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Synthesis of terminally perfluorinated long-chain alkanethiols, sulfides and disulfides from the corresponding halides

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Abstract

Semifluorinated *n*-alkanethiols, symmetrical sulfides and disulfides bearing the chain(s) $F(CF_2)_n(CH_2)_m$ with n=4, 6, 8, 10, and m=2, 11 have been prepared by various synthetic methods, starting from the corresponding iodides or bromides. Methods based on sodium hydrogen sulfide, commonly used to accomplish this conversion, treatment of the Bunte salt obtained from sodium thiosulfate, the basic hydrolysis of isothiouronium salts, the hydrolysis under mild conditions of thiophosphorates formed from sodium thiophosphate and the basic hydrolysis of thiol acetic acid derivatives, have been investigated and compared relatively to the selective synthesis of the title compounds. The thiolacetic route yields essentially the thiols with some amounts of disulfides. Results from thiourea appears similar. Sodium thiophosphate constitutes an excellent route for the synthesis of thioethers, particularly when starting from the bromides. The two classical methods based on sodium hydrogen sulfide and sodium thiosulfate exhibit poor selectivity. It has been possible to obtain all the sulfur compounds reported in the pure state.

Keywords: Terminally perfluorinated long — chain alkanethiols; Sulfides; Disulfides

1. Introduction

The generation, based on the SAM technique, of organised monomolecular films from sulfur molecules bearing perfluorinated chains and perhydrogenated spacers, e.g., $F(CF_2)_n(CH_2)_mSH$, offers the opportunity to study fundamental properties of fluorinated interfaces, such as wetting, adhesion and friction. In this field the influence of the length of the fluorinated and hydrogenated segments on such properties is of great interest [1,2].

However, the impact of impurity levels on the formation and structure of these adlayers recently appeared critical, particularly for the presence of sulfides or disulfides. The importance of purifying these precursors to unexpectedly high levels is critical when examining issues related to the formation and structures of these monolayers, which can be dominated by the trace components [3].

An important method for the synthesis of terminally fluorinated thiols, based on the formation of isothiouronium salts was first reported in the sixties [4,5] and developed more recently [6,7,8]. These syntheses have been limited to short hydrogenated spacers (m=2). The synthesis of a thiol bearing a long hydrogenated spacer (n=8, m=11) has been reported by Tsao, using the Bunte salt method [9]. An emerging new route based on thiolacetic acid was recently developed by Radford and applied to molecules bearing a short hydrogenated spacer: n=4, 6, 8, 10 and m=2 [10]. A new strategy involving the radical addition of fluorinated alkyl iodides to long chain ω-olefins α-functionalized with the thioacetate group (n=1, 2, 3, 4 and m=9–15 (relatively short fluorinated chains)) has been reported recently, the acidic deprotection used avoiding the formation of disulfides as by-products [2].

The aim of this work was to select the most pertinent synthetic routes to the title compounds and to clearly assess their identification and purification.

Semifluorinated *n*-alkanethiols, symmetrical sulfides and disulfides bearing the chain(s) $F(CF_2)_n(CH_2)_m$ with n=4, 6, 8, 10 and m=2, 11 have been prepared by various synthetic pathways, starting from the corresponding iodides or bromides. Five methods to accomplish this conversion have been studied. The basic hydrolysis of the thiol acetic acid derivatives, the hydrolysis in mild conditions of thiophosphorates formed from sodium thiophosphate, the basic hydrolysis of isothiouronium salts, a method based on

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sodium hydrogen sulfide, treatment of the Bunte salt obtained from sodium thiosulfate, have been investigated and are compared for the selective synthesis of the title compounds.

2. Experimental

2.1. General information

1-Iodo-2-perfluoroalkylethanes, 1-iodoperfluoroalkanes, 11-bromoundecanoic acid, undecyl-10-en-1-ol were supplied by Elf-ATOCHEM and used without further purification. Sodium metal, thiolacetic acid, azo-bis-*iso*-butyronitrile (AIBN), toluene, hexane, KF, tributyltin fluoride, tributylhexadecylphosphoniumbromide, thiophosphoryl chloride (98%), *n*-bromoundecane (Aldrich), 30% ammonia (Carlo Erba), triphenylphosphine (Merck), red phosphorus (Fluka), iodine, sodium thiosulfate (Prolabo), silica gel 60 (0.063–0.2 mm/70–230 mesh ASTM) for column chromatography (MACHEREY–NAGEL) were used as received.

2.2. Measurements and instruments

^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were obtained in $CDCl_3$, ^{31}P NMR in D_2O, using a Bruker AC-250 spectrometer operating at 250.13 MHz for ^{1}H, at 235.36 MHz for ^{19}F, at 101.25 MHz for ^{31}P and a Bruker DRX 400 operating at 400.13 MHz for ^{13}C. Chemical shifts δ are given in ppm, using as internal standards $Si(Me)_4$ for ^{1}H NMR and ^{13}C NMR, CCl_3F for ^{19}F NMR, H_3PO_4 for ^{31}P NMR. Mass spectra were obtained from a Jeol JMS D100 apparatus. Fusion points were obtained from differential scanning calorimetry (DSC) Mettler TA 4000.

2.3. Synthesis of the fluorinated starting halides

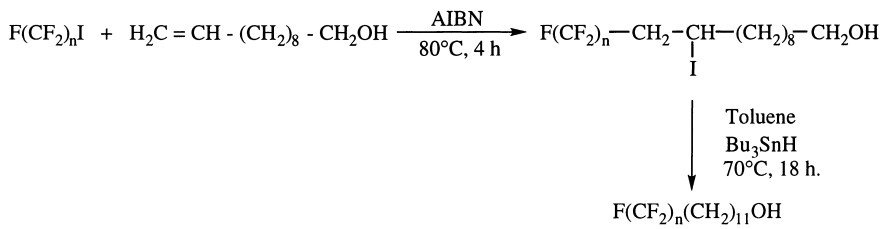
F-alkyl halides corresponding to the general formula $F(CF_2)_n(CH_2)_mX$ (X=I or Br) with n=4, 6, 8, 10 and m=2 have been supplied by Elf-ATOCHEM, those for m=11 have been prepared through the synthesis of 11-perfluoroalkylundecanols followed by their conversion to halides. As depicted in detail below iodides have generally been prepared when a long fluorinated chain is present (n=6, 8, 10) and bromides for the shorter chains (n=4, 6, 8), because of the drastic thermal conditions for the iodide syntheses, and the lower yields of the bromide routes.

2.3.1. Synthesis of 11-perfluoroalkylundecanols $F(CF_2)_n(CH_2)_{11}OH$: general procedure

For the synthesis of the alcohols we have chosen the route depicted in Scheme 1 [11] other possible routes have been reported recently [12].

1-Iodoperfluoroalkanes (0.1 mole), undecyl-10-en-1-ol (0.12 mole) and azo-bis-*iso*-butyronitrile (1%, 0.0012 mole AIBN) chosen as initiator [13–14] were placed under a nitrogen atmosphere in a 250 ml two-necked flask equipped with a reflux condenser. The reaction mixture was stirred for 4 h at 80°C. 11-perfluoroalkyl-10-iodoundecan-1-ol, $F(CF_2)_nCH_2CHI(CH_2)_9OH$, was not isolated, but directly reduced by tri-*n*-butyltin hydride. At room temperature, AIBN (10%, 0.1 mole) was dissolved in 10 ml of toluene and added under a purge of nitrogen to the reaction mixture, followed by a dropwise addition of tributyltin hydride [15] (0.2 mole) through a septum. The mixture was stirred and heated for 18 h at 80°C. Toluene was vacuum evaporated under reduced pressure at room temperature, then the mixture was treated by extraction with ether and washed with saturated aqueous NaCl three times. The ethereal layer was dried with sodium sulfate, filtered, and evaporated under reduced pressure. The crude product was dissolved in an ethereal suspension of KF and stirred 18 h, in order to transform the excess of reductive agent tri-*n*-butyltin hydride to tributyltin fluoride which is insoluble in ether, thus permitting its efficient removal [16]. The solution appeared as a milk-white suspension which was filtered using a filtration flask. The filtrate was vacuum evaporated. The residue was purified by crystallization in heptane to give the 11-perfluoroalkylundecanols, $F(CF_2)_n(CH_2)_{11}$ OH.

