A Ziegler–Natta type mechanism (Scheme III) is proposed for the present polymerization of acrylonitrile. In this scheme, five-coordinate cobalt(I)–methyl complexes are involved, which are formed by the reduction of cobalt(III) methyl with $NaBH_4$. Reduction of alkylcobalt(III) complex with $NaBH_4$ or Na(Hg) to give alkylcobalt(I) complex has been reported for other ligand systems.[18,42]

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The flexible bidentate ligand di-2-pyridylamine plays an important role of providing a vacant coordination site for acrylonitrile to form cobalt(I)–acrylonitrile π-complexes in the catalytic cycle.

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Registry No. 1, 81985-22-0; 3·I, 105763-88-0; 5·I, 105763-87-9; 5·ClO_4, 105763-90-4; 5·PF_6, 105763-91-5; acetonitrile, 107-13-1.

Stereochemistries and Mechanisms of Reactions of Electrophiles with Organotin Compounds

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The effect of solvent and electrophile on halodemetalation reactions of carbon–tin bonds has been investigated. Both stereochemical results and ^{119}Sn NMR have been used as mechanistic probes. The effect of solvent is extreme; reactions performed in polar solvents such as acetonitrile and dimethylformamide yield cleavage products with predominantly inversion of configuration, whereas nonpolar solvents yield products with predominantly retention. Polar-aprotic solvents appear to be highly efficient in promoting inversion stereochemistry. Polar-protic solvents are not as efficient. This is explained in terms of some very specific solvation phenomena. Also, ^{119}Sn NMR studies of several trialkyltin halides in various solvents show that these specific solvation phenomena can be qualitatively assessed. The nature of the electrophile also plays an important role in eventual stereochemistry; Br_2, I_2, ICl, and IBr are compared and discussed.

Early work investigating electrophilic cleavages of organomercurials indicated that retention of configuration at carbon was the general stereochemical outcome for S_E2 reactions.[1] In an attempt to demonstrate the viability of an inversion mechanism, Jensen and Davis[2] sought to devise a system which would have properties favorable to an inversion pathway. An examination of the possible transition states for S_E2 reactions, Figure 1, reveals that the transition state leading to inversion of configuration at carbon, Figure 1c, would require (a) sufficient charge stabilization of both leaving groups Y and M and (b) steric hindrance to frontside attack by the electrophile Y–Z. Thus, Jensen and Davis synthesized trineopentyl-*sec*-butyltin, reacted it with bromine in methanol with added sodium bromide, and obtained inversion at carbon.[2] Since this finding, other groups have also demonstrated inversion stereochemistry for S_E2 processes at carbon–tin bonds. Rahm and Pereyre demonstrated that the severe steric congestion caused by neopentyl substitution on tin resulted in an abnormal stereochemical outcome and that retention was still the preferred pathway.[3] In a later study performed by McGahey and Jensen it was found that inversion pathways compete with retention pathways and there is *no* general preferred stereochemistry.[4] They studied the bromodemetalation of a series of tetraalkyltins of the form (*sec*-butyl)Sn(isopropyl)$_{3-N}$(neopentyl)$_N$, N = 0–3, in carbon tetrachloride, acetonitrile, and methanol. They observed that reactions in carbon tetrachloride gave predominantly retention of configuration, reactions in methanol yielded *sec*-butyl bromide with either net retention or inversion of configuration depending on alkyl substitution, and reactions performed in acetonitrile gave products with predominantly net inversion of carbon. This work demonstrated the separate influences exerted by alkyl substitution on tin and solvent on the eventual stereochemical pathway.

Gielen and Fosty also observed a dramatic medium effect for the bromodemetalation of tetraalkyltins in chlorobenzene: inversion of configuration at carbon in the presence of "naked" fluoride ion and retention in the absence of the fluoride salt.[5]

These media effects raised crucial questions about the role of media participation in determining the eventual stereochemistry of electrophilic cleavages at the carbon–tin bond. The primary questions are the following: what role does solvent play in determining the stereochemistry of reaction, and what solvent properties are especially important in this participation? Reported herein are the results of a systematic study of the effects of solvent on the halodemetalation of tetraalkyltin compounds. Both stereochemistry at carbon and ^{119}Sn NMR are utilized as mechanistic probes.

Also, it has been demonstrated that alkyl substitution on tin is vitally important in determining the stereochemistry of electrophilic cleavage,[2-4] and preliminary results indicate that solvent also plays a major role.[4,5] However, the effect of the electrophile has not yet been systematically investigated. The stereochemistry of S_E2 reactions at carbon–tin bonds by bromine has been studied fairly

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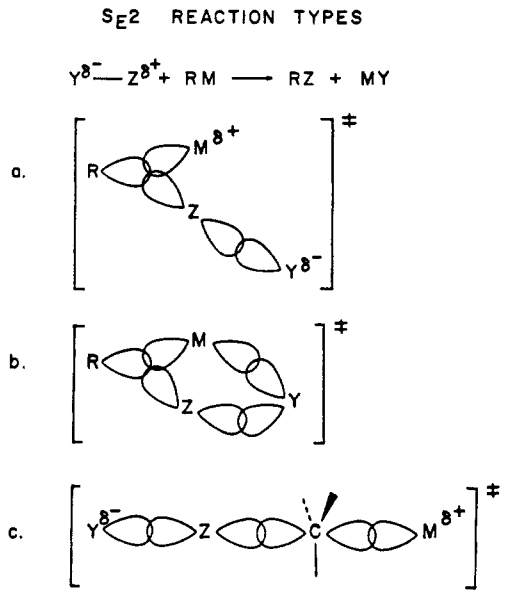

Figure 1.

extensively,[2-6] but little has been reported concerning other halogens. It might be expected that the nature of the electrophile would also exert some influence on the relative rates of the competing retention and inversion pathways. This expectation is realized in the results presented herein.

