Electrolytic Partial Fluorination of Organic Compounds. 31.[1] Regioselective Anodic Fluorination of 2-Quinolyl and 4-(7-Trifluoromethyl)quinolyl Sulfides and the Factors Affecting Its Optimization

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Electrochemical fluorination of 2-quinolyl and 4-(7-trifluoromethyl)quinolyl sulfides bearing an electron-withdrawing group at the position α to the sulfur atom was studied. Fluorination was successfully carried out using $Et_4NF{\cdot}nHF$ ($n = 3, 4$) and $Et_3N{\cdot}3HF$ as a supporting electrolyte and a fluoride ion source in dimethoxyethane in a divided cell to provide the corresponding α-fluorinated sulfides in good yields. A trifluoromethyl group positioned on the quinoline ring significantly enhanced anodic α-fluorination. 4-(Methylthio)-7-(trifluoromethyl)quinoline was also found to undergo anodic fluorination efficiently. Solvent effects of various donor numbers were also established.

Introduction

Recently, the discovery of many potent clinically important antitumor drugs having a quinoline moiety has been reported.[3] Also, a large number of quinoline derivatives are involved in the manufacture of a wide variety of medicinals and pharmaceuticals, including antibiotic,[4] antimalarial,[5] antibacterial,[6] antimicrobial,[7] and analgesic[8] drugs. The quinoline derivatives also have been shown to have important cytotoxic,[9] genotoxic,[10] and mutagenic[11] activities. Elsewhere, fluorinated organic compounds have received much interest due to the increased recognition of their biological importance.[12] Therefore, from a structure−activity relationship (SAR) viewpoint, the introduction of fluorine atom(s) into the quinoline ring (or its side chain) may provide medicinals and pharmaceuticals with increased or new functionality. However, conventional chemical fluorination processes are not easy to perform and often require hazardous reagents.[13] On the other hand, it was reported that anodic fluorination was a convenient method to accomplish this objective.[14]

In continuation of our current efforts directed toward exploring the regioselective anodic fluorination of organic compounds,[14b,15] we successfully carried out regioselective anodic α-fluorination of 2-pyridyl and 2-benzothiazolyl sulfides having an electron-withdrawing group (EWG) at the position α to the sulfur atom in an undivided cell.[16,17] However, we failed to fluorinate related sulfides devoid of an EWG. α-Fluoro sulfides serve as useful synthetic intermediates to medicinally active compounds.[18] With

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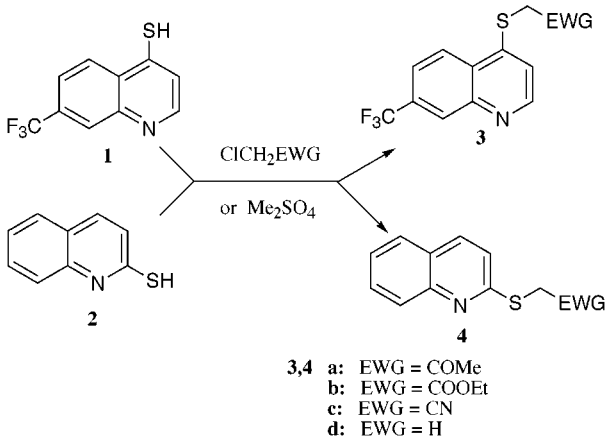
Scheme 1



these facts in mind, we have attempted the anodic fluorination of various 2- and 4-quinolyl sulfides using various supporting flouride salts and solvents in this work.

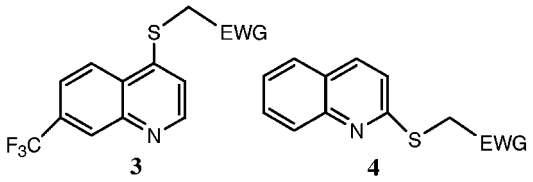
Results and Discussion

Synthesis of the Quinolyl Sulfides 3a−d and 4a−d. Reaction of the appropriate mercaptoquinoline **1** or **2** with α-chloroacetone, ethyl α-chloroacetate, and α-chloroacetonitrile in refluxing THF, in the presence of K_2CO_3, provided 4- and 2-quinolyl sulfides **3a−c** and **4a−c**, respectively, in high yields (Scheme 1). Compounds **1** and **2** were treated with Me_2SO_4 in aqueous NaOH solution at room temperature to provide the corresponding methylthio derivatives **3d** and **4d**, respectively, in excellent yields.

Oxidation Potentials of Quinolyl Sulfides. The oxidation potentials of quinolyl sulfides **3a−d** and **4a−d** were measured using cyclic voltammetry. The anhydrous acetonitrile solution containing $Bu_4N{\cdot}BF_4$ (0.1 M), platinum electrodes, and a SSCE reference electrode were used in this study. All sulfides showed irreversible oxidation peaks in the cyclic voltamograms. Generally, the 4-(7-trifluoromethyl)quinolyl sulfides **3a−d** have 0.2−0.3 V higher oxidation potentials than the corresponding 2-quinolyl sulfides **4a−d** due to the strongly electron-withdrawing CF_3 group. The presence of the electron-withdrawing groups at the position α to the sulfur atom caused the oxidation potentials to increase in the ascending order H < COMe < COOEt < CN as shown in Table 1.

