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REVIEWS

Reduction of Organic Compounds by Organotin Hydrides

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Reductions of organic compounds by organotin hydrides are reviewed to a depth intended to indicate scope and synthetic utility. Among the classes of compounds whose reductions are considered are alkyl halides, acyl halides, aldehydes, ketones, esters, and compounds containing other hetero multiple bonds.

Die Sn—H-Bindung der Organozinn-hydride ist schwächer und weniger polar als die B—H- und Al—H-Bindung der komplexen Bor- und Aluminium-hydride. Die hierdurch bedingten besonderen Eigenschaften erklären die zunehmende Bedeutung der Organozinn-hydride als Zwischenstufen in der Synthese anderer zinn-organischer Verbindungen und als selektiv wirkende Reduktionsmittel. In der folgenden Übersicht wird die präparative Anwendbarkeit der Organozinn-hydride zur Reduktion von Halogenalkanen, Säurehalogeniden, Aldehyden, Ketonen, Estern und einigen anderen Verbindungen besprochen.

Organotin hydrides have assumed increasing importance in recent years as intermediates in the synthesis of organotin compounds and as selective reducing agents in organic synthesis. Their special characteristics can be attributed in large measure to the fact that the tin-hydrogen bond is both weaker and less polar than the boron-hydrogen and the aluminum-hydrogen bonds found in the more familiar complex boro- and alumino-hydrides. These characteristics are manifested in reactions which may proceed by either free radical chain or polar mechanisms depending on the substrate, catalysts or reaction conditions. Consequently it is of particular importance to bear mechanistic considerations in mind in using organotin hydrides in synthesis.

Reductions by organotin hydrides which will be considered in this review may be formulated as displacements (equation *1*) or as two-step processes involving hydrostannation of a multiple bond followed by replacement of the organotin group by hydrogen (equation *2*). As will be seen below H-Y may be a protonic acid or an organotin hydride:

(*1*) $R-X + Sn-H \longrightarrow R-H + Sn-X$

$A=B + Sn-H \longrightarrow H-A-B-Sn$

(*2*) $H-A-B-Sn + H-Y \longrightarrow H-A-B-H + Sn-Y$

$Sn = SnR_3$

where R = alkyl, aryl

[1] G. WITTIG, F.J. MEYER, G. LANGE, Liebigs Ann. Chem. **571**, 167 (1951).

[2] H. GILMAN, J. EISCH, J. Org. Chem. **20**, 763 (1955).

[3] G.J.M. VAN DER KERK, J.G. NOLTES, J.G.A. LUIJTEN, J. Appl. Chem. **7**, 366 (1957).

Of the several methods available for the preparation of organotin hydrides, the most generally useful one involves the reduction of organotin halides by lithium aluminum hydride. Triphenyltin hydride is usually prepared in this way from triphenyltin chloride[1,2,3]:

$$4\ (C_6H_5)_3SnCl + LiAlH_4 \longrightarrow 4\ (C_6H_5)_3SnH + LiAlCl_4 \quad (3)$$

The procedure used in the author's laboratory is described[4].

Triphenyltin Hydride[4]: *To anhydrous ether (150 ml) in a three-neck* flask, which is cooled in an ice-water bath and fitted with a nitrogen inlet tube, a dropping funnel and stirrer, is added lithium aluminum hydride (1.56 g, 40.9 mmol) and triphenyltin chloride (32.5, 100 mmol). The mixture is stirred at the bath temperature for 15 min., and then at room temperature for 3 hr. The reaction mixture is slowly hydrolyzed with 100 ml of water with cooling *by the ice-water bath. The ether layer is washed with* ice-water (2×100 ml) and dried over magnesium sulfate. The ether is distilled off and the hydride distilled very rapidly, using an oil bath preheated to 200°; yield: 27–29 g (77–85%); b.p. 162–168°/0.5 mm. Because of the thermal instability of the hydride, low distillation pressures with a high-capacity vacuum pump are desirable.

Tributyltin Hydride is prepared in the same way; yield: 87%; b.p. 68–74°/0.3 mm.

Bis-[tributyltin] oxide is the most accessible source of the tributyltin group, and can be used in the *preparation of tri-n-butyltin hydride (in the follow*ing referred to as tributyltin hydride) in good yield[5]:

$$2\ [(n\text{-}C_4H_9)_3Sn]_2O + LiAlH_4 \longrightarrow 4\ (n\text{-}C_4H_9)_3SnH + (LiAlO_2) \quad (4)$$

Tributyltin Hydride[5]: The procedure is the same as that above with the exception that 1.90 g (50 mmol) of lithium aluminum hydride and 27.7 g (50 mmol) of bis-[tributyltin] oxide are used.

The *organotin dihydrides and trihydrides are pre*pared in the same way as the monohydrides. These are generally less stable than the monohydrides and so are used only when circumstances require. All of the hydrides are oxidized on exposure to air; their thermal stability decreases as the number of hydrogens increases. The monohydrides can be stored for reasonable periods of time if protected from oxygen and kept cold. Since some organotin compounds are quite toxic it is well to avoid inhalation of vapors and contact with the skin, and to carry out most operations in the hood.

[4] H.G. KUIVILA, O.F. BEUMEL, J. Amer. Chem. Soc. **83**, 1246 (1961).
[5] W.J. CONSIDINE, J.J. VENTURA, Chem. & Ind. **1962**, 1683.
[6] H.G. KUIVILA, L.W. MENAPACE, C.R. WARNER, J. Amer. Chem. Soc. **84**, 3584 (1962).
[7] L.W. MENAPACE, H.G. KUIVILA, J. Amer. Chem. Soc. **86**, 3047 (1964).

1. Reduction of Alkyl Halides

The reduction of alkyl halides by organotin hydrides can be best understood in terms of a free radical chain mechanism for which substantial evidence has been presented[6,7,8]. A reaction scheme which is fully consistent with results is shown in equations (*5*)–(*10*):

(*5*) Initiation: $SnH + Q\bullet \rightarrow Sn\bullet + QH$

(*6*) Propagation: $Sn\bullet + RX \rightarrow R\bullet + SnX$

(*7*) $R\bullet + SnH \rightarrow RH + Sn\bullet$

(*8*) Termination: $R\bullet + R\bullet \rightarrow R\text{-}R$

(*9*) $R\bullet + Sn\bullet \rightarrow R\text{-}Sn$

(*10*) $Sn\bullet + Sn\bullet \rightarrow Sn\text{-}Sn$

Of particular importance in the synthetic application of this reaction is the intermediacy of an *alkyl free radical. If it is ambident as is an allyl* or propargyl radical then two products are to be expected in reaction (*7*). Furthermore, some radicals tend to isomerize or fragment: if reaction (*7*) is sufficiently fast simple reduction products will result; if it is slow, rearranged or fragmented products will form.