Results and Discussion

Solvent Effects: Stereochemical Results. In studying the effect of solvent, the bromodemetalation of diisopropylneopentyl-*sec*-butyltin and triisopropyl-*sec*-butyltin were performed in ten different solvents. These two tetraalkyltin substrates were specifically chosen since McGahey and Jensen had previously shown that either compound has no overwhelming preference to either retention or inversion pathways.[4] The two requisite optically active tin compounds were synthesized via Scheme I.

Scheme I

$$Ph_3SnCl + 2M \xrightarrow[THF/NH_3]{-78\ ^\circ C} Ph_3Sn^-M^+ + MCl$$

$$Ph_3Sn^-M^+ + R^*\text{–}OMs \xrightarrow[THF/NH_3]{-33\ ^\circ C} Ph_3Sn\text{–}R^* \text{ (inversion)}$$

$$Ph_3Sn\text{–}R^* + 2Br_2 \xrightarrow[MeOH/CCl_4]{} R^*\text{–}SnPhBr_2$$

$$R^*SnPhBr_2 + 2R'MgBr \xrightarrow{Et_2O} R^*SnPhR_2'$$

$$R^*SnPhR_2' + Br_2 \xrightarrow{MeOH/CCl_4} R^*SnR_2'Br$$

$$R^*SnR_2'Br + R''MgBr \xrightarrow{Et_2O} R^*SnR_2'R''$$

R* = *sec*-butyl; M = Li, Na, K

The optical purities of the final tetraalkyltin compounds were assigned on the basis of the known optical purity and configuration of *sec*-butyltriphenyltin.[7]

In general the reactions were performed in the dark, at room temperature, under an air atmosphere with a ~0.2 M solution of the organotin substrate. Due to potentially bothersome and competing free-radical processes, when chlorinated hydrocarbon solvents were studied, the radical inhibitor bis(3-*tert*-butyl-4-hydroxy-5-methylphenyl) sulfide was used at a concentration one-tenth that of the organotin. The configuration and optical purity of the resulting *sec*-butyl bromide was determined, and the results are summarized in Table I.

Table I. Stereochemistry[a] of the Bromination of R_3Sn-*sec*-butyl

	obsd stereochemistry	
	i-Pr_3Sn[b]	*i*-Pr_2NpSn[b]
methanol	9% ret	4% ret
ethanol	33% ret	5% ret
1-propanol	25% ret	8% ret
acetonitrile	15% inv	66% inv
dimethylformamide	4% inv (76% inv)[c]	49% inv
benzonitrile	12% ret	4% ret
1,2-dichloroethane	8% ret	24% ret
chlorobenzene	28% ret	33% ret
tetrahydrofuran	24% ret	52% ret
carbon tetrachloride	57% ret	74% ret

[a] Defined as optical purity of 2-bromobutane/optical purity of organotin; 15.8° used as maximum rotation of starting *sec*-butyltriphenyltin and 34.2° for *sec*-butyl bromide.[7] [b] R_3Sn: Np = neopentyl; *i*-Pr = isopropyl; ret = retention; inv = inversion. [c] If the reaction is carried out at 0.02 M instead of 0.2 M concentration of tin compound to assure absolute homogeniety.

The results further support the work of earlier studies;[4,5] i.e., solvent or medium plays an important role in the mechanism of S_E2 bromodemetalation of carbon–tin bonds. The importance of solvent can be readily appreciated by comparing the transition states for the inversion (Figure 1c) and retention (Figure 1a,b) pathways. Though Figure 1a shows some charge separation, it is most likely that some internal charge stabilization exists to the point of possibly being the cyclic four-centered transition state, Figure 1b. Certainly the inversion pathway, Figure 1c, has complete charge separation and would require substantial solvation in order to be competitive with retention pathways. In accordance with this thought is the observation that net retention is observed in nonpolar solvents (exclusive of free-radical chains) whereas in polar solvents such as acetonitrile or dimethylformamide net inversion is observed. Thus the relative rates of the two competing pathways can be drastically altered by solvent changes.

