γ-Silicon Stabilization of Carbonium Ions in Solvolysis. 3. Solvolysis of 4-(Trimethylsilyl)-3-methyl-2-butyl *p*-Bromobenzenesulfonates

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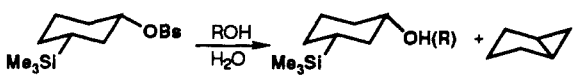
Abstract: It has been found that the rates of limiting solvolysis of 4-(trimethylsilyl)-3-methyl-2-butyl brosylate are accelerated relative to those of the corresponding 3,3-dimethyl-2-butyl and 4-(trimethylsilyl)-2-butyl esters. The relatively low α- and β-deuterium effects on the rates suggest a mechanism involving silicon-promoted γ-carbon participation. In order to determine the preferred stereochemical course of solvolytic substitution and of cyclopropane formation the threo and erythro alcohols were prepared separately, and the structure of the *p*-nitrobenzoate ester of the threo alcohol was established by X-ray crystallographic examination. Solvolysis of the brosylate esters of each diastereoisomeric alcohol produced mainly substitution products having exclusively retained configuration; the minor yields of 1,2-dimethylcyclopropane formed from the threo ester were predominantly of the cis configuration, and those from the erythro isomer were predominantly of the trans configuration. It is concluded that the mechanism involves the formation of an intermediate carbocation stabilized by the γ-silicon substituent through a "percaudal" interaction. The transition states for the formation and destruction of the intermediate ion are predominantly of the "W" conformation, but the "endo-sickle" also contributes and in each case nucleophilic attack apparently occurs from the front side of the bridged ion.

The role of γ-silicon in solvolysis reactions has been studied in some detail recently. In studies of the solvolysis of *cis*- and *trans*-3-(trimethylsilyl)cyclohexyl brosylates (eq 1 and 2) it was found that the diequatorial cis compound was accelerated by a factor of 452 relative to the diequatorial *trans*-4-*tert*-butylcyclohexyl brosylate in 97% 1,1,1-trifluoroethanol (97 T) at 25 °C, while the *trans*-3-(trimethylsilyl)cyclohexyl ester, with an axial leaving group, was only accelerated by a factor of 1.20.[1] The



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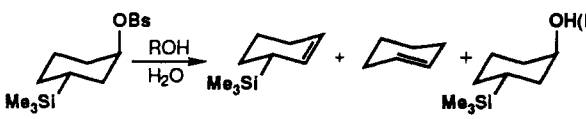

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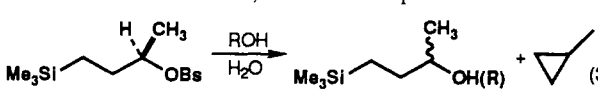
β-d_4 isotope rate effects were also vastly different for the two isomers. The cis isomer showed inverse or small β-d_4 effects, while the trans isomer showed a β-d_4 effect of over 2. The cis compound gave mainly direct substitution products with retained configuration, but a significant fraction of bicyclo[3.1.0]hexane was formed by 1,3-elimination. The trans isomer showed substitution with retention of configuration along with 1,2-elimination products and cyclohexene formed by hydrogen migration followed by trimethylsilyl elimination.

It was concluded that the two isomers react by two different mechanisms and that these mechanisms are determined by the different conformations of the molecules. The trans isomer with the axial leaving group reacts by ionization followed by, or concurrent with, neighboring hydrogen participation or elimination; the carbonium ion formed by hydrogen migration is stabilized by a β silyl group which subsequently eliminates rapidly to form cyclohexene. The cis compound with the equatorial leaving group undergoes ionization assisted by silicon-promoted carbon participation through the back lobe of the silicon–carbon bond in a "W" conformation.[2] Nucleophilic attack can then occur at C-1 to form the substitution products with retention of configuration or at silicon to form the 1,3-elimination product.



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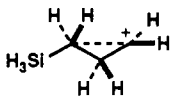
It has also been shown that 4-(trimethylsilyl)-2-butyl brosylate (eq 3) solvolyzed 8 to 10 times faster than pinacolyl brosylate, an analogue which reacts by a non-nucleophilically accelerated mechanism.[3] The α- and β-deuterium isotope rate effects were smaller than expected for nonassisted rate-determining ionization. The β-d_3 rate effect (k_H/k_{D3}) was 1.14–1.16 indicating a significant, but reduced, development of positive charge at the α-carbon in the transition state. The inverse or small β-d_2 effects at C-3 showed that although there is significant positive charge being developed at C-2 in the transition state, the carbon–deuterium bonds at C-3 are held in a conformation that allows little hyperconjugative overlap. The products from the solvolysis of 4-(trimethylsilyl)-2-butyl brosylate are mainly from nonstereospecific substitution with a small but significant amount of methylcyclopropane formed by 1,3-elimination.

The mechanism of this reaction was proposed to be similar to that for the solvolysis of *cis*-3-(trimethylsilyl)cyclohexyl brosylate except that two transition state conformations must be involved, the "W" and the "end-stickle".[2] In order to explain nonstereospecific substitution, it was postulated that reaction proceeded through both the "W" and the "endo-sickle" with nucleophilic attack coming from both the front and the back side of the carbonium ion. These two conformations must have nearly equal energies in order to give, within experimental error, racemic products.

Computation of the energies of some model γ-silyl stabilized carbonium ions using ab initio techniques showed that the trans perpendicular carbonium ion, 1, formed from the "W" or the "endo-sickle" conformation was stabilized by several kcal per mol relative to the trans planar conformation, 2, with the carbonium ion center rotated 90°.[4] It was also noted that the greatest proportion of the formal charge in the stabilized conformation of the ion resided on the silicon atom. These calculations reinforce the experimental evidence for the conformational dependence of γ-silicon stabilization of carbonium ions and establish the theoretical explanation for silicon-promoted carbon participation.



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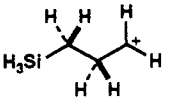

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(1) Shiner, V. J., Jr.; Ensinger, M. W.; Kriz, G. S. *J. Am. Chem. Soc.* **1986**, *108*, 842–844.
(2) Nickon, A.; Werstiuk, N. H. *J. Am. Chem. Soc.* **1967**, *89*, 3914–3915.
(3) Shiner, V. J., Jr.; Ensinger, M. W.; Rutkowske, R. D. *J. Am. Chem. Soc.* **1987**, *109*, 804–809.
(4) Davidson, E. R.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 3135–3137.

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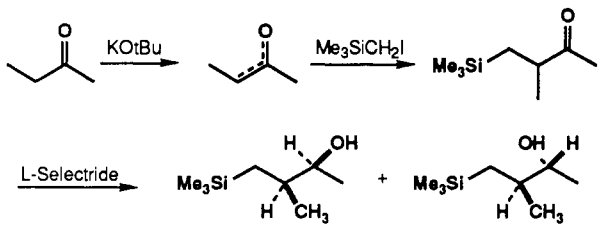
Scheme I. Preparation of 4-(Trimethylsilyl)-3-methyl-2-butanol



Grob and Sawlewicz recently found that solvolysis of 3-(trimethylsilyl)-1-adamantly bromide was accelerated by a factor of 8.6 in 80E at 70 °C relative to the unsubstituted compound. They also found that an additional acceleration factor of 3.8 was associated with a second γ-trimethylsilyl substituent at the 5 position of the adamantane ring. They suggest that the symmetrically bridged cation, where both trimethylsilyl groups are involved in promoting bridging, is consistent with these results.[5]

To characterize further the nature of the γ-silyl interaction in solvolysis reactions and especially to probe the question of its conformational dependence, we have examined the solvolysis of 4-(trimethylsilyl)-3-methyl-2-butyl brosylate. The behaviors of the individual diastereoisomers of this compound provide further insight into the conformational requirements of silicon-promoted carbon participation.

