and in solution that is due to the small change in molecule size (which is much more important for charged species because of the Born ionic solvation term in total energy) can be noticed. However, this is not observed experimentally[11] (cf. Table II), which indicates either that there is practically no change in the volume of the acetate ion due to the C-H bond cleavage or the gas-phase experiment is in error. It is worth while to note in this connection that the AM1 prediction for the solution is in a very good agreement with experimental BDE, whereas the data for the isolated species are more inconsistent (difference between calculated and experimental BDE is 6.6 kcal/mol).

As mentioned before,[5,9] the additional stabilization of the captodative radicals in solution is supported by the increase of their dipole moments. However, the data presented in Table III on the calculated dipole moments of molecules and radicals do not stress the specifically enhanced dipole moment change of cyanohydroxymethyl radical in comparison with other species.[18] Remarkably enough, the largest change (by 84% as calculated using AM1 parametrization) is obtained for the closed-shell cyanomethanol molecule. The large increase of AM1, PM3, and MNDO calculated dipole moments of the radical resulting from the C-H bond dissociation of ethylene glycol and MNDO calculated dipole moment of ethylene glycol itself are mainly due to the conformational change in these species (from trans conformation of OH groups in gas phase to gauche conformation in solution), but not to the electron redistribution in this radical. Altogether the calculated dipole moments of the closed-shell molecules are higher than the corresponding radicals (cf. Table III). In part this is caused by significant geometry changes at the carbon atom from a nearly tetrahedral configuration in the molecule to a planar configuration in the radical.

In conclusion, our results show that the AM1 SCRF ROHF method describes satisfactorily the homolytic dissociation energies (however, not the dissociation paths., cf. ref 19) of carbon-hydrogen bonds in polar solvents. More direct experimental data on bond cleavage energies are needed to validate the prediction of the merostabilization of captodative radicals in these media.

Registry No. H_3COH, 67-56-1; $HO^{\bullet}CH_2$, 2597-43-5; H_3CCH_2OH, 64-17-5; $H_3CC^{\bullet}HOH$, 2348-46-1; $(H_3C)_2CHOH$, 67-63-0; $(H_3C)_2C^{\bullet}OH$, 5131-95-3; $(H_2C)_3COH$, 75-65-0; $(CH_3)_2(C^{\bullet}H_2)COH$, 5723-74-0; CH_3CN, 75-05-8; $^{\bullet}CH_2CN$, 2932-82-3; $H_3CCO_2^-$, 71-50-1; $H_2C^{\bullet}CO_2^-$, 19513-45-2; $(CH_2OH)_2$, 107-21-1; $H_2C^{\bullet}(OH)CHOH$, 36730-46-8; $H_2C^{\bullet}(CN)OH$, 107-16-4; $(CN)C^{\bullet}HOH$, 27924-05-6.

(18) Remarkably enough, the largest change (by 84% as calculated using AM1 parametrization was obtained for the closed-shell cyanomethanol molecule. The large increase of the AM1, PM3, and MNDO calculated dipole moments of the radical resulting from the C-H bond dissociation of thylene and MNDO calculated dipole moment of ethylkene glycol itself are mainly due to conformational change in these species (from trans conformation of OH groups in gas phase to gauche conformation in solution), but not to the electron redistribution in this radical.

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Electrolytic Reactions of Fluoro Organic Compounds. 7.[1] Anodic Methoxylation and Acetoxylation of 2,2,2-Trifluoroethyl Sulfides. Preparation of Highly Useful Trifluoromethylated Building Blocks

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Anodic methoxylation and acetoxylation of 2,2,2-trifluoroethyl sulfides and the corresponding nonfluorinated sulfides were comparatively studied. It was found that a trifluoromethyl group remarkably promoted anodic substitution and methoxy and acetoxy groups were introduced adjacent to the trifluoromethyl group of the sulfides. Longer perfluoroalkyl groups also promoted these anodic substitutions. These products were shown to be highly useful building blocks for the synthesis of fluoro organic compounds.

Recently, a great deal of interest has been focused on trifluoromethylated compounds because of their possible biological activities.[2] However, methods for their synthesis are limited in many cases.[3] For example, nucleophilic substitution hardly occurs at the position α to a trifluoromethyl group due to its strong electron-withdrawing effect,[4,5] although sulfur nucleophiles undergo such substitution efficiently (Scheme I).[6] Therefore, the realization of substitution at the α-position is one of the most important subjects in modern organo fluorine chemistry. Electrochemical reactions have recently been shown to be

Scheme I

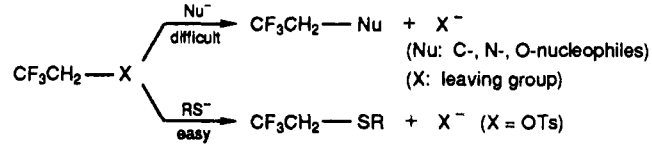

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Table I. Oxidation Potentials (Peak Potentials, E_p^{ox}) of Trifluoroethyl Sulfides[a]

$[PhSCH_2R_f]$

sulfide no.	R_f	E_p^{ox} (V) vs $Ag/AgNO_3$ sat.
1a	CF_3	1.35
4	CH_2CF_3	1.20
5	CH_3	1.05

[a] 2 mM of sulfide in 0.1 M Bu_4NBF_4/MeCN. Sweep rate: 100 mV/s.

useful new tools in organic synthesis.[7] With regard to fluoro organic compounds, extensive studies on the electrofluorination of organic compounds[8] and the synthesis of trifluoromethylated compounds by the anodic oxidation of trifluoroacetic acid in the presence of the appropriate unsaturated compounds[9] have been performed. Although anodic substitution is known to be a characteristic of certain electrochemical reactions, no results pertaining to the electrolytic substitution of trifluoromethylated compounds have been reported so far.[10]

Therefore, we successfully carried out the anodic methoxylation and acetoxylation of 2,2,2,-trifluoroethyl sulfides to trifluoroacetaldehyde equivalents. Trifloroacetaldehyde is a versatile building block for the synthesis of a variety of fluoro organic compounds. On the other hand, either chemical or electrochemical oxidative transformation of trifluoroethanol to trifluoroacetaldehyde has been unsuccessful (Scheme II). Trifluoroacetaldehyde is generally produced by the reduction of trifluoroacetic acid ester or acid chloride using an excess of LAH.

