Stereochemistry of Trifluoroacetolysis and Brominolysis of the Cyclohexyl–Tin Bond†

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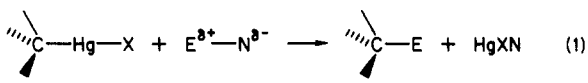
Trifluoroacetolyses of *cis*- and *trans*-(4-methylcyclohexyl)- and *cis*- and *trans*-(4-*tert*-butylcyclohexyl)triisopropylstannanes proceed stereospecifically with retention of configuration at carbon, on the basis of direct ^2H NMR examination of the reactions. Brominolysis was conducted under various conditions, and electrophilic brominolysis (methanol solvent) is characterized by a fine energetic balance between inversion and retention pathways, with the former favored for *equatorial* and the latter for *axial* carbon–tin bonds. Free radical brominolysis yields a statistical mixture of the *cis*- and *trans*-4-alkylcyclohexyl bromides, a result appropriate for bromine atom transfer to a 4-alkylcyclohexyl free radical.

Introduction

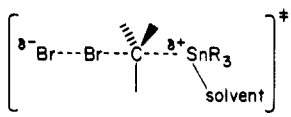
Until relatively recently, the most informative studies of electrophilic aliphatic substitution utilized organomercurials,[1] and retention of configuration was established as the normal stereo outcome for (electrophilic) cleavage of the carbon–mercury bond (eq 1). (A detailed discussion



(1)

of this area is available.) However, studies with other carbon–metal systems had indicated that a stereochemical "rule" (as applies to S_N2 reactions, for example) probably would not emerge for S_E2 reactions,[2] despite the fact that the significance of most of these studies was unclear for various reasons, which have been outlined elsewhere.[3] That retention of configuration was not the universal stereooutcome for bimolecular electrophilic substitution (S_E2) at non-carbanionic centers was shown by Jensen and Davis who reported a kinetically and stereochemically secure demonstration that electrophilic bromodestannylation (eq 2) of certain alkylstannanes could have a preferred inversion pathway (e.g., I).[3,4] This report has

$$(S)\text{-}(+)\text{-}s\text{-BuSn(neo-Pent)}_3 \xrightarrow[CH_3OH]{Br_2,\ Br^-} (R)\text{-}(-)\text{-}s\text{-BuBr} \quad (2)$$



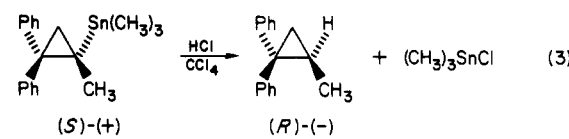
I

stimulated considerable activity,[5-8] and some of the factors that influence the balance between inversion and retention pathways are now apparent. A review of this subject has appeared recently.[3]

Because of our interest in cyclohexyl–metal systems and because of the key role played by cyclohexylmercurials in early studies of S_E2 reactions,[1] it appeared that comparative studies of cyclohexylmercurials and -stannanes would be especially instructive and provide further insight into destannylation stereochemistry. The availability[9] of various stereochemically pure (alkylcyclohexyl)stannanes has permitted such studies, and in this paper we report the stereochemistry of protonolysis (deuteriolysis) and brominolysis of the cyclohexyl–tin bond.

Results and Discussion

Protonolysis (Deuteriolysis) of the Cyclohexyl–Tin Bond. With respect to the cyclohexyl–mercury bond, Jensen and co-workers determined that retention is the preferred stereochemical course for cleavage by DCl in dioxane solvent.[10] Other combinations of acid/solvent presented considerable problems related to isomerization of the starting dicyclohexylmercurials. These authors further concluded that *equatorial* carbon–mercury bonds were cleaved more readily than the corresponding axial bonds.[10] There is no general stereochemical information available for protodestannylation of carbon–tin bonds, although HCl cleavage (CCl_4) of (*S*)-(+)-(1-methyl-2,2-diphenylcyclopropyl)trimethylstannane (eq 3) proceeds stereospecifically with retention, not surprising in view of the large barrier to inversion in cyclopropyl derivatives.[11-14]



(3)

Protonic acid cleavage of a carbon–metal bond is formally the simplest electrophilic aliphatic substitution, and previous studies with cyclohexylmercurials (using DX) have utilized C–D stretching frequencies (which differ for axial and equatorial C–D bonds) as the analytical method.[10] Directness (direct observation) and higher preci-

† Some of this work has appeared in preliminary form.[8]

(1) See: Jensen, F. R.; Rickborn, B. "Electrophilic Substitution of Organomercurials"; McGraw-Hill: New York, 1968. Sayre, L. M.; Jensen, F. R. *J. Am. Chem. Soc.* **1979**, *101*, 6001. For a more general discussion, see: Matteson, D. S. *Organomet. Chem. Rev. A* **1969**, *4*, 263.

(2) For example, see: Walborsky, H. M.; Impastato, F. J.; Young, A. E. *J. Am. Chem. Soc.* **1964**, *86*, 3283. Applequist, D. F.; Chimurny. G N. *Ibid.* **1967**, *89*, 875. Glaze, W. H.; Selman, C. M. *J. Org. Chem.* **1968**, *33*, 1987.

(3) Fukuto, J. M.; Jensen, F. R. *Acc. Chem. Res.* **1983**, *16*, 177. In this account, the tribromide ion cleavage of (*sec*-butylneopentyl)thallium bromide was reported to proceed with inversion. See also: Chambers, R. L.; Jensen, F. R. In "Aspects of Mechanism and Organometallic Chemistry"; Brewester, J., Ed.; Plenum Press: New York, 1978.

(4) Jensen, F. R.; Davis, D. D. *J. Am. Chem. Soc.* **1971**, *93*, 4048.

(5) Rahm, A.; Pereyre, M. *J. Am. Chem. Soc.* **1977**, *99*, 1672.

(6) Gielen, M.; Fosty, R. *J. Chem. Res., Minipr.* **1977**, 2373.

(7) McGahey, L. F.; Jensen, F. R. *J. Am. Chem. Soc.*, **1979**, *101*, 4397.

(8) Olszowy, H. A.; Kitching, W. *J. Org. Chem.* **1982**, *47*, 5230.

(9) Olszowy, H. A.; Kitching, W., preceding paper in this issue.

(10) Reference 1. pp 66–69. The interesting statement is made (p 69) that "80% retention in the case of *trans*- and 73% retention in the case of *cis*-bis(4-methylcyclohexyl)mercury (DCl/dioxane) should represent well the specificity of the protic acid cleavage". For stereochemical results with *di-sec*-butylmercury, see: Gale, L. H.; Jensen, F. R.; Landgrebe, J. M. *Chem. Ind. (London)* **1960**, 118.

(11) Sisido, K.; Kozima, S.; Tokizawa, T. *Tetrahedron Lett.* **1967**, *33*.

