

Novel Synthesis of Fluorinated Vinyl 1,2-Bis-Sulfides¹

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Although many efforts to develop new synthetic methodologies in organofluorine chemistry have been devoted in recent years, there are still many synthetic limitations to prepare the fluoroorganic compounds some of which may possess biological properties. Among them, synthetic routes to alkylthio or arylthio substituted fluoroolefins,²⁻¹⁰ which are very useful synthetic intermediates and potential enolate equivalents, have been quite restricted. In particular, there are only limited reports on the synthesis of fluorinated vinyl bis-sulfides and most of these methods refer to the synthesis of 1,1-bis-sulfides.^{2,5,9} On the other hand, only one example² has been reported on the preparation of fluorinated vinyl 1,2-bis-sulfides, but this method lacks generality and efficiency. The scarcity of general synthetic methods for the preparation of fluorinated vinyl 1,2-bis-sulfides and of their synthetic utilities prompted us to exploit new synthetic routes to those compounds, because these compounds would be useful and versatile synthetic intermediates for the preparation of new fluoroorganic compounds.

Recently, we have developed a general and an efficient method for the synthesis of perfluoroalkylated dithioketals.¹¹ As a part of our continuing studies on the chemistry and application of perfluoroalkylated dithioketals **1**, we have found that **1** was smoothly reacted with arylthio or alkylthio anions under mild condition to provide fluorinated vinyl 1,2-bis-sulfides **2**. We herein wish to report our preliminary results on the synthesis of **2**.

Initially, we began our studies by examining the reaction of **1** with two electron transfer reagents,¹² such as lithium naphthalenide (LN), lithium biphenylide (LB), and so on, because β,β -perfluoroalkylated vinyl sulfides (II), which are precursors of **2**, can be generated *via* β -defluorination of carbanion I bearing perfluoroalkyl group which may be prepared from the reaction of **1** with two electron transfer reagents. It has been well known that the reaction of nonfluorinated dithioketals with lithium di-*tert*-butylbiphenylide (LDBB)¹³ resulted in the formation of carbanions *via* cleavage of carbon-sulfur bond.¹⁴

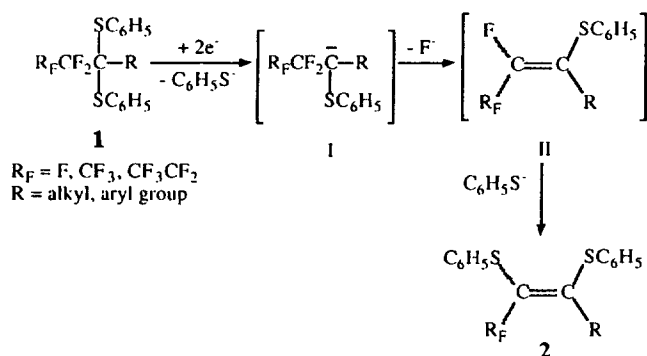


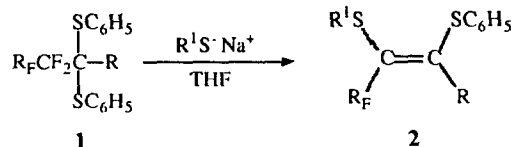
Table 1. Reactions of 1,1-Bis(phenylthio)-2,2,2-trifluoroethylbenzene **1a** with Electron Transfer Reagents

Entry No.	R ¹ M (eq.)	T (°C)	Yield (%) ^{a,b}
1	LB (2.5)	25	31 ^c
2	LN (2.5)	25	33 ^d
3	LN (3.5)	25	35 ^e
4	LN (4.5)	25	38
5	LN (4.5)	-78→25	51
6	LB (4.5)	-78→25	49
7	LDBB (4.5)	-78→25	43
8	SmI ₂ (4.5)	-78→25	NR ^f
9	C ₆ H ₅ S ⁻ Na ⁺ (2.5)	0→25	98

^a Isolated yield. ^b All products are *E* & *Z* isomeric mixtures. ^c Starting material (47%) was recovered. ^d Starting material (48%) was recovered. ^e Starting material (22%) was recovered. ^f No reaction.

When the reaction of **1a** (1 eq.) with LB (2.5 eq.) was carried out at 25°C, corresponding 1,2-bis-sulfides **2a** was isolated in 31% yield based on 53% conversion of the starting material. The use of LN (2.5 eq.) instead of LB (2.5 eq.) did not give any different result. However, the use of more excess of LN (4.5 eq.) in this reaction caused not only to increase the isolated yield (38%) of **2a**, but also to complete the reaction. To optimize the reaction condition, the reaction was performed at lower temperature. Therefore, **1a** was reacted with LN (4.5 eq excess) at -78 °C, followed by slow warming to room temperature, to afford **2a** in 51% isolated yield. The reaction of **1a** with LDBB, which is a stronger electron transfer reagent than LB or LN, did not bring about the improvement of yield of **2a**. To our surprise, SmI₂ did not initiate the reaction at all even at higher temperature. Finally, we found that the reaction of **1a** with sodium thiophenoxide at 0°C, followed by warming to room temperature, provided **2a** in almost quantitative yield. The reaction was clean and was completed in one hour. The results of these reactions are summarized in Table 1.

