Preparation of and Fluoroalkylation with (Chlorodifluoromethyl)trimethylsilane, Difluorobis(trimethylsilyl)methane, and 1,1,2,2-Tetrafluoro-1,2-bis(trimethylsilyl)ethane

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Abstract: CF_2BrCl reacts with aluminum/*N*-methylpyrrolidinone in the presence of chlorotrimethylsilane to give Me_3SiCF_2Cl in high yield. Similarly, CF_2Br_2 gives Me_3SiCF_2Br with bromotrimethylsilane. Chlorodifluoromethylation of aldehydes using Me_3SiCF_2Cl and a catalytic amount of TBAF in polar solvents occurs at room temperature, providing difluoromethylated alcohols in two steps. Electroreduction of Me_3SiCF_2Cl in the presence of chlorotrimethylsilane gives $Me_3SiCF_2SiMe_3$ (anion-derived product) and $Me_3SiCF_2CF_2SiMe_3$ (radical-derived product). Using THF/HMPA strongly favors the former, whereas THF/TDA-1 (tris(3,6-dioxaheptyl)amine) the latter. $Me_3SiCF_2SiMe_3$ difluoromethylates aldehydes acting as a difluoromethylene dianion ("CF_2^{2-}" equivalent), whereas $Me_3SiCF_2CF_2SiMe_3$ acts at room temperature as an in situ source for the perfluorovinyl anion (due to β-elimination of fluorotrimethylsilane). However, at low temperature the elimination pathway is suppressed and tetrafluoroethylene dianion ("$^-CF_2CF_2^-$" equivalent) behavior is observed. The structure of $Me_3SiCF_2CF_2SiMe_3$ was analyzed by X-ray diffraction. All of the studied fluoroalkylating reagents are moisture- and air-stable and can be readily obtained from a single convenient precursor (CF_2BrCl).

Introduction

Partially fluorinated organic compounds often possess properties making them suitable for diverse applications in materials science, agrochemistry, and the pharmaceutical industry.[1] Generally, the unique behavior of fluorinated systems can be attributed to the high electronegativity of the fluorine atom (4.0 on Pauling's electronegativity scale) combined with its close size to hydrogen (the van der Waal's radii of F and H atoms are 1.35 and 1.2 Å, respectively) leading to the increase in oxidative, hydrolytic, and thermal stability (the C−F bond energy averages about 116 kcal/mol). In many instances fluorinated compounds were shown to have minimal steric difference from their parent hydrido analogs. Among fluorine-containing groups, trifluoromethyl, difluoromethylene, and difluoromethyl groups are of the most interest and use. For example, many trifluoromethylated compounds are known to increase lipid solubility and, therefore, enhance *in vivo* transport rates.[2] The replacement of the methylene for difluoromethylene group has been shown to markedly increase the hydrolytic stability of some labile biologically active molecules. At the same time since very little steric perturbation takes place as hydrogen is replaced for fluorine, the substitution preserves or even increases the biological activity. In a recent example, Matsumura et al. have demonstrated that the difluorinated prostacyclin analog exhibits high stability along with the highest known inhibitory activity on ADP-induced human platelet aggregation.[3]

The CF_2 group is also recognized for its isosteric and isopolar relation to ethereal oxygen, a property which has been widely investigated in the area of difluorinated analogs of sugars and other oxygenated biomolecules.[2] The difluoromethyl group (CF_2H) is believed to act as an isopolar and isosteric analog of the hydroxyl group.[4] The CF_2H group was reported to act as a hydrogen bond donor which is useful in applications where a more lipophilic hydrogen bond donor other than OH is required. For example, chiral secondary alcohols bearing the lipophilic difluoromethyl group have been targeted as inhibitors of certain enzymes[5] and as precursors for the preparation of liquid crystalline materials.[6]

Compared with interest in the development of trifluoromethylation methods in recent years, introduction of the chlorodifluoromethyl as well as difluoromethyl and difluoromethylene groups has received less attention. Convenient procedures for introducing these latter groups are particularly desirable. Currently available methods are based on (a) synthesis of difluoromethyl- and difluoromethylene-containing compounds from the corresponding fluorinated building blocks, (b) nucleophilic difluorination of carbonyl compounds,[7] and (c) electro-

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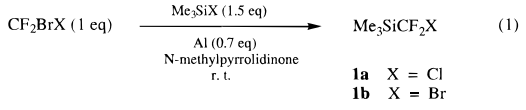
philic difluorination of carbanions and related nucleophiles.[3] Our interest in this field began with studies on the development of (trifluoromethyl)trimethylsilane (Me_3SiCF_3) and other (perfluoroalkyl)(trialkyl)silanes as reagents for nucleophilic trifluoromethylation and perfluoroalkylation.[8] Organosilicon fluoroalkylating reagents are especially attractive due to their relative nontoxicity, stability, ease of handling, and low cost. Since little is known about nucleophilic difluoromethylation using organosilicon reagents, we extended our investigations to these systems. We now report on the preparation and use of fluoroalkylating reagents of the general formula Me_3SiCF_2X (X = Cl (**1a**), Br (**1b**), $SiMe_3$ (**2**), CF_2SiMe_3 (**3**)) readily obtained from bromochlorodifluoromethane (CF_2BrCl) and dibromodifluoromethane (CF_2Br_2), respectively. The use of **1a**, **2**, and **3** in fluoroalkylation reactions is also described .

Results and Discussion

Preparation of Me_3SiCF_2X (X = Cl (1a) and Br (1b)). Use of Me_3SiCF_3 for the nucleophilic trifluoromethylation of various electrophiles is well documented.[8] Under initiation by tetrabutylammonium fluoride (TBAF) or other nucleophiles such as tris(dimethylamino)sulfur trimethylsilyl difluoride (TASF) or potassium *tert*-butoxide, Me_3SiCF_3 transfers the CF_3 group to ketones, aldehydes, esters, acid halides, and other substrates. Consequently, we investigated **1a** under similar reaction conditions in order to develop a convenient and mild protocol for the chlorodifluoromethylation of aldehydes to afford the corresponding secondary alcohols bearing the chlorodifluoromethyl group. The importance of these compounds for the preparation of difluoromethylated enzyme inhibitors is well established. Recently, the synthesis and microbial resolution of the CF_2Cl-containing alcohols from ethyl chlorodifluoroacetate were reported by Kitazume et al.[9] Reduction of the C−Cl bond of the resulting carbinols proceeds readily, providing the corresponding difluromethylated derivatives. The target compounds could be obtained in 5−6 steps. The silylated reagents were expected to provide a much simpler way.

Initially our efforts were directed to developing an efficient synthesis of **1a**, avoiding the complications associated with the use of a Ruppert-type procedure.[10] Recently aluminum-induced reductive methods for the preparation of Me_3SiCF_3 were reported, suggesting that readily available CF_2BrCl could be used similarly to CF_3Br in the reactions with chlorotrimethylsilane (Me_3SiCl) and aluminum.[11] In fact, we have found that the carbon−bromine bond of CF_2BrCl was selectively reduced by aluminum powder in *N*-methylpyrrolidinone (NMP) in the presence of Me_3SiCl, and **1a** was obtained in 80% isolated yield according to eq 1. No formation of **1b** was observed under



(1)

these conditions. The process appears to involve a two-electron reduction of the C−Br bond of CF_2BrCl followed by trapping of the resulting "CF_2Cl^-" anion by Me_3SiCl (Scheme 1). Aluminum powder, corresponding to a net consumption of two

Scheme 1

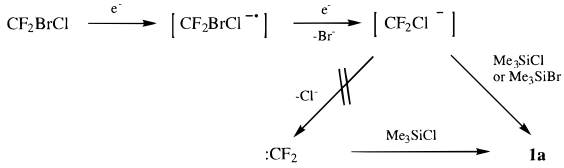


Table 1. Experimental Conditions for the Preparation of Me_3SiCF_2Cl and Me_3SiCF_2Br[a]

entry	halosilane (equiv)	Al (equiv)	difluoro-dihalomethane (equiv)	product (yield, %)[b]
1	Me_3SiCl (1.5)	0.7	CF_2BrCl (1.0)	Me_3SiCF_2Cl (80)
2	Me_3SiCl (1.5)	1.0	CF_2BrCl (1.0)	Me_3SiCF_2Cl (77)
3	Me_3SiCl (1.0)	1.5	CF_2BrCl (2.0)	Me_3SiCF_2Cl (15)
4	Me_3SiCl (1.5)	0.7	CF_2BrCl (1.0)	Me_3SiCF_2Br (30)[c]
5	Me_3SiCl (1.5)	1.0	CF_2BrCl (1.0)	Me_3SiCF_2Cl (65)
6	Me_3SiCl (1.5)	0.7	CF_2BrCl (1.0)	Me_3SiCF_2Br (55)
7[d]	Me_3SiCl (1.5)	1.0	CF_2BrCl (1.0)	Me_3SiCF_2Br (5)

[a] All reactions except entry 6 were carried out in sealed tubes at room temperature. [b] Isolated yield after distillation. [c] A 4:1 mixture of **1a** and **1b** was obtained. [d] Ultrasound-promoted reaction.

electrons per mole of CF_2BrCl, was needed for the reduction. The use of excess aluminum led to the increase in the undesired formation of fluorotrimethylsilane (Me_3SiF), which lowered the yield. Results of the optimization of the reaction parameters are presented in Table 1.