Scheme II

$$CF_3CH_2OH \xrightarrow{\text{oxidation}} CF_3CHO \xleftarrow{\text{LAH}} CF_3COOR \text{ or } CF_3COCl$$

In addition, the effect of longer perfluoroalkyl groups on these anodic substitutions was also investigated.

Results and Discussion

Oxidation Potentials of Fluoroalkyl Sulfides. In order to investigate the effect of the trifluoromethyl group on the oxidation potentials of sulfides, the anodic peak potentials of 2,2,2-trifluoroethyl and 3,3,3-trifluoropropyl sulfides **1a** and **4** together with the nonfluorinated sulfides **5** were measured at a platinum anode in acetonitrile. These sulfides exhibited multiple anodic waves, and the first peak potentials are summarized in Table I.

The fluorinated sulfides were found to be oxidized at a more positive potential than the corresponding nonfluorinated sulfides due to the electron-withdrawing effect of the trifluoromethyl group. It was also found that the anodic peak potentials shifted in the anodic direct as follows: E_p^{ox} **5** < **4** < **1a**.

Anodic Methoxylation of Fluoroalkyl Sulfides. The anodic methoxylation of various 2,2,2-trifluoroethyl sulfides **1a–d** together with 1,1-dihydroperfluoroalkyl sulfides **2** and **3** was carried out at a constant current in anhydrous methanol using an undivided cell under various conditions. Also the anodic methoxylation of the 3,3,3-trifluoropropyl sulfide **4** and the nonfluorinated ethyl sulfide **5** was also comparatively investigated in a similar manner. The results are summarized in Table II.

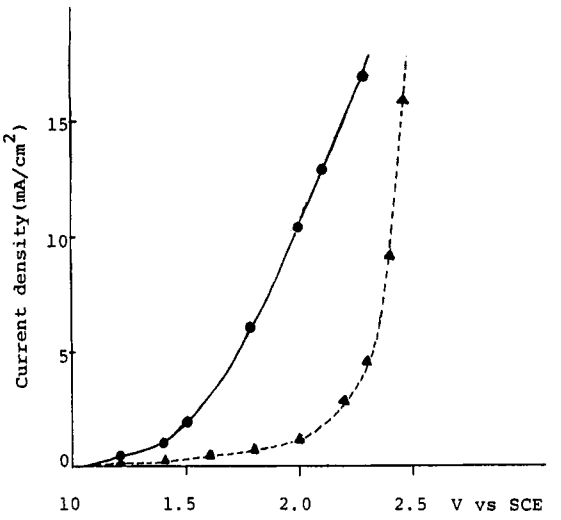

Figure 1. Current-potential curves: 0.2 M Et_4NOTs–MeOH solution (▲); in the presence of 0.2 M **1a** (●).

Anodic methoxylation of aryl 2,2,2-trifluoroethyl sulfides **1a** and **1b** smoothly proceeded to give the α-methoxy sulfides, **6a** and **6b** in high yields (runs 1 and 5). Similarly, 1,1-dihydroperfluoroalkyl phenyl sulfides **2** and **3** provided α-methoxylated products **7** and **8**, respectively, in good yields. In contrast, methoxylation did not occur in the case of the nonfluorinated sulfide **5** (run 11). Benzyl 2,2,2-trifluoroethyl sulfide **1c** gave the α-methoxylated product in a reasonable yield (run 6) while the aliphatic trifluoroethyl sulfide **1d** did not (run 7). It is notable that a perfluoroalkyl group strongly affected this anodic methoxylation as follows: α-trifluoromethyl and α-perfluoroalkyl groups remarkably promoted the anodic methoxylation while a β-trifluoromethyl group did not facilitate the substitution reaction. Furthermore, the sulfides **5**, devoid of a perfluoroalkyl group, failed to give a methoxylated product. Interestingly, the longer perfluoroalkyl group showed less substitution (runs 8 and 9) when compared with the trifluoromethyl group (run 1) although these longer perfluoroalkyl groups displayed a similar effect on the oxidation potentials of the sulfides as the trifluoromethyl group.[11]

It was also found that the anode material and supporting electrolyte significantly affected the reaction. A platinum anode was suitable for this methoxylation but a graphite one was not. Efficient anodic methoxylation of **1** was achieved using Et_4NOTs while the methoxylation was unsuccessful using either Bu_4NClO_4 or MeONa. The anodic methoxylation of **1c** resulted in the formation of two regioisomers **4c** and **4c′**. However, regioselectivity was not observed, and almost equal amounts of **4c** and **4c′** were formed. It was expected that the methoxylation should occur predominantly at the benzylic position of **1c** since benzylic anodic substitution is known to easily take place.[12] Therefore, it should be noted that the methoxylation took place to the same extent at both α-positions of the sulfide **1c**.