(12) Sisido, K.; Miyanisi, T.; Isida, T. *J. Organomet. Chem.* **1970**, *23*, 117.

(13) Sisido, K.; Ban, K.; Isida, T. *J. Organomet. Chem.* **1971**, *29*, C7.

(14) Gielen, M.; Backelmans, P.; Nasielski, J. *J. Organomet. Chem.* **1972**, *34*, 329.

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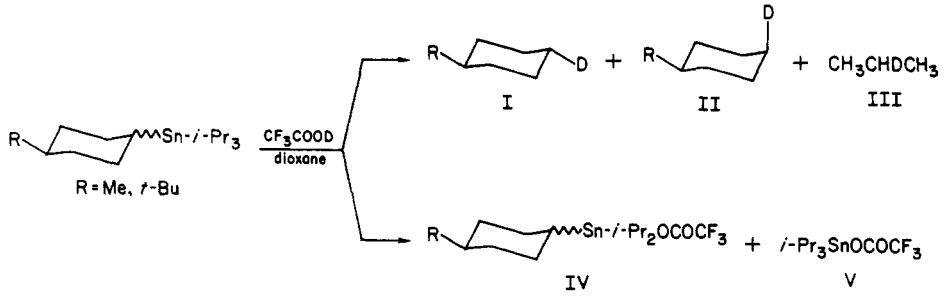
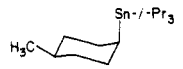
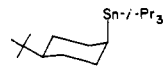
Table I. Stereochemical Outcome in the Reactions of (4-Alkylcyclohexyl)triisopropylstannanes with Trifluoroacetic Acid-*d* in Dioxane at 100 °C (after 12 Days)

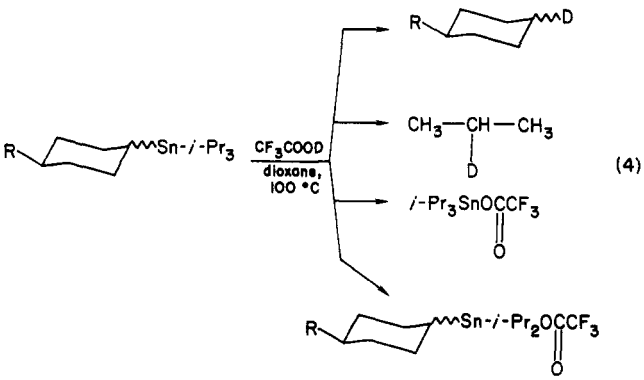


item	substrate	relative proportions,[d] % I[a]	II[a]	III[a]	IV[b]	V[b]	stereochem
1		36	<0.1[c]	64	68	32	100% retentn
2		<0.1[c]	34	66	70	30	100% retentn
3		23	<0.1[c]	77	80	20	100% retentn
4		<0.1[c]	8	92	94	6	100% retentn

[a] Relative proportions based on ^2H NMR signal intensity. [b] Relative proportions based on ^{119}Sn NMR signal intensity. [c] Not detected by ^2H NMR. [d] The ratio of I:II:III remained essentially constant after 2, 4, and 12 days (^2H NMR).

sion are virtues of ^2H NMR spectroscopy, as signals for axial ^2H are well resolved from corresponding equatorial ^2H signals in 4-alkylcyclohexane-*1-d*.[15] Our studies were conducted by using anhydrous 1,4-dioxane as solvent and trifluoroacetic acid-*d* as cleaving agent because of its acidity, ease of handling, and desirable solubility characteristics.

The general equation for the deuterolysis of the *cis*- and *trans*-(4-alkylcyclohexyl)triisopropylstannanes is shown in eq 4, and it is evident the stereochemical outcome can



(4)

be determined by direct ^2H NMR examination and assigning resonances to axially or equatorially disposed ^2H in the 4-alkylcyclohexane-*1-d*.[15] Preliminary experiments indicated that deuteriodestannylations were very slow under conditions where the acid and stannane were reacted as dilute (equimolar) solutions in dioxane at room temperature. A more convenient rate was achieved by using a 2:1 acid to stannane ratio at 100 °C. A typical procedure is described in the Experimental Section. After 12 days at 100 °C, the reaction mixture exhibited no signs of decomposition and reactions were judged to be ca. 80% complete, on the basis of ^{119}Sn NMR signal intensities of the (product) trialkyltin trifluoroacetates (+80 to +120 ppm range) and unreacted cyclohexylstannane (−40 to −50 ppm range).[9] Redistribution processes of the alkyl groups

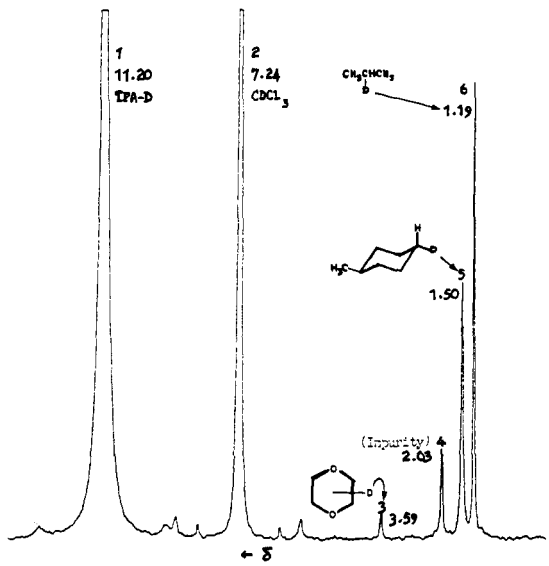
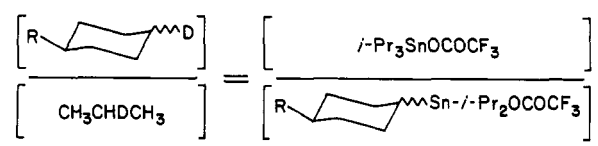


Figure 1. ^2H NMR spectrum of the total reaction mixture: *trans*-(4-methylcyclohexyl)triisopropylstannane with trifluoroacetic acid-*d* in dioxane at 100 °C, after 12 days.

on tin were not significant on the basis that only three ^{119}Sn NMR resonances were observed throughout the reaction, i.e., two for the trialkyltin trifluoroacetates and one for starting stannane. ^{119}Sn NMR examination also established that isomerization of starting stannane (i.e., cis ⇌ trans) was not detectable. Examination of the reaction was conducted after 2, 4, and 12 days.

