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NMR CONFORMATIONAL ISOMERIZATION STUDIES IN SOME 6-MEMBERED HETEROCYCLIC COMPOUNDS*

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Abstract—Analysis of low temperature line broadening in the NMR spectrum of 1,1,4,4-tetramethyl-1,4-disilacyclohexane suggests that some exchange broadening may be occurring. The kinetic process is attributed to chair-to-chair conformational isomerization. The barrier to inversion is estimated to be <6 kcal/mole. It is suggested that the low barrier is due mostly to the greater length of the carbon-silicon bonds. The barrier in N,N,N',N'-tetramethylpiperazinium diiodide was found to have a $\Delta F^{\ddagger}_{cb}$ of 12·7 kcal/mole.

HIGH resolution NMR spectroscopy has been used to study conformational izomerization in a number of 6-membered ring systems containing two or more adjacent hetero atoms. Generally speaking the introduction of adjacent hetero atoms has two consequences important to these kinds of studies, namely, a simplification of the NMR spectrum and an increase in the barrier to isomerization. We have taken advantage of these consequences in determining the isomerization barrier in acetone diperoxide (1,1,4,4-tetramethyl-2,3,5,6-tetraoxacyclohexane),[1] **1**, for example. Other 6-membered ring systems containing two or more adjacent hetero atoms, whose isomerization barriers have been determined, include 3,3,6,6-tetramethyl-1,2-dithiane,[2] **2**, 3,3,6,6-tetramethyl-1,2-dioxane,[2] **3**, and tetramethyl-*s*-tetrathiane,[3] **4**. In all of these cases the barrier to isomerization is higher than in the carbon analog, 1,1,4,4-tetramethylcyclohexane.[4–6]

We report here the results of out attempts to extend these studies to two other systems in which the hetero atoms are not adjacent, namely, N,N,N',N'-tetramethylpiperazinium diiodide, **5**, and 1,1,4,4-tetramethyl-1,4-disilacyclohexane, **6**. Abraham and MacDonald[7] have since reported all of the transition state parameters for N,N,N',N'-tetramethylpiperazinium dichloride, **7**, so that a complete temperature range study of the corresponding diiodide was not continued. Nevertheless, from the methyl resonance coalescence temperature (-30°C) and $\Delta\nu$, the maximum axial-equatorial methyl peak separation (6 Hz) the residence time, τ, was calculated from Equation (1).[8]

$$\tau = \frac{\sqrt{2}}{2\pi\Delta\nu} \tag{1}$$

The residence time was then used to calculate the rate constant for isomerization, and the Eyring formulation used to calculate $\Delta F^{\ddagger}_{cb} = 12{\cdot}7$ kcal/mole at the coalescence

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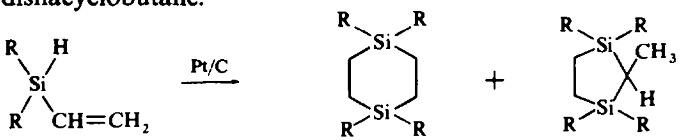
temperature. This value compares well with that of 12·9 ± 0·3 (0°C) given by Abraham and MacDonald for the dichloride,[7] and suggests that anion size has no pronounced effect on the barrier to inversion.

The synthesis of **6** and its ethyl analog, 1,1,4,4-tetraethyl-1,4-disilacyclohexane, **8**, followed, in general, the method given by Curry.[9] Thus, dimethylvinylchlorosilane was reduced to dimethylvinylsilane using lithium aluminum hydride. The dimethylvinylsilane was then dimerized by heating it neat with a catalyst of platinum on carbon. Total volatiles present were then distilled out of the reaction mixture and analyzed by GPC. It was found that the total yield of volatiles, could be improved from 21·2%, using the Curry procedure, to 33·1% by diluting the dimethylvinylsilane with diphenylether. The synthesis of **8** began with trichlorovinylsilane which was converted to diethylvinylchlorosilane with ethylmagnesium bromide. The dimerization and workup were carried out as with **6**.

