Organometallics **1993,** *12,* 697–703

The γ and δ Effects of Tin

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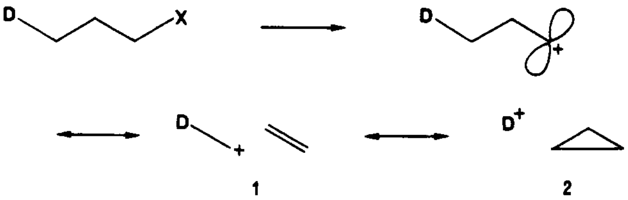
Received September 29, 1992

The trimethylstannyl group either γ (four bonds) or δ (five bonds) from a tosylate leaving group in the simple cyclohexane framework can alter the mechanism from nucleophilic assistance by solvent to intermediacy of a hyperconjugatively stabilized carbocation. The mechanistic change is indicated by rate accelerations (compared with the analogous ring lacking tin), by stereochemical dependence, by insensitivity to solvent nucleophilicity, by sensitivity to solvent ionizing power, by products resembling the hyperconjugative resonance structure, and (in the δ case) by the α-deuterium kinetic isotope effect. For the γ effect, stabilization of the carbocation occurs when tin is anti-anti to the leaving group (W geometry) and involves homohyperconjugation or cyclopropyl–(no-bond) conjugation. For the δ effect, stabilization occurs when tin is anti-gauche-anti (zigzag) to the leaving group and involves double hyperconjugation, i.e., (double-bond)–(no-bond) conjugation twice over. These results extend the concepts of delocalization of positive charge over σ bonds within the simple cyclohexane ring.

The interactions of orbitals over an intervening σ framework were first systematized by Hoffmann and coworkers almost 25 years ago.[2] The optimal situation in which to study such interactions has proved to be carbocations, because strong electron demand tends to magnify the effects. By the same token, highly polarizable and electron-donating substituents capable of receiving the positive charge also bring about enhanced effects. The best match therefore would seem to be observing the effects of strong donors such as trimethylstannyl or -silyl on carbocation production. If simple through-bond σ inductive effects were the only mechanism for transmission of information from silicon or tin to nucleofuge, effects would die off very rapidly after more than about two bonds. Over three bonds, e.g., Sn–C–C–X, very substantial effects have been observed and attributed to σ–π conjugation or hyperconjugation ($\mathrm{Sn{-}C{-}C^+ \leftrightarrow Sn^+\ C{=}C}$).[3,4] These three-bond interactions have been collectively referred to as β effects, because the perturbing substituent (Sn here) is β to the carbocation. The ability of a β-tin atom to stabilize a carbocation has been estimated from solvolysis studies to be at least 10^{15} times greater than that of hydrogen.[4] Because this is one of the largest electronic effects on record, we have used the tin atom as a probe to investigate orbital interactions over more than three bonds.

The four-bond or γ effect of substituents on carbocation formation has been studied most extensively with silicon as the donor.[3,5] In the case of tin, the first observations were made by Davis and co-workers.[6] They studied primary and secondary open-chain systems as well as secondary norbornyl systems and found accelerations up to 10^3 for tin in comparison with analogous structures containing hydrogen. Such effects were later studied by Grob and his group in adamantyl systems[6] and have found synthetic applications.[7] These γ effects have been attributed to standard hyperconjugation (**1** in Scheme I) or to percaudal ("through the tail") homohyperconjugation (represented by **2**). The relative merits of the two modes of interaction have been discussed by Adcock and Kok in the context of fluorine-19 chemical shift substituent effects.[8]

Scheme I



Initial attempts to uncover a five-bond or δ effect of silicon were negative,[9] but later investigations of a more favorable geometry led to observation of a modest acceleration.[10] Much more impressive results, however, have been obtained by the groups of Adcock and Shiner with tin as the donor.[10] These investigations examined systems with very favorable orientations between donor and leaving group that can lead to double or second sphere hyperconjugation (see **3** and **4** in Scheme II). Both the donor D and the leaving group X must be anti to the central carbon in the pathway, but the bonds around this central carbon that connect the end fragments may be anti (**3**), gauche (as in cyclohexyl below), or even syn (**4**). A large δ effect in the cubane skeleton has been attributed to a different phenomenon.[11]

Previous studies of tin-induced homohyperconjugation and double hyperconjugation (the γ and δ effects of tin,

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[1] This work was supported by the National Science Foundation, Grant No. CHE-8910841.

[2] Hoffmann, R.; Iwamura, A.; Hehre, W. J. *J. Am. Chem. Soc.* **1968,** *90,* 1499–1509.

[3] For a review of three-bond interactions of Si, see: Lambert, J. B. *Tetrahedron* **1990,** *46,* 2677–2689.

[4] For a discussion of the three-bond interactions of Sn, see: Lambert, J. B.; Wang, G.; Teramura, D. H. *J. Org. Chem.* **1988,** *53,* 5422–5428.

[5] Shiner, V. J., Jr.; Ensinger, M. W.; Rutkowske, R. D. *J. Am. Chem. Soc.* **1987,** *109,* 804–809. Grob, C. A.; Gründel, M.; Sawlewicz, P. *Helv. Chim. Acta* **1988,** *71,* 1502–1507. Bentley, T. W.; Kirmse, W.; Llewellyn, G.; Söllenböhmer, F. *J. Org. Chem.* **1990,** *55,* 1536–1540.

[6] Davis, D. D.; Black, R. H. *J. Organomet. Chem.* **1974,** *82,* C30–C34. Davis, D. D.; Johnson, H. T. *J. Am. Chem. Soc.* **1974,** *96,* 7576–7577. Fischer, W.; Grob, C. A. *Helv. Chim. Acta* **1978,** *61,* 1588–1608.

[7] Fleming, I.; Urch, C. J. *J. Organomet. Chem.* **1985,** *285,* 173–191. Plamondon, L.; Wuest, J. D. *J. Org. Chem.* **1991,** *56,* 2066–2075.

[8] Adcock, W.; Kok, G. B. *J. Org. Chem.* **1987,** *52,* 356–364.

[9] Fessenden, R. J.; Seeler, K.; Dagani, M. *J. Org. Chem.* **1966,** *31,* 2483–2487.

[10] Adcock, W.; Coope, J.; Shiner, V. J., Jr.; Trout, N. A. *J. Org. Chem.* **1990,** *55,* 1411–1412. Adcock, W.; Kristic, A. R.; Duggan, P. J.; Shiner, V. J., Jr.; Coope, J.; Ensinger, M. W. *J. Am. Chem. Soc.* **1990,** *112,* 3140–3145.

[11] Eaton, P. E.; Zhou, J. P. *J. Am. Chem. Soc.* **1992,** *114,* 3118–3120.