4-(Trimethylsilyl)-3-methyl-2-butanone was prepared by two separate methods. In the first, 2-(3,3-dimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline was prepared by the reaction of 2-amino-2-methyl-1-propanol with 4,4-dimethyl-4-silapentanoic acid at reflux. This oxazoline was deprotonated with *n*-butyllithium and methylated with methyl iodide to form 2-(1,3,3-trimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline. The quaternary ammonium salt of this material was formed by stirring with excess methyl iodide. 3,5,5-Trimethyl-5-sila-2-hexanone (4-trimethylsilyl-3-methyl-2-butanone) was prepared by reaction of the quaternary ammonium salt with methyllithium. The second method for formation of the ketone entailed deprotonation of 2-butanone with potassium *tert*-butoxide and the displacement reaction of this anion with 1-iodo-2,2-dimethyl-2-silapropane. This procedure gave poorer yields but was much simpler and required less time overall to complete.

The β-d_4 ketone was prepared by acid-catalyzed exchange of the ketone in deuterium oxide. A mixture of the diastereoisomeric alcohols was prepared by reaction of the ketones (deuterated or undeuterated) with lithium aluminum hydride. The mixture of α-*d* alcohols was prepared by reaction of the ketone with lithium aluminum deuteride.

A 70:30 mixture of the diastereoisomeric alcohols[6] was prepared by reduction of the ketone with lithium tri-*sec*-butylborohydride (L-Selectride). Since this reducing agent favors production of the less stable alcohol,[7] it was predicted that the predominant component would be the threo alcohol. Neither the mixture of alcohols nor the derived brosylates were easily separated. The *p*-nitrobenzoates, prepared by reaction with triethylamine and *p*-nitrobenzoyl chloride, were separated by repeated high-pressure liquid chromatography. The isomer with the shortest retention time corresponded to the major isomer from the L-Selectride reduction and was identified by X-ray crystallographic structure determination as having the threo configuration. The separate threo and erythro alcohols were prepared by treatment of the specific *p*-nitrobenzoate with lithium hydroxide in methanol. The *p*-bromobenzenesulfonates were prepared from the alcohols by reaction with *p*-bromobenzenesulfonyl chloride in pyridine. The brosylate esters were purified by high-pressure liquid chromatography on a silica gel column by using a hexane–ethyl acetate mixture as solvent. ^{1}H NMR (360 and 60 MHz) spectra were consistent with the assigned structures and could be used to distinguish the isomeric alcohols and esters. (See Experimental Section.)

Table I. Rate Constants for Solvolysis of 4-(Trimethylsilyl)-3-methyl-2-butyl-2-*d* Brosylate at 25 °C

	80E[a]	90E[a]	97T[a]
1:1 mixture of isomers	30.814 (0.054)[c]	9.108 (0.014)	1100 (50)[b]
threo	33.81 (0.10)	10.030 (0.008)	
erythro	27.289 (0.036)	7.951 (0.025)	

[a] Solvents are as follows: 80E and 90E represent 80 and 90 volume % ethanol, 20 and 10 volume % water, respectively; 97T represents 97 weight % 2,2,2-trifluoroethanol, 3 weight % water. [b] Rate constant for the undeuterated compound. [c] Numbers in parentheses indicate estimated errors.

Table II. Relative Rates for Solvolysis of 4-(Trimethylsilyl)-3-methyl-2-butyl Brosylate[a] at 25 °C

	80E[b]	90E[b]	97T[b]
$k/k_{\text{pinacolyl OBs}}$	48.5	47.9	138
$k/k_{\text{4-TMS-2-BuOBs}}$	6.89	5.95	13.0

[a] Values are quoted relative to the rates of solvolysis of the 1:1 mixture of the diastereoisomers. [b] Solvents are as noted in Table I.

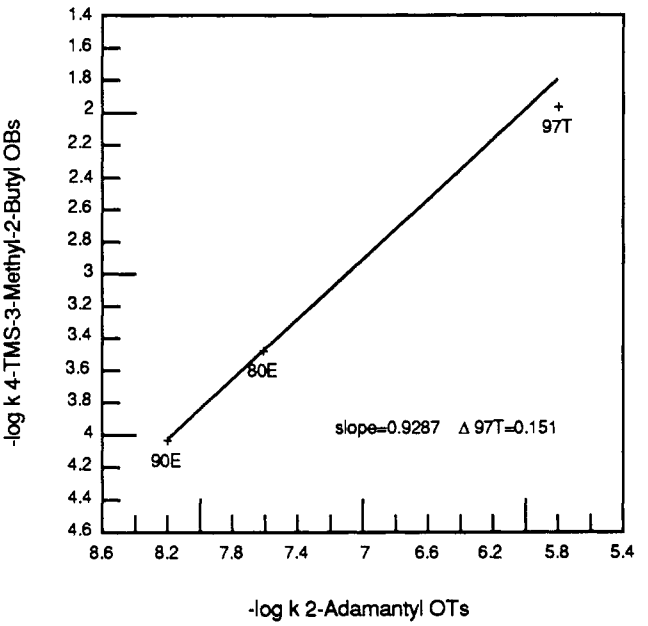


Figure 1. The EtOH–TFE plot for 4-(trimethylsilyl)-3-methyl-2-butyl brosylate.

Kinetic measurements were done conductometrically using a bipolar pulsed conductance apparatus. The rate constants for the solvolysis of 2-deutero-4-(trimethylsilyl)-3-methyl-2-butyl brosylate at 25 °C in various solvents are reported in Table I. The threo isomer is approximately 25% faster than the erythro isomer in ethanolic solvents. This difference is larger than and opposite in direction from that in the classical example of the 3-phenyl-2-butyl tosylates, where the rate of the solvolysis of the diastereoisomers differ by about 15% in acetone in 49 °C with the erythro isomer solvolysing faster.[8]

The rates of solvolysis relative to 4-(trimethylsilyl)-2-butyl brosylate and to pinacolyl brosylate are shown in Table II. Since the solvolyses are accelerated relative to the pinacolyl analogues, we conclude that there is a significant rate enhancement caused by the trimethylsilyl substituent. The acceleration factor of 6–13 relative to 4-(trimethylsilyl)-2-butyl brosylate is larger than would be expected from the inductive influence of the additional single

(5) Grob, C. A.; Sawlewicz, P. *Tetrahedron Lett.* **1987**, *28*, 951–952.
(6) The diastereoisomeric alcohols referred to are (2*R**,3*S**)-4-(trimethylsilyl)-3-methyl-2-butanol ("threo") and (2*R**,3*R**)-4-(trimethylsilyl)-3-methyl-2-butanol ("erythro"). Because each isomer of each pair reacts identically in the achiral environment of all experiments performed, for convenience, the compounds will be referred to as simply threo and erythro.
(7) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159–7161.
(8) Winstein, S.; Morse, B. K.; Grunwald, E.; Schreiber, K. C.; Corse, J. *J. Am. Chem. Soc.* **1952**, *74*, 1113–1120.