One significant trend, which becomes obvious in looking at the results, is the propensity of the polar-aprotic solvents acetonitrile and dimethylformamide to give the products with the greatest inversion, whereas polar-aprotic solvents such as methanol or ethanol are not nearly as efficient in stabilizing the inversion transition state. Certainly the protic solvents would be more efficient at stabilizing the anionic leaving group, bromide ion, in the inversion transition state due to their hydrogen-bonding capabilities (acetonitrile and dimethylformamide would stabilize bromide ion only via ion–dipole interactions). The difference in inversion transition state stabilization between the two classes of solvent, protic vs. aprotic, most likely lies in their abilities to solvate the tin cation. Space-filling models suggest that tremendous steric hindrance to solvation of the nascent trialkyltin cation exists. It would be expected that both acetonitrile and dimethylformamide would be more efficient at tin cation stabilization than methanol or ethanol on the basis of purely steric grounds. The polar-aprotic solvents have their donor atoms in a less sterically hindered form and are able to physically "reach" the cationic tin center. The protic solvents, methanol and ethanol, have their donor atom in a bivalent, doubly substituted form, thus making it more difficult to solvate the

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Table II. ^{119}Sn NMR Shifts of R_3SnBr in Various Solvents[a]

R	concn	solv	δ
methyl	neat[b]		129.6
methyl	~0.1 M	DMF	-3.7
ethyl	neat[b]		147.6
ethyl	~0.1 M	DMF	24.4
isopropyl	neat[b]		115.5
isopropyl	~0.1 M	DMF	32.4
neopentyl	~0.1 M	CCl_4	79.5
neopentyl	~0.1 M	DMF	6.0

[a] Ref = external standard $(CH_3)_4Sn$. [b] Not corrected for magnetic susceptibility, maximizing effect on the order of 2–3 ppm.

Table III. ^{119}Sn NMR Shifts of R_3SnX as a Function of Solvent

	chemical shift, δ[a]		
substrate	nonpolar	methanol	DMF
$(i\text{-Pr})_3SnBr$	115.5 (neat)[b]	92.2	32.4
$(Np)_3SnBr$	79.5 (CCl_4)	69.0	6.0
$(i\text{-Pr})_3SnCl$	100.4 (neat)[b]	64.6	10.3
$(Np)_3SnCl$	122.8 ($CDCl_3$)	94.6	22.4

[a] In ppm from $(CH_3)_4Sn$ (external standard). [b] Not corrected for magnetic susceptibility.

sterically hindered tin cation.

^{119}Sn NMR Results. It might be expected that the degree of tin atom solvation by these various solvents can be measured by ^{119}Sn NMR, since the electronic environment around the tin atom can be qualitatively determined by observing the ^{119}Sn resonance frequency in various solvents. It was previously stated that the tin cation is extremely crowded. Thus, the degree of solvation by a solvent should be dependent on both the structure of the solvent and the bulkiness of the alkyl groups on tin. Trialkyltin halides have a partial positive charge on tin, just as in the inversion transition state, and can thus act as Lewis acids. The bulkiness of the alkyl group on tin has already been shown to affect the Lewis acidity of various trialkyltin halides when complexing iodide.[9] Thus the ^{119}Sn shifts of a series of trialkyltin halides have been observed in a noncomplexing solvent, carbon tetrachloride or neat trialkyltin halide, and in a complexing solvent, dimethylformamide (DMF) (Table II).

The results in Table II indicate that increasing the bulkiness of the alkyl groups on tin decreases the degree of interaction between the complexing vs. noncomplexing solvents and show the following trend: R = methyl, $\Delta\delta$ = 133 ppm; R = ethyl, $\Delta\delta$ = 123 ppm; R = isopropyl, $\Delta\delta$ = 83 ppm; R = neopentyl, $\Delta\delta$ = 74 ppm. Although $\Delta\delta$ does decrease along the series, clearly the systems under study are not so hindered as to prevent some interaction with the solvent. These results thus support the idea that substitution on tin is important when the magnitude of solvent effects is discussed and that, in general, steric requirements must always be considered.

If the ^{119}Sn shifts are now compared for triisopropyl- and trineopentyltin bromides and chlorides in a nonpolar environment, CCl_4, $CDCl_3$, or neat solution, a polar-protic environment, methanol, and a polar-aprotic environment, DMF, a definite trend emerges (Table III). In all cases, dimethylformamide complexes the tin atom better than does methanol, which in turn interacts better than CCl_4, $CDCl_3$, or the trialkyltin halide itself. This is also the order of increasing inversion transition state stabilization, as obtained from the stereochemical results. Thus it is clear that a solvent capable of strongly solvating or complexing the tin center is important in obtaining inversion configuration at carbon.

It should be noted that interpretation of these results with ^{119}Sn NMR should be approached carefully since many factors can influence ^{119}Sn chemical shifts.[9] For example, ionization of the tin halide could lead to erroneous interpretation of the data. Also autoassociation of the substrate can lead to irregular results (though we have found there is no significant change in ^{119}Sn shifts upon dilution). Certainly these NMR results are purely qualitative but are clearly of value in conjunction with the stereochemical results.

In previous work it was found that bromide ion does not participate (coordinate to tin in the transition state) up to 1 M.[2] Therefore solvation of tin was expected to be relatively unimportant. This is not the case, however, and the observed greater degree of inversion in acetonitrile and DMF is likely the result of relative anionic and cationic solvation effects. Apparently the solvation of tin by acetonitrile or DMF more than offsets the lesser solvation of bromide ion (compared to methanol or ethanol).

Table IV. Stereochemistry[a] of the Halodemetalation of R_3Sn-*sec*-butyl

		obsd stereochemistry	
solvent	electrophile	$i\text{-Pr}_3Sn$[b]	$i\text{-Pr}_2NpSn$[b]
methanol	I_2	15% ret	11% ret
methanol	IBr	31% ret	73% ret
methanol	ICl	43% ret	41% ret
methanol	Br_2	9% ret	4% ret
acetonitrile	I_2	5% inv	13% inv
acetonitrile	IBr	41% inv	100% inv
acetonitrile	ICl	63% inv	100% inv
acetonitrile	Br_2	15% inv	66% inv

[a] Defined as optical purity of 2-iodobutane/optical purity of organotin; 38.5° used as maximum rotation of *sec*-butyl iodide[16] and 15.8° for *sec*-butyltriphenyltin.[7] [b] R_3Sn: Np = neopentyl; *i*-Pr = isopropyl; ret = retention; inv = inversion.

