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[(Polyfluoroalkoxy)methyl]thiiranes and 2-Anilinoethanethiols

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Abstract—By reaction of appropriate oxiranes with thiourea [(polyfluoroalkoxy)methyl]-substituted thiiranes were obtained that are key compounds for the synthesis of perfluoro-containing 1,2-aminopropanethiols.

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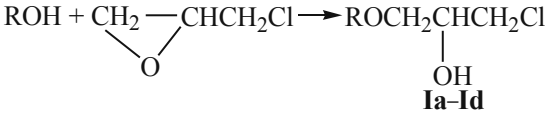
Many thiiranes attract a special attention of researchers as valuable initial synthons for the synthesis of versatile physiologically active substances, antidotes of heavy metals, radioprotectors, psychotropic and neurotropic compounds, pharmaceuticals used in the therapy of cancer in combination with alkylating antitumor preparations. They are also employed as monomers in production of specialty rubbers, as regulators of polymerization processes, antioxidants, and for other purposes [1–3].

In this connection the synthesis of new representatives of perfluoro-containing thiiranes, their amino derivatives, and the study of their functional properties is an urgent problem.

The key compounds for the preparation of [(polyfluoroalkoxy)methyl]fluoro-substituted oxiranes served polyfluoro-containing chlorohydrins **Ia–Id** obtained by reaction of 1,2-epoxy-3-chloropropane with various polyfluoro-containing aliphatic alcohols in the presence of sodium.

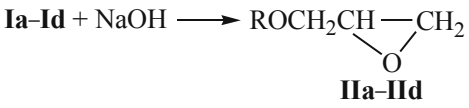
In the second stage by reaction of chlorohydrins **Ia–Id** with alkali oxiranes **IIa–IId** were synthesized. The latter are synthons for preparation of the thiiranes in question.



Ia–Id

R = CF_3CH_2 (**a**), $C_2F_5CH_2$ (**b**), $C_3F_7CH_2$ (**c**), $CHF_2CF_2CH_2$ (**d**).

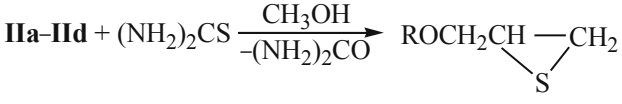
The reaction was carried out in the presence of a fine powder of potassium or sodium hydroxide in ether or by treating with 20% solution of these alkali.



IIa–IId

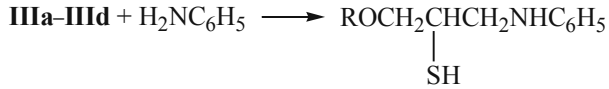
We formerly established [2–7] that anionotropic substitution of the oxygen atom in oxiranes by sulfur in the presence of sulfuric acid resulted in increased yields of alkoxy-substituted thiiranes. However the attempt to synthesize polyfluoroalkyl-substituted thiiranes by this procedure was unsuccessful. The reaction led predominantly to the formation of the side polymeric product decreasing the yield of the target compound.

Therefore we synthesized polyfluoroalkyl-containing thiiranes **IIIa–IIId** by the reaction of the corresponding oxiranes **IIa–IId** with thiourea in methanol solution.



IIIa–IIId

In order to study the effect of the polyfluoroalkyl moiety on the antioxidant and antimicrobial activity of 1,2-aminopropanethiols we carried out reactions of thiiranes **IIIa–IIId** with aniline.



IVa–IVd

The synthesized [(polyfluoroalkoxy)methyl]-substituted thiiranes and 1,2-aminopropanethiols are color-

less fluids with a specific odor. 1,2-Aminopropanethiols get yellow at prolonged storage.

The purity of compounds obtained was checked by elemental analysis, TLC, and GLC, and their structure was proved by IR and ^{1}H NMR spectroscopy.

In the IR spectra of perfluoro-containing thiiranes **IIIa–IIId** a strong absorption band is present in the region 640–660 cm^{-1} characteristic of the three-membered thiirane ring, and in the regions 1110–1130 and 160–1375 cm^{-1} appear absorption bands of the stretching vibrations of C–F bond.

