronkov, M. G.; Kuznetsova, G. A. *J. Organomet. Chem.* **1988**, *346*, 315.
(5) Hencsei, P.; Parkanyl, L. *Rev. Silicon, Germanium, Tin Lead Compd.* **1985**, *8*, 191.
(6) Dráger, M.; Ross, L.; Simon, D. *Rev. Silicon, Germanium, Tin Lead Compd.* **1983**, *7*, 299.
(7) Gerr, R. G.; Yanovskii, A. I.; Struchkov, Y. T. *Kristallografiya* **1983**, *28*, 1029.
(8) Iwamiya, J. H.; Maiciel, G. E. *J. Am. Chem. Soc.* **1993**, *115*, 6835
(9) Voronkov, M. G.; Baryshok, V. P.; Lazareva, N. F.; Saraev, V. V.; Vakulskaya, T. I.; Hencsei, P.; Kovacs, L. *J. Organomet. Chem.* **1989**, *368*, 155.
(10) Lee, Y.-A.; Chung, Y. K.; Kim, Y.; Jeong, J. H.; Chung, G.; Lee, D. *Organometallics* **1991**, *10*, 3707.
(11) Gudat, D.; Daniels, L. M.; Verkade, J. G. *J. Am. Chem. Soc.* **1989**, *111*, 8520.
(12) Parkanyl, L.; Fulop, V.; Hencsei, P.; Kovacs, I. *J. Organomet. Chem.* **1991**, *418*, 173.
(13) Nasim, M.; Livantsova, L. I.; Krut'ko, D. P.; Zaitseva, G. S.; Lorbeth, J.; Otto, M. *J. Organomet. Chem.* **1991**, *402*, 313.
(14) Voronkov, M. G.; Platonova, R. N.; Svarinskaya, R. A.; Karpova, N. I.; Dyakov, V. M. *Kokl. Akad. Nauk SSSR* **1978**, *242*, 1407.
(15) Voronkov, M. G. *Top. Curr. Chem.* **1979**, *84*, 77.
(16) Turley, J. W.; Boer, F. P. *J. Am. Chem. Soc.* **1968**, *90*, 4026.

S0020-1669(96)00349-7 CCC: $12.00 © 1996 American Chemical Society

distances (r_{Si-N}) has been found to range from 2.02 Å for the chloro derivative (X = Cl) to 2.89 Å[17] for the (*trans*-dimethylphenylphosphino)platinum derivative.[5,18] These distances are considerably shorter than the sum of the van der Waals radii of 3.5 Å for silicon and nitrogen. Hence, these structures have a transannular bond between silicon and nitrogen. The Si−N bond distances are variable according to the properties of the apical substituent (X) on silicon. The relationship between the Si−N distance and the axial substituent is well-understood, a stronger electron-withdrawing substituent generally resulting in a shorter Si−N distance.[19]

Voronkov has reported that the LD_{50} values depend on the cage structure.[15] Although silatranes have been much studied, 4-alkyl-substituted silatrane derivatives have received little attention. To our knowledge, there has been only one report about the synthesis of 4-ethylsilatrane derivatives.[20] Here, we report on the preparation, characterization, molecular structures, and MM2 calculations of these silatrane derivatives and discuss the effect of the 4-substitution on the molecular geometry by comparison with those of the nonsubstituted silatranes.

Experimental Section

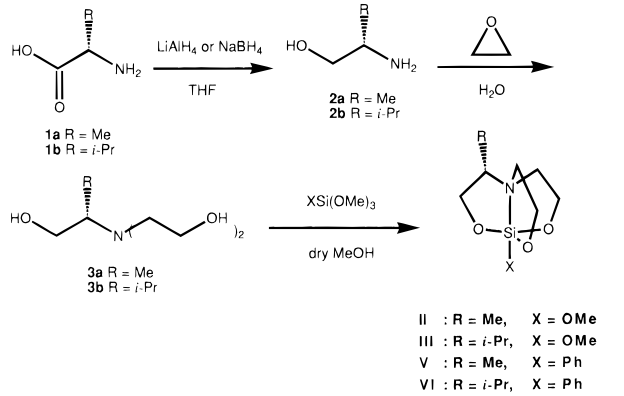
Materials. Tetrahydrofuran (THF) and diethyl ether were dried by passage through a column of activated alumina followed by drying with sodium benzophenone ketyl prior to use. MeOH was dried with an Mg ribbon. These solvents were stored under N_2. L-Valine, Si(OMe)$_4$, and PhSi(OMe)$_3$ were purchased from Tokyo Kasei Co. Ltd. L-Alanine, $LiAlH_4$, ethylene chlorohydrin, and triethanolamine were obtained from Wako Co. Ltd. $NaBH_4$ and alumina activated 300 were purchased from Nacalai Tesque Co. Ltd. These reagents were used without further purification.

