

**Table XI.** Kinetic Isotope Effect for Charge-Transfer Nitration<sup>a</sup>

| time,<br>min | conv,<br>% | ratio of molecular ions ( <i>m/z</i> ) |                     |                      | NA/NP <sup>b</sup> |
|--------------|------------|--|---------------------|----------------------|--------------------|
|              |            | 122/124                                | 167/168             | 153/154              |                    |
| 0            | 0          | 97/100                                 |                     |                      |                    |
| 10           | 4          | 82/100                                 | 67/68               | 97/100               | 1.32               |
| 25           | 10         | 93/100                                 | 57/54               | 96/100               | 1.27               |
| 55           | 20         | 93/100                                 | 58/61               | 90/100               | 1.50               |
| 145          | 41         | 100/71                                 | 58/58               | 100/96               | 1.56               |
|              |            | $\Phi_{MA}^c = 0.94$                   | $\Phi_{NA}^d = 1.0$ | $\Phi_{NP}^e = 0.97$ |                    |

<sup>a</sup> From CT irradiation of a solution of 0.05 M 4-methylanisole and 0.05 M 4-methylanisole-2,6-*d*<sub>2</sub> in 5 mL of acetonitrile containing 0.83 M TNM at  $\lambda > 480$  nm. <sup>b</sup> NA = 4-methyl-2-nitroanisole; NP = 4-methyl-2-nitrophenol. <sup>c</sup> Average kinetic isotope effect for the disappearance of 4-methylanisole, excluding entries 2 and 5. <sup>d</sup> Average kinetic isotope effect for nitroanisole. <sup>e</sup> Average kinetic isotope effect for nitrophenol, excluding entry 3.

[abundance of *m/z* = 124 after photolysis]. The relative amounts of the products formed were also determined by GC-MS analysis using peaks *m/z* = 167 and 168 for 4-methyl-2-nitroanisole (NA) and 4-methyl-2-nitroanisole-6-*d*<sub>1</sub> (NA-*d*<sub>1</sub>), respectively, i.e.,  $\Phi_{NA} = [\text{abundance of } m/z = 167]/[\text{abundance of } m/z = 168]$ , and using peaks *m/z* = 153 and 154 for 4-methyl-2-nitrophenol (NP) and 4-methyl-2-nitrophenol-6-*d*<sub>1</sub> (NP-*d*<sub>1</sub>), respectively, i.e.,  $\Phi_{NP} = [\text{abundance of } m/z = 153]/[\text{abundance of } m/z = 154]$ . The results obtained at various conversions are included in Table XI.

**Spectral Evidence for Olefinic Intermediates in the CT Alkylation of Anisoles.** A solution containing 0.06 M *p*-methylanisole and 0.28 M TNM in hexane (3 mL) was irradiated at 0 °C for 2 h with  $\lambda > 425$  nm. The solvent and excess TNM were removed in vacuo at 0 °C, and the crude reaction mixture was dissolved in CDCl<sub>3</sub>. The <sup>1</sup>H NMR spectrum

of this solution contained the characteristic resonances of the unreacted starting material and 4-methyl-2-(trinitromethyl)anisole (vide supra). In addition, the <sup>1</sup>H NMR spectrum showed olefinic resonances as a multiplet occurring between 5 and 6.5 ppm and new methoxy and methyl resonances at 3.63 and 1.91 ppm, respectively. The integration of the methoxy and methyl resonances indicated the ratio of the olefinic intermediate to the alkylation product to be ~1:2.5. Attempts to isolate the olefinic intermediate were unsuccessful, since it decomposed at room temperature to give 4-methyl-2-(trinitromethyl)anisole. In the case of the 4-haloanisoles, the irradiation of the complexes in dichloromethane at 0 °C for a short duration was followed immediately by the <sup>1</sup>H NMR spectral analysis of the crude product. It indicated the presence of olefinic resonances and the corresponding methoxy and methyl resonances as minor components of the crude reaction mixture. Upon allowing the solutions to stand at room temperature, the olefinic resonances gradually disappeared and were replaced with those of the 4-halo-2-(trinitromethyl)anisoles. These unstable olefinic components could be the TNM adducts to the anisoles similar to the 1:1 adducts previously isolated with anthracene donors.<sup>36</sup>

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**Registry No.** D<sub>2</sub>, 7782-39-0; anisole, 100-66-3; 2-methylanisole, 578-58-5; 3-methylanisole, 100-84-5; 4-methylanisole, 104-93-8; 4-fluoroanisole, 459-60-9; 4-chloroanisole, 623-12-1; 4-bromoanisole, 104-92-7; 4-(trinitromethyl)anisole, 110175-17-2; 3-methyl-4-(trinitromethyl)anisole, 110175-18-3; 4-fluoro-2-(trinitromethyl)anisole, 110175-19-4; 4-chloro-2-(trinitromethyl)anisole, 110175-20-7; 4-bromo-2-(trinitromethyl)anisole, 110175-21-8; 4-methyl-2-(trinitromethyl)anisole, 108088-84-2.

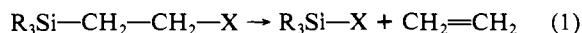
## Stabilization of Positive Charge by $\beta$ Silicon

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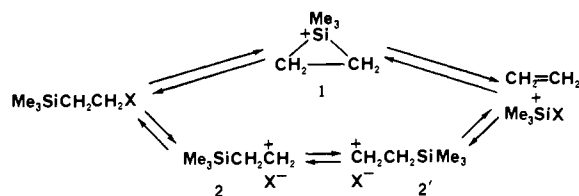
**Abstract:** The largest acceleration by a trimethylsilyl group in the formation of  $\beta$  positive charge has been measured in *r*-4-*tert*-butyl-*c*-2-(trimethylsilyl)cyclohex-*t*-yl (**6**). As the trifluoroacetate, this molecule reacts 10<sup>12</sup> times faster than cyclohexyl trifluoroacetate at 25 °C in 97% aqueous trifluoroethanol. Measurements for **6** were carried out on the 3,5-dinitrobenzoate, and the leaving group ratio was obtained from the closely related *cis*-2-(trimethylsilyl)cyclohexyl (**3**), for which the rates of both trifluoroacetate and 3,5-dinitrobenzoate could be measured. The trifluoroacetate of **3**, with a 60° disposition between the trimethylsilyl and leaving groups, reacted 7.2 × 10<sup>7</sup> more slowly than **6** with its 180° disposition of the analogous groups, but still 10<sup>4</sup> times faster than cyclohexyl. The rate ratios of both **3** and **6** were resolved into contributions from hyperconjugation and induction by analogy with the mathematics of  $\beta$  secondary deuterium isotope effects. In this way, it was determined that the antiperiplanar trimethylsilyl group causes an acceleration of 10<sup>10</sup> from the hyperconjugative interaction and 10<sup>2</sup> from induction, and the skew geometry causes an acceleration of about 10<sup>2</sup> from hyperconjugation and 10<sup>2</sup> from induction.

Extrusion of the elements of R<sub>3</sub>Si-X from a two-carbon fragment, in which X is a nucleofuge (eq 1), is a well-known and



well-studied procedure for generating a double bond.<sup>2,3</sup> The interesting role of silicon appears to parallel that of lone-pair-bearing or unsaturated substituents in anchimeric assistance. Scheme I depicts two mechanistic possibilities. In the upper

Scheme I



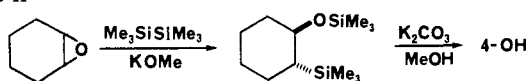
portion, silicon serves as a true internal nucleophile, engaging in nonvertical participation, to form the siliconium (pentavalent) intermediate **1**. In the lower portion, silicon provides stabilization of the  $\beta$  positive charge without nuclear movement (vertical

(1) Supported by the National Science Foundation (Grant No. CHE83-12285).

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Scheme II



stabilization) by means of hyperconjugation. In addition, because silicon is electropositive with respect to carbon, the  $\text{Me}_3\text{Si}$  group can stabilize either pathway in Scheme I via induction. Although our primary interest is the reaction of eq 1 under ionizing conditions, it has also been studied as an elimination reaction ( $\text{X} = \text{OCH}_3$ ), which may take place via a four-centered transition state.<sup>4</sup>

The most widely accepted mechanism for the reaction of eq 1 is silicon-assisted cleavage of the C-X bond. Thus the Winstein-Grunwald  $m$  value in ethanol-water is 1.02, characteristic of a reaction that is roughly as ionic as the solvolysis of *tert*-butyl chloride.<sup>5</sup> From product analysis of the solvolysis of *erythro*-(1,2-dibromopropyl)trimethylsilane, Jarvie, Holt, and Thompson showed that the reaction prefers the antiperiplanar arrangement of the Si-C-C-X atoms.<sup>6</sup> This observation is consistent with either mechanism of Scheme I, since both anchimeric assistance and hyperconjugation are optimal in the antiperiplanar geometry. The observation of scrambling in recovered, deuterium-labeled starting material,  $\text{Me}_3\text{SiCH}_2\text{CD}_2\text{Br}$  in methanol-water, indicates reversibility of the first step but is consistent with either mechanism of Scheme I; the siliconium ion **1** requires scrambling of deuterium between the two positions, as does rapid equilibration of ions **2** and **2'** via a 1,2-shift of silicon.<sup>7</sup> The  $\alpha$  deuterium isotope effect in the same substrate is consistent with C-X cleavage in the rate-determining step.<sup>8</sup> Hammett analysis of substrates of the form  $\text{ArMe}_2\text{SiCH}_2\text{CH}_2\text{Cl}$  yielded negative  $\rho$  values,<sup>5,9</sup> consistent with the buildup of some positive charge on silicon.