The IR spectra of polyfluoroalkyl-containing 1,2-aminopropanethiols **IVa–IVd** in contrast to initial thiiranes **IIIa–IIId** lack the absorption band characteristic of the thiirane ring in the region 640–660 cm^{-1}, but contain the characteristic absorption band in the region 3340–3360 cm^{-1} corresponding to the stretching vibrations of NH bonds of secondary amino groups. The stretching vibrations of SH bond give rise to a weak band in the region 2540–2545 cm^{-1}. Alongside the above bands all spectra contain strong absorption bands in the regions 1445–1460, 1500–1510, and 1590–1610 cm^{-1} characteristic of the stretching vibrations of the C=C bonds in benzene ring.

In the ^{1}H NMR spectrum of compound **IIId** two protons of the methylene group of thiirane ring appear in the strong field as two doublets at δ 2.1 and 2.4 ppm corresponding to *cis*- and *trans*-positions of hydrogen atoms. The signal of methine proton due to coupling with the protons of two adjacent methylene groups appears at 2.9 ppm as a quintet. The protons of two methylene groups linked to oxygen (CH_2OCH_2) give rise to a multiplet at 3.8 ppm. The signal from the proton of CHF_2 fragment appears downfield at 5.9 ppm. The ^{1}H NMR spectra of the other perfluoro-containing thiiranes have similar patterns.

^{1}H NMR spectra of perfluoroalkyl-containing 1,2-aminopropanethiols **IVa–IVd** resemble the spectra of the corresponding thiiranes but the signals of protons of SH and NH groups and also of three protons of the $CHCH_2$ fragment are observed in all the spectra as multiplets in the 2.9–3.7 ppm, and nonequivalent protons of the benzene ring give rise to a multiplet in the region 6.0–7.2 ppm.

It was shown by special investigation that the synthesized perfluoro-containing thiiranes possess high antiwelding properties, and their amino derivatives exhibit antimicrobial activity in lubricants.

EXPERIMENTAL

^{1}H NMR spectra were registered on a spectrometer Bruker AM-300 at operating frequency 300 MHz, solvent $CDCl_3$, internal reference TMS. IR spectra were recorded on a spectrophotometer UR-20. The purity of reaction products was checked by TLC on Silufol UV-254 plates.

3-(2,2,2-Trifluoroethoxy)-1-chloropropan-2-ol (Ia). To a cooled mixture of 10 g (0.1 mol) of 2,2,2-trifluoroethanol, 2.3 g (0.1 g-atom) of sodium, and 9.25 g (0.1 mol) of 1,2-epoxy-3-chloropropane was added at vigorous stirring a solution of 8 g of NaOH in 30 ml of H_2O, and the mixture was left standing at room temperature for 10 h. Then the organic layer was separated, washed twice with water, and dried with Na_2SO_4. The reaction product was subjected to vacuum distillation. Yield 9.6 g, bp 86–87°C (20 mm Hg), n_D^{20} 1.3971, d_4^{20} 1.3791. MR_D 33.67, calc. 33.33. IR spectrum, ν, cm^{-1}: 3155–3250 (OH), 675 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 3.21 m (2H, OCH_2), 3.74 m (1H, CH), 3.57 m (2H, CH_2Cl). Found, %: C 31.03; H 4.02; Cl 18.27. $C_5H_8ClF_3O_2$. Calculated, %: C 31.17; H 4.15; Cl 18.44.

Compounds **Ib–Id** were similarly obtained.

3-(3,3,3,2,2-Pentafluoropropoxy)-1-chloropropan-2-ol (Ib) was obtained from 15 g (0.1 mol) of 3,3,3,2,2-pentafluoropropanol and 9.25 g (0.1 mol) of 1,2-epoxy-3-chloropropane. Yield 13.8 g (57%), bp 87°C (22 mm Hg), n_D^{20} 1.3823. IR spectrum, ν, cm^{-1}: 3165–3230 (OH), 670 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 3.25 m (2H, OCH_2), 3.69 m (1H, CH), 3.60 m (2H, OCH_2). Found, %: C 29.53; H 3.14; Cl 14.48. $C_6H_8ClF_5O_2$. Calculated, %: C 29.69; H 3.29; Cl 14.64.