Alternatively to the anionic pathway, reaction 1 can be considered to be due to difluoromethylene insertion into the silicon−chlorine bond (generation of the CF_2 carbene via α-elimination from the CF_2Cl^- anion is regarded as a facile process[12]). However, this possibility was ruled out when Me_3SiBr was used instead of Me_3SiCl as an electrophile. No formation of Me_3SiCF_2Br (an expected product of carbene insertion) was observed, despite the fact that the silicon−bromine bond is considerably more reactive than the silicon−chlorine bond (Table 1, entry 5). This suggests that the reaction does not follow the carbene insertion pathway. Considering the high propensity of the CF_2Cl^- for an α-chloride elimination,[12] the cationic aluminum species formed during the oxidation of aluminum in the system must efficiently stabilize the intermediate chlorodifluoromethyl anion CF_2Cl^-.

The byproducts of the preparation of **1a** are CF_2ClH, CF_2BrH (formed from CF_2ClH by Cl/Br exchange), and Me_3SiF. CF_2ClH arises from quenching the CF_2Cl^- by residual acid. Its formation is minimized by using anhydrous NMP and acid-free Me_3SiCl. Some Me_3SiF is always produced in this system due to the thermodynamic preference for formation of the Si−F bond (the Si−F bond energy averages 193 kcal/mol).

The preparation of **1a** was carried out on a preparative scale (50 mmol). In order to withstand the pressure of the gaseous CF_2BrCl, the thick-walled glass reaction tubes equipped with magnetic stirrers were employed. The reaction tube was sealed, and the reaction mixture was stirred at room temperature overnight. After the volatile components were pumped off followed by hydrolysis and distillation of the products, **1a** was obtained as a colorless liquid contaminated with a small amount of disiloxane. Due to its inertness, disiloxane did not interfere with the chemistry of **1a** (*vide infra*) and the mixture could be further used without purification. Analytically pure samples of **1a** were obtained by washing the mixture with 98% sulfuric acid that quantitatively removed any traces of the disiloxane without affecting **1a**.

(8) For a review, see: (a) Prakash, G. K. S. In *Synthetic Fluorine Chemistry;* Olah, G. A., Chambers, R. D., Prakash, G. K. S., Eds.; Wiley: New York, 1992; Chapter 10. (b) Prakash, G. K. S; Yudin, A. K. *Chem. Rev.*, in press.

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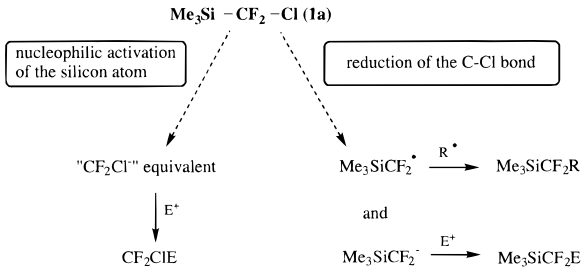
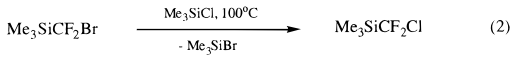
Scheme 2



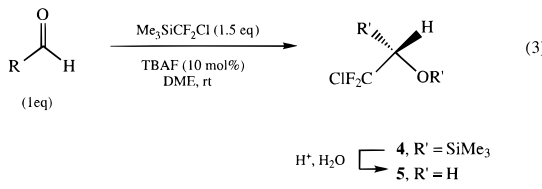
Under similar conditions CF_2Br_2 gave **1b** (Table 1, entry 6). In this case, however, Cl/Br exchange between Me_3SiCF_2Br and Me_3SiCl also led to the concurrent formation of **1a**. In a control experiment, when **1b** was heated with Me_3SiCl, a quantitative conversion into **1a** and Me_3SiBr took place (eq 2). In order to



eliminate this exchange, Me_3SiBr was subsequently employed instead of Me_3SiCl in the reaction, giving a 55% isolated yield of **1b** (Table 1, entry 6).

Reactivity of 1a. Two major pathways for the synthetic use of **1a** can be considered. Nucleophilic activation of the silicon atom (by fluoride ion) in the presence of a suitable electrophile in polar media should result in transfer of the chlorodifluoromethyl group to the electrophilic center (Scheme 2). Alternatively, the presence of carbon−chlorine bond suggests the possibility of reductive coupling to obtain new perfluoroalkylating agents such as difluorobis(trimethylsilyl)methane and 1,1,2,2-tetrafluoro-1,2-bis(trimethylsilyl)ethane.

Nucleophilic Activation of 1a. Me_3SiCF_2Cl was expected to serve as a source for CF_2Cl^-, similar to Me_3SiCF_3 being a convenient synthetic equivalent of CF_3^-.[8] However, during its preparation and subsequent purification, **1a** was found to be unaffected by water even upon prolonged exposure at more elevated temperatures. This is surprising for a silane with a highly polarized Si−CF_2Cl bond. Similar results were reported by Fuchikami et al. in their studies on the bromodifluoromethylating properties of $PhMe_2SiCF_2Br$.[13] In reactions with aldehydes under TBAF initiation in THF (the conditions usually employed in Me_3SiCF_3 chemistry), **1a** turned out to be much less reactive than Me_3SiCF_3. Only 30% of **1a** was consumed within the first 4 h of the reaction with benzaldehyde (Table 2, entry 1). Arguably, this reflects the difference in polarity between the Si−CF_3 and Si−CF_2Cl bonds which renders **1a** less susceptible to nucleophilic attack. We consequently examined more polar and more coordinating solvents that could further activate the silicon center toward nucleophilic attack and at the same time help in stabilizing the anionic intermediates. The addition of an equal volume of NMP to the reaction mixture greatly accelerated the chlorodifluoromethylation process (eq 3) (the mechanistic pathway is presented in Scheme 3). 1,2-



Dimethoxyethane (DME) was also found to be more suitable than THF as the reaction medium (Table 2). Moreover, its lower boiling point than NMP greatly simplifies the workup procedure. Compared to trifluoromethylation, the chlorodifluoromethylation requires higher amounts of initiator (10 mol % vs 2−3 mol % TBAF) for efficient conversion.

The finding that strongly polar solvents are needed for the nucleophilic activation of **1a** is in agreement with our earlier findings of the trans-trifluoromethylation of the disilyl sulfides where NMP was more effective than THF.[14] The polar solvents help stabilize a putative pentavalent silicon intermediate (Scheme 3). Mechanistically, the reaction is considered to involve initial formation of such a pentavalent complex via fluoride anion (of TBAF) attack on the fluorophilic silicon center in **1a**. Transfer of the chlorodifluoromethyl group to the electrophilic carbon center of the aldehyde then occurs. It is likely that precoordination of the aldehyde oxygen to the silicon center takes place at this stage. This step yields gaseous Me_3SiF and an alkoxide adduct, stabilized by tetrabutylammonium cation. Only a catalytic amount of TBAF is needed for the reaction because the overall catalytic cycle is further maintained by the silicon's affinity to the anionic oxygen center in tetrabutylammonium alkoxide obtained from an initial reaction between TBAF and **1a**. The term "autocatalytic" in this case refers to the continuous regeneration of the catalytic species that carries the whole process.[8]

A series of aromatic and aliphatic aldehydes were chlorodifluoromethylated (eq 3) at room temperature, providing an efficient pathway to the valuable class of difluoromethyl-containing secondary alcohols under mild conditions (Table 2). Tetrabutylammonium fluoride (TBAF) was found to be superior to KF and CsF as an initiating species. However, due to its hygroscopic properties, TBAF should be dried beforehand by azeotropic removal of water with 2-propanol or by other methods in order to minimize the formation of CF_2ClH during the reaction.[15] The mixture of **1a** and disiloxane, obtained directly upon the initial workup of the reaction mixture, is generally suitable for use in the reactions since the byproduct disiloxane is inert under the conditions. In some cases the silylated adducts **4** turned out to be quite resistant toward acidic workup (HCl, water) usually employed to remove the trimethylsilyl group. In these cases a 40% HF solution in acetonitrile was found suitable for the desilylation.[16] Ketones also reacted with **1a** at room temperature under TBAF initiation in the THF/NMP solvent system, furnishing the corresponding chlorodifluoromethylated adducts. Not unexpectedly, lower reactivity was observed compared to aldehydes (Table 2, entry 9).