Curry originally assigned the structures **6** and **8** to the volatile materials he obtained in his synthesis along with the desired polymeric products.[9] He subsequently altered these structure assignments on the basis of the NMR spectra.[10] Curry concluded that the dimerization of dimethylvinylsilane had actually given both **6** and an isomer, 1,1,2,3,3-pentamethyl-1,3-disilacyclopentane, **9**, in a 27:73 ratio, respectively, as determined from the NMR spectrum of the mixture. We have confirmed this conclusion on the basis of the NMR spectra of the separated components which were found to be present in a ratio of 20:80 (**6**:**9**) from GPC peak areas.

Again using the NMR spectrum of the mixed volatiles Curry concluded that diethylvinylsilane dimerization gave largely **8** along with a small amount of 1,1,3,3-tetraethyl-2-methyl-1,3-disilacyclopentane, **10**. He also concluded that the multiplicity of the methyl peaks indicated that **8** may exist in a fixed chair conformation. Having separated the mixture into its components we were able to conclude that **8** is in fact probably undergoing rapid isomerization and that the apparent multiplicity of the methylene protons in Curry's work is due to the presence of three major components as well as higher order splittings. The higher order splittings are expected since the presence of the silicon atom tends to reduce the chemical shift difference between the Me and Et groups.

The presence of the three major components in the ratio of 3:5:2 in the diethylvinylsilane dimerization was determined from GPC peak area. The components present to the extent of 50 and 20% were determined to be **10** and **8** respectively. Thus we find the 5-membered ring compound to be the dominant isomer, contrary to Curry's observation. The third component, which makes up 30% of the total volatiles has a mol. wt. which indicates that it is an isomer of the other two. At present no structure assignment is made for this material although reasonable possibilities would include 1,1,2,2-tetraethyl-1,2-disilacyclohexane and 1,1,3,3-tetraethyl-2,4-dimethyl-1,3-disilacyclobutane.



6: R = Me
8: R = Et

9: R = Me
10: R = Et

The 60 mHz NMR spectrum (CS_2) of **10** consists of a complex multiplet at 9·03 and a quartet at 9·9. The complex multiplet is made simpler by observing it with a 220 mHz spectrometer (CCl_4). Here the total spectrum consists of a doublet at 8·67 (J = 8·0 Hz), a triplet at 8·75 (J = 8·0 Hz), a multiplet at 9·17, and a quartet at 9·76 (J = 8·0 Hz). These absorptions can now be assigned to the ring Me, Et group Me, combined methylene, and methine protons of **10**, respectively. An even more striking example of the spectrum simplification which can be achieved by use of the 220 mHz spectrometer was found in **8** (Fig. 1). Here the 60 mHz spectrum consists of a highly complex multiplet centered at 9·2 (CS_2). The 220 mHz spectrum (CCl_4) is quite simple with apparently only first order splittings. It consists of a triplet at 9·12 (J = 8·0 Hz), a singlet at 9·35, and a quartet at 9·45 (J = 8·0 Hz). These absorptions are readily assigned to the Me, ring methylene and Et group methylene protons of **8**, respectively. It should be noted that the methylene group in the Et chain now absorbs at higher field than the Me because it is closer to the electropositive silicon atom.[11] The singlet