3-(4,4,4,3,3,2,2-Heptafluorobutoxy)-1-chloropropan-2-ol (Ic) was obtained from 20 g (0.1 mol) of 4,4,4,3,3,2,2-heptafluorobutanol and 9.25 g (0.1 mol) of 1,2-epoxy-3-chloropropane. Yield 17.5 g (60%), bp 91°C (15 mm Hg), n_D^{20} 1.3739. IR spectrum, ν, cm^{-1}: 3170–3225 (OH), 635 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 3.35 m (2H, OCH_2), 3.75 m (1H, CH), 3.67 m (2H, CH_2Cl). Found, %: C 28.61; H 2.59; Cl 11.98. $C_7H_8ClF_7O_2$. Calculated, %: C 28.72; H 2.74; Cl 12.14.

3-(3,3,2,2-Tetrafluoropropoxy)-1-chloropropan-2-ol (Id) was obtained from 13.2 g (0.1 mol) of 3,3,2,2-tetrafluoropropanol and 9.25 g (0.1 mol) of 1.2-epoxy-3-chloropropane. Yield 9.7 g (60%), bp 80–82°C (15 mm Hg), n_D^{20} 1.3875. IR spectrum, ν, cm^{-1}: 3145–3220 (OH), 638 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 3.28 m (2H, OCH_2), 3.80 m (1H, CH), 3.60 m (2H, CH_2Cl). Found,

%: C 31.95; H 3.83; Cl 15.63. $C_6H_9ClF_4O_2$. Calculated, %: C 32.07; H 4.01; Cl 15.81.

2-[(2,2,2-Trifluoroethoxy)methyl]oxirane (IIa). To a solution of 19.25 g (0.1 mol) of 3-(2,2,2-trifluoroethoxy)-1-chloropropan-2-ol (**Ia**) in 50 ml of anhydrous ether at vigorous stirring was added by portions 11.2 g (0.2 mol) of powdered potassium hydroxide. Therewith the reaction mixture strongly heated. Then it was heated to 60°C for 1.5 h. On cooling the ether layer was separated, the residue was extracted with anhydrous ether (3×30 ml). The ether was distilled off, the reaction product was distilled at ordinary pressure. Yield 9.36 g (60%), bp 132–135°C, d_4^{20} 1.2669, n_D^{20} 1.3581. MR_D 26.93, calc. 26.62. IR spectrum, ν, cm^{-1}: 829, 880, 910, 1220, 1285 (oxirane). ^{1}H NMR spectrum, δ, ppm: 2.65 m (2H, CH_2O), 3.35 m (3H, CH, CH_2O). Found, %: C 38.32; H 4.36. $C_5H_7F_3O_2$. Calculated, %: C 38.46; H 4.49.

Compounds **IIb–IId** were similarly obtained.

2-[(3,3,3,2,2-Pentafluoropropoxy)methyl]oxirane (IIb) was obtained from 24.3 g (0.1 mol) of compound **Ib** and 11.2 g (0.2 mol) of potassium hydroxide. Yield 16 g (52%), bp 80–81°C (83 mm Hg), n_D^{20} 1.3419. IR spectrum, ν, cm^{-1}: 817, 875, 915, 1280 (oxirane). ^{1}H NMR spectrum, δ, ppm: 2.55 m (2H, CH_2O), 3.25 m (3H, CH, CH_2O). Found, %: C 34.78; H 3.25. $C_6H_7F_5O_2$. Calculated, %: C 34.95; H 3.40.

2-[(4,4,4,3,3,3,2,2-Heptafluorobutoxy)methyl]-oxirane (IIc) was obtained from 29.2 g (0.1 mol) of compound **Ic** and 11.2 g (0.2 mol) of potassium hydroxide. Yield 11 g (43%), bp 79°C (50 mm Hg), n_D^{20} 1.3352. IR spectrum, ν, cm^{-1}: 825, 880, 919, 1215, 1275 (oxirane). ^{1}H NMR spectrum, δ, ppm: 2.60 m (2H, CH_2O), 3.35 m (3H, CH, CH_2O). Found, %: C 32.68; H 2.58. $C_7H_7F_7O_2$. Calculated, %: C 32.80; H 2.73.

