Table II. Elapsed Times for Conversion[a] of Selected Substrate Alcohols

alcohol (entry)	time,[b] min (PCC/ultrasound)	time,[b] min (PCC/silica gel)
2	240[d]	2160[c]
4	5	60
8	20	135
9	15	150
10	20	90
11	15	60

[a] 100% conversion unless otherwise indicated. [b] Reactions monitored by TLC at 5–10-min intervals unless otherwise indicated. [c] Reaction monitored by TLC at 0.5–1-h intervals. [d] 71% conversion.

CH_2), 1.02 (t, 3 H, CH_3), 0.92 (t, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 197, 95, 32, 24, 10, 7 ppm. Anal. Calcd for $C_6H_{11}NO_3$: C, 49.64; H, 7.63. Found: C, 49.32; H, 7.59.

2-Octanone (entry 3, Table I): purified (>99%, TLC) by flash column chromatography (30% Et_2O/hexanes) and Kugelrohr distilled, bp 170–172 °C (760 mm) [lit.[18] bp 170–172 °C (760 mm)].

3,4-Dimethoxybenzaldehyde (entry 4, Table I): purified (>99%, TLC) by flash column chromatography (EtOAc/hexane, 1:1) and recrystallized (Et_2O/pentane), mp 43–44 °C (lit.[19] mp 44 °C).

Nonanaldehyde (entry 5, Table I): purified (>99%, TLC) by flash column chromatography (30% Et_2O/hexanes) and Kugelrohr distilled, bp 49–50 °C (1 mm) [lit.[20] bp 49–50 °C (1 mm)].

(−)-Camphor (entry 6, Table I): purified (>99%, TLC) by flash column chromatography (30% Et_2O/hexanes) and recrystallized from ethanol–water: mp 176–177.5 °C; $[\alpha]^{20}_D$ −44° (c = 10, ethanol) [lit.[21] mp 176 °C; $[\alpha]^{20}_D$ −41° (c = 10, ethanol)].

3,7-Dimethyl-2,6-octadienal (entry 7, Table I): purified (>99%, TLC) by flash column chromatography (30% Et_2O/hexane) and Kugelrohr distilled, bp 84–85 °C (2 mm) [lit.[22] bp 84–85 °C (2 mm)].

3-(*N*-Phthaloyl)propionaldehyde (entry 8, Table I): purified (>99%, TLC) by standard column chromatography (30% toluene/EtOAc) and recrystallized from hexanes: mp 105–107 °C; IR ν_{max} ($CHCl_3$) 1760, 1720, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.8 (t, 1 H, aldehyde), 7.85 (dd, 2 H, aromatic), 7.75 (dd, 2 H, aromatic), 4.05 (5, 2 H, CH_2), 2.9 (t, 2 H, CH_2); mass spectrum, $M^{•+}$ (relative intensity) 203 (57), 175 (43), 160 (100), 147 (39), 130 (17), 104 (44), 76 (45). Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 64.85; H, 4.47; N, 6.74.

6-(Tetrahydropyran-2-yloxy)hexanal (entry 9, Table I): purified (>99%, TLC) by flash column chromatography (25% EtOAc/hexanes) and Kugelrohr distilled, bp 122–124 °C (2 mm) [lit.[23] bp 135–140 °C (7–8 mm)].

5-[(*tert*-Butyldimethylsilyl)oxy]-1-pentanal (entry 10, Table I): purified (>99%, TLC) by flash column chromatography (30% Et_2O/hexanes) and Kugelrohr distilled, bp 50–55 °C (0.2 mm) [lit.[24] bp 50–55 °C (0.2 mm)].

3-[2-[(*tert*-Butyldimethylsilyl)oxy]ethyl]cyclopentanone (entry 11, Table I): purified (>99%, TLC) by flash column chromatography (30% Et_2O/hexanes) and Kugelrohr distilled, bp 130–132 °C (1 mm) [lit.[25] bp 137 °C (1 mm)].

Acknowledgment. We thank Professor William G. Dauben and Professor Kenneth S. Suslick for suggestions and advice. Financial assistance from the University of Louisville, College of Arts and Sciences Research Committee, is also gratefully acknowledged.

