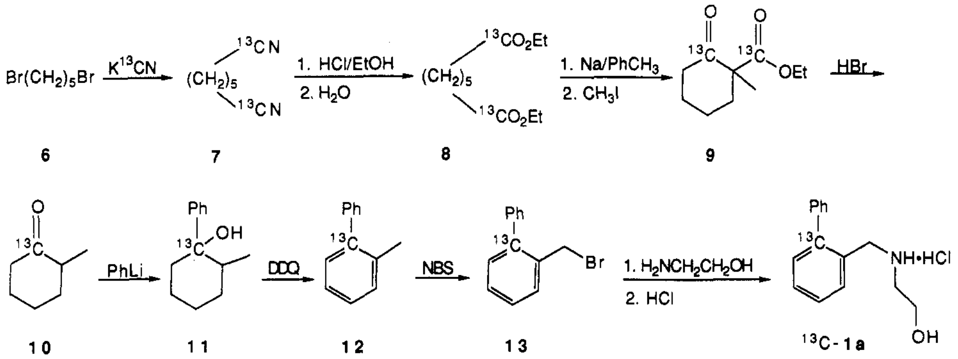
Scheme III



The conclusive demonstration of ^{13}C–H splitting in both the meta and para isomers umambiguously defines path B as the functioning pathway.

The simplicity of the ^{13}C NMR spectra in both examples demonstrated that only one route or rearrangement, path B, is operative. From this set of experiments, we may conclude that, prior to ring formation, the phenyl group of **1a** undergoes a series of 1,2-migrations, which contributes to the preponderant formation of 7-phenyl-1,2,3,4-tetrahydroisoquinoline **3**, rather than the anticipated 8-phenyl isomer **2**.

Experimental Section

General. All ^{13}C-labeled intermediates were identified by gas chromatographic comparison with their unlabeled analogues. The percentage of ^{13}C incorporation was determined by electron-impact mass spectroscopy. ^{13}C NMR experiments were performed at 20 MHz on a Varian FT-80A as gated decoupled spectra with full C–H coupling and retention of NOE. Tetramethylsilane was used as an internal standard. The ^{13}C NMR experiments were run on the hydrochloride salts in DMSO-d_6.

Synthesis of *N*-(2-Hydroxyethyl)-2-phenyl-*2*-^{13}*C*-benzylamine Hydrochloride (^{13}C-1a). The source of ^{13}C labeling was potassium cyanide-^{13}*C* obtained from Prochem/Isotopes. Steps in the synthesis of ^{13}C-**1a** are shown in Scheme III. All of the steps are from the literature and are not described here in detail. 1,5-Dibromopentane (**6**) was treated with potassium cyanide-^{13}*C* and heated under reflux in 4:1 (v/v) ethanol–water to form the labeled 1,5-dicyanopentane (**7**) in 87% yield.[8] Treatment with gaseous hydrogen chloride in ethanol formed the iminoester, and subsequent hydrolysis in water–ethanol gave diethyl pimelate (**8**) with the desired carboxyl label in 55% yield. Cyclization with concomitant methylation occurred with sodium metal and methyl iodide in refluxing toluene, forming labeled ethyl 2-methylcyclohexanone-2-carboxylate (**9**).[9] Upon heating in 48% aqueous hydrobromic acid, *1*-^{13}*C*-2-methylcyclohexanone (**10**) was formed. The yield from **8** to **10** was 40%. Reaction with phenyllithium in tetrahydrofuran at −78 °C gave 1-phenyl-1-hydroxy-*1*-^{13}*C*-2-methylcyclohexane (**11**). Aromatization by treating **11** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in refluxing toluene for 16 h yielded *1*-^{13}*C*-2-methylbiphenyl (**12**). Bromination of the methyl group with *N*-bromosuccimide in refluxing carbon tetrachloride gave **13**. Subsequent treatment with an excess of 2-aminoethanol in 1,2-dimethoxyethane and acidification with gaseous hydrogen chloride in ethanol gave ^{13}*C*-**1a** in 26% yield from **10**, without the necessity of purification of any intermediate. ^{13}C-**1a** was purified by the formation of the hydrochloride salt and the recrystallization from ethanol (mp 128 °C; isotopic enrichment: ^{13}C = 95.2%).

