On the Mechanism of the Reduction of Some Ketones by Organotin Hydrides. Hydride Transfer, Electron-Transfer–Hydrogen-Atom Abstraction, or Free Radical Addition

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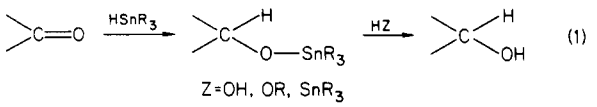
Three aromatic–aliphatic ketones, cyclopropyl phenyl ketone, α,α,α-trifluoroacetophenone, and α-fluoroacetophenone, are reduced by triphenyltin hydride by an initiated homolytic reaction to yield organic stannoxides. The reactivity is not markedly dependent upon solvent polarity. The uninitiated reduction with triphenyltin hydride of the more reactive electronegatively substituted fluorinated alkyl–aromatic ketones show a solvent-dependent reactivity. The reactivity increases as the solvent becomes more polar. Both homolytic and heterolytic processes occur in the more polar solvents. The homolytic reaction appears to be initiated by an electron-transfer process, and the propagation sequence, likewise, contains an electron-transfer step. It appears that in the propagation step the donor–acceptor ability of the reagents determine whether the homolytic reaction proceeds by a radical addition of a tin radical to the carbonyl oxygen or whether electron transfer occurs prior to tin–oxygen bond formation. A consideration of the timing of these processes suggests a merged mechanism where the donor–acceptor ability of the reagents determines the extent of electron transfer in or after the transition state.

Recently the homolytic chemistry of trialkyltin hydride reductions with a variety of substrates has been proposed to involve an electron-transfer process in both its initiation and chain propagation reactions. A free radical mechanism, involving electron transfer, was suggested for the reduction of benzyl iodides with tri-*n*-butyltin hydride in solvent benzene.[3] Subsequentyly, the results of a study of the reduction of methyl iodide by trialkyltin hydrides have been interpreted by an electron-transfer mechanism.[4] More recently, the replacement of the nitro group for a hydrogen in tertiary nitro compounds, using tri-*n*-butyltin hydride under free radical conditions, was shown to proceed by electron transfer.[5] Since the electron-transfer process appears to be involved in tin hydride reductions, it was of interest to reexamine the reduction of some organic carbonyl compounds by these reagents.

The reduction of aldehydes and ketones to their corresponding alcohol by organotin hydrides is well documented.[6-15] The synthetic utility of this reaction has, likewise, been demonstrated.[16,17] The yields obtained from the reductions, carried out in either neat solutions or in a variety of solvents, are usually high.

It is generally accepted that the reduction of ketones may proceed by either homolytic or heterolytic pathways. In both cases the process involves a formal addition of $HSnR_3$ to the carbonyl group to generate an alkoxystannane which upon hydrolysis, solvolysis, or hydrostannolysis, gives the corresponding alcohol.[13,18,19]



(1)

Z=OH, OR, SnR_3

The heterolytic mechanism, which involves a hydride transfer, was initially suggested by Newmann and Heymann[9] and subsequently confirmed by other workers.[8] This pathway was proposed to explain the observations that the rate of reduction increased with increasing solvent polarity and that electron-releasing substituents at tin and electron-withdrawing substituents adjacent to the carbonyl group, likewise, increased the rate of reduction. The reactions were found to be catalyzed by $ZnCl_2$ and by protic acids. Reactions conducted in solvent methanol, in the absence of light or AIBN (a radical initiator), were not affected by the presence of galvinoxyl (a radical inhibitor). The homolytic pathway has been shown to be initiated by either light or AIBN and is proposed to involve a free radical chain addition.[9,15]

During the course of a systematic study of the reactions of several ketones with trialkyltin hydrides, the half-wave reduction potentials of some ketones and trialkylstannyl cations were estimated.[20] The importance of the electron-donor and electron-acceptor properties of the reactants upon their propensity to react was substantiated. This relationship is a necessary, but not sufficient, requirement for an electron-transfer process, since the other proposed mechanisms also fit this requirement. It was concluded from the electrochemical results that the tri-*n*-butylstannyl radical would be harder to oxidize than the triphenylstannyl radical (from the measurement of the reduction of their cations, $\Delta G_{1/2} = 0.08$ V). In accord with