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Table II. Anodic Methoxylation of Fluoro Sulfides

$$\underset{\mathbf{1-5}}{RSCH_2R_f} \xrightarrow[\substack{MeOH\\10\ F/mol}]{-2e\ -H^+} \underset{\mathbf{6-9}}{RSCH(OMe)R_f}$$

run	sulfide no.	R	R_f	anode	supporting electrolyte	yield, %
1	**1a**	Ph	CF_3	Pt	Et_4NOTs	93 (**6a**)
2	**1a**	Ph	CF_3	C	Et_4NOTs	13 (**6a**)
3	**1a**	Ph	CF_3	Pt	Bu_4NClO_4	0
4	**1a**	Ph	CF_3	Pt	MeONa	0
5	**1b**	*p*-ClC_6H_4	CF_3	Pt	Et_4NOTs	80 (**6b**)
6	**1c**	$PhCH_2$	CF_3	Pt	Et_4NOTs	23[a] (**6c**, **6c'**)
7	**1d**	Et	CF_3	Pt	Et_4NOTs	0
8	**2**	Ph	CF_2CF_3	Pt	Et_4NOTs	72 (**7**)
9	**3**	Ph	$(CF_2)_2CF_3$	Pt	Et_4NOTs	58 (**8**)
10	**4**	Ph	CH_2CF_3	Pt	Et_4NOTs	trace (**9**)[b]
11	**5**	Ph	CH_3	Pt	Et_4NOTs	0

[a] Regioisomers [$PhCH_2SCH(OMe)CF_3$ (**6c**), $PhCH(OMe)SCH_2CF_3$ (**6c'**) (1:1)] were formed. [b] Formation of the product **9** was confirmed by mass spectrometry of the electrolytic solution of **4**: *m/e* 205 (M^+), 153 ($PhSCH{=}^+OMe$), 110 ($PhSH^+$), 109 (PhS^+), 77 (Ph^+), 69 (CF_3^+).

Table III. Anodic Acetoxylation of Fluoro Sulfides

$$\underset{}{PhSCH_2R_f} \xrightarrow[AcO^-]{-2e\ -H^+} \underset{\mathbf{10-13}}{PhSCH(OAc)R_f}$$

run	sulfide no.	R_f	supporting electrolyte[a]	current density, A/dm	electricity passed, F/mol	product yield, %
1	**1a**	CF_3	L	1.2	4.0	60 (**10**)
2[b]	**1a**	CF_3	H	5.0	3.0	70 (**10**)
3	**2**	CF_2CF_3	L	1.2	4.0	46 (**11**)
4	**3**	$CF_2CF_2CF_3$	L	1.2	4.0	43 (**12**)
5	**5**	CH_3	L	1.2	5.0	0 (**13**)
6[b]	**5**	CH_3	H	5.0	2.5	45 (**13**)

[a] L: 0.2 M AcONa/AcOH (30 mL) containing 2 mmol of sulfide. H: 1.2 M AcONa/AcOH (5 mL) containing 17 mmol of sulfide. [b] The electrolysis was carried out at ca. 50 °C to dissolve NaOAc in AcOH completely.

Hitherto, very few successful examples of anodic methoxylation of sulfides such as cephalosporin derivatives,[13] cyanomethyl sulfides,[14] and α-silylmethyl sulfides[15] have been reported. In this sense, it is significant that α-fluoroalkyl groups promoted the anodic methoxylation.

In order to elucidate the reaction mechanism of the anodic methoxylation, current-potential curves of the sulfides were measured. Figure 1 shows a typical example. It was found that the oxidation of the sulfide **1a** occurred at a much more cathodic potential than that of a Et_4NOTs–MeOH electrolytic solution itself. This fact suggests that the anodic methoxylation is initiated by the direct oxidation of a sulfide. Constant potential electrolysis of **1a** was carried out at the potential (2.0 V vs SCE), where the solvent could not be oxidized. Expectedly, the desired product was obtained in good yield (74%).

Considering the above results, the reaction seems to proceed via an electrogenerated cationic species, similar to that proposed for the anodic substitution of nonfluorinated sulfides[16,17] as follows. Deprotonation of cation radical A formed by initial one-electron oxidation of sulfides followed by effective reoxidation leads to the catinic intermediate C and successively the methoxylation takes place as shown in Scheme III. Since a perfluoroalkyl (R_f) group is strongly electron-withdrawing, the deprotonation of the cation radical A should be facilitated by the R_f group. In addition, a sort of captodative effect of the stabilization of the radical intermediate B would also contribute to this reaction.

Scheme III

$$R_fCH_2SAr \xrightarrow{-e} \underset{(A)}{[R_fCH_2\overset{+\bullet}{S}Ar]} \xrightarrow{-H^+} \underset{(B)}{[R_f\overset{\bullet}{C}HSAr]} \xrightarrow{-e}$$

$$\underset{(C)}{[R_f\overset{+}{C}HSAr \leftrightarrow R_fCH{=}\overset{+}{S}Ar]} \xrightarrow[MeO^-]{} R_fCH(OMe)SAr$$

Scheme IV

$$\underset{\mathbf{1a}}{CF_3CH_2SPh} \xrightarrow{m\text{-}ClC_6H_4CO_3H} \underset{\substack{\mathbf{14}\\95\%}}{CF_3CH_2\overset{O}{\overset{\downarrow}{S}}Ph} \xrightarrow[120\ °C]{Ac_2O} \underset{\substack{\mathbf{10}\\42\%}}{CF_3CH\overset{OAc}{\overset{\downarrow}{S}}Ph}$$

Therefore, it is not surprising that methoxylation at positions α to the perfluoroalkyl group preferably takes place.

Anodic Acetoxylation of Fluoroalkyl Sulfides. The anodic acetoxylation of fluorinated sulfides and a nonfluorinated sulfide was similarly carried out in acetic acid containing sodium acetate.

