An Internally Activated Tin Hydride with Enhanced Reducing Ability

E. Vedejs,* S. M. Duncan, and A. R. Haight

Chemistry Department, University of Wisconsin, Madison, Wisconsin 53706

Received January 20, 1993

Tin hydride 1 is activated for nucleophilic hydride transfer and also for radical chain reduction, depending on solvent. The nucleophilic hydride pathway is favored in methanol, and 1 can be used as a selective reducing agent for ketones. Simple ketones are not reduced in aprotic solvents, but β-hydroxy ketones are activated internally by the hydroxyl group and can be reduced in THF with good control of stereochemistry, as in the conversion from 7 to 9 (30:1 9:8). A catalytic version of the nucleophilic hydride reductions in methanol has been developed using $PhSiH_3$ as the stoichiometric hydride source. Radical chain dehalogenations can also be achieved with 1 at room temperature and without added radical initiators. Simple xanthates are not reduced efficiently in the absence of an initiator, but the reaction proceeds in the presence of AIBN.

Tributyltin hydride is commonly used for radical chain reductions.[1] It can also serve as a mild source of nucleophilic hydride, but the uncatalyzed reduction of simple ketones is slow and requires many hours in refluxing methanol.[2] Improved reaction rates can be achieved by using Lewis acid catalysts[3] or by adding $Bu_3P{=}O$[4a] or tetrabutylammonium halides as nucleophilic activating agents.[4b] The latter methods probably involve anionic, pentacoordinated tin hydride intermediate as the reactive reducing agents.

During a study of internally coordinated tin reagents,[5] we noticed that [*o*-[(dimethylamino)methyl]phenyl]tin hydride 1 (available from the corresponding halide by $LiAlH_4$ reduction)[6a] is considerably more reactive than is the parent compound 3.[3b] Thus, 1 was rapidly destroyed by exposure to mineral acids (vigorous foaming!) or more slowly by treatment with methanol (hydrogen evolution, complete within 6 h at 20 °C). By comparison, 3 survived with <5% decomposition after 20 h in methanol at 20 °C. As will be shown, 1 also reacted as a nucleophilic hydride donor with ketones, or as a radical chain reducing agent with organic halides, depending on the solvent and the substrate. These properties suggested the possible involvement of 2 in the reductions. Several previous reports mention increased nucleophilic hydride reactivity for internally coordinated tin hydrides,[7] but the nucleophilic hydride and radical chain mechanisms have been documented more extensively for structurally analogous silicon hydrides.[8] In particular, the anionic siliconate reagents described recently by Corriu et al. are comparable in terms of reactivity profile.[9] Since 1 is relatively nonbasic and more soluble in nonpolar solvents by comparison with the siliconate hydrides, we have explored its synthetic potential for representative reductions.

The new reagent reduced a variety of simple ketones to the alcohols (acetophenone, pinacolone, cyclohexenone, etc.) under the standard conditions (1.3–1.5 equiv of 1, 20 °C, methanol). Some of the more highly functionalized examples are summarized in Table I. Conjugated enones or ynones were reduced by 1,2-addition (<5% of 1,4-reduction, NMR assay), and chloride, bromide, and benzoyloxy substituents survived the conditions required to reduce ketones. No attempt was made to force the more sluggish reductions to completion by adding a larger excess of 1 to compensate for losses due to the reaction of 1 with methanol. A more practical solution to this problem was explored in several examples using a catalytic version of the reduction process with 10 mol % of 1 together with excess $PhSiH_3$ as the stoichiometric hydride source. These experiments generally allowed high conversions to the alcohols, presumably because of the continuous regeneration of 1 by the silane. Thus, phenacyl bromide (97%), cyclohexenone (99%), or 4-*tert*-butylcyclohexanone (84%) were all reduced efficiently at room temperature (GLPC assay). Phenylsilane did not reduce ketones in control

(1) (a) Kuivila, H. G. *Acc. Chem. Res.* **1968**, *1*, 299. Neumann, W. P. *Synthesis* **1987**, 665. Pereyre, M.; Quintard, J.-P;.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: Boston, 1987; Chapter 3. (b) Curran, D. P. *Synthesis* **1988**, 417. Ramiah *Tetrahedron* **1987**, *43*, 3541.

(2) (a) Pereyre, M.; Godet, J.-Y. *Tetrahedron Lett.* **1970**, *11*, 3653. (b) Quintard, J.-P.; Pereyre, M. *Bull. Soc. Chim Fr.* **1972**, 1950.

(3) Neumann, W. P.; Heymann, E. *Liebigs Ann. Chem.* **1965**, *683*, 11. Xian, Y. T.; Four, P.; Guibe, F.; Balavoine, G. *Nouv. J. Chim.* **1984**, *8*, 611.