Anodic Fluorination of 4- and 2-Quinolyl Sulfides, 3a−d and 4a−d. The anodic oxidation of 4-(7-trifluoromethyl)quinolyl acetonyl sulfide (**3a**) was examined in detail as it serves as a model for the related quinolyl sulfides. Anodic oxidation of **3a** was studied in the presence of a variety of fluorine sources under various electrolytic conditions. The results are summarized in Table 2. From these results, it is clear that anodic fluorination of **3a** took place regioselectively at the position α to the sulfur atom. The yield was extremely high especially when an $Et_4NF{\cdot}3HF$ supporting electrolyte in a DME electrolytic solvent was used under constant current electrolysis in a divided H-type cell fitted with an anion-exchange membrane. Regardless of supporting electrolytes, the α-monofluorinated product **5a** was obtained in a high yield and a small amount of α,α-difluorinated byproduct **6a** was generated with a

Table 1. Oxidation Potentials of Quinolyl Sulfides 3a−d and 4a−d



sulfide no.	EWG	E_p^{ox} (V vs SSCE)[a]
3a	COMe	1.92
3b	COOEt	2.04
3c	CN	2.14
3d	H	1.82
4a	COMe	1.70
4b	COOEt	1.76
4c	CN	1.91
4d	H	1.65

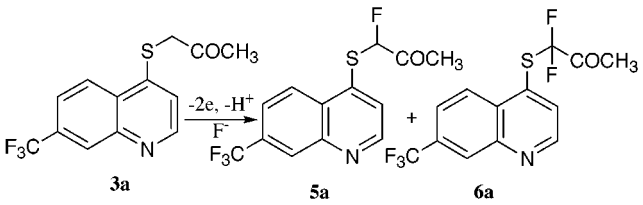
[a] In 0.1 M Bu_4BF_4/MeCN. Anode: Pt plate. Sweep rate: 100 mV s^{-1}.

Table 2. Anodic Fluorination of 4-(7-Trifluoromethyl)quinolyl Acetonyl Sulfide (3a)[a]

run	supporting electrolyte	solvent	charge passed (F/mol)	yield (%)[b] **5a**	**6a**
1	$Et_4NF{\cdot}4HF$	DME	4	80 (52)[c]	6
2	$Et_4NF{\cdot}3HF$	DME	4	96 (78)[c]	7
3[d]	$Et_4NF{\cdot}3HF$	DME	4	14	*e*
4	$Et_4NF{\cdot}3HF$	MeCN	2.7	28	3
5	$Et_4NF{\cdot}3HF$	CH_2Cl_2	3.5	23	9
6	$Et_3N{\cdot}3HF$	DME	4	84	6

[a] Constant current electrolysis (5 mA cm^{-2}). Anode and cathode were Pt plate (3 × 2 cm^2). A divided H-type cell with an anion-exchange membrane was used. [b] Calculated on the basis of ^{19}F NMR. [c] Isolated yield. [d] Using an undivided cell. [e] A considerable amount of bis[4-(7-trifluoromethyl)quinolyl] disulfide [MS: *m/e* 456 (M^+), 228 ($M^+/2$)] was detected.

Scheme 2



ratio of 15:1 (Scheme 2). Ring fluorination did not occur at all. The formation of **6a** was confirmed by mass spectroscopy, *m/e* 321 (M^+), 278 ($M^+ - COCH_3$), 228 ($M^+ - CF_2COCH_3$), and 196 ($M^+ - SCF_2COCH_3$), and ^{19}F NMR spectra, δ +13.64 (s, 3F) and −4.71 (s, 2F) ppm. On the other hand, the yield and selectivity of α-fluorinated product **5a** decreased sharply as shown in Table 2 (runs 3−5) when the electrolytic solvent and/or the cell type were changed.

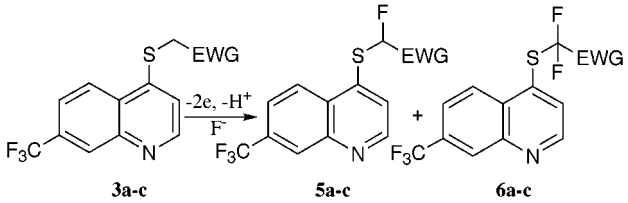
Previously, we demonstrated that acetonitrile was suitable for anodic fluorination of 2-pyridyl sulfides;[16] however, it was not effective for anodic fluorination of 4-quinolyl sulfide **3a**. The use of an undivided cell resulted in the formation of large amounts of bis[4-(7-trifluoromethyl)quinolyl] disulfide due to the **3a** C−S bond cleavage. This indicates that the reductive cleavage of the **3a** C−S bond took place at the cathode during electrolysis. This is sharp contrast to the previously reported successful anodic fluorination of 2-pyridyl acetonyl sulfide in an undivided cell.[16]

Table 3. Anodic Fluorination of 4-(7-Trifluoromethyl)quinolyl Sulfides Using DME as a Solvent

sulfide		supporting	charge passed	yield (%)[a]	
no.	EWG	electrolyte	(F/mol)	**5**	**6**
3a	COMe	$Et_4NF·3HF$	4	96 (78)[b]	7
3b	COOEt	$Et_4NF·4HF$	2.5	62	
3b	COOEt	$Et_4NF·3HF$	4.5	83	
3b	COOEt	$Et_3N·3HF$	6	67	
3c	CN	$Et_4NF·4HF$	4	86 (74)[b]	
3c	CN	$Et_4NF·3HF$	4	87 (81)[b]	
3c	CN	$Et_3N·3HF$	6	77	

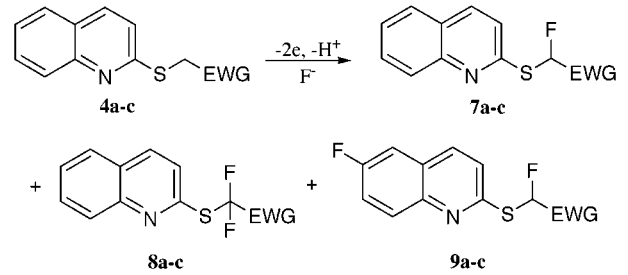
[a] Calculated on the basis of ^{19}F NMR. [b] Isolated yield.