Reduction of the Carbon-Halogen Bond of 1a,b. The efficient preparation of **1a** and **1b** prompted us to study the reactivity of the carbon−halogen bond of these compounds in reductive coupling with electrophiles. The attachment of a second trimethylsilyl group to the CF_2 moiety of **1a** furnishes bis(trimethylsilyl)difluoromethane (**2**), a synthetic equivalent of "CF_2^{2-}". Previously, preparation of **2** was briefly described by Fritz et al.[17] It was obtained via insertion of the singlet CF_2 (difluorocarbene), produced from (trifluoromethyl)(trimethyl)tin at elevated temperatures, into the silicon−silicon bond of $FMe_2SiSiMe_2F$ (the absence of the silicon-bound fluorine atoms renders the Si-Si bond in $Me_3SiSiMe_3$ unreactive toward difluorocarbene). The resulting $FMe_2SiCF_2SiMe_2F$, isolated by gas chromatography, was reacted with methyl-

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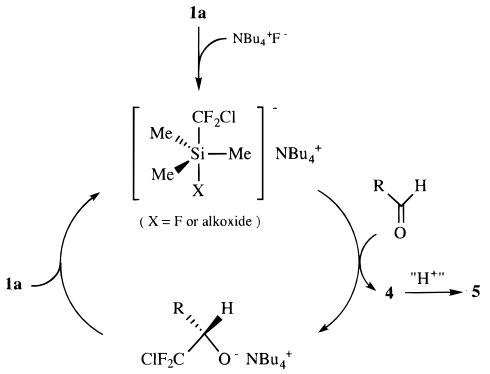
Table 2. Chlorodifluoromethylation of Carbonyl Compounds with Me_3SiCF_2Cl (**1a**)

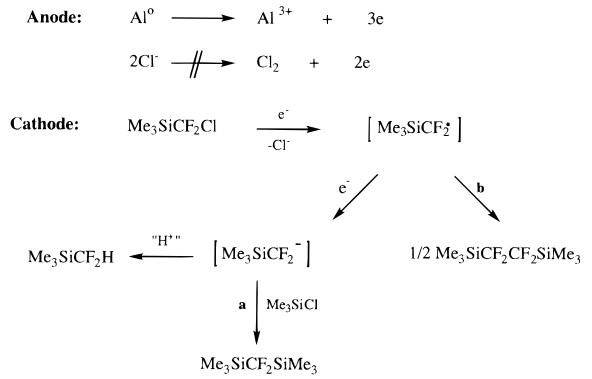
entry	aldehyde	product	solvent	initiator[b]	yield[c] (%)
1	PhC(O)H	$PhCH(OH)CF_2Cl$ (**5a**)	THF	TBAF	35[d]
2	PhC(O)H	$PhCH(OH)CF_2Cl$ (**5a**)	THF/NMP (1:1)	TBAF	68
3	PhC(O)H	$PhCH(OH)CF_2Cl$ (**5a**)	DME	TBAF	75[d]
4	$PhCH_2CH_2C(O)H$	$PhCH_2CH_2CH(OH)CF_2Cl$ (**5b**)	DME	KF	30
5	$PhCH_2CH_2C(O)H$	$PhCH_2CH_2CH(OH)CF_2Cl$ (**5b**)	NMP	CsF	45
6	$PhCH_2CH_2C(O)H$	$PhCH_2CH_2CH(OH)CF_2Cl$ (**5b**)	DME	TBAF	80
7	$PhCH_2C(O)H$	$PhCH_2CH(OH)CF_2Cl$ (**5c**)	DME	TBAF	85
8	n-$C_6H_{13}C(O)H$	n-$C_6H_{13}CH(OH)CF_2Cl$ (**5d**)	DME	TBAF	64
9	PhC(O)H	$Ph_2C(OH)CF_2Cl$ (**5e**)	THF/NMP (1:1)	TBAF	32[d]

[a] All reactions were carried out at room temperature for 24 h. [b] 10 mol% initiator was utilized. [c] Isolated yield after column chromatography. [d] Based on ^{19}F-NMR analysis.

Scheme 3

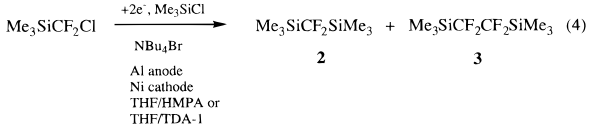


Scheme 4



lithium to afford **2** as a product of *Si*-alkylation. The apparent experimental difficulties in this procedure did not allow the synthesis of **2** on a preparative scale, which would have permitted investigation of its properties as a synthetic equivalent of CF_2^{2-}.

During the aluminum-induced synthesis of **1a** from CF_2BrCl, no products were formed derived from the reduction of the carbon−chlorine bond. Apparently, the aluminum/NMP combination was not sufficient to reach the reduction potential of the C−Cl bond and convert **1a** into anionic $Me_3SiCF_2^{2-}$. An attempt to use magnesium/THF and magnesium/THF/HMPA combinations resulted in very sluggish reactions between **1a** and Me_3SiCl, giving the disilylated difluoromethane **2** not exceeding 3−5% after one week (based on the NMR analysis).[18] The relative ineffectiveness of these reagents, traditionally employed for the reduction of alkyl halides, is not surprising in view of the difficulties generally encountered in the preparation of C_1-perfluorinated organometallics (the strong metal−fluorine bonds make these species extremely susceptible toward disproportionation).[19] This prompted us to study **1a** under conditions employed earlier by us in the electroreduction of CF_3Br using the sacrificial aluminum anode technique. The readily oxidizable aluminum anode prevents the formation of elemental chlorine (through the oxidation of chloride ions, Scheme 4).[11,20] This ensures that halogenation and other side reactions of the reduced species are largely suppressed, allowing the preparation in an undivided cell.[11a] The reduction of **1a** occurs on the surface of a nickel cathode, wherein the anions, electrogenerated from **1a**, are coupled with Me_3SiCl, present in the system. The electrolysis of a mixture of **1a**/Me_3SiCl in the THF/HMPA solvent system resulted in the formation of **2** along with that of unexpected 1,2-bis(trimethylsilyl)-1,1,2,2-tetrafluoroethane (**3**) (according to eq 4).[18] The results obtained in the electrochemi-



cal experiments are given in Table 3. Tetrabutylammonium hexafluorophosphate or bromide (3−4 mol %) was used as an electrolyte support to provide conductivity at the initial stages of the reaction. A current density of 100 mA was applied until NMR analysis of samples indicated the complete consumption of **1a**. The amount of electric current passed through the solution was equivalent to a slight excess of two electrons per mole of substrate, which is theoretically necessary to convert **1a** into the corresponding anion. Formation of the homocoupled byproduct **3** indicates the intermediacy of radicals in the course of the reduction (Scheme 4). An alternative mechanism suggested by one of the reviewers involving singlet difluoromethylene insertion into $Me_3SiCF_2^-$ followed by trimethylsilyation appears to be unlikely as no other difluoromethylene-derived products are observed. We have found that using an excess of Me_3SiCl and a 15:1 THF/HMPA mixture results in a 15:2 molar ratio of **2** and **3**, thus strongly favoring the anionic pathway of reduction. These conditions are optimal for the preparation of **2**. The obtained products were fully characterized by ^{19}F, ^{1}H, ^{13}C, and ^{29}Si NMR. Table 4 summarizes these data on compounds **2** and **3** as well the starting materials **1a** and **1b**.

Among the byproducts, Me_3SiCF_2H (formed via protonation of $Me_3SiCF_2^-$ by residual acid) and Me_3SiF were also detected. **3** is a low-melting solid compound (mp 38 °C) that crystallized out of the mixture of **2** and **3** upon cooling. Large (1.5 × 2 in.!) transparent crystals were deposited on the walls of the flask by slow room temperature sublimation of **3** from the mother liquid. In contrast, related Me_3SiCF_3 is a volatile liquid (bp 45 °C). This intriguing difference warranted X-ray structure analysis. Crystals of **3**, suitable for a single-crystal X-ray

(18) The disilyl derivative $PhMe_2SiCF_2CF_2SiPhMe_2$, containing a perfluoroethylene unit, was obtained by Ojima et al. via nickel-catalyzed reductive dimerization of $PhMe_2SiCF_2Br$: Fuchikami, T.; Ojima, I. *J. Organomet. Chem.* **1982**, *212*, 195.