Aluminum Chloride Induced Migration of ^{13}C-1a. ^{13}C-labeled **1a** (0.42 g, 1.59 mmol) was diluted with unlabeled compound **1a** (0.33 g, 1.25 mmol) and intimately mixed with aluminum chloride (1.10 g, 8.25 mmol) and ammonium chloride (0.25 g, 4.67 mmol). This material was heated to a melt at 132 °C while being stirred for 45 min. After this time, TLC (Baker silica gel, EtOAc/MeOH/NH$_4$OH = 10/10/0.01) showed the reaction to be complete (**1a**, R_f = 0.57; **4**, R_f = 0.57; **5**, R_f = 0.53). The reaction was quenched in 12 N hydrochloric acid and diluted with water. Toluene and ammonium tartrate were added to the solution. Sodium hydroxide pellets were added to adjust the pH to 10. The organic phase was dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give the crude product mixture as an oil (0.55 g, 85%). The three isomers were separated by column chromatography (Baker silica gel; EtOAc/MeOH/NH$_4$OH = 93/7/1) and converted to their respective hydrochloride salts by treatment with gaseous hydrogen chloride in 2-propanol.

Acknowledgment. We acknowledge our indebtedness to David Staiger of the Physical and Structural Chemistry Department for NMR spectral data and interpretation and Lewis Killmer for GC/MS spectral data.

Supplementary Material Available: ^{13}C NMR spectra of compounds **1a**, **4**, and **5** (Figures 1–3) (2 pages). Ordering information is given on any current masthead page.

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Rate Constants for the Reactions of Tris(trimethylsilyl)silyl Radicals with Organic Halides[1]

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We recently discovered that organic halides can be reduced in good yields to their corresponding dehalogenated compounds by using tris(trimethylsilyl)silane.[3] The procedure is straight-forward and involves a two-step free-radical chain process, eq 1 and 2. These findings

$$R^{\bullet} + (Me_3Si)_3SiH \rightarrow RH + (Me_3Si)_3Si^{\bullet} \qquad (1)$$

$$(Me_3Si)_3Si^{\bullet} + RX \rightarrow (Me_3Si)_3SiX + R^{\bullet} \qquad (2)$$

suggest that tris(trimethylsilyl)silane might be an effective substitute for tributyltin hydride. The tin compound is used extensively in laboratory syntheses but is unsatisfactory for widespread use because of its toxicity.

In support of the concept, we have found that the bond dissociation energy of the silicon–hydrogen bond in

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[2] (a) Consiglio Nazionale delle Ricerche. (b) National Research Council of Canada.

[3] Chatgilialoglu, C.; Griller, D.; Lesage, M. *J. Org. Chem.*, in press.

$(Me_3Si)_3SiH$ is 79 kcal mol^{-1} and is 11 kcal mol^{-1} less than those in simple trialkylsilanes so that reaction 1 is quite efficient.[4] To complete the picture, we needed to test the efficacy of reaction 2 and to compare the results with those obtained for tributylstannyl radicals.

We now describe the measurement of rate constants for reaction 2 that were obtained by using laser flash photolysis and competition techniques. The most striking feature of the data is the very large range of reactivities observed for different types of halides. Moreover, the results establish that tris(trimethylsilyl)silane is a perfectly satisfactory substitute for tributyltin hydride in radical chain reductions.

Results

The laser flash photolysis apparatus that was used in this work had a time resolution that covered the range 0.1–10 μs. As a result, the lowest rate constants that would be conveniently measured by using the technique were ca. 10^6 M^{-1} s^{-1}.

This constraint was only a significant limitation for the least reactive halides used in this work. In these cases, competition experiments coupled with product analyses were used to tie the reactivities of the less labile materials to the absolute rate constants measured by the flash photolysis approach.

