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Synthesis of Sterically Hindered Fluorous Aryl Perfluoroalkyl Sulfides

Antal Harsányi, Gitta Schlosser and József Rábai*

Institute of Chemistry, Eötvös Loránd University, Pázmány Péter sétány 1-A, Budapest, H-1117, Hungary

e-mail: rabai@elte.hu

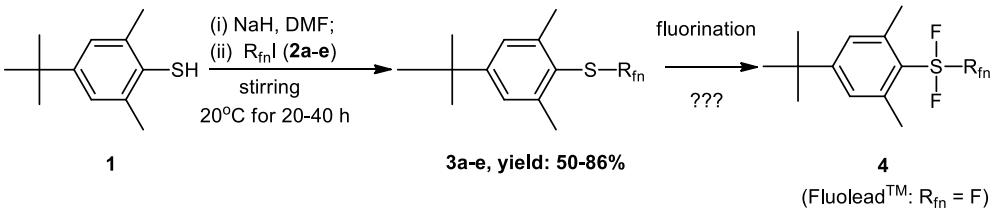
Abstract: *The sodium salt of 2,6-dimethyl-4-tert-butyl-benzenethiol was reacted in dimethyl formamide with a series of perfluoroalkyl iodides and 1,8-diiodoperfluorooctane to afford the corresponding perfluoroalkyl sulfides and 1,8-bis(arylthio)perfluorooctane in good yields.*

Keywords*:* fluorous sulfides, perfluoroalkyl iodides, perfluoroalkylation

Inspired by the introduction of Fluolead™ by Umemoto *et al.* [1] as a novel fluorinating reagent and with the early publication on the preparation of some aryl(trifluoromethyl)difluorosulfuranes by Yagupolskii *et al.* [2] we aimed at to synthesize $ArSF_2R_{fn}$ type sulfuranes (**4**) (Scheme 1).

Such perfluoroalkyl substituted reagents are expected to have unique physical-chemical properties similar to that of fluorocarbons and allowing easy separation of used reagents from products [3].

Here we disclose the optimized synthesis of precursor aryl perfluoroalkyl sulfides (**3a-e**) based on spontaneous perfluoroalkylation of thiols without initiators under similar conditions that reported for simple thiols by Feiring and Boiko [4](Scheme 1).



Scheme 1. Planned synthesis of novel *fluorous* aryl perfluoroalkyl difluorosulfuranes **4**.

Sterically hindered aryl perfluoroalkyl sulfides **3a-e** were prepared in good to excellent isolated yields using the reaction of the sodium salt of **1** with a slight excess of 1-iodoperfluoroalkanes ($R_{fn}I$, **2a-d**) or with that of 1,8-diiodoperfluorooctane (**2e**) in absolute DMF at room temperature for 20 to 40 h. The purified new fluorous sulfides **3a-e** were appropriately characterized. It is worth to mention that mass spectrometric measurements by APCI technique were highly facilitated by using a 1:1 vol/vol solvent mixture of CH_3CN and CF_3CH_2OH for sample preparation. The synthesis of the analogue trifluoromethyl sulfide ($R_{fn} = CF_3$) was effected by using CF_3I dissolved in DMF as a perfluoroalkylating reagent and reported earlier by us [5].

Our attempts for oxidative fluorination of **3** to **4** ($R_{fn} = CF_3$) with the use of $Br_2/KF/CH_2Cl_2$ and some other reagent systems however has not succeeded yet [6].

Experimental

^{1}H-, ^{13}C- and ^{19}F-NMR spectra were recorded on Bruker Avance 250 instrument using a 5 mm inverse $^{1}H/^{13}C/^{31}P/^{19}F$ probe head at room temperature. Chemical shifts (δ) are given in parts per million (ppm) units relatively solvent ($CDCl_3$) residual peaks (δ=7.26 for ^{1}H, δ=77.0 for ^{13}C) and to $CFCl_3$ as external standard (δ=0.00 for ^{19}F). Determination of molecular mass was performed by atmospheric pressure chemical ionization mass spectrometry (APCI-MS) on a Bruker Daltonics Esquire 3000 plus (Germany) ion trap mass spectrometer. Samples were dissolved in acetonitrile – trifluoroethanol solvent mixture (50:50, V/V). Mass spectra were acquired in the 50-1500 m/z range yielding singly charged radical cations ($M^{\bullet+}$). Nebulizer gas pressure was 25 psi, drying gas flow was 5 L/min, the heated capillary temperature was 250 °C and the vaporizer temperature was 450 °C. Samples were injected into the ion source in a flow rate of 10 μL/min using a syringe pump. Melting points were determined on a Böetius micro-melting point apparatus and are uncorrected. Gas chromatographic analysis of volatile products was performed using a Hewlett-Packard 5890 Series II instrument with PONA [crosslinked methylsilicone gum] 50 m x 0.2mm x 0.5 mm column, H_2 carrier gas, FID detection; Program: 120 °C, 5 min, 10 °C/min, 250 °C, 5 min, Inj.: 250°C, Det.: 280°C.

