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Physical-organic Studies of Organotin Compounds

By

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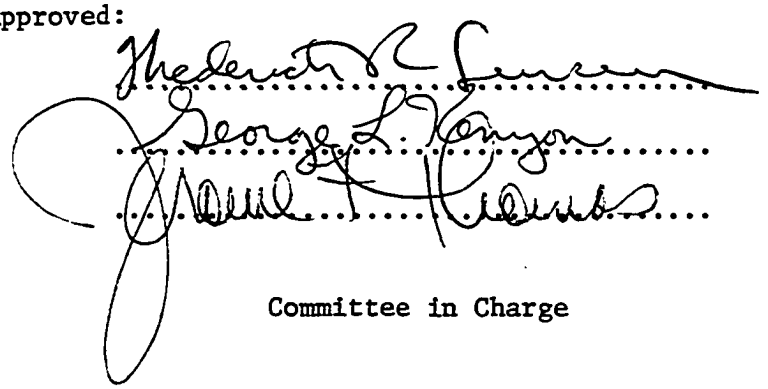

Committee in Charge

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To Sylvia

who fills each day with love

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Physical-Organic Studies of Organotin Compounds

Victor Seth Krimsley

ABSTRACT

The mechanism of the bromodemetallation of organotin compounds has been investigated. The stereochemistry of the reaction of tetraalkyltin compounds and trialkyltin halides with bromine has been carried out in methanol. Davis' result (D. Davis, Ph.D. Thesis, University of California, Berkeley, 1966) that the bromodemetallation of trineopentyl-sec-butyltin proceeds with inversion of configuration has been confirmed. It has further been shown that the reaction proceeds with greater than 80% inversion of configuration. Evidence is presented which indicates that this reaction may occur with complete inversion of configuration. The bromodemetallation of dineopentyl-sec-butyltin bromide was found to proceed with at least 60% retention of configuration. It is concluded that tetraalkyltin compounds are bromodemetallated via an S_E2 pathway with inversion of configuration. The results of the stereochemical study of the trialkyltin halide are interpreted in the light of existing kinetic data. It is proposed that trialkyltin halides are bromodemetallated via a four-centered, S_Ei transition state.

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The rate of bromodemetallation of a series of substituted-benzyltrineopentyltin compounds was carried out. It was anticipated that this investigation would provide a detailed knowledge of the charges present in the transition state of the bromodemetallation of tetraalkyltin compounds. A rather unusual rate sequence was observed. It is proposed that the bromodemetallation of the more reactive derivatives proceeds via an attack by bromine on the aromatic nucleus of the benzylic group. A change in mechanism is suggested to account for the rates of reaction of the less reactive derivatives. Kinetic data is presented which suggest that these compounds are bromodemetallated via the usual S_E2 pathway. Evidence is given that the bromodemetallation of tetraalkyltin compounds proceeds with little charge development at the carbon center undergoing attack (i.e. $\rho = -0.6$).

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FOREWORD

The following work deals with various mechanistic studies of electrophilic substitution reactions of organotin compounds:

$$R\text{-}Sn\lessgtr + E^{+} \longrightarrow R\text{-}E + {}^{+}Sn\lessgtr$$

The bulk of the work discussed and all of the work carried out by this worker deal with the bromodemetallation reaction:

$$R\text{-}Sn\lessgtr + Br_2 \longrightarrow R\text{-}Br + BrSn\lessgtr$$

Since both experimental portions of the thesis (Chapters II and III) draw heavily from the same literature, a general discussion of the pertinent literature will be found in the Introduction (Chapter I), while the Historical sections of Chapters II and III will deal with work more directly related to the experimental portions of those chapters. Since much of the new work discussed is an offshoot of the work of an earlier worker in this group (D. Davis, Ph.D. Thesis, Univ. of California (Berkeley), 1966), the important aspects of his work will be discussed in some detail.

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Chapter I

Introduction

I. Electrophilic Substitution Reactions

The electrophilic substitution reaction is well-documented in organic chemistry, and most chemists are familiar with the common aromatic electrophilic substitutions. For example, the Friedel-Crafts reaction,

(1) $(CH_3)_3C\text{-}Br$ + $\xrightarrow{\text{cat.}}$ + HBr

involves the substitution of a tertiary butyl cation, the electrophile, for a proton on the aromatic system.

In its most generalized form, the reaction:

$$X{:})Y + E(:N \longrightarrow X{:}E + Y{:}N$$

is promoted by the affinity of the electrophile, E, for the electrons of the X-Y bond. In the products X and N retain their electron pairs.

While most chemists think of aromatic substitution reactions when they hear the expression "electrophilic substitution" reaction, the electrophilic substitution reaction is much more general and the literature abounds with examples of a non-aromatic nature. For example, (1) the acid hydrolysis of a Grignard reagent:

$$R\text{-}MgCl + HCl \longrightarrow R\text{-}H + MgCl_2 ,$$

(2) the preparation of an organomercurial:

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$$R\text{-}MgCl + HgCl_2 \quad R\text{-}HgCl + MgCl_2$$

or (3) the chlorination of an organomercurial:

$$R\text{-}HgCl + Cl_2 \longrightarrow R\text{-}Cl + HgCl_2$$

are all electrophilic substitutions.

Charman, Hughes, and Ingold[1] visualized three pathways for electrophilic substitution reactions. These paths are analogous to those for nucleophilic substitutions:

(1) The S_E1 pathway involves a rate determining ionization of the substrate, followed by rapid reaction of the carbanion with the electrophile:

$$R\text{-}M \xrightarrow{\text{slow}} R^- + M^+$$

$$R^- + E\text{-}N \xrightarrow{\text{fast}} R\text{-}E + N^-$$

(2) The S_E2 reaction involves the rate determining attack of the electrophile upon the bond undergoing scission:

$$R\text{-}M + E\text{-}N \xrightarrow{\text{slow}} \left[R \div M \quad E\text{-}N \right]^{\ddagger} \longrightarrow \begin{matrix} R\text{-}E \\ + \\ M\text{-}N \end{matrix}$$

(3) The S_Ei pathway, frequently referred to as a four-center mechanism, involves a concerted rate-determining attack of the electrophile upon the substrate, with the nucleophilic portion assisting in the scission of bond undergoing cleavage:

$$R\text{-}M + E\text{-}N \xrightarrow{\text{slow}} \left[\begin{matrix} R & \text{----} & M \\ \vdots & & \vdots \\ E & \text{----} & N \end{matrix} \right]^{\ddagger} \longrightarrow \begin{matrix} R\text{-}M \\ + \\ E\text{-}N \end{matrix}$$

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Since the S_E2 and S_Ei reactions both have a kinetic dependence which is first order in substrate and first order in electrophile, they are indistinguishable kinetically. However, as we shall see in Chapter II, these pathways might be distinguishable stereochemically since the S_E2 pathway could occur with either inversion or retention of configuration, while the S_Ei mechanism is constrained to proceed with retention of configuration.

It is only in recent years that quantitative mechanistic studies of electrophilic substitution reactions have been carried out. In general, most studies involve measurement of the selectivity with which various groups, R, are cleaved from a given metal: $R\text{-}M + E^+ \xrightarrow[\text{solvent}]{} R\text{-}E + M^+$. The results vary considerably with electrophile, substrate, and solvent. Table 1 summarizes the relative rate data for several systems under various conditions. It is apparent that one cannot meaningfully discuss "electrophilic substitution reactions" without specifying the specific reaction and conditions. An organometallic substrate, R-M, has at least five major pathways by which it may be cleaved by an electrophile: (1) S_Ei (concerted), (2) S_E2 (with inversion of configuration), (3) S_E2 (with retention of configuration), (4) SH_1 (some radical process), and (5) S_E1 (unimolecular rate determining step).

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Table 1

Relative Rates of Organometallic Cleavage Reactions

Reaction:	$RSnR_3'$ Br_2 MeOH	R_2Hg HCl, DMSO Dioxane	RHgI $HClO_4$ H_2O	RHgBr $HgBr_2$ EtOH	R_4Sn HCl PhH	R_4Sn Br_2 CCl_4	R_4Sn I_2 MeOH	R_4Sn Br_2 PhCl	R_4Sn I_2 AcOH	R_4Sn Br_2 DMF	R_4Sn Br_2 AcOH	R_4Pb AcOH	R_4Pb $HClO_4$ AcOH	R_2Hg HCl, DMSO H_2O
Ref.	19	2	3	4	5	6	7	8	8	8	8	9	9	10
R														
Me	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Et	0.14	7.7	.44	.42	7.5	93	.118	12.0	.37	.46	.84	.79	.11	5.95
Pr	0.041	4.6	.22	--	3.0	45	.015	4.5	.043	.061	.12	.19	.04	3.2
i-Pr	0.0075	5.1	.13	--	3.0	800	--	13.0	--	--	.025	--	--	-3.5

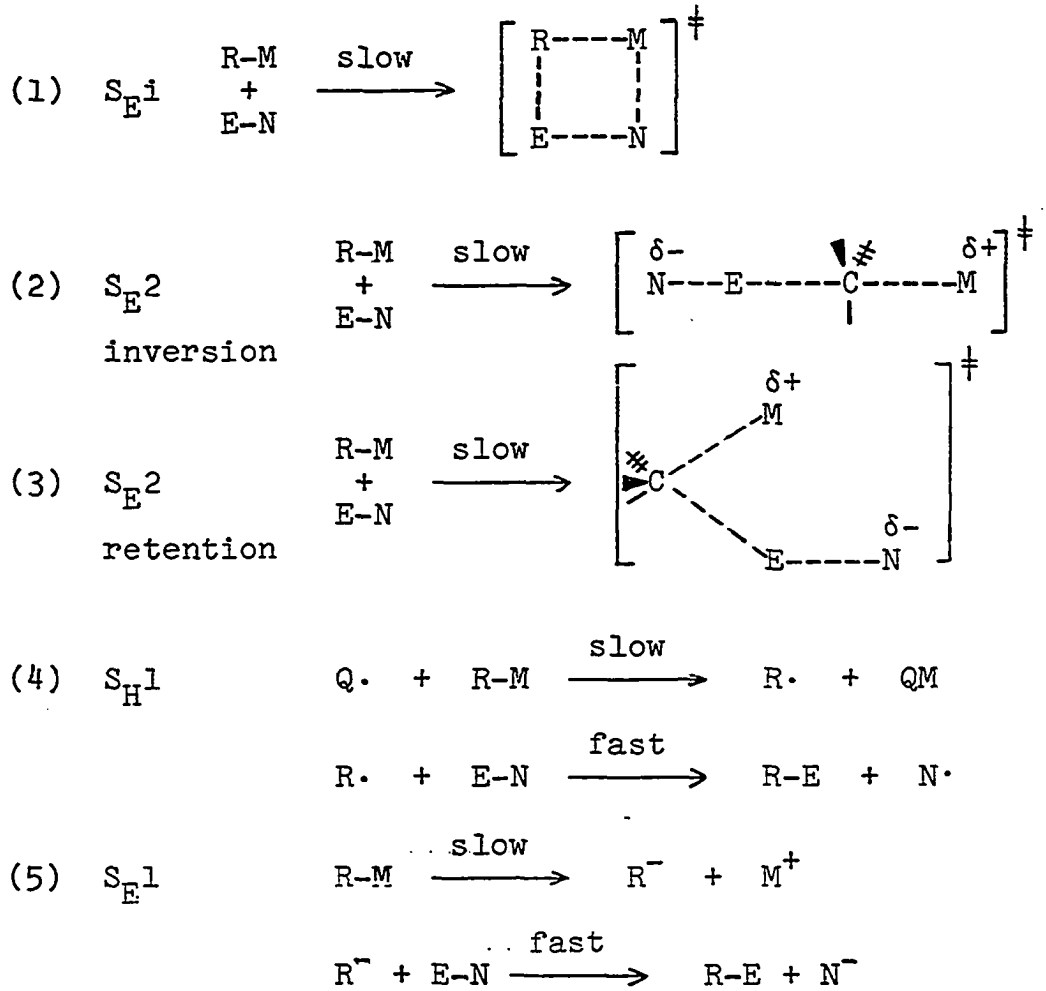

Figure 1. Pathways for Substitution Reactions on Organometallic Compounds

For a given substrate, the preferred pathway by which it is cleaved may depend upon the nature of the substrate itself, the particular electrophile, solvent, and reaction conditions. Moreover, several mechanisms may compete under any given set of conditions. The current work is concerned predominantly with halodemetallations of organotin compounds.

The Bromodemetallation of Organotin Compounds:

The halodemetallation of organotin compounds has been the subject of numerous studies by Gielen and Nasielski.[11-18]

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To summarize their data and conclusions very briefly, the authors have found[13] that for tetraalkyltin compounds, R_4Sn, bromo- or iodo-demetallation in polar solvents leads to a relative rate sequence $k_{rel}(R)$: Me > Et > n-Pr > i-Pr. However, in non-polar solvents, one observes the relative rate sequence: $k_{rel}(R)$: Me <Et> n-Pr < iso-Pr. In addition, for the polar solvents, CH_3OH, DMF, CH_3COOH, DMSO, the authors observed an increasing rate of reaction with increasing solvent nucleophilicity. From these observations they concluded that the reaction must proceed by two pathways. In polar solvents, they postulate an open, S_E2 transition state:

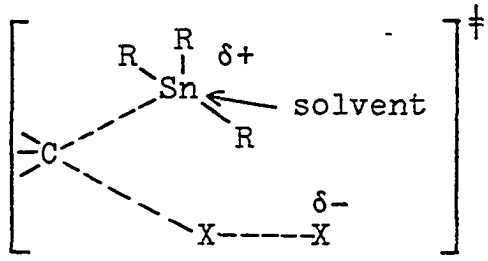

Figure 2.- Open S_E2 transition state (Retention of Configuration)

They attribute the rate sequence primarily to steric effects, the more bulky alkyl groups being cleaved most slowly. For this pathway, solvent assistance to the leaving tin-group is extremely important. Thus, the more nucleophilic the solvent, the greater the stabilization of the transition state. They assume by analogy to other electrophilic substitution reactions[13] that the reaction proceeds with retention of configuration and draw the transition state indicated.

For the non-polar solvents, where charge separation is

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more difficult to achieve, they postulate the four-centered S_Ei pathway:

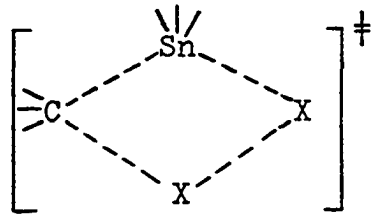

Figure 3. S_Ei transition state.

In this case, the nucleophilic portion of the electrophile – nucleophile pair can give greater stabilization to the developing positive charge on tin than can solvent. Whereas, in polar solvents, the solvent can provide much greater stabilization. For the polar, S_E2 pathway, the bulk of the solvent added to the transition state causes steric effects to be the major factor in determining the rate sequence. However, they consider the S_Ei pathway to be less crowded, and they explain the non-polar sequence on the basis of a balance between inductive and steric effects.

More recently Gilen and Nasielski[15] have looked into the bromo- and iododemetallation of several tetraalkyltin compounds in chlorobenzene, acetic acid, and methanol. They studied the rates of reaction of $RSnR_3'$ where R' = Me, Et and R = Me, Et, n-Pr, n-Bu, i-Pr, t-Bu. They find that in polar solvents, the rate expression is: rate = $k_2(R_4Sn)(X_2)$. However, in chlorobenzene, they claim to observe a third order term: rate = $k_2(R_4Sn)(X_2) + k_3(R_4Sn)(X_2)^2$. The authors attribute the third order contribution to a prior nucleophilic complexation:

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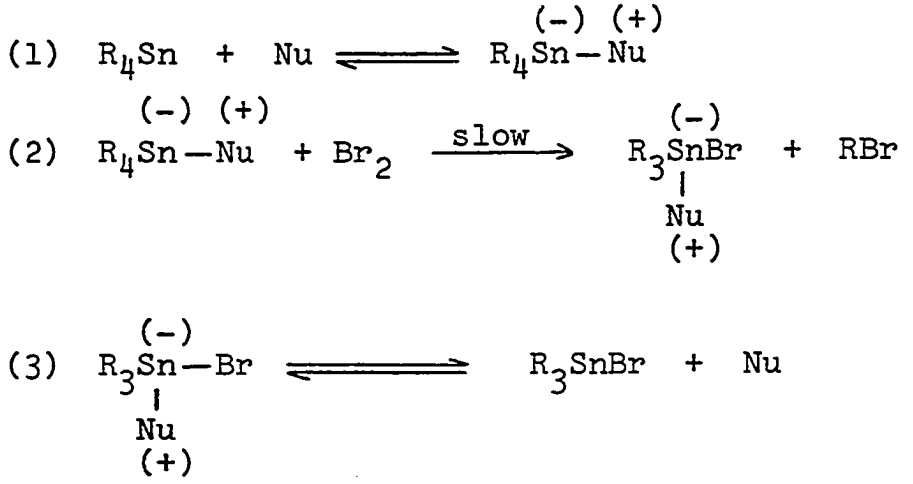
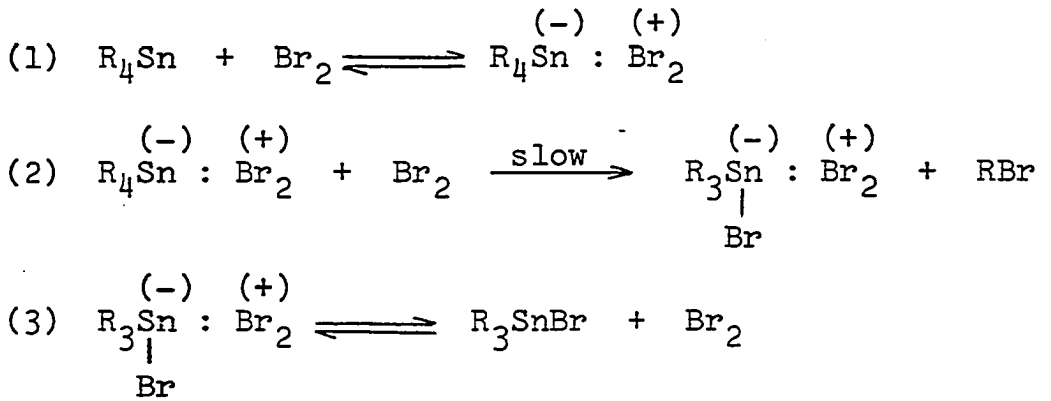


Although in polar solvents the nucleophile is the solvent, in chlorobenzene, the nucleophile is Br_2:



In the polar solvents, the authors find a rate sequence, $k_{rel}(R)$: Me > Et > n-Bu > n-Pr > i-Pr > t-Bu. Whereas in the non-polar chlorobenzene they find $k_{rel}(R)$: t-Bu > Me > Et=i-Pr > n-Pr=n-Bu. In addition, the authors find several somewhat unusual results, such as a rate dependence for the group cleaved upon the substrate from which the group is cleaved.

For example, in the iododemetallation in methanol, they observed the following relative rates for the cleavage of the group indicated from the substrate indicated:

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k_2(Me, Me_4Sn) = 1.77 >> k_2(Me, Me_3Sn-t-Bu) = 0.01

k_2(Et, Me_3SnEt) = 0.26 > k_2(Et, Et_4Sn) = 0.2

k_2(n-Pr, n-Pr-$SnEt_3$) = 0.06 > k_2(n-Pr, n-Pr_4Sn) = 0.025

k_2(n-Bu, Me_3Sn-n-Bu) = 0.132 > k_2(n-Bu, Et_3Sn-n-Bu) = 0.05 > k_2(n-Bu, n-Bu_4Sn) = 0.01

k_2(i-Pr, Me_3Sn-i-Pr) = 0.01 > k_2(i-Pr, i-Pr_4Sn) = 0.001

Again, the authors explain each result upon the competition of steric and electronic effects.

Perhaps the most definitive piece of work concerning halodemetallations of organotin compounds is that of Davis.[19] The pertinent aspects of his work are summarized here. To simplify the meaning of kinetic and stereochemical results, Davis studied the bromodemetallation in methanol of a series of unsymmetrical tin compounds, $RSnR_3'$, where the leaving tin group, $-SnR_3'$, would always be the same. Using R'= neopentyl and R=Me, Et, n-Pr, iso-Pr, sec-Bu, and neopentyl, Davis found the relative rate sequence to be: Me > Et > n-Pr > i-Pr > sec-Bu > neopentyl. In addition Davis found the reaction to proceed with inversion of configuration (see Chapter II). These results are in qualitative agreement with those of Gielen and Nasielski. Davis applied a linear free energy treatment to his data using Taft's $\sigma^*\rho^*$. The data (summarized in Table 2) is shown graphically in Figure 4.

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$$RSnR'_3 + Br_2 \rightarrow RBr + R'_3SnBr$$

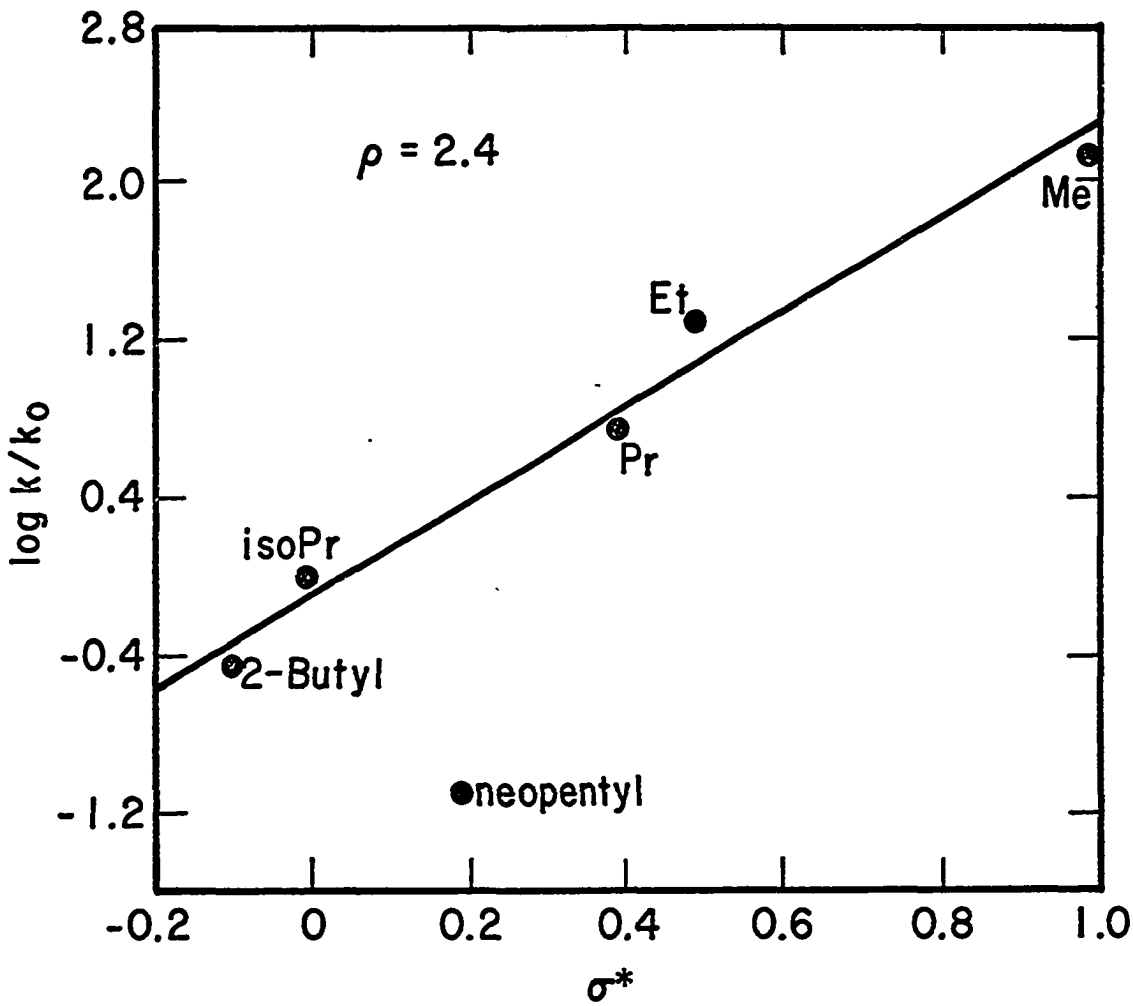

Figure 4. Bromodemetallation of $RSnR'_3$[a]

[a]Reference 19

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Table 2[a]

Bromodemetallation of R_3SnR' Correlation with σ* Relative Rate

R'	MeOH, 45°	log k/ko	σ*
Me	133	2.12	+0.98
Et	19.1	1.28	+0.49
n-Pr	5.42	0.734	+0.39
i-Pr	1.00	0.00	0.00
sec-Bu	.352	-0.10	-0.10
neopentyl	.0776	+0.19	+0.19

[a]Ref. 19

Since Davis also found the reaction to proceed with inversion of configuration, this data is reinterpreted here, comparing the relative rates of the bromodemetallation reaction to the relative rates of the well-known S_N2 halogen exchange reaction:[20]

$$Br^- + RCl \xrightarrow{k^{exch}} RBr + Cl^-$$

The data (summarized in Table 3) is shown in Figure 5. The plot shows an excellent correlation between these two reactions and further supports the stereochemical studies which accompanied it. The plot (Fig. 5) clearly demonstrates that for displacement reactions, one must be very careful about interpreting rate data in terms of quantitative inductive parameters if steric effects may play a part. It is well-known that steric effects are the major contributing factor in determining the relative rates of S_N2 reactions.

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Table 3

Rate Data for $R\text{-}SnR'_3 + Br \longrightarrow RBr + BrSnR'_3$[a]			Rate Data for $R\text{-}Cl + Br^- \longrightarrow R\text{-}Br + Cl^-$[b]	
RR	Relative Rate	$\log(k/k_o)$	Relative Rate	$\log(k/k_o)$
Me	6.96	0.84	37.2	1.57
Et	1.00	0.00	1.0	0.00
n-Pr	0.28	-0.546	0.69	-0.16
i-Pr	0.052	-1.28	0.018	-1.74
neopentyl	0.004	-2.39	0.0000063	-5.20

[a] See Ref. 19

[b] See Ref. 20

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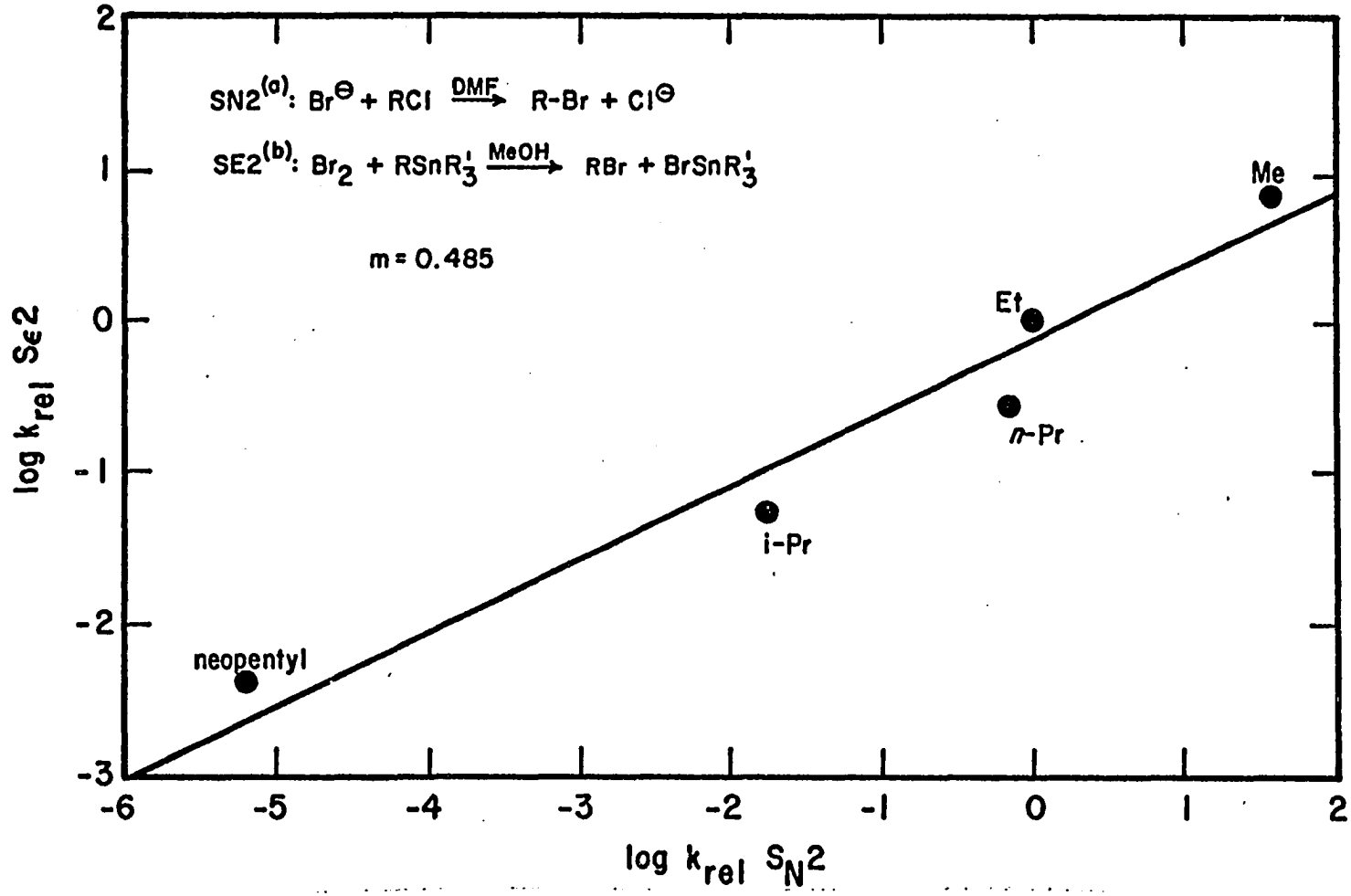

Figure 5. Comparison of S_E2 and S_N2 reactions.
(a) Reference 20
(b) Reference 19

From this data, it appears that the same is true of S_E2 inversion reactions. However, other factors must also be involved, or the slope in Fig. 5 would be unity. The fact that the S_E2 sequence is compressed relative to the S_N2 sequence may indicate that differing inductive sequences are involved in these two reactions. However, one cannot say a priori what they are. (See Introduction, Chapter III.)

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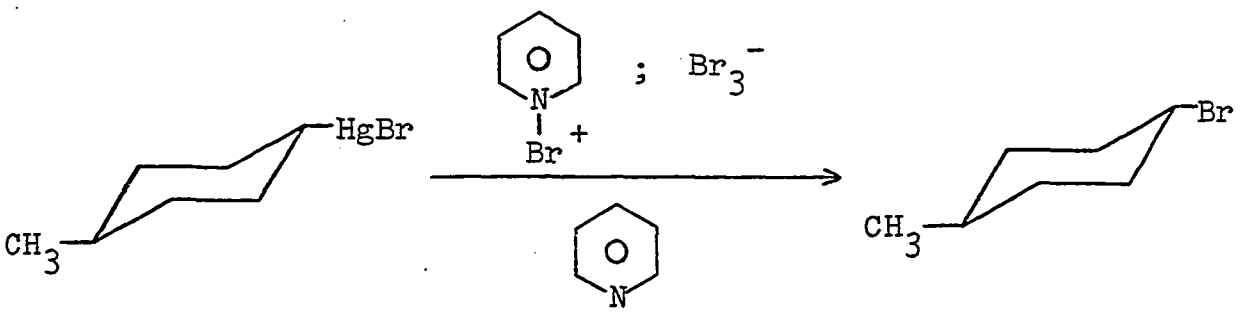
Chapter II

The Stereochemistry of Electrophilic Cleavage of Organotin Compounds

I. Historical

The question of the stereochemistry of electrophilic substitution reactions has received considerable attention in recent years. In general, where stereochemical studies were carried out, early workers reported retention of configuration.

For example, Jensen and Gale[1] studied the bromodemetellation of cis- and trans-4-methylcyclohexylmercuric bromides under a variety of conditions. In polar media, they observed retention of configuration:



100% retn. of configuration

Jensen and Nakamaye[2] have successfully prepared isomerically pure (>95%) endo-norbornylmagnesium bromide. Treatment of this Grignard reagent with either carbon dioxide or mercuric bromide leads to a product with retained stereochemistry:

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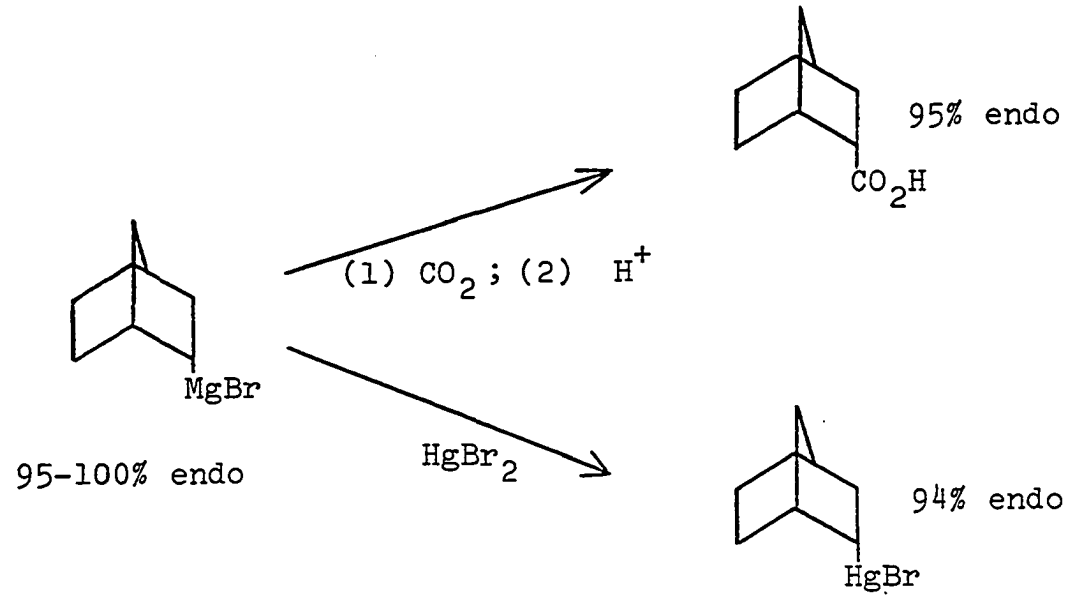
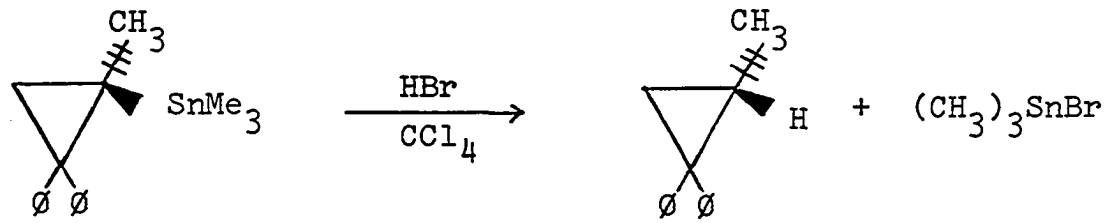


Sisido and coworkers[3,4] have prepared optically active (1-methyl-2,2-diphenylcyclopropyl) trimethyltin. Treatment of this compound with anhydrous HBr in carbon tetrachloride cleaves the cyclopropyl group with complete retention of configuration.