Scheme 3



3a-c **5a-c** **6a-c**

Scheme 4



4a-c **7a-c** **8a-c** **9a-c**

Next, the anodic fluorination of the other 4-(7-trifluoromethyl)quinolyl sulfides **3b**,**c** was carried out using DME in a divided cell. As shown in Table 3, fluorination took place selectively at the position α to the sulfur atom. No α,α- difluorination was detected regardless of the fluoride sources used in this work. As compared with **3a**, compounds **3b**,**c** have higher oxidation potentials; therefore, their corresponding α-fluorinated products **5b**,**c** should be more difficult to oxidize than **5a**. This seems to be one of the main reasons why **5b**,**c** were not susceptible to further oxidation leading to the α,α-difluorosulfides **6b**,**c**.

These results suggested further exploration of anodic fluorination of 2-quinolyl sulfides **4a**−**c** which are devoid of CF_3 groups on the quinoline ring. Anodic fluorination of sulfide **4a** was performed using various fluoride salts and solvents. Regardless of the electrolytic solutions, α-monofluorinated product **7a** was formed preferentially with byproducts including the ring fluorinated and α,α-difluorinated products **8a** and **9a** (Scheme 4).[19] However, pulse-controlled potential electrolysis in $Et_3N·3HF$/DME provided **7a** in a better yield and eliminated the byproducts. In contrast, $Et_3N·3HF$/MeCN gave much lower **7a** yield even when pulse electrolysis was used.

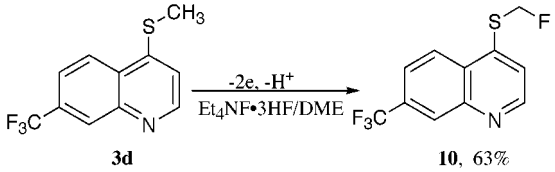
(19) Due to the extremely low yield of **8a** and **9a**,**b**, their structures were confirmed by MS and ^{19}F NMR spectra. **8a**: *m/e* 253 (M^+); ^{19}F NMR δ −9.45 (s). **9a**: *m/e* 253 (M^+); ^{19}F NMR δ −45.47 (dd, 1F, J = 10.12, 9.19 Hz), −89.09 (dq, 1F, J = 49.63, 3.68 Hz). **9b**: *m/e* 283 (M^+), 238 (M^+ − OEt), 210 (M^+ − COOEt), 191 (M^+ − FCOOEt), 178 (M^+ − CHFCOOEt), 146 (M^+ − SCHFCOOEt); ^{19}F NMR δ −45.64 (dd, 1F, J = 10.11, 9.19 Hz), −88.45 (d, 1F, J = 50.56 Hz) ppm. The 6-position at the quinoline ring of **9a**,**b** seems to be fluorinated in addition to α to the sulfur atom similarly to the case of **9c**.

Table 4. Anodic Fluorination of 2-Quinolyl Sulfides 4a−c[a]

	sulfide		supporting	charge passed	yield (%)[d]		
run	no.	EWG	electrolyte	(F/mol)	**7**	**8**	**9**
1	**4a**	COMe	$Et_4NF·4HF$	4	54	8	5
2	**4a**	COMe	$Et_4NF·3HF$	6	50	8	5
3	**4a**	COMe	$Et_3N·3HF$	7	55	8	5
4[b]	**4a**	COMe	$Et_3N·3HF$	6	64		
5[c]	**4a**	COMe	$Et_3N·3HF$	4	28		
6	**4b**	COOEt	$Et_4NF·4HF$	4	62		5
7	**4b**	COOEt	$Et_4NF·3HF$	4	54		5
8	**4b**	COOEt	$Et_3N·3HF$	6	69		7
9	**4c**	CN	$Et_4NF·4HF$	8	61		12
10	**4c**	CN	$Et_4NF·3HF$	8	52		12
11	**4c**	CN	$Et_3N·3HF$	8	62		12

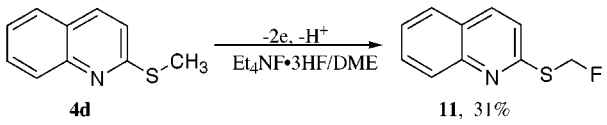
[a] Constant current electrolysis using DME as an electrolytic solvent. [b] Pulse electrolysis [1.7 V (50 s)/0.0 V (10 s)] was applied using DME as a solvent. [c] Pulse electrolysis [1.7 V (50 s)/0.0 V (10 s)] was applied using MeCN as a solvent. [d] Calculated on the basis of ^{19}F NMR.

