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Synthesis of Chloropolyfluoroarenes from Polyfluoroarenethiols and PCl_5

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Abstract—Replacement of the thiol group in polyfluoroarenethiols with chlorine was performed by treating with PCl_5 as chlorinating agent. By heating in ampules at 200–220°C polyfluoro- and polyfluorochloroarenethiols with PCl_5 mono- and dichloropolyfluoroarenes and also 1,2,4-trifluorotrichlorobenzene were synthesized. Dichloropolyfluoroarenes contain chlorine atoms in *ortho*- and *para*-positions.

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It is known that thiol group in aliphatic thiols can be substituted by chlorine atom in mild conditions under the action of chlorinating agents and triphenylphosphine. For instance, in reactions of these thiols with CCl_4 and triphenylphosphine the corresponding chloroalkanes are obtained [1, 2]. The configuration inversion is observed in the process [1]. In patent [2] the ionic mechanism of such transformation was suggested. At the same time the substitution of the thiol group with chlorine in butanethiol under the treatment with CCl_4, triethyl phosphite, and benzoyl peroxide was described. The process evidently involved radical intermediates [3].

Aliphatic thiols were converted in chloroalkanes in reactions with chlorocarbonylsulfenyl chloride and triphenylphosphine. Therewith the reaction between thiols and chlorocarbonylsulfenyl chloride first provided in high yields alkyl chlorocarbonyl disulfides and then these compounds reacted with triphenylphosphine with the formation of chloroalkanes [4].

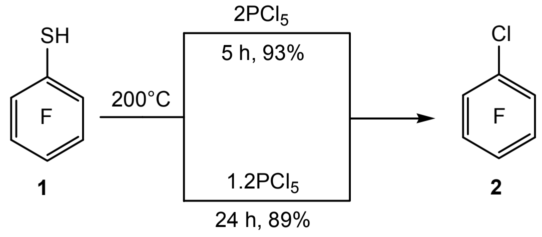
A method providing haloalkanes in high yields was developed applying the reaction of thiols with *N*-chlorosuccinimide and triphenylphosphine. The process was believed to occur with the participation of an intermediately generated quaternary phosphonium salt containing an alkyl sulfide group. This salt via S_N2 reaction with the chloride anion gives the chloroalkane [5].

The thiol group in aliphatic thiols may also be substituted by chlorine atom in mild conditions under treatment with sulfuryl chloride and triphenylphosphine [6]. First the aliphatic thiols are processed with sulfuryl chloride then follow the reaction of intermediately generated sulfenyl chloride with triphenylphosphine affording the chloroderivative. A similar process occurred with dialkyl disulfide. In the aromatic series for this system only the transformation is described of benzenethiol, diphenyl disulfide, and *para*-thiocrezole into chlorobenzene and *para*-chlorotoluene in low yields [6]. Still et al. mentioned in this publication a very limited possibility of such type transformations in aromatic compounds compared to aliphatic series and in this connection did not suggest any considerations on the reaction mechanism in the aromatic compounds.

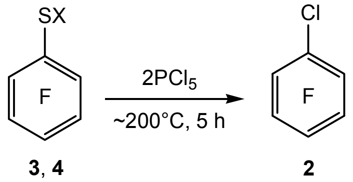
Recently we developed a convenient method of introducing chlorine atoms into polyfluoroarenes by thermal replacement of a thiol group for a chlorine atom. The thiol function is easily and selectively introduced into polyfluoroarenes by reactions of nucleophilic substitution [7, 8]. By this method a series of chloropolyfluoroaromatic compounds was synthesized in high yields [7, 8]. This reaction proceeds at high temperatures (~400°C) in a flow system.

In the present study the selective substitution of thiol group in polyfluoro- and polyfluorochloroarenethiols by the chlorine atom using PCl_5 as chlorineting reagent is described. This process occurs at ~200°C.