96% yield 96% yield

Baekelmans, Gielen, and Nasielski[5] have reported on the cleavage of cis- and trans-(2-methylcyclopropyl) trimethyltin in several solvents with iodine and bromine. The authors claim a retention pathway:

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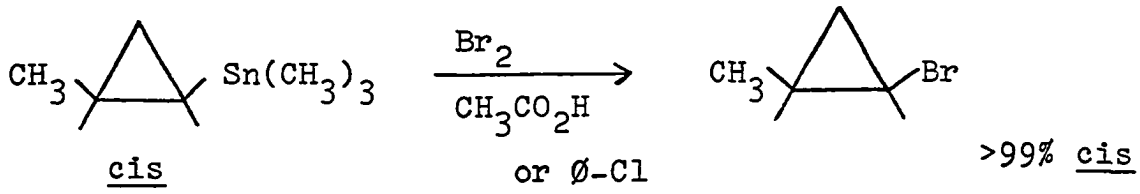
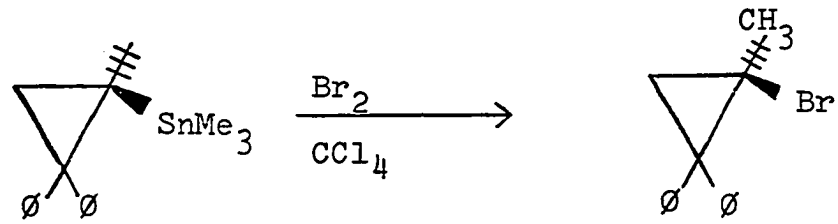


cis >99% cis

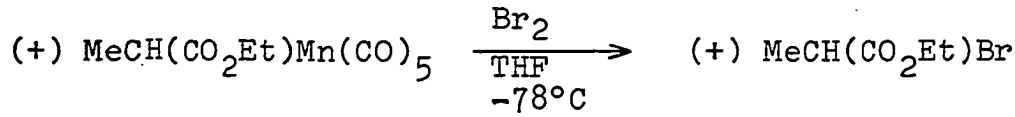
However, these results are in disagreement with Sisido who observed racemization for the bromodemetallation of (1-methyl-2,2-diphenylcyclopropyl) trimethyltin:



(+) (±)

Since both of these papers relate to the work of Davis and this worker, they will be discussed in considerable detail later (see Discussion).

Recently, Johnson and Pearson[6] have reported retention of configuration in the bromodemetallation of an alkyl manganese compound:



Although many early studies reported retention of configuration, recent studies have shown that inversion of configuration can also occur.

Davis[7] bromodemetallated optically active sec-butyl-trineopentyltin in methanol and found 37% inversion of configuration:

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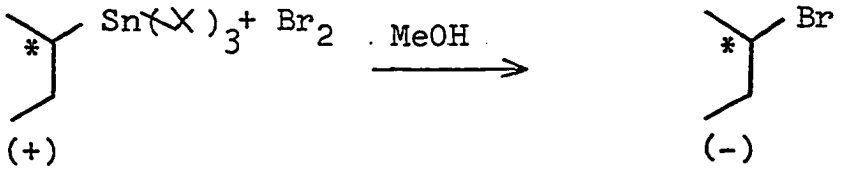
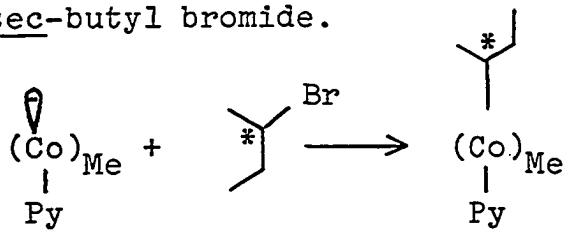
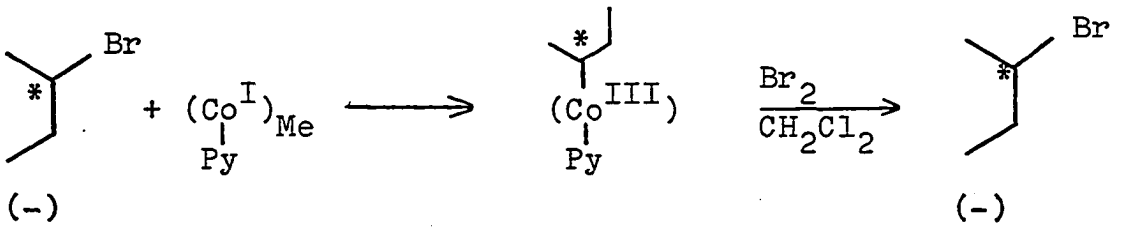


In addition, Jensen and Madan[8] have prepared an optically active sec-butyl cobalt derivative from cobaloxime (i.e. pyridine [bis(dimethylglyoximato)] cobalt I) and optically active sec-butyl bromide.



Because the compound has an intense visible absorption the determination of its absolute configuration has been rendered unfeasible. However, in other studies, Jensen, Buchanan, and Madan[9] have shown that alkylation of cobaloxime proceeds with inversion of configuration. Bromodemetallation of the sec-butyl cobalt derivative yields 2-bromobutane of the same configuration as the original starting material:



Since the alkylation studies show an inversion stereochemistry for step (1), step (2), the bromodemetallation must occur with inversion of configuration.

Molecular orbital calculations[10] have been performed which indicate that compared to the enormous preference shown

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for inversion of configuration in nucleophilic displacements, electrophilic substitutions show only a slight preference for inversion in the proton exchange of CH_4. Since these calculations are actually rather crude, their quantitative conclusions cannot be taken too seriously. However, qualitatively, the calculations do show that electrophilic substitutions (unlike nucleophilic displacements) are not likely to have a marked stereochemical preference, and they suggest that the stereochemical pathway may vary from system to system. Furthermore, while for simple carbon and hydrogen systems, such as CH_5^+, one need only accurately know the energy parameters of first and second row orbitals, for organometallic compounds, a knowledge of the higher row (i.e. fifth row for tin) orbitals is essential. These energies are not well-known. Thus, calculations from second row systems cannot be extended with any confidence to the more complex organometallics.

Since most stereochemical studies of electrophilic substitution reactions involve compounds which are prepared by an alkylation step, the stereochemistry of the alkylation reaction warrants some discussion here. Although it is accepted that most common nucleophiles displace a leaving group with inversion of configuration, the use of metals as nucleophiles has been investigated only recently. Because of the unique chemistry often observed for metallic compounds, simple stereochemical assumptions may not hold. Thus, the stereochemical course of the alkylation must be determined in each case by physical means.

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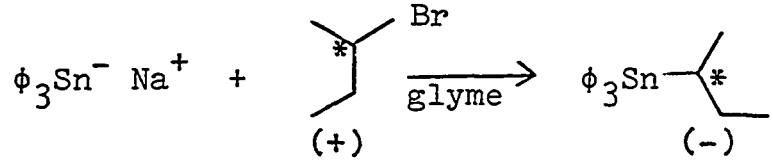
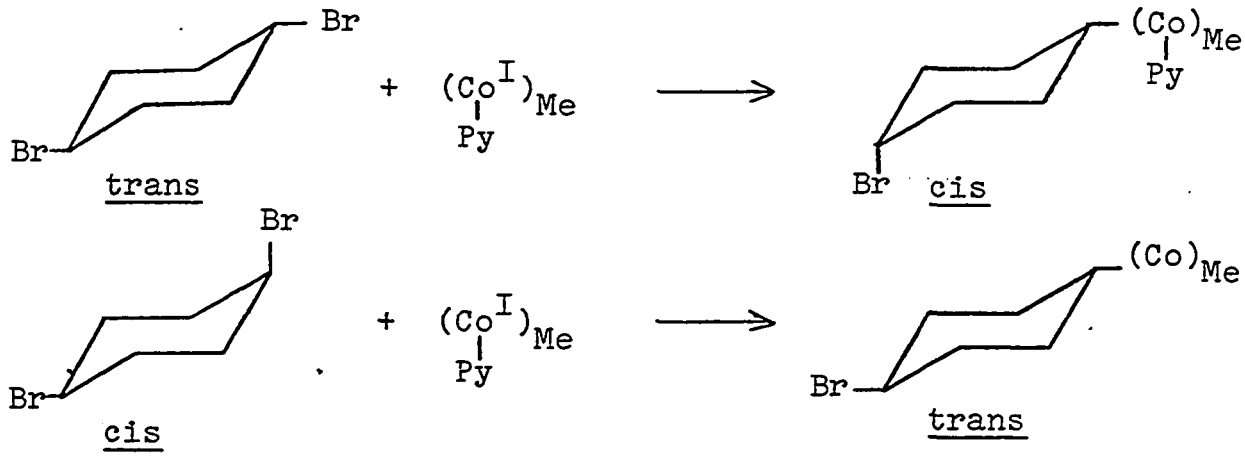
Davis and Jensen[11] have made use of Brewster's[12] Rules to correlate the signs and magnitudes of rotation of numerous organic compounds with their absolute configurations. Using this correlation, the stereochemical course of the displacement reaction between sodium triphenyltin and sec-butyl bromide was shown to be inversion of configuration.



Davis has similarly shown[7] that displacements with sodium triphenylsilicon and sodium triphenylgermanium occur with inversion of configuration.

Jensen, Madan, and Buchanan used nmr techniques to determine the stereochemistry of the alkylation of cobaloxime. The cis- and trans-1,4-dibromocyclohexanes were used to alkylate cobaloxime. The 100 MHz spectra of the products were compared with those of known cis- and trans-4-t-butyl-cyclohexyl bromides in order to assign the stereochemistry of the product:



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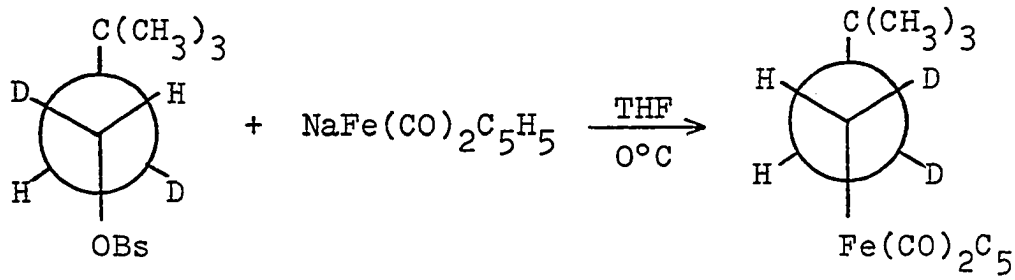
In all cases studied, displacement occurred with inversion of configuration.

Whitesides and Boschetto[13] have shown by nmr coupling constants of the vicinal protons that displacement at carbon by iron proceeds with inversion of configuration:



erythro threo

Johnson and Pearson[6] have used ord to show that displacement by $Mn(CO)_5^-$ on (-) PhMeCHBr proceeds with inversion.

Although Osborn and coworkers[14] have reported that iridium displaces bromide from trans-1-bromo-2-fluorocyclohexane with inversion of configuration, Pearson[15] has claimed retention for the reaction of a similar iridium complex with optically active ethyl 2-bromopropanoate.

In general, however, it appears that as nucleophiles, metals displace groups at carbon with inversion of configuration.

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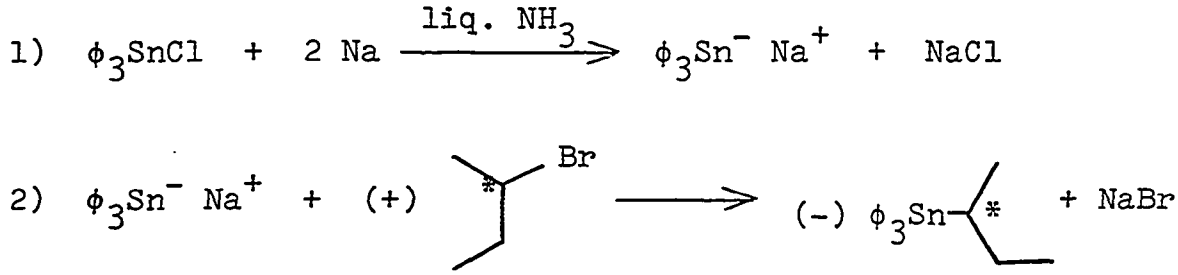
II. Results

The current study is concerned solely with the bromodemetallation of organotin compounds. Davis[7] has earlier shown that the bromodemetallation of (-) trineopentyl-sec-butyltin proceeds with at least 35% inversion of configuration in methanol. In addition, he found that (-) dicyclohexyl-sec-butyltin bromide was cleaved by bromine with 42% retention of configuration in carbon tetrachloride. These results have been expanded upon and clarified somewhat in the present study.

Optically active (-) triphenyl-sec-butyltin is readily prepared in liquid ammonia by the following sequence of reactions:



The generation of the triphenyltin anion in liquid ammonia is a facile and very quick reaction. The stereospecificity of the second step seems to vary somewhat from reaction to reaction but generally proceeds with at least 70% stereospecificity. One would expect step (2) to proceed via an S_N2 reaction in the highly polar liquid ammonia solvent. The prediction is confirmed experimentally by relating the sign of rotation to the absolute configuration. For

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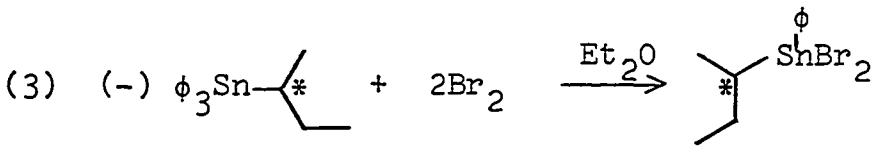
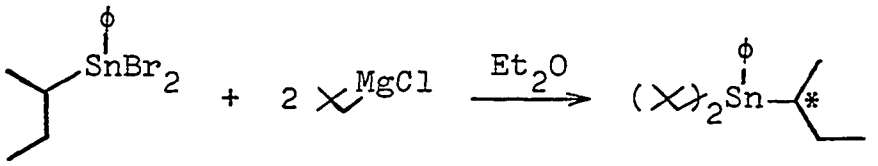
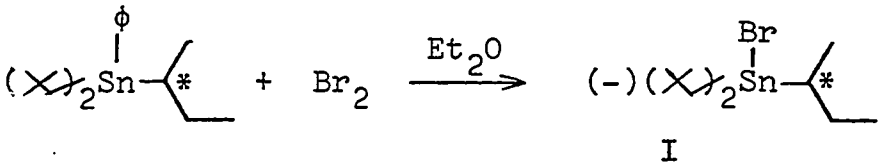
sec-butyl compounds, Brewster's rules[11,12] predict that triphenyl-sec-butyltin of the same absolute configuration as sec-butylbromide should have the same sign of rotation. These results are based on both empirical observations and theoretical considerations, and since no exceptions to these rules have ever been shown for 2-butyl compounds, it is reasonable to assign an inversion stereochemistry to this reaction. (See Historical.)

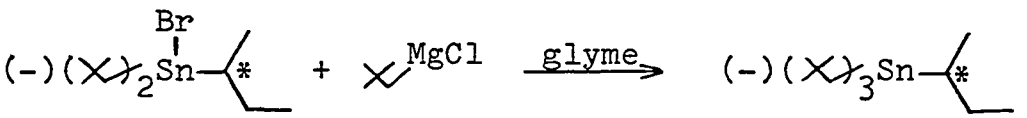
From this key intermediate, (-)ϕ_3-Sn- , both (-)-trineopentyl-sec-butyltin and (-)-dineopentyl-sec-butyltin bromide were prepared. (Since the asymmetric center is not involved in this sequence, one would expect both products to exhibit the same sign of rotation as the starting compound.)

(3) 

(4) 

(5) 

I

(6) 

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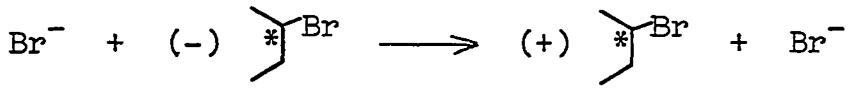
The tetraalkyltin ((-) trineopentyl-sec-butyltin) was cleaved by bromine in methanol under a variety of conditions. Run #1 was performed in the light at room temperature (22°) in the absence of sodium bromide. Run #2 was run in the dark at room temperature in the absence of sodium bromide. Run #3 was performed at 25° in the dark with 0.122 M sodium bromide concentration. All three runs showed inversion of configuration, but the third run gave at least 80% inversion for the bromodemetallation step. Since the maximum rotation for triphenyl-sec-butyltin is not known, it is not known in which step the racemization occurs. However, the increased racemization in the presence of light and the absence of sodium bromide suggest that radical pathways may affect the stereochemistry. When sodium bromide is present, the radical pathways appear to be quenched. However, racemization may then arise from Finkelstein reaction on the product:



A careful analysis of Davis' data (see Historical) strongly suggests that the bromodemetallation step occurs with 100% inversion of configuration. The excellent correlation of Davis' kinetic data[19] with the S_N2 data of Cook and Parker[20] (a known inversion reaction) strongly suggests that the bromodemetallation step occurs with complete inversion of configuration.

The trialkyltin bromide ((-) dineopentyl-sec-butyltin bromide) was cleaved in methanol twice, once at 45° and once at 0°. The reaction is extremely sluggish, and the

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addition of sodium bromide would have made the reaction stereochemistry impossible to determine under the conditions employed because of product racemization. Since the stereospecificity of the bromodemetallation of (-) trineopentyl-sec-butyltin was observed to vary depending upon the reaction conditions employed, it is assumed that radical formation plays at least some part in the lack of complete stereospecificity observed. Consequently, the degree of stereospecificity observed for the bromodemetallation of (-) dineopentyl-sec-butyltin bromide should be considered to be only a minimum for the reaction. At 45° 61% retention of configuration was observed whereas at 0° only 21.7% retention was observed. In both cases, unreacted starting material was reisolated and found to be less than 7% racemized under the reaction conditions.

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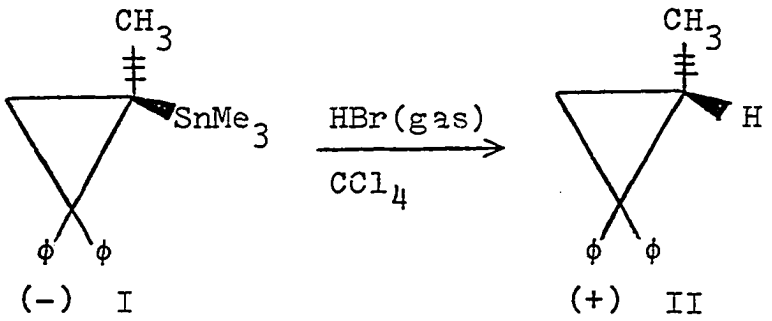
III. Discussion

The stereochemical results reported for organotin compounds seem contradictory. However, it will be shown that in fact the data are mutually consistent. All of the stereochemical results will be summarized first.

Sisido and coworkers[3,4] carried out several reactions on optically active (1-methyl-2,2-diphenylcyclopropyl) trimethyltin. These may be categorized as: (1) acid cleavage; (2) halodemetallation in non-polar solvent; (3) halodemetallation in polar solvent.

Bubbling anhydrous HBr through carbon tetrachloride[3] yielded a product with complete rention of configuration.



(-) I (+) II

Similarly, treatment of I in carbon tetrachloride with concentrated hydrochloric acid results in a product of completely retained stereochemistry. Thus, acid cleavage appears to proceed in highly stereospecific fashion with retention of configuration.

Treatment of I with one equivalent of bromine in carbon tetrachloride afforded a mixture of products:

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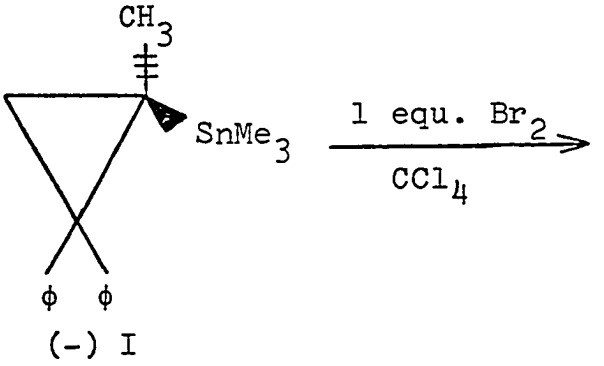
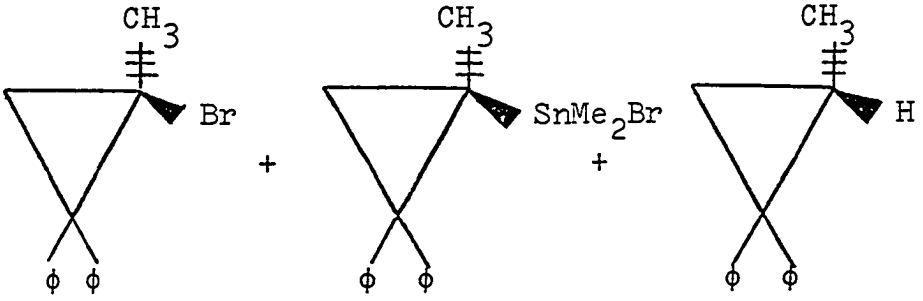


(-) I

yield : ---

optical purity: 87%



(-)	(-) III	(+) II
20%	30%	29%
1.3%	87%	87%

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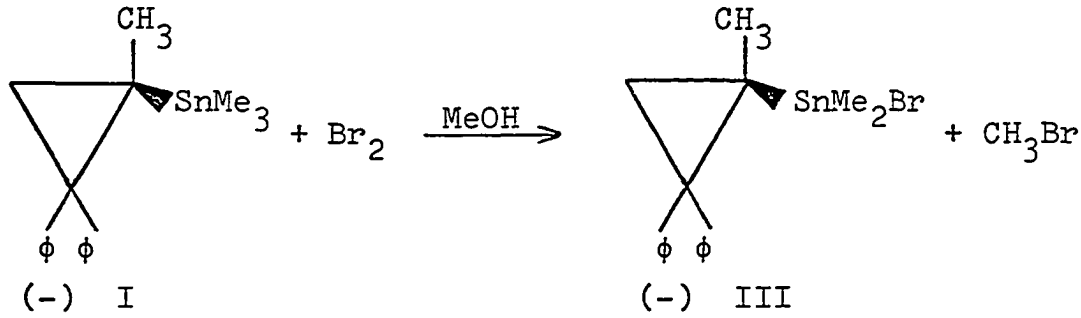
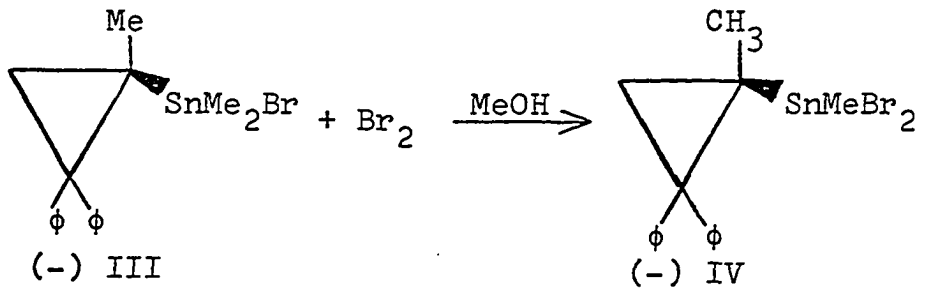
The cyclopropyl bromide produced was essentially racemic. It is probable that the slight retention of configuration represents a slight preference along the reaction path in the capture of the cyclopropyl radical. Slight stereochemical preferences such as this have already been observed.[16,17] Sisido believes that the reduction product II arises from the reaction of III and/or I with hydrogen bromide generated in the system. Sisido observes ostensibly the same stereochemical results for the iododemetallation of I. Thus, in non-polar solvent, Sisido observes a racemization course for the halodemetallation reaction.

When Sisido bromodemetallates I with one equivalent of bromine in methanol, he observes only one product in 97% yield:



Further treatment of (-) III with one more equivalent ov bromine removes an additional methyl group. Sisido isolates (-) IV in 74% yield but does not report any other products:



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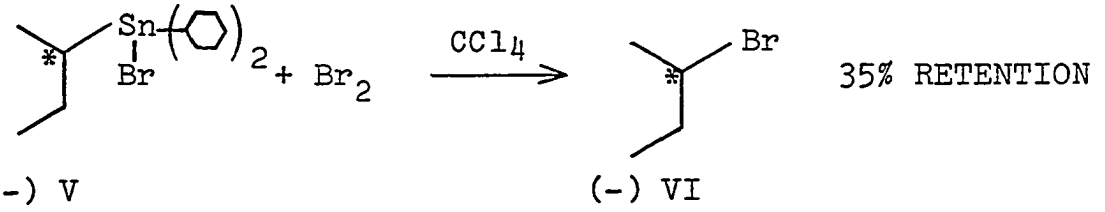
Thus, in polar solvents, Sisido observes high selectivity for the halodemetallation reaction.

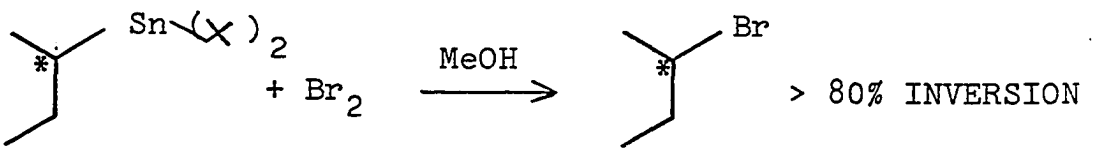
In addition to his stereochemical work in methanol, Davis[7] found that bromodemetallation of (-) trineopentyl-sec-butyltin with one equivalent of bromine proceeded with complete racemization in carbon tetrachloride. This is in agreement with Sisido's result. However, treatment of (-)sec-butyldicyclohexyltin bromide, (-) V, with one equivalent of bromine in carbon tetrachloride results in a product with 35% retention of configuration:



(-) V (-) VI

Thus, Davis found that while in non-polar solvents, tetra-alkyltins are bromodemetallated with complete loss of stereo-chemistry, trialkyltin halides are cleaved with retention of configuration.

In the current study it has been shown that tetraalkyltins are cleaved by bromine in the polar solvent methanol with an extremely high degree of stereospecificity, and that the reaction proceeds with at least 80% inversion of configuration:



(-) VII (+) VI

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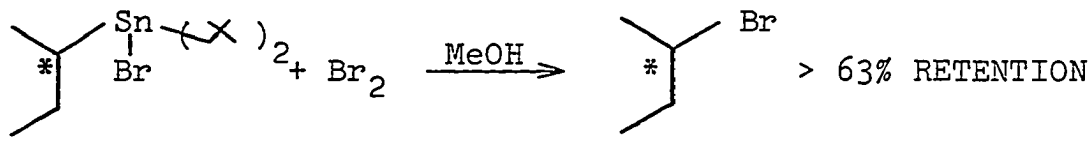
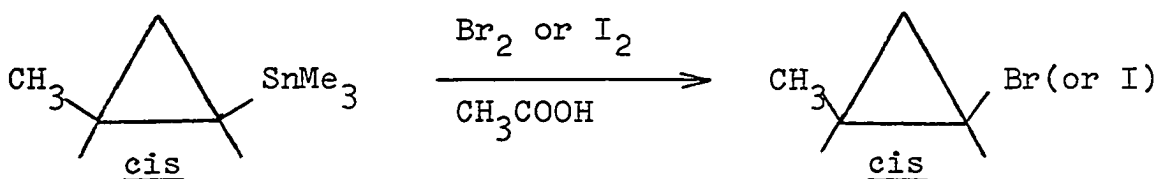
It has further been shown that the reaction is rather sensitive to racemization. It has already been shown (see Historical) that there is an excellent correspondence between this electrophilic displacement reaction and nucleophilic displacements upon the same alkyl groups. Thus, it is reasonable to assume that if sources of racemization could be removed completely one would observe complete inversion of configuration for the bromodemetallation reaction in methanol.

The current study has also shown that trialkyltin bromides are bromodemetallated in methanol with retention of configuration:



(-) VIII (-) VI

Baekelmans, Gielen, and Nasielski[5] have reported that the bromodemetallation and iododemetallation of cis- and (trans-2-methylcyclopropyl) trimethyltin proceeds with retention of configuration in a variety of solvents:



cis cis

IX x

> 99% RETENTION

The results are summarized in Table 3.

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Table 3[a]

Halodemetallation of cis- and (trans-2-methylcyclopropyl) trimethyltin

Substrate	$I_2/MeOH$	I_2/CH_3COOH	Br_2/CH_3COOH	Br_2/C_6H_5CL
$MeC_3H_4SnMe_3$	MeC_3H_4-I	Me-C_3H_4-I	Me-C_3H_4-Br	Me-C_3H_4-Br
Trans	>95% trans	>99% trans	>99% trans	>99% trans
Cis	>95% cis	>99% cis	>99% cis	>99% cis

[a] Ref. 5.

Unfortunately, absolutely no experimental details were reported either with the work or subsequently.

This report is in contrast to our results of inversion of configuration in polar solvents and racemization in non-polar media in the bromodemetallation of tetraalkyltins. However, it is now well substantiated that depending upon the substrate, halodemetallations of tetraalkyltin compounds may occur with enormous selectivity. In polar solvents, This selectivity is believed to arise primarily from steric effects. Thus, in polar solvents one would predict (based upon Davis' kinetic studies) that the methyl group would be the only group cleaved. In fact, Sisido's results help to verify this prediction (see p. 30) as he observes at least 97% removal of the methyl group when I is brominated in methanol.

The high selectivity with which the methyl group is removed from a tetraalkyltin has already been noted by Boué, Gielen, and Nasielski[18] who found that only the methyl

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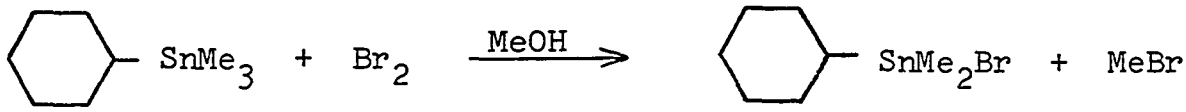
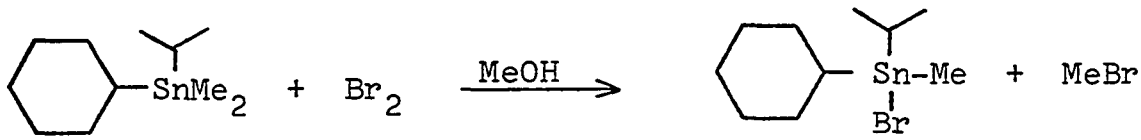
groups were removed when treating cyclohexyltrimethyltin, XI, or cyclohexyl-isopropyldimethyltin, XII, with one equivalent of bromine in methanol.



XI



XII XIV

Even in non-polar solvents, the selectivity may be very high. Although Sisido observed a 20% yield of 1-methyl-2,2-diphenylcyclopropyl bromide when I was brominatedin carbon tetrachloride, it is likely that this reaction proceeds through a cyclopropyl radical. Compound I is capable of giving a tertiary cyclopropyl radical, whereas compound IX (used by Gielen and Nasielski) would give a less stable secondary cyclopropyl radical. Thus, it would not be too surprising if compound IX gave only methyl cleavage even in non-polar media.

Consequently, the question of experimental details must be raised. In the absence of experimental details it is suggested that perhaps excess bromine was used in the bromodemetallation, and the following set of reactions actually occurred:

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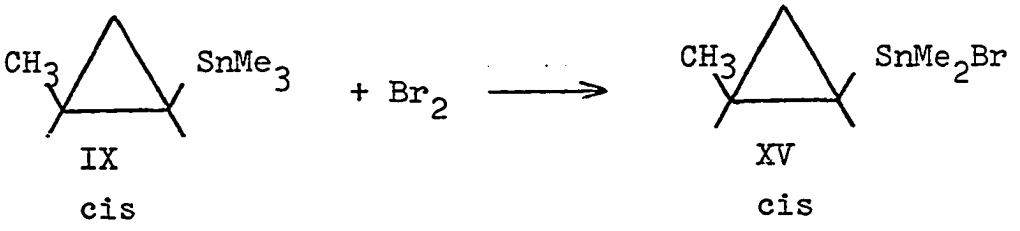
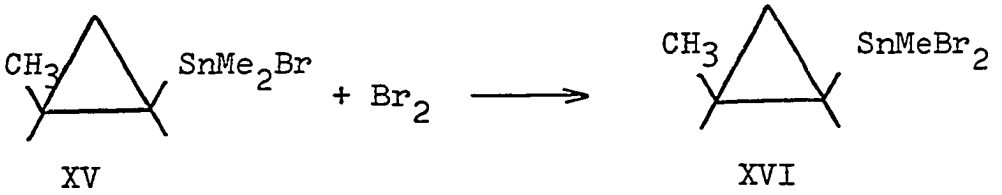
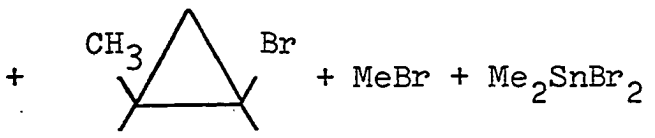
(1) 

IX cis — XV cis

(2) 

XV — XVI



If this is the case, Gielen and Nasielski actually observed the halodemetallation of a trialkyltin halide rather than a tetraalkyltin. This interpretation would agree with the current study and that of Davis, which have shown that trialkyltin halides are bromodemetallated with retention of configuration in both polar and non-polar media.