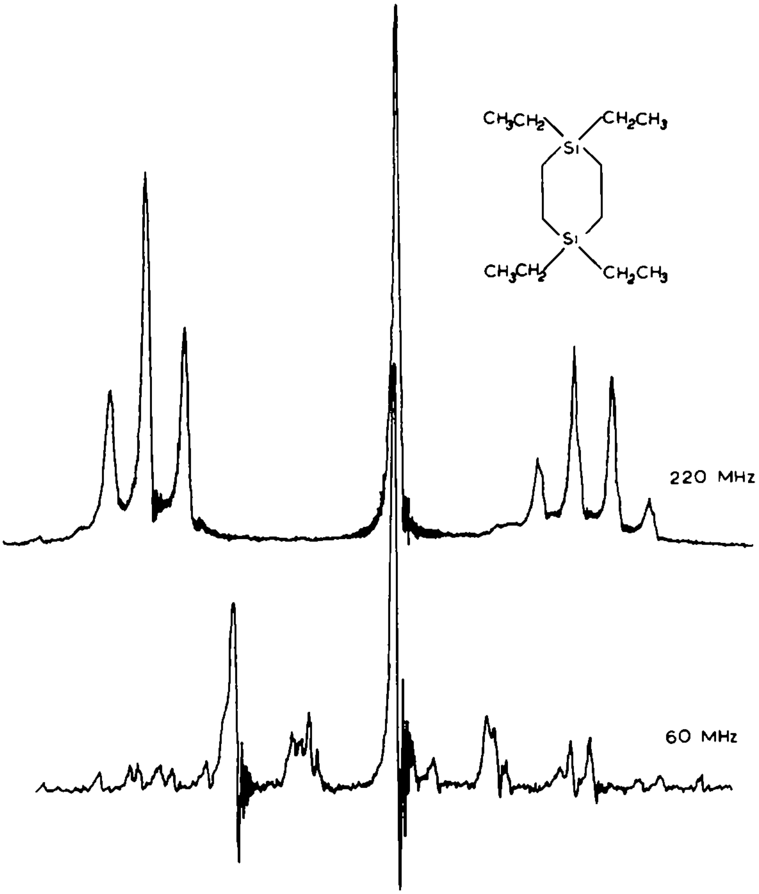


FIG. 1 The 60 mHz and 220 mHz NMR spectra of **8**.

absorption of the ring methylene protons also indicates that the ring is not in a fixed chain conformation as suggested by Curry,[10] but may be undergoing rapid isomerization.

The variable temperature line width study was done over the range −120° to −160° on a specially modified[12] Varian HR-60 spectrometer. Compound **6** was chosen for this study because its spectrum is simpler than that of **8**. Even at the lowest temperature used the Me group absorption does not split indicating that if conformational isomerization is occurring the barrier may be quite low. In order for the isomerization process to be reflected in the NMR spectrum, however, the chemical shift difference between the exchange positions must be sufficient to affect the line shape.

In this case since the absorption does not split at low temperatures, we cannot determine the $\Delta\nu$ difference for the axial and equatorial Me groups in **6**. Intuitively we might expect this difference to become smaller as the bond length between the Me group and the ring atom is increased since the attached Me groups are then further removed from the effect of the diamagnetic anisotropy of the ring C—C bonds which

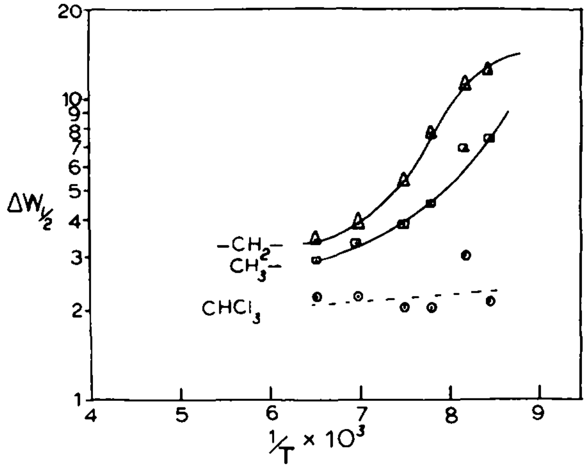


FIG. 2 A plot of line width versus $1/T$ for the methyl and methylene group NMR absorptions in **6**.

presumably is largely responsible for the axial-equatorial chemical shift difference.[13]