General Procedure for the Synthesis of Aryl Perfluoroalkyl Sulfides (GP) [7]

4-(*tert*-Butyl)-2,6-dimethylbenzenethiol [8] (1.93 g, 10 mmol) was suspended in absolute DMF (15 mL) and reacted with sodium hydride (11 mmol) in small portions, prepared by washing under an argon atmosphere a 57% w/w sodium hydride – white oil dispersion with pentane (3 x 5 mL). When the evolution of hydrogen ceased the perfluoroalkyl iodide (**2a-d**, $C_nF_{2n+1}I$, [n=4,6,8,10], 11.0 mmol) or 1,8-diiodoperfluorooctane (**2e**, $I(CF_2)_8I$, 5.50 mmol) was added and the mixture was stirred at room temperature for 20 h (**3a-c**) or 40 h (**3d-e**) under an N_2 atmosphere. Then the reaction mixture was poured into water (100 mL) and extracted with diethyl ether (3 x 20 mL), the combined organic extracts were washed with water (3 x 20 mL) and saturated aq-NaCl solution (20 mL). The ether phase was separated and dried (Na_2SO_4), then the ether was removed by distillation and the product was purified by vacuum distillation or crystallization.

(4-(tert-Butyl)-2,6-dimethylphenyl)(perfluorobutyl)sulfide (3a)

Yield: 2.90 g (71 %) colourless liquid, obtained by short path distillation; 20 Hgmm@160°C bath. It solidifies in the freezer. GC assay: 98%+, t_{RET}: 14.47 min. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.33 (s, 9H, $C(CH_3)_3$), 2.57 (s, 6H, CH_3), 7.22 (s, 2H, Ar CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 22.88, 31.43, 34.97, 118.81, 126.34, 145.98, 154.82. ^{19}F NMR (243 MHz, $CDCl_3$): δ -81,50 (m, 3F, CF_3), -85,96 (m, 2F, CF_2), -121,29 (m, 2F, CF_2), -126,01 (m, 2F, CF_2). MS (APCI, $M^{\bullet+}$): calcd. for $C_{16}H_{17}F_9S$ = 412.1; measured: 412.0.

(4-(tert-Butyl)-2,6-dimethylphenyl)(perfluorohexyl)sulfide (3b)

Yield: 3.50 g (68 %) white waxy solid with mp = 32-34 °C, obtained by short path distillation; 20 Hgmm@170°C bath. GC assay: 98%, t_{RET}: 15.90 min. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.32 (s, 9H, $C(CH_3)_3$), 2.56 (s, 6H, CH_3), 7.21 (s, 2H, Ar CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 22.89, 31.44, 34.97, 118.81, 126.34, 145.99, 154.82. ^{19}F NMR (243 MHz, $CDCl_3$): δ -81.33 (m, 3F, CF_3), -85.74 (m, 2F, CF_2), -120.38 (m, 2F, CF_2), -121.85 (m, 2F, CF_2), -123.28 (m, 2F, CF_2), -126.63 (m, 2F, CF_2). MS (APCI, $M^{\bullet+}$): calcd. for $C_{18}H_{17}F_{13}S$ = 512.1; measured: 511.9.

(4-(tert-Butyl)-2,6-dimethylphenyl)(perfluorooctyl)sulfide (3c)

Yield: 5.30 g (86 %) white crystals with mp = 53-54 °C, obtained by short path distillation; 0.5 Hgmm@120°C bath. GC assay: 98%, t_{RET}: 17.31 min. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.31 (s, 9H, $C(CH_3)_3$), 2.55 (s, 6H, CH_3), 7.20 (s, 2H, Ar CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 22.90, 31.45, 34.98, 118.82, 126.34, 145.98, 154.81. ^{19}F NMR (243 MHz, $CDCl_3$): δ -81.28 (m, 3F, CF_3), -85.72 (m, 2F, CF_2), -120.33 (m, 2F, CF_2), -121.65 (m, 2F, CF_2), -122.35 (m, 4F, CF_2), -123.24 (m, 2F, CF_2), -126.62 (m, 2F, CF_2). MS (APCI, $M^{\bullet+}$): calcd. for $C_{20}H_{17}F_{17}S$ = 612.1; measured: 611.8.

(4-(tert-Butyl)-2,6-dimethylphenyl)(perfluorodecyl)sulfide (3d)

Yield: 5.70 g (76 %) white crystals with mp = 72-75 °C, obtained by short path distillation; 0.5 Hgmm@140°C bath. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.31 (s, 9H, $C(CH_3)_3$), 2.55 (s, 6H, CH_3), 7.20 (s, 2H, Ar CH). ^{13}C NMR (62,5 MHz, $CDCl_3$): δ 22.90, 31.46, 34.98, 118.82, 126.33, 145.97, 154.81. ^{19}F NMR (243 MHz, $CDCl_3$): δ -81.26 (m, 3F, CF_3), -85.72 (m, 2F, CF_2), -120.33 (m, 2F, CF_2), -121.64 (m, 2F, CF_2), -122.24 (m, 8F, CF_2), -123.20 (m, 2F, CF_2), -126.58 (m, 2F, CF_2). MS (APCI, $M^{\bullet+}$): calcd. for $C_{22}H_{17}F_{21}S$ = 712.1; measured: 711.8.

(Perfluorooctane-1,8-diyl)bis((4-(tert-butyl)-2,6-dimethylphenyl)sulfide (3e)

The crude product was recrystallization from acetone (15 mL). Yield: 2.80 g (50 %) white crystals with mp = 100-101 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (s, 9H, $C(CH_3)_3$), 2.56 (s, 6H, CH_3), 7.21 (s, 2H, Ar CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 22.90; 31.45; 34.98; 118.82; 126.34; 145.98; 154.81. ^{19}F NMR (243 MHz, $CDCl_3$): δ = -85.67 (m, 4F, CF_2), 120.31 (m, 4F, CF_2), -121.62 (m, 4F, CF_2), -122.22 (m, 4F, CF_2). MS (APCI, $M^{\bullet+}$): calcd. for $C_{32}H_{34}F_{16}S_2$ = 786.2; measured: 786.0.

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