The stereochemical results reported here suggest some other tentative conclusions concerning electrophilic substitutions. Replacement of an electron-donating (or neutral) alkyl group by an electron-withdrawing halide on the leaving group, $-SnY_3$, has two effects: a) the stereochemical course of the reaction changes from inversion to retention; b) the rate of reaction is slowed drastically. Although the actual rate difference for the compounds studied is not known, Gielen and Nasielski[22] have compared the bromodemetallation

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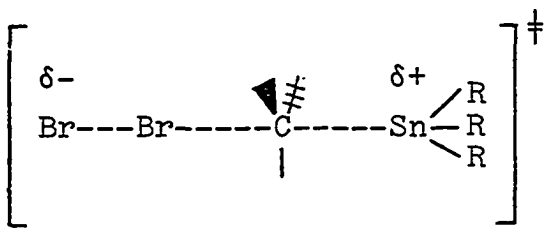
rates of R_4Sn and R_3SnBr (R=Me, Et, n-Pr) and they report a ratio for R_4Sn : R_3SnBr = ca. 10,000. The rate difference suggests that the reaction center is sensitive to electron withdrawal from tin and that rho, for the leaving group is negative.

It is known that for a tetraalkyltin compound, inversion of configuration:

i.e.

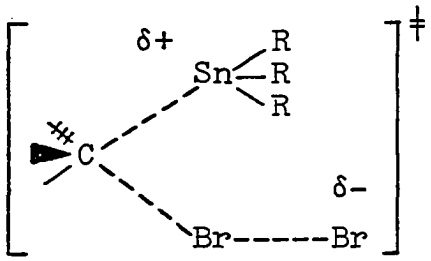


S_E2
(inversion)

XVII

is preferred to retention of configuration:

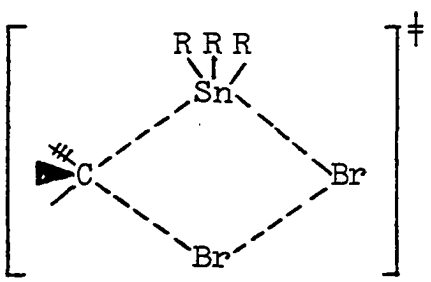
i.e.



S_E2
(retention)

XVIII

or



S_Ei

XIX

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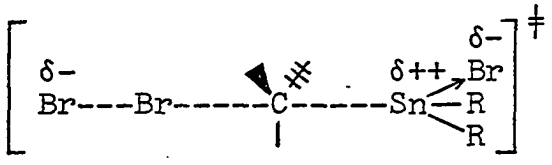
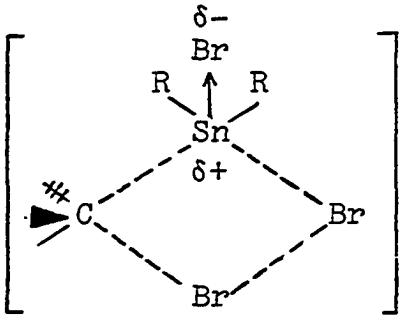
When an alkyl group on the tin group is replaced by an electron withdrawing halide, the reaction rate is slowed enormously and the stereochemical course is altered. Since XVIII and XVII have identical charge types, there is no compelling reason to ever prefer XVIII over XVII on the basis of their geometry, otherwise tetraalkyltin compounds would cleave with retention of configuration. The inversion results for the tetraalkyltin case suggest that XVII is favorable to XVIII on geometrical grounds. However, the large decrease in rate when going to the trialkyltin halide suggests that the competition between XX



XX

and XXI



XXI

may be such that the stabilization of the large charge upon tin in the transition state can best be accomplished via an S_Ei transition state. The concerted nature of this transition state would considerably lower the build-up of charge on tin. Thus, for the trialkyltin halide there is

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good reason to postulate XXI being superior to XX for electronic reasons. However, without other evidence to the contrary, there is no longer any compelling reason to consider the S_E2 retention pathway more favorable than the S_Ei in this case.

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IV. Experimental

(-) sec-Butyl alcohol was prepared by stereospecific hydroboration of cis-2-butene according to Brown.[19]

(+) sec-Butyl bromide was prepared as follows: Following the procedure of Wiley,[20] and Schaefer,[21] 49.33 g (0.667 mole) (-) sec-butyl alcohol ($[\alpha]_D$=- 7.694) and 225 g ϕ_3P (p.86 mole) was dissolved in 500 ml diglyme. To this solution 41 ml (∿0.75 mole) Br_2 (neat) was added over a one hour period, maintaining a temperature of 30-40°. The mixture was stirred an additional hour. The product was then distilled out of the reaction vessel at ∿40°/13 mm using a water bath whose temperature was ∿53°. The distillate was fractionated through a Todd column, b.p. 89-91°, 74.5 g (81.5%) sec-butyl bromide $[\alpha]_D$=+ 18.614. The sec-butyl bromide was checked for purity by g.c. and found to be free of sec-butyl alcohol.

Preparation of optically active (-) triphenyl-sec-butyltin: Using mechanical stirring, 88.3 g (0.23 moles) of triphenyltin chloride was suspended in 600 ml of liquid ammonia. To this mixture, 11.0 g of sodium chunks was added until the blue color (characteristic of the solvated electron in liquid ammonia) persisted. To this solution was added 33.0 g (0.24 moles) of (+) sec-butylbromide ($[\alpha]_D$= +21.14, neat) all at once. The blue color discharged immediately, leaving a deep yellow solution (believed to be characteristic of triphenyltin anion in liquid ammonia). The deep yellow color

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faded over about a fifteen minute period to a pale yellow color which never disappeared. The solution was stirred for four hours, allowing the liquid ammonia to boil off. Water and ether were used to extract the soluble materials remaining. An insoluble yellow material (which was not identified) was filtered off, and the organic layer was dried and the solvent evaporated in vacuo, leaving the crude product. The product was tested with ethanolic silver nitrate, and found to contain ditin. The crude material was dissolved in a minimum amount of acetone, and saturated potassium permanganate in acetone was added resulting in a voluminous brown precipitate. Permanganate addition was continued until the supernatant remained purple for several minutes, indicating that no further ditin or tin halide was present. The solution was filtered with the aid of supercel, and the filtrate was evaporated in vacuo. The residue was dissolved in ether and extracted with water. The organic layer was dried and filtered again with supercel, leaving a water-white filtrate. The solvent was removed in vacuo, and the residue was recrystallized from 95% ethanol to yield 47.5 g (50.9%) of (-) triphenyl-sec-butyltin; $[\alpha]_D = -9.92$ (c. 20.7, CH_2Cl_2) and $[\alpha]_D = -10.01$ (c. 5.09, benzene). This material tested negatively with ethanolic silver nitrate for ditin or tin halide.

Preparation of optically active (-) trineopentyl-sec-butyltin: An ethereal solution, containing 150 g (0.37 moles) of (-) triphenyl-sec-butyltin ($[\alpha]_D = -7.32$, corresponding to a

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minimum activity of 46.8%) was prepared and cooled to 0°. To this solution, 40 ml (0.74 moles) neat bromine was added slowly. After the persistence of orange color was observed, 1.11 moles of neopentylmagnesium chloride was added. The reaction mixture was quenched with dilute hydrochloric acid, and the organic layer was separated, dried, and the solvent was evaporated in vacuo. The oil was taken up in monoglyme and cooled to 0°. To this solution 20 ml (0.37 moles) of bromine was added, followed by 0.55 moles of neopentylmagnesium chloride. The reaction mixture was stirred at room temperature for 12 hours and quenched with aqueous ammonium chloride. The organic layer was dried and evaporated in vacuo. The resulting oil was recrystallized from 95% ethanol to yield 30.0 g (20.9%)of white crystals; m.p. 44.0-45.0°; $[\alpha]_D$ = -1.565 (c. 36.3, benzene).

Calc. % C 58.63 % H 10.88

found % C 58.84 % H 10.54

Preparation of (-) dineopnetyl-sec-butyltin bromide: A solution containing 45.0 g (0.11 moles) of (-) triphenyl-sec-butyltin ($[\alpha]_D$=-10.0; c.5,benzene) in 200 ml ether was cooled with an ice bath. To this was added 11.45 ml of neat bromine (0.22 moles) until the persistence of an orange color. The ice bath was removed, and 150 ml of 2.0 M neopentylmagnesium chloride (0.30 molees) was added rapidly. After 15 minutes, the reaction mixture was quenched with aqueous ammonium chloride, the organic layer dried, and the solvent removed in vacuo. The resulting oil (dineopentyl-sec-butylphenyltin)

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was dissolved in 200 ml ether and cooled to 0°. To this solution, 5.50 ml of Br_2 (0.104 moles) was added slowly until the persistence orange color of bromine remained. The reaction was quenched with 25 ml of 1 M sodium thiosulfate, and the organic layer was separated, dried, and the solvent removed in vacuo. The viscous organic product was bulb-to-bulb distilled, collecting the fraction of b.p. 92°/0.2 mm. A yield of 39.0 g (87.0%) of (-) dineopentyl-sec-butyltinbromide ($[\alpha]_D$ = 7.59 neat) was isolated.

Calc. %C 42.25; % H 7.85

Found: %C 42.53; % H 7.79

Bromodemetallation of (-) trineopentyl-sec-butyltin in methanol: Several procedures were used to bromodemetallate the optically active tin compound. All procedures gave optically active sec-butyl bromide whose activity was greater than 30% that of the starting material. However, the procedure given here, which gave the highest degree of stereospecificity, is comparable in concentrations to those used under kinetic conditions and was done in the dark to help eliminate radical pathways. A solution was prepared containing 11.64 g (0.04 moles) of (-) trineopentyl-sec-butyltin in 750 ml of 0.122 M sodium bromide in methanol. To this solution 0.04 moles of bromine was added. The vessel, which was completely black and further wrapped to keep out light, was kept at 25° for 24 hrs. The mixture was added to 250 ml of 0.2 M sodium thiosulfate and extracted with two 25 ml portions of pentane. The pentane solution was dried and filtered, and the pentane was slowly

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distilled off on a Podbelniak distillation apparatus. The concentrated solution was vacuum transferred, and the liquid which came over was preparatively gas chromatographed on a 5' × 1/2" - 5% SE-30 on 60/80 firebrick column, collecting the (+)-sec-butyl bromide.

The product had a rotation of $[\alpha]_D$ = +12.55.

Pseudo-Finkelstein Reaction:

To find out whether the trialkyltin bromide formed as a product racemized the (+)-sec-butylbromide formed in the stereochemical study, 3.56 g (0.02 moles) of tetramethyltin was dissolved in 50 ml of methanol and bromodemetallated by the addition of 1.09 ml (0.02 moles) of bromine. To this solution, 1.5 ml (-)-sec-butylbromide (α_{578} = -5.68) was added and the resulting mixture heated to 45° for 100 minutes. After cooling for an additional 80 minutes, the mixture was worked up exactly as in the cleavage study. The resulting (-)-sec-butylbromide isolated (α_{578} = -5.72) had not been racemized.

Bromodemetallation of (-) dineopentyl-sec-butyltin bromide in methanol: Using a black flask to exclude light, 18.0 g (0.045 moles) (-)dineopentyl-sec-butyltin bromide (α_D = 8.39) in 200 ml of methanol was heated to 45°. To the solution 2.0 ml (0.038 moles) bromine was added, and the reaction mixture was allowed to react for 36 hours. (This was not to completion.) The reaction was quenched by addition of 500 ml dilute (approx. 0.1 M) sodium thiosulfate, and the organic

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products were extracted with three 25 ml portions of pentane. The volatiles were vacuum transferred. The residue which contained unreacted starting material, was bulb-to-bulb distilled. The unreacted starting material (b.p. 88-90°/0.2 mm) had a rotation (α_D = 8.10) which indicated less than 4% racemization under the reaction conditions. The volatiles from the vacuum transfer were fractionated on a Podbelniak distillation apparatus to remove most of the pentane. The residue was preparatively gas chromatographed on a 5' × 1/2" 5% SE-30 on 60/80 firebrick column, collecting the product, (-) sec-butyl bromide ($[\alpha]_D$ = -12.93). The product indicated 61.16% overall inversion (from the starting (+) sec-butyl bromide) or at least 61.2% retention of configuration for the bromodemetallation step.

Using the same procedure, the reaction was carried out for one week at 0°. The unreacted starting material recovered (α_D = 7.83) was 6.7% racemized, while the (-) sec-butyl bromide isolated ($[\alpha]_D$ = -4.59) showed a minimum of 21.7% retention of configuration for the bromodemetallation step.

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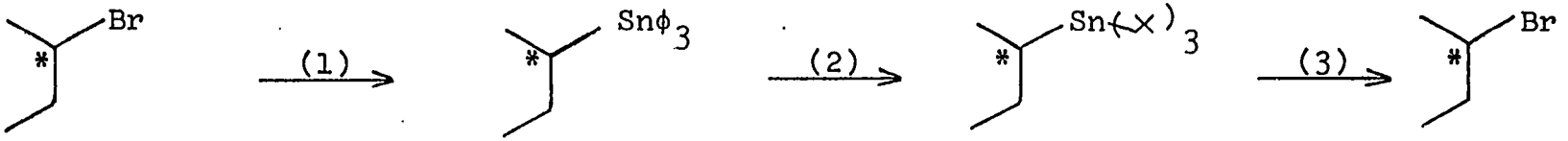
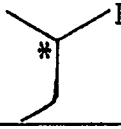
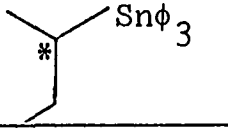
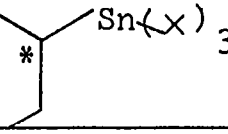
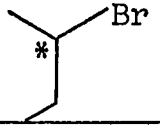
Table 1[a]

Bromodemetallation of (-) trineopentyl-sec-butyltin



Compound						% INVERSION STEP(3)
$[\alpha]_D$	(+) 33.6	(-) 13.21	(-) 2.83	(+) 8.92 (+)15.09 (+)22.64		
% activity	100.0%	83.38%[b]	83.38%	26.55 44.91 67.38		31.84 53.86 80.81

[a] All values normalized, assuming a value of $[\alpha]_D$ = 33.6 for 100% active 2-bromobutane. For actual rotations measured, see Experimental.

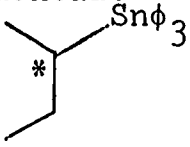
[b] See Table 2. This value based on highest known value for  of 15.84.

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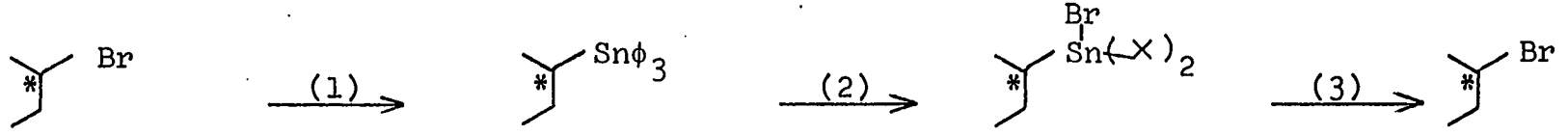
Table 2[a]

Bromodemetallation of (-) dineopentyl-sec-butyltin bromide



Compound	Br	Snϕ3	Br Sn(X)2	Br	//	% RETENTION STEP (3)
$[\alpha]_D$	(+) 33.6	(-) 15.84	(-) 12.06[c] (α_D=13.34)	(-) 20.55 (45°) (-) 7.29 (0°)	//	
% activity	100.0%	100.0%[b]	100.0%	61.2 21.7	//	61.2 21.7

[a] All values normalized assuming a value of α_D = 33.6 for 100% active 2-bromobutane. For actual rotations measured see Experimental.

[b] To date, this is the highest observed value for ϕ_3Sn-

[c] This value based on a density ρ =1.1060, measured by weighing 0.5 ml of (-)dineopentyl-sec-butyltin bromide.

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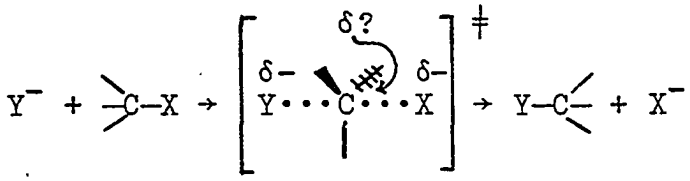
Chapter III

The Bromodemetallation of a Series of Substituted Benzyltin Compounds

I. Introduction

Despite the large number of studies concerning S_N2 reactions, certain features of the detailed mechanism are still somewhat elusive to experimental proof. In the transition state, I, a knowledge of the charge upon the central carbon atom undergoing attack would be desirable:



I

A priori, there is no way to tell whether the charge upon carbon is positive, negative, or neutral. The sign of the charge should depend upon the extent of bond-making (of C-Y) and bond-breaking (of C-X) in the transition state. The situation is further clouded by the fact that for the same reaction, changing the substituents bound to carbon may alter the sign of charge on carbon in the transition state.

Typically, Taft's $\sigma^*\rho^*$ treatments are used to determine charge types for reactions of aliphatic systems. However, use of the σ^* parameters cannot be applied to this case.

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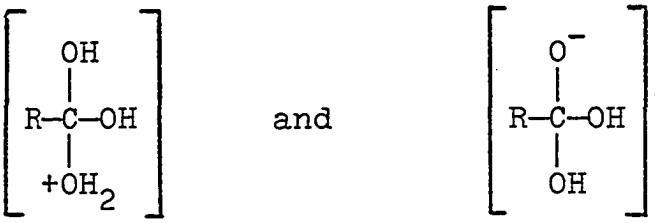
The $\sigma^*\rho^*$ parameters were derived by comparison of the rates of acid and base hydrolysis of a series of esters. The intermediates for these two reactions:



II and III

Intermediate for Acid Hydrolysis

Intermediate for Base Hydrolysis

differ only by their charge and two protons. Since the two protons are considered to have a negligible steric effect when comparing the two transition states (or intermediates shown), the σ^* parameters are used as a measure of the inductive or field effects of the aliphatic groups, R, upon the rates of reactions where steric effects do not effect the rate. However, for a bimolecular displacement upon R: $Y^- + R\text{-}X \rightarrow Y\text{-}R + X^-$, steric effects cannot be neglected.

Cook and Parker[1] have determined the rates of halide exchange (i.e. S_N2 displacement) on alkyl systems. Their data are summarized in Table 1 along with σ^* parameters for each substituent.

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Table 1

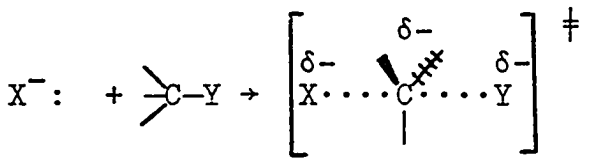
Relative Rate of Halide Exchange on Alkyl Systems

$$Br^- + R\text{-}Cl \rightarrow R\text{-}Br + Cl^-$$

R	σ^{*a}	log k_{rel}
Me	+.98	1.57
Et	+.49	0.00
n-Pr	+.39	-0.16
i-Pr	0.00	-1.74
i-Bu	+.29	-1.48
neo-Pentyl	+.19	-5.20

[a]Taken from reference 2.

The data, which are illustrated graphically in Figure (1), show that if one does not select a wide enough group of alkyl substituents, one can be falsely led into treating the data as a good linear free energy correlation. Consideration of only Me, Et, n-Pr, and i-Pr (the most common substituents to study) might lead one to conclude that S_N2 reactions proceed with a reasonably large (ρ = +3.40) negative charge on carbon:



III

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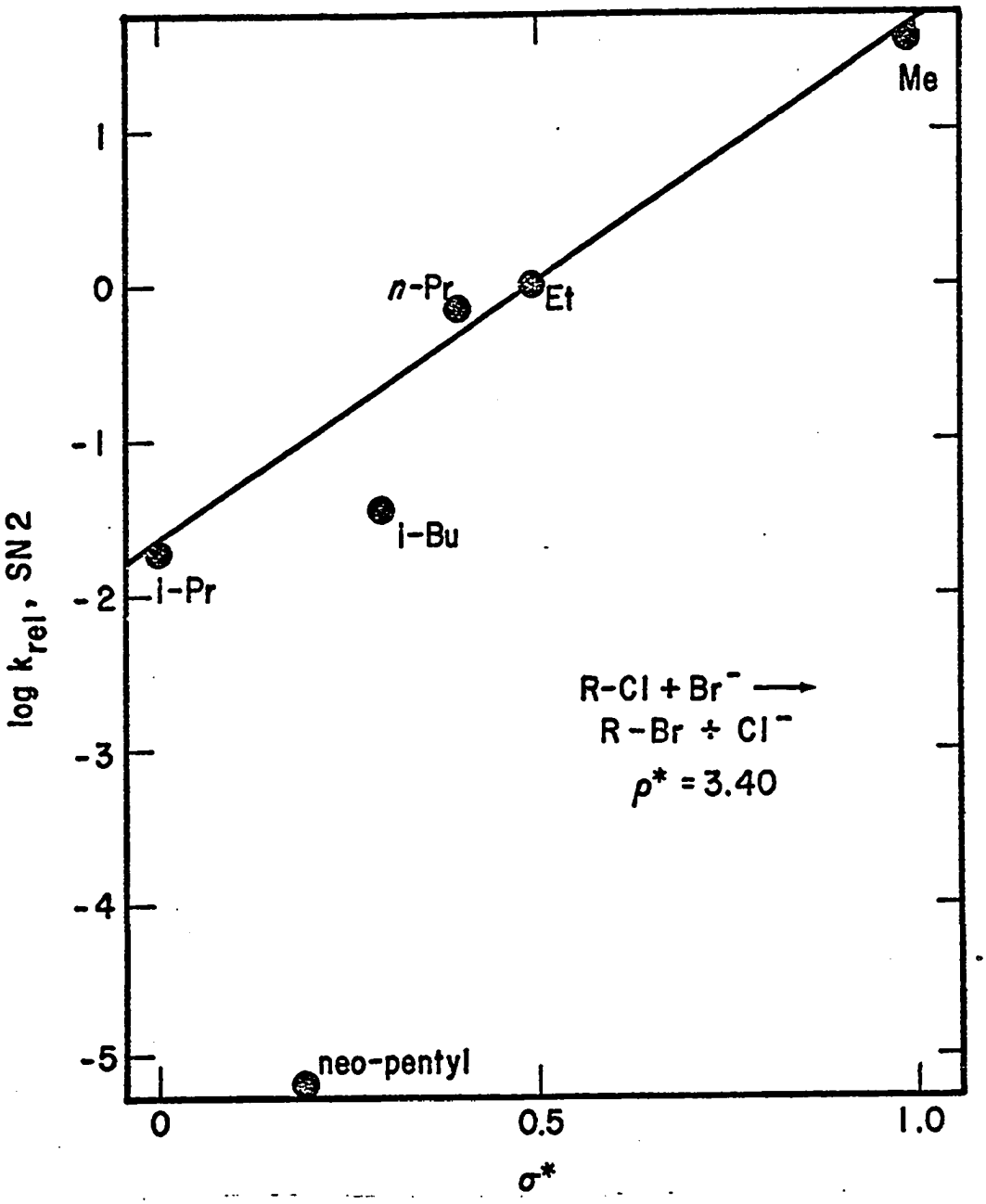

Figure 1. σ*ρ* treatment of S_N2 reaction.

(See Table 1)

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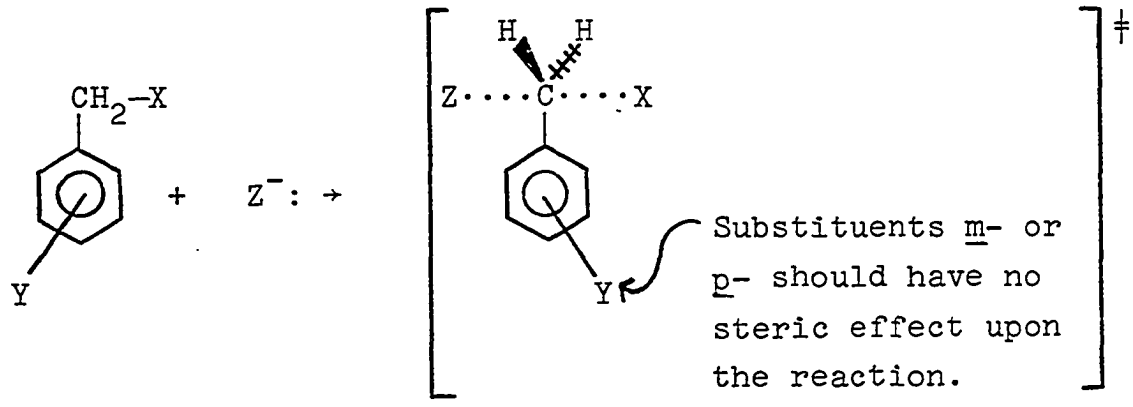
However, if all of the data are considered, it becomes apparent that what we are observing is a steric trend. Thus, neopentyl is four powers of ten (10^4) slower than it should be if the $\sigma^*\rho^*$ relationship is to hold, and isobutyl is 63 times too slow. We cannot with any confidence use varying alkyl groups to gather the information desired.

The use of substituted benzyl compounds should be more reliable, since steric effects at the benzylic reaction center should not be affected by m- or p- substituents on the ring:



V

Streitwieser[4] has compiled the available data for S_N2 reactions upon substituted benzyl compounds. The data for two of these reactions are summarized in Tables 2 and 3, along with Hammett's values of σ. The data, plotted in Figures 2 and 3, show that in both cases ρ is small ($-1<\rho<+1$). One may conclude that for S_N2 reactions the charge upon the carbon atom undergoing attack is small, and that this charge may vary in sign, depending upon the exact nature of the

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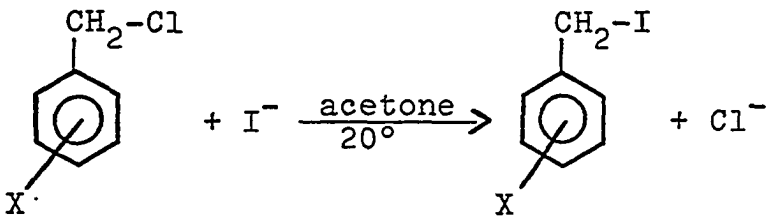
Table 2



X	k_{rel}	log k_{rel}	σ
H	1.00	0.00	0.00
m-F	1.39	0.14	+0.337
m-Cl	1.64	0.21	+0.373
m-Br	1.87	0.27	+0.391
m-I	1.77	0.25	+0.352
p-F	1.44	0.16	+0.062
p-Cl	2.12	0.33	+0.226
p-Br	2.36	0.37	+0.232
p-I	2.24	0.35	+0.170
p-CH_3	1.17	0.07	-0.170
m-NO_2	3.66	0.56	+0.710
p-NO_2	6.19	0.79	+0.778

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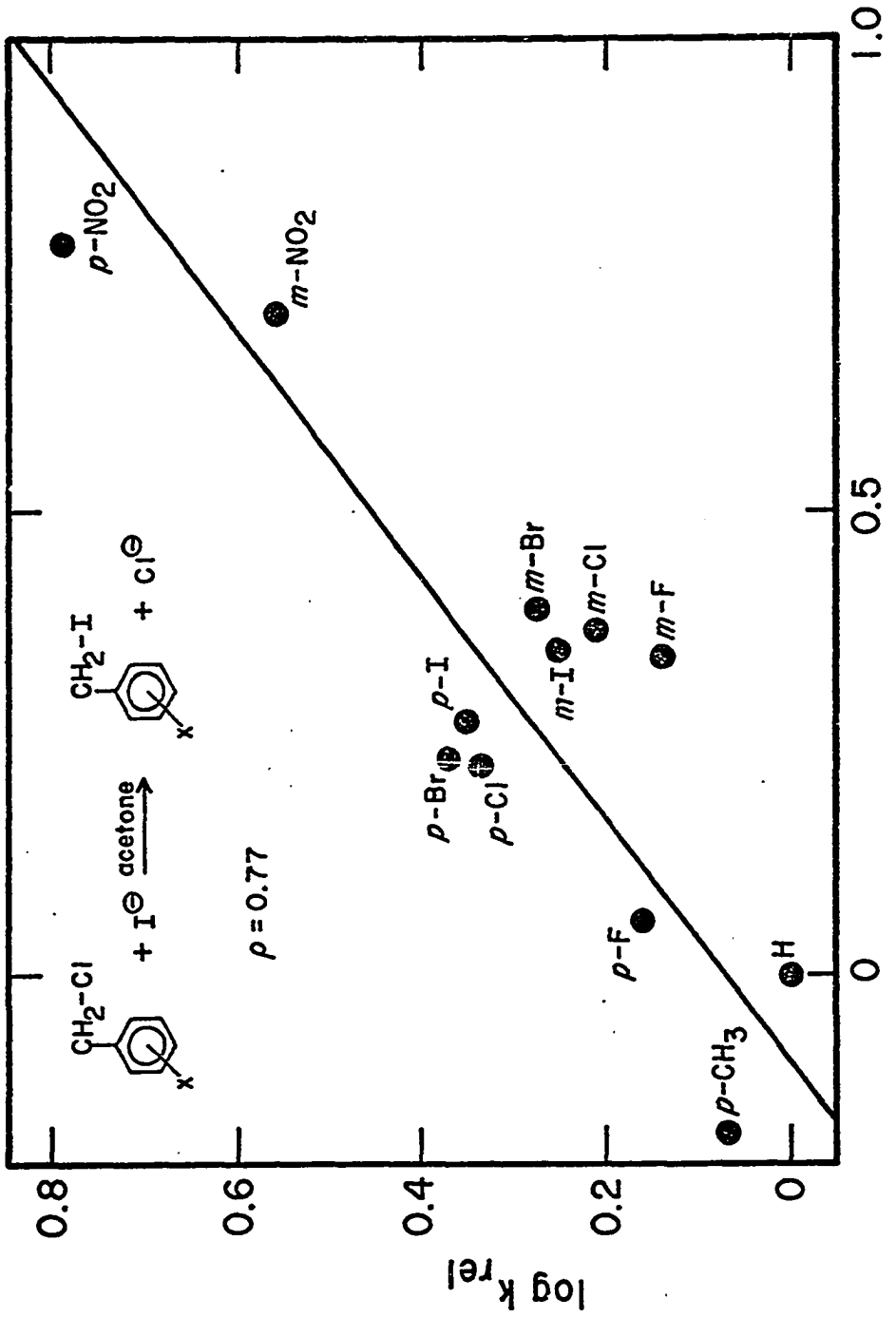

Figure 2. Hammett's σρ treatment.

