A New Approach to β-Fluoropyrroles Based on the Michael Addition of Isocyanomethylide Anions to α-Fluoroalkenyl Sulfones and Sulfoxides

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The reactions of 2-aryl-1-fluorovinyl phenyl sulfones with carbanions derived from isocyanoacetates gave mixtures of 3-aryl-4-fluoro-2-pyrrolecarboxylates and 3-aryl-4-fluoro-4-phenylsulfonyl-2-isocyanobutanoates, simple Michael addition products, in variable ratios depending upon the conditions employed. On the other hand, the reaction of 1-fluoro-1-propenyl phenyl sulfone afforded mainly the simple Michael addition products in moderate yields as well as a small amount of 4-phenylsulfonyl-3-methyl-2-pyrrolecarboxylates and a trace amount of 4-fluoro-3-methyl-2-pyrrolecarboxylates. 1-Fluoropropenyl phenyl sulfoxide underwent mainly the simple Michael addition to give butenoates and a small amount of 4-fluoro-2-pyrrolecarboxylates.

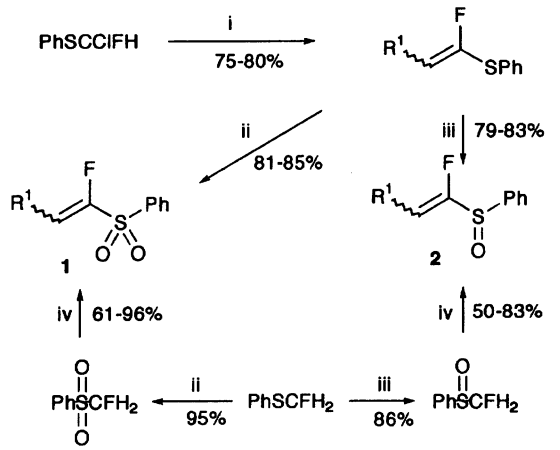
Substitution of a hydrogen atom of biologically important molecules for fluorine has proven to be not only making useful medicinals but also a powerful tool in fundamental studies of biochemical and metabolic processes[1] and in vivo imaging studies of a certain kind of receptors by positoron emission tomography[2] using positoron emitting ^{18}F nucleus.[3] Although a pyrrole skeleton is often found in biologically active compounds, studies on the fluorine-containing analogues are rare probably due to the lack of efficient methods for the introduction of a fluorine atom into the pyrrole nucleus.[4] The Shiemann reaction of pyrroles, which would be thought to be the most reliable method led to low yields. For example, the photochemical Shiemann reaction of 2-ethoxycarbonyl-4-pyrrolediazonium tetrafluoroborates was reported to give the corresponding 4-fluoropyrroles in 12—17% yields.[5]

We thought that fluoropyrroles might be prepared from α-fluoroalkyl phenyl sulfones by applying the new successful synthesis of pyrroles based on the addition of stabilized isocyanomethylide anions to appropriate Michael acceptors followed by the spontaneous ring closure.[6] From a mechanistic point of view, this reaction may contain some interesting problems; whether do the intermediate α-fluoro-α-phenylsulfonyl carbanions formed by the Michael addition of isocyanomethylide anions to α-fluoroalkenyl sulfones behave as carbanionoids or as carbenoids? Which group of fluorine or benzenesulfinate leaves from the carbenoid intermediates in the latter case[7] or from the pyrroline intermediates in the former case? In this paper, we discuss about our study on the reaction of α-fluoroalkenyl phenyl sulfones and sulfoxides with isocyanomethylide anions giving 2,3,4-trisubstituted pyrroles and 3-fluoro-substituted isocyanides.

Results and Discussion

Preparation of α-Fluoroalkenyl Phenyl Sulfones 1 and Sulfoxides 2. The sulfones **1** and sulfoxides **2** were easily prepared according to the reported procedures: i) condensation of chlorofluoromethyl phenyl sulfide with aldehydes followed by oxidation with one or two equiv of *m*-chloroperbenzoic acid (mCPBA)[8] or ii) condensation of fluoromethyl phenyl sulfone or sulfoxide with aldehydes[9] (Scheme 1). Both routes gave the similar results except for *E*: *Z* selectivity. The former route provided about 1:1 mixtures of *E*: *Z* isomers, whereas *E*-isomers were preferentially obtained by the latter route (*E*: *Z* ratio was ca. 2:1 for aliphatic aldehydes and >9:1 for aromatic ones).

Reaction of Sulfones 1 with Isocyanoacetates. Initially, we applied the reaction conditions used in the reaction of nitroolefins with isocyanoacetates.[6a—6c] Thus, 2-(4-biphenylyl)-1-fluorovinyl phenyl sulfone (**1a**) was refluxed with ethyl isocyanoacetate (2.8 equiv) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 2 equiv). However, the reaction did not take place and the starting sulfone was recovered in a 70% yield. This result is attributed that the vinyl sulfone **1a** is a poorer Michael acceptor than nitroolefins[6a—6c] and α,β-unsaturated carbonyl compounds.[6d] Next, we



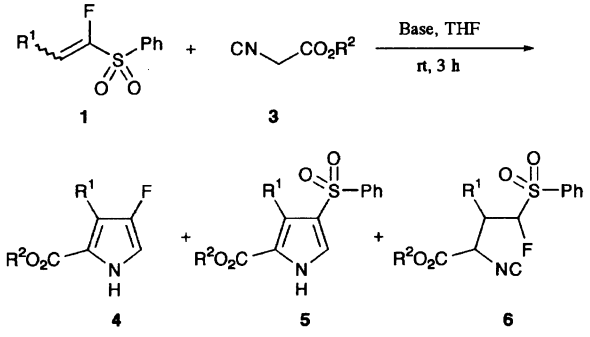
Scheme 1. Reagents and conditions: i) Ph_3P, MeLi–LiBr, R^1CHO, THF, −78 °C. ii) mCPBA (2 equiv), CH_2Cl_2, 0 °C→r.t. iii) mCPBA (1 equiv), CH_2Cl_2, 0 °C→r.t. iv) LDA (2 equiv), ClP(O)-$(OEt)_2$, THF, −78 °C; R^1CHO, −78 °C→r.t.

Table 1. Reaction of Sulfones **1** with Isocyanoacetates **3**

Entry	Sulfone[a]		Isocyanoacetate		Base	Yield/%			
	1	R^1	**3**	R^2 (equiv)	(equiv)	**1**[b]	**4**	**5**	**6**
1	**1a**	4-Ph-C_6H_4	**3a**	Et (2.0)	NaH (2.0)	30	5	Trace	25[c]
2	**1a**	4-Ph-C_6H_4	**3a**	Et (2.4)	NaH (4.0)	3	15	Trace	14[d]
3	**1a**	4-Ph-C_6H_4	**3a**	Et (4.2)	NaH (4.2)	35	8	Trace	—
4	**1a**	4-Ph-C_6H_4	**3a**	Et (2.0)	KH (2.0)	63	10	—	10[d]
5	**1a**	4-Ph-C_6H_4	**3a**	Et (3.5)	KH (3.5)	59	14	—	14[d]
6	**1a**	4-Ph-C_6H_4	**3a**	Et (4.0)	KH (4.0)	3	15	—	14[d]
7	**1a**	4-Ph-C_6H_4	**3a**	Et (2.8)	KH (2.8)[e]	48	35	—	—
8	**1b**	4-MeO-C_6H_4	**3a**	Et (2.0)	KH (2.0)	60	8	—	6[d]
9	**1c**	Me	**3a**	Et (1.0)	NaH (1.0)[f]	23	—	—	36[g]
10	**1c**	Me	**3a**	Et (2.0)	NaH (1.5)	—	Trace	21	58[d]
11	**1c**	Me	**3a**	Et (2.2)	NaH (1.8)	—	Trace	33	58[d]
12	**1c**	Me	**3a**	Et (2.0)	NaH (4.0)	—	Trace	33	—
13	**1c**	Me	**3b**	*t*-Bu (2.0)	NaH (2.0)	30	—	30	—
14	**1c**	Me	**3b**	*t*-Bu (2.0)	KH (2.0)	31	—	28	—

a) $E:Z=1:1$—$9:1$. b) $E:Z=>9:1$. c) The diastereomer ratio was $37:7:1:1$. d) The ratio was not determined. e) Kriptofix 222® (0.4 equiv) was added. f) DMF was used as a solvent. g) The diastereomer ratio was $6:4:3:2$.

changed the base for sodium hydride. The sulfone **1a** was treated with 2 equiv of ethyl sodioisocyanoacetate in THF at room temperature to give a mixture of fluoropyrrole **4aa** (5%) and butanoate **6aa** (25%) as well as 30% recovery of the starting sulfone ($E:Z=>9:1$; Eq. 1). A higher temperature (reflux) or a longer reaction time (2 d) did not improve either yield or selectivity but only brought about consumption of **1a**.