(19) Prakash, G. K. S.; Krishnamurti, R.; Olah, G. A. *J. Am. Chem. Soc.* **1989**, *111*, 393 and references cited therein.

(20) For a review, see: Chaussard, J.; Folest, J.-C.; Nedelec, J.-Y.; Perichon, J.; Sibille, S.; Troupel, M. *Synthesis* **1990**, 369.

Table 3. Experimental Conditions for the Electrocoupling between Me_3SiCF_2X (X = Cl, Br) and Me_3SiCl[a]

entry	Me_3SiCF_2X (equiv)	Me_3SiCl (equiv)	solvent mixture	supporting electrolyte (equiv)	electron density (mA)	yield (%) (ratio of **2** to **3**)
1	**1a** (1.0)	6.0	THF/HMPA (15:1)	NBu_4PF_6 (0.04)	100	80 (10:1)
2	**1a** (1.0)	6.0	DMF	NBu_4PF_6 (0.04)	100	0
3	**1a** (1.0)	6.0	NMP	NBu_4PF_6 (0.04)	50	0
4[b]	**1a** (1.0)	18.0	THF/HMPA (6:1)	NBu_4PF_6 (0.1)	150	27 (3.5:1)
5	**1a** (1.0)	10.0	THF/HMPA (12:1)	NBu_4PF_6 (0.03)	100	56 (6:1)
6	**1a** (1.0)	0.0	THF/HMPA (10:1)	NBu_4PF_6 (0.03)	100	0
7	**1a** (1.0)	3.0	THF/TDA-1 (1:1)	NBu_4Br (0.03)	100	75 (1:8.5)

[a] All reactions were carried out in a 100 mL undivided cell equipped with an aluminum (rod) anode and nickel grid cathode. [b] A syringe pump was used to introduce the **1a**/Me_3SiCl mixture.

Table 4. NMR Parameters of **1a**, **1b**, **2**, and **3**

silane	$\delta(^1H)$	$\delta(^{19}F)$	$\delta(^{13}C)$	$\delta(^{29}Si)$
1a	0.27 (s)	−63.8 (s)	−4.71 (s) 135.20 (t) ^1J(C−F) 327.0 Hz	10.21 (t) ^2J(Si−F) 32.0 Hz
1b	0.27 (s)	−58.0 (s)	−4.45 (s) 132.11 (t) ^1J(C−F) 338.5 Hz	12.30 (t) ^2J(Si−F) 29.3 Hz
2	0.13 (s)	−137.3 (s)	−4.12 (t) ^1J(C−F) 2.9 Hz 138.73 (t) ^1J(C−F) 260.7 Hz	1.65 (t) ^2J(Si−F) 29.0 Hz
3	0.22 (s)	−122.2 (s)	−400 (m) 126.63 (tt) ^1J(C−F) 264.5 Hz ^2J(C−F) 45.8 Hz	5.18 (tt) ^2J(Si−F) 34.3 Hz ^3J(Si−F) 17.2 Hz

Table 5. (a, top) Experimental Details of the X-ray Analysis of **3** and (b, bottom) Geometric Parameters of **3**

crystal size, mm	0.6 × 0.48 × 0.26	V, Å^3	644.0(3)
chem form	$C_8H_{18}F_4Si_2$	d_{calc}, gm cm^{-3}	1.271
fw	246.4	radiation	Cu Kα (λ = 1.541 78 Å)
cyst syst	monoclinic	no. of data colltd	1852
space group	$P2_1/n$	no. of data used	641 ($F > 4.0\sigma(F)$)
a, Å	6.474(2)	R	0.0456
b, Å	10.024(2)	R_w	0.0517
c, Å	9.924(2)	largest peak, e/Å^3	0.24
β, deg	90.33(2)	no. of parameters	64
Z	2		

Bond Distances (Å)

Si(1)−C(3)	1.935(4)	Si(1)−C(4)	1.847(4)
Si(1)−C(5)	1.857(5)	Si(1)−C(6)	1.846(5)
F(1)−C(3)	1.393(5)	F(2)−C(3)	1.394(4)
C(3)−C(3A)	1.499(8)		

Bond Angles (deg)

C(3)−Si(1)−C(4)	103.3(2)	C(3)−Si(1)−C(5)	108.7(2)
C(4)−Si(1)−C(5)	112.2	C(3)−Si(1)−C(6)	108.9(2)
C(4)−Si(1)−C(6)	111.6(2)	C(5)−Si(1)−C(6)	111.8(2)
Si(1)−C(3)−F(1)	108.3(2)	Si(1)−C(3)−F(2)	108.0(3)
F(1)−C(3)−F(2)	104.0(3)	Si(1)−C(3)−C(3A)	123.6(4)
F(1)−C(3)−C(3A)	105.7(4)	F(2)−C(3)−C(3A)	105.6(4)

analysis, were grown by recrystallization. The details of the X-ray structure analysis are given in the Experimental Section. Table 5 gives the structural parameters of **3**. An ORTEP diagram and a packing diagram of the monoclinic cell of **3** are presented in Figures 1 and 2, respectively. Experimental details of the structure analysis, and selected distances and angles in **3**, are given in parts a and b, respectively of Table 5. The unusually large value of 123.6° for the Si−C−C bond angle is possibly caused by the repulsion between the fluorine atoms and trimethylsilyl groups. The dihedral angle Si−C−C−Si of 180° indicates the perfect *trans* arrangement. The bond length as well as other bond angle values in the observed *trans* conformation of **3** are within the normal range. No intermolecular distances that would be indicative of the presence of stabilizing hydrogen contacts (C−H−F) that could result in

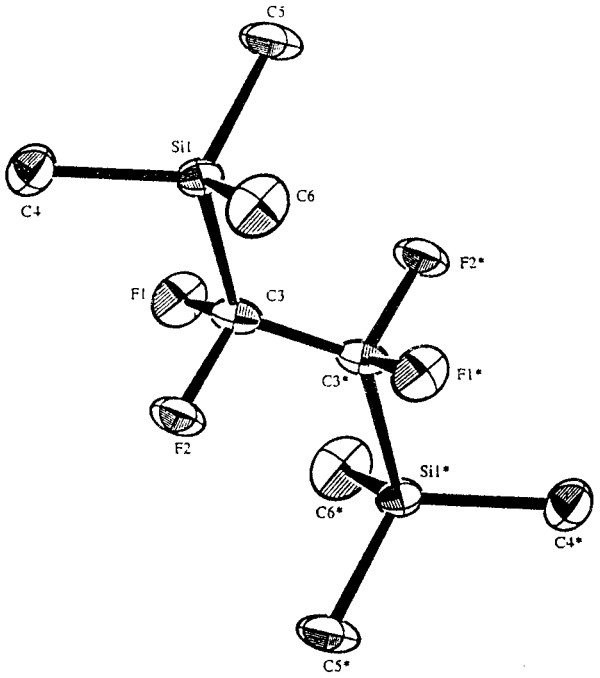


Figure 1. ORTEP drawing of **3** (the methyl hydrogens are not shown for clarity).

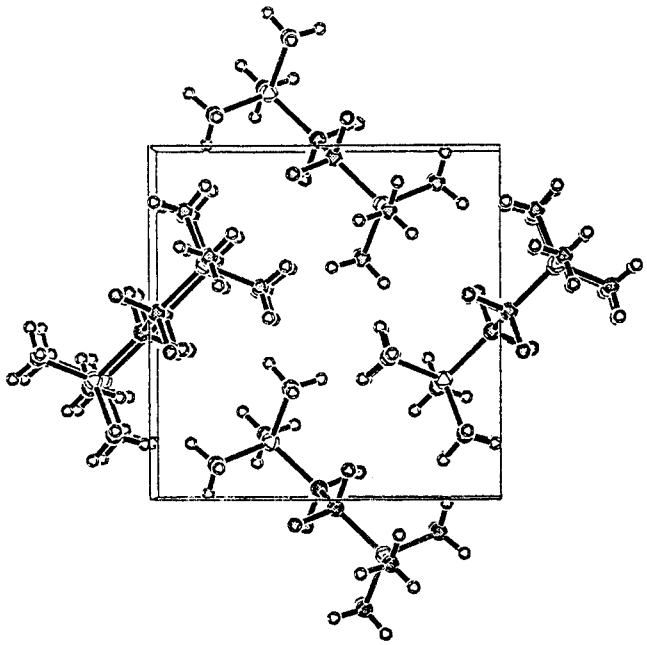


Figure 2. Packing diagrams along the *a*-axis of **3**.