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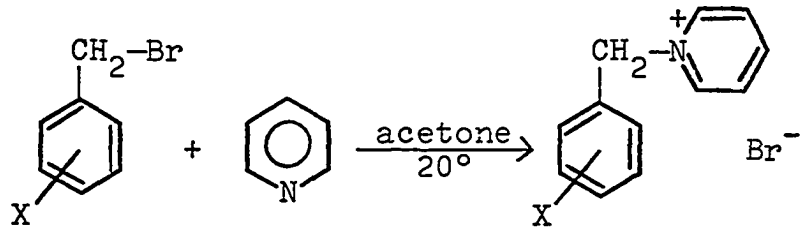
Table 3



X	k_{rel}	log k_{rel}	σ
H	1.00	0.00	0.00
m-F	0.78	-0.11	+0.337
m-Cl	0.88	-0.06	+0.373
m-Br	0.88	-0.06	+0.391
m-I	0.93	-0.03	+0.352
p-F	1.21	+0.08	+0.062
p-Cl	1.04	+0.02	+0.226
p-Br	1.06	+0.03	+0.232
p-I	1.21	+0.08	+0.276
m-CH_3	1.17	+0.09	-0.069
p-CH_3	1.65	+0.22	-0.170
m-NO_2	0.81	-0.09	+0.710
p-NO_2	0.92	-0.04	+0.778

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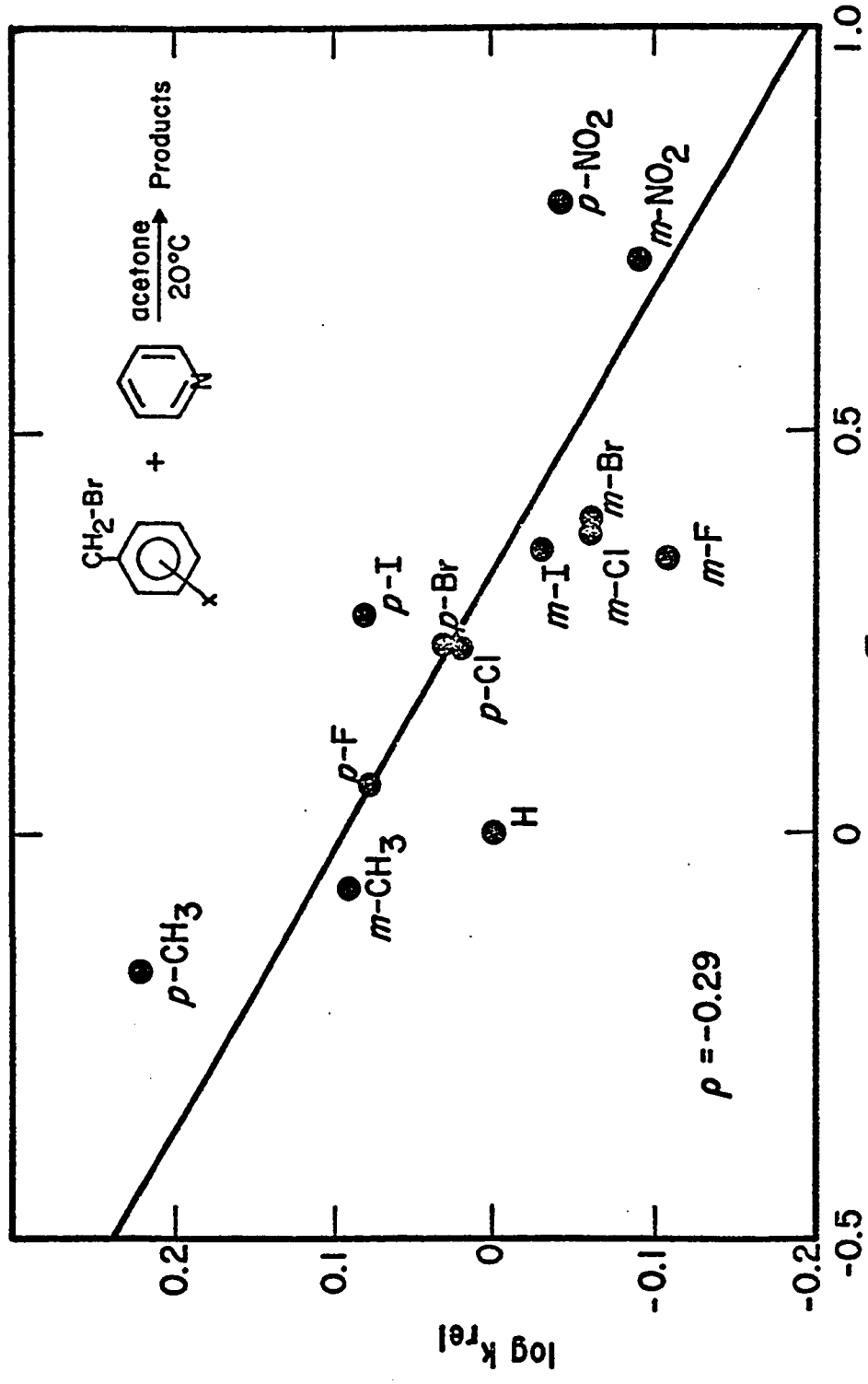

Figure 3. Hammett's σρ treatment. . .

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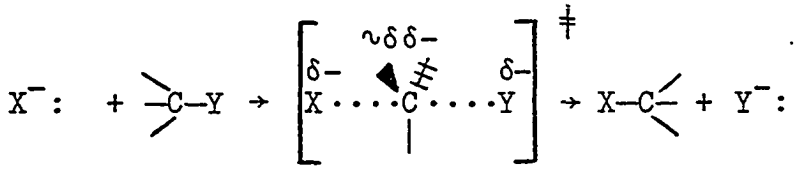
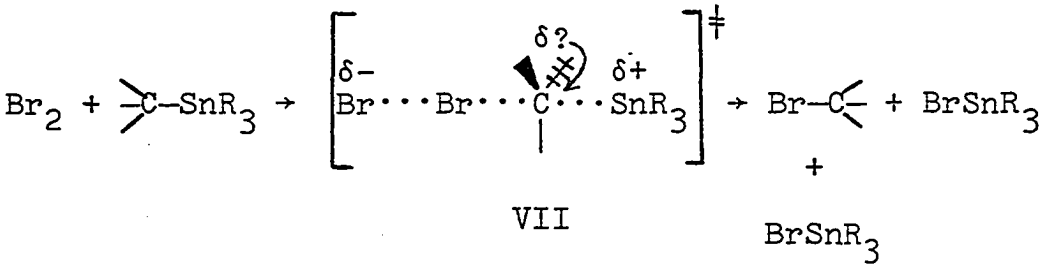
substrates undergoing reaction.



VI

In chapters I and II, the work of Davis[2] was discussed in detail. From the results of his work it was concluded that in polar solvents the bromodemetallation of tetraalkyltin compounds proceeds with inversion of configuration <u>via</u> an S_E2 pathway:



VII

It was also noted that the same failure of Taft's $\sigma^*\rho^*$ which we observe in S_N2 reactions applies to this S_E2 reaction. Since the relative rate sequence for Davis' bromodemetallation reaction parallels Cook and Parker's S_N2 reaction, it was hoped that the study of the bromodemetallation of a series of substituted-benzyltin compounds, $Y\text{-}C_6H_4\text{-}CH_2\text{-}SnR_3$ (R = neopentyl), would permit us to more precisely define the nature of the transition state in the bromodemetallation of tetraalkyltin compounds.

It was with this goal in mind that the rates of bromodemetallation of numerous substituted benzyltrineopentyltin

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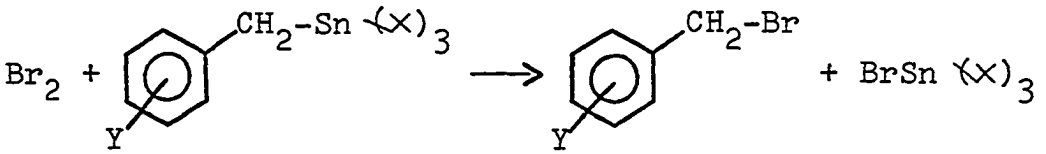
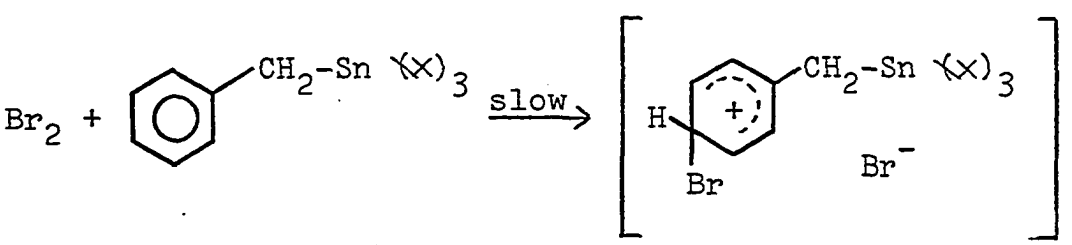
compounds, VIII, were determined:



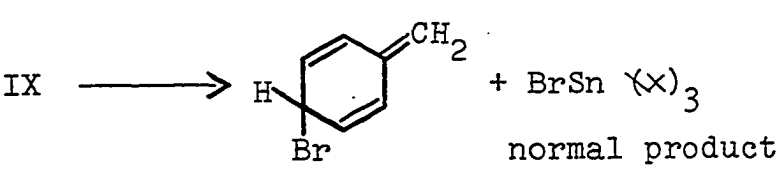
VIII

(Y = H, p-Me, p-MeO, p-Br, p-Cl, p-F, p-t-Bu, m-Me, m-MeO, m-CF_3, 2,4,6-Me_3)

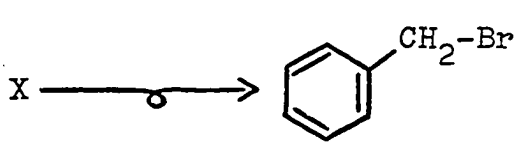
The results (summarized in a later section) do not permit any definite conclusions concerning the transition state of Davis' bromodemetallation reaction (although tentative conclusions may be drawn). However, the rate sequence provides compelling evidence that for at least some of the compounds studied this bromodemetallation reaction proceeds *via* an unusual pathway involving bromine attack upon the aromatic ring to give the same expected products of the normal bromodemetallation pathway:



IX



X normal product



XI normal product

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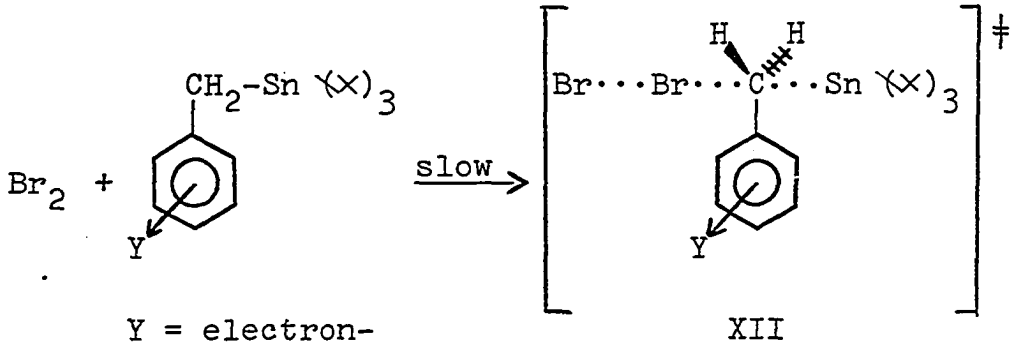
The data strongly suggest the operation of this mechanism for all but those compounds bearing electron-withdrawing substituents. Although ring attack cannot be definitely ruled out for those derivatives, certain features of the data strongly suggest a change in mechanism back to the normal S_E2 bromodemetallation pathway:



Y = electron-withdrawing

XII

XII ⟶ products

The postulate of a rate determining attack upon the ring requires that the R_3SnCH_2- group must be a strong electron-donating group, capable of activating the aromatic system to a comparable or greater extent than the methoxy-group [$(\sigma_\rho^+)_{MeO} = -0.764$].

In the next section, the validity of this assumption as well as a discussion of its theoretical basis will be presented.

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II. Historical

The electron-donating ability of the $M-CH_2-$ group is well substantiated. Early workers[5] noted that the ability of R_3M- (M = C, Si, Ge, Sn) to donate electrons was considerably smaller than that of the R_3M-CH_2- grouping. For example, while vinyl-metallic compounds do not exhibit large U.V. shifts as the metal is changed, the corresponding allyl derivatives show large bathochromic shifts as M, the group IV metal, is varied (Table 4).

Table 4[a]

Frequencies of the Lowest Energy Bands in the U.V. Spectra of Vinyl ($Me_3MCH = CH_2$) and Allyl ($Me_3MCH_2CHCH_2$) Derivatives of the Elements of Group IV (cm^{-1})

	Vinyl		Allyl	
M	ν_{max}	ε	ν_{max}	ε
C	55,600	14,000	54,600	11,000
Si	55,600	17,000	52,100	10,000
Ge	55,300	20,000	51,000	11,000
Sn	53,500	26,000	47,600	13,000

[a]Reference 5, p. 33.

Much of the early work concerning the electron-donating abilities of these groups was carried out on organosilicon compounds. Benkeser and Krysiak[6] found that the trimethylsilyl group, Me_3Si-, could act either as an

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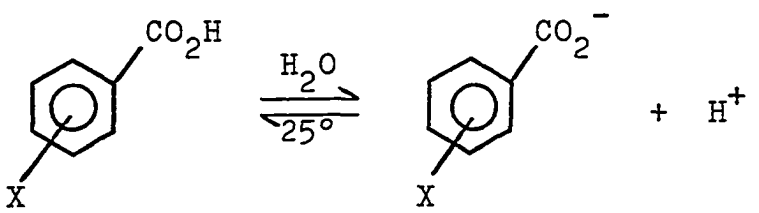
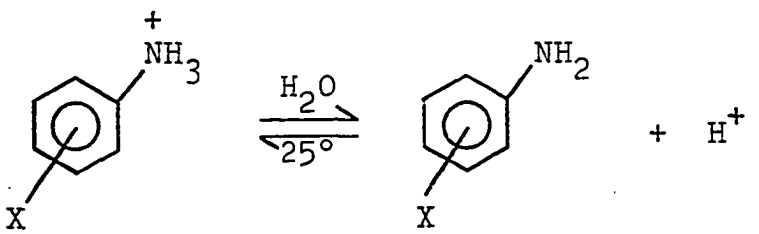
electron-donating group or as an electron-withdrawing group, depending upon the demand for electrons. Thus, m- and p-trimethylsilylbenzoic acids are slightly weaker acids than benzoic acid (i.e. Me_3Si- is slightly electron-donating):



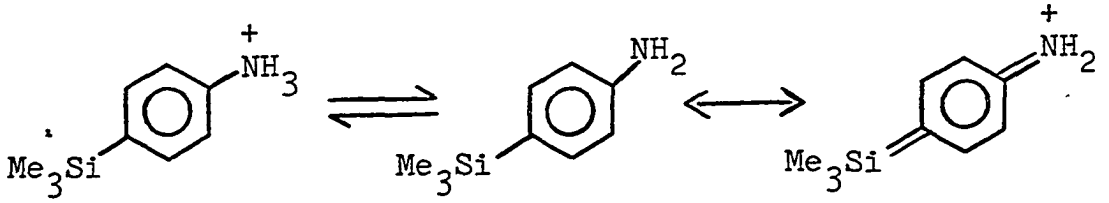
X:	H	m-Me_3Si-	p-Me_3Si-
pKa:	4.20	4.24	4.27

However, the para-substituted trimethylsilyl-anilinium ion is a stronger acid than the anilinium ion:



X:	H	m-Me_3Si-	p-Me_3Si-
pKa:	4.62	4.64	4.36

Presumably, the greater acidity of the para-substituted derivative is due to resonance stabilization in the free base:



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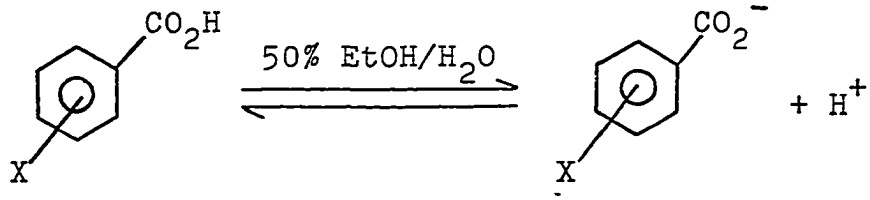
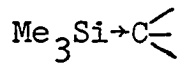
In this case, the trimethylsilyl group behaves as a mildly electron-withdrawing group.

Eaborn[7] studied the acidity of both the trimethylsilyl- (Me_3Si-), and trimethylsilylmethyl- (Me_3SiCH_2-) benzoic acids. He found that compared to the modest electron-donating ability of the trimethylsilyl- group, the trimethylsilylmethyl- group was a powerful electron donor, almost as strong as the methoxy group:



X:	H	m-Me_3SiCH_2-	p-Me_3SiCH_2-	p-OCH_3
pKa:	5.70	6.00	6.80	---
σ:	0.00	-0.205	-0.260	-0.268

These effects were considered to be consistent with the postulate that the trimethylsilyl- group has a large electron-donating effect (+I):



However, when this group is bound directly to a π-system (such as an aromatic ring), back donation of electrons from the π-system to the empty d-orbitals of silicon (-E) can neutralize the inductive effect:

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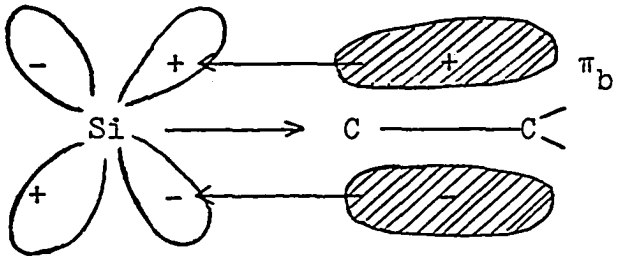

This back-donation of electrons (often referred to as either $Si^{d} \leftarrow C^{\pi}$ or d^{π}-p^{π} -bonding) is eliminated by the introduction of a methylene group between the silicon atom and the π-system. Although the inductive effect is reduced, the elimination of back-donation was believed to result in a net electron-donating inductive effect (+I).

However, additional work on the protodesilylation of substituted aromatic systems led Eaborn[8] to consider the possibility that hyperconjugation might play an important role in this phenomenon.

He observed that in the protodesilylation reaction, the stabilizing effect of the p-trimethylsilylmethyl- group was considerably larger than that of the m-substituent:

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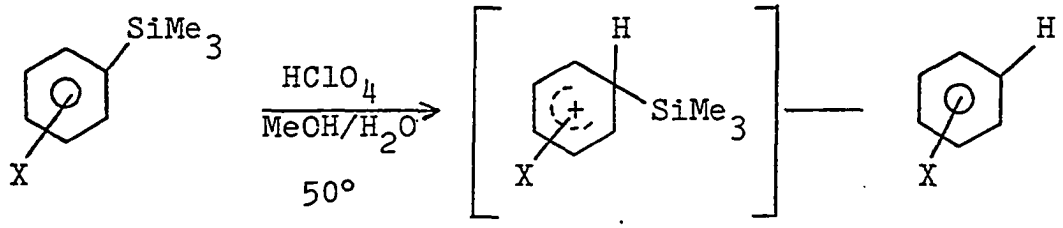
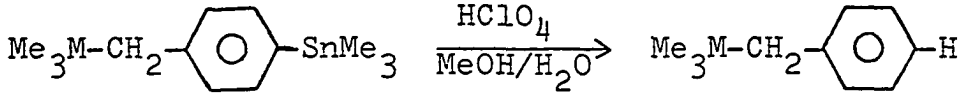


X:	H	p-Me_3Si-	p-Me_3SiCH_2-	m-Me_3SiCH_2-
k_{rel}:	1	2.5	315	6.2

By protodestannylating similar derivatives, R_3M-CH_2-$C_6H_4SnMe_3$,[9,10] Eaborn showed that germanium and tin behave in a similar fashion to silicon. The results of the perchloric acid destannylation[9] are shown below:



M:	Si	Ge	Sn
k_{rel}:	1	1.36	3.21

It is apparent that the electron-donating ability of the group, R_3MCH_2-, increases as one goes down the periodic chart.

Although the question concerning hyperconjugation versus inductive effects remained open for some time, more recent work seems to favor the hyperconjugative explanation for this phenomenon. Traylor[11] has studied the TCNE (tetra-

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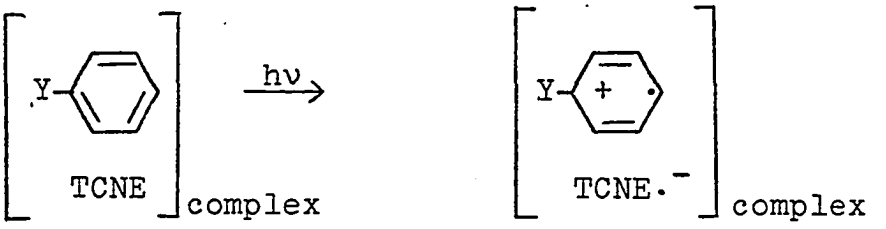
cyanoethylene) and DCMA (dichloromaleic anhydride) charge transfer complexes of numerous substituted benzenes, and he has correlated the wavelength of the charge transfer band with σ_p^+ of known substituents. The data, shown in Table 5, permit the empirical determination of σ_p^+ for new substituents according to the equations:

$$\nu_{TCNE} = 9,300\ \sigma^+ + 26,200 \pm 500\ cm^{-1}$$

$$\nu_{DCMA} = 10,400\ \sigma^+ + 36,400 \pm 600\ cm^{-1}$$

This empirical correlation has several limitations which become apparent upon considering why it works. The charge transfer absorption frequencies are known to be related to the ionization potentials of the aromatic donors. This is reasonable since both processes involve the removal of an electron from the highest filled molecular orbital on the aromatic system.



For benzene, the filled aromatic orbitals look like:

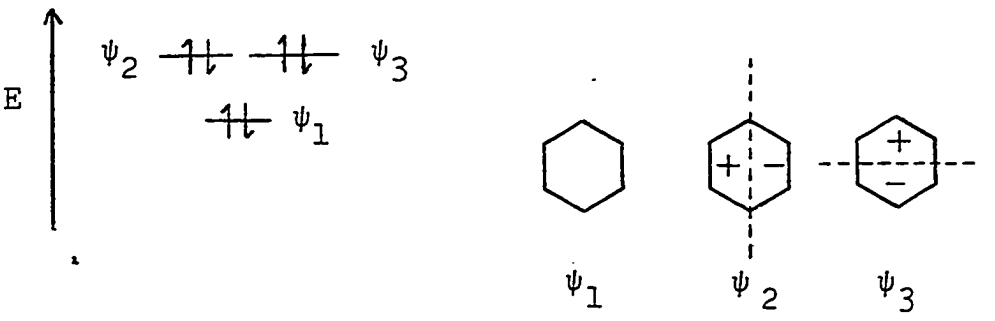


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Table 5[a]

Frequencies for Charge-Transfer Absorptions in Complexes of Tetracyanoethylene (TCNE) or Dichloromaleic Anhydride (DCMA) with Substituted Benzenes

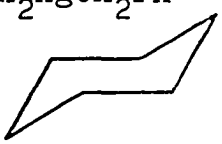
No.	π base	λ_{max}(mμ) (TCNE)	ν_{TCNE} cm^{-1}	ν_{DCMA}
1	PhH	387	25,800	
2	Ph-t-Bu	415	24,100	
3	Ph-i-Pr	415	24,130	
4	Ph-Et	412	24,200	
5	Ph-Me	411	24,300	33,560
6	$PhNHCOCH_3$	480	20,800	
7	$PhOCH_3$	507	19,700	28,600
8	$PhCH_2Cl$	380	26,300	
9	$PhCH_2Br$	382	26,200	
10	$PhCH_2OCH_2Ph$	396	25,300	
11	$PhCH_2CN$	360	27,800	
12	$PhCH_2Ph$	410	24,400	
13	Ph_3CH	405	24,700	
14	$PhCH_2SiMe_3$	486	20,100	29,940
15	$PhCH_2HgCH_2Ph$	635	15,780	24,940
16	Ph- 	413	24,200	
17	PhOH	481	20,800	
18	$PhCH=CH_2$	480	20,800	
19	$PhNMe_2$	520	19,200	21,230

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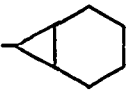
Table 5 (continued)

No.	π base	λ_{max} (mμ) (TCNE)	ν_{TCNE} cm^{-1}	ν_{DCMA}
20	PhOPh	495	20,200	
21	Ph-Ph	498	20,100	
22	$PhCH_2CO_2Et$	381	26,200	
23	$PhCH_2NHCOCH_3$	410	24,400	
24	$PhCH_2SnMe_3$			26,700
25	$PhCH_2CH_2PbPh_3$	396	25,200	
26	$PhCH_2CH(CH_3)HgCH(CH_3)CH_2Ph$	415	24,100	
27	Ph-  (mostly trans)	500	20,000	
28	Ph-	470	21,300	
29	$PhCH_2PbPh_3$	615	16,300	25,840

[a]Taken from reference 11.

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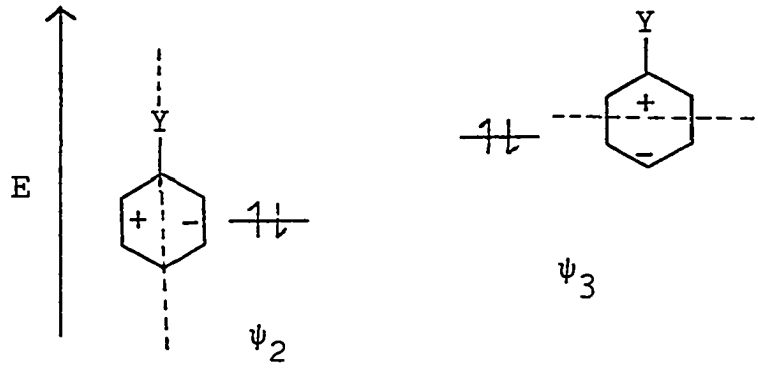
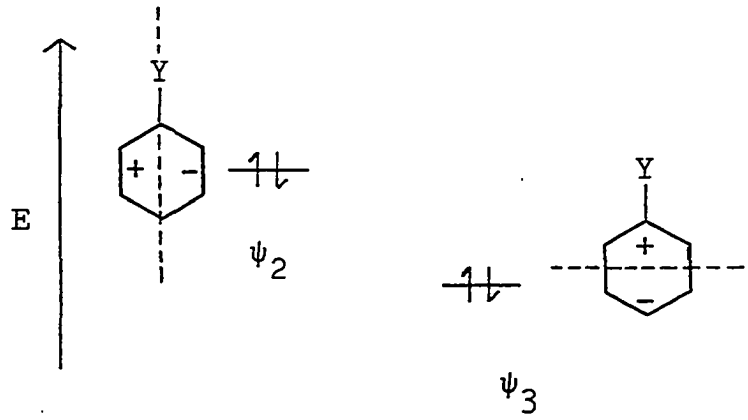
However, addition of a substituent, Y, removes the degeneracy of ψ_2 and ψ_3. If Y is electron donating, the MO's look like:



The electron removed will come from ψ_3, and the effect of Y upon the energy of ψ_3 will be observed.

However, if Y is electron withdrawing, the MO's look like:



The electron will be removed from ψ_2, where Y lies in a nodal plane. The effect of Y will not be observed. Thus, electron-withdrawing substituents may not be analyzed in this manner.

Electrophilic substitutions at the <u>para</u> position,

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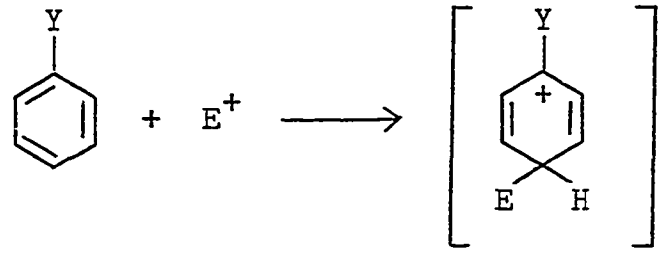
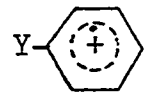


are analogous to the charge transfer process since they involve a perturbation of the same molecular orbital. Presumably, both processes involve an intermediate with a positive charge at the carbon bearing the substituent Y.

A naive way to picture the phenomenon is to consider the radical cation:



The positive charge will always reside in the most favorable location. If Y is electron-donating, this will be: Y→ rather than Y→ , etc. In addition, the greater the donating capacity of Y, the easier (i.e. less energy required) the formation of the radical cation will be, since its stability will increase with the donor strength of Y. This is exactly the same reasoning used to explain the effect of electron-donation on electrophilic aromatic substitution reactions.

As Traylor points out, the use of charge-transfer complexes permits one to separate hyperconjugative and inductive effects from those commonly referred to as participation. Since the charge-transfer occurs according to the Franck-Condon principle, it must involve no

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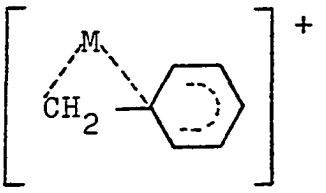
geometrical rearrangement in going from the ground state to the excited state. Thus, for any stabilizing effect observed in this manner, participation of the type shown in XIII may be ruled out.



XIII

From his charge-transfer data, Traylor has determined σ_p^+ values for numerous organometallic substituents. These are compiled in Table 6.

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Table 6[a]

Values of σ_p^+ for Various Groups, Y, on Benzenes as Determined by Reaction Rates and by Charge-Transfer Spectra

Group Y	σ^+ (from reactions)	σ^+ (from CT)
H-	0.0	-0.03
CH_3O-	-0.778	-0.74 (-0.75)
CH_3CONH-	-0.58	-0.60
$(CH_3)_3SiCH_2$-	-0.61	-0.66 (-0.63)
$(CH_3)_3SnCH_2$-	-0.76	-0.9
CH_3CH_2-	-0.295	-0.25
Ph_3PbCH_2-	---	-1.08
$Ph_3PbCH_2CH_2$-	∿(-0.3)	-0.22
$PhCH_2HgCH_2$-	-1.11	-1.12
$PhCH_2\underset{\displaystyle CH_3}{\underset{\vert}{C}}HHg\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2$-	∿(-0.3)	-0.25

[a]Taken from Reference 11.

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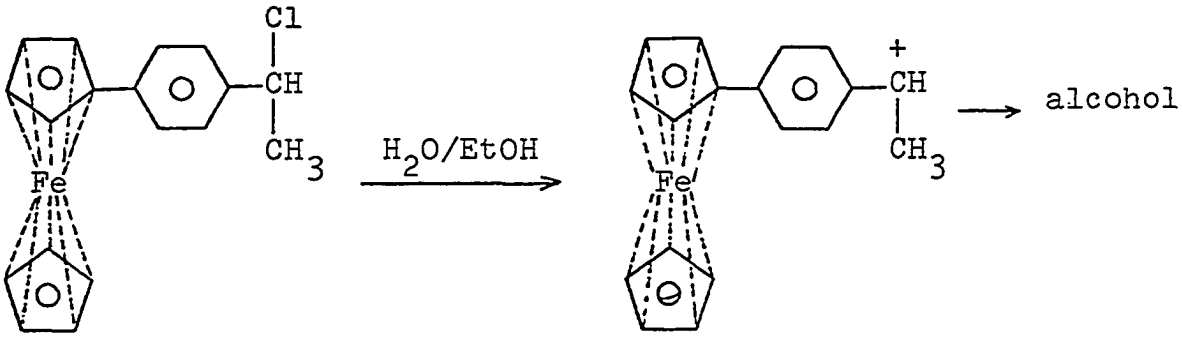
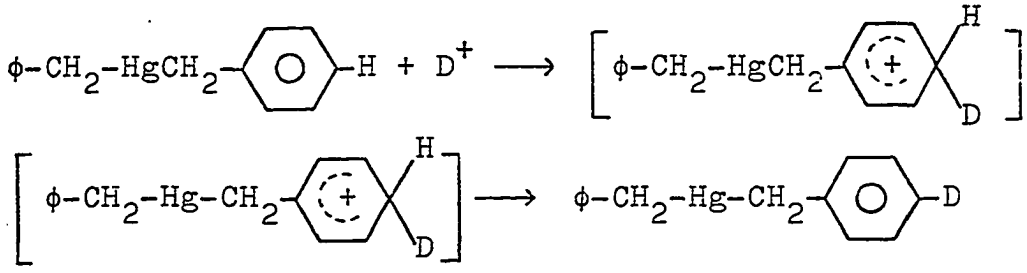
It is apparent from this table that electron-donation from the M-CH_2- group is a general phenomenon. Traylor had earlier observed its accelerating effect on chemical reactions such as the solvolysis of certain ferrocenyl derivatives[12] and the proton exchange of benzyl mercurials:[13]





A careful analysis of the data also makes the inductive explanation of the phenomenon seem dubious. Traylor interprets the values of the parameters for ϕ_3PbCH_2-, σ^+ = -1.08; ϕ_3PbCH_2-CH_2-, σ^+ = -0.25; and CH_3CH_2-, σ^+ = -0.25 in the following manner: the ϕ_3Pb- group on ϕ_3PbCH_2- differs from the CH_3- group on CH_3-CH_2- by -0.83. Insertion of an additional methylene, -CH_2-, between ϕ_3PbCH_2- and the aromatic ring should cause a decrease of this difference to -0.83/2.8 = -0.3 greater than CH_3-; or $\phi_3PbCH_2CH_2$- should have σ^+ = -0.55 if the phenomenon is caused by an inductive

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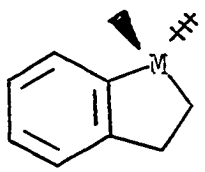
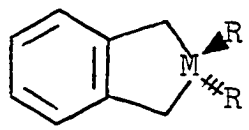
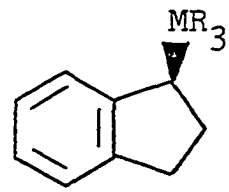
effect. However, if the effect is hyperconjugative, the additional methylene would completely eliminate the hyperconjugating ability of the substituent, and it should behave like other alkyl groups (i.e. $\sigma^+ \simeq -0.25$). The experimental value of -0.22 indicates a hyperconjugative mechanism.

This notion is given powerful support by the recent work of Pitt,[14] who has studied the ionization potentials of several cyclic derivatives.







	I	II	III
a	$MR_2=CH_2$	$MR_2=CMe_2$	$MR_3=SiMe_3$
b	CHMe	$SiMe_2$	Si_2Me_5
c	CMe_2	$Si(Me)SiMe_3$	$GeMe_3$
d	$SiMe_2$	$GeMe_2$	

The ionization potentials, which were derived from their TCNE complexes are given in Table 7.

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Table 7[a]

Frequencies and Ionization Potentials Derived from Charge Transfer Complexes with Tetracyanoethylene

Compound	$\bar{\nu}_1$, x 10^{-4} cm^{-1}	$\bar{\nu}_2$, x 10^{-4} cm^{-1}	IP, (eV)
o-xylene	2.20	2.49	8.61
o-diethylbenzene	2.13	2.43	8.51
indane (Ia)	2.14	2.48	8.52
tetralin	2.10	2.38	8.47
Ib	2.10	2.46	8.47
Ic	2.10	2.48	8.47
Id	2.15	2.44	8.54
IIa	2.10	2.46	8.47
IIb	2.07	2.37	8.41
IIc	2.04	2.89	8.37
IId	2.05	2.37	8.39
IIIa	1.88	2.38	8.13
IIIb	1.84	2.38	8.07
IIIc	1.80	2.33	8.02
toluene	2.26	2.56	8.71
$PhCH_2SiMe_3$	2.04	2.51	8.37
$PhCH_2Si_2Me_5$	1.97	2.51	8.27
$PhCH_2GeMe_3$	1.96	2.52	8.26

[a]Reference 14.

