Tris(trimethylsilyl)silane as a Radical-Based Reducing Agent in Synthesis[1,2]

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Tris(trimethylsilyl)silane is an effective reducing agent for organic halides, selenides, xanthates, and isocyanides, as well as an effective hydrosilylating agent for dialkyl ketones and alkenes. The silane functions as a mediator in the formation of intermolecular carbon–carbon bonds via radicals and allows a variety of organic substrates to be used as alkyl radical percursors. Absolute rate constants for the reaction of $(Me_3Si)_3Si^•$ radicals with a variety of organic compounds have been measured in solution by laser flash photolysis. At 294 K rate constants are $>5 \times 10^7\ M^{-1}\ s^{-1}$ for C=C double bonds that are activated by neighboring π-electron systems or by electron-withdrawing groups. For other substrates, reactivities decreased in the order xanthate > selenide > isocyanide > nitro > sulfide.

It has been recently shown that tris(trimethylsilyl)silane is a valuable reducing agent for organic halides (eq 1).[3,4]

$$RX + (Me_3Si)_3SiH \xrightarrow[\text{initiator}]{\text{radical}} RH + (Me_3Si)_3SiX \quad (1)$$

The procedure is straightforward and involves a two step free radical chain process (see Scheme I). Absolute rate constants for the two propagation steps have been obtained.[5,6] Tris(trimethylsilyl)silane can also be used as a mediator in the formation of C–C bonds either intermolecularly or intramolecularly using iodides or bromides as starting materials.[7] Furthermore, $(Me_3Si)_3SiH$ functions as a catalyst in the reduction of iodide and bromides, via radicals, when sodium borohydride is the consumable reagent.[8] These results, together with the fact that silanes are more acceptable than triorganotin compounds from ecological and toxicological perspectives,[9,10] suggest that tris(trimethylsilyl)silane could be an attractive alternative to tributyltin hydride in other radical chain reactions.[11-13]

In the present work, we have extended the use of $(Me_3Si)_3SiH$ as a reducing agent and as a mediator in the intermolecular C–C bond formation. We have also employed optical absorption techniques to study mechanistic aspects of these radical chain processes. Our results suggest that this reagent could be an important tool for organic chemists.

Scheme I

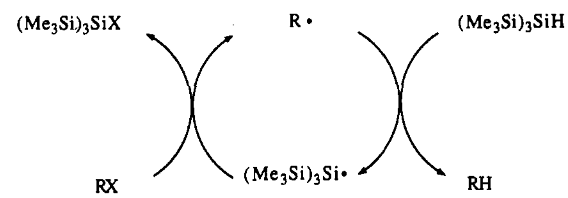
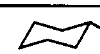
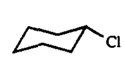
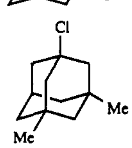
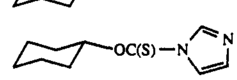
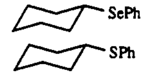
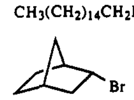
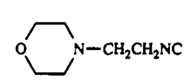
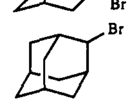
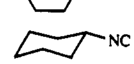
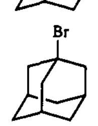


Table I. Reduction of Some Organic Compounds by Tris(trimethylsilyl)silane

RZ	yield RH (%)[a]	RZ	yield RH (%)[a]
$CH_3(CH_2)_{14}CH_2Cl$	68[b]		97
	82		86
	93		95
			99
			20[c]
$CH_3(CH_2)_{14}CH_2Br$	96		
	90	$CH_3(CH_2)_8CH_2NC$	94
			96
	96		95
	93	$(CH_3)_3CCH_2C(CH_3)_2NC$	85
$CH_3(CH_2)_{14}CH_2I$	98		

[a] Yields by GC analysis based on formation of RH. [b] Conversion 75%, yield 90%. [c] Conversion 38%, yield 53%.

Results

Reduction of Organic Derivatives. Reduction of a variety of organic derivatives were carried out by using

(1) Issued as NRCC publication No. 32307.
(2) Taken in part from the Ph.D work of B. Kopping.
(3) Chatgilialoglu, C.; Griller, D.; Lesage, M. *J. Org. Chem.* **1988**, *53*, 3641.
(4) Chatgilialoglu, C. In *Free Radicals in Synthesis and Biology*; Minisci, F., Ed.; Kluwer: Dordrecht, 1989; pp 115–123.
(5) Chatgilialoglu, C.; Griller, D.; Lesage, M. *J. Org. Chem.* **1989**, *54*, 2492.
(6) Chatgilialoglu, C.; Dickhaut, J.; Giese, B., manuscript in preparation.
(7) Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681.
(8) Lesage, M.; Chatgilialoglu, C.; Griller, D. *Tetrahedron Lett.* **1989**, *30*, 2733.
(9) Ricci, A.; Seconi, G.; Taddei, M. *Chimica Oggi* **1989**, *7*, 15 and references cited therein.
(10) Evans, C. J.; Karpel, S. *Organic Compounds in Modern Technology*; Elsevier: New York, 1985; Chapter 10.
(11) Neumann, W. P. *Synthesis* **1987**, 665.
(12) Curran, D. P. *Synthesis* **1988**, 417 and 489.
(13) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, 1986.

