Journal of Organometallic Chemistry, 159 (1978) 255—278

SELECTIVE SYNTHESES AND REACTIONS OF EPOXY-, HYDROXY-, AND KETO-SUBSTITUTED CYCLOHEXYLTRIPHENYLTIN COMPOUNDS *

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(Received April 4th, 1978)

Summary

The epoxidation of cyclohex-3-enyltriphenyltin gave a 40/60 mixture of *cis*- and *trans*-3,4-epoxycyclohexyltriphenyltin. The reaction of the *cis*- and *trans*-epoxides, separately with lithium aluminum hydride, gave *cis*-3-hydroxycyclohexyltriphenyltin (>99%) and *trans*-3-hydroxycyclohexyltriphenyltin (100%) respectively. Hydroboration (BH_3) followed by basic oxidation of cyclohex-3-enyltriphenyltin gave *cis*-3-hydroxy- (~42%), *trans*-3-hydroxy- (~42%) as well as *trans*-4-hydroxy- (~12%) and *cis*-4-hydroxy-cyclohexyltriphenyltin (~4%).

The attempted epoxidation of cyclohex-2-enyltriphenyltin gave only destannylation products due to the reactivity of allylic organotin compounds under electrophilic reaction conditions. Alternative hydroboration-oxidation of the allylic organotin compound also gave destannylation as well as 3- and 4-hydroxycyclohexyltriphenyltin compounds from rearrangement of the allylic to the homoallylic cyclohexenyltriphenyltin compound.

Epoxidation of cyclohex-1-enyltriphenyltin gave 1,2-epoxycyclohexyltriphenyltin, which upon reaction with lithium aluminum hydride, gave destannylated compounds arising from hydride attack at C(2) and elimination of cyclohexanone and triphenyltin anion.

cis-2-Methoxycyclohexyltriphenyltin was prepared stereospecifically by reaction of *trans*-1-bromo-2-methoxycyclohexane with triphenylstannylsodium, while the *trans*-2-hydroxycyclohexyltriphenyltin was also prepared in a stereospecific manner by reaction of *cis*-cyclohexene epoxide with triphenylstannylsodium.

A discussion of these reactions as well as the reactivity of all the substituted

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* Presented in part at the 172nd National Meeting of the American Chemical Society August 29—September 3, 1976, San Francisco, CA (U.S.A.), INOR 99 and at the Eighth International Conference on Organometallic Chemistry Sept. 12—16, 1977 Kyoto, Japan, Abstract 5A08. For a preliminary communication see Ref. 1.

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cyclohexyltriphenyltin compounds with electrophilic reagents and their gas phase protonolysis reactions via chemical ionization mass spectroscopy will be presented.

Introduction

While the number of organotin compounds that have been synthesized is substantial, it is particularly surprising to find that this fact does not extend to carbon-substituted cyclohexyltin compounds [1,2a—e]. Our interest in this area stemmed from the need to have available specific *cis*- and *trans*-hydroxycyclohexyltin derivatives for the biological oxidation studies we were conducting with cyclohexyltin compounds [3a—d]. After surveying the literature, we were further surprised to find that studies similar to those reported on the regio- and stereo-selectivity of metal hydride ring openings with alkyl-substituted cyclohexene epoxides [4a—d] as well as on the hydroboration-oxidation of alkyl- and trimethyl-silicon-substituted cyclohexenyl compounds [5a,b,11] had not been attempted with the corresponding organotin-substituted compounds [1].

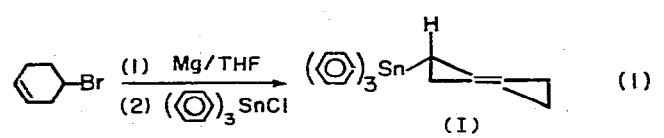
In this paper we wish to present results on the above-mentioned reactions with triphenyltin substituted derivatives and report on other selective reactions used to synthesize *cis*- and *trans*-2,3 and 4-hydroxycyclohexyltriphenyltin compounds. The reactivity of the hydroxycyclohexyltriphenyltin and all the other substituted cyclohexyltriphenyltin compounds with electrophilic reagents as well as their gas phase protonolysis reactions using chemical ionization mass spectrometry will also be presented.

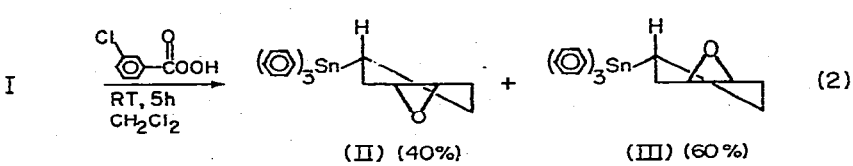
Results

Olefin epoxidation-metal hydride ring opening

Our approach was to prepare all of the possible cyclohexenyltriphenyltin isomers and study the epoxidation-lithium aluminum hydride ($LiAlH_4$) ring openings in order to discern the regio and stereoselectivity involved and then compare the results to those found for the corresponding alkyl-substituted cyclohexenyl compounds.

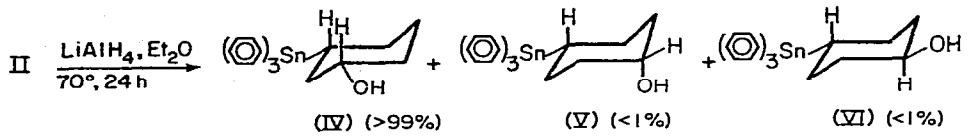
Cyclohex-3-enyltriphenyltin (I) which was prepared in 30% yield by reaction of cyclohex-3-enylmagnesium bromide with triphenyltin chloride (eq. 1), was treated with *m*-chloroperbenzoic acid to give a 90% yield of two epoxides (40/60), II and III (eq. 2). Fortunately, we were able to separate epoxides II and III





by preparative thin-layer chromatography (TLC) and study the reaction of $LiAlH_4$ with each epoxide.

The results from the $LiAlH_4$ reactions allowed one useful method for assigning the stereochemistry to each epoxide. Thus, II reacts with $LiAlH_4$ in diethyl ether (sealed tube, 70°C) to give in a highly regio and stereospecific manner *cis*-3-hydroxycyclohexyltriphenyltin (IV) (>99%) and a trace (<1%) of *cis*- and *trans*-4-hydroxycyclohexyltriphenyltin (V and VI) (40 and 60%) (eq. 3). The



(3)

stereochemistry of IV, V and VI was primarily based on their 360 MHz ^1H FT NMR spectra (Table 1) and comparison to compounds of known stereochemistry. Compound IV had a 360 MHz NMR spectrum ($CDCl_3$, TMS) with a multiplet at 3.93 ppm, which was assigned to the methine proton bearing the hydroxyl

TABLE 1

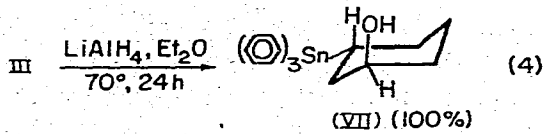
^1H NMR SPECTRAL DATA FOR COMPOUNDS I—XIX [a,i]

I [b]	2.06 (CH_2)(bm) [e], 2.43 (bm) (CH_2—C=), 5.68 (C=C), 7.43 (Ph)
II [d]	1.24 (H—C—Sn), 1.72 (m) [e], 1.86 (m), 2.08 (m), 2.30 (m), 3.11 (Singlet), 3.15 (m, J(H—H) 4.7, 1.6), 7.34, 7.53 (Ph)
III [d]	1.55 (H—C—Sn), 1.89 (m), 2.13 (m), 2.44 (m) 3.06 (, Singlet), 7.36, 7.5 (Ph)
IV [d]	1.23 (H—C—Sn), 1.53 (m) 1.64 (m), 1.85 (m), 2.02 (m), 2.15 (m), 3.93 (H—C—OH, bw [f] 36 Hz; J_{ax}—J_{ax} 8.7; $J_{ax\text{-}eq}$ 3.2)
V [d]	1.24 (H—C—Sn), 1.66 (H_{2a}) [g], 1.81 (H_{2e}), 2.02 (H_{3a}), 2.17 (H_{3e}), 3.73 (H—C—OH, bw 16 Hz), 7.36 7.5 (Ph)
VI [d]	1.24 (H—C—Sn), 1.66 (H_{2a}), 1.81 (H_{2e}), 2.02 (H_{3a}), 2.17 (H_{3e}), 3.54 (H—C—OH; Nonet: J_{ax}—J_{ax} 11.1; J_{ax}—J_{eq} 4.0), 7.36, 7.5 (Ph)
VII [d]	1.24 (H—C—Sn), 1.46—1.64 (m), 1.74 (m), 2.0 (m), 3.91 (H—C—OH, bw 23 Hz; $J_{ax\text{-}eq}$ 3.2)
VIII [b]	1.5—2.87 (CH_2), 7.25 (Ph)
IX [b]	2.0—2.5 (CH_2), 7.37 (Ph)
X [b]	1.75 (CH_2—)C=2.15 (CH_2), 2.95 (Sn—C—H), 5.6, 6.05 (C=C) 7.25—7.95 (Ph)
XI [b]	1.44 (CH_2), 1.66 (CH_2), 2.08 (CH_2—C=), 2.29 (CH_2—C=C), 5.98 (C=C ; $J_{117,119}$ Sn—H 54, 56 Hz)
XII [d]	1.24 (H—C—Sn), 1.47 (m), 1.92 (m), 2.06 (m), 2.33 (m), 3.18 (; $J_{117,119}$ Sn—H 54, 56 Hz), 7.56 7.37 (Ph)
XIII [d]	1.1 (H—C—Sn), 1.28 (4a, e), 1.62 (5a, e), 1.76 (6e), 1.90 (3a), 2.02 (6a), 2.11 (3e), 3.68 (H—C—OH J_{ax}—J_{ax} 10.1, J_{ax}—J_{eq} 3.67, bw 40 Hz), 7.33 7.56 (Ph)
XV [c]	1.12—2.2 (CH_2), 2.99 (OCH_3), 3.48 (H—C—O, bw 13 Hz), 7.32 7.54 (Ph)
XVII [b]	1.0—2.0 (CH_2), 3.9 (H—C—OH, bw 20 Hz), 7.2—7.6 (Ph)
XVIII [b]	1.0—2.0 (CH_2), 3.68 (H—C—OH, bw 30 Hz), 7.2—7.6 (Ph)
XIX [b]	1.2—2.3 (CH_2), 3.6 (H—C—OH, bw 27 Hz), 7.2—7.8 (Ph)

[a] $CDCl_3$, TMS, values in ppm. [b] 90 MHz. [c] 100 MHz. [d] 360 MHz. [e] Multiplet, m; broad multiplet, bm; [f] Band width, bw. [g] 2a, axial proton, C(2). [h] 3e, equatorial proton, C(3). [i] All compounds gave the correct integrations for the designated protons.

