Electrolytic Partial Fluorination of Organic Compounds. 17.[1] Regiospecific Anodic Fluorination of Sulfides Bearing Electron-Withdrawing Substituents at the Position α to the Sulfur Atom

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Regiospecific monofluorination of various sulfides bearing electron-withdrawing substituents, cyano, ester, acyl, amino, and phosphonate groups, at their α-positions was successfully carried out by the anodic oxidation of the sulfides in $Et_3N{\cdot}3HF$/MeCN using an undivided cell. Fluorine was introduced at the position α to the sulfur atom selectively. Fluorination of α-(phenylthio)-substituted cyclic carbonyl compounds was also successful. Furthermore, anodic α,α-difluorination of ethyl α-(phenylthio)acetate was also successfully carried out although a large amount of electricity was required.

Introduction

Selective fluorination of organic molecules is of great interest to not only organic chemists but also to biochemists because partially fluorinated organic molecules have unique physical and biological properties.[2–5] Although direct fluorination is the most simple procedure for the synthesis of such compounds, the methods are not always straightforward. Recently, various new fluorinating reagents such as CF_3OF, XeF_2, Et_2NSF_3 (DAST), and *N*-fluoropyridinium triflates have been developed.[6–9] However, they are still dangerous, difficult to handle, or very costly. On the contrary, electrochemical fluorination is an ideal method for direct fluorination because it can be done in one step under safe conditions.[10,11] However, electrochemical partial fluorination has been underdeveloped owing to lack of selectivity and the low nucleophilicity of fluoride ions.[12] In fact, hitherto reported electrochemical partial fluorination has been of little use because yields and product selectivity are mostly limited.[10,11]

Recently, we carried out successfully regioselective anodic monofluorination of fluoroalkyl and simple alkyl sulfides[13] and we proposed a Pummerer type mechanism *via* fluorosulfonium ions as key intermediates.[14,15] Since it was found that electron-withdrawing fluoroalkyl groups markedly promoted the anodic fluorination, anodic fluorination of sulfides bearing various electron-withdrawing substituents other than fluoroalkyl was attempted in this study and we found that this anodic fluorination is widely applicable and highly useful.[16]

At almost the same time, Brigaud and Laurent reported anodic α-monofluorination and α,α-difluorination of sulfides having electron-withdrawing groups by use of $Et_3N{\cdot}3HF$ as a supporting electrolyte:[17] They performed successfully anodic monofluorination of α-(phenylthio)-acetophenone, ethyl α-(phenylthio)-α-phenylacetate, and bis[(ethoxycarbonyl)methyl] sulfide. They also demonstrated efficient anodic difluorination of α-(phenylthio)-acetophenone together with desulfurization/fluorination of ethyl α-fluoro-α-(phenylthio)-α-phenylacetate providing ethyl α,α-difluoro-α-phenylacetate. In all cases, the yields are generally good. Although their fluorination was quite efficient, their successful examples were limited.

Results and Discussion

Oxidation Potentials of Sulfides Bearing an Electron-Withdrawing Group. Although systematic study has been done on the substituent effect on the cathodic reduction potentials of sulfides,[18] no report on the effect on the anodic oxidation potentials has been reported to date, outside of our work.[19] Therefore, the anodic peak potentials of the sulfides having an electron-withdrawing group, **1a,f–j,n,** and simple methyl phenyl sulfide were

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Table 1. Oxidation Potentials (Peak Potentials, E_p^{ox}) of Sulfides and Fluorinated Sulfides[a]

sulfide	E_p^{ox} (V vs SSCE)	α-fluorinated sulfide	E_p^{ox} (V vs SSCE)
$PhSCH_2COOEt$ (**1a**)	1.53	**2a**	1.86
$PhCH_2SCH_2COOEt$ (**1f**)	1.91	**2f**	2.31
n-$C_7H_{15}SCH_2COOEt$ (**1g**)	1.90	**2g**	2.45
$PhSCH_2CN$ (**1h**)	1.75	**2h**	2.11
$PhSCH_2COMe$ (**1i**)	1.53	**2i**	–
$PhSCH_2COPh$ (**1j**)	1.48	**2j**	1.87
$PhSCH_2Ph$ (**1n**)	1.43	**2n**	–
$PhSCH_3$	1.41	–	–

[a] 5 mM of sulfide in 0.1 M $NaClO_4$/MeCN. Sweep rate: 100 mV/s.

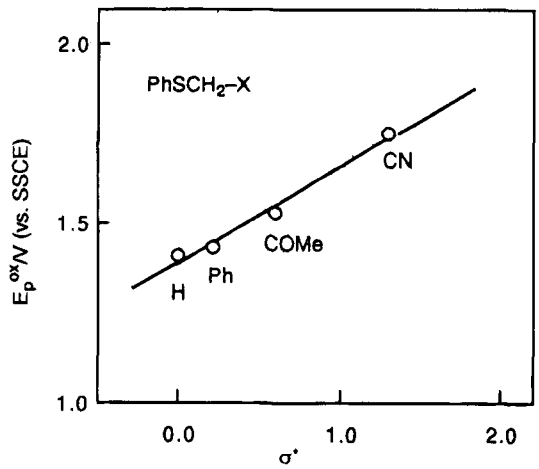

Figure 1. Relationship between oxidation potentials (E_p^{ox}) and substituent constants (σ^*).