crystallinity were detected. The shortest nonbonded distance between a fluorine atom and methyl hydrogen of a trimethylsilyl group is 2.88 Å, which is 0.33 Å longer than the van der Waals distance of 2.55 Å for the hydrogen−fluorine contact. Appar-

ently, the rigidity of the tetrafluoroethylene subunit within the *trans* conformation of **3** is responsible for efficient packing. A quite long value of 1.935 Å for the $Si-CF_2$ bond is indicative of its relative weakness. In comparison, a value of 1.923 Å was obtained by Burger et al. for the $Si-CF_3$ bond in CF_3SiH_3 using the electron diffraction study combined with the normal coordinate analysis.[21]

The preparative separation of **2** and **3** by distillation turned out to be rather tedious and impractical. Since our initial goal was the preparation of **2**, the experimental conditions were tailored toward its selective preparation, giving **3** as an insignificant byproduct. In order to obtain analytically pure **2** for synthetic purposes, the products collected following the workup of the electroreduction mixture (**2**, **3**, and disiloxane) were treated with a catalytic amount of tetrabutylammonium fluoride to remove **3** (*vide infra*) and partitioned between 98% sulfuric acid and pentane to remove traces of disiloxane. Evaporation of pentane yielded **2** as an analytically pure colorless liquid. Using the conditions where formation of **3** is minimized (Table 3, entry 1) allows the preparation of **2** on a preparative scale and in high yield. Similar to **1a**, the remarkable hydrolytic and thermal stabilities of the silylated derivatives **2** and **3** are noteworthy. They do not show any tendency for hydrolysis to give disiloxane and the corresponding gaseous CF_2HX (X = H, Cl).[22] Thermal stability of these molecules with respect to fluorine migration from carbon to silicon is also rather unusual. **3** does not show any tendency to extrude Me_3SiF even at high temperatures.

The described notable properties of the $SiCF_2Si$ moiety deserve further investigation. We believe that since the difluoromethylene group is considered isosteric with ethereal oxygen, CF_2 incorporation into an oxygenated polysiloxane framework might yield novel materials with unexpected and useful properties.[21] The rigidity of the backbone is one of the parameters that the difluoromethylene group is expected to alter. It should be noted, however, that the observed stability is most probably of kinetic, rather than thermodynamic origin due to the anticipated electrophilic character of the silicon atom adjacent to the highly electron-withdrawing difluoromethylene group.

In its own right, disilylated **3** is attractive for synthetic purposes as a source of the tetrafluoroethylene unit. Therefore, we needed conditions that would yield **3** as a major, rather than side, product. Conditions preferring the homocoupling were expected to provide a preferential path to **3**.

Preferential Preparation of 3. The behavior of alkyl halides with respect to electrochemical homocoupling has been previously investigated by Fry et al.[23] It is recognized that the first electron transfer in the reduction process is usually potential-determining. Dimerization of radicals occurs to some extent, but it is generally difficult to control since the second electron transfer to the radical generating the corresponding anion proceeds more readily. In other words, for alkyl halides E_1 (potential of the first electron transfer) is the *negative* of E_2 (potential of the second electron transfer). This fact precludes the efficient use of the controlled potential method which could otherwise be applied to provide the amount of electric current which is theoretically required in order to reach the first reduction potential and, therefore, favor dimerization. Similarly, in the constant current method used in our study, one assumes that the presence of a bromodifluoromethyl group in **1b** should facilitate the dimerization process since the brominated compounds generally have lower E_1 values.[23] However, we have found that when **1b** was treated under similar conditions, a complicated mixture of products was obtained, resulting in a very low isolated yield of **3**. It was reported that, in the electroreduction of alkyl halides even when a coupling process does result in a preferential formation of a dimer, the S_N2 reaction between the intermediate carbanion and alkyl halide is the actual mechanistic path.[24] For organofluorine compounds this path, however, is unlikely due to their known resistance to nucleophilic substitution. Therefore, to obtain high yields of the dimer **3**, the local concentration of the radicals near the electrode surface as well as their lifetime should be enhanced. An increase in the current density and, therefore, the concentration of the starting material (**1a**) near the electrode surface would be a step toward favoring dimerization. We have indeed found that under these conditions the formation of **3** increased based on the NMR analysis (Table 3, entry 4). Further, optimization of the reaction conditions for the formation of **2** and **3** led to the realization of a profound solvent effect on the ratio between **2** and **3**. Tris(3,6-dioxaheptyl)amine (TDA-1) as a cosolvent with THF highly favored the formation of the homocoupled product **3** (Scheme 4, path a), whereas when HMPA was used, the anionic product **2** was dominant (Scheme 4, path b). Both experiments were conducted under identical conditions. *Thus, by choosing a different solvent mixture during electroreduction, the reaction could be funneled through a predominantly anionic or radical pathway.* We believe that the solvent TDA-1 increases the lifetime of the radical cage formed during the first electron transfer step of the reduction, permitting the dominance of the radical-derived product **3**, whereas HMPA, well known for its great stabilizing effect on the anionic species, favors the formation of anion-derived product **2**.[12] Although the exact nature of the involved processes is speculative, the correlation with a donor number (DN) of the solvent is, nevertheless, conceivable. The dependence of the radical cage stability on the DN parameter was noted by Chen et al.[24] It was shown that, in copper-mediated reductions of perfluorinated alkyl iodides, solvents with small DN (DN < 17) led to diffusional control of the caged ion pair, permitting the trapping of a radical by an appropriate olefin. On the other hand, in solvents with DN higher than 31 (such as HMPA) the collapse of the ion pair led to further reduction of radicals, absorbed on the surface of the copper metal, giving anionic products.

The direct electrochemical conversion of CF_2BrCl or CF_2Br_2 into $Me_3SiCF_2SiMe_3$ without the isolation of **1a** would be the easiest for the preparation of **2**. However, in an attempted direct electrocoupling of CF_2Br_2 with Me_3SiCl, the formation of significant amounts of Me_3SiF drastically lowered the yield. Electrocoupling did occur, but the conversion and selectivity were low (15% of the 1:1.5 mixture of **2** and **3** was isolated). Structurally, the disilylated derivatives **2** and **3** are the first two homologs in the series $Me_3Si(CF_2)_nSiMe_3$ ($n = 1-10$). Higher members were used by Farnham in copolymerization with perfluoroalkenes, initiated by trialkylsilyl carboxylates.[25] These higher homologs are readily accessible via Barbier-type reactions between the corresponding perfluorinated dihalides and trimethylsilyl chloride. Analogous organometallic routes to **2** and **3** from CF_2Br_2 and CF_2BrCF_2Br suffer from the competition

(21) Beckers, H.; Burger, H.; Eujen, R.; Rempfer, B.; Oberhammer, H. *J. Mol. Struct.* **1986**, *140*, 281.

(22) Pawlenko, S. *Organosilicon Chemistry*; W. de Gruyter: Berlin, New York, **1986**.

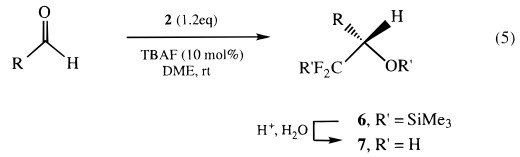
(23) (a) Fry, A. J.; Porter, J. M.; Fry, P. F. *J. Org. Chem.* **1996**, *61*, 3191. (b) Peters, D. G.; Willett, B. C. *J. Electroanal. Chem.* **1981**, *123*, 291.

(24) Chen, Q.-Y.; Yang, Z.-Y.; He, Y.-B. *J. Fluorine Chem.* **1987**, *22*, 171.

(25) Farnham, W. B. *Synthetic Fluorine Chemistry*; In Olah, G. A., Chambers, R. D., Prakash, G. K. S., Eds.; Wiley: New York, 1992; Chapter 11.

of α- and β-elimination of the halide ions.[26] Even generally milder and more selective electrochemical routes would be problematic. For example, an attempt to prepare the parent $Me_3SiCH_2CH_2SiMe_3$ by electroreduction of CH_2BrCH_2Br in the presence of Me_3SiCl leads to the preferential formation of ethylene by elimination of bromide anion. Ruppert's procedure was also found to be unsuitable for the preparation of **2**.[8] Our electrochemical methodology thus seems to be a method of choice for the straightforward preparation of the reagents **2** and **3** from readily available starting materials on a preparative scale.