2.3.1.1. 15,15,15,14,14,13,13,12,12-Nonafluoropentadecanol $F(CF_2)_4(CH_2)_{11}OH$. White solid, yield: 27.3 g, 70% relative to the starting 1-iodoperfluorobutane. mp: 33.5°C. ^{1}H NMR: δ 1.29 (m, 14 H, $(CH_2)_7$ and s, 1H, OH); 1.56 (m, 4H, $\underline{CH_2}CH_2OH$ and $\underline{CH_2}CH_2CF_2$); 2.05 (m, 2H, CH_2CF_2); 3.64 (t, 2H, J=6.6 Hz, $\underline{CH_2}OH$). ^{19}F NMR: δ −126.61 (m, 2F, $\underline{CF_2}CF_3$); −123.07 (m, 2F, $\underline{CF_2}CF_2CH_2$); −115.19 (m, 2F, $\underline{CF_2}CH_2$); −81.57 (m, 3F, $\underline{CF_3}$). MS (FAB +, matrix NBA) (m/z): 391 (40) $(M+H)^+$; 373 (5) $(M+H-H_2O)^+$.



Scheme 1. Synthesis of perfluoroalkylundecanols.

2.3.1.2. 17,17,17,16,16,15,15,14,14,13,13,12,12-Tridecafluoroheptadecanol $F(CF_2)_6(CH_2)_{11}OH$. White solid, yield: 34.3 g, 70% relative to the starting 1-iodoperfluorohexane. mp: 51.1°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.7 (m, 2F, $\underline{CF_2}CF_3$); −125.43 (m, 2F, $CF_2\underline{CF_2}CF_3$); −123.45 (m, 2F, $\underline{CF_2}(CF_2)_2CH_2$); −122.51 (m, 2F, $\underline{CF_2}CF_2CH_2$); −114.99 (m, 2F, $\underline{CF_2}CH_2$); −81.32 (m, 3F, $\overline{CF_3}$). MS (FAB +, matrix NBA) (*m/z*): 491 (40) $(M+H)^+$; 473 (5) $(M+H-H_2O)^+$.

2.3.1.3. 19,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-Heptadecafluorononadecanol $F(CF_2)_8(CH_2)_{11}OH$. White solid, yield: 35.4 g, 60% relative to the starting 1-iodoperfluorooctane. mp: 77.2°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.62 (m, 2F, $\underline{CF_2}CF_3$); −124.06 (m, 2F, $CF_2\underline{CF_2}CF_3$); −123.24 (m, 2F, $\underline{CF_2}(CF_2)_4CH_2$); −122.37 (m, 6F, $(\underline{CF_2})_3CF_2CH_2$); −114.99 (m, 2F, $\underline{CF_2}CH_2$); −81.26 (m, 3F, $\overline{CF_3}$). MS (FAB +, matrix NBA) (*m/z*): 591 (40) $(M+H)^+$; 573 (5) $(M+H-H_2O)^+$.

2.3.1.4. 21,21,21,20,20,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-Heneicosafluoroheneicosanol $F(CF_2)_{10}(CH_2)_{11}OH$. White solid, yield: 34.5 g, 50% relative to the starting 1-iodoperfluorododecane. mp: 104.9°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.77 (m, 2F, $\underline{CF_2}CF_3$); −124.16 (m, 2F, $CF_2\underline{CF_2}CF_3$); −123.33 (m, 2F, $\underline{CF_2}(CF_2)_6CH_2$); −122.39 (m, 6F, $(\underline{CF_2})_5CF_2CH_2$); −115.07 (m, 2F, CF_2CH_2); −81.42 (m, 3F, $\overline{CF_3}$). MS (FAB +, matrix NBA) (*m/z*): 691 (40) $(M+H)^+$; 673 (5) $(M+H-H_2O)^+$.

2.3.2. Conversion of the 11-perfluoroalkylundecanols into bromides and iodides

For the synthesis of bromides we use a route [17–18] different from that reported by Tsao et al. [9]. Iodides synthesis is adapted from [19] (Scheme 2).

2.3.3. Synthesis of 1-bromo-11-perfluoalkylundecanes $F(CF_2)_n(CH_2)_{11}Br$ (with n=4, 6, 8): general procedure

0.01 mole of alcohol and 0.62 g (0.01 mole) of triphenylphosphine dissolved in 20 ml of acetonitrile were placed in a 250 ml round-bottomed flask equipped with a reflux condenser and deoxygenated with nitrogen. The mixture was stirred and heated at 60°C. At this temperature 0.01 mole of bromine was added drop by drop. The mixture was allowed to react for 5 h. At room temperature, the mixture was extracted with ether and washed with saturated hot aqueous NaCl three times. The ethereal layer was dried over anhydrous sodium sulfate, filtered and then vacuum evaporated. The crude product was dissolved in 20 ml dichloromethane and 10 g of silica was added. The mixture was stirred 2 h in order to eliminate unreacted alcohol and traces of triphenylphosphine oxide remaining after the extraction step. The mixture was filtered and the solvent removed on a rotary evaporator. The bromides $F(CF_2)_n(CH_2)_{11}Br$ were obtained in 80% yield relative to the starting alcohol for all the *n* values studied.

2.3.3.1. 1-Bromo-15,15,15,14,14,13,13,12,12-nonafluoropentadecane. $F(CF_2)_4(CH_2)_{11}Br$, colorless liquid (3.62 g). ^{1}H NMR: δ 1.30 (m, 14H, $(CH_2)_7$); 1.6 (m, 2H, $\underline{CH_2}CH_2CF_2$); 1.8 (m, 2H, $\underline{CH_2}CH_2Br$); 2 (m, 2H, $\underline{CH_2}CF_2$); 3.4 (t, 2H, J=6.8 Hz, $CH_2\overline{Br}$). ^{19}F NMR: δ −126.62 (m, 2F, $\underline{CF_2}CF_3$); −125.17 (m, 2F, $CF_2\underline{CF_2}CH_2$); −115.2 (m, 2F, $\underline{CF_2}CH_2$); −81.57 (m, 3F, CF_3). MS (EI, 70 eV, 30°C) (*m/z*): 372 (0.1) $(M-HBr)^{+\bullet}$; 331 (0.6) $(M-(CH_2)_3Br)^+$; 317 (2.5) $(M-(CH_2)_4Br)^+$; 289 (2.7) $(M-(CH_2)_6Br)^+$; 275 (0.5) $(M-(CH_2)_7Br)^+$; 69 (5.0) $(CF_3)^+$; 55 (100) $(C_4H_7)^+$.

2.3.3.2. 1-Bromo-17,17,17,16,16,15,15,14,14,13,13,12,12-tridecafluoroheptadecane $F(CF_2)_6(CH_2)_{11}Br$. Colorless liquid (4.42 g). ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −124.63 (m, 2F, CF_2CF_3); −123 (m, 2F, $\underline{CF_2}CF_2CF_3$); −122.4 (m, 2F, $\underline{CF_2}(CF_2)_2CH_2$); −121.4 (m, 2F, $(\underline{CF_2})CF_2CH_2$); −113.7 (m, 2F, $\underline{CF_2}CH_2$); −80.6 (m, 3F, CF_3). MS (EI, 70 eV, 31.7°C) (*m/z*): 472 (0.08) $(M-HBr)^+$; 431 (0.64) $(M-(CH_2)_3Br)^+$; 417 (1.68) $(M-(CH_2)_4Br)^+$; 389 (2.08) $(M-(CH_2)_6Br)^+$; 375 (0.72) $(M-(CH_2)_7Br)^+$; 69 (5.76) $(CF_3)^+$; 55 (100) $(C_4H_7)^+$.

2.3.3.3. 1-Bromo-19,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-heptadecafluorononadecane $F(CF_2)_8(CH_2)_{11}Br$. White solid (5.22 g). mp: 37.6°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.62 (m, 2F, $\underline{CF_2}CF_3$); −124.5 (m, 2F, $\underline{CF_2}CF_2CF_3$); −123.5 (m, 2F, $\underline{CF_2}(CF_2)_4CH_2$); −122.37 (m, 6F, $(CF_2)_3CF_2CH_2$); −115 (m, 2F, $\underline{CF_2}CH_2$); −81.26 (m, 3F, CF_3). MS (EI, 70 eV, 69.4°C) 573 (0.375) $(M-Br)^+$; 531 (2.5) $(M-(CH_2)_3Br)^+$; 517 (8.75) $(M-(CH_2)_4Br)^+$; 489 (12.75) $(M-(CH_2)_6Br)^+$; 475 (3.37) $(M-(CH_2)_7Br)^+$; 69 (9.62) $(CF_3)^+$; 55 (100) $(C_4H_7)^+$.

