A Novel Trimerization of 1-Phenylsulfanyl-2,2,2-trifluoroethyl Isocyanide Giving a Dihydropyrimidine Derivative

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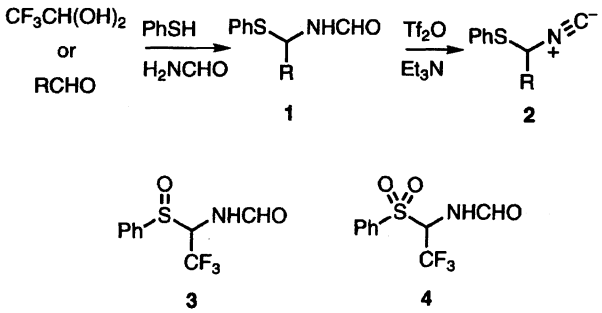
1-Phenylsulfanyl-2,2,2-trifluoroethyl isocyanide (**2a**) readily and selectively trimerized to 4,6-bis(phenylsulfanyl)-1-(1-phenylsulfanyl-2,2,2-trifluoroethyl)-5-(2,2,2-trifluoroethylideneamino)-2-trifluoromethyl-1,2-dihydropyrimidine (**5**) at room temperature, while other α-phenylsulfanyl isocyanides such as phenyl(phenylsulfanyl)methyl isocyanide (**2b**) are stable. Heating of **2b** resulted in formation of the corresponding nitrile as well as diphenyl disulfide and [bis(phenylsulfanyl)methyl]benzene.

Introduction of a trifluoromethyl group into a molecule has attracted much attention in pharmaceutical and agrochemical fields because it often imparts an important bioactivity to the parent molecule. Although many useful methods of direct trifluoromethylation represented by (trifluoromethyl)carcogenonium[1] and trifluoromethyl metallic reagents[2] have been reported, indirect methods using a trifluoromethyl-containing compound as a building block are also very important due to their versatility.[3] We planned to develop trifluoroacetaldehyde hemiacetal compounds for this purpose, because they could be easily prepared from readily available trifluoroacetic acid. During the course of this study, we have found unique trimerization of 1-phenylsulfanyl-2,2,2-trifluoroethyl isocyanide (**2**) to 4,6-bis(phenylsulfanyl)-1-(1-phenylsulfanyl-2,2,2-trifluoroethyl)-5-(2,2,2-trifluoroethylideneamino)-2-trifluoromethyl-1,2-dihydropyrimidine (**5**). In this paper, we will present a detailed characterization of this compound and discuss the reactivity of the related isonitriles.

Results and Discussion

Preparation of Trifluoroacetaldehyde Hemiacetal Derivatives. We tried to introduce nitrogen and sulfur functionalities in the trifluoroethyl compound because the sulfur-containing group might be helpful for the construction of nitrogen-containing heterocycles in the later stage. First, nucleophilic replacement of a chlorine atom of known 1-chloro-2,2,2-trifluoroethyl phenyl sulfide[4] by formamide was attempted and a very trace amount of formamide **1a** was formed. Next, 2,2,2-trifluoro-1,1-ethanediol[5] readily obtained by the reduction of trifluoroacetic acid with $LiAlH_4$ was refluxed in benzene with thiophenol and formamide using a Dean–Stark apparatus (Scheme 1). The desired formamide **1a** was obtained simply, by concentration of the reaction mixture followed by rinsing with EtOAc/hexane. The isolated yield was 61% based on thiophenol. Other formamides **1** could be prepared from the corresponding aldehydes by a similar method in the presence of a catalytic amount of *p*-toluenesulfonic acid (Table 1). In the case of chloral hydrate, however, 2,2,2-trichloroethylidene bisformamide was obtained instead of *N*-(1-phenylsulfanyl-2,2,2-trichloroethyl)formamide.



Scheme 1.

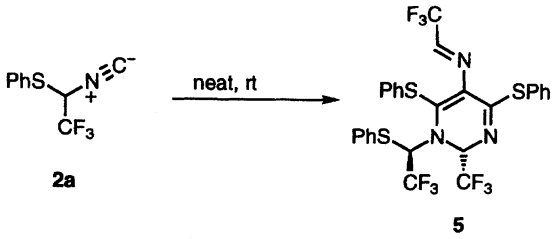
Oxidation of **1a** with one equivalent of dimethyldioxirane gave sulfoxide **3** as a 58 : 19 diastereomeric mixture estimated by ^1H and ^{19}F NMR of the reaction mixture. Chromatographic purification followed by recrystallization gave the major isomer of **3** in 60% yield. The minor isomer of **3**, however, could not be obtained in a pure form and it decomposed and partially isomerized to the major isomer. Exhaustive oxidation of **1a** with dimethyldioxirane gave sulfone **4** in 92% yield. *m*-Chloroperbenzoic acid is less effective and oxidations of **1a** with 3 and 6 equivalents of mCPBA gave

Table 1. Yields of Amide **1** and Isonitrile **2**

	R	Yield / %	
		1	**2**
a	CF_3	61	79
b	Ph	58	71
c	$PhCH_2CH_2$	59	79
d	C_6F_5	56	76

the major isomer of **3** and the sulfone **4** in respective yields of 44 and 33%, probably due to the partial decomposition of the minor sulfoxide during the reaction.