Physical Measurements. Solution NMR spectra were recorded on a JEOL EX270 FT NMR spectrometer. ^{1}H (270 MHz) NMR spectra were referenced to the chemical shift of the residual proton signal of the deuterated solvent (7.26 ppm for $CDCl_3$) or tetramethylsilane (TMS) as the internal reference. ^{13}C (67.9 MHz) NMR spectra were referenced to the solvent signals (77.0 ppm for $CDCl_3$). ^{29}Si (53.7 MHz) NMR spectra were referenced to TMS in $CDCl_3$ (10% by volume) as an external standard. ^{13}C NMR spectra of compounds were assigned with the C−H COSY technique. The recording temperature was 20 °C. Elemental analyses were carried out at the Chemical Materials Center, Institute for Molecular Science. Mass spectra were obtained with a Shimadzu GCMS-QP1000EX spectrometer (low resolution, 70 eV, EI) at the Chemical Materials Center, Institute for Molecular Science. GC analyses were performed on a Shimadzu GC-14A spectrometer equipped with a flame ionization detector using a Shimadzu capillary column (CBP1-M25-025). Melting points were determined with a Yanagimoto MP instrument.

Syntheses. The present compounds were obtained as shown in Scheme 1. At first the carboxyl group of the L-amino acids (**1a**,**b**) was reduced to give the amino alcohols, followed by *N*-alkylation with ethylene oxide to give the optically active triethanolamine derivatives (**3a**,**b**). They were finally allowed to react with XSi(OMe)$_3$ to give the silatrane derivatives.

Synthesis of 2-(*S*)-Amino-1-propanol, 2a. To a solution of L-alanine **1a** (50.6 g, 0.57 mol) in dry THF (250 mL) was added lithium aluminum hydride (21.0 g, 0.55 mol) little by little for 1.5 h at 0 °C. Simultaneously to the solution dry THF (200 mL) was added little by little. The mixture was refluxed for 17 h. The yellow solvent containing **2a** was decanted and concentrated. To the white Al(OH)$_3$ residue was added a mixture of THF and water (3:1). The mixture was refluxed for 12 h to extract **2a** in the residue. This procedure was repeated 5 times. To the combined extracts was added the above concentrate from decantation, and the solvent of the mixture was removed under reduced pressure (20 mmHg) to give **2a** (12.5 g, 29%) as a yellow syrup. ^{1}H NMR ($CDCl_3$): δ 1.04 (d, 3H, $J_{2,3}$ = 6.26 Hz, H-3), 2.97−3.03 (m, 1H, H-2), 3.23 (dd, 1H, $J_{1,1'}$ = 10.56 Hz, $J_{1,2}$ = 7.92 Hz, H-1), 3.52 (dd, 1H, $J_{1',2}$ = 3.96 Hz, H-1′).

Scheme 1



Synthesis of 2-(*S*)-Amino-3-methylbutanol, 2b. To a stirred suspension of $NaBH_4$ (20.1 g, 0.53 mol) in THF (200 mL, reagent grade without further purification) was added L-valine (25.2 g, 0.22 mol). The flask was immersed in an ice-water bath, and a solution of concentrated H_2SO_4 (13 mL, 0.23 mol) in ether (total volume of 50 mL) was added dropwise at such a rate as to maintain the reaction mixture temperature below 20 °C (addition time, approximately 3 h). Stirring of the reaction mixture was continued at room temperature for 15 h, and then MeOH (20 mL) was added carefully to decompose excess B_2H_6. The mixture was concentrated to ca. 100 mL, and then 5 M NaOH (200 mL) was added. After organic solvents were removed by distillation below 100 °C, the mixture was refluxed for 3 h. The turbid aqueous mixture was cooled to room temperature. The resulting precipitate was filtered through a thin pad of Celite and washed with water. The filtrate and the washings were combined. The solution was further diluted with additional water. The CH_2Cl_2 extraction (4 × 100 mL) followed by evaporation of the solvent left the pure product, **2b** (12.7 g, 57%) as yellow syrup. ^{1}H NMR ($CDCl_3$): δ 0.89 (d, 3H, $J_{3,4}$ = 6.6 Hz, H-4), 0.91 (d, 3H, $J_{3,4'}$ = 6.9 Hz, H-4′), 1.49−1.62 (m, 1H, $J_{2,3}$ = Hz, $J_{2',3}$ = Hz, $J_{3,4}$ = 8.8 Hz, H-3), 2.50−2.57 (m, 1H, H-2), 3.28 (dd, 1H, $J_{1,1'}$ = 10.4 Hz, $J_{1,2}$ = 8.8 Hz, H-1), 3.62 (dd, 1H, $J_{1',2}$ = 4.0 Hz, H-1′).

Synthesis of 2-(*S*)-(Bis(hydroxyethyl)amino)propanol Hydrochloride, 3a·HCl. To a solution of **2a** (12.0 g, 0.16 mol) in water (10 mL) was added ethylene oxide at atmospheric pressure at room temperature for 5 h. To the mixture was added hydrochloric acid (36%, 20 mL), and the solvent was evaporated in vacuo. The residue was washed with EtOH to give **3a·HCl** (25.2 g, 79%) as white crystals. ^{1}H NMR (D_2O): δ 1.27 (d, 3H, $J_{2,3}$ = 6.3 Hz, H3), 3.15−3.20 (m, 1H, H-2), 3.46 (t, 4H, $J_{1',2'}$ = 5.0 Hz, H-2′), 3.65−3.87 (m, 2H, H-1), 3.92 (t, 4H, H-1′).