Synthetic Applications of Bis(trimethylsilyl)difluoromethane (2) and 1,2-Bis(trimethylsilyl)-1,1,2,2-tetrafluoroethane 3. Similar to **1a**, bis(trimethylsilyl)difluoromethane (**2**) displayed rather sluggish reactivity toward carbonyl compounds in THF. This was observed despite the fact that the formation of the "$Me_3SiCF_2^-$" species (the *de facto* difluoromethylating agent) upon nucleophilic activation of **2** should be somewhat facilitated by partial stabilization of the resulting anionic center by the α-trimethylsilyl group (even if the anion has significant pyramidal character). For efficient conversion, the addition of NMP as a cosolvent was again found to be crucial.[14] This promoted the reaction between **2** and aldehydes to afford the difluoromethylated alcohols after the usual acidic workup (according to eq 5). DME was also effective as the reaction



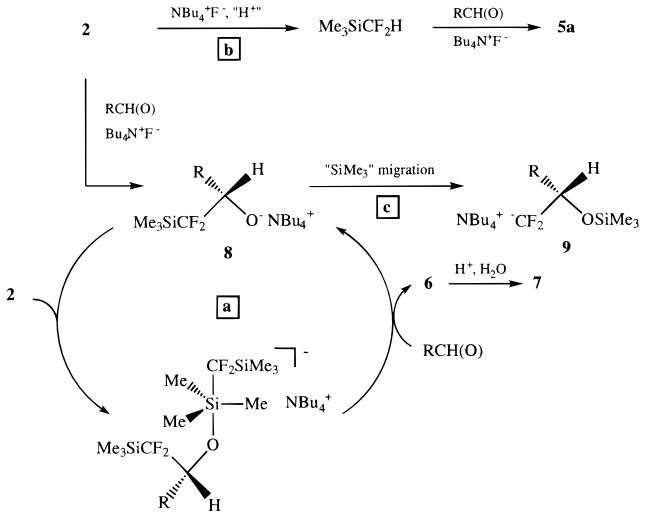
(5)

medium. Polar solvents apparently accelerate the reaction by stabilizing the charged species involved in the catalytic cycle similar to the reactions of **1a**. Benzophenone reacted with **2** at room temperature, albeit much slower, giving the difluoromethylated adduct after the usual workup.

As in the case of **1a**, TBAF turned out to be superior to KF as an initiator (10−15 mol % was necessary to ensure complete conversion). The only detectable byproducts were CF_2H_2 (t, δ_F −143 ppm) and $TMSCF_2H$ (d, δ_F −140 ppm) formed by the protonation of CF_2H^- and $TMSCF_2^-$, respectively, by the residual water present in TBAF solution. From a mechanistic point of view, the overall process can be considered as an initial formation of the silylated adduct **8** which starts the catalytic cycle (Scheme 5, path a). The aldehyde moiety is then siladifluoromethylated as indicated. Acidic workup of the adduct furnishes the desired difluoromethylated carbinol **7** (Table 6). Alternatively, Me_3SiCF_2H formed *in situ* from **2**, TBAF, and residual moisture could be regarded as a species that is at least in part involved in the present transformation (Scheme 5, path b). However, since no reaction occurred when **2** was exposed to TBAF in THF/H_2O (separation of **2** from traces of **3** was performed by using TBAF, *vide supra*), this possibility is less likely. Nevertheless, the process does occur to some extent which is evident by the traces of CF_2H_2 detected in the crude reaction mixture. Higher amounts of TBAF compared to trifluoromethylation were necessary for efficient conversion of an aldehyde into the corresponding difluoromethylated carbinol. This fact is mainly attributed to the inhibition through the competitive migration of the oxophilic trimethylsilyl group in **8,** generating **9** (Scheme 5, path c), which is not capable of further maintaining the reaction due to the lack of a nucleophilic oxygen center but does yield the desired difluoromethylated carbinols upon acidification.

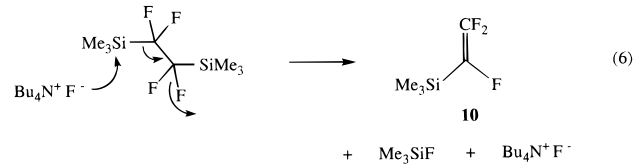
(26) Fry, A. J. *Synthetic Organic Electrochemistry*, 2nd ed.; Wiley: New York, 1989; Chapter 5, p 151.

Scheme 5



Compared to Me_3SiCF_2H (bp 50 °C), which can also be considered as a "CF_2H^-" equivalent,[10,22] **2** is hydrolytically stable and less volatile (bp 130 °C). Additionally, the silylated adducts **6** can be envisioned to react with other electrophiles besides "H^+" (acidic workup) which would permit **2** to have general "CF_2^{2-}" character. We are further investigating this aspect. Fuchikami et al. recently reported on the difluoromethylating properties of a related silane, $PhMe_2SiCF_2H$,[13] which reacts with aldehydes but only at elevated temperatures in polar solvents (100 °C, DMF) with KF as an initiator. Also, the observed relative inertness might be a result of the presence of the phenyl substituent. The formation of silyl enol ethers in reactions with enolizable carbonyl compounds was reported by Hiyama et al. as a side reaction.[27] This unwanted reaction path is also facilitated due to the presence of the phenyl substituent. Probably, its stabilizing effect on the developing negative charge during enolization is one of the reasons responsible for it. In fact, the perfluorophenyl derivative $Me_3SiC_6F_5$ is used for the preparation of silyl enol ethers from enolizable carbonyl compounds.[28] In any case, the ease of preparation of **2** from readily available starting materials (CF_2BrCl and Me_3SiCl) along with the displayed mild chemistry makes it a convenient CF_2H^- equivalent.

In contrast to both **1a** and **2**, 1,2-bis(trimethylsilyl)-1,1,2,2-tetrafluoroethane (**3**) was completely used up within 3 h when reacted with a variety of aldehydes and ketones in THF under TBAF initiation at room temperature. The analysis of this exothermic reaction revealed the net transfer of the *perfluorovinyl* group to the carbonyl carbon accompanied by Me_3SiF elimination. We have found that only a catalytic amount of TBAF was needed to convert **3** into (perfluorovinyl)trimethylsilane (**10**) (eq 6 and Table 7). The reaction of **3** regenerates



(6)

TBAF, making the process catalytic. Upon addition of an aldehyde or a ketone to the reaction mixture, addition of a perfluorovinyl unit readily occurs similar to the previously

(27) Fujita, M.; Obayashi, M.; Hiyama, T. *Tetrahedron* **1988**, *44*, 4135.
(28) Gostevskii, B. A.; Vyazankina, O. A.; Kalikhman, I. D.; Bannikova, O. B.; Vyazankin, N. S. *Zh. Obshch. Khim.* **1983**, *53*, 229; *J. Gen. Chem. USSR (Engl. Transl.)* **1983**, *53*, 200.

Table 6. Difluoromethylation of Carbonyl Compounds with $Me_3SiCF_2SiMe_3$ (**2**)

entry[a]	aldehyde	product	solvent	yield[b] (%)
1	PhC(O)H	PhCH(OH)CF_2H (**7a**)	THF	20
2	PhC(O)H	PhCH(OH)CF_2H (**7a**)	THF/NMP (1:1)	70
3	PhC(O)H	PhCH(OH)CF_2H (**7a**)	DME	75
4	$PhCH_2CH_2C(O)H$	$PhCH_2CH_2CH(OH)CF_2H$ (**7b**)	DME	66
5	$PhCH_2C(O)H$	$PhCH_2CH(OH)CF_2H$ (**7c**)	DME	78
6	*n*-$C_6H_{13}C(O)H$	*n*-$C_6H_{13}CH(OH)CF_2H$ (**7d**)	DME	55
7	PhC(O)H	$Ph_2C(OH)CF_2H$ (**7e**)	NMP	40

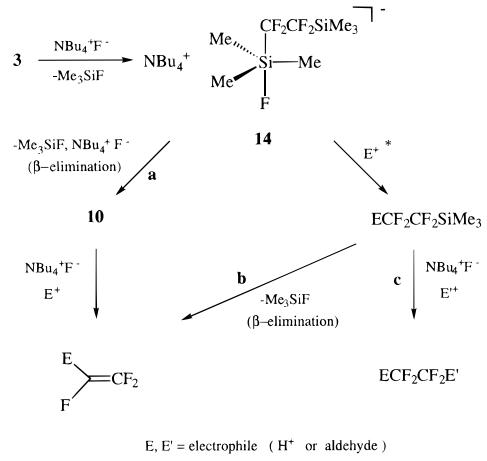
[a] All reactions were carried out at room temperature for 24 h using 10 mol % TBAF as an initiator. [b] Isolated yield after column chromatography.