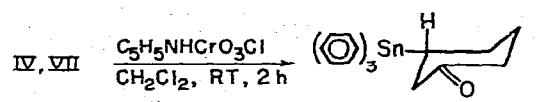
group. The coupling pattern for this multiplet reveals that an interesting conformational process is present and that a 1,3-diaxial interaction of the hydroxyl and the tin atom seems to be responsible for this fluxionality. While the 1,3-diequatorial conformer is predominant and is thermodynamically more stable, this Sn ← O interaction could lower the activation energy for ring flip [6]. Consistent with this result is the fact that similar interactions of the epoxide oxygen and the tin atom are responsible for the stereochemistry in eq. 3. This point will be discussed more fully later in the paper.

The corresponding *trans*-epoxide (III) reacts with $LiAlH_4$, under similar conditions, to give exclusively *trans*-3-hydroxycyclohexyltriphenyltin (VII) (eq. 4). The 360 MHz ^1H NMR spectrum gives a multiplet at 3.91 ppm and again from

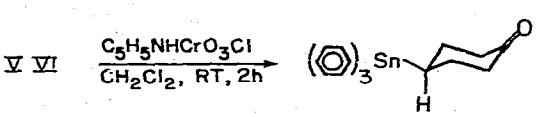


(VII) (100%) (4)

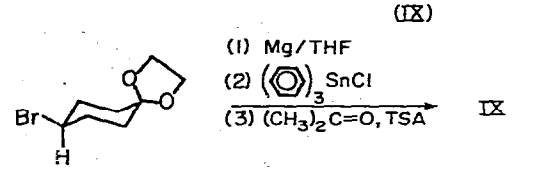
coupling and low temperature NMR experiments compound VII is also fluxional with the predominant conformation as shown. The assigned position of the hydroxyl group in IV, VII and V, VI was further ascertained by oxidation to the ketones VIII, and IX, one of which, IX, was prepared in an unequivocal fashion (eqs. 5—7). It was of interest in the formation of compound IV to ascertain



(VIII) (5)



(IX) (6)



IX (7)

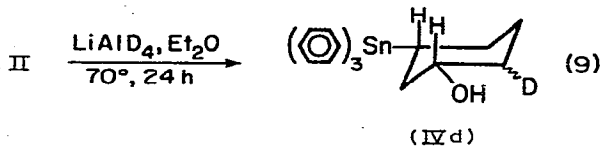
whether the corresponding ketone, compound VIII, was an intermediate in the ring opening reaction with $LiAlH_4$ (eq. 2). Since the result for this reaction was quite unexpected with regard to the regiochemistry shown, and in fact opposite to that found for the corresponding *cis*-3,4-epoxy-4-t-butylcyclohexane *, we decided to do two experiments. Reduction of VIII with $LiAlH_4$ gave predominantly compound IV (>95%) with a small amount of VII (<5%) (eq. 8). Thus

VIII $\xrightarrow{LiAlH_4}$ IV (>95%) + VII (<5%) (8)

to provide definitive information concerning the intermediacy of VIII in the ring opening reaction of II to IV, we repeated the latter reaction with lithium alumi-

* This epoxide was found to give predominantly *cis*-4-hydroxy-t-butylcyclohexane [4a].

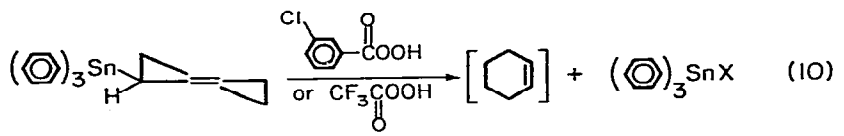
num deuteride ($LiAlD_4$). If the ketone was the intermediate in the ring opening of II, then two deuteriums would be incorporated, while only one deuterium if



(IVd)

no ketone was formed (eq. 9). Our results confirm that II ring opens to IVd with $LiAlD_4$ without going through VIII since only one deuterium was found, by chemical ionization mass spectrometry, to be incorporated into the product (see Experimental section).

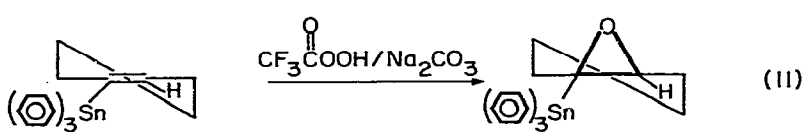
To further extend our synthetic scheme to *cis*- and *trans*-2-hydroxycyclohexyltriphenyltin compounds, we attempted to epoxidize the allylic isomer of I, cyclohex-2-enyltriphenyltin (X). Unfortunately, we only observed an electrophilic cleavage reaction giving the triphenyltin derivative and presumably cyclohexene (eq. 10). This is consistent with the reactivity of allytin compounds [7],



(X)

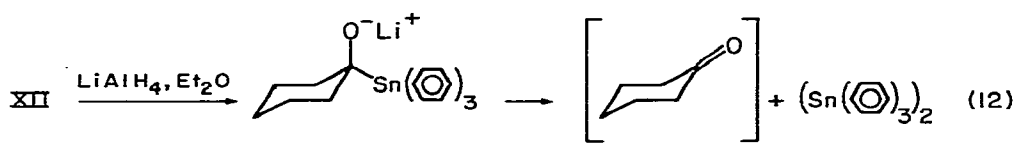
since considerable positive charge on the carbon β to the tin—carbon σ bond is being generated in the transition state. This leads to σ—π interactions and rapid elimination of the triphenyltin cation.

We were able to prepare the vinyl analog of I, cyclohex-1-enyltriphenyltin (XI) and successfully epoxidize it with pertrifluoroacetic acid [76,8] (eq. 11). Com-



(XI) (XII)

pound XII reacted with $LiAlH_4$ in a highly regiospecific reaction to give an intermediate oxyanion that went on to eliminate the triphenyltin anion and eventually gave hexaphenylditin as the only tin containing product (eq. 12). No attempt



was made to identify the carbon fragment, but we looked for the occurrence of any *cis*-2-hydroxycyclohexyltriphenyltin and none was found.

Hydroboration-oxidation

The alternative method for the preparation of hydroxycyclohexyltin compounds is through the use of the hydroboration-oxidation reaction procedure.

TABLE 2

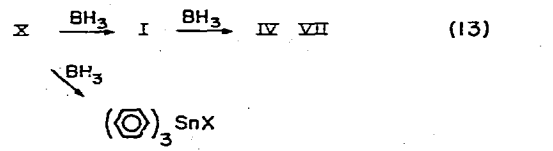
HYDROBORATION-OXIDATION OF I[a]

Compound	~%		~*cis*/*trans* C(3)	~*cis*/*trans* C(4)
IV	42 (32)[b]	(24)[c]	1 (1.6)[b]	(.5)
VII	42 (20)	(49)		
V	4 23	(?)		0.3 (0.9)[b] (~0)[c]
VI	12 (25)	(25)		

[a] Diborane in THF at 25°C for 24 h followed by oxidation with alkaline hydrogen peroxide. [b] This value in parentheses represents that formed with t-butylcyclohex-3-ene [5a]. [c] Represents that formed with cyclohex-3-enyltrimethylsilicon [11].

In this regard, we studied the hydroboration of compound I (Table 2) with diborane and found this procedure gives compounds IV—VII in ~42, 4, 12 and 42%, respectively.

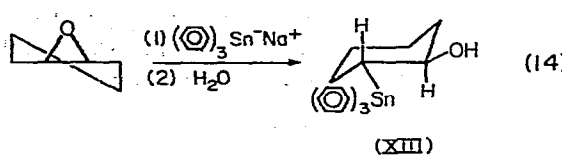
Unfortunately, attempts to hydroborate compound X lead only to isomerization to compound I and elimination reactions (eq. 13). No 2-hydroxycyclo-



hexyltin compounds were formed. Only products IV—VII which must emanate from I were produced.