Scheme 5



3d **10**, 63%

Scheme 6



4d **11**, 31%

Anodic fluorination of other 2-quinolyl sulfides **4b**,**c** was attempted in DME. Spectral data indicated that $Et_3N·3HF$ and $Et_4NF·4HF$ were more effective than $Et_4NF·3HF$ for selective fluorination giving only two fluorinated products. These two products were identified as α-fluorinated and α,6-difluorinated sulfides **7b**,**c** and **9b**,**c**, respectively (Scheme 4).[19] The $^1H-^1H$ COSY NMR spectrum of **9c** indicated that the ring fluorination took place at the 6-position of the quinoline moiety. α,α-Difluorination was not detected at all during fluorination of sulfides **4b**,**c** (Table 4).

Moreover, anodic fluorination of 4-(methylthio)-7-(trifluoromethyl)quinoline (**3d**) devoid of EWG using $Et_4NF·3HF$/DME under constant current electrolysis resulted in the formation of the isolable 4-((fluoromethyl)thio)-7-(trifluoromethyl)quinoline (**10**) (Scheme 5) selectively in a good yield along with a small amount (8%) of its ring-fluorinated analogue. The position of the additional fluorine atom in the latter product could not be determined exactly, although ^{19}F NMR signals at δ +13.89 (s, 3F), −40.19 (d, 1F, J = 6.44 Hz), and 108.50 (t, 1F, J = 51.47 Hz) ppm were found and the mass spectrum fragment of *m/e* 279 (M^+) and 260 (M^+ − F) were identified.

Similar anodic oxidation of 2-(methylmercapto)quinoline (**4d**) with $Et_3N·3HF$/DME under pulse electrolysis resulted in a reasonable α-fluorinated yield (product **11** in Scheme 6). Thus, **3d** provided a much higher α-fluorinated yield compared with **4d**. This is probably due to the strong electron-withdrawing effect of the quinoline ring CF_3 group. Recently, it has been reported that anodic α-fluorination of alkyl phenyl sulfides could be markedly

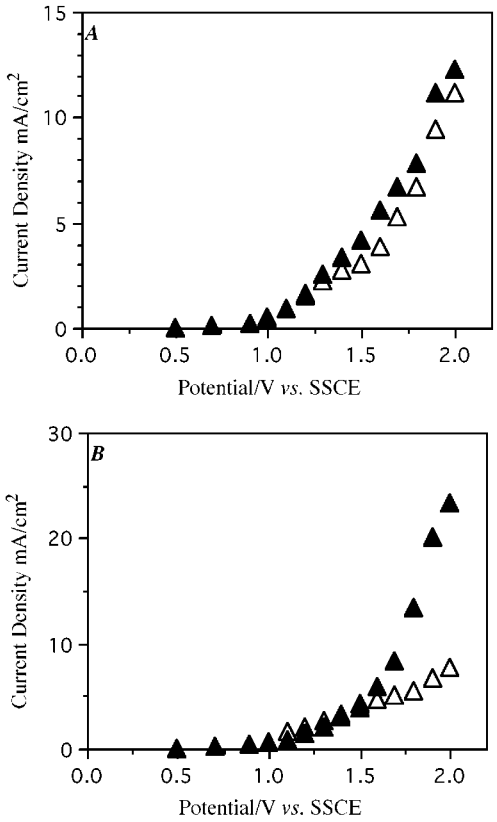


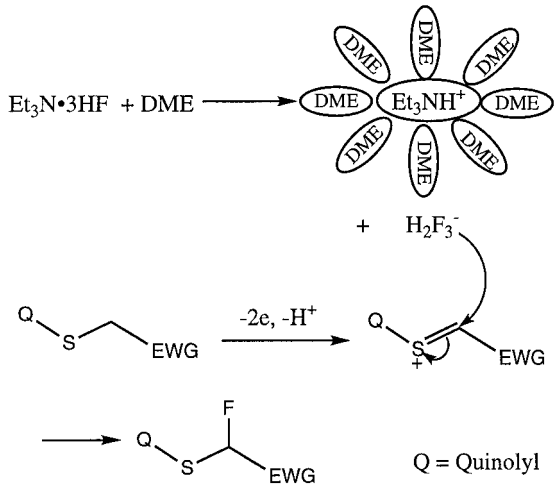
Figure 1. Current−potential curves of the electrolytic solutions 0.5 M $Et_3N{\cdot}3HF$/DME (20 mL) (*A*) and 0.5 $Et_3N{\cdot}3HF$/MeCN (20 mL) (*B*) in the presence (▲) and the absence (△) of substrate **4a** (1.0 mmol).

improved by a strongly electron-withdrawing group at the benzene ring.[20] Previously, we successfully carried out anodic α-fluorination of methyl phenyl sulfide in DME.[21] However, we failed to fluorinate methyl 2-pyridyl sulfide.[16] Therefore, these successful anodic fluorinations of **3d** and **4d** in DME are significant.

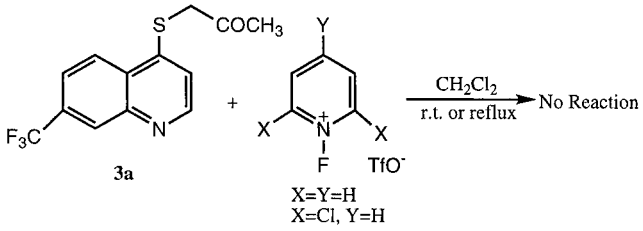
DME was found to be the most suitable electrolytic solvent. From the I−E curves shown in Figure 1, it is clear that the addition of **4a**, for example, to the $Et_3N{\cdot}$3HF/DME solution resulted in a much smaller cathodic shift as compared with the case of $Et_3N{\cdot}3HF$/MeCN. This suggested that acetonitrile should be a more suitable electrolytic solvent than DME. However, the experimental results were the inverse. The superiority of DME may be explained in terms of its ability to solvate the cationic part of the fluoride salt in which a naked fluoride anion is left for easy attack on the anodically generated cationic intermediate. In support of this, DME has much higher donor number (23.9) than acetonitrile (14). A possible mechanism is outlined in Scheme 7.[22]

N-Fluoropyridinium salts are known to be powerful fluorinating reagents.[23] However, fluorination of **3a**, as a model compound, with *N*-fluoropyridinium salts in dichloromethane even under reflux resulted in no formation of the expected fluorinated products (Scheme 8).