As shown in Table III, successful acetoxylation of fluoroalkyl sulfides **1a**, **2**, and **3** was achieved to give the corresponding α-acetoxy sulfides **10–12** (runs 1, 3, and 4).

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In these reactions, the longer 1,1-dihydroperfluoroalkyl sulfides **2** and **3** gave lower yields similarly to the case of the anodic methoxylation. In contrast, no acetoxylated sulfide was obtained from nonfluorinated sulfide **5** under the same electrolytic conditions (run 5). It was observed that the anodic acetoxylation of **5** proceeded to give the α-acetoxylated sulfide **13** in a low yield only when the concentration of both substrate **5** and the electrolyte was extremely high (run 6).[18,19] It was also found that the yield of **10** increased to 70% under high concentration conditions, although the amount of the consumed electricity decreased (run 2). Thus, it was demonstrated that the anodic acetoxylation of fluorinated sulfides was a highly current efficient process when compared to the corresponding nonfluorinated substrates.

Pummerer rearrangement is a well-known reaction for the preparation of α-acetoxy sulfides from sulfoxides.[20] Preparation of **10** from the sulfoxide **14** derived from **1a** was attempted by Pummerer rearrangement as shown in Scheme IV. However, the sulfoxide **14** provided **10** in low yield even after heating at 120 °C for 24 h in acetic anhydride.[21]

Cyanomethyl phenyl sulfide is known to give the corresponding α-acetoxy sulfide in good yield by Pummerer rearrangement of the sulfoxide by heating at the same temperature for several hours.[22] Therefore, a trifluoromethyl group was found to interfere with the rearrangement although its electron-withdrawing effect is similar to that of a cyano group. Thus, the electrochemical acetoxylation was found to be superior to the Pummerer reaction since the acetoxylation proceeded under mild conditions with higher yields.

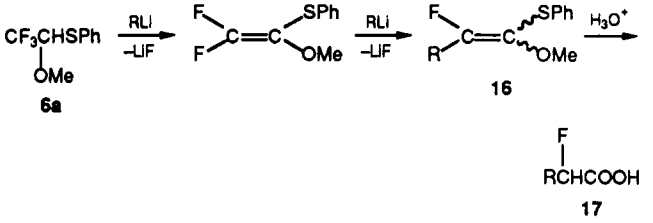
Synthetic Utilization of α-Methoxy and α-Acetoxy Sulfides as Trifluoromethylated Building Blocks. In order to demonstrate the synthetic utility of the electrolytic products **6** and **10** as trifluoroacetaldehyde equivalents, we first attempted their transformation into hydrazone derivatives since they are known to be useful building blocks for the preparation of heterocyclic compounds bearing a trifluoromethyl group.[23] Thus, **10** was easily converted into trifluoroacetaldehyde phenylhydrazone **15** (70% yield) without any defluorination in the course of alkali hydrolysis (Scheme V).

Scheme V

$$\underset{\mathbf{10}}{CF_3CH(OAc)SPh} \xrightarrow{\text{aqueous } K_2CO_3} [CF_3CHO] \xrightarrow{PhNHNH_2} \underset{\mathbf{15}\ 70\%}{CF_3CH{=}NNHPh}$$

Furthermore, we sucessfully attempted the transformation of **6a** into α-monofluoroalkanoic acids, a class of compounds with current biological interest.[2] Thus, treatment of **6a** with 2 equiv of alkyl- or phenyllithium in tetrahydrofuran at −78 °C followed by warming to room temperature for 3 h provided monofluoroketene hemiacetal **16** in high yields as shown in Table IV. The stereochemical structure of **16** has not yet been established. In this reaction, *n*-butyl- and phenyllithium gave one isomer

Table IV. Transformation of α-Methoxy Sulfide 6a into α-Fluoroalkanoic Acids



R	yield, % 16	yield, % 16 → 17
n-Bu	70 (**16a**)	95 (**17a**)
s-Bu	84 (**16b**)[a]	80 (**17b**)
Ph	85 (**16c**)	31 (**17c**)

[a] Stereoisomers (2:5).

whereas *sec*-butyllithium provided two isomers, whose stereochemistry has not yet been determined. Successful transformation of **16** into α-monofluoroalkanoic acids **17** could be achieved in moderate to excellent yields by acidic hydrolysis as shown in Table IV. Nakai et al. reported similar reaction using trifluoroacetaldehyde dithioacetal derived from trifluoroacetaldehyde and ethanthiol.[24]

Finally, we tried nucleophilic substitution of **6** with carbon nucleophiles. Generally, generation of carbocations bearing an α-triflurometlhyl group is difficult due to the strong electron-withdrawing effect.[25,26] Since **6** has an acetal structure, it was expected that Lewis acid catalyzed elimination of the methoxy group of **6** would generate the corresponding carbocation which should be stabilized by the neighboring sulfur atom. Using aromatic compounds as a nucleophile, the substitution reaction of **6a** and **6b** was attempted. The reaction with benzene was greatly affected by a Lewis acid as shown in Table V.

It was found that the more stronger Lewis acid gave the better results. Aluminum trichloride was the most effective for this reaction, and a phenyl group was successfuly introduced into the α-position to the trifluoromethyl group (runs 4–6). The substituted phenyl group such as *p*-isobutylphenyl was also introduced in moderate yield (run 7). Since the desulfurization of the product **18** thus obtained can be easily performed using Bu_3SnH (Scheme VI)

Scheme VI

$$CF_3CH(Ar')SAr \xrightarrow[-Bu_3SnSAr]{Bu_3SnH} CF_3CH_2Ar'$$

as reported by Uneyamat et al.,[27] the present procedure seems to be useful for the preparation of 2,2,2-trifluoroethyl aromatics.

