

Even this crystal contained some disordered atoms, as described above.

The lack of symmetry in the film characterization implied space groups $P1$ or $P\bar{1}$. The final triclinic cell parameters determined from least-squares analysis of 22 reflections centered with Mo $K\alpha_1$ radiation on a Picker four-circle diffractometer were found to be $a = 10.757$ (8), $b = 10.141$ (8), $c = 11.698$ (9) Å, and $\alpha = 104.95$ (2), $\beta = 114.83$ (2), $\gamma = 81.33$ (2). The density, assuming two chemical species per unit cell, calculated to be 1.30 g/cc which is in agreement with the observed density of 1.29 (± 0.03) g/cc.

Intensity data were collected by the moving counter-moving crystal ($\theta - 2\theta$) method with scan range of 1.70° (0.75 before the peak maximum and 0.95 after) (DATA) and backgrounds of 15 sec each (BK1 and BK2). Zr-filtered Mo $K\alpha$ radiation was used and the

pulse height analyzer was set to accept 90% of the radiation. Data were collected in the region $+h, \pm k, \pm l$ out to 2θ of 45°. An equivalent data set was taken in the region $-h, \pm k, \pm l$ but was not used due to instrument problems which developed during the collection. Throughout the data collection, six standard reflections (004, 222, 115, 040, 500, and 422) were checked and indicated a 3.1% loss of intensity per 1000 reflections. Fourteen of the reflections in the unique set of data diffracted with intensities beyond the linear range of the detector and were rerun with an attenuator which had been standardized with reflections in the linear range. Of the 2933 data in the independent set, 2212 were found to have intensities greater than 1.5 standard deviations, where $\sigma(I) = [\text{DATA} + \text{BK1} + \text{BK2} - 0.03^2(\text{DATA} - \text{BK1} - \text{BK2})^2]^{1/2}$. No corrections were made for the absorption of the crystal.

The Conformational Preferences of the *N*-Trimethylsilyl and *O*-Trimethylsilyl Groups¹

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Abstract: *O*-Trimethylsilylcyclohexanol (I), *N*-trimethylsilylcyclohexylamine (II), and the *cis*- and *trans*-4-methyl and *cis*- and *trans*-4-*tert*-butyl derivatives of these molecules have been synthesized. Measurements at 100 and 220 MHz of the nmr chemical shifts of the α protons of the unsubstituted and *cis*- and *trans*-4-*tert*-butyl-substituted compounds were used to obtain values of 1.21 and 0.88 kcal mol⁻¹ for the conformational free energy preferences (A values) of the $-\text{NHSiMe}_3$ and $-\text{OSiMe}_3$ groups, respectively. In addition, A values of 1.15 and 0.93 kcal mol⁻¹, respectively, for these same groups were estimated from the chemical shift data for the *cis*-4-methyl compounds, assuming an A value of 1.70 kcal mol⁻¹ for the methyl group. The close agreement between these two methods suggests that in the present case, at least, accurate measurement of conformational preferences may be obtained by the chemical shift method. The present results are discussed in light of recent criticism of this method. An unusually large value for a HCNH proton-proton coupling of 10 Hz was observed for II.

Increasing use is being made of trimethylsilylation techniques to volatilize large molecules and polar hydrogen bonded molecules,² especially those of biological interest such as steroids³ and amino acids.⁴ In a recent article³ Chambaz and Horning described the reactions of several trimethylsilylating reagents and discussed the effect of reaction conditions and the influence of steric effects on reaction rates and on the structure of products. They showed that under similar silylating conditions, the axial hydroxyl of 5 β -androstan-3 β -ol-17-one reacted more slowly than the equatorial hydroxyl of 5-androstan-3 α -ol-17-one. Wilson and Ripley have attributed the physical behavior of $-\text{OSiMe}_3$ derivatives of steroids during gas chromatographic analysis to conformational changes wrought on the steroid nucleus by conversion of a hydroxyl group to what one might anticipate to be a more bulky trimethylsilyl ether.^{5,6} Eaborn⁷ has summarized data

which show that reaction rates and equilibria of various trialkylsilyl compounds are subject to steric effects. When a $-\text{SiMe}_3$ group is bonded to a ring carbon in substituted cyclohexanes its steric influence appears to be similar to that of a *tert*-butyl group.^{8,9} However, when the silicon atom is not bonded directly to a ring carbon but is separated by a nitrogen or oxygen atom, the steric requirements of the resulting silylamine or silyl ether are less certain. To clarify this situation we report in detail the determinations of the equatorial-axial free energy differences (A values)¹⁰ of the $-\text{OSiMe}_3$ and $-\text{NHSiMe}_3$ groups by two proton nmr methods.