In general, the overall rate of reduction seems to be determined by the rate of abstraction of halogen from the alkyl halide, and follows the order

$RF < RCl < RBr < RJ.$

Bromides and iodides tend to react spontaneously with tributyltin hydride in the absence of solvent; chlorides require heating or catalysis by a free radical source such as azobisisobutyronitrile or by irradiation; fluorides do not react[7]. Variation of the alkyl group reveals the expected sequence:

primary < secondary < teriary;

also if R• is a relatively stable radical reactivity of R-X is high: benzyl, allyl, trichloromethyl[7]. Increased electronegativity of *R* increases reactivity to a modest degree: propargyl halides are three to four times as reactive as allyl halides. Hydride reactivity follows the order:

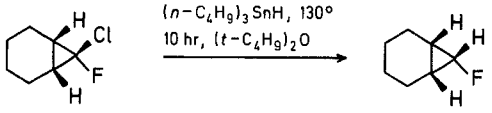
$$(n\text{-}C_4H_9)_3SnH < (n\text{-}C_4H_9)_2SnH_2 < (C_6H_5)_3SnH < (C_6H_5)_2SnH_2$$

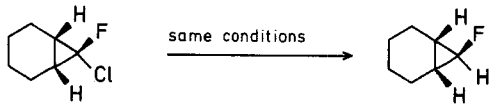
In practice, the monohydrides are used almost exclusively because the dihydrides are somewhat less stable. No systematic study has been reported on *interference by other reducible functional groups.* However, it is known that the nitro group is

[8] D.J. CARLSSON, K.U. INGOLD, J. Amer. Chem. Soc. **90**, 1055, 7047 (1968).

reduced more rapidly but that carbonyl, cyano, and alkoxycarbonyl groups and carbon-carbon multiple bonds do not usually interfere in the reduction of bromides. Results on the reduction of some monohalides are given in Table 1.

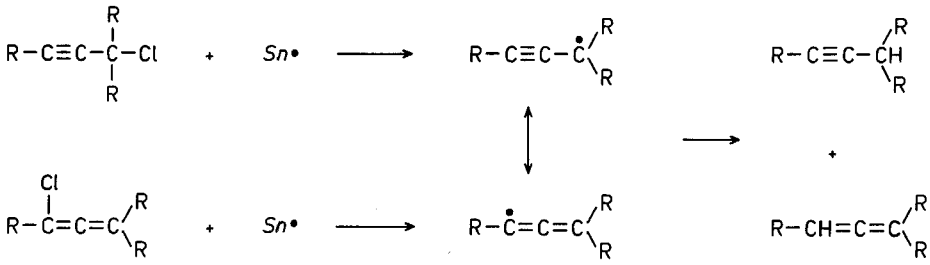
Simple carbon free radicals lose their stereochemical identity either because they are planar or undergo extremely rapid inversion. Thus, it is not surprising that reduction of optically active 1-chloro-1-phenylethane with triphenyltin deuteride leads to racemic α-deuterioethylbenzene. On the other hand, the α-fluorocyclopropyl radical in norcarane type systems appears to retain its configuration completely on the time scale of the reductions, for reactions (*11*) and (*12*) proceed with 100 % retention in configuration[10]:

(*11*) 

(*12*) 

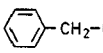
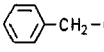
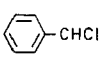
The utility of the reduction of organic halides by organotin deuterides as a means of preparing selectively deuterated compounds has been emphasized[11], and is discussed below.

The ambident radical formed by abstraction of chlorine from a propargyl or allenyl chloride could react with organotin hydride to form either allene or acetylene (equation *13*):

(*13*) 

A mechanistically oriented study of the reduction of ten alkyl substituted propargyl chlorides showed that both allene and acetylene are formed, with the latter predominating by a factor ranging from 1.1 to 25. The magnitude of this ratio depends upon several factors whose individual contributions are not easy to assess[12]. The single allenyl chloride used in this study, 1-chloro-3-methyl-1,2-butadiene, gave a very poor yield of reduction product as anticipated from the fact that vinyl halides are reduced only with difficulty by organotin hydrides.

Table 1. Reduction of Alkyl Halides with Tributyltin Hydride[19].

Halide	Conditions[a]	Yield %[b]
	4 *M* in ether, ex., 12 hr	68
	100°, 4 hr	85
	ex., 1 hr	71
	4 *M* in ether, 12 hr	84
	1.5 *M* in bromobenzene, 60 hr	95[c]
	1.5 *M* in ether, 9 days	88[c]
	180 hr	76
	100°, 17 hr	77
	100°, 17 hr triphenyltin hydride	77
	ex., 19 hr	89
	150°, 45 min.	71
	0.8 *M* in benzene, 80°, 1.5 *M* % azobisisobutyronitrile	99
	100°, 1 hr	86

[a] Neat reaction, ambient temperature when not specified; ex. = exothermic.
[b] Isolated, except where specified.
[c] By gas chromatography.

The early observation[6] that benzotrichloride can be reduced stepwise in good yields to benzylidene dichloride, benzyl chloride, and toluene has been exploited by several investigators for the selective reduction of geminal dihalides to monohalides and then to alkanes. Dihalocarbenes can be generated over a broad temperature range depending upon their precursors. Additions to olefins of widely varying reactivity can thus be effected making this reaction one of the most versatile available for the preparation of the cyclopropane ring. The resulting geminal dihalocyclopropanes can then be reduced selectively and in high yield to the monohalides and

[9] H.G. Kuivila, L.W. Menapace, J. Org. Chem. **28**, 2165 (1963).