(1)

In order to improve the yield and selectivity of **4aa**, various reaction conditions were examined and some of them are listed in Table 1. The best selectivity of **4aa** was obtained by using 2.8 equiv each of potassium hydride and ethyl isocyanoacetate (**3a**) in the presence of 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane (Kriptofix 222®; 0.4 equiv), although the conversion was still low (Entry 7). In these reactions, another expected pyrrole **5aa** was formed in very small amount (<5%). The bad material valance observed is due to formation of considerable numbers of by-products, some of which were identified as **7aa**, **8aa**, and **9aa** by diagnosis of ^{1}H NMR and GC-MS (Chart 1). Isomerization of the starting **1** was observed under basic reaction conditions employed: when *Z*-rich **1a** ($E:Z=1:4$)

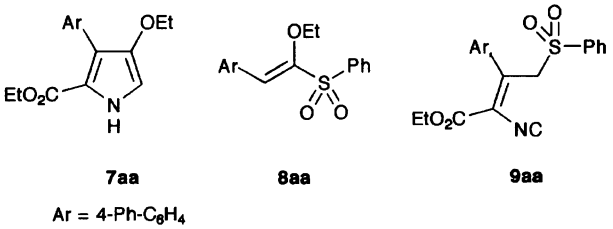


Chart 1.

was treated with 2 equiv each of **3a** and sodium hydride at room temperature for 3 h, a similar result as Entry 1 was obatained and the isomer ratio of the recovered **1a** (44%) was $E:Z=7:2$.

On the other hand, the reaction of aliphatic **1c** with the same Michael donor proceeded fairly well to give 58% of butanoate **6ca**, 21% of phenylsulfonylpyrrole **5ca**, and a trace amount of fluoropyrrole **4ca** (Entry 10). Use of an excess amount of potassium hydride against the isocyanoacetate led to complete disappearance of **6ca** almost without affecting the yields of pyrroles (Entry 12). The reaction of **1c** with *t*-butyl isocyanoacetate **3b** afforded **5cb** as the only identifiable product.

Reaction of Sulfoxides 2 with Isocyanoacetates 3.

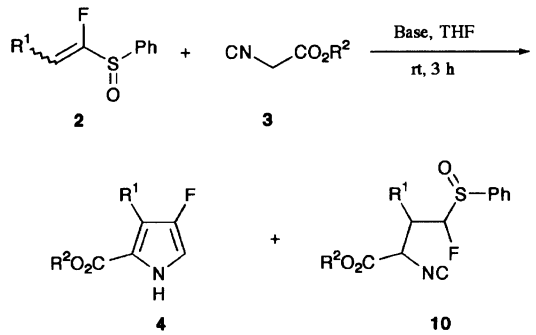
The similar reaction of α-fluoroalkenyl sulfoxides **2**, which were considered as poorer Michael acceptors than **1**, was conducted (Eq. 2, Table 2). We anticipated that the reaction would give simple addition product **10** and 4-phenylsulfinylpyrrole, because a benzenesulfenate anion is though as a poorer leaving group than a benzenesulfinate anion. The reaction of **2a** with **3a**, however, proceeded sluggishly and gave only fluoropyrrole **4aa** and a very trace amount of a simple Michael addition

Table 2. Reaction of Sulfoxides **2** with Isocyanoacetates **3**

Entry	Sulfoxide[a]		Isocyanoacetate		Base	Yield/%		
	2	R^1	**3**	R^2 (equiv)	(equiv)	**2**[b]	**4**	**10**
1	**2a**	4-Ph-C_6H_4	**3a**	Et (1.8)	NaH (2.0)	54	14	—
2	**2a**	4-Ph-C_6H_4	**3a**	Et (2.0)	NaH (5.0)	35	10	—
3	**2a**	4-Ph-C_6H_4	**3a**	Et (2.8)	KH (2.8)	44	12	—
4	**2a**	4-Ph-C_6H_4	**3a**	Et (3.5)	KH (3.4)	Trace	22	—
5	**2c**	Me	**3a**	Et (1.2)	KH (1.2)	30	3	43[c]
6	**2c**	Me	**3a**	Et (1.7)	KH (1.7)	—	9	51[d]
7	**2c**	Me	**3a**	Et (3.4)	KH (3.4)	—	5	58[d]
8	**2c**	Me	**3b**	*t*-Bu (1.8)	KH (4.0)	—	7	50[e]
9	**2d**	$PhCH_2CH_2$	**3a**	Et (2.0)	NaH (5.0)	—	15	9[d]
10	**2d**	$PhCH_2CH_2$	**3a**	Et (3.0)	KH (2.2)	—	5	50[f]

a) $E:Z=1:1$—$9:1$. b) $E:Z=>9:1$. c) The major four-diastereomer ratio was 8:4:3:2. d) The ratio was not determined. e) The major four-diastereomer ratio was 25:11:5:4. f) The major four-diastereomer ratio was 10:7:3:2.

product in addition to a large amount of the starting material. On the other hand, the simple addition products **10** were obtained from the reactions of **2c** and **2d** in moderate yields as well as a small amount of 4-fluoropyrroles **4**.

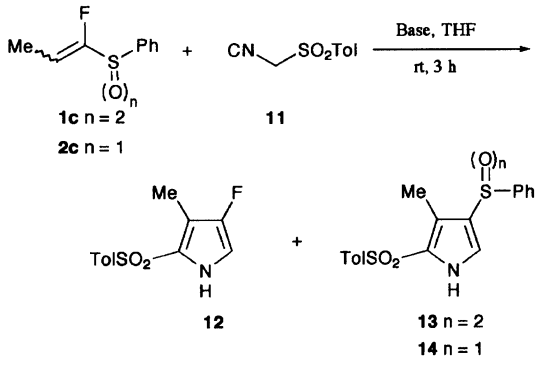


(2)

Reaction with Tosylmethyl Isocyanide (11). The reaction of tosylmethyl isocyanide (**11**) giving 2,5-unsubstituted pyrroles was extensively studied by van Leusen and other groups.[10] The tosyl group was usually eliminated during the course of reactions. The reaction of 1-fluoro-1-propenyl sulfone **1c** with **11**, however, gave mixtures of 4-fluoro-2-tosylpyrrole **12** and 4-phenylsulfonyl-2-tosylpyrrole **13** in low yields (Eq. 3, Table 3). 2,5-Unsubstituted pyrroles could not be obtained. A similar mixture of 4-fluoro-2-tosylpyrrole **12** and 4-phenylsulfinyl-2-tosylpyrrole **14** was obtained in the reaction of 1-fluoro-1-propenyl sulfoxide **2c**. It is worth of noting that none of simple Michael addition product was obtained in both reactions of **1c** and **2c** with **11**.