Synthesis of 2-(*S*)-(Bis(hydroxyethyl)amino)butanol, 3b. To a solution of **2b** (12.7 g, 0.12 mol) in water (13 mL) was added ethylene oxide at atmospheric pressure at room temperature for 8 h. The solvent was evaporated in vacuo to give **3b** (21.2 g, 90%) as yellow syrup. ^{1}H NMR ($CDCl_3$): δ 0.85 (d, 3H, $J_{1,2}$ = 6.6 Hz, H-4), 0.95 (d, 3H, $J_{1,2}$ = 6.9 Hz, H-4′), 1.71−1.83 (m, 1H, H-3), 2.50−2.57 (m, 1H, H-2), 3.23 (dd, 1H, $J_{1,1'}$ = 10.6 Hz, $J_{1,2}$ = 7.9 Hz, H-1), 3.52 (dd, 1H, $J_{1',2}$ = 4.0 Hz, H-1′).

1-Methoxysilatrane, I. White powder was obtained by the literature method:[1] mp 155−156 °C (lit.[1] 155−156 °C). ^{1}H NMR ($CDCl_3$): δ 2.85 (t, 6H, $J_{3,4}$ = 5.94 Hz, NCH_2), 3.49 (s, 3H, OCH_3), 3.84 (t, 6H, OCH_2). ^{13}C NMR ($CDCl_3$): δ 57.59 (CH_2O), 51.18 (CH_2N), 50.89 (CH_3O). ^{29}Si NMR ($CDCl_3$): δ −94.5. LRMS (70 eV, EI) *m*/*z* (relative intensity, proposed ion): 205 (18.8, M^+), 174 (80.3, M^+ - OCH_3), 162 (100.0, M^+ - C_2H_5N), 132 (17.9). Anal. Calcd for $C_7H_{15}NO_4Si$: C, 40.95; H, 7.36; N, 6.82. Found: C, 40.43; H, 7.00; N, 6.77.

(17) Eaborn, C.; Odell, K. J.; Pidcock, A.; Scollary, G. R. *J. Chem. Soc., Chem. Commun.* **1976**, 317.
(18) Hencsei, P.; Csonka, G.; Kovács, I. *J. Organomet. Chem.* **1987**, *329*, 305.
(19) Kemme, A. A.; Bleidelis, J. J.; Petsunovich, V. A.; Baryshok V. P.; Voronkov, M. G. *Dokl. Akad. Nauk SSSR* **1978**, *243*, 688.
(20) Yang, Y.; Yin, C. *Gaodeng Xuexiao Huaxue Xuebao* **1986**, *7*, 430.

Table 1. Crystallographic Data

	I R = H; X = OMe	**II** R = Me; X = OMe	**III** R = *i*-Pr; X = OMe	**V** R = Me; X = Ph	**VI** R = *i*-Pr; X = Ph
chem formula	$C_7H_{15}NO_4Si$	$C_8H_{17}NO_4Si$	$C_{10}H_{21}NO_4Si$	$C_{13}H_{19}NO_3Si$	$C_{15}H_{23}NO_3Si$
fw	205.29	219.31	247.37	265.38	293.44
space group	$Pna2_1$ (No. 33)	$P2_12_12_1$ (No. 19)	$P2_1$ (No. 4)	$P2_12_12_1$ (No. 19)	$P2_12_12_1$ (No. 19)
a,	13.407(1)	10.110(3)	8.481(1)	8.813(1)	8.365(1)
b,	8.761(2)	11.083(2)	7.805(1)	11.137(2)	13.538(2)
c,	8.191(1)	9.474(2)	10.218(2)	13.757(1)	13.841(2)
β, deg			111.31(1)		
V, Å^3	962.2(2)	1061.6(3)	630.1(2)	1350.2(2)	1567.3(3)
Z	4	4	2	4	4
T, °C	20	20	20	20	20
λ, Å	0.7107	0.7107	0.7107	0.7107	0.7107
ρ_{calc}, g cm^{-3}	1.417	1.372	1.304	1.305	1.243
abs coeff (Mo Kα), mm^{-1}	0.229	0.212	0.186	0.175	0.157
R/R_w[a]	0.038/0.040	0.043/0.026	0.040/0.024	0.032/0.034	0.045/0.054

[a] Relevant expressions are as follows, where F_o and F_c represent respectively the observed and calculated structure factor amplitudes. Function minimized was $w(|F_o| - |F_c|)^2$, where $w = 1/\sigma^2(F_o)$. $R = \sum||F_o| - |F_c||/\sum|F_o|$. $R_w = [(\sum w(|F_o| - |F_c|)^2/\sum wF_o^2]^{1/2}$.