(4) (a) Shibata, I.; Suzuki, T.; Baba, A.; Matsuda, H. *J. Chem. Soc., Chem. Commun.* **1988**, 882. (b) Shibata, I.; Yoshida, T.; Kawakami, T.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1992**, *57*, 4049. (c) For reductions using Bu_2SnH_2, see: Shibata, I.; Nakamura, K.; Baba, A.; Matsuda, H. *Tetrahedron Lett.* **1990**, *31*, 6381.

(5) Vedejs, E.; Haight, A. R.; Moss, W. *J. Am. Chem. Soc.* **1992**, *114*, 6556.

(6) (a) Van Koten, G.; Schaap, C. A.; Noltes, J. G. *J. Organomet. Chem.* **1975**, *99*, 157. (b) Wilt, J. W.; Belmonte, F. G.; Zieske, P. A. *J. Am. Chem. Soc.* **1983**, *105*, 5665.

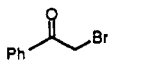
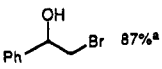
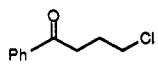
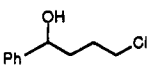
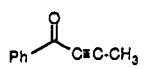
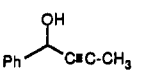
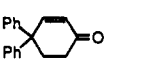
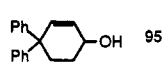
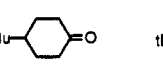
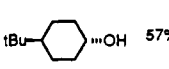
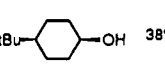
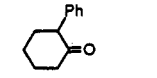
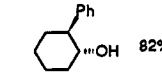
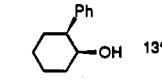
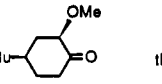
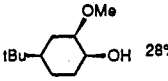
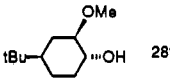
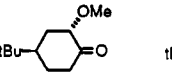
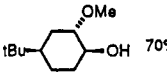
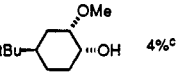
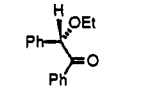
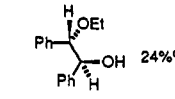
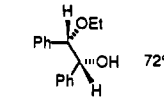
(7) (a) Neumann, W. P.; Niermann, H.; Sommer, R. *Liebigs Ann. Chem.* **1962**, 27. Knocke, R.; Neumann, W. P. *Liebigs Ann. Chem.* **1974**, 1486. Kuivila, H. G. *Adv. Organomet. Chem.* **1964**, *1*, 47.

(8) Silicon hydride analogies: (a) Boyer, J.; Breliere, C.; Corriu, R. J. P.; Kpoton, A.; Poirier, M.; Royo, G. *J. Organomet. Chem.* **1986**, *311*, C39. Corriu, R. J. P.; Lanneau, G. F.; Perrot-Petta, M.; Mehta, V. D. *Tetrahedron Lett.* **1990**, *31*, 2585. (b) Helmer, B. J.; West, R.; Corriu, R. J. P.; Poirier, M.; Royo, G.; DeSaxce, A. *J. Organomet. Chem.* **1983**, *251*, 295. (c) Corriu, R. J. P.; Royo, G.; DeSaxce, A. *J. Chem. Soc., Chem. Commun.* **1980**, 892. (d) Breliere, C.; Carre, F.; Corriu, R. J. P.; Poirier, M.; Royo, G. *Organometallics* **1986**, *5*, 388. (e) Boyer, J.; Corriu, R. J. P.; Kpoton, A.; Mazhar, M.; Poirier, M.; Royo, G. *J. Organomet. Chem.* **1986**, *301*, 131. (f) Breliere, C.; Corriu, R. J. P.; Royo, G.; Zwecker, J. *Organometallics* **1989**, *8*, 1834. (g) Fry, J. L.; McAdam, M. A. *Tetrahedron Lett.* **1984**, *25*, 5859. (h) Corriu, R. J. P.; Guerin, C.; Henner, B.; Wang, Q. *J. Organomet. Chem.* **1989**, *365*, C-7. (i) Hosomi, A.; Hayashida, H.; Kohra, S.; Tominaga, Y. *J. Chem. Soc., Chem. Commun.* **1986**, 1411. Kohra, S.; Hayashida, H.; Tominaga, Y.; Hosomi, A. *Tetrahedron Lett.* **1988**, *29*, 89. (j) Kira, M.; Sato, K.; Sakurai, H. *J. Org. Chem.* **1987**, *52*, 948. Kira, M.; Sato, K.; Sakurai, H. *Chem. Lett.* **1987**, 2243. (k) Perozzi, E. F.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1591. Chopra, S. K.; Martin, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 5342. (l) Attar-Bashi, M. T.; Eaborn, C.; Vencl, J.; Walton, D. R. M. *J. Organomet. Chem.* **1976**, *117*, C-89.