Table 3. Reaction of 1-Fluoro-1-propenyl Sulfone **1c** and Sulfoxide **2c** with Tosylmethyl Isocyanide (**11**)

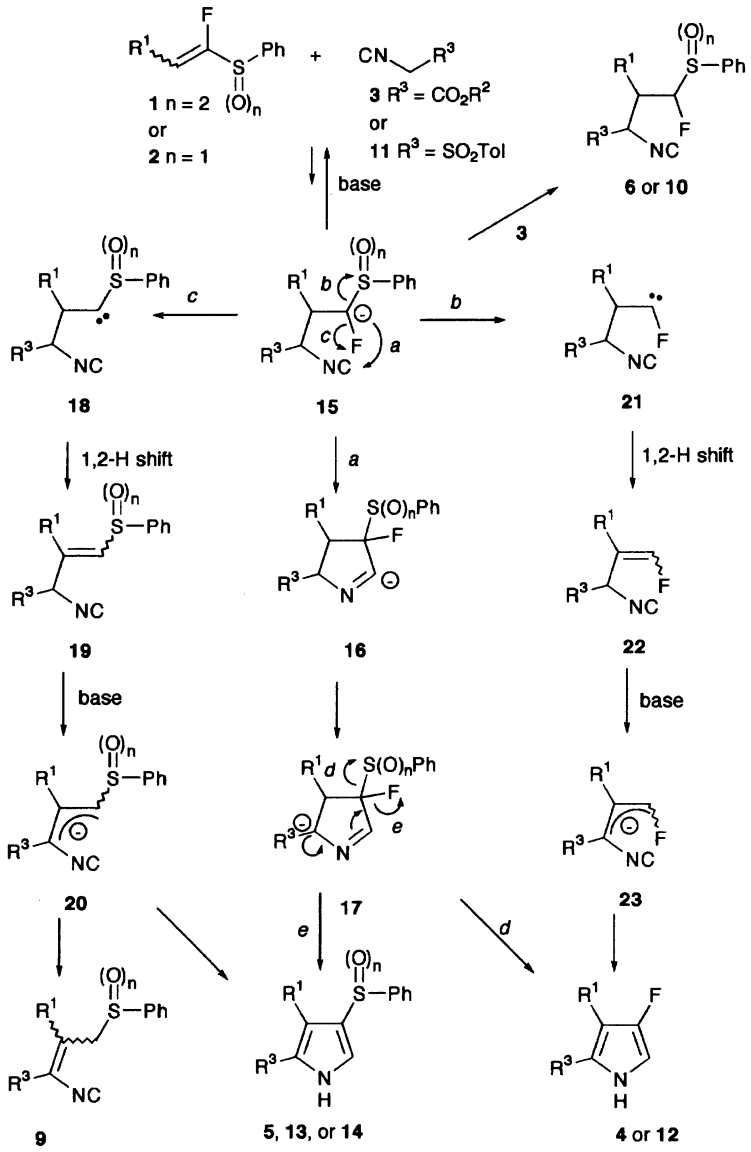
Entry	Substrate	**11**	NaH	Yield/%		
		equiv	equiv	**1c/2c**	**12**	**13/14**
1	**1c**	2.0	2.0	60	8	23
2	**1c**	2.0	4.0	46	7	18
3	**2c**	2.0	2.0	40	18	17
4	**2c**	2.0	4.0	35	24	24



(3)

Reaction Mechanism Consideration. Michael adduct anion **15** is thought to decompose in three different ways: Proton abstraction forming **6** or **10**; intramolecular addition to the isocyano group giving pyrrolinide **17**, which then undergoes 1,4-elimination of benzenesulfinate, benzenesulfenate, or fluoride to afford **4** or **5**; and α-elimination of fluoride, benzenesulfinate, or benzenesulfenate followed by 1,2-hydrogen shift of the resulting carbenes to give **19** or **22** (Scheme 2). The Michael addition of the stabilized carbanions derived from **3** or **11** to the fluorovinyl sulfones **1** or sulfoxides **2** is considered to be a rather unfavorable process especially in the case of 2-aryl derivatives, where sterically bulky aryl groups decrease the reactivity at the β-position. Thus, concentration of the Michael intermediate **15** would be very low and it would tend to undergo the cyclization or α-elimination rather than capture of an acidic proton from **3** or **11**. Thus yields of **6** and **10** were low in cases of **1a**, **1b**, and **2a**, and yields of **6ca** were greatly increased in the presence of neutral **3a** (Table 1, Entries 10 and 11). Moreover when tosylmethyl isocyanide (**11**), of which methylene protons are less acidic than **3**, was employed, the formation of simple Michael addition products was completely suppressed.

The tendency observed in the pyrrole formation (**4**



Scheme 2. Possible reaction pathways.

vs. **5**) from **1** Table 1, Entries 1—8 vs. Entries 10—14) would be understood by assuming that the pathway ***a*** is the main route to the pyrroles **4** and **5**. In the case of 2-aryl-1-fluorovinyl sulfones **1a** and **1b**, steric interaction between R^1 and benzenesulfonyl groups in **17** would be expected and thus would facilitate departure of the benzenesulfinate anion from **17**. The carbene routes to pyrroles via **19** and **22**, however, could not be excluded because **9aa**, which was derived from the carbene **18**, was obtained from the reaction mixture.[11] In the reaction of sulfoxides **2** with **3**, selective formation of fluoropyrroles rather than sulfinylpyrroles is interesting, but mechanism remains unclear.

Summary. We have shown that β-fluoropyrroles which are very difficult to access can be prepared from the reaction of α-fluoroalkenyl sulfones and sulfoxides with isocyanomethylide anions, although the yields are low. Studies on respective transformations of 4-fluoropyrrolecarboxylates and 4-fluorobutanoates into fluorinated porphyrins and α-amino acids[12] are under way and the results will be reported elsewhere.

Experimental

Melting points are uncorrected. Unless otherwise specified, NMR spectra were obtained with a JEOL GSX-270 spectrometer at ambient temperature by using $CDCl_3$ as a solvent, tetramethylsilane as an internal standard for ^1H and ^{13}C, and $CFCl_3$ as an internal standard for ^{19}F. Mass spectra were measured with a Hitachi M80B-LCAPI spectrometer under the following ionizing conditions: EI (electron impact, 20 eV) and CI (chemical ionization, 70 eV, methane or isobutane as CI gas). Column chromatography was carried out using Wakogel C-200. Ether and THF were distilled from sodium benzophenone ketyl. Other commercially available materials were used without further purification. Fluoromethyl phenyl sulfide was prepared in good yields (75—85%) from the reaction of chloromethyl phenyl sulfide with spray-dried KF[13] according to the literature procedure.[14] Isocyanoacetates **2a** and **2b** were prepared from the cor-

responding *N*-fomylglycine esters using $POCl_3$ and triethylamine.[15] Tolylmethyl isocyanide **11** was prepared according to the literature method.[16]

2-(4-Biphenylyl)-2-fluoroethenyl Phenyl Sulfone (1a): Colorless crystals, mp 165—167 °C (*E* isomer, hexane/CH_2Cl_2). ^{1}H NMR δ=6.94 (1H of *Z* isomer, d, *J*=22.3 Hz), 7.10 (1H of *E* isomer, d, *J*=34.8 Hz), and 7.3—8.1 (both 14H, m); ^{19}F NMR δ=−111.78 (*Z* isomer, d, *J*=22 Hz) and −125.08 (*E* isomer, d, *J*=35 Hz); IR (KBr) 3044, 1486, 1440, 1408, 1310, 1086, and 1040 cm^{-1}; MS (EI) *m/z* (rel intensity) 339 (M^++1, 19), 338 (M^+, 83), 213 (14), 194 (100), 185 (59), and 125 (21). Found: C, 70.92; H, 4.46%. Calcd for $C_{20}H_{15}FO_2S$: C, 70.99; H, 4.47%.