Synthesis of 1-Methoxy-4-(*S*)-methylsilatrane, II. **3a**·HCl (4.12 g, 20.6 mmol) was neutralized with NaOH (2.11 g, 52.8 mmol) in MeOH. The solvent was evaporated to give **3a** as yellow syrup and NaCl. Then **3a** was extracted with chloroform. The chloroform layer was evaporated to give **3a** as yellow syrup. The syrup was dried over P_2O_5. To a solution of the above whole syrup (**3a**) in dry MeOH (20 mL) was added $Si(OMe)_4$ (4 mL, 27.1 mmol). The mixture was refluxed for 2 days under a nitrogen atmosphere and evaporated in vacuo to yield brown syrup. The syrup was chromatographed on silica gel, by the use of a MeOH−$CHCl_3$ (1:99) mixture. The eluate containing the yellow layer was concentrated in vacuo, and the residue was recrystallized from $CHCl_3$−hexane to give **II** (2.04 g, 45%) as the white powder: mp 155−156 °C. ^{1}H NMR ($CDCl_3$): δ 1.11 (d, 3H, $J_{4,12}$ = 6.6 Hz, H-12), 2.51 (dd, 1H, $J_{6,6'}$ = 12.2 Hz, $J_{6,7}$ = 4.0 Hz, H-6), 2.70−2.90 (m, 3H, H-6′, H-9, H-9′), 2.97−3.10 (ddq, 1H, $J_{3,4}$ = 11.2 Hz, $J_{3',4}$ = 5.9 Hz, H-4), 3.46 (dd, 1H, $J_{3,3'}$ = 10.9 Hz, H-3), 3.47 (s, 3H, O-CH_3), 3.74−3.92 (m, 4H, H-7, H-7′, H-10, H-10′, dd, H-3′). ^{13}C NMR ($CDCl_3$): δ 62.70 (O*C*H_2CH(CH_3)N), 57.03, 56.97 (CH_2O), 53.44 (OCH$_2$*C*H(CH_3)N), 50.35 (CH_3O), 47.47, 44.57 (CH_2N), 9.50 (CH(*C*H_3)). ^{29}Si NMR ($CDCl_3$): δ −94.5. LRMS (70 eV, EI) *m/z* (relative intensity, proposed ion): 219 (7.3, M^+), 188 (40.0, $M^+ - OCH_3$), 176 (100.0, $M^+ - C_2H_5N$). Anal. Calcd for $C_8H_{17}NO_4Si$: C, 43.81; H, 7.81; N, 6.39. Found: C, 43.54; H, 7.53; N, 6.40.

Synthesis of 4-(*S*)-Isopropyl-1-methoxysilatrane, III. To a solution of **3b** (3.21 g, 16.2 mmol) in dry MeOH (10 mL) was added $Si(OMe)_4$ (3.2 mL, 21.7 mmol). The mixture was refluxed for 21 h under a nitrogen atmosphere and evaporated in vacuo to yield brown syrup. The syrup was chromatographed on silica gel, by the use of a MeOH−$CHCl_3$ (1:99) mixture. The yellow organic layer was concentrated in vacuo, and the residue was recrystallized from $CHCl_3$−hexane to give **III** (2.19 g, 53%) as white powder: mp 112−113 °C. ^{1}H NMR ($CDCl_3$): δ 0.91 (d, 3H, $J_{12,13}$ = 6.6 Hz, H-13), 1.14 (d, 3H, $J_{12,14}$ = 6.6 Hz, H-14), 1.82−1.90 (m, 1H, H-12), 2.50−2.60 (m, 1H, H-4), 2.70−2.95 (m, 3H, H-6, H-6′, H-9), 3.08−3.13 (m, 1H, H-9′), 3.42 (dd, 1H, $J_{3,3'}$ = 11.1 Hz, $J_{3,4}$ = 11.1 Hz, H-3), 3.48 (s, 3H, O-CH_3), 3.80−3.90 (m, 4H, H-7, H-7′, H-10, H-10′), 3.95 (dd, 1H, $J_{3',4}$ = 5.9 Hz, H-3′). ^{13}C NMR ($CDCl_3$): δ 64.33 (*C*(*i*-Pr)N), 62.16 (O*C*H_2CH(*i*-Pr)N), 57.97 (CH_2O), 50.82 (CH_3O), 50.98, 45.93 (CH_2N), 28.77 (*C*H(CH_3)$_2$), 21.82, 19.82 (CH(*C*H_3)$_2$). ^{29}Si NMR ($CDCl_3$): δ −90.8. LRMS (70 ev, EI) *m/z* (relative intensity, proposed ion): 247 (23.0, M^+), 216 (49.2, $M^+ - OCH_3$), 204 (100.0, $M^+ - C_2H_5N$), 172(31.6), 148(11.2). Anal. Calcd for $C_{10}H_{21}NO_4Si$: C, 48.55; H, 8.56; N, 5.66. Found: C, 48.43; H, 8.38; N, 5.62.