Propane-2-*d* is a cleavage product, and some may have been lost during transfer processes (see Experimental Section). Thus, the relative proportions (based on ^2H NMR data) of 4-alkylcyclohexane-*1-d* and propane-2-*d* quoted should be regarded as approximate (eq 5). How-



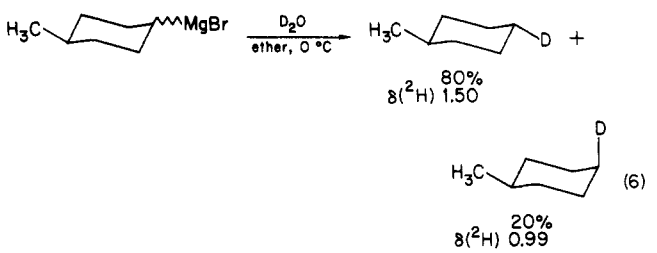
(5)

ever, the relative proportions are more accurately reflected

(15) See, for example: Kitching, W.; Atkins, A. A.; Wickham, G.; Alberts, V. J. *J. Org. Chem.* **1981**, *46*, 563.

by the ^{119}Sn NMR signal intensities of the trialkyltin trifluoroacetates. Nevertheless, the data in Table I shows excellent agreement between the two analytical methods.

Figure 1 represents the ^2H NMR spectrum of the total reaction mixture resulting from deuterolysis of *trans*-(4-methylcyclohexyl)triisopropylstannane. (The solvent system at this stage is ca. CF_3COOD (8%), dioxane (32%), and $CHCl_3$ (60%) (the latter added to increase volume in the 10-mm NMR tube) with some $CDCl_3$ for referencing purposes (δ 7.24 was assigned to $CDCl_3$ in this system.) Peaks 1 (δ 11.20) and 2 (δ 7.24) correspond to CF_3COOD and $CDCl_3$, respectively, while peak 3 (δ 3.59) is due to 1,4-dioxane. (Neat 1,4-dioxane exhibits a (natural abundance) ^2H signal at δ 3.59, and the ^1H shift of 1,4-dioxane is δ 3.60.) The signal at δ 2.03 (peak 4) is derived from added chloroform or the slight amount of ethanol in it. A mixture comprising CF_3COOD, dioxane, and chloroform (and C^2HCl_3) affords ^2H signals at δ 11.2, 3.59, 7.24, and 2.03. Furthermore, this latter signal was absent when chloroform was not added to the reaction mixture, thus confirming this signal is not associated with the reaction under scrutiny. Peak 6 (δ 1.19) was due to propane-*2-d* on the basis of coincidence with the shift of authentic propane-*2-d* (i-C_3H_7MgBr + D_2O) in the same solvent system and attentuation of this signal (in the reaction medium) when propane-*2-d* was added. The remaining signal 5 (δ 1.50) was assigned to *trans*-4-methylcyclohexane-*1-d* that was independently prepared by D_2O quenching of 4-methylcyclohexyl magnesium bromide (eq 6).



This mixture of isomers, in which trans is known to predominate,[15] exhibited signals at δ 1.50 (major) and 0.99 (minor) in the presently utilized solvent system. Furthermore, the addition of this 80/20 trans/cis mixture caused the signal at δ 1.50 to increase substantially relative to peak 6. It is clear, then, that only *trans*-4-methylcyclohexane-*1-d* is detectable, confirming stereospecific (retention) cleavage of the cyclohexyl–tin bond.

Figure 2 represents the ^2H NMR spectrum of the reaction mixture for *cis*-(4-methylcyclohexyl)triisopropylstannane, and only *cis*-4-methylcyclohexane-*1-d* is formed, again a stereospecific (retention) process. Similar approaches were employed in the cases of the (4-*tert*-butylcyclohexyl)stannanes and authentic *trans*- and *cis*-4-*tert*-butylcyclohexane-*1-d* were obtained (75% trans/cis mixture) by the Grignard route. ^2H shifts for the dioxane/CF_3COOD/$CHCl_3$ solvent system were as follows: trans, δ 1.49; cis, δ 0.93, $\Delta\delta$ = 0.56. ($\Delta\delta$ values of 0.56 and 0.55 have been reported previously.[15,19])

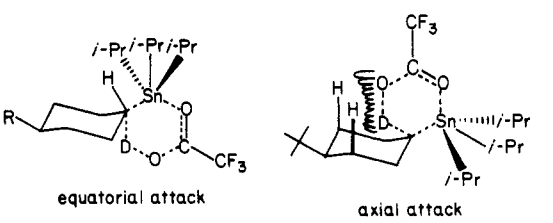
The stereochemical course of those deuteriodestannylations are summarized below in Table I, and clean retention is observed.

^{13}C and ^{119}Sn NMR spectra of reaction mixture were obtained and confirmed the well-behaved course of these reactions. In particular, the ^{13}C spectra (and ^{119}Sn shift) confirm the unchanged nature of unreacted stannane, and the identities of the hydrocarbon and trialkyltin trifluoroacetates (products), mostly by comparison with the spectra of authentic samples (Table II). It is to be noted that cleavage of two alkyl groups from tin was not detected.

Selectivity of Alkyl Group Cleavage. Deuteriolysis of *trans*-(4-alkylcyclohexyl)triisopropylstannanes (items 1 and 3, Table I). Proceeds with approximately equal rates of cleavage of isopropyl and cyclohexyl groups (after statistical correlation) i.e., $k_{i\text{-Pr}} \approx k_{Cy}$. However, in the conformationally "immobile" *cis*-(4-*tert*-butylcyclohexyl)-stannane (with tin group overwhelmingly axial), $k_{i\text{-Pr}}$ is 4–5 times greater than k_{Cy} (axial), although *retention* is still the stereo course. Frontside axial approach by the electrophile would be expected to experience severe nonbonded interactions with axial 3,5 hydrogens, as shown below. On the other hand, conformationally inhomogeneous *cis*-(4-methylcyclohexyl)stannane (Table I) affords a product distribution very similar to that obtained with the *trans*-4-alkyl systems. This is explicable in terms of reaction proceeding predominantly through the conformer with an equatorial tin group, such conformer calculated to be ca. 30% at 100 °C.

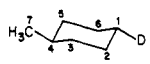
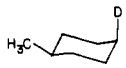
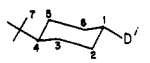
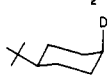
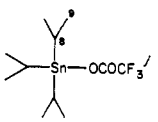
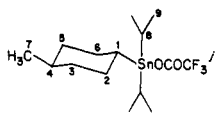
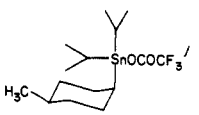
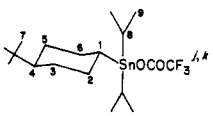
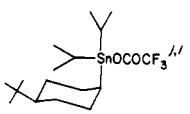
The relative rate of cleavage of axial and equatorial C–Sn bonds was determined by ^2H NMR examination of the product mixture resulting from deuteriolysis of an equimolar mixture of *trans*- and *cis*-(4-*tert*-butylcyclohexyl)triisopropylstannanes. The usual reaction conditions were employed, and after 12 days at 100 °C, the mixture exhibited signals for *trans*- and *cis*-4-*tert*-butylcyclohexane-*1-d* in an ca. 4:1 ratio, indicating that the equatorial C–Sn bond is more reactive, assuming isopropyl cleavage from axially and equatorially oriented $Sn(i\text{-}C_3H_7)_5$ proceed at the same rate. (Note Table I) that the rate of cleavage of an equatorial C–Sn bond (in *trans*-4-*tert*-butyl isomer) is essentially the same as that for isopropyl cleavage, after statistical correction.) Thus, the prediction is made that deuterolysis of the *cis*-4-*tert*-butyl isomer should afford cycloalkane and propane in a ratio of 1:3 (× 4) = 1:12, in excellent agreement with the observed ratio of 8:92 or 1:11.5.