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tris(trimethylsilyl)silane. Reactions of each derivative with $(Me_3Si)_3SiH$ at 75–90 °C in toluene and in the presence of a radical initiator, i.e. AIBN (azoisobutyronitrile), gave the corresponding hydrocarbons in excellent yields (see Table I). Sample analyses were carried out using GC and authentic samples as calibrants. Yields were quantified by using an internal standard.

Reductions of bromides and iodides were straightforward, and the reactions were complete after a short time (ca. 0.5 h). For tertiary, secondary, and primary chlorides the reductions became increasingly difficult due to the shorter chain lengths. Thus, for the reduction of primary chlorides a longer reaction time and periodic addition of initiator was necessary. Photochemical initiation of chloride reduction was used and proved to be quite efficient.[3]

The reduction of thionoesters and especially xanthates using tributyltin hydride is a mild, general method used for the deoxygenation of secondary alcohols.[14] By replacing tributyltin hydride with tris(trimethylsilyl)silane the reduction of thionoesters is still efficient and goes to completion after 1 h with good yields (Table I).

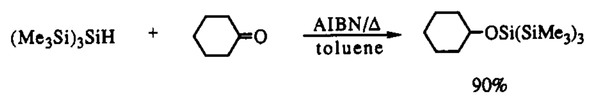
Secondary alkyl selenides and sulfides were also reduced by the silane, as expected in view of the affinity of silyl radicals for sulfur- and selenium-containing substrates. However, while reductive cleavage of the C–Se bond was effective, the corresponding cleavage of the C–S bond was inefficient.

The most unexpected results came from the reduction of alkyl isocyanides by a procedure similar to the one employed by Barton and his co-workers[15] for Bu_3SnH. The reduction yields of tertiary, secondary, and primary isocyanides by Bu_3SnH are dependent on the temperature, i.e. the yields are good in boiling toluene or benzene for secondary and tertiary isocyanides, whereas primary isocyanides can be reduced in acceptable yields only in refluxing xylene with periodic additions of initiator. Using tris(trimethylsilyl)silane this function can be replaced by hydrogen independently of the nature of the alkyl substituent. That is, primary, secondary, and tertiary isocyanides at ca. 80 °C gave the corresponding hydrocarbon in excellent yields (Table I). The silicon-containing product has been isolated in a pure form and the infrared spectrum indicates an equilibrium between nitrile and isonitrile isomers, viz.,[16]

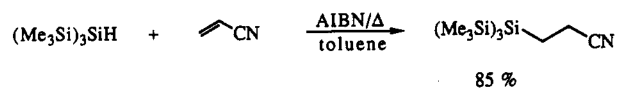
$$(Me_3Si)_3Si\text{-}NC \rightleftharpoons (Me_3Si)_3Si\text{-}CN \qquad (2)$$

Finally, the replacement of a tertiary nitro group by hydrogen, which can be effectively achieved using tributyltin hydride,[17] is not observed in the reactions between 4-nitro-2,2,4-trimethylpentane, *p*-cyano-α-nitrocumene, and tris(trimethylsilyl)silane. The fact that the conversions of nitro derivatives are relatively high, i.e. 70% of the starting materials are consumed after 3 h under normal reduction conditions, indicates that the reaction path is different from that with tin hydride.[18]

Hydrosilylation of Double Bonds. Additions of silyl radicals to multiple bonds are generally very fast processes.[19] Tris(trimethylsilyl)silane, being a good hydrogen donor, is capable of substaining radical hydrosilylations of dialkyl ketones[20,21] and olefins.[20] When a mixture of $(Me_3Si)_3SiH$ and cyclohexanone or acrylonitrile was heated at 80–90 °C for 1–2 h in the presence of catalytic amounts of AIBN as initiator, addition of the silane across the double bond occurs, affording the hydrosilylated compounds in good yields, viz.,



(3)



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Absolute Rate Constants for the Reaction of $(Me_3Si)_3Si^{\bullet}$ Radicals with Various Organic Compounds. A convenient method for generating tris(trimethylsilyl)silyl radicals involves the photodecomposition of di-*tert*-butyl peroxide in the presence of the silane, viz.,[22]

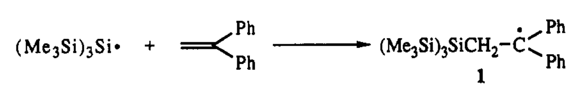
$$t\text{-BuOOBu-}t \xrightarrow{h\nu} 2\,t\text{-BuO}^{\bullet} \qquad (5)$$

$$t\text{-BuO}^{\bullet} + (Me_3Si)_3SiH \rightarrow t\text{-BuOH} + (Me_3Si)_3Si^{\bullet} \qquad (6)$$

The rate constant for reaction 6 was found to be $(1.1 \pm 0.2) \times 10^8\ M^{-1}\ s^{-1}$ at 295 K.[22] At high $(Me_3Si)_3SiH$ concentration the formation of the tris(trimethylsilyl)silyl radical will therefore be an essentially instantaneous process on our laser flash photolysis time scale, so that time-resolved studies on its subsequent reactions can be made. Two kinetic procedures were employed.

Direct Method. The laser flash photolysis technique allows rate constants to be measured directly by monitoring either the decay of the reactant or the growth of the product of a reaction. The transient optical spectra due to the tris(trimethylsilyl)silyl radical show weak absorption below 340 nm[22] and preclude detailed kinetic studies. 1,1-Diphenylethylene proved to be well suited to the direct measurement of product radical growth.