Method

The first approach used (method 1) is that originally described by Eliel.^{11,12} In this method the nmr chemical shift of the α -proton of a conformationally mobile cyclohexyl compound is compared with the shifts of the α -protons in the corresponding conformationally rigid *cis*- and *trans*-4-*tert*-butylcyclohexyl derivatives (see Figure 1). The A value is then calculated from the equation¹³

(1) This paper presents the results of one phase of research carried out at the Jet Propulsion Laboratory, California Institute of Technology, under Contract No. NAS 7-100, sponsored by the National Aeronautics and Space Administration.

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(3) E. Chambaz and E. C. Horning, *Anal. Biochem.*, **30**, 7 (1969).

(4) J. F. Klebe, H. Finkbeiner, and D. M. White, *J. Amer. Chem. Soc.*, **88**, 3390 (1966).

(5) W. E. Wilson and J. E. Ripley, *Anal. Chem.*, **41**, 810 (1969).

(6) W. J. A. Vandenhuevel, *J. Chromatogr.*, **27**, 85 (1967).

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(8) R. J. Fessenden, K. Seeler, and M. Dagaini, *J. Org. Chem.*, **31**, 2483 (1966).

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(10) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, **77**, 5562 (1955).

(11) E. L. Eliel, *Chem. Ind. (London)*, 568 (1959).

(12) E. L. Eliel and M. Gianni, *Tetrahedron Lett.*, 97 (1962).

Table I. Proton Chemical Shifts of the α -Proton of Unsubstituted and 4-Alkyl-Substituted $-\text{NHSiMe}_3$ and $-\text{OSiMe}_3$ Cyclohexanes

Compound ^a	$S^{b,c}$ (100 MHz), Hz				$S^{b,c}$ (220 MHz), Hz			
	$\sigma,^d$ Hz	δ^e	n^f	$\sigma,^d$ Hz	δ^e	n^f		
I	84.3	1.4	3.57	3	295.7	1.0	3.55	2
<i>cis</i> -4-Me I	54.6	0.1	3.87	2				
<i>trans</i> -4-Me I	93.5	0	3.48	2				
<i>trans</i> -4- <i>tert</i> -butyl I	92.7	2.0	3.49	3	316.9	1.6	3.46	3
<i>cis</i> -4- <i>tert</i> -butyl I	44.0	2.0	3.98	2	206.1	0.1	3.96	2
II	187.0	0	2.54	2	518.2	2.5	2.54	2
<i>cis</i> -4-Me II ^h	149.4		2.92	1				
<i>trans</i> -4-Me II ^h	194.4		2.47	1				
<i>trans</i> -4- <i>tert</i> -butyl II	194.4	0.1	2.47	2	533.5	0.7	2.47	2
<i>cis</i> -4- <i>tert</i> -butyl II	131.5	0.5	3.10	3	394.9	0.9	3.10	3

^a 20 vol % solutions in CH_2Cl_2 (see *h*). ^b Chemical shift is measured in hertz upfield from the high-field ^{13}C satellite of the solvent, CH_2Cl_2 . ^c Measured at 29°. ^d This estimate of the standard deviation includes all measurements of different solutions on different days. ^e For the convenience of the reader, the approximate chemical shift in parts per million downfield from tetramethylsilane (TMS) is also given. TMS was not included in the nmr tubes so chemical shift calculations are based on the chemical shift of CH_2Cl_2 (5.30 ppm downfield) [N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, p 9] and the measured spacing between CH_2Cl_2 and its high-field ^{13}C satellite (88.5 Hz). $J_{^{13}\text{C}\text{H}}$ measures 176.5 Hz for our solutions compared with 178 Hz given by J. W. Emsley, J. Feeney, and L. H. Sutcliffe ["High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, New York, N. Y., 1966, p 1014]. ^f Number of measurements. ^g Measured at 18°. ^h Measurements were made on a 1:1 mixture of the *cis* and *trans* isomers. The mixture of isomers was made up as a 40 vol % solution in CH_2Cl_2 ; *i.e.*, 20 vol % in each isomer.

$$A = -\Delta G^\circ = RT \ln \frac{S_a - S}{S - S_e}$$

where S (see Experimental Section. Nmr Measurements) denotes the chemical shift of the α -proton in the conformationally flexible cyclohexyl system, and S_a and S_e denote the shifts of the equatorial and axial α -protons in the *cis*-4-*tert*-butyl- and *trans*-4-*tert*-butyl-cyclohexyl compounds, respectively.