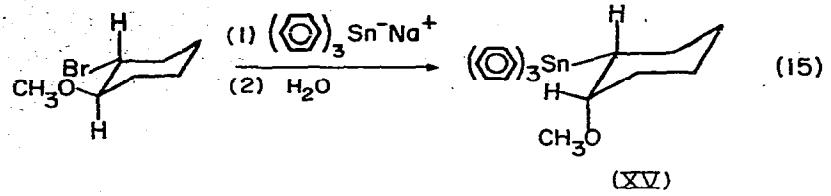
Triphenylstannylsodium reactions

The stereospecific reactions of triphenylstannylsodium with acyclic epoxides and alkyl halides have been previously studied [9a,b]. However, the reaction of this reagent was not attempted with a cyclic epoxide [1]. Thus, reaction of triphenylstannylsodium with *cis*-cyclohexene epoxide gave, with inversion of configuration, *trans*-2-hydroxycyclohexyltriphenyltin XIII (eq. 14). The *trans*-stereochemistry was established by 360 MHz ^{1}H NMR spectroscopy (3.68 ppm,



band width 35 Hz) and this result is consistent with that recently obtained with trimethylstannylsodium and *cis*-cyclohexene epoxide [2e].

In previous attempts to prepare *cis*-2-hydroxycyclohexyltriphenyltin (XIV, eq. 13), we were, unfortunately, not successful. It was shown that the cobalt(I) anion reacted with *trans*-1-bromo-2-methoxycyclohexane, with total inversion of configuration, giving a *cis*-2-methoxycyclohexylcobalt derivative [10]. We repeated this reaction with triphenylstannylsodium and the only tin product we obtained was *cis*-2-methoxycyclohexyltriphenyltin (XV) by strictly inversion of configuration (eq. 15). Any elimination products, such as cyclohexene, that

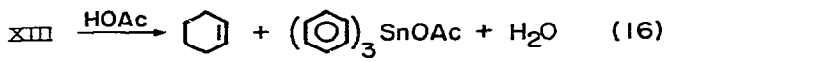


(15)

(XV)

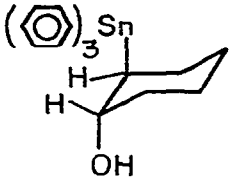
might have been produced in this reaction were not identified but are known to occur [2e].

The *cis*-stereochemical assignment for XV was based on its 100 MHz ^{1}H NMR spectrum which notably gave a narrow multiplet (13 Hz) at 3.48 ppm. The methoxyl singlet at 2.99 ppm was also accompanied by a smaller singlet at 3.07 ppm, which we at first thought was due to the *trans*-isomer of XV. However, after comparing the reactivity of both compounds XIII and XV with glacial acetic acid, we decided that the small singlet at 3.07 ppm is probably due to a ring inversion process that is occurring with XV. Thus, compound XIII reacted instantaneously with glacial acetic acid to give cyclohexene and triphenyltin acetate (eq. 16) as one would expect for a *trans*-2-hydroxycyclohexyltin compound



(16)

that could assume the *trans*-diaxial conformation (XVI) in the transition state. This result is also consistent with the corresponding *trans*-2-hydroxycyclohexyl-



(XVI)

trimethylsilicon compound, which also reacts instantaneously with dilute acid to provide cyclohexene [11].

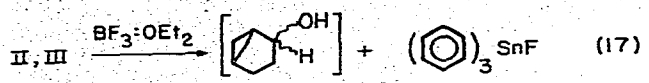
Alternatively, reaction of XV with glacial acetic acid gave no discernable cyclohexene even after 3 days and is totally consistent with a *cis* orientation of both the triphenyltin and methoxyl groups, i.e., a *trans* diaxial conformation such as XVI is not possible with compound XV.

Consequently, the possibility of a slow ring inversion giving the predominant equatorial tin (XV) conformer might be involved to explain the presence of the small singlet at 3.07 ppm. This ring inversion will be discussed in more detail in a future publication [6].

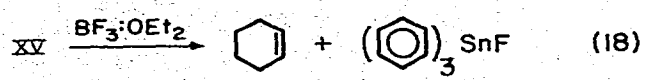
Reactivity of oxygen substituted cyclohexyltriphenyltin compounds in solution and the gas phase

It was of interest to ascertain whether various electrophilic reagents could react with the epoxides, alcohols, etc., that we just described without causing a loss of triphenyltin group. Compounds II and III were treated with boron trifluoride etherate with instantaneous loss of the triphenyltin group. Although we

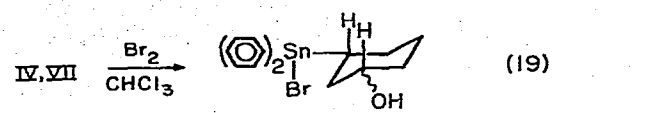
did not identify the carbon product, we assume that loss of the triphenyltin group emanates from boron trifluoride attack on the epoxide oxygen followed by cyclodestannylation as previously observed with 3,4-epoxybutyltin derivatives [12a,b] (eq. 17).



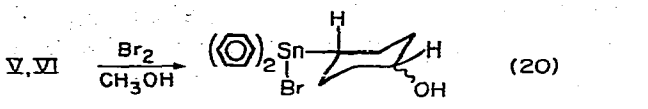
Similarly, reaction of compound XV with boron trifluoride etherate gave cyclohexene and a triphenyltin derivative (eq. 18).



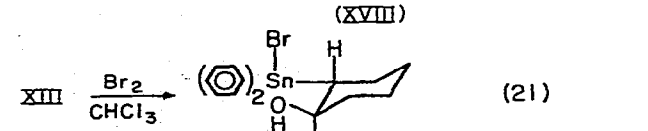
Bromination of compounds IV, VII and V, VI gave the corresponding 3- or 4-hydroxycyclohexyldiphenyltin bromides (XVII and XVIII) in good yields (eqs. 19, 10), while similar results with XIII also gave the corresponding bromide, XIX (eq. 21).



(XVII)

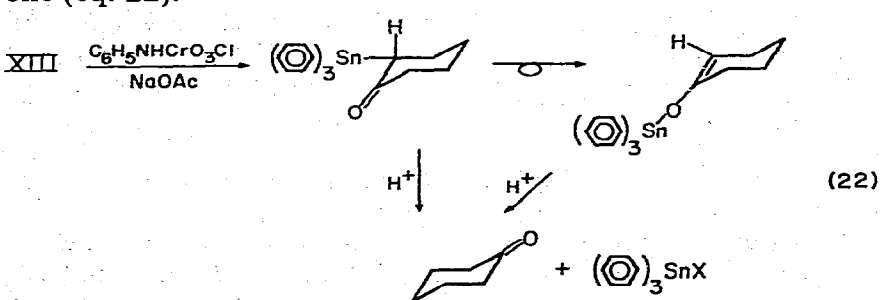


(XVIII)



(XIX)

As stated previously, oxidation of the *cis*- and *trans*-3- or -4-hydroxycyclohexyltriphenyltin compounds (IV, VII and V, VI) to their common ketones (VIII and IX) was conveniently carried out with pyridium chlorochromate (eqs. 5 and 6). However, similar attempts to oxidize *trans*-2-hydroxycyclohexyltriphenyltin (XIII) to the corresponding 2-keto derivative gave instead cyclohexanone (eq. 22).



We have been interested in the gas phase protonolysis reactions of organotin

TABLE 3

CHEMICAL IONIZATION MASS SPECTRA OF SUBSTITUTED CYCLOHEXYLTIN COMPOUNDS

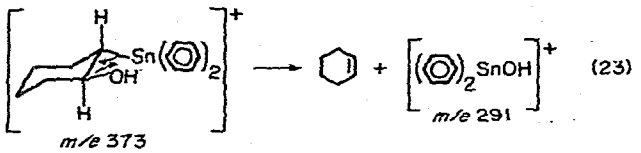
Compound	A Isobutane B Methane	*m/e* (relative intensity) [a]				
		$[Ph_3Sn]^+$	$[M\text{-}Ph]^+$ [b]	$[M+1]^+$	$[Ph_2SnOH]^+$	Other ions
I	A	351(68)	355(100)			
	B	351(77)	355(33)			
II	A	351(100)	371(23)			
	B	351(47)	371(33)			
III	A	351(100)		449(83)		
	B	351(70)	371(33)	449(7.4)		
IV	A	351(26)	373(33)			
	B	351(63)	373(33)	451(6)		
V and VI	A	351(100)	373(10)			
VII	A	351(100)	373(14)			
	B	351(100)	373(29)		291(17)	
VIII	A	351(8)	369(100)	447(6)		
	B	351(35)	369(33)	447(6)		
IX	A	351(100)	369(56)			
	B	351(41)	369(32)			
X	A	351(100)	355(40)			
	B	351(100)	355(70)	433(28)		
XI	A	351(100)	355(77)			
XII	A	351(100)	371(10)			
XIII	A	351(42)	373(33)			431(8, $[M-17]^+$)
	B	351(63)	373(33)		291(21)	431(4, $[M-17]^+$)
XV	A	351(20)	387(33)			
	B	351(15)	387(50)			305(12, $[Ph_2SnOCH_3]^+$)
XVII	A		375(16)			373(100, $[M-Br]^+$)
XVIII	B					353(100, $[Ph_2SnBr]^+$)
XIX	A		375(38)			353(96); 373 (60, $[M-Br]^+$)
IVd	B		374(33) [c]			

[a] Total ion current based on ^{120}Sn isotope. [b] Normalized for three phenyl groups. [c] Incorporation of one deuterium.

compounds [13a—13c] and wanted to see whether the various stereoisomers, i.e., compounds II—VII showed significant differences in their chemical ionization mass spectra. The reagent gases methane and isobutane were utilized to see if a selectivity prevailed upon lowering the exothermicity of the proton transfer reaction.