1-Fluoro-2-(4-methoxyphenyl)ethenyl Phenyl Sulfone (1b): Colorless crystals: mp 75—77 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=3.83 (3H of *E* isomer, s), 3.85 (3H of *Z* isomer, s), 6.86 (1H of *Z* isomer, d, *J*=22.7 Hz), 6.91 (2H of *E* isomer, d, *J*=8.8 Hz), 6.92 (2H of *Z* isomer, d, *J*=8.8 Hz), 7.01 (1H of *E* isomer, d, *J*=35.4 Hz), 7.46 (2H of *Z* isomer, d, *J*=8.8 Hz), 7.54 (2H of *E* isomer, d, *J*=8.8 Hz), 7.59 (both 2H, m), 7.68 (both 1H, m), 7.90 (2H of *Z* isomer, m), and 8.00 (2H of *E* isomer, m); ^{19}F NMR δ=−114.01 (*Z* isomer, d, *J*=23 Hz) and −128.82 (*E* isomer, d, *J*=35 Hz); IR (KBr) 2832, 1656, 1606, 1512, 1344, 1312, 1256, 1168, 1098, 1054, and 1036 cm^{-1}; MS (EI) *m/z* (rel intensity) 293 (M^++1, 13), 292 (M^+, 74), 167 (26), 156 (27), 150 (100), and 139 (77). Found: C, 61.51; H, 4.39%. Calcd for $C_{15}H_{13}FO_3S$: C, 61.63; H, 4.48%.

1-Fluoro-1-propenyl Phenyl Sulfone (1c): Colorless oil, oven temp 100 °C/0.2 mmHg (1 mmHg≈133.322 Pa). ^{1}H NMR δ=1.81 (3H of *E* isomer, dd, *J*=7.3 and 3.1 Hz), 2.14 (3H of *Z* isomer, dd, *J*=7.9 and 3.1 Hz), 5.93 (1H of *Z* isomer, dq, *J*=23.5 and 7.9 Hz), 6.31 (1H of *E* isomer, dq, *J*=32.0 and 7.3 Hz), 7.5—7.7 (both 3H, m), and 7.9—8.0 (both 2H, m); ^{13}C NMR δ=9.45 (*E* isomer, d, *J*=4 Hz), 10.05 (*Z* isomer, d, *J*=4 Hz), 113.92 (*E* isomer, d, *J*=7 Hz), 115.67 (*Z* isomer, d, *J*=15 Hz), 128.01 (*Z* isomer), 128.32 (*E* isomer), 129.25 (both), 134.20 (*E* isomer), 134.32 (*Z* isomer), 137.33 (*E* isomer), 138.28 (*Z* isomer), 152.49 (*Z* isomer, d, *J*=280 Hz), and 154.67 (*E* isomer, d, *J*=294 Hz); ^{19}F NMR δ=−116.82 (*Z* isomer, dq, *J*=22 and 3 Hz) and −129.78 (*E* isomer, dq, *J*=32 and 3 Hz); IR (neat) 1676, 1450, 1336, 1310, 1296, 1176, 1142, 1088, 1038, 1024, and 1000 cm^{-1}; MS (EI) *m/z* (rel intensity) 200 (M^+, 3), 125 (100), 109 (3), 97 (18), and 77 (48). Found: C, 53.60; H, 4.45%. Calcd for $C_9H_9FO_2S$: C, 53.99; H, 4.53%.

1-Fluoro-1-propenyl Phenyl Sulfoxide (2c): Colorless oil, oven temp 75 °C/0.2 mmHg, ^{1}H NMR δ=1.78 (3H of *E* isomer, dd, *J*=7.5 and 2.9 Hz), 2.06 (3H of *Z* isomer, dd, *J*=7.5 and 3.2 Hz), 5.80 (1H of *Z* isomer, dq, *J*=17.2 and 7.6 Hz), 5.85 (1H of *E* isomer, dq, *J*=34.5 and 7.2 Hz), and 7.5—8.0 (both 5H, m); ^{13}C NMR δ=9.37 (*E* isomer d, *J*=4 Hz), 10.62 (*Z* isomer, d, *J*=5 Hz), 110.63 (*E* isomer, d, *J*=7 Hz), 113.90 (*Z* isomer, d, *J*=14 Hz), 124.46 (*E* isomer*), 124.85 (*Z* isomer*), 129.14 (both), 131.28 (*Z* isomer*), 131.56 (*E* isomer*), 139.51 (*Z* isomer*, d, *J*=2 Hz), 140.19 (*E* isomer*), 157.48 (*Z* isomer*, d, *J*=312 Hz), and 158.46 (*E* isomer*, d, *J*=311 Hz) (*The assignment may be changable); ^{19}F NMR δ=−127.02 (*Z* isomer, dq, *J*=17 and 2 Hz) and −129.98 (*E* isomer, dq, *J*=34 and 2 Hz); IR (neat) 1668, 1480, 1448, 1306, 1154, 1088, 1054, 1022, and 1000 cm^{-1}; MS (EI) *m/z* (rel intensity) 184 (M^+, 10), 167 (35), 136 (44), 125 (30), 109 (100), 97 (15), and 77 (60).

General Procedure for the Reaction of Sulfones 1 and Sulfoxides 2 with Isocyanoacetates 3 and Tosylmethyl Isocyanide (11). Sodium hydride or potassium hydride (washed by dry hexane to remove the mineral oil) was suspended in 10 ml of THF under a nitrogen atmosphere. To the suspension was slowly added isocyanide at 0—5 °C and then the mixture was stirred for 10 min. A solution of α-fluoroalkenyl sulfone **1** or sulfoxide **2** (0.5 mmol) in 1 ml of THF was added to the milky yellow suspension at room temperature. After 3 h, the reaction was quenched with saturated aq ammonium chloride and the mixture was extracted with ether (3×30 ml). The ethereal extract was dried over Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (CH_2Cl_2–ether).

Ethyl 3-(4-Biphenylyl)-4-fluoro-2-pyrrolecarboxylate (4aa): Colorless crystals, mp 142—143 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=1.26 (3H, t, *J*=7.2 Hz), 4.27 (2H, q, *J*=7.2 Hz), 6.81 (1H, t, *J*=3.4 Hz), 7.3—7.7 (9H, m), and 8.89 (1H, br); ^{13}C NMR δ=14.16, 60.67, 106.45 (d, *J*=28 Hz), 115.55 (d, *J*=3 Hz), 117.70 (d, *J*=12 Hz), 126.42, 127.09, 127.24, 128.74, 129.35 (d, *J*=3 Hz), 130.71 (d, *J*=1 Hz), 140.17, 140.96, 149.98 (d, *J*=244 Hz), and 160.75 (d, *J*=3 Hz); ^{19}F NMR δ=−166.29 (t, *J*=3 Hz); IR (KBr) 3292, 1668, 1486, 1424, 1288, 1198, 1104, and 1022 cm^{-1}; MS (EI) *m/z* (rel intensity) 310 (M^++1, 15), 309 (M^+, 72), 305 (14), 291 (67), 263 (100), 245 (71), 234 (16), and 217 (20). HRMS Found: *m/z* 309.1158. Calcd for $C_{19}H_{16}FNO_2$: M, 309.1165.