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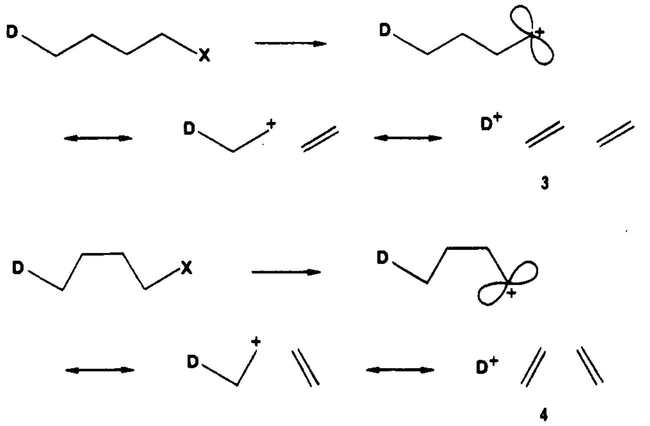
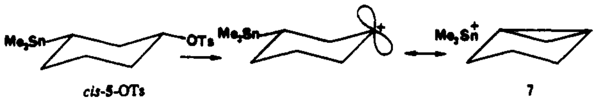
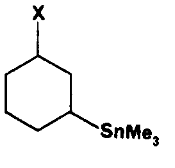
Scheme II



Scheme III



respectively) have examined either open-chain systems[6] or polycyclic systems.[10] We decided to examine these effects in the fundamental cyclohexyl geometries, as exemplified by **5** and **6**.[12] They represent an intermediate



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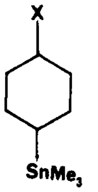


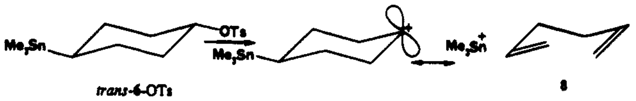
6

situation, in which the geometry is more restricted than in the open-chain systems of Davis but less restricted than in the rigid polycyclic cases of Adcock and Shiner. Moreover, the cyclohexyl system permits competition with backside nucleophilic attack by solvent, the k_s mechanism, which is prohibited for bridgehead and adamantyl geometries and is inhibited at other polycyclic positions. Thus, **5** and **6** can demonstrate whether homohyperconjugation and double hyperconjugation can compete with nucleophilic processes, a comparison not possible in the Adcock–Shiner systems. We report herein that both homohyperconjugation and double hyperconjugation are viable phenomena within the cyclohexyl framework.

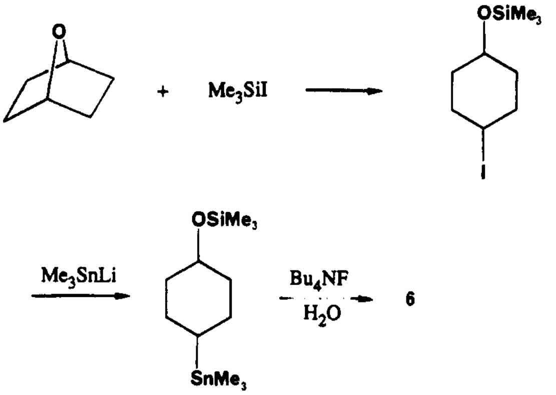
Results

Synthesis. The cis stereoisomer of the subject for the study of the γ effect of tin (**5**) has the planar W arrangement of the Sn–C–C–C–X moiety of the molecule, in which the percaudal or homohyperconjugative interaction has the optimal opportunity (**7** in Scheme III). The trans isomer offers the nonplanar sickle arrangement that prohibits the percaudal interaction. Both isomers could be obtained by selective reduction of the known 3-(trimethylstannyl)cyclohexanone.[13] Reduction with lithium aluminum hydride proceeds by axial attack of hydride to give predominantly the cis isomer.[13] Reduction with the more bulky lithium tri-*sec*-butylborohydride on the other hand proceeds by equatorial attack to give predominantly the trans isomer.[14] A similar procedure was used by Shiner et al. to obtain the analogous trans silyl substrate.[15] For purposes of obtaining reaction rates, the two alcohols were purified and converted to the tosylates or trifluoroacetates.

Scheme IV



Scheme V



The trans stereoisomer of the subject for study of the δ effect (**6**) has the anti-gauche-anti arrangement of the Sn–C–C–C–C–X moiety that permits double hyperconjugation of the type **3** (**8** in Scheme IV). The cis isomer, however, has a gauche-gauche-anti arrangement in which such overlap is not possible. The two isomers were obtained in a cis/trans ratio of about 1/2 by the procedure of Scheme V. Separation of the isomers required a sequence of sublimation and flash column chromatography. The alcohols were converted to the tosylates for kinetic measurements. In order to measure the α secondary deuterium isotope effect, the mixture of alcohols was oxidized to the ketone with chlorochromate and then reduced back to a mixture of alcohols (predominantly the desired trans isomer) with lithium aluminum deuteride.

Kinetics. Rates were measured by conductance with tosylate as the leaving group for the δ systems and for the trans γ system. The cis tosylate in the γ series (**5**) proved to be too reactive, so that the trifluoroacetate was substituted as the leaving group. Relative rates from the latter leaving group were converted to values for the tosylate with the factor 1940 measured previously.[16]

In order to obtain information on the roles of solvent nucleophilicity and ionizing power and hence on the relative contributions of carbocation (k_c) and solvent-participation (k_s) mechanisms, rates were measured in both ethanol and trifluoroethanol at several levels of water content (Tables I and II). The values for each substrate

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[12] One aspect of this work has been communicated: Lambert, J. B.; So, J.-H.; Salvador, L. A. *Tetrahedron Lett.* **1990**, *27*, 3841–3844.

[13] Kitching, W.; Olszowy, H.; Waugh, J. *J. Org. Chem.* **1978**, *43*, 898–905. Wickham, G.; Olszowy, H. A.; Kitching, W. *J. Org. Chem.* **1982**, *47*, 3788–3793.

[14] Ochiai, M.; Iwaki, S.; Ukita, T.; Matsuura, Y.; Shiro, M.; Nagao, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4606–4610.

[15] Shiner, V. J., Jr.; Ensinger, M. W.; Kriz, G. S.; Halley, K. A. *J. Org. Chem.* **1990**, *55*, 653–661.

[16] Lambert, J. B.; Wang, G.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838–7845.

