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SCOPE AND MECHANISM OF THE ORGANOTIN HYDRIDE REDUCTION OF ALKYL HALIDES

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BY

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INTRODUCTION

INTRODUCTION

REDUCTION OF ALKYL HALIDES

This dissertation deals with a reaction involving alkyl halides which results in the replacement of the halogen atom by a hydrogen atom. There are available several methods other than the one being described in this dissertation which can bring about the same transformation. In this section several of these methods will be enumerated. Some of their characteristics, which have a bearing on the utility of organotin hydrides for the reduction of alkyl halides, will be mentioned.

Carey and Smith[1] investigated the reduction of alkyl halides using zinc and acetic acid. Although this method gave good yields when the halogen was iodine, it seemed to be less suitable for the less reactive bromides and chlorides. For example, the reduction of cetyl (hexadecyl) iodide produced a 95% yield of cetane after three hours. Under similar conditions, the corresponding bromide yielded a product which still contained 7.8% bromine after ten hours. Cetyl chloride was mostly unchanged after twenty hours. Carey and Smith[1] also investigated the use of zinc-copper couple as a reducing agent. The only reported example was the reduction of cetyl iodide which proceeded in 90% yield.

Catalytic hydrogenation has also been used as a method for reducing alkyl halides. Again, Carey and Smith[1] investigated the hydrogenolysis of cetyl iodide using a paladium-calcium carbonate catalyst. The reaction proceeded in 90% yield. Horner, Schlafer and Kammerer[2] made a study of the scope of Raney nickel catalyzed hydrogenolysis of alkyl halides. Some of their observations will be mentioned.

Simple bromides and iodides produced fair yields of the corresponding hydrocarbons while the chlorides proved to be very unreactive. The reduction of 3-chloro-1-hexene produces n-hexane while 4-chloro-1-hexene produces 4-chlorohexane. The trichloromethyl group was very readily reduced to the corresponding methyl group as indicated by the reduction of benzotrichloride to toluene. Chloroacetone was reduced to isopropyl alcohol.

One can effect the replacement of a halogen by a hydrogen by preparation of the Grignard reagent followed by the addition of a proton donor. However, it has been shown that this process is often accompanied by products formed from disproportionation and coupling. A comparison made between chlorides and iodides indicates that the chlorides give the desired product in the higher yield.[3]

The use of lithium aluminum hydride as a reducing agent for alkyl halides has been investigated.[4] The reaction is sluggish and in some cases does not occur in a reasonable time in refluxing diethyl ether, conditions which are usually sufficient for other lithium aluminum hydride reductions. Higher boiling solvents such as tetrahydrofuran and di-n-butyl ether can sometimes be used to speed up the reaction. Alkyl bromides are reduced more readily than the chlorides. Primary halides react more readily than secondary halides which in turn are more reactive than tertiary halides. Cyclic and aromatic halides prove to be very unreactive. The reaction can be further accelerated by the addition of lithium hydride. It has been proposed that not all four hydrogens exhibit the same reactivity toward alkyl halides and that the reaction of the first hydrogen is a much faster process than the reaction of the next three. The presence of lithium hydride serves to

regenerate lithium aluminum hydride by reaction with aluminum hydride. In this system, lithium aluminum hydride acts as a hydrogen carrier as shown by the fact that no reaction was found to occur with lithium hydride alone.

The reaction of α-haloketones with lithium aluminum hydride results in the reduction of the carbonyl group and produces the corresponding α-halohydrin as the initial product. In the presence of excess reducing agent, the halohydrin is reduced further to the alcohol.[5]

The inertness of alkyl halides toward alkali metal hydrides was also demonstrated by Cristol.[6] Sodium hydride did not react with any of eight halides studied even under forcing conditions. Included among the eight halides was the normally reactive benzyl bromide.

ORGANOTIN HYDRIDE REDUCTION OF ALKYL HALIDES

In 1957 van der Kerk and his co-workers[7,8,9] reported the first examples of the reduction of alkyl halides by organotin hydrides. These workers were investigating the addition of organotin hydrides to olefinic double bonds. However, the reaction of triphenyltin hydride with allyl bromide did not produce the expected addition product, Eq. (1), but produced instead propene and triphenyltin bromide, Eq. (2).

$$CH_2{=}CHCH_2Br + (C_6H_5)_3SnH \rightarrow (C_6H_5)_3SnCH_2CH_2CH_2Br \qquad (1)$$

$$CH_2{=}CHCH_2Br + (C_6H_5)_3SnH \rightarrow CH_2{=}CHCH_3 + (C_6H_5)_3SnBr \qquad (2)$$

The purpose of this work was to examine the scope and mechanism of the reduction of alkyl halides by organotin hydrides. At the time this work was started the only publications concerning this work were

those of van der Kerk. Since then several investigators have published data pertinent to the scope of this reaction. As has already been mentioned, van der Kerk and co-workers reported the first example of this reaction. Subsequently, in 1958, these investigators reported the reduction of methallyl chloride, 4-bromobutene and n-butyl bromide by triphenyltin hydride.[8,9] Kupchik and Connelly[10], in 1961, reported the reduction of benzyl chloride and dl-α-phenylethyl chloride by triphenyltin hydride to the corresponding unhalogenated hydrocarbons. The following year, Lorenz and Becker[11] reported the step-wise reduction of carbon tetrachloride to chloroform, methylene chloride and methyl chloride using triphenyltin hydride. Also in 1962, Kupchik and Kiesel[12] reported the reduction of 1-bromonorbornane to norbornane using triphenyltin hydride. In 1963, a preliminary communication concerning this present work was published[13], and Seyferth[14] and co-workers published data on the reduction of a series of gem-dihalocyclopropanes using tri-n-butyltin hydride. There is in press at the present time in Volume I of "Recent Advances in Organometallic Chemistry" edited by F. G. A. Stone and R. West[15], a chapter by Henry G. Kuivila on the reactions of organotin hydrides with organic compounds.* The efforts made during this work to further expand the scope and utility of this reaction and to understand the mechanism involved will be presented in this dissertation.

* The author is grateful to Dr. Kuivila for making this chapter available to him prior to publication.

RESULTS AND DISCUSSION

RESULTS AND DISCUSSION

SCOPE

General.

Organotin hydrides are usually prepared by reducing the corresponding organotin chlorides with lithium aluminum hydride.

$$\frac{1}{4-n} R_nSnCl_{4-n} + \frac{1}{4} LiAlH_4 \rightarrow \frac{1}{4-n} R_nSnH_{4-n} + \frac{1}{4} LiAlCl_4 \qquad (3)$$

Once prepared, the hydrides must be protected from the atmosphere since they are readily oxidized. Tri-n-butyltin hydride, the most stable of the hydrides used in this work, was stored in scrupulously clean, evacuated ampoules. For the most part, the hydride resisted decomposition even after several months. However, in a few cases appreciable decomposition was apparent as indicated by the relief of excess pressure on opening the ampoules.

Beumel[16], investigating the reduction of aldehydes and ketones with organotin hydride, commented on the stability of butyl and phenyl substituted tin hydrides. Triorganotin hydrides of low molecular weight are clear, colorless, viscous liquids which are thermally stable at room temperature and decompose slowly at about 125°C. The corresponding diorganotin dihydrides are clear, colorless liquids. Di-n-butyltin dihydride is relatively stable at room temperature. It is readily distilled under pressures below 10 mm., but decomposes very rapidly if heated near 125°C. Diphenyltin dihydride is unstable at room temperature and can be prepared and handled only near 0°C. Neumann and Niermann[17], investigating the preparation of organotin hydrides from the corresponding

organotin chlorides and alkyl aluminum hydrides, reported that diphenyltin dihydride is distillable without decomposition only in extremely clean fat-free glass vessels. The organotin trihydrides are also clear, colorless, liquids which are unstable at room temperature. Phenyltin trihydride can be distilled at 39°C/6 mm. with some decomposition occurring during the distillation. At room temperature it becomes noticeably discolored in an hour. Butyltin trihydride is more stable than phenyltin trihydride and can be distilled at atmospheric pressure with some decomposition. Distillation under reduced pressure greatly increases the yield. The pure, vacuum distilled hydride is stable at 0°C and discolors slightly only after several hours at room temperature.

A number of alkyl halides have been reduced by tri-n-butyltin hydride and di-n-butyltin dihydride. Iodides and bromides react exothermically. Chlorides are less reactive and require a catalyst for reaction in a reasonable time. Reactions were usually carried out at room temperature, neat or in solution, using ordinary laboratory apparatus and maintained under an atmosphere of prepurified nitrogen. Table I, which contains a list of the compounds reduced by tri-n-butyltin hydride and di-n-butyltin dihydride during the course of this work, provides an indication of the scope of this reaction.

Alkyl iodides, bromides and chlorides can be reduced conveniently and in good yields. The reduction of α-haloketones produces the corresponding ketones in good yield. In only one case was any alcohol observed and then in a very small amount (item 8). As already indicated, lithium aluminum hydride reduces α-haloketones to the corresponding halohydrins. Allylic and homoallylic halides undergo removal of the

TABLE I

Reduction of Alkyl Halides by Organotin Hydrides

Item	Alkyl Halide	Organotin Hydride	Product	% Yield Reduction Product	% Yield Organotin Halide
1	1-BrC_8H_{17}	$(\underline{n}\text{-}C_4H_9)_2SnH_2$	$\underline{n}\text{-}C_8H_{18}$	84	87
2	2-BrC_8H_{17}		$\underline{n}\text{-}C_8H_{18}$	99	90
3	Cyclo-$C_6H_{11}Br$		Cyclo-C_6H_{12}	82	87
4	$C_6H_5CH_2Br$		$C_6H_5CH_3$	60	97
5	$C_6H_5CH_2Cl$		$C_6H_5CH_3$	82	96
6	$C_6H_5CCl_3$		$C_6H_5CHCl_2$	88	b
			$C_6H_5CH_2Cl$	9	b
7	3-Bromocamphor		Camphor	70	b
8	$C_6H_5COCH_2Cl$		$C_6H_5COCH_3$	95	b
			$C_6H_5CH(OH)CH_3$	3	b
9[a]	$C_6H_5COCH_2Cl$	$(\underline{n}\text{-}C_4H_9)_3SnH$	$C_6H_5COCH_3$	99	b
10	$C_6H_5CHCl_2$		$C_6H_5CH_2Cl$	75	b
			$C_6H_5CH_3$	2	b
11	$C_6H_5CCl_3$		$C_6H_5CHCl_2$	88	b
12	1-IC_7H_{15}		$\underline{n}\text{-}C_7H_{16}$	95	b
13[a]	$C_6H_5C(CH_3)_2CH_2Cl$		$C_6H_5C(CH_3)_2CH_3$	95	b

[a] Initiated by 1.6 mole percent azobisisobutyronitrile

[b] Yield not determined

halogen atom only, as observed by van der Kerk, et al. The double bond is not affected. One of the most valuable characteristics of organotin hydride reductions is selectivity among geminal polyhalides. Benzotrichloride can be reduced successively in high yields to benzal chloride, benzyl chloride and toluene. The reduction is remarkably free from steric effects as indicated by the reduction of neophyl chloride (item 13) under relatively mild conditions. The series of relative rate constants in Table XI which will be presented in the section Results and Discussion of Mechanism shows that iodides are more readily reduced than the corresponding bromides which are more readily reduced than corresponding chlorides. Benzotrifluoride was inert to the tri-n-butyltin hydride even at 80°C.

Catalysis.

Alkyl chlorides are reduced much more slowly than the corresponding bromides. However, it was observed during the course of this work that the presence of approximately 1.6 mole percent azobisisobutyronitrile exerts a profound catalytic effect. In Table II are gathered the results obtained using azobisisobutyronitrile at 80°C. The halides chosen were those which react slowly, if at all, at this temperature in the absence of a catalyst. In the case of benzyl chloride, chlorocyclohexane and bromobenzene, the presence of 1.6 to 1.8 mole percent of the initiator was sufficient to bring about substantial reduction within thirty minutes. With chlorobenzene 18.5 mole percent of the initiator was required to bring about 76% reduction in 21.5 hours; however, no reaction occurs at the reflux temperature even with the more reactive triphenyltin

TABLE II

Effect of Azobisisobutyronitrile on the Rate of Reaction of Tri-n-Butyltin Hydride and Various Organic Halides at 80 ± 2°C

Exp. No.	Substrate[a]	Mole % Azobisisobutyronitrile	Reaction Time (Minutes)	Percent Reaction Uninitiated	Percent Reaction Initiated
1	$C_6H_5CH_2Cl$	1.6	30	26.0	100
			60	36.0	-
			570	78.0	-
2	Cyclo-$C_6H_{11}Cl$	1.6	35	1.0	69.5
			70	1.0	89.3
			185	-	100.0
			2880	10.2	-
3	C_6H_5Br	1.5	30	4.7	41.0
			70	6.7	58.4
			210	13.1	69.5
			690	13.3	72.7
4	C_6H_5Br	3.5	1880	-	90.4
			2195	-	89.5
5	C_6H_5Cl	1.8	30	No Rxn.	No Rxn.
			610	No Rxn.	1.3
			2275	No Rxn.	-
6	C_6H_5Cl	8.0	1280	-	36.0
7[b]	C_6H_5Cl	9.2	1140	-	40.2
			2430	-	36.1
8	C_6H_5Cl	18.5	1290	-	75.9

[a] Approximately 0.9 M in substrate and tri-n-butyltin hydride used in experiments 1-5; experiments 6-8 were carried out neat.

[b] Experiment No. 7 run at 130 ± 2°C

hydride in the absence of the catalyst.[18] The catalytic effect of this free radical initiator makes possible the reduction of even the most unreactive halides.

"Hydride Carrier" Method of Reduction.

During the course of this work, a simple method for the reduction of alkyl halides by organotin hydrides which avoids the preparation and isolation of the organotin hydride was developed. This method takes advantage of several facts. It is known that lithium aluminum hydride reacts with organotin halides very rapidly to produce organotin hydrides and the reduction of alkyl halides by lithium aluminum hydride, which proceeds via a nucleophilic displacement mechanism, is slow. However, the reduction of alkyl halides by organotin hydrides, which proceeds by a free radical mechanism as will be shown in the section Results and Discussion of Mechanism, is relatively fast. These facts suggest the use of an organotin halide as a "hydride carrier" for the reduction of organic halides by lithium aluminum hydride. The reaction sequence is given by Eqs. (4-5).

$$LiAlH_4 + 4R_3SnX \longrightarrow LiAlX_4 + 4R_3SnH \qquad (4)$$

$$R_3SnH + RX \longrightarrow RH + R_3SnX \qquad (5)$$

At least one equivalent of lithium aluminum hydride is added to a solution containing one mole of the organic halide and about 3 mole percent of the organotin halide. The organotin hydride is generated as is indicated in Eq. (4). It reduces the organic halide, Eq. (5), thus regenerating organotin halide. The organotin halide is then reduced with

more lithium aluminum hydride. The method has been applied to the reduction of bromocyclohexane and used as a method for determining the relative effectiveness of several organotin hydrides as reducing agents. The results are shown in Table III. As is indicated there is very little reaction between lithium aluminum hydride and bromocyclohexane under the conditions used. The order of effectiveness of the hydrides is as follows:

$(C_6H_5)_2SnH_2 \cong \underline{n}\text{-}C_4H_9SnH_3 > (C_6H_5)_3SnH \cong (\underline{n}\text{-}C_4H_9)_2SnH_2 > (\underline{n}\text{-}C_4H_9)_3SnH$

Phenyltin trihydride and stannic hydride were found to undergo decomposition too rapidly to be effective reducing agents.

MECHANISM

General.