Thus, we have shown α-methoxy and α-acetoxy sulfides anodically formed from 2,2,2-trifluoroethyl sulfides are highly useful trifluoroacetaldehyde equivalents and versatile fluorobuilding blocks.

In summary, this work serves to illustrate successful examples of the potential utility of the electrochemical technique in the synthesis of fluoro organic compounds.

Experimental Section

^1H NMR and ^{19}F NMR spectra were recorded at 60 MHz on Varian EM 360 NMR and Hitachi R-24F NMR spectrometers, respectively. The chemical shifts for ^1H and ^{19}F NMR are given in δ ppm downfield from internal Me_4Si and upfield from external

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Table V. Nucleophilic Substitution of α-Methoxy Sulfide 6 with Aromatic Compounds

$$\underset{\mathbf{6a,b}}{ArSCH(OMe)CF_3} \xrightarrow[-MeO^-]{\text{Lewis acid}} [ArSCHCF_3^+ \leftrightarrow ArS{=}CHCF_3^+] \xrightarrow[-H^+]{Ar'H} \underset{\mathbf{18}}{ArSCH(Ar')CF_3}$$

run	Ar	Ar'	Lewis acid	reaction temp, °C	reaction time, h	yield, %
1	Ph	Ph	$SnCl_4$	reflux	10	7 (18a)
2	Ph	Ph	$BF_3{\cdot}OEt_2$	reflux	6	35 (18a)
3	Ph	Ph	$TiCl_4$	reflux	3	29 (18a)
4	Ph	Ph	$AlCl_3$	room temp	1	63 (18a)
5	Ph	Ph	$AlCl_3$	-78	2.5	83 (18a)
6	p-ClC_6H_4	Ph	$AlCl_3$	room temp	2	53 (18b)
7	Ph	p-(i-Bu)C_6H_4	$AlCl_3$	-78	8	48 (18c)

CF_3COOH, respectively. IR spectra were obtained with a Hitachi 295 infrared spectrometer. Mass spectra were obtained with a JEOL JMS-D100 GC–mass spectrometer. High-resolution mass spectra were obtained with a Hitachi M-80B GC–mass spectrometer. Cyclic voltammetric and preparative electrolysis experiments were carried out using a Hokutodenko HA-501 Potentiostat/Galvanostat equipped with a Hokutodenko HF-201 digital coulombmeter.

Fluoroalkyl Sulfides. α-Trifluoroethyl sulfide **1** and 1,1-dihydroperfluoroalkyl sulfides **2** and **3** were prepared from thiols and 2,2,2-trifluoroethyl and 1,1-dihydroperfluoroalkyl *p*-toluenesulfonates similar to the reported procedure.[6,28] Phenyl 3,3,3-trifluoropropyl sulfide (**4**) was prepared from thiophenol and 1,1,1-trifluoropropyl iodide.[29]

***p*-Chlorophenyl 2,2,2-trifluoroethyl sulfide (1b):** ^1H NMR ($CDCl_3$) δ 3.40 (q, 2 H, CH_2, J_{H-F} = 10 Hz), 7.2–7.6 (m, 4 H, C_6H_4Cl); MS *m/e* 228 (M^+ + 2), 226 (M^+) calcd for $C_8H_6F_3ClS$ *m/e* 225.9831, found 225.9830.

Phenyl 2,2,3,3,3-pentafluoropropyl sulfide (2): ^1H NMR (CCl_4) δ 3.40 (t, 2 H, CH_2, J_{H-F} = 16 Hz), 7.1–8.0 (m, 5 H, Ph); MS *m/e* 242 (M^+), 123 ($M^+ - CF_3CF_2$), 109 (SPh^+); calcd for $C_9H_7F_5S$ *m/e* 242.0188, found 242.0090.

Phenyl 2,2,3,3,4,4,4-heptafluorobutyl sulfide (3): ^1H NMR (CCl_4) δ 3.46 (t, 2 H, CH_2, J_{H-F} = 16.4 Hz), 7.1–8.0 (m, 5 H, Ph); MS *m/e* 292 (M^+), 123 ($M^+ - CF_3CF_2CF_2$), 104 (PhS^+); calcd for $C_9H_9F_3S$ *m/e* 206.0377, found 206.0302.

Electrolysis and Product Analysis. Electrolysis was carried out mainly at a constant current using platinum plates (3 × 2 cm) as an anode and a cathode in an undivided cylindrical cell equipped with a magnetic stirrer. Electrolytic conditions in each electrolysis are shown in Tables II and III.

(a) Anodic Methoxylation. Constant current (3.3 A/cm^2) electrolysis of sulfides **1–5** (2 mmol) was carried out in 0.2 M Et_4NOTs–MeOH (30 mL) at room temperature. After passing 10 F/mol of electricity (monitoring unreacted **1–5** by silica gel TLC), the electrolyte was mixed with 60 mL of water and extracted three times with 30-mL portions of ether and then washed with 30 mL of brine. The extracts were dried over anhydrous sodium sulfate, and the solvent was evaporated. The remaining oil was chromatographed on silica gel (hexane–AcOEt, 95:5) to provide α-methoxy products **6–9**.

(b) Anodic Acetoxylation. After electrolysis under the conditions shown in Table III, the electrolyte was mixed with 60 mL of water and extracted three times with 30-mL portions of ether. The extracts were washed with sodium bicarbonate, water, and brine and then dried over anhydrous sulfate. After evaporation of the solvent, the residue was chromatographed on silica gel (hexane–AcOEt, 9:1) to provide α-acetoxy products **10–13**.