1-Phenylsilatrane, IV. White powder was obtained by the literature method:[1] mp 211−212 °C (lit.[1] 210−211 °C). ^{1}H NMR ($CDCl_3$): δ 2.91 (t, 6H, $J_{3,4}$ = 5.9 Hz, NCH_2), 3.90 (t, 6H, OCH_2), 7.24−7.26 [m, 3H, Ph(*o,p*)], 7.71 [m, 2H, Ph(*m*)]. ^{13}C NMR ($CDCl_3$): δ 134.05 [Ph(*m*)], 127.74, 127.29 [Ph(*o,p*)], 57.70 (CH_2O), 50.98 (CH_2N). ^{29}Si NMR ($CDCl_3$): δ −81.6. LRMS (70 eV, EI) *m/z* (relative intensity, proposed ion): 251 (9.4, M^+), 174 (100.0, $M^+ - C_6H_5$), 130 (4.2, $M^+ - C_6H_5 - C_2H_5N$). Anal. Calcd for $C_{12}H_{17}NO_3Si$: C, 57.30; H, 6.81; N, 5.57. Found: C, 56.69; H, 6.61; N, 5.54.

Synthesis of 4-(*S*)-Methyl-1-phenylsilatrane, V. This compound was synthesized by the same method as that for **II** except $PhSi(OMe)_3$ was used instead of $Si(OMe)_4$: mp 136−137 °C. ^{1}H NMR ($CDCl_3$): δ 1.14 (d, 3H, $J_{4,12}$ = 6.6 Hz, H_3-12), 2.57 (ddd, 1H, $J_{6,6'}$ = 12.5 Hz, $J_{6,7}$ = 3.3−3.6 Hz, $J_{6,7'}$ = 1.0 Hz, H-6), 2.82−2.95 (m, 3H, H-6′, H-9, H-9′), 3.07−3.20 (ddq, 1H, $J_{3,4}$ = 11.2 Hz, $J_{3',4}$ = 5.9 Hz, H-4), 3.54 (dd, 1H, $J_{3,3'}$ = 10.9 Hz, H-3), 3.81 (dd, 1H, H-3′), 7.21−7.29 [m, 3H, Ph(*o, p*)], 7.69−7.73 [m, 2H, Ph(*m*)]. ^{13}C NMR ($CDCl_3$): δ 134.00 [Ph(*m*)], 127.49, 127.12 [Ph(*o,p*)], 63.15 (O*C*H_2CH(CH_3)N), 57.47 (CH_2O), 53.66 (OCH$_2$*C*H(CH_3)N), 47.85, 44.98 (CH_2N), 9.92 (CH(*C*H_3)). ^{29}Si NMR ($CDCl_3$): δ −80.5. LRMS (70 eV, EI) *m/z* (relative intensity, proposed ion): 265 (18.1, M^+), 222 (100.0, $M^+ - C_2H_5N$), 188 (67.5, $M^+ - C_6H_5$). Anal. Calcd for $C_{13}H_{19}NO_3Si$: C, 58.82; H, 7.22; N, 5.28. Found: C, 57.94; H, 7.25; N, 5.15.

Synthesis of 4-(*S*)-Isopropyl-1-phenylsilatrane, VI. This compound was synthesized by the same method as that for **III** except $PhSi(OMe)_3$ was used instead of $Si(OMe)_4$: mp 132−133 °C. ^{1}H NMR ($CDCl_3$): δ 0.93 (d, 3H, $J_{12,13}$ = 6.6 Hz, H-13), 1.16 (d, 3H, $J_{12,13'}$ = 6.6 Hz, H-14), 1.81−1.95 (m, 1H, H-12), 2.57−2.67 (m, 1H, H-4), 2.74−3.16 (m, 4H, H-6, H-6′, H-9, H-9′), 3.49 (dd, 1H, $J_{3,3'}$ = 11.1 Hz, $J_{3,4}$ = 11.1 Hz, H-3), 3.75 (dd, 1H, $J_{3',4}$ = 5.94 Hz, H-3′), 7.24−7.26 [m, 3H, Ph(*o,p*)], 7.68−7.72 [m, 2H, Ph(*m*)]. ^{13}C NMR ($CDCl_3$): δ 134.05 [Ph(*m*)], 127.96, 127.28 [Ph(*o,p*)], 64.29 (OCH$_2$*C*H(*i*-Pr)N), 62.19 (O*C*H_2CH(*i*-Pr)N), 58.22 (CH_2O), 51.12, 45.99 (CH_2N), 29.02 (*C*H(CH_3)$_2$), 22.03, 19.97 (CH(*C*H_3)$_2$). ^{29}Si NMR ($CDCl_3$): δ −75.4. LRMS (70 eV, EI) *m/z* (relative intensity, proposed ion): 293 (36.6, M^+), 250 (100.0), 216 (33.1, $M^+ - C_6H_5$), 172 (24.2, $M^+ - C_2H_5N$), 148(13.6). Anal. Calcd for $C_{15}H_{23}NO_3Si$: C, 61.41; H, 7.90; N, 4.77. Found: C, 60.53; H, 7.80; N, 4.59.

WARNING: Some silatranes are toxic[3] and should be handled with caution.