Charge buildup may be achieved by either vertical or nonvertical interactions (Scheme I). Most authors currently favor vertical stabilization, as depicted in the lower part of Scheme I. Traylor and co-workers<sup>10</sup> found good evidence for hyperconjugation by the  $\text{Me}_3\text{SiC}$  unit, and Davis and Jacocks<sup>11</sup> found that two  $\text{Me}_3\text{Si}$  groups provide an additive effect, not expected for nonvertical participation. As Jarvie et al. pointed out, there has been no estimation of the extent of the inductive contribution to the mechanism.<sup>6</sup> Moreover, the full kinetic acceleration has not been measured, since previous studies were carried out on open-chain systems and in solvents with relative high nucleophilicity. Indeed, Vencel et al.<sup>9</sup> found that the Hammett  $\rho$  value decreases in solvents of increased nucleophilicity, suggesting a larger contribution from a  $k_s$ -type mechanism. By calculation, Jorgensen and co-workers<sup>12</sup> found that stabilization in the gas phase of positive charge on carbon by a  $\beta$ -silyl group is 38 kcal/mol, of which about 9 kcal/mol is from the inductive effect and the remainder from hyperconjugation.

We have reported preliminary data on separation of the inductive and participative contributions.<sup>13</sup> By using systems that are fully biased conformationally, we now report the quantitative separation of the inductive and hyperconjugative portions in solution. Moreover, these systems provide the first measurement of the full kinetic acceleration caused by an antiperiplanar  $\beta$ -silyl group in the production of positive charge on carbon.

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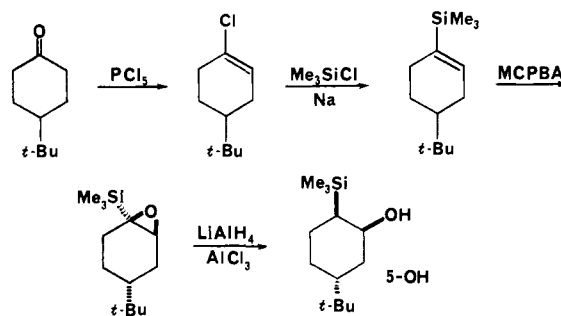
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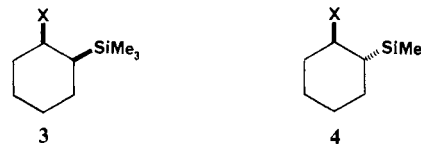
(13) Lambert, J. B.; Finzel, R. B. *J. Am. Chem. Soc.* **1982**, *104*, 2020-2022.

Scheme III



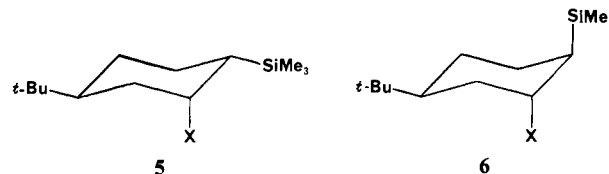
## Results

**Synthesis.** Preliminary measurements were carried out on esters of the *cis*- and *trans*-2-(trimethylsilyl)cyclohexanols (**3** and **4**,  $\text{X} = \text{OH}$ ).<sup>13</sup> These could provide  $60^\circ$  and  $180^\circ$  dihedral angles



between  $\text{Me}_3\text{Si}$  and  $\text{X}$ , respectively. Molecule **3** provided the first example of the *gauche* geometry, since all earlier work had been carried out on open-chain systems that presumably favored anti forms. The *cis* form was prepared as described in footnote 13 of ref 13. The initial preparation<sup>13</sup> of the *trans* form had been completed only one time and in very low yield. Consequently, we required a new synthesis of **4**, which is given in Scheme II. Ring opening of cyclohexene oxide with (trimethylsilyl)potassium gave a 5/1 *trans/cis* mixture of the indicated siloxysilane. Subsequent treatment with potassium carbonate produced pure *trans* alcohol, **4-OH**, after recrystallization. This two-step procedure, based on the work of Dervan and Shippey,<sup>14</sup> uses 2 equiv of hexamethylsilane to protect the initially formed oxyanion from decomposing to alkene.

Compound **3** can exist in two conformations, both with a dihedral angle of about  $60^\circ$ . In order to obtain data on a system with a known conformation, we prepared *trans*-5-*tert*-butyl-*trans*-2-(trimethylsilyl)cyclohexan-*trans*-*ol* (**5**,  $\text{X} = \text{OH}$ ) by the procedure of

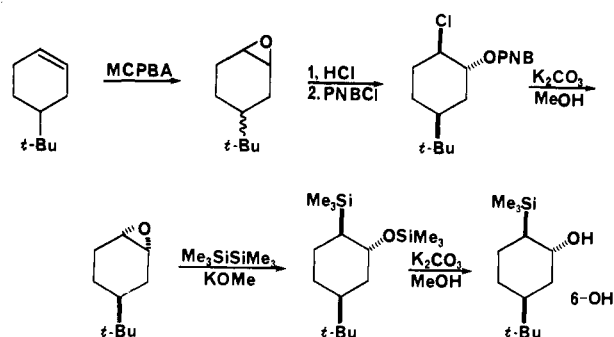


Scheme III. This compound has the leaving group constrained to the axial position. Epoxidation of 4-*tert*-butyl-1-(trimethylsilyl)cyclohexane gave a mixture of diastereomers, of which the major component had the desired *trans* relationship between the epoxide and the *tert*-butyl group. Ring opening with lithium aluminum hydride in a 1/1 mixture with aluminum trichloride gave predominantly the desired product. In the absence of aluminum trichloride, the major mode of hydride attack was at the undesired 2-position, to give 4-*tert*-butyl-1-(trimethylsilyl)cyclohexan-1-ol. The advantage of the mixed-hydride formulation had been discovered by Paquette and co-workers.<sup>15</sup> The stereochemistry follows from the mode of preparation, from the shorter retention time of **5** in comparison with the minor isomer (formed by *cis* epoxidation, followed by hydride ring opening to the isomer with hydroxyl equatorial), and the <sup>13</sup>C position of the carbon  $\alpha$  to hydroxyl. As found for the 3-*tert*-butylcyclohexanols, the carbinol resonance of **5** ( $\delta$  69.0) was upfield from that of the minor

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Scheme IV



isomer with hydroxyl equatorial ( $\delta$  74.6).<sup>16</sup>

Similarly, compound **4** exists as a mixture of diaxial and diequatorial conformations. The desired diaxial form may be obtained by use of the *tert*-butyl biasing group in *r*-4-*tert*-butyl-*c*-2-(trimethylsilyl)cyclohexan-*t*-ol (**6**, X = OH). This material, with a frozen dihedral angle of about 180° between Me<sub>3</sub>Si and X, has the optimal geometry for either vertical or nonvertical stabilization. This material was prepared by the method of Scheme IV. Separation of the isomers of the epoxide could not be carried out effectively, so the method of Rickborn and Quartucci was used.<sup>17</sup> The epoxide ring was opened with HCl, and the resulting chloro alcohols were treated with *p*-nitrobenzoyl chloride to give the chloro esters, the isomers of which could be separated. Re-formation of the epoxide ring followed by cleavage with (trimethylsilyl)potassium and hydrolysis gave the desired isomer. The chemical shift for the proton  $\alpha$  to OH was  $\delta$  4.20, consonant with an equatorial proton (axial OH). For comparison, the methine protons in the 3-*tert*-butylcyclohexanols were observed at  $\delta$  4.17 for the trans isomer (axial OH, as here) and at  $\delta$  3.43 for the cis isomer (equatorial OH).<sup>18</sup> The carbinol carbon resonated at  $\delta$  68.8 for **6** and at  $\delta$  69.0 for **5**, in good agreement since both alcohols have axial hydroxyls.

**Kinetics.** Our first choice of leaving group was tosylate, but these materials decomposed rapidly on formation. The *p*-nitrobenzoates of **3** and **4**, on the other hand, were unreactive. We finally settled on the trifluoroacetates, which have a reactivity that is intermediate between tosylate and *p*-nitrobenzoate. Unlike halogens, the trifluoroacetate group can replace hydroxyl stereospecifically. All rates were measured conductometrically. The rates of the cis trifluoroacetates (**3** and **5**, X = O(CO)CF<sub>3</sub>) were measured in nonnucleophilic trifluoroethanol (TFE) in order to minimize solvent interactions. For the unbiased 3-O(CO)CF<sub>3</sub>, rates were measured in 60, 80, and 97% TFE and were found to be relatively insensitive to these solvent changes. For 97% TFE, rates were measured at three temperatures (40–60 °C) in order to permit a modest extrapolation to 25 °C, the temperature at which all rates are being compared. These rates are listed in Table I. The rate of the biased 5-O(CO)CF<sub>3</sub> was measured only in 90% TFE at two temperatures, with extrapolation to 25 °C (Table I).