Analysis of the methane and isobutane CIMS of compounds II and III revealed dramatic differences between the two compounds (Table 3). For instance, with methane as the reagent gas, electrophilic cleavage (CH_5^+) of II gave the triphenyltin ion (*m/e* 351, 47%) and the 3,4-epoxycyclohexyldiphenyltin ion (*m/e* 371, 33%), while isobutane ($(CH_3)_3C^+$) provided these two ions in 100 and 23% (relative abundances), respectively. In contrast to this result, compound

III with methane gave ions *m/e* 351 (70%), *m/e* 371 (33%), and a quasimolecular *M* + 1 ion at *m/e* 449 (7%), while with isobutane the *m/e* 351 ion (100%) was evident and the *m/e* 371 ion was absent. More importantly, the quasimolecular *M* + 1 ion, *m/e* 449, had a relative abundance of 83%. This latter result provides added confirmation for the assignment of the stereochemistry of II as *cis*-epoxide and III as the *trans*-epoxide. This point will be elaborated on in the discussion section. The various *cis*- and *trans*-2,3- and -4-hydroxycyclohexyltin compounds (IV—VII) were not as distinct in their reactivity; however, some interesting reactions took place. Notably, the *trans*-2-hydroxycompound (XIII) with methane, gave ions at *m/e* 351 (63%), 373 (33%), 431 (4%) and 291 (21%). The latter we postulate is derived from a rearrangement of the hydroxyl group to the tin cation (eq. 23). Compound XV also showed a similar rearrange-



(23)

ment but in lower relative abundance, *m/e* 305 (11.5%), for the methoxydiphenyltin cation. The *cis*-3- and *trans*-3-hydroxy compounds IV and VII also provided some differences. For example, the methane CIMS of IV gave ions at *m/e* 351 (63%), 373 (33%) and 451 (6%), with the latter ion being the *M* + 1 quasi-molecular ion. Compound VII had ions at *m/e* 351 (100%), 373 (29%) and 291 (17%) with methane. This latter ion with VII is the hydroxydiphenyltin cation which must be formed by a rearrangement of hydroxyl to tin. This ion, however, is not present in the CIMS of IV and reflects the stereochemical differences between the two isomers.

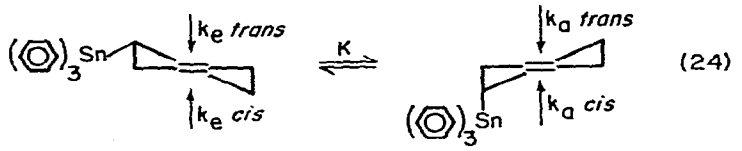
Since compounds V and VI could not be separated, no interpretation of their spectrum will be attempted. Interestingly, the ketones from IV, VII and V, VI, compounds VIII and IX, had different spectra with methane as the reagent gas. Thus with VIII, ions at *m/e* 351 (35%), 369 (33%) and 447 (6%) [*M* + 1] were evident, while IX had only the *m/e* 351 and 369 ions with relative abundance of 41 and 100%, respectively.

The olefins, compounds I, X and XI, gave results as expected with loss of the phenyl group (*m/e* 355) and loss of the cyclohexenyl group (*m/e* 351) as the only ions formed (Table 3). Both X and XI gave the triphenyltin cation as the base ion (*m/e* 351, 100%) while I gave the $M - C_6H_5$ (*m/e* 355, 100%) as the base ion, reflecting the differences between the allylic and vinyl isomers (X and XI) and that of the homoallylic I in their reactivity in gas phase electrophilic cleavage reactions [7].

Discussion

A comparison of the results of compounds I and II, III in the epoxidation and $LiAlH_4$ ring opening reactions with the 4-alkyl-substituted cyclohexenyl derivatives [4a,d] would be informative in order to ascertain the role of the triphenyltin group in these selective transformations.

The epoxidation of I gave compounds II and III in a ratio of 40 to 60% * showing a predominance of *trans*-epoxide. This can be rationalized by the fact that the conformational preference of groups attached to a cyclohexene ring in the 4 position [14] (we designate the triphenyltin as I in our nomenclature) are less selective than the cyclohexane system. Since the *A* value for a triphenyltin group on a cyclohexyl ring was found to be ~1.5, then that for cyclohex-3-enyltriphenyltin (designated as E_4 by Jensen and Bushweller) should be considerably lower. This means that the quasi-axial conformer should be more pronounced making the transition state for *cis*-epoxidation less favorable overall than that for *trans*-epoxidation (eq. 24).



(24)

where k_e *cis* ≈ k_e *trans* ≈ k_a *trans* ≫ k_a *cis*

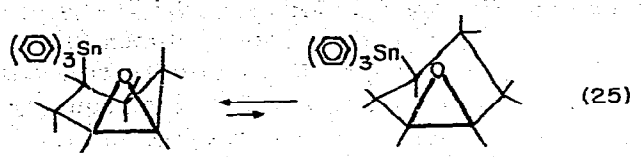
These arguments were used by Rickborn and Lwo [4c] to explain the decreased rates in *cis*- versus *trans*-epoxidation with alkyl-substituted cyclohexene derivatives. Additionally, the longer carbon—tin bond length, 2.18 Å versus 1.54 Å for the carbon—carbon bond also strengthens the argument for greater conformational flexibility than in either the t-butyl or methyl analogs. This is borne out by the fact that t-butylcyclohex-3-ene gives an ~60/40 ratio of *cis*- to *trans*-epoxide [4a], while the methylcyclohexene analog gives a 46/54 *cis* to *trans* ratio [4c].

From the results obtained by Rickborn and Lwo [4c], the approximate E_4 value for the triphenyltin group in I, based on the 60% *trans*-epoxide and an equatorial population of ~60%, is ~0.24. Thus, even though this is a purely qualitative estimate of the E_4 value for the triphenyltin group, it does reflect the large axial population present in I.

The ring opening reaction with $LiAlH_4$ for II and III can also be compared to their alkyl-substituted analogs. We will assume that the diaxial ring opening reaction is prevalent with II and III as shown by Rickborn et al. [4a]. Interestingly enough, compound II gives the equatorial not the axial product. If one compares this to the corresponding methyl and t-butyl compounds, then the letter results are diametrically opposite. Accordingly, the t-butyl or methyl derivatives gave *cis*-4-hydroxyalkylcyclohexane derivatives, while II gave predominantly (>99%) *cis*-3-hydroxycyclohexyltriphenyltin (IV). We attempted to rationalize this result by a conformational difference between II and the corresponding alkyl analogs. Specifically, interaction of the epoxide oxygen and the tin atom could account for a pronounced diaxial half chair conformation which, if rate

* In our preliminary communication [1] we stated a ratio of 50/50 for II/III based on preparative TLC isolation and correction for errors using this method. However, the more accurate ratio, as reported, is now based on a ^{119}Sn NMR spectrum (37.317 MHz) of II and III with shifts based on tetramethyltin of —115.37 ppm and —108 ppm, respectively. The area of each signal normalized to 100% gave the 40/60 ratio for II/III.

determining in the ring opening, could account for the observed result. Analysis of low temperature ^{1}H and room temperature ^{119}Sn NMR spectra of II as well as coupling constants of the product reflect the possibility of Sn ← O interaction in both epoxide II and *cis*-3-alcohol IV [6] (eq. 25 and 26).



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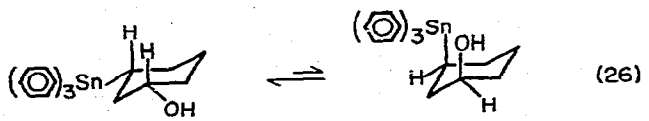

(26)

Reaction of $LiAlH_4$ with conformer A would give *cis*-3-alcohol via a diaxial ring opening mechanism. The latter postulate was further strengthened by the following results. The ketone VIII was eliminated as a precursor to compound IV by reaction of II with $LiAlD_4$ giving incorporation of only one deuterium per molecule of IV (eq. 9), while on the other hand, the corresponding *trans*-epoxide III gave a result similar to the alkyl-substituted *trans*-epoxide, i.e., the *trans*-3-alcohol was produced.

The epoxidation of the allyl derivative X failed, but interestingly, the vinyl derivative XI reacted with pertrifluoroacetic acid to give epoxide XII. We were somewhat surprised that epoxidation rather than destannylation occurred in this reaction. Presumably, the tin—carbon σ electrons are orthogonal to any positive charge developed in the epoxidation transition state precluding destannylation. It was hoped that XII would be the precursor to *cis*-2-hydroxycyclohexyltriphenyltin. However, the regiochemistry in the $LiAlH_4$ reaction was opposite to that recently reported for the corresponding trimethylsilicon derivative [15], but consistent with alkyl-substituted derivatives [4d] of XII; that of hydride attack at the least-substituted 2 position to give the 1-oxycyclohexyltriphenyltin anion intermediate (eq. 12). One obvious difference between a trimethylsilicon and a triphenyltin group could be steric in origin, where we would assume the longer tin—carbon bond would place the latter group further from the reaction center. However, the ring opening in XII provides hydride attack at the least substituted carbon atom suggesting that the triphenyltin group might be contributing the larger steric effect. Alternatively, the loss of the triphenyltin anion or an electron-withdrawing effect by the trimethylsilicon group [16] could also be the determining factors between the reactivity difference of triphenyltin and trimethylsilicon compounds.

The hydroboration-oxidation results with I can be compared to the corresponding alkyl- and trimethyl-silicon substituted-cyclohexenyl derivatives (Table 2). It can be pointed out that I provides the higher regiospecificity (84% C(3) and 16% C(4)) than with the t-butyl analogue XX (52% C(3) and 48% C(4)). The stereospecificity is higher at C(3) for t-butylcyclohex-3-ene (XX) (*c*/*t* 1.6) versus (*c*/*t* 1), while at C(4) I is more stereospecific (*c*/*t* 0.3) versus XX (*c*/*t* 0.9). Comparing I to the trimethylsilicon compound XXI [11] reveals similarities in the overall regiochemistry (XXI, 73% C(3) and 25% C(4)), while differences in

the *cis*/*trans* ratios at C(3) and C(4) are evident. The *c*/*t* ratio for XXI at C(3) is 0.5 and that at C(4) ~0.