By heating of pentafluorobenzenethiol **1** with ~1 mole of PCl_5 in an ampule at ~200°C during 5 h the substitution of the thiol group for the chlorine atom occurs while the reaction mixture contains along with chloropentafluorobenzene **2** bis(pentafluorophenyl) disulfide **3** and pentafluorobenzenesulfenyl chloride **4** (ratio of **2**–**3**–**4** ~83 : 9 : 8, according to ^{19}F NMR data). By increasing the time of the reaction to 16 h the fraction in the reaction mixture of compound **2** grows and the fractions of compounds **3** and **4** decrease (ratio of **2**–**3**–**4** ~91 : 5 : 4, according to ^{19}F NMR data). After heating for 24 h we managed to obtain almost individual arene **2** in 89% yield. This may prove that ~1 mole of PCl_5 is sufficient for the use in the reaction, however it requires longer heating compared to reaction of compound **1** with 2 moles of PCl_5. In this case the reaction takes 5 h and leads to practically individual compound **2** in a high yield.

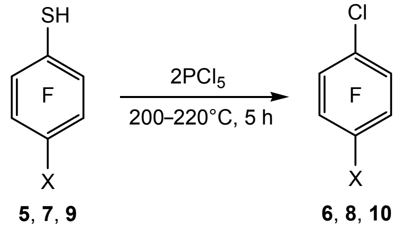


By heating compounds **3** and **4** with PCl_5 chloroarene **2** was also obtained.



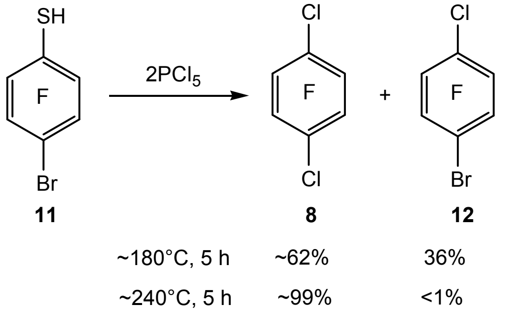
X = SC_6F_5 (**3**), Cl (**4**).

In similar way reactions of *para*-substituted thiol **1** derivatives proceed. Hence, by heating 2,3,5,6-tetrafluorobenzenethiol **5** with PCl_5 we obtained 1-chloro-2,3,5,6-tetrafluorobenzene **6**, and from 4-chlorotetrafluorobenzenethiol **7**, 1,4-dichlorotetrafluorobenzene **8**. 4-Trifluoromethyl-2,3,5,6-tetrafluorobenzenethiol **9** in reaction with PCl_5 gives a high yield of 4-chloroheptafluorotoluene **10**.

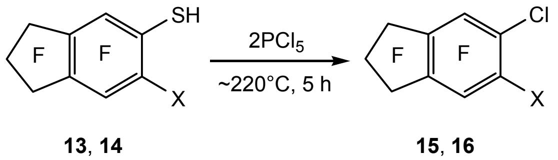


X = H (**5**, **6**), Cl (**7**, **8**), CF_3 (**9**, **10**).

At the same time the attempt to obtain 1-bromo-4-chlorotetrafluorobenzene **12** by chlorinating 4-bromotetrafluorobenzenethiol **11** at 180°C resulted as well in considerable substitution of bromine by the chlorine atom. By increasing the reaction temperature to ~240°C practically individual compound **8** was obtained.



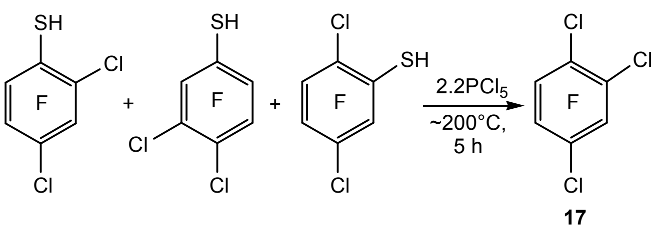
From nonafluoroindane- and 6-chlorooctafluoroindane-5-thiols **13** and **14** we obtained 5-chlorononafluoro- and 5,6-dichlorooctafluorindanes **15** and **16**.



X = F (**13**, **15**), Cl (**14**, **16**).

By heating in ampule the mixture of 2,4-, 3,4-, and 2,5-dichlorotrifluorobenzenethiols in the ratio 70 : 18 : 12 (^{19}F NMR) with PCl_5 we obtained practically individual 1,2,4-trichlorotrifluorobenzene **17** in 90% yield (Scheme 1).