The initially reported<sup>13</sup> rate at 25 °C in 97% TFE for the unbiased trans compound 4-O(CO)CF<sub>3</sub> was not able to be repeated. Possibly owing to impurities, that rate proved to be much too slow. The actual rate of purified **4**, obtained by the new pathway of Scheme II and repeated by two individuals, initially was too fast to be measured with the trifluoroacetate leaving group, nor was the rate of the biased trans compound **6** ever able to be measured for the trifluoroacetate. Use of the 3,5-dinitrobenzoate group (ODNB) permitted direct measurement of the rates of both the unbiased 4-ODNB and the biased 6-ODNB for several TFE–water mixtures (Table I). Measurements at two temperatures permitted the short extrapolation to 25 °C. In order to place the unbiased cis and trans compounds on a common basis, however, the rate ratio for the trifluoroacetate and 3,5-dinitrobenzoate

Table I. Rate Measurements in Aqueous Trifluoroethanol

| system                  | leaving group           | % TFE                | temp, °C           | corr coeff        | $k$ , s <sup>-1</sup>   |                          |                         |
|-------------------------|-------------------------|----------------------|--------------------|-------------------|-------------------------|--------------------------|-------------------------|
| cyclohexyl              | O(CO)CF <sub>3</sub>    | 60                   | 99.9               | 0.99994           | 8.36 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 90.2               | 0.99995           | 6.82 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 1.23 × 10 <sup>-5</sup> |                          |                         |
|                         |                         | 70                   | 99.8               | 0.99987           | 4.23 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 90.2               | 0.9996            | 3.07 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 2.02 × 10 <sup>-6</sup> |                          |                         |
|                         | 3 (cis)                 | O(CO)CF <sub>3</sub> | 80                 | 99.8              | 0.9997                  | 2.55 × 10 <sup>-5</sup>  |                         |
|                         |                         |                      |                    | 90.2              | 0.99994                 | 1.21 × 10 <sup>-5</sup>  |                         |
|                         |                         |                      |                    | 25.0 <sup>a</sup> |                         | 2.15 × 10 <sup>-8</sup>  |                         |
|                         |                         | ODNB                 | 97                 | 25.0 <sup>a</sup> |                         | 7.05 × 10 <sup>-10</sup> |                         |
|                         |                         |                      |                    | 60                | 49.6                    | 0.9999                   | 3.40 × 10 <sup>-4</sup> |
|                         |                         |                      |                    | 80                | 49.6                    | 0.9999                   | 3.01 × 10 <sup>-4</sup> |
| 5 ( <i>t</i> -Bu cis)   | O(CO)CF <sub>3</sub>    | 60                   | 60.0               | 0.999             | 6.66 × 10 <sup>-4</sup> |                          |                         |
|                         |                         |                      | 50.0 <sup>b</sup>  |                   | 2.43 × 10 <sup>-4</sup> |                          |                         |
|                         |                         |                      | 49.6 <sup>b</sup>  | 0.9988            | 2.42 × 10 <sup>-4</sup> |                          |                         |
|                         |                         | 70                   | 40.5               | 0.999             | 1.16 × 10 <sup>-4</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 2.36 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 2.98 × 10 <sup>-8</sup> |                          |                         |
|                         | ODNB                    | 65                   | 90.0               | 0.998             | 3.00 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 80.0               | 0.994             | 1.14 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 1.75 × 10 <sup>-8</sup> |                          |                         |
|                         |                         | 70                   | 90.0               | 0.994             | 1.43 × 10 <sup>-5</sup> |                          |                         |
|                         |                         |                      | 80.0               | 0.996             | 5.38 × 10 <sup>-6</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 7.70 × 10 <sup>-9</sup> |                          |                         |
| 4 (trans)               | O(CO)CF <sub>3</sub>    | 90                   | 90.0               | 0.98              | 8.33 × 10 <sup>-4</sup> |                          |                         |
|                         |                         |                      | 80.0               | 0.996             | 2.97 × 10 <sup>-6</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 2.97 × 10 <sup>-9</sup> |                          |                         |
|                         |                         | ODNB                 | 97                 | 25.0 <sup>a</sup> |                         | 9.77 × 10 <sup>-11</sup> |                         |
|                         |                         |                      |                    | 43.8              | 0.9988                  | 1.98 × 10 <sup>-4</sup>  |                         |
|                         |                         |                      |                    | 35.0              | 0.9995                  | 1.78 × 10 <sup>-4</sup>  |                         |
|                         | 6 ( <i>t</i> -Bu trans) | O(CO)CF <sub>3</sub> | 97                 | 25.0              | 0.9998                  | 2.84 × 10 <sup>-5</sup>  |                         |
|                         |                         |                      |                    | 25.0              | 0.9994                  | 1.22 × 10 <sup>-4</sup>  |                         |
|                         |                         |                      |                    | 25.0              | <i>c</i>                | 1.13 × 10 <sup>-4</sup>  |                         |
|                         |                         | ODNB                 | 97                 | 25.0              | 0.996                   | 1.09 × 10 <sup>-4</sup>  |                         |
|                         |                         |                      |                    | 25.0              | 0.996                   | 9.25 × 10 <sup>-5</sup>  |                         |
|                         |                         |                      |                    | 25.0              | 0.993                   | 8.26 × 10 <sup>-5</sup>  |                         |
| 6 ( <i>t</i> -Bu trans) | O(CO)CF <sub>3</sub>    | 97                   | 50.0               | <i>c</i>          | 4.63 × 10 <sup>-3</sup> |                          |                         |
|                         |                         |                      | 40.0               | <i>c</i>          | 5.43 × 10 <sup>-4</sup> |                          |                         |
|                         |                         |                      | 25.0 <sup>a</sup>  |                   | 1.67 × 10 <sup>-5</sup> |                          |                         |
|                         | ODNB                    | 97                   | 25.0 <sup>d</sup>  |                   | 4.0 × 10 <sup>0</sup>   |                          |                         |
|                         |                         |                      | -24.0 <sup>e</sup> | 0.998             | 1.54 × 10 <sup>-3</sup> |                          |                         |
|                         |                         |                      | -21.0 <sup>f</sup> | 0.997             | 2.39 × 10 <sup>-3</sup> |                          |                         |
| 6 ( <i>t</i> -Bu trans) | ODNB                    | 97                   | 25.0 <sup>g</sup>  |                   | 6.7 × 10 <sup>-1</sup>  |                          |                         |
|                         |                         |                      | 40.0               | <i>c</i>          | 1.81 × 10 <sup>-2</sup> |                          |                         |
|                         |                         |                      | 35.0               | <i>c</i>          | 1.15 × 10 <sup>-2</sup> |                          |                         |
|                         | O(CO)CF <sub>3</sub>    | 97                   | 25.0 <sup>a</sup>  |                   | 7.1 × 10 <sup>-3</sup>  |                          |                         |
|                         |                         |                      | 25.0 <sup>d</sup>  |                   | 1.7 × 10 <sup>3</sup>   |                          |                         |

<sup>a</sup>Extrapolated from the higher temperatures. <sup>b</sup>Measured by two different individuals. <sup>c</sup>Average of three or four runs. <sup>d</sup>Calculated from the O(CO)CF<sub>3</sub>/ODNB ratio of 2.42 × 10<sup>5</sup>. <sup>e</sup>Temperature from a dry ice/diethyl sulfate bath. <sup>f</sup>Temperature from a dry ice/carbon tetrachloride bath. <sup>g</sup>Calculated directly from the measurements on the trifluoroacetate at -21 and -24 °C.

leaving groups was needed. The rate of the unbiased cis compound, **3**, therefore was measured for both leaving groups, and the trifluoroacetate/dinitrobenzoate ratio in 97% TFE was found to be 2.42 × 10<sup>5</sup>, in good agreement with a value of 4.6 × 10<sup>5</sup> reported for trifluoroacetate/*p*-nitrobenzoate.<sup>19</sup> Table II summarizes these rate measurements in terms of rate ratios based on trifluoroacetates in 97% TFE at 25 °C. It is seen that the conformationally frozen trans compound 6-O(CO)CF<sub>3</sub> is a phenomenal 12 orders of magnitude faster than cyclohexyl trifluoroacetate, which was chosen as the point of comparison for a system lacking the C–Si bond entirely. The rates for the trans trifluoroacetates calculated from the trifluoroacetate/dinitrobenzoate ratio for the cis compounds indicate extremely short half-lives. For example, the calculated rate for 4-O(CO)CF<sub>3</sub> of 4.0 s<sup>-1</sup> corresponds to a half-life of only 0.17 s at 25 °C.

(16) Buchanan, G. W.; Stothers, J. B. *Can. J. Chem.* **1969**, *47*, 3605–3610.

(17) Rickborn, B.; Quartucci, J. *J. Org. Chem.* **1964**, *29*, 2476–2477.

(18) Pasto, D. J.; Gontarz, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 6902–6908.

(19) Noyce, D. S.; Virgilio, J. A. *J. Org. Chem.* **1972**, *37*, 2643–2647.

Table II. Rate Ratios for Trifluoroacetates in 97% Trifluoroethanol at 25 °C

| system                             | $k_{rel}$                         | $k_{rel}$         |
|------------------------------------|-----------------------------------|-------------------|
| cyclohexyl                         | 1                                 |                   |
| 3 (cis)                            | $3.3 \times 10^4$                 | 1                 |
| 5 <sup>a</sup> ( <i>t</i> -Bu cis) | $4.0 \times 10^4$                 | 1.2               |
| 4 (trans)                          | $5.7 \times 10^9$ <sup>b</sup>    | $1.7 \times 10^5$ |
|                                    | $9.5 \times 10^8$ <sup>c</sup>    | $2.8 \times 10^4$ |
| 6 ( <i>t</i> -Bu trans)            | $2.4 \times 10^{12}$ <sup>b</sup> | $7.2 \times 10^7$ |

<sup>a</sup> Measured in 90% TFE. <sup>b</sup> Measured as the 3,5-dinitrobenzoate and converted to the trifluoroacetate. <sup>c</sup> Measured at low temperatures as the trifluoroacetate

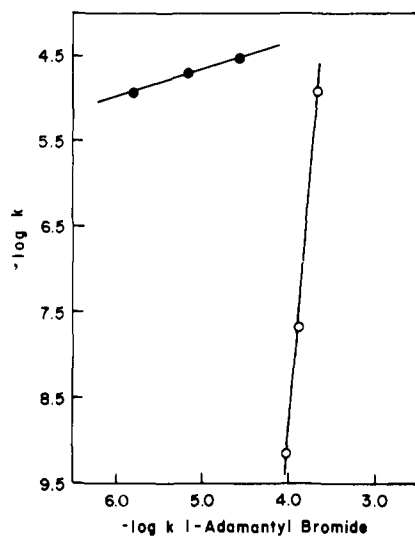


Figure 1. Raber-Harris plot for cyclohexyl trifluoroacetate.

Concern over unknown drawbacks of relying on the leaving group ratio prompted us to look into faster kinetic methods and low-temperature methods, so that the rate of the unbiased trans compound, 4-O(CO)CF<sub>3</sub>, could be measured directly in 97% TFE. We were successful in obtaining the rate of this trans compound at -21.0 and -24.0 °C (Table I), and the rate was then calculated from these values for 25 °C ( $6.7 \times 10^{-1} \text{ s}^{-1}$ ). This value is a factor of 6 smaller than that ( $4.0 \text{ s}^{-1}$ ) obtained from the dinitrobenzoate. Since both values involve extrapolations, we consider that this agreement is excellent. It also confirms that the trifluoroacetate/dinitrobenzoate rate conversion is reasonably accurate, so that the rate calculated for the biased trans system 6-O(CO)CF<sub>3</sub> is reliable.