X-ray Structure Analysis. The single crystals were obtained by diffusing hexane over a CH_2Cl_2 solution of each compound. Crystals were mounted on a glass fiber with epoxy resin. Crystal data are summarized in Table 1. The reflections were collected on an Enraf-Nonius CAD4 (**I**, **V**, **VI**) and a Rigaku AFC5S (**II**, **III**) automated four-circle diffractometer with graphite-monochromatized Mo Kα radiation. The unique reflections with $I > 3\sigma(I)$ were used for the structure refinements. All of the calculations were performed using the teXsan[21] crystallographic software package of Molecular Structure Corp. The structures of **I**, **III**, **V**, and **VI** were solved by heavy-atom Patterson methods[22] and expanded using Fourier techniques.[23] The structure of **II** was solved by direct methods[24] and expanded using Fourier techniques.[23] The non-hydrogen atoms were refined anisotro-

(21) *teXsan*: Crystal Structure Analysis Package; Molecular Structure Corp.: 1985 and 1992.

(22) Beurskens, P. T.; Admiraal, G.; Beurskens, G.; Bosman, W. P.; Garcia-Granda, S. R.; Gould, O.; Smits, J. M. M.; Smykalla, C. *PATTY*: The DIRDIF program system, Technical Report of the Crystallography Laboratory, University of Nijmegen: Nijmegen, The Netherlands, 1992.

Table 2. Force Field Parameters Used in the Present Calculations (LP = lone pair, O_{ax} = O (axial), C2 = C (sp2), C3 = C (sp3))

Stretching

	force constant, mdyn Å^{-1}	equilib value, Å
C3−O_{ax}	5.36	1.402
N−Si	5.1	2.186
Si−O_{ax}	5.5	1.626
LP−O_{ax}	4.6	0.6

Bending

	force constant, mdyn Å rad^{-2}	equilib value, deg
C3−N−Si	0.63	107.7
C3−O_{ax}−Si	0.77	106.8
C3−O_{ax}−LP	0.35	105.16
C2−Si−O	0.7	90.0
C2−Si−N	1.045	180.0
H−C3−O_{ax}	0.54	106.7
O−Si−O	0.46	120.0
O−Si−N	0.8	90.0
O−Si−O_{ax}	0.46	90.0
N−Si−O_{ax}	0.8	180.0
Si−O_{ax}−LP	0.35	105.16
LP−O_{ax}−LP	0.24	131.0

Out of Plane Bending

	force constant, mdyn Å rad^{-2}
C2−Si	0.05

Torsional

	force constant, kJ mol^{-1}		
	V1	V2	V3
C3−C3−N−Si	−0.84	3.05	3.35
H−C3−N−Si	0.0	0.0	2.18
H−C3−O_{ax}−Si	0.0	0.0	2.22
H−C3−O_{ax}−LP	0.0	0.0	0.0
C2−C2−Si−O	0.0	0.0	0.0
C2−C2−Si−N	0.0	0.0	0.0
C3−O−Si−C2	0.0	0.0	1.69
C3−O−Si−N	0.0	0.0	0.96
C3−O−Si−O_{ax}	−0.71	−5.02	0.0
LP−O−Si−C2	0.0	0.0	0.0
LP−O−Si−N	0.0	0.0	0.0
LP−O−Si−O_{ax}	0.0	2.09	−0.84
C3−N−Si−C2	0.0	0.0	0.0
C3−N−Si−O	0.0	0.0	0.96
C3−N−Si−O_{ax}	0.0	0.0	0.96
O−Si−O_{ax}−C3	−0.71	−5.02	0.0
O−Si−O_{ax}−LP	0.0	2.09	−0.84
N−Si−O_{ax}−C3	0.0	0.0	0.96
N−Si−O_{ax}−LP	0.0	0.0	0.0

van der Waals

	van der Waals radius, Å	ϵ, kJ mol^{-1}
O_{ax}	1.74	0.21

pically. Hydrogen atoms of **V** were refined isotropically, and those of **I**, **II**, **III**, and **VI** were placed at idealized positions. Refinements were carried out using full-matrix least-squares procedures.

MM2 Calculation. Molecular mechanics (strain-energy minimization) calculations were carried out by employing a modification[25] of the MM2 computer program.[26] The used force field parameters are given in Table 2. MM2 parameters were set up for a trigonal bipyramid model. Figure 2 shows the plots of the calculated final strain energy of silatrane species (kJ mol^{-1}). Energies calculated for (equatorial) and (axial) (kJ mol^{-1}) are plotted in Figure 3. The MM2 calculations thus give relative conformer populations for the axial (A) and equatorial (B) species. The final strain energy of axial conformers was obtained as follows: On the minimized structure (equatorial), the hydrogen (H4) and the substituent (Me or *i*-Pr) were exchanged with each other. Then the structure was minimized under the fixed conformation.

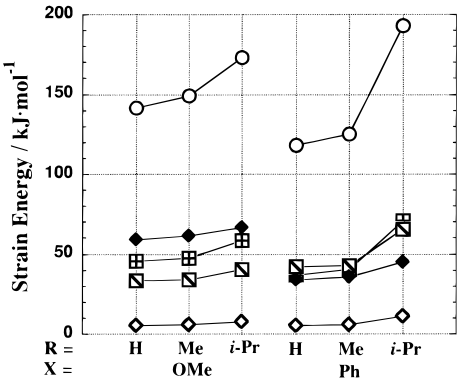


Figure 2. Final strain energies of silatrane species (kJ mol^{-1}); E_{total} (open circles), $E_{stretching}$ (open diamonds), $E_{bending}$ (squares with crossed lines), $E_{van\ der\ Waals}$ (squares with diagonal lines), and $E_{torsional}$ (filled diamonds).