If this is the case then the difference observed in **5** ($\Delta\nu_{a-e}$ = 6 Hz) and 1,1,4,4-tetramethylcyclohexane, **11**, ($\Delta\nu_{a-e}$ = 3·85 Hz), suggest that $\Delta\nu_{a-e}$ for **6** may indeed be very low and perhaps of the order of 0·5–1·5 Hz. Thus one expects any exchange broadening to be small. In order to determine whether there is in fact any exchange broadening we have measured the line width of the Me and methylene absorption over the range −120° to −160°. The total line width is made up of contributions from field inhomogeneity and stability and T_2^0, the transverse relaxation time in the absence of exchange, as well as any exchange broadening. Since T_2^0 may itself be temperature dependent, it is necessary to use a standard which permits an approximation of the total contribution of all non-exchange broadening to the line width throughout the temperature range studied. Additional temperature dependent broadening is then considered to be due to some kinetic process. In this case we have used chloroform as a standard to assess non-exchange broadening.

As shown in Fig. 2, the Me and methylene absorptions in **6** undergo considerably greater line broadening as the temperature is reduced than does the proton absorption in chloroform. Provided that the chloroform broadening is a good measure of non-exchange broadening in **6**, we can then conclude that there is a kinetic process occurring. This process is presumably chair-to-chair conformational isomerization. The effect of temperature on the spectrum of **6** over the range $-130°$ to $-160°$ is shown in Fig. 3.

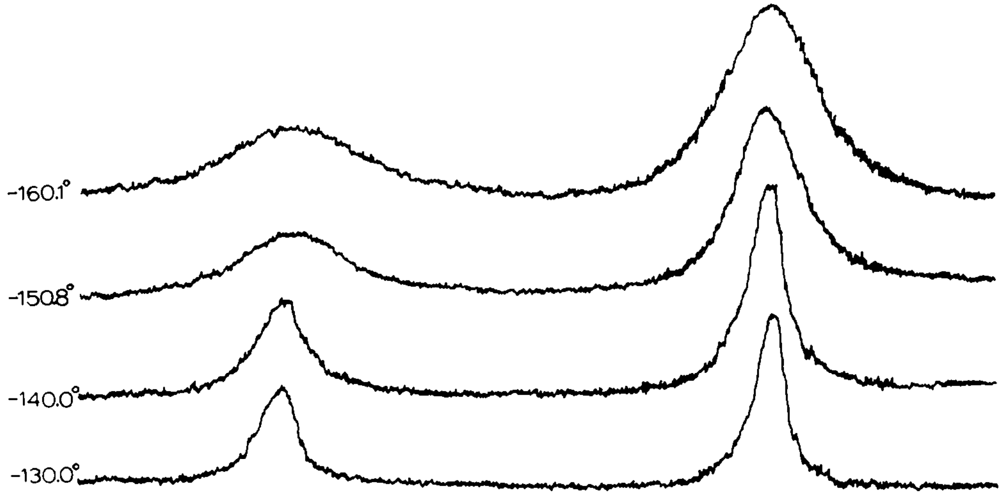
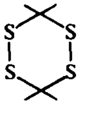
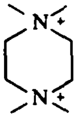
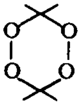
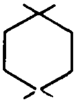
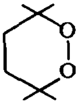
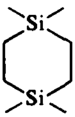
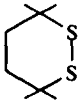
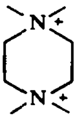


FIG. 3 The 60 mHz NMR spectrum of **6** at a series of temperatures.

Since coalescence of the Me group absorptions must have occurred at or below $-160°$ it is only possible to place an upper limit on the value of $\Delta F^{\ddagger}_{cb}$ for the ring inversion process. If it is assumed that $\Delta\nu_{a-e}$ in **6** is 1·0 Hz then use of Eq. (1) and the Eyring formulation gives $\Delta F^{\ddagger}_{cb} < 6$ kcal/mole. Actually the value of $\Delta\nu_{a-e}$ used has only a small effect on the value of $\Delta F^{\ddagger}$ in this approximation method. Thus a variation in this value from 0·2 to 5·0 Hz gives values of $\Delta F^{\ddagger}_{cb}$ of 6·4–5·7 kcal/mole. Very recently Jensen and Bushweller[14] have reported the barrier in 1,1-dimethyl-1-silacyclohexane, **12**, to be 5·50 ± 0·25 kcal/mole ($-157·1°$). In this work a lower temperature ($-177°$) was achieved and line separation in the combined C_3, C_4, and C_5 methylene absorption was observed. A summary of the $\Delta F^{\ddagger}$ values for **6** and a number of related compounds is given in Table 1.