Another procedure (method 2) of assessing conformational preferences assumes additivity of A values for substituents attached to the cyclohexyl ring. Here, *cis*-4-methylcyclohexyl derivatives are used as the conformationally mobile systems with the two groups, methyl and $-\text{NHSiMe}_3$ or methyl and $-\text{OSiMe}_3$, competing for the energetically favored equatorial position. The conformationally rigid model compounds are the same *cis*- and *trans*-4-*tert*-butylcyclohexyl derivatives used in the first method. From the *cis*-4-methyl compounds, the A values are calculated (eq 2) as the difference between the A value of, *e.g.*, $-\text{NHSiMe}_3$ and the A value of methyl. The A value of the latter is taken as 1.70 kcal mol⁻¹.¹⁴

$$A_{\text{NHSiMe}_3} - A_{\text{CH}_3} = -\Delta G^\circ = RT \ln \frac{S_a - S}{S - S_e}$$

Additionally, we have compared α -proton chemical shifts of *trans*-4-methyl I and II with the corresponding *trans*-4-*tert*-butyl I and II and found the shifts to be experimentally indistinguishable. The *trans*-4-methyl compounds are essentially conformationally pure since the *trans* diequatorial conformer is favored by at least 2.5 kcal mol⁻¹¹⁵ over that of the *trans* diaxial. The significance of these measurements of the *trans*-4-methyl systems will be considered in more detail as we discuss Eliel's nmr chemical shift method, whose validity has been questioned recently by Jensen¹⁶ (see below).

(13) E. L. Eliel and R. J. L. Martin, *J. Amer. Chem. Soc.*, **90**, 682 (1968).

(14) J. A. Hirsch in "Topics in Stereochemistry," Vol. 1, N. H. Allinger and E. L. Eliel, Ed., Interscience, New York, N. Y., 1967, p 204.

(15) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 236.

(16) (a) F. R. Jensen and B. H. Beck, *J. Amer. Chem. Soc.*, **90**, 3251 (1968); see also ref 13; (b) F. R. Jensen, C. H. Bushweller, and B. H.

The raw chemical shift data are given in Table I, and the A values for the $-\text{NHSiMe}_3$ and $-\text{OSiMe}_3$ groups calculated for both methods are given in Table II.

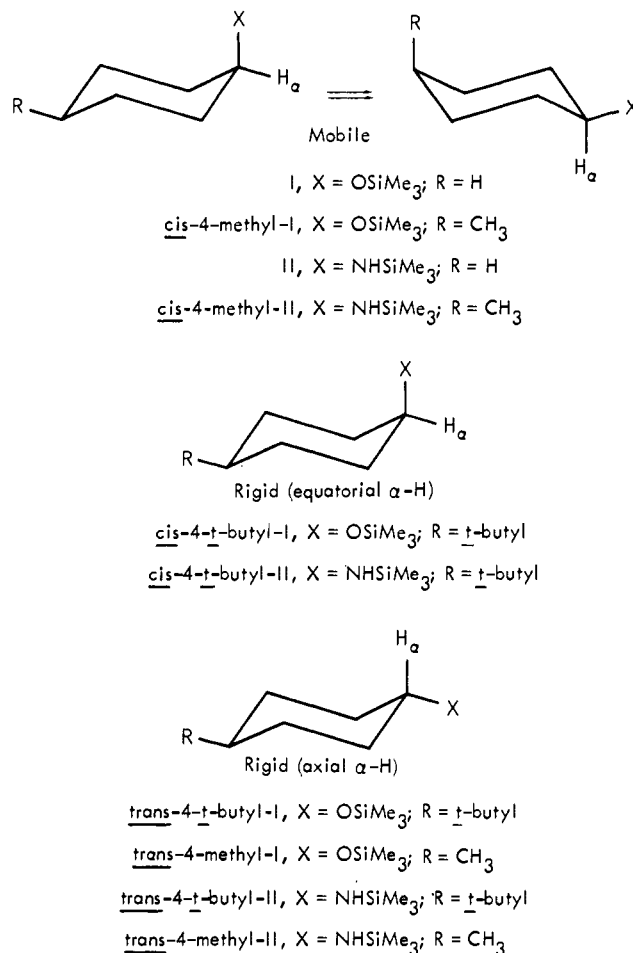


Figure 1. Mobile and rigid conformers of $-\text{OSiMe}_3$ and $-\text{NHSiMe}_3$ substituted cyclohexanes.