(1) Taken in part from the Ph. D. Disstertation of G. E. Diaz, University of Alberta, Demonton, Alberta 1983.
(2) Postdoctoral Fellow, University of Alberta, 1982–84.
(3) Blackburn, E. V.; Tanner, D. D. *J. Am. Chem. Soc.* **1980**, *102*, 692.
(4) Tamblyn, W. H.; Vogler, E. A.; Kochi, J. K. *J. Org. Chem.* **1980**, *45*, 3912.
(5) Tanner, D. D.; Blackburn, E. V.; Diaz, G. E. *J. Am. Chem. Soc.* **1981**, *103*, 1557.
(6) Van der Kerk, G. J. M.; Noltes, J. C. *J. Appl. Chem.* **1959**, *9*, 106.
(7) Leusink, A. J.; Budding, H. A.; Drenth, W. *J. Organomet. Chem.* **1968**, *13*, 163.
(8) Leusink, A. J.; Budding, H. A.; Marsman, J. M. *J. Organomet. Chem.* **1968**, *13*, 155.
(9) Newmann, W. P.; Heymann, E. *Justus Leibigs, Ann. Chem.* **1965**, *683*, 11.
(10) Quintard, J. P.; Pereyre, M. J. *J. Organomet. Chem.* **1974**, *82*, 103.
(11) Brimage, D. R. G.; Davidson, R. S.; Lambeth, P. F. *J. Chem. Soc.* **1971**, 1241.
(12) Cullen, W. R.; Styan, G. E. *Inorg. Chem.* **1965**, *4*, 1437.
(13) Quintard, J. P.; Pereyre, M. *Bull. Soc. Chim. Fr.* **1972**, 1950.
(14) Pommier, J. C.; Valade, J. *Bull Soc. Chim. Fr.* **1965**, 975.
(15) Pereyre, M.; Valade, J. *C.R. Acad. Sci. Paris* **1965**, *258*, 4785; **1965**, *260*, 581.
(16) Kuivila, H. G.: Beumal, O. F., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1246.
(17) Kuivila, H. G. *Synthesis* **1970**, *2*, 499.
(18) (a) Creemers, H. M. J. C.; Verbeek, F.; Noltes, J. G. *J. Organomet. Chem.* **1967**, *8*, 469. (b) Creemers, H. M. J. C.; Noltes, J. C. *Recl. Trav. Chim. Pays-Bas* **1964**, *84*, 1589.
(19) Pereyre, M.; Godet, J. Y. *Tetrahedron Lett.* **1970**, *42*, 3653.
(20) Ph.D. Thesis. G. E. Diaz, University of Alberta, 1983.

0022-3263/85/1950-2149$01.50/0

Table I. Reduction of α,α,α-Trifluoroacetophenone with Triphenyltin Hydride

reaction[a]	solvent	conditions[b]	% product yield: $CF_3CH(OH)Ph$	% product yield: unreacted ketone
1	benzene		4.4 ± 0.7	91.0 ± 0.5
2	benzene	*m*-DNB (6%)	traces	95.1 ± 1.4
3	benzene	AIBN (4%)	90.6 ± 0.2	8.4 ± 0.4
4	acetonitrile		31.6 ± 3.4	62.6 ± 1.6
5	acetonitrile	*m*-DNB (6%)	10.0	71.0
6	acetonitrile	AIBN (4%)	61.5 ± 1.2	34.3 ± 1.8
7	methanol		66.3 ± 6.8	32.6 ± 5.4
8	methanol	*m*-DNB (6%)	38.7 ± 1.8	57.5 ± 1.2
9	methanol	AIBN (4%)	68.4 ± 3.8	28.8 ± 1.7

[a] A mole ratio of 1:1 of ketone and triphenyltin hydride was used. [b] All reactions were run at 61 °C.

this observation triphenyltin hydride has been demonstrated to be more reactive than tri-*n*-butyltin hydride in reducing ketones to their corresponding alcohols. When electron-withdrawing groups are present the ketones had, as expected,[21] a lower reduction potential: acetophenone, $E_{1/2}$ = −2.61 V; α-fluoroacetophenone, $E_{1/2}$ = −2.05 V; α,α,α-trifluoroacetophenone, $E_{1/2}$ = −2.00 V.[20]

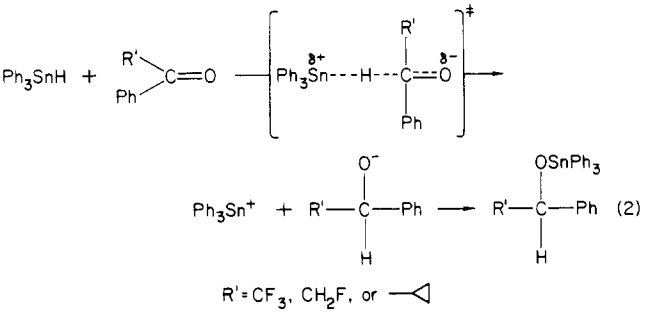
Preliminary experiments from this laboratory[20] showed that acetophenone is unreactive with trialkyltin hydride in the absence of light or a radical initiator. However, under the same conditions α-fluoroacetophenone reacted readily to form two products, not only α-(fluoromethyl)-benzyl alcohol but also a second unexpected product, acetophenone. Similarly, α,α,α-trifluoroacetophenone reacted readily to produce the corresponding trifluoro alcohol. Cyclopropyl phenyl ketone had been shown by Pereyre and Godet[19,22,23] to react with trialkyltin hydrides to yield two products, butyrophenone proposed to be the sole product of a radical reaction and cyclopropylbenzyl alcohol which was proposed to arise by a slower ionic process. Cyclopropyl phenyl ketone was therefore chosen as another mechanistic probe for the processes involved in carbonyl reduction by trialkyltin hydride. A detailed study of the reduction of α,α,α-trifluoroacetophenone, α-fluoroacetophenone, and cyclopropyl phenyl ketone is the subject of this paper.