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Conformational Preferences of the Silane and Methylsilane Groups

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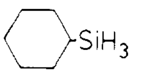
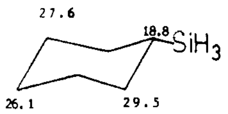
Although the silane group (SiH_3) is one of the cornerstones of organosilane conformational analysis, a parameter as fundamental as the free energy difference between the axial and equatorial conformers of cyclohexylsilane (1) has not been measured ($A_{SiH_3} = -\Delta G° = RT \ln K$ for the axial ⇄ equatorial equilibrium). This $\Delta G°$ value can be related to the gauche–trans free energy difference in 1-silabutane in the normal way. A number of calculations[1,2] suggest A_{SiH_3} is of such a magnitude (1.26; 1.1–1.2 kcal/mol) that determination should be possible from NMR spectra of cyclohexylsilane under slow-exchange conditions, but attempts[1] have been thwarted by the near-coincident ^1H chemical shifts of axial and equatorial SiH_3 at lower field strengths (60 100 MHz). In view of the importance of these free energy values, we wish to report that A_{SiH_3} = 1.45 and $A_{SiH_2CH_3}$ = 1.65 kcal/mol.



(1)))



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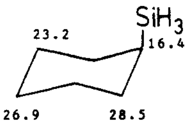

(3)

The 400-MHz ^1H spectrum of cyclohexylsilane (1; CD_2Cl_2 solvent) exhibits signals at δ 3.45 (3 H, d, $^3J_{H-H}$ = 3 Hz, $^1J_{^{29}Si-H}$ = 190.2 Hz; ^{29}Si = 4.7%) for SiH_3, δ 1.06 (>CHSi) and ring protons at δ 1.3 (5 H, ax H) and δ 1.77 (5 H, eq H) (In CH_3SiH_3, $^1J_{^{29}Si-H}$ = 194 Hz). The spectrum of the cooled sample (188 K) contained a new, broadened signal in the SiH_3 region, some 27.5 Hz (ca. 0.07 ppm) to the low-field side of the major (equatorial) SiH_3 signal. (Axial CH_3 in methylcyclohexane is ca. 0.1 ppm to low field of the equatorial CH_3 signal.)[3] This new signal was comparable in intensity with the low-field satellite resulting from ^{29}Si coupling ($^1J_{^{29}Si-H}$ = 190.2 Hz) within the major SiH_3 signal, and integration provided K = 50 for the axial ⇄ equatorial equilibrium, leading to $-\Delta G°_{188}$ = 1.45 ± 0.03 kcal/mol (A_{SiH_3} = 1.45 kcal/mol).

The ^{13}C NMR spectrum of 1 (CD_2Cl_2 solvent) is noticeably broadened at 213 K, and at 188 K, a set of sharp signals has emerged for the equatorial conformer, and four new, low-intensity, somewhat broadened signals are ascribed to the axial conformer. On the basis of chemical shifts, relative intensities (two are about double the intensity of the other two) and broadening patterns as the temperature is lowered, assignments as shown in 2 and 3 are arrived at. Careful integration of the 16.4 ppm signal (in 3) and the lower field ^{29}Si satellite around the 18.8 ppm signal (in 2; $^1J_{^{29}Si-C}$ = 58 Hz) led to K = 47.5 and A_{SiH_3} = 1.44 kcal/mol, in excellent agreement with the value based on ^1H NMR measurements. (At 188 K and under the conditions employed (30° pulse angle, 3-s pulse delay and bilevel decoupling) relative signal areas should accurately

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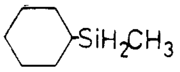
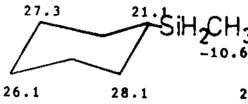
reflect the conformational proportions.) The significant upfield γ-effect of SiH_3 (−3.8 ppm, based on cyclohexane, $\delta_C = 27.0$ ppm) is noteworthy and should be compared with −6.4 ppm for (axial) methyl in methylcyclohexane.[4] However, the patterns of ring carbon shifts for **3** and **2** resemble those for axial and equatorial methylcyclohexane, i.e., in both axial conformers all ring carbons except C_4 are to higher field than the corresponding signals in the equatorial conformers. These trends can be rationalized in terms of the γ-gauche effect, and anti-vicinal hydrogen–hydrogen interactions.[4]

Cyclohexylmethylsilane (**4**) was also examined, but the 400-MHz ^{1}H spectrum (188 K) did not provide a useful measure of the conformational ratio, although broad minor signals at δ 3.47 (SiH_2, axial) and δ 0.08 (SiH_2CH_3) were discernible. (The corresponding signals for the equatorial conformer were δ 3.43 and 0.02, respectively.) Examination of the dideuterio derivative (SiD_2CH_3) did not afford improved resolution. Fortunately, the 100-MHz ^{13}C spectrum at 188 K was more revealing, and a set of minor broadened signals, with appropriate relative intensities, could be ascribed to the minor form and are assigned in **5** and **6**. Two measures of conformational populations were possible. Integration of the axial CH_3 signal (−9.5 ppm) against the lower field ^{29}Si satellite of the (major) equatorial CH_3 signal ($^1J_{^{29}SiCH_3}$ = 50 Hz) provided $-\Delta G^\circ_{188} = 1.6 \pm 0.05$ kcal/mol, whereas similar treatment of the C1 signal (19.3 ppm in **6**) and the lower field satellite about C1 (21.1 ppm in **5** ($J_{^{29}Si\text{-}C}$ = 56 Hz)) led to $-\Delta G^\circ_{188} = 1.65$ kcal mol. The almost identical γ-gauche effects of axial SiH_3 and SiH_2CH_3 (in **3** and **6**) are expected on the basis that the asymmetric conformation of **6** (i.e., **7**) is more favoured than arrangement **8**, on both enthalpic and statistical grounds.[1]