Beck, *J. Amer. Chem. Soc.*, **91**, 344 (1969); (c) F. A. L. Anet and P. M. Henricks, *Tetrahedron Lett.*, 741 (1969).

Table II. Calculated A Values for $-NHSiMe_3$ and $-OSiMe_3$ Groups

Compound ^a	A^b (100 MHz), kcal mol ⁻¹	σ^c	A^d (220 MHz), kcal mol ⁻¹	σ^c
I	0.94	0.09	0.83	0.01
<i>cis</i> -4-Me I	0.93	0.08		
II	1.21	0.01	1.21	0.08
<i>cis</i> -4-Me II ^e	1.15	0.02		

^a 20 vol % solutions in CH_2Cl_2 (see footnote *e*). ^b Measured at 29°. ^c This estimate of the standard deviation in the A value is based on the estimates of the standard deviation of the S measurements, Table I. ^d Measured at 18°. ^e Measurements were made in a 1:1 mixture of the *cis* and *trans* isomers. The mixture of isomers was made up as a 40 vol % solution in CH_2Cl_2 ; *i.e.*, 20 vol % in each isomer.

Discussion

We shall first consider the validity of the methods we employed to measure A values, then discuss the significance of our results, and finally mention our finding of an unusually large HCNH proton-proton coupling.

Validity of the Measurements. The chief assumption of method 1 is that introduction of a 4-*tert*-butyl group does not affect the chemical shift of the α -proton. That is, if an unsubstituted cyclohexyl derivative could be restrained from inverting and then examined while the substituent was in, for example, the equatorial position, the axial α -proton's chemical shift would be the same as the shift of the analogous *trans*-4-*tert*-butyl derivative where the α -proton is always axial. The same assumption applies to method 2 where the chemical shift of the axial α -proton of the mobile *cis*-4-methyl derivative, if the mobile system could be restrained from inverting, is assumed to be the same as the α -proton shift in the *trans*-4-*tert*-butyl model. However, Jensen^{16a} has found that at low temperatures (-80 to -105°) substitution of a *tert*-butyl group for hydrogen at the 4 position of several cyclohexyl derivatives shifts the axial or equatorial α -proton resonance by 2.6–8.3 Hz (100 MHz). These measurements were made by comparing conformationally rigid 4-*tert*-butyl systems with analogous unsubstituted cyclohexyl derivatives which are present as two conformational forms at the low temperatures.

With this evidence, questioning the basic assumption of the nmr shift measurement method, Jensen determined the effect which such uncertainties have on calculated A values. He accomplished this by calculating A values for several cyclohexyl systems using what we have designated as method 1. That is, he used the shift measurements of *trans*-4-*tert*-butyl model systems as reference values for pure axial and pure equatorial protons. He recalculated the A values using this time the shift measurements of frozen unsubstituted cyclohexyl systems, corrected for the temperature dependence of this shift, as reference values for pure axial or equatorial protons. The A values from this latter method were compared with and agree with (± 0.08 kcal mol⁻¹) A values determined from an independent measurement of relative areas of the α -proton resonances (-80°) arising from the two frozen cyclohexyl conformers. The significant A value differences be-

tween method 1 and the other two methods of calculation ranged from 0.14 to 0.27 kcal mol⁻¹.

We felt it was important, then, to assess the precision of our measurements to determine whether an inaccuracy of the magnitude found by Jensen, 0.14–0.27 kcal mol⁻¹, would be greater than our experimental precision and thus establish whether the complications exposed by Jensen's work would affect our determination of conformational preferences. In Table I we have indicated our precision (estimated standard deviations) of S measurements to be less than 2.5 Hz for all cases. This precision results in experimental uncertainties in calculated A values which range from 0.01 to 0.09 kcal mol⁻¹ (Table II). These variations are quite similar to the experimental uncertainties reported by Jensen^{16b} which ranged from 0.01 to 0.14 kcal mol⁻¹ and which were generally proportional to the calculated A values. We conclude, then, that our A values are determined with approximately the same precision as those reported by Jensen and that chemical shift inaccuracies of the magnitude found by Jensen, 2.6–8.3 Hz, would produce significant inaccuracies in our calculated A values. In this discussion we are observing the distinction between precision and accuracy, the former being a measure of repeatability and the latter a measure of how closely our calculations agree with a "true" value.