2-[(3,3,2,2-Tetrafluoropropoxy)methyl]oxirane (IId) was obtained from 22.5 g (0.1 mol) of compound **Id** and 11.2 g (0.2 mol) of potassium hydroxide. Yield 19 g (48%), bp 79–80°C (90 mm Hg), n_D^{20} 1.3568. IR spectrum, ν, cm^{-1}: 820, 885, 915, 1220, 1278 (oxirane). ^{1}H NMR spectrum, δ, ppm: 2.75 m (2H, CH_2O), 3.55 m (3H, CH, CH_2O), 5.9 m (1H, CHF_2). Found, %: C 38.13; H 4.11. $C_6H_8F_4O_2$. Calculated, %: C 38.30; H 4.26.

2-[(2,2,2-Trifluoroethoxy)methyl]thiirane (IIIa). A mixture of 8.6 g (0.1 mol) of thiourea, 15.6 g (0.1 mol) of compound **IIa**, and 30 ml of methanol was stirred for 2 h at 50°C, then it was cooled, washed with water, extracted with tetrachloromethane, and dried with anhydrous magnesium sulfate. On distilling off the solvent the reaction product was subjected to vacuum distillation. Yield 11 g (63%), bp 80°C (18 mm Hg), n_D^{20} 1.4083. IR spectrum, ν, cm^{-1}: 645 (thiirane), 1115, 1365 (C–F). ^{1}H NMR spectrum, δ, ppm: 2.15, 2.30 d (2H, *cis*- and *trans*-CCH_2), 2.90 q (1H, CH), 3.8 m (4H, CH_2OCH_2). Found %; C 34.72; H 3.91; S 18.45. $C_5H_7F_3OS$. Calculated, %: C 34.88; H 4.07; S 18.60.

Compounds **IIIb–IIId** were similarly obtained.

2-[(3,3,3,2,2-Pentafluoropropoxy)methyl]thiirane (IIIb) was obtained from 20.6 g (0.1 mol) of oxirane **IIb** and 7.6 g (0.1 mol) of thiourea. Yield 12 g (57%), bp 100°C (50 mm Hg), n_D^{20} 1.3967. IR spectrum, ν, cm^{-1}: 650 (thiirane), 1118, 1350 (C–F). ^{1}H NMR spectrum, δ, ppm: 2.10, 2.35 d (2H, *cis*- and *trans*-CCH_2), 2.85 q (1H, CH), 3.85 m (4H, H_2COCH_2). Found, %: C 32.26; H 3.02; S 14.25. $C_6H_7F_5OS$. Calculated, %: C 32.43; H 3.15; S 14.41.

2-[(4,4,4,3,3,2,2-Heptafluorobutoxy)methyl]-thiirane (IIIc) was obtained from 25.6 g (0.1 mol) of oxirane **IIc** and 7.6 g (0.1 mol) of thiourea. Yield 13 g (49%), bp 98°C (50 mm Hg), n_D^{20} 1.3879. IR spectrum, ν, cm^{-1}: 655 (thiirane), 1120, 1365 (C–F). ^{1}H NMR spectrum, δ, ppm: 2.15, 2.30 d (2H, *cis*- and *trans*-CCH_2), 2.90 q (1H, CH), 3.80 m (4H, H_2COCH_2). Found, %: C 30.71; H 2.41; S 11.59. $C_7H_7F_7OS$. Calculated, %: C 30.88; H 2.57; S 11.76.

2-[(3,3,2,2-Tetrafluoropropoxy)methyl]thiirane (IIId) was obtained from 18.7 g (0.1 mol) of oxirane **IId** and 7.6 g (0.1 mol) of thiourea. Yield 8.5 g (42%), bp 79–80°C (3 mm Hg), n_D^{20} 1.4120. IR spectrum, ν, cm^{-1}: 645 (thiirane), 1130, 1370 (C–F). ^{1}H NMR spectrum, δ, ppm: 2.10, 2.25 d (2H, *cis*- and *trans*-CCH_2), 2.85 q (1H, CH), 3.85 m (4H, H_2COCH_2), 5.90 (1H, CHF_2). Found, %: C 35.11; H 3.78; S 15.56. $C_6H_8F_4OS$. Calculated, %: C 35.29; H 3.92; S 15.69.