Ethyl 4-Fluoro-3-(4-methoxyphenyl)-2-pyrrolecarboxylate (4ba): Colorless crystals, mp 65—67 °C. ^{1}H NMR δ=1.25 (3H, t, *J*=7.2 Hz), 3.85 (3H, s), 4.25 (2H, q, *J*=7.1 Hz), 6.78 (1H, t, *J*=3.5 Hz), 6.94 (2H, m), 7.47 (2H, m), and 8.80 (1H, br); ^{13}C NMR δ=14.19, 55.25, 60.53, 106.31 (d, *J*=28 Hz), 113.18, 115.31 (d, *J*=4 Hz), 122.61, (d, *J*=2 Hz), 128.42, 131.49 (d, *J*=1 Hz), 149.93 (d, *J*=243 Hz), 158.95, and 160.82 (d, *J*=3 Hz); ^{19}F NMR δ=−166.82 (t, *J*=3.3 Hz); IR (KBr) 3292, 1666, 1536, 1496, 1426, 1292, 1260, 1104, and 1020 cm^{-1}; MS (EI) *m/z* 264 (M^++1, 10), 263 (M^+, 55), 217 (100), 202 (8), 174 (19), and 146 (9). Found: *m/z* 263.0955. Calcd for $C_{14}H_{14}FNO_3$: M, 263.0955.

Ethyl 4-Fluoro-3-methyl-2-pyrrolecarboxylate (4ca): Colorless crystals, mp 59—60 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=1.37 (3H, t, *J*=7.2 Hz), 2.26 (3H, s), 4.32 (2H, q, *J*=7.2 Hz), 6.65 (1H, t, *J*=3.5 Hz), and 8.58 (1H, br); ^{13}C NMR δ=7.84 (d, *J*=1 Hz), 14.38, 60.31, 106.09 (d, *J*=28 Hz), 113.39 (d, *J*=14 Hz), 116.29 (d, *J*=5 Hz), 151.17 (d, *J*=240 Hz), and 161.69 (d, *J*=3 Hz); ^{19}F NMR δ=−168.21 (t, *J*=3 Hz); IR (KBr) 3288, 1682, 1472, 1430, 1282, 1154, and 1102 cm^{-1}; MS (EI) *m/z* (rel intensity) 172 (M^++1, 7), 171 (M^+, 72), 142 (25), 125 (100), 97 (29), and 70 (15). HRMS Found: *m/z* 171.0696. Calcd for $C_8H_{10}FNO_2$: M, 171.0695.

***t*-Butyl 4-Fluoro-3-methyl-2-pyrrolecarboxylate (4cb):** Colorless crystals, mp 97—99 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=1.57 (9H, s), 2.23 (3H, s), 6.61 (1H, t, *J*=3.5 Hz), and 8.61 (1H, br); ^{13}C NMR δ=7.89, 28.42, 81.14, 105.23 (d, *J*=28 Hz), 112.66 (d, *J*=14 Hz), 117.52 (d, *J*=5 Hz), 151.20 (d, *J*=239 Hz), and 160.97 (d, *J*=3 Hz); ^{19}F NMR δ=−168.31 (t, *J*=3 Hz); IR (KBr) 3308, 1674, 1528, 1464, 1416, 1400, 1372, 1286, 1262, 1146, and 1098 cm^{-1}; MS (EI) *m/z* (rel intensity) 199 (M^+, 16), 143 (74),

125 (100), 97 (7), and 71 (3). HRMS Found: m/z 199.0994. Calcd for $C_{10}H_{14}FNO_2$: M, 199.1006.

Ethyl 4-Fluoro-3-(2-phenylethyl)-2-pyrrolecarboxylate (4da): Pale yellow crystals, mp 120 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=1.37 (3H, t, J=7.1 Hz), 2.86 (2H, m), 3.05 (2H, m), 4.31 (2H, q, J=7.1 Hz), 6.64 (1H, t, J=3.7 Hz), 7.1—7.3 (5H, m), and 8.64 (1H, br); ^{19}F NMR δ=−168.04 (t, J=3 Hz); IR (KBr) 2984, 2940, 2164, 1758, 1694, 1526, 1468, 1428, 1390, 1272, 1216, 1034, and 738 cm^{-1}; MS (EI) m/z (rel intensity) 261 (M^+, 34), 170 (100), 142 (57), 126 (18), 124 (81), and 91 (50). HRMS Found: m/z 263.1232. Calcd for $C_{19}H_{16}FNO_2$: M, 263.1231.

Ethyl 3-(4-Biphenylyl)-4-phenylsulfonyl-2-pyrrolecarboxylate (5aa): Obtained as an impure form; ^{1}H NMR δ=1.35 (3H, t, J=7.0 Hz), 4.20 (2H, q, J=7.0 Hz), 7.26 (1H, d, J=4.3 Hz), 7.3—7.8 (12H, m), and 8.00 (2H, m) (NH could not be seen). HRMS Found: m/z 405.1070. Calcd for $C_{19}H_{16}FNO_2$: M, 405.1045.

Ethyl 3-Methyl-4-phenylsulfonyl-2-pyrrolecarboxylate (5ca): Pale yellow crystals, mp 129—130 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=1.33 (3H, t, J=7.0 Hz), 2.40 (3H, s), 4.31 (2H, q, J=7.0 Hz), 7.45—7.55 (3H, m), 7.58 (1H, d, J=3.4 Hz), 7.92 (2H, m), and 9.99 (1H, br); ^{13}C NMR δ=10.19, 14.26, 60.90, 121.88, 125.23, 126.04, 126.31, 126.97, 129.01, 132.74, 142.47, and 161.14; IR (KBr) 3240, 3120, 2936, 1680, 1484, 1448, 1420, 1390, 1358, 1314, 1262, 1146, 1098, 1052, and 1000 cm^{-1}; MS (EI) m/z (rel intensity) 293 (M^+, 100), 264 (12), 248 (23), 246 (25), and 149 (27). HRMS Found: m/z 293.0735. Calcd for $C_{14}H_{15}NO_4S$: M, 293.0721.

***t*-Butyl 3-Methyl-4-phenylsulfonyl-2-pyrrolecarboxylate (5cb):** Pale yellow crystals, mp 165 °C (hexane/CH_2Cl_2). ^{1}H NMR δ=1.55 (9H, s), 2.38 (3H, s), 7.45—7.55 (3H, m), 7.56 (1H, d, J=3.7 Hz), 7.91 (2H, m), and 10.49 (1H, br); ^{13}C NMR δ=10.20, 28.18, 82.25, 122.97, 124.65, 125.41, 125.69, 126.83, 128.90, 132.60, 142.48, and 160.79; IR (KBr) 3324, 2980, 2932, 1696, 1556, 1480, 1450, 1400, 1370, 1304, 1258, 1178, 1052, and 1000 cm^{-1}; MS (EI) m/z (rel intensity) 321 (M^+, 0.8), 265 (100), 221 (77), 183 (14), 170 (14), 156 (17), and 154 (25); (CI) 350 (M^++Et, 9), 322 (M^++1, 100), 294 (8), 266 (46), 222 (16), and 188 (12). HRMS Found: m/z 321.1038. Calcd for $C_{16}H_{19}NO_4S$: M, 321.1033.

Ethyl 3-(4-Biphenylyl)-4-fluoro-2-isocyano-4-phenylsulfonylbutanoate (6aa): Obtained as a mixture of four diastereomers (A : B : C : D=31 : 7 : 1 : 1), pale yellow oil. ^{1}H NMR (isomer A) δ=1.15 (3H, t, J=7.2 Hz), 4.13 (2H, q, J=7.2 Hz), 4.2—4.3 (1H, m), 5.05 (1H, d, J=3.4 Hz), 5.66 (1H, dd, J=47.3 and 8.6 Hz), and 7.3—7.9 (14H, m); (isomer B, typical signals) δ=1.28 (3H, t, J=7.0 Hz), 4.14 (2H, q, J=7.0 Hz), 4.61 (1H, d, J=3.1 Hz), and 5.87 (1H, dd, J=47.9 and 10.6 Hz); ^{13}C NMR (isomer A) δ=13.87, 44.81 (d, J=18 Hz), 57.43 (br, d, J=6 Hz), 63.23, 100.06 (d, J=225 Hz), 127.04, 127.51, 127.72, 127.75, 128.83, 129.40, 129.46, 129.73, 134.90, 135.47, 139.96, 142.27, and 163.89; (isomer B, typical signals) δ=46.53 (d, J=17 Hz), 57.52, 63.40, 100.90 (d, J=225 Hz), 134.79, and 164.10; ^{19}F NMR δ=−175.59 (B, dd, J=48 and 5 Hz), −178.46 (A, dd, J=47 and 11 Hz), −179.64 (C, dd, J=46 and 9 Hz), and −186.64 (D, dd, J=48 and 30 Hz); IR (KBr) 2148, 1758, 1334, 1290, 1216, 1156, 1088, 1064, and 1040 cm^{-1}; MS (EI) m/z (rel intensity) 451 (M^+, 26), 309 (47), 255 (9), 198 (100), 179 (12), 141 (25), and 83 (55).