Now, the chemical shift measurements of *cis*- and *trans*-4-methylcyclohexyl systems provide us with two pieces of information relating to the accuracy of our A value calculations. First, the α -proton chemical shifts of *trans*-4-methyl I and II give us an independent measurement of S_e . These methyl-substituted compounds exist with the substituents disposed entirely in the diequatorial conformation, and Table I indicates that the differences in α -proton shifts between the *trans*-4-methyl and *trans*-4-*tert*-butyl compounds are insignificant (0.8 and 0.0 Hz). Thus, while Jensen^{16a} finds that substituting hydrogen for a *tert*-butyl group in the 4 position causes a chemical shift change in the α -proton of several hertz, we find for our systems that substituting a methyl group for a *tert*-butyl causes a change in the α -proton chemical shift of a fraction of a hertz. Jensen's data^{16a} show that axial and equatorial α -proton resonances are affected more or less to the same extent at low temperature by introduction of a 4-*tert*-butyl group; hence we presume that our S_a measurement should be affected as little as our S_e measurements.

The second piece of information comes from the A value determined by method 2 which uses the mobile compounds *cis*-4-methyl I and II. The importance of this measurement is seen when we consider that the A value is derived by comparing chemical shifts of three cyclohexyl derivatives, each of which has a 4-alkyl substituent. Certainly, if substituting an alkyl group for hydrogen in the 4 position causes a significant difference in the α -proton resonance position, then method 2 should not agree with method 1. Table II shows that the A values calculated separately by methods 1 and 2 agree within ± 0.06 kcal mol⁻¹.

If the inaccuracies discussed by Jensen are manifested in our systems, then we are left with two possibilities: (i) substituting a *tert*-butyl or a methyl for hydrogen in the 4 position introduces the same error, because the S_e measurements are the same for *trans*-4-*tert*-butyl

and *trans*-4-methyl, or (ii) for our particular compounds and solvent systems, the chemical shift error associated with substituting an alkyl group for hydrogen is smaller than our experimental error and smaller in magnitude than that found by Jensen. We feel the latter (ii) is the case because of the excellent agreement between method 1 and method 2. Recall that method 2 compares all 4-alkyl substituted compounds, while method 1 compares an unsubstituted mobile cyclohexyl system with two 4-*tert*-butyl rigid models. We conclude, then, that the *A* values calculated in this work represent a reasonably accurate measure of the equatorial-axial free energy preference of the -NHSiMe₃ and -OSiMe₃ groups. Our judgment of Eliel's nmr method is not as harsh as that of Jensen¹⁶—that the method is invalid—but we are reminded of the common difficulties associated with using model systems for physical measurements.

Significance of the Results. The most obvious feature of our results is that the conversion of cyclohexanol or cyclohexylamine to its corresponding trimethylsilyl derivative produces no dramatic change in the conformational preference of the derivative. If we assume that the *A* values (see Table III) are an indication of the

Table III. Selected *A* Values^a

Group	<i>A</i> , kcal mol ⁻¹
OH	0.52 ^c
OCH ₃	0.60
OSiMe ₃	0.89 ^b
NH ₂	1.20
NHCH ₃	1.0
NHSiMe ₃	1.21 ^b
CH ₃	1.70

^a *A* values were taken from ref 14. The tabulated values are those designated by Hirsch as the "best values" for aprotic solvents (accurate to ±0.1 kcal mol⁻¹). Any solvent dependent differences in *A* values is smaller than the scatter of values reported for different methods. ^bThis work. ^cThis value is probably low by 0.1 kcal mol⁻¹: E. L. Eliel, D. G. Neilson, and E. C. Gilbert, *Chem. Commun.*, 360 (1968).

relative sizes of the -NHSiMe₃ and -OSiMe₃ groups, then the -NHSiMe₃ group is approximately the same size as -NH₂ and slightly larger (0.2 kcal mol⁻¹) than -NHCH₃, while -OSiMe₃ is slightly larger (0.3 kcal mol⁻¹) than -OH or -OCH₃. All of these groups are significantly smaller than the methyl group (1.7 kcal mol⁻¹). Certainly the total volume of the -NHSiMe₃ or -OSiMe₃ group is greater than -CH₃, but since the -SiMe₃ group is separated from the ring by a heteroatom, its steric influence on ring conformation is diminished.