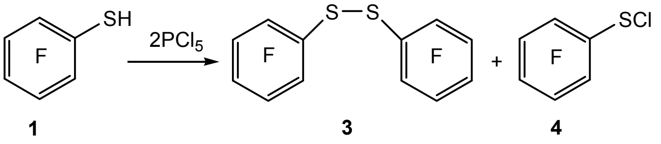
Scheme 1.



To understand the process of substitution of the thiol group for chlorine atom in reactions of polyfluoroarenethiols with PCl_5 we studied the behavior of compound **1** in reactions with PCl_5 at various temperatures.

At 20ºC thiol **1** and PCl_5 afforded only disulfide **3**, in keeping with the data of thiols transformations into disulfides in reactions with PCl_5 [9]. By heating thiol **1** with PCl_5 in an ampule at 100°C a mixture formed of sulfenyl chloride **4** and compound **3**, while arene **2** was not obtained according to ^{19}F NMR data, (Scheme 2).

Scheme 2.



	3		**4**
~20°C	~100	:	0
~100°C, 5 h	~69	:	31

From disulfide **3** and PCl_5 at 100ºC a mixture was obtained of initial compound **3** and pentafluorophenylsulfenyl chloride **4** in a ratio 68 : 32 (according to ^{19}F NMR data).

The generation of disulfide **3** from thiol **1** and PCl_5 at 20°C may occur through the transformations shown in Scheme 3. Considering that in crystalline state PCl_5 has ionic structure $[PCl_4]^+[PCl_6]^-$ [10], the generation of sulfenyl chloride **4** may occur involving cation $[PCl_4]^+$. Compound **4** while interacting with thiol **1** transforms in disulfide **3**, as has been proved by a special experiment. The formation of disulfide **3** from thiol **1** and PCl_5 without participation of sulfenyl chloride **4**, evidently, is also possible. The interaction of disulfide **3** with Cl_2 may cause the formation of sulfenyl chloride **4** in the reaction of thiol **1** with PCl_5 at ~100°C. The participation of Cl_2 in this process may be due to the decomposition of PCl_5 at heating [11–13].

Scheme 3.

$$\underset{\mathbf{1}}{C_6F_5SH} \xrightarrow[\text{~20°C, –HCl, –}PCl_3]{PCl_5} \underset{\mathbf{4}}{[C_6F_5SCl]} \xrightarrow[\text{–HCl}]{C_6F_5SH} \underset{\mathbf{3}}{C_6F_5SSC_6F_5}$$

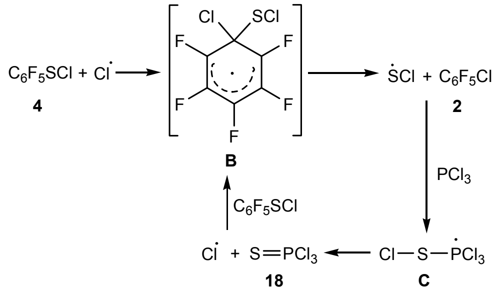
Previously it was assumed that in reactions of PCl_5 with olefins the transfer from heterolytic to homolytic mechanism was possible as the temperature of reaction was raised [14]. In this connection the substitution of thiol group in polyfluoroarenethiols by chlorine atom at higher temperatures (180–220°C) could proceed by the homolytic mechanism. Here the source of chlorine is PCl_5 (eq. 1). Cl_2 may also dissociate to chlorine atoms (eq. 2) [11, 12, 15]. Sulfenyl chloride **4** formed at heating disulfide **3** with PCl_5 (eq. 3) may decompose to chlorine atom and thiyl radical **A** (eq. 4). The formation of compound **2** from sulfenyl chloride **4** goes, probably, through the radical σ-complex **B** (eq. 5) [7]. Radical SCl eliminated at the decomposition of σ-complex **B** could generate the phosphoranyl radical **C** by interaction with PCl_3. The latter at β-decomposition results in thiophosphoryl chloride **18** that we have registered by ^{31}P NMR spectrum and GC-MS. It is known that phosphoranyl radicals, despite their relative stability, may undergo β-decomposition, including the one with generation of S=P bond [16].