Scheme 1

$$PhSCH_2COOEt \xrightarrow[F^-/MeCN]{-2e,\ -H^+} PhSCHFCOOEt$$
1a **2a**

measured by cyclic voltammetry using a platinum anode in anhydrous acetonitrile. These sulfides showed irreversible multiple anodic waves. The first peak potentials E_p^{ox} are summarized in Table 1. The sulfides bearing an electron-withdrawing group were found to be oxidized at more positive potentials than simple methyl phenyl sulfide owing to the electron-withdrawing effect.

As shown in Figure 1, a good linear correlation of oxidation potentials E_p^{ox} with Taft's σ^* values for substituent groups was obtained. This clearly indicates that the polar effect of the substituent group plays a significant role in the electron-transfer step from the sulfide to the anode. It is noted that a strong electron-withdrawing cyano group increased E_p^{ox} significantly (0.34 V) as compared to methyl phenyl sulfide while benzoyl and acetyl groups increased slightly (0.07–0.12 V).

Anodic Fluorination of Sulfides. First, anodic fluorination of α-(phenylthio)acetate (**1a**) was investigated (Scheme 1) at constant potential in acetonitrile containing various fluorides as supporting electrolytes and the fluoride ion source, using an undivided cell.

As shown in Table 2, $Et_3N{\cdot}3HF$ and pyridine polyhydrogen fluoride gave the desired monofluorinated sulfide **2a** (runs 1 and 2) while the other two were not effective (runs 3 and 4). Although pyridine polyhydrogen fluoride is an effective fluorinating reagent, this fluoride was found to be less suitable for the anodic fluorination as compared to $Et_3N{\cdot}3HF$. Consequently, we chose $Et_3N{\cdot}3HF$/MeCN as an electrolytic system for our purpose.

Table 2. Effect of Supporting Electrolytes on Anodic Monofluorination of (Phenylsulfenyl)acetate 1a

run	supporting electrolyte	anodic potential, V vs SSCE	charge passed, F/mol	product yield, %
1	$Et_3N{\cdot}3HF$	1.6	2.5	76
2	$C_5H_5N{\cdot}(HF)_n$	1.8	2.1	49
3	$Bu_4NF{\cdot}3H_2O$	*a*	2.0	0
4	$PhCH_2NMe_3{\cdot}HF_2$[b]	2.4	3.4	0

[a] Constant current (10 mA/cm^2) electrolysis. [b] Divided cell.

Scheme 2

$$R^1SCH_2COOR^2 \xrightarrow[Et_3N{\cdot}3HF/MeCN]{-2e,\ -H^+} R^1SCHFCOOR^2$$
1b ~ 1g **2b ~ 2g**

Table 3. Anodic Monofluorination of α-Thio-Substituted Esters 1

	sulfide					
run	no.	R^1	R^2	anodic potential, V vs SSCE	charge passed, F/mol	product yield, %
1	**1b**	*p*-MeC_6H_4	Et	1.6	2.1	78 (**2b**)
2	**1c**	*p*-$MeOC_6H_4$	Et	1.6	2.5	62 (**2c**)
3	**1d**	*p*-ClC_6H_4	Et	1.9	2.2	56[a] (**2d**)
4	**1e**	Ph	CH_2Ph	1.8	2.5	80 (**2e**)
5	**1f**	$PhCH_2$	Et	2.1	5.0	44 (**2f**)
6	**1g**	C_7H_{15}	Et	2.1–2.3	16.1	70 (**2g**)

[a] *p*-$ClC_6H_4CHFCONH_2$ (32%) was also formed by ammonolysis of the initial product **2g** during the workup with aqueous NH_4OH.

Next, anodic fluorination of α-(*para*-substituted phenylthio)acetates **1b–d** was carried out (Scheme 2).

They underwent monofluorination quite well regardless of the substituent X groups on the benzene ring. In the case of α-[(*p*-chlorophenyl)thio]acetate **1d**, the corresponding monofluoroamide was also formed considerably beside monofluoro ester **2d**. This amide was formed by ammonolysis of the initial product **2d** during the workup because aqueous ammonia was used in order to neutralize the electrolytic solution. Anodic fluorination of other types of α-thio-substituted esters was also successful. Even though the sulfides **1b**, and **1e–g** each have multiple positions susceptible to substitution by a fluorine, regiospecific fluorination took place: a fluorine was introduced exclusively α to the ester group and no fluorination of the *p*-tolyl, benzyl, or heptyl groups was observed.

Figure 2 shows a typical example of current-potential curves of the substrate and the electrolytic solution itself. A cathodic shift was observed in the curve when **1a** was added to the electrolytic solution. This suggests that the fluorination should be initiated by direct electron transfer from sulfides to the anode. This anodic fluorination may proceed with a Pummerer-type mechanism *via* a fluorosulfonium cation as observed in the case of fluoroalkyl sulfides.[15]

The reaction was extended to sulfides bearing various electron-withdrawing substituents other than ester (Scheme 3). The results are summarized in Table 4.