The Effect of the Electrophile. The halodemetalation of triisopropyl-*sec*-butyltin and diisopropylneopentyl-*sec*-butyltin has been carried out in methanol and acetonitrile by using iodine, iodine monochloride, and iodine monobromide as electrophiles, utilizing the same reaction conditions as for the bromodemetalation reactions. The results are summarized in Table IV.

The rate law for iododemetalation of tetraalkyltin compounds has been determined previously.[10] In both methanol and dimethyl sulfoxide the rate expression was found to be purely second order, first order in tetraalkyltin and first order in iodine

$$\text{rate} = k_2[R_4Sn][I_2]$$

Studies have also been performed on the relative rates of iododemetalation of a series of R_4Sn compounds in acetic acid (R = methyl, ethyl, propyl).[11] The results are identical with those found with bromine; i.e., $k_{Me} > k_{ethyl} > k_{propyl}$. These findings are explained in terms of steric effects involving the trialkyltin leaving group. Thus these previous studies show that iodine behaves similarly to bromine in that it appears to be a well-behaved S_E2 process. (One group, however, does bring up the possibility of electron-transfer processes for the iododemetalation of tetraalkyltins in nonpolar solvents,[12] but it is not clear that this is relevant to these results in polar solvents.)

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Data on the mixed dihalogen cleavage of organotins are limited; for example, the rate laws in polar solvents have yet to be determined. Because only second-order kinetics have been observed in polar solvents for both bromine and iodine, for the sake of discussion, we assume the interhalogens behave similarly. Though limited in number, previous studies have demonstrated that reactions of organotins with iodine monobromide and iodine monochloride yield only alkyl iodides and trialkyltin bromides or chlorides as products.[13] This suggests that the reactions occurred via exclusively polar mechanisms.

Nonetheless, it is difficult to accurately describe the mechanism or mechanisms by which these mixed halogens or iodine cleave tetraalkyltins without supporting stereochemical evidence. Sisido et al. iododemetalated optically active (+)-(1-methyl-2,2-diphenylcyclopropyl)trimethyltin in carbon tetrachloride but obtained only racemized products.[14] This is not surprising considering the available radical pathways in carbon tetrachloride when no measures are taken to eliminate them.

A comparison of the results with the previous stereochemical studies with bromine reveals that iodination proceeds with greater net retention under identical conditions. This is not surprising if one closely examines the possible retention transition states in Figure 1. The transition states (Figure 1a,b) are subject to severe steric interactions between the alkyl groups on tin and the incoming electrophile. As was shown by McGahey and Jensen[4] and in this study, steric interactions are vitally important in determining stereochemistry. Any factor reducing these unfavorable steric interactions is expected to lower the energy of the retention pathway. Thus the ability of iodine to form bonds at longer distances than bromine decreases the hindrance by bulky groups on tin in the retention transition state. (The *A* value for iodine is slightly less than for bromine.)

Cleavage of carbon–tin bonds by the mixed halogens IBr and ICl in methanol consistently occurs with yet greater net retention than with iodine. The three electrophiles differ only in the anionic leaving group since the electrophile atom is in each case iodine. The propensity of the mixed-atom electrophiles ICl and IBr to yield products with higher retention of configuration at carbon may be ascribed to stronger interaction between chloride or bromide and the incipient tin cation in the retention transition state (see Figure 1b). Remember that methanol is not efficient at solvating the tin cation. Thus such increased internal complexation between the cationic and anionic leaving groups should favor retention stereochemistry.

By contrast, all halodemetalations in acetonitrile investigated here occur with inversion. Inversion pathways are dominant in acetonitrile presumably due to the solvent's ability to solvate the large, sterically hindered tin cation, thus lowering the activation energy of the reaction. With the tin cation adequately solvated by the solvent acetonitrile, the stability of the anionic leaving group thus becomes an important consideration in the overall energetics of the inversion pathway. On the basis of anodic dissolution potentials of mercury vs. an external calomel electrode, it has been determined that the order of stability for halide ions in acetonitrile is[15] $Cl^{\theta} > Br^{\theta} > I^{\theta}$. This is the same order as the increased preference for the inversion pathway. Accordingly, the energy of the inversion transition state is lowered as the leaving halide ion is changed from iodide to bromide to chloride, accounting for the increased net inversion of the series I_2, IBr, and ICl.

Conclusion. The results presented here and previously[3-5] indicate that the stereochemistry of S_E2 processes at carbon–tin bonds can be independently altered by judicious choice of (a) alkyl substitution on tin, (b) solvent or medium, and (c) electrophile. Furthermore, there appears to be no preferred, general stereochemical pathway. Both the retention and inversion processes are competing, and the relative rates of each can be altered with the above-mentioned factors.