The generation of $(Me_3Si)_3Si^{\bullet}$ in a 4:1 (v/v) mixture of di-*tert*-butyl peroxide and tris(trimethylsilyl)silane containing 0.02–0.03 M of 1,1-diphenylethylene (DPE) led to a transient spectrum of adduct radical 1 with maxima at ca. 330 nm.[23]



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(7)

The rate constant for reaction 7 was obtained from a study of the buildup traces of 1 at different concentrations of DPE. Under these conditions the pseudo-first-order rate constant associated with the buildup, k_{obsd}, is given by

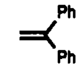
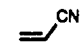
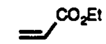
$$k_{obsd} = k_0 + k_7[DPE] \qquad (8)$$

where k_0 reflects the lifetime of the tris(trimethylsilyl)silyl radical in the absence of DPE. At 294 K we obtained $k_7 = (1.04 \pm 0.14) \times 10^8\ M^{-1}\ s^{-1}$.

Probe Technique. The direct method described above is inappropriate for most reactions in which carbon-centered radicals are produced since they are not easily detected at wavelengths >300 nm. For this reason, rate

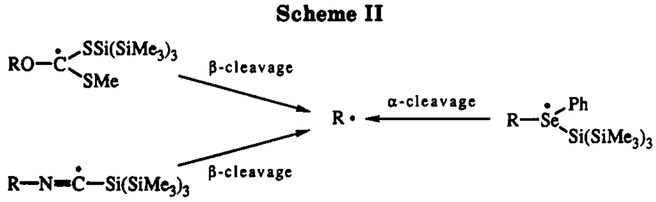
(14) For reviews see: Barton, D. H. R.; Motherwell, W. B. *Pure Appl. Chem.* **1981**, *53*, 15. Hartwig, W. *Tetrahedron*, **1983**, *39*, 2609.
(15) Barton, D. H. R.; Bringmann, G.; Lamotte, G.; Hay-Motherwell, R. S.; Motherwell, W. B. *Tetrahedron Lett.* **1979**, 2291.
(16) Seckar, J. A.; Thayer, J. S. *Inorg. Chem.* **1976**, *15*, 503.
(17) Ono, N.; Miyake, H.; Kanimura, A.; Hamamoto, I.; Tamura, R.; Kaji, A. *Tetrahedron* **1985**, *41*, 4013.
(18) Further work on the reaction of tris(trimethylsilyl)silane with nitro alkanes, under free radical conditions, is in progress.
(19) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5119; **1983**, *105*, 3252.
(20) Kulicke, K. J.; Giese, B. *Synlett* **1990**, 91.
(21) For rate constants of $(Me_3Si)_3Si^{\bullet}$ addition to ketones see: Alberti, A.; Chatgilialoglu, C. *Tetrahedron*, **1990**, *46*, 3963.
(22) Chatgilialoglu, C.; Rosini, S. *Bull. Soc. Chim. Fr.* **1988**, 298.
(23) McPhee, D. J.; Campredon, M.; Lesage, M.; Griller, D. *J. Am. Chem. Soc.* **1989**, *111*, 7563 and references therein.

Table II. Absolute Rate Constants at 294 K for the Reactions of $(Me_3Si)_3Si^•$ Radicals with Some Organic Substrates

substrate	k, M^{-1} s^{-1}
	$(1.04 \pm 0.14) \times 10^8$
	$(5.93 \pm 0.28) \times 10^7$
	$(6.31 \pm 0.70) \times 10^7$
	$(9.67 \pm 0.94) \times 10^7$
c-$C_6H_{11}NC$	$(4.68 \pm 0.16) \times 10^7$
c-$C_6H_{11}OC(S)SMe$	$(1.05 \pm 0.06) \times 10^9$
$^tBuNO_2$	$(1.16 \pm 0.04) \times 10^7$
$PhSeC_{10}H_{21}$	$(9.63 \pm 1.26) \times 10^7$
$PhSC_{10}H_{21}$	$\leq 5 \times 10^6$
$(CH_3)_3CBr$[a]	$(1.2 \pm 0.2) \times 10^8$
$CH_3CH_2CH(CH_3)Br$[a]	$(4.6 \pm 1.3) \times 10^7$
$CH_3(CH_2)_4Br$[a]	$(2.0 \times 0.2) \times 10^7$

[a] Taken from ref 5.

Scheme II



constants for a variety of organic substrates were measured by using reaction 7 as a probe. Under competitive conditions where the tris(trimethylsilyl)silyl radicals can react with an organic substrate, S, or with DPE, the formation of adduct 1 follows pseudo-first-order kinetics which can be described by eq 9. Values of k at ca. 294 K were

$$k_{obsd} = k_0 + k_7[DPE] + k[S] \quad (9)$$

determined at constant [DPE] for a variety of organic substrates.

Both procedures yield absolute rate constants but do not distinguish between sites or modes of attack. Assignment of the rate constants to given paths must be based on chemical knowledge derived from other techniques, e.g., product analysis or EPR spectroscopy. The results are summarized in Table II.

Competitive Reactions. For the reduction of xanthates, isocyanides, and perhaps selenides with $(Me_3Si)_3SiH$, the key step of the chain reactions is expected to be the fragmentation of the intermediate radical derived from the fast addition of the tris(trimethylsilyl)silyl radical to the specific substrate (cf. Scheme II).

