Organofluorine sulfur-containing compounds

3.* Preparation of difluoromethylpolyfluoroaryl sulfides. Reactions of difluoromethylpentafluorophenyl sulfide with oxidants

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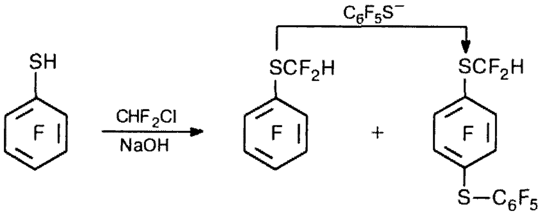
Polyfluorinated aryldifluoromethyl sulfides have been obtained by treatment of polyfluorinated 4-X-substituted thiophenols with chlorodifluoromethane in an alkaline medium. Reactions of difluoromethylpentafluorophenyl sulfide with H_2O_2, $KMnO_4$, and HNO_3, giving the corresponding sulfoxide and sulfone, were studied.

Key words: polyfluorinated thiophenols, difluorochloromethane, reactions; aryldifluoromethyl sulfides, oxidation.

Phenol, thiophenol, and their derivatives react with chlorodifluoromethane as a source of difluorocarbene in alkaline media to give aryldifluoromethyl ethers and aryldifluoromethyl sulfides.[2,3] The interaction of pentafluorophenol with chlorodifluoromethane under similar conditions results in difluoromethyl pentafluorophenyl ether.[4] With the purpose of expanding knowledge on the reactions of functional derivatives of polyfluoroarenes with dihalocarbenes and synthesizing polyfluorinated arylmethyl sulfides, it seemed interesting to study the possibility of using polyfluorinated thiophenols in transformations of this type.

In the present work we studied the reactions of polyfluorothiophenols with chlorodifluoromethane in an alkaline medium. We showed that the reaction of pentafluorothiophenol with chlorodifluoromethane in the presence of an alkali at 45 °C results in difluoromethyl(pentafluorophenyl) sulfide (**1**) as the main product, along with a small amount of 4-(difluoromethylthio)nonafluorodiphenyl sulfide (**2**). However, even a small increase in temperature (60 °C) results in the formation of compound **2** in a considerable amount (Table 1).



1 **2**

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* For Part 2, see Ref. 1.

Table 1. Conditions of the reactions of 4-X-substituted polyfluorothiophenols with chlorodifluoromethane. Physicochemical properties of the resulting difluoromethyl(polyfluoroaryl) sulfides

X	Amounts of the reagents				Time of passing CHF_2Cl/h	T_{exp} /°C	Products			
	4-X-C_6F_4SH /g	NaOH /g	H_2O /mL	Dioxane /mL			Yield/g (%)	B.p./°C (14—16 Torr)	Mol. mass, found calculated	Empirical formula
F	19.91	10.01	36	42	3.3	45	21.92 (89)*	46	249.9697 249.9687	C_7HF_7S
F	79.91	41.98	126	149	3.6	60	46.42 (47)**	46		
H	19.69	10.01	36	42	2.2	45	30.14 (92)	43	231.9784 231.9795	$C_7H_2F_6S$
CF_3	60.18	31.00	56	132	3.0	45	72.18 (96)	50	299.9655 299.9655	C_8HF_9S

* The yield of sulfide **2** was 7 %. ** The yield of sulfide **2** was 48 %.

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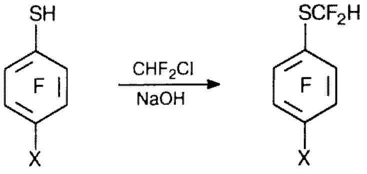
Sulfide **2** is probably a product of the reaction between compound **1** and the pentafluorophenylthiolate anion. As shown in separate experiments, sulfide **1** reacts with NaOH and C_6F_5SH in aqueous dioxane to give compound **2**.

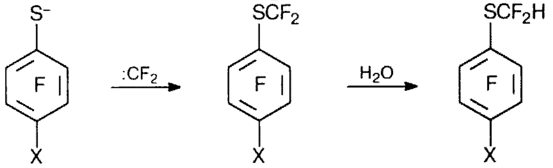
In order to reveal the relation between the reactions leading to formation of difluoromethylpolyfluoroaryl sulfides, we also studied the interaction of 2,3,5,6-tetrafluorothiophenol and 2,3,5,6-tetrafluoro-4-trifluoromethylthiophenol with chlorodifluoromethane. In both cases, the reactions occur similarly to give difluoromethyl-2,3,5,6-tetrafluorophenyl sulfide (**3**) and difluoromethyl(*p*-heptafluorotolyl) sulfide (**4**), respectively.