Rate measurements at multiple temperatures provided data for the calculation of activation parameters, which are given in Table IV.

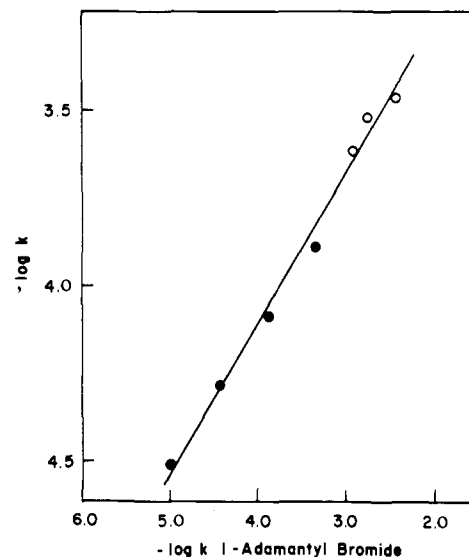
**Molecularity.** Use of mixed solvents according to the method of Raber and Harris<sup>20</sup> provides a convenient test for the molecularity of the reaction. This procedure takes advantage of the fact that trifluoroethanol does not change ionizing power appreciably when mixed with variable amounts of water, whereas ethanol does not change nucleophilicity appreciably when mixed with variable amounts of water. For a unimolecular reaction, a log-log plot of the rate of a substrate vs that of 1-adamantyl bromide (a model for a unimolecular reaction) gives a single line for both solvent mixtures, since solvent nucleophilicity is not important for the reaction plotted on both axes. For a bimolecular reaction, however, two distinct lines are obtained for the ethanol and trifluoroethanol mixtures, since solvent nucleophilicity becomes an important factor.

Table I contains the kinetic data required for aqueous trifluoroethanol, and Table III contains the additional kinetic data

Table III. Rate Measurements in Aqueous Ethanol

| system     | leaving group        | % ethanol | temp, °C        | corr coeff | $k, \text{ s}^{-1}$   |
|------------|----------------------|-----------|-----------------|------------|-----------------------|
| cyclohexyl | O(CO)CF <sub>3</sub> | 50        | 90 <sup>a</sup> | 0.99992    | $3.47 \times 10^{-4}$ |
|            |                      |           | 70 <sup>a</sup> | 0.9998     | $1.80 \times 10^{-4}$ |
|            |                      |           | 25 <sup>b</sup> |            | $2.98 \times 10^{-5}$ |
|            |                      |           | 60              | 0.9999     | $2.42 \times 10^{-4}$ |
|            |                      |           | 70 <sup>a</sup> | 0.9998     | $1.26 \times 10^{-4}$ |
|            |                      |           | 25 <sup>b</sup> |            | $2.01 \times 10^{-5}$ |
|            |                      | 70        | 90 <sup>a</sup> | 0.9997     | $1.62 \times 10^{-4}$ |
|            |                      |           | 70 <sup>a</sup> | 0.997      | $7.83 \times 10^{-5}$ |
|            |                      |           | 25 <sup>b</sup> |            | $1.18 \times 10^{-5}$ |
|            |                      |           | 80              | 0.9991     | $2.28 \times 10^{-4}$ |
|            |                      |           | 90              | 0.999      | $1.67 \times 10^{-4}$ |
|            |                      |           | 84.8            | 0.9997     | $1.22 \times 10^{-4}$ |
| 3 (cis)    | O(CO)CF <sub>3</sub> | 50        | 49.6            | 0.9999     | $1.30 \times 10^{-4}$ |
|            |                      |           | 60              | 0.9999     | $8.02 \times 10^{-5}$ |
|            |                      |           | 70              | 0.9999     | $5.20 \times 10^{-5}$ |
|            |                      |           | 80              | 0.999      | $3.33 \times 10^{-4}$ |
|            |                      |           | 60              | 0.9991     | $1.67 \times 10^{-4}$ |
|            |                      |           | 55              | 0.999      | $1.02 \times 10^{-4}$ |
|            |                      | 60        | 49.6            | 0.99991    | $3.14 \times 10^{-5}$ |
|            |                      |           | 45              | 0.999      | $2.83 \times 10^{-5}$ |
|            |                      |           | 50              | 0.9996     | $3.44 \times 10^{-4}$ |
|            |                      |           | 40              | 0.9993     | $1.36 \times 10^{-4}$ |
|            |                      |           | 25 <sup>b</sup> |            | $2.99 \times 10^{-5}$ |
|            |                      |           | 60              | 0.998      | $2.21 \times 10^{-4}$ |
| 4 (trans)  | 3,5-DNB              | 50        | 50              | 0.9996     | $3.44 \times 10^{-4}$ |
|            |                      |           | 40              | 0.9993     | $1.36 \times 10^{-4}$ |
|            |                      |           | 25 <sup>b</sup> |            | $2.99 \times 10^{-5}$ |
|            |                      |           | 60              | 0.998      | $2.21 \times 10^{-4}$ |
|            |                      |           | 40              | 0.996      | $8.33 \times 10^{-5}$ |
|            |                      |           | 25 <sup>b</sup> |            | $1.71 \times 10^{-5}$ |
|            |                      | 70        | 55              | 0.998      | $4.00 \times 10^{-4}$ |
|            |                      |           | 45              | 0.997      | $1.30 \times 10^{-4}$ |
|            |                      |           | 25 <sup>b</sup> |            | $1.09 \times 10^{-5}$ |
|            |                      |           | 80              | 0.991      | $2.63 \times 10^{-4}$ |
|            |                      |           | 45              | 0.991      | $8.33 \times 10^{-5}$ |
|            |                      |           | 25 <sup>b</sup> |            | $6.58 \times 10^{-6}$ |

<sup>a</sup> Average of two runs. <sup>b</sup> Extrapolated from the higher temperatures.

Figure 2. Raber-Harris plot for *cis*-2-(trimethylsilyl)cyclohexyl trifluoroacetate (3-O(CO)CF<sub>3</sub>).

needed for aqueous ethanol to construct the Raber-Harris plots. The plots for cyclohexyl trifluoroacetate, *cis*-2-(trimethylsilyl)cyclohexyl trifluoroacetate (3, X = O(CO)CF<sub>3</sub>), and *trans*-2-(trimethylsilyl)cyclohexyl 3,5-dinitrobenzoate (4, X = ODNB) are given in Figures 1-3.<sup>21</sup>

**Product Studies.** Product studies were carried out in 97% trifluoroethanol and in 80% ethanol. All compounds gave only

(20) Raber, D.; Neal, W. C., Jr.; Dukes, M. D.; Harris, J. M.; Mount, D. L. *J. Am. Chem. Soc.* **1978**, *100*, 8137-8146. Harris, J. M.; Mount, D. L.; Smith, M. R.; Neal, W. C., Jr.; Dukes, M. D.; Raber, D. J. *Ibid.* **1978**, *100*, 8147-8156.

(21) There may be a systematic error in the values for the unbiased trans system 4-ODNB measured in aqueous ethanol solvent, associated with determination of the infinity point. The measured values may be somewhat too large. If so, the solid circles for Figure 3 would move downward, thereby improving the linearity of the plot.

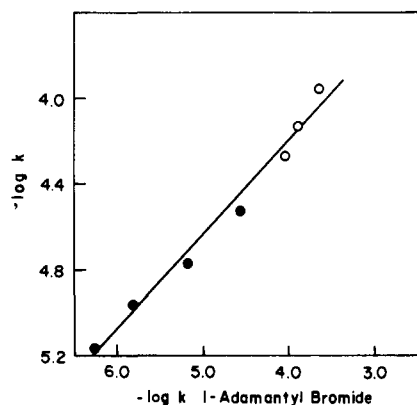


Figure 3. Raber-Harris plot for *trans*-2-(trimethylsilyl)cyclohexyl 3,5-dinitrobenzoate (4-ODNB).

Table IV. Activation Parameters in 80% Ethanol

| system           | leaving group        | no. of temperatures | $\Delta G^\ddagger$ , kcal mol <sup>-1</sup> | $\Delta H^\ddagger$ , kcal mol <sup>-1</sup> | $\Delta S^\ddagger$ , eu | corr coeff |
|------------------|----------------------|---------------------|--|--|--------------------------|------------|
| cyclohexyl       | O(CO)CF <sub>3</sub> | 4                   | 25.9   | 17.9   | -27                      | 0.998      |
| <b>3</b> (cis)   | O(CO)CF <sub>3</sub> | 4                   | 25.3   | 25.8   | 1.6                      | 0.998      |
| <b>4</b> (trans) | ODNB                 | 2                   | 23.4   | 23.1   | -1.0                     |            |

cyclohexene and cyclohexanol. The unbiased cis substrate **3** as the dinitrobenzoate gave only cyclohexene in both solvents, as did the biased trans substrate **6** as the dinitrobenzoate in 97% trifluoroethanol. The unbiased trans substrate **4** as the dinitrobenzoate gave only cyclohexene in 80% ethanol but also 2% of alcohol in 97% trifluoroethanol. The unbiased cis substrate **3** as the trifluoroacetate gave 92% cyclohexene (the remainder being alcohol) in 97% trifluoroethanol and 98% cyclohexene in 80% ethanol. Cyclohexyl trifluoroacetate gave 13% and 0.4% cyclohexene, respectively, in the two solvents, the remainder being alcohol.