Experimental Section

General Data. Unless otherwise noted starting materials were obtained from commercial suppliers and used without further purification. Melting points and boiling points are uncorrected. NMR spectra were generally determined on a Varian T-60, a Varian EM 390, or a UCB 200 spectrometer. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Proton-decoupled ^{119}Sn NMR spectra were measured at 67.16 MHz on the UCB 180 spectrometer. Chemical shifts are expressed as parts per million downfield from tetramethyltin as reference. Melting points were determined on a Büchi melting point apparatus. Gas–liquid partition chromatography (GLC) was conducted on a Varian Aerograph A-90-P3 gas chromatograph or a Varian Aerograph 1200 capillary chromatograph. Mass spectra were obtained with an AEI MS-12 spectrometer. Mass spectral data are tabulated as *m/e* (intensity expressed as percent of total ion current). Optical rotations were measured directly at the sodium D line or at the mercury lines of 578 and 546 nm with a Perkin-Elmer Model 241 polarimeter. Quantitative elemental analysis were performed by the Microanalytical Laboratory of the College of Chemistry of the University of California at Berkeley.

Resolution of (±)-2-Butanol. Optically active 2-butanol was obtained from resolution of the Brucine salt of 2-butyl hydrogen phthalate according to the procedure of Kantor and Hauser.[16]

Preparation of (*R*)-(−)-*sec*-Butyltriphenyltin. A 1-L, 3-necked, round-bottomed flask equipped with a dry ice condenser, self-equalizing addition funnel, mechanical stirrer, and a nitrogen inlet bubbler was flame dried under a stream of nitrogen (nitrogen was dried by passage through Drierite and potassium hydroxide). The flask was charged with 163.05 g (0.4235 mol) of triphenyltin chloride and 200 mL of tetrahydrofuran freshly distilled from Na/benzophenone. The system was again flushed with nitrogen and then immersed in a dry ice bath. Approximately 350 mL of ammonia was then distilled into the reaction vessel from potassium. A milky white solution resulted when all of the ammonia had been transferred. Under positive nitrogen pressure, 20.37 g (0.8855 mol) of freshly cut sodium was added slowly. After 4 h of stirring, the reaction mixture turned blood-red. The dry ice bath was removed, and the reaction mixture was allowed to reflux over a 2-h period. Then, 58.5 g (0.385 mol) of *sec*-butylmethanesulfonate, prepared by the method of Crossland and Servis[17] from 2-butanol, $[\alpha]^{26}_D$ +11.03°, was added neat to the tin anion solution over 5 min. The reaction mixture was allowed to reach room temperature and stirred overnight. To the resulting gray solution was added 500 mL of water and 250 mL of ether, and the resulting layers were separated. The aqueous phase was extracted once with 100 mL of ether. The combined organic extracts were washed successively with 250 mL of 20% potassium fluoride and 250 mL of brine and dried over anhydrous potassium carbonate. Removal of the solvent by rotary evaporation gave a white oil consisting of a mixture of the desired product and hexaphenylditin. The crude product was taken up in hot absolute ethanol, and the insoluble ditin was removed by filtration. When the filtrate was cooled, the product crystallized as white needles. The precipitate was washed with cold ethanol and dried in a

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vacuum oven (1 mm, <50 °C) for several hours. The white solid was further purified by silica gel (Merck 60) column chromatography (5 × 30 cm column) with pentane as the eluant. This afforded 69.33 g (44%) of (*R*)-(−)-triphenyl-*sec*-butyltin: mp 70–72 °C; $[\alpha]^{26}_D$ −11.468°; l = 1; ρ = 0.0489 g/mL in benzene. This rotation corresponds to 73% optical purity and a stereospecificity of 89% in the tin anion displacement of the methanesulfonate ester of 2-butanol. Anal. Calcd for $C_{22}H_{24}Sn$: C, 64.90; H, 5.87. Found: C, 64.85; H, 5.87.

Preparation of Diisopropylphenyl-*sec*-butyltin Compounds. In a typical procedure, triphenyl-*sec*-butyltin, 35.0 g (0.086 mol), was placed in a 500-mL, round-bottomed flask containing a magnetic stirring bar. The compound was dissolved in a minimum amount of carbon tetrachloride (about 120 mL). Then 250 mL of methanol was slowly added with vigorous stirring to obtain a 0.3 M solution. A selfequalizing funnel, containing 8.9 mL of bromine (0.172 mol) in 28.5 mL of carbon tetrachloride, was then attached to the flask. With the exclusion of light, the bromine solution was slowly added over a period of 5 h and the solution was stirred overnight. Additional bromine was added, if necessary, until a faint yellow color persisted. Excess bromine was destroyed by the addition of pentene. The solvents were removed by rotary evaporation, and residual bromobenzene was removed on a high-vacuum line overnight. Further purification of *sec*-butylphenyltin dibromide was not necessary.

The required isopropylmagnesium bromide was prepared to give 4 mol of Grignard reagent/mol of the *sec*-butylphenyltin dibromide (2-fold excess). The Grignard reagent was prepared from isopropyl bromide, 32.9 mL (0.35 mol), in either ether or THF, 175 mL, freshly distilled from Na/benzophenone. Commercially available magnesium turnings, 8.36 g (0.35 mol), were used. When reaction initiation was required, either 1,2-dibromoethane or an iodine crystal was used.