Results and Discussion

Reduction of α,α,α-Trifluoroacetophenone. The reduction of α,α,α-trifluoroacetophenone to α-(trifluoromethyl)benzyl alcohol can be effected by triphenyl- or tri-*n*-butyltin hydride. As anticipated from the measurement of reduction potentials, triphenyltin hydride is more reactive than tri-*n*-butyltin hydride. In order to observe the effect of changes in reaction conditions, the reactions were carried out in a manner such that incomplete reaction occurred (61 °C; over 16 h; in solvents of different polarity, benzene, acetonitrile, and methanol; with or without a radical inhibitor, *m*-dinitrobenzene, *m*-DNB). The yields of products and unreacted starting materials were determined by GLPC (see Table I).

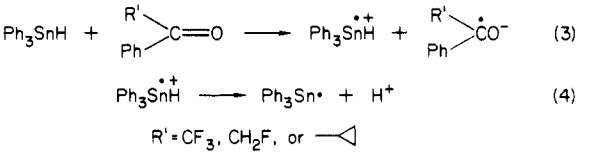
In the absence of an initiator *or* radical inhibitor in solvents benzene, acetonitrile, or methanol, the corresponding alcohol was formed in increasing yields as the solvent polarity increased (reactions 1, 4, and 7; Table I). When the reactions were repeated in the presence of 6% *m*-dinitrobenzene, the yields of the product alcohol were substantially reduced (reactions 2, 5, and 8). The dependence of solvent polarity upon reactivity suggests that

Scheme I. Hydride-Transfer Process

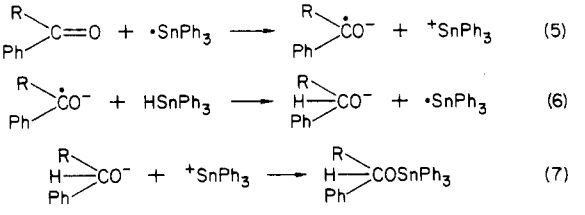


Scheme II

a. Electron-Transfer Initiation Process



b. Electron Transfer-Hydrogen Abstraction Process



either ionic intermediates or radical ions produced from an electron-transfer process are involved. The partial inhibition of the reaction by a well-documented[5,24] radical and/or electron-transfer inhibitor, *m*-DNB, indicates that the reaction must follow, at least in part, a radical or radical ion mechanism. Previous reports[8,10,13] on the reductions of ketones in methanol concluded that the products were formed by a hydride transfer process (see Scheme I). The partial inhibition of an uninitiated reduction is, however, inconsistent with the proposal that the reaction proceeds solely by a hydride-transfer process. However, competing homolytic and heterolytic pathways can be invoked to explain the less than complete inhibition of the reaction by *m*-DNB in the more polar solvents.

Since the thermal homolysis of the tin–hydride bond ($D(R_3Sn–H)$ = 65.0 kcal/mol) is not significant under the reaction conditions (61 °C), an alternative radical initiation process is necessary to explain the thermal radical reduction reaction.[3] By analogy with the initiation step proposed for the reduction of benzyl iodides and tertiary

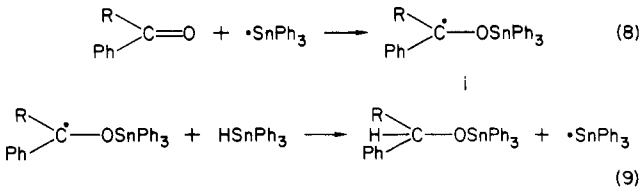
(21) Zuman, P.; Barnes, D.; Ryvolvá-Kejharova, A. *Discuss. Faraday Soc.* **1968**, *45*, 203.
(22) Godet, J. Y.; Pereyre, M. *J. Organomet. Chem.* **1972**, *40*, C23.
(23) Godet, J. Y.; Pereyre, M. *C.R. Acad. Sci. Paris.* **1973**, *277*, 211.
(24) Kornblum, N. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 734.

Table II. Reduction of α-Fluoroacetophenone with Triphenyltin Hydride

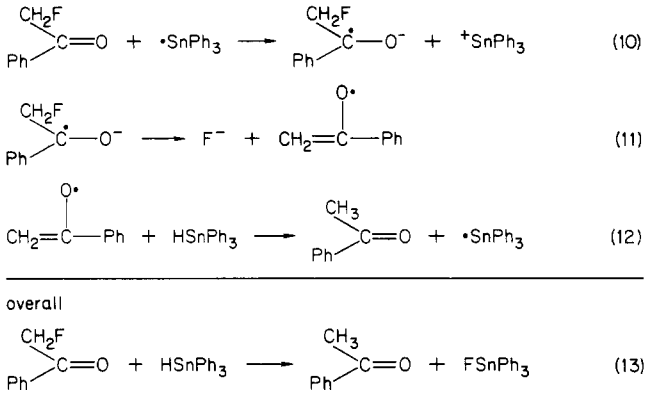
reaction[a]	solvent	conditions	% product yield: $CH_3\overset{O}{\overset{\|}{C}}Ph$	% product yield: $H_2FC\overset{OH}{\overset{\|}{C}}HPh$	% product yield: unreacted ketone
1	benzene		4.9 ± 0.0	1.2 ± 0.1	91.0 ± 0.6
2	benzene	*m*-DNB (6%)	traces	traces	99.0 ± 0.6
3	benzene	AIBN (4%)	87.0 ± 0.3	<1.0	6.8 ± 0.0
4	acetonitrile		3.2 ± 1.1	1.3 ± 0.1	90.1 ± 2.0
5	acetonitrile	*m*-DNB (6%)	0.8 ± 0.0	0.1 ± 0.0	93.7 ± 0.7
6	acetonitrile	AIBN (4%)	84.6 ± 0.8	0.64 ± 0.0	14.3 ± 1.0
7	methanol		5.3 ± 0.0	41.4 ± 0.6	51.8 ± 0.4
8	methanol	*m*-DNB (6%)	0.6 ± 0.1	39.4 ± 0.3	59.9 ± 0.3
9	methanol	AIBN (4%)	65.8 ± 0.5	1.8 ± 0.0	28.8 ± 0.1