Laser Flash Photolysis

Direct Method: A convenient method for generating $(Me_3Si)_3Si^\bullet$ radicals involves the photodecomposition of di-*tert*-butyl peroxide in the presence of tris(trimethylsilyl)silane, eq 3 and 4.[5] The transient optical spectra due to *tert*-butoxyl and tris(trimethylsilyl)silyl radicals show weak absorptions below 340 nm.[5]

$$\mathrm{Me_3COOCMe_3} \xrightarrow{h\nu} \mathrm{2Me_3CO^\bullet} \tag{3}$$

$$\mathrm{Me_3CO^\bullet + (Me_3Si)_3SiH \rightarrow Me_3COH + (Me_3Si)_3Si^\bullet} \tag{4}$$

At 298 K in isooctane or in benzene–di-*tert*-butyl peroxide (1:2, v/v) as solvents, the rate constant for reaction 4 is rather high ($k_4 = (1.0 \pm 0.1) \times 10^8$ M^{-1} s^{-1}[5]). Thus, at high $(Me_3Si)_3SiH$ concentrations, the formation of the tris(trimethylsilyl)silyl radical was an essentially instantaneous process on our laser flash photolysis time scale so that time-resolved studies on its subsequent reactions were easily made.

In principle, the laser flash photolysis technique allows rate constants to be measured directly by monitoring either the decay of a reactant or the growth of the product of a reaction. The transient optical absorption of the tris(trimethylsilyl)silyl radical is weak in the accessible wavelength range (vide supra) and precluded detailed kinetic studies. However, 9-bromofluorene proved to be well suited for the direct measurement of product 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 5.3×10^{-4} to 3.2×10^{-3} M 9-bromofluorene led to the transient spectrum of 9-fluorenyl radical, Fl$^\bullet$, with maxima at 503 (strong), 470 (weak), and 440 (weak).[6]

$$\mathrm{(Me_3Si)_3Si^\bullet + Fl{-}Br \rightarrow (Me_3Si)_3SiBr + Fl^\bullet} \tag{5}$$

The rate constant for reaction 5 was obtained by measuring the pseudo-first-order rate constants, k_{obsd}, for the growth of the fluorenyl radical as a function of the concentration of 9-bromofluorene. The relationship is given in eq 6 where k_0 reflects the lifetime of the tris(trimethylsilyl)silyl radical in the absence of the substrate. At 294 K we obtained $k_5 = (2.1 \pm 0.1) \times 10^9$ M^{-1} s^{-1} (Figure 1).

Table I. Absolute Rate Constants at 293 K for Halogen Atom Abstraction by $(Me_3Si)_3Si^\bullet$ Radicals

substrate	k_2, M^{-1} s^{-1}	substrate	k_2, M^{-1} s^{-1}
Fl–Br[a]	$(2.1 \pm 0.1) \times 10^9$	$CH_3(CH_2)_4Br$	$(2.0 \pm 0.2) \times 10^7$
$C_6H_5CH_2Br$	$(9.6 \pm 1.4) \times 10^8$	CCl_4	$(1.7 \pm 0.4) \times 10^8$
$(CH_3)_3CBr$	$(1.2 \pm 0.2) \times 10^8$	$CHCl_3$	$(6.8 \pm 1.8) \times 10^6$
$CH_3CH_2CH(CH_3)Br$	$(4.6 \pm 1.3) \times 10^7$	$C_6H_5CH_2Cl$	$\leq 2 \times 10^6$

[a] 9-Bromofluorene.

Table II. Relative Rate Constants at 298 K for Halogen Atom Abstractions by $(Me_3Si)_3Si^\bullet$ Radicals

substrate	k^{rel}	substrate	k^{rel}
$CH_3(CH_2)_4Br$	1.0	$CH_3(CH_2)_5C(CH_3)_2Cl$	0.02
C_6H_5Br	0.23	$CH_3(CH_2)_4Cl$	*a*
$C_6H_5CH_2Cl$	0.24		

[a] Reaction chain length too short for accurate measurement.