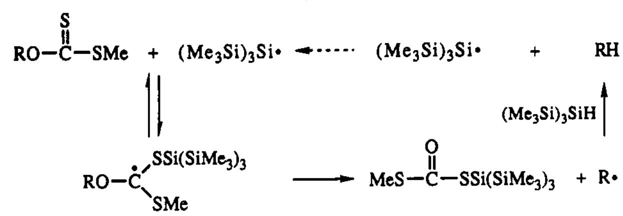
In view of the relevance of the mechanistic knowledge to synthetic applications, we have designed a series of competitive experiments to determine the actual mechanism involved. In particular, the experiment involved competition reactions between the following pairs: c-$C_6H_{11}NC/CH_3(CH_2)_7Br$, c-$C_6H_{11}OC(S)SMe/CH_3(CH_2)_7Br$, c-$C_6H_{11}SePh/CH_3(CH_2)_7Br$. Relative reactivities were obtained by GC analysis following the thermally initiated radical reaction between tris(trimethylsilyl)silane and the two organic substrates (1:1:1 equiv) at 90 °C. The relative reactivities were calculated from the loss of starting material and the appearance of corresponding hydrocarbons by using internal standard. Table III shows the conversion and yield ratios obtained from these experiments together with the ratio of the related rate constants taken from Table II.

Table III. Competitive Reactions Using Tris(trimethylsilyl)silane as the Reducing Agent

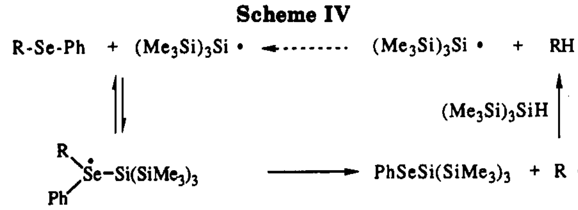
pairs of substrates	time, min	c-$C_6H_{11}X/CH_3(CH_2)_7Br$[a,c]	c-hexane/ n-octane[b,c]	rate constant ratio[d,e]
c-$C_6H_{11}NC/$ $CH_3(CH_2)_7Br$	10	1.14	1.22	2.3
	20	1.18	1.24	
	30	1.15	1.19	
c-$C_6H_{11}OC(S)SMe/$ $CH_3(CH_2)_7Br$	10	2.00	2.38	50
	20	1.57	1.85	
	30	1.43	1.63	
c-$C_6H_{11}SePh/$ $CH_3(CH_2)_7Br$	10	0.10	0.08	4.8
	20	0.12	0.08	
	30	0.16	0.09	

[a] Disappearance of the starting material (%) ratio. [b] Product formation (%) ratio. [c] At 90 °C. [d] Rate constants taken from Table II. [e] At 20 °C.

Scheme III



Scheme IV



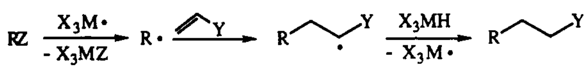
The data indicate that the mechanistic schemes of some of these reactions are complex. For example, in the competitive experiments between n-octyl bromide and cyclohexyl isocyanide the conversion and product ratios are very close to the rate constant ratio being obtained at 90 and 20 °C, respectively (see Table III). Therefore, we can safely assume that the reversible step of the $(Me_3Si)_3Si^•$ radical addition to isocyanides is not important. On the other hand, the competition experiments with cyclohexyl xanthate/n-octyl bromide and cyclohexyl selenide/n-octyl bromide indicate that the relative reactivities are very different from those expected on the basis of the absolute rate constants. That is, for the former pair of substrates, product studies indicate the xanthate to be ca. 2 times more reactive than the primary alkyl bromide instead of ca. 50 times (cf. Table III). Product studies for the latter show the selenide to be ca. 10 times less reactive than primary alkyl bromides, although absolute rate constants indicate that it reacts with tris(trimethylsilyl)silyl radical 5 times faster. These results suggest that the first propagation step is reversible. In fact, if the additions of tris(trimethylsilyl)silyl radicals to thiocarbonyl are irreversible, then cyclohexane should have been formed in more than 90% yield. The mechanism that we conceive for the reduction of xanthates is outlined in Scheme III. That is, tris(methylsilyl)silyl radicals, initially generated by small amounts of AIBN, attack alkyl xanthate to form in a reversible manner, a radical intermediate that undergoes β-scission to form alkyl radicals. Hydrogen abstraction from the silane gives the alkane and $(Me_3Si)_3Si^•$ radicals, thus completing the cycle of this chain reaction. In the selenide case, we believe that a selenanyl radical[24]

Table IV. Radical-Based Reaction of Cyclohexyl Derivatives with Acrylonitrile Using Tris(trimethylsilyl)silane as Mediator[a]

RZ	time, min	RCH_2CH_2CN yield,[b] %	$(Me_3Si)_3SiCH_2CH_2CN$ yield,[b] %	c-C_6H_{12} yield,[b] %
c-$C_6H_{11}I$	10	10	–	57
	20	13	–	68
	30	14	–	76
c-$C_6H_{11}Br$	10	18	13	10
	20	29	15	18
	30	31	17	19
c-$C_6H_{11}NC$	10	5	6	5
	20	12	13	9
	30	19	17	13
c-$C_6H_{11}SePh$	10	1.5	11	17
	20	1.5	18	45
	30	1.6	19	52
c-$C_6H_{11}OC(S)SMe$	10	2	1	7
	20	6	3	18
	30	10	5	40

[a] At 90 °C. [b] Yields by GC analysis based on products formation.