Table I. Rate Measurements for the γ Effect

system[a]	solvent[b]	temp, °C	r^2 [c]	rate, s^{-1}
cis-**5**-Tfa	97% TFE	75.0	0.9995	3.10×10^{-4}
		65.0	0.9995	1.20×10^{-4}
		50.0	0.9999[d]	2.50×10^{-5}
		25.0	*e*	1.42×10^{-6} [f]
	85% TFE	75.0	0.9998	2.49×10^{-4}
	80% TFE	75.0	0.9998	2.59×10^{-4}
	70% TFE	75.0	0.9999	3.13×10^{-4}
	70% ethanol	75.0	0.9992	1.36×10^{-4}
	60% ethanol	75.0	0.9997	2.23×10^{-4}
	50% ethanol	75.0	0.9998	3.94×10^{-4}
trans-**5**-OTs	97% TFE	75.0	0.9999	2.54×10^{-3}
		50.0	0.9998	2.10×10^{-4}
		40.0	0.9999	6.82×10^{-5}
		25.0	*e*	1.12×10^{-5}
	80% TFE	50.0	0.9999	3.04×10^{-4}
	60% TFE	50.0	0.9999	5.12×10^{-4}
	80% ethanol	75.0	0.9996	6.64×10^{-4}
		50.0	0.9998	4.54×10^{-5}
		25.0	*e*	1.98×10^{-6}
	70% ethanol	50.0	0.9995	9.67×10^{-5}
	60% ethanol	50.0	0.9994	1.76×10^{-4}

[a] Tfa stands for trifluoroacetate and OTs for *p*-toluenesulfonate. [b] TFE stands for trifluoroethanol (w/w %); ethanol values are v/v %. [c] Correlation coefficient squared; mean of two runs. [d] One run. [e] Rates extrapolated from higher temperatures. [f] Extrapolated only from runs at 65.0 and 75.0 °C.

Table II. Rate Measurements for the δ Effect

system	solvent[a]	temp, °C	r^2 [b]	rate, s^{-1}
trans-**6**-OTs	97% TFE	75.0	0.9996	7.98×10^{-3}
		50.0	0.9999	8.17×10^{-4}
		25.0	*c*	5.72×10^{-5}
	80% TFE	50.0	0.9999	9.44×10^{-4}
	60% TFE	50.0	0.9999	1.33×10^{-3}
	80% ethanol	75.0	0.9998	3.62×10^{-4}
		65.0	0.9999	1.21×10^{-4}
		50.0	*c*	2.15×10^{-5}
	70% ethanol	50.0	0.9999	5.00×10^{-5}
	60% ethanol	50.0	0.9996	1.04×10^{-4}
trans-**6**-OTs-*d*	97% TFE	50.0	0.9999	6.84×10^{-4}
cis-**6**-OTs	97% TFE	75.0	0.9998	1.70×10^{-3}
		50.0	0.9999	1.44×10^{-4}
		25.0	*c*	8.08×10^{-6}
	80% TFE	50.0	0.9999	2.65×10^{-4}
	60% TFE	50.0	0.9999	5.26×10^{-4}
	80% ethanol	75.0	0.9999	7.56×10^{-4}
		65.0	0.9999	2.72×10^{-4}
		50.0	0.9999	5.28×10^{-5}
	70% ethanol	50.0	0.9999	1.07×10^{-4}
	60% ethanol	50.0	0.9999	2.04×10^{-4}
	50% ethanol	50.0	0.9999	4.04×10^{-4} [d]

[a] See footnote *b*, Table I. [b] See footnote *c*, Table I. [c] Rates extrapolated from higher temperatures. [d] One run.

were plotted versus the rates of 1-adamantyl bromide according to the procedure of Raber and Harris[17] (Figures 1–4).

Rates were collected at multiple temperatures, and activation parameters were calculated (Table III). Some of these figures were used to calculate rates and rate ratios at 25 °C (Table IV).

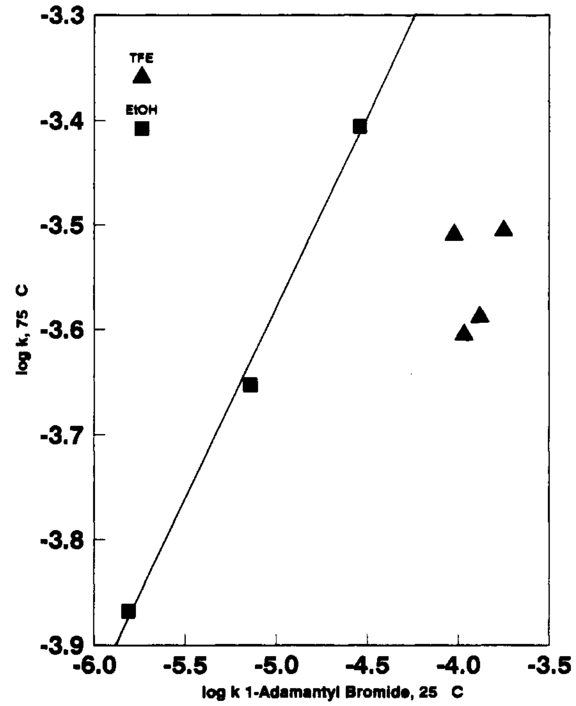

Figure 1. Raber–Harris plot for *cis*-3-(trimethylstannyl)cyclohexyl trifluoroacetate (*cis*-**5**-OTfa).

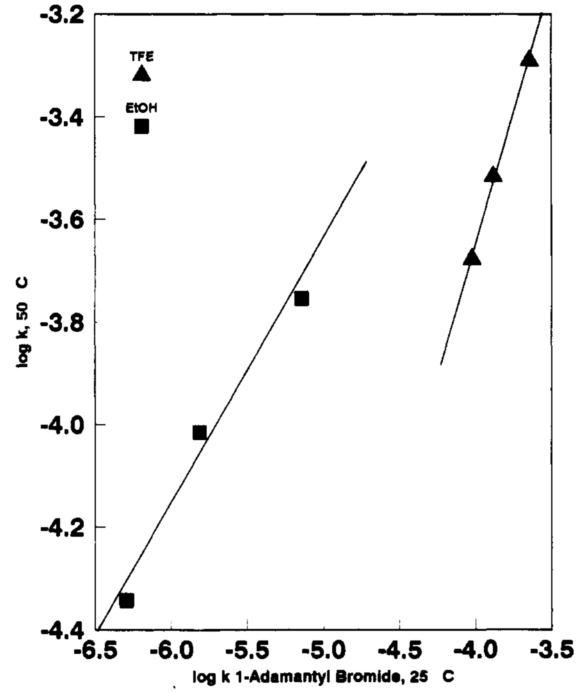

Figure 2. Raber–Harris plot for *trans*-3-(trimethylstannyl)cyclohexyl tosylate (*trans*-**5**-OTs).

Products. Determination of products was carried out in two solvents, 97% trifluoroethanol and 80% ethanol. *cis*-3-(Trimethylstannyl)cyclohexyl tosylate (*cis*-**5**-OTs) gave entirely bicyclo[3.1.0]hexane in both solvents. The analogous trifluoroacetate gave 88% of the hydrolysis product with retention in ethanol, *cis*-3-(trimethylstannyl)cyclohexanol. In trifluoroethanol, it gave 60% of bicyclo[3.1.0]hexane. The remaining products were of undetermined structure, the largest proportion of which (18%) was a material that retained the ring and the trimethylstannyl group. *trans*-3-(Trimethylstannyl)cyclohexyl tosylate (*trans*-**5**-OTs) in ethanol produced 48% of cyclohexene, 25% of probably 4-(trimethylstannyl)cyclohexene, and 15% of a material containing the C–Sn bond. In trifluoroethanol it produced 60% of cyclohexene and no products containing the C–Sn bond.

trans-4-(Trimethylstannyl)cyclohexyl tosylate (*trans*-**6**-OTs) in trifluoroethanol gave 60% of 1,5-hexadiene and

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(17) Raber, D., Jr.; 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. *J. Am. Chem. Soc.* **1978**, *100*, 8147–8156.