[10] T. Ando, F. Namigata, H. Yamanaka, W. Funasaka, J. Amer. Chem. Soc. **89**, 5719 (1967).
However, see L.J. Altman, B.W. Nelson, J. Amer. Chem. Soc. **91**, 5162 (1969), for a different result with another cyclopropyl system.

unhalogenated analogs by organotin hydrides. Table 2 lists results of typical applications of this procedure. The stereochemistry of reduction of most geminal dihalocyclopropanes depends, not upon which of the two halogen atoms is removed in reaction (*6*), but rather upon steric factors in the hydrogen transfer reaction (*7*). Thus, the major product in the reduction of 1,1-diiodo-*cis*-2,3-dimethylcyclopropane is the all-*cis* monoiodide: the less hindered direction for attack by the organotin hydride on the intermediate radical is *trans* to the two methyl groups. A similar degree of selectivity is shown in the reduction of the 7,7-dihalonorcaranes. One isomer is formed to the virtual exclusion of the other in the reduction of 9,9-dibromobicyclo[6.1.0]nonane[13] with tributyltin hydride and of the 9-chloro-7-phenylnorcaranes with triphenyltin hydride[16].

Reduction of 1,1-Dibromo-2,2-dimethyl-3-ethylidenecyclopropane[15]: The cyclopropane derivative (19 g, 0.074 mol) is placed into a flask fitted with stirrer, condenser, and dropping funnel. The contents are cooled in an ice bath and tributyltin hydride (21.7 g, 0.074 mol) is added over 2 hr. The reaction mixture is then warmed to ~ 35° and allowed to stand until a test of an aliquot with acid indicates disappearance of the hydride (~ 24 hr). Distillation provides 9.2 g (70%) of 1-bromo-2,2-dimethyl-3-ethylidenecyclopropane; b.p. 47°/10 mm. A residue of 27 g of tributyltin bromide remains in the distillation flask.

Reduction of 7,7-Dichlorobicyclo[4.1.0]heptane[13]: A mixture of 7,7-dichlorobicyclo[4.1.0]heptane (0.08 mol) and tributyltin hydride (0.08 mol) is heated at 140° for 3 hr. Distillation gives 8.65 g (83%) of a 1.8:1 mixture of 7-chlorobicyclo[4.1.0]heptanes; b.p. 56–58°/11 mm; n_D^{25}: 1.4860; and 23.6 g (91%) of tributyltin chloride; b.p. 80–83°/0.07 mm; n_D^{25}: 1.4894.

Trihalomethyl derivatives of mercury, $RHgCX_3$[18], and of tin, R_3SnCX_3[19], have been reduced selectively in good yields to the dihalides.

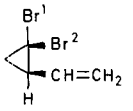
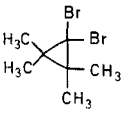
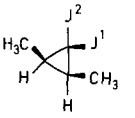
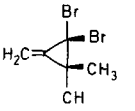
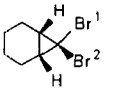
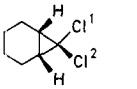
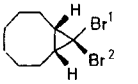
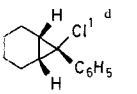
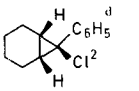
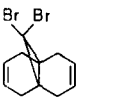
The course of reaction of organotin hydrides with vicinal dihalides depends upon the nature of the halogen[20]. For example, 2,3-dibromobutanes undergo partially stereospecific *anti*-elimination with tributyltin hydride. On the other hand, compounds such as 2,3-dichlorobutanes and 1-bromo-1-phenyl-2-chloroethane undergo simple reduction as shown in equations (*14*) and (*15*):

(*14*) $H_3C-\underset{Cl}{CH}-\underset{Cl}{CH}-CH_3 \xrightarrow{SnH} H_3C-CH_2-\underset{Cl}{CH}-CH_3 \xrightarrow{SnH} H_3C-CH_2-CH_2-CH_3$

(*15*) $C_6H_5-\underset{Br}{CH}-CH_2-Cl \xrightarrow{SnH} C_6H_5-CH_2-CH_2-Cl$

This reaction has potential synthetic utility because most dehalogenating agents tend to cause elimination instead of reduction in systems such as these.

Table 2. Reduction of Geminal Dihalocyclopropanes

Compound	% Yield in replacement of X	% Yield in replacement of both X	References
	*1* 45 *2* 17	—	13
	84	69[b]	13
	*1* 17.5 *2* 52.5		14
	70	53[c]	15
	*1* 23.5 *2* 58.5	—	13
	*1* 29.5 *2* 53.5	—	13
	*1* 84 *2* 0	—	13
 and 	*1* 1 *2* 80	—	16
	[e]	—	17

[a] Tributyltin hydride used except were specified.
[b] One-step process from dibromide.
[c] From monobromide.
[d] Epimer mixture of unspecified composition reduced with triphenyltin hydride.
[e] Yield not given.

[11] F.D. GREENE, N.N. LOWRY, J. Org. Chem. **32**, 882 (1967).

[12] R.M. FANTAZIER, M.L. POUTSMA, J. Amer. Chem. Soc. **90**, 5490 (1968).

[13] D. SEYFERTH, H. YAMAZAKI, D.L. ALLESTON, J. Org. Chem. **28**, 703 (1963).

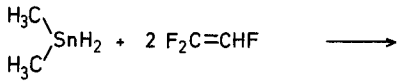
[14] J.P. OLIVER, U.V. RAO, J. Org. Chem. **31**, 2696 (1966).

[15] W. RAHMAN, H.G. KUIVILA, J. Org. Chem. **31**, 772 (1966).

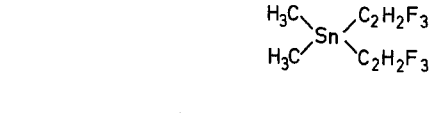
[16] F.R. JENSEN, D.B. PATTERSON, Tetrahedron Letters **1966**, 3837.

[17] E. VOGEL, W. GRIMME, S. KORTE, Tetrahedron Letters **1965**, 3625.