Both I and XXI afford predominant boron attack at C(3) reflecting some similar conformational and electronic effects for their substituents, although these effects are difficult to assess fully. The length of the carbon—tin versus the carbon—silicon bond (2.18 versus 1.94 Å) might explain the differences in stereochemistry at C(3) with the trimethylsilicon group exerting the greater steric effect, hence the larger ratio of *trans*-3-hydroxyl compound to its *cis* isomer. The results at C(4) for I and XXI cannot be fully assessed, because no *cis*-4-hydroxy isomer was detected for XXI, but again, the *trans*-4-hydroxyl isomer is predominant in both cases.

We wish to emphasize the use of high field NMR spectroscopy concerning this latter result, because we could not separate V and VI by TLC (even the corresponding acetates would not separate by TLC) and had to find a spectroscopic method to do the job. At 100 MHz only one isomer (VI) was evident. Fortuitously, we ran the 360 MHz ^{1}H FT NMR spectrum on the same sample from the hydroboration of I and found that our pure *trans* compound VI at 100 MHz had, at 360 MHz, 25% of its *cis* isomer V (Fig. 1).

The reactions of organotin anions with cyclic epoxides had not been previously attempted [1]. We treated triphenyltinsodium with cyclohexene epoxide and obtained compound XIII, which was assigned the *trans* stereochemistry by NMR spectroscopy. A similar stereochemical result was also obtained by Kitching and co-workers [2e] using trimethyltinlithium. Thus, inversion of configuration occurs consistently with both organotin anions.

While the stereochemical consequences of trimethyltinlithium reactions with alkyl halides has been reinvestigated [2e], reaction with 1-bromo-2-methoxycyclohexyl derivatives has not been previously studied (eq. 15). In this regard, it was recently found [2e] that the reaction of trimethyltinlithium with 4-alkylcyclohexyl halides gave both *cis*- and *trans*-4-alkyicyclohexyltrimethyltin compounds. We, on the other hand, find that with *trans*-1-bromo-2-methoxycyclo-

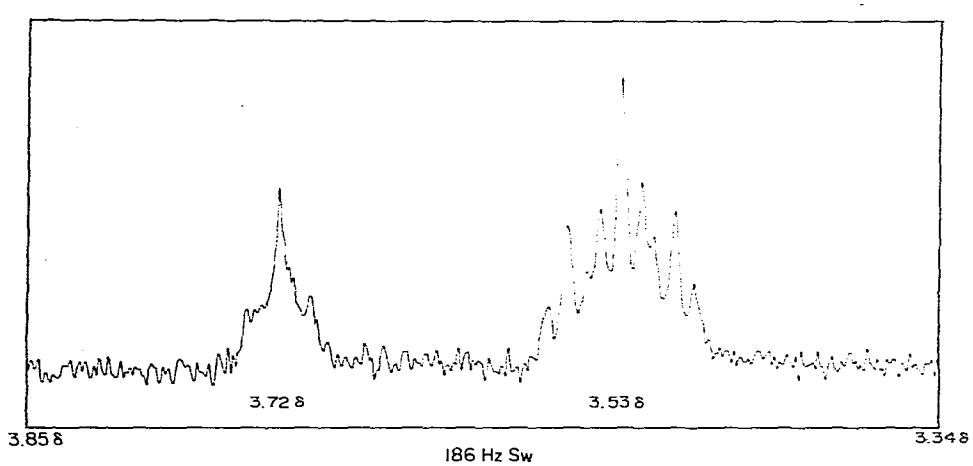

Fig. 1. The 360 MHz ^{1}H NMR spectrum of compounds V and VI with δ 3.72 ppm the *cis*-H—C—OH and δ 3.53 ppm the *trans*-H—C—OH multiplet.

hexane and triphenyltinsodium (eq. 15) the tin-containing product is *cis*-2-methoxycyclohexyltriphenyltin (XV), which indicates strictly inversion of configuration for this class of compounds *. Conceivably, approach of the triphenyltin anion must occur from the axial side proceeding by an S_N2 mechanism giving inversion of configuration. Alternatively, if attack of the triphenyltin anion also occurred on bromide (bromide—sodium exchange), then this would give the carbanion, which would presumably eliminate methoxide ion to produce cyclohexene. If this occurred then the possible retention product (*trans*) would not be seen. We did not look for cyclohexene, but presume it was produced by the exchange reaction, as expected, from other examples [9b].

We verified the *cis* stereochemistry of XV by the fact that this compound did not react with glacial acetic acid even after three days and by the NMR pattern of the methine proton on the carbon with the methoxyl group.

Several of the various electrophilic reagents provided loss of the triphenyltin group. Both the epoxides, II and III, reacted with boron trifluoride etherate to form the triphenyltin derivative via a presumed cyclodestannylation reaction [12] (eq. 17). The interesting fact that a transition state that develops positive charge on the 3 position of a cyclohexyltriphenyltin derivative must involve an axial triphenyltin substituent enhances the concept of interaction of various nucleophiles in that position with a tin atom at the 1 position. Dreiding models also confirm the close proximity of the axial triphenyltin group, both in the *cis*- and *trans*-epoxides II and III, with the 3 carbon atom.

While XV failed to react with glacial acetic acid, it reacted instantaneously with boron trifluoride etherate to give cyclohexene and the triphenyltin derivative. Again, considerable carbonium ion character must be present at the 2 carbon atom before elimination can occur.

As expected, bromine cleavage of the phenyl—tin bond was the only reaction with compounds IV—VII (eq. 19 and 20) and is consistent with the facile reactions of these bonds with electrophiles [17].

The use of CIMS in providing stereochemical information has received limited attention [18]; however, the examples in the literature show promise for differentiating between configurational isomers using this technique. We have stated our results with the various hydroxy, keto, and olefinic cyclohexyltriphenyltin compounds, but one result with the epoxides II and III deserves special comment. The methane and isobutane CIMS of these compounds showed dramatic differences, which enabled us to further elucidate the stereochemistry of each epoxide.

Our premise was that the *cis*-epoxide oxygen's nonbonding electrons would interact with the tin *d*-orbitals precluding gas phase protonation on the epoxide. Alternatively, the *trans*-epoxide should be free from this interaction and be protonated. Indeed, this was shown by the isobutane spectra of each epoxide, where the *cis*-epoxide II provides no $M + 1$ ion, while the *trans*-epoxide III had the $M + 1$ ion in 83% relative abundance. This also strengthened the hypothesis that the pseudo diaxial conformation for II predominates, although extrapolation from gas phase to solution concerning such interaction may not always be con-

* Prof. Kitching has experiments underway to elucidate the stereochemistry of this reaction with trimethyltinlithium. (Personal communication)

clusive (eq. 25). This type of interaction and other conformational aspects of substituted cyclohexyltin compounds in solution, as studied by NMR spectroscopy, will be fully discussed in a future publication [6].

It is clearly evident that the conformational requirements of the triphenyltin group on a cyclohexyl ring system greatly influences the reactivity of these systems and we hope that our contribution will provide stimulus to others to conduct studies in this new and exciting area of organotin chemistry.

Experimental

Instrumentation and materials

^{1}H NMR spectral data was recorded on a Perkin—Elmer R32 NMR spectrometer operating at 90 MHz and equipped with a Nicolet TT7 pulse and computer unit for operation in the FT mode; a Bruker HXS-360 located at the Stanford Magnetic Resonance Laboratory operating in the FT mode at 360 MHz and a Varian HA-100. The infrared (IR) spectra were recorded on a Perkin—Elmer 457 double grating spectrometer and the chemical ionization mass spectra were recorded on a Finnigan 1015D instrument with a Control Data 150 computer system. Elemental analyses were carried out by the Microanalytical Laboratory, College of Chemistry, University of California, Berkeley, CA and were ±0.3% unless stated otherwise. Melting points are uncorrected and triphenyltin chloride was a gift from M & T Chemicals Inc., Rahway, N.J.

Preparation of cyclohex-3-enyl bromide [14]

To a stirred, refluxing solution of 58 g (0.5 mol) 1,4-cyclohexanediol in 300 ml of benzene was added dropwise 103 g (0.38 mol) of phosphorus tribromide. The hydrogen bromide that was formed was trapped in a 20% potassium hydroxide solution. The reaction mixture was refluxed overnight then poured onto 250 ml of an ice/water mixture. The benzene layer was washed with a 10% sodium carbonate solution (4 × 120 ml); water (1 × 120 ml) and dried over anhydrous potassium carbonate. The benzene was removed by distillation at atmospheric pressure. The crude product was then vacuum distilled to give 34 g (b.p. 50—52°C (22 mmHg) of product. This was dissolved in 75 ml of methanol along with 2 g of calcium carbonate and then refluxed for 30 min. The mixture was cooled and filtered. Then 45 ml of methylene chloride was added and this solution was washed thrice with 40 ml portions of water and then dried over anhydrous magnesium sulfate. The methylene chloride was distilled at atmospheric pressure and the residue distilled under vacuum to give 23.7 g (29%) b.p. 49—52°C (28 mmHg) of product.

GLC on 6′ × 0.25″ SF 90 Chrom G column at 100°C showed one pure compound. NMR (90 MHz, $CDCl_3$, TMS) 2.12 ppm (4 H multiplet); 2.56 ppm (2 H multiplet); 4.30 ppm (1 H multiplet), and 5.58 ppm, (2 H multiplet).