(9) Corriu, R. J. P.; Guerin, C.; Henner, B. J. L.; Wang, Q. *Organometallics* **1991**, *10*, 3574.

0022-3263/93/1958-3046$04.00/0

Table I. Ketone Reduction in Methanol (20 °C)

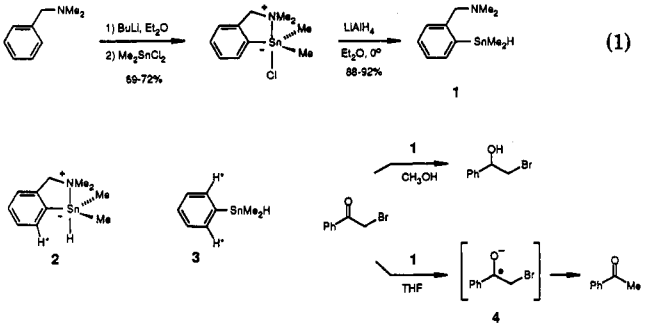
entry	ketone	products		
1		 87%[a]		0.5-1%[b]
2		 61%[a]		
3		 81%[a]		
4		 95%[a]		
5		 57%[c]		38%[c]
6		 82%[c]		13%[c]
7		 28%[c]		28%[c]
8		 70%[c]		4%[c]
9		 24%[c]		72%[c]

[a] Isolated yield. [b] Yield estimated by GLPC analysis of the mixture. [c] Mixture of two diastereomers isolated; yield estimated by NMR assay.

experiments where 1 was not present. Several other silanes such as Et_3SiH, Ph_2SiH_2, $(MeO)_3SiH$, or PMHS ($[MeSiHO]_n$) were also tested, but these proved to be relatively unreactive and practical turnover of the tin catalyst (1) was not observed. On the other hand, $(MeO)_2SiMeH$ afforded results comparable to those obtained with $PhSiH_3$.

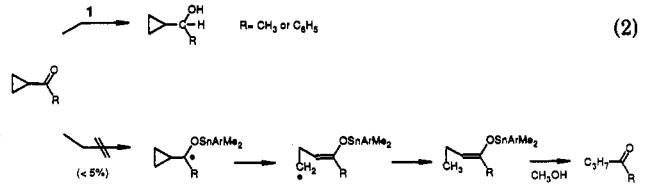
No clear pattern has emerged with respect to ketone facial selectivity in the reductions in methanol. Most of the standard test cases gave diastereomer mixtures, including 4-*tert*-butylcyclohexanone (1.5:1 axial/equatorial attack). The most highly face-selective reduction encountered in this study (Table I, entry 8) was in the case of *trans*-2-methoxy-4-*tert*-butylcyclohexanone. Equatorial hydride delivery was favored by a ratio of 19:1, syn to the axial methoxy group. Lithium aluminum hydride reduction of the same substrate affords a contrasting 15:85 ratio with axial hydride delivery preferred, a result that follows the Felkin–Nguyen selectivity pattern.[10] The syn reduction with 1 can be interpreted as evidence for coordination of tin at the α-methoxy group. However, an acyclic α-alkoxy ketone (Table I, entry 9) reacted with 1 to give a modest 3:1 preference for the erythro product that formally corresponds to the Felkin–Nguyen pathway. This result is not consistent with the carbonyl facial selectivity observed in the conformationally locked ketone of entry 8. No dominant "alkoxy effect" is apparent in these reductions.

An ionic process (nucleophilic hydride delivery) is most likely for the reductions in methanol. A radical mechanism can be ruled out because cyclopropyl methyl ketone and cyclopropyl phenyl ketone are reduced cleanly by 1 to give unrearranged cyclopropylcarbinols (eq 1). Pereyre



(1)

and Godet have shown that cyclopropane ring opening occurs when trialkyltin radicals attack carbonyl oxygen in cyclopropyl ketones (eq 2), while reduction via an ionic



(2)

hydride transfer process takes place without ring cleavage.[11] A single-electron transfer (SET) initiated reduction[12] via the ketyl radical anion is also ruled out for reductions performed in methanol. The key observation in this context is given in Table I, entry 1, where phenacyl bromide is reduced to the bromohydrin (87% isolated) and traces (0.5–1%) of acetophenone. Tanner et al. report that the ketyl intermediate 4 expected from an SET process undergoes rapid loss of bromide ion on the nanosecond time scale.[13] Reduction with 1 in methanol must therefore take place by a different mechanism, presumably by nucleophilic hydride transfer. However, this conclusion does not apply to reactions in aprotic solvents. Thus, phenacyl bromide reacts with 1 in THF to produce acetophenone and only traces of alcohol products.