Dehydration of the Formamide 1. Transformation of a formamino group to an isocyano group is usually accomplished by Ugi's methods by using phosphoryl chloride, phosgene, or its equivalents in the presence of a tertiary amine.[6] These methods, however, were not effective for the dehydration of **1a** and decomposition of **1a** occurred to give only diphenyl disulfide as an identifiable product. On the other hand, **1a** was cleanly dehydrated as −78 °C by a powerful method[7] using trifluoromethanesulfonic anhydride and Et_3N to give the isonitrile **2a** as a pale reddish brown oil in 79% yield, which was contaminated with ca. 20% of a by-product. As the R_f values of **2a** and the by-product were very close, the purification of **2a** was attempted by using GPC. The by-product, which proved to be trimer **5** (vide post), was easily obtained in a pure form by the GPC, while concentration of the fractions of **2a** again gave impure **2a** contaminated with the by-product. Nevertheless, structure of **2a** was unambiguously determined by diagnosis of its spectroscopic data [ν_{NC} 2136 cm^{-1} and *m/z* 217 (M^+)]. The formamides **1b—d** were converted to **2b—d** in the similar manner (Table 1), while none of isocyano products was obtained in the cases of **3** and **4**.



2a **5** (1)

When **2a** stood at room temperature for several days, yellow crystals were formed. From the IR analysis of the syrup, the absorption due to the isocyano group almost disappeared. The crystals were isolated in 30% yield by filtration followed by washing with ether/hexane. Spectral data of the crystalline compound were completely different from those of the isonitrile **2a** and showed that the crystals were isomerically pure. GC-MS spectra revealed it to be a trimer of **2a** (M^+ 651 under EI conditions). In the IR spectra, no isocyano, NH, or CO absorption was observed. From $^{13}C\{^1H\}$ and DEPT spectra, three quartets due to the methine carbons adjacent to CF_3 appeared at δ=70.4 (J=32 Hz), 71.2 (J=32 Hz), and 147.4 (J=41 Hz). Two of the three methine hydrogen atoms resonated at δ=6.08 and 6.27 as quartets of J=6.4 and 7.3 Hz, respectively in the ^1H NMR spectra and the last one was found to be hidden in the aromatic proton region at δ=7.62 in CH-COSY. Thus, the trimer has three trifluoroethylidene units, one of which has an sp^2-carbon. Emphasis should be put on the ^{19}F NMR spectra. There were three signals of doublet of quartets, doublet, and quintet at δ=−71.27 (J=7 and 6 Hz), −71.63 (J=3 Hz), and −76.43 (J=6 Hz), respectively. The unexpected coupling should be caused by the through-space mechanism[8] between fluorine atoms. In fact, cross peaks between the trifluoromethyl signals at δ=−71.27 and −76.43 were observed in the ^{19}F–^{19}F COSY spectra. This suggests that these two trifluoromethyl groups are spatially very close to each other. Fortunately, a single crystal with good quality was obtained by recrystallization from toluene. The crystal was subject to X-ray analysis and the structure was solved to be **5** as a racemate in Eq. 1 (One enantiomer is depicted). The molecular drawing of **5** is shown in the Fig. 1 (ORTEP without hydrogen atoms; Table 2). Intramolecular distances between fluorine atoms of the two trifluoromethyl groups are 2.874(8) and 3.040(7) Å which are very close to the double (2.70 Å) of the fluorine van der Waals radius. This must be the reason for the unusually large long-range coupling (^6J coupling).

Although the isonitrile **2a** could be stored in a freezer for a week without the trimerization in a solution of toluene, CH_2Cl_2, or ether, the partial trimerization already occurred even during the purification of the isonitrile **2a**, probably in the condensation steps. The trimerization to **5** was highly stereoselective, judged from the ^{19}F NMR analysis of "purified" isonitrile **2a** which was always contaminated with the trimer to some extent. Signals due to other compound(s) than **2a** and **5** are very weak (less than 1/10 compared to the signals of **5**).