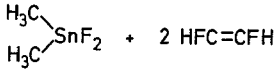
Although simple alkyl fluorides cannot be reduced by organotin hydrides, fluorovinyl compounds can be reduced by an addition-elimination mechanism, an example of which is shown in equations (*16*) and (*17*)[21,22,23]:



(*16*)

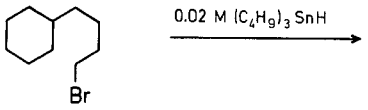


(*17*)

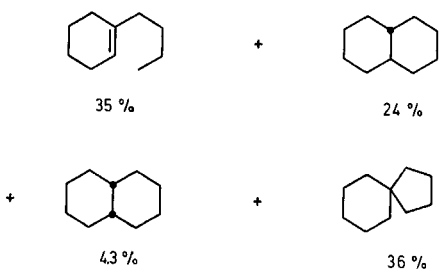


Aryl bromides and iodides undergo reduction with triphenyltin hydride at temperatures around 125° in excellent yields[24,25]. Simple derivatives were used in the studies reported so that the practical scope of the reaction remains to be established.

The fact that some intermediate radicals may rearrange may be a boon or a bane from the synthetic standpoint. Among the rearrangements which may occur are cyclizations of radicals formed from alkenyl halides to five[26,27] or six-membered[27] rings, cyclization of acetylenyl radicals to five- or six-membered rings[28], and opening[29,30] of cyclopropylcarbinyl radicals to allylcarbinyl radicals or the reverse[30]. An example is given in equation (*18*) showing the reduction of 1-bromo-4-cyclohexylbutane by tributyltin hydride[27] in benzene:



(*18*)

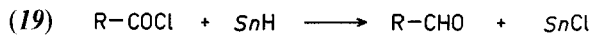


The yield of the butylcyclohexene could be increased to 78% by changing the concentration of bromide to 0.10 *M* and of the hydride to 0.14 *M*.

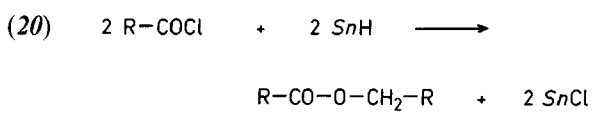
[18] D. Seyferth, J.M. Burlitch, H. Dertouzos, H.D. Simmons, J. Organometal. Chem. **7**, 405 (1967).
D. Seyferth, H.D. Simmons, L.J. Todd, J. Organometal. Chem. **2**, 282 (1964).

2. Reduction of Acyl Halides

On the basis of the foregoing, it might be expected that aldehydes could be conveniently prepared by the reduction of acyl halides by organotin hydrides as in reaction (*19*). However, competing ester formation (equation *20*) also occurs[31]:

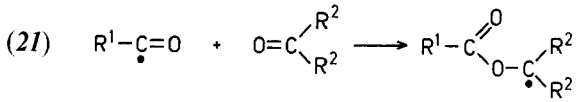


(*19*)

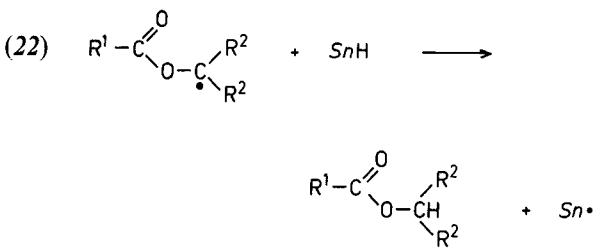


(*20*)

Although the mechanism of ester formation has not been rigorously established, and may be complex[31], reactions (*21*) and (*22*) serve to account for its formation from the expected intermediate acyl radical:



(*21*)



(*22*)

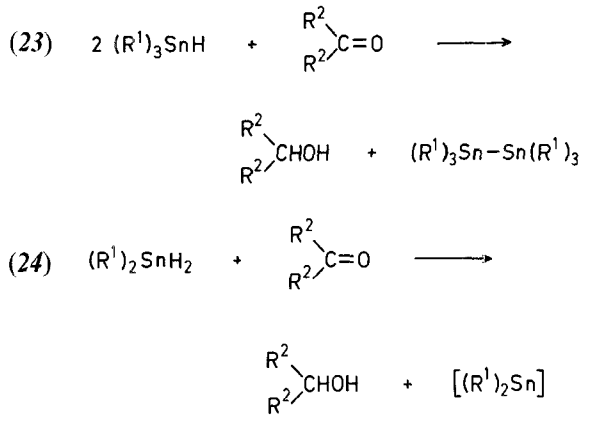
When acyl halides are reduced with tributyltin hydride, neat, the product may be only ester (propanoyl chloride) or only aldehyde (benzoyl bromide), but is more commonly a mixture[31]. Similar results are obtained with triphenyltin hydride[32]. The roles which the various reaction parameters play in directing the course of the reaction are not yet understood. However, if an aldehyde or ketone is present when triphenyltin hydride and certain acid chlorides react virtually quantitative yields of esters can be obtained[33].

1-Phenylethyl acetate[33]: A mixture of acetyl chloride (31.1 mg, 0.396 mmol), acetophenone (49.2 mg, 0.410 mmol), triphenyltin hydride (148 mg, 0.528 mmol), and benzene (0.148 g) is allowed to stand for 30 min. at room temperature. Quantitative conversion of the acetophenone into 1-phenylethyl acetate is obtained.

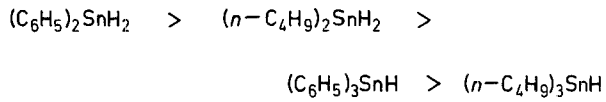
[19] A.G. Davies, T.N. Mitchell, J. Chem. Soc. [C] **1969**, 1896.
[20] R.J. Strunk, P.M. DiGiacomo, K. Aso, H.G. Kuivila, J. Amer. Chem. Soc. **92**, 2849 (1970).
[21] H.C. Clark, S.G. Furnival, J.T. Kwon, Canad. J. Chem. **41**, 2889 (1963).
[22] W.R. Cullen, G.E. Styan, J. Organometal. Chem. **6**, 633 (1964).
[23] M. Akhtar, H.C. Clark, Canad. J. Chem. **46**, 633 (1968).
[24] L.A. Rothman, E.I. Becker, J. Org. Chem. **24**, 294 (1959); **25**, 2204 (1960).
[25] D.H. Lorenz, P. Shapiro, A. Stern, E.I. Becker, J. Org. Chem. **28**, 2332 (1963).