Tanner and Singh have shown that the reduction of phenacyl chloride by Ph_3SnH in methanol affords a 3:2 mixture of chlorohydrin (hydride transfer) and acetophenone (SET-initiated radical chain),[12] while the latter pathway is strongly favored in THF, benzene, or acetonitrile. In the case of phenacyl bromide, acetophenone is formed exclusively, regardless of solvent. Nucleophilic hydride transfer from Ph_3SnH to carbonyl no longer competes with the SET radical chain in the aprotic solvent. The proposed SET mechanism invokes electron transfer in the initiation step and also in a propagation step.[12] Since 1 gave bromohydrin and only traces of acetophenone in methanol, the rate of nucleophilic hydride transfer is strongly enhanced relative to the radical chain process.

(10) Battioni, J.-P.; Chodkiewicz, W. *Bull. Soc. Chim. Fr.* **1977**, 320.

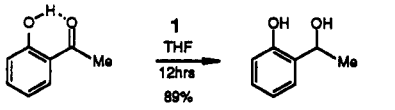
(11) Pereyre, M.; Godet, J. Y. *Tetrahedron Lett.* **1970**, 3653.

(12) (a) Tanner, D. D.; Diaz, G. E.; Potter, A. *J. Org. Chem.* **1985**, *50*, 2149. (b) Tanner, D. D.; Singh, H. K. *J. Org. Chem.* **1986**, *51*, 5182.

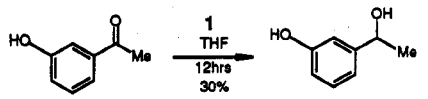
(13) Tanner, D. D.; Chen, J. J.; Chen, L.; Luelo, C. *J. Am. Chem. Soc.* **1991**, *113*, 8074.

However, the radical chain reduction using 1 in THF occurs at room temperature and is also fast by comparison with the Ph_3SnH reaction which requires heating to 60 °C. Furthermore, the solvent effect is more pronounced with 1 and allows control over the competing pathways by changing the experimental procedure.

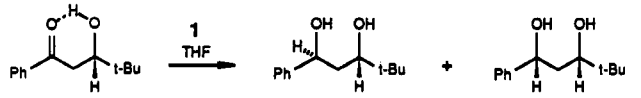
Simple ketones were relatively unreactive with 1 in aprotic solvents. Thus, treatment of acetophenone with 1.2 equiv of 1 gave the following conversions (24 h, rt): THF (<2%), CH_3CN (5%), DMF (30%). Nucleophilic attack by the hydride source is apparently facilitated by protonation of the ketone carbonyl oxygen, an observation that suggests the possibility of carbonyl activation by a suitably placed internal hydroxyl group. As expected, the internally H-bonded ketone 5 was reduced faster in THF



5

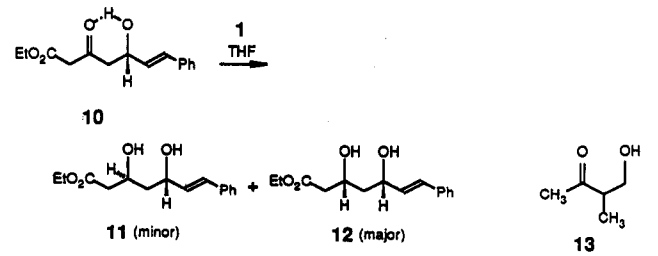


6



7 8 (minor) 9 (major)

solution than was the meta isomer 6 (89% vs 33% conversion after 12 h). Furthermore, aliphatic β-hydroxy ketones also were reduced under aprotic conditions in THF. In the best example, 7 reacted with 30:1 selectivity for the diol 9 (91% isolated after 72 h), a result that corresponds to hydride delivery from the less hindered face of an internally H-bonded carbonyl group.[14,15] A faster reaction was observed in alcohol solvents, but selectivity decreased as conversion rates increased (2-methyl-2-propanol, 18:1 9:8, 85% after 29 h; 2-propanol, 15:1 9:8, 87% after 14 h). The same carbonyl facial preference was also observed in the reduction of 10,[14g] but the ratio of



10

11 (minor) 12 (major)

13

(14) For other examples of analogous stereocontrolled hydroxy ketone reductions see: (a) Narasaka, K.; Pai, H. C. *Chem. Lett.* **1980**, 1415. (b) Sletzinger, K.; Verhoeven, T. R.; Volante, J. M.; McNamara, J. M.; Corley, E. G.; Liu, T. M. H. *Tetrahedron Lett.* **1985**, *26*, 2951. (c) Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, *27*, 5939. Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560. (d) Rosslein, L.; Tamm, C. *Helv. Chim. Acta* **1988**, *71*, 47. (e) Hanamoto, T.; Hiyama, T. *Tetrahedron Lett.* **1988**, *29*, 6467. (f) Paterson, I.; Rawson, D. J. *Tetrahedron Lett.* **1989**, *30*, 7463. (g) Kathawala, F. G.; Prager, B.; Prasad, K. P.; Repic, O.; Shapiro, M. J.; Stabler, R. J.; Wilder, L. *Helv. Chim. Acta* **1986**, *69*, 803.