The *sec*-butylphenyltin dibromide was taken up in a small volume of ether (~100 mL) and added to the stirred solution of Grignard reagent at a rate to maintain reflux. Upon complete addition, the solution was stirred an additional 2 h. The reaction mixture was then immersed in an ice bath, and water was slowly added to destroy excess Grignard reagent. The organic and aqueous phases were separated, and the aqueous phase was extracted twice with 100-mL portions of ether. The organic phases were combined and washed twice with 150 mL of 20% aqueous potassium fluoride and twice with 150 mL of brine. After being dried with anhydrous potassium carbonate, the solution was filtered and the ether was removed by rotary evaporation. This procedure afforded 22.25 g of crude diisopropylphenyl-*sec*-butyltin (76.3%). This material was used without further purification.

Preparation of *sec*-Butyltriisopropyltin. Diisopropylphenyl-*sec*-butyltin, 22.25 g (0.066 mol), was placed in a 500-mL, round-bottomed flask. The compound was dissolved in 70 mL of carbon tetrachloride, and 150 mL of methanol was added to obtain a ~0.3 M solution. A self-equalizing addition funnel containing 3.41 mL of bromine (0.066 mol) in 20 mL of carbon tetrachloride was attached to the flask. With the exclusion of light, the bromine solution was added with stirring over 2 h. When necessary, additional bromine was added until a faint yellow color persisted. Excess bromine was destroyed with pentene, and the solvent was removed by rotary evaporation. The remaining clear liquid was placed on a high-vacuum line to remove any residual bromobenzene.

Isopropylmagnesium bromide was prepared as above. A 2 M solution of the Grignard reagent in ether corresponding to a 2-fold excess was prepared. Diisopropyl-*sec*-butyltin bromide was taken up in 30 mL of ether and slowly added to the Grignard reagent. The solution was refluxed for 2 h after the addition was completed. The reaction mixture was then cooled in an ice bath, and the excess Grignard reagent was destroyed by the slow addition of 80 mL of water. The aqueous and organic layers were separated, and the aqueous phase was extracted twice with 100 mL of ether. The combined ether extracts were then washed twice with 80 mL of aqueous 20% potassium fluoride and twice with 80 mL of brine. The solution was dried over anhydrous potassium carbonate and filtered, and the solvent was removed by rotary evaporation. The remaining clear, viscous liquid was vacuum distilled through a short-path Vigreaux column; bp 83 °C at 2.0 mm. This procedure afforded 20.7 g (78%) of (*R*)-(−)-triisopropyl-*sec*-butyltin: $[\alpha]^{26}_D$ −11.356°; l = 1; ρ = 0.1798 g/mL in carbon tetrachloride. Mass spectrum (70 eV): m/e (relative intensity) 306 (0.06), 263 (0.69), 207 (1.07), 165 (1.40), 125 (0.89), 111 (1.52), 97 (2.60), 83 (2.68), 57 (5.69). Anal. Calcd for $C_{13}H_{30}Sn$: C, 51.12; H, 9.85. Found: C, 51.11; H, 9.68.

Preparation of Diisopropylneopentyl-*sec*-butyltin. Diisopropylneopentyl-*sec*-butyltin was synthesized from diisopropylphenyl-*sec*-butyltin and neopentyl Grignard in a manner directly analogous to that of triisopropyl-*sec*-butyltin. The neopentyl Grignard was synthesized by similar methods to those used for the preparation of the isopropyl Grignard (neopentyl chloride freshly purified by distillation from P_2O_5). The crude diisopropylneopentyl-*sec*-butyltin, a yellow oil, was vacuum distilled through a short-path Vigreaux column; bp 65–67 °C at 0.10 mm. This procedure afforded a 69% yield of (*R*)-(−)-diisopropylneopentyl-*sec*-butyltin: $[\alpha]^{26}_D$ −7.168; l = 1; ρ = 0.2033 g/mL in carbon tetrachloride. The precursor triphenyl-*sec*-butyltin had $[\alpha]^{26}_D$ −11.468°, l = 1, and ρ = 0.0489 g/mL. Mass spectrum (70 eV): m/e (relative intensity) 334 (0.04), 291 (3.85), 277 (1.64), 263 (1.00), 235 (4.33), 191 (2.50), 135 (4.12), 121 (1.63). Anal. Calcd for $C_{15}H_{32}Sn$: C, 54.10; H, 10.22. Found: C, 54.42; H, 10.12.

General Method for Stereochemical Analysis of Bromodemetalation Reactions. For stereochemical studies, the concentration of *sec*-butyl bromide in the polarimetry cells was determined by quantitative gas chromatography using toluene as an internal standard. The toluene/*sec*-butyl bromide gas chromatographic response ratio was determined in the following way. (*S*)-(+)-Bromobutane, prepared from *R*-(−)-2-butanol ($[\alpha]^{26}_D$ −4.80°) by using bromine and triphenylphosphine in diglyme,[17,19] and 0.050 mL of toluene were diluted to 5 mL in a volumetric flask. The calculated rotation, based on 0.0878 g of (*S*)-(+)-2-bromobutane, $[\alpha]^{26}_D$ +11.718°, was $[\alpha]^{26}_D$ +0.212°. The observed value was $[\alpha]^{26}_D$ −0.217°. Samples of this solution were analyzed by gas chromatography (15 ft × 0.5 in. glass column in 10% SE-52 on Chromosorb W), and the area ratio of toluene/*sec*-butyl bromide was determined to be 0.695. The response factor is defined as

$$\frac{\text{area of toluene}}{\text{area of } sec\text{-butyl bromide}} \times \text{factor} = \frac{\text{weight of toluene}}{\text{weight of } sec\text{-butyl bromide}}$$

A factor of 0.710 was obtained. This can be compared with factors of 0.728 and 0.744 determined by Davis[18] and McGahey,[19] respectively.