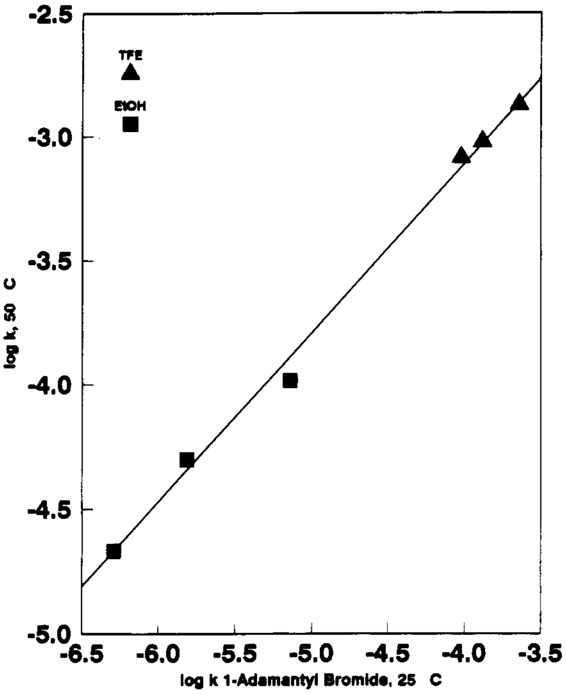


Figure 3. Raber–Harris plot for *trans*-4-(trimethylstannyl)cyclohexyl tosylate (*trans*-6-OTs).

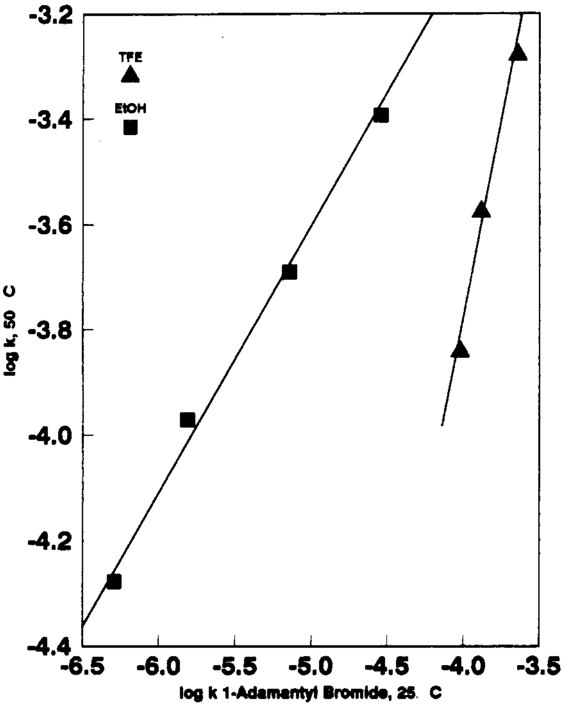


Figure 4. Raber–Harris plot for *cis*-4-(trimethylstannyl)cyclohexyl tosylate (*cis*-6-OTs).

a host of other products, which lacked trimethylstannyl groups on carbon. In ethanol the yield of 1,5-hexadiene was reduced to 15%. In addition there were 30% of the retained *trans*-4-(trimethylstannyl)cyclohexanol, 14% of the retained ethyl *trans*-4-(trimethylstannyl)cyclohexyl ether, and 22% of (trimethylstannyl)cyclohexenes. *cis*-4-(Trimethylstannyl)cyclohexyl tosylate (*cis*-6-OTs) in trifluoroethanol gave only 10% of 1,5-hexadiene. The remaining products were not determined, although alkenic protons were present (suggesting cyclohexenes) and resonances from trimethylstannyl on carbon were absent. In ethanol there was 60% of 4-(trimethylstannyl)cyclohexene, 10% of the inverted *trans*-4-(trimethylstannyl)cyclohexanol, and 9% of the inverted ethyl *trans*-4-(trimethylstannyl)cyclohexyl ether.

Table III. Activation Parameters

system[a]	solvent[a]	$\Delta H^{\ddagger}$,[c] kcal mol^{-1}	$\Delta S^{\ddagger}$,[c] cal deg^{-1} mol^{-1}	$\Delta G^{\ddagger}$,[c] kcal mol^{-1}
cis-**5**-OTfa	97% TFE	21.6	−12.8	25.4
trans-**5**-OTs	97% TFE	21.8	−8.1	24.2
	80% EtOH	23.4	−6.2	25.2
trans-**6**-OTs	97% TFE	19.8	−11.5	23.2
	80% ethanol	24.5	−4.2	25.8
cis-**6**-OTs	97% TFE	21.5	−9.7	24.4
	80% ethanol	23.2	−6.4	25.1
cyclohexyl-OTs[b]	97% TFE	22.2	−10.4	25.3

[a] See footnotes *a* and *b*, Table I. [b] From ref 17. [c] Estimated error is ±0.1.

Table IV. Rate Ratios for Tosylates in 97% Trifluoroethanol at 25 °C

system	rel rate	system	rel rate
cyclohexyl	1.0[a]	*trans*-**6**-OTs	42
cis-**5**-OTs	>2010[b]	*cis*-**6**-OTs	5.9
trans-**5**-OTs	8.2		

[a] Absolute rate calculated to be 1.37 × 10^{-6} s^{-1} from parameters in Table III measured in this study. [b] The tosylate/trifluoroacetate factor was measured to be 1940 by ref 16.

Discussion

Molecularity. The rate data of Tables I and II, when plotted versus analogous data for 1-adamantyl bromide, provide a visual criterion for distinguishing between the unimolecular k_c pathway and the bimolecular, solvent-assisted k_s pathway, as described by Raber, Harris, and their co-workers.[17] They recognized that aqueous mixtures of trifluoroethanol vary in nucleophilicity but not in ionizing power. Thus, a reaction occurring by a k_c pathway would show little dependence on trifluoroethanol concentration. In contrast, aqueous mixtures of ethanol vary in ionizing power but not in nucleophilicity. Plotting the rates of a k_c reaction vs those of 1-adamantyl bromide should yield a single straight line, as both materials follow the same mechanism. Moreover, there should be a strong variation of both rates in the ethanol mixtures and little variation in the trifluoroethanol mixtures. Because a reaction following a k_s pathway shows a dependence on solvent nucleophilicity, its rate varies in trifluoroethanol and the Raber–Harris plot shows two separate lines for the two solvents. Methyl and cyclohexyl tosylates provide classic examples of this type of plot.[17]

We shall first examine the 4-(trimethylstannyl)cyclohexyl tosylates (**6**-OTs), as the interpretation of their Raber–Harris plots is quite straightforward. Figure 4 shows the plot for the cis isomer, in which the conformational arrangement of the two substituents does not permit hyperconjugative interaction in the transition state. This is a typical plot for a k_s pathway. There are two distinct lines, and the trifluoroethanol data are spread out over almost 1 order of magnitude. Introduction of the cis trimethylstannyl group thus has little influence on the mechanism, as the Raber–Harris plot of Figure 4 is essentially identical with that of cyclohexyl tosylate.