Synthesis of cyclohex-3-enyltriphenyltin (I)

To a mixture of 0.6 g (0.0214 g-atom) magnesium metal in 5 ml of dry tetrahydrofuran (THF) was added dropwise 3.3 g (0.0204 mol) of 4-bromocyclohexene in 5 ml THF. The resulting Grignard reagent was refluxed for 1 h and to this was added 7.9 g (0.0204 mol) of triphenyltin chloride in 10 ml of dry THF.

The reaction mixture was refluxed for 5 h and then stirred overnight. The reaction mixture was hydrolyzed with a saturated solution of ammonium chloride followed by exhaustive extraction of the solids with ether (1000 ml). The combined ether extracts were washed with water and dried over magnesium sulfate. Ether removal and recrystallization of the solids from ethanol/benzene yielded 4.59 g (50%) of product, m.p. 161—163°C. Anal. $C_{24}H_{24}Sn$ calcd.: C, 66.86; H, 5.61% (satisfactory).

Synthesis and separation of cis- and trans-3,4-epoxycyclohexyltriphenyltin (II and III)

To a solution of 0.75 g (0.002 mol) cyclohex-3-enyltriphenyltin in 15 ml of methylene chloride was added 0.48 g (0.003 mole) of *m*-chloroperbenzoic acid portionwise over a ten minute period. After stirring for 3 h, and additional 0.05 g of *m*-chloroperbenzoic acid was added and the resulting solution stirred for 16 h. The *m*-chlorobenzoic acid was filtered and the methylene chloride solution washed with dilute sodium carbonate and then dried over magnesium sulfate. Concentration of the solution yielded 0.5 g of a product, which after recrystallization from ethanol/benzene, had a m.p. 171.5—173°C. Analysis of this product by thin layer chromatography (TLC) using hexane/diisopropyl ether (70/30) showed the presence of two epoxides. Preparative TLC was accomplished on 0.250 mm plates using 22 mg of the mixture of II and III and the above mentioned solvents (elution of the plate was done three times to increase resolution between II and III). The epoxides II and III were detected using the standard procedure [3c]. This procedure entails covering the plate with aluminum foil with an edge exposed. The plate is placed under a UV light, and then sprayed with hydroxyquinolinesulfonic acid (HQ) to visualize under UV light both the bands. The area was scraped and each band eluted with chloroform. Separation was checked and shows purities of 99%. The upper band (8.0 mg, 42%) was found to be the *cis*-epoxide II and the lower band (10.7 mg, 57%) the *trans*-epoxide III. (See text for NMR and CIMS data on the structure assignments for II and III.)

The infrared spectrum (CCl_4) showed bands at 3020, 2970, 2900, 1420, 1470, 1070, and 700 cm^{-1} consistent with an epoxide. Anal. II and III $C_{24}H_{24}SnO$ calcd.: C, 64.57; H, 5.38% (satisfactory).

Reaction of cis-3,4-epoxycyclohexyltriphenyltin with lithium aluminum hydride

In initial experiments with a mixture of II and III, it was found that ring opening of the epoxides with lithium aluminum hydride was best accomplished in diethyl ether, however, the reaction was complete only if carried out in a sealed tube placed in an oil bath at ~70°C for 24 to 48 h. Thus, each of the epoxides were then separated by preparative TLC (see above) and then treated separately with $LiAlH_4$ in a sealed ampoule.

The *cis*-epoxide II (2 mg) dissolved in 1.0 ml of anhydrous diethyl ether was placed in an ampoule containing 2.5 mg of $LiAlH_4$. The ampoule was stirred and heated in an oil bath at ~70°C for 48 h and then the ampoule cooled and the contents hydrolyzed with 1 ml of a saturated solution of ammonium chloride. TLC analysis using diisopropyl ether/acetic acid (99/1) indicated predominantly one compound (>99%) and a trace amount of another component. Subsequent

reductions, followed by preparative TLC and NMR analysis, indicated the predominate product to be *cis*-3-hydroxycyclohexyltriphenyltin (IV) (~60%). The *cis*- and *trans*-4-hydroxy isomers V and VI were not separable by TLC, but 360 MHz ^{1}H NMR spectra allowed analysis based on the areas of the methine protons attached to the carbon bearing the hydroxyl group (see text) in each compound.

Reaction of trans-3,4-epoxycyclohexyltriphenyltin with lithium aluminum hydride

As previously described (vide supra) the *trans*-epoxide (2 mg) was placed in a sealed ampoule with 2.3 mg of $LiAlH_4$ in 1 ml of anhydrous diethyl ether while similar workup as described above and TLC analysis revealed one pure compound. The spectral analysis indicated it to be *trans*-3-hydroxycyclohexyltriphenyltin (XII) (see text).

Synthesis of trans-2-hydroxycyclohexyltriphenyltin (XIII)

To a mixture of 5.25 g (0.41 mol) of naphthalene and 4.6 g (0.2 mol) of sodium metal in 125 ml of dry dimethoxyethane, stirred at room temperature for 30 min, was added 38.5 g (0.10 mol) of triphenyltin chloride in 100 ml of dimethoxyethane dropwise over a 4 h period. After stirring for 1.5 h, a solution of 9.8 g (0.10 mol) cyclohexene oxide in 25 ml of dimethoxyethane was added over a 1 h period and the resulting solution stirred for 16 h at room temperature. The reaction mixture was cooled to 0°C and 125 ml of a saturated ammonium chloride solution was added. The insoluble salts were filtered and the water layer separated and extracted with ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and concentrated yielding a white solid to which 75 ml of hot heptane was added and the insoluble solid filtered yielding 28.6 g of crude product. Recrystallization twice from ether/heptane yielded 15 g (34%) of XIII (m.p. 120—121.5°C).

The infrared spectrum ($CHCl_3$) showed bands at 3580, 3060, 2000, 2920, 2850, 1560, 1480, 1450, 1075, 1050, and 700 cm^{-1}; NMR ($CDCl_3$) δ 7.8—6.9 (m, 15 H, phenyl protons), 3.8—3.2 (m, 1 H, H—C—OH), and 2.3—0.7 ppm (m, 9 H, cyclohexyl). Anal. $C_{24}H_{26}OSn$ calcd.: C, 64.27; H, 5.84% (satisfactory).

Synthesis of trans-2-hydroxycyclohexyldiphenyltin bromide from trans-2-hydroxycyclohexyltriphenyltin

To a cooled solution (—35°C) of XIII (0.51 g, 0.01 mol) in 10 ml of chloroform, was added dropwise 0.160 g (0.001 mol) of bromine in 8 ml chloroform. The chloroform and bromobenzene were removed under a vacuum resulting in a clear oil which solidified on cooling at —5°C for two days to give XIX (m.p. 61—64°C). (See Tables for NMR and CIMS data.) Anal. $C_{18}H_{21}BrOSn$ calcd.: C, 47.83; H, 4.68% (satisfactory).

Hydroboration of cyclohex-3-enyltriphenyltin with diborane

In a four-necked flask equipped with an inlet for Argon, addition funnel, reflux condenser and magnetic stirring bar was placed 0.5 g (1.16 mmol) of cyclohex-3-enyltriphenyltin in 5 ml of dry THF.

To this stirring solution was added 1.13 ml of a 1 *M* diborane solution in THF.

The reaction mixture was stirred overnight at room temperature and found by TLC to still contain starting material. Thus, additional diborane (0.6 ml 1 *M* solution in THF) was added and stirring continued for 1 h with the solution being refluxed. The excess diborane was hydrolyzed with water and then 1 ml of 3 *N* sodium hydroxide was added followed by 1 ml of 30% hydrogen peroxide. The reaction mixture was extracted with ether. The ether was evaporated and TLC of the crude product (diisopropyl ether/acetic acid, 99/1) showed three components. Separation by preparative TLC (1 mm plates and eluted twice with the above mentioned solvent system) of ~100 mg of crude product gave ~50 mg of a 1/1 mixture of two isomeric alcohols (IV and VII) m.p. 123—125°C and 10 mg of a component that gave only one spot by TLC, but was found to be a mixture of two isomeric alcohols (V and VI) m.p. 138—141°C in the ratio of 1/3 using 360 MHz ^{1}H NMR spectroscopy (see text).

The 1/1 mixture of IV and VII was separated using the following conditions: 20 mg of a 1/1 mixture of IV and VII in 1 ml of THF was placed on ten 0.25 mm silica-gel 60 TLC plates which represents ~2 mg/plate. The TLC plates were eluted three times with diisopropyl ether/acetic (99/1). The separated tin compounds were detected as previously reported [3c] and scraped and eluted with chloroform to give 7.7 mg of the upper band which was found by NMR spectroscopy to be compound VII and 5.1 mg of a lower band identified as compound IV. A middle band (~5.7 mg) contained both IV and VII. See Table 1 for pertinent NMR spectroscopic analysis. Anal. IV and VII, V and VI, $C_{24}H_{26}OSn$ calcd.: C, 64.27; H, 5.84% (satisfactory).

Preparation of trans-1-bromo-2-methoxycyclohexane [19]

In a round-bottom flask was placed 1.78 g (0.01 mol) of *N*-bromosuccinimide and to this was added 1.78 g (0.022 mol) cyclohexene in 50 ml of methanol. The solution was stirred for 1 h and then stood overnight. The workup included addition of ether; a 10% sodium carbonate solution was then used to extract the succinimide, followed by a water wash of the ether layer. The ether layer was dried over anhydrous magnesium sulfate and then the ether removed and the residue distilled to give 0.7 g (36%) b.p. 50°C/20 mmHg of product. The 90 MHz NMR (CCl_4) had multiplets at 3.95 ppm (H—C—Br) 3.35 ppm (OCH_3), 3.25 ppm (H—C—O) and 1.0 to 2.5 ppm for the cyclohexyl ring protons. GLC analysis (6′ × 0.25″ SF 90 at 100°C) revealed one single peak. This reaction on a 0.1 mol scale gave yields of ~60%.