(15) Kiyooka, S.-I.; Kuroda, H.; Shimasaki, Y. *Tetrahedron Lett.* **1986**, *27*, 3009. Hoffmann, R. W.; Weidman, U. *Chem. Ber.* **1991**, *124*.

Table II. Radical Chain Dehalogenation with 1 (THF, 20 °C)

entry	halide	product	yield (%)
1	phenacyl bromide	acetophenone	86[a]
2	o-(bromoethyl)benzene	ethylbenzene	100[b]
3	γ-iodobutyrophenone	butyrophenone	98[b]
4	3-bromo-1-phenylpropene	β-methylstyrene	100[b]
5	p-bromoanisole	anisole	78[c]
6	p-iodoanisole	anisole	85[d]

[a] Isolated yield within 1 h reaction time. [b] Conversion within 12 h (GLPC analysis). [c] Conversion after 3 days. [d] Conversion after 1 day.

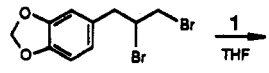
12:11 was only 3.9:1 (63% after 48 h). The β-hydroxy ketone 13 was not reduced efficiently under the THF conditions (<5% yield after 72 h, rt). Lower reactivity in this case can be attributed to an increase in eclipsing methyl–methyl interactions in the conformation necessary for internal H-bonding. We also encountered difficulties in attempts to apply the catalytic reduction method (excess $PhSiH_3$ + 0.1 equiv of 1 in THF) to the β-hydroxy ketones. The catalytic cycle did take with 7 in THF, but there was a substantial decrease in the diastereomer ratio (to ca. 3:1).

A brief survey of functional group compatibility has been made. Thus, 1 did not reduce esters, simple enoates, nitriles, epoxides, sulfones, saturated nitro alkanes, or simple halides in methanol solution, at least in part because the reagent itself is destroyed by the protic solvent within a few hours. However, halides and other typical radical chain reduction substrates did react in aprotic solvents. As already mentioned, phenacyl bromide was rapidly dehalogenated with 1 in THF to give acetophenone. Simple alkyl bromides were considerably less reactive, but dehalogenations occurred efficiently at room temperature on a time scale of hours, or days for the aryl halide substrates. Good yields were obtained in THF in the absence of any added initiators or catalysts (Table II). A primary selenide ($PhSeCH_2CH(Ph)CH_3$) was also reduced at 20 °C, but the rate was marginal and only ca. 30% conversion was seen after 2 days.

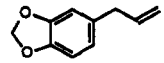
Several standard test systems were examined to establish that radical intermediates are involved in these reductions.[16] Thus, cyclopropylcarbinyl bromide was reduced cleanly to 1-butene using 1 in deuterated tetrahydrofuran. The absence of significant deuterium incorporation (NMR assay; ca. 5% detection limit) supports direct participation by 1 in the hydrogen transfer step, and the exclusive formation of the rearranged product is consistent with rapid ring opening of a cyclopropylcarbinyl radical intermediate.[16] Furthermore, a radical elimination was demonstrated in the reaction of 1 with saffrole dibromide 14 to give saffrole 15 (>95% isolated yield). On the other hand, the bromohydrin ether 16 was dehalogenated to phenetole without elimination (54% conversion after 24 h; GLPC assay). Reductive trapping of the radical intermediate in this case is faster than elimination of the phenoxyl radical.

In all of the halide examples, reductions proceeded at room temperature without added initiators. No special precautions were necessary to achieve useful reduction rates, although we saw some indication of nonreproducible

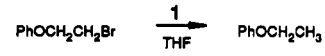
(16) Maillard, B.; Forrest, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7024. Kinney, R. J.; Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 7902. Curran, D.; Newcomb, M. *Acct. Chem. Res.* **1988**, *21*, 206. Castaing, M.; Pereyre, M.; Ratier, M.; Blum, P. M.; Davies, A. G. *J. Chem. Soc., Perkin Trans. 2* **1979**, 287.



14



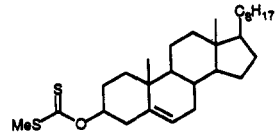
15



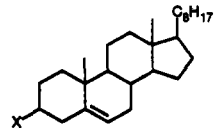
16

induction periods that may reflect the presence of unknown chain terminators. Deliberate addition of galvinoxyl suppressed the reductive dehalogenation of phenacyl bromide or 1-(bromoethyl)benzene as expected for a chain process.