Scheme V

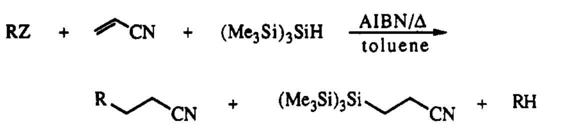


$X_3M\bullet$ = $Bu_3Sn\bullet$ or $(Me_3Si)_3Si\bullet$

is formed as intermediate followed by α-cleavage leading to formation of alkyl radical. In other words, our results indicate that the reaction should be designated as S_H2 (stepwise) rather than as an S_H2 (synchonous) process.[25] Scheme IV shows the mechanism for the reduction of secondary alkyl phenyl selenide.

Carbon–Carbon Bond Formation. In the last decade, the intermolecular C–C bond formation has been increasingly achieved by radical addition to alkenes. In such reactions, the adduct radicals have to be trapped, generally by a hydrogen donor, subsequent to the C–C bond formation in order to prevent polymerization (see Scheme V).[12,13] These complex reactions have often been accomplished using tributyltin hydride. To test the use of tris(trimethylsilyl)silane as mediator in the formation of C–C bond (cf. Scheme V), we designed a series of experiments using different organic substrates as alkyl radical percursors.

The reactions of c-$C_6H_{11}Z$ (where Z = I, Br, NC, OC(S)SMe, SePh), tris(trimethylsilyl)silane and acrylonitrile in 1:1:1 equivalent ratio and under the same conditions were studied, viz.,



(10)

2 3 4

The formation of the products **2**, **3**, and **4** are derived from the C–C bond formation, hydrosilylation of alkene, and the reduction of the organic substrate, respectively. The results are summarized in Table IV. These data further attempt to reconcile conflicting kinetic and product studies. That is, based on the absolute kinetic data it is expected that the behavior of xanthate and selenide will be similar to iodide and bromide respectively. However, the observed discrepancies are in accordance with the relative rates. These results confirm the reversible addition of the $(Me_3Si)_3Si^\bullet$ radicals to xanthate and selenide as shown in Schemes III and IV, respectively.

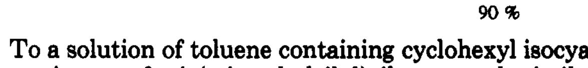
Table V. Carbon–Carbon Bond Formation via Radicals Using Tris(trimethylsilyl)silane as Mediator

RZ	T, °C	2,[a] %	3,[a] %	4,[a] %
c-$C_6H_{11}I$	80	81	5	10
c-$C_6H_{11}Br$	80	64	18	11
c-$C_6H_{11}NC$	80	50	38	10
	110	70	20	10
	140	65	18	17
c-$C_6H_{11}OC(S)SMe$	80	26	51	17
	110	45	14	35
	140	38	14	37
c-$C_6H_{11}SePh$	80	9	75	10
	110	36	40	14
	140	46	18	15

[a] Yields by GC analysis based on products formation.

The success of C–C bond formation by means of this methodology depends upon addition of nucleophilic alkyl radicals to alkenes substituted with electron-withdrawing substituents. Unfortunately silyl radicals are also nucleophilic and add rapidly to such alkenes. To overcome this problems, and to decrease the direct reduction product, i.e. cyclohexane, we performed a new series of experiments by slowly adding a mixture of silane and alkene to a solution of cyclohexyl derivative. Table V shows the results obtained under these conditions. Furthermore, in order to obtain information about the cleavage of intermediate, which in some cases is present prior to the formation of the cyclohexyl radical (cf. Scheme II), we also ran the same experiments at higher temperatures.

The information described above is of importance in designing reactions for syntheses. Two examples now will be illustrated. To a solution containing cyclohexyl iodide and acrylonitrile in toluene, a mixture of tris(trimethylsilyl)silane and AIBN in toluene was added slowly over the period of 2 at 80 °C. Normal workup followed by flash chromatography on silica afforded 90% of the desired product, viz.,



(11)

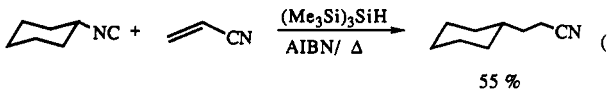
90 %

To a solution of toluene containing cyclohexyl isocyanide, a mixture of tris(trimethylsilyl)silane, acrylonitrile, and AIBN in toluene was added slowly over the period of 2 h at 110 °C. Normal workup followed by flash chromatog-

(24) Evidence for selenanyl type radicals has been obtained in single crystal EPR experiments. For example see: Symons, M. C. R. In *Electron Spin Resonance Vol. 6*; Ayscough, P. B., Ed.; The Royal Society of Chemistry: Letchworth, 1981; p 114.

(25) Ingold, K. U.; Roberts, B. P. *Free Radicals Substitution Reactions*; Wiley: New York, 1971.

raphy on silica afforded 55% of the desired product, viz.,



(12)

Discussion

Reduction of organic functional groups by organotin hydrides via radicals has continued to increase in importance since its discovery in the 1960s.[26] Free radicals are reactive intermediates of considerable importance in the development of organic chemistry,[11-13] and many methodologies in synthesis via radicals have employed tributyltin hydride.[27] However, organotin compounds are generally toxic and create disposal problems, and it is often difficult to remove the tin-containing byproducts from the reaction mixtures. Therefore, tris(trimethylsilyl)silane should be an attractive alternative for organotin compounds in many of these free radical reactions.