2.3.4. Synthesis of 1-iodo-11-perfluoroalkylundecanes $F(CF_2)_n(CH_2)_{11}I$ (with n=4, 6, 8, 10): general procedure

The 1-iodo-11-perfluoroalkylundecanes $F(CF_2)_n(CH_2)_{11}I$ were formed from the corresponding alcohols as follows: the alcohol (0.02 mole), red phosphorus (8×10^{-3} at.) and

$$F(CF_2)_n(CH_2)_{11}OH + Ph_3P + Br_2 \xrightarrow[70°C,\ N_2,\ 5\ h]{\text{Acetonitrile}} F(CF_2)_n(CH_2)_{11}Br + Ph_3P{=}O + HBr$$

$$3\ F(CF_2)_n(CH_2)_{11}OH + 3/2\ I_2 + P \xrightarrow{5\ h,\ 140\ °C} 3\ F(CF_2)_n(CH_2)_{11}I + H_3PO_3$$

Scheme 2. Synthesis of perfluoroalkylundecane halides.

iodine (2×10^{-2} at.) were introduced into a 250 ml Erlenmeyer flask equipped with a reflux condenser and a magnetic stirrer, and heated at 140°C for 5 h. The reaction mixture was cooled to room temperature and the solid product treated three times with ether (3 ml×125 ml). The combined ether extracts were filtered and washed with saturated aqueous NaCl three times. The ethereal solution was dried over sodium sulfate and freed from solvent on a rotary evaporator. Iodides $F(CF_2)_n(CH_2)_{11}I$ were, thus, obtained in the pure state, in 95% yield relative to the starting alcohols, as white solids.

2.3.4.1. 17,17,17,16,16,15,15,14,14,13,13,12,12-Tridecafluoro-1-iodoheptadecane, $F(CF_2)_4(CH_2)_{11}I$. Colorless liquid (9.5 g). ^{1}H NMR: δ 1.35 (m, 14H, $(CH_2)_7$); 1.6 (m, 2H, $\underline{CH_2}CH_2CF_2$); 1.8 (m, 2H, $\underline{CH_2}CH_2I$); 2.2 (m, 2H, $\underline{CH_2}CF_2$); 3.2 (t, 2H, J=7 Hz, $\underline{CH_2}I$). ^{19}F NMR: δ −124.63 (m, 2F, $\underline{CF_2}CF_3$); −123 (m, 2F, $\underline{CF_2}CF_2CF_3$); −122.4 (m, 2F, $\underline{CF_2}(CF_2)_2$ CH_2); −121.4 (m, 2F, $(\underline{CF_2})CF_2CH_2$); −113.7 (m, 2F, $\underline{CF_2}CH_2$); −80.6 (m, 3F, CF_3).MS (EI; 70 eV; 68°C) (m/z): 499 (1) $(M-H)^+$; 373 (2) $(C_4F_9(CH_2)_{11})^+$; 317 (10) $(C_4F_9(CH_2)_7)^+$; 289 (15) $(C_4F_9(CH_2)_5)^+$; 275 (5) $(C_4F_9(CH_2)_4)^+$; 155 (13) $(C_{11}H_{22}+H)^+$; 55 (100) $(C_4H_7)^+$.

2.3.4.2. 17,17,17,16,16,15,15,14,14,13,13,12,12-Tridecafluoro-1-iodoheptadecane, $F(CF_2)_6(CH_2)_{11}I$. White solid (11.4 g). mp: 22.1°C. ^{1}H NMR: δ 1.35 (m, 14H, $(\underline{CH_2})_7$); 1.6 (m, 2H, $\underline{CH_2}CH_2CF_2$); 1.8 (m, 2H, $\underline{CH_2}CH_2I$); 2.2 (m, 2H, CH_2CF_2); 3.2 (t, 2H, J=7 Hz, $\underline{CH_2}I$). ^{19}F NMR: δ −126.7 (m, 2F, $\underline{CF_2}CF_3$); −124.5 (m, 2F, $CF_2CF_2CF_3$); −123.5 (m, 2F, $\underline{CF_2}(CF_2)_2CH_2$); −122.30 (m, 2F, $\underline{CF_2}CF_2CH_2$); −115 (m, 2F, $\underline{CF_2}CH_2$); −81. 6 (m, 3F, CF_3). MS (EI; 70 eV; 72.2°C) (m/z): 599 (1) $(M-H)^+$; 473 (2.5) $(C_6F_{13}(CH_2)_{11})^+$; 417 (13) $(C_6F_{13}(CH_2)_7)^+$; 389 (13) $(C_6F_{13}(CH_2)_5)^+$; 375 (4) $(C_6F_{13}(CH_2)_4)^+$; 155 (13) $(C_{11}H_{22}+H)^+$; 55 (100) $(C_4H_7)^+$.

2.3.4.3. 19,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-Heptadecafluoro-1-iodononadecane, $F(CF_2)_8(CH_2)_{11}I$. White solid (13.3 g). mp: 42.8°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.62 (m, 2F, $\underline{CF_2}CF_3$); −124.06 (m, 2F, $CF_2CF_2CF_3$); −123.24 (m, 2F, $\underline{CF_2}(CF_2)_4CH_2$); −122.37 (m, 6F, $(CF_2)_3CF_2CH_2$); −115 (m, 2F,CF_2CH_2); −81.26 (m, 3F, CF_3). MS (EI; 70 eV; 69.8°C) (m/z): 699 (0.5) $(M-H)^+$; 573 (1) $(C_8F_{17}(CH_2)_{11})^+$; 517 (2.6) $(C_8F_{17}(CH_2)_7)^+$; 489 (4) $(C_8F_{17}(CH_2)_5)^+$; 475 (1) $(C_8F_{17}(CH_2)_4)^+$; 155 (8) $(C_{11}H_{22+}1)^+$; 55 (100) $(C_4H_7)^+$.

2.3.4.4. 21,21,21,20,20,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-Heneicosafluoro-1-iodoheneicosane, $F(CF_2)_{10}(CH_2)_{11}I$. White solid (15.2 g). mp: 69.2°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.77 (m, 2F, $\underline{CF_2}CF_3$); −124.16 (m, 2F, $\underline{CF_2}CF_2CF_3$); −123.33 (m, 2F, $\underline{CF_2}(CF_2)_6CH_2$); −122.39 (m, 10F, $(CF_2)_5CF_2CH_2$); −115.07 (m, 2F, $\underline{CF_2}CH_2$); −81.42 (m, 3F, CF_3). MS (EI; 70 eV; 83.7°C) (m/z): 673 (0.8) $(C_{10}F_{21}(CH_2)_{11})^+$; 617 (1.3) $(C_{10}F_{21}(CH_2)_7)^+$; 589 (4.6) $(C_{10}F_{21}(CH_2)_5)^+$; 575 (1) $(C_{10}F_{21}(CH_2)_4)^+$; 155 (4) $(C_{11}H_{22}+1)^+$; 55 (100) $(C_4H_7)^+$.

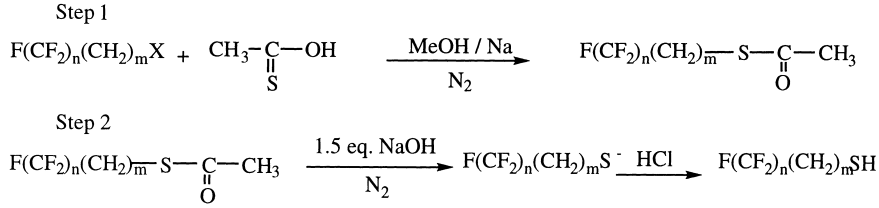
2.4. Conversion of F-alkyl halides of general formula $F(CF_2)_n(CH_2)_mX$ (X=I or Br; n=4,6,8,10; m=2,11) to sulfur compounds by various methods

2.4.1. Thiolacetic acid derivatives

The synthesis of perhydrogenated alkanethiols from the corresponding halides using thiolacetic acid has been largely described by Whitesides et al. [20]. A similar technique has been applied by Radford et al. [10] to semifluorinated halides bearing a short hydrogenated spacer. Here we report the application of the thiolacetic route to the halides $F(CF_2)_n(CH_2)_mI$ (n=4, 6, 8, 10; m=2 and n=6, 8, 10; m=11), including some differences in the process compared with the literature (Scheme 3).