The use of radical chain initiators was not explored in the dehalogenations because initiation was not necessary, but we did encounter evidence that AIBN initiation can expand the scope of reductions using 1. As already mentioned, 1 reacted very slowly with sulfur or selenium derivatives at room temperature. Xanthate 17[17] behaved

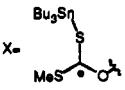


17

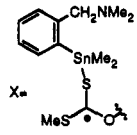


18 X = OH
19 X = H

20a X =



20b X =



similarly, but it could be reduced using a large excess of 1 in THF at room temperature to give several products including cholesterol 18 and cholestene 19. The reaction was much faster in the presence of an initiator (AIBN; sunlamp irradiation), but the same complex mixture was formed. Reduction of 17 using Bu_3SnH is known to give sideproducts if the intermediate radical **20a** is generated at temperatures where it does not undergo rapid fragmentation.[17] Apparently, premature capture of **20a** by the tin hydride affords an unstable hemithioacetal intermediate that decomposes to 18 during workup. Barton et al. controlled this problem by slowly adding the tin hydride to 17 in refluxing toluene. At the higher temperature, **20a** fragments rapidly, resulting in good yields of the deoxygenation product 18. With 1 as the reducing agent, an improvement in product ratios was obtained simply by heating the reaction mixture to 80 °C to encourage fragmentation of **20b**. However, conversion was modest because 1 is thermally unstable. Ultimately, it was found that addition of AIBN accelerated the desired reduction at 80 °C sufficiently to give >90% conversion after 30 min using 2.3 equiv of 1 in benzene. Slow addition of the hydride was not necessary, and no special precautions were required. Polar materials (1 and its decomposition products) were easily removed by filtration through silica gel, and conventional purification methods afforded crystalline 19 in 75% yield. A trace of cholesterol was also detected by analytical TLC, together with minor unidentified sulfur-containing byproducts. Nearly identical results were obtained using the procedure of Barton et al.[17] We assume that the AIBN-initiated reaction proceeds by the same radical chain pathway with 1 as the reducing agent as with Bu_3SnH.[17]

(17) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

Table III. Spectroscopic Comparisons of 1 and 3 (Benzene-d_6)

	1	3
^{1}H-NMR		
δ SnH	5.64 ppm	5.45 ppm
δ SnCH	0.30 ppm	0.19 ppm
$^1J_{SnH}$	1696/1777[a] Hz	1724/1804[a] Hz
$^2J_{SnCH}$	51/53[a] Hz	53/55[a] Hz
$^3J_{SnC-CH}$	55[b] Hz	51/53[a] Hz
^{119}Sn-NMR		
δ Sn	−30.2 ppm (vs Me_4Sn)	−42.2 ppm (vs Me_4Sn)
^{13}C-NMR		
δ SnMe	−8.99 ppm	−11.6 ppm
$^1J_{SnMe}$	361[b] Hz	354[b] (346/362)[a] Hz

[a] ^{117}Sn/^{119}Sn coupling values resolved. [b] Average value; ^{117}Sn/^{119}Sn splittings not resolved.

In the absence of AIBN, the qualitative reaction rates were not sensitive to variables such as the exclusion of light or oxygen. Apparently, no species other than 1 is necessary to initiate the radical chain reductions of the halide substrates. Although we cannot rule out participation by unknown impurities in the chain initiation event, all of the evidence suggests that 1 is capable of initiating radical chains spontaneously in the case of halide substrates. An SET process similar to that suggested by Corriu et al.[9] and by Tanner et al.[12] is the most likely explanation, but a conventional radical chain mechanism is not ruled out.

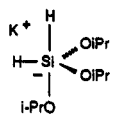
The pentavalent structure 2 could be the species responsible for electron transfer. In an attempt to determine whether 2 is a better description for bonding in the ground state than is the tetracoordinated structure 1, NMR comparisons have been performed between 1 and the parent system 3.[6b] A trend toward pentavalent tin should be reflected by increased $^1J_{SnC}$ in 1,[18a] but only a modest difference was seen in the relevant coupling constants: $^1J_{SnMe}$ = 361 Hz for 1 and 354 Hz for 3 (average of ^{117}Sn and ^{119}Sn satellites). The three-bond coupling (55 Hz vs 52 Hz, average of ^{117}Sn and ^{119}Sn coupling) between tin and the *o*-aryl proton (marked H*) was also marginally larger in 1 vs 3. High-field chemical shifts for the ^{119}Sn nucleus relative to carefully chosen reference structures can also be used as evidence for pentavalent tin.[18] However, the small difference in δ values for 1 and 3 (δ ^{119}Sn, −30.2 and −11.6 ppm, respectively, Table III) is in the opposite direction. These data do not establish that 2 is the best structural representation, although they could be consistent with a small ground-state contribution from a trigonal bipyramidal structure.[18a] Judging from the reactivity of 1, tin–nitrogen coordination becomes more important in the transition state for electron transfer as well as for hydride delivery.