Table III. Absolute Rate Constants for Halogen Atom Abstractions by Group 14 Centered Radicals

substrate	$Et_3Si^\bullet$	$(Me_3Si)_3Si^\bullet$	$Bu_3Sn^\bullet$
$C_6H_5CH_2Br$	2.4×10^9	9.6×10^8	1.5×10^9
$(CH_3)_3CBr$	1.1×10^9	1.2×10^8	1.7×10^8
$CH_3(CH_2)_4Br$	5.4×10^8	2.0×10^7	2.6×10^7
$C_6H_5CH_2Cl$	2.0×10^7	4.6×10^6	1.1×10^6
$(CH_3)_3CCl$	2.5×10^6	4.0×10^5[a]	2.7×10^4
$CH_3(CH_2)_4Cl$	3.1×10^5		1.4×10^3

[a] $CH_3(CH_2)_5C(CH_3)_2Cl$ used as an example of a tertiary alkyl chloride.

$$k_{\mathrm{obsd}} = k_0 + k_5[\mathrm{Fl^\bullet}] \tag{6}$$

Probe Technique: Many organic halides readily react with tris(trimethylsilyl)silyl radicals, reaction 2, but the radicals R$^\bullet$ that are produced are often not easily detected by optical means. For these compounds, the rate constants for halogen substraction, k_2, were measured by making use of reaction 5 as a probe of the lifetime of the silyl radical. Under these competitive conditions, the $(Me_3Si)_3Si^\bullet$ radicals abstracted halogen from RX or from 9-bromofluorene and the formation of the 9-fluorenyl radical (which was monitored at 503 nm) followed pseudo-first-order kinetics, which are described in eq 7, where the terms have the same meaning as those in eq 6.

$$k_{\mathrm{obsd}} = k_0 + k_5[\mathrm{Fl^\bullet}] + k_2[\mathrm{RX}] \tag{7}$$

Values of k_2 at ca. 294 K were determined by this procedure for a variety of organic halides. The results are summarized in Table I.

Competition Reactions

Relative rate constants were obtained by GC analyses following the photochemically initiated radical reaction between tris(trimethylsilyl)silane and two organic halides at 25 °C. These relative rate constants were calculated from the loss of starting materials (or the appearance of corresponding hydrocarbons) by using the method of Ingold and Shaw[7] and are given in Table II. They were converted to absolute rate constants by taking $CH_3(CH_2)_4Br$ as a standard since this was investigated by laser

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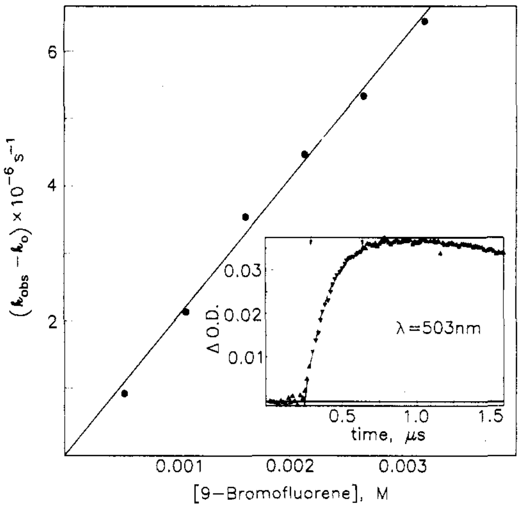

Figure 1. Plot of $k_{obsd} - k_0$ for the reaction of tris(trimethylsilyl)silyl radicals with 9-bromofluorene. Insert: Representative trace monitored at 503 nm for the growth of the 9-fluorenyl radical, [9-bromofluorene] = 1.59×10^{-3} M. The section between the arrows corresponds to the points used for kinetic calculations.

flash photolysis methods (Tables I–III).

Discussion

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, for a particular R group the rate constants decrease on going from bromide to chloride, while for a given halogen, X, the rate decrease along the series R = benzyl > tertiary alkyl > secondary alkyl > primary alkyl > phenyl. However, our quantitative kinetic data revealed that there was an enormous spread in the reactivities of different types of organic halides since rate constants varied by more than 6 orders of magnitude.