Reaction of trans-1-bromo-2-methoxycyclohexane with triphenylstannylsodium

In a 500 ml flask equipped with a stirring bar, drying tube and nitrogen inlet was placed 2.62 g (0.02 mol) naphthalene and 2.3 g (0.19 g-atom) of sodium metal in 100 ml of dimethoxyethane. The reaction mixture was stirred for 1.5 h after which 19.3 g (0.05 mol) of triphenyltin chloride was added dropwise in 50 ml of dimethoxyethane, maintaining at all times, the green color. This took ~4 h and then the solution was cooled in an ice-bath and 10 g (0.52 mol) *trans*-1-bromo-2-methoxycyclohexane in 40 ml of dimethoxyethane was added dropwise over 1 h. The reaction mixture was allowed to come to room temperature and stirring was continued for 17 h. Hydrolysis with a saturated ammonium chloride solution was followed by extraction with ether. The ether was washed

thrice with water and dried over anhydrous magnesium sulfate. The ether was removed to give oily crystals (9.0 g) which remained oily after recrystallization. TLC showed it to be one compound and further purification by preparative TLC (diisopropyl ether/hexane 1/1) gave a product with m.p. 44—47°C. Further proof for the *cis*-stereochemistry was forthcoming by the attempted reaction of this compound with glacial acetic acid. No reaction took place even after 19 h as evidenced by the lack of any cyclohexene protons in the NMR spectrum of the reaction mixture. In contrast to this result, the corresponding *trans* alcohol reacts instantaneously with glacial acetic acid to give cyclohexene and triphenyltin acetate (NMR).

The NMR spectrum (100 MHz, $CDCl_3$) gave the usual multiplet for an equatorial hydrogen (H—C—OCH_3) at 3.48 ppm (band width 13 Hz) and the methoxyl signal at 2.99 ppm. A smaller signal at 3.07 ppm cannot be attributed to the corresponding *trans* isomer, since upon reaction with glacial acetic acid the NMR remained the same. However, it is possible that this is the inverted conformer, i.e., methoxy equatorial and triphenyltin axial. If this is correct, then the ratio of equatorial to axial conformers (CH_3O) would be ~5. Anal. $C_{25}H_{28}OSn$ calcd.: C, 64.79; H, 6.04% (satisfactory).

Preparation of cyclohex-1-enyltriphenyltin

In a flask was placed 500 mg (0.048 g-atom) magnesium metal in 25 ml of anhydrous tetrahydrofuran. To this was added ~6 drops of ethylene dibromide and to this refluxing solution was added dropwise 2.0 g (0.0124 mol) cyclohex-1-enyl bromide [20] dissolved in 5 ml of anhydrous tetrahydrofuran. The resulting reaction mixture was refluxed for 24 h and then 4.8 g (0.013 mol) of triphenyltin chloride dissolved in 10 ml of anhydrous tetrahydrofuran was added dropwise over a 20 min period. After addition, the reaction mixture was refluxed for 3 h. The reaction mixture was diluted with diethyl ether and the solids filtered and washed thoroughly with ether. The ether was removed and the residue extracted with hexane to separate hexaphenyltin, which is insoluble in hexane. The hexane soluble material was recrystallized from ethanol/benzene (9/1) to give a compound m.p. 146—150°C. This compound (78 mg ~2% yield) had a 90 MHz NMR spectrum ($CDCl_3$, TMS) with signals at 1.61 and 1.44 ppm (5 H), 2.29 and 2.08 ppm (3 H), 5.98 ppm (1 H) and 7.24 ppm (15 H). Anal. $C_{24}H_{24}Sn$ calcd.: C, 66.86; H, 5.61% (satisfactory).

Epoxidation of cyclohex-1-enytriphenyltin with pertrifluoroacetic acid [8]

In a flask was placed 78 mg (0.181 mmol) of cyclohex-1-enyltriphenyltin and 339 mg (3.2 mmol) anhydrous sodium carbonate in 5 ml of methylene chloride. To this was added 0.905 mmol of pertrifluoroacetic acid (prepared from 190 mg trifluoroacetic anhydride and 34 mg of 90% hydrogen peroxide in 2 ml of methylene chloride) in 2 ml of methylene chloride over a 15 min period. The resulting reaction mixture was stirred for 24 h after which it was filtered and dried over magnesium sulfate. After removal and solvent 40 mg (50%) of product was obtained. Purification by column chromatography on florasil with pentane and then pentane/ether (98/2) gave the epoxide (20 mg) which had a m.p. 142—143°C. The 90 MHz NMR spectrum ($CDCl_3$, TMS) had a signal at 3.18 ppm with $J(^{117/119}Sn—H)$ coupling 54/56 Hz for the oxirane proton as well as the complete

absence of the vinyl proton at 5.98 ppm. The CIMS (isobutane) gave ions at *m/e* 351 (100%) and *m/e* 371 (10%), the latter the $M - C_6H_5$ ion. Anal. $C_{24}H_{24}OSn$ calcd.: C, 64.51; H, 5.38% (satisfactory).

Reaction of 1,2-epoxycyclohexyltriphenyltin with lithium aluminum hydride

To 6.0 mg (0.0134 mmol) of 1,2-epoxycyclohexyltriphenyltin in 3 ml anhydrous ether was added ~2 mg of lithium aluminum hydride and placed in an ampoule. The ampoule was sealed and placed in an oil bath for 48 h at 75°C. The ampoule was opened and hydrolysis of excess hydride was accomplished with a saturated ammonium chloride solution. The ether layer was separated and dried, after washing with water, with anhydrous magnesium sulfate. TLC analysis revealed hexaphenyltin and no discernible *cis*-2- or -1-hydroxycyclohexyltriphenyltin compounds.

Oxidation of trans-2-hydroxycyclohexyltriphenyltin (XIII) with pyridinium chlorochromate [21]

In a flask was placed 0.37 g (1.7 mmol) pyridinium chlorochromate and 27.8 mg (0.34 mmol) of sodium acetate in 2 ml of methylene chloride. To this was added rapidly 0.5 g (1.1 mmol) of *trans*-2-hydroxycyclohexyltriphenyltin (XIII).

The reaction mixture was analyzed after 2 h to show the appearance of triphenyltin acetate and no tin containing ketone. The reaction was diluted with ether and filtered through florasil. An IR of the solution showed the presence of a carbonyl at 1710 cm^{-1} and consistent with cyclohexanone. GLC analysis on a dexil column gave a compound with the same retention time as cyclohexanone and a 2,4-dinitrophenylhydrazone derivative was isolated and purified by washing with ether and drying to give m.p. 160—161°C, which was identical in melting point and mixing melting point with an authentic 2,4-D derivative of cyclohexanone.

Oxidation of compounds IV and VII with pyridinium chlorochromate [21]

In a flask was placed 29 mg (0.064 mmol) of a ~1/1 mixture of compounds IV and VII in 2 ml of methylene chloride along with 21 mg (0.097 mmol) pyridinium chlorochromate. The reaction mixture was followed by TLC (diisopropyl ether/acetic acid 99/1) and after 2 h the starting alcohols IV and VII had disappeared and two new products, one major and the other minor, had appeared at a higher R_f. The reaction mixture was diluted with ~20 ml of ether and filtered through florasil. Preparative TLC (0.25 mm plates silica gel GF) gave the major compound (10 mg) with m.p. 113.5—115.5°C and an IR spectrum with ($CHCl_3$) C=O 1710 cm^{-1} (strong); 90 MHz NMR ($CDCl_3$, TMS) 7.18—7.7 ppm (*M*/15 H) 1.6—2.87 ppm (*M*/10 H); and CIMS (methane) $M + 1$, *m/e* 449 (5%), *m/e* 371 (100%) ($M - C_6H_5$) and M — cyclohexonyl, *m/e* 351 (30%) consistent with cyclohex-3-onyltriphenyltin. The minor product was found to be cyclohex-3-onyldiphenyltin chloride formed by an electrophilic cleavage reaction of a phenyl group by hydrochloric acid. We found by buffering the oxidation with sodium acetate that this cleavage reaction could be prevented. Anal. $C_{24}H_{24}OSn$ calcd.: C, 64.57; H, 5.38% (satisfactory).

Oxidation of cis- and trans-4-hydroxycyclohexyltriphenyltin with pyridium chlorochromate [21]

In a 10 ml flask was placed 2.16 mg (0.01 mmol) of pyridinium chlorochromate along with 1.0 mg (0.012 mmol) of anhydrous sodium acetate in 1 ml of methylene chloride. To this mixture was added rapidly 3.1 mg (0.007 mmol) of a 3/1 mixture of *trans*- and *cis*-4-hydroxycyclohexyltriphenyltin dissolved in 1.0 ml of methylene chloride. The reaction mixture was stirred at room temperature for 3 h and then the reaction mixture analyzed by TLC (2% diisopropyl ether/ acetic acid) to show a new product and no discernible starting alcohols. The reaction mixture was diluted with 20 ml of ether and filtered through florasil. The ether was removed and the ketone, m.p. 180—183°C, had an IR ($CHCl_3$) spectrum with C=O 1708 cm^{-1}, CIMS (methane) *m/e* 369 (33%) 351 (41%) and 90 MHz NMR ($CDCl_3$, TIMS) 2.0—2.5 ppm (9 H) 7.37 ppm (15 H). Anal. $C_{24}H_{24}OSn$ calcd.: C, 64.57, H, 5.38% (satisfactory).