The specific rotations were determined by calculating the concentration of *sec*-butyl bromide in a known volume containing a known quantity of toluene. Thus

$$\text{g of } sec\text{-butyl bromide} = \text{g of toluene} \Big/ \frac{\text{area of toluene}}{\text{area of } sec\text{-butyl bromide}}(0.710)$$

Since the (+) rotamers of all *sec*-alkyl compounds are of the *S* configuration,[18] any change in sign represents a change in stereochemistry. Optical purities of the tetraalkyltins are taken to be those of *sec*-butyltriphenyltin. The optical purities of the alkyl halides and *sec*-butyltriphenyltin compounds were assigned by using the following maximum rotations: for *sec*-butyltriphenyltin, 15.9°;[7] for *sec*-butyl bromide, 34.1°;[3] for *sec*-butyl iodide, 38.5°.[20]

General Method for the Bromodemetalation of (*R*)-(−)-*sec*-Butyltrialkyltin Compounds in Ten Solvents. The bromodemetalation of (*R*)-(−)-*sec*-butyltriisopropyltin and *R*-(−)-*sec*-butylneopentyldiisopropyltin was performed in ten different solvents: methanol, ethanol, *n*-propyl alcohol, acetonitrile, dimethylformamide, benzonitrile, 1,2-dichloroethane, chlorobenzene, tetrahydrofuran, and carbon tetrachloride. The alcohols were purified by distillation from magnesium. Acetonitrile was

(18) Davis, D. D. Ph.D. Thesis, University of California, Berkeley, 1966.
(19) McGahey, L. F. Ph.D. Thesis, University of California, Berkeley, 1979.
(20) Hudson, H. R. *Synthesis* **1969**, 112.

purified by first stirring over calcium hydride and then distilling from phosphorus pentoxide. Dimethylformamide was distilled from barium oxide. Halogenated solvents were distilled from phosphorus pentoxide. THF was distilled from Na/benzophenone. Bromine was not purified. In a typical procedure for the bromodemetalation, 2.0 g (0.0066 mol) of (*R*)-(−)-*sec*-butyltriisopropyltin was taken up in 25 mL of the selected solvent and placed into a 50-mL, round-bottomed flask equipped with a self-equalizing addition funnel. To the addition funnel was added 0.34 mL (0.0066 mol) of bromine in 5 mL of the selected solvent. For reactions performed in the halogenated solvents, the radical inhibitor 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide was used in a concentration one-tenth that of the organotin. With the absolute exclusion of light, the bromine solution was added slowly over 2 h with stirring. After the addition of bromine was completed, the reaction was quenched by the addition of 2 mL of 10% aqueous sodium bisulfite. Then, 10 mL of methylene chloride was added followed by 50 mL of water. The layers were separated, and the aqueous phase was extracted twice with 3 mL of methylene chloride. The combined organic extracts were washed twice with 3 mL of water and dried over calcium chloride. The solution was filtered, and the volatiles were bulb-to-bulb vacuum transferred. The volatiles were then concentrated to 2 mL by distilling off excess methylene chloride through an 18-in. tantalum spiral column. To the remaining solution was added 50 μL of toluene, and the solution made up to 2 mL with methylene chloride in a volumetric flask. The optical rotation was then taken. The concentration of *sec*-butyl bromide in solution was determined by quantitative gas chromatography. The stereospecificity of each reaction is determined by calculating the optical purity of the resultant *sec*-butyl bromide and comparing it to the optical purity of the precursory (*R*)-(−)-*sec*-butyltriphenyltin.

Reactions performed in acetonitrile were carried out in an identical manner except that the concentration of the volatiles after vacuum transfer afforded *sec*-butyl bromide in the distillate. Apparently *sec*-butyl bromide will azeotrope with acetonitrile. This was not a hindrance since the appropriate fraction of the distillate containing *sec*-butyl bromide was subjected to the above-mentioned analytical procedure.

General Method for Stereochemical Analysis of Iododemetalations. As with the bromodemetalation studies, the concentration of *sec*-butyl iodide in polarimetry cells was determined by quantitative gas chromatography using ethylbenzene as an internal standard. The ethylbenzene/*sec*-butyl iodide gas chromatographic response ratio was determined in the following manner. Various concentration ratios of ethylbenzene and toluene were made up, and peak area ratios were determined after gas chromatography. The response factor is defined as

$$\frac{\text{area of ethylbenzene}}{\text{area of } sec\text{-butyl iodide}} \times \text{factor} = \frac{\text{weight of ethylbenzene}}{\text{weight of } sec\text{-butyl iodide}}$$

The response factor was found to be 0.586. The data for the iododemetalation was manipulated in the same manner as with the bromodemetalations except for the newly acquired response factor for *sec*-butyl iodide.