It is clear that with the exception of **6** the presence of two or more hetero atoms in the ring has raised the barrier to inversion in this series. While it is true that the hetero atoms in **6** are non-adjacent, the reduction in the barrier is so large that this fact, in itself, would not seem to be responsible. While both bond deformation and eclipsing interactions must contribute to the barrier, it seems likely that the drastic drop in the barrier to inversion in **6** may be largely associated with the increased bond

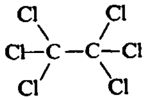
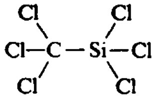
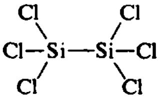
Table 1. A summary of $\Delta^{\ddagger}_{cb}$ values for various six-membered ring compounds

Compound	Temp.	$\Delta F^{\ddagger}_{cb}$ kcal/mole	Ref.	Compound	Temp.	$\Delta F^{\ddagger}_{cb}$ kcal/mole	Ref.
 **4**	50	16	3	 $2I^-$ **5**	−30	12·7	this work
 **1**	30	15·0	1	 **11**	−53 −62	11·3 11·1	5 6
 **3**	12	14·6	2	 **6**	−160	<6	this work
 **2**	−2	13·4	2	 **12**	−157·1	5·5	14
 $2Cl^-$ **7**	0	12·9	7				

length of the carbon–silicon bond in **6** as compared to the corresponding carbon–carbon bond in **11**, for example. Some support for this possibility can be found in the work of Morino and Hirota[15] who determined the effect of substituting silicon for carbon on the potential barrier to rotation in some ethane derivatives. A summary of some of their findings is given in Table 2. In this system the rotation barrier was found to decrease markedly as silicon was successively substituted for carbon. The barrier in the compounds studied is considered to be due largely to the interaction between substituents and thus should be particularly sensitive to interatomic distance.

If for comparison purposes, one makes the assumption that similar considerations are dominant in determining the barrier to inversion in **6**, then it is possible to make a rough prediction of what this barrier might be. Thus an increase in bond length of 0·47 Å in going from hexachloroethane, **13**, to trichloromethyl-trichlorosilane, **14**, had the effect of reducing the barrier by 6·5 kcal/mole.[15] Using standard lengths for the appropriate bonds in **6** and **11** shows that the affected bond length has increased by 0·33 Å in the silicon-containing compound. One would then approximate that the barrier in **6** would be reduced by 4·56 kcal/mole on the basis of rotational considerations alone. Given that $\Delta F^{\ddagger}_{cb}$ for **11** is 11·1 kcal/mole[6] one would then predict a maximum barrier of 6·5 kcal/mole for **6**. This value is to be compared with the experimental value of $<6{\cdot}0$ kcal/mole. Since the procedure used to predict the barrier is rather tenuous, the closeness of the predicted and observed values may be entirely fortuitous. Nevetherless, it is felt that it is instructive to review the results of Morino and Hirota[15] and that it is reasonable to suggest that the low barrier to isomerization in **6** is due largely to the increased length of the carbon–silicon bonds involved.

TABLE 2. THE EFFECT OF BOND LENGTH ON ROTATION BARRIER IN SOME ETHANE DERIVATIVES (FROM REF. 14)

Compound	Bond length	Potential barrier kcal/mole
 **13**	1·46 Å	10·8
 **14**	1·93 Å	4·3
 **15**	2·02 Å	1·0

EXPERIMENTAL

M.ps were taken on a Kofler hot stage and are uncorrected. NMR spectra were taken on a Varian A-60, Varian HR-220, or on a modified[12] DP-60 high resolution NMR spectrometer. Gas chromatographic analyses were done on a Varian-Aerograph A-700 Gas Chromatograph. Mass spectral analyses were performed by Dr. J. Wright of Harvard University.