3. Reduction of Aldehydes and Ketones

Reductions of aldehydes and ketones by organotin hydrides were initially observed to proceed according to equations (*23*) and (*24*):



Diphenyltin hydride was found to react readily at ambient temperature with a variety of aldehydes and ketones[4,31]. The diphenyltin formed as a product was polymeric and could be filtered off, and the reduction product readily obtained by appropriate work-up. This reduction procedure had a distinct advantage over others because no hydrolysis step was necessary. The reactivity of hydrides examined followed the order



with the latter requiring temperatures of 100° or higher for reduction in a reasonable time. High isolated yields of alcohols have been obtained with simple compounds using diphenyltin dihydride and dibutyltin dihydride (see Table 3)[34].

Table 3. Reductions of Aldehydes and Ketones with Diphenyltin Dihydride and Dibutyltin Dihydride[34,35]

Carbonyl compound	Yield (%) of alcohol with $(C_6H_5)_2SnH_2$	Yield (%) of alcohol with $(n\text{-}C_4H_9)_2SnH_2$
Cyclohexanone	82	
Benzophenone	59	85
2-Methylcyclohexanone	83	94
4-Methylcyclohexanone	82.5	76.5
4-*t*-Butylcyclohexanone	85.5	93.5
l-Menthone	81.5	81.5
d-Carvone	83.5	70.5
Benzaldehyde	62	
Benzoquinone	59	66
Benzil	87.5[a]	93[a]

[a] Product was *meso*-hydrobenzoin.

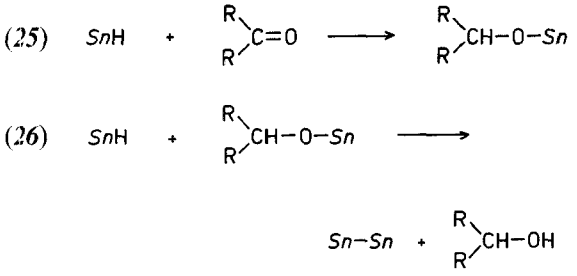
[26] C. Walling, J.H. Cooley, A.A. Ponaras, E.J. Racah, J. Amer. Chem. Soc. **88**, 5361 (1966).

Examination of the stereochemistry of reduction by four different organotin hydrides reveals a preference for formation of the more stable epimer as shown in Table 4. The stereoselectivity differs little from that observed with lithium aluminum hydride or sodium borohydride.

Reductions with Diphenyltin Dihydride[34,35]: To a slurry of lithium aluminum hydride (1.90 g, 0.050 mol) in dry ether (35 ml) at 0° is added dropwise over 30 min. a solution of diphenyltin dichloride (17.2 g, 0.05 mol) in ether (50 ml). The mixture is stirred with continued cooling for another 30 min. and excess lithium aluminum hydride is destroyed by dropwise addition of water (100 ml). After essentially all of the solids are dissolved, the ether layer is separated and washed thrice with 100 ml portions of ice-water. The ether solution is dried over calcium chloride and concentrated under reduced pressure, to 1 *M* on the assumption of a quantitative yield in its preparation. Generally, 50 ml of this solution is added to 45.0 mmol of carbonyl compound, the 10% excess being used in case yields were not quantitative, and to ensure complete reduction, particularly in those cases where the isomeric composition of the product alcohol is to be determined. Within ~5 min., a white precipitate appears; after standing overnight, the precipitate usually becomes yellow and is covered by a colorless supernatant. Diethylamine (1 ml) is added in order to destroy the remaining hydride, and further polymerize the diphenyltin and thus diminish its solubility. If the amine is not added more diphenyltin precipitates during the work-up of the reaction product. For maximum recovery of product, since the volume of the diphenyltin is substantial, the reaction mixture is tranferred into a Soxhlet cup and extracted with ether for 2 hr or more. The extract is then concentrated and the product recovered by distillation of crystallization.

Another form of selectivity which has been examined briefly[36] comes into play in the reduction of compounds containing two or more different carbonyl groups as illustrated by ketosteroids. Results obtained when one mole of diphenyltin dihydride was allowed to react with one mole of steroid are shown in Table 5. The products formed were mixtures of epimers or diastereomers whose configurations were not established unambiguously.

These reductions undoubtedly proceed by a two-step mechanism:

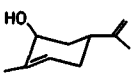
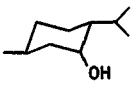


[27] D.L. Struble, A.L.J. Beckwith, G.E. Gream, Tetrahedron Letters **1968**, 3701.

[28] J.K. Crandall, D.J. Keyton, Tetrahedron Letters **1969**, 1653.

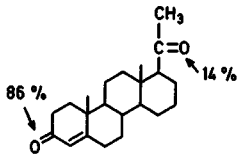
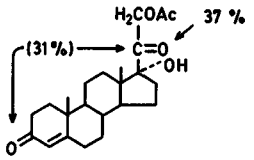
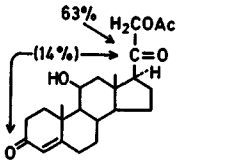
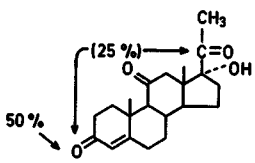
[29] S.J. Cristol, R.V. Barbour, J. Amer. Chem. Soc. **90**, 2832 (1968).

Table 4. Stereochemistry of Reduction of Cyclohexanones by Organotin Hydrides, Complex Metal Hydrides, and Aluminum Isopropoxide[34].

Reducing agent	% *trans*-alcohol obtained in the reduction of			
	4-*t*-butyl-cyclohexanone	4-methyl-cyclohexanone	yield (%) from carvone	yield (%) from menthone
n-$C_4H_9SnH_3$	92	73		
$(n\text{-}C_4H_9)_2SnH_2$	88	75	94.7	
$(C_6H_5)_2SnH_2$	87	76	97.1	48
$(C_6H_5)_3SnH$	87	70		
$LiAlH_4$	91–93[a]	79–81[a]	94	71[b]
$NaBH_4$	75		49	
$Al(O\text{-}i\text{-}C_3H_7)_3$	77–81	67	58[c]	30
(Equilibrium)	77–81[a]	60–71[a]		

[a] E.L. ELIEL, R.S. RO, J. Amer. Chem. Soc. **79**, 5992 (1957).
[b] A.K. MACBETH, J.S. SHANNON, J. Chem. Soc. **1952**, 2852.
[c] R.H. REITSEMA, J. Amer. Chem. Soc. **75**, 1996 (1953).