Step 1: anhydrous methanol (100 ml), except for n=10 where anhydrous ethanol was employed, was added to a 250 ml round-bottomed flask and deoxygenated with nitrogen. Sodium metal (38 mmol) was added and allowed to react under a nitrogen atmosphere. The sodium methoxide solution was cooled with an ice bath, and thiolacetic acid (38 mmol) was added drop by drop followed by 1-iodoperfluoroalkylalkane (20 mmol). After stirring for 5 h at 70°C, the mixture was extracted with ether (150 ml) and washed with saturated hot aqueous NaCl three times. The organic phase was dried over sodium sulfate, filtered, and evaporated under reduced pressure. All the starting iodide was converted. The yield of pure 2-perfluoroalkylthiolacetate ($F(CF_2)_n(CH_2)_mSC(O)CH_3$) was in the range 85/90% for all the n and m values studied relative to the starting 1-iodoperfluoroalkylalkane.

2-perfluoroalkylethanethiolacetates($F(CF_2)_n(CH_2)_2SC(O)CH_3$) yellow oil, (except for n=10 yellow solid); ^{1}H



Scheme 3. Synthesis of perfluoroalkylalkanethiols with thiolacetic acid.

NMR: δ 2.3 (s, 3H, CH_3); 2.4 (m, 2H, $CF_2\underline{CH_2}CH_2$); 3.05 (m, 2H, $\underline{CH_2}SC(O)CH_3$). ^{13}C NMR: δ 20.55 (s,CH_2−S), 30.72 (s, CH_3); 31.9 (m, $\underline{CH_2}$−CF_2); between 105 and 128 broad peak corresponding to the fluorinated carbons; 195.14 (s, C=O). Similar spectroscopic data have been observed for 2-perfluoroalkyundecanethiolacetates.

Step 2: $F(CF_2)_n(CH_2)_mSC(O)CH_3$ was dissolved in methanol (50 ml for 0.01 mole of starting product) in a 250 ml three-necked flask, equipped with a reflux condenser and a dropping funnel containing 1.5 eq of NaOH in a minimum of water, and kept under nitrogen at room temperature. The aqueous solution of NaOH was added to the reaction flask and the mixture was allowed to reflux for 3 h. The reaction was cooled in an ice bath and poured with stirring into a 250 ml beaker containing ice water (100 ml), concentrated HCl (10 ml) and diethyl ether (150 ml). The ethereal layer was separated and washed with saturated aqueous NaCl (3 ml×150 ml), dried over anhydrous sodium sulfate, filtered and then vacuum evaporated. The crude product was purified by distillation of the thiol under vacuum for n=4, 6, 8 m=2 and n=6 m=11. For n=10 m=2 and for n=8, 10 m=11 the disulfides are separated from the corresponding thiols, taking advantage of the poor solubility of the disulfides in ethanol (1 g of crude product for 50 ml of ethanol, except for n=10, m=11: 100 ml). Indicated yields are relative to the starting 1-iodoperfluoroalkylalkane.

2.4.1.1. 6,6,6,5,5,4,4,3,3- Nonafluorohexanethiol $F(CF_2)_4(CH_2)_2SH$. Colorless liquid, yield: 3.36 g, 60%. bp: 35°C 10 mmHg. ^1H NMR: δ 1.6 (t, 1H, J=8 Hz, SH); 2.4 (m, 2H, $CF_2\underline{CH_2}CH_2$); 2.75 (m, 2H, CH_2SH).^{19}F NMR: δ −126.83 (m, 2F, $\underline{CF_2}CF_3$); −125.18 (m, 2F, $\underline{CF_2}CF_2CH_2$); −115.4 (m, 2F, $\underline{CF_2}CH_2$); −81.9 (m, 3F, $\underline{CF_3}$). MS (EI, 70 eV, 24.1°C) (*m/z*): 280 (54.5) $(M)^{+\bullet}$; 69 (21) $(CF_3)^+$; 61 (20) $(C_2H_5S)^+$; 47 (100) $(CH_3S)^+$.

2.4.1.2. 8,8,8,7,7,6,6,5,5,4,4,3,3-Tridecafluorooctanethiol $F(CF_2)_6(CH_2)_2SH$. Colorless liquid, yield: 4.5 g, 60%. bp: 61°C 10 mmHg. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −126.94 (m, 2F, $\underline{CF_2}CF_3$); −124.55 (m, 2 F, $\underline{CF_2}CF_2CF_3$); −124 (m, 2F, $\underline{CF_2}(CF_2)_2CH_2$); −122.6 (m, 2 F, $\underline{CF_2}CF_2CH_2$); −115.5 (m, 2 F, $\underline{CF_2}CH_2$); −81.64 (m, 3 F, $\underline{CF_3}$). MS (EI, 30 eV, 48.7°C) (*m/z*): 380 (58.2) $(M)^{+\bullet}$; 69 (29) $(CF_3)^+$; 61 (53.6) $(C_2H_5S)^+$; 47 (100) $(CH_3S)^+$.

2.4.1.3. 10,10,10,9,9,8,8,7,7,6,6,5,5,4,4,3,3-Heptadecafluorodecanethiol $F(CF_2)_8(CH_2)_2SH$. Colorless liquid, yield: 7.68g, 80%. bp: 89°C 10 mm Hg. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −127.1 (m, 2F, $\underline{CF_2}CF_3$); −124.37 (m, 2F, $\underline{CF_2}CF_2CF_3$); −123.67 (m, 2 F, $\underline{CF_2}(CF_2)_4CH_2$); −122.83 (m, 6 F, $(\underline{CF_2})_3CF_2CH_2$); −115.55 (m, 2F, $\underline{CF_2}CH_2$); −81.61 (t, 3 F, $\underline{CF_3}$). MS (EI, 30 eV, 48.7°C) (*m/z*): 480 (55) $(M)^{+\bullet}$; 69 (21) $(CF_3)^+$; 61 (54) $(C_2H_5S)^+$; 47 (100) $(CH_3S)^+$. Anal. Calc. for $C_{10}H_5F_{17}S$: C,25.01; H, 1.05; F, 67.26; S, 6.67. Found: C, 24.85; H, 1.02; F, 66.93; S, 6.61%.

2.4.1.4. 12,12,12,11,11,10,10,9,9,8,8,7,7,6,6,5,5,4,4,3,3-Henreicosafluorododecanethiol $F(CF_2)_{10}(CH_2)_2SH$. White solid, yield: 8.12 g, 70%. mp 68°C. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −126.77 (m, 2F, $\underline{CF_2}CF_3$); −124.16 (m, 2 F, $\underline{CF_2}CF_2CF_3$); −123.33 (m, 2 F, $CF_2(\underline{CF_2})_6CH_2$); −122.39 (m, 10 F, $(\underline{CF_2})_3CF_2CH_2$); −115.07 (m, 2 F, $\underline{CF_2}CH_2$); −81.42 (m, 3 F, CF_3). MS (EI, 70 eV, 29.2°C) (*m/z*): 579 (10) $(M)^+$; 69 (8) $(CF_3)^+$; 61 (20) $(C_2H_5S)^+$; 47 (100) $(CH_3S)^+$.

2.4.1.5. 15,15,15,14,14,13,13,12,12-Nonafluoropentadecanethiol $F(CF_2)_4(CH_2)_{11}SH$. Colorless liquid. bp: 85°C 0.1 mmHg. ^1H NMR: δ 1.3 (m, 15 H, $(CH_2)_7$ and SH); 1.55 (m, 4H, $\underline{CH_2}CH_2CF_2$ and 2H, $\underline{CH_2}CH_2SH$); 2 (m, 2H, CH_2CF_2); 2.52 (td, 2H, J_{H-H}=J_{H-SH}=7.3 Hz, CH_2SH). ^{19}F NMR: δ −126.61 (m, 2F, $\underline{CF_2}CF_3$); −125.07 (m, 2F, $\underline{CF_2}CF_2CH_2$); −115.19 (m, 2F, $\underline{CF_2}CH_2$); −81.57 (m, 3F, $\underline{CF_3}$). MS (FAB +, matrix NBA) (*m/z*): 405 (10) $(M-H)^+$; 403 (6.6) $(C_4F_9(CH_2)_{10}CS)^+$; 55 (100) $(C_4H_7)^+$.