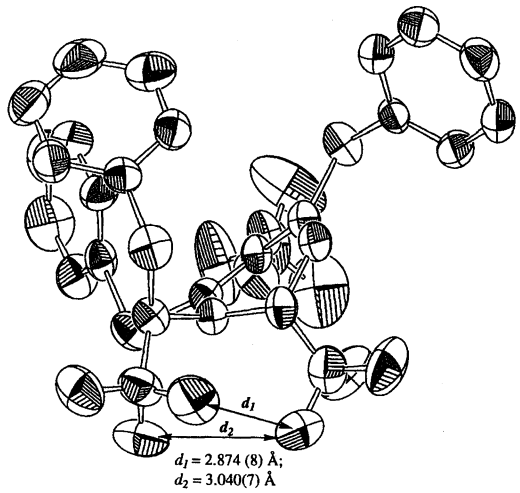
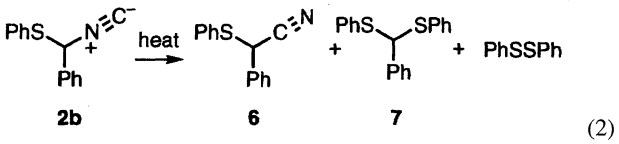


Fig. 1. ORTEP drawing of **5**. Hydrogen atoms are omitted.

Table 2. Crystal Data of the Trimer **5**

Empirical formula	$C_{27}H_{18}F_9N_3S_3$
Formula weight M	651.62
Crystal system	Monoclinic
Space group	$P2_1/c$
Z value	4
R value	0.048
Lattice parameters	
a/Å	9.420 (4)
b/Å	11.678 (4)
c/Å	26.090 (6)
β/°	94.99 (2)
V/Å^3	2859 (3)



2b **6** **7** (2)

Other isonitriles **2b**—**d** were prepared in a similar manner as **2a** but they were stable at room temperature. When the isonitrile **2b** was heated in toluene under reflux for 1.5 h, the starting **2b** was entirely consumed. GC-MS analysis of the reaction mixture revealed no indication of a trimer of **2b**. Products identified in the reaction mixture were nitrile **6**, dithioacetal **7**, and diphenyl disulfide and the isolated yields (column chromatography) based on the phenylsulfanyl moiety were 40, 36, and 22%, respectively (Eq. 2). A similar result was obtained when **2b** was heated without a solvent.

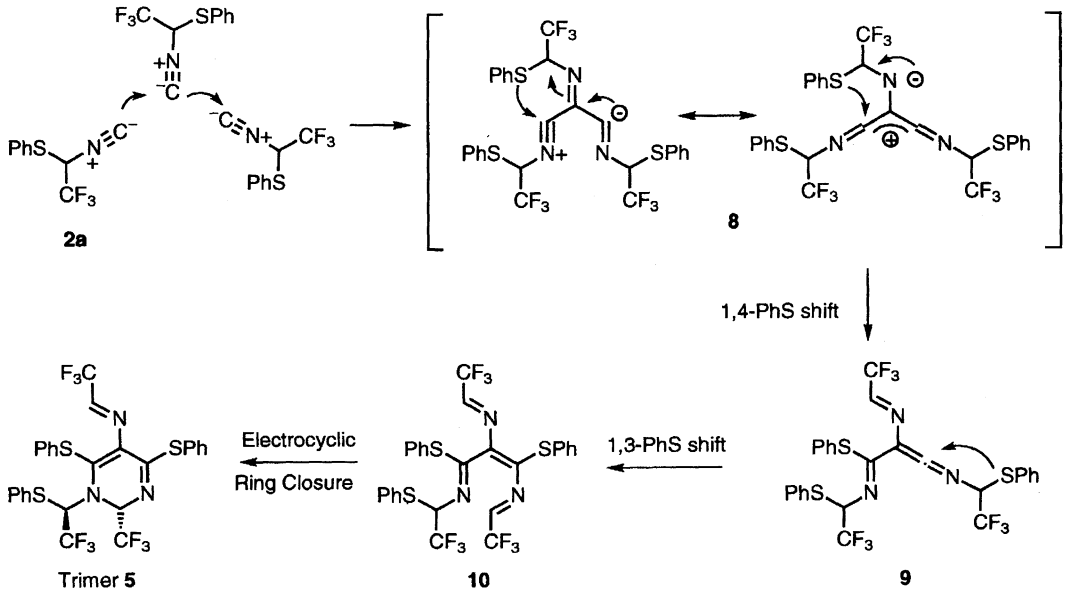
Mechanistic Consideration of the Trimerization. A possible reaction pathway to the trimer **5** is illustrated in Scheme 2. Polyfluorinated isonitriles are known to be thermally unstable and readily oligomerize due to the electron-withdrawing character of fluorine, so generally this reaction is highly dependent upon the bulkiness and electronic character of a monomer.[9] Thus, the isonitrile **2a** may react with itself and the oligomerization would be interfered with probably by steric requirement of the bulky 1-phenylsulfanyl-2,2,2-trifluoroethyl group to give dipole intermediate **8**.[10] 1,4-Migration of the phenylsulfanyl group would take place to afford **9**, which would be subjected to the 1,3-migration of another phenylsulfanyl group to afford diazatriene **10**. 6π-Electrocyclic ring closure of **10** would provide the observed trimer **5**, although the stereochemical course remains unclear.