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Although there is a small stabilization of 0.1 eV when replacing carbon by a metal in series II, this effect is small compared with 0.4-0.5 eV stabilizations in series III. Clearly, there is an angular requirement for the stabilization to occur. It is well known that while hyperconjugation has an angular dependence, inductive effects are not subject to such a dependence. Thus, in series II, where the C-M bond is perpendicular to the plane of the aromatic ring, no hyperconjugative stabilization can occur. However, in series III, the C-M bond is in good geometrical position to overlap with the π-system and stabilization occurs. Pitt notes that series I, which has the M-C bond oriented properly does not show any hyperconjugative effect. He suggests that for this case, the metal-carbon bond is located further from the aromatic ring (1.87 Å) than the C-M bond in series III (1.54 Å from the ring). While this may play a part, he is probably observing direct back donation of the p^{π}-d^{π} type described earlier.

Bock and Alt[15,16,17] have also studied the ionization potentials, charge transfer complexes, and reduction potentials of numerous silyl-derivatives and have observed the same phenomena as Traylor. Although they suggest that the effect is inductive, their argument[15] is based on a molecular orbital model. Considering the compelling experimental data of Traylor and Pitt, their conclusions must be considered doubtful.

Thus, it appears that through hyperconjugation of the

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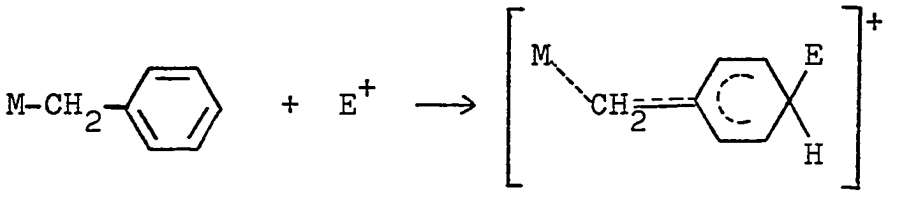
type shown below, XIV, the M-CH_2- group is capable of powerful electron-donation to the aromatic ring:



hyperconjugation

XIV

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III. Results

Davis[2] carried out a detailed kinetic investigation of the bromodemetallation of methyltrineopentyltin in methanol with added sodium bromide. In order to simplify the kinetics, sodium bromide was added in swamping excess:

$$Br^- + Br_2 \underset{}{\overset{K_{equ}}{\rightleftharpoons}} Br_3^-$$

$$K_{equ} = 177 \ (25° \text{ in MeOH})$$

He found that the reaction was first order in organotin and tribromide. In addition, he found the observed rate to have an inverse dependence upon added bromide. The kinetic data is consistent with the following:

$$\text{observed rate} = k_2^{obs} [R_3SnR'] [Br_2]_t = k_2 [R_3SnR'] [Br_2]$$

$$\text{where } k_2 = k_2^{obs} (1 + K_{equ}[Br^-]); \text{ and } [Br_2]_t = [Br_3^- + Br_2]$$

Thus, the true rate is first order in tin compound and first order in bromine.

Since all rates were carried out at swamping sodium bromide concentrations ([NaBr] = 0.366 M; $[Br_2]_t \cong 2 \times 10^{-3}$ M), and since the equilibrium with bromine lies heavily to the tribromide side ($Br^- + Br_2 \overset{K=177}{\rightleftharpoons} Br_3^-$), the total bromine concentration, $(Br_2)_t = (Br_3^- + Br_2)$ is always approximately equal to tribromide concentration. To simplify future discussions, the term "bromine" may be employed instead of "tribromide" or"total bromine." Since the concentration of free bromine, Br_2, is never discussed, this should lead to

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no ambiguity.

In the current study, it was assumed that Davis' kinetic conclusions would hold for the various benzyltrineopentyltin compounds studied. This assumption appears valid since (1) changes in organotin concentration did not significantly affect the rate, and (2) all rates were found to be first order in bromine. In general, rates were run under pseudo-first-order conditions (excess organotin), and second-order conditions (comparable organotin and bromine concentrations). In no case did the bromine concentration exceed that of organotin ($[Sn] \geq [Br_2]_t$).

To standardize the running of kinetics, all runs were carried out at 0.366 M NaBr concentration. To avoid errors all runs were done uniformly. A stock solution which was approximately 4×10^{-3} M in bromine and 0.732 M in sodium bromide was prepared in absolute methanol. For each run a methanolic solution of known concentration of organotin compound was prepared, and several milliliters of this and the stock solution were equilibrated to the desired temperature. Equal volumes of each solution were then syringed into the cuvette and the absorbance monitored as a function of time. For all runs the initial $[Br_2]_t$ was approximately 2×10^{-3} M.

The rates were computed in one of three ways, depending upon the conditions employed:

(1) When the organotin compound was in swamping excess, a pseudo-first-order treatment was employed:

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$$\ln \left(\frac{a}{a-x}\right) = (k_1^{obs})t$$

A plot of log O.D. vs. t gives a straight line whose slope is $m = -k_1^{obs} / 2.303$.

Since $k_2^{obs}=k_1^{obs}/[Sn]$, k_2^{obs} is readily computed from the pseudo-first order rate.

(2) When the initial organotin compound concentration was in excess but in comparable concentration to bromine, a second order rate expression was employed:

$$\left(\frac{1}{a-b}\right) \ln \left(\frac{b}{a} \frac{(a-x)}{(b-x)}\right) = (k_2^{obs})t$$

A plot of $\log \left(\frac{b}{a} \frac{(a-x)}{(b-x)}\right)$ vs. t gives a straight line whose slope is

$$m = \frac{(a-b)\ k_2^{obs}}{2.303}$$

(3) When the initial concentrations of organotin and bromine were equal, the appropriate rate expression used was:

$$\left(\frac{1}{a-x}\right) - \left(\frac{1}{a}\right) = k_2^{obs}\ t$$

A plot of $\frac{1}{a-x}$ vs. t gives a straight line whose slope, $m = k_2^{obs}$.

For pseudo-first order rates (case 1), only the absorbance or optical density is necessary at each time. However, under second order conditions (cases 2 and 3) a knowledge of the instantaneous concentrations of bromine and organotin compound were necessary. Instantaneous bromine concentrations were

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determined from Beer's Law: $A = (\varepsilon)(c)(d)$. The extinction coefficient, ε, was determined to be $\varepsilon = 734$ (see below). The instantaneous organotin concentrations were determined from the instantaneous bromine concentrations.

The extinction coefficient for Br_3^- at 385 nm was determined by measuring the absorbance of several solutions as a function of their Br_3^- concentration: $A = (\varepsilon)\ (Br_3^-)\ (d)$.

The data is summarized in Table 8.

Table 8

Extinction Coefficient of Br_3^- at 385 nm

(NaBr) = 1.0 M

Br_3^-	A	ε
2.56×10^{-3}	1.880	742
1.28×10^{-3}	0.940	741
0.512×10^{-3}	0.365	718
0.256×10^{-3}	0.185	723
		734 (mean)

The mean value of $\varepsilon = 734$ is in reasonably good agreement with Davis' value of 782.

Activation parameters were determined for all but two of the tin compounds studied. The m-methyl- and m-methoxy derivatives react too rapidly to be measured conveniently at a variety of temperatures.

Since all kinetic runs were carried out in the presence

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of added sodium bromide, it was necessary to compute the true rate, k_2, from the observed rate, k_2^{obs} :

$k_2 = k_2^{obs}(1 + K_{equ}[Br^-])$.

In order to determine the activation parameters, it is necessary to know how K_{equ} varies with temperature. Herzog and DuBois[18] have studied this equilibrium as a function of temperature in methanol, and their data are shown in Table 9.

Table 9

Equilibrium Constant in Absolute Methanol

$$Br_2 + Br^- \underset{}{\overset{K_{equ}}{\rightleftharpoons}} Br_3^-$$

Temperature (°C)	K_{equ} ($l \cdot mole^{-1}$)
-15	355 ± 24
+ 5	260 ± 9
+18	204 ± 13
+25	177 ± 18

Since Herzog and DuBois did not determine K_{equ} at the same temperatures at which the kinetics were carried out, it was necessary to determine these values graphically.

Thermodynamics equates equilibra with temperature according to the equation:

$$K_{equ} = e^{+\Delta S/R} \cdot e^{-\Delta H/RT}$$

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or

$$\log K_{equ} = \frac{\Delta S}{2.303R} - \frac{\Delta S}{2.303R}\left(\frac{1}{T}\right)$$

Consequently, a plot of ($\log K_{equ}$) versus (1/T) should give a straight line from which K_{equ} may be determined for any temperature. However, when the data of Herzog and DuBois is plotted in this way, the points are non-linear (see Fig. 4). Apparently, the data needs some improvement.

Nevertheless, it was found that a plot of (K_{equ}) versus (1/T) gave a very good straight line (see Fig. 5). Thus, as a reasonable approximation, values of K_{equ} were taken from this non-termodynamic plot.

The values selected are summarized in Table 10.

Table 10

Extrapolated Values of K_{equ}

Temperature (°C)	K_{equ} ($l \cdot mole^{-1}$)
0	280.3
25	177.0
35	144.7

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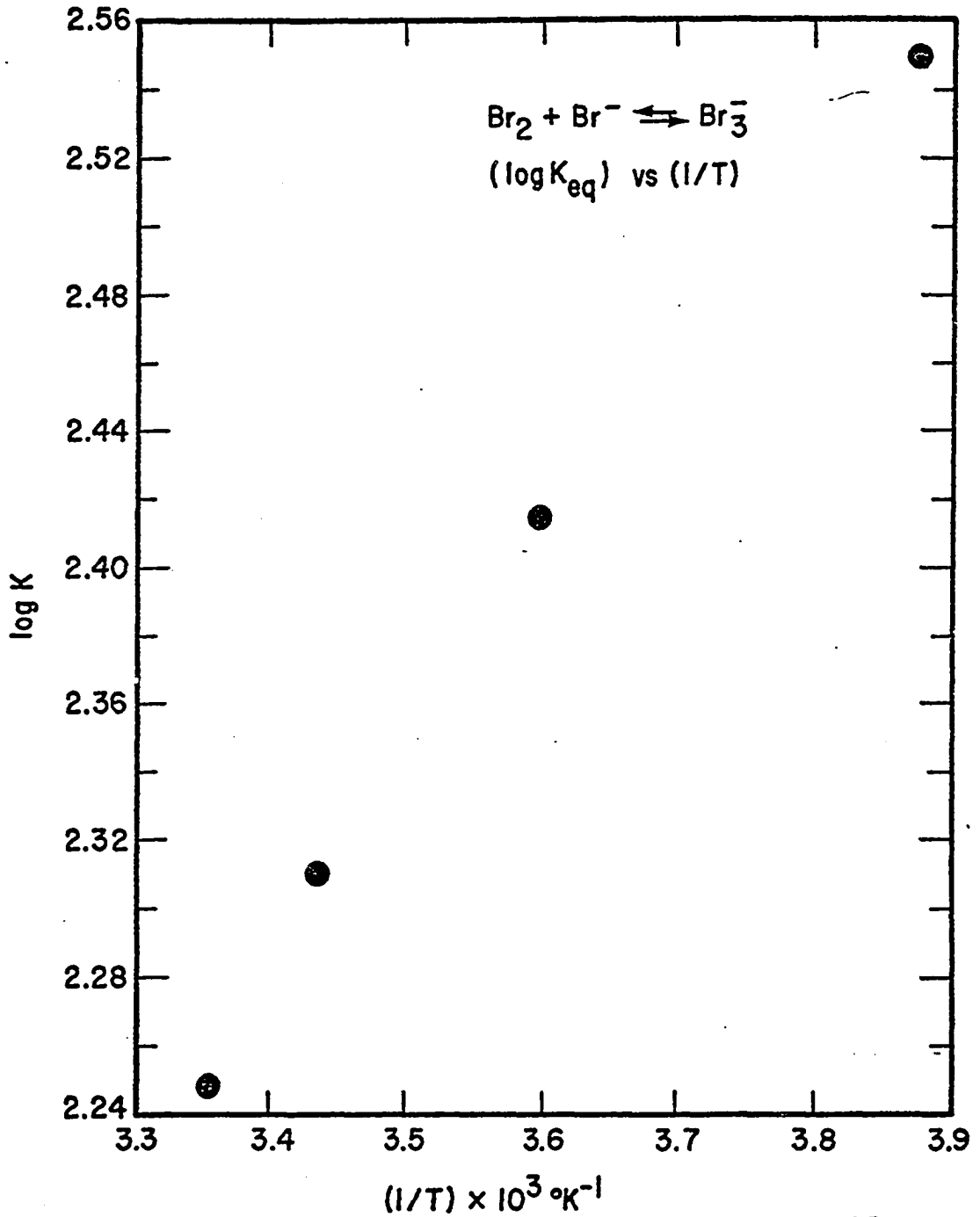

Figure 4. Tribromide Equilibrium in Methanol (Reference 18).

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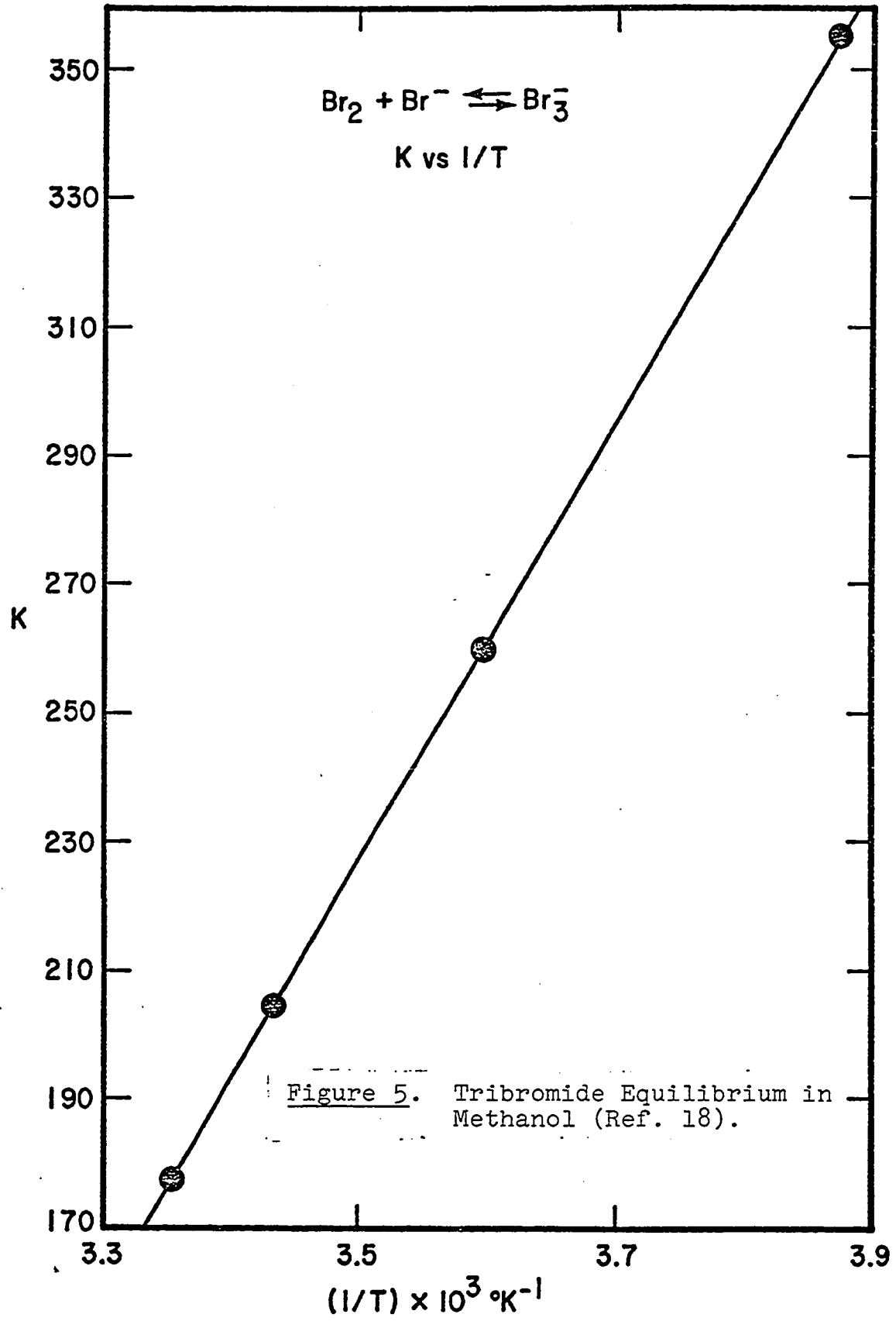

Figure 5. Tribromide Equilibrium in Methanol (Ref. 18).

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Methyltrineopentyltin:

In order to check the accuracy of the method, several runs were carried out at 25° on methyltrineopentyltin, a compound studied by Davis. The results, summarized in Table 11, have reasonably good internal consistency, and give an idea of the magnitude of error in the experimental method. Davis' value of 4.50 $\underline{M}^{-1} \cdot sec^{-1}$ for k_2 is about 10% different from the value reported here of 4.11 $\underline{M}^{-1} \cdot sec^{-1}$. Since all conclusions drawn from the kinetic data are based upon relative rates, this small discrepancy need not concern us, as all results carried out by this worker had reasonably good internal consistency.

Table 11

Bromodemetallation of Methyltrineopentyltin

MeOH; [NaBr] = 0.366 $\underline{M}$, μ = 0.366, $[Br_2]_t \cong 2 \times 10^{-3}$ $\underline{M}$

Run#	T (°C)	[Sn]	$k_2^{obs} \times 10^2$ $\underline{M}^{-1} \cdot sec^{-1}$	k_2 $\underline{M}^{-1} \cdot sec^{-1}$
16	25	7.01×10^{-2}	5.91	3.89
17	25	6.01×10^{-2}	6.24	4.11
19	25	6.01×10^{-2}	6.32	4.16
20	25	6.01×10^{-2}	6.34	4.17
21	25	6.01×10^{-2}	6.29	4.14
22	25	4.43×10^{-2}	6.30	4.15
23	25	6.05×10^{-2}	5.98	3.93
24	25	6.11×10^{-2}	6.56	4.32
mean			6.24 ± .15	4.11 ± .10

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Benzyltrineopentyltin:

The parent benzyl compound was bromodemetallated in similar fashion to methyltrineopentyltin, and ironically had an observed rate, k_2^{obs}, at 25° of exactly 1.00 $\underline{M}^{-1} \cdot sec^{-1}$. Thus, relative rates for all compounds are merely their observed rate at 25°.

Table 12

Bromodemetallation of Benzyltrineopentyltin

MeOH; [NaBr] = 0.366 $\underline{M}$, μ = 0.366, $[Br_2]_t \cong 2 \times 10^{-3}$ $\underline{M}$

Run #	T (°C)	[Sn] × 10^3	k_2^{obs} $\underline{M}^{-1} \cdot sec^{-1}$	$k_2(\times 10^{-1})$ $\underline{M}^{-1} \cdot sec^{-1}$
10	25	20.1	1.02	6.71
11	25	4.01	0.948	6.24
25	25	2.87	1.04	6.84
39	0	16.0	0.108	1.12
50	35	7.44	2.06	10.82
52	35	3.72	2.37	12.44
53	35	3.98	2.30	12.08

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Table 13

Variation of Rate Constant with Temperature

Benzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2 $M^{-1} \cdot sec^{-1}$	$k_2^a \times 10^{-1}$ $M^{-1} \cdot sec^{-1}$	$\log(k_2/T)$	K
39	0	0.108	1.12	-1.3873	280.3
10,11,25	25	1.00	6.58	-0.6560	177.0
50,52,53	35	2.24	11.76	-0.4182	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

The thermodynamic parameters determined from this were:

$\Delta H^{\pm}$ = 10.51 kcal/mole ± 0.36

$\Delta S^{\pm}$ = -14.97 e.u. ± 1.76

$\Delta G^{\pm}$ = 14.97 kcal/mole

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p-Methylbenzyltrineopentyltin:

Table 14

Bromodemetallation of p-Methylbenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs}(× 10) $M^{-1} \cdot sec^{-1}$	k_2(× 10^{-1}) $M^{-1} \cdot sec^{-1}$
12	25	19.6	3.66	2.41
101	25	16.4	3.71	2.44
78	0	26.3	0.415	0.430
79	0	23.9	0.413	0.428
51	35	7.42	7.76	4.07
89	35	4.72	7.33	3.85
91	35	5.73	8.10	4.25

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Table 15

Variation of Rate Constant with Temperature

p-Methylbenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} (× 10) $M^{-1} \cdot sec^{-1}$	k_2[a] $M^{-1} \cdot sec^{-1}$	log(k/T)	K
78,79	0	0.414	4.29	-1.8038	280.3
12,101	25	3.68	24.2	-1.0903	177.0
51,89,91	35	7.73	40.6	-0.8801	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

From this data, the activation parameters were determined:

$\Delta H^{\pm}$ = 9.87 kcal/mole ± 0.70

$\Delta S^{\pm}$ = -19.12 e.u. ± 2.33

$\Delta G^{\pm}$ = 15.57 kcal/mole

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p-t-Butylbenzyltrineopentyltin:

Table 16

Bromodemetallation of p-t-Butylbenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs}(× 10) $M^{-1} \cdot sec^{-1}$	k_2(× 10^{-1}) $M^{-1} \cdot sec^{-1}$
40	25	17.2	5.13	3.38
102	25	13.12	4.41	2.90
103	25	14.74	4.01	2.64
74	0	27.3	0.600	0.622
81	0	20.8	0.588	0.609
54	35	5.43	8.87	4.66
90	35	4.64	8.77	4.60

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Table 17

Variation of Rate Constant with Temperature

p-t-Butylbenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} (× 10) $M^{-1} \cdot sec^{-1}$	k_2[a] $M^{-1} \cdot sec^{-1}$	log(k/T)	K
74,81	0	0.594	6.15	-1.6472	280.3
40,102,103	25	4.52	29.7	-1.0014	177.0
54,90	35	8.82	46.3	-0.8230	140.7

[a] $k_2 = k_2^{obs} (1+K[Br^-])$

From this data, the activation parameters were determined:

$\Delta H^{\pm}$ = 8.73 kcal/mole ± 0.49

$\Delta S^{\pm}$ = -22.56 e.u. ± 2.73

$\Delta G^{\pm}$ = 15.45 kcal/mole

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p-Methoxybenzyltrineopentyltin:

Table 18

Bromodemetallation of p-Methoxybenzyltrineopentyltin

MeOH: [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs} (× 10) $M^{-1} \cdot sec^{-1}$	k_2 (× 10^{-1}) $M^{-1} \cdot sec^{-1}$
6	25	16.0	1.78	1.17
7	25	10.1	1.79	1.18
26	25	5.76	1.77	1.16
77	0	22.2	0.233	0.241
80	0	24.0	0.231	0.239
55	35	11.45	3.48	1.83
106	35	10.77	3.93	2.06
107	35	13.01	3.38	1.77

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Table 19

Variation of Rate Constant with Temperature

p-Methoxybenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} (× 10) $M^{-1} \cdot sec^{-1}$	k_2^a $M^{-1} \cdot sec^{-1}$	log(k/T)	K
77,80	0	0.232	2.40	-2.0560	280.3
6,7,26	25	1.78	11.7	-1.4071	177.0
55,106,107	35	3.60	18.9	-1.2120	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

From this data, the activation parameters were determined:

$\Delta H^{\pm}$ = 8.90 kcal/mole ± 0.51

$\Delta S^{\pm}$ = -23.85 e.u. ± 1.77

$\Delta G^{\pm}$ = 16.01 kcal/mole

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p-Fluorobenzyltrineopentyltin:

Table 20

Bromodemetallation of p-Fluorobenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs}(× 10^2) $M^{-1} \cdot sec^{-1}$	k_2 $M^{-1} \cdot sec^{-1}$
14	25	50.4	4.17	2.74
31	25	7.71	3.99	2.63
72	0	28.3	0.790	0.818
76	0	26.4	0.744	0.771
57	35	27.9	7.43	3.90

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Table 21

Variation of Rate Constant with Temperature

p-Fluorobenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	$k_2^{obs}(\times 10^2)$ $M^{-1} \cdot sec^{-1}$	k_2 [a] $M^{-1} \cdot sec^{-1}$	log(k/T)	K
72,76	0	0.767	0.795	-2.5358	280.3
14,31	25	4.08	2.69	-2.0444	177.0
57	35	7.43	3.90	-1.8972	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

From this data, the activation parameters were determined:

$\Delta H^{\pm}$ = 6.84 kcal/mole ± 0.44

$\Delta S^{\pm}$ = -33.87 e.u. ± 1.75

$\Delta G^{\pm}$ = 16.93 kcal/mole

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p-Chlorobenzyltrineopentyltin:

Table 22

Bromodemetallation of p-Chlorobenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	$[Sn]^2 \times 10^3$	$k_2^{obs}(\times 10^2)$ $M^{-1} \cdot sec^{-1}$	k_2 $M^{-1} \cdot sec^{-1}$
15	25	42.7	3.82	2.51
30	25	9.22	3.98	2.62
69	0	34.4	0.823	0.853
71	0	34.6	0.839	0.869
48	35	40.2	6.65	3.49

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Table 23

Variation of Rate Constant with Temperature

p-Chlorobenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} ($\times 10^2$) $M^{-1} \cdot sec^{-1}$	k_2^a $M^{-1} \cdot sec^{-1}$	log(k/T)	K
69,71	0	0.831	0.861	-2.5011	280.3
15,30	25	3.90	2.57	-2.0643	177.0
48	35	6.67	3.50	-1.9446	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

From this data the activation parameters were determined:

$\Delta H^{\pm}$ = 5.89 kcal/mole ± 0.57

$\Delta S^{\pm}$ = -36.94 e.u. ± 1.89

$\Delta G^{\pm}$ = 16.90 kcal/mole

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p-Bromobenzyltrineopentyltin:

Table 24

Bromodemetallation of p-Bromobenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs} (× 10^2) $M^{-1} \cdot sec^{-1}$	$M^{-1} \cdot sec^{-1}$
64	25	22.9	3.71	2.44
65	25	30.8	4.15	2.73
66	25	23.2	3.60	2.37
68	0	24.4	0.786	0.814
60	35	21.7	6.25	3.28
61	35	22.9	6.93	3.64
62	35	30.8	6.83	3.59

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Table 25

Variation of Rate Constant with Temperature

p-Bromobenzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} ($\times 10^2$) $M^{-1} \cdot sec^{-1}$	k_2[a] $M^{-1} \cdot sec^{-1}$	log(k/T)	K
68	0	0.786	0.814	-2.5258	280.3
64,65,66	25	3.82	2.51	-2.0747	177.0
60,61,62	35	6.67	3.50	-1.9446	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

From this data the activation parameters were determined:

$\Delta H^{\pm}$ = 6.19 kcal/mole ± 0.49

$\Delta S^{\pm}$ = -35.97 e.u. ± 1.61

$\Delta G^{\pm}$ = 16.91 kcal/mole

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m-(Trifluoromethyl)benzyltrineopentyltin:

Table 26

Bromodemetallation of m-(Trifluoromethyl)benzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs} (× 10^2) $M^{-1} \cdot sec^{-1}$	k_2 $M^{-1} \cdot sec^{-1}$
9	25	35.2	2.36	1.55
29	25	4.50	2.78	1.83
104	25	19.8	2.64	1.74
70	0	19.8	0.529	0.548
58	35	25.2	4.68	2.46
108	35	19.8	5.08	2.67

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Table 27

Variation of Rate Constant with Temperature

m-(Trifluoromethyl)benzyltrineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} ($\times 10^2$) $M^{-1} \cdot sec^{-1}$	k_x [a] $M^{-1} \cdot sec^{-1}$	log(k/T)	K
70	0	0.529	0.548	-2.6985	280.3
9,29,104	25	2.59	1.70	-2.2438	177.0
58,108	35	4.88	2.56	-2.0803	140.7

[a] $k_2 = k_2^{obs} (1+K[Br^-])$

From this data the activation parameters were determined:

$\Delta H^{\pm}$ = 6.81 kcal/mole ± 0.03

$\Delta S^{\pm}$ = 34.62 e.u. ± 0.10

$\Delta G^{\pm}$ = 17.13 kcal/mole

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(2,4,6-Trimethylbenzyl)trineopentyltin:

Table 28

Bromodemetallation of (2,4,6-Trimethylbenzyl) trineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	[Sn] × 10^3	k_2^{obs} $M^{-1} \cdot sec^{-1}$	$k_2(\times 10^{-1})$ $M^{-1} \cdot sec^{-1}$
99	25	4.37	1.34	8.82
100	25	3.60	1.42	9.34
109	0	4.24	0.205	2.12
97	35	4.37	2.82	14.81
98	35	3.47	2.98	15.65

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Table 29

Variation of Rate Constant with Temperature

(2,4,6-Trimethylbenzyl) trineopentyltin

MeOH; [NaBr] = 0.366 M; μ = 0.366; $[Br_2]_t \cong 2 \times 10^{-3}$ M

Run #	T (°C)	k_2^{obs} $M^{-1} \cdot sec^{-1}$	$k_2^{a}(\times 10^{-2})$ $M^{-1} \cdot sec^{-1}$	log(k/T)	K
109	0	0.205	0.212	-1.1090	280.3
99,100	25	1.38	0.908	-0.5161	177.0
97,98	35	2.90	1.52	-0.3059	140.7

[a] $k_2 = k_2^{obs}(1+K[Br^-])$

From this data the activation parameters were determined:

$\Delta H^{\pm}$ = 8.83 kcal/mole ± 0.01

$\Delta S^{\pm}$ = -19.95 e.u. ± 0.02

$\Delta G^{\pm}$ = 14.78 kcal/mole

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m-Methylbenzyltrineopentyltin:

The bromodemetallation of m-methylbenzyltrineopentyltin proceeds too rapidly to determine its activation parameters conveniently. Its rate at 0° was found to be k_2^{obs} = 10.33 $\underline{M}^{-1}$ sec^{1} at 0°. This corresponds to a relative rate of 95.6 (compared to the parent compound at 0°).

m-Methoxybenzyltrineopentyltin:

The bromodemetallation of m-methoxybenzyltrineopentyltin proceeded too rapidly for measurement under normal conditions. Its rate was measured on a Cary 14 at 0° using a 10 cm cell. Although a reasonably good kinetic plot was obtained, the reaction was 90% complete in 1.2 seconds under the conditions used. Thus, it is possible that the rate measured is really a rate of mixing. Nevertheless, a minimum value of k_2^{obs} = 5.14×10^4 $\underline{M}^{-1}$ sec^{-1} was observed at 0°. This corresponds to a relative rate of $\geq 4.76 \times 10^5$.

The relative rates of all the compounds studied are compiled along with the activation parameters in Table 30.

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Table 30

Relative Rates of Bromodemetallation of Substituted Benzyltrineopentyltin Derivatives

Substituent (Y)	Relative Rate	$\Delta G^{\ddagger}\left(\frac{kcal}{mole}\right)$	$\Delta H^{\ddagger}\left(\frac{kcal}{mole}\right)$	$\Delta S^{\ddagger}$(e.u.)
H	1	14.97	10.51	-14.97
p-CH_3	0.368	15.57	9.87	-19.12
p-t-Bu	0.452	15.45	8.73	-22.56
p-CH_3O	0.178	16.01	8.90	-23.85
2,4,6-$(CH_3)_3$	1.38	14.78	8.83	-19.95
p-F	4.08×10^{-2}	16.93	6.84	-36.50
p-Cl	3.90×10^{-2}	16.90	5.89	-36.94
p-Br	3.82×10^{-2}	16.91	6.19	-35.97
m-CF_3	2.59×10^{-2}	17.13	6.81	-34.47
m-CH_3	95.6	-----	-----	------
m-CH_3O	$\geq 4.76 \times 10^{5}$	-----	-----	------

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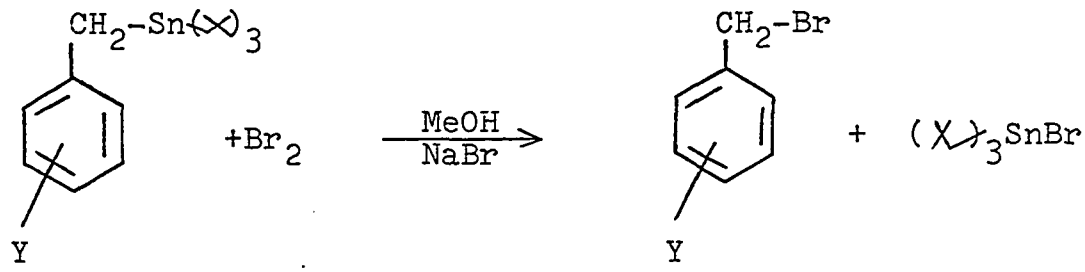
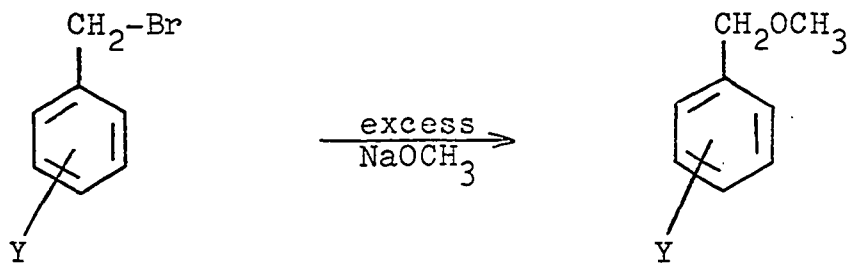
Product Study

Product studies were carried out for three of the derivatives, p-CH_3, m-CH_3, and H-. The reaction was found to be quantitative as written:



Since benzyl bromides are unstable to gas chromatography conditions, the product benzyl halide was converted to the corresponding benzyl methyl ether before analysis:



To insure that the benzyl methyl ether did not arise from the bromodemetallation reaction itselt, the reaction mixture was gas chromatographed before and after treatment with sodium methoxide. Although no benzyl methyl ether could be detected prior to the addition of methoxide, the same reaction mixture gave the ether in quantitative yield after its addition.