Scheme 7



Scheme 8



Therefore, the electrochemical fluorination offers a safe alternative to conventional chemical methods which can be carried out under mild conditions.

In conclusion, we have successfully carried out selective fluorination of 2- and 4-quinolyl sulfides in DME containing $Et_3N{\cdot}3HF$ and $Et_4NF{\cdot}nHF$ ($n = 3, 4$) using a divided cell. Such electrolytic systems are widely applicable to selective fluorination of various heterocyclic sulfides.

Experimental Section

Caution! $Et_3N{\cdot}3HF$ was purchased from Aldrich, and $Et_4NF{\cdot}nHF$ ($n = 3, 4$)[24] was obtained from Morita Chemical Industries Co. Ltd. *They are toxic and skin contact can result in a serious burn, so proper safety precautions should be taken at all times. It is recommended to practice good laboratory safety procedures including, using rubber gloves for hand protection.*[25]

^1H NMR, ^{19}F NMR, and ^{13}C NMR spectra were recorded at 270, 254, and 68 MHz, respectively, in $CDCl_3$ as a solvent. The chemical shifts for ^1H and ^{13}C NMR are given in δ ppm downfield from internal TMS, and those for ^{19}F NMR are given in δ ppm downfield from internal C_6F_6 [$\delta(CFCl_3)$ of the C_6F_6 reference is −162.2 ppm].

Synthesis of Quinolyl Sulfides. General Procedure. An α-chloro compound (20 mmol) was added to a stirred solution of mercaptoquinoline **1** or **2** (20 mmol) in tetrahydrofuran (40 mL), in the presence of potassium carbonate (3.4 g, 25 mmol). The mixture was refluxed for 30 min and then left to cool to the room temperature. The inorganic salts were filtered off, and the filtrate was evaporated under vacuum. The solid product was recrystallized from methanol or ethanol to give the corresponding quinolyl sulfides **3a−c** and **4a-c,** respectively.

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(22) We have already proposed that the fluorination of sulfides proceeds *via* a fluorosulfonium ion as a key intermediate.[21]
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Compounds **3d** and **4d** were prepared according to the known synthetic procedure of **4d**.[26a]

1-[4-(7-(Trifluoromethyl)quinolyl)thio]-2-propanone (3a): 92% yield, mp 126−127 °C; ^{1}H NMR δ 2.37 (s, 3H), 3.96 (s, 2H), 7.24 (d, 1H, J = 4.62 Hz), 7.74 (dd, 1H, J = 8.91, 1.98 Hz), 8.26 (d, 1H, J = 8.91 Hz), 8.38 (s, 1H), 8.79 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.73 (s); MS *m/e* 285 (M^+), 242 ($M^+ - COCH_3$). Anal. Calcd for $C_{13}H_{10}F_3NOS$: C, 54.73; H, 3.53; N, 4.91. Found: C, 54.68; H, 3.26; N, 4.62.

Ethyl α-[4-(7-(trifluoromethyl)quinolyl)thio]acetate (3b): 83% yield, mp 48−49 °C; ^{1}H NMR δ 1.28 (t, 3H, J = 7.26 Hz), 3.90 (s, 2H), 4.24 (q, 2H, J = 7.26 Hz), 7.37 (d, 1H, J = 4.62 Hz), 7.74 (dd, 1H, J = 8.91, 1.32 Hz), 8.25 (d, 1H, J = 8.91 Hz), 8.37 (s, 1H), 8.81 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.71 (s); ^{13}C NMR (DEPT) δ 13.98 (CH_3), 33.75, 62.26 (CH_2), 118.13, 122.17, 124.80, 127.85, 150.58 (CH), 121.71, 125.70, 131.39, 131.87, 146.61, 168.14 (C); MS *m/e* 315 (M^+), 242 ($M^+ - COOEt$). Anal. Calcd for $C_{14}H_{12}F_3NO_2S$: C, 53.33; H, 3.84; N, 4.44. Found: C, 53.40; H, 3.83; N, 4.12.

α-[4-(7-(Trifluoromethyl)quinolyl)thio]acetonitrile (3c): 90% yield, mp 180−181 °C; ^{1}H NMR δ 3.88 (s, 2H), 7.50 (d, 1H, J = 4.62 Hz), 7.80 (dd, 1H, J = 8.91, 1.65 Hz), 8.23 (d, 1H, J = 8.91 Hz), 8.45 (s, 1H), 8.96 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.67 (s); ^{13}C NMR (DEPT) δ 16.03 (CH_2), 119.25, 122.44, 125.19, 127.24, 151.36 (CH), 116.93, 120.80, 130.01, 130.50, 143.56, 146.60 (C); MS *m/e* 268 (M^+), 228 ($M^+ - CH_2CN$). Anal. Calcd for $C_{12}H_7F_3N_2S$: C, 53.73; H, 2.63; N, 10.44. Found: C, 53.69; H, 2.35; N, 10.41.