Phenyl 1-methoxy-2,2,2-trifluoroethyl sulfide (6a): ^1H NMR ($CDCl_3$) δ 3.60 (s, 3 H, CH_3), 4.80 (q, 1 H, CH, J_{H-F} = 6 Hz), 7.1–7.7 (m, 5 H, C_6H_5); ^{19}F NMR ($CDCl_3$) δ -3.1 (d); MS *m/e* 222 (M^+); calcd for $C_9H_9F_3OS$ *m/e* 222.0326, found 222.0375.

***p*-Chlorophenyl 1-methoxy-2,2,2-trifluoroethyl sulfide (6b):** ^1H NMR ($CDCl_3$) δ 3.60 (s, 3 H, CH_3), 4.70 (q, 1 H, CH, J_{H-F} = 6 Hz), 7.16–7.60 (m, 4 H, C_6H_4Cl); ^{19}NMR ($CDCl_3$) δ -3.4 (d); MS *m/e* 258 (M^+ + 2), 256 (M^+); calcd for $C_9H_8F_3ClOS$ *m/e* 255.9936, found 255.9902.

Benzyl 1-methoxy-2,2,2-trifluoroethyl sulfide (6c): ^1H NMR ($CDCl_3$) δ 3.35 (s, 3 H, CH_3), 3.80 (s, 2 H, CH_2), 4.45 (q, 1 H, CH, J_{H-F} = 7 Hz), 7.28 (s, 5 H, C_6H_5); MS *m/e* 236 (M^+); calcd for $C_{10}H_{11}F_3OS$ *m/e* 236.0408, found 236.0503.

1-Methoxy-1-phenylmethyl 2,2,2-trifluoroethyl sulfide (6c′): ^1H NMR δ 2.85 (q, 2 H, CH_2, J_{H-F} = 19 Hz), 3.39 (s, 3 H, CH_3); 5.50 (s, 1 H, CH), 7.19 (s, 5 H, C_6H_5); MS *m/e* 236 (M^+); calcd for $C_{10}H_{11}F_3OS$ *m/e* 236.0408, found 236.0445.

Phenyl 1-methoxy-1*H*-pentafluoropropyl sulfide (7): ^1H NMR (CCl_4) δ 3.62 (s, 3 H, CH_3), 4.85 (dd, 1 H, CH, J_{H-F} = 18, 5.0 Hz), 7.2–7.7 (m, 5 H, C_6H_5); MS *m/e* 272 (M^+); 163 ($M^+ - PhS$), 153 ($M^+ - CF_3CF_2$), 109 (PhS^+). Anal. Calcd for $C_{10}H_9F_5OS$: C, 44.12; H, 3.33. Found: C, 44.2; H, 3.43.

Phenyl 1-methoxy-1*H*-heptafluorobutyl sulfide (8): ^1H NMR (CCl_4) δ 3.59 (s, 3 H, CH_3), 4.83 (dd, 1 H, CH, J_{H-F} = 19, 5.6 Hz), 7.1–7.7 (m, 5 H, C_6H_5); MS *m/e* 322 (M^+), 213 ($M^+ - SPh$), 153 ($M^+ - CF_3CF_2CF_2$), 109 (SPh^+). Anal. Calcd for $C_{11}H_9F_7OS$: C, 41.00; H, 2.81. Found: C, 41.15; H, 2.93.

Phenyl 1-acetoxy-2,2,2-trifluoroethyl sulfide (10): ^1H NMR ($CDCl_3$) δ 2.10 (s, 3 H, CH_3), 6.30 (q, 1 H, CH, J_{H-F} = 6 Hz), 7.1–7.6 (m, 5 H, C_6H_5); ^{19}F NMR ($CDCl_3$) δ -3.5 (d); IR 1770 cm^{-1} (C=O); MS *m/e* 250 (M^+); calcd for $C_{10}H_9O_2S$ *m/e* 250.0275, found 250.0270.

Phenyl 1-acetoxy-1*H*-pentafluoropropyl sulfide (11): ^1H NMR (CCl_4) δ 2.09 (s, 3 H, CH_3), 6.22 (q, 1 H, CH, J_{H-F} = 8 Hz), 7.1–7.8 (m, 5 H, C_6H_5); IR 1780 cm^{-1} (C=O); MS *m/e* 300 (M^+). Anal. Calcd for $C_{11}H_9F_5O_2S$: C, 44.01; H, 3.02. Found: C, 43.81; H, 3.11.

Phenyl 1-acetoxy-1*H*-heptafluorobutyl sulfide (12): ^1H NMR (CCl_4) δ 2.14 (s, 3 H, CH_3), 6.30 (dd, 1 H, CH, J_{H-F} = 17, 6.9 Hz), 7.2–7.9 (m, 5 H, C_6H_5); IR 1790 cm^{-1} (C=O); MS *m/e* 350 (M^+). Anal. Calcd for $C_{12}H_9F_7O_2S$: C, 41.15; H, 2.59. Found: C, 41.15; H, 2.66.

Preparation of 10 by Pummerer Rearrangement. Phenyl 2,2,2-trifluoroethyl sulfoxide (14): To a stirred solution of 10 mmol of *m*-chloroperbenzoic acid in 45 mL of dichloromethane was added dropwise sulfide **1a** at 0 °C. After 1 h, the reaction mixture was mixed with water and extracted repeatedly with dichloromethane. The extracts were washed with water and dried with anhydrous sodium sulfate. After evaporation, the residual solid was recrystallized from hexane to provide pure sulfoxide **14** in 95% yield; mp 77–78 °C; ^1H NMR ($CDCl_3$) δ 3.50 (q, 2 H, CH_2, J_{H-F} = 6 Hz), 7.4–7.9 (m, 5 H, C_6H_5); IR (CCl_4) 1060 cm^{-1} (S–O); MS *m/e* 208 (M^+), 192 ($M^+ - O$), 125 ($PhSO^+$), 109 (PhS^+), 83 ($CF_3CH_2^+$). Anal. Calcd for $C_8H_7F_3OS$: C, 46.15; H, 3.39. Found: C, 46.16; H, 3.40.