Mechanism of Deuteriodestannylation. The strict retention stereochemistry observed requires either an S_E2 (open) or S_E2 (cyclic) transition-state geometry, but distinction between these is difficult. Although tetraalkylstannanes have virtually no acceptor properties (Lewis base), displacement of the (formal) R_3Sn^+ requires charge stabilization, and if dioxane can function efficiently in this way, S_E2 (open) could be operative. Alternatively, molecular CF_3COOD could provide acetate interaction with the departing tin group, so that the S_E2 (cyclic) configuration was operative. The apparently greater steric requirement of the cleavage of an axial C–Sn bond (mentioned earlier) is reminiscent of the situation with axial C–Hg bonds.[1] It should be recognized that the rate differences encountered in these cleavages are small, and a number of subtle factors such as electronic differences between axial and equatorial bonds (as reflected possibly by differing ^{119}Sn shifts) could be responsible, in addition to nonbonded effects.



Brominolysis of the Cyclohexyl–Tin Bond. The bromine cleavage reactions of each isomerically pure (4-methylcyclohexyl)- and (4-*tert*-butylcyclohexyl)triisopropylstannane were carried out in methanol, acetonitrile,

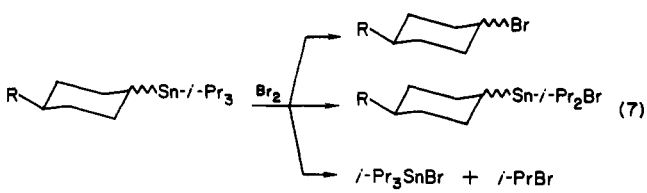
Table II. ^2H, ^{119}Sn, and ^{13}C NMR Data for Hydrocarbons and Trialkyltin Trifluoroacetates Obtained from Reactions of (4-Alkylcyclohexyl)triisopropylstannanes with Trifluoroacetic Acid-*d* in Dioxane at 100 °C (12 Days; Alkyl = Me, *t*-Bu)

			$\delta(^{13}C)^{a,d}$ ($J(^{13}C-^{119}Sn$, Hz)						
product	$\delta(^2H)^{a,b}$	$\delta(^{119}Sn)^{a,c}$	C1	C2,6	C3,5	C4	C7	C8	C9
CH_3CHDCH_3	1.19							16.1[e]	16.1[e-g]
	1.50		26.48[g,h]	26.48	35.61	32.92	22.91		
	0.99		^{13}C NMR data as above						
	1.49		26.95[g,h]	27.36	28.06	48.59	27.59		
	0.93		^{13}C NMR data as above						
		92.8						22.7 (331.1, 316.5)	20.75 (14.7)
		85.2	33.91	37.36	30.69	32.86	22.79	22.79	20.75
		111.3	37.22 (312, 298)	29.03	36.14 (24.4)	31.66	21.86	23.57 (317.4, 302.7)	20.64
		83.8	34.55	31.39 (14.6)	29.81 (76.2)	48.24	27.47	22.79 (342, 325)	20.80 (14.6)
		117.2	38.38	29.03 (14.6)	30.78 (29.31)	48.52	27.57	23.86 (314, 299)	20.64

[a] Observed chemical shifts in a solvent mixture consisting of TFA-*d*, dioxane, and chloroform (8:32:60 approximately). [b] Referenced to $CDCl_3$ ($\delta(^2H)$ 7.24). [c] Referenced to the unreacted (4-alkylcyclohexyl)triisopropylstannane that was still present in the reaction mixture; ^{119}Sn chemical shifts for tetraalkylstannanes are as follows: *trans*-(4-methylcyclohexyl)triisopropylstannane, $\delta(^{119}Sn)$ −53.81; *cis*-(4-methylcyclohexyl)triisopropylstannane, $\delta(^{119}Sn)$ −48.78; *trans*-(4-*tert*-butylcyclohexyl)triisopropylstannane, $\delta(^{119}Sn)$ −54.39; *cis*-(4-*tert*-butylcyclohexyl)triisopropylstannane, $\delta(^{119}Sn)$ −44.17. [d] Referenced to 1,4-dioxane ($\delta(^{13}C)$ 67.14); values in parentheses are $^{13}C-^{119}Sn$ coupling constants. [e] Broad signal. [f] ^{13}C chemical shifts for propane $CH_3CH_2CH_3$ are $\delta(^{13}C)$ 15.6 (CH_3), 16.1 (CH_2). It is known that the replacement of a proton by deuterium in unactivated alkanes causes the α-carbon to shift to high field by ≃ 0.5 ppm; therefore the ^{13}C resonance of CHD in CH_3CHDCH_3 is assumed to overlap with CH_3. [g] The anticipated 1:1:1 triplet, due to the one bond $\alpha(^{13}C-^2H)$ coupling ($^1J(^{13}C-^2H)$), was unresolved probably due to an increased spin-lattice relaxation time (T_1) and a decrease in the NOE. [h] Uncertain assignment. [i] $\delta(^{13}CMe_3)$ 32.68. [j] ^{13}C NMR data for $OCOCF_3$ ligand as follows: C=O 1:3:3:1 quartet centered at 158.11 ppm with $^2J(^{13}CO-CF_3)$ = 41.03 Hz; CF_3 1:3:3:1 quartet centered at 115.10 ppm with $^1J(^{13}C-F_3)$ = 288.09 Hz. [k] $\delta(^{13}CMe_3)$ 32.62. [l] $\delta(^{13}CMe_3)$ 32.83.

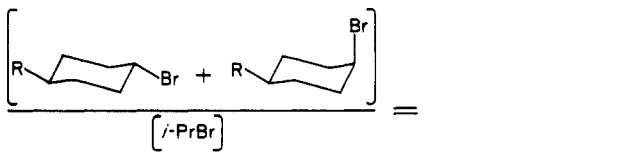
and chlorobenzene under varying reaction conditions. In all cases, a standard bromine solution was freshly prepared in solvent of choice and added dropwise to a slight excess of the tetraalkylstannane, at 0 °C in the dark. A typical procedure is described in the Experimental Section.