[a] A mole ratio of 1:1 of ketone to triphenyltin hydride was used. [b] All reactions were run at 61 °C.

Scheme III. Radical Addition Process



Scheme IV. Conversion of α-Fluoroacetophenone to Acetophenone



nitro compounds[3,5] with tin hydrides, an initiation step presumably occurs by electron transfer (see Scheme IIa).

The AIBN-induced reactions of α,α,α-trifluoroacetophenone with triphenyl- and tri-*n*-butyltin hydride, carried out in benzene, proceeded by a chain process whose chain lengths were 46 and 24, respectively,[25] and produced the alkoxystannane prior to hydrolysis. Prior to hydrolysis, a comparison of the ^1H NMR spectrum of the reaction mixture obtained from an initiated reaction of α,α,α-trifluoroacetophenone with triphenyltin hydride (in solvent benzene-d_6) with that of authentic α-(trifluoromethyl)benzyl alcohol suggested that the final product in the reaction mixture was the alkoxystannane. The multiplet for the α-hydrogen was observed at δ 5.17 and was assigned to $HC(CF_3)(OSnPh_3)Ph$, since the α-hydrogen in the alcohol showed a similar multiplet at δ 4.35 (Δδ = 0.72). This difference in chemical shift can be compared with the chemical shifts of the α-hydrogen absorbances of authentic samples of tri-*n*-butylstannyl methoxide and tri-*n*-butylstannyl ethoxide and the α-hydrogen absorbances of their parent alcohols. They showed similar chemical shift differences of Δδ = 0.38 and Δδ = 0.37.

The initiated formation of the alkoxystannane, in the presence of AIBN, could be the result of either radical addition–hydrogen abstraction, or electron transfer–hydrogen abstraction (see Schemes III and IIb). The ketyl radical anion–stannyl cation pair could collapse to form the carbon centered radical i and would be indistinguishable from the intermediate formed from radical addition. However, a reduction process occurring by an electron-transfer mechanism would be expected to be affected by the polarity of the solvent due to the charge separation in the transition state of the rate-controlling step. The reduction of α,α,α-trifluoroacetophenone by triphenyltin hydride in the presence of AIBN (reactions 3 and 6, Table I) showed an increased yield of alcohol compared to the corresponding uninitiated reaction. However, reactions run in methanol showed almost the same yields as found in the uninitiated reaction (cf. reactions 7 and 9). Since the yield of reduction product was only partially inhibited by the addition of *m*-DNB, the reaction in methanol appears to be better explained by the suggestion that the increased polarity of the solvent was not only effecting an electron-transfer process but was also favoring a concomitant hydride-transfer mechanism.

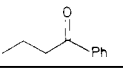
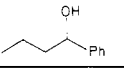
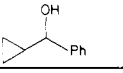
Reduction of α-Fluoroacetophenone. The reactions of α-fluoroacetophenone with triphenyltin hydride were carried out under the same conditions as those used for the reduction of α,α,α-trifluoroacetophenone. Two products could be observed: α-(fluoromethyl)benzyl alcohol and acetophenone (Table II).

When the reactions were carried out in the absence of a radical initiator or a radical inhibitor in either benzene or acetonitrile, low yields of α-(fluoromethyl)benzyl alcohol were observed. However, when the reaction was carried out in the more polar solvent, methanol, a high yield of alcohol (41%) was found. Accompanying the α-(fluoromethyl)benzyl alcohol in all three solvents was a detectable amount of acetophenone, a product which had been shown to be unreactive under the reaction conditions[20] (reactions 1, 4, and 7; Table II). When the reactions were repeated in the presence of a radical inhibitor, the yield of acetophenone was reduced in all three solvents whereas the yields of α-(fluoromethyl)benzyl alcohol was essentially unaffected by the presence of inhibitor when the reaction was carried out in solvent methanol (reaction 8, Table II). In the presence of AIBN the comparative yields were reversed: acetophenone was the major product in all solvents and α-(fluoromethyl)benzyl alcohol was formed in very low yields (reactions 3, 6, and 9, Table II). Unlike the reactions of α,α,α-trifluoroacetophenone, reduction showed very little solvent effect upon changing from benzene to acetonitrile, whereas the highly polar solvent, methanol, caused an appreciable increase in the yield of the alcohol under uninitated conditions.