The main purpose of this work has been to attempt to elucidate the mechanism involved in the organotin hydride reduction of alkyl halides. Several mechanisms can be considered for this reaction. A multicenter mechanism involving a four center transition state might seem to be a likely one.

$$R_3SnH + R'_3CX \longrightarrow \left[\begin{array}{ccc} R_3Sn & \cdots\cdots & H \\ \vdots & & \vdots \\ X & \cdots\cdots & CR'_3 \end{array}\right] \longrightarrow R_3SnX + R'_3CH$$

If one makes an analogy between the complex metal hydrides and organotin hydrides, then a nucleophilic displacement of the S_N2 type becomes a possible mechanism. The two mechanisms mentioned above as well as

TABLE III

Reduction of Bromocyclohexane by Organotin Hydrides Generated *in situ*[a]

Experiment Number	Organotin Halide	Reaction Time (Minutes)	Percent Reaction
1[b]	None	100	0.6
		185	0.8
		1450	1.0
		2645	1.4
2	$(C_6H_5)_3SnCl$	30	18.1
		150	79.7
		240	83.0
		300	80.3
		380[c]	81.0
		495	90.1
		615	93.2
		1350	98.0
3	$(n\text{-}C_4H_9)_3SnCl$	45	1.0
		230	5.6
		1610	47.2
4	$(C_6H_5)_2SnCl_2$	30	22.4
		65	63.5
		110	89.4
		145	92.4
		175	91.3
		1290	95.8
5	$(n\text{-}C_4H_9)_2SnCl_2$	40	7.0
		95	15.9
		155	38.8
		230	51.7
		315	64.5
		780	80.2
		1380	88.0
6	$C_6H_5SnCl_3$[d,e]	30	6.7
		70	5.3
		120	5.6
		180	6.1

Table III (continued)

Experiment Number	Organotin Halide	Reaction Time (Minutes)	Percent Reaction
7	n-$C_4H_9SnCl_3$ [e]	35	22.2
		60	71.6
		90	98.6
		195	100.0
8	$SnCl_4$ [e,f]	30	0.7
		90	0.7

[a] In refluxing diethyl ether; 2.5 mole percent of organotin halide used; bromocyclohexane 1.2 M.

[b] This experiment was run in order to observe the extent of reaction between bromocyclohexane and lithium aluminum hydride.

[c] After 340 minutes an additional 0.001 moles of $LiAlH_4$ was added.

[d] The reaction mixture turned white upon addition of $LiAlH_4$ solution but turned red and then black within 15 minutes.

[e] Reaction mixture kept under nitrogen atmosphere.

[f] Within 30 minutes the reaction mixture turned black.

others such as S_N1 can be eliminated on the basis of a variety of experimental observations which have been made. All the information concerning the mechanism which is available as the result of this work is consistent only with a free radical chain process. Equations (6-8) comprise a mechanistic hypothesis which is consistent with all experimental observations. In this scheme, Q• is a free radical which reacts by abstracting a hydrogen atom from an organotin hydride molecule. The organotin free radical abstracts a halogen atom from the alkyl halide thus producing an alkyl free radical. This free radical reacts in turn by abstracting a hydrogen atom from an organotin hydride molecule thus regenerating the organotin free radical. The last two reactions constitute a chain process. An analogy to organotin free radicals is the production of organosilicon free radicals which has been reported in the literature. For example, Curtice, Gilman and Hammond[19] made a study of triphenylsilyl free radicals produced by the action of peroxides or azobisisobutyronitrile on triphenylsilane.

$$R_3SnH + Q\bullet \longrightarrow R_3Sn\bullet + Q\text{-}H \qquad (6)$$

$$R_3Sn\bullet + R\text{-}X \longrightarrow R_3SnX + R\bullet \qquad (7)$$

$$R\bullet + R_3SnH \longrightarrow R_3Sn\bullet + R\text{-}H \qquad (8)$$

During the course of this investigation no attempt was made to determine the process by which termination occurs. It is assumed that termination occurs by coupling of free radicals.

Formation of an Alkyl Fragment.

Evidence for the formation of an alkyl fragment and thus elimination of the four center mechanism as a possibility is based on two sets

of experimental observations. The first of these is that the reduction of propargyl bromide by tri-n-butyltin hydride produced a mixture consisting of 84% propyne and 16% allene as determined by gas chromatography. The presence of allene was demonstrated by infrared spectroscopy (spectra nos. 3444, 3479), the characteristic allene band appearing at 1975 cm.$^{-1}$. The four center mechanism would be expected to lead to the formation of propyne exclusively. However, resonance stabilization of the propargylic radical could lead to the formation of the two observed products. (Figure 1).

Figure 1

Formation of Propyne and Allene

$$HC{\equiv}CCH_2Br + (n\text{-}C_4H_9)_3Sn\cdot$$

$$\downarrow$$

$$H_2C{=}C{=}\dot{C}H \longleftrightarrow HC{\equiv}C{-}\dot{C}H_2$$

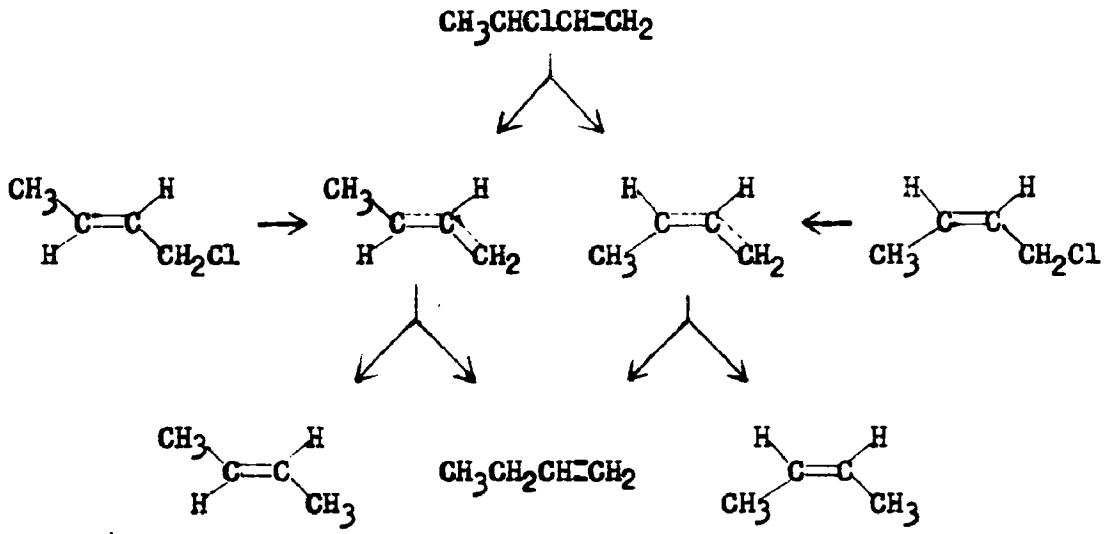
$$\downarrow R_3SnH$$

$$H_2C{=}C{=}CH_2 + HC{\equiv}CCH_3$$

The second set of experimental observations which lends support to the formation of an alkyl fragment is the results obtained from the reduction of isomeric methallyl chlorides with triphenyltin hydride. Mixtures consisting of different proportions of the isomeric methallyl chlorides produce mixtures of all three normal butenes. The ratios of the products are different from the ratios of the starting materials. The production of a resonance stabilized allylic radical would be expected to lead to a mixture of products as is indicated in Figure 2.

Figure 2

Reduction of Isomeric Methallyl Chlorides by Triphenyltin Hydride



Walling and Thaler[20] have studied the stereochemistry of the same allylic radicals and found that the allylic radical is capable of retaining its configuration. Bartlett[21] confirmed this observation concerning the stereochemistry of allylic radicals. Walling's work was concerned with allylic chlorination by t-butyl hypochlorite, Eq. (9).

$$RCH_2CH{=}CH_2 + t\text{-}C_4H_9OCl \longrightarrow RCH(Cl)CH{=}CH_2 + RCH{=}CHCH_2Cl + t\text{-}C_4H_9OH \qquad (9)$$

Among the substrates used were 1-butene and cis- and trans-2-butene. The ratio of isomeric methallyl chlorides produced from each substrate was reported. If one can predict the configurations of the allylic radicals being formed from each methallyl chloride and if it can be assumed that the allylic radicals once formed will react in the same manner in our system as in Walling's system, then one should be able to calculate the ratio of products formed in this work using Walling's

data. The compositions of the starting chlorides are given in Table IV. The possibility of isomerization of the chlorides catalyzed by triphenyltin chloride was investigated by storing a sample of each mixture of chlorides over triphenyltin chloride for a length of time equal to that which was allowed for the reduction. As is indicated also in Table IV, triphenyltin chloride had little, if any, effect on the chlorides. The ratio of 3-chloro-1-butene to 1-chloro-2-butene was measured by gas chromatography. The ratio of trans to cis-1-chloro -2-butene was approximated by infrared spectroscopy (spectrum no. 4487) using the spectra of each isomer published by Hatch and Nesbitt.[22]

In Table V are presented the ratios of the butenes obtained from each mixture of chlorides as determined by gas chromatography and the ratios of the butenes which should have been produced on the basis of Walling's data. The calculated values were arrived at by multiplying the ratio of the products obtained by Walling from each isomeric butene by the fraction of the corresponding methallyl chloride present in each of our reaction mixtures. For example, consider the two corresponding substrates, trans-2-butene used by Walling and trans-1-chloro-2-butene used by us. Walling reported that trans-2-butene reacts to give a mixture consisting of 73.2% 1-chloro-2-butene and 26.8% 3-chloro-1-butene. The reaction mixture used by us in Reaction II (Table IV) contained 74.3% trans-1-chloro-2-butene. To calculate the theoretical product distribution which should be obtained from this isomer, we multiplied 73.2 and 26.8 by 0.743. These results were added to give the calculated product distribution. As can be seen, the agreement is good for the mixture which was predominantly trans- and cis- 1-chloro-2-butene. However, the

TABLE IV

Composition of Isomeric Methallyl Chlorides

Chloride	Reaction I		Reaction II	
	% Before Start of Reaction	% After Standing Over $(C_6H_5)_3SnCl$	% Before Start of Reaction	% After Standing Over $(C_6H_5)_3SnCl$
3-Chloro-1-butene	86.0	77.6	9.5	10.7
cis-1-Chloro-2-butene	2.5	22.4[a]	16.2	89.3[a]
trans-1-Chloro-2-butene	11.5		74.3	

[a] This figure represents the combined percentage of both cis- and trans- 1-chloro-2-butene.

TABLE V

Composition of Isomeric Butenes

(Relative Percent)

	Reaction I		Reaction II	
Butene	Observed	Calculated[a]	Observed	Calculated[a]
1-Butene	27.0	30.6	26.9	28.8
cis-2-Butene	13.8	22.4	11.5	12.5
trans-2-Butene	59.2	47.0	61.6	58.7

[a] Calculated on the basis of Walling's data

calculated results for the mixture containing predominantly 3-chloro-1-butene is high for the estimation of cis-2-butene. The fact that the agreement is good for the case in which the stereochemistry of the resulting allylic radicals are known for the most part implies that our assumption concerning a characteristic reactivity of the allylic radical in both systems may be correct. If this is the case, then the difference between observed and calculated ratios must be due to the fact that the ratio of trans- to cis- allylic radicals produced in Reaction I is not the same as that produced in the chlorination. Walling proposes that the ratio of cis- to trans- 1-chloro-2-butene formed from 1-butene may be determined by the conformational distribution of the olefin. He assumes a staggered conformation of the groups at C_3 and the double bond about C_1-C_2, thus allowing for a trans- and gauche conformation, conformations I and II, respectively in Figure 3. Radical attack on the trans form should give rise to trans-allylic radical, while the gauche-structure should give the cis- radical. The conformations in our system, however, are different. The most stable conformations for 1-chloro-2-butene are most likely those in which the double bond about C_1-C_2 is staggered between the methyl group and the hydrogen atom (conformation III) in one case and between the chlorine atom and the hydrogen atom in the second case (conformation IV). The third possible conformation (V), is unlikely since the double bond would be staggered between the methyl group and the chlorine atom. Abstraction of the chlorine atom from a molecule which is in the first conformation (III) requires that there be a rotation about the C_2-C_3 bond in order for the developing p orbital to overlap with the pi orbital of the double bond. The direction of rotation will determine the configuration of the resulting free radical.

One would therefore expect tc produce a mixture of cis- and trans- allylic radicals which would then react as indicated in Figure 2. Abstraction of a chlorine atom from the second conformation (IV) appears to be more favorable since the geometry of the molecule is such that the developing p orbital is able to overlap with the pi orbital of the double bond without any rotation. It is also to be noted that this conformation leads exclusively to the trans- radical. It is therefore not at all surprising that 1-chloro-2-butene produces more trans-2-butene than is calculated. The surprising fact is that there is not even more of the trans product formed. As was mentioned above, the last conformation is very unlikely. However, if a molecule did react in this conformation, it would produce a cis radical.

Stereochemistry.

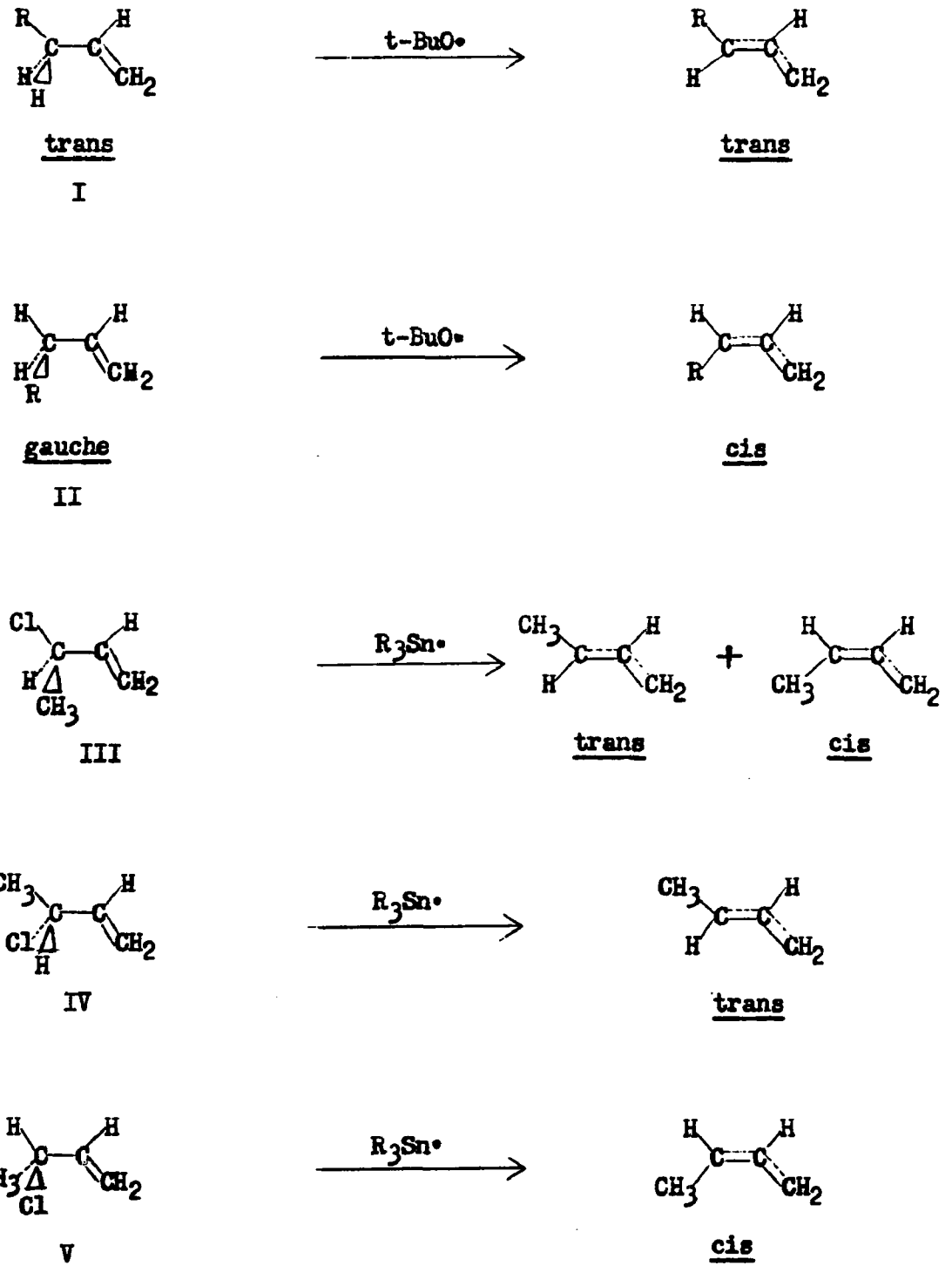
An observation made by Kuivila[23] which is pertinent to the mechanism is that optically active α-phenylethyl chloride reacts with triphenyltin deuteride to produce racemic α-deuteriophenylethane. This observation is inconsistent with an S_N2 or four-center mechanism, either of which would be expected to lead to a single enantiomorph.

Catalysis by Azobisisobutyronitrile.

Evidence which strongly suggests that free radicals are involved in the organotin hydride reduction of alkyl halides is the fact that the reaction is subject to catalysis by a free radical source. In Table II which has already been presented (page 11) have been gathered the results obtained using azobisisobutyronitrile as the free radical source at 80°C.

Figure 3

Formation of Allylic Radicals



As can be seen, the azo compound exerts a profound catalytic effect.

Effect of Azobisisobutyronitrile on Relative Rate Constants.