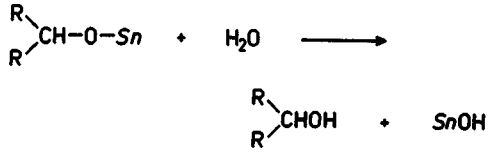
Table 5. Reduction of Ketosteroids with Equimolar Diphenyltin Dihydride[a].

 progesterone	 Reichstein's compound S acetate
 hydrocortisone acetate	 cortisone acetate

[a] Figures outside of parentheses indicate percentage of product reduced at the given carbonyl group. Figures in parentheses indicate percentages of diols formed[36].

The first step can be catalyzed by light[37,38,39], by azobisisobutyronitrile[40], by zinc chloride[40], or thermally[40]. The second step represents an example of a general reaction between organotin hydrides and organotins containing electronegative groups bonded to tin (RO-[41,42], R_2N-[43]). Depending upon conditions only reaction (*25*), or both (*25*) and (*26*) may occur. The latter is a polar reaction whose rate is increased by electron withdrawal by R, suggesting that the reaction is initiated by electrophilic attack on oxygen by hydrogen of the organotin hydride[44].

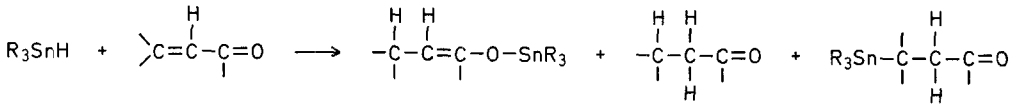
On the other hand, it appears not to be accelerated by the catalysts mentioned above to a significant degree. Thus, if one wishes to prepare the organotin alkoxide he will use a catalyst at low temperature. A free radical mechanism can be promoted by use of irradiation or a free radical source such as azobisisobutyronitrile, and a polar mechanism by use of zinc chloride, or, in the case of electron deficient carbonyl groups, by use of a polar solvent[45,46]. Addition of triethyltin hydride to ω,ω,ω-trifluoroacetophenone is virtually complete in 20 minutes in butyronitrile at 20°, whereas less than 5% reaction occurs in 2 hours in cyclohexane at the same temperature[45]. Formation of the alkoxide, followed by the facile hydrolysis (reaction *27*) results in overall reduction of the carbonyl group involving use of only one equivalent of hydride instead of the 2 equivalents required by the two-step process:



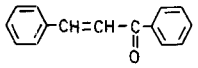
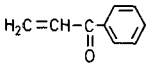
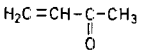
(27)

[30] C.R. WARNER, R.J. STRUNK, H.G. KUIVILA, J. Org. Chem. **31**, 3381 (1966).
[31] H.G. KUIVILA, E.J. WALSH, J. Amer. Chem. Soc. **88**, 571 (1966);
E.J. WALSH, H.G. KUIVILA, J. Amer. Chem. Soc. **88**, 576 (1966).
[32] E.J. KUPCHIK, R.J. KIESEL, J. Org. Chem. **29**, 3690 (1964); **31**, 456 (1966).

Table 6. Reaction of Organotin Hydrides with Some α,β-Unsaturated Ketones[48]

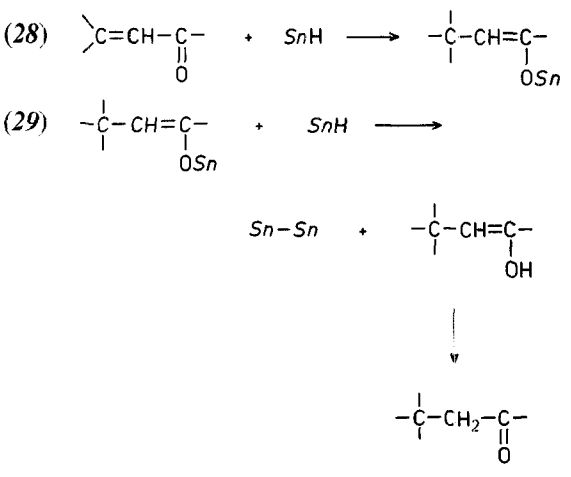


1 2 3

Ketone	Tin hydride	Molar ratio ketone:hydride	Reaction conditions	Yield %	Molar ratio 1:2:3
	$(n\text{-}C_4H_9)_3SnH$	1:1	5 hr, 70°	90	90: 10[a]: 0
	$(C_6H_5)_3SnH$	3:1	3 hr, 55°	70	40: 60 : 0
	$(C_6H_5)_3SnH$	1:3	3 hr, 55°	75	50: 50 : 0
			5 hr, 55°[b]	80	0:100[b]: 0
	$(C_6H_5)_2SnH_2$	1:1	3 hr, 55°	55	
	$(n\text{-}C_4H_9)_3SnH$	1:1	6 hr, 55°	60	95: 5[a]: 0
	$(n\text{-}C_4H_9)_3SnH$	3:4	20 hr, 55°	45	85: 15[a]: 0
	$(C_6H_5)_3SnH$	3:4	3 hr, 55°	60	70: 30 : 0
	$(C_6H_5)_3SnH$	1:2	4 hr, 55°	85	0:100 : 0
	$(C_6H_5)_2SnH_2$	3:4	2 hr, 55°	25	0:100 : 0
	$(n\text{-}C_4H_9)_3SnH$	1:1	12 hr, 55°	0	
	$(C_6H_5)_3SnH$	2:1	3 hr, 55°	80	0: 45 :55
	$(C_6H_5)_3SnH$	1:2	3 hr, 55°	80	0: 35 :65
	$(C_6H_5)_2SnH_2$	1:1	1 hr, 55°	40	0:100 : 0

[a] The presence of compound **2** in these reaction mixtures most probably is the result of hydrolysis of compound **1**.
[b] N.M.R.-spectrum run after standing overnight.