X = H (**3**), CF_3 (**4**) **3, 4**

The formation of compounds **1**, **3**, and **4** can be represented similarly to the scheme suggested for the reactions of phenol, thiophenol, their derivatives, and pentafluorophenol with chlorodifluoromethane.[2—4]

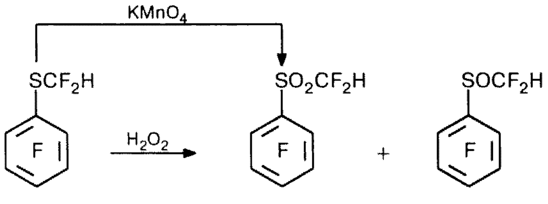
$$HCF_2Cl \longrightarrow :CF_2$$



X = F, H, CF_3

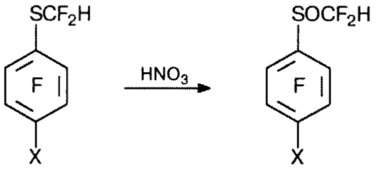
Treatment of chlorodifluoromethane with an alkali generates difluorocarbene, which reacts with the polyfluorophenylthiolat anion to give the (polyfluorophenylthio)difluoromethyl anion. The latter adds a proton to yield difluoromethyl(polyfluorophenyl) sulfide.

We studied some chemical properties of difluoromethyl(polyfluoroaryl) sulfides, in particular, their reactions with oxidants. The oxidation of compound **1** with hydrogen peroxide in acetic acid results in difluoromethyl(pentafluorophenyl)sulfone (**5**) along with difluoromethyl(pentafluorophenyl)sulfoxide (**6**). The reaction of compound **1** with $KMnO_4$ gives only sulfone **5**.



1 **5** **6**

It is known that treatment of sulfides with HNO_3 affords sulfoxides.[5] In view of this, we studied the reaction of sulfide **1** with HNO_3 and showed that it yields compound **6** without sulfone **5**. A similar reaction of compound **3** results in difluoromethyl(2,3,5,6-tetrafluorophenyl)sulfoxide (**7**).



1, 3 **6, 7**

X = F (**1, 6**), H (**3, 7**)

The structures of the compounds obtained were established using high resolution mass spectrometric and ^{19}F and ^1H NMR spectral data (Tables 1—3).

Experimental

^{19}F and ^1H NMR spectra were recorded on a Bruker WP-200SY instrument (~10 mol. % solutions in CCl_4 and $CDCl_3$; C_6F_6 and $SiMe_4$ as internal standards, respectively). Mass spectra were obtained on a Finnigan MAT 8200 mass spectrometer (temperature of the inlet system 70—110 °C; energy of ionizing electrons ~70 eV). Mass spectra were used for determining the exact molecular weights and the molecular formulas of the compounds. GLC analyses were performed on an LKhM-72 instrument (a thermal conductivity detector, linear programming of the temperature (10 °C min^{-1}), 4000×4 mm columns filled with SKTFV-803 silicone (*A*), SKTFT-50 silicone (*B*), or QF-1 fluorosilicone (*C*) on Chromosorb W, ratio of the amounts of the fixed phase and the solid carrier 15 : 100, column temperature 50—250 °C, detector temperature 250 °C, feed rate of the carrier gas (He) 10 mL min^{-1}).

Synthesis of difluoromethyl(polyfluoroaryl)sulfides (general procedure). Polyfluorothiophenol was added dropwise with stirring to a solution of NaOH in aqueous dioxane, and then chlorodifluoromethane was added at a rate of 3 L h^{-1}. After the reaction ceased, the mixture was acidified with HCl to pH < 1

Table 2. ^{19}F and ^1H NMR spectra of difluoromethyl(polyfluoroaryl)sulfides and their derivatives

Compound	δ ^{19}F				δ ^1H	
	F(2), F(6)	F(3), F(5)	F(4)	CF_2H	CF_2H	H(4)
1	32.7	2.2	14.4	70.7	6.82	—
2*	32.7	30.6	—	70.9	6.89	—
3	31.1	25.1	—	70.7	6.90	7.24
4**	33.5	23.4	—	71.2	6.98	—
5	29.9	4.6	22.8	39.6	6.32	—
6	25.6	4.4	18.9	43.8, 46.7	6.77	—
7	27.4	24.4	—	43.5, 47.1	6.82	7.37

* For the pentafluorophenyl ring of compound **2**, δ: 29.7 (F_o); 2.3 (F_m); 12.7 (F_p). ** δ CF_3 105.1.