The possibility exists that the presence of a free radical source would bring about a change in the mechanism of the reduction and, although it could be assumed that the catalyzed reaction was proceeding by a free radical mechanism, the thermal reaction may be proceeding by some other mechanism. This possibility was investigated by allowing pairs of alkyl halides to compete for an insufficient amount of tri-n-butyltin hydride in the presence and absence of azobisisobutyronitrile and determining the relative rate constants. If the catalyzed and uncatalyzed reactions were not proceeding by the same mechanism, it would be expected that the relative rate constants would, in general, be different. In Table VI are gathered the results of these experiments. The difference between the relative rate constants for each set is within experimental error as would be expected if both thermal and catalyzed reactions proceed by a free radical mechanism.

TABLE VI

Effect of Azobisisobutyronitrile on Relative Rate Constants

Competitor A	Competitor B	k_A/k_B Catalyzed	k_A/k_B Thermal
$2\text{-}BrC_4H_9$	$C_6H_5CH_2Cl$	32.1	34.4
$BrCH_2Cl$	$2\text{-}BrC_8H_{15}$	8.20	8.66

Inhibition by Hydroquinone.

A study was made concerning the effect of hydroquinone, a free radical inhibitor, on the rate of reduction of two alkyl halides. In order to test whether hydroquinone could function as an inhibitor in a free radical reaction involving an organotin hydride, experiments with hydroquinone as an inhibitor were conducted in the presence of approximately 1 mole percent azobisisobutyronitrile (Table VII, runs 1, 2). Other experiments (runs 3-8) were carried out in the absence of the azonitrile. Simultaneous reactions were carried out in each case under identical conditions except that one reaction contained about 1.5 mole percent hydroquinone. With the exception of runs 7 and 8, the experiments were conducted by placing all reactants and solvent in a flask, removing aliquots and sealing these in ampoules which were flushed with nitrogen prior to sealing. All ampoules were then placed in an oil bath at $80 \pm 2^{\circ}C$. Runs 7 and 8 were each conducted in a 50 ml. round bottom flask equipped with two stopcocks which enabled one to withdraw aliquots while nitrogen was flowing through the system during the sampling process. The extent of reaction was determined by gas chromatography as outlined in the experimental section. Curve I is a graphic representation of runs 7 and 8. It is evident from Table VII and Curve I that hydroquinone can retard the reduction. This is consistent with a free radical mechanism.

Effect of Oxygen on Rate of Reduction.

The effect of varying the amount of oxygen in the atmosphere over a reaction mixture was studied and our results indicate that

TABLE VII

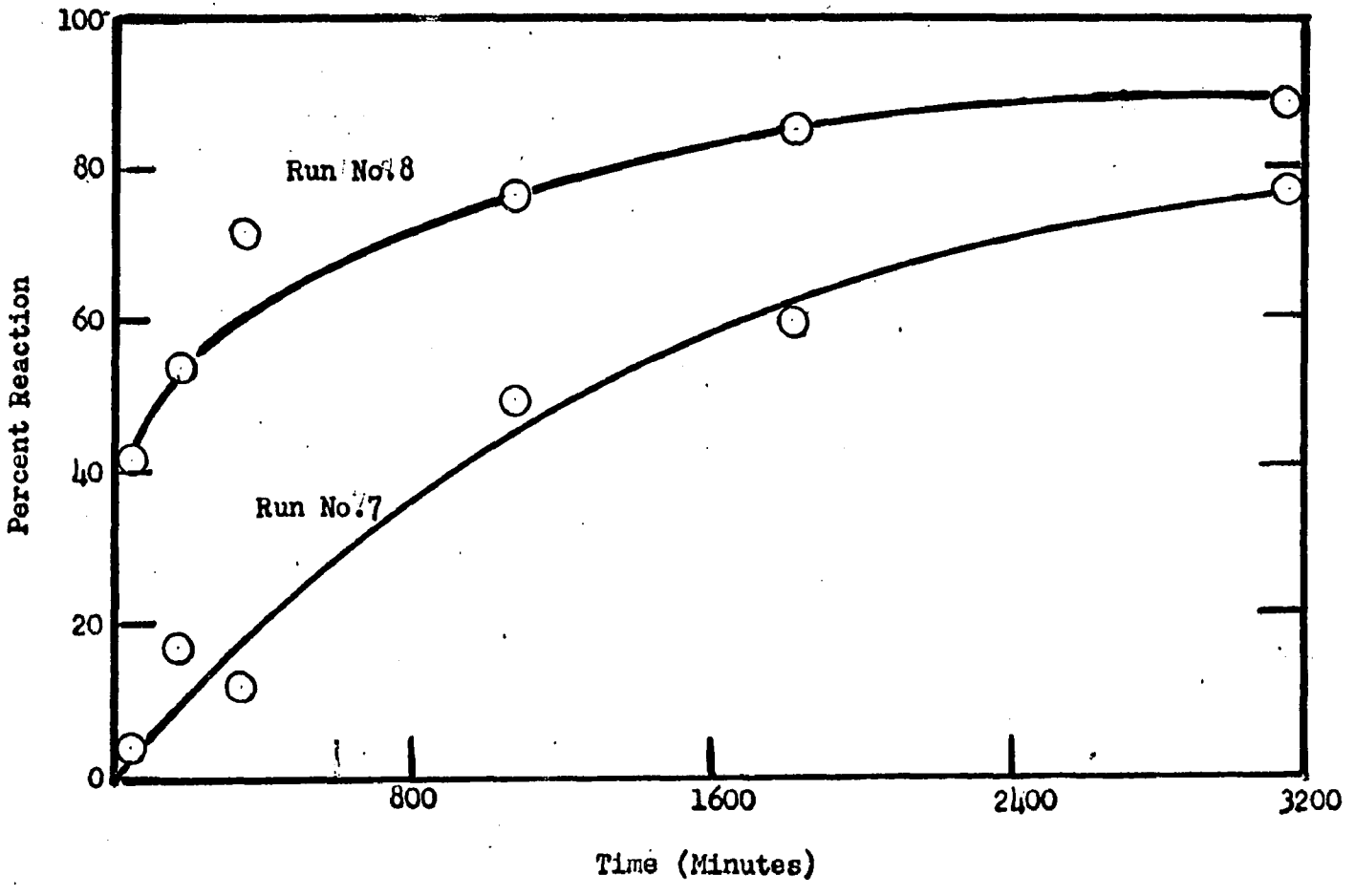
Inhibition of Tri-n-Butyltin Hydride Reduction of Alkyl Halides by Hydroquinone at 80 ± 2°C[a]

Run No.	Substrate	Time (Min.)	Percent Reaction[c] Inhibited	Percent Reaction[c] Uninhibited
1,[b] 2[b]	Cyclo-$C_6H_{11}Cl$	24	4	10
		73	10	24
		151	15	35
		220	18	41
		569	16	52
		1551	22	50
3, 4	$C_6H_5CH_2Cl$	436	No Reaction	75.1
		1222	No Reaction	76.1
5, 6	$C_6H_5CH_2Cl$	65	No Reaction	36.2
		127	No Reaction	49.2
		269	No Reaction	58.6
		445	No Reaction	70.6
		602	No Reaction	73.5
7, 8	$C_6H_5CH_2Cl$	60	3.7	41.4
		185	16.9	53.2
		360	11.8	71.6
		1085	47.8	76.7
		1830	60.2	85.0
		3155	77.5	89.2

[a] Approximately 0.4 M in substrate and organotin hydride; approximately 1.5 mole percent hydroquinone used; anisole used as solvent

[b] Runs 1 and 2 were conducted in the presence of approximately 1 mole percent azobisisobutyronitrile.

[c] Percent reaction for reactions 1 and 2 are based on a comparison of reduction product and internal standard peak height; all others were determined by the internal standard method.



Effect of Hydroquinone on Reaction Rate

Run No. 7, Hydroquinone Present
Run No. 8, Hydroquinone Absent

oxygen, which is a diradical, can function as a catalyst when present in small amounts and as an inhibitor when it is present in amounts approaching 20%. The reactants used were n-butyl bromide and tri-n-butyltin hydride in chlorobenzene as solvent, at 45°C. The reaction was followed using gas chromatography.

The procedure used was to mix n-butyl bromide and tri-n-butyltin hydride in a solvent, freeze the contents of the reaction flask in Dry Ice - acetone, evacuate to approximately 1 mm. pressure, bleed into the flask the desired pressure of oxygen and bring to atmospheric pressure by bleeding prepurified nitrogen into the flask. In those cases where the atmosphere was uniform, the reaction flask was merely flushed with the appropriate gas.

TABLE VIII

Gross Effect of Oxygen on Reaction Rate at 45°C

Reaction Number	Atmosphere	Reaction Time (Hours)	Percent Reaction
1	N_2	22	21.2
2	Air	22	50.0
3	O_2	22	1.1

The above reaction mixtures were exposed to air for about a minute, the flasks were resealed and returned to the constant temperature bath.

Table VIII (continued)

Reaction Number	Atmosphere	Reaction Time (Hours)	Percent Reaction
1	Exposed to air	18	55.4
2	Exposed to air	18	61.6
3	Exposed to air	18	1.1

The above data indicate that oxygen can both catalyze and inhibit the reaction. The reaction mixture stored under air gave appreciably more reaction than that stored under nitrogen whereas pure oxygen strongly inhibited the reaction. When some oxygen was allowed to enter the flask containing pure nitrogen, the reaction seemed to be catalyzed.

Our efforts then turned to controlling the amount of oxygen in the flask according to the procedure described above. The results are summarized in Table IX.

TABLE IX

Effect of Varying Amounts of Oxygen on Reaction Rate at 45°C

Reaction Number	% Oxygen in Reaction Flask [a]	Reaction Time (Hours)	Percent Reaction
4	4.2	15	42.4
5	10.1	15	54.5
6	20.5	15	0.79
7	31.0	15	1.85

[a] Remainder of atmosphere consists of prepurified nitrogen.

After 15 hours the atmospheres in the flasks were adjusted to contain about 4.5% oxygen by the procedure described above and were returned to the constant temperature bath. Results are summarized below.

Table IX (continued)

Reaction Number	% Oxygen in Reaction Flask	Reaction Time (Hours)	Percent Reaction
4	4.2	35	70.9
5	4.5	35	64.0
6	4.5	35	44.4
7	4.5	35	51.1

These results again indicate that oxygen can function as both catalyst and inhibitor depending on concentration. Inspection of the upper half of Table IX shows that when present in amounts up to 10%, oxygen functions as a catalyst. When present in amounts approaching 20%, it functions as an inhibitor. When the excess oxygen was removed and the amount of oxygen adjusted to about 4.5%, there was a marked increase in the percent reaction in those flasks which initially contained 20.5 and 31.0% oxygen and which had shown little, if any, reaction.

One explanation which seems to be compatible with the observations concerning the effect of oxygen is outlined in Eqs.(10-20). Represented are some of the reactions which can occur in a system containing

$$R_3SnH + O_2 \longrightarrow R_3Sn\cdot + \cdot O\text{-}OH \qquad (10)$$

$$R_3Sn\cdot + O_2 \longrightarrow R_3SnO\text{-}O\cdot \qquad (11)$$

$$R_3SnO\text{-}O\cdot + R_3Sn\cdot \longrightarrow R_3SnO\text{-}OSnR_3 \qquad (12)$$

$$R_3SnO\text{-}OSnR_3 \longrightarrow 2R_3SnO\cdot \quad (13)$$

$$R_3SnO\cdot + R_3Sn\cdot \longrightarrow R_3SnOSnR_3 \quad (14)$$

$$R_3Sn\cdot + RX \longrightarrow R_3SnX + R\cdot \quad (15)$$

$$R\cdot + R_3SnH \longrightarrow RH + R_3Sn\cdot \quad (16)$$

$$R\cdot + \cdot O\text{-}OH \longrightarrow RO\text{-}OH \quad (17)$$

$$R\cdot + O_2 \longrightarrow RO\text{-}O\cdot \quad (18)$$

$$RO\text{-}O\cdot + R_3SnH \longrightarrow RO\text{-}OH + R_3Sn\cdot \quad (19)$$

$$RO\text{-}O\cdot + R\cdot \longrightarrow RO\text{-}OR \quad (20)$$

organotin hydride, alkyl halide and oxygen. Omitted are reactions involving free radicals which produce other free radicals. The formation of one free radical by the consumption of another should not have any overall effect with regards to termination. The initiation step, Eq. (10), involves the abstraction of a hydrogen atom from the organotin hydride by oxygen producing an organotin radical and a hydroperoxy radical. The organotin radical can then react with oxygen, which is the start of a process which terminates by the production of the bis oxide, Eqs. (11-14). The overall effect is the consumption of two organotin radicals. The organotin radical can also react with the alkyl halide producing an alkyl radical, Eq. (15). The fate of the alkyl radical is determined by three competing reactions, Eqs. (16-18). Equation (16) is the normal propagation step and leads to formation of the reduction product and an organotin radical. Equation (17) is a termination step since it leads to non-radical products. Equation (18) involves the reaction of an alkyl radical with oxygen and produces an alkyl peroxy radical. The alkyl peroxy radical can then react, in a propagation step, with the organotin hydride or it can couple with another radical, such as an alkyl radical,

to give a peroxide. This is another termination step. It is assumed that the rate constants for termination steps, which involve coupling of radicals, are greater than the rate constants for either initiation or propagation steps, which involve bond cleavage. For example, the rate constant for the reaction represented by Eq. (20) would be greater than that for Eq. (19).

Doubling the concentration of the oxygen doubles the rate of any reaction which involves oxygen. This means that the rate at which the organotin radical is being formed has been doubled, Eq. (10). The rate of any reaction involving the organotin radical is also doubled. Therefore, the rates at which the alkyl radical are produced, Eq. (15) and consumed, Eqs. (16-18), are also doubled. Considering only these effects, one would predict an increase in the rate at which the product is formed, since the rate of the product forming reaction, Eq. (16), has been doubled. However, these are not the only reactions which are affected. The rate of Eq. (11), which is the start of a process which consumes two organotin radicals, quadruples since the concentrations of both reactants have been doubled. The rate of Eq. (18) which is also the start of a process which ends in the consumption of two alkyl radicals is also quadrupled. In this case, likewise, the concentration of both reactants has been doubled by doubling the concentration of the oxygen. One can conclude, then, that the rate of termination is increasing faster than the rate of initiation or propagation. It is to be expected that catalysis should change to retardation and finally to inhibition as the oxygen concentration is increased.

Effect of Structure on Reactivity.

A method which often provides much useful information concerning the mechanisms of organic reactions is a study of the effect of structure on reactivity. If it can be assumed that the rate determining step in the reaction under consideration is the abstraction of the halogen atom from the alkyl halide, then any change in the structure of the halide which affects the stability of the incipient free radical should also affect the rate at which the free radical is formed. Thus, one should be able to predict qualitatively the relative reactivity of various substrates if indeed the formation of a free radical is involved in the rate determining step.

One of the major efforts involved in this work has been a study of the relative reactivities of a number of halides. The procedure used in this study was to allow the halides to compete in pairs for an insufficient amount of organotin hydride and to analyze the resulting reaction mixtures for unreacted starting materials, products or both. Analysis was by gas chromatography using the internal standard method which is described by Keulemans.[24] Results were calculated using the usual equation which was first described by Ingold[25]:

$$\frac{\log A_o - \log A}{\log B_o - \log B} = \frac{k_A}{k_B}$$

where k_A/k_B represents the ratio of rate constants for the abstraction of a halogen atom by an organotin radical from alkyl halides A and B, respectively. A_o and B_o represent the initial concentrations of each halide and A and B represent final concentrations of each halide.

In deriving the above mentioned log expression for the determination of relative rate constants, one assumes that both competing reactions are irreversible and proceed by the same mechanism and, therefore, have the same kinetic order. To test the assumption concerning the order, a study was made involving the effect of varying the concentration of each competitor and organotin hydride on a relative rate constant. If the relative rate constant does not vary as the result of a change in the concentration of any of the reactants, the assumption is considered valid. Results obtained are presented in Table X.

TABLE X

Effect of Varying Concentrations on The Relative Rate Constant

Bromodichloromethane vs. Benzyl bromide

Initial Conc. $BrCHCl_2$ (mmoles)	Initial Conc. $C_6H_5CH_2Br$ (mmoles)	Initial Conc. $(n\text{-}C_4H_9)_3SnH$ (mmoles)	Volume of Solvent (ml.)	$k_{BrCHCl_2}/k_{C_6H_5CH_2Br}$
3.70	15.07	3.78	5	3.18
3.87	4.07	3.78	5	3.50
3.75	7.50	3.78	5	3.30
7.40	7.46	3.78	5	3.26
7.59	7.48	3.78	10	3.42
8.86	14.97	7.56	5	3.50

As can be seen from Table X, there is no definite trend in the relative rate constants over the range of concentrations used.