Table I shows that the reductions of a variety of organic functional groups by tris(trimethylsilyl)silane are very efficient. Yields are excellent for most of the precursors, i.e. iodides, bromides, chlorides, secondary selenides and xanthates, primary, secondary, and tertiary isocyanides. Tertiary alkyl nitro derivatives are not reduced. Hydrosilylations of dialkyl ketones and olefins are also quite efficient processes.[20,21]

Absolute rate constants for the reaction of tris(trimethylsilyl)silyl radicals with a variety of organic substrates are now available (Table II). It is also worth mentioning that the difference in reactivity between $(Me_3Si)_3Si^{\bullet}$ and $Et_3Si^{\bullet}$ radicals is not large, the former being 4–10 times less reactive.[28] As we have already shown,[5] the trends in reactivity for halogen atom abstraction from RX by $(Me_3Si)_3Si^{\bullet}$ radicals are those which would be expected on thermochemical grounds. That is, rate constants depend upon the strength of the carbon–halogen bond being broken and are around 10^5 for chlorides, 10^7–10^8 for bromides, and larger than 10^9 ($M^{-1}\ s^{-1}$) for iodides, and they also depend to a limited extent on the kind of R.[5]

The addition of tris(trimethylsilyl)silyl radicals to multiple bonds is a facile process. Thus, olefins in which the double bond is activated either by conjugation with a neighboring π-electron system or by electron-withdrawing groups are very reactive ($k > 5 \times 10^7\ M^{-1}\ s^{-1}$). The addition of $(Me_3Si)_3Si^{\bullet}$ radicals to isocyanide and nitro groups are also rapid, rate constrants being larger than $10^7\ M^{-1}\ s^{-1}$. It has been shown by EPR spectroscopy that $(Me_3Si)_3Si^{\bullet}/t$-$BuNO_2$ and $Et_3Si^{\bullet}/t$-BuNC reactions yield the siloxy nitroxide[30] and the imidoyl[31] radical, respectively.

The reaction of $(Me_3Si)_3Si^{\bullet}$ radicals with cyclohexyl xanthate occurs with a rate constant of $1 \times 10^9\ M^{-1}\ s^{-1}$ at room temperature. In view of the affinity of silyl radicals for sulfur (bond dissociation energy for Si–S is ca. 100 kcal mol^{-1}),[32] there are two possible sites of attack. That is, the addition to the sulfur of the thiocarbonyl moiety and a direct S_H2 attack on the sulfide sulfur.[33] However, the fact that the sulfide $C_{10}H_{21}SPh$ reacts with a rate constant of less than $5 \times 10^6\ M^{-1}\ s^{-1}$ implies that addition to C=S π-bond is favored.

The replacement of isocyanide by hydrogen warrants further comments. Isocyanides, which are obtained from primary amines via formylation and dehydration by phosphorus oxychloride/triethylamine at low temperatures,[35] can be reduced to the corresponding hydrocarbon by Bu_3SnH.[15,36] The reduction yields of tertiary, secondary, and primary isocyanides by Bu_3SnH are dependent on the temperature, i.e. the yields are good in boiling toluene or benzene for secondary and tertiary isocyanides, whereas primary isocyanides can be reduced in acceptable yields only in refluxing xylene. Although very little is known about the overall mechanism and, in particular, about the structural characteristics of the intermediate imidoyl radicals, it is believed that the effect is due to the increase of the activation energy for the β-scission step in the order tertiary, secondary, primary. In replacing tributyltin hydride by tris(trimethylsilyl)silane, the reduction of isocyanides becomes more facile, that is the reactivity is independent of the nature of the alkyl substituent at 75 °C. It has been shown by EPR spectroscopy[37] that the triethylsilyl adduct, which has a linear or close to linear arrangement of bonds about C_α, form $R^{\bullet} + Et_3SiCN$ readily. From the available kinetic data,[37] we calculate (at 75 °C) rate constants of 5×10^5 and $2 \times 10^7\ s^{-1}$ for β-scission of n-$BuN{=}\dot{C}SiEt_3$ and t-$BuN{=}\dot{C}SiEt_3$ radicals, respectively.

Tris(trimethylsilyl)silane can also be used as a mediator in intermolecular C–C bond formation using a variety of organic substrates as precursors for the alkyl radicals. These processes occurring via radical chain reactions similar to the tin method (cf. Scheme V). For successful syntheses, it is important that (i) the $R_3M^{\bullet}$ radicals react faster with the radical precursor than with the alkene and (ii) the $R^{\bullet}$ radicals attack alkene to form the adduct radical prior to reaction with the hydrogen donor. The kinetic information gathered in this paper should be of value in the design of new syntheses involving tris(trimethylsilyl)silane. In fact, we showed in two examples, i.e. cyclohexyl iodide and isocyanide, that it is possible to control these complex chain reactions and to obtain good to excellent yields.