## Discussion

The Raber-Harris plots demonstrate conclusively that the introduction of  $\beta$  silicon changes the solvolytic mechanism from  $k_s$  to  $k_C$ . Cyclohexyl trifluoroacetate gives a two-line plot (Figure 1) that is characteristic of a bimolecular reaction.<sup>20</sup> Both the cis (Figure 2) and the trans (Figure 3)<sup>21</sup> unbiased systems (**3**-O(CO)CF<sub>3</sub> and **4**-ODNB) give one-line plots characteristic of unimolecular reactions. The activation parameters corroborate these results (Table IV). The bimolecular reaction of cyclohexyl trifluoroacetate has a large, negative entropy of activation, whereas the two silicon-containing substrates give activation entropies close to zero. Thus in both cases (cis and trans) we may proceed with consideration of carbocation-generating mechanisms, as in Scheme I.

Given the much larger rate for the unbiased trans **4** than we previously reported<sup>13</sup> and the even larger value for the biased trans **6**, it is clear that nonvertical or vertical participation vastly outweighs induction as a mechanism for stabilization of positive charge by  $\beta$  silicon, as concluded by Jorgensen and co-workers<sup>12</sup> and contrary to our earlier conclusions.<sup>13</sup> Our experiments do not distinguish nonvertical and vertical contributions. Provided that the widely accepted hyperconjugative model (vertical stabilization) is the best description, the stereochemical dependence of the rate acceleration from the  $\beta$  C-Si bond should follow the same mathematical expression as the hydrogen-deuterium  $\beta$  secondary kinetic isotope effect, which is given by eq 2.<sup>22</sup> In this

$$\log(k_H/k_{D,\theta}) = \cos^2 \theta [\log(k_H^V/k_{D,0}^V)] + \log(k_H^I/k_b^I) \quad (2)$$

expression,  $k_H$  is the observed rate for a parent compound (no

deuterium),  $k_{D,\theta}$  is the observed rate for a deuteriated variety in which the D-C-C-X dihedral angle is  $\theta$ , V indicates the vertical contribution to the rate, and I indicates the inductive contribution to the rate. In isotope effect theory, the inductive part normally is disregarded, so that the second term on the right is set to zero.<sup>22</sup> The cosine-squared factor is multiplied by the maximum hyperconjugative contribution, as present at  $\theta = 0^\circ$ .

The isotope expression may be adapted to the present context in the form of eq 3, in which  $k_{Si,\theta}$  is for the silylated molecule,

$$\log(k_{Si,\theta}/k_H) = \cos^2 \theta [\log(k_{Si,0}^V/k_H^V)] + \log(k_{Si}^I/k_H^I) \quad (3)$$

$k_H$  is for the unsilylated model (cyclohexyl), and  $\theta$  is the Si-C-C-X dihedral angle (other symbols are analogous). If the inductive term is set equal to zero, eq 3 reduces to eq 4, in which

$$\log(k_{Si,\theta}/k_H) = \cos^2 \theta [\log(k_{Si,0}^V/k_H^V)] \quad (4)$$

the superscript V may be dropped. Division of two such expressions for different dihedral angles leads to eq 5, since the factor

$$\frac{\log(k_{Si,\theta}/k_H)}{\log(k_{Si,\theta'}/k_H)} = \frac{\cos^2 \theta}{\cos^2 \theta'} \quad (5)$$

$\log(k_{Si,0}^V/k_H^V)$  divides out. For the present case, the dihedral angle provided by the biased system **6** is about  $180^\circ$ . The dihedral angle in **3** or **5** is about  $60^\circ$ . For these angles, eq 5 leads to eq 6, from

$$\frac{\log(k_{Si,180^\circ}/k_H)}{\log(k_{Si,60^\circ}/k_H)} = \frac{\cos^2 180^\circ}{\cos^2 60^\circ} = 4.0 \quad (6)$$

which it is seen that the ratio of the logarithms of relative rates expected for the systems under study should be 4.0. The figures from Table II indicate that the observed ratio, however, is  $\log(2.4 \times 10^{12})/\log(3.3 \times 10^4) = 2.7$ , well short of the theoretical ratio of 4.0. Given the cis ratio of  $3 \times 10^4$ , the trans ratio would have to be about  $10^{18}$  in order to give the 4.0 of eq 6.

We can suggest several reasons for this discrepancy. (1) The trans molecule is deformed away from a perfect  $180^\circ$  dihedral angle. In order to obtain the observed value of 2.7 instead of 4.0, eq 5 and 6 require an angle of about  $145^\circ$  for the trans case instead of  $180^\circ$  ( $\cos^2 145^\circ/\cos^2 60^\circ = 2.7$ ). A deformation to  $145^\circ$  is entirely unreasonable. Similar large and unlikely distortions would be required for the cis system. (2) The predominant mechanism is not described by eq 3 but by some other theory, as might be the case, for example, if nonvertical stabilization were the predominant mechanism. In light of other evidence,<sup>10,11</sup> we are not willing to come to this conclusion, but it is not excluded. (3) Elimination of the inductive term in eq 3 is unjustified, so that the simplifications of eq 4-6 are incorrect.

The third explanation results in an acceptable explanation of the data. Equation 3 may be treated as an equation in two unknowns,  $\log(k_{Si,0}^V/k_H^V)$  and  $\log(k_{Si}^I/k_H^I)$ , the vertical and inductive contributions to the rate acceleration. Since two values of  $k_{Si,\theta}/k_H$  and  $\theta$  are available, the two unknowns may be obtained readily. In exponential form, the total acceleration of  $2.4 \times 10^{12}$  for the trans system may be resolved into the vertical acceleration of  $2.4 \times 10^{10}$  and the inductive acceleration of  $1.0 \times 10^2$ . The figure for vertical acceleration corresponds to the maximum value, since  $\cos^2 \theta$  is at a maximum for  $0^\circ$  (as well as for  $180^\circ$ ). If the inductive contribution is independent of dihedral angle, then the total acceleration of  $3.3 \times 10^4$  for the cis system is composed of a vertical acceleration of  $3.3 \times 10^2$  and the same induction acceleration of  $1.0 \times 10^2$ .

It should be pointed out that the rate ratios in the middle column of Table II compare the silyl systems, which react by a  $k_C$  mechanism, with cyclohexyl trifluoroacetate, which reacts by a  $k_s$  mechanism. The  $k_C$  mechanism for cyclohexyl trifluoroacetate must be slower than the observed rate. To that extent, all the rate ratios in the middle column are too small and therefore are minima.

Jorgensen and co-workers<sup>12</sup> have carried out a theoretical study on this same problem and have obtained similar results to those of our experiments. They found that a  $\beta$ -silyl group stabilizes

(22) Melander, L.; Saunders, W. H. *Reaction Rates of Isotopic Molecules*; Wiley: New York, 1980; pp 174-180. Sunko, D. E.; Szele, I.; Hehre, W. J. *J. Am. Chem. Soc.* 1977, 99, 5000-5005.

a carbocation center by a total of 38 kcal/mol, of which 8.9 kcal/mol is through induction. These figures correspond to an overall acceleration of  $10^{27}$ , of which  $10^{21}$  is hyperconjugation and  $10^6$  is induction at 25 °C. It would be expected that the process of stabilization is more effective in the gas phase, as used for the calculation. Comparison of our experimental factors with Jorgensen's theoretical factors shows that hyperconjugation has been attenuated by a factor of  $10^9$  and induction by a factor of  $10^4$  in the trans form. It is interesting that through-bond stabilization (induction) is subject to less dilution in going from the gas phase to solution than is the  $\pi$  component (hyperconjugation).

Our original report on the unbiased system<sup>13</sup> underestimated the hyperconjugative contribution because of the incorrectly measured rate of the unbiased trans compound **4**. It is now clear that hyperconjugation provides the vast majority of stabilization of positive charge by a  $\beta$  silicon in the antiperiplanar case ( $10^{10}$ ) and that induction provides a smaller but significant contribution ( $10^2$ ). The unusually large rate reported earlier<sup>13</sup> for the unbiased cis compound **3** has been confirmed, so that our original conclusions about the importance of the inductive effect in this system have been confirmed and quantified.

The *tert*-butyl-substituted system with the trimethylsilyl and leaving groups trans to each other (**6**) reacts some 400 times faster than the unbiased trans system lacking the *tert*-butyl group (**4**). In the cis compounds (**3** and **5**), the presence of the *tert*-butyl group has a very small effect. Thus the leaving group is probably axial in the unbiased cis system (**3**) as well as in the biased cis case (**5**). The factor of 400 for the trans systems, however, seems too large to result from a freezing out of the diaxial form for **6**, in comparison with the predominantly diequatorial **4**. A simple Winstein-Holness calculation<sup>23</sup> from the known *A* values for  $\text{Me}_2\text{Si}$  and  $\text{O}(\text{CO})\text{CF}_3$  suggests that complete biasing into the diaxial position should cause a rate increase of only 20–50. It is possible that the extremely rapid reaction of **4** means that the conditions for the Curtin-Hammett principle do not hold. Thus the interconversion of the diaxial and diequatorial forms may not be sufficiently faster than the reaction itself, so that for **4** this interconversion becomes kinetically significant.

## Summary

The rate acceleration provided by a  $\beta$ -silyl group in the formation of a carbocation has proved to be much larger than expected. At 25 °C in 97% trifluoroethanol, molecule **6** ( $\text{X} = \text{O}(\text{CO})\text{CF}_3$ ), in which trimethylsilyl is frozen into the antiperiplanar (diaxial) relationship with respect to the leaving group, reacts about  $10^{12}$  times faster than cyclohexyl trifluoroacetate. In this arrangement, hyperconjugation should be maximized. Thus trimethylsilyl is one of the most active groups for anchimeric assistance on record, and the C–Si bond may provide the largest rate acceleration yet attributed to hyperconjugation. An even larger rate ratio might be observed in a solvent with lower nucleophilicity than trifluoroethanol. Use of theory developed for isotope effect analysis permits decomposition of the overall acceleration for the trans compound **6** into a hyperconjugative factor of about  $10^{10}$  and an inductive factor of  $10^2$ . A large acceleration ( $3.3 \times 10^4$ ) was also observed for the cis system **3** ( $60^\circ$  dihedral angle), and this factor is composed of essentially equal hyperconjugative and inductive factors.<sup>24</sup>

## Experimental Section

**Tosylhydrazone of Cyclohexanone.** Cyclohexanone (Aldrich) (9.8 g, 0.10 mol) was added to a stirred solution of 20.5 g (0.11 mol) of *p*-toluenesulfonhydrazide in 24 mL of absolute ethanol. After refluxing for 3 h, the mixture was cooled to 0 °C with an ice bath, and yellow crystals precipitated. The product was then filtered and air-dried to give 24.8 g (94%) of the crude tosylhydrazone, which was purified by recrystallization from absolute ethanol (mp 152–155 °C): <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.4–1.8 (br m, 6,  $\text{CH}_2$ ), 2.0–2.4 (br m, 5, NH,  $\text{N}=\text{CCH}_2$ ),

2.40 (s, 3,  $\text{CH}_3$ ), 7.37, 7.85 (AB q, 4,  $\text{C}_6\text{H}_4$ ).