Table 7. Perfluorovinylation of Carbonyl Compounds with $Me_3SiCF_2CF_2SiMe_3$ (**3**)

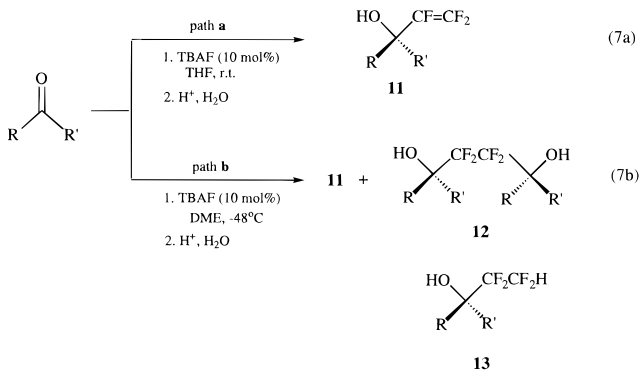
entry[a]	carbonyl compound	product	solvent	yield[b] (%)
1	PhC(O)H	PhCH(OH)CF=CF_2 (**11a**)	THF	75
2	$PhC(O)CH_3$	$PhCCH_3$(OH)CF=CF2 (**11b**)	THF	80
3	$C_6H_{13}C(O)H$	$C_6H_{13}CH(OH)CF=CF_2$ (**11c**)	THF	64

[a] All reactions were carried out at room temperature for 2 h using 10 mol % TBAF as an initiator. [b] Isolated yield after column chromatography.

Scheme 6



described processes (Scheme 6, path a). Consequently, **3** acts as a convenient, *in situ* source of "CF_2=CF^-".[29] The corresponding secondary and tertiary perfluorovinylated alcohols were obtained in high yields according to eq 7a. Scheme 6



depicts some considerations of reactivity. After the initial attack of fluoride on the silicon atom of **3**, the transient species **14** can undergo β-fluoride ion elimination, forming perfluorovinylsilane **10** which further reacts with electrophiles present in the reaction mixture. At the same time, **14** itself can undergo addition to an aldehyde followed by β-fluoride ion elimination, giving the trifluorovinyl products (Scheme 6, path b).

(29) For perflurovinylation using Me_3SiCF=CF_2, obtained from CF_2=CFCl, BuLi, and Me_3SiCl, see ref 27.

Although β-fluoride ion elimination in **14** is highly favored at room temperature, it was possible to find the conditions where the elimination was suppressed and 2 equiv of a carbonyl compound was able to react with 1 equiv of **3** ("$^-CF_2CF_2^-$" equivalent, Scheme 6, path c). We have found that when the reaction was carried out at −48 °C in DME as a solvent in the presence of 3 equiv of benzaldehyde, the formation of the diol **12** containing the perfluoroethylene unit occurred. At the same time, competitive protonation resulted in the formation of tetrafluoroethylated carbinol **13**. Recently, Fuchikami has shown that $PhMe_2SiCF_2CF_2SiPhMe_2$ undergoes reaction with carbonyl compounds, affording mixtures of perfluorovinyl alcohol, tetrafluoroethylene-containing diol, and tetrafluoroethylated alcohol.[30] However, again elevated temperatures were required in order to activate the silicon center of this phenylated derivative. Little selectivity with respect to perfluorovinylation was observed at the needed higher temperatures. Along with the more convenient method of preparation of **3** adaptable for a preparative synthetic scale, **3** also shows high reactivity as well as selectivity for obtaining perfluorovinyl carbinols at room temperature while giving alcohols **12** and **13** at low temperatures.

Experimental Section

General Procedures. Preparation of compounds **1a** and **1b** was carried out in oven-dried sealed tubes. Synthesis of compounds **2** and **3** was performed in an oven-dried one-compartment electrochemical cell. Reactions of **1a**, **2**, and **3** with carbonyl compounds were performed under an argon atmosphere in flame-dried glassware with magnetic stirring. The boiling points are uncorrected. ^{1}H, ^{13}C, ^{19}F, and ^{29}Si NMR spectra were recorded at 500, 125, 470, and 99 MHz, respectively, using $CDCl_3$ as solvent. All chemical shifts are reported in parts per million (δ) and are relative to residual $CHCl_3$ for ^{1}H, $CDCl_3$ for ^{13}C, $CFCl_3$ for ^{19}F, and $(CH_3)_4Si$ for ^{29}Si NMR. The fluorinated alcohols **5a**−**d**,[9] **7a**−**d**,[9] **11a**−**c**,[27,33] **12**,[30] and **13**[30] were characterized by comparison of their spectral properties with the literature data.

THF and DME were distilled from sodium/benzophenone ketyl. *N*-Methylpyrrolidinone (anhydrous), aluminum powder, chlorotrimethylsilane and TBAF (hydrate) were purchased from Aldrich Chemical Co., Inc. Chlorotrimethylsilane was distilled from calcium hydride to remove traces of hydrochloric acid. Aldehydes were pretreated with aqueous sodium hydroxide to remove acid impurities. Bromochlorodifluoromethane and dibromodifluoromethane were purchased from PCR, Inc.

Preparation of (Chlorodifluoromethyl)trimethylsilane (1a). A 100 mL thick-walled, high-pressure glass tube equipped with a magnetic stirring bar and dried in an oven overnight was charged with 0.9 g (52 mmol) of fresh aluminum powder. The tube was then purged with dry argon three times followed by addition of 30 mL of dry *N*-methylpyrrolidinone via syringe. The resulting slurry was stirred and degassed under vacuum followed by purging with argon. An 8 g (74 mmol) sample of freshly distilled chlorotrimethylsilane was then added, and the resulting mixture was frozen at −196 °C. An 8.1 g (49 mmol) portion of bromochlorodifluoromethane was condensed into the cooled tube followed by sealing under vacuum. The sealed tube was

(30) Fuchikami, T.; Hagiwara, T. Jpn. Kokai Tokkyo Koho JP06,228,-030[94,228,030] (CL.C07C33144).

allowed to reach room temperature after which the mixture was stirred overnight. The reaction was accompanied by the formation of a yellow-brown dense cake. During the workup, the tube was precooled to −196 °C and then opened on the vacuum line. After warming to room temperature, the volatile contents were condensed in another flask using a standard vacuum line technique. The colorless mixture thus obtained contained the product **1a**, traces of CF_2HCl, and fluorotrimethylsilane along with unreacted chlorotrimethylsilane. Further purification included hydrolysis, neutralization, and fractional distillation of the organic phase using a 15 cm column packed with glass helices. This procedure afforded **1a** as a colorless liquid containing 5−10 mol % of disiloxane. The traces of disiloxane were removed by partitioning between 98% sulfuric acid and pentane[31] at 0 °C . The pentane was then removed by distillation, giving pure **1a** as a colorless liquid, 6.2 g (80% yield of the theoretical yield, based on bromochlorodifluoromethane): bp 80−82 °C (lit.[10] bp 87 °C); ^{1}H NMR δ 0.27; ^{13}C NMR δ −4.71, 135.20 (t, ^1J(C−F) 327.0 Hz); ^{19}F NMR δ −63.8; ^{29}Si NMR δ 10.21 (t, ^2J(Si−F) 32.0 Hz).

Preparation of (Bromodifluoromethyl)trimethylsilane (1b). Compound **1b** was prepared similarly to **1a** by reacting 9.45 g of CF_2Br_2 (45 mmol), 10 g (65 mmol) of Me_3SiBr, and 0.85 g of aluminum powder in a sealed tube. A 60 mL sample of NMP was used in this case in order to facilitate stirring of the dense reaction mixture. Compared to the preparation of **1a**, a faster rate of thickening of the reaction mixture in the case of **1b** is observed. This is probably due to the complexation of NMP with the $AlBr_3$ formed during the oxidation of aluminum metal (the reaction is accompanied by the formation of a dense "cake" due to this complexation). To some extent, larger amounts of solvent alleviate the problem. The workup of the contents of the tube followed by 98% H_2SO_4/pentane partition and fractional distillation of the organic phase using a 15 cm column packed with glass helices afforded 5.1 g of **1b** (55% yield of the theoretical yield, based on bromochlorodifluoromethane) as a colorless liquid: bp 112 °C (lit.[10] bp 105−106 °C); ^{1}H NMR δ 0.27; ^{13}C NMR δ −4.45, 132.11 (t, ^1J(C−F) 339.0 Hz); ^{19}F NMR δ −58.3; ^{29}Si NMR δ 12.45 (t, ^2J(Si−F) 29.0 Hz).

Reaction of 1b with Chlorotrimethylsilane. A 300 mg (1.5 mmol) sample of (bromodifluoromethyl)trimethylsilane (**1b)** (neat) was heated with excess chlorotrimethylsilane in a closed round-bottom flask at 100 °C for 2 h. The NMR analysis of the reaction mixture showed a quantitative conversion of **1b** into **1a**.