2.4.1.6. 17,17,17,16,16,15,15,14,14,13,13,12,12-Tridecafluoroheptadecanethiol $F(CF_2)_6(CH_2)_{11}SH$. Colorless liquid. bp: 115°C 0.1 mmHg. ^1H NMR: δ 1.3 (m, 15 H, $(CH_2)_7$ and SH); 1.55 (m, 4H, $\underline{CH_2}CH_2CF_2$ and 2H, $\underline{CH_2}CH_2SH$); 2 (m, 2H, CH_2CF_2); 2.52 (td, 2H, J_{H-H}=J_{H-SH}=7.3 Hz, CH_2SH). ^{19}F NMR: δ −126.7 (m, 2F, CF_2CF_3); −125.13 (m, 2F, $CF_2CF_2CF_3$); −123.45 (m, 2F, $\underline{CF_2}(CF_2)_2CH_2$); −122.5 (m, 2 F, CF_2 CF_2CH_2); −115 (m, 2F, $\underline{CF_2}CH_2$); −81.34 (m, 3F, CF_3). MS (FAB +, matrix NBA) (*m/z*): 505 (10) $(M-H)^+$; 503 (6.6) $(C_6F_{13}(CH_2)_{10}CS)^+$; 55 (100) $(C_4H_7)^+$.

2.4.1.7. 19,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-heptadecafluorononadecanethiol $F(CF_2)_8(CH_2)_{11}SH$. White solid, yield: 6.06 g, 50%. mp. 49.7°C. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −126.57 (m, 2F, $\underline{CF_2}CF_3$); −123.99 (m, 2F, $\underline{CF_2}CF_2CF_3$); −123.17 (m, 2F, $\underline{CF_2}(CF_2)_4CH_2$); −122.37 (m, 6 F, $(CF_2)_3CF_2CH_2$); −114.86 (m, 2F, CF_2CH_2); −81.13 (m, 3F, CF_3). MS (FAB +, matrix NBA) (*m/z*): 605 (10) $(M-H)^+$; 603 (6.6) $(C_8F_{17}(CH_2)_{10}CS)^+$; 55 (100) $(C_4H_7)^+$. HRMS: caldfor 605, 1171$(M-H)^+$. Obsd for $C_{19}H_{22}F_{17}S$: 605, 1125.

2.4.1.8. 21,21,21,20,20,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-Heneicosafluoroheneicosanethiol $F(CF_2)_{10}(CH_2)_{11}SH$. White solid, yield: 5.65 g, 40%. mp: 73.4°C. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −126.77 (m, 2F, CF_2CF_3); −124.16 (m, 2F, $CF_2CF_2CF_3$); −123.33 (m, 2F, $CF_2(CF_2)_6CH_2$); −122.39 (m, 10 F, $(CF_2)_5CF_2CH_2$); −115.07 (m, 2F, CF_2CH_2); −81.42 (m, 3F, CF_3). MS (FAB +, matrix NBA) (*m/z*): 705 (20) $(M-H)^+$; 703 (11, 4) $(C_{10}F_{21}(CH_2)_{10}CS)^+$; 55

Table 1
Synthesis of perfluoroalkylalkanethiols, starting from the corresponding iodides, through the thiolacetic acid route

Starting compound RI	Recovered fluorinated compounds (%)	Relative molar percentage determined by NMR		Yield of RSH isolated after purification (%)[a]
		RSSR	RSH	
$F(CF_2)_4(CH_2)_2I$	60	5	95	50
$F(CF_2)_6(CH_2)_2I$	61	7	93	50
$F(CF_2)_8(CH_2)_2I$	80	4	96	68
$F(CF_2)_{10}(CH_2)_2I$	81	5	95	70
$F(CF_2)_4(CH_2)_{11}I$	75	6	94	69
$F(CF_2)_6(CH_2)_{11}I$	75	7	93	68
$F(CF_2)_8(CH_2)_{11}I$	79	10	90	60
$F(CF_2)_{10}(CH_2)_{11}I$	66	7	93	50

[a]After distillation or recrystallisation.

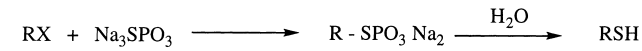
(100) $(C_4H_7)^+$. HRMS: cald for 705, 1107 $(M-H)^+$. Obsd. for $C_{21}H_{22}F_{21}S$: 705, 1205.

Identification of the disulfides: disulfides appearing in Table 1 have been identified by comparison of their ^1H and ^{19}F spectra with the equivalent compounds obtained in larger amounts in the pure state when working with thiourea or sodium thiophosphate (see below).

2.4.2. Reaction of F-alkyl halides with sodium thiophosphate

A simple and safe method of converting primary aliphatic halides to the corresponding mercaptans has been reported by Bieniarz [21]. Sodium thiophosphate tribasic dodecahydrate reacts with the halide in methanol or aqueous DMF, thus affording the desired mercaptans. We prepared the thiophosphate tribasic dodecahydrate in the laboratory [22], compound which in reference [21] is purchased from Aldrich, and in order to control its reactivity we have performed the reaction on the 11-bromoundecanoic acid, a compound equivalent to the 10-bromodecanoic acid studied in the cited reference, and observed a result very similar to the one reported by Bieniarz (reaction in DMF/water, formation of the corresponding thiols in 90% yield without any sulfide) (Scheme 4).

In the case of the semifluorinated halides studied in this work we observed very different results, reaction time being largely higher for a significant conversion and sulfides being



Scheme 4. Formation of alkyl-S-phosphorothiolate and thier hydrolysis to thiols.

mainly produced in the place of thiols, as summarized in Table 2.

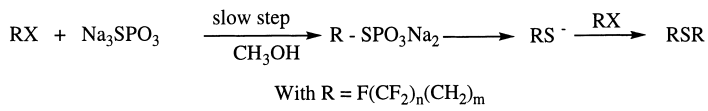
Experiments here reported have been run in methanol. Experiments in DMF/water failed completely. Moreover, it is essential to mention that the reaction times used for the perfluorinated alkyl halides are greater than in the literature [21]. Thiols when observed appeared in low yields. The main compounds formed are the sulfides with significant amounts of disulfides. In his original paper, Bieniarz [21] states that the mercaptan is prepared in the first step in a phosphate protected form, which also obviates the oxidative dimerisation of the thiolates. Moreover, the phosphorothioate hydrolysis occurs under very mild conditions, thus lowering the risk of oxidative dimerization (disulfide) or thioether formation.

In the case of the semifluorinated halides used, the method appears as an excellent one for the direct preparation of thioethers, obtained in good yields and easily purified as shown in the experimental part.

Note that the results on compounds bearing a long hydrogenated spacer are essentially for starting bromides; yields from iodides appeared lower. Satisfactory yields are

Table 2
Reaction of semifluorinated halides with sodium thiophosphate

Halide/Na_3PO_3S 1/1	Time of reaction	Recovered fluorinated compounds (%)	Relative molar percentage determined by NMR			
			RX	RSSR	RSR	RSH
$F(CF_2)_6(CH_2)_{11}Br$	24 h	85	90	3	0	7
$F(CF_2)_6(CH_2)_{11}Br$	48 h	62	62	2	31	4
$F(CF_2)_6(CH_2)_{11}Br$	72 h	59	39	5	56	Traces
$F(CF_2)_6(CH_2)_{11}I$	72 h	39	72	3	20	5
$F(CF_2)_8(CH_2)_2I$	24 h	57	50	0	50	0
$F(CF_2)_8(CH_2)_2I$	48 h	59	10	6	84	0
$F(CF_2)_8(CH_2)_2I$	72 h	70	Traces	28	72	0
$F(CF_2)_8(CH_2)_2I$	72 h under nitrogen	63	Traces	20	80	0



Scheme 5. Synthesis of perfluoroalkyl alkylsulfides with sodium thiophosphate.

obtained for iodide compounds bearing a short hydrogenated spacer. We consider that these results can be interpreted as follows: phosphorothioate formation is particularly slow in the case of the compounds studied. Consequently, their mild hydrolysis occurs in a relatively basic medium and in the presence of unreacted starting halide. Under such conditions the observed formation of thioether and disulfide is not unexpected. In addition, we have run an experiment starting from the *n*-undecylbromide, experiment run in methanol, and observed essentially the formation of sulfide with only 2% of disulfide and traces of the thiol (on the basis of NMR data). Thus, it can be considered that the results of Bierniaz are only for relatively activated halides (Scheme 5).