It is possible, however, that the steric effects of -SiMe₃ derivatives would be more prominent in long-range interactions as in steroid systems. We refer particularly to the 11β-OH steroids³ where the axial hydroxyl, sandwiched between two axial methyl groups, is not readily trimethylsilylated under conditions in which "normal" axial cyclohexyl hydroxyls react fairly rapidly. Fieser and Fieser¹⁷ have reported a corresponding lack of reactivity for acylation reactions in similar 11β-OH steroid systems. It is important,

(17) L. F. Fieser and M. Fieser, "Steroids," Reinhold, New York, N. Y., 1959, p 216.

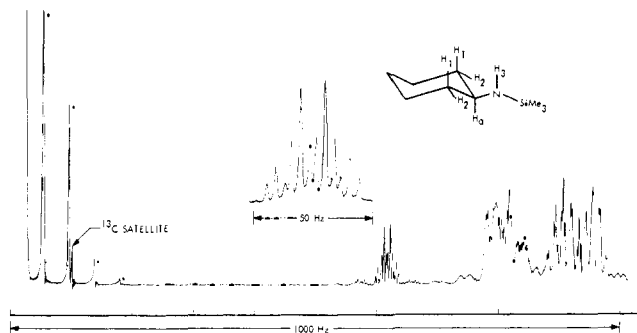


Figure 2. Proton nmr spectrum (220 MHz) of *N*-trimethylsilyl-cyclohexylamine; 20 vol % solution in CH₂Cl₂. The SiMe₃ proton resonance is upfield and is not shown. Inset shows the expanded α-proton region. Note the satellite signal due to ¹³CH₂Cl₂ among the spinning side bands (denoted by an asterisk) of the main ¹³CH₂Cl₂ signal.

however, to make the distinction between rates of reaction and the equilibrium composition of reactants. Indeed, it was the desire to be able to make such a distinction which originally prompted us to undertake our investigation. Our measurements give us information only about the equilibrium composition of reactants.

HCNH Proton-Proton Coupling

We wish to comment briefly on an interesting experimental feature, namely the coupling between the proton on nitrogen and the cyclohexyl α-proton. This coupling is best seen (Figure 2) in the 220-MHz spectrum of II. Considering solely the first-order spin-spin splittings, the α-proton pattern may be analyzed to give $J_{H_1H_\alpha} \approx J_{H_3H_\alpha} = 10$ Hz, and $J_{H_2H_\alpha} = 3.7$ Hz. This HCNH proton-proton coupling, $J_{H_1H_\alpha}$, is roughly twice as large as other values reported in the literatures.¹⁸⁻²⁰ Such a large coupling is, perhaps, indicative of a *trans*-coplanar arrangement of the H_α-C and N-H₃ bonds. An examination of CPK molecular models indicates that such an arrangement is sterically reasonable and is perhaps the favored spatial arrangement for the conformer with the -NHSiMe₃ group disposed equatorially.

Experimental Section

Nmr Measurements. Each of the trimethylsilyl compounds was dissolved in CH₂Cl₂ to make a 20 vol % solution, except for *cis*- and *trans*-4-methyl II. These two trimethylsilylamines, which we were unable to separate, were analyzed as a 1:1 mixture. The mixture of the latter isomers was made up as a 40 vol % solution in CH₂Cl₂—20 vol % in each isomer. Methylene chloride was chosen as a solvent for these studies since it is a moderately polar aprotic solvent in which trimethylsilylation reactions can be very conveniently carried out. Furthermore, it has no interfering nmr signals and it is sufficiently volatile to offer no interference in gas chromatographic analysis.

The various trimethylsilyl compounds were shown by gas chromatography to be at least 95% pure. The nmr spectra also were consistent with an isomeric purity of at least 95% as shown by examination of the X-H region of the spectra. Solutions, degassed and sealed under nitrogen, did not deteriorate with time.

Spectra were recorded at 100 and 220 MHz for all compounds except the 4-methyl-substituted compounds which were analyzed only at 100 MHz. Since chemical shift separations are increased

(18) M. Barfield and M. Karplus, *J. Amer. Chem. Soc.*, **91**, 1 (1969).

(19) E. W. Randall and J. D. Baldeschwieler, *J. Mol. Spectrosc.*, **8**, 365 (1962).