Pummerer Rearrangement of 14. A solution of 0.5 mmol of **14** in 2 mL of acetic anhydride was stirred at 120° for 24 h. The reaction mixture was poured into water, and the resulting solution was extracted repeatedly with ether and washed with aqueous potassium carbonate and water. The solution was dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on silica gel (hexane–AcOEt, 9:1) to provide **10** in 42% yield.

Transformation of 10 into Trifluoroacetaldehyde Phenylhydrazone (15). To a stirred solution of 2 mmol of **10** in 10 mL of ethanol was added dropwise 1 mL of aqueous potassium carbonate (4 mmol) at room temperature. After the reaction mixture was stirred overnight a solution of 3 mmol of phenylhydrazine in 1 mL of acetic acid was added dropwise. After being stirred overnight, the solution was extracted repeatedly with dichloromethane. The extracts were washed with water and dried

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over anhydrous sodium sulfate. After evaporation, the residue was chromatographed on silica gel (hexane–dichloromethane, 4:1) to provide the corresponding hydrazone **15** in 68%. The product **15** was identified by spectroscopic comparison with the authentic sample.[23]

Transformation of 6a into Monofluoro Carboxylic Acids. 1-Methoxy-1-(phenylthio)-2-fluoro-1-hexene (16a). To a stirred solution of 0.5 mmol of **6a** in 0.5 mL of ether was added dropwise a solution of 1 mmol of butyllithium in hexane solution (1.8 M) at −78 °C under a nitrogen atmosphere. After 3 h, the temperature was raised to room temperature, and then saturated aqueous ammonium chloride was added to the reaction mixture. The solution was extracted repeatedly with ether and washed with brine and then dried over anhydrous sodium sulfate. After evaporation, the residue was chromatographed on silica gel (hexane–AcOEt, 95:5) to provide **16a** in 70% yield: ^{1}H NMR ($CDCl_3$) δ 0.6–1.8 (m, 7 H, C_3H_7), 2.50 (dt, 2 H, CH_2CF=, J_{H-H} = 6 Hz, J_{H-F} = 22 Hz), 3.50 (s, 3 H, OCH_3), 7.1–7.5 (m, 5 H, C_6H_5); IR 1660 cm^{-1} (C=O); MS m/e 240 (M^+), 197 ($M^+ - C_3H_7$). Anal. Calcd for $C_{13}H_{17}FOS$: C, 64.97; H, 7.13. Found: C, 64.85; H, 7.18.

The other ketene hemiacetals **16b** and **16c** were prepared similarly.

1-Methoxy-1-(phenylthio)-2-fluoro-3-methyl-1-hexene (16b, isomer 1): ^{1}H NMR δ 0.93 (t, 3 H, CH_3CH_2, J_{H-H} = 7 Hz), 1.15 (d, 3 H, CH_3CH, J_{H-H} = 7 Hz), 1.47 (q, 2 H, CH_2, J_{H-H} = 7 Hz), 2.93 (sextet d, 1 H, CH, J_{H-H} = 7 Hz, J_{H-F} = 32 Hz), 3.55 (s, 3 H, OCH_3), 7.13–7.57 (m, 5 H, C_6H_5); MS m/e 240 (M^+), 255 ($M^+ - CH_3$), 211 ($<M^+ - C_2H_5$). Anal. Calcd for $C_{13}H_{17}FOS$: C, 64.97; H, 7.13. Found: C, 64.62; H, 7.12.

1-Methoxy-1-(phenylthio)-2-fluoro-3-methyl-1-hexene (16b, isomer 2): ^{1}H NMR δ 0.90 (t, 3 H, CH_3CH_2, J_{H-H} = 7 Hz), 1.13 (d, 3 H, CH_3CH, J_{H-H} = 7 Hz), 1.45 (q, 2 H, CH_2, J_{H-H} = 7 Hz), 3.03 (sex d, 1 H, CH, J_{H-H} = 7 Hz, J_{H-F} = 32 Hz), 3.63 (s, 3 H, OCH_3), 7.13–7.43 (m, 5 H, C_6H_5); MS m/e 240 (M^+), 225 ($M^+ - CH_3$), 211 ($M^+ - C_2H_5$). Anal. Calcd for $C_{13}H_{17}FOS$: C, 64.97; H, 7.21. Found: C, 64.88; H, 7.21.

1-Fluoro-1-phenyl-2-methoxy-2-(phenylthio)ethene (16c): ^{1}H NMR ($CDCl_3$) δ 3.70 (s, 3 H, OCH_3), 7.1–8.0 (m, 10 H, C_6H_5, SC_6H_5); ^{19}F NMR ($CDCl_3$) δ 28.3 (s). Anal. Calcd for $C_{15}H_{13}FOS$: C, 69.21; H, 5.03. Found: C, 69.24; H, 5.17.

2-Fluorohexanoic acid (17a): A mixture of **16a** and 5 mL of 90% H_2SO_4 was heated at 50 °C for 5 h. After cooling, the solution was extracted repeatedly with ether, washed with water, and then dried over anhydrous sodium sulfate. Evaporation of the solvent provided **17a** in 95% yield. Its spectral data were completely identical with those of the authentic sample.[24,30]

The other fluoro carboxylic acids **17b** and **17c** were similarly prepared and **17c** was identified by spectroscopic comparison with the authentic sample.[24,30]

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2-Fluoro-3-methylpentanoic acid (17b): ^{1}H NMR ($CDCl_3$) δ 0.77–1.70 (m, 9 H, s-Bu), 4.85 (dd, 1 H, CH, J_{H-H} = 4 Hz, J_{H-F} = 50 Hz), 8.73 (s, 1 H, CO_2H); ^{19}F NMR ($CDCl_3$) δ 116 (dd). Anal. Calcd for $C_6H_{11}FO_2$: C, 53.72; H, 8.26. Found: C, 53.42; H, 8.54.