These observations would seem to argue that the reduction proceeds by an ionic process (favored by solvent polarity) to yield α-(fluoromethyl)benzyl alcohol and a competing radical process (which can be inhibited by

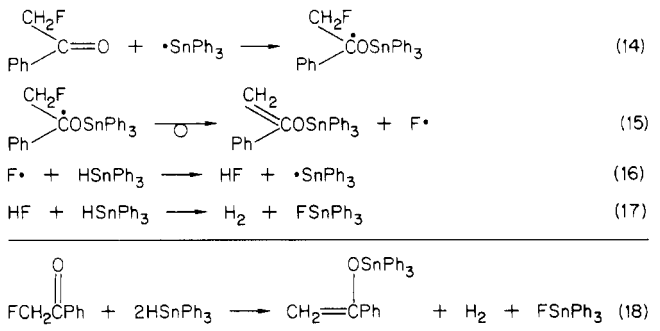
(25) Chain length was estimated from [products]/[AIBN]2*f*, where the initiator efficiency, *f*, was taken as 0.5.

Table III. Radical Initiated (AIBN, 4%) Reaction of Cyclopropyl Phenyl Ketone (0.05 M) with Organotin Hydride at 68 °C

reaction[a]	solvent	R_3SnH	$[R_3SnH]$, mol L^{-1}	% product yield				
							unreacted ketone	open/ closed chain
1	toluene	Ph_3SnH	0.02	7.1	trace	2.9	89.0	2.45
2	toluene	Ph_3SnH	0.05	19.6	3.0	5.4	66.4	4.19
3	toluene	Ph_3SnH	0.08	34.1	18.2	10.8	33.9	4.84
4	toluene	Ph_3SnH	0.30	13.7	66.0	12.2		6.53
5	toluene	Bu_3SnH	0.05	18.9		1.3	85.0	14.5
6	toluene	Bu_3SnH	0.08	71.4	trace	2.5	32.0	28.5
7	methanol	Ph_3SnH	0.03	11.8	8.1	2.6	72.8	7.65
8	methanol	Ph_3SnH	0.05	17.1	14.4	4.4	63.8	7.16
9	methanol	Ph_3SnH	0.07	15.5	39.9	7.1	38.0	7.80
10	methanol	Ph_3SnH	0.08	6.8	82.3	11.1	2.5	8.03
11	methanol	Ph_3SnH	0.25		91.1	10.1		9.02
12	methanol	Bu_3SnH	0.05	9.8	trace	1.5	90.2	6.53
13	methanol	Bu_3SnH	0.08	26.3	13.5	6.4	48.8	6.22

[a] A mole ratio of 1:1 of ketone to organotin hydride was used.

Scheme V. Alternative Mechanism for the Conversion of α-Fluoroacetophenone to Acetophenone



(14) (15) (16) (17) (18)

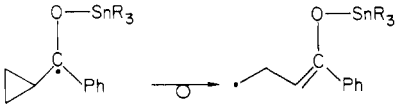
m-DNB or initiated by AIBN) to produce acetophenone. Scheme IV, involving an electron-transfer process, is suggested as a plausible radical mechanism. However, an alternative radical addition process must also be considered (see Scheme V).

In such a mechanism acetophenone could not be formed in higher than 50% yield in a 1:1 molar reaction mixture since the stoichiometry is 2:1. When the products of the initiated reaction in solvent benzene were subjected to analysis, a higher than 50% (87%) yield of acetophenone was observed, and the condensible gases were found to correspond to 4–7%, i.e., the amount of nitrogen produced from the decomposition of the initiator AIBN. This evidence discounts the alternative mechanism and strongly favors the electron-transfer process depicted in Scheme IV.

Although the results suggested that the reduction of α,α,α-trifluoroacetophenone involved an electron-transfer process, only the reduction of the α-fluoroacetophenone gave a strong evidence for such a mechanism. It can be argued, however, that since the less favored acceptor α-fluoroacetophenone is reduced by an electron-transfer process, then the reduction of α,α,α-trifluoroacetophenone will most likely proceed by a similar mechanism. Since the initiated reactions were shown to proceed at faster rates in benzene and acetonitrile than any heterolytic process (see Tables I and II), the assumption that the two fluorinated substrates proceeded by a similar mechanism was substantiated by carrying out a competitive reaction of α-fluoroacetophenone and α,α,α-trifluoroacetophenone with triphenyltin hydride under radical-initiating conditions in the two solvents. A substantial solvent effect was observed, the values of the relative rates $k_{\alpha,\alpha,\alpha\text{-trifluoroacetophenone}}/k_{\alpha\text{-fluoroacetophenone}}$ in benzene and acetonitrile were 2.30 and 9.86, respectively. This solvent effect is consistent with an electron-transfer process which should heavily depend upon the solvent polarity and is not consistent with a process involving neutral radical species.