The results obtained from this study are listed in Table XI.

TABLE XI

Relative Rates of Reduction of Organic Halides

by Tri-n-Butyltin Hydride

At 45°C			At 80 ± 2°C[a]		
No.	Halide	Relative Rate[b]	No.	Halide	Relative Rate[b]
1.	$C_6H_5CH_2Cl$	0.05	19.	$C_6H_5CH_2Cl$	1.00
2.	n-C_4H_9Br	1.00	20.	C_6H_5Br	0.72 ± 0.07
3.	1-BrC_8H_{17}	1.10	21.	m-$CF_3C_6H_4CH_2Cl$	1.64 ± 0.04
4.	Cyclo-$C_6H_{11}Br$	1.46	22.	$H_2C{=}CHCH_2Cl$	1.83
5.	Cyclo-C_5H_9Br	2.37	23.	$HC{\equiv}CCH_2Cl$	6.11 ± 0.77
6.	2-BrC_8H_{17}	2.63	24.	2-BrC_8H_{17}	30.0 ± 3.8
7.	2-BrC_4H_9	2.99	25.	2-BrC_4H_9	33.3 ± 1.28
8.	t-C_4H_9Br	7 ± 1	26.	$BrCH_2Cl$	250 ± 22
9.	$BrCH_2Cl$	25.8 ± 1.4			
10.	$CH_2{=}CHCH_2Br$	30.5 ± 1.6			
11.	$C_6H_5CH_2Br$	33.5 ± 1.8			
12.	m-$BrC_6H_4CH_2Br$	36.2 ± 4.6			
13.	$BrCH_2COOC_2H_5$	60.4 ± 3.3 42.9 ± 2.3			
14.	1-IC_7H_{15}	61.1 ± 5.7			
15.	CCl_4	75.1 ± 4.7			
16.	$BrCHCl_2$	112 ± 6			

Table XI (continued)

At 45°C

No.	Halide	Relative Rate[b]
17.	$HC{\equiv}CCH_2Br$	139 ± 7
18.	$BrCCl_3$	226 ± 12

[a] Competitive reactions conducted at $80 \pm 2°C$ were all initiated by approximately 1.7 mole percent azobisisobutyronitrile except for numbers 20, 25 and 26. For numbers 20 and 25, four experiments were carried out, two with and two without azobisisobutyronitrile. For number 26, three experiments were carried out, two with and one without azobisisobutyronitrile.

[b] Relative rate constants which are the result of more than one competitive experiment include the standard deviation which is arrived at using the following expression:[28]

$$S.D. = \sqrt{\frac{d_1^2 + d_2^2 + \cdots d_n^2}{n-1}}$$

where: d = deviation of each experiment from the average

n = number of experiments

Qualitatively, the relative reactivities are those expected for a reaction leading to the production of a free radical in the rate determining step. The series eliminates S_N2 as a possible mechanism since branching on the carbon bearing the halogen increases the reactivity of the substrate. The S_N1 mechanism follows the same general reactivity trend as is observed in Table XI with two major differences. From Table XI it can be seen that benzyl bromide is more reactive than t-butyl bromide by a factor of about five, whereas t-butyl chloride solvolyzes faster than benzyl chloride by a factor which is strongly dependent upon the solvent.[26] Also, propargyl halides are more reactive than the corresponding allyl halides by a factor of from three to four (Table XI). However, the solvolysis rate ratio of α,α-dimethylallyl chloride to α,α-dimethylpropargyl chloride is approximately 10^5 in aqueous ethanol.[26] Szwarc and co-workers[27] have published a relative rate series for the abstraction of bromine atoms by methyl radicals (Eq. 21). Since the rate determining step is the formation of an alkyl radical, we should find a similarity between Szwarc's series and ours. Szwarc's

$$CH_3\cdot + R\text{-}Br \longrightarrow CH_3Br + R\cdot \qquad (21)$$

data is reproduced in Table XII. Although the range of our series is considerably smaller, the two sets of data seem to parallel each other with one exception. This exception concerns the reactivity of carbon tetrachloride. In our series carbon tetrachloride reacts faster than benzyl bromide while in Szwarc's there is a reversal for these two substrates. The possible reason for this difference will be discussed below.

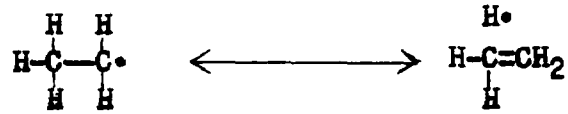
TABLE XII

Relative Rate Constants for Halogen Atom Abstraction

	Methyl radical[a]			Tin Hydride Reduction		
R	I	Br	Cl	I	Br	Cl
CH_3	45	6×10^{-3}				
C_2H_5	180					
n-C_4H_9					1.00	
n-C_7H_{15}				61.1		
s-C_3H_7	870					
s-C_4H_9					2.99	
t-C_4H_9	1680				7	
$C_6H_5CH_2$	7560	6.5			33.5	0.05
CH_2Cl	6400	1.4			25.8	
$CHCl_2$		131			112	
CCl_3		7400	4.4		226	75.1
CF_3	20,000					

[a] Relative Rate constants for reactions $RX + CH_3\cdot \longrightarrow R\cdot + CH_3X$ (k_2) expressed as a ratio k_2/k_1, where k_1 refers to the reaction $CH_3\cdot + C_6H_5CH_3 \longrightarrow CH_4 + C_6H_5CH_2\cdot$.[27]

The reactivity sequence for the halogens is as follows: iodine > bromine > chlorine. This follows from the facts that 1-iodoheptane is about sixty times as reactive as the n-alkyl bromides and that benzyl bromide is more reactive than the chloride by a factor of 670. Replacement of hydrogen by either methyl groups or chlorine atoms increases the reactivity. Both these observations can be attributed to increased stability of the incipient free radical and relief of steric strain in going from tetrahedral sp^3 hybridization to the planar sp^2 hybridization. Stabilization by the methyl groups can come from hyperconjugation:



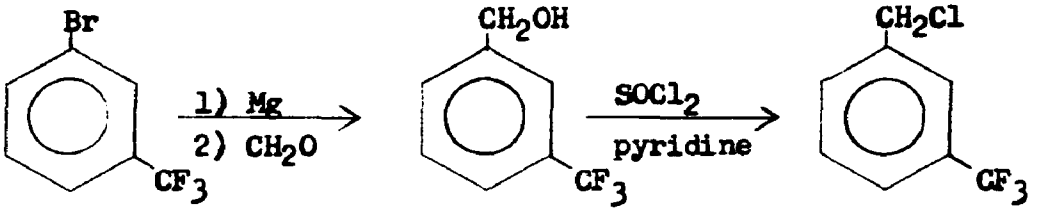
Chlorine atoms can stabilize a free radical by resonance:

Conjugation of the free radical with a π system also offers resonance stabilization, thus explaining the reactivity of the benzyl and allyl halides.

There is some evidence for suspecting that polar factors play an important role in determining the reactivity. For this reason m-trifluoromethylbenzyl chloride was synthesized and allowed to compete against benzyl chloride. The synthetic scheme is shown below.

Figure 4

Synthesis of m-Trifluoromethylbenzyl Chloride



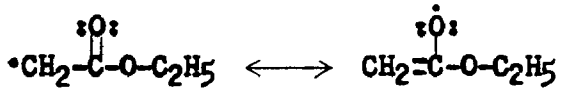
It was found that m-trifluoromethylbenzyl chloride reacts faster than benzyl chloride by a factor of 1.6. Therefore, electron withdrawing groups have an accelerating effect on the rate of reaction. The fact that m-bromobenzyl bromide is slightly more reactive than benzyl bromide also bears this out. This is not too surprising in view of the electropositive nature of the organotin radical. Polar contributors may play an important part in the transition state as is shown below:

$$\left[R_3C\text{-}X \quad \cdot SnR'_3\right] \longleftrightarrow \left[R_3C\cdot \quad X\text{-}SnR'_3\right] \longleftrightarrow \left[R_3C:^{\ominus} \; X\cdot \; ^{\oplus}SnR'_3\right]$$

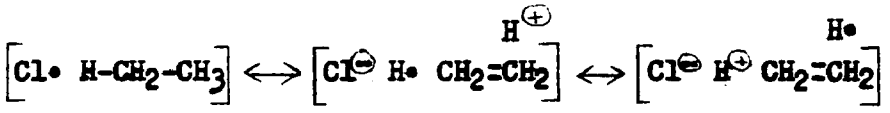
This polar contribution could account for the abnormally high reactivity of carbon tetrachloride. The incipient trichloromethyl radical has three electronegative chlorine atoms attached to it which would stabilize any negative charge which develops on the carbon atom. The propargyl halides also seem to be abnormally reactive when compared with the corresponding allyl halide. Propargyl bromide is 4.5 times as reactive as allyl bromide and propargyl chloride is 3.3 times as reactive as allyl chloride. The polar effect could again be used to explain this high reactivity. The electronegative sp hybridized carbon atom of the propargyl system

would be more effective than the sp^2 hybridized carbon atom of the allyl system in stabilizing any negative charge developing on the halogen bearing carbon. There is also an entropy loss involved in the allylic system which must become planar for maximum stabilization.

The reactivity of ethyl bromoacetate can be explained as the result of inductive acceleration as well as resonance stabilization as shown below.



The polar effect observed for the reaction of the electropositive tin radical is not surprising in view of the information available on the polar effects of reactions which involve electronegative radicals such as chlorine atom and t-butoxy radical. In both these cases, electron- withdrawing substituents decreased the reactivity of the substrates which were studied; an effect opposite to that observed for the reaction of an organotin radical. Walling[29], making a survey of polar effects observed for reactions involving chlorine atoms, proposes that the deactivation by electron withdrawing groups on substituted toluenes and the primary > secondary >tertiary order observed for alkanes could be explained by stabilization of the transition state which involves a polar contributor having a partial negative charge on the chlorine atoms and partial positive charge on the organic molecule.



Walling and Jacknow[30] studied the free radical chlorination of

substituted toluenes using t-butyl hypochlorite. This reaction involves abstraction of a hydrogen atom by a t-butoxy radical in the rate limiting step. The data were obtained in terms of a relative reactivity series and showed that electron withdrawing substituents made the substrate less reactive. According to the authors, these data imply that the t-butoxy radical is an electron accepting species preferentially attacking points of high electron availability. The polar properties of the t-butoxy radical are thus comparable to the chlorine atom.

Patmore and Gritter[31] studied the ease of attack of a t-butoxy radical on a series of monosubstituted cyclohexanes. Their data indicate that the substituents govern the breaking of a carbon-hydrogen bond through their inductive effect. The authors propose a transition state in which one of the contributors has a positive charge developing on the carbon atom from which the hydrogen is being abstracted and a negative charge on the t-butoxy radical.

$$X\cdot + RH \longrightarrow (R{:}H\cdot\ X \longleftrightarrow R\cdot^{\oplus} H X{:}^{\ominus} \longleftrightarrow R\cdot\ H{:}X) \longrightarrow R\cdot\ HX$$

Their data show that electron-releasing substituents such as methyl and ethyl yield relative reactivities greater than that of cyclohexane, whereas electron- withdrawing substituents, such as cyano and nitro produce reactivities less than cyclohexane. It would seem, therefore, that the structure described above which has a charge separation, is an important contributor to the transition state, since methyl and ethyl would stabilize a positive charge on the organic molecule which has lost the hydrogen atom.

Russel[32] also has presented evidence that the transition state

for the attack of bromine atoms or N-succinimidyl radicals on benzyl hydrogens involves separation of charge.

The fact that bromocyclopentane is 1.6 times as reactive as bromocyclohexane is probably a steric acceleration. Removal of a bromine atom from cyclopentane relieves steric strain which is not present in cyclohexane.

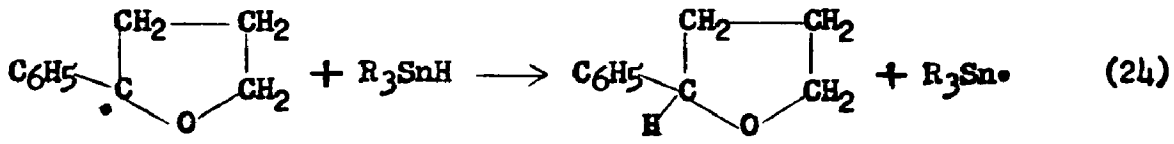
The fact that secondary alkyl halides are only about forty times as reactive as bromobenzene is quite surprising. We are not able to account for this rather small difference.

Intramolecular Alkyl Radical Trapping.

During the course of this work attempts were made to trap the alkyl radicals postulated as intermediates in the alkyl halide reduction. In these laboratories, Kuivila and Walsh[33] have demonstrated that aldehydes and ketones are good traps for acyl radicals. However, attempts to trap the alkyl radical by added cyclohexanone were unsuccessful. In order that the radical carbon be favorably situated sterically, the azobisisobutyronitrile catalyzed reduction of γ-chlorobutyrophenone with tri-n-butyltin hydride was undertaken. Analysis of the reaction mixture showed the major product to be 2-phenyltetrahydrofuran, whose formation can be rationalized according to Eqs. (22-24).

$$C_6H_5CCH_2CH_2CH_2Cl + R_3Sn\cdot \longrightarrow C_6H_5CCH_2CH_2CH_2\cdot + R_3SnCl \qquad (22)$$

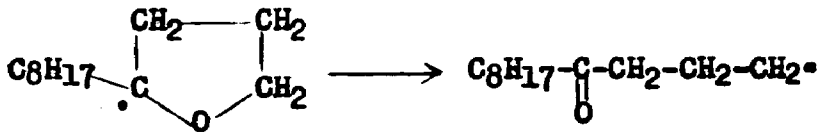
$$C_6H_5CCH_2CH_2CH_2\cdot \longrightarrow \qquad (23)$$



(24)

The reduction yielded 64% of a mixture of ketone and ether. The ketonic material was separated from the ether using Girard's T reagent. It was calculated that the mixture consisted of 80% ether and 20% ketone. The infrared spectrum of the ether was identical with the spectra of 2-phenyltetrahydrofuran which was sent to us through the courtesy of Dr. R. L. Letsinger.

Wallace and Gritter[34] studied the mechanism of the tert-butyl peroxide-induced free radical addition of four-, five-, and six-membered cyclic ethers to 1-octene. The products were always a ketone and an ether, the ketone predominating. Two mechanisms were proposed. One involved formation of a cyclic radical which decyclizes to give an open chain radical containing a carbonyl group on the delta carbon. This radical then abstracts a hydrogen atom. In the reduction of γ-chloro-



butyrophenone we have reversed this process and formed predominantly the product from the cyclic radical. However, we have a phenyl group instead of an alkyl side chain. The cyclic radical in this case is a stable benzyl radical which is probably the reason for the reversal.

EXPERIMENTAL

EXPERIMENTAL

All experiments involving organotin hydrides were conducted in an atmosphere of prepurified nitrogen unless otherwise indicated. The infrared spectra were determined with a Perkin-Elmer model 21 recording double-beam spectrophotometer with sodium chloride optics. Proton magnetic resonance spectra were determined with a Varian model A-60 Analytical Nuclear Magnetic Resonance Spectrometer. Experiments involving gas chromatography were carried out using an F. and M. model 300 gas chromatograph.

MATERIALS

Organic Halides.

The organic halides used were commercially available in most cases. They were purified by distillation when more than 5% impurities were present or when highly colored. Purity was determined by gas chromatography.

Solvents.

Solvents used were commercially available and were usually purified by distillation.

Organotin Hydrides.

The organotin hydrides were prepared by reduction of the appropriate organotin chlorides with lithium aluminum hydride. Tri-*n*-butyltin hydride was also prepared by reduction of bis(tri-*n*-butyltin) oxide.

The procedures followed were those described by Kuivila and Beumel[35] and by Considine and Ventura.[36] Tri-n-butyltin chloride and bis(tri-n-butyltin oxide) were obtained through the courtesy of M and T Chemicals, Inc.

Tri-n-butyltin Hydride from Tri-n-Butyltin Chloride. A 500 ml. flask in an ice bath was fitted with a stirrer, a dropping funnel and a nitrogen inlet. To the flask was added 3.8 g. (0.1 moles) of lithium aluminum hydride followed by 150 ml. of anhydrous ether. Tri-n-butyltin chloride, 65.0 g. (0.2 moles) in 150 ml. of anhydrous ether was added dropwise over a period of 60 minutes. The ice bath was removed and the mixture was allowed to stir at room temperature for a period of from two to eight hours. The mixture was then hydrolyzed with 50 ml. of water and the ether layer separated and washed with two 50 ml. portions of water and then two 50 ml. portions of saturated calcium chloride solution. The ether layer was then dried over magnesium sulfate for one hour. The ether layer was decanted, the solvent stripped off. The residue was distilled, the main fraction distilling at 91.5-93°C/0.9 mm. The hydride was then stored in evacuated ampoules. The yield was 60-80%.