Ethyl 4-Fluoro-2-isocyano-3-(4-methoxyphenyl)-4-phenylsulfonylbutanoate (6ba): Obtained as an impure mixture of four diastereomers (A : B : C : D=5 : 4 : 1 : <1); ^{1}H NMR (isomer A) δ=1.18 (3H, t, J=7.3 Hz), 3.77 (3H, s), 4.0—4.3 (3H, m), 4.97 (1H, d, J=3.6 Hz), 5.58 (1H, dd, J=47.5 and 9.0 Hz), and 6.7—7.9 (9H, m); (isomer B, typical signals) δ=1.24 (3H, d, J=7.3 Hz), 3.84 (3H, s), 5.30 (1H, d, J=3 Hz), and 5.80 (1H, dd, J=48 and 3 Hz).

Ethyl 4-Fluoro-2-isocyano-3-methyl-4-phenylsulfonylbutanoate (6ca): Obtained as a mixture of four diastereomers (A : B : C : D=6 : 4 : 3 : 2), pale yellow oil. ^{1}H NMR (isomer A) δ=1.34 (3H, t, J=7.2 Hz), 1.37 (3H, dd, J=7.0 and 1.2 Hz), 3.15 (1H, m), 4.33 (2H, q, J=7.2 Hz), 4.72 (1H, d, J=2.8 Hz), 5.03 (1H, dd, J=47.8 and 9.3 Hz), and 7.6—8.0 (5H, m); (isomer B) δ=1.23 (3H, dd, J=7.0 and 2.8 Hz), 1.34 (3H, t, J=7.2 Hz), 3.15 (1H, m), 4.33 (2H, q, J=7.2 Hz), 5.03 (1H, dd, J=4.0 and 1.2 Hz), 5.14 (1H, dd, J=47.0 and 7.6 Hz), and 7.6—8.0 (5H, m); (isomer C, typical signals) δ=1.29 (3H, t, J=7.2 Hz), 1.52 (3H, d, J=7.0 Hz), 4.26 (2H, q, J=7.2 Hz), 4.43 (1H, d, J=2.8 Hz), and 5.18 (1H, dd, J=47.5 and 9.9 Hz); (isomer D, typical signals) δ=4.51 (1H, d, J=5.5 Hz), and 5.36 (1H, dd, J=48.1 and 3.5 Hz); ^{13}C NMR δ=9.81 (B, d, J=8 Hz), 10.47 (A, d, J=5 Hz), 10.57 (D*, d, J=9 Hz), 13.05 (C*, d, J=6 Hz), 13.86 (C*), 13.93 (D*), 13.99 (B), 14.01 (A), 34.71 (B, d, J=21 Hz), 35.21 (A, d, J=17 Hz), 35.71 (D*, d, J=20 Hz), 36.64 (C*, d, J=16 Hz), 57.10 (A, br d, J=6 Hz), 58.48 (C*, br), 58.82 (B, br d, J=6 Hz), 58.88 (D*, br), 63.10 (C*), 63.34 (B), 63.37 (A), 63.40 (D*), 99.79 (D*, d, J=225 Hz), 100.70 (B, d, J=223 Hz), 101.39 (A, d, J=221 Hz), 101.51 (D*, d, J=220 Hz), 129.2—129.6 (*o*-, *m*-, and *p*-aromatic carbons), 134.98 (C*), 135.06 (A), 135.11 (B), 135.39 (D*), 161.05 (B, br), 162.77 (D*, br), 162.85 (A, br), 162.94 (C*, br), 164.39 (B, d, J=1 Hz), 164.54 (C*), 164.63 (A, d, J=1 Hz), and 164.74 (D*) (*The assignment may be changable.); ^{19}F NMR δ=−172.99 (C, dd, J=48 and 4 Hz), −175.78 (A, dd, J=48 and 7 Hz), −185.28 (B, dd, J=48 and 10 Hz), and −188.77 (D, dd, J=48 and 20 Hz); IR (KBr) 2148, 1756, 1450, 1332, 1212, and 1158 cm^{-1}; MS (CI) m/z (rel intensity) 314 (M^++1, 100), 287 (15), 243 (9), 172 (46), 144 (68), 125 (60), 88 (44), and 77 (26).

Ethyl 3-(4-Biphenylyl)-4-ethoxy-2-pyrrolecarboxylate (7aa): Obtaied as an impure form; ^{1}H NMR δ=1.23 (3H, t, J=7.3 Hz), 1.33 (3H, t, J=7.0 Hz), 3.90 (2H, q, J=7.0 Hz), 4.24 (2H, q, J=7.3 Hz), 6.60 (1H, d, J=3.0 Hz), 7.3—7.7 (14H, m), and 8.78 (1H, br s); MS (EI) m/z (rel intensity) 336 (M^++1, 20), 335 (M^+, 86), 289 (100), 260 (48), 232 (8), and 205 (18).

(*E*)-2-(4-Biphenylyl)-1-ethoxyethenyl Phenyl Sulfone (8aa): Obtained as an impure form; ^{1}H NMR δ=1.34 (3H, t, J=7.3 Hz), 4.18 (2H, q, J=7.3 Hz), 5.27 (1H, s), 7.3—7.7 (10H, m), 7.70 (2H, m), and 7.98 (2H, m), ^{13}C NMR δ=15.36, 70.79, 122.24, 126.95, 127.31, 127.80, 128.34, 128.84, 129.07, 130.24, 130.62, 133.52, 139.03, 139.97, 142.29, and 152.19; MS (EI) m/z (rel intensity) 364 (M^+, 22), 195 (17), 194 (100), 167 (8), 165 (26), and 125 (8). HRMS Found: m/z 364.1115. Calcd for $C_{22}H_{20}O_3S$: M, 364.1131.

Ethyl 3-(4-Biphenylyl)-2-isocyano-4-phenylsulfonyl-2-butenoate (9aa): Obtained as an impure form; ^{1}H NMR δ=1.02 (3H, t, J=7.3 Hz), 4.10 (2H, q, J=7.3 Hz),

5.29 (2H, s), 7.1—7.3 (4H, m), 7.3—7.6 (8H, m), and 7.65 (2H, m); ^{13}C NMR δ=13.74, 53.41, 60.92, 122.04, 125.79, 126.65, 127.02, 127.37, 127.47, 128.40, 128.80, 129.34, 130.08, 131.00, 132.57, 140.46, 140.82, 141.57, and 160.51; MS (EI) m/z (rel intensity) 432 (M^++1, 29), 431 (M^+, 100), 385 (22), 267 (13), 244 (26), 216 (15), 193 (16), and 167 (11). HRMS Found: m/z 431.1195. Calcd for $C_{25}H_{21}NO_4S$: M, 431.1190.