(20) E. Grunwald, *J. Phys. Chem.*, **67**, 2208 (1963).

linearly with field strengths, measurement of the α -proton chemical shifts at higher field are more accurate. The α -proton spectra are complex multiplets due to coupling with adjacent ring protons. In the case of amine derivatives there is also coupling with the proton on nitrogen (see Figure 2). Owing to this complexity, chemical shifts were measured from the estimated centers of gravity of the multiplets. This estimation was undoubtedly the least accurate aspect of our measurements. For some of the compounds we were able to simplify the α -proton region by decoupling (100 MHz) and consequently make more accurate shift measurements of the narrow and symmetrical peaks. At 220 MHz the α -protons exhibited more nearly first-order splitting patterns; hence centers of gravity of the more symmetrical multiplets could be estimated with increased accuracy.

We chose not to employ the conventional internal standard tetramethylsilane (TMS) since its presence would complicate the spectra of samples containing $-\text{SiMe}_3$ groups. Instead, we measured the chemical shifts in hertz upfield from the high-field ^{13}C satellite of the CH_2Cl_2 solvent. For the purpose of our discussion this shift has been designated S .

Synthesis. *cis*- and *trans*-4-*tert*-Butylcyclohexanecarboxylic Acid. In general, we followed the method of Tichy, *et al.*,²¹ to synthesize and separate these isomers. The hydrogenation of *p*-*tert*-butylbenzoic acid by Adam's catalyst was successfully scaled up fourfold. It was found that the catalyst could be recycled with no appreciable loss in activity by filtering it off from the reaction mixture after use and storing it under glacial acetic acid between hydrogenations. After reaction, the acetic acid solvent was removed on a rotary evaporator, and the solid acids were air dried on a filter, washed with water, and thoroughly dried over KOH in a vacuum desiccator. The dried product was recrystallized directly from ethyl acetate to yield pure *cis*-4-*tert*-butylcyclohexanecarboxylic acid, mp 117.2–117.7° (lit.²¹ mp 117.5–118°). Three additional recrystallizations did not change the melting point.

The crude *trans*-4-*tert*-butylcyclohexanecarboxylic acid was recovered from the mother liquors and equilibrated in refluxing KOH–ethylene glycol. This treatment converted the remaining *cis* isomer into *trans*; the latter was recrystallized from ethyl acetate and gave a product with mp 175° (lit.²¹ mp 174.5–175.5°). Three additional recrystallizations did not change the melting point.

***cis*- and *trans*-4-*tert*-Butylcyclohexylamine.** The *cis*- and *trans*-4-*tert*-butylcyclohexanecarboxylic acids were separately converted to the corresponding amines by the Schmidt reaction.^{21,22} All manipulations were carried out in a nitrogen atmosphere or under vacuum. Each of the isolated amines distilled at approximately 68° (4–5 mm) (lit.²¹ bp 76–77° (11 mm)).

Trimethylsilyl Derivatives. General. A comprehensive review of silylation procedures is contained in Pierce's² book. Most of the trimethylsilyl derivatives were synthesized using trimethylsilyl chloride (Me_3SiCl) and either an amine base or hexamethyldisilazane (HMDS). After removal of precipitated amine hydrochloride by filtration, the derivative was purified by distillation or preparative gas chromatography. We will describe a typical synthesis for each method (procedure 1, 2, 3, and 4) employed and list pertinent physical properties for all compounds. All manipulations were performed in a dry nitrogen atmosphere.

***N*-Trimethylsilyl-*cis*-4-*tert*-butylcyclohexylamine (Procedure 1).** To 1 g (6.4 mmol) of *cis*-4-*tert*-butylcyclohexylamine was added 1.5 ml (12 mmol) of Me_3SiCl (Pierce Chemical) and 40 ml (29 mmol) of Et_3N . A copious precipitate of $\text{Et}_3\text{N} \cdot \text{HCl}$ formed immediately; to ensure complete mixing of any occluded reactants the mixture was refluxed for 2 hr. The solid was filtered off and the desired trimethylsilylamine was concentrated in the filtrate by distilling through a 15-cm Vigreux column. The *N*-trimethylsilyl-*cis*-4-*tert*-butylcyclohexylamine was fractionated through an efficient, 30 cm, center rod column, bp 88–91° (3.3 mm).

***N*-Trimethylsilyl-*trans*-4-*tert*-butylcyclohexylamine.** *trans*-4-*tert*-butylcyclohexylamine was converted to the *N*-trimethylsilyl derivative as in procedure 1, bp 93–96° (3.3 mm).