N,N,N',N'-*Tetramethylpiperazinium diiodide* (**5**). To an ice-cold soln of N,N'-dimethylpiperazine (1·0 g, 8·8 mmoles) in 30 ml *p*-dioxane was added 10 ml (160 mmole) MeI. The reaction mixture was refluxed for

1 hr during which time it became mostly solid. The solid was filtered off; yield was 3·94 g (87%). Recrystallization from EtOH–water gave material with m.p. 275° (d) lit.[16] m.p. 278°. The NMR spectrum of this material in liquid SO_2 showed just two singlets at 6·36 and 6·72* with integrated areas of 8·0 and 11·7, respectively.

Dimethylvinylsilane. Into a 1000 ml round bottom flask fitted with an ice–water cooled reflux condenser was placed a slurry of LAH (15·5 g, 0·41 mole) in 200 ml freshly distilled THF. A soln of dimethylvinylchlorosilane (200 g, 1·65 mole, Peninsular) in 200 ml dry THF was added, dropwise, to the slurry. When addition was complete, stirring was continued for ~12 hr at room temp and 2 hr at reflux. The product was distilled from the reaction mixture, b.p. 37–38°, lit.[9] b.p. 36·7° (738 mm). The NMR spectrum (CCl_4) had a doublet at 9·92 and multiplets at 5·98 and 4·14 with integrated areas of 6·1, 0·93, and 3·0, respectively, yield was 116 g (81·7%).

1,1,4,4-*Tetramethyl*-1,4-*disilacyclohexane* (**6**). Dimethylvinylsilane (2·98 g, 0·346 mole) and 0·65 g 1% Pt/C were heated at reflux under N_2 for 3·5 hr at the end of which time the temp of the mixture was 200°. The reflux condenser was replaced with a distilling head and volatiles removed at 190° (25 mm) and 173° (0·7 mm). Total yield of volatiles was 7·32 g (21·2%). This mixture was analyzed by GPC on a 20 ft × $\frac{3}{8}$ in, 20% XE-60 cyanosilicone column at 80° and 200 ft/sec He flow. The two major components present at retention times of 35 min and 39·5 min and relative peak areas of 4:1 were collected for further analysis.

The first material collected had NMR absorptions (CCl_4) at 9·10 (d,† $J = 7·8$ Hz), 9·42 (s), 10·03 (d), and 10·27 (qu) with integrated intensities of 3·0, 4·0, 12·1, and 0·94, respectively. These are assigned to the ring Me, methylene, silicon Me and methine protons, respectively, of 1,1,2,3,3-pentamethyl-1,3-disilacyclopentane by analogy with the results of Curry.[10]

The second fraction had two singlet NMR absorptions (CCl_4) at 9·19 and 9·95 with relative areas of 7·6 and 12·0, respectively. These are assigned to the methylene and Me protons of 1,1,4,4-tetramethyl-1,4-disilacyclohexane, respectively. (Found: C, 55·81; H, 11·92; Si, 32·42; Mol. Wt. 172·1095 (exact mass). $C_8H_{20}Si_2$ requires: C, 55·73; H, 11·69; Si, 32·58%; Mol. Wt. 172·1103).

The total yield of volatiles was increased to 33·1% by carrying out the dimerization in diphenylether solvent. The relative gpc peak areas of the major products remained at 4:1.

Diethylvinylchlorosilane. To a soln of trichlorovinylsilane (80·5 g, 0·5 mole, Peninsular, b.p. 93°) in 250 ml of dry ether was added, dropwise, a soln of EtMgBr (1·0 mole) in ether. The reaction mixture was refluxed and stirred vigorously during the addition. When addition was complete, the reaction mixture was allowed to stand at room temp overnight. It was then filtered and the solid washed with ether. After removal of solvent the residue was distilled on a spinning band column to give product boiling at 138–142°, lit.[9] b.p. 139–141; yield 18·47 g (24·8%). This material had multiplets in its NMR spectrum (CCl_4) at 4·0 and 9·1 with relative areas of 3·0 and 10·5, respectively.