The desired monofluoro products were obtained in fairly good yields in the six cases. Although anodic methoxylation is well known to take place at the *N*-alkyl group of amides,[20] this fluorination occurred exclusively α to the sulfur atom (runs 4 and 5). On the other hand,

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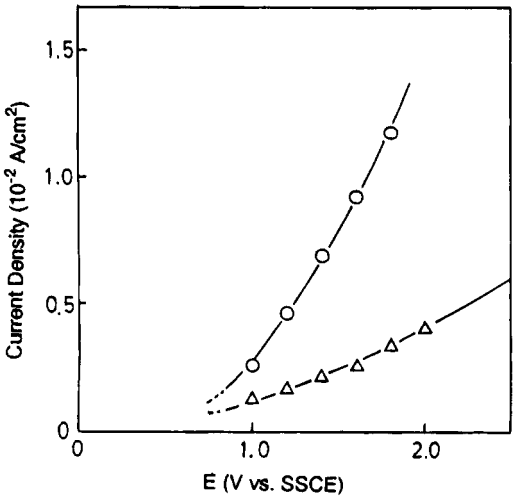


Figure 2. Current–potential curves: 0.37 M Et_3N·3HF/MeCN (△), 0.1 M $PhSCH_2COOEt$ in 0.37 M Et_3N·3HF/MeCN (○).

Scheme 3

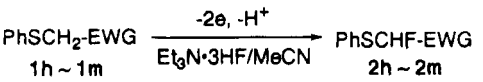
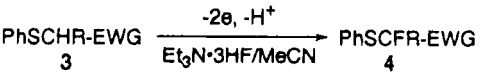


Table 4. Anodic Monofluorination of Sulfides Bearing Electron-Withdrawing Substituents

run	sulfide no.	EWG	anodic potential, V vs SSCE	charge passed, F/mol	product yield, %
1	**1h**	CN	1.7	5.0	75 (**2h**)
2	**1i**	COMe	1.6–1.8	7.6	80 (**2i**)
3	**1j**	COPh	1.5	5.0	55 (**2j**)
4	**1k**	CONHPr	1.7	2.8	88 (**2k**)
5	**1l**	$CONEt_2$	1.7	5.8	80 (**2l**)
6	**1m**	$PO(OEt)_2$	1.9	2.7	78 (**2m**)
7	**1n**	CH_2Ph	1.6	2.2	0[a]

[a] PhSSPh (91%) was formed.

Scheme 4



benzyl phenyl sulfide (**1n**) did not give any fluorinated products, and a large amount of diphenyl disulfide was formed beside of benzaldehyde and benzyl phenyl sulfoxide. Anodic benzylic substitution easily takes place, and benzylic fluorinated compounds are known to be generally very unstable. Presumably anodic fluorination of **1n** at the benzylic position is followed by hydrolysis providing disulfide and aldehyde.

Among the products obtained here, α-fluorophosphonate **2m** should be a promising building block because it has been shown that the corresponding α-chloro derivative is versatile starting material for the preparation of α-chlorovinyl sulfides.[21]

Anodic fluorination was further extended to sulfides bearing an additional functional group (Scheme 4, Table 5).

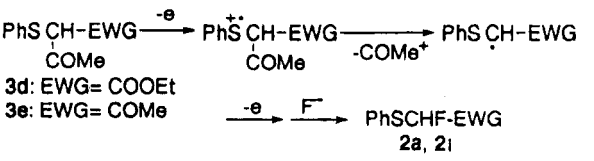
α-Chloro sulfide **3b** gave an extremely low yield of the desired fluorinated product in an undivided cell because **3b** was easily cathodically reducible. But, anodic fluorination of **3b** was successfully carried out in a divided cell to give a rather good yield (run 2). An electron-donating methyl group did not affect the fluorination (run 1). Fluorination of malonic ester **3c** provided the expected product **4c** (run 3). However, in the case of keto ester **3d**, elimination of an acetyl group was accompanied to provide **2a** in addition to the formation of the expected product **4d** (run 4). It is noted that diketone **3e** gave α-fluoro monoketone **2i** solely and the expected α-fluoro diketone was not formed at all (run 5). This can be explained as follows: Since an acetyl cation is readily generated, anodically generated radical cation intermediate of **3d** and **3e** splits into an acetyl cation and a radical as shown in Scheme 5.

Table 5. Anodic Monofluorination of Sulfides Bearing Two Functional Groups

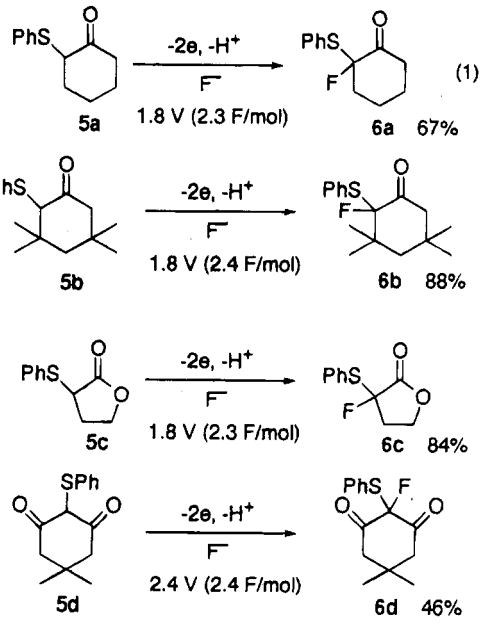
run	sulfide no.	R	EWG	anodic potential, V vs SSCE	charge passed, F/mol	product yield, %
1	**3a**	Me	COOEt	1.8	2.9	83 (**4a**)
2[a]	**3b**	Cl	COOEt	2.2	2.3	66 (**4b**)
3	**3c**	COOEt	COOEt	2.0	15.4	77 (**4c**)
4	**3d**	COMe	COOEt	1.6	3.3	16 (**4d**) 32 (**2a**)
5	**3e**	COMe	COMe	1.7	3.0	55 (**2i**)

[a] A divided cell was used.