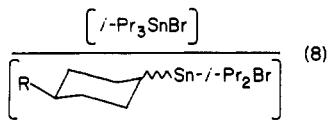
The products which could possibly result from the brominolysis are shown in eq 7. Capillary VPC exami-



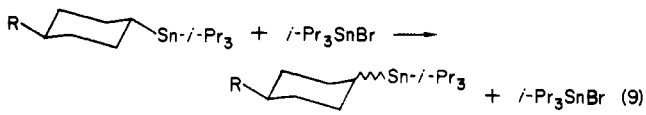
(7)

nation of the product mixture was well-suited for the determination of alkyl bromides as mixtures of *cis*- and *trans*-4-methyl- and *cis*- and *trans*-4-*tert*-butylcyclohexyl bromides were readily separable on the column employed. This analysis therefore provided an accurate distribution of the alkyl bromides, after slight corrections for predetermined response factors. ^{13}C NMR examination of the product mixture served two purposes: first, to confirm the presence of all possible cleavage products and, second, to provide an independent measure of the proportions of the various product bromoalkanes. In addition, the ratio of the two possible trialkyltin bromides may be determined by considering the ^{13}C signals of the well-resolved methine carbons of the isopropyl groups attached to tin (Sn–CH-$(CH_3)_2$). ^{119}Sn NMR examination of the total reaction mixture was particularly useful, as this would provide another measure of the ratio of the two possible trialkyltin bromides, which should be equal to the ratio of alkyl-bromides as shown in eq 8. Furthermore, the absence of a ^{119}Sn NMR signal corresponding to a (4-alkylcyclohexyl)triisopropylstannane of opposite configuration to that of starting stannane confirmed that a redistribution reaction as shown in eq 9 is unimportant.





(8)

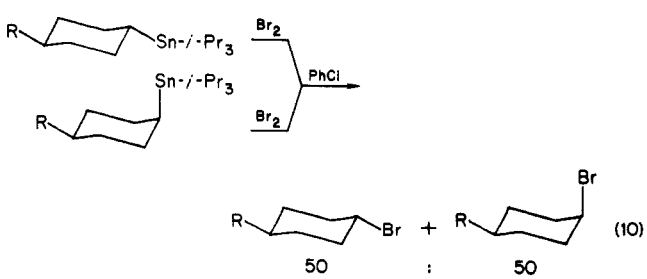


(9)

The results of the bromodestannylation experiments are gathered in Table III, and the NMR data are summarized in Table IV (^{13}C data for alkyl bromides) and Table V (^{13}C and ^{119}Sn data for trialkyltin bromides). Assignments were made from consideration of ^{13}C–^{119}Sn couplings, signal intensities, chemical shifts, etc.

Inspection of the data in Table III reveals that two types of reaction conditions were employed for the bromodestannylation, viz., one in which a polar (electrophilic) process would be favored (items 1–7) and the other in which free radicals are likely to be involved (item 8–12). Existing information accords with this categorizing of the reaction conditions.[3]

Brominolysis in chlorobenzene (items 8–12) of all four stannanes provides a near statistical distribution of the product 4-alkylcyclohexyl bromides, a result appropriate for the intermediacy of the corresponding 4-alkylcyclohexyl radical, known to possess low (or no) selectivity in the product forming (bromine abstraction) step.[16] The cyclohexyl and isopropyl radicals possess no special stabilizing features so that selectivity in homolytic cleavage of these stannanes would be very low, as is observed. There appears to be a slight preference for cleavage of the cyclohexyl–tin bond. Other studies support the conclusion that free radicals would be involved under the conditions employed in items 8–12. Optically active *sec*-butyltrineopentyltin, on treatment with bromine in chlorobenzene, yields (largely) racemic *sec*-butyl bromide,[5] and similar treatment of *erythro*-(1,2-dideuterio-3,3-dimethyl butyl)-triisopropylstannane results in complete loss of stereochemical integrity in the bromide product (eq 10).[6] We



(10)

attempted to observe the result for electrophilic destannylation in a nonnucleophilic solvent by suppressing the radical route by hydroquinone and air, but a statistical distribution of bromides was still obtained (item 12). While this type of result may be attributable to competing inversion and retention pathways,[3] it may simply indicate a failure to suppress the radical route in the cyclohexyl system, although more efficient radical traps may lead to

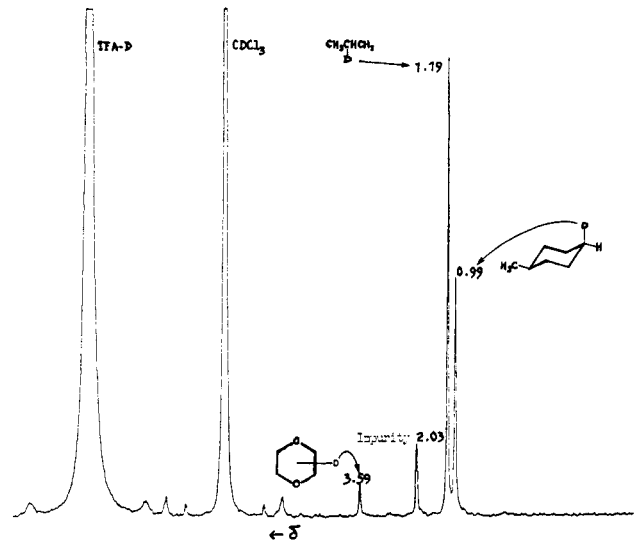
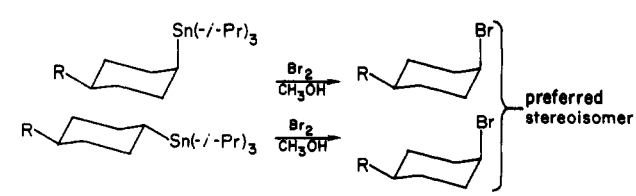


Figure 2. ^{2}H NMR spectrum of the total reaction mixture: *cis*-(4-methylcyclohexyl)triisopropylstannane with trifluoroacetic acid-*d* in dioxane at 100 °C, after 12 days.

a different stereochemical result. It should be pointed out, that trineopentyl-*sec*-butylstannane can be bromodestannylated in carbon tetrachloride in the presence of a radical inhibitor with retention (92%) stereochemistry.[17]

Solvent has been demonstrated to exert a major influence on the course of bromodestannylation by a number of workers, and the careful studies of Jensen and coworkers reveal methanol (with added bromide ion) to be a suitable solvent in which to conduct electrophilic bromodestannylation.[3] Indeed, essentially 100% configurational inversion was observed for bromodestannylation of *sec*-butyltrineopentylstannane in methanol containing added sodium bromide. This and related results constitute the major reason for believing that the items 1–7 in Table III represent the outcomes of authentic electrophilic substitutions of the cyclohexyl–tin bonds. Additionally the results are quite different from those in items 8–12, and also added bromide ions (item 5), a known free radical suppressor, had no significant effect (cf. items 1, 5). Electrophilic bromodestannylations in the present systems are not stereospecific; i.e., the energy difference between inversion and retention pathways is finely balanced, and the preferred stereochemistry is dependent on the orientation of the tin moiety. When $(i\text{-Pr})_3Sn$ is axially oriented (items 2, 4, 6, 7) retention is favored, but predominant inversion prevails for equatorially oriented C–Sn bonds (eq 11).