Table III. Isotope Rate Effects in the Solvolysis of 4-(Trimethylsilyl)-3-methyl-2-butyl Brosylate at 25 °C

	90E[a]	80E
α-d	1.132 (0.007)[b]	1.127 (0.004)
β-d_4	1.157 (0.008)	1.132 (0.002)

[a] Solvents are as noted in Table I. [b] Errors are indicated in parentheses.

β-methyl group. This suggests that the methyl group may be acting to favor the conformation required for silicon-promoted participation.

Plotting the log of the rate constants against the log of the rate constants for 2-adamantyl tosylate according to the method of Raber and Harris[9] (Figure 1) shows an ethanol correlation line with a slope of approximately unity with the point for the 97T rate being very close to the line. This plot is similar to those for 4-(trimethylsilyl)-2-butyl and *cis*-3-(trimethylsilyl)cyclohexyl brosylates and is consistent with a non-nucleophilically assisted mechanism.

The isotope effects on solvolysis are shown in Table III. The α-d isotope rate effects are reduced relative to those for the pinacolyl analogue (1.15–1.16) and are slightly smaller than those for 4-(trimethylsilyl)-2-butyl brosylate. This indicates that there is participation promoted by silicon giving delocalization of the carbonium ion positive charge onto the silicon and that the participation is enhanced in this compound relative to 4-(trimethylsilyl)-2-butyl brosylate. The β-d_4 isotope rate effects are also smaller than those (1.19–1.22) expected for simple rate-determining ionization without participation and smaller than those found in 4-(trimethylsilyl)-2-butyl brosylate. It should be noted that if silicon participates as proposed, the deuterium on carbon-3 would be held in a position such that little hyperconjugative interaction with the developing p-orbital would be possible resulting in a small rate effect as is observed for the β-d_2 effects in 4-(trimethylsilyl)-2-butyl brosylate and the β-d_4 effects in *cis*-3-(trimethylsilyl)cyclohexyl brosylate. It is thus assumed that most of the effect noted in the β-d_4 compound comes from the deuteriums on the methyl group. This significant, but relatively small, isotope effect indicates that there is positive charge being generated at the α-carbon in the transition state but that the charge is reduced by the silicon-promoted participation.

The structure and yields of the products of the solvolysis of each separate diastereoisomer of 4-(trimethylsilyl)-3-methyl-2-butyl brosylate and of the 1:1 mixture are shown in Table IV. The identity and ratios of the products were determined by examination of the ^{2}H NMR of the products resulting from the solvolysis of the α-deuterated isomer in various solvents. The identities of the cyclopropane products were confirmed by comparison of the deuterium chemical shift with reference spectra of known *cis*- and *trans*-1,2-dimethylcyclopropane.[10,11] The product studies were reproduced to ensure that the small yield of the cyclopropane products were not artifacts of the experiments. Deuterium chemical shifts varied slightly with solvent and are as follows in 97T (relative to external $CDCl_3$ at 7.2600 ppm): 4-(trimethylsilyl)-3-methyl-2-butyl-*2-d* trifluoroethyl ether, 3.645 ppm; 4-trimethyl-3-methyl-2-butan-*2-d*-ol, 3.841 ppm; *cis*-1,2-dimethylcyclopropane-*1-d*, 0.876 ppm; *trans*-1,2-dimethylcyclopropane-*1-d*, 0.546 ppm; 2-methyl-1-butene-*3-d*, 2.383 (in 90E). The stereochemistry of the substitution reaction was determined by isolation of the product alcohol from the reaction of the threo isomer in 90E and the erythro isomer in 80E. From comparison of the ^{1}H NMR of the recovered alcohol with alcohol of known stereochemistry, it was determined that in both cases the recovered alcohol was exclusively of the same configuration as the starting brosylate. This conclusion can be made with confidence since the methyl β to the reaction center shows a chemical shift difference

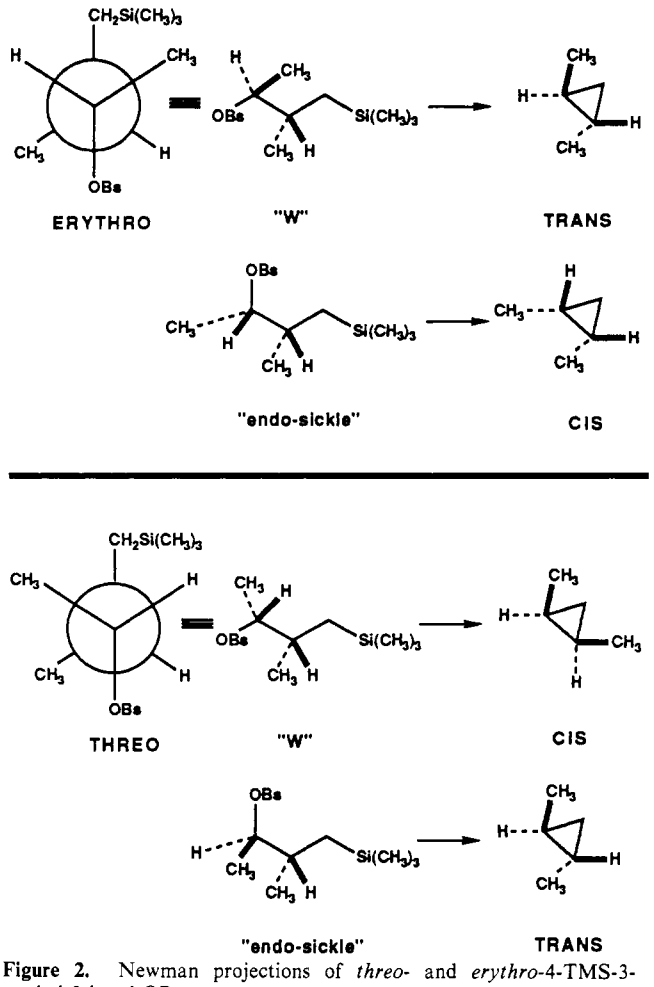


Figure 2. Newman projections of *threo*- and *erythro*-4-TMS-3-methyl-2-butyl OBs.

of 0.011 ppm between the diastereomers, and any amount over 3–5% of a minor isomer could easily be detected. It would be expected that if inversion of stereochemistry occurred in the same proportion as formation of the minor cyclopropane product (*cis*-1,2-dimethylcyclopropane for the erythro and *trans*-1,2-dimethylcyclopropane for the threo), there would be approximately 20% substitution with inversion from the erythro diastereomer. Since the minor cyclopropane product was formed in such small percentages in 97T, the amount of inversion expected would be too small to see using the NMR technique.

The stereochemistry of the 1,3-deoxysilylation can be deduced from the relationship between the configurations of the reacting ester and the cyclopropane products. For the threo isomer, *cis*-1,2-dimethylcyclopropane is the major 1,3-elimination product. Only a trace of the *trans*-cyclopropane is seen and only in 97T. The erythro isomer on the other hand yields predominantly the trans but also some *cis*-1,2-dimethylcyclopropane, except in 97T where only the *trans*-cyclopropane was found. As seen in Figure 2, the threo isomer can produce the *cis*-cyclopropane by reacting through the "W" conformation. The *trans*-cyclopropane can be formed from the "endo-sickle" conformation of the threo isomer or from the "W" conformation of the erythro isomer. The small but significant fraction of the *cis*-cyclopropane can be formed from the erythro isomer by reaction from the "endo-sickle" conformation. It is interesting to note that for the threo isomer, the only solvent which facilitates the formation of any detectable amount of the *trans*-cyclopropane ("endo-sickle" transition state conformation) is 97T, while in the erythro isomer 97T is the only solvent in which no *cis*-cyclopropane ("endo-sickle" transition state conformation) is formed. In other words, 97T seems to favor the formation of the trans product in both cases. In both isomers it is clear that the "W" conformation is favored, but the "endo-sickle" is still significant. By using this rationalization for the formation

(9) Raber, D. J.; Neal, W. C., Jr.; Dukes, M. D.; Harris, J. M.; Mount, D. L. *J. Am. Chem. Soc.* **1978**, *100*, 8137–8146.
(10) TRC Spectral Data, ^{1}H NMR; Beach, L. B., Ed.; 1982; Vol. 1, Serial Number 148C.
(11) *Sadtler Standard NMR Spectra Collection*; 1980; Number 8174M.