Scheme 5



Scheme 6



The products **4a–d** have a multifunctional carbon structure, therefore, they seem to be highly useful in synthetic chemistry.[22]

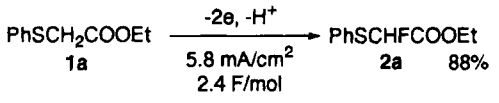
Fluorination was also successful using α-(phenylthio)-substituted cyclic ketones **5a–d** as shown in Scheme 6.

The yield of fluorinated product **6a** was not so satisfactory because elimination of HF of **6a** easily takes place.

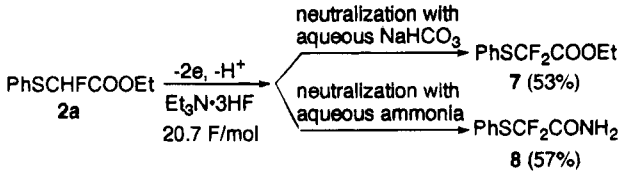
(21) Loutrot, P.; Laurenco, C.; Petrova, J.; Savignac, P. *Synthesis* **1976**, 107.

(22) Takeuchi, Y.; Itoh, N.; Koizumi, T.; Yamaguchi, K. *J. Am. Chem. Soc.* **1991**, *113*, 6318.

Scheme 7



Scheme 8



In contrast, **5b** gave much higher yield because **5b** has no β-hydrogen. Although **6c** has β-hydrogens, elimination of HF is not so fast compared with **6a**. So, much better yield was obtained from **5c**. Cyclic diketone **5d** was also fluorinated though the yield was less than 50%. It is noted that anodic fluorination of open-chain diketone **3e** caused ready elimination of an acetyl group while that of cyclic diketone did not cause such carbon–carbon bond cleavage.

As mentioned in the introduction section, Brigaud and Laurent also found a similar fluorination of sulfides.[17] In almost all cases, they used an undivided cell but they employed a divided cell for fluorination of α-benzoyl sulfide **1j** because the benzoyl group is usually easily reducible. On the contrary, we found that sulfides such as **1i,j, 3d,e,** and **5a,b,d** having reducible carbonyl groups underwent anodic fluorination selectively even in an undivided cell. Because the acidic proton of $Et_3N·3HF$ is discharged at a relatively early stage of the electrolysis, the carbonyl groups are not reduced.

Selective anodic monofluorination could also be achieved by constant-current electrolysis because the fluorinated products have much higher oxidation potentials than the starting materials as shown in Table 1. Thus, for example, monofluorinated product **2a** was obtained in excellent yield (88%) from ethyl α-(phenylthio)acetate (**1a**) as shown in Scheme 7. This finding that constant-current electrolysis with an undivided cell was effective for the fluorination, is important from a practical point of view.[23]

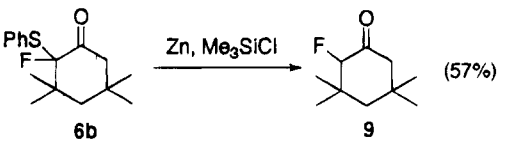
The procedure was also applied to the preparation of difluoro derivatives. For example, anodic oxidation of monofluoro ester **2a** at 2.2 V vs SSCE provided the difluoro ester **7** in good yield (Scheme 8). In this case, after electrolysis was complete, the electrolysis solution was neutralized with aqueous $NaHCO_3$. If, instead, the solution was neutralized with aqueous ammonia, α,α-difluoro-α-(phenylthio)acetamide (**8**), formed by ammonolysis of the initial product, was isolated. Similar reaction took place when the electrolytic solution of **1d** was treated with aqueous ammonia (see Table 3, run 3).

Although our anodic difluorination was successful, the current efficiency was unsatisfactory. In contrast, as mentioned already in the introduction, Brigaud and Laurent achieved anodic difluorination of α-(phenylthio)-acetophenone with good current efficiency (58%) in a similar electrolytic solution in a divided cell.[17]

Traditional methods for the preparation of α-fluoro sulfides require expensive, unstable, or troublesome reagents, such as xenon difluoride,[24] (diethylamino)sulfur trifluoride (DAST),[25] or potassium fluoride.[26,27]

N-Fluoropyridinium triflate is also a useful fluorinating reagent.[28] However, fluorination of **1a**, for example, with the latter reagent resulted in only low (38%) yield. In contrast, anodic fluorination does not require any special reagents, the procedure is very simple, and the desired products can be obtained directly in almost pure form.

Scheme 9



The fluorinated products are versatile building blocks,[29] and, furthermore, desulfurization can be easily achieved with various reducing reagents. For example, reductive desulfurization of **6b** with zinc metal in the presence of trimethylchlorosilane[30] readily provided the corresponding monofluoro cyclic ketone **9** in moderate yield (Scheme 9) although optimization of reaction conditions has not been done yet.

Thus, anodic fluorination should be highly promising for the preparation of a variety of fluoroorganic compounds. Further application of this method is now under investigation.

Experimental Section

^1H NMR and ^{19}F NMR spectra were recorded at 60 MHz on Varian EM 360 NMR and Hitachi R-1200F NMR spectrometers, respectively, using $CDCl_3$ as a solvent. The chemical shifts for ^1H and ^{19}F NMR are given in δ (ppm) downfield from internal Me_4Si and upfield from external 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 spectra were obtained with a Hitachi M-80B GC-mass spectrometer. Cyclic voltammeteric and preparative electrolysis experiments were carried out using a Hokutodenko HA-501 Potentiostat/Galvanostat equipped with a Hokutodenko HF-201 digital coulombmeter.