It was stated in the Introduction to Chapter III that the relative rate sequence leads us to postulate the following mechanism for at least some of the compounds studied:

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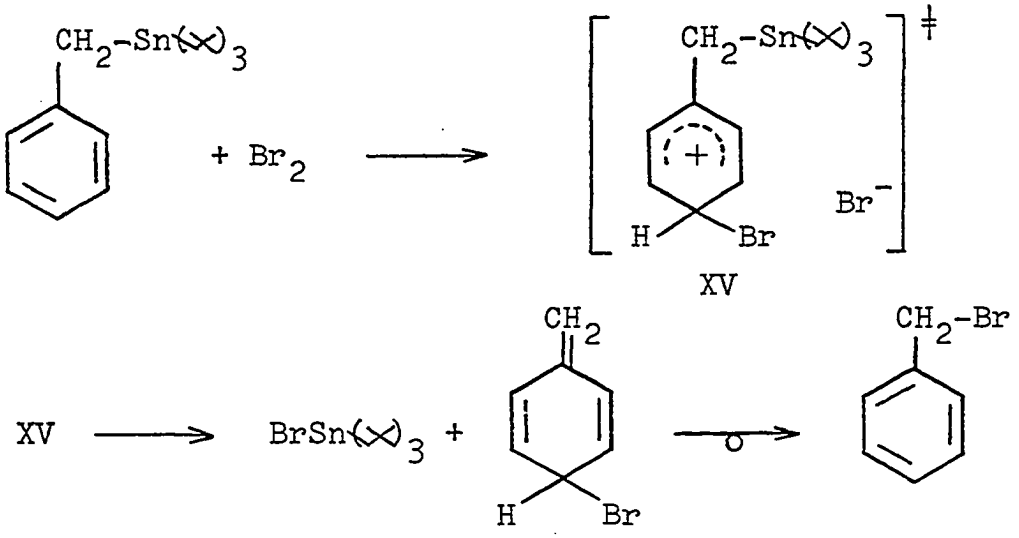

XV

The relative rates for the monosubstituted compounds are compiled along with their Hammett's σ parameters in Table 31.

The relative rate data, shown graphically in Figure 6, clearly do not correlate with Hammett's σ. However, the enormous acceleration provided by the m-methyl- and m-methoxy-substituents leads us to propose that the grouping, R_3SnCH_2-, acting as a powerful ortho-, para- director to electrophilic attack upon the aromatic system enables the reaction to proceed through the unusual mechanism presented earlier. Although a complete analysis of this postulate will be delayed until the Discussion section, the remaining experiments discussed here will serve to provide a more solid basis for this postulate.

Additional Results:

σ^+ of $R_3SnCH_2^-$

Following the method of Traylor[11], the TCNE charge-transfer band was measured for benzyltrineopentyltin and

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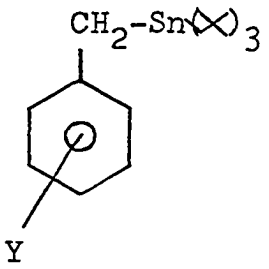
Table 31

Relative Rates of Bromodemetallation



Substituent (Y)	Relative Rate	log k_{rel}	σ^a
H	1.00	0.00	0.00
p-CH_3	0.368	-0.43	-0.170
p-t-Bu	0.452	-0.34	-0.197
p-CH_3O	0.178	-0.75	-0.268
p-F	4.08×10^{-2}	-1.39	+0.062
p-Cl	3.90×10^{-2}	-1.41	+0.226
p-Br	3.82×10^{-2}	-1.42	+0.232
m-CF_3	2.59×10^{-2}	-1.59	+0.415
m-CH_3	95.6	+1.98	-0.069
m-CH_3O^-	$\geq 4.76 \times 10^5$	+5.68	+0.115

[a] Taken from Ref. 3.

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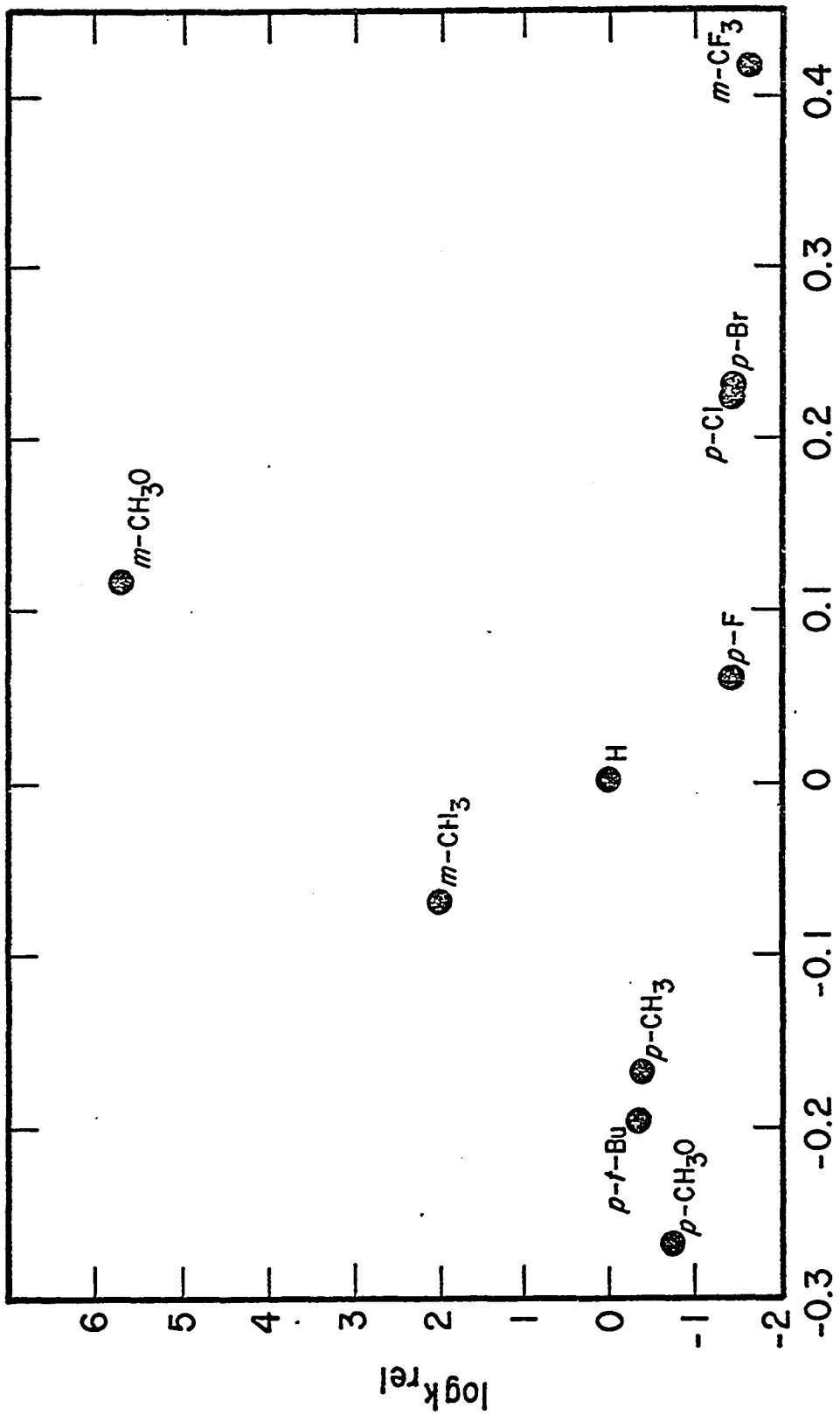

Figure 6. Bromodemetallation of Substituted Benzyltrineopentyltin Compounds. Hammett's σρ Treatment.

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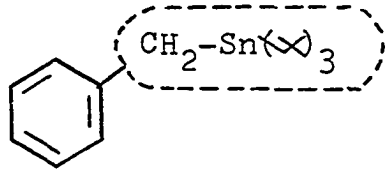
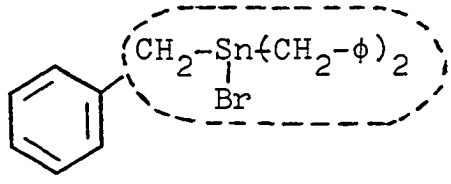
tribenzyltin bromide.

The longest wavelength band, λ_{max}, determined for each compound was:



λ_{max} = 582 ± 2 nm



λ_{max} = 513 ± 2 nm

Using Traylor's empirical correlation:

$$\nu_{TCNE} = (9300\ \sigma^{+} + 26{,}200) \pm 500\ cm^{-1}$$

The values of σ_p^+ were determined to be:

$(\phi)_3Sn-CH_2-$, $\sigma_p^+ = -0.97 \pm 0.01$

$(\phi)_2\ Br\ Sn-CH_2-$, $\sigma_p^+ = -0.72 \pm 0.01$

As one would predict, the replacement of an alkyl group on tin by an electron withdrawing halogen reduces the value of σ^+ by a substantial amount. $(\Delta\sigma_p^+) = -0.25$.) This large difference adds more support to the notion that the large σ^+ values are due to a hyperconjugative effect. If we consider σ_p (essentially the inductive or field effect) for CH_3CH_2- and Br:

$$\Delta\sigma_p = (\sigma_p^{Et} - \sigma_p^{Br}) = [(-0.151) - (+0.232)] = -0.383$$

This should be a reasonable approximation for the

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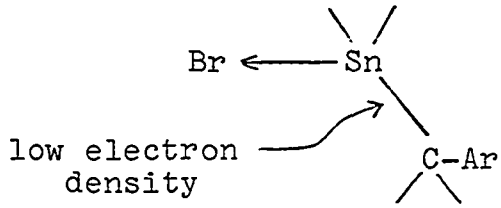
difference in inductive effect between a neopentyl- and bromo- group attached directly to an aromatic ring. For the groups under consideration, $[(\phi)_3 SnCH_2-$ and $(\phi-CH_2)_2\underset{Br}{Sn}-CH_2-]$,=the neopentyl- and bromo- groups are insulated from the aromatic nucleus by two atoms ($Y-Sn-CH_2-Ar$). Thus, we should observe an inductive difference of about

$$\frac{\Delta\sigma_p}{(2.8)^2} \quad \text{or} \quad \frac{-.383}{7.84} = -.049$$

if the fall-off were due to inductive effects. It is more reasonable that the large falloff is due to a large decrease in the electron density of the carbon-tin bond when a halogen is bound directly to tin:



Attempted Incorporation of ^{79}Br:

The bromodemetallation of p-bromobenzyltrineopentyltin was carried out under kinetic conditions using Br_2 and NaBr whose isotopic abundances were 80:20 ^{79}Br : ^{81}Br. Naturally occurring bromine is 50.54:49.46 ^{79}Br : ^{81}Br. The organotin compound was prepared with a natural abundance of bromine isotopes in the para position. The purpose of the experiment was to determine whether the bromine which brings about the bromodemetallation would be incorporated into the aromatic

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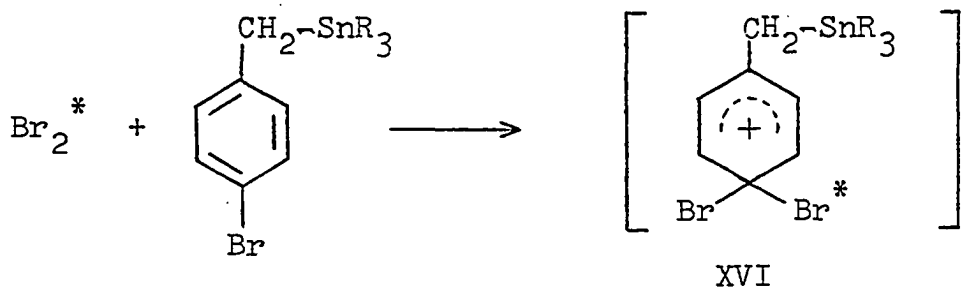
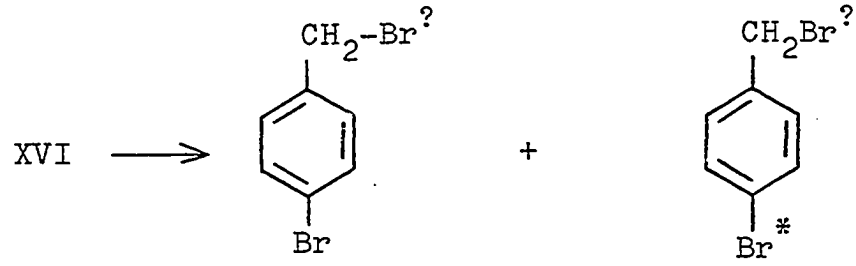
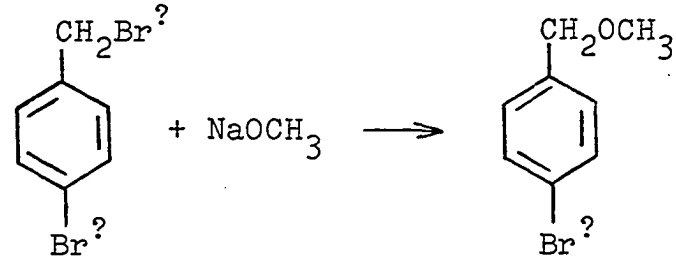
nucleus via the following mechanism:



XVI



The p-bromobenzylbromide was converted to p-bromobenzyl-methyl ether for isolation and mass spectral analysis:



Analysis of the parent ions (Mass Nos. 199 and 201) and the $C_7H_6Br^+$ ions (Mass Nos. 169 and 171) ions revealed that within the experimental uncertainty, none of the label was incorporated into the aromatic ring.

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Table 32

Relative Peak Heights for Product (p-bromobenzyl) methyl ether

169	171
14.9	12.75
15.1	13.8
14.8	13.75
14.9	13.9
14.7	13.9
14.88 (mean)	13.82 (mean)
14.88	13.78 (relative abundance after correction for ^{13}C)
$\%^{79}Br = 51.9\%$	

199	201
13.7	12.8
13.4	12.7
13.2	12.4
13.1	12.8
13.5	12.5
13.38 (mean)	12.64 (mean)
13.38	12.59 (relative abundance after correction for ^{13}C)
$\%\ ^{79}Br = 51.52$	

Using the identical procedure, naturally occurring Br_2 and NaBr was used to check the accuracy of the method. For the parent ions (Mass Nos. 199 and 201), the bromine-79 content was determined to be 51.93% and for the p-bromobenzyl

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ion (Mass Nos. 169 and 171), the ^{79}Br content was determined at 50.92%.

As a check on the method and on the labelled bromine used, tetraphenyltin was bromodemetallated with 81.3:18.7 ^{79}Br : ^{81}Br. Since the product, bromobenzene, must incorporate the bromine used, the results are unambiguous:

$$\phi_4Sn + Br_2^* \longrightarrow \phi Br^* + Br^*Sn\phi_3$$

The results indicate that the method is valid and the bromine-79 used has the isotopic content indicated by the manufacturer.

Table 33

Relative Peak Heights for Product Bromobenzene

P (156)	P+2 (158)
13.1	3.5
14.8	3.9
14.1	3.7
10.7	2.8
11.2	3.0
12.1	3.1
12.2	3.1
11.7	3.1
12.49 (mean)	3.28 (mean)
12.49	3.27 (relative abundance after correction for ^{13}C)
% ^{79}Br = 79.10	

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Bromination of Anisoles:

In order to evaluate the reactivity of the bromine - sodium bromide - methanol system towards aromatic nuclei, several derivatives of anisole were brominated under the conditions used for studying the bromodemetallation reactions (i.e. [substrate] = 10^{-1} - 10^{-2} M; [NaBr] = 0.366 M; $[Br_2]_t \cong 2 \times 10^{-3}$ M). Although a detailed kinetic study was not carried out, using pseudo-first order conditions (excess anisole), all rates were found to be first order in bromine. The rates of bromination of four anisoles were carried out at 25°. The results are summarized in Table 34. No product studies were carried out. (Note: k_2^{obs} is also the relative rate, k_{rel}, compared to the bromodemetallation of benzyltrineopentyltin.)

Table 34

Bromination of Substituted Anisoles,

$X\text{-}C_6H_4\text{-}OCH_3$ MeOH; [NaBr] = 0.366 M

μ = 0.366; $[Br_2] \cong 2 \times 10^{-3}$ M

Substituent (X)	$[X\text{-}C_6H_4OCH_3] \times 10^2$	k_2^{obs} ($\times 10^3$)
H-	7.07	23.40
p-OCH_3	10.26	1.93
p-CH_3	20.86	1.05
p-Cl	10.82	No Reaction*

* No detectable change in O.D. after 18 hrs.

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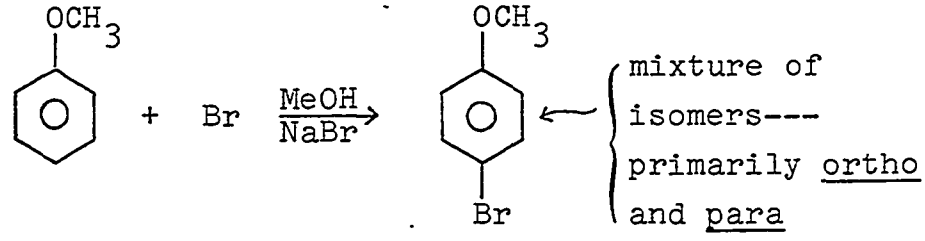
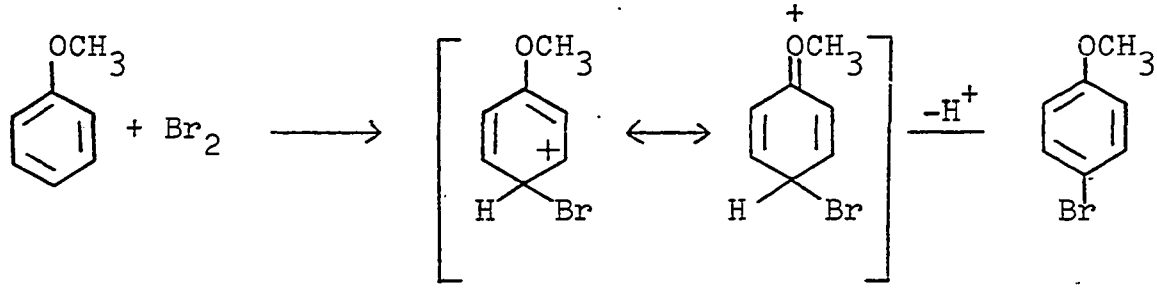
IV. Discussion

In an earlier section (see Historical), compelling evidence was presented to support the contention that the R_3SnCH_2- group is a powerful electron donor to aromatic systems. Using Traylor's empirical correlation is has been shown that this group has a σ^+ value of $\sigma_p^+ = -0.97$. While it is well known that benzene and toluene are unreactive to bromine under ordinary conditions, anisole has been shown to be readily brominated under the reaction conditions employed in the bromodemetallation study.



The strongly electron donating methoxy group ($\sigma^+ = -0.78$) is capable of permitting this reaction to occur. The ability of the methoxy group to stabilize the intermediate along the reaction coordinate is of primary importance:



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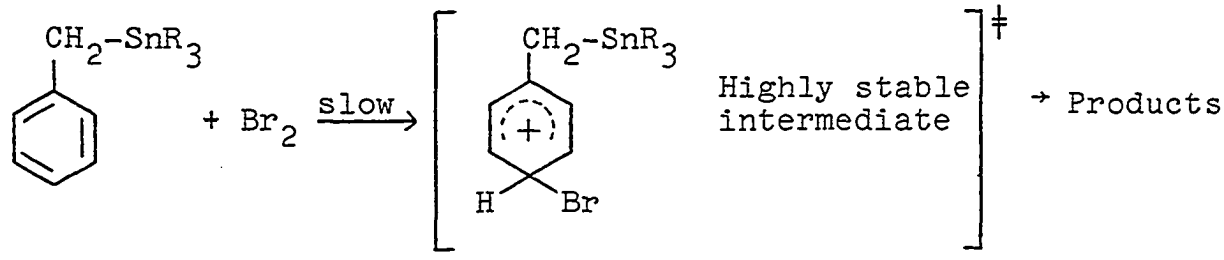
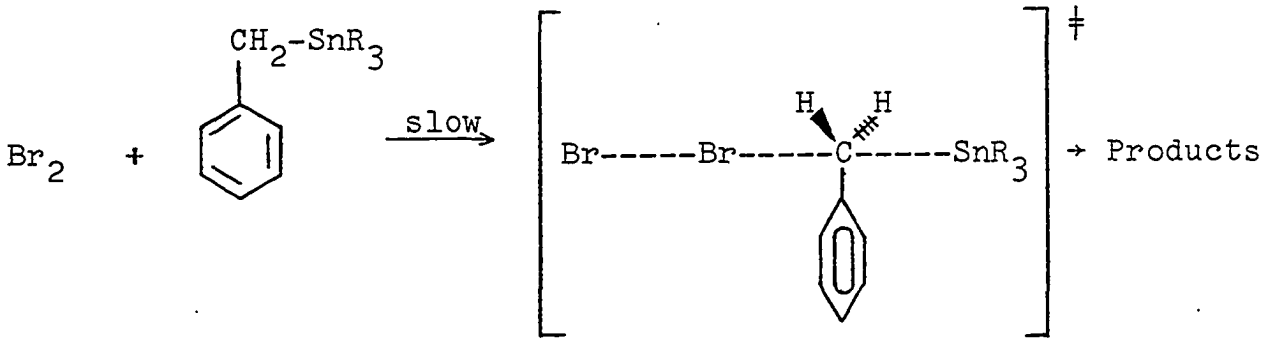
For reasons which have been discussed at length, it appears that the R_3SnCH_2- group, (hereafter referred to as the "tin-methylene" group), is capable of providing enormous stabilization to the same type of intermediates:



Nevertheless, it still remains to be shown that these intermediates are involved in the reaction under discussion, rather than the normal S_E2 pathway:



Several pieces of kinetic data strongly support this view. Let us first consider the relative rates of the <u>para</u>-substituted compounds:

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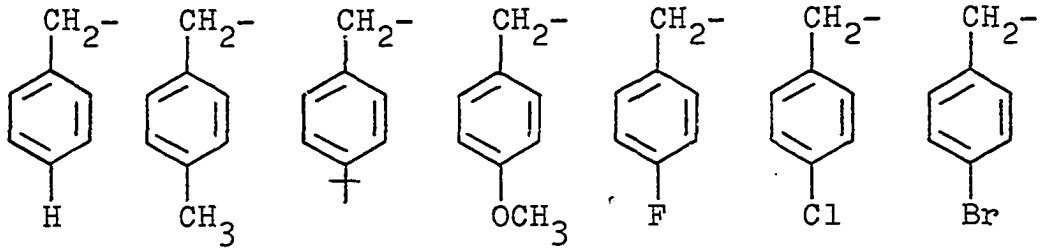

	H	CH_3		OCH_3	F	Cl	Br
k_{rel}	1.00	0.368	0.452	0.178	0.041	0.039	0.038
σ	0.00	-0.170	-0.197	-0.268	+0.062	+0.226	+0.232

These relative rates are shown in Figure 7. Several features are noteworthy: (1) p-H, the parent compound, is the most reactive compound, although the σ value of hydrogen is intermediate between the values of the other substituents; (2) the para-halo derivatives all have approximately the same rate, although the σ value of p-F is much closer to that of the parent compound, p-H, than it is to that of p-Cl or p-Br; (3) if the electron-donating substituents are considered alone, it would appear that the reaction rate is slowed considerably by electron donation. This would be extremely unusual for a reaction which involves the attack of an electron deficient species (i.e. the electrophile). Considering the data as a whole, this possibility may be rejected with a fair amount of certainty.

If one considers the possibility that at least some of the more reactive compounds proceed via a rate determining attack upon the ring, the data becomes more consistent with the current body of fact concerning substituent effects.

The parent compound has the potential of attack at three sites, two ortho and one para:

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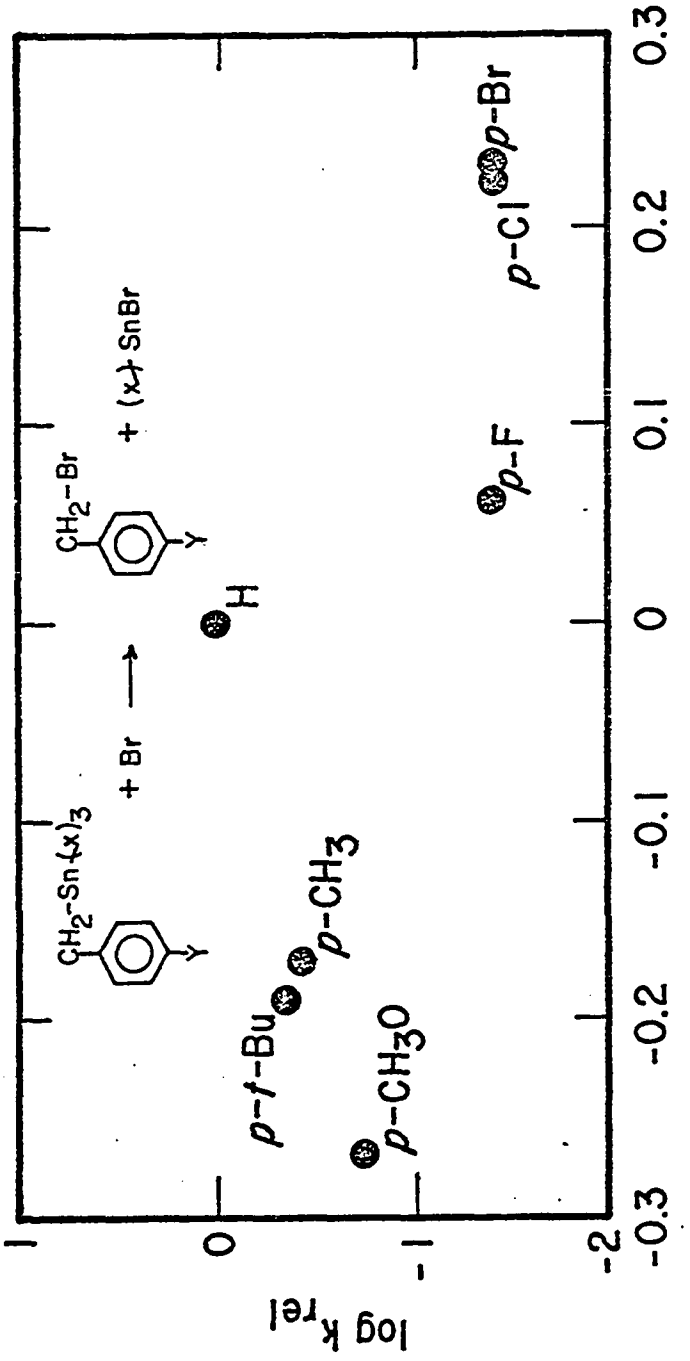

Figure 7. Bromodemetallation of Para-Substituted Derivatives. Hammett's σp Treatment.

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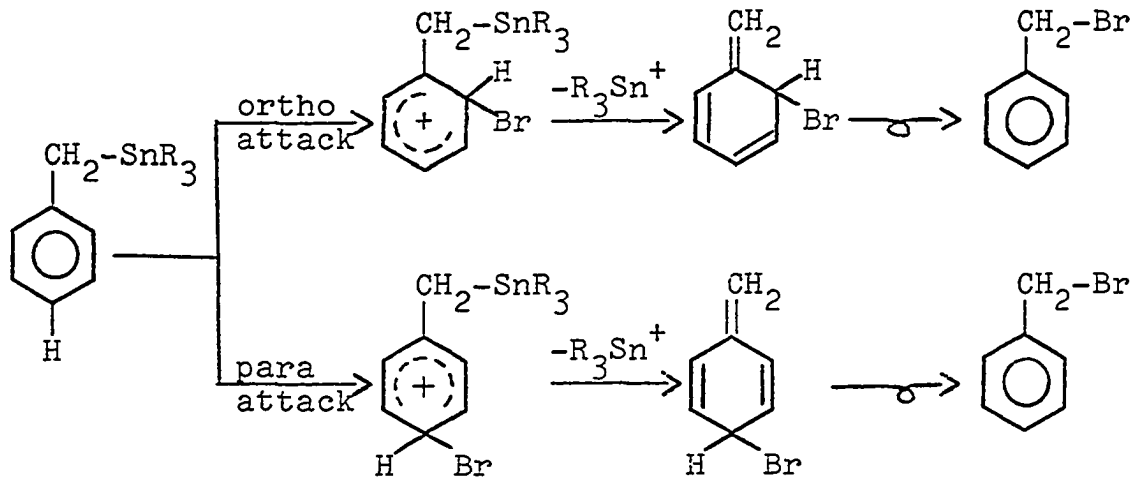
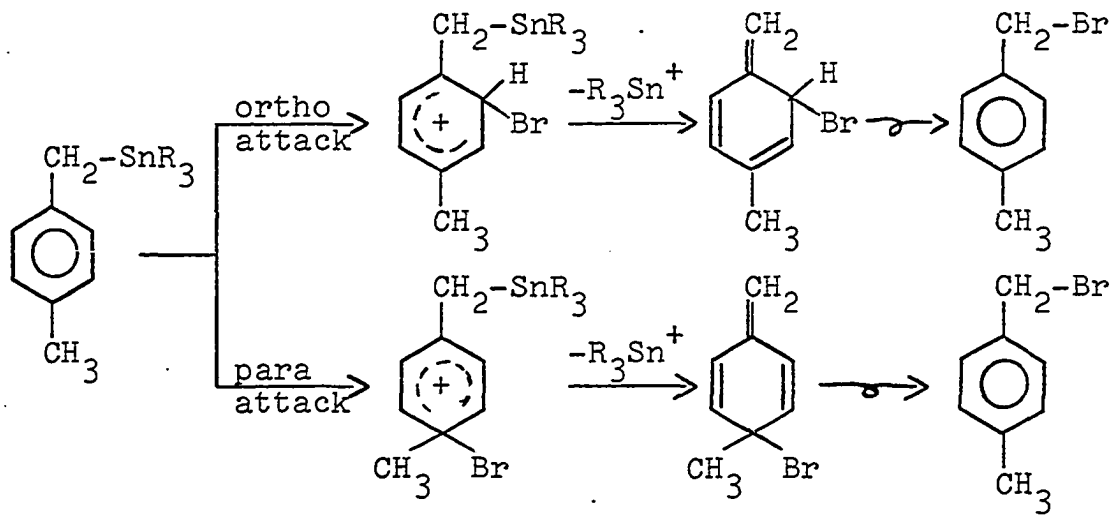


It must be pointed out that the para-substituted compounds may also have three positions available:



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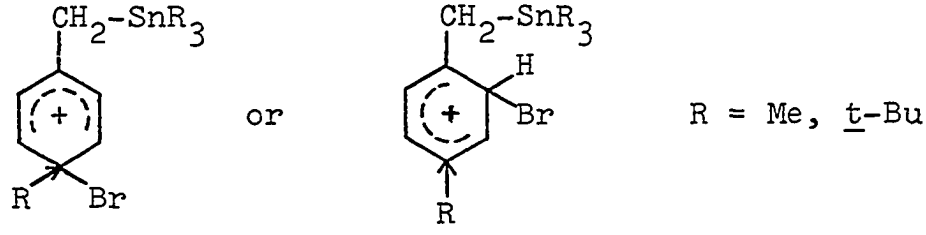
The question of whether or not attack does occur at a carbon bearing a substituent will be discussed at some length a little later. However, even if it does occur, it would not be too surprising if steric considerations rendered the reaction of the substituted compounds somewhat slower than the unsubstituted parent. This would help explain why the parent is the fastest compound in this group.

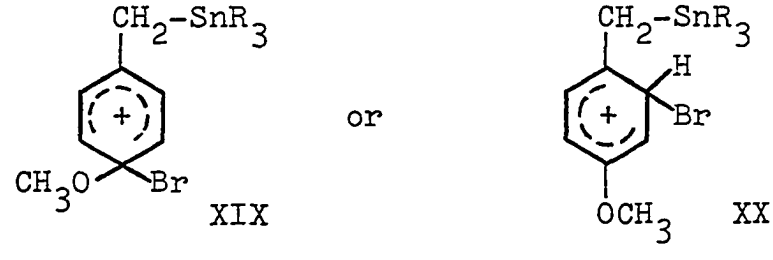
If we now consider the electron-donating compounds, the para-methyl- or para-t-butyl- derivatives can give two possible intermediates:



XVII XVIII

For both intermediates XVII and XVIII the alkyl substituent is electron-donating. For structure XVIII, we must consider the σ_m^+ value for methyl- or t-butyl. Both substituents have a small electron-donating effect for attack upon a position meta to them.

However, the para-methoxy group does not have this stabilizing influence:



XIX XX

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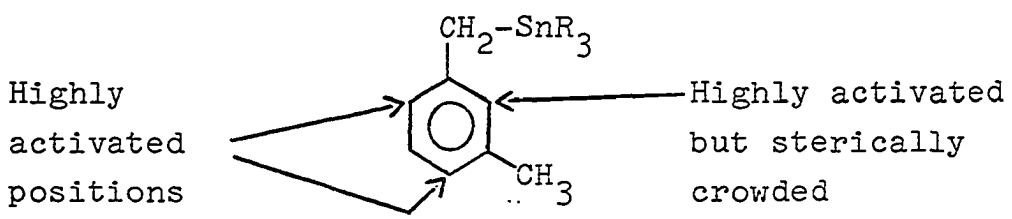
The σ_m^+ value for methoxy ($\sigma_m^+ = +0.047$) shows that it is slightly electron-withdrawing for attack meta to it.

Thus, ring attack could also explain the anomalous sequence among the electron-donating substituents.

For the para derivatives, the two substituents attached to the aromatic ring may work in opposition to each other (as in the p-methoxy case). Even if the substituents enhance each other (as in the methyl case) the enhancement will be small. However, two o-, p- directors situated meta to each other may enormously enhance the reactivity of the molecule since their effects will be working together.



If the original postulate of ring attack is correct, the m-methyl derivative should be more reactive than the parent, and the m-methoxy should be more reactive still. Voila! The m-methyl derivative is ca. 100 times as fast as the parent, and the m-methoxy compound is ca. 500,000 times the parent. Clearly, these striking rate differences can only be explained by a rate determining attack of the electrophile on the ring.