Table IV. Product Yields for Solvolysis of 4-(Trimethylsilyl)-3-methyl-2-butyl Brosylate[a]

	80E[b,c]		90E		97T	
	threo	erythro	threo	erythro	threo	erythro
$Me_3SiCH_2CHMeCHMeOR$	25.0	24.5	38.1	35.7	56.5	35.2
$Me_3SiCH_2CHMeCHMeOH$	52.5	55.7	35.9	42.2	31.1	30.6
cis-$Me_2C_3H_4$	18.3	3.0	18.5	3.8	12.1	0.0
trans-$Me_2C_3H_4$	0.0	12.9	0.0	12.8	0.4	34.3
$H_2C{=}CMeCHDMe$	4.3	4.0	7.4	5.6		

[a] Products, given as percentages, were identified by ^2H NMR of the α-deuterated materials. Product ratios were determined by using a curve fitting analysis program to integrate the NMR signals. [b] All reactions were run in solutions buffered with 2,6-dimethylpyridine. [c] Solvents are as noted in Table I.

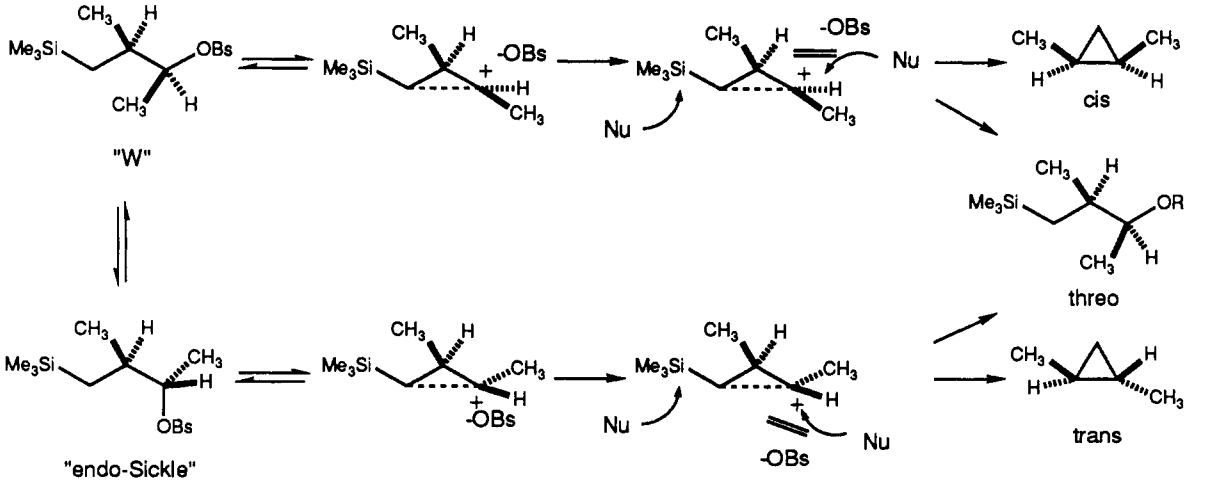


Figure 3. Mechanism for the solvolysis of *threo*-4-(trimethylsilyl)-3-methyl-2-butyl brosylate.

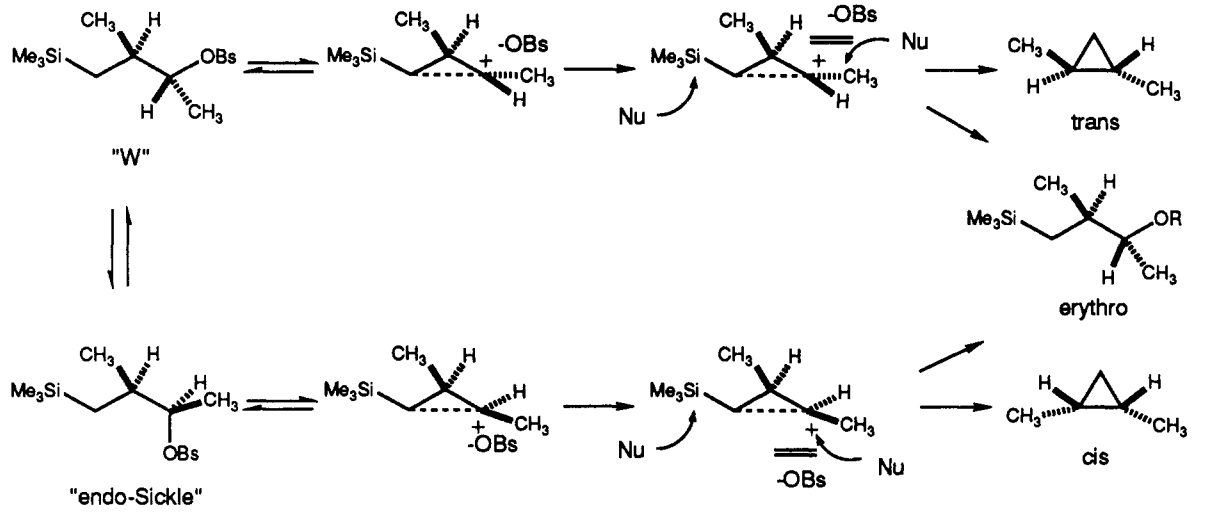


Figure 4. Mechanism for the solvolysis of *erythroh4*-(trimethylsilyl)-3-methyl-2-butyl brosylate.

of the cyclopropane products, it would be expected that the stereochemistry of the substitution products would follow the same pattern. The experimental evidence clearly shows, however, that the configuration of the substitution products is retained. This would seem to indicate that if the compound reacts through the "W" conformation, then nucleophilic attack also occurs through the "W" conformation. Similarly if the compound reacts from the "endo-sickle", nucleophilic attack occurs through the "endo-sickle". This is different from the mechanism suggested for the 4-(trimethylsilyl)-2-butyl brosylate where nucleophilic attack from either side in both conformations must be present in order to produce racemic products but similar to the mechanism suggested for *cis*-3-trimethylsilylcyclohexyl brosylate where all substitution products are of retained stereochemistry. This is a point which is not clearly understood and remains open for further investigation. One possible explanation for this difference is that in 4-(trimethylsilyl)-3-methyl-2-butyl brosylate and *cis*-3-(trimethylsilyl)cyclohexyl brosylate there is more silicon-promoted carbon participation, with the intermediate having more cyclopropane-like character (stronger participation) than in the 4-(trimethylsilyl)-2-butyl case. This may shield the back side of the carbonium ion from nucleophilic attack more effectively.