Ethyl 4-Fluoro-2-isocyano-3-methyl-4-phenylsulfinylbutanoate (10ca): Obtained as a mixture of eight diastereomers (A : B : C : D : E : F : G : H=16 : 8 : 6 : 4 : 2 : 2 : <1 : <1), a pale yellow oil. ^{1}H NMR (isomer A) δ=1.12 (3H, d, J=6.7 Hz), 1.31 (3H, t, J=7.0 Hz), 2.94 (1H, m), 4.28 (2H, q, J=7.0 Hz), 4.80 (1H, d, J=3.1 Hz), 5.00 (1H, dd, J=48.2 and 7.9 Hz), and 7.3—7.8 (5H, m); (isomer B, typical signals) δ=4.64 (1H, d, J=4.0 Hz) and 5.04 (1H, dd, J=49.1 and 1.7 Hz); (isomer C, typical signals) δ=4.49 (1H, d, J=4.0 Hz) and 5.16 (1H, dd, J=48.2 and 8.9 Hz); (isomer D, typical signals) δ=4.36 (1H, d, J=7.0 Hz) and 5.01 (1H, dd, J=48.2 and 4.2 Hz); ^{13}C NMR δ=7.38 (E*, d, J=9 Hz), 8.93 (C*, d, J=7 Hz), 9.26 (F*, d, J=9 Hz), 9.23 (D*, d, J=6 Hz), 10.37 (A, d, J=5 Hz), 12.51 (B, d, J=5 Hz), 13.73 (B), 13.80 (D*), 13.86 (C*), 13.88 (A), 35.82 (D*, d, J=16 Hz), 35.91 (A, d, J=16 Hz), 35.99 (C*, d, J=20 Hz), 37.65 (B, d, J=16 Hz), 56.83 (A, br d, J=5 Hz), 58.3—58.7 (B, C, and D, br), 62.87 (B), 63.06 (D*), 63.14 (A and C*), 105.37 (D*, d, J=226 Hz), 106.24 (B and C*, d, J=226 Hz), 106.82 (A, d, J=225 Hz), 124.73 (C*, d, J=2 Hz), 124.76 (D*, d, J=2 Hz), 124.92 (A, d, J=2 Hz), 125.16 (B, d, J=2 Hz), 129.1—129.7, 131.5—132.3, 138.90 (A, d, J=5 Hz), 138.95 (B, d, J=5 Hz), 139.82 (C and D), 162.32 (B), 162.46 (A), 162.55 (C*), 164.57 (C*), 164.62 (B), 164.69 (D*), and 164.87 (A) (*The assignment may be changable.); ^{19}F NMR δ=−178.93 (B, dd, J=48 and 7 Hz), −180.33 (A, dd, J=49 and 11 Hz), −188.74 (C, dd, J=48 and 22 Hz), −189.21 (E, dd, J=50 and 28 Hz), −190.97 (F, dd, J=47 and 5 Hz), −191.62 (D, dd, J=49 Hz and J=29 Hz), −195.9 (G, m), and −196.3 (H, m); IR (neat) 2940, 2148, 1754, 1704, 1634, 1276, 1210, 1088, 1050, and 1024 cm^{-1}, MS (CI) m/z (rel intensity) 298 (M^++1, 2), 271 (2), 235 (1), 210 (3), 198 (6), 170 (100), 144 (21), 142 (41), 117 (21), and 86 (6).

***t*-Butyl 4-Fluoro-2-isocyano-3-methyl-4-phenylsulfinylbutanoate (10cb):** Obtained as a mixture of eight diastereomers (A : B : C : D : E : F : G : H=25 : 11 : 5 : 4 : 3 : < 1 : <1 : <1), a pale yellow oil. ^{1}H NMR (isomer A) δ=1.13 (3H, d, J=7.0 Hz), 1.50 (9H, s), 2.88 (1H, br), 4.66 (1H, d, J=2.8 Hz), 4.95 (1H, dd, J=48.5 and 8.6 Hz), and 7.3—7.7 (5H, m); (isomer B, typical signals) δ=1.40 (3H, d, J=7.0 Hz), 4.35 (1H, d, J=4.0 Hz), and 5.16 (1H, dd, J=48.2 and 8.6 Hz); (isomer C, typical signals) δ=1.23 (3H, d, J=6.1 Hz), 4.48 (1H, d, J=4.0 Hz), and 5.05 (1H, dd, J=49 and 2 Hz); (isomer D, typical signals) δ=1.27 (3H, d, J=7.0 Hz), 4.21 (1H, d, J=7.0 Hz), and 4.97 (1H, dd, J=48.2 and 4.0 Hz); ^{13}C NMR δ=7.20 (D*, d, J=8 Hz), 8.70 (C*, d, J=7 Hz), 9.51 (E*, d, J=6 Hz), 10.02 (A, d, J=5 Hz), 12.54 (B, d, J=5 Hz), 27.36 (B), 27.50 (A), 27.61 (C*), 35.79 (C*, d, J=20 Hz), 35.90 (A, d, J=17 Hz), 37.31 (B, d, J=16 Hz), 37.52 (D*, d, J=17 Hz), 57.24 (A, br m), 59.20 (B, C, and D, br m), 84.21 (B), 84.47 (A), 84.52 (C*), 84.60 (D*), 105.38 (D*, d, J=228 Hz), 105.44 (C*, d, J=233 Hz), 106.27 (B, d, J=228 Hz), 106.67 (A, d, J=226 Hz), 124.64 (C*, d, J=1 Hz), 124.66 (D*, d, J=1 Hz), 124.87 (A, d, J=1 Hz), 125.18 (B, d, J=1 Hz), 129.1—129.4, 132.0—132.2, 138.68 (B, d, J=5 Hz), 138.80 (A, d, J=5 Hz), 139.69 (D*, d, J=4 Hz), 139.71 (C*, d, J=5 Hz), 161.7—162.1 (br m), 162.93 (C*), 163.20 (B), 163.31 (D*), and 163.56 (A) (*The assignment may be changable.); ^{19}F NMR δ=−179.44 (B, dd, J=48 and 7 Hz), −180.43 (E, dd, J=48 and 10 Hz), −188.48 (D, dd, J=48 and 24 Hz), −188.57 (C, dd, J=48 and 24 Hz), and −191.99 (E, dd, J=50 and J=30 Hz); IR (neat) 2980, 2148, 1748, 1372, 1308, 1260, 1156, 1080, and 1052 cm^{-1}; MS (CI) m/z (rel intensity) 326 (M^++1, 4), 270 ($MH^+ - CH_2$=CMe_2, 90), 252 (M^+ − O-*t*-Bu, 23), 250 (54), 144 (85), 127 (90), and 166 (100). HRMS Found: m/z 326.1199. Calcd for $C_{16}H_{20}FNO_3S+H^+$: M, 326.1224.