The use of isocyanides as precursors for C–C bond is without precedence.[13] In fact, C–C bond formation does not take place when alkyl isocyanides are used together with tributyltin hydride in the presence of alkenes.[13] Presumably, the addition of stannyl radicals is slow or readily reversible. We should also emphasize that up to now no method exists in which primary alkylamines can be used as alkyl radical percursors in the formation of C–C bonds.[38]

(26) Kuivila, H. G. *Acc. Chem. Res.* **1968**, *1*, 299.
(27) In his recent review of free radical chain reactions in organic synthesis[12] Curran dedicates almost half of the several hundred citations to tin hydride based chemistry.
(28) For absolute rate constants of $Et_3Si^{\bullet}$ radical reactions see references 19 and 29.
(29) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5123.
(30) Alberti, A.; Dellonte, S.; Paradisi, C.; Roffia, S.; Pedulli, G. F. *J. Am. Chem. Soc.* **1990**, *112*, 1123.
(31) Blum, P. M.; Roberts, B. P. *J. Chem. Soc., Chem. Commun.* **1976**, 535.
(32) Walsh, R. *Acc. Chem. Res.* **1981**, *14*, 246.
(33) The mechanism of deoxygenation of primary and secondary alcohols by meams of the reaction of their derived dithiocarbonate esters with tributyltin hydride (Barton-McCombie reaction[14]) has been the subject of considerable discussion recently.[34]
(34) For recent review, see: Minisci, F. In *Sulfur-Centered Reactive Intermediates in Chemistry and Biology*; Chatgilialoglu, C., Asmus, K.-D., Eds.; Plenum: New 1990; pp 303–317.
(35) Barton, D. H. R.; Bringmann, G.; Motherwell, W. B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2665.
(36) Barton, D. H. P.; Bringmann, G.; Lamotte, G.; Motherwell, W. B.; Hay-Motherwell, R. S.; Porter, A. E. A. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2657. Barton, D. H. R.; Bringmann, G.; Motherwell, W. B. *Synthesis* **1980**, 68.
(37) Blum, P. M.; Roberts, B. P. *J. Chem. Soc. Perkin Trans. 1* **1978**, 1313.
(38) Chatgilialoglu, C.; Giese, B.; Kopping, B. *Tetrahedron Lett.*, in press.

Conclusions

Free radicals ar of considerable importance in the development of organic chemistry, and many methodologies in radical-based synthesis employed tributyltin hydride. However, there are problems associated with triorganotin compounds. Tris(trimethylsilyl)silane should be an attractive alternative of tributyltin hydride for the majority of these reactions although in few instances the two reagents complement each other. The results obtained in this work should provide useful data for the design of new syntheses.

Experimental Section

Materials. Tris(trimethylsilyl)silane, TTMSS, was prepared by reaction of trichlorosilane with trimethylchlorosilane as described by Burger and Kilian.[39] Cyclohexyl selenide,[40] cyclohexyl xanthate,[41] 4-nitro-2,2,4-trimethylpentane,[42] and *p*-cyano-α-nitrocumene[43] were prepared following literature procedures. All other materials were commercially available and were used as received.

General Procedure for Reduction of Organic Derivatives. A solution, containing the compound to be reduced, TTMSS (1.2 equiv), and AIBN (3–10%) as initiator in toluene was heated at 75–90 °C for 0.5–2 h and then analyzed by GC. Yield were quantified by GC using dodecane or tetradecane as an internal standard.

Preparation of Tris(trimethylsilyl) Cyanide. A solution of 327 mg (3 mmol) cyclohexyl isocyanide, 896 mg (3.6 mmol) TTMSS, and 59 mg (0.36 mmol) AIBN in 30 mL of toluene was heated at 90 °C for 2 h. The mixture was concentrated in vacuo. The residue was dissolved in 10 mL of pentane. 790 mg (80%) adduct crystallized as a white solid. Tris(trimethylsilyl)silyl cyanide: mp 89 °C (pentane); ^{13}C NMR ($CDCl_3$) δ 0.2714 (9 C, $SiMe_3$), 125.19 (1 C, CN); GC/MS 273 (M^+), 258 ($M^+ - 15$), 174 ($(Me_3Si)_2Si^+$), 73 (Me_3Si^+); IR (CH_2Cl_2) ν 2200 (CN), 2050 (NC). Anal. Calcd for $C_{10}H_{27}NSi_4$ (273.67): C, 43.88; H, 9.94; N, 5.11. Found: C, 43.24; H, 9.54; N, 4.98.

Hydrosilylation of Cyclohexanone. A 10-mL two-necked round-bottomed flask equipped with a magnetic stirring bar, nitrogen inlet, reflux condenser, and septum was flushed with nitrogen and was charged with 245 mg (2.5 mmol) cyclohexanone, 747 mg (3.0 mmol) of TTMSS, and 29 mg (0.18 mmol) of AIBN in 1 mL of toluene. After 3 h another portion of 29 mg (0.18 mmol) of AIBN in toluene was added. After 6 h the mixture was concentrated. Distillation gave 704 mg (81%) of [[tris(trimethylsilyl)silyl]oxy]cyclohexane (bp 75–125 °C, 0.4 mbar). [[Tris(trimethylsilyl)silyl]oxy]cyclohexane: ^1H NMR ($CDCl_3$) δ 0.18 (s, 27 H, $SiMe_3$), 1.21–1.31 (m, 5 H), 1.42–1.46 (m, 1 H), 1.63–1.72 (m, 4 H), 3.25–3.29 (m, 1 H, H-1); ^{13}C NMR ($CDCl_3$ δ 0.69 (9 C, $SiMe_3$), 23.6 (2 C, C-3, C-5), 25.4 (1 C, C-4), 35.3 (2 C, C-2, C-6), 74.8 (1 C, C-1); GC/MS *m/z* 331 ($M^+ - 15$), 273 ($M^+ - 73$), 263 ($M^+ - 83$), 249 ($M^+ - 97$), 247 ($M^+ - 99$), 233 ($M^+ - 113$), 83 $(C_6H_{11})^+$. Anal. Calcd for $C_{15}H_{38}OSi_4$ (346.81): C, 51.95; H, 11.04. Found: C, 52.09; H, 11.22.