**1-(Trimethylsilyl)cyclohexene.** A solution of 26.64 g (0.10 mol) of cyclohexanone tosylhydrazone in 750 mL of tetramethylethylenediamine was cooled to –60 °C and treated under Ar with 163 mL of a 2.4 M solution (4 equiv) of butyllithium in hexane. The deep red solution was allowed to warm to room temperature and was stirred for 3 h. The solution was cooled to 0 °C, and 43.47 g (50.7 mL, 0.4 mol) of trimethylsilyl chloride was added slowly. The resulting mixture was stirred overnight, 200 mL of  $\text{H}_2\text{O}$  was then added, and the mixture was extracted with diethyl ether. The organic phase was washed with  $\text{H}_2\text{O}$ , and the combined aqueous layers were reextracted with ether. The ether portions were washed with saturated aqueous  $\text{CuSO}_4$  and saturated NaCl solutions and were dried over  $\text{MgSO}_4$ . The solvent was removed by careful distillation through a Vigreux column. Subsequent distillation of the remaining liquid yielded 9.4 g (61%) of 1-(trimethylsilyl)cyclohexene (bp 94–98 °C (75 mmHg)): IR (mull) 1617  $\text{cm}^{-1}$  ( $\text{C}=\text{C}$ ); <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  0.15 (s, 9,  $\text{SiCH}_3$ ), 1.0–2.5 (br m, 8,  $\text{CH}_2$ ), 6.05 (br s, 1,  $\text{C}=\text{CH}$ ).

**1-(Trimethylsilyl)cyclohexene Oxide.** To a cold solution (0 °C) of 4.74 g (0.022 mol) of 80% *m*-chloroperoxybenzoic acid in 750 mL of  $\text{CH}_2\text{Cl}_2$  was added 3.08 g (0.020 mol) of 1-(trimethylsilyl)cyclohexene in 25 mL of  $\text{CH}_2\text{Cl}_2$  over a 1.5-h period with the temperature kept below 5 °C. Stirring was continued overnight at 0 °C. *m*-Chloroperoxybenzoic acid was removed by filtration, and the solution was extracted with 10% aqueous NaOH and  $\text{H}_2\text{O}$ . The solution was dried ( $\text{MgSO}_4$ ) and the solvent removed by rotary evaporation to yield 2.8 g (83%) of the desired 1-(trimethylsilyl)cyclohexene oxide: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  –0.02 (s, 9,  $\text{SiCH}_3$ ), 1.0–2.1 (br s, 8,  $\text{CH}_2$ ), 2.96 (br s, 1, CH).

**cis-2-(Trimethylsilyl)cyclohexanol (3-OH).** 1-(Trimethylsilyl)cyclohexene oxide (2.55 g, 0.015 mol) in 6 mL of anhydrous diethyl ether was slowly added to a cooled suspension of 0.3 g (0.075 mol) of  $\text{LiAlH}_4$  in 25 mL of anhydrous ether while the temperature was not allowed to exceed 5 °C. The solution was stirred overnight at room temperature and was quenched with 2 mL of  $\text{H}_2\text{O}$ . The salts were filtered off and washed with hot ether. The ethereal solution was dried with  $\text{MgSO}_4$ , and the solvent was removed by rotary evaporation to yield 1.85 g (72%) of crude *cis*-2-(trimethylsilyl)cyclohexanol. Recrystallization from pentane yielded long white needles (mp 59–60 °C): <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  0.02 (s, 9,  $\text{SiCH}_3$ ), 1.1–1.9 (br m, 10,  $\text{CH}_2$ ,  $\text{SiCH}_2\text{OH}$ ), 4.13 (br s, 1, OCH); mass spectrum *m/e* 91 (13.3), 82 (37.5), 75 (100.0), 73 (35.4), 67 (57.1), 54 (12.1). Anal. Calcd for  $\text{C}_9\text{H}_{20}\text{OSi}$ : C, 62.73; H, 11.63; Si, 16.27. Found: C, 62.87; H, 11.74; Si, 16.11.

**cis-2-(Trimethylsilyl)cyclohexyl Trifluoroacetate (3-O(CO)CF<sub>3</sub>).** A solution of trifluoroacetic anhydride (Aldrich) (0.23 g, 0.15 mL, 0.0011 mol) in 1 mL of anhydrous diethyl ether was added slowly to a solution of pyridine (0.088 g, 0.9 mL, 0.0011 mol) and *cis*-2-(trimethylsilyl)cyclohexanol (3-OH, 0.172 g, 0.001 mol) in 2 mL of ether cooled to 0 °C. The resulting mixture was stirred at 0 °C for 30 min. The solid was filtered off, and the solution was washed with cold saturated aqueous  $\text{CuSO}_4$  and 10% aqueous  $\text{NaHCO}_3$  and was dried over  $\text{MgSO}_4$  in the refrigerator. The solvent was removed by rotary evaporation at about 5 °C to give the desired material as an oil: IR (mull) 1778  $\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ); <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  –0.07 (s, 9,  $\text{SiCH}_3$ ), 0.6–2.4 (br m, 9,  $\text{CH}_2$ ,  $\text{SiCH}$ ), 5.35 (br s, 1, CH).

**cis-2-(Trimethylsilyl)cyclohexyl 3,5-Dinitrobenzoate (3-ODNB).** 3,5-Dinitrobenzoyl chloride (0.56 g, 2.4 mmol) was dissolved in 5 mL of dry pyridine to form a slurry. The solution was cooled with an ice bath, and a solution of *cis*-2-(trimethylsilyl)cyclohexanol (3-OH, 0.344 g, 2 mmol) in 1 mL of dry pyridine was added to the flask dropwise. The mixture was stirred for 3 h and was then poured into 5 mL of  $\text{H}_2\text{O}$  and extracted with  $\text{CHCl}_3$  ( $3 \times 50$  mL). The extract was dried ( $\text{MgSO}_4$ ). Evaporation of the solvent produced a solid that was recrystallized from ethanol: 0.57 g, 78%; mp 104–106 °C; IR (KBr) 3100, 1716 ( $\text{C}=\text{O}$ )  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  0 (s, 9), 0.9–2.1 (m, 9), 5.5 (m, 1), 9.2–9.4 (m, 3).

**Cyclohexyl Trifluoroacetate.** A solution of trifluoroacetic anhydride (2.10 g, 0.01 mol) in 10 mL of anhydrous diethyl ether was added dropwise over a period of 1 h to a solution of pyridine (0.79 g, 0.01 mol) and cyclohexanol (1.00 g, 0.01 mol) in 10 mL of ether. The reaction mixture was maintained at 0 °C throughout the addition. After addition was complete, the solid was filtered off and the ethereal solution was washed with cold dilute HCl, saturated aqueous  $\text{CuSO}_4$ , and 10% aqueous  $\text{NaHCO}_3$ . After drying over  $\text{MgSO}_4$ , the ether was removed by rotary evaporation to give 1.17 (60%) of the trifluoroacetate as an oil: IR (mull) 1688  $\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ); <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.1–2.2 (br m, 10,  $\text{CH}_2$ ), 5.02 (br s, 1, CH).

**trans-2-(Trimethylsilyloxy)-1-(trimethylsilyl)cyclohexane.** A solution of hexamethyldisilane (4.4 g, 30 mmol) in anhydrous THF (6 mL) was added slowly to a mixture of potassium methoxide (1.06 g, 15 mmol) and 18-crown-6 (4.00 g, 15 mmol) in anhydrous THF (30 mL) cooled in an

(23) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; pp 234–239.

(24)  $\beta$ -Silyl stabilization of positive charge has recently been used to help generate aryl cations solvolitically. Himeshima, Y.; Kobayashi, H.; Sonoda, T. *J. Am. Chem. Soc.* **1985**, *107*, 5286–5288.

ice bath with stirring under  $N_2$ . The resultant mixture was stirred overnight, and cyclohexene oxide (1.51 g, 15 mmol) in THF (2 mL) was added slowly. After stirring overnight, the mixture was added to  $H_2O$  (30 mL) and extracted with diethyl ether ( $3 \times 10$  mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous  $MgSO_4$ , filtered, and concentrated by rotary evaporation. Vacuum distillation of the residue provided the product as a 5/1 trans/cis mixture (3.24 g, 13.25 mmol, 88%); bp 108 °C (23 mmHg);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.05 (s, 9), 0.08 (s, 9), 0.25–2.18 (br m, 9), 3.48 (m, 1);  $^{13}C$  NMR ( $CDCl_3$ ) (trans isomer)  $\delta$  -1.6, 1.1, 25.4, 26.6, 26.9, 35.1, 38.0, 74.5, (cis isomer)  $\delta$  -1.7, 1.1, 25.3, 26.5, 26.8, 35.0, 38.1, 73.2.