Experimental

General Details. Melting points are uncorrected. Unless otherwise specified, NMR spectra were obtained with a JEOL-GSX270 or JNM400 spectrometer at ambient temperature by using $CDCl_3$ as a solvent and tetramethylsilane and $CFCl_3$ as internal standards for ^1H, ^{13}C, and ^{19}F. Mass spectra and high resolution mass spectra were measured with a Hitachi M80B-LCAPI spectrometer under the following ionizing conditions: EI (electron impact, 20 eV; 70 eV for HRMS; high boiling perfluorokerosine as a standard) and CI (chemical ionization, 70 eV, isobutane as CI gas). Column chromatography and TLC analysis were carried out using BM-127ZH (Fuji-Davison) and Kieselgel 60 F_{254} (Merk), respectively. Ether and THF were freshly distilled from sodium benzophenone ketyl. Dichloromethane, benzene, toluene, and triethylamine were distilled from CaH_2 under an inert atmosphere. Other commercially available materials were used without further purification.

Typical Procedure for *N*-(1-Phenylsulfanyl-2,2,2-trifluoroethyl)formamide (1a). A solution of 2,2,2-trifluoro-1,1-ethanediol (4.64 g, 40 mmol), thiophenol (2.20 g, 20 mmol) and formamide (1.80 g, 40 mmol) in 50 ml of dry benzene (50 ml) was refluxed with a Dean–Stark apparatus overnight. Removal of the solvent left a crystalline solid. Trituration of the solid with ether/hexane gave 2.87 g (61% based on thiophenol) of pure **1a** as colorless needles: Mp 98—101 °C; R_f 0.5 (40% EtOAc/hexane); ^1H NMR (This compound exists as a mixture of rotational isomers in a solution at ambient temperature in a ratio of 9 : 1.) major isomer: δ=5.86 (1H, dq, J=10.1 and 7.3 Hz, H^1), 6.59 (1H, br, NH), 7.3—7.55 (5H, m, Ar), and 8.11 (1H, s, CHO); typical signals of minor isomer: δ=4.98 (1H, dq, J=10.3 and 7.0 Hz, H^1) and 6.25 (1H, br, NH); ^{13}C NMR major isomer: δ=56.0 (q, J=34 Hz, C1), 123.6 (q, J=281 Hz, C2), 129.5, 129.5, 134.6, 135.8 (ipso), and 159.9 (CHO); a typical signal of minor isomer: δ=162.6 (CHO); ^{19}F NMR major isomer: δ=−74.13 (d, J=8 Hz); minor isomer: δ=−74.3 (d, J=7 Hz); IR (KBr) 3268s, 1666vs, 1262s, 1226s, 1206s, and 1114s cm^{-1}; MS (EI) *m/z* (rel intensity) 235 (M^+; 14) and 110 (100). HRMS Found: *m/z* 235.0278. Calcd for $C_9H_8F_3NOS$: M, 235.0279.

***N*-[Phenyl(phenylsulfanyl)methyl]formamide (1b):** Colorless needles: Mp 141—142 °C; ^1H NMR (This compound exists as a mixture of rotational isomers in a solution at ambient temperature in a ratio of 3 : 1.) major isomer: δ=6.22 (1H, br, NH), 6.60 (1H, d, J=9.5 Hz, H^1), 7.3—7.5 (10H, m, Ar), and 8.11 (1H, s, CHO); minor isomer: δ=5.80 (1H, d, J=10.0 Hz, H^1), 6.22 (1H, br, NH), 7.3—7.5 (10H, m, Ar), and 7.64 (1H, d, J=12.0 Hz, CHO); ^{13}C NMR major isomer: δ=57.6 (C1), 126—138 (Ar), and 159.8



Scheme 2. Possible reaction pathway.