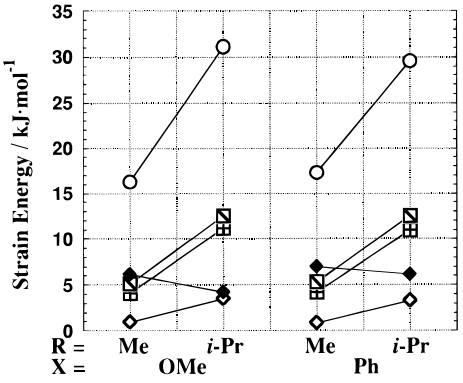


Figure 3. Difference in energy between the equatorial and axial conformers: E_{total} (open circles), $E_{stretching}$ (open diamonds), $E_{bending}$ (squares with crossed lines), $E_{van\ der\ Waals}$ (squares with diagonal lines), and $E_{torsional}$ (filled diamonds).

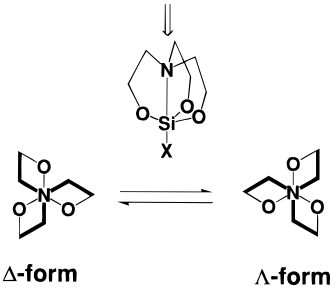


Figure 4. Definition of Δ-form and Λ-form.

Results and Discussion

Nonsubstituted Silatrane. Figure 4 shows silatrane viewed from the nitrogen atom on the N−Si axis. Silatrane has three five-membered chelate rings. Figure 4 shows the definition of the absolute configurations of silatrane. The Δ- and Λ-forms have a left- and right-handed propeller, respectively. We can

(23) Beurskens, P. T.; Admiraal, G.; Beurskens, G.; Bosman, W. P.; Garcia-Granda, S.; Gould, R. O.; Smits, J. M. M.; Smykalla, C. *DIRDIF92*: The DIRDIF program system; Technical Report of the Crystallography Laboratory; University of Nijmegen: Nijmegen, The Netherlands, 1992.
(24) Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Polidori, G.; Spagna, R.; Viterbo, D. SIR88. *J. Appl. Cryst.* **1989**, *22*, 389.
(25) Yoshikawa, Y. *J. Comput. Chem*. **1990**, *11*, 326.
(26) Allinger, N. L.; Yuh, Y. H. *QCPE* **1980**, *11*, 395.

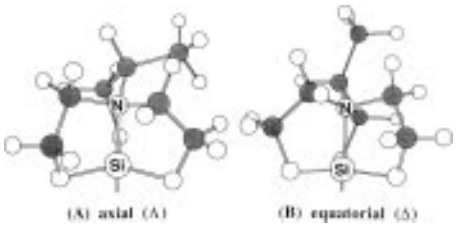


Figure 5. Conformation of (A) axial (Λ) and (B) equatorial (Δ). Phenyl group is omitted for clarity.

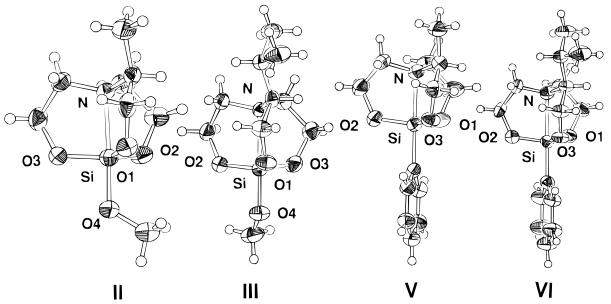


Figure 6. Perspective view of the structures of **II**, **III**, **V**, and **VI**.

Table 3. ^{1}H NMR Coupling Constants for Silatrane Derivatives

compound	R	X	$J_{3',4}$, Hz	$J_{3,4}$, Hz	$J_{3,3'}$, Hz
II	Me	OMe	5.9	11.2	10.9
III	*i*-Pr	OMe	5.9	11.1	11.1
V	Me	Ph	5.9	11.2	10.9
VI	*i*-Pr	Ph	5.9	11.1	11.1

guess that the conformation (δ or λ) of each chelate ring is exchangeable in nonsubstituted silatrane, and therefore the absolute configurations are not fixed. The relative abundance of the Δ- and Λ-forms at equilibrium can be changed by the introduction of a substituent into the triethanolamine moiety.

4-Substituted Silatrane. There can exist two conformers (with a substituent in an axial (A) and equatorial (B) orientation) in the optically active silatrane derivatives with the substituent on 4-carbon (Figure 5). We carried out MM2 calculations on 4-methyl-1-phenylsilatrane (**V**) (Figure 5). The calculations estimate B to be more stable than A by 17.3 kJ mol^{-1}, and the result suggests that conformer B with the equatorial substituent exists predominantly at equilibrium. ((A) axial, 142.3 kJ mol^{-1}; (B) equatorial, 125.0 kJ mol^{-1}).

We also carried out X-ray analyses on 4-substituted compounds **II**, **III**, **V**, and **VI**.