2.4.2.1. Synthesis of bis(perfluoroalkylalkane)sulfides $[F(CF_2)_n(CH_2)_m]_2S$ (with n=4, 6, 8 and m=2, 11): general procedure. To sodium thiophosphate dodecahydrate (0.01 mole, itself synthesized following the Wurtz method [22], (characterizated by NMR ^{31}P: −35 ppm [23]) dissolved in 60 ml of refluxing methanol was added semifluorinated halide (0.01 mole) dissolved in 60 ml of methanol. Refluxing was continued for 72 h. The solution was cooled to room temperature and concentrated to about 2 ml. The mixture was recovered by extraction with diethylether, washed with saturated aqueous NaCl three times, dried over sodium sulfate, filtered, and evaporated under vacuum. The crude products were purified as follows: in the case of the compounds bearing a short hydrogenated chain the separation sulfide/disulphide was performed by column chromatography R_f (hexane)=0.24 for the sulfides and 0.35 for the disulfides; in the case of the compounds bearing a long hydrogenated chain: selective recrystallization of the sulfides in dichloromethane (1 g for 10 ml).

2.4.2.2. Sulfides: bis(6,6,6,5,5,4,4,3,3-nonafluorohexyl)sulfide $[F(CF_2)_4(CH_2)_2]_2S$. Colorless liquid, yield: 2.63 g, 50%. ^1H NMR: δ 2.35 (m, 4H, 2 CH_2CF_2); 2.7 (m, 4H, 2 CH_2S). ^{19}F NMR: δ −126.83 (m, 4F, 2 $\underline{CF_2}CF_3$); −125.18 (m, 4F, 2 $\underline{CF_2}CF_2CF_3$); −115.37 (m, 4F, 2 $\underline{CF_2}CH_2$); −81.9 (m, 6F, 2 CF_3). MS (FAB +, matrix GT) (*m/z*): 526 (20) $(M)^+$; 525 (16.6) $(M-H)^+$; 293 (100) $(M-CH_2C_4F_9)^+$.

2.4.2.3. Bis(8,8,8,7,7,6,6,5,5,4,4,3,3-tridecafluorooctyl)sulfide $[F(CF_2)_6(CH_2)_2]_2S$. Colorless liquid, yield: 3.63 g, 50%. ^1H NMR: δ 2.4 (m, 4H, 2 CH_2CF_2); 2.6 (m, 4H, 2 CH_2S). ^{19}F NMR: δ −126.94 (m, 4F, 2 CF_2CF_3); −124.55 (m, 4F, 2 $CF_2CF_2CF_3$); −124 (m, 4F, 2 $CF_2(CF_2)_2CH_2$); −122.6 (m, 4F, 2 $CF_2CF_2CH_2$); −115.5 (m, 4F, 2 $\underline{CF_2}CH_2$); −81.64 (m, 6F, 2 $\underline{CF_3}$). MS (FAB +, matrix GT) (*m/z*): 726 (100) $(M)^+$; 725 (56) $(M-H)^+$; 393 (96) $(M-CH_2C_6F_{13})^+$. Anal. Calc. for $C_{16}H_8F_{26}S$: C, 26.46; H, 1.11; F, 68.01; S, 4.41. Found: C, 26.21; H, 1.51; F, 68.00; S, 4.81%.

2.4.2.4. Bis(10,10,10,9,9,8,8,7,7,6,6,5,5,4,4,3,3-heptadecafluorodecy)lsulfide $[F(CF_2)_8(CH_2)_2]_2S$. White solid, yield: 3.89 g, 42%. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −127.1 (m, 4F, 2 $\underline{CF_2}CF_3$); −124.37 (m, 4F, 2 $\underline{CF_2}CF_2CF_3$); −123.67 (m, 4F, 2 $\underline{CF_2}(CF_2)_4CH_2$); −122.83 (m, 12F, 2 $(\underline{CF_2})_3CF_2CH_2$); −115.55 (m, 4F, 2 $\underline{CF_2}CH_2$); −81.61 (m, 6F, 2 CF_3). MS (FAB +, matrix GT) (*m/z*): 926 (100) $(M)^+$; 493 (70) $(M-CH_2C_8F_{17})^+$. Anal. Calc. for $C_{20}H_8F_{32}S$: C, 25.93; H, 0.87; F, 69.73; S, 3.46. Found: C, 25.62; H, 1.3; F, 69.54; S, 3.45%.

2.4.2.5. Bis(17,17,17,16,16,15,15,14,14,13,13,12,12-tridecafluoroheptadecyl)sulfide $[F(CF_2)_6(CH_2)_{11}]_2S$. White solid, yield: 2.93 g, 30%. mp: 64.2°C. ^1H NMR: δ 1.3 (m, 28 H, 2 $(CH_2)_7$); 1.55 (m, 8H, 2 $\underline{CH_2}CH_2CF_2$) and 2 $\underline{CH_2}CH_2S$); 2 (m, 4H, 2 CH_2CF_2); 2.5 (t, 4H, J=7.2 Hz, 2 $\underline{CH_2}S$). ^{19}F NMR: δ −126.7 (m, 4F, 2 $\underline{CF_2}CF_3$); −125.13 (m, 4F, 2 $CF_2CF_2CF_3$); −123.45 (m, 4F, 2 $CF_2(CF_2)_2CH_2$); −122.5 (m, 4F, 2 $\underline{CF_2}CF_2CH_2$); −115 (m, 4F, 2 $\underline{CF_2}CH_2$); −81.34 (m, 6F, 2 $\underline{CF_3}$). MS (FAB +, matrix GT) (*m/z*): 977 (100) $(M-H)^+$; 533 (66) $(M-(CH_2)_{10}-C_6F_{13})^+$; 503 (62) $(C_6F_{13}(CH_2)_{10}CS)^+$. Anal. Calc. for $C_{34}H_{44}F_{26}S$: C, 41.72; H, 4.53; F, 50.47; S, 3.27. Found: C, 42.04; H, 4.45; F, 50.47; S, 3.61%.

2.4.2.6. Bis(19,19,19,18,18,17,17,16,16,15,15,14,14,13,13,12,12-heptadecafluorononadecyl)sulfide $[F(CF_2)_8(CH_2)_{11}]_2S$. White solid, yield: 2.36 g, 20%. mp: 83°C. ^1H NMR: as for the preceding compound. ^{19}F NMR: δ −126.57 (m, 4F, 2 $\underline{CF_2}CF_3$); −123.99 (m, 4F, 2 $\underline{CF_2}CF_2CF_3$); −123.17 (m, 4F, 2 $\underline{CF_2}(CF_2)_4CH_2$); −122.37 (m, 12 F, 2 $(\underline{CF_2})_3CF_2CH_2$); −114.86 (m, 4F, 2 CF_2CH_2); −81.13 (m, 6F, 2 CF_3). MS (FAB +, matrix GT) (*m/z*) 1177 (100) $(M-H)^+$; 618 (65) $(M-(CH_2)_{10}C_8F_{17})^+$; 602 (60) $(C_8F_{17}(CH_2)_{10}CS)^+$. Anal. Calc. for $C_{38}H_{44}F_{32}S$: C, 38.72; H, 3.76; F, 54.8; S, 2.72. Found: C, 38.14; H, 3.86; F, 54.6; S, 3.04%.