Reduction of Cyclopropyl Phenyl Ketone. The reduction of cyclopropyl phenyl ketone by organotin hydride was examined in two solvents, nonpolar toluene and polar methanol, and allowed to react at 68 °C (the same solvents and temperature used by Pereyre and Godet for the reduction of the same ketone)[22] for 16 h in the absence of light (see Table III).

Three products were observed in the radical-initiated reaction: butyrophenone, α-propylbenzyl alcohol, and α-cyclopropylbenzyl alcohol. The α-propylbenzyl alcohol presumably arises from the further reduction of the product butyrophenone. The open chain ketone can only arise from a radical process. A radical addition intermediate (ii) can be anticipated to ring open readily.



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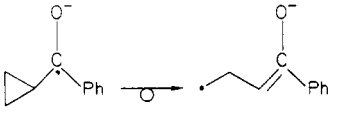
Similarly, a ketyl radical anion (iii), the result of an electron-transfer process, could also be anticipated to ring



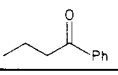
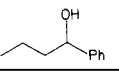
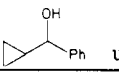
iii

open. An ionic process would not be expected to yield a ring-opened product. α-Cyclopropylbenzyl alcohol can presumably arise from either a homolytic or heterolytic process.

Consistent with the above predictions, when the reaction was carried out in the presence of a radical initiator, the open ring compounds are the major products (see Table III). A series of reactions was carried out by using increasing concentrations of organotin hydride in an attempt to trap the close ring intermediate (ii).

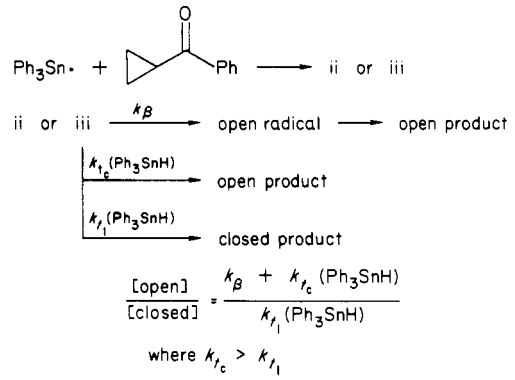
Since a common intermediate (i.e., ii or iii), if present, can undergo either unimolecular ring opening, or bimolecular transfer with tin hydride and since the ratio of rates for the two processes, at the concentrations of tin hydride used, must be comparable (since both products are formed), increasing the absolute concentration of tin hydride would be expected to decrease the ratio of the open to closed products. In fact, the effect observed is the

Table IV. Reaction of Cyclopropyl Phenyl Ketone with Organotin Hydride

				% product yield			
reaction[a]	solvent	conditions	$[R_3SnH]$, mol L^{-1}				unreacted ketone
1	methanol	Ph_3SnH	0.50	15.3	trace	0.12	83
2	methanol	Ph_3SnH *p*-DNB(3%)	0.50			trace	97 ± 3[b]
3	methanol	Ph_3SnH *p*-DCB(6%)	0.50			trace	97 ± 3[b]
4	methanol	Bu_3SnH	0.50	trace	trace	29.5	66
5	methanol	Bu_3SnH *p*-DNB(3%)	0.50			28.4	71
6	methanol	Bu_3SnH *p*-DCB(6%)	0.50			22.5	77

[a] A mole ratio of 1:1 of ketone to organotin hydride was used. [b] The values quoted are averages of two independent reactions. [c] All reactions were run at 65 °C.

Scheme VI



opposite (see ratio open/closed product in Table III). The observation that the ratio does not decrease appears to rule out a mechanism proceeding by just one radical species, i.e. ii or iii.

Previously, Pereyre and Godet had concluded, on the basis of detecting only ring-opened material from the reactions in toluene, and on their interpretation of the effect of placing substituents on the cyclopropyl ring upon the products formed, that ring-opened material was formed by a concerted addition–ring opening. This does not appear to be the case for the unsubstituted cyclopropyl phenyl ketone since both products are found.

As the ratio of open chain to closed reduction product increases with tin hydride concentration, it can tentatively be proposed that in the AIBN-initiated reduction a second bimolecular reaction (dependent upon tin hydride concentration) can also lead to ring-opened product (see Scheme VI).

The results in Table III also confirm earlier observations that triphenyltin hydride is more reactive than tri-*n*-butyltin hydride. Under similar reaction conditions there is usually more unreacted ketone left when tri-*n*-butyltin hydride is used (cf. reactions 5, 6, 12, and 13 with reactions 3, 4, 8, and 10, Table III).

When the reaction with triphenyltin hydride was carried out under the same conditions in the absence of a radical initiator, there was no detectable formation of product. However, when the reaction was repeated under more concentrated conditions in refluxing methanol over 4 days, the three reaction products were observed (see Table IV). The major product was butyrophenone. When this reaction was repeated in the presence of radical inhibitors (*p*-DNB or *p*-DCB) the formation of the ring-opened products was completely inhibited. When a tin hydride which is less likely to function as an electron-transfer reagent, tri-*n*-butyltin hydride, was used, the main product was α-cyclopropylbenzyl alcohol, the product observed by Pereyre and Godet with tri-*n*-butyltin hydride.[19] The yield of this product was not appreciably inhibited by the presence of radical inhibitors. But traces of ring-opened product were observed to be suppressed by the addition of *p*-DNB or *p*-DCB.