α-β-Unsaturated aldehydes and ketones are readily reduced by organotin hydrides. Early reports[4,34,47] that the carbonyl group is selectively reduced have been followed by others[33,48,49] showing that 1,4-addition of the organotin hydride to the conjugated system and reduction of the double bond occur as the major reactions in most cases. Results are most easily understood in terms of the reaction sequence (*28*–*29*):

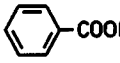


The product distribution depends simply on the relative rates of (*28*) and (*29*) and upon the concentration of the hydride; the nature of the hydride also plays a role as shown by the data in Table 6. Methyl vinyl ketone appears to be unique in undergoing 4,3-addition to the double bond with triphenyltin hydride.

4. Reduction of Esters

By analogy with aldehydes and ketones, esters might be expected to undergo addition of organotin hydrides to the carbonyl group to form hemiacetals or hemiketals. Although reaction does occur (under conditions more drastic than those necessary for ketones) the overall course of the reaction can be

[33] L. KAPLAN, J. Amer. Chem. Soc. **88**, 1833, 4970 (1966).
[34] H.G. KUIVILA, O.F. BEUMEL, J. Amer. Chem. Soc. **80**, 3798 (1958).
[35] H.G. KUIVILA, A.K. SAWYER, A.G. ARMOUR, J. Org. Chem. **26**, 1426 (1961).

Table 7. Reduction of Benzoates,  -COOR with Tributyltin Hydride[50]

R (mmol)[a]	Source[b]	Reaction conditions	Unreacted benzoate recovered (mmol)	Yield of $(n\text{-}C_4H_9)_3SnO—CO—C_6H_5$[d] (hydrocarbon)[e] (mmol)	% Reduction[f]
$-CH(C_6H_5)_2$ (9.1)[g]	azoisobutyronitrile	80°, 24 hr	2.4	7.1 (5.6)	78
$-CH_2-CH=CH_2$ (7.3)	U.V.	80°, 7 hr	1.8	2.2. (3.0)[h]	30
$-n\text{-}C_4H_9$ (11.9)	U.V.	130°, 50 hr	9.4	1.2	10
$-sec\text{-}C_4H_9$ (7.6)	U.V.	130°, 44 hr	5.2	2.2	29
$-t\text{-}C_4H_9$ (7.1)	U.V.	130°, 30 hr	3.1	4.3	61
$-C_6H_5$ (7.2)	U.V.	130°, 6.4 hr	4.4	2.3	33
$-CH_2-C_6H_5$ (12.1)	U.V.	130°, 3.5 hr	2.9	9.3 (9.1)	77
$-CH(C_6H_5)_2$ (8.2)	di-*t*-butyl peroxide	130°, 6 hr	1.3	7.3 (6.4)	89
$-C(C_6H_5)_3$ (2.2)[g]	U.V.	130°, 2 hr	0.6	1.7 (1.5)[h]	77
$-CH_2-CH=CH-C_6H_5$ (5.1)	U.V.	130°, 2.5 hr	1.4	3.8 (3.3)[i]	75

[a] Unless otherwise stated, equivalent amount of tributyltin hydride was used without solvent.
[b] For U.V., a G.E. 275-Watt sunlamp was used; azobisisobutyronitrile added was 20 mol %, and di-*t*-butyl peroxide used was 3–5 mol %.
[c] Reaction was followed to the disappearance of the Sn-H band at $\sim 1815 cm^{-1}$ in the I.R. region.
[d] By quantitative I. R. spectrophotometric analysis with estimated accuracy of ±5%.
[e] By G.L.C. analysis with an internal standard, unless otherwise stated.
[f] Based on $(n\text{-}C_4H_9)_3SnO—CO-C_6H_5$ obtained.
[g] *t*-Butylbenzene was used as solvent.
[h] Isolated by column chromatography.
[i] Mixture consists of allylbenzene and *trans*-propenylbenzene in the ratio of 1.6:1 and trace amount of *cis*-propenylbenzene.

formulated as the hydrostannolysis of the alkyl-oxygen bond[50]. Since the reaction is catalyzed by light and free radical sources the mechanism may be formulated as shown in reactions (*30*)–(*32*):

(*30*) $Sn\bullet + R^1-\overset{\overset{O}{\|}}{C}-OR^2 \longrightarrow R^1-\overset{\overset{OSn}{|}}{\overset{\bullet}{C}}-OR^2$

(*31*) $R^1-\overset{\overset{OSn}{|}}{\overset{\bullet}{C}}-OR^2 \longrightarrow R^1-\overset{\overset{OSn}{|}}{C}=O + R^2\bullet$

(*32*) $R^2\bullet + SnH \longrightarrow R^2-H + Sn\bullet$

Consistent with this scheme is the fact that benzoate esters in which $R^2\bullet$ is a relatively stable radical (benzyl, benzhydryl, triphenylmethyl, cinnamyl) give better yields of products than those in which $R^2\bullet$ is less stable ($n\text{-}C_4H_9$, C_6H_5). Selected results from a survey are gathered in Table 7.

One of the more useful reactions of organotin hydrides from the organometallic chemist's point of view is the addition to carbon-carbon multiple bonds. α,β-Unsaturated esters and nitriles may give either or both of two adducts (equation *33*):

(*33*) $\rangle C=\overset{|}{C}-R + SnH \longrightarrow$

$-\overset{|}{\underset{Sn\,H}{\overset{|}{C}}}-\overset{|}{C}-R$ and / or $-\overset{|}{\underset{H\,Sn}{\overset{|}{C}}}-\overset{|}{C}-R$

R = -CN, -COOR' β-adduct α-adduct

The α-adducts are rapidly solvolyzed by hydroxylic reagents to form the saturated esters or nitriles. These two reactions have been combined as a means of selectively reducing the double bonds by allowing the unsaturate to react with tributyltin hydride in methanol as solvent, equation (*34*) for example[51]:

(*34*) $H_3C-CH=CH-CN + (n-C_4H_9)_3SnH + CH_3OH \xrightarrow{150°,\ 20\ hr} H_3C-CH_2-CH_2-CN + (n-C_4H_9)_3SnOCH_3$ 90 %

[36] O.F. BEUMEL, Ph. D. Thesis, University of New Hampshire, 1960.
[37] M. PEREYRE, J. VALADE, Compt. Rend. **258**, 4785 (1964).
[38] M. PEREYRE, J. VALADE, Compt. Rend. **260**, 581 (1965).