Diethylvinylsilane. To a stirred slurry of LAH (1·18 g, 0·031 mole) in 10 ml of abs ether was added, dropwise, a soln of diethylvinylchlorosilane (18·5 g, 0·124 mole) in 30 ml abs ether. The reaction mixture was refluxed for 3·5 hr and then allowed to stand overnight. Water was then added slowly and the ether layer was separated and washed with the water. After drying (Na_2SO_4) solvent was removed and the residue distilled on a spinning band column. The product had b.p. 100–101°, lit.[9] b.p. 100·5° (794 mm); yield was 4·73 g (32%). This material had NMR (CCl_4) absorptions at 4·15 (m), 6·23 (m) and 9·25 (m) with integrated areas of 3·0, 0·9, and 10·5 respectively. The relative gpc peak areas of the major products remained at 4:1.

1,1,4,4-*Tetraethyl*-1,4-*disilacyclohexane* (**8**). Diethylvinylsilane (7·0 g, 0·061 mole) was heated under reflux with ~0·02 g 1% Pt/C until the temp of the mixture reached 190°. Volatiles were removed by distillation at 185° (0·7 mm); yield was 2·43 g (34·7%). The total volatile product was analyzed by GPC on a 30 ft × $\frac{3}{8}$ in 5% XF-1150 cyanosilicone column at 130° and 200 ft/sec He flow. The three major products of retention times 21, 26, and 29 min and relative yields of 3:5:2 were collected.

The product of shortest retention time shows a complex multiplet at 9·1 in its NMR spectrum (CS_2). It has mol. wt. = 228·1727 and thus is apparently an isomer of the other two products. At present no structure is assigned to this product.

The product of intermediate retention time has a multiplet at 9·03 and a quartet at 9·9 in its NMR spectrum (CS_2). (Found: C, 63·4; H, 12·9; Si, 23·5. $C_{12}H_{28}Si_2$ requires: C, 63·1; H, 12·4; Si, 24·6%). The 220 mHz NMR spectrum (CCl_4) of this material had a doublet at 8·67 ($J = 8·0$ Hz), a triplet at 8·75 ($J = 8·0$ Hz), a multiplet at 9·17, and a quartet at 9·76 ($J = 8·0$ Hz). These absorptions are assigned to the ring Me, the Et group Me, the combined methylene groups, and the methine protons of 1,1,3,3-tetraethyl-2-methyl-1,3-disilacyclopentane, respectively.

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* NMR tau values given are relative to external tetramethylsilane.

† d = doublet; s = singlet; qu = quartet, etc.

The third product had a very complex multiplet in the 60 mHz NMR (CS_2) spectrum centered at 9·2. The 220 mHz NMR spectrum (CCl_4) was much simpler with a triplet at 9·12 (J = 8·0 Hz), a singlet at 9·35, and a quartet at 9·45 (J = 8·0 Hz). These absorptions are assigned to the Me ring methylene, and Et group methylene protons, respectively, of 1,1,4,4-tetraethyl-1,4-disilacyclohexane. Mol. Wt. 228·1736 (exact mass): $C_{12}H_{28}Si_2$ requires 228·1730.

Variable temperature NMR *measurements.* The variable temp spectra were run on a modified Varian DP-60 NMR spectrometer with field frequency provided by a Hewlett-Packard frequency synthesizer. The variable temp probe has been described elsewhere.[12] The sample was dissolved in dichlorodifluoromethane (Freon 12). Temp measurements were made with a thermocouple which was located in an NMR tube in the probe. Precise line width measurements were made in the range from −120°C to −160°. At least four measurements were made at each temp on the methylene and Me protons of **6** as well as on the chloroform standard.

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