(CHO); typical signals of minor isomer: δ=65.1 (C1) and 162.7 (CHO); IR (KBr) 3268s, 1646vs, 748s, and 694s cm^{-1}; MS (CI) *m/z* (rel intensity) 244 (M^++1; 1), 199 (61), 134 (100), and 111 (83). Found: C, 69.09; H, 5.49; N, 5.75%. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.39; N, 5.76%.

***N*-(3-Phenyl-1-phenylsulfanylpropyl)formamide (1c):** Colorless needles: Mp 92—93 °C; ^{1}H NMR (This compound exists as a mixture of rotational isomers in a solution at ambient temperature in a ratio of 2 : 1.) major isomer: δ=1.95—2.2 (2H, m, H^2), 2.7—2.9 (2H, m, H^3), 5.52 (1H, dt, *J*=9.5 and 6.7 Hz, H^1), 5.89 (1H, d, *J*=9.5 Hz, NH), 7.15—7.45 (10H, m, Ar), and 8.04 (1H, d, *J*=0.6 Hz, CHO); minor isomer: δ=1.95—2.3 (2H, m, H^2), 2.7—2.9 (2H, m, H^3), 4.54 (1H, ddd, *J*=10.7, 8.3, and 5.8 Hz, H^1), 6.05 (1H, t, *J*=11 Hz, NH), and 7.15—7.45 (11H, m, Ar and CHO); ^{13}C NMR δ=32.5 (major C2), 32.2 (minor C2), 36.9 (minor C3), 37.4 (major C3), 54.8 (major C1), 61.3 (minor C1), 126.2, 126.5, 127.9, 128.4, 128.5, 128.7, 129.1, 129.2, 129.4, 132.6, 135.5, 139.6, 140.4, 159.9 (major CHO), and 165.5 (minor CHO); IR (KBr) 3204s, 1658vs, and 754s cm^{-1}; MS (EI) *m/z* (rel intensity) 271 (M^+; 2), 162 (16), 117 (100), and 91 (92). Found: C, 71.00; H, 6.36; N, 5.14%. Calcd for $C_{16}H_{17}NOS$: C, 70.82; H, 6.31; N, 5.16%.

***N*-[Pentafluorophenyl(phenylsulfanyl)methyl]formamide (1d):** Colorless powder: Mp 136—138 °C; ^{1}H NMR (This compound exists as a mixture of rotational isomers in a solution at ambient temperature in a ratio of 7 : 1.) major isomer: δ=6.53 (1H, br, NH), 6.83 (1H, d, *J*=10.0 Hz, H^1), 7.3—7.5 (5H, m, Ar), and 8.12 (1H, s, CHO); minor isomer: δ=6.43 (1H, d, *J*=10.0 Hz, H^1), 6.53 (1H, br, NH), 7.3—7.5 (5H, m, Ar), and 7.52 (1H, d, *J*=12.0 Hz, CHO); ^{13}C NMR δ=49.0 (major C1), 49.1 (minor C1), 128—131, 137.6 (m), 141.3 (m), 144.4 (m), 159.7 (major CHO), and 162.1 (minor CHO); IR (KBr) 3324m, 1660vs, 1526s, and 1506s cm^{-1}; MS (EI) *m/z* (rel intensity) 333 (M^+; 1), 314 (2), 224 (100), 196 (85), 110 (11). Found: C, 50.72; H, 2.54; N, 4.13%. Calcd for $C_{14}H_8F_5NOS$: C, 50.45; H, 2.42; N, 4.20%.

Typical Procedure for Dehydration of 1a. To a solution of formamide **1a** (235 mg, 1 mmol) and triethylamine (0.84 ml, 6 mmol) in dry CH_2Cl_2 (10 ml) was dropwisely added 0.34 ml (2 mmol) of trifluoromethanesulfonic anhydride at −78 °C over 15 min under a nitrogen atmosphere. After the mixture was stirred for 30 min at the temperature, water (10 ml) was added to quench the reaction. TLC analysis of the mixture revealed the existence of a new spot at R_f 0.9 (40% EtOAc) and only **2a** could be detected by the GC-MS analysis. The organic phase was separated and the aqueous phase was extracted with ether (3×10 ml). The combined organic extracts were washed with water (20 ml), sat. aq-$NaHCO_3$ (20 ml), and brine (20 ml), dried over Na_2SO_4, and concentrated. The residual oil was purified by column chromatography on silica gel using 10—30% EtOAc/hexane as an eluent system to give 172 mg (79%) of 1-phenylsulfanyl-2,2,2-trifluoroethyl isocyanide (**2a**) as a pale reddish brown oil, which was already contaminated with ca. 20% of (2*S**)-4,6-bis(phenylsulfanyl)-1-[(1*R**)-1-phenylsulfanyl-2,2,2-trifluoroethyl]-5-(2,2,2-trifluoroethylideneamino)-2-trifluoromethyl-1,2-dihydropyrimidine (**5**) determined from ^{19}F NMR. **2b**: ^{1}H NMR δ=4.97 (1H, q, *J*=5.9 Hz, H^1), 7.35—7.55 (3H, m), and 7.66 (2H, m); ^{13}C NMR δ=60.5 (q, *J*=36 Hz, C1), 121.4 (q, *J*=282 Hz, C2), 129.8, 131.0, 135.0 (ipso), 136.0, and the isocyano carbon is not seen; ^{19}F NMR δ=−73.99 (d, *J*=6 Hz); IR (neat) 2136vs, 1336s, 1256vs, 1198vs, and 1128vs cm^{-1}; MS (EI) *m/z* (rel intensity) 217 (M^+; 33), 197 (13), 148 (9), and 109 (100).