Hydrosilylation of Acrylonitrile. A solution of 796 mg (3.2 mmol) of TTMSS, 169 mg (3.2 mmol), acrylonitrile, and 52 mg (0.32 mmol) of AIBN in 15 mL of toluene was heated at 90 °C for 2 h. The reaction mixture was concentrated in vacuo. Distillation gave 85% yield of 3-[tris(trimethylsilyl)silyl]propionitrile. The adduct crystallized as a white solid [bp (sublimes) 100 °C (10^{-1}) mbar]. 3-[Tris(trimethylsilyl)silyl]propionitrile: ^1H NMR ($CDCl_3$) δ 0.19 (27 H, $SiMe_3$), 1.56 (2 H, H-3), 2.36 (2 H, H-2); ^{13}C NMR ($CDCl_3$) δ 0.72 (9 C, $SiMe_3$), 4.71 (1 C, C-3), 15.78 (1 C, C-2), 121.65 (1 C, C-1). Anal. Calcd for $C_{12}H_{31}NSi_4$ (301.73): C, 47.76; H, 10.35; N, 4.64. Found: C, 47.78; H, 10.40; N, 4.64.

Competition between *n*-Octyl Bromide and Cyclohexyl Isocyanide, Xanthate, and Selenide (Table III). A solution of 1 equiv of *n*-octyl bromide, 1 equiv of the cyclohexyl derivate, 1 equiv of TTMSS, and AIBN (5–10%) as initiator in toluene was heated at 90 °C. After 10, 20, and 30 min the yields were quantified by GC using dodecane as an internal standard.

Addition of Cyclohexyl Iodide, Bromide, Isocyanide, Xanthate, and Selenide to Acrylonitrile (Table IV). A solution of 1 equiv of precursor, 1 equiv of acrylonitrile, 1 equiv of TTMSS, and AIBN (5–10%) as initiator was heated at 90 °C. After 10, 20, and 30 min the yields were quantified by GC using dodecane as an internal standard.

Addition of Cyclohexyl Iodide, Bromide, Isocyanide, Xanthate, and Selenide to Acrylonitrile (Table V). To a solution of 0.5 mmol of the precursor in 5 mL of toluene at 80 °C, 110 °C, and in 5 mL of xylene at 140 °C was added over 2 h a solution of 0.6 mmol of TTMSS, 0.6 mmol of acrylonitrile, and 0.05 mmol of AIBN in 4 mL of toluene. Yields were quantified by GC using dodecane as an internal standard.

Addition of Cyclohexyl Iodide to Acrylonitrile. A 100-mL round-bottomed flask equipped with a magnetic stirring bar, dry argon inlet, reflux condenser, and septum was flushed with argon and charged with 840 mg (4.0 mmol) of cyclohexyl iodide and 212 mg (4.0 mmol) of acrylonitrile in 40 mL of toluene. The mixture was brought to reflux; 1.19 g (4.8 mmol) of TTMSS and 157 mg (0.96 mmol) of AIBN dissolved in 6 mL of toluene were added over 2 h through a long needle using a syringe pump. The reaction mixture was cooled, concentrated in vacuo, and flash chromatographed on silica gel using pentane.

Addition of Cyclohexyl Isocyanide to Acrylonitrile. A solution of 3 mmol of precursor in 20 mL of toluene was placed in a two-necked round-bottom flask equipped with a magnetic stirring bar, argon inlet, reflux condenser, and septum; 190 mg (3.6 mmol) of acrylonitrile, 896 mg (3.6 mmol) of TTMSS, and 114 mg (0.7 mmol) of AIBN dissolved in 6 mL of toluene were added by means of a syringe over 3–4 h. During the addition the solution was heated at 90 °C. After 4 h the heating was stopped and the reaction mixture was cooled, concentrated in vacuo, and flash chromatographed on silica gel using pentane.

Laser Flash Photolysis. The laser flash photolysis experiments were carried out under oxygen-free conditions using pulses (337.1 nm, 8 ns, up to 10 mJ) from a Molectron UV 24 nitrogen laser for excitation. The experimental system was interfaced with PDP/03L computer that controlled the experiment and provided data gathering, storage, and hard copy facilities. Complete details have been given elsewhere.[44]

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(39) Bürger, H.; Kilian, W. *J. Organomet. Chem.* **1969**, *18*, 299.
(40) Liotta, D. *Acc. Chem. Res.* **1984**, *17*, 28.
(41) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.
(42) Kornblum, N.; Jones, W. J. *Org. Synth.* **1963**, *43*, 87.
(43) Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A. *J. Org. Chem.* **1976**, *41*, 1560.
(44) Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7747.