Table 3. Spin-coupling constants (J) in difluoromethyl(polyfluoroaryl)sulfides and their derivatives

Compound	J/Hz						
	F(α)—H	F(α)—F(2)	F(4)—F(3)	F(4)—F(2)	H(4)—F(3)	H(4)—F(2)	F(α)—F(α)
1	56	4.5	20.5	4.0	—	—	—
2	57	4.5	21.0	3.5	—	—	—
3	56	4.0	—	—	9.5	7.5	—
4*	56	4.5	—	—	—	—	—
5	53	5.0	20.5	9.0	—	—	—
6	55	5.0	20.5	6.0	—	—	268
7	55	4.5	—	—	9.0	7.5	270

* $J_{CF_3-F_o}$ = 22.5 Hz.

and distilled with steam. The organic layer was separated, washed with aqueous Na_2CO_3 and water, dried with $MgSO_4$, and analyzed by GLC (columns *A* and *B*). The precipitate that remained after distillation was filtered off and washed with water. The product was distilled *in vacuo* (except sulfide **2**, which was recrystallized). The results are presented in Table 1.

Reaction of sulfide 1 with pentafluorothiophenol. Pentafluorothiophenol (1.60 g, 0.008 mol) was added to a solution of NaOH (1.56 g, 0.039 mol) in 55 % aqueous dioxane (11 mL). Sulfide **1** (2.00 g, 0.008 mol) was added dropwise over a period of 10 min; the mixture was kept for 2 h at 40 °C, acidified with concentrated HCl to pH < 1, and distilleld with steam to give 3.10 g of a product containing 97 % of sulfide **2** (according to GLC on column *B*). Yield 87 %, m.p. 45—47 °C (from pentane). Found: M = 429.9338. $C_{13}HF_{11}S_2$. Calculated: M = 429.9344.

Reaction of compound 1 with H_2O_2. Compound **1** (4.20 g, 0.017 mol) was added dropwise to a mixture of glacial acetic acid (70 mL) and 33 % H_2O_2 (15.5 mL). The mixture was heated to 105—110 °C and vigorously stirred for 15 h at the same temperature. The acetic acid was distilled off. The residue was neutralized with aqueous Na_2CO_3 and extracted with chloroform; the extract was dried with $MgSO_4$. The sovlent was distilled off to give 3.62 g of a mixture containing (according to GLC on column *B*) 72 % of sulfone **5** and 24 % of sulfoxide **6**.

Reaction of compound 1 with $KMnO_4$. Compound **1** (5.16 g, 0.021 mol) in acetic acid (30 mL) was added dropwise to a mixture of acetic acid (120 mL) and $KMnO_4$ (6.94 g, 0.044 mol). The mixture was kept for 18 h at 25 °C and treated with aqueous solutions of Na_2SO_3 and Na_2CO_3. The precipitate was filtered off, and the aqueous solution was extracted with chloroform. The solvent was distilled off to give 4.70 g of a product containing 96 % of compound **5** (according to GLC on column *B*). Yield 78 %, m.p. 58 °C (sublimation at 45 °C/10 Torr). Found: M = 281.9585. $C_7HF_7O_2S$. Calculated: M = 282.1318.

Reactions of compounds 1 and 3 with HNO_3. ***A.*** Compound **1** (24.35 g, 0.092 mol) was added dropwise to freshly distilled HNO_3 (~100 %, 80 mL). The mixture was kept for 32 h at 40 °C. Excess HNO_3 was distilled off *in vacuo*; the residue was poured into $CHCl_3$ and washed with aqueous Na_2CO_3 until neutral pH was attained. The organic phase was separated and dried with $CaCl_2$. The solvent was distilled off to give 26.13 g of a product containing 98 % of compound **6** (according to GLC on column *B*). Yield 98 %. Found: M = 265.9659. C_7HF_7OS. Calculated: M = 266.1328.

B. Compound **3** (1.16 g, 0.005 mol) was added dropwise to freshly distilled HNO_3 (~100 %, 4.2 mL). The mixture was kept for 20 h at 50 °C, poured onto ice, and extracted with chloroform. The extract was dried with $MgSO_4$. The solvent was distilled off to give 0.52 g of a product containing 91 % of compound **7** (according to GLC on column *C*). Yield 40 %. Found: M = 248.0050. $C_7H_2F_6OS$. Calculated: M = 248.1424.

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