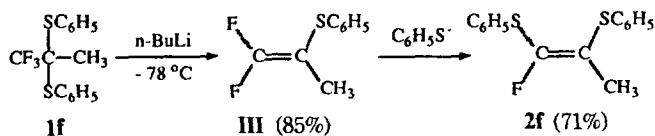
We performed the reaction of **1a** with other types of thio anions under the same reaction condition. Therefore, **1a** was reacted with allylthio and alkylthio anion to afford the corresponding 1,2-bis-sulfides **2b** and **2c** in 92% and 93% yields, respectively. When the reaction of 1,1-bis(phenylthio)-2,2,3,3,3-pentafluoropropylbenzene **1d** with sodium thiophenoxide was performed under the employed reaction condition, corresponding 1,2-bis-sulfide **2d** was obtained in 94% yield. In contrast, a prolonged time (3 days) was needed in the reaction of 1,1-bis(phenylthio)-2,2,3,3,4,4,4-heptafluorobutylbenzene **1e** with sodium thiophenoxide to give corresponding 1,2-bis-sulfide **2e** in 60% yield. This result indicated that β -fluoro- β -pentafluoroethylvinyl sulfide, possible precursor of **2e**, was very reluctant to react with thiophenoxide probably due to steric hindrance between pentafluoroethyl group and

Table 2. Reactions of Perfluoroalkylated Dithioketals **1** with Allylthio, Alkylthio, and Phenylthio Anions

Compound No.	R _f	R	R ¹	Yield(%) ^{a,b}
2a	F	C ₆ H ₅	C ₆ H ₅	98
2b	F	C ₆ H ₅	CH ₂ =CHCH ₂	92
2c	F	C ₆ H ₅	<i>n</i> -C ₃ H ₇	93
2d	CF ₃	C ₆ H ₅	C ₆ H ₅	94
2e	CF ₃ CF ₃	C ₆ H ₅	C ₆ H ₅	60 ^c
2f	F	CH ₃	C ₆ H ₅	NR ^d

^a Isolated yield. ^b All products are *E* & *Z* isomeric mixtures. ^c The reaction took 3 days. ^d No reaction.

thiophenoxide in addition step. Finally, no reaction occurred between 1,1,1-trifluoro-2,2-bis(phenylthio)propane **1f** and sodium thiophenoxide. However, 1-methyl-2-fluorovinyl 1,2-bisulfide **2f** can be prepared from the reaction of β,β-difluorovinyl sulfide (III), which was obtained in 85% yield from the reaction of **1f** with *n*-BuLi at -78°C, with sodium thiophenoxide at room temperature. The results of these reactions are summarized in Table 2.



Since thiophenoxide ion has been known as electron-transfer reagent in many reactions,^{15,16} it is necessary to clarify the reaction pathway, *p*-Dinitrobenzene (*p*-DNB), which is a powerful one-electron acceptor and thus inhibits the electron-transfer process, was used in the reaction of **1a** with sodium thiophenoxide. If this reaction involved the electron-transfer process, the use of *p*-DNB would inhibit the electron-transfer process and no reaction should be observed. However, the reaction of **1a** with sodium thiophenoxide in the presence of *p*-DNB (1 eq.) at 25°C resulted in the formation of **2a** in 97% yield. This result indicated that the reaction of **1a** with sodium thiophenoxide did not involve the electron-transfer process. Therefore, thiophenoxide ion may attack phenylthio group of dithioketals to form carbanion I bearing perfluoroalkyl group, which quickly undergoes β-defluorination to afford β,β-perfluorinated vinyl sulfides (II). Then, intermediates II undergo addition reaction with another one equivalent of thiophenoxide anion, followed by β-defluorination to give fluorinated vinyl 1,2-bisulfides **2**.

In a typical procedure, a 50 ml two-neck flask, equipped with a septum, a magnetic stirring bar, and a nitrogen tee connected to a source of nitrogen, was charged with NaH

(60% dispersion in mineral oil, 0.20 g, 5.0 mmol). After washing NaH with pentane twice and drying, 10 ml dry THF was added and then the mixture was cooled to 0°C by using an ice bath. Thiophenol (0.53 g, 4.8 mmol) was added dropwise at 0°C and the mixture was stirred at 0°C for 30 min. 1,1-Bis(phenylthio)-2,2,2-trifluoroethylbenzene (0.75 g, 2.0 mmol) dissolved in 4 ml dry THF was added at 0°C and then the mixture was warmed slowly to room temperature. After stirring at room temperature for 1 hour, the mixture was quenched with H₂O (20 ml), extracted with ether (30 ml×2), and the ether layers dried with anhydrous MgSO₄. Column chromatography (hexane) provided 0.66 g (98% yield) of 1,2-bis(phenylthio)-1-phenyl-2-fluoroethene **2a**: oil; ¹H-NMR (CDCl₃) 7.60-7.00 (m, 15H); ¹⁹F-NMR (standard vs CF₃COOH) 5.35 (s), 6.05 (s) (*E* & *Z* isomers); IR (neat) 3050, 1580, 1475, 1440, 1100, 1070, 1025, 740, 690 cm⁻¹; MS, *m/e* (relative intensity) 338 (100, M⁺), 229 (65), 196 (28), 185 (17), 165 (30), 152 (15), 121 (20), 77 (13).

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