Nucleophilic Substitution of 6 with Benzenes.

Phenyl 1-Phenyl-2,2,2-trifluoroethyl Sulfide (18a). To a stirred solution of 2.25 mmol of aluminum trichloride and 12 mmol of benzene in 3 mL of CH_2Cl_2 was added dropwise 1.5 mmol of **6a** at −78 °C under a nitrogen atmosphere. After 2.5 h of stirring, the solution was warmed to room temperature and 8 mL of water was added. The resulting solution was extracted repeatedly with ether and washed with aqueous sodium bicarbonate, water, and brine. The extracts were dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on silica gel (hexane–AcOEt, 20:1) to provide pure **18a** in 83% yield: ^{1}H NMR (CCl_3) δ 4.37 (q, 1 H, CH, J_{H-F} = 8 Hz), 7.0–7.5 (m, 10 H, C_6H_5); MS m/e 268 (M^+), 199 ($M^+ - CF_3$), 159 ($M^+ - C_6H_5S$); calcd for $C_{14}H_{11}F_3S$ m/e 268.0533, found 268.0522.

The other derivatives **18b** and **18c** were similarly prepared.

4-Chlorophenyl 1-Phenyl-2,2,2-trifluoroethyl Sulfide (18b). Sixty equivalents of benzene was used to react with the substrate **6b**, and the product **18b** was separated using hexane–AcOEt (9:1) as an elution solvent; ^{1}H NMR (CCl_4) δ 4.37 (q, 1 H, CH, J_{H-F} = 8 Hz), 6.8–7.9 (m, 9 H, C_6H_5 and C_6H_4); MS m/e calcd for $C_{14}H_{10}ClF_3S$ m/e 302.0143, found 302.0156.

1-(4-Isobutylphenyl)-2,2,2-trifluoroethyl phenyl sulfide (18c): ^{1}H NMR ($CDCl_3$) δ 0.91 (d, 6 H, CH_3, J_{H-H} = 6.6 Hz), 1.86 (m, 1 H, $CH(CH_3)_2$), 2.46 (d, 2 H, CH_2, J_{H-H} = 7.1 Hz), 4.45 (q, 1 H, $CHCF_3$, J_{H-F} = 8.6 Hz), 7.09–7.50 (m, 9 H, C_6H_5 and C_6H_4); ^{19}F NMR ($CDCl_3$) δ 10.6 (d); MS m/e 324 (M^+), 215 ($M^+ - C_6H_5S$); calcd for $C_{18}H_{19}F_3S$ m/e 324.1159, found 324.1161.

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Registry No. **1a**, 2262-07-9; **1b**, 129264-94-4; **1c**, 77745-03-0; **1d**, 5187-62-2; **2**, 129264-95-5; **3**, 129264-96-6; **4**, 102687-64-9; **5**, 622-38-8; **6a**, 108200-49-3; **6b**, 129285-45-6; **6c**, 129264-97-7; **6c'**, 129264-98-8; **7**, 129264-99-9; **8**, 129265-00-5; **9**, 129265-01-6; **10**, 108200-50-6; **11**, 129265-02-7; **12**, 129265-03-8; **13**, 91922-48-4; **16a**, 108200-51-7; **16b**, 129265-04-9; **16c**, 129265-05-0; **17a**, 1578-57-0; **17b**, 6087-16-7; **17c**, 1578-63-8; **18a**, 123228-00-2; **18b**, 129265-06-1; **18c**, 129265-07-2; MeOH, 67-56-1; MeONa, 124-41-4; Et_4NOTs, 35895-69-3; AcONa, 127-09-3; AcOH, 64-19-7; *n*-BuLi, 109-72-8; *s*-BuLi, 598-30-1; PhLi, 591-51-5; $SnCl_4$, 7646-78-8; $BF_3{\cdot}OEt_2$, 109-63-7; $TiCl_4$, 7550-45-0; $AlCl_3$, 7446-70-0; Pt, 7440-06-4; carbon, 7440-44-0; benzene, 71-43-2; isobutylbenzene, 538-93-2.

Lewis Acid Mediated Fluorinations of Aromatic Substrates

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Direct fluorination of aromatic substrates, PhZ (Z = Cl, CHO, $CH(OCH_2)_2$, NO_2, $CO_2CH_2CH_3$, OH, $NHCH_3$, OCH_3, CH_3), in the presence and absence of BCl_3 or $AlCl_3$, has been investigated. For PhCl and PhOH, inclusion of boron trichloride increased the percent conversion and the amount of para product. However, $AlCl_3$ caused an increase in the ortho regioselectivity in the reaction with chlorobenzene. For PhCHO, inclusion of a Lewis acid decreased the percent conversion. In the presence of BCl_3, the ethylene glycol acetal of PhCHO gave only ortho and para fluorinated derivatives with improved conversion. $PhCO_2CH_2CH_3$ was unaffected by the inclusion of Lewis acid while the percentage conversion of $PhNO_2$ increased only slightly. Fluorination of $PhNHCH_3$, $PhOCH_3$, or $PhCH_3$ gave complex reaction mixtures. *p*-Nitroanisole gave rise to only 2-fluoro-4-nitroanisole in the presence or absence of either Lewis acid.

Selective fluorination of organic molecules is of great interest to many biochemists and organic chemists because of the biological importance of these species. Within the last 10 years new reagents have been developed that

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