Reduction of cis-3,4-epoxycyclohexyltriphenyltin with lithium aluminum deuteride

In an ampoule was placed 2 mg (0.0045 mmol) of the TLC purified *cis*-3,4-epoxycyclohexyltriphenyltin (II) and 2 mg (0.042 mmol) of lithium aluminum deuteride in 1 ml of anhydrous diethyl ether. The ampoule was heated for 48 h at ~75°C and then hydrolyzed with deuterium oxide. The product was isolated and submitted to CIMS (methane) analysis. The mass spectrum showed the $M - C_6H_5$ ion; *m/e* 374, as the base ion (100%) which indicated incorporation of one deuterium atom.

Reduction of cyclohex-3-onyltriphenyltin with lithium aluminum hydride

In a flask was placed 1 mg of cyclohex-3-onyltriphenyltin along with 6 mg (excess) lithium aluminum hydride in 1 ml of anhydrous diethyl ether.

The reaction mixture was stirred overnight and then several drops of a saturated ammonium chloride solution was added. The ether layer was separated and dried over anhydrous magnesium sulfate. The products were analyzed by TLC to show *cis*-3-hydroxycyclohexyltriphenyltin (>95%) and a trace (<5%) of the corresponding *trans* isomer.

Preparation of cyclohex-2-enyl bromide [11]

In a 500 ml round bottom flask was placed 21 g of cyclohexene (0.5 mol), 33.5 g (0.19 mol) *N*-bromosuccinamide in 125 ml of carbon tetrachloride along with 0.125 g of benzoyl peroxide.

The reaction mixture was refluxed for 2 h and then cooled in an ice bath. The reaction mixture was filtered to remove the succinamide and then the carbon tetrachloride distilled at reduced pressure through a 6" vigreux column. The residue was distilled to give 16 g (50%) of cyclohex-2-enyl bromide b.p. 38°C/22 mmHg.

Preparation of cyclohex-2-enyltriphenyltin (X)

In a four-necked flask was placed 1.31 g (0.01 mol) naphthalene and 1.15 g (0.05 g-atom) sodium metal in 50 ml of dimethoxyethane. This reaction mixture was stirred for 3 h at room temperature and then to this was added dropwise

(2.5 h) 9.6 g (0.025 mol) of triphenyltin chloride. The reaction mixture was cooled to −50°C (dry-ice/acetone) and to this was added 4.0 g (0.025 mol) of freshly distilled cyclohex-2-enyl bromide over a 1 h period. The reaction mixture was allowed to come to room temperature and stirred for 17 h. The usual workup gave 1.0 g of solid which was found by TLC (hexane/diisopropyl ether 7/3) to be product along with triphenyltin chloride. One can remove the naphthalene by recrystallization from ethanol/benzene (10/1); however, removal of triphenyltin chloride is best achieved by dry column chromatography with hexane as the solvent. This procedure gave pure product m.p. 81.5—83°C. See Tables 1 and 2 for spectroscopic data on X. Anal. $C_{24}H_{24}Sn$ calcd.: C, 66.86; H, 5.61% (satisfactory).

Attempted reaction of cyclohex-2-enyltriphenyltin (X) with m-chloroperbenzoic acid

In a two-necked flask was placed 64 mg (1.5×10^{-4} mol) of X in 6 ml of methylene chloride along with 1 g of anhydrous potassium carbonate. To this cooled solution (0°C) was added 29.2 mg (1.6×10^{-4} mol) of *m*-chloroperbenzoic acid portionwise over a 10 min period. The reaction mixture was stirred at room temperature for 4 h. The analysis indicated a triphenyltin derivative and no epoxidation product was formed.

Hydroboration-oxidation of cyclohex-2-enyltriphenyltin (X)

In a similar setup as described for the hydroboration of compound I, compound X was hydroborated and then oxidized to give 3 and 4-hydroxycyclohexyltriphenyltin compounds. Thus, it was evident that compound X was isomerized under the reaction conditions to compound I. No 2-hydroxycylohexyltriphenyltin compounds were formed.

Preparation of cyclohex-4-onyltriphenyltin

In a flask equipped with a magnetic stirring bar, two dropping funnels, a reflux condenser and a nitrogen inlet was placed 0.4 g (0.015 g-atom) magnesium metal in 10 ml of anhydrous tetrahydrofuran. To this was added 3.0 g (0.014 mol) of the ethylene glycol ketal of 4-bromocyclohexanone [22] dissolved in 5 ml of tetrahydrofuran.

The Grignard reaction was started by entrainment with dibromoethylene and reflux was continued for 0.5 h. To this Grignard was added 5.0 g (0.0126 mol) triphenyltin chloride and the resulting solution refluxed overnight. The reaction mixture was hydrolyzed with a saturated ammonium chloride solution then washed with water and finally dried over magnesium sulfate. Removal of the ether followed by thin-layer chromatography revealed product contaminated with triphenyltin chloride. The contaminated product (~4.0 g) was placed on a florasil column and eluted with hexane. This removed the triphenyltin chloride. The product (~1.0 g) was placed in 50 ml benzene along with 10 ml of acetone and 50 mg of toluenesulphonic acid to remove the protecting group. The solution was refluxed and water removed azeotropically. The residue, after addition of water and separating the layers, was subjected to preparative thin-layer chromatography (hexane/diisopropyl ether (1/1)) to give 200 mg of a product that had a similar R_f and spectroscopic data to the ketone that was prepared by oxidation of compounds V and VI.

Reaction of cis- and trans-3,4-epoxycyclohexyltriphenyltin with boron trifluoride etherate

To a benzene solution (5 ml) of 50 mg (0.11 mmol) of the *cis*- and *trans*-epoxides II and III was added 14 μl of freshly distilled boron trifluoride etherate. TLC analysis (50/50 hexane/diisopropyl ether) revealed formation of a triphenyltin derivative.

Attempted demethylation of cis-2-methoxycyclohexyltriphenyltin (XV)

In a three-necked flask equipped with a drying tube, inlet for argon and a dropping funnel was placed 327 mg (0.705 mmol) of XV in 5 ml of dry methylene chloride. The solution was cooled (0°C) and to this was added dropwise a solution of boron tribromide (177 mg) in 3 ml of methylene chloride. After addition, the reaction mixture was allowed to warm to room temperature and the solvent removed on a rotary evaporator. The residue was taken up in methanol several times and evaporated to remove boric acid.

The residue showed by TLC (50/50 hexane/diisopropyl ether) only triphenyltin bromide as also confirmed by NMR spectroscopy.

Preparation of cis- and trans-3-hydroxycyclohexyldiphenyltin bromide (XVII)

In a flask was placed 40 mg of a mixture of IV and VII in 4 ml of chloroform. To this stirring solution, maintained at −35°C during addition, was added 14 mg of bromine in 3 ml of chloroform. TLC analysis (diisopropyl ether/acetic acid (1%)) revealed a new product and further destannylated products. Preparative TLC (1 mm silica gel GF plate using the above stated solvent) gave ~3 mg of product whose 90 MHz FT NMR (Table 1) and CIMS (Table 3) confirm its structure. Anal. $C_{18}H_{21}BrOSn$ calcd.: C, 47.82; H, 4.68% (satisfactory).

Preparation of cis- and trans-4-hydroxycyclohexyldiphenyltin bromide (XVIII)

To a flask containing 5 mg (0.0067 mmol) of a 25/75 mixture of V and VI in 2 ml of methanol was added ~1.0 mg of bromine. The reaction mixture was stirred overnight then analyzed by TLC to show a new compound and a trace of starting material. Preparative TLC on a 0.25 mm silica gel G plate using diisopropyl ether/acetic acid (2%) gave pure product. The CIMS (Table 3) and 90 MHz FT NMR (Table 1) were in agreement with the structure. Anal. $C_{18}H_{21}BrOSn$ calcd.: C, 47.82; H, 4.68% (satisfactory).

Reaction of trans-2-hydroxycyclohexyltriphenyltin (XIII) with glacial acetic acid

In an NMR tube was placed 78.1 mg of XIII in 0.4 ml of deuterochloroform. The NMR (90 MHz) spectrum was recorded and then 10.5 mg of glacial acetic acid was added. The spectrum ran immediately after the addition of HOAc showed the olefinic protons of cyclohexene (5 ppm) and the disappearance of the methine H—C—OH proton at 3.68 ppm. GLC analysis (OV 101 at 50°C) also confirmed the presence of cyclohexene.

Attempted reaction of cis-2-methoxycyclohexyltriphenyltin (XV) with glacial acetic acid

In an NMR tube was placed 78 mg of XV in 0.4 ml of deuterochloroform.

The NMR spectrum (90 MHz) was recorded and then ~7.4 μl of glacial acetic acid was added. After 19, 40 and 64 h the spectrum was unchanged.

Acknowledgements

The authors wish to thank Dr. W. Conover of the Stanford Magnetic Resonance Laboratory for recording the 360 MHz ^{1}H FT NMR spectra. SMRL is supported by grants NSF GR 23633 and NIH RR00711. We acknowledge Dr. Roy Holmstead of this laboratory for recording all the CIMS spectra. This study was made possible by grants from the National Institute of Environmental Health Sciences (NIH 5 P01-ES00049). Dr. J.E. Casida is gratefully acknowledged for encouragement of this aspect of the bioorganotin program, and the important exchange of information with Dr. William Kitching (Univ. of Queensland) was especially useful in preparation of this manuscript.

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