In conclusion, any proposed mechanism for the solvolysis of 4-(trimethylsilyl)-3-methyl-2butyl brosylate must account for an acceleration of the rate similar to the accelerations found for *cis*-3-(trimetylsilyl)cyclohexyl brosylate and 4-(trimethylsilyl)-2-butyl brosylate and attributed to silicon-promoted carbon participation. Because of the smaller isotope effects and the observed accelerations relative to those for 4-(trimethylsilyl)-2-butyl brosylate, we conclude that the methyl group in the 3 position must favor the conformations needed for participation and enhances the effects of participation. The configuration of the cyclopropane products shows that there are two conformations through which participation occurs, the "W" and the "endo-sickle" with the "W" being strongly favored. Finally the configurations of the substitution products show that nucleophilic substitution

occurs with retention of configuration. From this information, the mechanisms for the solvolysis of *threo*- and *erythro*-4-(trimethylsilyl)-3-methyl-2-butyl brosylate are proposed in Figures 3 and 4.

The small amount of the product not accounted for by this mechanism apparently comes from either hydrogen migration followed by trimethylsilyl elimination or trimethylsilylmethyl migration. In either case this is a minor product and does not influence the conclusions drawn here.

Experimental Section

2-(3,3-Dimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline was prepared by the method of Allen and Ginos.[12] Freshly distilled 2-amino-methyl-1-propanol (12.18 g, 0.1367 mol) was added to 20.00 g (0.1369 mol) of 4,4-dimethyl-4-silapentanoic acid. This mixture was stirred at reflux (at 175 °C) until the temperature fell to 145 °C. The crude product was distilled through a short Vigreux column into 30 mL of hexane. The aqueous layer was separated and extracted several times with chloroform. All organic layers were combined in chloroform and dried over sodium hydroxide pellets. The volatile solvents were evaporated with a rotary evaporator, leaving a white semisolid. This material was distilled through a 16-cm vacuum-jacketed column packed with glass helices. Four fractions were collected: the first three being chloroform, water, and unreacted starting material, in that order. Fraction four distilled at 201 °C (16.44 g collected, 60.4%): ^{1}H NMR ($CDCl_3$, 60 MHz) δ −0.05 (s, 9 H), 0.8 (m, 2 H), 1.20 (s, 6 H), 2.2 (m, 2 H), 3.85 (s, 2 H).

2-(1,3,3-Trimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline was prepared by the method of Meyers.[13] 2-(3,3-Dimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline (5.02 g, 0.0252 mol) was placed in a dry round-bottomed flask containing about 45 mL of dry tetrahydrofuran under an argon atmosphere. The solution was cooled to −78 °C, and 10 mL of a 2.68 M *n*-butyllithium solution (0.0268 mol) was added dropwise, resulting in a bright yellow solution. Methyl iodide (4.24 g, 0.0299 mol) was added dropwise with stirring. The reaction mixture was allowed to stir at −78 °C for approximately 5 h. It was the allowed to warm to room temperature and poured onto approximately 100 mL of ice water. The organic layer was separated, and the aqueous layer was extracted several times with diethyl ether. The combined organic layers were washed with saturated sodium bicarbonate and dried over calcium sulfate, and the volatile organics were removed in vacuo. The crude product was not purified further but was carried on to the next step: ^{1}H NMR ($CDCl_3$ at 60 MHz) δ −0.1 (s, 9 H), 0.9 (m, 2 H), 1.20 (d, overlapping), 1.25 (s, overlapping), doublet + singlet = 9 H, 1.8 (m, 1 H), 3.8 (s, 2 H).

3,5,5-Trimethyl-5-sila-2-hexanone (method A) was prepared by the method of Meyers.[14] The crude 2-(1,3,3-trimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline was placed in a round-bottomed flask, and 10 mL of methyl iodide was added. The mixture was stirred at room temperature under argon for approximately 44 h. The excess methyl iodide was removed in vacuo, and the residual material was washed several times with diethyl ether (pipetting the diethyl ether from the solid). The remaining salt (suspended in diethyl ether) was transferred to a larger flask, and 65 mL of 0.94 M methyllithium was added. This was allowed to stir at room temperature under argon from approximately 2 days. The solution was then poured onto approximately 50 mL of cold water. The organic layer was separated, and the aqueous layer was extracted several times with diethyl ether. The combined organic layer was concentrated and placed in approximately 100 mL of water containing 10 g of oxalic acid. The two-phase mixture was refluxed for 1 h. The organic layer was separated, the aqueous layer was extracted several times with diethyl ether, and the combined organic layer was washed with saturated sodium bicarbonate, dried over magnesium sulfate, and filtered through activated charcoal, and the solvent was removed in vacuo, giving 2.6 g of product (0.0164 mol, 65.2% from 2-(3,3-dimethyl-3-silabutyl)-4,4-dimethyl-1,3-oxazoline): ^{1}H NMR ($CDCl_3$) δ −0.1 (s, 9 H), 0.8 (m, 2 H), 1.1 (d, J = 6 Hz, 3 H), 2.0 (s, 3 H), 2.4 (m, 1 H).

1-Iodo-2,2-dimethyl-2-silapropane was prepared according to the method of Sommer.[15] Sodium iodide (75 g, 0.50 mol) was dissolved in 500 mL of dry acetone. 1-Chloro-2,2-dimethyl-2-silapropane (36 g, 41 mL, 0.29 mol) was added with stirring. This solution was stirred at reflux overnight (18 h). After cooling, precipitated sodium chloride was filtered, and most of the acetone was distilled. The remaining material was washed (3 × 50 mL) with water. The water washes were extracted (2 × 10 mL) with diethyl ether, and all organic layers were combined. This material was fractionally distilled with 1-iodo-2,2-dimethyl-2-silapropane (48.34 g, 0.226 mol, 76.9%) distilling at 139 °C: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.03 (s, 9 H), 1.93 (s, 2 H).

3,5,5-Trimethyl-5-sila-2-hexanone (Method B). 1-Iodo-2,2-dimethyl-2-silapropane (25.00 g, 0.1168 mol) was added to a solution of 2-butanone (8.00 g, 0.111 mol) in 200 mL of tetrahydrofuran and cooled to 0 °C in an ice bath. Also cooled to 0 °C was a solution of potassium *tert*-butoxide (13.15 g, 0.1173 mol) in 150 mL of tetrahydrofuran. This first solution was quickly added to the second, and the resulting light yellow solution was stirred at 0 °C for 30 min. This was allowed to warm to room temperature and then heated to reflux with stirring overnight. After cooling, the solution was washed with 10% hydrochloric acid (2 × 10 mL), water (1 × 10 mL), saturated sodium bicarbonate (1 × 10 mL), 20% sodium thiosulfate (2 × 10 mL), and saturated sodium chloride (1 × 10 mL) and then dried over magnesium sulfate. Volatile materials were fractionally distilled leaving 21.02 g of a mixture containing 3,5,5-trimethyl-5-sila-2-hexanone (major product by NMR), 6,6-dimethyl-6-sila-3-heptanone, tetrahydrofuran, and possibly 2,2-dimethyl-2-silapropyl *tert*-butyl ether. This material was not purified further but was carried on to the next reaction for future purification.