Discussion

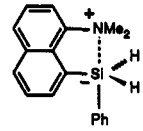
Internal activation of structurally analogous silicon hydrides has been studied extensively.[8,9] Most of these

(18) (a) Jastrzebski, J. T. B. H.; Grove, D. M.; Boersma, J.; van Koten, G.; Ernsting, J.-M. *Magnetic Resonance in Chemistry* **1991**, *29*, S25. (b) Smith, P. J.; Tupciaukas, A. P. *Annual Reports on NMR Spectroscopy* **1978**, *8*, 291. Wrackmeyer, B. *Annu. Rep. NMR Spectrosc.* **1985**, *16*, 73.
(19) Abraham, M. H.; Andonian-Haftvan, J. *Bull. Soc. Chim. Belg.* **1980**, *89*, 819.

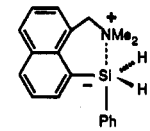
reports implicate pentacoordinated siliconate species as the reactive hydride sources, and **21–25** have been suggested to have pentacoordinated solution structures based on X-ray and NMR evidence.[8c,d] These silicon hydrides



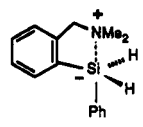
21



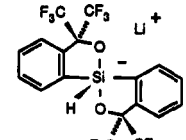
22



23



24



25

have increased hydride donor reactivity, and **21–23** and **25** are sufficiently activated to reduce ketones.[8a,j,k,9] Since the NMR evidence for **1** indicates little contribution by a pentacoordinated tin species **2**, the details of bonding in the ground state appear not to play a decisive role in the enhanced hydride reactivity of **1**. More likely, the activating effect functions in the transition state leading to Sn–H bond cleavage and may well involve a bonding interaction between nitrogen and tin. An SET-initiated radical chain mechanism is consistent with available evidence for the dehalogenations, but further details of the activation process cannot be specified at this time.

The amino tin hydride reagent **1** can serve as a selective nucleophilic hydride source in protic solvents or as a radical chain reducing agent under aprotic conditions. The room temperature reactivity of **1** should be an advantage with thermally sensitive substrates. No initiator is necessary for the radical reductions of halides, and the tin byproduct in dehalogenations is the crystalline and easily recycled tin halide. A modified Barton deoxygenation is also possible with **1**, although optimum results require AIBN initiation at 80 °C. The combination of easy workup and control over selectivity using simple solvent effects may prove useful in complex synthetic applications.

Experimental Section

[2-[(Dimethylamino)methyl]phenyl]dimethyltin Hydride (1). The method of Noltes et al.[6a] was used to prepare [2-[(dimethylamino)methyl]phenyl]dimethyltin bromide or the corresponding chloride (mp 120–123 °C from ether–hexane). To a 0 °C slurry of lithium aluminum hydride (900 mg, 23.7 mmol; Aldrich) in 30 mL of Et_2O was slowly added the tin chloride (4.5 g, 14.1 mmol) in 30 mL of THF. After being stirred at 0 °C for 15 min the reaction was quenched by slow addition into ca. 50 mL ice water and the product extracted with ether (150 mL) and washed with ice water. The organic layer was dried ($MgSO_4$) and concentrated (aspirator) at <20 °C to give 3.5 g (88%) of **1** as a clear colorless oil which was used without further purification. The hydride could be handled for short periods without special precautions, but long-term storage at −15 °C was necessary to avoid decomposition. A characteristic fragment ion was detected in the mass spectrum for $C_{11}H_{19}NSn$, M − 16, 266.0132, error = 4.5 ppm; base peak = 91.0592 amu. IR (C_6D_6, cm^{-1}): 2800, =CH; 1820, SnH; 1500, =CH. 200-MHz NMR (C_6D_6, ppm) δ: 7.70 (1 H, dd, J = 5.3, 3.5 Hz, $^3J_{SnCCH}$av = 55 Hz), 7.20–7.10 (2 H, m), 6.95–6.85 (1 H, m), 5.64 (1 H, sept, J = 2.2 Hz, $^1J_{SnH}$ = 1777/1696 Hz), 3.13 (2 H, s), 1.84 (6 H, s), 0.30 (6 H, d, J = 2.2 Hz, $^2J_{SnCH}$ = 51/53 Hz). ^{13}C NMR ($\{^1H\}$, C_6D_6, ppm) δ: 145.6, 141.3, 137.8, 128.5, 127.7, 127.2, 65.8, 44.3, −9.0 ($^1J_{SnC}$ = 361 Hz). ^{119}Sn NMR ($\{^1H\}$, C_6D_6, ppm) δ: −30.2 vs Me_4Sn.