After the oil was left for 3 d, yellow crystals appeared. A small amount of ether was added, followed by hexane and the mixture was filtered to give 52 mg (30%) of **5** as yellow crystals. ^{1}H NMR δ=6.08 (1H, q, *J*=6.4 Hz, H^2), 6.27 (1H, q, *J*=7.3 Hz, $H^{1'}$), 6.66 (2H, m, Ar), and 7.25—7.65 (14H, m, Ar and N=C*H*CF_3); ^{13}C NMR δ=70.4 (q, *J*=32 Hz, C1′), 71.2 (q, *J*=32 Hz, C2), 118.6 (q, *J*=275 Hz, N=CH*C*F_3), 122.4 (q, *J*=282 Hz, PhSCH*C*F_3), 123.3 (q, *J*=289 Hz, 2-*C*F_3), 128.2 (C5), 128.3, 128.4, 129.0, 129.2, 129.2, 129.5, 129.7, 129.9, 130.2, 133.5 (N=*C*HCF$_3$), 135.0, 135.2 (C4), 135.7, 147.4 (q, *J*=41 Hz), and 166.9 (C6); ^{19}F NMR δ=−71.27 (dq, *J*=7 and 6 Hz, 2-C*F*$_3$), −71.67 (d, *J*=3 Hz, N=CHC*F*$_3$), and −76.43 (quint, *J*=6 Hz, PhSCHC*F*$_3$); IR (KBr) 1580s, 1272vs, 1192s, 1168vs, 1132vs, 1110vs, and 1070s cm^{-1}; MS (EI) *m/z* (rel intensity) 651 (M^+; 15), 582 (13), 543 (17), and 191 (100). Found: C, 49.96; H, 2.86; N, 6.53%. Calcd for $C_{27}H_{18}F_9N_3S_3$: C, 49.78; H, 2.78; N, 6.45%.

Phenyl(phenylsulfanyl)methyl Isocyanide (2b): ^{1}H NMR δ=5.83 (1H, s, H^1) and 7.3—7.5 (10H, m); ^{13}C NMR δ=62.7 (C1), 126.3, 128.7, 129.1, 129.3, 129.8, 130.4, 133.9 (ipso), 135.0 (ipso), and 160.6 (NC); IR (neat) 3060m, 2128vs, 1442m, 748vs, and 694vs cm^{-1}; MS (EI) *m/z* (rel intensity) 225 (M^+; 11), 198 (100), and 110 (42).

Phenyl(phenylsulfanyl)propyl Isocyanide (2c): ^{1}H NMR δ=2.16 (2H, m, H^2), 2.86 (2H, m, H^3), 4.51 (1H, t, *J*=7.0 Hz, H^1), and 7.2—7.8 (10H, m); ^{13}C NMR δ=32.0 (C2), 36.8 (C3), 59.1 (C1), 126.6, 128.5, 128.6, 128.7, 129.4, 129.5, 134.6 (ipso), 139.2 (ipso), and 158.9 (NC); IR (neat) 2128vs, 1442m, 750vs, and 702vs cm^{-1}; MS (EI) *m/z* (rel intensity) 253 (M^+; 22), 226 (36), and 117 (100).

Pentafluorophenyl(phenylsulfanyl)methyl Isocyanide (2d): ^{1}H NMR δ=5.98 (1H, s, H^1) and 7.3—7.6 (5H, m); ^{19}F NMR δ=−140.8 (2F, m, ortho), −151.1 (1F, m, para), and −160.3 (2F, m, meta); IR (neat) 2128vs, 1512vs, 1128vs, 1000vs, 920vs, and 746vs cm^{-1}; MS (EI) *m/z* (rel intensity) 315 (M^+; 49), 238 (20), 206 (46), and 109 (100).