Tri-n-butyltin Hydride from Bis(Tri-n-Butyltin) Oxide. The procedure followed was the same as that for the preparation from tri-n-butyltin chloride; however, the stoiciometry is different. Two moles of the hydride are produced for every mole of oxide. The yields were 91-92%.

Di-n-Butyltin Dihydride. The procedure followed was the same as that described for tri-n-butyltin hydride. The main fraction distilled

at 32.5-34.5°C/.01 mm. The yields were 67-72%.

Triphenyltin Hydride. The procedure followed was the same as that described for tri-n-butyltin hydride except that the triphenyltin chloride was added directly into the reaction flask. The product was distilled using an oil bath preheated to 200°C. The main fraction distilled at 168°C/0.5 mm. The yield was 60%.

REDUCTION OF ALKYL HALIDES

Procedure.

Reductions were carried out in ordinary laboratory apparatus usually at room temperature. The organic halide was placed in an Erlenmeyer flask followed by the solvent when used. The organotin hydride was added using a pipette. The flask was then flushed with prepurified nitrogen and stoppered. If the reaction was exothermic, the flask was cooled in an ice bath. In those cases where a catalyst was used, aliquots of the reaction mixture were removed and sealed in ampoules which were flushed with prepurified nitrogen prior to sealing. Yields were determined either by isolation or by gas chromatography. Identity of the product was usually established by infrared spectroscopy when the product was isolated or by retention time when gas chromatography was used.

Di-n-butyltin Dihydride Reductions.

1-Bromooctane. A mixture of 3.86 g. (20.0 mmoles) 1-bromooctane and 2 ml. (10.0 mmoles) di-n-butyltin dihydride was prepared. The

reaction, which was exothermic, was allowed to proceed at room temperature for twelve days, and was distilled. After redistillation the yield of n-octane boiling at 35-37°C/22 mm. was 1.91 g. (84%) (infrared spectrum no. 2132). The second fraction yielded 3.42 g. (87%) di-n-butyltin dibromide.

2-Bromooctane. A mixture of 5.88 g. (30.0 mmoles) 2-bromooctane and 3 ml. (15.0 mmoles) di-n-butyltin dihydride was prepared. The reaction, which was exothermic, was allowed to proceed for six days and was distilled. The yield of n-octane collected in two fractions, boiling at 40-41°C/28 mm. and 31-33°C/0.3 mm. was 3.41 g. (99%) (infrared spectrum no. 2121). The third fraction yielded 5.30 g. (90%) di-n-butyltin dibromide.

Bromocyclohexane. A mixture of 3.28 g. (20.0 mmoles) bromocyclohexane and 2 ml. (10.0 mmoles) di-n-butyltin dihydride was prepared. The reaction, which was exothermic, was allowed to proceed for twelve days and was distilled. After redistillation, the yield of cyclohexane, boiling at 77°C, was 1.34 g. (82%) (infrared spectrum no. 2133). The second fraction yielded 3.41 g. (87%) di-n-butyltin dibromide.

Benzyl bromide. A mixture of 3.54 g. (20.0 mmoles) benzyl bromide and 2 ml. (10.0 mmoles) di-n-butyltin dihydride was prepared. The reaction, which was exothermic, was allowed to proceed for six days and was distilled. After redistillation the yield of toluene, boiling at 30°C/30 mm. was 1.11 g. (60%) (infrared spectrum no. 2119). The yield of di-n-butyltin dibromide, boiling at 130°C/0.3 mm., was 3.82 g. (87%).

Benzyl chloride. A mixture of 2.54 g. (20.0 mmoles) benzyl chloride and 2 ml. (10.0 mmoles) di-n-butyltin dihydride was prepared. The reaction, which was exothermic, was allowed to proceed for six days and was distilled. The yield of toluene, boiling at 28°C/28 mm. was 1.52 g. (82%) (infrared spectrum no. 2120). The yield of di-n-butyltin dichloride, boiling at 145°C/1 mm., was 2.88 g. (96%). It was identified by a mixture melting point (m.p. 42-44°C).

Benzotrichloride. A mixture of 1.96 g. (10.0 mmoles) benzotrichloride and 1 ml. (5.0 mmoles) di-n-butyltin dihydride was prepared. The reaction was complete after 16.5 hours. Benzal chloride (88%) and benzyl chloride (9%) were produced as determined by gas chromatography using a 4 foot column packed with 20% silicone oil on celite. The yield was estimated by comparing the peak heights of the product and unreacted starting material.

3-Bromocamphor. A mixture of 6.94 g. (30.0 mmoles) 3-bromocamphor and 3 ml. (15.0 mmoles) di-n-butyltin dihydride was prepared. The reaction was complete after 60 hours. Camphor was isolated by sublimation from the reaction mixture under reduced pressure followed by resublimation. The yield was 3.19 g. (70%). Its melting point was 171-176°C (reported 176-177°C).

Phenacyl chloride. A mixture of 1.62 g. (10.5 mmoles) phenacyl chloride and 1 ml. (5.1 mmoles) di-n-butyltin dihydride was prepared in 5 ml. diethyl ether. The reaction, which was exothermic, was complete after one day. Acetophenone (95%) and α-phenylethyl alcohol (3%) were produced as determined by gas chromatography using a 4 foot column packed

with 20% carbowax 20 M on Chromosorb P (42-60 mesh). Yields were estimated by comparing the peak heights of the products and unreacted starting material.

Tri-n-butyltin Hydride Reductions.

Phenacyl chloride. A mixture of 0.589 g. (3.78 mmoles) phenacyl chloride, 0.010 g. (0.061 mmoles) azobisisobutyronitrile and 1 ml. (3.78 mmoles) tri-n-butyltin hydride was prepared in 5 ml. benzene. Cumene was added as an internal standard. A 1 ml. aliquot was sealed in a nitrogen flushed ampoule and placed in an oil bath at 80 ± 2°C. The reaction was complete after one hour. Acetophenone (99%) was produced as determined by gas chromatography using a column packed with 20% carbowax 20 M on Chromosorb P (42-60 mesh). The yield was arrived at by using the internal standard method.

Benzal chloride. A mixture of 0.622 g. (3.86 mmoles) benzal chloride and 1 ml. (3.78 mmoles) tri-n-butyltin hydride was prepared. The reaction was allowed to proceed at 45°C for seven days. Benzyl chloride (75%) and toluene (2%) were produced as determined by gas chromatography using a column packed with 20% silicone oil on celite. Yields were estimated by comparing the peak heights of the products and unreacted starting material.

Benzotrichloride. A mixture of 0.757 g. (3.87 mmoles) benzotrichloride and 1 ml. (3.78 mmoles) tri-n-butyltin hydride was prepared in 2.5 ml. diethyl ether. The reaction was complete after ten days. Benzal chloride (90%) was produced as determined by gas chromatography

using a column packed with 20% silicone oil on celite. The yield was arrived at by comparing the peak heights of the product and unreacted starting material.

1-Iodoheptane. A mixture of 0.860 g. (3.68 mmoles) 1-iodoheptane and 1 ml. (3.78 mmoles) tri-n-butyltin hydride was prepared in 2.5 ml. benzene. Chlorobenzene was added as an internal standard. The reaction, which was exothermic, was complete after four days. n-Heptane (96%) was produced as determined by gas chromatography using a column packed with 20% paraffin oil on Chromosorb P (80-100 mesh). The yield was determined using the internal standard method.

Neophyl chloride. A mixture of 0.636 g. (3.79 mmoles) neophyl chloride, 0.010 g. (0.061 mmoles) azobisisobutyronitrile and 1 ml. (3.78 mmoles) tri-n-butyltin hydride was prepared in 5 ml. toluene. A 1 ml. aliquot was sealed in a nitrogen flushed ampoule and placed in an oil bath at 80± 2°C. t-Butylbenzene was produced (95%) as determined by gas chromatography using a column packed with 20% silicone oil on celite. The yield was estimated by comparing the peak heights of the product and unreacted starting material. The product was identified by its proton magnetic resonance spectra (spectrum no. 24).

RELATIVE RATE DETERMINATIONS

Procedure.

The relative rate constants for the halides listed in Table VIII were determined by allowing the halides to compete in pairs for an

insufficient amount of organotin hydride and analyzing the resulting reaction mixture for unreacted starting materials, products or both. Gas chromatography was used for the analyses. With only one exception, a 4 foot column packed with 20% paraffin oil on Chromosorb P (80-100 mesh) was used. The exception was the competitive reactions between m-trifluoromethylbenzyl chloride and benzyl chloride in which case a 4 foot column packed with 17% nitrile silicone fluid on Chromosorb P (60-80 mesh) was used.

The two competitors and an internal standard were weighed out into the reaction flask. The solvent was then added and the organotin hydride introduced using a pipette. The flask was then flushed with nitrogen, tightly stoppered and placed in a constant temperature bath set for $45 \pm 0.01^{\circ}C$. The flask remained in the bath until all the organotin hydride was consumed. The solution was tested for the presence of organotin hydride by removing an aliquot and introducing it into an etheral solution of sulfuric acid. Evolution of hydrogen indicated a positive test.

The final concentration of the competitors was determined by gas chromatography using the internal standard method described by Keulemans.[24] Calibration curves were prepared by chromatographing synthetic mixtures containing the pure component whose concentration was to be determined and an internal standard in several accurately known proportions. The ratios of the areas of the peaks for the component and the internal standard were then plotted against the ratios of the amounts actually present (moles). The reaction mixture which contained a known amount of the internal standard was then chromatographed and the ratio

of the component to internal standard peak areas was determined. The concentration of the component was then calculated. The areas were determined by multiplying the peak height by the peak width at the mid point.[24]

The relative rate constants were determined according to the method published by Ingold and Stow.[25] The expression used in these determinations is as follows:

$$\frac{\log \frac{Ao}{A}}{\log \frac{Bo}{B}} = \frac{k_A}{k_B}$$

in which: Ao = the initial concentration of halide A

A = the final concentration of halide A

Bo = the initial concentration of halide B

B = the final concentration of halide B

In deriving this expression, one assumes that both competitive reactions proceed by the same mechanism and therefore have the same kinetic order. In order to observe whether this assumption was valid, a study was made concerning the effect of varying the concentration of each competitor and organotin hydride on a relative rate constant. If the relative rate constant does not vary as the result of a change in the concentration of any of the reactants, the assumption is considered valid. These data have been summarized in Table X.

The relative rate constants obtained for each set of competitors is given in Tables XIII and XIV. Initial and final concentrations for all competitive reactions are given in Table XV. The data used in plotting

TABLE XIII

Relative Rates of Reduction of Organic Halides

by Tri-n-butyltin Hydride at 45°

Exp. No.	Competitor A	Competitor B	Solvent	k_B/k_A	Internal Standard Curve No.
1	n-C_4H_9Br	2-BrC_8H_{15}	$C_6H_5CH_3$	2.63	8, 4
2	1-BrC_8H_{15}	2-BrC_4H_9	$C_6H_5CH_3$	2.72	1, 5
3	n-BrC_4H_9	1-BrC_8H_{15}	$C_6H_5CH_3$	1.10	10, 1
4	n-C_4H_9Br	t-C_4H_9Br	$C_6H_4(CH_3)_2$	7.56	7, 6
5	n-C_4H_9Br	t-C_4H_9Br	$C_6H_4(CH_3)_2$	6.79	7, 6
6	n-C_4H_9Br	Cyclo-$C_6H_{13}Br$	Cyclo-C_6H_{13}	1.46	2, 9
7	n-C_4H_9Br	Cyclo-$C_5H_{11}Br$	Cyclo-C_6H_{13}	2.37	3, 9
8	$BrCH_2Cl$	$C_6H_5CH_2Br$	C_6H_5Cl	1.30	17, 18
9	$BrCH_2Cl$	$C_6H_5CH_2Br$	C_6H_5Cl	1.30	17, 18
10	$C_6H_5CH_2Br$	CCl_4	C_6H_5Cl	2.16	18, 22
11	$C_6H_5CH_2Br$	CCl_4	C_6H_5Br	2.38	24, 37
12	$C_6H_5CH_2Br$	CCl_4	C_6H_5Br	2.14	24, 37
13	$C_6H_5CH_2Br$	$BrCHCl_2$	C_6H_5Br	3.18	24, 23
14	$C_6H_5CH_2Br$	$BrCHCl_2$	C_6H_5Br	3.50	24, 23
15	$C_6H_5CH_2Br$	$BrCHCl_2$	C_6H_5Br	3.30	24, 23
16	$C_6H_5CH_2Br$	$BrCHCl_2$	C_6H_5Br	3.26	24, 23
17	$C_6H_5CH_2Br$	$BrCHCl_2$	C_6H_5Br	3.42	24, 23
18	$C_6H_5CH_2Br$	$BrCHCl_2$	C_6H_5Br	3.50	24, 23
19	$CH_2=CHCH_2Br$	$C_6H_5CH_2Br$	C_6H_5Cl	1.15	21, 18
20	$CH_2=CHCH_2Br$	$C_6H_5CH_2Br$	C_6H_5Cl	1.09	21, 18

Table XIII (continued)

Exp. No.	Competitor A	Competitor B	Solvent	k_B/k_A	Internal Standard Curve No.
21	$CH_2=CHCH_2Br$	$C_6H_5CH_2Br$	C_6H_5Cl	1.04	21, 18
22	$CH_2=CHCH_2Br$	$C_6H_5CH_2Br$	C_6H_5Cl	1.13	21, 18
23	$C_6H_5CH_2Br$	$BrCH_2CO_2C_2H_5$	C_6H_5Cl	1.28	18
24	$C_6H_5CH_2Br$	$BrCH_2CO_2C_2H_5$	2,3-Dimethyl butane	1.80	24
25	$2\text{-}BrC_4H_9$	$C_6H_5CH_2Br$	C_6H_5Br	10.4	31, 24
26	$2\text{-}BrC_4H_9$	$C_6H_5CH_2Br$	C_6H_5Br	11.1	31, 24
27	$2\text{-}BrC_4H_9$	$C_6H_5CH_2Br$	C_6H_5Br	11.3	31, 24
28	$2\text{-}BrC_4H_9$	$C_6H_5CH_2Br$	C_6H_5Br	12.0	31, 24
29	$C_6H_5CH_2Br$	$1\text{-}IC_7H_{15}$	C_6H_5Br	1.95	24, 28
30	$C_6H_5CH_2Br$	$1\text{-}IC_7H_{15}$	C_6H_5Br	1.70	24, 28
31	$C_6H_5CH_2Cl$	$2\text{-}BrC_4H_9$	C_6H_5Br	54.6	24, 31
32	$\underline{m}\text{-}BrC_6H_4CH_2Br$	$CH_2=CHCH_2Br$	C_6H_5Cl	1.01	29, 21
33	$C_6H_5CH_2Br$	$\underline{m}\text{-}BrC_6H_4CH_2Br$	C_6H_5Cl	1.21	18
34	$C_6H_5CH_2Br$	$\underline{m}\text{-}BrC_6H_4CH_2Br$	C_6H_5Cl	1.18	18
35	$BrCHCl_2$	$BrCCl_3$	C_6H_5Br	1.97	23, 35
36	$BrCHCl_2$	$BrCCl_3$	C_6H_5Br	2.06	23, 35

TABLE XIV

Relative Rates of Reduction by Tri-n-butyltin Hydride at 80± 2°

Catalyzed by 1.6% Azobisisobutyronitrile

Exp. No.	Competitor A	CompetitorB	Solvent	k_B/k_A	Internal Standard Curve No.
37	C_6H_5Br	$C_6H_5CH_2Cl$	i-$C_3H_7C_6H_5$	1.21	30, 24
38	C_6H_5Br	$C_6H_5CH_2Cl$		1.26	30, 24
39[a]	C_6H_5Br	$C_6H_5CH_2Cl$		1.48	30, 24
40[a]	C_6H_5Br	$C_6H_5CH_2Cl$		1.55	30, 24
41	$C_6H_5CH_2Cl$	2-BrC_4H_9		34.4	24, 31
42	$C_6H_5CH_2Cl$	2-BrC_4H_9		34.5	24, 31
43[a]	$C_6H_5CH_2Cl$	2-BrC_4H_9		32.2	24, 31
44[a]	$C_6H_5CH_2Cl$	2-BrC_4H_9		32.0	24, 31
45	$CH_2=CHCH_2Cl$	2-BrC_8H_{17}		15.4	32, 26
46	$CH_2=CHCH_2Cl$	2-BrC_8H_{17}		17.3	32, 26
47	$C_6H_5CH_2Cl$	$CH_2=CH_2-CH_2Cl$		1.83	18, 32
48	$HC\equiv C-CH_2Cl$	2-BrC_8H_{17}		4.71	27, 26
49	$HC\equiv C-CH_2Cl$	2-BrC_8H_{17}		5.57	27, 26
50	$HC\equiv C-CH_2Cl$	2-BrC_8H_{17}		4.46	27, 26
51	$C_6H_5CH_2Cl$	m-$CF_3C_6H_4CH_2Cl$		1.60	38, 39
52	$C_6H_5CH_2Cl$	m-$CF_3C_6H_4CH_2Cl$		1.68	38, 39
53	2-BrC_8H_{17}	$BrCH_2Cl$		7.95	26, 17
54	2-BrC_8H_{17}	$BrCH_2Cl$		8.40	26, 17
55[a]	2-BrC_8H_{17}	$BrCH_2Cl$	C_6H_5Br	8.66	26, 17

[a] Reactions conducted without the addition of azobisisobutyronitrile.