In contrast, the plot for the trans isomer (Figure 3), in which hyperconjugative overlap of the type illustrated by **3** is possible, shows a dramatic change with respect to those of the cis isomer and of cyclohexyl tosylate. The trifluoroethanol rates now show little sensitivity to changes in water content, and the overall plot is a single line, indicating a mechanism like that of 1-adamantyl bromide (k_c). Solvent involvement has been replaced by internal stabilization. Thus, the Raber–Harris plot gives strong evidence for double hyperconjugation in the trans δ isomer.

In the 3-(trimethylstannyl)cyclohexyl tosylates (5-OTs), the trans isomer is not capable of homohyperconjugation. Indeed, the Raber–Harris plot of Figure 2 exhibits the traditional characteristics of a k_s mechanism, with two distinct lines and with the trifluoroethanol points spread out. Introduction of a trans trimethylstannyl group apparently does not alter the mechanism from that of cyclohexyl tosylate.

Unfortunately, the cis tosylate reacted too rapidly for our kinetic methods; therefore, we had to have recourse to the slower trifluoroacetate. The Raber–Harris plot (Figure 1) gave an intermediate form, neither the single line of k_c nor two lines of k_s. Our product studies (vide infra) suggest that in ethanol the reaction occurs by nucleophilic attack on the carbonyl group, leading to ester hydrolysis, a reaction that would exhibit sensitivity to solvent nucleophilicity. The Raber–Harris plot shows much lower sensitivity of the rate to nucleophilicity in trifluoroethanol. We believe that the plot of Figure 1 is consistent with a change in mechanism, in which the high nucleophilicity of aqueous ethanol leads to a k_s-like ester hydrolysis, whereas the high ionizing power and low nucleophilicity of aqueous trifluoroethanol leads to a k_c reaction with homohyperconjugative participation. It is noteworthy that 97% trifluoroethanol is not linear in rate with the other trifluoroethanol mixtures, contrary to the examples of Figures 2–4, again suggesting a more complex situation in which a change in mechanism takes place with solvent. It is possible that the observed rate in 97% trifluoroethanol represents that of the k_c process, but the mechanism may not have been fully transformed even in this solvent mixture, so that the true k_c rate is faster than what we observed. It is likely, because of its rapid rate, that the cis tosylate would give a normal single-line Raber–Harris plot, indicative of a k_c mechanism.

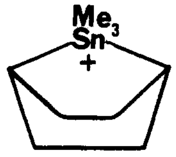
Rate Accelerations. Rate comparisons were made for tosylates in 97% trifluoroethanol at 25 °C relative to cyclohexyl, since this solvent represents the highest ionizing power. For the γ system in which homoconjugation is stereoelectronically prohibited (*trans*-3-(trimethylstannyl)cyclohexyl tosylate, *trans*-5-OTs), the rate is about 8 times faster than that of cyclohexyl (Table IV). This factor is appropriate for the rate of a predominantely axial k_s system in comparison with a predominantely equatorial k_s system and arises because of the different steric environments of the two positions. Thus, the rate ratio for axial and equatorial leaving groups in simple biased cyclohexyl systems (*cis*- to *trans*-4-*tert*-butylcyclohexyl tosylate or brosylate) is between 3 and 6.[9,18] In contrast, the analogous cis system reacts at least 2010 times faster than cyclohexyl (Table IV). Even without consideration of the point made in the above section on molecularity that the rate of the cis isomer as measured for the trifluoroacetate in 97% trifluoroethanol may not be entirely k_c but may still have an admixture of k_s, this acceleration is quite large. The acceleration for the analogous silicon brosylate is 460.[15] Therefore, tin is more effective than silicon in supporting homohyperconjugation, or, to express it differently, the γ effect of tin is stronger than that of silicon.

For the delta system in which double hyperconjugation is stereoelectronically prohibited (*cis*-4-(trimethylstannyl)cyclohexyl tosylate, *cis*-6-OTs), the rate is about 6 times faster than that of cyclohexyl (Table IV), a factor that again is within the range expected for a predominantely axial leaving group when compared with a predominately equatorial leaving group.[9,18] In contrast, the analogous trans system reacts more than 40 times faster, a figure that represents a substantial acceleration for an equatorial leaving group. Moreover, it is much larger than the negligible factor observed by Fessenden et al. for the analogous silicon system.[9]

Products. The cis γ tosylate gave exclusively bicyclo[3.1.0]hexane in both 97% trifluoroethanol and 80% ethanol. This product resembles the homoconjugatively stabilized transition state or intermediate (7). The trifluoroacetate in 97% trifluoroethanol gave 60% of the same material. In ethanol the apparent change of mechanism to nucleophilic attack by water at the carbonyl group is indicated by predominant formation of the retained alcohol (*cis*-5-OTfa → *cis*-5-OH). The trans isomer produced a mixture of unsaturated products and none of the bicyclohexane. It also is noteworthy that the cis γ silicon substrate with weaker homohyperconjugation produced only 16% of the same bicyclohexane.[15]

The trans δ tosylate in 97% trifluoroethanol gave 60% of 1,5-hexadiene, the product that resembles the double hyperconjugatively stabilized transition state or intermediate (8). The cis isomer gave only 10% of 1,5-hexadiene. Thus, the products of the respective γ and δ systems that show rate accelerations corroborate hyperconjugative interactions. The systems that did not show rate accelerations gave products that are consistent with normal solvent attack.

Isotope Effect. The isotope effect of 1.19 that was measured for the trans δ system (*trans*-6-OTs) is normal for a change from an sp^3 ground state to an sp^2 transition state, as in a carbocation.[19] Nucleophilic displacement reactions, such as direct reaction of the solvent with tosylate or displacement of the leaving group by tin (nonvertical or anchimeric assistance by tin, as in 9), normally give small or inverse secondary deuterium isotope effects.



9

Summary. The γ and δ effects of tin are negligible when the steric arrangement between tin and the leaving group is inappropriate for long-range hyperconjugation. Thus, *trans*-3-(trimethylstannyl)cyclohexyl tosylate (*trans*-5-OTs) and *cis*-4-(trimethylstannyl)cyclohexyl tosylate (*cis*-6-OTs) react by the same k_s mechanism as cyclohexyl tosylate. This mechanism is proved by the absence of significant rate accelerations compared with cyclohexyl,

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[18] Shiner, V. J., Jr.; Jewett, J. G. *J. Am. Chem. Soc.* 1965, *87*, 1382–1384.