Oxidation of 1a with Dimethyldioxirane Giving *N*-(1-Phenylsulfinyl-2,2,2-trifluoroethyl)formamide (3) and *N*-(1-Phenylsulfonyl-2,2,2-trifluoroethyl)formamide (4). To a solution of **1a** (235 mg, 1 mmol) in acetone (5 ml) was added 11.6 ml (1.1 mmol) of 0.095 M solution (1 M=1 mol dm^{-3}) of dimethyldioxirane in acetone[11] at room temperature. After 2 h, the solvent was removed by a rotary evaporator. NMR analysis of the residue revealed existence of the isomeric sulfoxides **3**, sulfone **4**, and the starting material **1a** in a 58 : 19 : 16 : 7 ratio and three spots in TLC (30% EtOAc/hexane; R_f=0.55, 0.3, and 0.15) were observed by UV and ammonium molybdate visualization. Column chromatography on silica gel (30—50% EtOAc/hexane) of the residue gave three fractions corresponding to the TLC spots. From the first fraction, **1a** was recovered in 7% (17 mg) yield and concentration of the second fraction gave 159 mg of a white solid which consisted of the major isomer of sulfoxide **3** and sulfone **4** in a ratio of 21 : 1. The third fraction gave 51 mg of a mixture of isomers of **3** and unidentified compounds in addition to a small amount of sulfone **4**. TLC of this concentrated fraction showed two spots which corresponded to polar two of the three spots in the reaction mixture. Chromatography of this material gave 25 mg of the major sulfoxide **3** with a small amount of sulfone **4** and 14 mg of a mixture. Recrystallization of the combined sulfoxide from ether/hexane gave 150 mg (60%) of an analytically pure **3** as white powdery crystals: Mp 140—141 °C; ^{1}H NMR δ=5.41 (1H, dq, *J*=10.6 and 7.8 Hz, H^1), 7.5—7.6 (5H, m, Ar), 7.97 (1H, br d, *J*=10.6 Hz, NH), and 8.18 (1H, s, CHO); ^{13}C NMR δ=67.7 (q, *J*=32 Hz, C1), 122.6 (q, *J*=282 Hz, C2), 124.0, 129.7, 132.6, 138.8 (ipso), and 160.4 (CHO); ^{19}F NMR δ=−71.28 (d, *J*=8 Hz); IR (KBr) 3188s, 1662vs, and 1126vs cm^{-1}; MS (CI) *m/z* (rel intensity) 252 (M^++1; 14), 206

(5), and 126 (100). Found: C, 43.12; H, 3.19; N, 5.61%. Calcd for $C_9H_8F_3NO_2S$; C, 43.03; H, 3.21; N, 5.58%. The unstable isomer of **3**: ^{1}H NMR (typical signals) δ=5.74 (1H, dq, J=10.7 and 7.3 Hz, H^1) and 8.31 (1H, s, CHO); ^{19}F NMR δ=−67.87 (d, J=8 Hz).

To a solution of **1a** (470 mg, 2 mmol) in acetone (10 ml) was added 57 ml (4.7 mmol) of 0.083 M solution of dimethyldioxirane in acetone at room temperature and the mixture was stirred for 30 min. After removal of the solvent, the residue was chromatographed on silica gel (30—50% EtOAc/hexane) to give 490 mg (92%) of sulfone **4** as white crystals: Mp 111—112 °C; ^{1}H NMR δ=5.86 (1H, dq, J=10.7 and 7.0 Hz, H^1), 6.95 (1H, br d, J=10.7 Hz, NH), 7.62 (2H, m, Ar), 7.76 (1H, m, Ar), 7.97 (2H, m, Ar), and 8.24 (1H, s, CHO); ^{13}C NMR δ=66.2 (q, J=33 Hz, C1), 121.1 (q, J=283 Hz, C2), 129.3, 129.7, 135.4, 136.0 (ipso), and 160.1 (CHO); ^{19}F NMR δ=−68.70 (d, J=7 Hz); IR (KBr) 3192 s, 1672vs, 1350s, 1330s, 1280s, 1200s, and 1158vs cm^{-1}; MS (CI) m/z (rel intensity) 268 (M^++1; 40), 183 (9), and 143. Found: C, 41.01; H, 3.15; N, 5.20%. Calcd for $C_9H_8F_3NO_3S$; C, 40.45; H, 3.02; N, 5.24%.