$$PCl_5 \rightleftharpoons PCl_3 + Cl_2 \qquad (1)$$

$$Cl_2 \rightleftharpoons 2Cl^{\bullet} \qquad (2)$$

$$\underset{\mathbf{3}}{C_6F_5SSC_6F_5} + PCl_5 \xrightarrow{\Delta} \underset{\mathbf{4}}{2C_6F_5SCl} + PCl_3 \qquad (3)$$

$$\underset{\mathbf{4}}{C_6F_5SCl} \rightleftharpoons \underset{\mathbf{A}}{C_6F_5\dot{S}} + Cl^{\bullet} \qquad (4)$$



(5)

Radical **A** also could have formed sulfenyl chloride **4** and radical PCl_4 (eq. 6) by abstracting chlorine from PCl_5. Interactions of this type were described in [11, 12]. Phosphoranyl radical PCl_4 decomposes into PCl_3 and Cl [11] (eq. 7).

$$\underset{\mathbf{A}}{C_6F_5\dot{S}} + PCl_5 \longrightarrow \underset{\mathbf{4}}{C_6F_5SCl} + \dot{P}Cl_4 \qquad (6)$$

$$\dot{P}Cl_4 \rightleftharpoons PCl_3 + \dot{Cl} \qquad (7)$$

A similar system may be suggested to describe the transformations of other polyfluoroarenethiols into chloropolyfluoroarenes.

EXPERIMENTAL

Analytic and spectral measurements were carried out in Chemical Service Center of joint usage of the Siberian Branch of the Russian Academy of Sciences.

NMR spectra were recorded on a Bruker AV-300 [282.4 (^{19}F) and 300 (^{1}H) MHz] spectrometer in CCl_4 with added $(CD_3)_2CO$, internal reference C_6F_6 and HMDS (0.04 ppm from TMS). ^{31}P NMR spectra were recorded on a Bruker AV-400 (162.0 MHz) spectrometer, external reference H_3PO_4. Positive values of chemical shifts correspond to the signal downfield shift. For GC-MS a chromatograph HP 5890 with mass-selective detector HP 5971 was used and a chromatograph Agilent 6890N with the system Agilent 5973N. Energy of ionizing electrons was 70 eV. The separation of substances was performed using column HP-5 30 m × 0.25 mm × 0.25 μm, carrier gas helium, flow rate 1 mL/min, column temperature 50–280°C, ion source temperature 173°C. GC analysis was carried out on a chromatograph HP 5890 with a column HP-5, 30 m × 0.52 mm × 2.6 μm and a detector of thermal conductivity.

Initial polyfluoroarenethiols were obtained by the method [17]. Isomeric mixture of dichlorotrifluorobenzenethiols was prepared from technical mixture of *o*-, *m*-, *p*-$C_6F_4Cl_2$ and KSH (yield 90%) [18].

The formation of compounds **3** and **4** and final products of polyfluoroarenethiols chlorination was proved by comparing their ^{19}F NMR spectra with published data [7, 8, 18].

Chlorination of polyfluoroarenes. Method 1. Polyfluoroarenethiol was charged in an ampule and PCl_5 was added by portions. After the gas evolution finished the ampule was sealed, placed into a metal case, and heated. After the reaction completed the ampule was cooled, opened, its content was placed into a flask under a layer of water with ice (80–100 g), stirred for 2 h by magnetic stirrer to hydrolyze the phosphorus compounds, then alkalinized with Na_2CO_3, stirred for 2 h more, and subjected to steam distillation. The reaction product was separated, dried with $CaCl_2$, and analyzed by GC and ^{19}F NMR methods. Compounds **2**, **6**, **8**, **10**, **12**, **15**, **16**, and **17** were obtained.

Chloropentafluorobenzene (2). From 3.16 g (15.79 mmol) of compound **1** and 6.69 g (32.13 mmol) of PCl_5 (201–203°C, 5 h) were obtained 2.96 g (93%) of compound **2** (content in the mixture according to GC data ~100%).