TABLE XV

Initial and Final Concentrations of Substrates Used in Relative Rate Determinations[a,b]

Exp. No.	Conc. I.S. (mmoles)	Initial Conc. Competitor A (mmoles)	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. A	Initial Conc. Comp. B	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. B
1	3.84	3.82	0.606	2.73	3.84	0.524	1.57
2	3.86	3.80	0.806	2.62	3.92	0.322	1.43
3	3.85	3.93	0.572	2.58	3.74	0.729	2.35
4	3.78	3.78	0.842	3.09	3.78	0.200	0.86
5	3.78	3.78	0.822	3.02	3.78	0.196	0.84
6	3.81	3.71	0.605	2.21	3.82	0.556	1.79
7	3.86	3.85	0.704	2.62	3.87	0.428	1.55
8	3.66	3.89	0.422	2.16	3.86	0.458	1.80
9	3.70	3.91	0.438	2.26	3.78	0.426	1.85
10	3.56	3.80	0.316	2.43	3.83	0.344	1.46
11	3.62	3.88	0.365	2.49	3.76	0.353	1.31
12	3.79	3.74	0.331	2.41	3.81	0.351	1.36
13	3.84	15.07	0.508	13.00	3.70	0.568	2.30

Table XV (continued)

Exp. No.	Conc. I.S. (mmoles)	Initial Conc. Competitor A (mmoles)	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. A	Initial Conc. Comp. B	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. B
14	3.64	4.07	0.294	2.94	3.87	0.327	1.24
15	3.85	7.50	0.396	5.89	3.75	0.419	1.69
16	7.54	7.46	0.122	6.50	7.40	0.596	4.72
17	3.78	7.48	0.241	6.52	7.59	1.182	4.74
18	7.35	14.97	0.371	12.08	8.86	0.542	4.19
19	3.45	4.02	0.440	2.14	3.82	0.464	1.86
20	3.82	3.91	0.393	2.10	3.75	0.393	1.91
21	3.79	4.04	0.436	2.32	3.72	0.436	2.09
22	3.82	3.97	0.382	2.05	3.68	0.412	1.75
23	3.45	3.89	0.412	2.16	3.88	-	1.83
24	3.28	3.80	0.430	2.31	3.87	-	1.58
25	3.70	11.27	2.505	10.03	3.81	0.684	1.11
26	3.87	15.28	3.298	13.75	3.74	0.625	1.17
27	3.80	15.11	3.332	13.70	3.78	0.628	1.24
28	3.82	11.28	2.478	10.21	3.76	0.646	1.14

Table XV (continued)

Exp. No.	Conc. I.S. (mmoles)	Initial Conc. Competitor A (mmoles)	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. A	Initial Conc. Comp. B	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. B
29	3.90	3.78	0.328	2.43	3.69	0.614	1.57
30	3.58	3.79	0.392	2.30	3.71	0.669	1.59
31	3.78	7.71	0.081	7.40	3.86	0.105	0.42
32	3.96	3.80	0.512	1.95	3.72	0.342	1.90
33	3.60	3.80	0.397	2.05	3.80	-	2.05
34	3.65	3.75	0.392	2.00	3.86	-	1.83
35	3.83	3.85	0.628	2.53	3.77	0.367	1.65
36	3.88	3.86	0.632	2.60	3.94	0.382	1.75
37[c]	3.66	3.99	0.282	2.61	3.96	0.400	2.42
38[c]	3.78	3.74	0.275	2.42	3.84	0.404	2.22
39	3.66	3.77	0.270	2.52	3.84	0.445	2.12
40	3.86	3.92	0.217	2.87	3.96	0.371	2.44
41	3.84	9.97	0.116	9.52	3.69	0.184	0.74
42	3.66	3.93	0.070	3.70	3.74	0.094	0.37

Table XV (continued)

Exp. No.	Conc. I.S. (mmoles)	Initial Conc. Competitor A (mmoles)	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. A	Initial Conc. Comp. B	Peak Area Comp.A(or product)/ Peak Area I.S.	Final Conc. Comp. B
43	3.51	7.66	0.116	7.24	3.62	0.154	0.59
44	3.56	10.63	0.136	10.13	3.78	0.212	0.81
45	3.79	4.16	0.628	3.56	3.63	0.628	0.33
46	3.71	4.19	0.672	3.73	3.67	0.936	0.49
47	3.71	3.32	0.265	2.13	4.21	0.340	1.87
48	3.63	4.15	0.541	3.10	3.68	0.822	0.93
49	3.81	3.89	0.510	3.06	3.63	0.766	0.95
50	3.63	4.10	0.534	3.06	3.67	0.807	0.99
51	1.53	2.08	0.364	1.30	1.87	0.578	0.88
52	1.73	2.06	0.314	1.30	1.88	0.510	0.87
53	3.87	11.34	0.255	9.95	3.88	0.393	1.37
54	3.78	11.32	0.398	9.96	3.78	0.246	1.29
55	3.80	11.32	0.269	10.38	4.75	0.420	2.24

Table XV (continued)

[a] Initial concentrations were determined by weight of starting material; final concentrations were determined by gas chromatography using the internal standard method[3] except for experiments 23, 24, 33 and 34 in which only the final concentration of one competitor was determined by gas chromatography and the final concentration of the second competitor was determined by difference assuming 100% reaction.

[b] 3.78 mmoles tri-n-butyltin hydride used in each case except experiment 18 which used 7.56 mmoles; experiments 1 through 7 used 20 cc. solvent, experiments 8, 9, 19, 20, 21 and 22 used 10 cc. of solvent. The remaining experiments used 5 cc. of solvent.

TABLE XVI

Internal Standard Curve Data

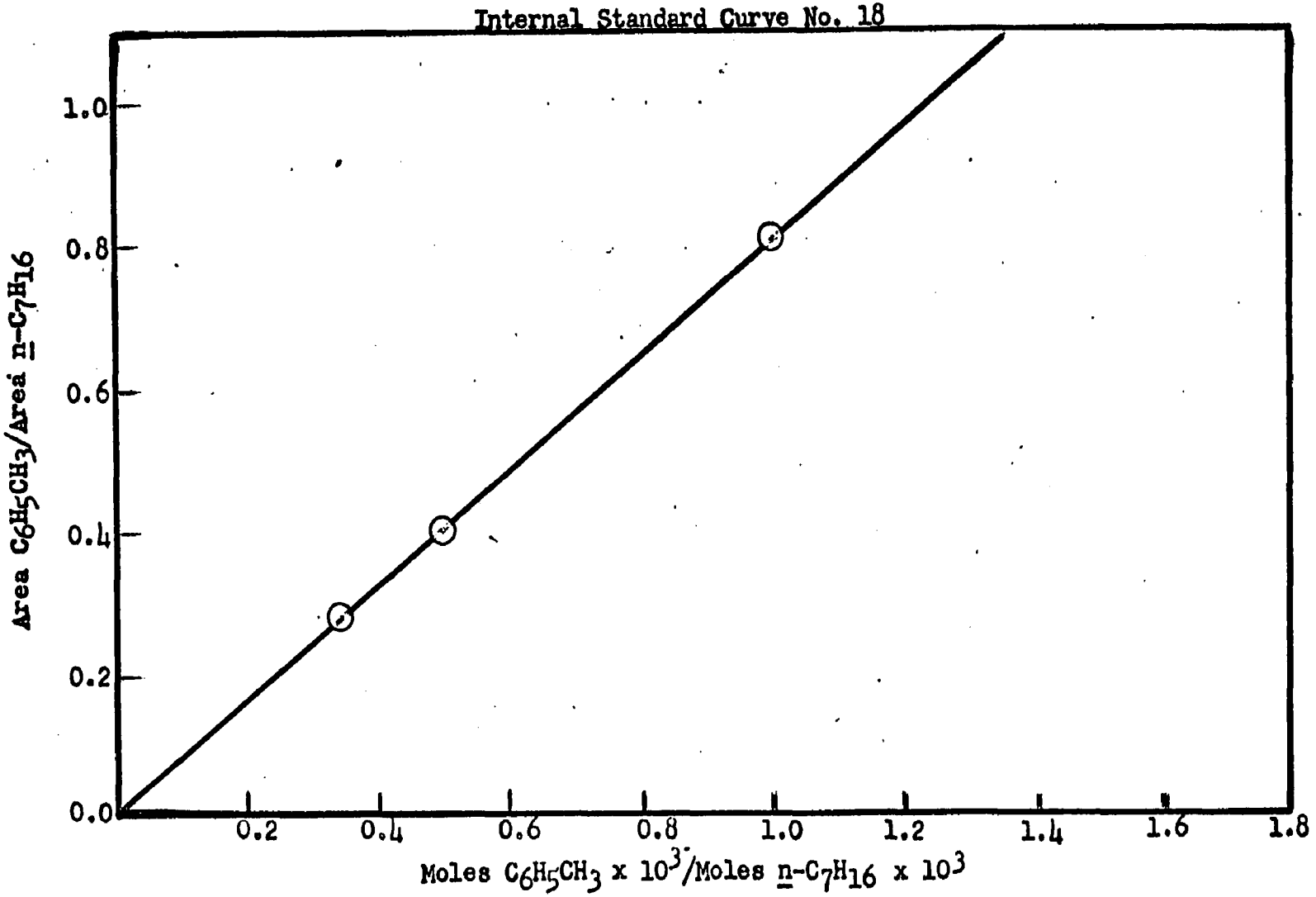
Curve No.	Substrate	Internal Standard	Mmoles Substrate/ Mmoles I.S.	Peak Area Substrate/ Peak Area I.S.
1	1-BrC_8H_{15}	n-C_7H_{16}	0.962 0.497 0.340	1.141 0.592 0.394
2	Cyclo-$C_6H_{13}Br$	$C_6H_5CH_3$	0.985 0.487 0.340	1.156 0.585 0.404
3	Cyclo-$C_5H_{11}Br$	$C_6H_5CH_3$	1.101 0.506 0.350	1.070 0.538 0.372
4	2-BrC_8H_{15}	n-C_7H_{16}	0.725 0.506 0.338	0.876 0.635 0.432
5	2-BrC_4H_9	n-C_7H_{16}	0.980 0.702 0.476	0.805 0.592 0.404
6	t-C_4H_9Br	$C_6H_5CH_3$	1.092 0.672 0.518 0.331	0.952 0.591 0.460 0.294
7	n-C_4H_9Br	$C_6H_5CH_3$	1.000 0.675 0.506 0.340	1.045 0.700 0.525 0.368
8	n-C_4H_9Br	n-C_7H_{16}	1.001 0.515 0.336	0.854 0.438 0.283
9	n-C_4H_9Br	$C_6H_5CH_3$	0.985 0.514 0.335	1.022 0.536 0.350
10	n-C_4H_9Br	n-C_7H_{16}	0.508 0.359 0.000	0.439 0.306 0.000

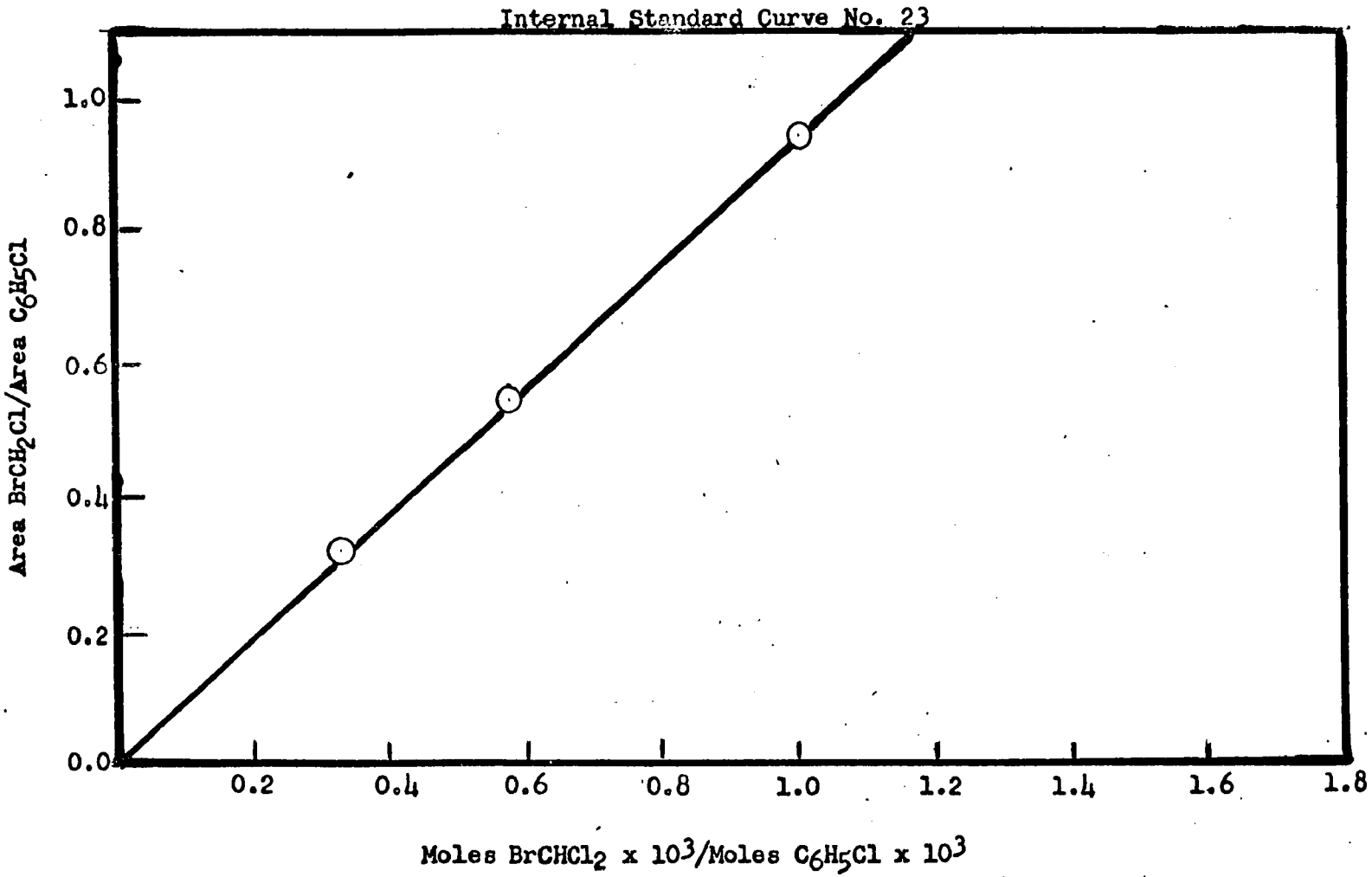
Table XVI (continued)

Curve No.	Substrate	Internal Standard	Mmoles Substrate/ Mmoles I.S.	Peak Area Substrate/ Peak Area I.S.
17	$BrCH_2Cl$	n-C_7H_{16}	1.040 0.477 0.329	0.754 0.333 0.234
18	$C_6H_5CH_3$	n-C_7H_{16}	1.002 0.498 0.342	0.812 0.400 0.280
22	CCl_4	C_7H_{16}	0.993 0.503 0.302	0.824 0.420 0.249
24	$C_6H_5CH_3$	C_6H_5Cl	0.994 0.474 0.332	0.929 0.451 0.314
37	CCl_4	C_6H_5Cl	0.941 0.442 0.000	0.916 0.435 0.000
23	$BrCHCl_2$	C_6H_5Cl	1.000 0.574 0.333	0.945 0.548 0.320
21	$CH_2=CHCH_2Br$	n-C_7H_{16}	0.990 0.506 0.323	0.694 0.365 0.228
31	2-BrC_4H_9	C_6H_5Cl	2.858 1.877 0.428	2.642 1.724 0.405
28	n-C_7H_{16}	C_6H_5Cl	0.977 0.472 0.000	1.099 0.537 0.000
29	m-$BrC_6H_4CH_2Br$	n-C_7H_{16}	1.071 0.494 0.000	1.178 0.539 0.000
35	$BrCCl_3$	C_6H_5Cl	0.993 0.494 0.298	0.940 0.434 0.230

Table XVI (continued)

Curve No.	Substrate	Internal Standard	Mmoles Substrate/ Mmoles I.S.	Peak Area Substrate/ Peak Area I.S.
30	C_6H_6	C_6H_5Cl	0.640	0.491
			0.411	0.330
			0.000	0.000
26	n-C_8H_{16}	n-C_7H_{14}	0.956	1.033
			0.491	0.538
			0.000	0.000
32	$CH_2{=}CHCH_2Cl$	C_6H_5Cl	1.005	0.883
			0.530	0.460
			0.000	0.000
27	$HC{\equiv}C\text{-}CH_2Cl$	n-C_7H_{16}	1.007	0.631
			0.487	0.315
			0.000	0.000
38	$C_6H_5CH_3$	n-C_7H_{16}	0.728	0.515
			0.461	0.327
			0.000	0.000
39	m-$CF_3C_6H_4CH_3$	n-C_7H_{16}	1.000	0.894
			0.660	0.575
			0.000	0.000


Internal Standard Curve No. 18
Area $C_6H_5CH_3$/Area n-C_7H_{16}
1.0
0.8
0.6
0.4
0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
Moles $C_6H_5CH_3$ x 10^3/Moles n-C_7H_{16} x 10^3


Internal Standard Curve No. 23
Area $BrCH_2Cl$/Area C_6H_5Cl
1.0
0.8
0.6
0.4
0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
Moles $BrCHCl_2$ x 10^3/Moles C_6H_5Cl x 10^3

the calibration curves are given in Table XVI. Two internal standard calibration curves have been reproduced (pages 67 and 68).