Method for Iododemtalation of (*S*)-(+)-*sec*-Butyltriisopropyltin in Acetonitrile. A 100-mL, round-bottomed flask was charged with 3.0 g (0.009 84 mol) of (*S*)-(+)-*sec*-butyltriisopropyltin ($[\alpha]^{26}_D$ +4.424°, optical purity = 30.5%) in 40 mL of acetonitrile. Also added to the solution was 0.352 g (0.000 985 mol) of the radical inhibitor 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide. With the exclusion of light, a slurry of 2.50 g of iodine (0.009 84 mol) in 10 mL of acetonitrile was added over 2 h with stirring. The reaction was stirred an additional hour. To the reaction mixture was added 10 mL of aqueous 10% sodium bisulfite to destroy unreacted iodine, followed by 30 mL of methylene chloride and 100 mL of water. The layers were separated, and the aqueous phase was extracted twice with 50 mL of methylene chloride. The combined organic extracts were dried over calcium chloride. The solution was concentrated to ~60 mL on a rotary evaporator, and the volatiles were bulb-to-bulb vacuum transferred. Distillation of the volatiles on an 18-in. spiral tantalum column afforded a fraction at 80 °C which, by GC analysis, contained substantial amounts of *sec*-butyl iodide. To this fraction of the distillate was added 20 μL of toluene, and the solution was made up to 2 mL in a volumetric flask. Determination of the rotation of the solution and quantitative gas chromatographic analysis afforded $[\alpha]^{26}_D$ −0.59°, optical purity = 1.53%. This corresponds to a stereospecificity of reaction of 5% inversion.

For iododemetalation of (*S*)-(+)-*sec*-butyltriisopropyltin in methanol the reaction was carried out in an analogous manner to that described for the reaction in acetonitrile with one minor modification. Distillation of the volatiles after vacuum transfer did not afford any *sec*-butyl iodide in the distillate. The *sec*-butyl iodide remained in the pot and did not azeotrope with either methylene chloride or methanol. The volatiles were concentrated to ~2 mL. To this remaining solution was added 15 μL of ethylbenzene, and the solution was made up to 2 mL with methylene chloride in a 2-mL volumetric flask. Determination of the rotation of this solution and quantitative gas chromatographic analysis afforded $[\alpha]^{26}_D$ 1.782°, optical purity = 4.62%. This corresponds to a stereospecificity of 15% retention.

Similar iododemetalations of (*S*)-(+)-*sec*-butyldiisopropylneopentyltin in acetonitrile afforded *sec*-butyl iodide, $[\alpha]^{26}_D$ −1.56°, optical purity = 4.0%, corresponding to a stereospecificity of 13% inversion, while in methanol $[\alpha]^{26}_D$ +1.30, optical purity = 3.4%, corresponding to a stereospecificity of 11% retention of configuration.

Synthesis and Stereochemical Integrity of Optically Active *sec*-Butyl Iodide. To establish the stereochemical integrity of *sec*-butyl iodide to reaction and workup conditions, optically active *sec*-butyl iodide was synthesized from *sec*-butyl alcohol by a slightly modified version[21] of the method of Berlak and Gerrard.[22] Trineopentylethyltin, 2.0 g (0.0055 mol), was taken up in 25 mL of methanol, and 0.197 g (0.000 55 mol) of 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide was added as a radical inhibitor. To this mixture was then added 0.500 g (0.002 75 mol) of optically active *sec*-butyl iodide: $[\alpha]^{26}_D$ 18.717°, optical purity = 49%. With the exclusion of light, 1.40 g (0.0055 mol) of iodine was slowly added over 48 h (a much longer reaction time than necessary). Workup of the reaction mixture was identical with that of the previously conducted iododemetalations. This afforded optically active *sec*-butyl iodide with $[\alpha]^{26}_D$ +14.70°, optical purity = 38%. Approximately 20% racemization had taken place. Identical reactions carried out in carbon tetrachloride, and acetonitrile gave *sec*-butyl iodide with 20% racemization. While some racemization does take place under these severe conditions, it would be minor under the normal reaction conditions.

Iododemetalation of Optically Active *sec*-Butyltriisopropyltin or *sec*-Butyldiisopropylneopentyltin Using Iodine Monohalides. As an example, for iodine monobromide in acetonitrile: to a 50-mL, round-bottom flask was added 25 mL of a 0.25 M solution of the appropriate optically active tetraalkyltin compound in acetonitrile. With the exclusion of light, 1 equiv of iodine monobromide in 5 mL of acetonitrile was added through a self-equalizing addition funnel. Addition was complete after 1 h, the reaction was quenched by the addition of 10 mL of saturated sodium thiosulfate, and the reaction mixture was then poured into 100 mL of water, followed by the addition of 40 mL of methylene chloride. The layers were separated, and the aqueous phase was extracted twice with 50 mL of methylene chloride. The combined organic phases were then washed twice with 100 mL of water and dried with calcium chloride. The volatiles were then bulb-to-bulb vacuum transferred. The volatiles were concentrated by removing by distillation excess methylene chloride on a 18-in. spiral tantalum column. To the remaining liquid was added a known amount of ethylbenzene (5–10 μL), and the solution was made up to 2 mL with methylene chloride in a volumetric flask. Determination of the optical rotation and quantitative gas chromatography gave the $[\alpha]^{26}_D$ value and, thus, optical purity. The stereochemistry of the reaction was determined by comparing the optical purity of the *sec*-butyl iodide with that of the starting *sec*-butyltrialkyltin.

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