3,5,5-Trimethyl-5-sila-2-hexanol. Lithium aluminum hydride (0.28 g, 0.00737 mol) was suspended in 25 mL of dry diethyl ether at 0 °C under an argon atmosphere. 3,5,5-Trimethyl-5-sila-2-hexanone (1.01 g, 0.00639 mol) was added dropwise with stirring. The reaction was allowed to stir at 0 °C for approximately 2 h and then allowed to warm to room temperature overnight. To the reaction mixture were added 0.24 g of water, 0.24 g (15%) of sodium hydroxide, and 0.80 g of water in that order. The inorganic salts were filtered, and the organic layer was dried with magnesium sulfate. The solid was removed by filtration, and the solvent was evaporated with a rotary evaporator. 3,5,5-Trimethyl-5-sila-2-hexanol (0.85 g, 83.1%) was recovered as a mixture of diastereoisomers which were analytically separated on a Varian 3700 gas chromatograph by using a 50-m DB5 capillary column with 20 psig head pressure with helium as the carrier gas and a split ratio of 100:1. The retention times of the two diastereomers were 15.21 and 15.34 min integrating to a 46%:54% ratio, respectively: ^{1}H NMR ($CDCl_3$ 360 MHz) δ −0.008 (s, 9 H), 0.320 (m, 1 H), 0.70 (m, 1 H), 0.899, 0.908 (d, J = 6.8 Hz, 3 H), 1.114, 1.124 (d, J = 6.5 Hz, 3 H), 1.33 (br s, 1 H), 1.64 (m, 1 H), 3.590, 3.713 (pentet, J = 6.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$ 75 MHz) δ −0.73 CH_3; 17.214, 17.509 CH_2; 18.999, 19.402 CH_3; 19.636 CH_3; 36.270, 36.445 CH; 73.377, 73.605 CH.

A 70/30 mixture of the diastereomeric alcohols was synthesized by the method of Brown.[7] Lithium tri-*sec*-butylborohyride (6.5 mL of a 1.0 N solution, 0.0065 mol) was placed in a 50-mL, round-bottomed flask under argon. This solution was cooled to −78 °C, and 1.00 g (0.00632 mol) of 3,5,5-trimethyl-5-sila-2-hexanone was added dropwise with stirring. This was allowed to stir at −78 °C for 2 h and then allowed to warm to room temperature overnight. The reaction mixture was then treated with 30 mL of 3 N sodium hydroxide, followed by 30 mL of 30% hydrogen peroxide. The organic layer was separated, and the aqueous layer was extracted several times with diethyl ether. The combined organic factors were dried over magnesium sulfate, and the solvent was removed in vacuo, yielding 0.61 g (0.386 mol, 61.0%) of an approximately 70/30 (by NMR) mixture of diastereomeric 3,5,5-trimethyl-5-sila-2-hexanol.

2-Deuterio-3,5,5-trimethyl-5-sila-2-hexanol (0.52 g, 70.9% yield) was prepared from 0.82 g (0.004554 mol) of 3,5,5-trimethyl-5-sila-2-hexanone and 0.1532 g (0.003652 mol) of lithium aluminum deuteride by the same procedure as cited for the preparation of 3,5,5-trimethyl-5-sila-2-hexanol (1:1 mixture of diastereoisomers). The product was purified by high-pressure liquid chromatography by using a 20 cm × 1 cm prepacked silica gel column with 70% hexane–30% ethyl acetate as the solvent: ^{1}H NMR ($CDCl_3$, 300 MHz) on mixture of diastereomers, δ −0.014, −0.021 (s, 9 H), 0.50 (m, 1 H), 0.68 (m, 1 H), 0.890, 0.900 (d, J = 7.5 Hz, 3 H), 1.108 (s, 3 H), 1.16 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz, proton decoupled) on same mixture, δ −0.702 CH_3; 17.201, 17.496 CH_2; 18.892, 19.294 CH_3; 19.616 CH_3; 36.176, 36.338 CH; 73.38, 73.60 (triplet J = 20 Hz) CD.

1,1,1,3-Tetradeuterio-3,5,5-trimethyl-5-sila-2-hexanone. A solution of deuterium chloride, deuterium phosphate, and deuterium oxide was prepared by slow addition of 4.5 g of phosphorus pentachloride to 40 mL of deuterium oxide. To 10 mL of this solution was added 0.7 g (0.004 mol) of 3,5,5-trimethyl-5-sila-2-hexanone. This was stirred at room temperature in a stoppered flask for 10 days. The partially exchanged ketone was separated from the aqueous layer, and the procedure was repeated. After an additional 12 days, the ketone was again separated from the aqueous layer, and the aqueous layer was extracted with diethyl ether. The organic layers were combined and dried over magnesium sulfate, and the solvent was removed in vacuo, yielding 0.2 g of (0.001

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mol, 30%) 1,1,1,3-tetradeuterio-3,5-trimethyl-5-sila-2-hexanone: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 0.04 (s, 9 H), 0.57 (d, J = 18 Hz, 1 H), 0.96 (d, J = 18 Hz, 1 H), 1.12 (s, 3 H).

1,1,1,3-Tetradeuterio-3,5,5-trimethyl-5-sila-2-hexanol (0.15 g, 74% yield) was prepared from 0.20 g (0.0012 mol) of 1,1,1,3-tetradeuterio-3,5,5-trimethyl-5-sila-2-hexanone and 0.10 g (0.0026 mol) of lithium aluminum hydride by the same procedure as cited for the preparation of 3,5,5-trimethyl-5-sila-2-hexanol (1:1 mixture of diastereoisomers). The product was carried out to the next step without further purification: ^{1}H NMR ($CDCl_3$, 360 MHz) on mixture of diastereomers, δ 0.23 (s, 9 H), 0.323 (m, 1 H), 0.675 (m, 1 H), 0.890, 0.900 (s, 3 H), 1.688 (br s, 1 H, OH), 3.571, 3.605 (s, 1 H).

2-Deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-Nitrobenzoate. Freshly distilled triethylamine (2.8 mL, 2.0 g, 0.020 mol) and a catalytic amount of (dimethylamino)pyridine was added to a solution of *p*-nitrobenzoyl chloride (2.30 g, 0.0125 mol) in 25 mL of dry methylene chloride. 2-Deuterio-3,5,5-trimethyl-5-sila-2-hexanol (1.25 g, 0.00776 mol) was added, and the solution was stirred at room temperature under an inert atmosphere. After 2 h, the reaction mixture was washed with cold 10% hydrochloric acid (2 × 15 mL) and saturated sodium bicarbonate (1 × 30 mL). The organic layer was dried over magnesium sulfate and filtered through decolorizing charcoal. The volatile material was removed in vacuo, and the resulting solid was purified by high-pressure liquid chromatography by using 95% hexane–5% ethyl acetate as solvent on a 10 mm i.d. × 25 cm length prepacked silica gel column. High-resolution NMR clearly shows the presence of two diastereomeric isomers of 2-deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-nitrobenzoate (1.52 g, 0.0490 mol, 63%). The diastereomers were separated by repeated high-pressure liquid chromatography by using 95% hexane–5% ethyl acetate as solvent at 2.00 mL per min, injecting between 0.050 and 0.120 mL of an approximately 10% solution of the benzoate on the same column used above for the purification. This separation was done using a second Rainin HPX pump as an autoinjector controlled by a Gilson 201 automated fraction collector. The first isomer to elute was also purified by recrystallization in petroleum ether. The second isomer did not crystallize well and was rechromatographed several times. An X-ray crystal structure of the isomer with the shorter retention time showed this isomer to be the *threo*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexyl-*p*-nitrobenzoate: ^{1}H NMR threo isomer ($CDCl_3$, 360 MHz) δ 0.052 (s, 9 H), 0.444 (d of d, J_1 = 10.5 Hz, J_2 = 14.4 Hz, 1 H), 0.716 (d of d, J_1 = 3.6 Hz, J_2 = 14.4 Hz, 1 H), 1.008 (d, J = 6.5 Hz, 3 H), 1.285 (s, 3 H), 1.974 (m, 1 H) 8.246 (AA'BB' m, 4 H); ^{1}H NMR erythro isomer ($CDCl_3$, 360 MHz) δ 0.026 (s, 9 H), 0.453 (d of d, J_1 = 10.5 Hz, J_2 = 14.4 Hz, 1 H), 0.746 (d of d, J_1 = 3.2 Hz, J_2 = 14.4 Hz, 1 H), 1.014 (d, J = 6.8 Hz, 3 H), 1.309 (s, 3 H), 1.950 (m, 1 H); 8.246 (AA'BB' m, 4 H).