In addition, the striking difference between meta- and para- derivatives rules out any type of π-complex formation

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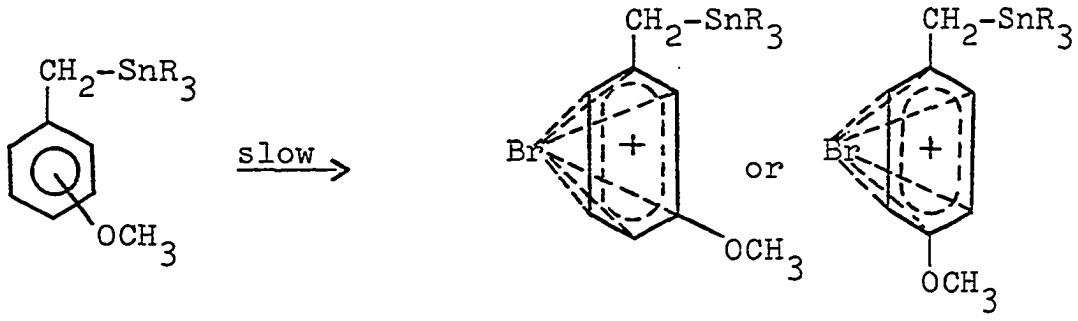
as the rate determining step: i.e.



XXI XXII

π-Complex formation should not be sensitive to the position of the substituents upon the ring. However, the m-methoxy derivative reacts more than 2 million times as fast as the p-methoxy derivative.

Clearly, for at least some of the compounds the reaction proceeds with a rate determining electrophilic attack upon the aromatic system.

It is possible to treat the para-substituted derivatives according to a linear free energy correlation. The value for substituents on a position on an aromatic system is merely the sum of the individual substituent parameters for that position:

$$\Sigma\sigma^{+}_{\text{position on the ring}} = \Sigma\sigma^{+}_{\text{substituents}}.$$

If one substituent is held constant, it is possible to analyze the reaction rates merely by looking at the other substituents. For the para-substituted benzyltin compounds, the tin-methylene group is held constant.

Let us assume that attack occurs ortho to this group:

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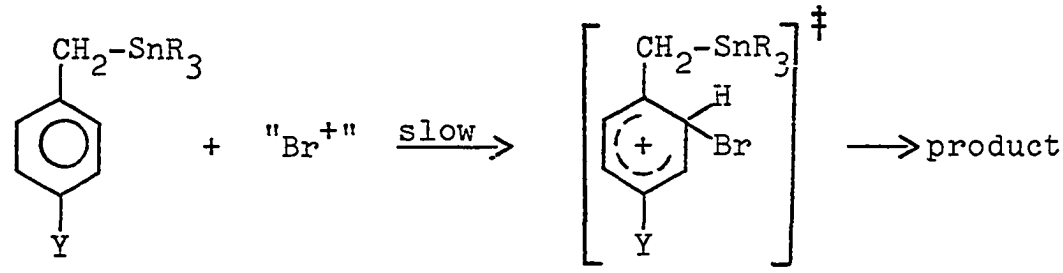
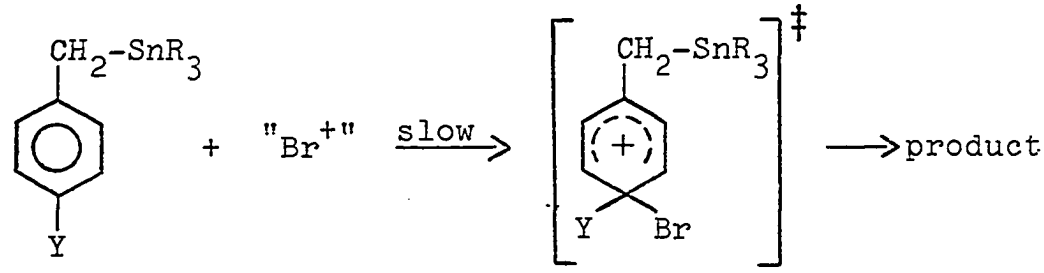


Since the other substituent, Y, is meta to the position of attack, the rates should be correlated with the σ_m^+ value of Y. Although the possibility of <u>para</u> attack further complicates this treatment:



for all of the derivatives studied, substituents which withdraw electrons from positions <u>meta</u> to them also are electron-withdrawing from the carbon to which they are bound (i.e. F, Cl, Br, MeO). Similarly, electron donating groups (i.e. Me, <u>t</u>-Bu), donate electrons to both of these positions. Thus, <u>para</u> attack, if it occurs, may not complicate the treatment since the effect at both positions may parallel each other.

Although it appears reasonable that <u>meta</u> attack could occur, this intermediate cannot lead to a benzyl bromide

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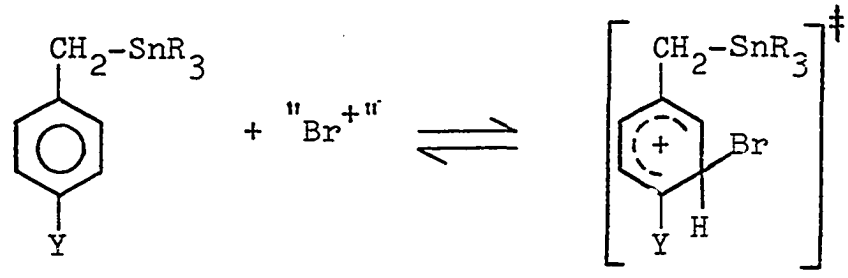
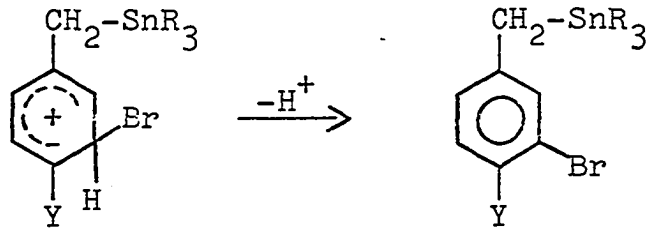


product. (Only ortho- and para- attack can lead to the correct product.) This intermediate can either reverse (in which case we never observe it), or it can lose a proton (but it cannot lose R_3Sn):



However, product studies indicate that the reaction gives a quantitative yield of benzyl bromide. (No m-bromobenzyltrineopentyltin is formed.) Thus one may assume the partial rate factor for meta- attack to be zero.

The relative rates and their corresponding σ_m^+ parameter are summarized in Table 35. The data, shown in Figure 8, appear to give a satisfactory linear free energy correlation. If one accepts this correlation, it follows that all of the derivatives studied are cleaved via the ring attack mechanism. However, several experimental facts cast doubt upon this interpretation.

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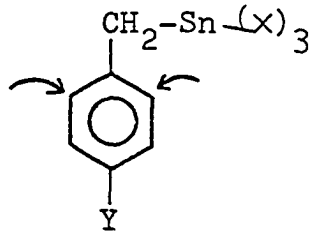
Table 35

Free Energy Correlation for para-Substituted Benzyltin Compounds



Correlation between σ_m^+ and k_{rel}

Y	log k_{rel}	σ_m^+ [a]
p-CH_3	-0.43	-0.069
p-t-Bu	-0.34	-0.058
p-CH_3O	-0.75	+0.047
p-F	-1.39	+0.337
p-Cl	-1.41	+0.373
p-Br	-1.42	+0.391

[a]Taken from reference

If the linear free energy relationship is valid, the reaction must proceed with an abnormally low charge build up since $\rho = -2.40$. Some typical reaction parameters for electrophilic substitution are shown in Table 36.

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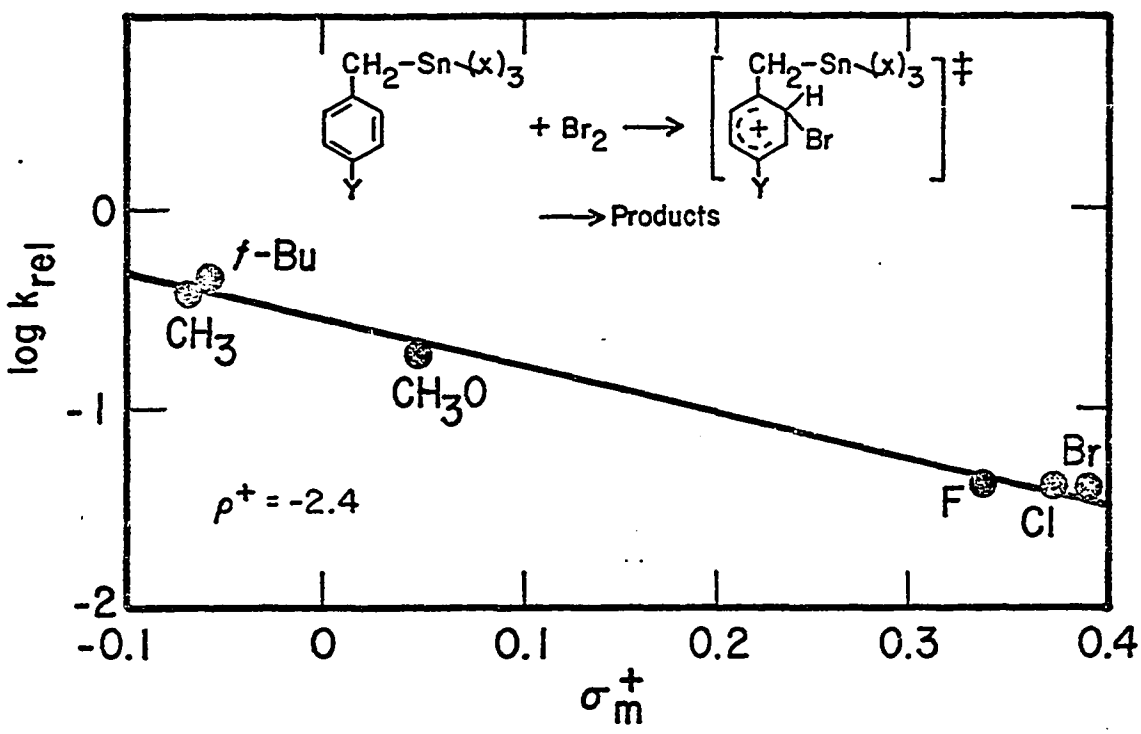

Figure 8. Bromodemetallation of Para-Substituted Derivatives.
$\sigma_m^+\rho^+$ Treatment.

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Table 36[a]

Electrophilic Aromatic Substitution Reactions

Reaction, conditions	ρ
Bromination, Br_2, HOAC-H_2O, 25°	-12.1
Bromination, Br_2, HOAC-$MeNO_2$, 30°	- 8.7
Chlorination, Cl_2, HOAC, 25°	-10.0
Acetylation, MeCOCl, $AlCl_3$, $C_2H_4Cl_2$, 25°	- 9.1
Bromination, HOBr, $HClO_4$, 50% dioxane, 25°	- 6.2
Bromo-Desilylation, $ArSiMe_3$, Br_2, HOAC, 25°	- 6.2
Proto-Desilylation, $ArSiMe_3$, $HClO_4$, MeOH-H_2O, 51°	- 4.6
Ethylation, EtBr, $GaBr_3$, ArH, 25°	- 2.4

[a]Reference 19.

The possibility was considered that the particular electrophile - solvent system might lead to low ρ values for some reason. (Actually, in a highly hydrogen-bonding solvent such as methanol, one would predict the opposite effect.) Thus, several anisole derivatives were brominated to evaluate the plausibility of this postulate. (See Results, Table 34.) Although these results can only be considered preliminary (in the absence of a full kinetic investigation and product study), a comparison of the relative rates of the following compounds casts considerable doubt upon the suggestion:

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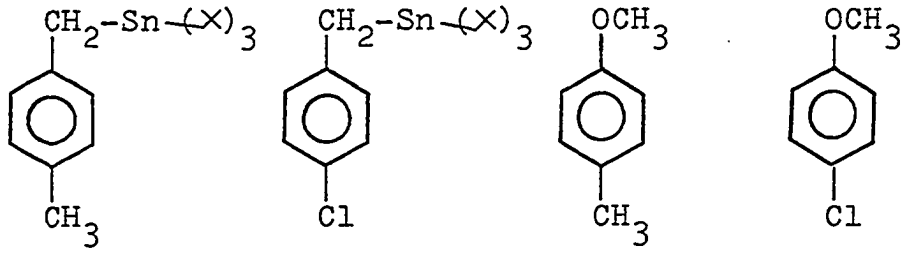

k_{rel} (x 10^3):	368	39.0	1.05	N.R. (after 18 hrs)

For the tin compounds, the chloro derivative reacts about 1/9 th as fast as the methyl derivative. If one were to observe the same ratio in the anisoles, the bromination of para-chloroanisole would have been 50% complete after 18 hrs under the reaction conditions employed. However, there was no evidence of any reaction at all after 18 hrs. Thus, ρ for the anisoles must be reasonably high as one would expect, even in the Br_2:NaBr:MeOH system.

The possibility was also considered that perhaps the linear free energy correlation breaks down when extremes of electron donation are present. For example, it would seem reasonable that if an extremely strong electron-donor is present, the transition state might occur early along the reaction coordinate, before a substantial charge has build up.

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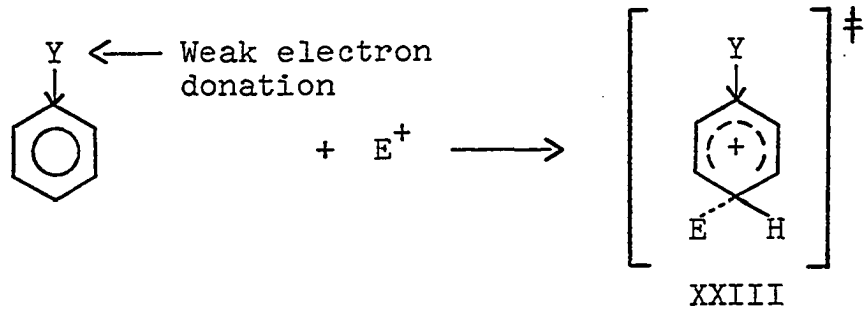
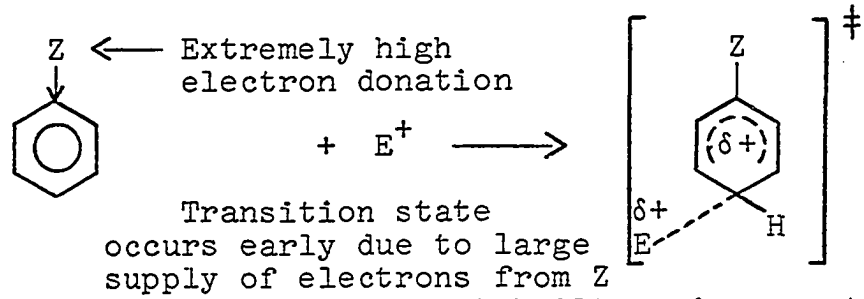


XXIII

Transition state occurs very close to the intermediate



XIV

Transition state occurs early due to large supply of electrons from Z -full charge not yet built up in aromatic ring.

This approach would suggest that if one considered a wide enough range of substituents, a $\sigma^+\rho^+$ plot might look like Figure 9.

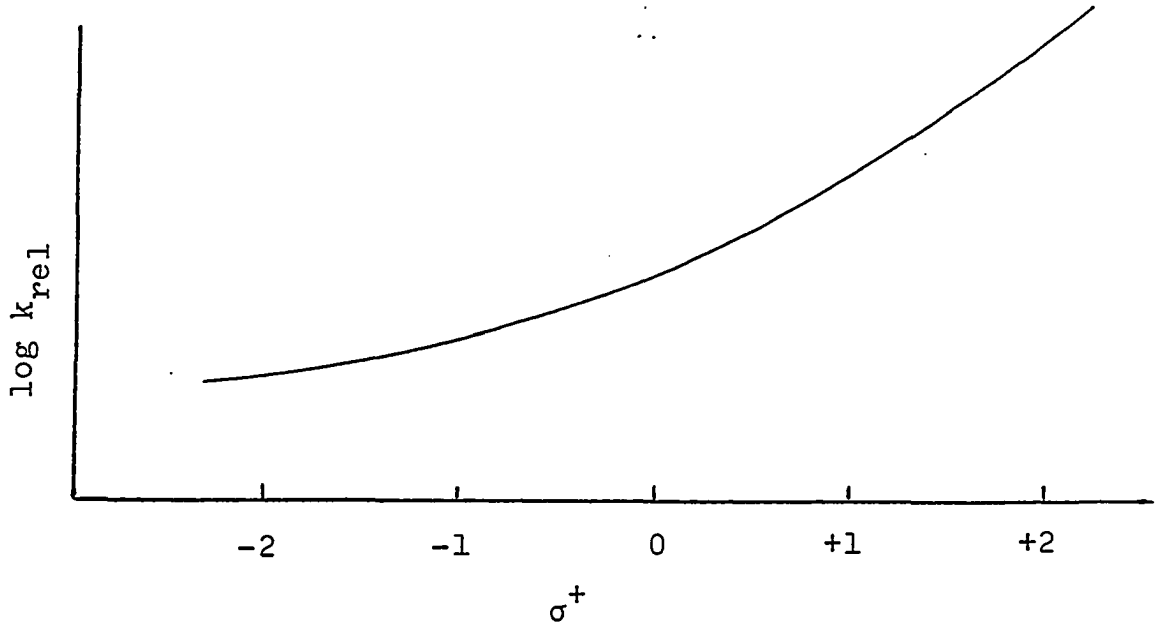


Figure 9. Hypothetical Free Energy Diagram Over a Large Range of σ^+

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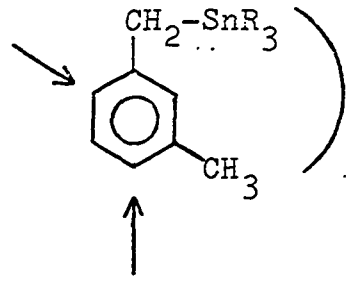
Normally, one deals with substituent changes between $(\sigma_p^+)_{OCH_3} = -0.764$ and $(\sigma_p^+)_{Cl} = +0.373$. Suppose non-linearity develops when the range is extended. Since the substituent parameters in Figure 8 are really -0.4 to -1.2 (i.e. $\sigma_p^+ = (-0.97) + (-0.306) = -1.28$ for p-methylbenzyltrineopentyltin), perhaps the slope is reduced. However, this possibility can also be dismissed if the meta derivatives, m-CH_3- and m-CH_3O- are considered.

$$\log k_{rel} = \log \frac{5.14 \times 10^4}{10.33} = \Delta\sigma^+\rho^+ = [(-0.764) - (-0.306)]\rho^+$$

$$\rho^+ = -8.1$$

(Values of σ_p^+ are used for σ_p^+ and σ_o^+ for CH_3- and CH_3O:



These two derivatives determine a $\rho^+ = -8.1$. In addition $\sigma_p^+ = -1.73$ for m-methoxybenzyltrineopentyltin, the largest σ^+ of any compound studied. Clearly, the ring attack model does not account for all of the facts.

A possible explanation which might account for the small ρ would involve a cyclic transition state for some of the compounds:

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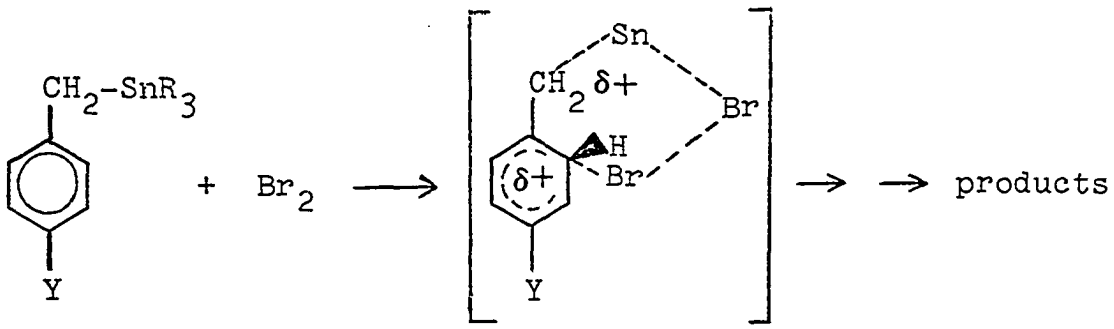
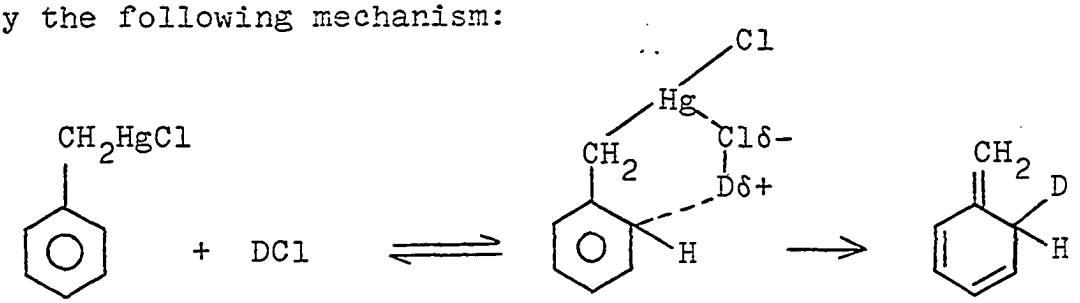


XXV

where the partial positive charge build up in the aromatic ring is reduced substantially by the concerted nature of the transition state.

A similar mechanism was proposed by Reutov and coworkers[26] to account for some of the products which arise during deuterodemetallation of benzylmercuric chloride. Reutov accounted for the extensive deuterium incorporation in the ortho position of the toluene formed during the reaction by the following mechanism:



XXVI

The isomerization of XXVI to toluene may be acid catalyzed, accounting for the large amount of toluene-d_2 formed:

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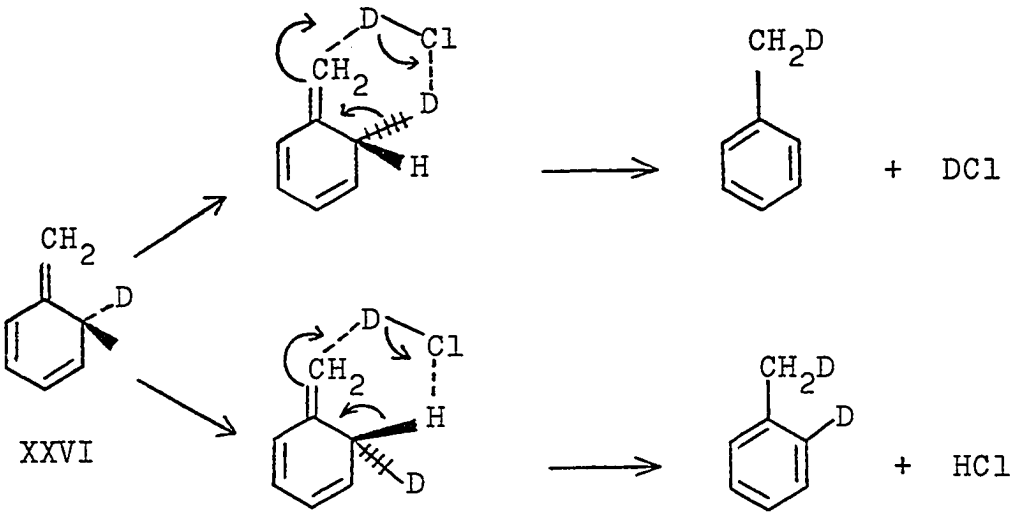

Although prior exchange of the benzylmercuric chloride accounts for some of the deuterium incorporation, the extent of deuterium incorporation in the product was always found to exceed that of the unreacted starting material. Therefore, prior exchange alone cannot account for all of the deuterium found in the aromatic nucleus.

Indeed, the cyclic transition state, XXV, gains some tentative support by considering the activation parameters for the bromodemetallation reaction (Table 37). If one considers the entropy contribution, the halo-derivatives exhibit a markedly higher (negative) entropy of activation than do the other derivatives. This might suggest the more constrained cyclic transition state for these derivatives.

While this possibility is certainly not ruled out, perhaps a more plausible explanation for the rate sequence is the following. The normal S_E2 pathway and the abnormal

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Table 37

Activation Parameters for the Bromodemetallation of Substituted-Benzyltrineopentyltin Compounds

$X-C_6H_4-CH_2-SnR_3$ R = neopentyl

Substituent X	k_{rel}	$\Delta H^{\ddagger}$ $\frac{k\,cal}{mole}$	$\Delta S^{\ddagger}$(e.u.)	$\Delta G^{\ddagger}$ $\frac{k\,cal}{mole}$
H	1.00	10.51	-14.97	14.97
p-CH_3	0.368	9.87	-19.12	15.57
p-t-Bu	0.452	8.73	-22.56	15.45
p-CH_3O	0.178	8.90	-23.85	16.01
2,4,6-Me_3	1.38	8.83	-19.95	14.78
p-F	0.041	6.84	-36.50	16.93
p-Cl	0.039	5.89	-36.94	16.90
p-Br	0.038	6.19	-35.97	16.91
m-CF_3	0.026	6.81	-34.47	17.13

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ring attack mechanism are in competition. For the more reactive derivatives, ring-attack is the mode, but as the ring is deactivated by electron-withdrawing substituents, the normal S_E2 pathway takes over. It was pointed out earlier that the normal S_E2 sequence for alkyltrineopentyltin compounds parallels that of S_N2 reactions, although the sequence is compressed by a factor of:

$$\frac{\log k_{rel}^{S_E2}}{\log k_{rel}^{S_N2}} = 0.486$$

Streitwieser[21] gives an average $k_{rel} = 4$ for S_N2 displacement reactions on benzyl compared to methyl. This would correspond to a $k_{rel} = 1.96$ for a normal S_E2 displacement reaction. From the known relative rate of bromodemetallation of methyltrineopentyltin ($k_2^{obs} = 6.24 \times 10^{-2}$ at [NaBr] = 0.366), one estimates a relative rate of $0.123 = k_2^{obs}$ for a normal S_E2 cleavage of benzyltrineopentyltin. If this estimate is approximately correct, then it would appear reasonable that the parent compound, m-MeO, m-Me, p-t-Bu, p-Me, and 2,4,6-Me_3- derivatives are bromodemetallated primarily through the ring-attack pathway. The p-methoxy derivative ($k_2^{obs} = 0.178$) may be bromodemetallated by a mixed mechanism, and the p-F, p-Cl, p-Br, and m-CF_3 derivatives undergo a normal S_E2 bromodemetallation. Once again, the striking differences in activation parameters for the halo-derivatives lends considerable support to this postulate.

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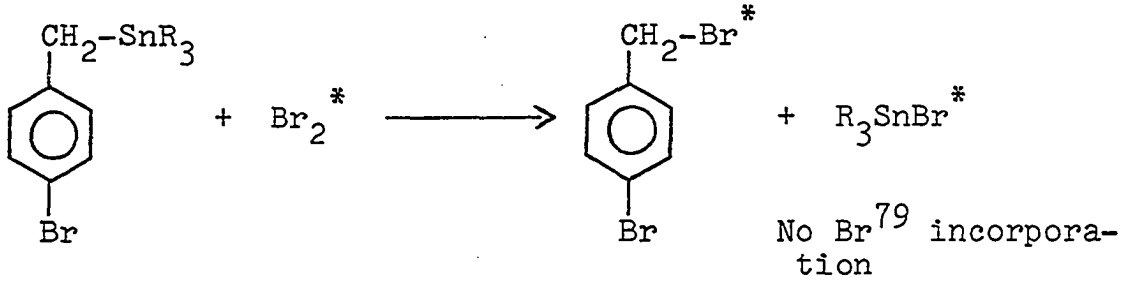
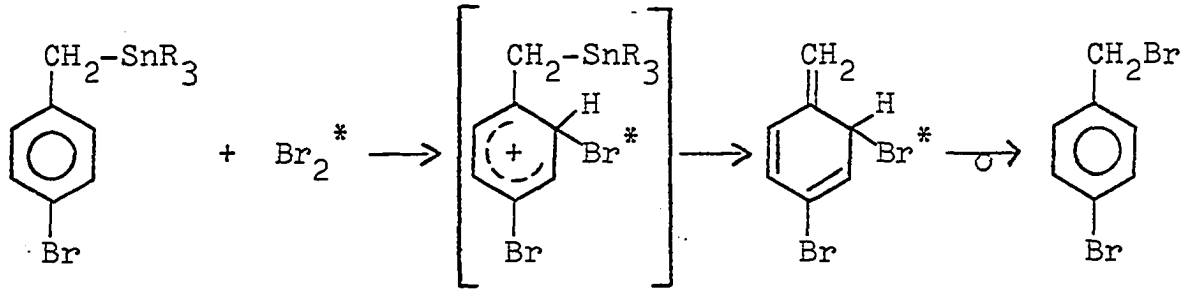
The failure of p-bromobenzyltrineopentyltin to incorporate bromine-79 into the ring lends some support to this interpretation:



However, this result in no way requires that a normal S_E2 pathway occurs. Attack at the ortho position would not result in ^{79}Br incorporation:



Exclusive ortho attack would not be unreasonable in this case, since the halogen already attached to the ring would render the para-position somewhat electron-deficient. Nevertheless, the failure of bromine-79 to be incorporated is consistent with the suggested change in mechanism.

It is difficult to assess the relative contribution of each pathway to the bromodemetallation of the methoxy derivative. The activation parameters for this compound

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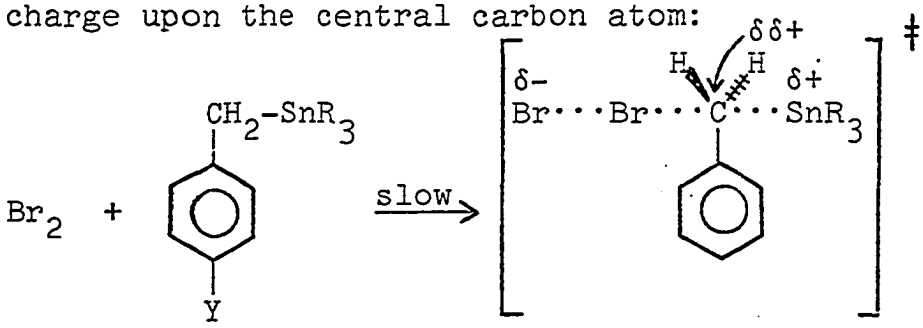
are not significantly different from the "ring-attacked" group. In the absence of additional data, it appears that the change in mechanism takes place when the ring is slightly more deactivated than is this derivative to aromatic attack.

If one accepts this postulate, then some tentative conclusions may be drawn concerning the transition state of the bromodemetallation of tetraalkyltin compounds. If in fact the p-F, p-Cl, p-Br, and m-CF_3 derivatives are bromodemetallated via an ordinary S_E2 pathway, a tentative assignment of ρ may be made. (See Figure 10) From this data, it would appear that ρ is small (ρ ≃ -0.6), and the reaction proceeds with a very small amount of positive charge upon the central carbon atom:



If this is correct, one must conclude that the transition state occurs early along the reaction coordinate, with bond-making proceeding bond-breaking. This is in accordance with the notion that the electrophile first comes into contact with the rear lobe of the sp^3 orbital undergoing inversion, and in the early stages of the reaction coordinate stabilizes itself by removing the electron-density from this

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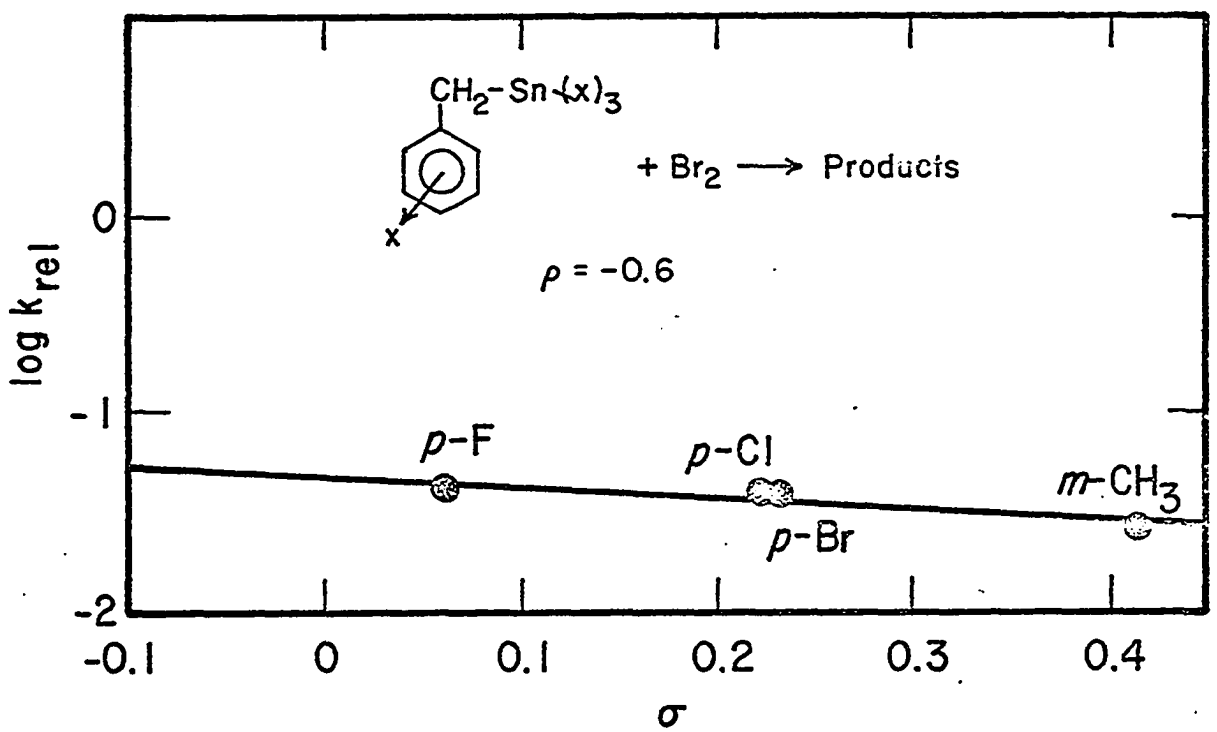

Figure 10. Bromodemetallation of Halo-Substituted Derivatives.
Hammett's σρ Treatment.