(4)



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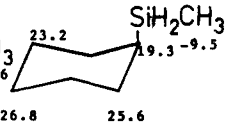

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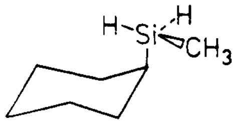

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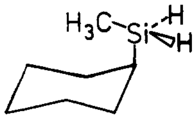

(8)

Certain calculated *A* values for SIH_3 and SiH_2CH_3 agree well with those reported here. For example, Ouellette[1] reported values of 1.26 and 1.62 kcal/mol on the basis of an early empirical force field, whereas Cartledge[2] arrived at 1.1–1.2 kcal/mol for SiH_3 on the basis of an MM2-82 parameter set and certain new torsion terms. That SiH_3 has a smaller *A* value than CH_3 (1.74 kcal/mol) can be understood in terms of lower nonbonded terms (E_{nb}) between the "over-the-ring" hydrogen and the C3,5 methylenes (in **3**) compared with axial methylcyclohexane, because of longer C–Si and Si–H bonds. Bending force constants involving silicon are lower than for carbon, and angle deformations about Si could lead to "opening-up" of the H–Si–C angle and a "closing-in" of the Si–C_1–H_1 angle, both of which would reduce E_{nb}.[5] $A_{Si(CH_3)_3}$ of 2.5 kcal/mol has been reported previously.[6]

Experimental Section

Compounds. Commercially available (Petrarch Systems) cyclohexyltrichlorosilane was slowly added, as an ether solution, to a well-stirred ether suspension of lithium aluminum hydride (2 mol equiv) at 0 °C. After addition was complete, the reaction was stirred at room temperature for about 30 min and then flash distilled, with all volatiles being condensed at −78 °C. Ether was carefully removed, and the residual oil was distilled (Kugelrohr apparatus) and then redistilled. Cyclohexylsilane thus obtained showed no impurities by capillary gas chromatography nor by the subsequent ^{1}H and ^{13}C NMR examinations, the details of which are discussed in the text.

An identical procedure was employed to convert cyclohexylmethyldichlorosilane to cyclohexylmethylsilane.

Cyclohexylsilane was purified by Kugelrohr distillation (oven temperature 55 °C/20 mmHg) (lit.[7] 119.5 °C/739.5 mmHg); accurate mass = 114.0860 (calcd for $C_6H_{14}{}^{28}Si$ = 114.0864).

Cyclohexylmethylsilane was also purified by Kugelrohr distillation (oven temperature 58 °C/20 mmHg); accurate mass = 128.1025 (calcd for $C_7H_{16}{}^{28}Si$ = 128.1021).

NMR spectra were obtained with a JEOL-GX-400 spectrometer using the 5-mm dual ^{1}H, ^{13}C probe. ^{13}C spectra were acquired by using 64K data points and bilevel decoupling, with a 3-s recycle time, 30° pulse, and 20-kHz spectral width. ^{1}H spectra were acquired by using 32K data points, a 5-s recycle time, 30° pulse, and 4-kHz spectral width. The temperature control unit for the probe was calibrated with reference to the temperature calibration curves[8] for a methanol sensor at low temperature (a Varian sealed tube sample of methanol). Temperatures are considered accurate to ±1.5 °C.

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Registry No. 1, 18162-96-4; 4, 2096-99-3; cyclohexyltrichlorosilane, 98-12-4; cyclohexylmethyldichlorosilane, 5578-42-7.

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Synthesis of Saframycins. 3. Preparation of a Key Tricyclic Lactam Intermediate to Saframycin A

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In the conduct of synthetic efforts on the antitumor antibiotics saframycins (**1–3**, Chart I), safracins (**4**, **5**), and saframycins Mx (**6**, **7**), we recentry reported a total synthesis of (±)-**2** from the tricyclic lactam **11**.[1] To extend the scope of the synthetic route of the saframycins, we have focused our attention on the synthetic studies of **1**.[3]

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