(11)

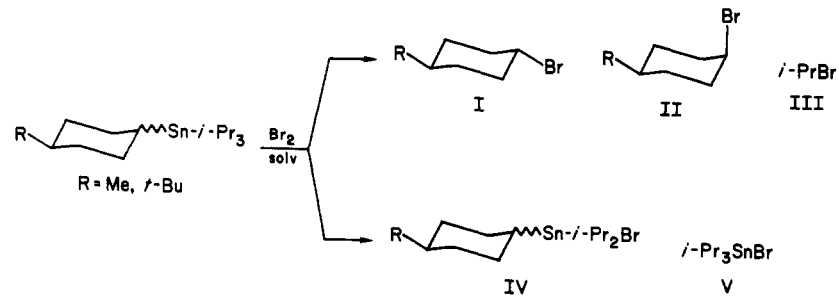
The data in Table III indicate also little discrimination between cyclohexyl and isopropyl in these polar destannylations.

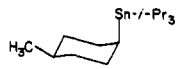
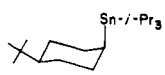
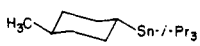
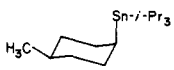
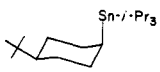
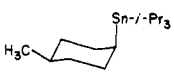
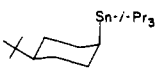
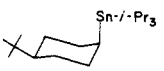
The essentially conformationally homogeneous *cis*-(4-*tert*-butylcyclohexyl)stannane is cleaved with predominant retention, despite significant interactions between the

(16) Jensen, F. R.; Gale, L. H.; Rodgers, J. E. *J. Am. Chem. Soc.* **1968**, *90*, 5793.

(17) The radical inhibitor bis(3-*tert*-butyl-4-hydroxy-5-methylphenyl) sulfide was employed. See Ref 3, p 180.

Table III. Stereochemical Results for Bromine Cleavage Reactions of (4-Alkylcyclohexyl)triisopropylstannanes under Various Reaction Conditions

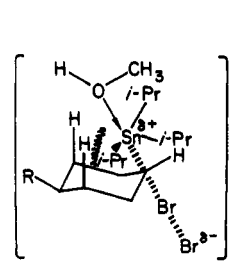


item	substrate	conditns	rel proportns, % I[a]	II[a]	III[a]	IV[b]	V[b]	preferred stereochem
1		MeOH, 0 °C, dark, air	11 (10)	14 (17)	75 (73)	68	32	inversn, 56%
2		MeOH, 0 °C, dark, air	10 (13)	16 (17)	74 (70)	75	25	retentn, 62%
3		MeOH, 0 °C, dark, air	15 (14)	25 (19)	60 (67)	62	38	inversn, 62%
4		MeOH, 0 °C, dark, air	10 (12)	15 (16)	75 (72)	68	32	retentn, 60%
5		MeOH, 0 °C, dark, +NaBr (2 equiv), air	10	13	77			inversn, 55%
6		MeOH, 0 °C, dark, +NaBr (2 equiv), air	10	20	70			retentn, 66%
7		CH_3CN, 20 °C, dark, air	3	3.5	93.5			retentn, 54%
8		PhCl, 20 °C, light,[c] air	17.5 (15)	16.5 (15)	66 (70)	64	36	none
9		PhCl, 20 °C, light,[c] air	16.6 (15)	16.4 (15)	67 (70)	65	35	none
10[d]		PhCl, 20 °C, light,[c] air	19.5 (18)	20.5 (18)	60 (64)	65	35	none
11[d]		PhCl, 20 °C, light,[c] air	14 (13)	15 (13)	71 (84)	71	29	none
2 12		PhCl, 20 °C, dark, hydroquinone,[e] air	14.8	15.2	70			none

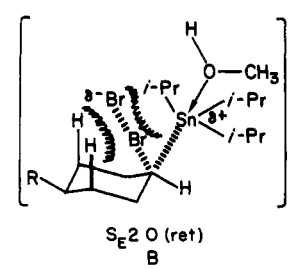
[a] Values obtained from capillary VPC examination. The values in parentheses were obtained from ^{13}C NMR examination and are based on the signal intensity of the carbon bearing the bromine. [b] The trialkyltin bromide distributions were derived from the integral of the respective ^{119}Sn NMR signal. [c] In daylight and irradiation with a fluorescent lamp. [d] The distribution of the alkyl bromides was largely unaltered when this reaction was performed in the dark. [e] The chlorobenzene solvent used in this experiment was the clear upper portion of a hydroquinone saturated solution. Air was passed through the solvent prior to addition of bromine.

attacking bromine and the axial 3,5 hydrogens, as well as the bulky triisopropyltin group. On the other hand, inversion entails displacement of the solvated $(i\text{-Pr})_3Sn$ group in an axial direction and nonbonded effects could be severe as well. On this basis, the predominant inversion for equatorial Sn bonds is understandable, in that departure is unimpeded, and, if there is stabilization gained from a tetrahedral → trigonal change around tin,[3,18] this is uninhibited also. *cis*-4-Methylcyclohexylstannane, as mentioned previously, requires treatment as a conformer equilibrium and use of data from items 1 and 4 for "fixed" equatorial and axial C–Sn bonds leads to a predicted ratio of 1.45 for *cis*-/*trans*-4-methylcyclohexyl bromide, which may be compared with the experimental value of 1.32.

On the very reasonable assumption, that the kinetics of bromodestannylation for bromine/methanol determined previously,[4] are applicable to the present cases, transition states for inversion and retention pathways can be formulated as A and B.



S_E2 O (inv)
A

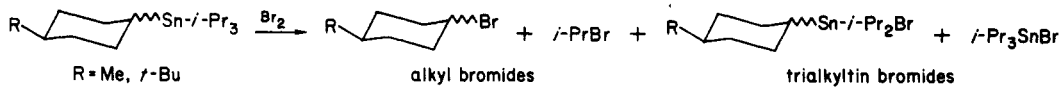


S_E2 O (ret)
B

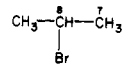
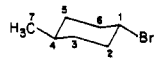
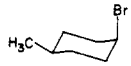
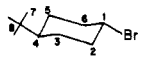
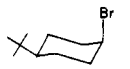
The nature of the groups of tin are known to exert a profound effect on stereochemistry.[3,7] With reaction conditions set, successive replacement of isopropyl with neopentyl promotes the inversion pathway. Thus with bromodestannylation of *s*-$BuSnR_3$, when R = isopropyl, 22% retention is observed, but this changes to net inver-

(18) Brown, H. C.; Berneis, H. L. *J. Am. Chem. Soc.* **1953**, *75*, 10.