**trans-2-(Trimethylsilyl)cyclohexanol (4-OH) (Method A).** A mixture of trans-2-(trimethylsilyloxy)-1-(trimethylsilyl)cyclohexane (3.24 g, 13.3 mmol) and  $K_2CO_3$  (1.0 g) in  $CH_3OH$  (50 mL) was stirred for 2 days. The mixture was poured into  $H_2O$  (50 mL) and extracted with diethyl ether ( $4 \times 25$  mL). The combined organic layers were dried over anhydrous  $K_2CO_3$ , filtered, and concentrated by rotary evaporation. Vacuum distillation provided the pure alcohol (2.02 g, 11.7 mmol, 88%). The material crystallized on standing. Recrystallization from pentane gave the pure trans isomer: bp 50 °C (0.1 mmHg); mp 48–50 °C;  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.02 (s, 9), 0.2–2.1 (br m, 10), 3.41 (m, 1);  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  -1.7, 25.3, 26.5, 26.8, 34.9, 38.2, 73.2.

**trans-2-(Trimethylsilyl)cyclohexanol (4-OH) (Method B).** A solution of hexamethyldisilane (1.51 mL, 7.5 mmol) in anhydrous THF (4 mL) was added slowly to a mixture of potassium methoxide (0.53, 7.5 mmol) and 18-crown-6 (1.41 g, 5.3 mmol) in THF (10 mL). After the solution had stirred for 10 min, cyclohexene oxide (0.5 mL, 5 mmol) was added slowly via syringe. After stirring overnight, the reaction mixture was cooled in an ice bath, and  $H_2O$  (2 mL) was added carefully. The aqueous portion was extracted with ether ( $2 \times 5$  mL), and the combined organic layers were dried over anhydrous  $MgSO_4$ , filtered, and concentrated by rotary evaporation. Vacuum distillation of the residue provided the product: 0.48 g, 2.8 mmol, 56%; bp 75–85 °C (15 mmHg). Anal. Calcd for  $C_8H_{20}OSi$ : C, 62.72; H, 11.70; Si, 16.30. Found: C, 62.55; H, 11.58; Si, 16.08.

**trans-2-(Trimethylsilyl)cyclohexyl Trifluoroacetate (4-O(CO)CF<sub>3</sub>).** This compound was prepared by the same method as that used for the cis isomer:  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.12 (s, 9), 0.7–2.1 (br m, 9), 4.8 (m, 1); IR (mull) 1775  $cm^{-1}$  (C=O).

**trans-2-(Trimethylsilyl)cyclohexyl 3,5-Dinitrobenzoate (4-ODNB).** 3,5-Dinitrobenzoyl chloride (0.141 g, 0.6 mmol) was dissolved in 5 mL of pyridine in a round-bottomed flask. A solution of trans-2-(trimethylsilyl)cyclohexanol (0.086 g, 0.5 mmol) was added dropwise to the flask with stirring. The mixture was then stirred for an additional 3 h,  $H_2O$  (25 mL) was added, and the solution was extracted with  $CHCl_3$  ( $4 \times 25$  mL). Solvent evaporation provided a solid that was purified by recrystallization from ethanol: 0.18 g, 100%, mp 91–93 °C; IR (KBr) 1728 (C=O)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.03 (s, 9), 1.0–2.1 (br m, 9), 5.18 (br m, 1), 9.3 (m, 3).

**1-Chloro-4-tert-butylcyclohexene.** A solution of 4-tert-butylcyclohexanone (30 g, 144 mmol) in  $CHCl_3$  (100 mL) was added dropwise with stirring to  $PCl_5$  (22 g, 106 mmol), cooled in an ice bath under a drying tube. The resultant orange solution was allowed to warm to room temperature and was stirred overnight. Cold  $H_2O$  (100 mL) was carefully added and the mixture was extracted with pentane ( $6 \times 50$  mL). The combined organic layers were washed with saturated aqueous  $NaHCO_3$  (50 mL) and brine (50 mL), dried over anhydrous  $MgSO_4$ , filtered, and concentrated by rotary evaporation. Vacuum distillation of the residue provided 1-chloro-4-tert-butylcyclohexene: 19.6 g, 120 mmol, 85%; bp 47 °C (0.1 mmHg);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.77 (s, 9), 1.20–2.53 (br m, 7), 5.68 (m, 1).

**4-tert-Butyl-1-(trimethylsilyl)cyclohexene.** After the method of Nagendrappa,<sup>25</sup> Na cuttings (10.0 g, 435 mmol) were added to a solution of 1-chloro-4-tert-butylcyclohexene (9.78 g, 61 mmol) and chlorotrimethylsilane (25 mL, 270 mmol) in anhydrous diethyl ether (250 mL). Workup and vacuum distillation provided the product: 10.39 g, 49 mmol, 81%; bp 75 °C (1.3 mmHg);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.0 (s, 9), 0.8 (s, 9), 1.0–2.1 (br m, 7), 5.6 (m, 1).

**4-tert-Butyl-1-(trimethylsilyl)cyclohexene Oxide.** A solution of 83% *m*-chloroperoxybenzoic acid (34.9 g, 167 mmol) in  $CH_2Cl_2$  (500 mL) was cooled in an ice bath under  $N_2$ . 4-tert-Butyl-1-(trimethylsilyl)cyclohexene (13.9 g, 66 mmol) was added dropwise with stirring. After 12 h, the mixture was filtered and the solid was washed with  $CH_2Cl_2$  (20 mL). The organic solution was washed with saturated aqueous  $NaHCO_3$  ( $3 \times 100$  mL) and brine (100 mL) and then was dried over anhydrous  $MgSO_4$ , filtered, and concentrated by distillative removal of solvent. Vacuum distillation of the residue provided the product: 12.76 g, 56 mmol, 85%; bp 86 °C (8 mmHg);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.0 (s, 9), 0.9 (s,

9), 1.0–2.0 (br m, 7), 2.9 (s, 1). The product was a mixture of isomers with the epoxide ring cis and trans to the *tert*-butyl group.

**r-5-tert-Butyl-t-2-(trimethylsilyl)cyclohexan-t-ol (5-OH).** After the method of Paquette,<sup>15</sup> a mixture of  $LiAlH_4$  (1.0 g, 26 mmol) and  $AlCl_3$  (1.0 g, 7.5 mmol) was stirred in anhydrous ether (150 mL) under  $N_2$  in an ice bath. 4-tert-Butyl-1-(trimethylsilyl)cyclohexene oxide (5.00 g, 22 mmol) was slowly added via syringe. The resultant mixture was allowed to warm to room temperature and stir overnight. Water (2 mL), 15% aqueous  $NaOH$  (2 mL), and additional water (5 mL) were added carefully to the chilled reaction mixture. The resultant salts were filtered and washed with diethyl ether ( $2 \times 20$  mL). The combined filtrate and washings were dried over anhydrous  $MgSO_4$ , filtered, and concentrated by distillative removal of solvent to provide a crystalline material of over 90% mass balance. Gas chromatography (3% DEGS column) revealed a component accounting for 84% (uncorrected for response of the thermal conductivity detector) of the material. Preparative gas chromatography provided pure 5-OH: mp 90 °C;  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.05 (s, 9), 0.74 (s, 9), 0.70–2.4 (br m, 9), 4.12 (br s, 1);  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  -2.36 ( $CH_2Si$ ), 20.60, 21.90, 28.46, 31.49, 32.26, 41.03 ( $SiCH_2CH_2CH_2CH_2$ ), 27.32 ( $(CH_3)_3C$ ), 69.04 (CHOH).

**r-5-tert-Butyl-t-2-(trimethylsilyl)cyclohex-t-yl Trifluoroacetate (5-O(CO)CF<sub>3</sub>).** This compound was synthesized by the same method as that used for the trifluoroacetate of 3 from the corresponding alcohol (0.228 g, 1 mmol):  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.10 (s, 9), 0.75 (s, 9), 0.7–2.3 (br m, 8), 5.42 (br s, 1).

**4-tert-Butylcyclohexene.** After the method of Sicher, Sipos, and Tichý,<sup>26</sup> 4-tert-butylcyclohexanol (78.0 g, 0.50 mol) was converted to an intermediate mesylate with methanesulfonyl chloride (67 mL, 0.88 mol) in anhydrous pyridine. Thermal elimination followed by workup provided the desired alkene: 55.4 g, 0.40 mol, 80%; bp 58 °C (14 mmHg) (lit.<sup>26</sup> bp 54–55 °C (10 mmHg));  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.51 (s, 9), 0.72–1.97 (br m, 7), 5.21 (s, 2).

**4-tert-Butylcyclohexene Oxide.** A solution of 4-tert-butylcyclohexene (20.0 g, 144 mmol) in anhydrous  $CH_2Cl_2$  (40 mL) was added dropwise to a solution of 82% *m*-chloroperoxybenzoic acid (30.8 g, 159 mmol) in  $CH_2Cl_2$  (500 mL) cooled in an ice bath. After stirring for 16 h, the mixture was filtered, washed with 10% aqueous  $NaOH$  ( $4 \times 100$  mL), dried over anhydrous  $MgSO_4$ , filtered, and concentrated by rotary evaporation. The residue was vacuum distilled to provide the product as a mixture of cis and trans isomers: 19.30 g, 0.125 mol, 87%; bp 90 °C (20 mmHg) (lit.<sup>26</sup> bp 78–80 °C (9 mmHg));  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.62 (s, 9), 0.76–2.03 (br m, 7), 2.83 (m, 2).

**r-2-Chloro-c-tert-butylcyclohex-t-yl p-Nitrobenzoate.** After the method of Rickborn and Quartucci,<sup>17</sup> 4-tert-butylcyclohexene oxide (7.52 g, 49 mmol) was treated with hydrogen chloride first and then *p*-nitrobenzoyl chloride (11.0 g, 59 mmol) in  $CHCl_3$  (40 mL) to provide a mixture of chloro esters. Five crystallizations from  $CH_3OH$  provided the desired isomer: 2.16 g, 6 mmol, 13%; mp 125–126 °C (lit.<sup>17</sup> mp 124.5–126 °C);  $^1H$  NMR ( $CCl_4$ )  $\delta$  0.95 (s, 9), 1.34–2.12 (br m, 7), 4.25 (m, 1), 5.32 (m, 1), 8.27 (m, 4).