Anodic Fluorination of Sulfides. The electrolysis was performed at a platinum anode and cathode (3 × 4 cm) in dry MeCN (50 mL) containing $Et_3N·3HF$ [3 mL (0.37 M): 10 equiv to sulfide] or pyridine polyhydrogen fluoride [(70% HF content) 1.5 mL: 10 equiv to sulfide] containing 5 mmol of the substrate, sulfide. In order to avoid deposition of polymerized products on the anode, pulse electrolysis [mainly, applied potential (90 s)/0 V (10 s)] was performed. During the electrolysis, the temperature was maintained at ca. 20 °C. After the starting material was completely consumed (silica gel, TLC monitoring), the electrolytic solution was neutralized with 50 mL of 12% aqueous ammonia (**2a–f,h,j, 4a, 8**) or 130 mL of 6% aqueous sodium bicarbonate (**2g,i,k–m, 7, 4b–d, 6a–d**). The acetonitrile was then removed by evaporation below 40 °C. The residue was extracted with ether (40 mL and then 20 mL ×

(23) In fact, we have shown that selective anodic fluorination of **1a** was successfully carried out at a constant current by using a flow cell: Konno, A.; Fuchigami, T. *J. Appl. Electrochem.* **1995**, *25*, 173.

(24) (a) Zupan, M. *J. Fluorine Chem.* **1976**, *8*, 305. (b) Marat, R. K.; Janzen, A. F. *Can. J. Chem.* **1977**, *55*, 3031. (c) Janzen, A. F.; Wang, P. M. C.; Lemire, A. E. *J. Fluorine Chem.* **1983**, *22*, 557.

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(26) Potassium fluoride is very hygroscopic, and the reaction requires heating in MeCN solution in the presence of an expensive crown ether, for as long as 4–5 days.[27]

(27) More, K. M.; Wemple, J. *Synthesis* **1977**, 791.

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(30) Kurozumi, S.; Toru, T. *Synth. Commun.* **1977**, *7*, 427.

4). The extracts were washed with brine (200 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2 for **2c**; $CHCl_3$ for **6c,d**; $CHCl_3/CCl_4$,1:1–6:4 for **2a,g,h,k, 4d, 2i,j, 7, 8**; $CHCl_3/CCl_4$,7:3–9:1 for **2b,d–f,l, 4a,c, 6b, 9**; hexane/AcOEt, 3:7 for **2m**) to provide the desired fluorinated product.

Ethyl α-fluoro-α-(phenylthio)acetate (2a): ^{1}H NMR δ 1.18 (t, 3H, J = 7.0 Hz), 4.12 (q, 2H, J = 7.0 Hz), 6.00 (d, 1H, J = 52.0 Hz), 7.2–7.7 (m, 5H); ^{19}F NMR δ-77.3 (d, J = 52.0 Hz); IR 1770 (CO), 1440, 1370, 1320, 1270, 1250, 1180, 1040, 1020, 750, 690 cm^{-1}; MS m/e 214 (M^+), 141 (M^+ − COOEt), 109 (PhS^+). Anal. Calcd for $C_{10}H_{11}FO_2S$: C, 56.06; H, 5.17. Found: C, 55.91; H, 5.35.

Ethyl α-fluoro-α-(*p*-tolylthio)acetate (2b): ^{1}H NMR δ 1.18 (t, 3H, J = 7.0 Hz), 2.32 (s, 3H), 4.08 (q, 2H, J = 7.0 Hz), 5.93 (d, 1H, J = 52.0 Hz), 6.9–7.5 (m, 4H); ^{19}F NMR δ-77.4 (d, J = 52.0 Hz); IR 1780 (CO), 1595, 1380, 1330, 1280, 1260, 1180, 1050, 805 cm^{-1}; MS m/e 228 (M^+), 155 (M^+ − COOEt), 123 ($MeC_6H_4S^+$), 92 (PhS^+). Anal. Calcd for $C_{11}H_{13}FO_2S$: C, 57.86; H, 5.74. Found: C, 57.58; H, 6.04.

Ethyl α-fluoro-α-[(*p*-methoxyphenyl)thio]acetate (2c): ^{1}H NMR δ 1.18 (t, 3H, J = 7.0 Hz), 3.73 (s, 3H), 4.05 (q, 2H, J = 7.0 Hz), 5.86 (d, 1H, J = 52.0 Hz), 6.6–7.6 (m, 4H); ^{19}F NMR δ-78.3 (d, J = 51.0 Hz); IR 2990, 2850, 1780 (CO), 1595, 1570, 1495, 1465, 1445, 1375, 1290, 1250, 1175, 1110, 1095, 1030, 835, 805, 640, 530 cm^{-1}; MS m/e 244 (M^+), 171 (M^+ − COOEt), 139 ($MeOC_6H_4S^+$); calcd for $C_{11}H_{13}FO_3S$ m/e 244.0568, found 244.0519.

Ethyl α-[(*p*-chlorophenyl)thio]-α-fluoroacetate (2d): ^{1}H NMR δ 1.18 (t, 3H, J = 7.0 Hz), 4.10 (q, 2H, J = 7.0 Hz), 5.94 (d, 1H, J = 52.0 Hz), 7.0–7.7 (m, 4H); ^{19}F NMR δ −77.6 (d, J = 51.0 Hz); IR 3000, 1770 (CO), 1575, 1480, 1395, 1370, 1325, 1270, 1185, 1095, 1040, 1020, 1015, 830, 740, 500 cm^{-1}; MS m/e 250 (M^+ + 2), 248 (M^+), 175 (M^+ − COOEt), 143 ($ClC_6H_4S^+$); calcd for $C_{10}H_{10}ClFO_2S$ m/e 248.0072, found 248.0005.