Table IV. ^{13}C NMR Data for Alkyl Bromides Formed in the Brominolysis of *cis*- and *trans*-(4-Alkylcyclohexyl)triisopropylstannanes in Methanol or Chlorobenzene

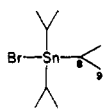
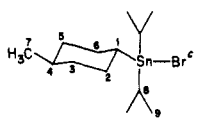
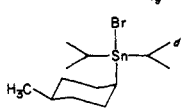
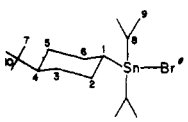
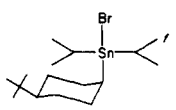


R = Me, *t*-Bu — alkyl bromides — trialkyltin bromides

alkyl bromide	$\delta(^{13}C)^{a,b}$ C1	C2,6	C3,5	C4	C7	C8
					28.93 [28.32]	46.13 [45.05]
	52.97 [52.01]	38.99 [38.35]	36.22 [35.86]	31.24 [31.18]	22.43 [22.47]	
	55.31 [54.23]	35.54 [34.58]	30.80 [30.31]	32.68 [31.65]	22.08 [21.88]	
	53.11 [52.30]	40.09 [38.91]	30.49 [28.67]	46.40 [46.63]	27.84 [27.38]	32.87 [32.35]
	55.99 [54.94]	36.27 [35.28]	22.77 [21.88]	48.04 [47.68]	27.88 [27.38]	33.11 [32.35]

[a] Referenced to either Me_4Si ($\delta(^{13}C)$ 0.0) or to CH_3OH ($\delta(^{13}C)$ 49.99 in methanol. [b] Values in brackets in chlorobenzene.

Table V. ^{13}C and ^{119}Sn NMR Characteristics for Trialkyltin Bromides Produced in the Reaction of *cis*- and *trans*-(4-Alkylcyclohexyl)triisopropylstannanes with Bromine in Methanol or Chlorobenzene

trialkyltin bromide	$\delta(^{119}Sn)^a$	$\delta(^{13}C)^b$ ($^2J(^{13}C-^{119}Sn$, Hz) C1	C2,6	C3,5	C4	C8	C9
	88.86 [116.7]					23.94 (357.42, 341.80) [21.41]	22.11 (17.58) [21.06]
	79.41 [104.8]	34.02 [32.18]	32.50 [31.42]	38.58 (73.27) [37.44]	34.95 [32.88]	23.78 (360.5, 342.9) [21.06]	22.08 (17.58) [21.41]
	97.49 [114.9]	36.48 [34.63]	29.34 [29.02]	35.89 (32) [35.22]	31.91 [31.42]	23.66 [21.35]	21.85 [21.88] [21.88]
	79.01 [104.8]	35.52 [32.82]	33.15 [32.00]	30.92 (74.22) [29.84]	49.52 [48.15]	23.67 (357.4, 339.8) [21.06]	22.11 (17.58) [21.41]
	109.5 [118.1]	36.93 [36.33]	28.70 [27.9]	31.86 (22.3) [30.95]	49.99 [48.50]	23.52 [22.17]	21.76 (15.63) [21.41]

[a] Referenced to TMT ($\delta(^{119}Sn)$ 0.0) in methanol. Values in brackets in chlorobenzene. [b] Referenced to Me_4Si ($\delta(^{13}C)$ 0.0) to CH_3OH ($\delta(^{13}C)$ 49.99) in methanol. Values in brackets in chlorobenzene. [c] $\delta(^{13}C)$ (C7) 23.47 (in MeOH), 23.05 (in PhCl). [d] $\delta(^{13}C)$ (C7) 22.79 (in MeOH), 21.88 (in PhCl). [e] $\delta(^{13}C)$ (C7) 27.88 (in MeOH), 27.38 (in PhCl); $\delta(^{13}C)$ (C10) 34.16 (in MeOH), 32.35 (in PhCl). [f] $\delta(^{13}C)$ (C7) 28.04 (in MeOH), 27.56 (in PhCl); $\delta(^{13}C)$ (C10) 33.42 (in MeOH), 32.59 (in PhCl).

sion (~65%) when R = neopentyl. This type of change has been ascribed predominantly to steric shielding of the frontside of carbon by the bulky ligands on tin, thus promoting rearward electrophilic attack. Jensen has drawn attention[3] to the fact that when R = isopropyl in *s*-$BuSnR_3$, the rate of the inversion process is nearly equal to the rate of the retention process, suggesting the use of this system for examining other factors that could influence the stereochemistry of S_E2 reactions. It is of interest that with cyclohexyltriisopropylstannanes, a similar closely balanced retention–inversion situation applies. It is thus of considerable interest to determine the stereochemical outcome with cyclohexylneopentylstannanes, and this study is planned.

A very limited study of brominolysis in acetonitrile was conducted (item 7) and a significant increase in selectivity was observed, in that isopropyl cleavage was now 93.5% (cf. 75% in methanol) and the preference for retention (54%) was reduced (from 60%). A similar trend has been reported for *sec*-butyltriisopropylstannane.[3]

Experimental Section

Compounds. The organostannanes employed in this work have been fully described in the accompanying paper, as have the cyclohexylbromides.

4-Methyl- and 4-*tert*-Butylcyclohexane-*1*-*d* and Propane-*2*-*d*. The procedure described below is typical: (4-methylcyclohexyl)magnesium bromide was prepared in anhydrous diethyl ether from *cis*-4-methylcyclohexyl bromide (12.4 g, 0.07 mol) and magnesium metal (1.95 g, 0.08-mol) in flame-dried glassware under a nitrogen atmosphere. A 1.6-g (0.08-Mol) sample of deuterium oxide (98% D) was dissolved in about 10 mL of diethyl ether and the mixture added slowly to the cooled (0 °C)

Grignard solution. The reaction mixture was stirred at room temperature for about 10 min after which a further 2.0 mL of deuterium oxide was added. The reaction mixture was extracted with diethyl ether, washed with water, dried ($MgSO_4$) and slowly concentrated by applying a mild vacuum. A crude oil (7.5 g) was obtained that was subsequently distilled. The first fraction (4.2 g, 60% yield) distilled at 101 °C and was shown to be pure trans (80%)/cis (20%) 4-methylcyclohexane-*1-d*.

4-*tert*-Butylcyclohexane-*1-d* was prepared in a similar fashion as a 75% trans/25% cis isomeric mixture from (4-*tert*-butylcyclohexyl)magnesium bromide and deuterium oxide in an overall yield of 80%. The observed boiling point was 169–170 °C (lit.[19] bp cis 171–172 °C, trans 170–171 °C).

Propane-*2-d* was also prepared via the Grignard procedure (isopropylmagnesium bromide and D_2O). The liberated gas was passed through two cold traps (−10 °C) to exclude ether vapour and then bubbled directly into a solvent mixture consisting of 8% TFA-*d*, 32% dioxane, and 60% chloroform.