Figure 6 shows the molecular structures. It can be seen in Figure 6 that the alkyl groups exist in the equatorial position in accord with molecular mechanics calculations.

The ^{1}H NMR coupling constants for compounds **II**, **III**, **V**, and **VI** are listed in Table 3. There are H3, H3′, and H4 protons in the chelate ring with the substituent (Figure 7). The values of vicinal coupling $J_{3',4}$ are 5.9 Hz for all compounds. These results show that the dihedral angles H3′−C−C−H4 are about 60°. The values of vicinal coupling $J_{3,4}$ are ranging from 11.1 to 11.2 Hz. These results show that the dihedral angles H3−C−C−H4 are about 180°. All of the results suggest the equatorial conformation as shown in Figure 7. From these results, it can be concluded that the substituents have a preference for the equatorial position both in crystals and in solution. These results are in good agreement with the expectation from the aforementioned MM2 calculations (Figure 5).

^{13}C NMR Measurements. Figure 1 shows the numbering for 4-alkylsilatranes. As shown in the Experimental Section, even though the ^{29}Si chemical shifts change from one compound to another, the ^{13}C chemical shifts of OCH_3 and C_6H_5 do not appreciably differ. The ^{13}C NMR signals of 3- and 4-carbon shift to a lower field than those of nonsubstituted silatranes, while ^{13}C NMR signals of 6- and 11-carbon shift to a higher field than those of nonsubstituted silatranes. We interpret these results are attributed to the γ-position (C6, C11) steric compression effect.

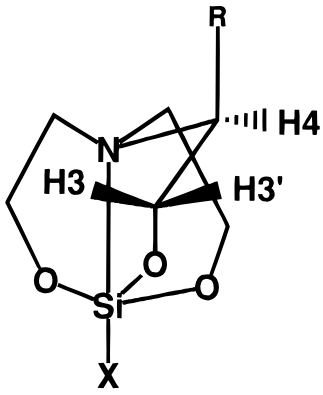


Figure 7. H3, H3′, H4 positions of silatrane.

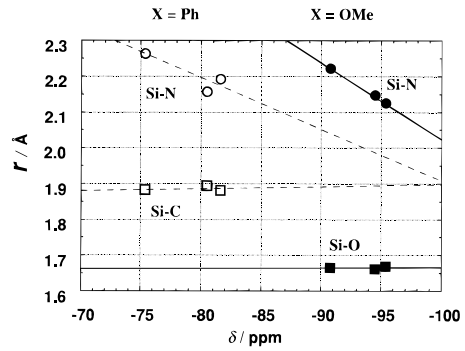


Figure 8. Correlation plots for r_{Si-N} and r_{Si-X} vs ^{29}Si NMR chemical shift values.

^{29}Si Chemical Shifts, r_{Si-N}, and r_{Si-X}. Figure 8 shows the correlation plots for the values of r_{Si-N} and r_{Si-X} for silatrane derivatives (**I**−**VI**) vs the ^{29}Si chemical shift values. The solid circles (●) show the r_{Si-N} values of **I**−**III** (X = OMe), and the open circles (○), the r_{Si-N} values of **IV**−**VI** (X = Ph). A tendency is observed that the bigger the steric hindrance of substituents are, the lower field the signals shift to. Another tendency of the r_{Si-N} values is also observed that the bigger the steric hindrance of substituents are, the larger the corresponding r_{Si-N} values are. Especially, the r_{Si-N} values of **III** and **VI** (R = *i*-Pr) are much larger than the others. Solid squares (■) show the r_{Si-X} values of **I**−**III** (X = OMe). Squares (□) show the r_{Si-X} values of **IV**−**VI** (X = Ph). Figure 8 shows that, even though the lengths of Si−N change, the Si−X bond lengths (X: trans position to nitrogen) do not appreciably differ from one another.

Conclusions

(1) A crystal of the nonsubstituted 1-methoxysilatrane contains equimolecular amounts of the Δ-form and the Λ-form.

(2) The substituents (R) have a preference to take the equatorial orientation both in the crystals and in the solution.

(3) The structures determined by X-ray analyses and by ^{1}H NMR spectroscopy are consistent with those from the MM2 calculations.

(4) The bigger the steric hindrance of substituents (R) are, the lower field the corresponding ^{29}Si NMR signals shift to.

(5) Even though the lengths of Si−N differ significantly in the five compounds, the individual Si−C and Si−O bond lengths (X: trans position to nitrogen) do not appreciably differ from one another.

Acknowledgment. This work was in part supported by a Grant-in-Aid for Scientific Research No. 05403009 from the Ministry of Education, Science, Sports and Culture. Dr. Kiyoshi Tsuge is thanked for his invaluable assistance in X-ray crystallography, and Mr. Yasuharu Ohmori is thanked for his contributions to the MM2 calculations.

Supporting Information Available: Text detailing data collection and structure refinement, tables listing details of the structure determination, bond lengths, bond angles, anisotropic thermal parameters, hydrogen atomic parameters, and figures showing ORTEP diagrams for **I**−**III**, **V**, and **VI** (44 pages). Ordering information is given on any current masthead page.

IC960349G