General Procedure for Ketone Reductions with 1 in Methanol. To a solution of ketone (0.3–1.0 mmol) in methanol (1–3 mL) was added **1** (1.3 equiv) via syringe. For catalytic reduction, this procedure was modified by using 0.1 equiv of **1** and 3 equiv of $PhSiH_3$ (Petrarch). The reaction mixture was stirred overnight at room temperature and was then concentrated (aspirator) and the residue purified by flash chromatography on silica gel, 1:5 EtOAc/hexane eluent, to remove unreacted ketone. The organotin residues were retained by the column. Authentic samples of *trans*-2-phenylcyclohexanol and α-cyclopropylbenzyl alcohol were obtained from Aldrich. Product structural assignments for 2-ethoxy-1,2-diphenylethanol,[20a] 4-phenyl-3-butyn-2-ol,[20b] 4,4-diphenylcyclohex-2-en-1-ol,[20c] *cis*- and *trans*-4-*tert*-butylcyclohexanol,[20d] *cis*-2-phenylcyclohexanol,[20e] 1-cyclopropylethanol,[20f] 2-bromo-1-phenylethanol,[20g] 4-chloro-1-phenylbutanol,[20h] and the 4-*tert*-butyl-2-methoxycyclohexanol isomers[10] were based on comparisons with literature spectral data.

Hydroxy Ketone Reductions. The procedure was the same as above, except that the reaction was performed in THF. 2-Hydroxyacetophenone, 3-hydroxyacetophenone, and 4-hydroxy-3-methylbutan-2-one were purchased from Aldrich and were used without further purification. 4,4-Dimethyl-3-hydroxy-1-phenylpentan-1-one (**7**)[21] and ethyl 5-hydroxy-3-oxo-7-phenylhept-6-enoate (**10**)[14g] were prepared by literature procedures. Authentic samples of 2-hydroxyphenethyl alcohol and 3-hydroxyphenethyl alcohol were obtained from Aldrich. NMR comparisons established the structures of the diastereomers (syn and anti) of 4,4-dimethyl-1-phenylpentane-1,3-diol[15] and ethyl 3,5-dihydroxy-7-phenylhept-6-enoate.[14g]

General Procedure for Radical Dehalogenation. Phenacyl bromide, 2-bromoethyl phenyl ether, 1-bromoethylbenzene, cinnamyl bromide, (bromomethyl)cyclopropane, 4-bromoanisole, and 4-iodoanisole were purchased from Aldrich and used without further purification. To a solution of organic halide (1.0 mmol) in THF (3 mL) at room temperature was added **1** (1.5 equiv) via syringe. Reaction times varied from 5 to 10 min in the case of phenacyl bromide to 12–24 h for typical primary or secondary bromides to 1–3 days for aryl halides or an alkyl selenide. After solvent removal (aspirator), the residue was triturated with 1:10 ether–hexane to remove the dehalogenated product. The residual tin halide was then separated by crystallization from ether. The organic layer was concentrated (aspirator), and the residue was purified by flash chromatography on silica gel, 1:5 EtOAc/hexane eluent. Phenetole, ethylbenzene, butyrophenone, saffrole, anisole, and isopropylbenzene were compared to authentic samples (Aldrich).

Radical Deoxygenation of Xanthate 17. A solution of **17**[17] (61 mg), hydride **1** (83 mg, 2.3 equiv), and AIBN (3 mg) was prepared in dry benzene (3 mL). This mixture was heated in an 80 °C bath and monitored by analytical TLC (silica gel, 10% EtOAc/hexane). After 30 min, the xanthate had disappeared, and the solution was cooled to room temperature, concentrated (aspirator), and purified by preparative layer chromatography (silica gel, 7.5% EtOAc/hexane). Several minor zones at R_f 0.2–0.5 were incompletely separated and could not be identified, but traces of cholesterol **18** were present according to analytical TLC comparisons. The zone at R_f = 0.8 was collected to give crystalline cholestene **19** (36 mg, 75%), identical by NMR spectroscopy with a commercial sample (Aldrich).

Acknowledgment. This work was supported by the National Institutes of Health (CA17918).

(20) (a) Inoue, M.; Taguchi, Y.; Sugita, T.; Ishikawa, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2098. (b) Grindley, T. B.; Johnson, K. F.; Katritzky, A. R.; Keogh, H. J.; Thirkettle, C.; Topsom, R. D. *J. Chem. Soc., Perkin Trans. 2* **1974**, 282. (c) Vittorelli, P.; Katalinic, J. P.; Mukherjee-Muller, G.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1975**, *58*, 1379. (d) Eliel, E. L.; Ro, R. S. *J. Am. Chem. Soc.* **1957**, *79*, 5992. (e) Verbit, L.; Price, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 5143. (f) Pierre, J.-L.; Perraud, R.; Arnaud, P. *Acad. Sci. Ser. C* **1970**, *270*, 1663. (g) Knipe, A. C. *J. Chem. Soc., Perkin Trans. 2* **1973**, 589. (h) Yamaguchi, S.; Kabuto, K. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 3033.

(21) Katayama, S.; Fukuda, K.; Watanbe, T.; Yamauchi, M. *Synthesis* **1988**, 178.