X-Ray Analysis. A yellow hexagonal crystal of **5** having approximate dimensions of 0.500×0.230×0.180 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo $K\alpha$ radiation and a 12 kW rotating anode generator. Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $24.18<2\theta<29.32°$ corresponded to a monoclinic cell with dimensions: a=9.420(4), b=11.678(4), c=26.090 Å, β=94.99(2)°, and V=2859(3) Å^3. For Z=4 and FW=651.62, the calculated density is 1.513 g cm^{-3}. Based on the systematic absences of $h0l$ ($l\neq 2n$) and $0k0$ ($k\neq 2n$) and the successful solution and refinement of the structure, the space group was determined to be $P2_1/c$ (#14). The data were collected at a temperature of 25±1 °C using the ω scan technique to a maximum 2θ value of 55.1°. Omega scans of several intense reflections, made prior to data collection, had an average width at half-weight of 0.20° with a taking-off angle of 6.0° min^{-1} (in omega). The weak reflections [$I<10.0\sigma(I)$] were rescanned (maximum of 2 rescans) and the counts were accumulated to assure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 1.0 mm and the crystal to detector distance was 25.8 cm. Of the collected 7304 reflections, 6895 were unique (R_{int}=0.045). An empirical correction for the absorption was made based on azimuthal (Ψ) scans of three reflections.[12] The structure was solved by the direct method using MITHRIL program.[13] The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were refined isotropically. Rotation of the trifluoromethyl group in trifluoroethylideneamino unit was solved as a disordered structure. Calculations were carried out on a VAX station 3200 computer with TEXSAN programs[14] which used the atomic scattering factors taken from "International Tables for X-Ray Crystallography".[15] The final cycle of full-matrix least-squares refinement yields R=0.048, R_w=0.047 and goodness-of-fit=1.56 for 2005 observed reflections [$I>3.00\sigma(I)$] and 480 variable parameters. The final atomic parameters are deposited as Document No. 69032 at the Office of the Editor of Bull. Chem. Soc. Jpn.

References

1) T. Umemoto and S. Ishihara, *Tetrahedron Lett.*, **31**, 3579 (1990).

2) G. S. K. Prakash, R. Krishnamurti, and G. Olah, *J. Am. Chem. Soc.*, **111**, 393 (1989); G. P. Stahly and D. R. Bell, *J. Org. Chem.*, **54**, 2873 (1989); Y. Kobayashi, K. Yamamoto, and I. Kumadaki, *Tetrahedron Lett.*, **20**, 4071 (1979); C. Francèse , M. Tordeux, and C. Wakselman, *J. Chem. Soc., Chem. Commun.*, **1989**, 642; T. Kitazume and N. Ishikawa, *J. Am. Chem. Soc.*, **107**, 5186 (1985).

3) For a review, see: K. Uneyama, *Yuuki Gosei Kagaku Kyokai Shi* (*J. Syn. Org. Chem.*), **49**, 612 (1991).

4) K. Uneyama, M. Momota, K. Hayashi, and T. Itoh, *J. Org. Chem.*, **55**, 5364 (1990).

5) D. R. Husted and A. H. Ahlbrecht, *J. Am. Chem. Soc.*, **74**, 5422 (1952).

6) S. R. Sandler and W. Karo, "Organic Functional Group Preparations," Academic Press, New York (1972), Vol. 3, p. 179.

7) J. E. Baldwin and I. A. O'Neil, *Synlett*, **1990**, 603.

8) J. Hilton and L. H. Sutcfiffe, *Prog. Nucl. Magn. Reson. Spectrosc.*, **10**, 27 (1975).

9) D. Lentz, *Angew. Chem., Int. Ed. Engl.*, **33**, 1315 (1994); D. Lentz, I. Brüdgam, and H. Hartl, *Angew. Chem., Int. Ed. Engl.*, **26**, 921 (1987).

10) Arylidenecarbenes and carbenoids were reported to undergo oligomerization to form butatrienes and/or radiarenes depending upon the electronic character, steric demand, and generation methods including metal additives, see: H. Hopf and G. Mass, *Angew. Chem., Int. Ed. Engl.*, **31**, 931 (1992).

11) J. K. Crandall, D. J. Batal, D. P. Sebesta, and F. Lin, *J. Org. Chem.*, **56**, 1153 (1991).

12) A. C. T. North, D. C. Phillips, and F. S. Mathews, *Acta Crystallogr., Sect. B*, **B36**, 575 (1980).

13) G. J. Gilmore, *J. Appl. Crystallogr.*, **17**, 42 (1984).

14) "TEXSAN-Texray Structure Analysis Package, Version 5.0," Molecular Structure Corporation, The Woodlands, TX. 77381 (1989).

15) "International Tables for X-Ray Crystallography," Kynoch Press, Birmingham (1974), Vol. IV, p. 71.