Benzyl α-fluoro-α-(phenylthio)acetate (2e): ^{1}H NMR δ 5.03 (s, 2H), 6.02 (d, 1H, J = 53.0 Hz), 7.0–7.6 (m, 10H); ^{19}F NMR δ −76.9 (d, J = 51.0 Hz); IR 3060, 3030, 2950, 1770 (CO), 1580, 1490, 1475, 1470, 1450, 1440, 1375, 1320, 1265, 1210, 1170, 1035, 1020, 995, 965, 740, 685, 605, 490 cm^{-1}; MS m/e 276 (M^+), 141 (M^+ − COOEt), 109 (PhS^+); calcd for $C_{15}H_{13}FO_2S$ m/e 276.06188, found 276.0616.

Ethyl α-(benzylthio)-α-fluoroacetate (2f): ^{1}H NMR δ 1.26 (t, 3H, J = 7.0 Hz), 3.92 (m, 2H), 4.15 (q, 2H, J = 7.0 Hz), 5.73 (d, 1H, J = 51.0 Hz), 7.24 (s, 5H); ^{19} F NMR δ −82.5 (d, J = 51.0 Hz); IR 2990, 1760 (CO), 1490, 1455, 1370, 1325, 1270, 1180, 1040, 700 cm^{-1}; MS m/e 228 (M^+), 155 (M^+ − COOEt), 123 ($PhCH_2S^+$); calcd for $C_{11}H_{13}FO_2S$ m/e 228.0620, found 228.0650.

Ethyl α-fluoro-α-(heptylthio)acetate (2g): ^{1}H NMR δ 0.7–1.9 (m, 16H), 2.6–3.0 (m, 2H), 4.28 (q, 2H, J = 7.0 Hz), 5.87 (d, 1H, J = 52.0 Hz); ^{19}F NMR δ −81.5 (d, J = 52.0 Hz); IR 2970, 2940, 2870, 1770 (CO), 1470, 1375, 1330, 1270, 1185, 1040 cm^{-1}; MS m/e 236 (M^+), 163 (M^+ − COOEt), 131 ($C_7H_{15}S^+$); calcd for $C_{11}H_{21}FO_2S$ m/e 236.1245, found 236.1245.

α-Fluoro-α-(phenylthio)acetonitrile (2h): ^{1}H NMR δ 6.12 (d, 1H, J = 49.0 Hz), 7.2–7.7 (m, 5H); ^{19}F NMR δ −71.5 (d, J = 49.0 Hz); IR 3070, 2960, 2260 (CN), 1480, 1445, 1030, 1000, 945, 735, 690 cm^{-1}; MS m/e 167 (M^+), 109 (PhS^+). Anal. Calcd for C_8H_6FNS: C, 57.47; H, 3.62; N, 8.38. Found: C, 57.56; H, 3.77; N, 8.09.

α-Fluoro-α-(phenylthio)acetone (2i): ^{1}H NMR δ 2.11 (d, 3H), 5.69 (d, 1H, J = 52.0 Hz), 7.1–7.7 (m, 5H); ^{19}F NMR δ −78.3 (dq, J = 52.0, 2.0 Hz); IR 3070, 2950, 1755 (CO), 1590, 1480, 1450, 1360, 1230, 1170, 1040, 1030, 1010, 960, 760, 730, 690 cm^{-1}; MS m/e 184 (M^+), 141 (M^+ − Ac), 109 (PhS^+), 77 (Ph^+), 43 (Ac^+); calcd for C_9H_9FOS m/e 184.0395, found 184.0350.

α-Fluoro-α-(phenylthio)acetophenone (2j): ^{1}H NMR δ 6.69 (d, 1H, J = 53.0 Hz), 7.1–8.1 (m, 10H); ^{19}F NMR δ −78.4 (d, J = 53.0 Hz); IR 3070, 1700 (C)), 1600, 1585, 1480, 1450, 1440, 1345, 1310, 1280, 1255, 1185, 1050, 1025, 1000, 960, 845, 820, 810, 740, 685, 670, 625, 505, 470 cm^{-1}; MS m/e 246 (M^+), 141 (M^+ − PhCO), 109 (PhS^+), 105 ($PhCO^+$), 77 (Ph^+); calcd for $C_{14}H_{11}FOS$ m/e 246.0513, found 246.0449.

α-Fluoro-α-(phenylthio)-*N*-propylacetamide (2k): ^{1}H NMR δ 0.6–1.7 (m, 5H), 3.06 (q, 2H, J = 6 Hz), 6.01 (d, 1H, J = 54.0 Hz), 6.08 (br s, 1H), 7.1–7.7 (m, 5H); ^{19}F NMR δ −74.7 (d, J = 52.0 Hz); IR 3300, 2980, 2950, 2880, 1660 (CO), 1530, 1480, 1470, 1465, 1455, 1440, 1385, 1305, 1275, 1205, 1155, 1080, 1065, 1025, 1000, 990, 940, 820, 805, 745, 690 cm^{-1}; MS m/e 227 (M^+), 141 ($PhSCHF^+$), 110 ($PhSH^+$), 109 (PhS^+), 86 ($C_3H_7NHCO^+$), 43 (C_3H_7). Anal. Calcd for $C_{11}H_{14}FNOS$: C, 58.13; H, 6.21. Found: C, 57.90; H, 6.48.