4-(Methylthio)-7-(trifluoromethyl)quinoline (3d): 90% yield, mp 79 °C; ^{1}H NMR δ 2.65 (s, 3H), 7.21 (d, 1H, J = 4.62 Hz), 7.73 (dd, 1H, J = 8.91, 1.65 Hz), 8.21 (d, 1H, J = 8.91 Hz), 8.37 (s, 1H), 8.81 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.74 (s); MS *m/e* 243 (M^+), 228 ($M^+ - CH_3$). Anal. Calcd for $C_{11}H_8F_3NS$: C, 54.32; H, 3.31; N, 5.76. Found: C, 54.07; H, 3.03; N, 5.82.

1-(2-Quinolylthio)-2-propanone (4a):[26b] 93% yield, mp 53−54 °C; ^{1}H NMR δ 2.42 (s, 3H), 4.12 (s, 2H), 7.26 (d, 1H, J = 8.58 Hz), 7.43 (ddd, 1H, J = 7.92, 7.26, 1.0 Hz), 7.64 (ddd, 1H, J = 8.25, 7.26, 1.32 Hz), 7.72 (d, 1H, J = 8.25 Hz)), 7.87 (d, 1H, J = 7.92 Hz), 7.91 (d, 1H, J = 8.58 Hz); ^{13}C NMR (DEPT) δ 28.75 (CH_3), 39.75 (CH_2), 120.14, 125.32, 127.24, 127.49, 129.65, 135.58 (CH), 147.79, 156.84, 203.56 (C); MS *m/e* 217 (M^+), 202 ($M^+ - CH_3$), 174 ($M^+ - COCH_3$), 128 ($M^+ - SCH_2COCH_3$). Anal. Calcd for $C_{12}H_{11}NOS$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.20; H, 4.79; N, 6.12.

Ethyl α-(2-quinolylthio)acetate (4b):[26c] 86% yield, mp 87−88 °C; ^{1}H NMR δ 1.28 (t, 3H, J = 7.26 Hz), 4.12 (s, 2H), 4.23 (q, 2H, J = 7.26 Hz), 7.24 (d, 1H, J = 8.91 Hz), 7.41 (ddd, 1H, J = 7.92, 6.93, 1.32 Hz), 7.62 (ddd, 1H, J = 8.25, 6.93, 1.65 Hz), 7.70 (d, 1H, J = 7.92 Hz)), 7.88 (d, 1H, J = 8.25 Hz), 7.90 (d, 1H, J = 8.91 Hz); ^{13}C NMR (DEPT) δ 14.17 (CH_3), 32.40, 61.55 (CH_2), 120.32, 125.42, 127.58, 127.94, 129.65, 135.63 (CH), 126.02, 148.07, 157.06, 169.70 (C); MS *m/e* 247 (M^+), 202 ($M^+ - OEt$), 173 ($M^+ - HCOOEt$), 160 ($M^+ - CH_2COOEt$), 128 ($M^+ - SCH_2COOEt$). Anal. Calcd for $C_{13}H_{13}NO_2S$: C, 63.14; H, 5.30; N, 5.66. Found: C, 63.01; H, 5.07; N, 5.34.

α-(2-Quinolylthio)acetonitrile (4c): 96% yield, mp 69−70 °C; ^{1}H NMR δ 4.20 (s, 2H), 7.23 (d, 1H, J = 8.57 Hz), 7.49 (ddd, 1H, J = 8.25, 7.92, 1.32 Hz), 7.69 (ddd, 1H, J = 8.57, 8.25, 1.32 Hz), 7.76 (d, 1H, J = 7.92 Hz), 7.99 (d, 1H, J = 8.57 Hz), 8.01 (d, 1H, J = 8.25 Hz); ^{13}C NMR (DEPT) δ 14.95 (CH_2), 119.87, 126.09, 127.65, 128.19, 130.15, 136.46 (CH), 116.99, 126.31, 148.01, 154.07 (C); MS *m/e* 200 (M^+), 173 ($M^+ - HCN$). Anal. Calcd for $C_{11}H_8N_2S$: C, 65.98; H, 4.03; N, 13.99. Found: C, 66.04; H, 3.96; N, 14.05.

Anodic Fluorination of Quinolyl Sulfides. Typical anodic fluorination conditions are as follows: Electrolysis was performed using platinum electrodes (3 × 2 cm^2) in 0.5 M $Et_4NF{\cdot}3HF$/DME (20 mL) to which the appropriate sulfide (1 mmol) was added. An H-type divided cell with an anion-exchange membrane (IE-DF 34-5 TOSOH) under a nitrogen atmosphere at ambient temperature was used. Constant current electrolysis (5 mA cm^{-2}) was applied until the starting sulfide was almost consumed (as monitored by TLC). After electrolysis, the electrolytic solution was purified by silica gel column chromatography employing ethyl acetate to remove the fluoride salts. The collected effluent was evaporated under reduced pressure, and the residue was further purified by passing it through a long silica gel column chromatograph using hexane/ethyl acetate (5:1) as an eluent.

Pulse electrolysis procedure [applied potential (50 s)/0.0 V (10 s)] was used instead of constant current electrolysis, when necessary.