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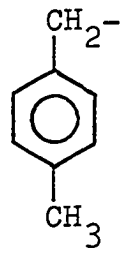
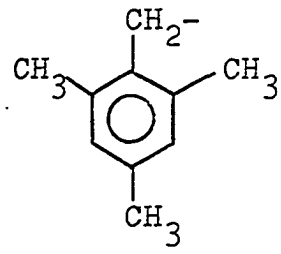
orbital prior to the breaking of carbon-tin bond. These conclusions must be considered tentative of course due to the uncertain nature of the data used.

At this point, only the bromodemetallation of the polymethylated compound remains to be discussed:





k_{rel} 0.368 1.38

The 2,4,6-trimethyl- derivative was prepared in the hope that by blocking the reaction positions, the certainty of ring-attack in the other derivatives might be demonstrated. However, rather than clear the air, this compound seems to have muddied the waters. Nevertheless, the overwhelming bulk of the data indicates that ring attack must be occurring in the more reactive compounds. A careful consideration of the data compels one to conclude that this reaction must take place with attack occurring at the positions bearing a methyl substituents. Compound I must be slower than the parent compound due to the reduced reactivity caused by the steric effect of a methyl group at the para-position. However, the rate difference is modest, because the methyl group (σ_m^+ = -0.069) slightly activates the positions meta to it. Similarly, the 2,4,6-trimethyl- derivative (III) is faster

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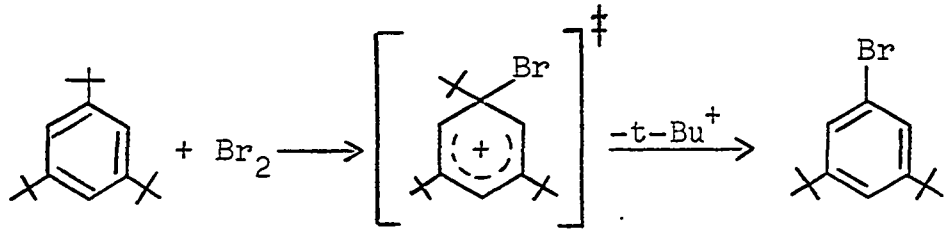
than (I), as all of the methyl groups act in conjunction to activate each position somewhat. Thus, the steric and electronic effects offset each other.

The concept of electrophilic attack by bromine at a position bearing a methyl group is rendered more plausible when one considers the fact that the catalytic bromination of 1,3,5-tri-t-butylbenzene leads to the isolation of only one product:[20]



71%

At present it is impossible to assess the relative amount of attack in the para position of compound I and the analogous t-butylbenzyltrineopentyltin. Bartlett's result seems to indicate that there is not a large steric inhibition to bromination of an aromatic ring. Thus, it appears plausible that both derivatives have a substantial partial rate for attack at the para position.

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V. Experimental

Materials:

Sodium bromide, Malinckrodt analytical reagent grade, was dried at 110° for two days prior to use.

Anhydrous methanol was prepared by either the method of Vogel or by refluxing for 24 hrs over CaH_2 prior to fractionation.

Bromine, Malinckrodt analytical reagent grade was washed with concentrated sulfuric acid and distilled from potassium bromide. Only the center cut was used (bp 58, lit. bp 58.8[22]). Anhydrous stannic chloride (Baker analytical reagent) was used directly.

Trineopentyltin chloride was prepared by the following general procedure:

> A solution of 600 ml of 3.3 N (1.98 moles) neopentylmagnesium chloride was prepared by treating 212 g (2.0 moles) of neopentyl chloride in ether with excess magnesium turnings (60 g, 2.5 moles). (1,2-dibromomethane is necessary to initiate this sluggish Grignard reaction.) The Grignard reagent was filtered from the remaining magnesium turnings into a 2-liter, 3-necked round-bottomed flask, equipped with mechanical stirrer, double-jacketed reflux condenser, and addition funnel. The solution was cooled with an ice bath and maintained at about 10° during the subsequent reaction.

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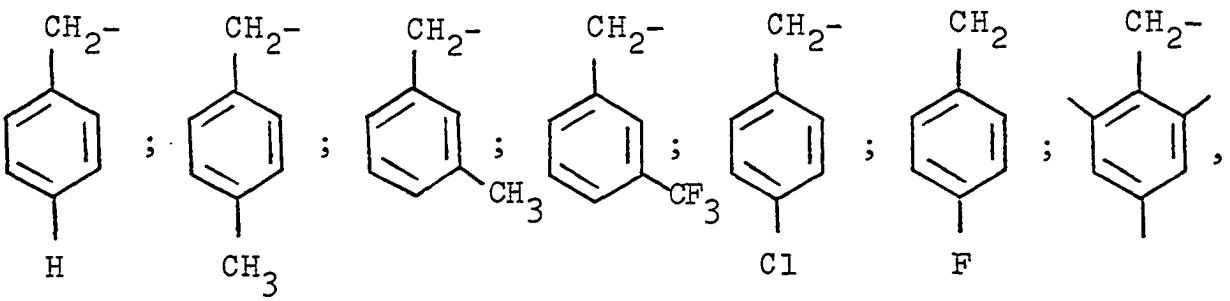
A solution of 129 g (0.5 moles) of stannic chloride in 250 ml of benzene was added slowly (45-60 min) to the Grignard reagent. The reaction mixture was allowed to stir for an additional 15 minutes before quenching with excess aqueous ammonium chloride. The organic layer was separated and the aqueous layer extracted twice with 150 ml portions of ethyl ether. The combined organic layers were dried with anhydrous magnesium sulfate, filtered, and the solvent removed in vacuo. The crude wet solid (162 g) was recrystallized twice from 95% ethanol to yield white needles (107 g, 62% yield), mp 110.5 - 111.0° (lit. 113.5 - 114.5°[23]).

General Method for Preparation of $R'Sn'R_3$ Compounds (R=neopentyl, R'=benzyl or substituted benzyl).

All compounds were prepared from the reaction of the appropriate benzylmagnesium chloride with trineopentyltin chloride. For the compounds, R'=



the Grignard reagents were prepared from the commercially available benzyl chlorides. For the compounds, R'=

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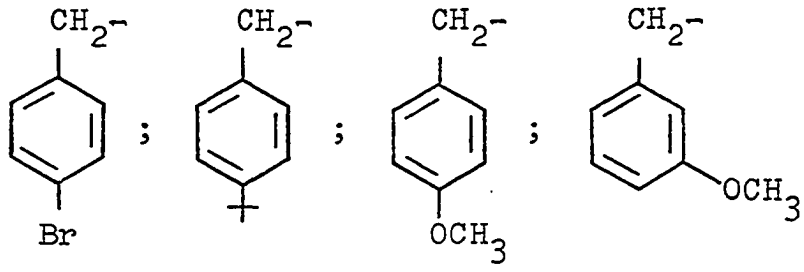

the chlorides and Grignard reagents were prepared by methods described below.) A typical procedure follows: 80 ml of 0.8 N (0.064 moles) benzylmagnesium chloride was added to 11.0g(0.03 moles) trineopentyltin chloride in 50 ml of ethyl ether. (The reaction was carried out in a vessel fitted with a reflux condenser to contain the exothermic reaction.) The reaction mixture was quenched with excess aqueous ammonium chloride. The organic layer was separated, and the aqueous layer was extracted twice with 50 ml portions of ether. The combined organic layers were dried over magnesium sulfate, filtered, and the solvent evaporated in vacuo. In the case of all compounds except R' = 2,4,6-Me_3-C_6H_2-CH_2-, the products were liquids. The solid was recrystallized twice from 95% ethanol. The liquids were all viscous and were purified only with difficulty. All products were contaminated with the corresponding bibenzyl which arises from coupling during Grignard formation. The products were purified on a one foot gold spinning-band column. Upon fractionation the bibenzyl sublimed under vacuum and collected in the condenser of the spinning band. The oil bath was lowered, the distillation flask removed, and the column cleaned. This procedure was repeated several times until

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no solid collected in the condenser. Approximately 20 drops forerun was taken, and the remainder of the liquid which distilled was collected. This material was rather viscous, and boiling points were difficult to obtain. For the parent compound, $C_6H_5CH_2-Sn(C_5H_{11})_3$, 11.15 g (87.7% yield), bp 99.5/0.07 mm was collected. This material gave only one spot with TLC elution on silica gel with hexane. Spectral properties and product studies (quantitative and qualitative) of its bromodemetallation reaction are all consistent with the desired structure and inconsistent with disporportionation products such as a 50:50 mixture of $(\phi-CH_2)_2SnR_2 + R_4Sn$, (R = neopentyl).

Preparation of p-Bromobenzylmagnesium chloride:

The reduction of 145 g methyl p-bromobenzoate (0.67 moles) was carried out by addition of the ester in 1000 ml ether over a one hour period to a two-fold excess of lithium aluminum hydride (25.3 g, 0.67 moles) in 500 ml ether. The reaction mixture was refluxed overnight and worked up by the careful addition of a saturated solution of sodium sulfate. The sodium sulfate solution serves to destroy the excess of $LiAlH_4$ and complexes with the resultant aluminum salts. The ethereal solution was decanted from the salts, dried with additional sodium sulfate and the solvent evaporated in vacuo. The residue was recrystallized from methyl alcohol to yield 67 g (0.36 moles, 53.7% yield) of white needles of p-bromobenzyl alcohol, mp 77.5-78.5° (lit. mp 76°[25]). p-Bromobenzyl alcohol (27.9 g, 0.15 moles)

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was added to 88.5 g (0.75 moles) thionyl chloride. The reaction mixture was refluxed for 5 hr and the complete removal of excess thionyl chloride was achieved by addition of 10 ml of toluene prior to distillation of the thionyl chloride. After the temperature of the liquid being distilled had risen to 110° (i.e. the bp of toluene) the system was evacuated, and the p-bromobenzyl chloride (bp 98-102/0.5 mm) was collected using a bulb-to-bulb distillation. The Grignard reagent was prepared as usual, taking care to use only one equivalent of magnesium in order to prevent formation of di-Grignard reagent (the benzylic chloride being more reactive than the aryl bromide).

p-t-Butylbenzylmagnesium chloride was prepared from methyl p-t-butylbenzoate following the same procedure as that outlined for p-bromobenzylmagnesium chloride.

m-Methoxybenzylmagnesium chloride was prepared using the same procedure as above, starting from the commercially available m-methoxybenzyl alcohol.

p-Methoxybenzylmagnesium chloride was prepared as follows:

> A solution containing 69.0 g (0.5 moles) p-methoxybenzyl alcohol was prepared in 500 ml dry benzene. Dry HCl gas was bubbled through the solution for 1.5 hr. (Use of other solvents such as ethyl ether can result in extensive polymerization.) A water layer separated. The organic layer was quickly washed, once with water and three times with 100 ml portions of 5% sodium bicarbonate,

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dried over magnesium sulfate, filtered, and the solvent evaporated *in vacuo*. The residue was bulb-to-bulb distilled (bp 93-94°/0.7 mm) giving a colorless liquid, *p*-methoxybenzyl chloride (56.7 g, 72.7% yield).

Using a high dilution cyclic Grignard maker (described by Campaigne and Yokley[24]), 0.044 moles (12.2%) of *p*-methoxybenzylmagnesium chloride was prepared.

Table 38

Preparation of Substituted Benzyltrineopentyltin Compounds

		Calculated		Found	
Y	Formula	%C	%H	%C	%H
H-	$C_{22}H_{38}Sn$	62.43	9.52	62.80	9.24
p-CH_3-	$C_{23}H_{42}Sn$	63.18	9.68	62.91	9.71
p-CH_3O	$C_{23}H_{42}SnO$	60.95	9.34	61.04	9.42
p-F	$C_{22}H_{37}FSn$	59.89	8.91	60.12	8.97
p-Cl	$C_{22}H_{37}ClSn$	57.73	8.59	57.83	8.34
p-Br	$C_{22}H_{37}BrSn$	52.62	7.82	52.71	7.52
m-CH_3-	$C_{23}H_{42}Sn$	63.18	9.68	63.19	9.62
m-CH_3O	$C_{23}H_{42}SnO$	69.95	9.34	60.67	9.15
m-CF_3	$C_{23}H_{39}F_3Sn$	56.24	8.00	56.13	7.97
2,4,6-$(CH_3)_3$	$C_{25}H_{46}Sn$	64.53	9.96	64.35	9.86
p-$(CH_3)_3C$-	$C_{26}H_{48}Sn$	65.16	10.09	64.98	9.96

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Kinetic Method:

The kinetics of the bromodemetallation of R_3SnR' compounds was followed by monitoring the disappearance of total bromine (as tribromide) in the solution at 385 nm (mμ). A Beckman DU Spectrophotometer with a thermostatted cell compartment was used to measure the optical density as a function of time.

Extinction Coefficient:

The extinction coefficient of tribromide has been previously determined by Davis to be 782. Using the equipment used in all of the kinetic runs described here, this value was checked as follows: Bromine was added to a solution which was already 0.972 M sodium bromide in methanol. Three 10 ml aliquots of this bromine solution were titrated with standard thiosulfate (0.1000 N). The aliquots consumed 5.13, 5.14, and 5.12 ml of thiosulfate. The bromine concentration was thus determined to be 5.13×10^{-2} N or 2.56×10^{-2} M. From this solution, samples of various concentrations were prepared and their absorbance measured in a 1 cm cell.

$c(Br_3^-)$	A	ε
2.56×10^{-3}	1.880	742
1.28×10^{-3}	0.940	741
0.512×10^{-3}	0.365	718
0.256×10^{-3}	0.185	723

Using Beer's Law, $A = (\varepsilon)(c)(d)$, ε. the extinction

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coefficient was obtained for each concentration, and a mean value of $\varepsilon = 734$ was determined. This value was used for computing concentrations in second-order kinetic runs.

The instantaneous optical density allows the determination of the total instantaneous bromine concentration, from which the rate constant was determined by the usual methods. For initial concentrations of similar magnitude the rate constant was determined from the integrated rate expression:

$$\frac{1}{a-b} \ln \frac{b}{a} \frac{(a-x)}{(b-x)} = k_2^{obs} t$$

A plot of log (a-x)/(b-x) vs. t yields a straight line with slope

$$m = \frac{(a-b)k_2^{obs}}{2.303} .$$

When the initial concentrations were equal the following rate expression was used:

$$\frac{1}{a-x} - \frac{1}{a} = k_2^{obs} t .$$

A plot of 1/(a-x) vs. t yields a straight line whose slope, $m = k_2^{obs}$. When organotin concentration was much larger than bromine concentration a pseudo-first order treatment was employed:

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$$\ln \frac{a}{a-x} = k_1^{obs} t$$

from which the second-order rate constant, k_2^{obs}, was obtained:

$$k_2^{obs} = \frac{k_1^{obs}}{[Sn]_o} .$$

A plot of log O.D. vs. t yields a straight line whose slope, $m = -k_1^{obs}/2.303$.

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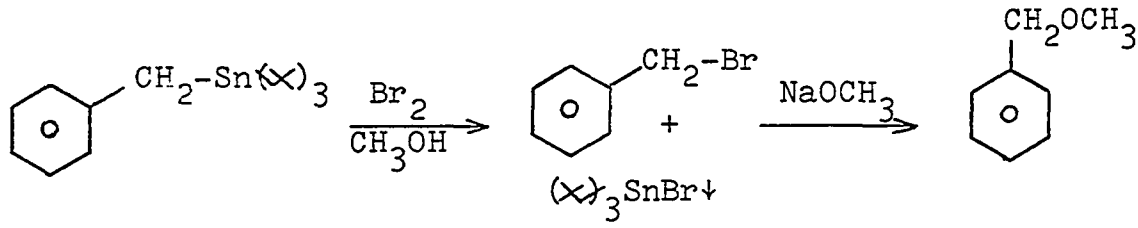
Product Study:

Since benzyl bromides decompose under gas chromatography conditions, product studies were carried out by treating the reaction mixtures with excess sodium methoxide and determining the product benzyl methyl ethers:



Studies were carried out on three compounds, the parent (p-H), p-methyl, and m-methyl derivatives. The following procedure for the parent compound illustrates the method: A Varian Aerograph Model 600-C Hy Fi instrument with a 10' × 1/8" 5% SE-30 on 80/100 chromosorb P column was used for the analysis. At least three samples were prepared containing known quantities of benzyl methyl ether and undecane (which was used as a marker) in methanol. Each sample was injected three times, and the area ratios were determined for each sample. From the combined data from all of the samples, a value,

$$\text{alpha} = \frac{\text{Area ratio } \bigcirc\!\!-CH_2OCH_3 \;/\; C_{11}H_{24}}{\text{Wt. ratio } \bigcirc\!\!-CH_2OCH_3 \;/\; C_{11}H_{24}},$$

was determined. Three samples of a known quantity of parent compound and undecane were dissolved in methanol, and a slight excess of neat bromine was added to each. Upon standing,

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a solid, which was identified by IR as trineopentyltin bromide, precipitated. The excess bromine was destroyed by the addition of an appropriate alkene; one whose product peaks did not interfere with those of the products being studied. (In the case of the parent compound, cyclohexene was employed.) Excess sodium methoxide was then added and the solutions allowed to sit for several hours. The reaction mixtures were then each injected three times, as in the determination of alpha. For each sample, the area ratios were measured. Alpha was then used to determine the quantity of benzyl methyl ether produced in the reaction, and this was compared to the theoretical amount of ether expected. Within the accuracy of the method, the reaction was found to be quantitive. Using a preparative instrument, the ethers were collected and identified as the desired product by IR comparison to authentic ethers.

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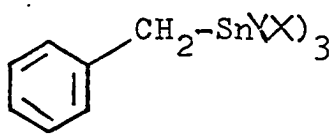
Table 39

Product Study Data for Benzyltrineopentyltin



$$\alpha = \frac{\text{Area ratio benzylmethyl ether/undecane}}{\text{Wt. ratio benzylmethyl ether/undecane}}$$

	Determination of α			
Sample #	W	X	Y	Z
	0.7387	0.7074	0.7626	0.7789
Values of α	0.7270	0.7346	0.7679	0.7605
	0.7765	0.7117	0.7725	0.7497
Mean Value of α: 0.7490	0.7474	0.7179	0.7677	0.7630

Weight of benzyl methyl ether produced as final product from bromodemetallation of benzyltrineopentyltin

Sample #	2	3	4
	0.0490	0.0488	0.0474
Wt. Found	0.0475	0.0481	0.0477
	0.0460	0.0494	0.0496
Mean Wt. Found	0.0475	0.0488	0.0482
Theor. Wt. Present*	0.0474	0.0487	0.0480
% Yield	100.2	100.2	100.4
Mean %	100.3%		

*based upon quantitative conversion of benzyltrineopentyltin to benzyl methyl ether.

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Table 40

Product Study for m-methylbenzyltrineopentyltin

$$\alpha = \frac{\text{Area ratio (m-methylbenzyl) methyl ether/dodecane}}{\text{Wt. ratio (m-methylbenzyl) methyl ether/dodecane}}$$

	Determination of α		
Sample #	A	B	C
	0.8023	0.8262	0.8421
Values of α	0.8095	0.8099	0.8706
	0.8230	0.8184	0.8173
Mean Values α:	0.8116	0.8182	0.8433
Mean α:	0.8244		

Weight of (m-methylbenzyl) methyl ether produced as product from bromodemetallation of m-methylbenzyltrineopentyltin:

Sample #	8	9	10
	0.0486	0.0487	0.0515
Values of α	0.0524	0.0558	0.0511
	0.0485	0.0485	0.0498
Mean Wt. Found	0.0498	0.0510	0.0508
Theor. Wt. Present	0.0493	0.0521	0.0498
% Yield	100.0	97.9	102.0
Mean %	100.0		

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Table 41

Product Study Data for p-Methylbenzyltrineopentyltin

$$\alpha = \frac{\text{Area ratio (p-methylbenzyl) methyl ether/dodecane}}{\text{Wt. ratio (p-methylbenzyl) methyl ether/dodecane}}$$

	Determination of α		
Sample #	G	H	J
	0.8050	0.7961	0.8018
Values of α	0.7799	0.7794	0.7595
	0.7896	0.8208	0.8442
Mean α:	0.7908	0.7988	0.8018
Mean Value of α:	0.7971		

Weight of (p-methylbenzyl) methyl ether produced as final product from bromodemetallation of p-methylbenzyltrineopentyltin:

Sample #	11	12	13
	0.0677	0.0352	0.0545
Values of α	0.0667	0.0341	0.0541
	0.0614	0.03	0.0599
Mean Wt. Found	0.0653	0.0347	0.0562
Theor. Wt. Present	0.0686	0.0366	0.0607
% Yield	95.2	94.8	94.2
Mean %	94.7%		

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Product Study:

I.R. data:

benzylmethyl ether (cm^{-1})

2950(s); 1600(w); 1500(m); 1450(m); 1375(m); 1200(m); 1100(s); 1050(m); 965(m); 930(m); 900(m); 740(s); 698(s).

(p-methylbenzyl) methyl ether (cm^{-1})

2950(s); 1900(w); 1800(w); 1625(w); 1510(m); 1450(m); 1375(m); 1200(m); 1100(s); 965(m); 920(m); 840(m); 805(s); 750(m).

(m-methylbenzyl) methyl ether (cm^{-1})

2950(s); 1625(w); 1450(m); 1380(m); 1200(m); 1160(m); 1100(s); 970(m); 930(m); 885(m); 785(s); 745(m); 697(s).

Bromine Label Experiment:

A solution of natural abundance bromine (50.54% ^{79}Br) in methanol was standardized with thiosulfate and found to be 0.0454 M in Br_2. A solution of 127.7 mg of $Na^{79}Br$ (whose ^{79}Br content was reported to be 95.06% ^{79}Br: 4.94% ^{81}Br by the manufacturer) in 10 ml methanol was added to 5 ml of this standardized bromine solution. The $NaBr:Br_2:CH_3OH$ solution was allowed to sit overnight to ensure exchange of the bromine. The final tribromide solution had a calculated content of 82.93% ^{79}Br. The mole ratio of sodium bromide to bromine (as Br_2) is 1.2119 mmoles NaBr/0.2270 mmoles

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Br_2 (or 5.341). This should reasonably approximate kinetic conditions.

A solution of 263.8 mg p-bromobenzyltrineopentyltin (0.5253 mmoles) in methanol was prepared, and this was added all at once to the bromine-79 solution. The bromine color took approximately thirty minutes to disappear completely. Upon completion the reaction mixture was added immediately to 50 ml of water (A), and this was extracted with 30 ml of methylene chloride. The methylene chloride layer was washed successively with 30 ml of water (B), and then 20 ml of water (C). Another 30 ml of methylene chloride were used to successively extract aqueous layers A, B, and C. Finally A, B, and C were extracted with an additional 15 ml of methylene chloride. The combined organic layers were filtered, removing any suspended water.

The organic layer was evaporated in vacuo and the residue chromatographed on a column packed with 9 g of silica gel, eluting first with 150 ml of hexane and then 150 ml of methylene chloride. The hexane contained unreacted starting tin compound and p-bromobenzyl bromide. The methylene chloride contained trineopentyltin bromide. Attempts to identify the bromine-79 content of the trineopentyltin bromide by mass spectroscopy were unsuccessful. The residue from the hexane eluant was dissolved in 25 ml of methanol, and 1.0 g sodium methoxide was added. This was refluxed for 15 minutes and added to 50 ml of water. The water was extracted with methylene chloride (as above), washing the

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successive extractions with portions of water (as above). The methylene chloride was filtered and evaporated *in vacuo*. The residue was chromatographed on 9 g of silica gel, eluting first with 150 ml of hexane removing unreacted starting tin compound , and then with 150 ml methylene chloride which eluted the desired (*p*-bromobenzyl) methyl ether. The solvents were evaporated, and both compounds were further purified by preparative gas chromatography. The mass spectral data for the $BrC_7H_6^+$ ion from the unreacted tin compound showed no bromine-79 exchange prior to the reaction. The bromine isotope ratio for the product ether was determined both for the parent ion (mass Nos.199 and 201) and the *p*-bromobenzyl ion (mass Nos. 169 and 171).

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Relative Peak Heights for Product (p-Bromobenzyl) Methyl Ether (Multiple Scans)

169	171
14.9	12.75
15.1	13.8
14.8	13.75
14.9	13.9
14.7	13.9
14.88	13.82
14.88	13.78 (relative abundance after correction for ^{13}C)
% ^{79}Br = 51.9%	

199	201
13.7	12.8
13.4	12.7
13.2	12.4
13.1	12.8
13.5	12.5
13.38	12.64
13.38	12.59 (relative abundance after correction for ^{13}C)
% ^{79}Br = 51.52	

Using the identical procedure, naturally occurring sodium bromide was used to check the accuracy of the method. For the parent ions (mass Nos. 199 and 201), the bromine-79 content was determined to be 51.93%, and for the p-bromobenzyl ion, the content was 50.92%.

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Check on Bromine Label Experiment:

A solution of natural abundance bromine in methanol was prepared and standardized. (The solution was 0.0495 M in bromine.) A 5 ml aliquot of this 0.0495 M standardized bromine solution was added to 114.3 mg (1.111 mmoles) of sodium bromide (which was 95.06% bromine-79). The resulting tribromide solution was permitted to sit overnight before use. The calculated composition of the solution was 81.3% ^{79}Br:18.7% ^{81}Br. The addition of 180 mg of tetraphenyltin, decolorized the bromine solution immediately. The solution was added to water and extracted with two 20 ml portions of chloroform. The chloroform extracts were dried with a calcium chloride chip and filtered. The chloroform was carefully removed by fractionation until only about 1.5 ml of solution remained. This preparatively gas chromatographed, and the bromobenzene which was isolated was analyzed for its bromine isotopic content by mass spectroscopy. The parent ions (mass Nos. 156 and 158) were used to determine the bromine isotopic ratio.

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Peak Heights of P and P+2 Peaks for Bromobenzene

P (156)	P+2 (158)
13.1	3.5
14.8	3.9
14.1	3.7
10.7	2.8
11.2	3.0
12.1	3.1
12.2	3.1
11.7	3.1
12.49	3.28
12.49	3.27 (relative abundance after ^{13}C correction)

79.10% ^{79}Br: 20.90% ^{81}Br

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Table 42

Sample Run (Run #25)

Bromodemetallation of Benzyltrineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2]_0=2.82\times10^{-3}$ M; $[Sn]_0=2.87\times10^{-3}$ M

t (sec)	O.D.
0	2.050
60	1.750
90	1.620
120	1.525
150	1.413
180	1.345
210	1.280
240	1.213
300	1.100
360	1.003
420	0.925
480	0.855
540	0.800
600	0.750
840	0.605
1080	0.495

$k_2^{obs} = 1.04\ M^{-1}\cdot sec^{-1}$

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Table 43

Sample Run (Run #28)

Bromodemetallation of p-Methylbenzyltrineopentyltin

MeOH; 25°; [NaBr] = 0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; [Sn] = 1.96×10^{-2} M

t (sec)	O.D.
0	0.913
60	0.588
120	0.395
180	0.250
240	0.160
300	0.110
420	0.048
540	0.020

$k_2^{obs} = 0.366\ M^{-1} \cdot sec^{-1}$

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Table 44

Sample Run (Run #102)

Bromodemetallation of p-t-Butylbenzyltrineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2]_0 = 1.71 \times 10^{-3}$ M; $[Sn]_0 = 13.12 \times 10^{-3}$ M

t (sec)	O.D.
0	1.218
24	1.035
48	0.893
72	0.775
96	0.673
120	0.583
144	0.513
168	0.448
192	0.393
216	0.345
240	0.305

$k_2^{obs} = 0.441\ M^{-1} \cdot sec^{-1}$

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Table 45

Sample Run (Run #9)

Bromodemetallation of p-methoxybenzyltrineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; $[Sn] = 1.60 \times 10^{-2}$ M

t (sec)	O.D.
0	1.118
48	0.950
108	0.800
168	0.668
228	0.565
288	0.475
408	0.350
528	0.250
708	0.150
828	0.100

$k_2^{obs} = 1.78 \times 10^{-1}\ M^{-1} \cdot sec^{-1}$

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Table 46

Sample Run (Run #99)

Bromodemetallation of (2,4,6-trimethylbenzyl) trineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2]_0=1.82\times10^{-3}$ M; $[Sn]_0=4.37\times10^{-3}$ M

t (sec)	O.D.
0	1.340
48	1.038
96	0.815
144	0.640
192	0.515
240	0.415
288	0.343
336	0.285
384	0.238
432	0.195
480	0.163

$k_2^{obs} = 1.34\ M^{-1} \cdot sec^{-1}$

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Table 47

Sample Run (Run #14)

Bromodemetallation of p-fluorobenzyltrineopentyltin

MeOH; 25°; [NaBr] = 0.366 M; $[Br_2] \simeq 2 \times 10^{-3}$ M; $[Sn] = 5.04 \times 10^{-2}$ M

t (sec)	O.D.
0	1.200
60	1.040
120	0.913
180	0.798
240	0.708
360	0.550
480	0.433
600	0.338
840	0.200
1080	0.125

$k_2^{obs} = 4.17 \times 10^{-2}\ M^{-1} \cdot sec^{-1}$

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Table 47

Sample Run (Run #14)

Bromodemetallation of p-Fluorobenzyltrineopentyltin

MeOH; 25°; [NaBr] = 0.366 M; $[Br_2] \simeq 2 \times 10^{-3}$ M; $[Sn] = 5.04 \times 10^{-2}$ M

t (sec)	O.D.
0	1.200
60	1.040
120	0.913
180	0.798
240	0.708
360	0.550
480	0.433
600	0.338
840	0.200
1080	0.125

$k_2^{obs} = 4.17 \times 10^{-2}\ M^{-1} \cdot sec^{-1}$

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Table 48

Sample Run (Run #15)

Bromodemetallation of p-Chlorobenzyltrineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; $[Sn] = 4.27 \times 10^{-2}$ M

t (sec)	O.D.
0	1.375
60	1.230
120	1.100
180	1.005
240	0.938
360	0.755
480	0.628
600	0.520
840	0.358
1080	0.233
1320	0.160
1560	0.108

$k_2^{obs} = 3.82 \times 10^{-2}\ M^{-1} \cdot sec^{-1}$

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Table 49

Sample Run (Run #64)

Bromodemetallation of p-Bromobenzyltrineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \approx 2 \times 10^{-3}$ M; $[Sn] = 2.29 \times 10^{-2}$ M

t (sec)	O.D.
0	1.745
60	1.663
120	1.578
180	1.495
300	1.345
420	1.220
600	1.048
900	0.813
1200	0.635
1500	0.493
1800	0.383
2400	0.233
3000	0.145

$k_2^{obs} = 3.71 \times 10^{-2}\ M^{-1} \cdot sec^{-1}$

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Table 50

Sample Run (Run #9)

Bromodemetallation of (m-trifluoromethylbenzyl) Trineopentyltin

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; $[Sn] = 3.52 \times 10^{-2}$ M

t (sec)	O.D.
0	1.350
120	1.218
240	1.080
360	0.965
480	0.870
600	0.785
900	0.595
1200	0.455
1500	0.348
2100	0.193
2700	0.115

$k_2^{obs} = 2.36 \times 10^{-2}\ M^{-1} \cdot sec^{-1}$

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Table 51

Sample Run (Run #36)

Bromodemetallation of m-Methylbenzyltrineopentyltin

MeOH; 0°; [NaBr]= 0.366 M; $[Br]_0=1.78\times10^{-3}$ M; $[Sn]_0=4.95\times10^{-3}$

t (sec)	O.D.
0	1.308
5	1.035
11	0.783
20	0.528
35	0.290
65	0.098

$k_2^{obs} = 10.68\ M^{-1} \cdot sec^{-1}$

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Table 52

Sample Run (Run #110)

Bromodemetallation of m-Methoxybenzyltrineopentyltin

MeOH; 0°; [NaBr]=0.366 M; $[Br_2]_0 = [Sn]_0 = 1.36 \times 10^{-4}$ M

t (sec)*	O.D.**
0	0.99
0.024	0.40
0.588	0.22
0.882	0.15
1.176	0.11

$k_2^{obs} = 5.7 \times 10^4\ M^{-1} \cdot sec^{-1}$

* Times read off chart paper with millimeter ruler chart speed set at 8 inches/min.

** Kinetics run in 10 cm cell, using Cary 14 spectrophotometer.

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Table 54

Sample Run (Run #118)

Bromination of p-Methyanisole

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; $[ArOCH_3] = 2.09 \times 10^{-1}$ M

t (sec)	O.D.
0	1.193
480	1.075
960	0.970
1440	0.875
1920	0.795
2400	0.708
2880	0.630
3360	0.570
3840	0.510
4320	0.460
4800	0.420
5280	0.378
5760	0.348
6240	0.318
6720	0.285
7200	0.250

$k_2^{obs} = 1.05 \times 10^{-3}\ M^{-1} \cdot sec^{-1}$

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Table 55

Sample Run (Run #114)

Bromination of Dimethoxybenzene

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; $[ArOCH_3] = 1.03 \times 10^{-1}$ M

t (sec)	O.D.
0	1.258
600	1.110
1200	0.983
1800	0.875
2400	0.783
3000	0.690
3600	0.613
4200	0.543
4800	0.485
5400	0.428
6000	0.385
6600	0.340
7200	0.303
7800	0.268

$k_2^{obs} = 1.93 \times 10^{-3}\ M^{-1} \cdot sec^{-1}$

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Table 56

Sample Run

Bromination of p-Chloroanisole

MeOH; 25°; [NaBr]=0.366 M; $[Br_2] \cong 2 \times 10^{-3}$ M; $[ArOCH_3] = 1.08 \times 10^{-1}$ M

No detectable change in O.D. over 18 hours.

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