2.4.2.7. Disulfides: bis(8,8,8,7,7,6,6,5,5,4,4,3,3-tridecafluorooctyloctyl)disulfide $[F(CF_2)_6(CH_2)_2S]_2$. White solid. mp: 39.2°C. ^1H NMR: δ 2.9 (m, 4H, CH_2S); 2.5 (m, 4H, CH_2CF_2). ^{19}F NMR: δ −126.94 (m, 4F, 2 $\underline{CF_2}CF_3$); −124.55 (m, 4F, 2 $\underline{CF_2}CF_2CF_3$); −124 (m, 4F, 2 $\underline{CF_2}(CF_2)_2CH_2$);

Table 3
Yields of semifluorinated sulfides, disulfides and thiols, when reacting corresponding halides with sodium thiophosphate (halide/Na_3PO_3S: 1/1)

Starting compound RX	Recovered fluorinated compounds after 72 h (%)	Relative molar percentage determined by NMR				Yield of RSR isolated after purification (wt.%)
		RX	RSSR	RSH	RSR	
$F(CF_2)_4(CH_2)_2I$	60	0	5	0	95	50
$F(CF_2)_6(CH_2)_2I$	70	Traces	11	0	88	50
$F(CF_2)_8(CH_2)_2I$	70	Traces	28	0	72	42
$F(CF_2)_6(CH_2)_{11}Br$	59	39	5	Traces	56	30
$F(CF_2)_8(CH_2)_{11}Br$	61	37	7	15	41	20

−122.6 (m, 4F, 2 $\underline{CF_2}CF_2CH_2$); −114.3 (m, 4F, 2 $\underline{CF_2}CH_2$); −81.64 (m, 6F, 2 $\underline{CF_3}$). MS (EI, 70 eV, 47.1°C) (*m/z*): 758 (100) $(M)^+$; 739 (15) $(M-F)^+$; 425 (30) $(M-CH_2C_6F_{13})^+$. HRMS: cald for 757.9652 $(M)^+$. Obsd for $C_{16}H_8F_{26}S_2$: 757.9747.

2.4.2.8. Bis(10,10,10,9,9,8,8,7,7,6,6,5,5,4,4,3,3-heptadecafluorodecyl)disulfide $[F(CF_2)_8(CH_2)_2S]_2$. White solid. mp: 76.4°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −127.1 (m, 4F, 2 CF_2CF_3); −124.37 (m, 4F, 2 $CF_2CF_2CF_3$); −123.67 (m, 4F, 2 $\underline{CF_2}(CF_2)_4CH_2$); −122.83 (m, 12F, 2 $(\underline{CF_2})_3CF_2CH_2$); −114.5 (m, 4F, 2 $\underline{CF_2}CH_2$); −81.61 (m, 6F, 2 $\underline{CF_3}$). MS (EI, 70 eV, 71.1°C) (*m/z*): 958 (74) $(M)^{+\bullet}$; 939 (12.3) $(M-F)^+$; 525 (32.3) $(M-CH_2C_8F_{17})+$; 512 (22.3) $(C_8F_{17}CH_2CH_2S_2H)^{+\cdot}$. HRMS: cald for 957.9525$(M)^+$. Obsd for $C_{20}H_8F_{32}S_2$: 957.9433.

Thiols when indicated in Table 3 have been identified on the basis of their ^{1}H and ^{19}F spectra by comparison with spectral data of the equivalent compounds obtained in the pure state when working with thiolacetic acid (see above).

Disulfides appearing in Table 3, and bearing a long hydrogenated spacer have been identified by comparison of their ^{1}H and ^{19}F spectra with the equivalent compounds obtained in the pure state when working with thiourea (see below).

2.4.2.9. Synthesis of 11-mercaptoundecanoic acid $HS(CH_2)_{10}COOH$. To 2 mmol of 11-bromoundecanoic acid in 2 ml of DMF was added 2 equiv. of sodium thiophosphate dodecahydrate in 10 ml of water. The mixture was stirred for 5 h and the pH was lowered to 4 with 3.5% HCl. Stirring was continued overnight. The reaction mixture was extracted three times with CH_2Cl_2, washed with brine and dried over anhydrous sodium sulfate, filtered and then vacuum evaporated. The crude product was purified by recrystallization in hexane, white solid (a compound previously described by Whitesides [20]).

^{1}H NMR: δ 1.28 (m, 13 H, $(CH_2)_6$ and SH); 1.65 (m, 4 H, $\underline{CH_2}CH_2SH$ and $\underline{CH_2}CH_2COOH$); 2.35 (t, 2 H, $\underline{CH_2}COOH$); 2.5 (q, 2H, $\underline{CH_2}SH$); 10.6 (1 H, COOH).

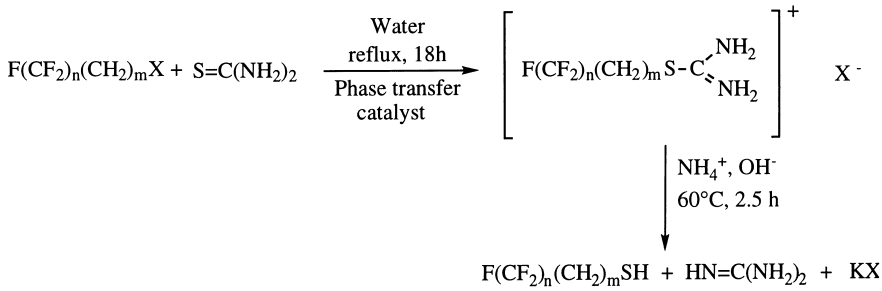
2.4.3. Preparation of thiouronium salts

An important method for the synthesis of terminally fluorinated thiols, based on the formation of isothiouronium salts was first reported in the sixties [4,5] and developed more recently [6–8]. In these reports only short hydrogenated spacers were used with a basic treatment of isothiouronium salt with ammonia [24]. We have applied this process to long hydrogenated spacers (m=11) with excellent yields as shown in Table 4 (Scheme 6).

Thiourea (0.03 mole), perfluoroalkyl halide (0.02 mole) tributylhexadecylphosphonium bromide (1 mmole) and 12 ml of water were placed in a 250 ml bi-necked flask equipped with a reflux condenser. The reaction mixture was stirred overnight at reflux. The basic hydrolysis of isothiouronium salts was performed at room temperature, under a nitrogen atmosphere. An aqueous solution of ammonia (0.02 mole, 30% in water) was added drop by drop through a septum. After stirring for 2.5 h at 60°C, the mixture was acidified with dilute HCl, extracted with ether (150 ml) and washed with saturated hot aqueous NaCl three times. The organic phase was dried over sodium sulfate, filtered, and evaporated under reduced pressure. The crude products when in the liquid state, were distilled under vacuum. Solid ones were dissolved in ethanol, thus eliminating the disulfide by recrystallization. In these cases final yields were very low (around 20%).

Table 4
Reaction of semifluorinated halides with thiourea

Starting compounds RX	Recovered fluorinated compounds (%)	Relative molar percentage determined by NMR		
		RX	RSSR	RSH
$F(CF_2)_4(CH_2)_2I$	61	6	4	90
$F(CF_2)_6(CH_2)_2I$	63	5	10	95
$F(CF_2)_4(CH_2)_{11}Br$	83	7	18	74
$F(CF_2)_6(CH_2)_{11}I$	87	6	19	75
$F(CF_2)_8(CH_2)_{11}I$	78	5	10	86



Scheme 6. Synthesis of perfluoroalkylalkanethiols from thiourea.

2.4.3.1. Bis(15,15,15,14,14,13,13,12,12-nonafluoropentadecyl)disulfide [F(CF$_2$)$_4$(CH$_2$)$_{11}$S]$_2$. White solid. mp: 34.9°C. ^{1}H NMR: δ 1.3 (m, 28 H, 2 $(CH_2)_7$); 1.55 (m, 8H, 2 $CH_2CH_2CF_2$ and 2 $\underline{CH_2}CH_2S$); 2 (m, 4H, 2 CH_2CF_2); 2.68 (t, 4H, J=7.3 Hz, 2 $\overline{CH_2}S$). ^{19}F NMR: δ −126.61 (m, 4F, 2 $\underline{CF_2}CF_3$); −125.07 (m, 4F, 2 $\underline{CF_2}CF_2CH_2$); −115 (m, 4F, 2 $\overline{CF_2}CH_2$); −81.57 (m, 6F, 2 $\overline{CF_3}$). MS (EI, 70 eV, 141.3°C) (*m/z*): 810 (7) $(M)^{+\bullet}$; 577 (0.8) $(M-CH_2(CF_2)_4F)^+$; 438 (10) $(C_4F_9(CH_2)_{11}S_2H)^+$; 405 $(C_4F_9(CH_2)_{11}S)^+$ (10); 403 (2.3) $(C_4F_9(CH_2)_{10}\ CS)^+$; 57 (100) $(C_4H_9)^+$. HRMS: cald for 810.2597. Obsd for $C_{30}H_{44}F_{18}S_2$: 810.2699.