Ethyl 3-[Fluoro(phenylsulfinyl)methyl]-2-isocyano-5-phenylpentanoate (10da): Obtained as a mixture of eight diastereomers (A : B : C : D : E : F : G : H=10 : 7 : 3 : 2 : 1 : <1 : <1 : <1), a pale yellow oil. ^{1}H NMR (isomer A) δ=1.20 (3H, t, J=7.2 Hz), 1.8—2.2 (2H, m), 2.6—2.9 (3H, m), 4.16 (2H, m), 4.54 (1H, d, J=3.5 Hz), 5.12 (1H, dd, J=48.5 and 8.1 Hz), and 7.2—7.7 (10H, m); ^{13}C NMR δ=13.67 (A), 13.69 (B), 26.21 (D*), 26.52 (B, d, J=6 Hz), 26.71 (A, d, J=6 Hz), 31.96 (C*), 32.72 (B), 33.00 (A, d, J=1 Hz), 33.92 (D*), 38.05 (C*, d, J=18 Hz), 39.45 (B, d, J=18 Hz), 40.34 (A, d, J=19 Hz), 40.9 (D*, d, J=18 Hz), 55.4 (C*, br), 56.2 (D*, br), 56.79 (B, br), 57.01 (A, br), 63.01 (A and B), 63.29 (C*), 104.2 (D*, d, J=227 Hz), 104.4 (C*, d, J=227 Hz), 105.78 (B, d, J=228 Hz), 106.11 (A, d, J=226 Hz), 123.62 (C*), 124.56 (B, d, J=2 Hz), 124.66 (A, d, J=2 Hz), 124.82 (D*), 126.15 (C*), 126.18 (A), 126.24 (D*), 126.29 (B), 128—128.3, 128.3—128.6, 129.26 (B), 129.34 (A), 129.41 (C*), 129.58 (D*), 131.83 (C*), 131.97 (B), 132.02 (D*), 132.12 (A), 139.61 (C), 139.65 (D*), 139.77 (B), 140.13 (A), 162.1 (C*, br), 162.54 (A, br), 162.6 (D*, br), 162.75 (B, br), 164.60 (A), 164.8 (D*), 164.88 (B), and 165.26 (C*) (*The assignment may be changable.); ^{19}F NMR δ=−181.80 (F, br d, J=49 Hz), −186.26 (C, dd, J=48 and 26 Hz), −187.26 (A, dd, J=48 and 24 Hz), −187.80 (B, dd, J=50 and 27 Hz), −187.99 (E, d, J=47 Hz), −190.23 (D, dd, J=47 and 9 Hz), and −193.32 (G, dd, J=46 and 13 Hz); IR (neat) 2980, 2148, 1752, 1604, 1086, 1048, 1024, and 1000 cm^{-1}, MS (CI) m/z (rel intensity) 388 (M^++1, 3), 283 (5), 267 (4), 262 (4), 255 (76), 238 (31), 143 (42), 129 (100), 127 (38), and 111 (70). HRMS Found: m/z 388.1381. Calcd for $C_{21}H_{23}FNO_3S+H^+$: M, 388.1381.

4-Fluoro-3-methyl-2-tosylpyrrole (12): Pale yellow crystals, mp 52 °C. ^{1}H NMR δ=2.15 (3H, s), 2.39 (3H, s), 6.67 (1H, t, J=3.7 Hz), 7.27 (2H, m), 7.75 (2H, m), and 9.48 (1H, br s); IR (KBr) 3144, 3010, 2920, 1595, 1506, 1320, 1304, 1204, 1146, 1096, 1084, 1058, and 912 cm^{-1}; MS (EI) m/z (rel intensity) 253 (M^+, 29), 223 (40), 159 (100), 139 (40), 131 (49), 107 (29), 92 (68), and 91 (81). HRMS Found: m/z 253.0571. Calcd for $C_{12}H_{12}FNO_2S$: M, 253.0572.

3-Methyl-4-phenylsulfonyl-2-tosylpyrrole (13): Pale yellow crystals, mp 162—164 °C. ^{1}H NMR δ=2.28 (3H, s), 2.38 (3H, s), 7.25 (2H, m), 7.44—7.57 (3H, m), 7.58 (1H, d, J=3.7 Hz), 7.72 (2H, m), 7.87 (2H, m), and 10.51 (1H, br s); IR (KBr) 2920, 1538, 1448, 1358, 1304, 1180, 1146, and 1088 cm^{-1}; MS (EI) m/z (rel intensity) 376 (M^++1, 22), 375 (M^+, 100), 361 (5), 311 (6), 169 (15), and 139 (24). HRMS Found: m/z 375.0597. Calcd for $C_{18}H_{17}NO_4S_2$: M,

375.0597.

3- Methyl- 4- phenylsulfinyl- 2- tosylpyrrole (14): Pale yellow viscous oil. ^{1}H NMR δ=2.20 (3H, s), 2.40 (3H, s), 7.04 (1H, d, J=3.4 Hz), 7.27 (2H, m), 7.48 (3H, m), 7.60 (2H, m), 7.71 (2H, m), and 10.0 (1H, br s); MS (EI) m/z (rel intensity) 359 (M^+, 31), 342 (43), 311 (32), 204 (20), 187 (100), and 139 (22). HRMS Found: m/z 359.0647. Calcd for $C_{18}H_{17}NO_3S_2$: M, 359.0648.

References

1) "Biomedicinal Aspects of Fluorine Chemistry," ed by R. Filler and Y. Kobayashi, Kodansha Ltd. and Elsevier Biochemical Press, Tokyo and New York (1982).

2) T. Suhara, in "Atarashii Nou No Reseputa," ed by N. Ogawa, Sekai Hoken Tsushinsha, Osaka (1989), Part III, Chap 3.

3) K. Watanabe, T. Fukumura, S. Sasaki, M. Maeda, and S. Takehara, *Chem. Pharm. Bull.*, **39**, 3211 (1991), and references cited therein.

4) For general aspects for fluorination of pyrroles, see: R. A. Jones, in "Comprehensive Heterocyclic Chemistry," ed by A. R. Katritzky and C. W. Rees, Pergamon Press (1984), Vol. 4, Chap. 3.05, p. 213, and for recent preparation of fluoropyrroles based on 1,3-dipolar cycloaddition of azomethine ylides, see: J. Leroy, M. Rubinstein, and C. Wakselman, *J. Fluorine Chem.*, **25**, 255 (1984).

5) A. Suzuki, H. Toi, Y. Aoyama, and H. Ogoshi, *Heterocycles*, **33**, 87 (1992); H. Onda, H. Toi, Y. Aoyama, and H. Ogoshi, *Tetrahedron Lett.*, **26**, 4221 (1985).

6) a) N. Ono, M. Bougauchi, and K. Maruyama, *Tetrahedron Lett.*, **33**, 1629 (1992); b) N. Ono, H. Kawamura, M. Bougauchi, and K. Maruyama, *J. Chem. Soc., Chem. Commun.*, **1989**, 1580; c) D. H. R. Barton and S. Z. Zard, *J. Chem. Soc., Chem. Commun.*, **1985**, 1098; d) A. M. van Leusen, "Lectures in Heterocyclic Chemistry," ed by R. N. Castle and S. W. Schneller, HeteroCoporation, Orem, Utah (1980), Vol. 5, p. S111.

7) A benzenesulfinate ion was reported to leave preferentially from a difluoro(phenylsulfonyl)methanide ion giving difluorocarbene, see: J. Hine and J. J. Porter, *J. Am. Chem. Soc.*, **82**, 6178 (1960).

8) H. Uno, K. Sakamoto, F. Semba, and H. Suzuki, *Bull. Chem. Soc. Jpn.*, **65**, 210 (1992).

9) J. R. McCarthy, D. P. Matthews, M. L. Edwards, D. M. Stemerick, and E. T. Jarvi, *Tetrahedron Lett.*, **31**, 5449 (1990).

10) For a recent report on pyrrole synthesis using tosylmethyl isocyanide, see: D. van Leusen, E. van Echten, and A. M. van Leusen, *J. Org. Chem.*, **57**, 2245 (1992), and extensive references cited therein.

11) A similar electrocyclic ring closure as **9** to **5** under basic conditions was reported: N. Engel and W. Steglich, *Angew. Chem., Int. Ed. Engl.*, **17**, 676 (1978).

12) J. T. Welch and S. Eswarakrishnan, "Fluorine in Bioorganic Chemistry," John Wiley & Sons, New York (1991).

13) N. Ishikawa, T. Kitazume, T. Yamazaki, Y. Mochida, and T. Tatsuno, *Chem. Lett.*, **1981**, 761.

14) K. N. Moore and J. Wemple, *Synthesis*, **1977**, 791. Another preparation of fluoromethyl phenyl sulfide based on the fluoro Pummerer reaction, see: J. R. McCarthy, N. P. Peet, M. E. LeTourneau, and M. Inbasekaren, *J. Am. Chem. Soc.*, **107**, 735 (1985).

15) U. Schöllkopf, D. Hoppe, and R. Jentsch, *Chem. Ber.*, **108**, 1580 (1975).

16) A. M. van Leusen, H. Siderius, B. E. Hoogenboom, and D. van Leusen, *Tetrahedron Lett.*, **1972**, 5337.