[19] Isaacs, N. *Physical Organic Chemistry*; Longman: Essex, U.K., 1987; pp 265, 394–395, 599–600. Harris, J. M. *Prog. Phys.-Org. Chem.* 1974, *11*, 103–108. Harris, J. M.; Hall, R. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* 1971, *93*, 2551–2553.

by the two-line Raber–Harris plots (Figures 2 and 4), and by the low proportion of the hyperconjugation-like products, respectively bicyclo[3.1.0]hexane and 1,5-hexadiene.

In contrast, when the four bonds (Sn–C–C–C–X) are properly aligned for the γ effect in *cis*-3-(trimethylstannyl)cyclohexyl tosylate (*cis*-**5**-OTs) and when the five bonds (Sn–C–C–C–C–X) are properly aligned for the δ effect in *trans*-4-(trimethylstannyl)cyclohexyl tosylate (*trans*-**6**-OTs), the trimethyltin group changes the mechanism of reaction to k_c. This is a remarkable alteration for such distant substituents in flexible systems. The k_c mechanism and its associated hyperconjugative interaction are substantiated by the respective rate accelerations of 2010 (for the γ effect) and 42 (for the δ effect), by the Raber–Harris plots (Figures 1 and 3), by the high proportions of hyperconjugation-like products, and by the α-deuterium isotope effect of 1.19 for the δ effect. These results indicate that the transition state to carbocation formation is stabilized by homohyperconjugation in the case of the δ effect (**7**) and by double hyperconjugation in the case of the δ effect (**8**). In both cases, the acceleration is larger for tin than it was for the analogous silicon systems.[5,9]

Interestingly, the γ effect of tin is greater in the cyclohexyl framework than was previously observed for open-chain and for polycyclic cases. It is reasonable that the degree of freedom lost by going from chain[6] to ring improves the stereoelectronic likelihood for homohyperconjugation. The relatively small acceleration found by Grob[6] in adamantyl systems may indicate that the rigid polycyclic system offers too great a C–C distance for this homo effect to be optimal. The interaction between the C–Sn bond and the empty carbocation orbital (**2**) may be weak in the rigid framework. The cyclohexyl system (**7**) then permits a lowering of the C–C–C bond angle and hence stronger homohyperconjugative overlap.

In contrast, double hyperconjugation does not involve the long bond of the three-membered ring and is accomplished in polycyclic systems very effectively. The rate accelerations of the tin systems compared with analogous systems lacking tin (Sn/H rate ratios) are considerably larger in polycyclic cases than in cyclohexyl: up to 7000 for 2-adamantyl and 2840 for 2-bicyclo[2.2.2]octyl, compared with 42 for cyclohexyl. It is possible that the higher rigidity of the polycyclic systems removes conformations lacking the optimal stereoelectronic arrangement and creates an environment that is superior to cyclohexyl. Examination of rigid cyclohexyls, e.g., with anchoring *tert*-butyl groups, might enhance the rate acceleration.

It also is important to appreciate differences in the reference systems. The systems lacking tin in the polycyclic cases are 2-adamantyl and 2-bicyclo[2.2.2]octyl. In 2-adamantyl, backside attack by solvent on the leaving group is excluded by geometry; in 2-bicyclo[2.2.2]octyl solvent attack is slowed by the hydrogens on the opposed bridges. Thus, these systems largely react by unassisted carbocation formation (k_c). In contrast, cyclohexyl tosylate reacts by solvent assistance, i.e., by nucleophilic attack by solvent (k_s). Therefore, the reference comparison in the cyclohexyl systems currently under study is relatively faster than the references in the polycyclic cases. Thus, rate accelerations by the tin substituents are diminished and cannot be compared directly with those in the polycyclic cases. We can conclude that homoconjugation from the γ effect of tin and double hyperconjugation from the δ effect of tin are much stronger than the ability of solvent to displace the leaving group and result in changes of mechanism with concomitant solvent effects, rate accelerations, and product alterations.

Experimental Section

3-(Trimethylstannyl)cyclohexanone.[13] (Trimethylstannyl)lithium was prepared by dropwise addition of chlorotrimethylstannane (11.98 g, 0.06 mol) in 20 mL of anhydrous, freshly distilled tetrahydrofuran (THF) to Li wire (2.08 g, 0.30 mol) in 15 mL of anhydrous THF, cooled on an ice bath, under N_2, followed by stirring for 3 h. The solution of (trimethylstannyl)lithium was transferred under N_2 by syringe to a round-bottomed flask. To this was added 2-cyclohexen-1-one (4.80 mL, 0.050 mol) in 15 mL of anhydrous THF at 0 °C under N_2. The mixture was stirred overnight at room temperature, quenched with aqueous HCl, and extracted with 2 × 15 mL of diethyl ether. The organic layer was washed with saturated aqueous NaCl (20 mL) and dried over anhydrous $MgSO_4$. The solvent was removed by rotary evaporation to give 12.20 g (94% crude) of a yellow oil. Distillation under reduced pressure of the crude product from two such preparations gave 3-(trimethylstannyl)cyclohexanone as a colorless oil (69%, >98% pure by GC): IR 2940 (s, C—H), 1715 (s, C=O), 530 (s, C—Sn) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 9H (^2J(Sn–H) = 50.4, 52.6 Hz), Me_3Sn), 1.5–1.8 (m, 3H, ring), 1.88 (br d, 1H, ring), 2.10 (m, 1H, ring), 2.26–2.42 (m, 4H, ring); ^{13}C NMR ($CDCl_3$) δ −11.63 (Me_3Sn), 25.17 (C3), 29.37 (C4), 30.90 (C5), 42.14 (C6), 45.78 (C2), 212.54 (C1); ^{119}Sn NMR ($CDCl_3$) δ 8.42.

***cis*-3-(Trimethylstannyl)cyclohexanol (*cis*-5-OH).**[13] 3-(Trimethylstannyl)cyclohexanone (10.43 g, 0.040 mol) in 15 mL of anhydrous diethyl ether was added to a slurry of excess $LiAlH_4$ (0.60 g, 0.015 mol) in 35 mL of ether in an ice bath under N_2 and stirred for 1 h. The mixture was warmed to room temperature and stirred for an additional 6 h. The reaction was quenched with aqueous H_2SO_4 and extracted with 3 × 20 mL of ether. The organic layer was washed with 3 × 15 mL of saturated aqueous NaCl and dried over anhydrous Na_2SO_4. Removal of solvent by rotary evaporation gave a colorless oil (10.14 g, 96% crude yield), which by ^1H NMR analysis was an 85/15 cis/trans mixture of alcohols. Distillation under reduced pressure and flash column chromatography (200 g of alumina, 1:1 hexane–ether eluant) of 2.00 g of material gave 0.34 g of pure cis alcohol: IR 3350 (OH), 1045 (C—O), 530 (C—Sn) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.00 (s, 9H (^2J = 50.8 Hz), Me_3Sn), 1.12–1.26 (m, 5H, SnCH and ring), 1.38 (d, 1H, OH), 1.68 (br d, 1H, ring), 1.76 (br d, 1H, ring), 1.97 (br d, 1H, ring), 2.02 (br d, 1H, ring), 3.49 (m, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ −12.02 (Me_3Sn), 22.03 (C3), 27.20 (C5), 29.46 (C4), 35.79 (C6), 39.71 (C2), 71.84 (C1); ^{119}Sn NMR δ 2.13; MS m/z 249 (M − CH_3, 15%), 247 (11), 165 (100), 151 (13), 135 (30).