**trans-4-tert-Butylcyclohexene Oxide.** After the method of Rickborn and Quartucci,<sup>17</sup> *r*-2-chloro-*c*-tert-butylcyclohex-t-yl *p*-nitrobenzoate (2.66 g, 7.8 mmol) was treated with  $K_2CO_3$  (3.2 g) and  $H_2O$  (4 mL) in  $CH_3OH$  (40 mL) to provide the desired epoxide: 0.90 g, 5.8 mmol, 74%; bp 86–90 °C (17 mmHg);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  0.62 (s, 9), 0.76–2.03 (br m, 7), 2.83 (s, 2).

**r-5-tert-Butyl-t-1-(trimethylsilyloxy)-c-2-(trimethylsilyl)cyclohexane.** A solution of hexamethyldisilane (5.31 mL, 26 mmol) in anhydrous THF (15 mL) was added slowly and dropwise with stirring under  $N_2$  to a mixture of KOMe (1.84 g, 26 mmol) and 18-crown-6 (6.86 g, 26 mmol) in anhydrous THF (35 mL) cooled in an ice bath. After the mixture was heated to room temperature and stirred overnight, a solution of trans-4-tert-butylcyclohexene oxide (2.00 g, 13 mmol) in THF (2 mL) was added. After stirring overnight, the mixture was added slowly to  $H_2O$  (30 mL) and extracted with diethyl ether ( $4 \times 15$  mL). The combined organic layers were washed with brine (15 mL), dried over anhydrous  $MgSO_4$ , filtered, and concentrated by rotary evaporation. Vacuum distillation of the residue provided pure product as a colorless oil: (3.26 g, 10.9 mmol), 75%; bp 112 °C (23 mmHg);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.25 (s, 9), 0.25 (s, 9), 0.79 (s, 9), 0.79–2.38 (br m, 8), 3.0–3.38 (br m, 1).

**r-5-tert-Butyl-c-2-(trimethylsilyl)cyclohexan-t-ol (6-OH).** A mixture of the above compound (3.26 g, 10.9 mmol) and  $K_2CO_3$  (1.0 g) in 95% aqueous ethanol (25 mL) was stirred for 2 days. The mixture was poured into  $H_2O$  (25 mL) and extracted with diethyl ether ( $3 \times 10$  mL). The combined organic layers were dried over anhydrous  $K_2CO_3$ , filtered, and concentrated by rotary evaporation. Vacuum distillation of the residue provided pure product: 1.50 g, 6.6 mmol, 61%; bp 95–106 °C (0.1

mmHg);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.05 (s, 9), 0.74 (s, 9), 0.74-2.53 (br m, 8), 4.12 (br s, 1);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.8 ( $\text{CH}_3\text{Si}$ ), 21.8, 25.2, 32.7, 32.8, 35.3, 40.8 ( $\text{SiCH}_2\text{CH}_2\text{CH}_2$ ), 27.5 ( $(\text{CH}_3)_3\text{C}$ ), 68.8 ( $\text{CHOH}$ ).

***r*-5-*tert*-Butyl-*c*-2-(trimethylsilyl)cyclohex-*f*-yl Trifluoroacetate (6-O(CO)CF<sub>3</sub>)**. The ester was synthesized by the same method as that used for the trifluoroacetate **3** from the corresponding alcohol (6-OH, 0.228 g, 1 mmol). An elimination reaction to form 4-*tert*-butylcyclohexene occurred quickly, but the  $^1\text{H}$  NMR spectrum prior to decomposition revealed a broad signal at  $\delta$  5.36 indicative of the trifluoroacetate.

***r*-5-*tert*-Butyl-*c*-2-(trimethylsilyl)cyclohex-*f*-yl 3,5-Dinitrobenzoate (6-ODNB)**. 3,5-Dinitrobenzoyl chloride (0.282 g, 1.2 mmol) was dissolved in 5 mL of pyridine, and the solution was cooled with an ice bath. A solution of the alcohol 6-OH (0.228 g, 1.0 mmol) in 1 mL of pyridine was added dropwise with stirring. The mixture was then stirred for 4 h at 0 °C. Water (5 mL) was added and the mixture was extracted with diethyl ether (4 × 15 mL). The combined organics were dried over  $\text{MgSO}_4$  and filtered. Evaporation of the solvent gave a solid that was recrystallized from absolute ethanol: 0.22 g, 60%; mp 96-98 °C (dec);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.2 (s, 9), 1.0 (s, 9), 0.7-2.0 (m, 7), 5.65 (m, 1), 9.1-9.3 (m, 3, arom); IR (KBr) 1713  $\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ). A sample was recrystallized from hexane for elemental analysis. Anal. Calcd for  $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_6\text{Si}$ : C, 56.87; H, 7.11; N, 6.64; Si, 6.65. Found: C, 56.65; H, 7.08; N, 6.46; Si, 6.22.

**Solvents.** Ethanol was distilled from magnesium ethoxide as described by Lund and Bjerrum.<sup>27</sup> Commercial 2,2,2-trifluoroethanol was distilled from aqueous  $\text{K}_2\text{CO}_3$ , dried with  $\text{P}_2\text{O}_5$ , and fractionally distilled through

a 10-in. vacuum-jacketed column packed with glass helices, bp 73.5-74.5 °C. Ethanol mixtures are quoted in volume percentage and trifluoroethanol mixtures in weight percentage.

**Kinetic Methods.** Rates in aqueous solvents were determined conductometrically with an Industrial Instruments Model RC 16B2 conductivity bridge. The conductivity cell (Industrial Instruments) had black Pt electrodes, cell constant 0.42  $\text{cm}^{-1}$ , and a volume of approximately 35 mL. In a typical experiment, enough substrate to make a solution approximately  $10^{-3}$  M was added to the cell, which contained almost 20 mL of solvent. The cell was then stoppered and equilibrated in a constant-temperature bath (Haake Model NB22) for at least 5 min with stirring. Solvolyses were followed by taking at least 10 readings approximately equally spaced in conductance over 1-3 half-lives. The raw conductance data were then fitted to a first-order rate equation by means of a least-squares computer program. The precision of the fit to first-order kinetics was satisfactory over up to 3 half-lives in the aqueous ethanol and aqueous trifluoroethanol solvents.

**Product Studies.** A 0.2-0.5 M solution of the substrate in the desired solvent (1 mL) was prepared in a Pyrex tube (0.8 mm in diameter). The tubes were sealed and placed in a constant-temperature bath at 90 °C. The dinitrobenzoates were mostly insoluble at room temperature but totally soluble at 90 °C. After 5 days, the tubes were cooled in an ice bath and opened. A filtration was then performed to remove any solid product formed. The mixtures were then analyzed with GC-MS: 20-m column with 3% Carbowax on Chromosorb W, FID detector, gas flow 10 mL/min. Under these conditions, all the components were well separated and the product alkene and alcohol had differences in retention times as much as 6 min. Cyclohexanol is characterized by peaks at *m/e* 100, 82, 67, and 57, cyclohexene by peaks at *m/e* 82, 67, and 54, and 4-*tert*-butylcyclohexene by peaks at *m/e* 138, 82, 67, and 57.

(27) Lund, H.; Bjerrum, J. *Chem. Ber.* 1931, 64, 210-213.

## Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an *Escherichia coli* Formylmethionine tRNA<sup>1</sup>

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**Abstract:** The synthesis of silyl-protected ribonucleoside 3'-O-phosphoramidites and the preparation of the controlled-pore glass supports needed for the solid-phase chemical synthesis of oligoribonucleotides are described. These reagents were evaluated in the synthesis of a series of oligomers consisting of the pentadecameric homopolymers of adenosine, cytidine, guanosine, uridine, and various sequences of mixed-base composition. Different reactivities were observed for the morpholino- and (diisopropylamino)phosphoramidites under actual synthesis conditions, and these were attributed to the relative ease of their activation by tetrazole as determined by  $^{31}\text{P}$  NMR. A comparison of the methyl- and cyanoethyl-protected phosphoramidites indicated that, although the cyanoethyl group was easier to remove, there was no significant difference between the two in terms of the quality of the final sequence. The purity of the 3'-phosphoramidites is easily determined by NMR. A full protocol for the deprotection, handling, and purification of synthetic oligoribonucleotides is also described. The results of these studies were applied to the successful chemical synthesis of the 43-mer 5'-CAU AAC CCG AAG AUC GUC GGU UCA AAU CCG GCC CCC GCA ACC A-3', corresponding to the 3'-terminus of a formylmethionine (fMet) tRNA of *Escherichia coli*, in which the modified bases have been substituted by their unmodified parent nucleosides. The 43-mer was fully characterized by polyacrylamide gel electrophoresis, enzymatic RNA sequencing, HPLC analysis of an enzymatic digest, and terminal nucleotide analysis, both 5' and 3', using enzymatic digestion followed by two-dimensional chromatography. The effectiveness of alkylsilyl ethers for the protection of the 2'-hydroxyl of the ribose ring, when used in conjunction with the phosphoramidite method for the formation of the phosphotriester linkages in RNA synthesis, is clearly established.

Intense interest in the development of facile, rapid, and high-yield RNA synthesis strategies has been fueled by its unique and sometimes unexpected biological activities, i.e., self-splicing RNA<sup>2</sup> antisense RNA in the translational control of the expression of

genes,<sup>3</sup> the formation of lariats during the splicing of eukaryotic mRNA,<sup>4</sup> recombinant RNA technology,<sup>5</sup> and involvement of a

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(1) Preliminary results of this work were presented: Usman, N.; Ogilvie, K. K. *Abstracts of Papers*, 191st National Meeting of the American Chemical Society, New York, NY, April 13-18, 1980; American Chemical Society: Washington, DC, 1986; ORGN 334.

(2) Bass, B. L.; Cech, T. R. *Nature (London)*. 1984, 308, 820.