α-Fluoro-α-(phenylthio)-*N,N*-diethylacetamide (2l): ^{1}H NMR δ 1.1 (t, 3H), 1.23 (t, 3H), 3.37 (q, 2H), 3.40 (q, 2H), 6.19 (d, 1H, J = 55.0 Hz), 7.1–7.7 (m, 5H); ^{19}F NMR δ −72.0 (d, J = 55.0 Hz); IR 2980, 2940, 1640 (CO), 1580, 1480, 1460, 1440, 1380, 1360, 1280, 1210, 1130, 1100, 1080, 1065, 1020, 995, 940, 915, 900, 800, 740, 715, 685 cm^{-1}; MS m/e 241 (M^+), 141 (M^+ − Et_2NCO), 100 (Et_2NCO^+), 72 (Et_2N^+); calcd for $C_{12}H_{16}FNOS$ m/e 241.0967, found 241.0951.

Diethyl [fluoro(phenylthio)methyl]phosphonate (2m): ^{1}H NMR δ 1.37 (t, 6H, J = 7.0 Hz), 4.19 (q, 2H, J = 7 Hz), 4.32 (q, 2H, J = 7.0 Hz), 5.92 (dd, 1H, $J_{H,F}$ = 52.7 Hz, $J_{H,P}$ = 6.5 Hz), 7.1–7.7 (m, 5H); ^{19}F NMR δ −90.71 (dd, $J_{P,F}$ = 85.6 Hz, $J_{H,F}$ = 52.7 Hz); IR 3000, 2960, 2930, 1590, 1490, 1450, 1400, 1380, 1290, 1270, 1170, 1100, 1060, 1030, 980, 840, 800, 750, 710, 690, 560 cm^{-1}; MS m/e 278 (M^+), 214 (M^+ − F − EtO), 141 ($PhSCHF^+$), 109 (PhS^+), 77 (Ph^+). Anal. Calcd for $C_{11}H_{16}FO_3PS$: C, 47.46; H, 5.80; S, 11.53. Found: C, 47.16; H, 5.78; S, 11.45.

Ethyl α-Fluoro-α-(phenylthio)propionate (4a): ^{1}H NMR δ 1.07 (t, 3H, J = 7.0 Hz), 1.89 (d, 3H, J = 18 Hz), 3.98 (q, 2H, J = 7.0 Hz), 7.1–7.6 (m, 5H); ^{19}F NMR δ −45.8 (q, J = 18 Hz); IR 3000, 1770, 1750, 1470, 1440, 1375, 1280, 1125, 1085, 1070, 1020, 930, 870, 850, 750, 690 cm^{-1}; MS m/e 228 (M^+), 155 (M^+ − COOEt), 109 (PhS^+), 77 (Ph^+); calcd for $C_{11}H_{13}FO_2S$ m/e 228.0619, found 228.0593.

Ethyl α-chloro-α-fluoro-α-(phenylthio)acetate (4b): ^{1}H NMR δ 1.23 (t, 3H, J = 7.0 Hz), 4.18 (q, 2H, J = 7.0 Hz), 7.1–7.8 (m, 5H); ^{19}F NMR δ −5.4 (s); IR 3000, 1780 (CO), 1475, 1445, 1395, 1370, 1300, 1260, 1090, 1080, 1065, 1025, 980, 870, 750, 705, 690 cm-1; MS m/e 250 (M^+ + 2), 248 (M^+), 175 (M^+ − COOEt), 109 (PhS^+), 77 (Ph^+); calcd for $C_{10}H_{10}ClFO_2S$ m/e 248.0073, found 248.0048.

Ethyl α-fluoro-α-(phenylthio)malonate (4c): ^{1}H NMR δ 1.22 (t, 6H, J = 7.0 Hz), 4.19 (q, 4H, J = 7.0 Hz), 7.2–7.8 (m, 5H); ^{19}F NMR δ −51.7 (s); IR 3000, 1780 (CO), 1480, 1450, 1400, 1370, 1270, 1235, 1095, 1045, 1020, 960, 855, 750, 690 cm^{-1}; MS m/e 286 (M^+), 213 (M^+ − COOEt), 167 (M^+ − COOEt − EtOH), 109 (PhS^+). Anal. Calcd for $C_{13}H_{15}FO_4S$: C, 54.54; H, 5.28. Found: C, 54.25; H, 5.49.

Ethyl α-fluoro-α-(phenylthio)acetoacetate (4d): ^{1}H NMR δ 1.20 (t, 3H, J = 7.0 Hz); 2.19 (d, 3H); 4.15 (q, 2H, J = 7.0 Hz); 7.1–7.7 (m, 5H); ^{19}F NMR δ −54.5 (s); IR 2990, 1770 (CO), 1750 (CO), 1470, 1440, 1365, 1355, 1250, 1190, 1095, 1065, 1040, 1020, 1010, 740, 700, 690 cm^{-1}; MS m/e 256 (M^+), 214 (M^+ − $COCH_2$), 167 (M^+ − Ac − EtOH), 141 ($PhSCHF^+$), 109 (PhS^+). Anal. Calcd for $C_{12}H_{13}FO_3S$: C, 56.24; H, 5.11. Found: C, 56.50; H, 5.02.