The high reactivity of CCl_4 and, presumably, of other polychlorinated alkanes relative to the monochlorinated substrates cannot be entirely attributed to more favorable thermodynamic factors.[8] For the triethylsilyl radical we have previously suggested that its high reactivity toward halogen donors, particularly CCl_4, reflected the importance of charge separation in the transition state.[9,10] The same explanation can be advanced to explain the high reactivity of $(Me_3Si)_3Si^{\bullet}$ toward CCl_4.

Some of the rate constants measured in this work are reported in Table III together with the corresponding values for triethylsilyl and tributyltin radicals.[9] The difference in reactivity between the $(Me_3Si)_3Si^{\bullet}$ and $Et_3Si^{\bullet}$ radicals increases as the absolute rate constants decrease, as would be expected. In general, triethylsilyl displays the highest reactivity toward all alkyl halides, whereas for bromides $(Me_3Si)_3Si^{\bullet}$ and $Bu_3Sn^{\bullet}$ display similar reactivities. However, the most striking feature of the data is that rate constants for the reactions of $Bu_3Sn^{\bullet}$ fall rapidly with chlorides. By contrast, the reactivity with silyl radicals is sustained at a substantially higher level and implies that tris(trimethylsilyl)silane ought to be a better reducing agent for alkyl chlorides than is tributyltin hydride.

Experimental Section

Materials. Tris(trimethylsilyl)silane was prepared by reaction of trichlorosilane with trimethylchlorosilane as described by Burger and Kilian.[11] Tris(trimethylsilyl)silane was purified by careful distillation followed by preparative GC. All other compounds used in this work were commercially available and, where necessary, were purified by standard methods.

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.[12]

Relative Rate Constants. Relative rate constants were measured by taking pairs of organic halides, each 0.1–0.5 M and tris(trimethylsilyl)silane (0.04 M) in hexadecane as solvent. The solutions (2 mL, volume) were placed in quartz test tubes and were carefully deoxygenated by using argon purging. They were then photolyzed in a Rayonet reactor (λ = 254 nm) and were analyzed as the reaction progressed. Products were identified by GC/mass spectrometry (Hewlett-Packard 5790) and were quantified by GC (Hewlett-Packard 5890). Both instruments were equipped with cross-linked methylsilicon columns. Decane and undecane were used as internal standards, and authentic samples of the starting materials and products were used as calibrants.

Product balances, based on the amount of hydrocarbon formed versus silane used, were normally in the range 110–120%. We presume that this excess is due to the photolysis of the tris(trimethylsilyl)silyl halides that are formed during the reaction. This process does not affect the relative rate constants since it simply constitutes an initiation step. The relative rate constants obtained in these experiments were cross-checked by taking different combinations of the organic halides under study. The variation in values measured for the relative rate constants was <10%.

Acknowledgment. Two of us, C.C. and D.G., thank NATO for a research grant (no. 86/678) that made this collaboration possible.

Registry No. $(Me_3Si)_3Si^{\bullet}$, 26121-01-7; $Me_3COOCMe_3$, 110-05-4; $(Me_3Si)_3SiH$, 1873-77-4; FlBr, 1940-57-4; $Fl^{\bullet}$, 2299-68-5; $C_6H_5CH_2Br$, 100-39-0; $(CH_3)_3CBr$, 507-19-7; $CH_3CH_2CH(CH_3)Br$, 78-76-2; $CH_3(CH_2)_4Br$, 110-53-2; CCl_4, 56-23-5; $CHCl_3$, 67-66-3; $C_6H_5CH_2Cl$, 100-44-7; C_6H_5Br, 108-86-1; $CH_3(CH_2)_5C(CH_3)_2Cl$, 928-60-9; $CH_3(CH_2)_4Cl$, 543-59-9; $(CH_3)_3CCl$, 507-20-0.

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[8] (a) Although the bond dissociation energies of $PhCH_2$–Cl and Cl_3C–Cl are 72 and 73 kcal mol^{-1}, respectively,[8b] the rate constant for $(Me_3Si)_3Si^{\bullet} + CCl_4$ reaction is about 300 times greater than that for $(Me_3Si)_3Si^{\bullet} + PhCH_2Cl$. (b) McMillen, D. R.; Golden, D. M. *Ann. Rev. Phys. Chem.* **1982**, *33*, 493.

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