***trans*-3-(Trimethylstannyl)cyclohexanol (*trans*-5-OH).**[14,15] 3-(Trimethylstannyl)cyclohexanone (5.26 g, 0.020 mol) in 10 mL of anhydrous THF was added dropwise to a solution of lithium tri-*sec*-butylborohydride (20 mL, 1.0 M in THF, Aldrich), and the mixture was stirred for 7 h at −78 °C. The reaction mixture was warmed to room temperature overnight and then was quenched with 30 mL of 3 M NaOH and then 30 mL of 30% H_2O_2. The mixture was saturated with K_2CO_3, ether (20 mL) was added, and the layers were separated. The mixture was again extracted with 2 × 30 mL of ether, and the organic layer was dried over $MgSO_4$. Removal of the solvent by rotary evaporation gave 5.42 g of a light yellow oil, which was a 92/8 trans/cis mixture of alcohols by ^1H NMR. Flash column chromatography (200 g of alumina, 1 L each of hexane, 1:1 hexane–CCl_4, CCl_4, and CCl_4–ether as eluants) of 5 g of crude product gave 1.85 g of pure alcohol (96/4 trans/cis) (the procedure also was carried out with K-Selectride with a similar result): ^1H NMR ($CDCl_3$) δ 0.01 (s, 9H (^2J = 49, 51 Hz), Me_3Sn), 1.40–1.85 (br m, 10H, ring and OH), 3.82 (m, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ −11.07 (Me_3Sn), 19.88 (C3), 23.01 (C5), 29.88 (C4), 34.06 (C6), 37.90 (C2), 67.80 (C1); ^{119}Sn NMR δ 3.87; MS m/z 249 (M − CH_3, 21%), 247 (21), 165 (100), 151 (22), 135 (35). Anal. Calcd for

$C_9H_{20}OSn$: C, 41.11; H, 7.67; Sn, 45.14. Found: C, 41.42; H, 7.61; Sn, 45.07.

***cis*-3-(Trimethylstannyl)cyclohexyl tosylate (*cis*-5-OTs)** was prepared by the standard Tipson procedure[20] to give 1.36 g (73%) of colorless crystals: ^{1}H NMR ($CDCl_3$) δ −0.03 (s, 9H (^2J = 52 Hz), Me_3Sn), 1.06–1.23 (m, 3H, SnCH and ring), 1.31–1.51 (m, 2H, ring), 1.62 (br d, 1H, ring), 1.76 (br d, 1H, ring), 1.90 (br d, 1H, ring), 1.97 (br d, 1H, ring), 2.42 (s, 3H, $ArCH_3$), 4.38 (m, 1H, CHO), 7.31 (d, 2H, Ar), 7.77 (d, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ −11.83 (Me_3Sn), 21.78 (C3), 27.36 (C5), 28.91 (C4), 32.92 (C6), 36.82 (C2), 83.57 (C1).

***cis*-3-(Trimethylstannyl)cyclohexyl trifluoroacetate (*cis*-5-OTfa)** was prepared by reaction of the alcohol with trifluoroacetic anhydride to give 0.10 g (56%): ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 9H (^2J = 50.0, 52.3 Hz), Me_3Sn), 1.17–1.51 (m, 5H, SnCH and ring), 1.73 (m, 1H, ring), 1.88 (br d, 1H, ring), 2.04–2.09 (m, 2H, ring), 4.84 (m, 1H, HCO); ^{13}C NMR ($CDCl_3$) δ −11.77 (Me_3Sn), 21.51 (C3), 27.09 (C5), 29.14 (C4), 31.61 (C6), 35.39 (C2), 79.65 (C1); ^{119}Sn NMR ($CDCl_3$) δ 6.19.

***trans*-3-(Trimethylstannyl)cyclohexyl tosylate (*trans*-5-OTs)** was prepared by the standard method of Tipson[20] to give 0.80 g (51%): ^{1}H NMR ($CDCl_3$) δ −0.05 (s, 9H (^2J = 50, 52 Hz), Me_3Sn), 1.34–1.88 (m, 9H, ring), 2.42 (s, 3H, $ArCH_3$), 4.62 (m, 1H, CHO), 7.30 (d, 2H, Ar), 7.78 (d, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ −11.56 (Me_3Sn), 18.44 (C3), 22.54 (C5), 29.23 (C4), 31.26 (C6), 35.04 (C2), 80.59 (C1); ^{119}Sn NMR ($CDCl_3$) δ 5.15.

4-Iodocyclohexyl Trimethylsilyl Ether. 7-Oxanorbornane (10.2 mL, 0.1 mol), anhydrous NaI (15 g, 0.1 mol), and freshly distilled acetonitrile (70 mL) were placed in a 250-mL three-necked flask. To this mixture was added chlorotrimethylsilane (13 mL, 0.1 mol) slowly under N_2 at room temperature with rapid stirring. A white precipitate formed immediately. The mixture was stirred overnight and then was refluxed for 5 h. The mixture was extracted with 5 × 50 mL of hexane. The solvent was removed by rotary evaporation, and the residue was distilled under vacuum to give 25.25 g of a light yellow liquid (bp 64–66 °C (0.05 mmHg), 85%): ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 9H, Me_3Si), 1.35 (q, 2H, ring), 1.71 (d, 2H, ring), 1.87 (q, 2H, ring), 2.22 (d, 2H, ring), 3.63 (septet, 1H, CHO), 4.16 (br s, 1H, CHI); MS *m/z* 298 (M^+, 0.6%), 283 (9.2), 171 (27), 91 (24.8), 81 (100), 73 (44).

4-(Trimethylstannyl)cyclohexyl Trimethylsilyl Ether. In a 250-mL three-necked flask was placed 3.12 g (450 mmol) of cut Li wire and 120 mL of THF. To this was added chlorotrimethylstannane (18 g, 90 mmol) in 50 mL of THF with rapid stirring at 0 °C. The mixture was stirred for 24 h and then allowed to sit overnight. The dark brown solution was transferred by syringe to an addition funnel and added with stirring to a 500-mL flask that contained 4-iodocyclohexyl trimethylsilyl ether (22.4 g, 75 mmol) in 150 mL of THF. The mixture was stirred for 2 days at room temperature. The solvent was removed by rotary evaporation, and the residue was extracted with hexane. Removal of the hexane and distillation at reduced pressure gave 21.5 g of colorless liquid (86%, bp 65–75 °C (0.1 mmHg)), which by ^{1}H NMR was a cis/trans mixture.