From 3.12 g (15.59 mmol) of compound **1** and 3.76 g (18.06 mmol) of PCl_5 (200–202°C, 24 h) were obtained 2.82 g (89%) of compound **2**, content in the mixture ~100% (GC).

Similarly from 3.21 g (8.06 mmol) of compound **3** and 3.58 g (17.91 mmol) of PCl_5 (203–205°C, 5 h) were obtained 2.94 g (88%) of compound **2**, content in the mixture 97.2% (GC).

From 3.50 g (14.92 mmol) of compound **4** and 6.40 g (30.73 mmol) of PCl_5 (203–205°C, 5 h) were obtained 2.62 g (85%) of compound **2**, purity 98.4% (GC).

1-Chloro-2,3,5,6-tetrafluorobenzene (6). From 3.33 g (18.28 mmol) of compound **5** and 7.93 g (38.08 mmol) of PCl_5 (198–200°C, 5 h) were obtained 3.10 g (92%) of compound **6**, purity 99.7% (GC).

1,4-Dichlorotetrafluorobenzene (8). By heating 3.29 g (15.19 mmol) of thiol **7** and 6.60 g (31.69 mmol) of PCl_5 (201–203°C, 5 h) were obtained 3.01 g (90%) of compound **8**, purity 99.5% (GC).

4-Chloroheptafluorotoluene (10). From 3.10 g (12.39 mmol) of compound **9** and 5.22 g (25.07 mmol) of PCl_5 (219–221°C, 5 h) were obtained 2.89 g (92%) of compound **10**, purity ~100% (GC).

Reactions of 4-bromotetrafluorobenzenethiol (11) with PCl_5. *a*. From 3.25 g (12.45 mmol) of thiol **11** and 5.35 g (25.69 mmol) of PCl_5 (179–181°C, 5 h) were obtained 2.64 g of a mixture containing compounds **8** 62.4% and **12** 36%, according to GC data.

b. At 238–240°C (5 h) from 3.48 g (13.33 mmol) of compound **11** and 5.48 g (26.32 mmol) of PCl_5 were obtained 2.62 g of a mixture containing compounds **8** 99.1% and **12** 0.6%, according to GC data.

1-Bromo-4-chlorotetrafluorobenzene (12). ^{19}F NMR spectrum (from the spectrum of a mixture of compounds **8** and **12**), δ, ppm: 22.6 m ($F^{3,5}$), 30.3 m ($F^{2,6}$). Found M^+ 262 1Cl, 1Br. Calculated *M* 261.88.

5-Chlorononafluoroindane (15). From 3.48 g (11.15 mmol) of compound **13** and 4.76 g (22.86 mmol) of PCl_5 (218–220°C, 5 h) were obtained 3.19 g (90%) of compound **15**, purity 99% (GC).

5,6-Dichlorooctafluoroindane (16). Similarly by heating (218–220°C, 5 h) 3.04 g (9.25 mmol) of compound **14** with 3.83 g (18.39 mmol) of PCl_5 were obtained 2.83 g (92%) of a substance containing compound **16** 99.1%, according to GC data.

1,2,4-Trichlorotrifluorobenzene (17) [18]. By chlorination of 3.26 g (13.99 mmol) of a mixture of 2,4-, 3,4- and 2,5-dichlorotrifluorobenzenethiols (~70 : 18 : 12 according to ^{19}F NMR data) and 6.51 g (31.26 mmol) of PCl_5 at 198–200°C (5 h) were obtained 2.97 g (90%) of a substance containing compound **17** 99.9%, according to GC data.

Compounds (2 and 18). *a*. In an ampule was charged 1.76 g (8.79 mmol) of thiol **1** and then by portions 2.13 g (10.22 mmol) of PCl_5 was added. After the end of gas evolution the ampule was sealed, placed into a metal case, and held for 18 h at 200°C. Then the ampule was cooled and opened. We obtained 3.40 g of a mixture of compound **2** (49%) and $PSCl_3$ **18** (45%) according to GC-MS data.

b. In an ampule was charged 3.15 g (15.74 mmol) of thiol **1** and then by portions 6.53 g (31.36 mmol) of PCl_5 was added. After the end of gas evolution the ampule was sealed, placed in a metallic case, and held for 5 h at 201–203°C. Then the ampule was cooled, opened, its content was placed into flask with ice (~70 g). To the mixture 10.51 g of Na_2CO_3 was added, the reaction products were subjected to steam distillation, separated, dried with $CaCl_2$. We obtained 3.60 g of a mixture containing according to GC-MS data 80.7% of compound **2** and 16.6% of $PSCl_3$ **18**.