1-Fluoro-1-[4-(7-(trifluoromethyl)quinolyl)thio]-2-propanone (5a): ^{1}H NMR δ 2.29 (d, 3H, J = 2.97 Hz), 6.28 (d, 1H, J = 52.79 Hz), 7.74 (d, 1H, J = 4.62 Hz), 7.81 (dd, 1H, J = 8.91, 1.98 Hz), 8.37 (d, 1H, J = 8.91 Hz), 8.44 (s, 1H), 8.93 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.69 (s, 3F), −82.84 (dq, 1F, J = 52.40, 2.76 Hz); ^{13}C NMR (DEPT) δ 26.02 (CH_3), 97.92 (d, CHF, J = 238 Hz), 123.13, 125.08, 125.84, 127.98, 150.87 (CH), 121.56, 129.22, 132.01, 140.41, 147.29, 198.24 (C); MS *m/e* 303 (M^+), 260 ($M^+ - COCH_3$), 241 ($M^+ - CH_3COF$), 196 ($M^+ - SCHFCOCH_3$); HRMS calcd for $C_{13}H_9F_4NOS$ *m/e* 303.0341, found *m/e* 303.0333. Anal. Calcd for $C_{13}H_9F_4NOS$: C, 51.49; H, 2.99; N, 4.62. Found: C, 51.80; H, 3.16; N, 4.54.

Ethyl α-fluoro-α-[4-(7-(trifluoromethyl)quinolyl)thio]acetate (5b): ^{1}H NMR δ 1.15 (t, 3H, J = 7.26 Hz), 4.14 (q, 2H, J = 7.26 Hz), 6.30 (d, 1H, J = 51.47 Hz), 7.79 (m, 2H), 8.38 (s, 1H), 8.42 (d, 1H, J = 5.61 Hz), 8.94 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.74 (s, 3F), −82.63 (d, 1F, J = 51.48 Hz); ^{13}C NMR (DEPT) δ 4.17 (CH_3), 63.36 (CH_2), 92.88 (d, CHF, J = 229.57 Hz), 123.41, 125.98, 126.79, 128.39, 151.37 (CH), 122.06, 130.05, 132.61, 140.52, 147.85, 164.95 (C); MS *m/e* 333 (M^+), 260 ($M^+ - COOEt$), 241 ($M^+ - FCOOEt$), 197 ($M^+ - SCHFCOOEt$). Anal. Calcd for $C_{14}H_{11}F_4NO_2S$: C, 50.45; H, 3.33; N, 4.20. Found: C, 50.16; H, 3.21; N, 3.83.

α-Fluoro-α-[4-(7-(trifluoromethyl)quinolyl)thio]acetonitrile (5c): mp 88−89 °C; ^{1}H NMR δ 6.43 (d, 1H, J = 48.83 Hz), 7.87 (m, 2H), 8.43 (d, 1H, J = 8.90 Hz), 8.51 (s, 1H), 9.06 (d, 1H, J = 4.29 Hz); ^{19}F NMR δ +13.66 (s, 3F), −78.18 (d, 1F, J = 48.72 Hz); MS *m/e* 286 (M^+), 228 ($M^+ - CHFCN$). Anal. Calcd for $C_{12}H_6F_4N_2S$: C, 50.35; H, 2.11; N, 9.79. Found: C, 50.64; H, 2.01; N, 9.67.

1-Fluoro-1-(2-quinolylthio)-2-propanone (7a): mp 50 °C; ^{1}H NMR δ 2.52 (d, 3H, J = 2.97 Hz), 7.15 (d, 1H, J = 49.81 Hz), 7.27 (d, 1H, J = 8.58 Hz), 7.51 (ddd, 1H, J = 7.92, 7.26, 1.0 Hz), 7.71 (ddd, 1H, J = 8.25, 7.26, 1.0 Hz), 7.77 (d, 1H, J = 7.92 Hz), 7.96 (d, 1H, J = 8.25 Hz), 8.03 (d, 1H, J = 8.58 Hz); ^{19}F NMR δ −88.93 (dq, J = 49.64, 2.76 Hz); ^{13}C NMR (DEPT) δ 26.15 (CH_3), 95.49 (d, CHF, J = 223.2 Hz), 120.23, 126.23, 127.48, 128.03, 130.15, 137.13 (CH), 126.56, 147.74, 153.06, 200.72 (C); MS *m/e* 235 (M^+), 215 ($M^+ - HF$), 192 ($M^+ - COCH_3$), 173 ($M^+ - CH_3COF$), 128 ($M^+ - SCHFCOCH_3$). Anal. Calcd for $C_{12}H_{10}FNOS$: C, 61.26; H, 4.28; N, 5.95. Found: C, 60.99; H, 4.44; N, 5.78.