5. Reduction of C=N Double Bonds

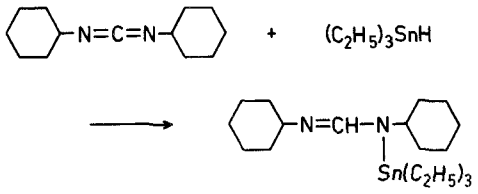
Isocyanates have been shown to undergo polar addition of triethyltin hydride to the C=N double bond, the direction of addition depending on the nature of the group attached to nitrogen. Two examples may be cited[52-55]:

(35) $(C_2H_5)_3SnH + C_6H_5-N=C=O \longrightarrow C_6H_5-N(Sn(C_2H_5)_3)-C(H)=O$

(36) $(C_2H_5)_3SnH + n-C_6H_{13}-N=C=O \longrightarrow n-C_6H_{13}-N(H)-C(Sn(C_2H_5)_3)=O$

The reason for the difference in direction of addition in the two cases is not at all clear.

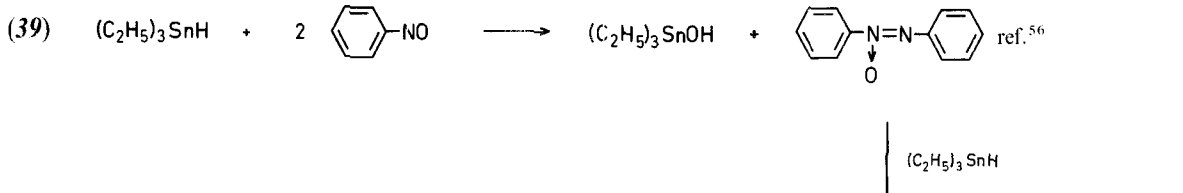
Azomethines and dicyclohexylcarbodiimide undergo straightforward addition to form compounds with the organotin group attached to nitrogen[56]. The triethyltin groups in the products of reactions (35)–(37) are easily replaced by hydrogen upon hydrolysis:

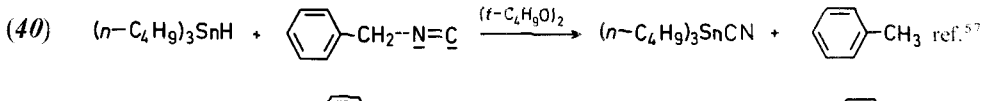
(37) 

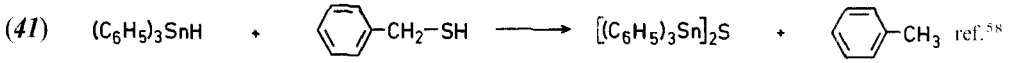
6. Miscellaneous Reductions

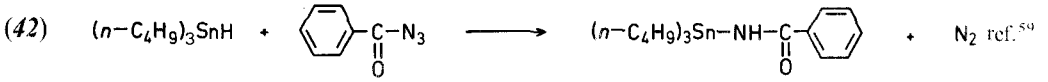
The reactions of several other functional groups with organotin hydrides have been examined briefly and are shown in the following equations. Their potential in organic synthesis needs to be explored more extensively:

(38) $(C_2H_5)_3SnH + C_6H_5-N=C=S \longrightarrow C_6H_5-N(H)-C(Sn(C_2H_5)_3)=S$ ref.[52]

(39) 

(40) 

(41) 

(42) 

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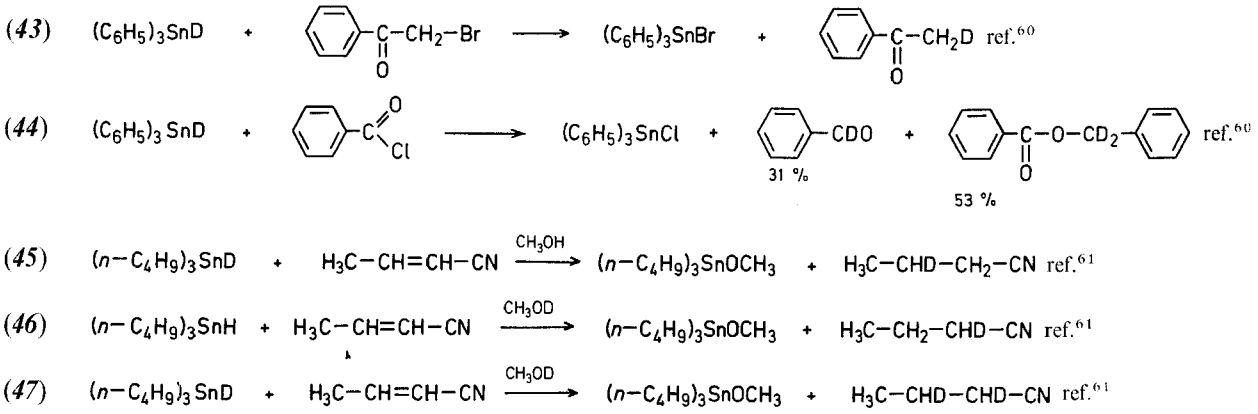
7. Specific Deuterium Labeling

Reductions and additions with organotin hydrides usually proceed with little side reactions. Because of this, and the fact that organotin deuterides are readily available by reduction of appropriate organotin derivatives with lithium aluminum deuteride, highly specific deuterations of organic compounds can be readily effected. Illustrative examples may be cited:



8. "One-Pot" Reduction Procedures

Hayashi et al. have shown[62] that organotin hydrides can be prepared by hydrogen-oxygen exchange between polymethylsiloxane and organotin oxides (equation *48*):

$$(R_3Sn)_2O + (H_3C-SiHO)_n \longrightarrow 2\ R_3SnH + (H_3C-SiO_{1.5})_n \quad (48)$$

The reaction product is distilled to produce virtually pure organotin hydride leaving the unreactive cross-linked silicone behind. Reactions of the hydride can be carried out *in situ*, thus obviating the need for isolating the hydride:

$$2\ R-X + (R'_3Sn)_2O + (H_3C-SiHO)_n \longrightarrow 2\ R-H + 2\ R'_3SnX + (H_3C-SiO_{1.5})_n \quad (49)$$

This method has been found to be successful for reducing aliphatic and aromatic halides, geminal dibromocyclopropanes, and 4-methylcyclohexanone[63].

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