Typical Procedure for the Chlorodifluoromethylation of Aldehydes Using 1a. To a mixture of (chlorodifluoromethyl)trimethylsilane (**1a**) (200 mg, 1.26 mmol) and benzaldehyde (90 mg, 0.85 mmol) in dry DME (4 mL) was added 10 drops of 1 M solution of TBAF in THF (ca. 10 mol %).[32] The reaction mixture was stirred for 24 h at room temperature. Gradually, the orange color evolved. When the TLC analysis indicated complete conversion of the starting benzaldehyde, the solution was quenched with 40% HF in acetonitrile in order to remove the trimethylsilyl group from the initial adduct **4a**. Column chromatography (hexanes/ethyl acetate, 10:1) yielded 121 mg of the product 2-chloro-2,2-difluoro-1-phenylethanol[9] (**5a**) in 75% yield based on benzaldehyde.

A similar procedure was used for the preparation of compounds **5b**−**d**. Their spectral properties are reported in the literature.[9]

Preparation of Bis(trimethylsilyl)difluoromethane (2). A 10 mL portion of chlorotrimethylsilane, 5 mL of HMPA, and 0.5 g of tetra-*n*-butylammonium bromide were dissolved under an argon atmosphere in 50 mL of THF in a single-compartment electrochemical cell equipped with an aluminum rod anode (99% pure) and nickel grid cathode. Preelectrolysis at 100 mA was performed until hydrogen evolution was no longer detectable, which corresponded to the removal of the residual hydrochloric acid. An amount of 6 g of **1a** (28 mmol) was introduced into the cell, and the electrolysis at 100 mA was carried out until approximately 2.1 F/mol of electric current was consumed. The reaction mixture was monitored by GC−MS and NMR. Upon completion, the reaction was quenched with water and extracted with pentane (4 × 100 mL). The combined pentane fractions were dried with sodium sulfate. At this point, NMR analysis showed the mixture to consist of pentane and disiloxane as well as products **2** and **3** in a 10:1 molar ratio. Tetrabutylammonium fluoride (1 M solution in THF) was added in order to transform **3** into volatile (perfluorovinyl)-trimethylsilane (**10**). Pentane and **10** were removed by distillation. In order to remove disiloxane, the mixture was treated with 98% sulfuric acid followed by fractionation using a 15 cm column packed with glass helices which afforded 4.1 g of **2** (65% yield of the theoretical yield, based on **1a**) as a colorless liquid: bp 120 °C; ^{1}H NMR δ 0.13; ^{13}C NMR δ −4.12 (t, ^3J(C−F) 2.9 Hz), 138.73 (t, ^1J(C−F) 260.7 Hz); ^{19}F NMR δ −137.3; ^{29}Si NMR δ 1.65 (t, ^2J(Si−F) 29.0 Hz).

Typical Procedure for the Difluoromethylation of Aldehydes Using 2. To a mixture of bis(trimethylsilyl)difluoromethane (**2**) (250 mg, 1.27 mmol) and benzaldehyde (90 mg, 0.85 mmol) in dry DME (4 mL) was added 10 drops of 1 M solution of TBAF in THF (ca. 10 mol %).[32] The reaction mixture was stirred for 24 h at room temperature. When the TLC analysis indicated complete conversion of the starting benzaldehyde, the solution was quenched with 4 N HCl in order to remove the trimethylsilyl group from the initial adduct **6a**. Column chromatography (hexanes/ethyl acetate, 10:1) yielded 140 mg of the product 2,2-difluoro-1-phenylethanol[9] (**7a**) in 70% yield based on benzaldehyde.

A similar procedure was used for the preparation of compounds **7b**−**d**. Their spectral properties are reported in the literature.[9]

Preparation of 1,2-Bis(trimethylsilyl)-1,1,2,2-tetrafluoroethane (3). A 10 mL sample of chlorotrimethylsilane, 50 mL of TDA-1, and 0.5 g of tetra-*n*-butylammonium bromide were added under an argon atmosphere to 50 mL of THF in a single-compartment electrochemical cell equipped with an aluminum rod anode (99% pure) and nickel grid cathode. Preelectrolysis at 100 mA was performed until hydrogen evolution commenced. An amount of 8 g (50 mmol) of **1a** was introduced into the cell, and the electrolysis at 100 mA was carried out until approximately 1.1 F/mol of electric current was consumed. The reaction mixture was monitored by GC−MS and NMR. Upon completion, the reaction was quenched with water and extracted with pentane (4 × 100 mL). The combined pentane fractions were dried with sodium sulfate. The NMR analysis showed the mixture to consist of pentane and disiloxane as well as products **2** and **3** in a 1:8.5 molar ratio. Pentane was removed by distillation. In order to remove disiloxane, the mixture was treated with 98% sulfuric acid and extracted with pentane or, alternatively, fractionated using a 15 cm column packed with glass helices. When most of the disiloxane was removed, the mixture was allowed to cool to room temperature. Crystallization at −20 °C resulted in the formation of white crystals of **3** that were separated from the mother liquid by filtration, furnishing 4.3 g of **3** (70% yield of the theoretical yield, based on **1a**) as a colorless liquid: bp 120 °C; ^{1}H NMR δ 0.22; ^{13}C NMR δ −4.00 (m), 126.63 (tt, ^1J(C−F) 264.5 Hz, ^2J(C−F) 45.8 Hz); ^{19}F NMR δ −122.2; ^{29}Si NMR δ 5.18 (tt, ^2J(Si−F) 34.3 Hz, ^3J(Si−F) 17.2 Hz).

X-ray Analysis of 3. Crystals of **3**, suitable for an X-ray structure determination, were grown via crystallization from the mixture of **2** and **3**. The compound crystallizes very well as large, beautiful needles, with some specimens reaching dimensions as large as 0.5 × 0.5 × 10.0 mm. X-ray diffraction data were collected on a small crystal using Cu Kα radiation on a Siemens P4/RA automated diffractometer at low temperature (−120 °C). The structure was solved by direct methods and refined to final agreement factors of $R = 4.6\%$ and $R_w = 5.2\%$ for 1852 nonzero reflections. Details of the structure analysis are given in Table 5.

Typical Procedure for the Perfluorovinylation of Carbonyls Using 3. To a mixture of 1,2-bis(trimethylsilyl)-1,1,2,2-tetrafluoroethane (**3**) (300 mg, 1.22 mmol) and benzaldehyde (90 mg, 0.85 mmol)

(31) A series of (perfluoroalkyl)trialkylsilanes were purified by partitioning between 98% sulfuric acid and hexane: Sekya, A.; Hoshi, N.; Kobayashi, T. Jpn. Kokai Tokkyo Koho JP06,228,164[94,228,164] (CL.C07F7/12).

(32) Tetrabutylammonium fluoride (TBAF) is known for its highly hygroscopic nature caused by the basicity of fluoride ion. However, the amount of water associated with fluoride ion can be drastically lowered using the procedure of Cox et al. (see ref 15) by heating the TBAF/H_2O complex at 40 °C under dynamic vacuum until ca. 20% loss of the sample weight occurs. Alternatively, we have found that anhydrous 2-propanol (0.005% H_2O, Aldrich) is suitable for azeotropic removal of water. Thereby, the yellow-brown TBAF/H_2O complex is mixed in a Schlenk flask with isopropanol which is removed under vacuum. The cycle is repeated 10−15 times. As a result of this treatment, an off-yellow powder is obtained which was found to be suitable for our synthetic purposes.

in dry THF was added 3 drops of 1 M solution of TBAF in THF (ca. 3 mol %).[32] The color instantaneously changed to dark-brown. The reaction mixture was stirred for 4 h at room temperature. When the TLC analysis indicated complete conversion of the starting benzaldehyde, the solution was quenched with 4 N HCl in order to remove the trimethylsilyl group from the initial adduct **6a**. Column chromatography (hexanes/ethyl acetate, 10:3) yielded 172 mg of the product 1-(trifluoroethenyl)-1-phenylmethanol (**11a**) in 75% yield based on benzaldehyde.

A similar procedure was used for the preparation of compounds **11b**−**c**. Their spectral properties are reported in the literature.[27]

Low-Temperature Reaction of 1,2-Bis(trimethylsilyl)-1,1,2,2-tetrafluoroethane (3) with Benzaldehyde. To a mixture of 1,2-bis-(trimethylsilyl)-1,1,2,2-tetrafluoroethane (**3**) (500 mg, 2 mmol) and benzaldehyde (646 mg, 6 mmol) in dry DME at −48 °C were added 5 drops of 1 M solution of TBAF in THF (ca. 3 mol %).[32] The reaction mixture was stirred for 4 h at −48 °C and then allowed to warm to room temperature. Usual workup, followed by column chromatography, afforded compounds **11**, **12**, and **13** in a 1:3:2 molar ratio, determined by ^{19}F NMR. The overall yield was 75%.

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