The identification of compound **18** was performed using the ^{31}P NMR data [19], and also by comparing the complete mass-spectrum, obtained by electronic ionization, with a spectrum from the library W8N08 [20], where a concise mass-spectrum of thiophosphoryl chloride was published. Complete mass spectrum of compound **18** synthesized by the method [21], *m/z* (I_{rel}, %): 174 (2.8), 172 (20.6), 170 (59.0), 168 (58.0) [Cl_3PS], 138 (1.5), 136 (2.0) [Cl_3P], 137 (13.8), 135 (70.6), 133 (100.0) [Cl_2PS], 105 (1.4), 103 (8.2), 101 (12.4) [Cl_2P], 100 (2.5), 98 (6.0) [ClPS], 68 (1.8), 66 (5.0) [ClP], 63 (9.0) [PS], 37 (0.7), 35 (1.9) [Cl].

Metod 2. In an ampule was charged compound **1**, **3**, and **4** and by portions PCl_5 was added. After the end of gas evolution the ampule was sealed, placed in a metal case, and heated. Then the ampule was cooled, opened, its content was dissolved in 2 mL of methylene chloride, and analyzed with ^{19}F NMR.

This method was applied to perform the reactions of compounds **1**, **3**, and **4** with PCl_5 in various conditions:

a. After mixing from 0.0905 g (0.45 mmol) of compound **1** and 0.1898 g (0.91 mmol) of PCl_5 at room temperature we obtained pure compound **3** (^{19}F NMR data).

b. From 0.1760 g (0.88 mmol) of compound **1** and 0.3677 g (1.77 mmol) of PCl_5 by heating at 100°C during 5 h a mixture was obtained of compounds **3** and **4** in a ratio ~69 : 31 (^{19}F NMR data).

c. By increasing the temperature to 198–200°C (5 h) from 0.2552 g (1.28 mmol) of compound **1** and 0.2638 g (1.27 mmol) of PCl_5 a mixture was obtained of compounds **2**, **3**, and **4** in a ratio ~83 : 9 : 8 (^{19}F NMR data).

d. Similarly from 0.1341 g (0.67 mmol) of compound **1** and 0.1570 g (0.75 mmol) of PCl_5 (199–201°C, 16 h) a mixture was obtained containing compounds **2**, **3**, and **4** in a ratio ~91 : 5 : 4 (^{19}F NMR data).

From 0.18 g (0.45 mmol) of compound **3** and 0.19 g (0.48 mmol) of PCl_5 at 100°C during 5 h a mixture was obtained of compounds **3** and **4** in a ratio ~68 : 32 (^{19}F NMR data).

Thermolys of compound (4). From 0.22 g (0.94 mmol) of compound **4** at 200°C during 24 h a mixture was obtained of compound **2** and decafluorodiphenyl polysulfides in a ratio ~83 : 17 (^{19}F NMR data).

Thermolys of compound (4) in the presence of PCl_3. From 0.25 g (1.08 mmol) of compound **4** and 0.15 g (1.09 mmol) of PCl_3 at 200°C during 24 h a mixture was obtained of compounds **2**, **3**, and bis(pentafluorophenyl) sulfide in a ratio ~83 : 15 : 2 (^{19}F NMR data). Formation of $PSCl_3$ was confirmed by the ^{31}P NMR data.

Reaction of thiol (1) with sulfenyl chloride (4). To 0.1416 g (0.60 mmol) of sulfenyl chloride **4** at room temperature was added dropwise 0.1167 g (0.58 mmol) of thiol **1**. After the gas evolution stopped the obtained mixture was dissolved in ~2 mL of CH_2Cl_2 and analyzed with ^{19}F NMR. The reaction mixture contained compounds **3** and **4** in a ratio ~ 93 : 7 (^{19}F NMR data).

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