2-Fluoro-2-(phenylthio)cyclohexanone (6a): ^{1}H NMR δ 1.3–3.3 (m, 8H), 7.1–7.7 (m, 5H); IR 3080, 2960, 2880, 1760 (CO), 1590, 1580, 1480, 1470, 1455, 1450, 1430, 1340, 1320, 1280, 1240, 1150, 1130, 1110, 1095, 1085, 1055, 1030, 960, 920, 895, 850, 770, 710, 695, 615, 515, 500 cm^{-1}; MS m/e 224 (M^+), 110 ($PhSH^+$); calcd for $C_{12}H_{13}FOS$ m/e 224.0671, found 224.0645.

2-Fluoro-3,3,5,5-tetramethyl-2-(phenylthio)cyclohexanone (6b): ^{1}H NMR δ 1.0–1.4 (m, 12H), 1.4–2.5 (m, 4H), 7.1–7.7 (m, 5H); ^{19}F NMR δ −70.30 (s); IR 2970, 2940, 1740 (CO), 1485, 1480, 1445, 1370, 1290, 1250, 1230, 1110, 1045, 1030, 920, 880, 750, 690 cm^{-1}; MS m/e 280 (M^+), 110 ($PhSH^+$), 109 (PhS^+). Anal. Calcd for $C_{16}H_{21}FOS$: C, 68.54; H, 7.55. Found: C, 68.84; H, 7.42.

α-Fluoro-α-(phenylthio)-γ-butyrolactone (6c): ^{1}H NMR δ 2.3–3.0 (m, 2H), 4.1–4.6 (m, 2H), 7.0–7.8 (m, 5H); IR 3080, 1795 (CO), 1450, 1390, 1310, 1230, 1190, 1140, 1105, 1050, 1030, 1020, 960, 880, 760, 745, 710, 695, 600, 500 cm^{-1}; MS

m/e 212 (M^+), 109 (PhS^+). Anal. Calcd for $C_{10}H_9FO_2S$: C, 56.59; H, 4.27. Found: C, 56.88; H, 4.07.

2-Fluoro-5,5-dimethyl-2-(phenylthio)-1,3-cyclohexanedione (6d): ^1H NMR δ 0.8–1.4 (m, 6H), 7.2–7.7 (m, 4H), 7.7–8.0 (m, 1H); ^{19}F NMR δ −72.5 (s); IR 2970, 1760, 1730, 1700, 1475, 1440, 1320, 1230, 1065, 970, 750, 680 cm^{-1}; MS *m/e* 266 (M^+), 110 ($PhSH^+$), 109 (PhS^+). Anal. Calcd for $C_{14}H_{15}FO_2S$: C, 63.13; H, 5.68. Found: C, 63.46; H, 5.69.

Ethyl α,α-difluoro-α-(phenylthio)acetate (7): ^1H NMR δ 1.25 (t, 3H, J = 7.0 Hz), 4.22 (q, 2H, J = 7.0 Hz), 7.0–7.8 (m, 5H); ^{19}F NMR δ −3.3 (s); IR 3010, 1785 (CO), 1480, 1450, 1380, 1300, 1135, 1120, 1075, 1025, 980, 760, 695 cm^{-1}; MS *m/e* 232 (M^+), 159 (M^+ − COOEt), 109 (PhS^+), 77 (Ph^+). Anal. Calcd for $C_{10}H_{10}F_2O_2S$: C, 51.72; H, 4.34. Found: C, 51.75; H, 4.51.

α,α-Difluoro-α-(phenylthio)acetamide (8): ^1H NMR δ 6.35 (br s, 2H), 7.2–7.8 (m, 5H); IR (KBr) 3420, 3200, 1665 (CO), 1480, 1445, 1430, 1120, 1095, 1060, 985, 800, 750, 690, 620 cm^{-1}; MS *m/e* 203 (M^+), 159 (M^+ − $CONH_2$), 110 ($PhSH^+$), 109 (PhS^+), 77 (Ph^+), 44 ($CONH_2$). Anal. Calcd for $C_8H_7F_2NOS$: C, 47.28; H, 3.47; N, 6.89. Found: C, 47.58; H, 3.74; N, 6.91.

2-Fluoro-3,3,5,5-tetramethylcyclohexanone (9).[31] To a stirred suspension of 0.2 g (0.003 g-atom) of zinc powder (activated by aqueous HCl)[30] in ether (2 mL) was added dropwise a solution of **6b** (0.5 mmol) in ether (1 mL) and then was added dropwise Me_3SiCl (5 mmol). After 24 h of stirring at room temperature, the solution was mixed with aqueous saturated $NaHCO_3$ (50 mL) and extracted with ether (10 mL × 3). The extracts were washed (aqueous saturated $NaHCO_3$/50 mL) and dried ($MgSO_4$) and then evaporated. The residue was chromatographed on silica gel ($CHCl_3/CCl_4$, 7:3) to provide pure **9** in 57% yield: ^1H NMR δ 1.0–1.2 (m, 12H), 1.6–1.8 (m, 2H), 2.3–2.32 (m, 2H), 4.62 (d, 1H, J = 50.1 Hz); IR 2970, 1750 (CO), 1480, 1460, 1395, 1375, 1090, 1060, 660 cm^{-1}; MS *m/e* 172 (M^+), 157 (M^+ − Me). Anal. Calcd for $C_{10}H_{16}FO$: C, 69.73; H, 9.95. Found: C, 69.98; H, 9.70.

(31) Barnett, W. E. *J. Am. Chem. Soc.* **1984**, *106*, 452.

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Supplementary Material Available: ^1H NMR spectra of **2c–g,i,j,l, 4a,b,** and **6a** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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