EFFECT OF VARYING AMOUNTS OF OXYGEN ON RATES OF REDUCTION

Procedure.

Approximately 3.7 mmoles of n-butyl bromide and toluene (internal) standard) were weighed out in the reaction flask. To this was added 20 cc. of solvent and 3.78 mmoles of tri-n-butyltin hydride. A stopcock was attached and the flask partially immersed in a dry ice-acetone bath. The flask was attached to a system which included a vacuum pump, a manometer and a reservoir flask containing a supply of the gas to be introduced. The reaction flask was evacuated to approximately 1 mm. Oxygen was allowed to bleed into the reaction flask until the desired pressure was attained. The reservoir flask was changed and nitrogen was allowed to bleed into the reaction flask until atmospheric pressure was reached. In those cases where the atmosphere in the flask was either all nitrogen or all oxygen, the gas was introduced simply by flushing the flask with the appropriate gas. The flask was then placed in a 45°C constant temperature bath. The reactions were monitored by gas chromatography using the internal standard method.[24] Pertinent data for these experiments are given in Table XVII.

TABLE XVII

Effect of Varying Amounts of Oxygen on Rate of Reduction of n-Butyl Bromide by Tri-n-butyltin Hydride at 45°C[a]

Exp. No.	Atmosphere in Reaction Flask	Conc. I. S. (mmoles)	Initial Conc. Substrate (mmoles)	Area $n\text{-}C_4H_9Br$ / Area $C_6H_5CH_3$	Final Conc. Substrate (mmoles)	Internal Standard Curve No.	Time (Hours)	% Rxn.
1	N_2	3.78	3.72	0.843	2.93	11	22	21.2
2	Air	3.79	3.78	0.542	1.89	11	22	50.0
3	O_2	3.79	3.72	1.055	3.68	11	22	1.1
4	4% O_2[b]	3.80	3.72	0.608	2.12	11	15	42.4
5	10% O_2[b]	3.90	3.69	0.432	1.56	11	15	54.5
6	20% O_2[b]	3.81	3.55	1.004	3.42	11	15	0.8
7	31% O_2[b]	3.82	3.76	1.028	3.69	11	15	1.8

[a] Internal standard was toluene; 20 ml. of chlorobenzene used as solvent.

[b] Remainder of the atmosphere was prepurified nitrogen.

After sampling each reaction, the flasks were either exposed to air for about one minute or adjusted to contain approximately 4% oxygen by freezing procedure outlined above. Data obtained for these experiments are continued below (Table XVII continued).

TABLE XVII (continued)

Exp. No.	Atmosphere in Reaction Flask	Area n-C_4H_9Br / Area $C_6H_5CH_3$	Final Conc. n-C_4H_9Br	Additional Time (Hours)	Percent Reaction
1	Exposed to air	0.473	1.66	18	55.4
2	Exposed to air	0.416	1.45	18	61.6
3	Exposed to air	1.061	3.68	18	1.1
4	4% O_2[a]	0.319	1.11	35	70.9
5	4% O_2[a]	0.332	1.20	35	64.0
6	4% O_2[a]	0.533	1.87	35	44.4
7	4% O_2[a]	0.518	1.83	35	51.1

[a] Remainder of the atmosphere was prepurified nitrogen.

REDUCTION OF PROPARGYL BROMIDE; DETERMINATION OF PROPYNE AND ALLENE

Procedure.

Propargyl bromide and tri-n-butyltin hydride (about 3.8 mmoles) were allowed to react in a flask which was connected to a gas burette. Three different procedures were used. In two cases the hydride was placed in the reaction flask, the system closed and propargyl bromide introduced with a hypodermic syringe through a rubber septum. In one

case the atmosphere was nitrogen and in the other case the atmosphere was air. In the third case, the atmosphere was nitrogen but the order of addition of reactants was reversed. The gaseous products were trapped in the gas burette. An infrared spectrum was determined for the products in the first two cases (spectra nos. 3444, 3479). Propyne and allene were identified by comparison of the infrared spectra with those published in the literature for the two compounds.[37] In the third case, the products were analyzed by gas chromatography using an 11 foot column packed with 17% nitrile silicone fluid on Chromosorb P (42-60 mesh). A comparison of the peak areas indicated that the mixture contained 84% propyne and 16% allene. The area ratio for propyne to allene was 14.9/2.86. The possibility of bromoallene being an impurity in the propargyl bromide was eliminated by determining the infrared spectrum for the starting material (spectrum no. 4692). There was no indication of any allene bond present.

CATALYSIS BY AZOBISISOBUTYRONITRILE

Procedure.

Samples of the organic halide were weighed in two flasks. Azobisisobutyronitrile was added to one of the flasks and 4 ml. of solvent was added to each flask. Tri-n-butyltin hydride was added to one flask and several one ml. aliquots were sealed in ampoules after flushing with nitrogen. Tri-n-butyltin hydride was added to the second flask and the process repeated. All ampoules were then placed in an oil bath at 80±2°C. After various time intervals, ampoules were removed and the

solutions were examined by gas chromatography using a two foot column packed with 20% silicone rubber on Chromosorb P (60-80 mesh). Percent reaction was arrived at by a comparison of product and reactant peak areas. In cases where the substrate was in large excess, an internal standard was added in order to determine the extent of reaction. The data pertinent to these experiments are given in Tables XVIII and XIX.

HYDRIDE CARRIER EXPERIMENTS

Procedure.

An ether solution of cyclohexyl bromide and the organotin chloride to be tested were placed in a flask equipped with a stirrer, reflux condenser and a heating mantle. An excess of an ether solution of lithium aluminum hydride was added by means of a syringe. In cases where it was known that the organotin hydrides were relatively unstable, a nitrogen atmosphere was maintained over the solution. This was done with phenyltin trichloride, butyltin trichloride and stannic chloride. The solution was allowed to reflux. After various time intervals, samples were removed and introduced into a test tube containing water and immersed in an ice bath. After the hydrolysis was complete, a few drops of ether was added to the test tube. The test tube was stoppered and shaken and the layers allowed to separate. A sample was drawn from the ether layer and investigated using gas chromatography. A two-foot column packed with 20% silicone rubber on Chromosorb P (60-80 mesh) was used. The percent reaction was arrived at by a comparison of product and reactant peak heights. The data

TABLE XVIII

Tri-n-butyltin Hydride Reduction of Organic Halides Catalyzed by Azobisisobutyronitrile

Exp. No.	Substrate	Solvent[a]	Internal Standard	Mmoles Internal Standard	Mmoles Initiator	Mmoles Tri-n-butyltin Hydride	Mmoles Substrate Uninitiated	Mmoles Substrate Initiated
1	$C_6H_5CH_2Cl$	C_6H_5Cl	-	-	0.061	3.78	3.80	3.80
2	Cyclo-$C_6H_{13}Cl$	$C_6H_5CH_3$	-	-	0.061	3.78	3.77	3.73
3	C_6H_5Br	$C_6H_5CH_3$	-	-	0.067	3.78	3.76	3.83
4	C_6H_5Br	$C_6H_5CH_3$	-	-	0.134	3.78	-	3.74
5	C_6H_5Cl	$C_6H_5CH_3$	-	-	0.067	3.78	3.82	3.75
6	C_6H_5Cl	-	-	-	0.304	3.78	-	48.8
7	C_6H_5Cl	-	$C_6H_5CH_3$	3.99	0.346	3.78	-	48.8
8	C_6H_5Cl	-	$C_6H_5CH_3$	3.67	0.906	4.91	-	48.8

[a] 4 ml. of solvent was used.

TABLE XIX

Extent of Reduction of Organic Halides by Tri-n-Butyltin Hydride Catalyzed and Uncatalyzed

Exp. No.	Substrate	Reaction Time (Minutes)	Uninitiated Reaction: Peak Area Product / (Peak Area Reactant + Peak Area Product) Uninitiated	Uninitiated Reaction: Percent[a] Reaction	Initiated Reaction: Peak Area Product / (Peak Area Reactant + Peak Area Product) Initiated	Initiated Reaction: Percent Reaction
1	$C_6H_5CH_2Cl$	30	0.218	26	.853	90 - 100
		60	0.305	36	.854	90 - 100
		570	0.665	78	-	-
2	Cyclo-$C_6H_{13}Cl$	35	-	1	0.658	69
		70	0.009	1	0.845	89
		185	-	-	0.947	100
		2880	0.097	10.2	-	-
3	C_6H_5Br	30	0.047	4.7	0.410	41
		70	0.067	6.7	0.584	58
		210	0.131	13.1	0.695	69
		690	0.133	13.3	0.727	73
4	C_6H_5Br	1880	-	-	0.904	90
		2195	-	-	0.895	89
5	C_6H_5Cl	30	-	No Rxn.	-	No Rxn.
		610	-	-	0.013	1.3
		2275	-	No Rxn.	-	-

Table XIX (continued)

Exp. No.	Substrate	Reaction Time (Minutes)	Uninitiated Reaction: Peak Area Product / (Peak Area Reactant + Peak Area Product) Uninitiated	Uninitiated Reaction: Percent[a] Reaction	Initiated Reaction: Peak Area Product / (Peak Area Reactant + Peak Area Product) Initiated	Initiated Reaction: Percent Reaction
6	C_6H_5Cl	1280	-	-	0.360	36
7	C_6H_5Cl	1140	-	-	0.312	40.2
		2430	-	-	0.281	36.1
8	C_6H_5Cl	1290	-	-	0.656	75.9

[a] In experiments 1-5, the percent reaction was determined by comparing the peak areas of the organic halide and its reduction product; in experiment 6, the peak areas of organotin hydride and organotin halide was compared; in experiments 7 and 8, the peak areas of the reduction product and an internal standard ($C_6H_5CH_3$) were compared.

pertinent to these experiments are presented in Table XX.

INHIBITION BY HYDROQUINONE

Procedure.

Preliminary experiments were conducted by weighing in two flasks the substrate to be reduced. Hydroquinone was added to one of the flasks followed by the solvent to both flasks. Tri-n-butyltin hydride was introduced into each of the flasks with a pipette. Several 1 ml. aliquots were removed from each flask and sealed in ampoules which had been flushed with nitrogen before sealing. The ampoules were then placed in an oil bath at $80 \pm 2^{\circ}C$. The initial experiment which demonstrated that hydroquinone could act as an inhibitor was conducted in the presence of azobisisobutyronitrile.

The experiments using benzyl chloride as a substrate were repeated in a manner which avoided sealing aliquots in ampoules. The method consisted of placing in two flasks the substrate and the solvent, adding the hydroquinone to one of the flasks and tri-n-butyltin hydride to both. The reaction flasks had two stopcocks attached in such a manner that the reaction mixture could be sampled while nitrogen continuously flowed through the system during the process of sampling. When the sampling was complete, the stopcocks were closed. The reactions were run in an oil bath at $80 \pm 2^{\circ}C$. Experiments involving benzyl chloride were quenched by destroying tri-n-butyltin hydride with concentrated sulfuric acid. This was done because it was determined that appreciable reaction was taking place after a sample was introduced into the gas

TABLE XX

Reduction of Bromocyclohexane by Organotin Hydrides

Generated *in situ* by Lithium Aluminum Hydride[a]

Exp. No.	Organotin Halide	Mmoles Organotin Halide	Moles Bromocyclo-hexane	Moles $LiAlH_4$	Reaction Time (minutes)	Peak Height Product / (Peak Height Reactant + Peak Height Product)	Percent Reaction
1	-	-	0.030	0.016	100	0.006	1.0
					185	0.006	1.0
					1450	0.011	1.0
					2645	0.014	1.4
2	Triphenyltin Chloride	0.771	0.030	0.015	30	0.181	18.0
					150	0.797	80.0
					240	0.829	83.0
					300	0.805	80.0
3	Tri-n-butyltin chloride	0.770	0.030	0.016	45	0.009	1.0
					230	0.056	5.6
					1610	0.472	47.0
4	Diphenyltin Dichloride	0.763	0.030	0.018	30	0.224	22.0
					65	0.635	64.0
					110	0.893	89.0
					145	0.925	92.0
					175	0.901	90.0
					1290	0.958	96.0

Table XX (continued)

Exp. No.	Organotin Halide	Mmoles Organotin Halide	Moles Bromocyclo-hexane	Moles $LiAlH_4$	Reaction Time (minutes)	Peak Height Product / Peak Height Reactant + Peak Height Product	Percent Reaction
5	Dibutyltin Dichloride	0.765	0.030	0.018	40	0.074	7.0
					95	0.159	16.0
					155	0.388	39.0
					230	0.516	52.0
					315	0.646	65.0
					780	0.802	80.0
					1380	0.879	88.0
6	Phenyltin[b,c] Trichloride	0.807	0.030	0.018	30	0.067	6.7
					70	0.053	5.3
					120	0.056	5.6
					180	0.061	6.1
7	Butyltin[c] Trichloride	0.802	0.030	0.018	35	0.222	22.0
					60	0.714	71.0
					90	0.986	99.0
					195	0.896	90.0
8	Stannic[c,d] Chloride	0.750	0.030	0.018	30	0.007	1.0
					90	0.007	1.0

[a] In 25 ml. refluxing diethyl ether

[b] The reaction mixture turned red and then black within 15 minutes.

[c] Reaction mixture kept over nitrogen atmosphere

[d] Within 30 minutes the reaction mixture turned black

chromatograph. After the hydride was destroyed the organic layer was washed with water and dried over potassium carbonate.

Extents of reaction were determined by gas chromatography using a four foot column packed with 20% paraffin oil on Chromosorb P (80-100 mesh). In experiments involving chlorocyclohexane as substrate, reduction product and internal standard peak heights were compared. For experiments involving benzyl chloride, the internal standard method was used[24] and the concentration of reduction product was determined. Pertinent data for these experiments are summarized in Tables XXI and XXII.