1-Anilino-3-(2,2,2-trifluoroethoxy)propane-2-thiol (IVa). Into a glass ampule of 50 ml capacity was charged 17.2 g (0.1 mol) of thiirane and 18.6 g (0.2 mol) of aniline. The ampule was sealed and heated for 10 h at 95–100°C. On cooling the ampule was opened, excess aniline and unreacted thiirane was distilled off, and the residue was subjected to vacuum distillation. Yield 19 g (72%), bp 122°C (0.3 mm Hg), n_D^{20} 1.4975. IR spectrum, ν, cm^{-1}: 1445, 1510, 1595 (C=C), 2450 (SH), 3350 (NH). ^{1}H NMR spectrum, δ, ppm: 2.90–3.50 m (7H, SH, NH, CH_2CHCH_2), 6.1–7.1 m (5H, C_6H_5). Found %; C 52.43; H 5.43; N 5.43; S 12.61. $C_{11}H_{14}F_3NOS$. Calculated, %: C 52.59; H 5.58; N 5.58; S 12.75.

Thiols **IVb–IVd** were similarly obtained.

1-Anilino-3-(3,3,3,2,2-pentafluoropropoxy)-propane-2-thiol (IVb) was obtained from 22.3 g (0.1 mol) of thiirane **IIIb** and 18.6 g (0.02 mol) of aniline. Yield 18.6 g (59%), bp 122°C (0.3 mm Hg), n_D^{20} 1.4863. IR spectrum, ν, cm^{-1}: 1450, 1515, 1590 (C=C), 2550 (SH), 3355 (NH). ^{1}H NMR spectrum, δ, ppm: 2.85–3.45 m (7H, SH, NH, CH_2CHCH_2), 6.1–7.1 m (5H, C_6H_5). Found, %: C 51.83; H 4.92; N 4.89; S 11.38. $C_{12}H_{14}F_3NOS$. Calculated, %: C 51.99; H 5.05; N 5.05; S 11.55.

1-Anilino-3-(4,4,4,3,3,2,2-heptafluorobutoxy)-propane-2-thiol (IVc) was obtained from 27.2 g (0.1 mol) of thiirane **IIIc** and 18.6 g (0.02 mol) of aniline. Yield 24 g (65%), bp 130°C (0.2 mm Hg), n_D^{20} 1.4775. IR spectrum, ν, cm^{-1}: 1470, 1520, 1585 (C=C), 2545 (SH), 3345 (NH). ^{1}H NMR spectrum, δ, ppm: 2.90–3.40 m (7H, SH, NH, CH_2CHCH_2), 6.15–7.15 m (5H, C_6H_5). Found, %: C 42.58; H 3.71; N 38.23; S 8.61. $C_{13}H_{14}F_7NOS$. Calculated, %: C 42.74; H 3.84; N 38.36; S 8.77.

1-Anilino-3-(3,3,2,2-tetrafluoropropoxy)propane-2-thiol (IVd) was obtained from 20.4 g (0.1 mol) of thiirane **IIId** and 18.6 g (0.02 mol) of aniline. Yield 18 g (61%), bp 130°C (0.3 mm Hg), n_D^{20} 1.5010. IR spectrum, ν, cm^{-1}: 1455, 1515, 1590 (C=C), 2550 (SH), 3355 (NH). ^{1}H NMR spectrum, δ, ppm: 2.85–3.45 m (7H, SH, NH, CH_2CHCH_2), 6.20–7.35 m (5H, C_6H_5). Found, %: C 48.32; H 4.92; N 4.56; S 10.61. $C_{12}H_{15}F_4NOS$. Calculated, %: C 48.48; H 5.05; N 4.71; S 10.77.

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