***cis*- and *trans*-4-(Trimethylstannyl)cyclohexanol (*cis*-6-OH and *trans*-6-OH).** The isomeric mixture of 4-(trimethylstannyl)cyclohexyl trimethylsilyl ether was placed in a 100-mL flask with 50 mL of THF. The mixture was stirred for 24 h at room temperature after about 0.1 mL of tetrabutylammonium fluoride (1 M in THF) had been added. After solvent had been removed by rotary evaporation, the ammonium salts were precipitated with 30 mL of hexane. The precipitate was removed by filtration, and the hexane was removed by rotary evaporation to give 4.56 g (93%) of a white solid. The initial step of purification was sublimation at 40 °C (0.1 mmHg). The isomers (10 g) were separated by flash column chromatography over alumina with elution with 2 L of hexane, 2 L of 1:1 hexane–CCl_4, 2 L of CCl_4, 2 L of 1:1 CCl_4–ether, 2 L of ether, 1 L of 1:1 ether–$CHCl_3$, and 2 L of $CHCl_3$. The cis isomer was collected primarily in the hexane–CCl_4 fractions and the trans isomer in the ether–$CHCl_3$ fractions. Characterization of the cis isomer: ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 9H, ^2J(Sn–H) = 49, 51 Hz), Me_3Sn), 1.3–1.85 (m, 10H, ring and OH), 3.80 (m, 1H, CHO); ^{13}C ($CDCl_3$) δ −10.85 (Me_3Sn), 24.84 (C4), 26.26 (C3, C5), 35.08 (C2, C6), 68.53 (C1); ^{119}Sn NMR ($CDCl_3$) δ −0.44; MS *m/z* 264 (M^+, 1%), 249 (16), 247 (12), 231 (12), 165 (100), 151 (33), 135 (37). Anal. Calcd for $C_9H_{20}OSn$: C, 41.11; H, 7.67; Sn, 45.14. Found: C, 40.99; H, 7.93; Sn, 45.34. Characterization of the trans isomer: ^{1}H NMR ($CDCl_3$) δ −0.03 (s, 9H (^2J(Sn–H) = 49, 52 Hz), Me_3Sn), 0.96 (t of t, 1H, SnCH) 1.28 (q of d, 2H, ring), 1.31 (q of d, 2H, ring), 1.64 (d, 1H, OH), 1.86 (br d, 2H, ring), 1.98 (br d, 2H, ring), 3.49 (m, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ −11.81 (Me_3Sn), 23.36 (C4), 29.10 (C3, C5), 37.98 (C2, C6), 70.86 (C1); ^{119}Sn NMR ($CDCl_3$) δ 2.69; MS *m/z* 264 (M^+, 2%), 249 (25), 247 (28), 231 (10), 221 (11), 165 (100), 151 (34), 135 (39). Anal. Calcd for $C_9H_{20}OSn$: C, 41.11; H, 7.67; Sn, 45.14. Found: C, 41.40; H, 7.87; Sn, 44.57.

***cis*-4-(Trimethylstannyl)cyclohexyl tosylate (*cis*-6-OTs)** was prepared by the Tipson procedure:[20] ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9H (^2J(Sn–H) = 51 Hz), Me_3Sn), 1.18 (m, 1H, CHSn), 1.45–1.8 (m, 8H, ring), 2.42 (s, 3H, $ArCH_3$), 4.68 (br s, 1H, CHO), 7.30 (d, 2H, Ar), 7.77 (d, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ −11.31 (Me_3Sn), 23.64 (C4), 25.42 (C3, C5), 32.70 (C2, C6), 80.65 (C1); ^{119}Sn NMR ($CDCl_3$) δ 0.68; MS *m/z* 403 (M − CH_3, 1%), 337 (55), 321 (21), 241 (16), 231 (28), 165 (100), 151 (22), 135 (17).

***trans*-4-(Trimethylstannyl)cyclohexyl tosylate (*trans*-6-OTs)** was prepared by the Tipson procedure:[20] ^{1}H NMR ($CDCl_3$) δ −0.03 (s, 9H (^2J(Sn–H) = 50, 52 Hz), Me_3Sn), 0.93 (t of t, 1H, CHSn), 1.28 (q of d, 2H, ring), 1.40 (q of d, 2H, ring), 1.85 (br d, 2H, ring), 1.93 (br d, 2H, ring), 2.42 (s, 3H, $ArCH_3$), 4.38 (m, 1H, CHO), 7.30 (d, 2H, Ar), 7.77 (d, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ −11.78 (Me_3Sn), 22.64 (C4), 28.90 (C3, C5), 34.90 (C2, C6), 82.48 (C1); ^{119}Sn NMR ($CDCl_3$) δ 3.62; MS *m/z* 403 (M − CH_3, <1%), 337 (69), 321 (48), 241 (25), 165 (100), 151 (13), 135 (20).

***trans*-4-(Trimethylstannyl)cyclohexyl-1-*d* Tosylate (*trans*-6-*d*-OTs).** The isomeric mixture of alcohols was oxidized in 69% yield with pyridinium chlorochromate in CH_2Cl_2 to 4-(trimethylstannyl)cyclohexanone. Reduction of this material with $LiAlD_4$ produced a 72% yield of *trans*-4-(trimethylstannyl)cyclohexyl-1-*d*, identical with the undeuterated material except for the absence of the proton α to hydroxyl. The alcohol was converted to the tosylate by the Tipson procedure[20] and purified by recrystallization from pentane (61%).

Kinetics. Conductance procedures have been detailed previously.[4]

Product Determination. The products of solvolysis in perdeuterated 80% ethanol or 97% 2,2,2-trifluoroethanol were obtained from ca. 0.2 M solutions of the ester in sealed NMR tubes after greater than 10 half-lives. Structures were determined by comparison of ^{1}H, ^{13}C, and ^{19}Sn spectra with those of authentic samples of cyclohexene, bicyclo[3.1.0]hexane, 1,5-hexadiene, and the 3- and 4-(trimethylstannyl)cyclohexanols. Product yields were calculated from the integration of ^{1}H resonances in 80% ethanol. We attributed a 25% component to 4-(trimethylstannyl)cyclohexene [^{1}H NMR δ 0.03 ($SnMe_3$), 5.6–5.7 (alkenic); ^{13}C NMR δ −11.66, 21.57, 26.58, 27.26, 29.66, 127.64, 128.61]. The destannylation products, Me_3SnOR, were assigned to peaks at 0.54–0.61 ppm in the ^{1}H spectra and to the ^{119}Sn resonances as follows: 97% TFE δ 97 ($Me_3SnO(CO)CF_3$), 84 ($Me_3SnOCD_2CF_3$), and 65 (Me_3SnOD); 80% ethanol δ 23 ($Me_3SnOCD_2CD_3$).

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[20] Tipson, R. S. *J. Org. Chem.* **1944**, *9*, 235. Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; pp 1179–1181.