Crystallographic Analysis. *threo*-2-Deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-nitrobenzoate was provided to the Indiana University Molecular Structure Center (IUMSC) for analysis. The sample occurred as colorless needles which tended to grow as multicrystalline bundles. A fragment was cleaved from a bundle and affixed to a glass fiber using the standard techniques employed by the IUMSC.[16] Crystal data are: space group $P2_1/n$; a = 8.319 (9) Å, b = 30.88 (6) Å, c = 6.911 (7) Å, β = 109.73 (7)°, Z = 4, D_{calc} = 1.230 g cm^{-3}. It was noted that the intensities were somewhat low, and the long b axis resulted in inaccurate background corrections for some reflections.

Data were collected and reduced in the usual manner. The averaging for equivalent data was only 0.085, indicative of the problems with the long axis and poor crystal shape.

The structure was solved by a combination of direct methods (MULTAN78) and Fourier techniques. Hydrogen atoms were located and refined. Final residuals for the 1523 observed data (out of 2196 unique) are $R(F)$ = 0.086 and $R_w(F)$ = 0.082.

A final difference Fourier was essentially featureless, with the largest peak being 0.3 e/A^3.

***threo*-2-Deuterio-3,5,5-trimethyl-5-sila-2-hexanol** was prepared by a base-catalyzed ester exchange of *threo*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-nitrobenzoate. Lithium hydroxide (0.12 g, 0.0050 mol) was dissolved in 20 mL of methanol. threo-2-Deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-nitrobenzoate (0.52 g, 0.0017 mol) was added with stirring. After 3 h, the reaction mixture was washed with saturated ammonium chloride (3 × 5 mL) and dried over magnesium sulfate, and the volatile organic materials were removed in vacuo. The remaining material was purified by high-pressure liquid chromatography using 70% hexane–30% ethyl acetate as solvent on a 10 mm i.d. × 25 cm length prepacked silica gel column yielding 0.26 g of (95%) *threo*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexanol: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 0.016 (s, 9 H), 0.3035 (d of d, J_1= 14.4 Hz, J_2 = 10.5 Hz, 1 H), 0.6785 (d of d, J_1 = 14.4 Hz, J_2 = 3.2 Hz, 1 H), 0.902 (d, J = 6.5 Hz, 3 H), 1.101 (s, 3 H), 1.628 (m, 1 H).

***erythro*-2-Deuterio-3,5,5-trimethyl-5-sila-2-hexanol** (0.24 g, 91%) was prepared from *erythro*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-nitrobenzoate (0.50 g, 0.0016 mol) and lithium hydroxide (0.12 g, 0.0050 mol) by the method outlined for the preparation of *threo*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexanol: ^{1}H NMR (Ccl_3, 360 MHz) δ 0.025 (s, 9 H), 0.3685 (d of d, J_1 = 14.4 Hz, J_2 = 10.5 Hz, 1 H), 0.675 (d of d, J_1 = 14.6 Hz, J_2 = 3.2 Hz, 1 H), 0.898 (d, J = 6.8 Hz, 3 H), 1.117 (s, 3 H), 1.64 (m, 1 H).

3,5,5-Trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate (1:1 mixture of the diastereoisomers) was prepared by a modification of the Tipson procedure.[17] *p*-Bromobenzenesulfonyl chloride (0.97 g, 0.0038 mol) was dissolved in a minimal amount of freshly distilled dry pyridine at 0 °C. 3,5,5-Trimethyl-5-sila-2-hexanol (0.61 g, 0.0038 mol) was slowly added to this mixture. This solution was allowed to stir at 0 °C for approximately 30 min. It was then allowed to stand at approximately −10 °C for 2 to 3 days. The progress of the reaction could be estimated from the quantity of pyridinium chloride crystals formed in the flask. After the reaction was deemed complete, the liquid was decanted from the white solid into a separatory funnel. The crystals were washed three times with diethyl ether. The combined organic materials were neutralized by successive washings with cold 2 N sulfuric acid. The mixture was kept cold by inserting ice chips into the funnel along with the acid. When the aqueous layer used for washing was no longer basic by pH paper, the organic layer was washed with cold, saturated sodium bicarbonate. The organic layer was separated, dried over magnesium sulfate, and filtered, and the solvent was evaporated by using a rotary evaporator. The compound was purified by high-pressure liquid chromatography using a 1 cm × 25 cm stainless steel prepacked silica gel column, and 95% hexane–5% ethyl acetate as solvent yielding 1.07 g (74.3%) of 1:1 *threo/erythro*-3,5,5-trimethyl-5-sila-2-hexyl brosylate: ^{1}H NMR ($CDCl_3$ 360 MHz) on mixture of diastereomers δ −0.037, −0.020 (s, 9 H), 0.29 (m, 1 H), 0.50 (m, 1 H), 0.844, 0.865 (d, J = 4.3 Hz, 3 H), 1.191, 1.209, (d, J = 6.5 Hz, 3 H), 1.80 (m, 1 H), 4.497, 4.510 (q, J = 6.5 Hz, 1 H), 7.731 (AA'BB' m, 4 H).

2-Deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate (0.62 g, 53% yield) was prepared from 0.52 g (0.0032 mol) of 3,5,5-trimethyl-5-sila-2-hexanol (1:1 mixture of diastereoisomers) and 0.79 g (0.0031 mol) of *p*-bromobenzenesulfonyl chloride, by the method outlined for the preparation of 3,5,5-trimethyl-5-sila--hexyl brosylate: ^{1}H NMR ($CDCl_3$, 360 MHz) on mixture of diastereoisomers δ −0.047, −0.031 (s, 9 H), 0.28 (m, 1 H), 0.50 (m, 1 H), 0.828, 0.854 (d, J = 6.8 Hz, 3 H), 1.171, 1.195 (s, 3 H), 1.783 (m, 1 H), 7.717 (AA'BB' m, 4 H).

1,1,1,3-Tetradeuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate (0.21 g, 61% yield) was prepared from 0.15 g (0.00091 mol) of 1,1,1,3-tetradeuterio-3,5,5-trimethyl-5-sila-2-hexanol (1:1 mixture of diastereoisomers) and 0.26 g (0.0010 mol) of *p*-bromobenzenesulfonyl chloride, by the method outlined for the preparation of 3,5,5-trimethyl-5-sila-2-hexyl brosylate: ^{1}H NMR ($CDCl_3$ 360 MHz) on mixture of diastereoisomers δ −0.035, −0.019 (s, 9 H), 0.28 (m, 1 H), 0.47 (m, 1 H), 0.832, 0.858 (s, 3 H), s, 1 H), 7.726 (AA'BB' m, 4 H).