***N*-Trimethylsilylcyclohexylamine (Procedure 2).** Freshly distilled cyclohexylamine (Matheson Coleman and Bell), 15 ml (133 mmol), and Me_3SiCl , 10 ml (79 mmol), were refluxed in 100 ml of dry benzene for 1 hr. Precipitated cyclohexylamine hydrochloride was removed by filtration and the filtrate was fractionated to give *N*-trimethylsilylcyclohexylamine, bp 55.5–56.2° (3 mm).

***N*-Trimethylsilyl-*cis*- and -*trans*-4-methylcyclohexylamine (Procedure 3).** *N*-Trimethylsilyldiethylamine, 2 ml (10.5 mmol), and freshly distilled *cis*- and *trans*-4-methylcyclohexylamine, 1 ml (7.6 mmol), were heated in a 25-ml round-bottomed flask fitted with a 15-cm Vigreux column until the reflux temperature reached 125°. The pot residue was injected in 50- μl aliquots directly onto a glpc column, 10 ft \times $\frac{3}{8}$ in., 20% SE-52 on 60–80 mesh acid washed Chromosorb W, operated with a 200 cm^3/min He carrier gas flow, 200° column oven, 202° injector, and 206° thermal conductivity detector. The gas chromatograph was a Varian Aerograph Model 1520-B. The *N*-trimethylsilylamine isomers, which were unresolved and which had a retention time of approximately 8 min, were collected directly in nmr tubes.

***O*-Trimethylsilylcyclohexanol (Procedure 4).** A 10-g (100 mmol) sample of cyclohexanol, 20 ml (96 mmol) of HMDS (Analabs), and 10 ml (79 mmol) of Me_3SiCl were refluxed for approximately 0.5 hr. The precipitated NH_4Cl was removed by filtration and the filtrate fractionated through an efficient 30-cm center rod column to yield *O*-trimethylsilylcyclohexanol, bp 170.8–171.5.

***O*-Trimethylsilyl-*cis*- and -*trans*-4-*tert*-butylcyclohexanol.** A mixture of *cis*- and *trans*-4-*tert*-butylcyclohexanols was converted to its *O*-trimethylsilyl ethers by procedure 4. The mixed ethers, bp 88–92° (4 mm), were separated by glpc using conditions described in procedure 3 except the He flow rate was reduced to 150 cm^3/min . Retention time of the *cis* ether was 6 min and that of the *trans* ether was 9.1 min.

***O*-Trimethylsilyl-*cis*- and -*trans*-4-methylcyclohexanol.** A mixture of *cis*- and *trans*-4-methylcyclohexanol was converted to its *O*-trimethylsilyl ethers by procedure 4. The mixed ethers, bp 183.1–184.9°, were separated by glpc using the same conditions described for procedure 3 except the column oven was at 150° and the He flow rate was 130 cm^3/min . The retention time of the *cis* ether was 14.4 min and that of the *trans* ether was 16.2 min.

High-Resolution Mass Spectral Analyses. All of the compounds studied are moisture sensitive, hydrolyzing rapidly in air and most likely reacting with glass surfaces. In spite of repeated attempts, we were unable to obtain satisfactory elemental analyses using microcombustion procedures. We have instead made high-resolution mass spectral measurements of the parent ions of the compounds using a peak matching technique²³ with perfluorokerosene fragments serving as reference masses. Measurements were made on an MS-902.

cis- and *trans*-4-*tert*-butyl I were analyzed as an epimeric mixture as were the epimeric pairs *cis*- and *trans*-4-methyl I and *cis*- and *trans*-4-methyl II. The exact molecular weights are listed: I, for $\text{C}_9\text{H}_{20}\text{OSi}$, 172.1278 (found, 172.1257); *cis*- and *trans*-4-Me I, calcd for $\text{C}_{10}\text{H}_{22}\text{OSi}$, 186.1440 (found, 186.1437); *cis*- and *trans*-4-*tert*-butyl I, calcd for $\text{C}_{13}\text{H}_{28}\text{OSi}$, 228.1902 (found, 228.1900); II, calcd for $\text{C}_9\text{H}_{21}\text{NSi}$, 171.1438 (found, 171.1420); *cis*- and *trans*-4-Me II, calcd for $\text{C}_{10}\text{H}_{23}\text{NSi}$, 185.1594 (found, 185.1602); *cis*-4-*tert*-butyl II, calcd for $\text{C}_{13}\text{H}_{29}\text{NSi}$, 227.2062 (found, 227.2048); *trans*-4-*tert*-butyl II, calcd for $\text{C}_{13}\text{H}_{29}\text{NSi}$, 227.2062 (found, 227.2048).

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