^2H and ^{13}C NMR characteristics for the above deuterated hydrocarbons are contained in Table II.

Bromodestannylations. A typical procedure is described below. A 194-mg (5-mmol) sample of *cis*-(4-*tert*-butylcyclohexyl)triisopropylstannane was added to a 5-mL single-necked flask containing a small stirring bar and 1.0 mL of methanol. A 0.95-mL sample of a 0.5 M methanolic bromine solution (4.75 mmol of Br) was then added dropwise in the dark to the vigorously stirred (cooled 0 °C) tin solution from a micro dropping funnel over a period of ca. 10 min. Stirring (1 h at 0 °C and 12 h at room temperature) followed, after which a VPC and NMR examination of the total reaction mixture followed.

VPC determinations for bromodestannylation experiments were carried out on a Varian 3740 Capillary GC utilizing a flame ionization detector with an OV101 column (50 metres) with internal diameter 0.25 mm (manufacturers claim 200 000 theoretical plates for this column when new). Carrier gas employed was helium set at 30 lbs of pressure and detector gases were hydrogen (40 lbs) and oxygen (40 lbs); flow rate 0.6 mL/min. Temperature programming was as follows: initial column temperature 60 °C, held for 2 min after injection; column temperature was then increased at a rate of 6 °C/min to a final temperature of 180 °C which was maintained for 10 minutes before recycle was commenced.

Peak heights for alkyl bromides from reaction mixtures were converted to relative per cent after a minor response factor correction; response factors for each alkyl bromide, viz, *cis*- and *trans*-4-alkylcyclohexyl bromides (alkyl = Me, *t*-Bu) and isopropyl bromide, were determined from freshly prepared mixtures of authentic alkyl bromides of known concentrations.

At the completion of each brominolysis experiment approximately two drops of the reaction mixture was added to 1 mL of carbon disulfide; after thorough mixing, 1 μL of the CS_2 solution was then injected into the GC (injections were carried out three times for each sample).

A typical procedure is described below. A 116-mg (mmol) sample of *cis*-(4-*tert*-butylcyclohexyl)triisopropylstannane was accurately weighed into a small screw cap bottle into which was then added 345 mg (5%) of freshly prepared CF_3COOD/dioxane solution (6 mmol of CF_3COOD), prepared by dissolving 0.80 g of TFA-*d* in 3.20 g of dioxane. The organostannane–acid solution was transferred into an ampule under a stream of nitrogen; the ampules were then sealed, wrapped in aluminium foil, and placed in an air oven maintained at 100 °C (±2 °C). Usually, three such reaction mixtures were prepared for each tetraalkylstannane and examined after 2, 4, or 12 days. At the appropriate time, ampules were withdrawn from the oven and cooled (0 °C) and reaction mixtures transferred to 10-mm NMR tubes. At this stage, it was necessary to add 0.5 mL of anhydrous chloroform to the reaction mixture for purposes of increasing the volume to the appropriate level for 10-mm NMR tubes. Control experiments indicated that the use of chloroform in this way had no noticeable effect on product distributions.

After 12 days at 100 °C, the reaction mixtures exhibited no signs of decomposition and reactions were judged to be about 80% complete (roughly estimated by consideration of the ^{119}Sn NMR signal integrals of the combined trialkyltin trifluoroacetates and unreacted tetraalkylstannanes). Even under the rather harsh conditions employed for these acid cleavage reactions, degenerate redistribution processes were not in evidence since all reaction mixtures consistently provided only three ^{119}Sn NMR resonances, viz, two signals corresponding to the alkyltin trifluoroacetates and one signal for starting material.

Tetramethyltin (TMT) and tetramethylsilane (Me_4Si) were not employed as NMR reference materials for ^{119}Sn and ^{13}C NMR spectra (respectively) since both these compounds react with unconsumed CF_3COOD. Signals in ^{119}Sn NMR spectra were referenced to the resonance of unreacted tetraalkylstannane, and it was unambiguously demonstrated that the stereochemistry of the starting stannane was unaltered by comparison of original ^{119}Sn NMR spectra of reaction mixtures with the ^{119}Sn NMR spectra of reaction mixtures that were intentionally spiked with the isomer of opposite configuration. ^{13}C NMR spectra were referenced to the sharp, 1,4-dioxane singlet (δ (^{13}C) 67.14) while ^2H NMR signals were referenced to added two drops) deuteriochloroform (δ (^2H) 7.24). Unfortunately, signal overlap in the ^{13}C NMR spectra precluded an estimation of the relative proportions of hydrocarbons and alkyltin trifluoroacetates. However, ^{13}C NMR spectra confirmed the presence of all reaction products. NMR spectra were acquired as described in the preceding paper.

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Registry No. CF_3COOD, 599-00-8; CH_3CHDCH_3, 20717-74-2; *i*-$Pr_3SnOCOCF_3$, 91312-01-5; *i*-PrBr, 75-26-3; *i*-Pr_3SnBr, 19464-54-1; *trans*-4-methylcyclohexane-*1-d*, 75768-10-4; *cis*-4-methylcyclohexane-*1-d*, 75768-09-1; *trans*-4-*tert*-butylcyclohexane-*1-d*, 17553-36-5; *cis*-4-*tert*-butylcyclohexane-*1-d*, 53042-76-5; *trans*-(4-methylcyclohexyl)triisopropylstannane, 82544-63-6; *cis*-(4-methylcyclohexyl)triisopropylstannane, 82544-62-5; *trans*-(4-*tert*-butylcyclohexyl)triisopropylstannane, 83802-06-6; *cis*-(4-*tert*-butylcyclohexyl)triisopropylstannane, 83802-07-7; *trans*-(4-methylcyclohexyl)diisopropylstannyl trifluoroacetate, 91311-97-6; *cis*-(4-methylcyclohexyl)diisopropylstannyl trifluoroacetate, 91311-98-7; *trans*-(4-*tert*-butylcyclohexyl)diisopropylstannyl trifluoroacetate, 91311-99-8; *cis*-(4-*tert*-butylcyclohexyl)diisopropylstannyl trifluoroacetate, 91312-00-4; *trans*-4-methylcyclohexyl bromide, 28046-91-5; *cis*-4-methylcyclohexyl bromide, 5009-37-0; *trans*-4-*tert*-butylcyclohexyl bromide, 28046-90-4; *cis*-4-*tert*-butylcyclohexyl bromide, 5009-36-9; *trans*-(4-methylcyclohexyl)diisopropylstannyl bromide, 91312-02-6; *cis*-(4-methylcyclohexyl)diisopropylstannyl bromide, 91312-03-7; *trans*-(4-*tert*-butylcyclohexyl)diisopropylstannyl bromide, 91312-04-8; *cis*-(4-*tert*-butylcyclohexyl)diisopropylstannyl bromide, 91312-05-9; 4-*tert*-butylcyclohexyl bromide, 7080-86-6.

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