Both the tin hydrides react with cyclopropyl phenyl ketone in methanol but apparently by significantly different mechanisms. Triphenyltin hydride produces ring-opened material by an uninitiated homolytic pathway (Scheme IIa, reactions 3 and 4, and/or Schemes IIb or III), whereas tri-*n*-butyltin hydride yields primarily ring-closed cyclobenzyl alcohol by a heterolytic pathway (see Scheme I).

Experimental Section

Materials. The internal standards *n*-tridecane (99% pure) *n*-heptadecane (99% pure) (Aldrich), and *n*-hexadecane (99% pure) (Eastman) were used as supplied.

Tri-*n*-butyltin hydride (Alfa) was distilled and the fraction with bp 68–74 °C (0.3 mm) was used. Triphenyltin hydride (Alfa) was used as supplied.

α,α-Azobis(isobutyronitrile) (Aldrich) was recrystallized from ethanol–water, mp 101–102 °C (lit.[26] mp 103 °C).

Butyrophenone (Matheson, Coleman and Bell) was used as supplied.

Cyclopropyl phenyl ketone (Aldrich) was redistilled, bp 90 °C (2.8 mm) (lit.[26] bp 121–123 °C (15 mm)).

α-Propylbenzyl alcohol was obtained by reduction of butyrophenone with lithium aluminum hydride in ether. α-Cyclopropylbenzyl alcohol was similarly prepared from the corresponding ketone; the fraction with bp 129–132 °C (18 mm) (lit.[26] bp 130–135 °C (18 mm)) was used.

α,α,α-Trifluoroacetophenone was prepared by treating trifluoroacetic acid with an ether solution of phenylmagnesium bromide.[27] Fractional distillation (69–70 °C (30 mm)) (lit.[28] bp 75 °C (37 mm)) gave the product in 58% yield: IR (neat) 5.78 (CO) μm; MS, *m/e* 174, 105.

α-(Trifluoromethyl)benzyl alcohol was prepared by reduction of its parent ketone with lithium aluminum hydride. The product from fractional distillation, 58 °C (2.3 mm), was further purified by gas chromatography (3 ft × $^1/_4$ in. stainless steel packed with 10% FFAP on Chromosorb WAW): NMR ($CDCl_3$) δ 2.95 (d, 1 H), 4.95 (m, 1 H), 7.30–7.56 (m, 5 H); MS, *m/e* 176, 107.

α-Fluoroacetophenone was prepared by treating fluoroacetyl chloride with benzene in the presence of aluminum trichloride.[29] Fractional distillation, 70–72 °C (1.5 mm) (lit. 65–70 °C (1 mm) gave the product in 81% yield: mp 26–27 °C (lit.[25] mp 27–28 °C); NMR ($CDCl_3$) δ 5.57 (d, 2 H, J = 47.5 Hz), 7.36–8.10 (m, 5 H); IR (neat) 5.86 (CO) μm; MS, *m/e* 183, 105.

Tri-*n*-butylstannyl methoxide was prepared from the reaction of tri-*n*-butylstannyl chloride with a methanolic solution of sodium methoxide.[30] Fractional distillation, 75–78 °C (0.25 mm (lit.[30] 101 °C (2 mm)) yielded a colorless liquid: NMR ($CDCl_3$) δ 0.65–1.8 (m, 27 H), 3.65 (s, 3 H). Anal. Calcd for $C_{13}H_{30}OSn$: C, 48.63;

(26) Aldrich Catalog Handbook of Fine Chemicals 1982–83.
(27) Dishart, K. T.; Levine, R. *J. Am. Chem. Soc.* **1956**, *78*, 2268.
(28) Simmons, J. H.; Ramler, E. O. *J. Am. Chem. Soc.* **1943**, *65*, 389.
(29) Bergmann, F.; Kalmus, A. *J. Am. Chem. Soc.* **1954**, *76*, 4137.
(30) Mack, G. P.; U.S. Pat. 2 475 800, May 15, 1956; *Chem. Abst.* **1957**, *51* 6219.

H, 9.41. Found: C, 48.94; H, 9.54.

Tri-*n*-butylstannyl ethoxide was prepared by a similar procedure, an ethanolic solution of sodium ethoxide being used. Fractional distillation, 97 °C (1 mm) yielded the product: NMR ($CDCl_3$) δ 0.65–1.8 (m, 27 H), 1.18 (t, 3 H), 3.78 (q, 2 H).

Solvents benzene, acetonitrile, and methanol were purified and dried by standard procedures.[31]

General Procedure. The typical procedure was to make a stock solution which was 0.1 M in ketone and 0.04 M in internal standard. Similarly, a stock solution which was 0.1 M in tin hydride was made. Equal aliquots of each stock solution were added to a reaction ampule, the mixture was degassed by three freeze–thaw cycles, and then the ampule was sealed under vacuum. The reaction mixture was thermostated in an oil bath at 61 °C for a standard time (16 h) in the dark. The ampule was then opened and the product mixture analyzed by GLPC using either a 5 ft × $^1/_8$ in. stainless steel column packed with 10% FFAP on Chromosorb WAW DMCS 60/80 mesh or a 25-m FFAP capillary column. Product peaks were identified by a comparison of their retention times, GLPC–mass spectra, and GLPC–IR with those of authentic samples. Duplicate experiments were run with each ketone to test the effects of inhibition by *m*-dinitrobenzene, initiation by AIBN, structure of the hydride, and polarity of the solvent.