***threo*-2-Deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate** (0.60 g crude, 98%) was prepared from *threo*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexanol (0.26 g, 0.0016 mol) and *p*-bromobenzenesulfonyl chloride (0.45 g, 0.0018 mol) by the method cited for the preparation of 3,5,5-trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate with freshly distilled pyridine. The product was purified by high-pressure liquid chromatography with 90% hexane–10% ethyl acetate as solvent on a 10 mm i.d. × 25 cm length prepacked silica gel column: ^{1}H NMR ($CDCl_3$, 360 MHz) δ −0.034 (s, 9 H), 0.2665 (d of d, J_1 = 14.4 Hz, J_2 = 10.5 Hz, 1 H), 0.493 (d of d, J_1 = 14.6 Hz, J_2 = 3.8 Hz, 1 H), 0.8675 (d, J = 6.9 Hz, 3 H), 1.188 (s, 3 H), 1.807 (m, 1 H), 7.728 (AA'BB' m, 4 H).

***erythro*-2-Deuterio-3,5,5-trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate** (0.50 g cride, 88%) was prepared from *erythro*-2-deuterio-3,5,5-trimethyl-5-sila-2-hexanol (0.24 g, 0.0015 mol) and *p*-bromobenzenesulfonyl chloride (0.42 g, 0.0016 mol) by the method cited for the preparation of 3,5,5-trimethyl-5-sila-2-hexyl *p*-bromobenzenesulfonate with freshly distilled pyridine. The product was purified by high-pressure liquid chromatography with 90% hexane–10% ethyl acetate as solvent on a 10 mm i.d. × 25 cm length prepacked silica gel column: ^{1}H NMR ($CDCl_3$, 360 MHz) δ −0.019 (s, 9 H), 0.290 (d of d, J = 14.4 Hz, J_2 = 11.2 Hz, 1 H), 0.582 (d of d, J_1 = 14.4 Hz, J_2 = 2.9 Hz, 1 H), 0.840 (d, J = 6.9 Hz, 3 H), 1.203 (s, 3 H), 1.795 (m, 1 H), 7.726 (AA'BB' m, 4 H).

Conductivity Water. Deionized water was prepared by the procedure described by Murr.[18]

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Ethanol (E) was prepared by the procedure described by Murr,[18] with modifications by Buddenbaum.[19]

2,2,2-Trifluoroethanol (TFE or T) was prepared by the procedure described by Shiner et al.[20]

Ethanol-Water. These volume percent solutions were prepared by weight with densities and buoyancy corrections as described by Murr.[18]

2,2,2-Trifluoroethanol-Water. These solutions were prepared as weight percent solutions by the method described by Shiner et al.[20]

Conductance Kinetics Procedure. Conductance measurements were made by using a bipolar pulsed conductance apparatus built in this laboratory based on the design of Caserta and Enke.[21] This instrument was calibrated by comparing the experiment resistances with known fixed resistors and fitting the curve to an eight-parameter equation with the simplex method.[22] Conductivity cells used were made in this laboratory based on the design of Murr,[18] by using modifications by Dowd,[23] Tomasik,[24] and Wilgis.[25] The data were recorded by a TI 980 computer with programs developed by McMullen[26] and Tomasik.[24] The instrument was later changed to an IBM PC with use of control and data acquisition programs written by Ensinger and Russ.[27] The data were analyzed on an IBM PC with a calibration program written by Tomasik[24] and Wilgis[25] and a nonlinear, doubly weighted least-squares program written by Buddenbaum,[19] with modifications by Vogel,[28] Pinnick,[29] Bowersox and Tomasik,[30] Wilgis,[25] Stoelting,[31] and Ensinger.[32]

Product Determination. Product studies by ^2H NMR spectroscopy were performed in the following manner. A 1.0-mL sample of reaction mixture (approximately 0.1 M in deuterium) was prepared in 1.0-mL volumetric flask with a molar excess of 2,6-lutedine. This was transferred to an NMR tube, sealed, and let react for more than 10 half-lives. The ^2H spectra were recorded by using a Nicolet 360 MHz spectrometer at 55.4 MHz. The Fourier transform NMR spectra were taken by using between 500 and 2000 scans. Product ratios were determined by integration of the peaks by using a curve fitting program on the Nicolet spectrometer. Comparison of this technique with the cut and weigh technique used in the past showed good agreement.

Deuterium chemical shifts varied slightly with solvent and are as follows in 97T (relative to external $CDCl_3$ at 7.2600 ppm): 4-(trimethylsilyl)-3-methyl-2-butyl-*2-d* trifluoroethyl ether, 3.645 ppm; 4-trimethyl-3-methyl-2-butanol-*2-d*, 3.841 ppm; *cis*-1,2-dimethylcyclopropane-1-*d*, 0.876 ppm; *trans*-1,2-dimethylcyclopropane-*1-d*, 0.546 ppm; 2-methyl-1-butene-*3-d*, or 4-(trimethylsilyl)-3-methyl-2-butanol-*3-d*, 2.383 (in 90E). The stereochemistry of the substitution reaction was determined by isolation of the product alcohol from the reaction of the threo isomer in 90E and the erythro isomer in 80E. For this determination the samples prepared from deuterium NMR analysis were opened, and the solvent was removed under high vacuum. The remaining material was filtered through a silica gel filter with diethyl ether rinses and separated by using high-pressure liquid chromatography on a prepacked 10 mm i.d. × 25 cm length silica gel column with 70% hexane-30% ethyl acetate as solvent. The peak corresponding to known 3,5,5-trimethyl-5-sila-2-hexanol was collected, and the high-resolution proton NMR spectra was recorded. Comparison of these spectra with known pure threo and erythro alcohols showed complete retention of configuration.

Acknowledgment. This material is based upon work supported by the National Science Foundation under Grant Nos. CHE 85-06682 (project support) and CHE 81-05004 (NMR).

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Dimers, Trimers, and Tetramers of Cytosine with Guanine

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Abstract: Cytosine and guanine have been shown previously to form Watson-Crick type base pairs in nonaqueous solvents, suggesting that the monomers can be used to understand and possibly to predict structures of the polymeric nucleic acids. Yet, the poor solubility properties of cytosine and guanine (and their corresponding nucleosides) have limited the utility of the monomeric model of polymeric nucleic acids. The 2′-deoxynucleosides, which are substituted at both ribose hydroxyls with triisopropylsilyl groups, have high solubilities (greater than 200 mM) in nonpolar solvents such as chloroform-*d*. These substituted nucleosides are appropriate for detailed ^1H NMR study of hydrogen bonding between cytosine and guanine over a wide temperature range. In this DNA model system, cytosine and guanine form the stable Watson-Crick type dimer, as would be expected from previous studies of bases in higher dielectric solvents or at lower concentrations. We report here that the bases form such dimers and additional, more intricate hydrogen-bonded complexes. Cytosine and guanine monomers form both trimers (cytosine:guanine$_2$) and tetramers [(cytosine:guanine)$_2$] in low-dielectric solution. Thus, the interactions of monomers are consistent with formation of two-, three-, and four-stranded nucleic acid polymers.

Much of biological specificity is derived from hydrogen bonding. In nucleic acids, selective hydrogen bonds between complementary bases direct the fidelity of replication/transcription processes and also stabilize secondary and tertiary structures. Forces that stabilize double-stranded nucleic acids can be conceptually and experimentally decomposed into base-base hydrogen-bonding interactions (horizontal) and stacking interactions (vertical). The two types of interaction can be modeled by monomers in the appropriate environments. In relatively low dielectric solvents such as chloroform or even in dimethyl sulfoxide, the bases primarily form hydrogen bonds,[1-13] while in aqueous solution the bases

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