REDUCTION OF γ-CHLOROBUTYROPHENONE BY TRI-n-BUTYLTIN HYDRIDE

The reaction was conducted in a 100 ml. flask fitted with a stirrer, a pressure equalizing addition funnel, a condenser, and a nitrogen inlet tube. To the flask was added 35.7 mmoles of γ-chlorobutyrophenone and 25 ml. of anhydrous ether. The reaction flask was placed in an oil bath set for 80°C. A solution containing 37.8 mmoles of tri-n-butyltin hydride and 0.061 mmoles of azobisisobutyronitrile in 25 ml. of anhydrous ether was added over a period of ten hours. The reaction mixture was allowed to stir at 80°C for an additional 34 hours, after which time the tri-n-butyltin hydride was consumed. Distillation gave a 65% yield of ketone - ether mixture as determined by infrared spectroscopy (spectra nos. 4185, 4734). The mixture distilled over the range 66 - 74°C/0.25 mm. and 3.40 mmoles was collected. It was determined that the mixture contained 80% 2-phenyltetrahydrofuran by removing the ketone with Girard's T reagent. An infrared spectrum was

TABLE XXI

Inhibition of Tri-n-Butyltin Hydride[a]

Reduction of Alkyl Halides by Hydroquinone[b]

			Hydroquinone Present[d]			Hydroquinone Absent	
Reaction No.	Substrate	Internal Standard	Mmoles Substrate	Mmoles Internal Standard	Mmoles Hydroquinone	Mmoles Substrate	Mmoles Internal Standard
1, 2[c]	$C_6H_{11}Cl$	$C_6H_5CH_3$	3.72	3.82	0.06	3.90	3.62
3, 4	$C_6H_{11}Cl$	$C_6H_5CH_3$	3.80	3.67	0.06	3.74	3.88
5, 6	$C_6H_5CH_2Cl$	n-C_7H_{16}	3.92	3.58	0.06	3.92	3.59
7, 8	$C_6H_5CH_2Cl$	n-C_7H_{16}	3.82	3.46	0.06	3.79	3.77

[a] 3.78 mmoles tri-n-butyltin hydride used in each case

[b] Solvent - 10 cc. anisole

[c] 0.032 and 0.034 mmoles azobisisobutyronitrile used respectively in reactions numbers one and two.

[d] Odd numbered reactions contain hydroquinone.

TABLE XXII

Extent of Reaction in Inhibition Experiments[a]

Reaction No.	Substrate	Time (Min.)	Peak Area Product / Peak Area Internal Standard	Mmoles Product Formed	Percent Reaction[c]
1[b]	Cyclo-$C_6H_{11}Cl$	24	0.037	-	4
		73	0.103	-	10
		151	0.148	-	15
		220	0.185	-	18
		569	0.162	-	16
		1581	0.218	-	22
2[b]	Cyclo-$C_6H_{11}Cl$	24	0.104	-	10
		73	0.241	-	24
		151	0.350	-	35
		220	0.406	-	41
		569	0.515	-	52
		1581	0.500	-	50
3	$C_6H_5CH_2Cl$	1222	-	-	No Rxn.
4	$C_6H_5CH_2Cl$	436	0.642	2.84	75.1
		1222	0.652	2.88	76.1
5	$C_6H_5CH_2Cl$	602	-	-	No Rxn.
6	$C_6H_5CH_2Cl$	65	0.308	1.37	36.2
		127	0.425	1.86	49.2
		269	0.506	2.22	58.6
		445	0.606	2.67	70.6
		602	0.633	2.78	73.5
7	$C_6H_5CH_2Cl$	60	0.038	0.14	3.7
		185	0.155	0.64	16.9
		360	0.109	0.45	11.8
		1085	0.443	1.89	49.8
		1830	0.536	2.28	60.2
		3155	0.687	2.93	77.5
8	$C_6H_5CH_2Cl$	60	0.340	1.56	41.4
		185	0.435	2.01	53.2
		360	0.584	2.71	71.6
		1085	0.625	2.90	76.7
		1830	0.691	3.21	85.0
		3155	0.726	3.38	89.2

Table XXII (continued)

[a] Reactions 1-8 were conducted by sealing aliquots in ampoules; reactions 9 and 10 were each conducted by keeping the reaction mixture in a flask and removed aliquots at the times indicated.

[b] Percent reaction is based on a comparison of peak heights of reduction product and internal standard.

[c] Odd numbered reactions contain hydroquinone.

taken of the residue (spectra nos. 4259, 4740) and it was found to be identical with an infrared spectrum of an authentic sample of 2-phenyltetrahydrofuran. The infrared spectrum of the authentic sample was provided by Dr. R. L. Letsinger.

TRIPHENYLTIN HYDRIDE REDUCTION OF 3-CHLORO-1-BUTENE AND 1-CHLORO-2-BUTENE

The 1-chloro-2-butene was obtained by treating 3-chloro-1-butene with a small amount of ferric chloride and distilling off the more volatile isomer.

The reactions were conducted in a sealed ampoule which had a side arm attached to it. Triphenyltin hydride in slight excess and the chloride were placed in an ampoule. The ampoule was flushed with nitrogen and sealed. The chloride used in each case was contaminated by some of the isomeric chlorides as indicated in Table XXIII. The ratio of 3-chloro-1-butene and 1-chloro-2-butene present in each mixture was determined by gas chromatography using an 11 foot column packed with 17% nitrile silicone fluid on Chromosorb P (42-60 mesh). The method used was to compare peak areas. The ratio of trans- to cis-1-chloro-2-butene was approximated using infrared spectroscopy. The infrared spectrum of each stereoisomer has been published by Hatch and Nesbitt.[22] A band which was characteristic for each isomer was found, i.e. 695 cm^{-1} for the trans isomer and 768 cm^{-1} for the cis isomer. These spectra were determined in the gas phase and at different concentrations, i.e. 50 mm. for the trans and 60 mm. for the cis. The area of each characteristic band was calculated by multiplying the height of the band by the width

TABLE XXIII

Composition of Isomeric Chloride

Reaction I	Before Start of Reaction		After Standing over Triphenyltin Chloride	
Chloride	Peak Area	Relative %	Peak Area	Relative %
3-Chloro-1-butene	13.41	86.0	12.21	76.2
cis-1-Chloro-2-butene	2.20	2.5	3.51	23.8[a]
trans-1-Chloro-2-butene		11.5		

Reaction II	Before Start of Reaction		After Standing Over Triphenyltin Chloride	
Chloride	Peak Area	Relative %	Peak Area	Relative %
3-Chloro-1-butene	1.19	9.5	1.37	10.7
cis-1-Chloro-2-butene	11.42	16.2	11.50	89.3[a]
trans-1-Chloro-2-butene		74.3		

[a] This figure represents the combined percentage of both cis- and trans- 1-chloro-2-butene.

at the mid-point. The area of the cis- isomer was multiplied by 0.83 to correct for the concentration difference. One now has the ratio of the peak areas when the ratio of the concentrations is unity. The infrared spectrum of a mixture of isomeric chlorides containing predominantly 1-chloro-2-butene was determined as a smear (spectrum no. 4487). The mixture was obtained by ferric chloride isomerization of 3-chloro-1-butene followed by the addition of potassium carbonate and distillation. The fraction boiling above 80°C was collected. The areas of the two characteristic bands were calculated. Knowing the ratio of the peak areas when the ratio of the concentrations was unity, we were able to calculate the ratio of trans- to cis-1-chloro-2-butene present in this mixture. It is assumed that the relative areas of the two bands being used do not change in going from the gaseous phase to the liquid phase.

During the course of the reaction a sample of each of the isomeric chlorides was stored over triphenyltin chloride in order to observe whether triphenyltin chloride can induce isomerization. The reduction was allowed to continue for forty days. After this period, the ampoule side arm was immersed in liquid nitrogen to condense the gaseous products. The side arm was opened and the composition of the products were determined by gas chromatography using a 15 foot column packed with 40% dimethyl sulfolane on firebrick (40 mesh). Results are given in Table XXIV.

PREPARATION OF m-TRIFLUOROMETHYLBENZYL CHLORIDE

Preparation of m-trifluoromethylbenzyl alcohol. A dry one liter three necked round-bottomed flask was equipped with a stirrer, a 500 ml.

TABLE XXIV

Composition of Isomeric Butenes

Reaction I

Butene	Peak Area	Relative %
1-Butene	7.69	26.8
	6.85	27.2
trans-2-Butene	16.98	59.4
	14.81	59.0
cis-2-Butene	3.94	13.8
	3.47	13.8

Reaction II

Butene	Peak Area	Relative %
1-Butene	4.22	27.4
	7.51	26.4
trans-2-Butene	7.51	61.2
	16.81	61.0
cis-2-Butene	1.85	11.4
	3.13	11.6

addition funnel and a reflux condenser which is fitted with a calcium chloride drying tube. In the flask was placed 10.7 g. (0.44 moles) of magnesium turnings, a crystal of iodine and 20 ml. of dry ether. A solution of 100 g. (0.44 moles) of m-trifluoromethylbromobenzene in 340 ml. of dry ether was added with stirring. The reaction started spontaneously. The addition took one hour. The mixture was stirred and heated in an 80°C oil bath for one hour after addition was complete.

The addition funnel was then replaced by a piece of 10 mm. glass tubing which reached almost to, but not below, the surface of the liquid. This tube was connected directly to a 250 ml. round-bottom flask containing 50 g. of paraformaldehyde which had been previously dried for two days in a vacuum desicator over phosphorous pentoxide. This flask contained an inlet tube for admitting prepurified nitrogen. The stirrer was started and the flask containing the paraformaldehyde was heated in an oil bath at 200°C. The formaldehyde formed by depolymerization is carried over into the Grignard reagent by a slow current of prepurified nitrogen. After two hours the reaction was complete, as indicated by a negative color test with Michler's ketone.

The reaction mixture was then cooled in ice, and hydrolyzed by adding dropwise 100 ml. of a 25% solution of ammonium chloride in water. The ether solution is filtered and the solid residue was washed with 100 ml. of ether. The ether fractions are combined and dried over sodium sulfate. The ether was stripped off and the product distilled under reduced pressure to give 60.0 g. (78%) of m-trifluoromethylbenzyl alcohol boiling at 77-78°C/0.8 mm.

Preparation of m-trifluoromethylbenzyl chloride. In a 100 ml. round-bottomed flask, fitted with a stirrer, an addition funnel, a condenser fitted with a calcium chloride drying tube and a thermometer, were placed 20 g. (0.11 moles) of m-trifluoromethylbenzyl alcohol and 9.5 g. (0.12 moles) of pyridine. To the rapidly stirred mixture, which is cooled in an ice bath, was added 14.3 g. (0.12 moles) of thionyl chloride. Addition lasted one-half hour and the temperature was not allowed to go above 60°C. The mixture was stirred for 2.5 hours at room temperature after the addition was complete. The mixture was poured into a separatory funnel and extracted seven times with 50 ml. portions of ether. The ether extracts were combined. The ether was removed using a Rinco evaporator and the residue was washed three times with 25 ml. portions of water, dried over calcium chloride and distilled under reduced pressure. The yield of m-trifluoromethylbenzyl chloride boiling at 44-45°C/0.85 mm. was 10.1 g. (47%) (infrared spectrum no. 4874, proton magnetic resonance spectrum no. 134).

PREPARATION OF m-METHYLBENZOTRIFLUORIDE

A small amount of m-methylbenzotrifluoride was isolated by reacting m-trifluoromethylbenzyl chloride with tri-n-butyltin chloride in the presence of azobisisobutyronitrile at 80°C. Distillation at atmospheric pressure yield m-methylbenzotrifluoride, micro boiling point 128.2°C (reported 127°C)[38], (proton magnetic resonance spectrum no. 135).

SUMMARY

The scope of the organotin hydride reduction of alkyl halides has been expanded. Reactions proceed in good yields. The selectivity of the hydride has been demonstrated by reducing functionally substituted alkyl halides and observing selective removal of the halogen atom. Also, in the case of geminal polyhalides, stepwise reduction occurs so that one can selectively remove one or more of the halogen atoms. The reduction of less reactive halides can be effected by the addition of a small amount of azobisisobutyronitrile which exerts a profound catalytic effect on the reaction. A "hydride carrier" method of reduction which avoids the prior preparation and isolation of the organotin hydride has been developed.

The mechanism of the reduction has been investigated. The formation of an alkyl fragment has been demonstrated. The reaction is subject to free radical catalysis and inhibition. The effect of structure on reactivity has been investigated. In addition to being consistent with the free radical mechanism, this study also demonstrated the influence of an important polar effect for this reduction. Finally, trapping of the alkyl radical was accomplished. All the evidence obtained is consistent with a free radical chain process.

BIBLIOGRAPHY

1. P. C. Carey and J. C. Smith, J. Chem. Soc., 1933, 346.

2. L. Horner, L. Schlafer and H. Kammerer, Chem. Ber., 92, 1700 (1959).

3. J. W. H. Oldham and A. R. Ubbelohde, J. Chem. Soc., 1938, 201.

4. E. Johnson, R. H. Blizzard and H. W. Corhart, J. Am. Chem. Soc., 70, 3664 (1948).

5. R. E. Lutz, R. J. Wayland, Jr., and H. G. France, J. Am. Chem. Soc., 72, 5511 (1950).

6. S. J. Cristol, J. W. Ragsdale and J. S. Meek, J. Am. Chem. Soc., 71, 1863 (1949).

7. G. J. M. van der Kerk, J. G. Noltes and J. G. A. Luijten, J. Appl. Chem., 7, 356 (1957).

8. J. G. Noltes and G. J. M. van der Kerk, "Functionally Substituted Organotin Compounds", Tin Research Institute, Greenford, England, 1956, p. 72.

9. J. G. Noltes and G. J. M. van der Kerk, Chem. and Ind. (London), 1959, 294.

10. E. J. Kupchik and R. C. Connolly, J. Org. Chem., 26, 4747 (1961).

11. D. H. Lorenz and E. I. Becker, J. Org. Chem., 27, 3370 (1962).

12. E. J. Kupchik and R. J. Kiesel, Chem. and Ind. (London), 1962, 1654.

13. H. G. Kuivila, L. W. Menapace and C. R. Warner, J. Am. Chem. Soc., 84, 3584 (1962).

14. D. Seyferth, H. Yamazaki and D. L. Alleston, J. Org. Chem., 28, 703 (1963).

15. H. G. Kuivila in F. G. A. Stone and R. West, Advances in Organometallic Chemistry, Vol. I, Academic Press, New York, New York, in press.

16. O. F. Beumel, Jr., Doctor of Philosophy Thesis, University of New Hampshire (1960).

17. W. P. Neumann and H. Nierman, Ann. Chem., 653, 164 (1962).

18. L. A. Rothmann and E. I. Becker, J. Org. Chem., 25, 2203 (1960).

19. J. Curtice, H. Gilman and G. S. Hammond, J. Am. Chem. Soc., 79, 4754 (1957).

20. C. Walling and W. Thaler, J. Am. Chem. Soc., 83, 3877 (1961).

21. P. D. Bartlett, Eighteenth National Organic Symposium of the American Chemical Society, June 16-20, 1963.

22. L. W. Hatch and S. S. Nesbitt, J. Am. Chem. Soc., 72, 727 (1950).

23. H. G. Kuivila, private communication.

24. A. I. M. Keulemans, Gas Chromatography, Reinhold Publishing Corporation, New York, 1957, pp. 32-33.

25. C. K. Ingold and F. R. Stow, J. Chem. Soc., 1927, 2918.

26. A. Streitwieser, Jr., Chem. Revs., 56, 616, 653 (1956).

27. F. W. Evans, R. J. Fox and M. Szwarc, J. Am. Chem. Soc., 82, 6414 (1960). R. J. Fox, F. W. Evans and M. Szwarc, Trans. Faraday Soc., 57, 1915 (1961).

28. A. F. Daggett and W. B. Meldrum, Quantitative Analysis, D. C. Heath and Company, Boston, Mass., 1955, p. 119.

29. C. Walling, Free Radicals in Solution, John Wiley and Sons, Inc., New York, N. Y., 1957, p. 365.

30. C. Walling and B. B. Jacknow, J. Am. Chem. Soc., 82, 6113 (1960).

31. E. L. Patmore and R. J. Gritter, J. Org. Chem., 27, 4196 (1962).

32. G. A. Russel, J. Org. Chem., 23, 1407 (1958).

33. H. G. Kuivila and E. J. Walsh, Jr., private communication.

34. T. J. Wallace and R. J. Gritter, J. Org. Chem., 27, 3067 (1962).

35. H. G. Kuivila and O. F. Beumel, Jr., J. Am. Chem. Soc., 83, 1246 (1961).

36. W. J. Considine and J. J. Ventura, Chem. and Ind., 1683 (1962).

37. R. C. Lord and P. Venkateswarlu, J. Chem. Phy., 20, 1237 (1952); R. H. Pierson, A. N. Fletcher and E. St. Clair Gantz, Anal. Chem. 28, 1218 (1956); American Petroleum Institute Research Project 44, Infrared Spectrum No. 45.

38. J. Wender, H. Greenfield, S. Metlin and M. Orchen, J. Am. Chem. Soc., 74, 4079 (1952).