GLPC analyses were carried out with either an HP5840A or a Varian Vista 6000 gas chromatograph. The area ratios were converted to mole ratios for quantitative determinations by using standard calibration curves. ^{1}H NMR high resolution spectra were obtained on a Brucker WH400 high-field spectrometer. GLPC/IR data were obtained on a Nicolet 7199 FT/IR spectrometer interfaced to a Varian 3700 gas chromatograph.

Competitive Reaction of α,α,α-Trifluoroacetophenone and α-Fluoroacetophenone with Triphenyltin Hydride. A stock solution which was 0.1 M in both α,α,α-trifluoroacetophenone and α-fluoroacetophenone, with a known amount of added internal standard, was made in solvent benzene. Equal aliquots of this solution and a stock solution 0.1 M in triphenyltin hydride, with 4% AIBN added, were added to a reaction ampule. The mixture was degassed and reacted at 61 °C for 3.5 h. The reaction was repeated in solvent acetonitrile. The relative rates of reduction in each solvent were determined from the relative rates of disappearance of the two substrates as found by GLPC analysis.

Reaction of Cyclopropyl Phenyl Ketone with Organotin Hydride in Refluxing Methanol. A solution which was 0.5 M in ketone and 0.5 M in organotin hydride was prepared in methanol. A known amount of *n*-hexadecane, an internal standard, was added. The methanolic solution was heated under total reflux for 4 days. The product solution was analyzed by GLPC on a 25-m 10% FFAP capillary column or a 10 ft × $^1/_6$ in. 10 FFAP on Chromosorb WAW stainless steel column. Results are reported in Table III.

Analysis of Noncondensible Gases in the Reduction of α-Fluoroacetophenone. A reaction mixture using the 0.1 M stock solutions in solvent benzene, with 4% AIBN, was added to a reaction vessel fitted with a break seal. The mixture was reacted at 61 °C for 16 h. The vessel was then attached to a vacuum line, the seal broken, and the noncondensible gases transferred, using a Toppler pump, to a bulb of known volume. The temperature and pressure of the gases were measured and the number of moles of product were estimated.

Registry No. $PhCH(OH)CH_2F$, 345-64-2; Ph_3SnH, 892-20-6; Bu_3SnH, 688-73-3; α,α,α-trifluoroacetophenone, 434-45-7; α-fluoroacetophenone, 450-95-3; cyclopropyl phenyl ketone, 3481-02-5; α-propylbenzyl alcohol, 614-14-2; α-cyclopropylbenzyl alcohol, 1007-03-0; trifluoroacetic acid, 76-05-1; phenyl bromide, 108-86-1; α-(trifluoromethyl)benzyl alcohol, 340-04-5; fluoroacetyl chloride, 359-06-8; benzene, 71-43-2; tributylstannyl chloride, 1461-22-9; butyrophenone, 495-40-9; tributylstannyl methoxide, 1067-52-3; tributylstannyl ethoxide, 682-00-8.

(31) Vogel, A. I. "Textbook of Practical Organic Chemistry", Longman: Birmingham, AL; 1956.

Reactions in the Solid State. 2.† The Crystal Structures of the Inclusion Complexes of 1,1,6,6-Tetraphenylhexa-2,4-diyne-1,6-diol with Benzylideneacetophenone and 2,5-Diphenylhydroquinone with Dibenzylideneacetone

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The crystal structures of the inclusion complexes of 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol with benzylideneacetophenone and 2,5-diphenylhydroquinone with dibenzylideneacetone show that in both complexes two molecules of the guest are linked by hydrogen bonds between the carbonyl oxygen atom and the hydroxyl groups of the host. The molecules in both structures are packed with parallel planar guest molecules related by an inversion center with double-bond center-to-center distances ranging from 3.787 to 3.947 Å. Those distances are within the limit for photochemical [2 + 2] cycloaddition in the solid state. Irradiation in the solid state should, in principle, reveal stereoselective cycloadditions to afford the syn head-to-tail dimers.

The courses of certain types of solid-state reactions are determined by the geometry of the reactant lattice. In a long survey by Cohen and Schmidt,[1] the dependence of photochemical reactions in the solid state on the relative geometry of the reactants in the crystal has been discussed. The postulate that such reactions occur with a minimum amount of atomic or molecular movement implies that the reactions are controlled by the relative fixed distances and orientations, determined by the crystal structure, between potentially reactive centers. The topochemical rules also

† Part 1: *J. Chem. Soc., Perkin Trans. 2*, **1984**, 757–765.

(1) Cohen, M. D.; Schmidt, G. M. J. *J. Chem. Soc.* **1964**, 1966.

0022-3263/85/1950-2154$01.50/0