Ethyl α-fluoro-α-(2-quinolylthio)acetate (7b): ^{1}H NMR δ 1.32 (t, 3H, J = 7.26 Hz), 4.34 (q, 2H, J = 7.26 Hz), 7.22 (d, 1H, J = 8.57 Hz), 7.44 (d, 1H, J = 50.47 Hz), 7.45 (ddd, 1H, J = 8.25, 6.93, 1.32 Hz), 7.67 (ddd, 1H, J = 8.25, 7.58, 1.32 Hz), 7.71 (dd, 1H, J = 8.25, 1.32 Hz)), 7.98 (dd, 1H, J = 8.25, 1.0 Hz), 8.00 (d, 1H, J = 8.57 Hz); ^{19}F NMR δ −85.31 (d, J = 50.56 Hz); ^{13}C NMR (DEPT) δ 13.91 (CH_3), 62.51 (CH_2), 90.01 (d, CHF, J = 225.80 Hz), 120.30, 126.20, 127.55, 128.19, 130.10, 136.80 (CH), 126.55, 147.78, 153.00, 166.50 (C); MS *m/e* 265 (M^+), 220 ($M^+ - OEt$), 192 ($M^+ - COOEt$), 173 ($M^+ - FCOOEt$), 128 ($M^+ - SCHFCOOEt$); HRMS calcd for $C_{13}H_{12}FNO_2S$ *m/e* 265.0573, found *m/e* 265.0568. Anal. Calcd for $C_{13}H_{12}FNO_2S$: C, 58.85; H, 4.56; N, 5.28. Found: C, 59.17; H, 4.50; N, 5.36.

α-Fluoro-α-(2-quinolylthio)acetonitrile (7c): mp 60 °C; ^{1}H NMR δ 7.22 (d, 1H, J = 8.57 Hz), 7.53 (ddd, 1H, J = 8.24, 7.92, 1.32 Hz), 7.73 (ddd, 1H, J = 8.58, 6.93, 1.32 Hz), 7.79 (d, 1H, J = 8.24 Hz), 7.89 (d, 1H, J = 48.83 Hz), 7.99 (d, 1H, J = 8.57 Hz), 8.07 (d, 1H, J = 8.58 Hz); ^{19}F NMR δ −83.13 (d, J =

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48.72 Hz); MS *m/e* 218 (M^+), 198 ($M^+ - HF$), 191 ($M^+ - HCN$), 160 ($M^+ - CHFCN$), 128 ($M^+ - SCHFCN$); HRMS calcd for $C_{11}H_7FN_2S$ *m/e* 218.0314, found 218.0321. Anal. Calcd for $C_{11}H_7FN_2S$: C, 60.54; H, 3.23; N, 12.84. Found: C, 60.52; H, 3.07; N, 12.84.

α,6-Difluoro-α-(2-quinolylthio)acetonitrile (9c): mp 82 °C; ^{1}H NMR δ 7.21 (d, 1H, J = 8.25 Hz), 7.31 (d, 1H, J = 8.91 Hz), 7.68 (dt, 1H, J = 8.57, 7.92 Hz), 7.82 (d, 1H, J = 8.57 Hz), 7.86 (d, 1H, J = 49.50 Hz), 8.38 (d, 1H, J = 8.91 Hz); ^{19}F NMR δ −45.00 (dd, 1F, J = 10.11, 9.19 Hz), −83.65 (d, 1F, J = 48.72 Hz); MS *m/e* 236 (M^+), 216 ($M^+ - HF$), 190 ($M^+ - HF - CN$), 178 ($M^+ - CHFCN$), 146 ($M^+ - SCHFCN$); HRMS calcd for $C_{11}H_6F_2N_2S$ *m/e* 236.0220, found *m/e* 236.0208. Anal. Calcd for $C_{11}H_6F_2N_2S$: C, 55.93; H, 2.56; N, 11.86. Found: C, 56.28; H, 2.66; N, 11.89.

4-((Fluoromethyl)thio)-7-(trifluoromethyl)quinoline (10): mp 107 °C; ^{1}H NMR δ 5.96 (d, 2H, J = 51.47 Hz), 7.68 (d, 1H, J = 4.62 Hz), 7.77 (dd, 1H, J = 8.91, 1.65 Hz), 8.23 (d, 1H, J = 8.91 Hz), 8.42 (s, 1H), 8.90 (d, 1H, J = 4.62 Hz); ^{19}F NMR δ +13.74 (s, 3F), −110.25 (t, 1F, J = 51.47 Hz); ^{13}C NMR (DEPT) δ 84.88 (d, CH_2F, J = 221 Hz), 120.54, 122.57, 125.19, 127.98, 150.94 (CH), 121.67, 125.69, 131.85, 144.71; 146.90 (C); MS *m/e* 261 (M^+), 242 ($M^+ - F$), 228 ($M^+ - CH_2F$), 196 ($M^+ - SCH_2F$). Anal. Calcd for $C_{11}H_7F_4NS$: C, 50.58; H, 2.70; N, 5.36. Found: C, 50.26; H, 2.66; N, 5.37.

2-((Fluoromethyl)thio)quinoline (11): ^{1}H NMR δ 6.33 (d, 2H, J = 51.47 Hz), 7.30 (d, 1H, J = 8.58 Hz), 7.48 (ddd, 1H, J = 8.25, 7.93, 1.0 Hz), 7.69 (ddd, 1H, J = 8.25, 6.93, 1.32 Hz), 7.76 (d, 1H, J = 7.93 Hz), 8.01 (d, overlapped 2H, J = 8.58 Hz); ^{19}F NMR δ −112.38 (t, J = 51.47 Hz); ^{13}C NMR (DEPT) δ 82.77 (d, CH_2F, J = 214.90 Hz), 120.70, 126.06, 127.62, 128.50, 130.03, 136.60 (CH), 126.60, 147.80, 153.00 (C); MS *m/e* 193 (M^+), 173 ($M^+ - HF$), 160 ($M^+ - CH_2F$), 129 ($M^+ - SCHF$). Anal. Calcd for $C_{10}H_8FNS$: C, 62.16; H, 4.17; N, 7.25. Found: C, 62.17; H, 4.40; N, 6.95.

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