2.4.3.2. Bis(17,17,17,16,16,15,15,14,14,13,13,12,12- tridecafluoroheptadecyl)disulfide [F(CF$_2$)$_6$(CH$_2$)$_{11}$S]$_2$. White solid. mp: 50.4°C. ^{1}H NMR: as for the preceding compound. ^{19}F NMR: δ −126.7 (m, 4F, 2 $\underline{CF_2}CF_3$); −125.13 (m, 4F, 2 $\underline{CF_2}CF_2CF_3$); −123.45 (m, 4F, 2 $\underline{CF_2}(CF_2)_2CH_2$); −122.5 (m, 4 F, 2 $\underline{CF_2}$ CF_2CH_2); −114.9 (m, 4F, 2 CF_2CH_2); −81.34 (m, 6F, 2 $\overline{CF_3}$). MS (EI, 70 eV, 159°C) (*m/z*): 1010 (10) $M^{+\bullet}$; 505 (29) $(M-S(CH_2)_{11}$-$C_6F_{13})^+$; 503 (0.8) $(C_6F_{13}(CH_2)_{10}-CS)^+$; 57 (100) $(C_4H_9)^+$.

Other compounds (thiols) appearing in Table 4 have been assigned by comparison of their spectral data with those obtained for identical compounds identified in the pure state above.

2.4.4. Reaction of sodium hydrogen sulfide NaSH with terminally perfluorinated alkyl iodides

Sodium hydrogen sulfide (NaSH) is a much better reagent for the formation of thiols from alkyl halides than H_2S. We have performed this process in two separate steps. In Step 1 sodium hydrogen sulfide has been prepared in the pure state according to the literature [25]. In the second step starting iodides are reacted with sodium hydrogen sulfide in methanol (Scheme 7).

We observed that in spite of the separation of the process into two steps, the reaction led to thiols, sulfides and disulfides. Thiols are favoured when starting from iodides bearing a long hydrogenated spacer, a result in accordance with literature data on perhydrogenated primary halides [26]. When starting from halides with a short hydrogenated spacer, formation of sulfide occurs predominantly.

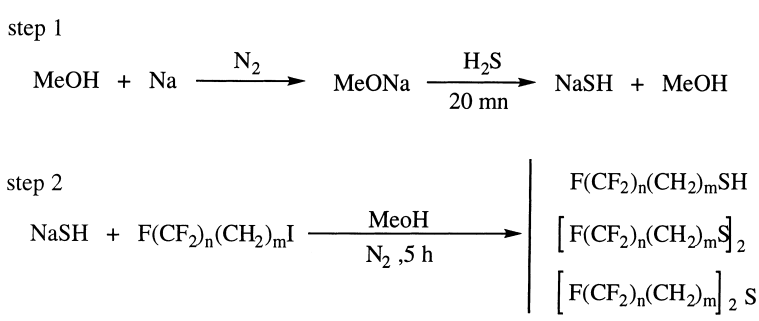
Under a nitrogen atmosphere, sodium hydrogen sulfide (0.01 mole), synthesized separately [23], perfluoroalkyl halide (0.01 mole) and 20 ml of anhydrous ethanol were placed in a 100 ml two-necked flask equipped with a reflux condenser. The reaction mixture was stirred for 5 h at reflux. The mixture was acidified (dilute HCl), extracted with ether (50 ml), and the organic phase washed with saturated hot aqueous NaCl three times, dried over sodium sulfate, filtered, and freed from solvent on a rotary evaporator.

Compounds appearing in Table 5 have been assigned by comparison of their spectral data with the ones obtained for identical compounds identified in the pure state above.

2.4.5. The Bunte salt reaction

Conversion of the 1-bromo-11-perfluoroalkylundecane $F(CF_2)_8(CH_2)_{11}Br$ to thiol via the Bunte salt reaction [27–28] has been recently reported by Tsao (yield 74%) [9]. In our hands the reaction gave a similar result for the $F(CF_2)_6(CH_2)_{11}Br$ bromide (Scheme 8).

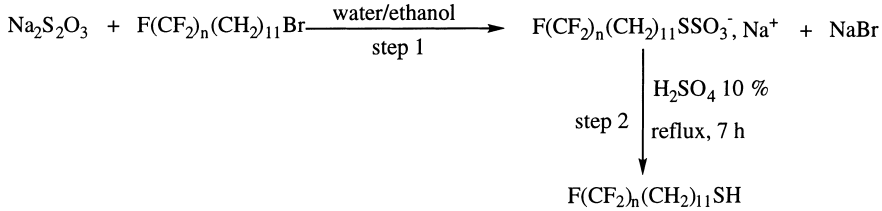
When starting from the corresponding iodides we observed competitive formation of disulfide and sulfide,



Scheme 7. Reaction of terminally fluorinated alkyl iodides with sodium hydrogen sulfide.

Table 5
Reaction of semifluorinated iodides with sodium hydrogen sulphide (molar ratio 1:1)

Starting compounds RI	Recovered fluorinated compounds (%)	Relative molar percentage determined by NMR			
		RI	RSSR	RSR	RSH
$F(CF_2)_6(CH_2)_2I$	66	5	8	60	27
$F(CF_2)_6(CH_2)_{11}I$	74	4	6	20	70



Scheme 8. The Bunte salt reaction.

Table 6
Reaction of semifluorinated alkyl halides with sodium thiosulfate (ratio $Na_2S_2O_3$/halide: 1/1)

Starting compounds RX	Recovered fluorinated compounds (%)	Relative molar percentage determined by NMR			
		RX	RSSR	RSR	RSH
$F(CF_2)_6(CH_2)_{11}Br$	70	5	Traces	Traces	95
$F(CF_2)_8(CH_2)_{11}I$	74	32	12	6	50
$F(CF_2)_6(CH_2)_{11}I$	72	22	11	7	60
$F(CF_2)_6(CH_2)_2I$	49	32	12	Traces	55

as shown in Table 6. Similar results are obtained when starting from an iodide bearing an short hydrogenated spacer $F(CF_2)_6(CH_2)_2I$.

Halide (3 mmol), was dissolved in 5 ml of ethanol in a 25 ml flask. Sodium thiosulfate (3 mmol) was dissolved in 5 ml of water, and the resulting solution was added to the ethanol one. The mixture was heated at reflux for 18 h. Hydrolysis was carried out by adding 3 ml of 10% aqueous sulfuric acid and refluxing for 7 h. The thiol product could be seen separating as a heavier liquid phase. The thiol was recovered by extraction with ether, washed with water three times, dried with sodium sulfate, filtered, and freed from solvent. Compounds appearing in Table 6 have been assigned by comparison of their spectral data with the ones obtained for identical compounds identified in the pure state above.

3. Conclusions

Results obtained for the five synthetic routes studied above for the synthesis of thiols, sulfides and disulfides, from the corresponding iodides are summarized in Table 7, taking the iodo-perfluorohexylalkanes $F(CF_2)_6(CH_2)_mI$, m=2, 11 as an example.

Methods based on thioacetic acid and thiourea yield very similar results and appear the best ones for thiol synthesis. Experiments with sodium thiophosphate constitute an

Table 7
Products distribution when starting from the iodides $F(CF_2)_6(CH_2)_mI$, m=2, 11 depending on the method used

Synthetic route	Relative product distribution in mole (%)							
	R=$F(CF_2)_6(CH_2)_2$				R=$F(CF_2)_6(CH_2)_{11}$			
	RI	RSH	RSR	RSSR	RI	RSH	RSR	RSSR
Thioacetic acid	0	93	0	7	0	90	0	10
Thiourea	5	85	0	10	6	75	0	19
Sodium thiophosphate	Traces	0	88	11	72	5	20	3
Sodium hydrogen sulfide	5	27	60	8	4	70	20	6
Sodium thiosulfate	32	55	Traces	12	22	60	7	11

excellent direct route to thioethers, at least when working with the short hydrogenated spacers. When starting from the long ones, conversion of the iodide appears severely limited. This difficulty is circumvented when starting from the equivalent bromides (see Table 2, 39% of remaining starting halide in the place of 72%). All the compounds reported have been identified unambiguously. Purification to a high level has been performed by distillation, selective recrystallization or column chromatography. The two other classical routes studied, sodium hydrogen sulfide and sodium thiosulfate (the Bunte reaction), yield a mixture of thiols, sulfides and disulfides.

These compounds should find use in the generation of well-defined fluorinated interfaces using the self-assembled monolayers (SAMs) technique.

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