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Reaction with Alcohols of 1-Bromo(chloro)-1,2-epoxyheptafluorobutanes and 1,2-Epoxyperfluorobutane. Preparation of α-Bromo-, α-Chloro-, and α-Alkoxyhexafluorobutyric Acids Esters

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Abstract—1-Bromo(chloro)-1,2-epoxyheptafluorobutanes reacted with primary and secondary alcohols by two concurrent routes giving a mixture of esters of α-alkoxy- and α-bromo(chloro)-hexafluorobutyric acids with growing content of the latter on increasing the bulk of the nucleophilic agent. 1,2-Epoxyperfluorobutane under the same conditions was converted into α-alkoxyhexafluorobutyric acid esters. Reaction of 1-bromo-1,2-epoxyheptafluorobutane and 1,2-epoxyperfluorobutane with potassium *tert*-butylate in *tert*-butanol resulted in *tert*-butyl α-bromohexafluorobutyrate and heptafluorobutyrate respectively due to the forced attack of the bulky nucleophile on the terminal carbon atom of the epoxy ring.

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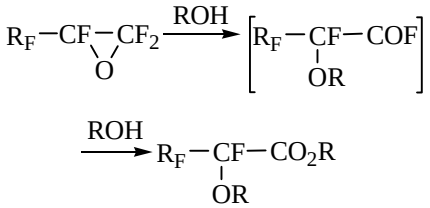
Oxides of terminal fluoroolefins are highly reactive compounds and important intermediates in preparation of substances endowed with versatile biological activuity and technically useful characteristics. Nucleophilic opening of the ring in polyfluoroepoxides is the key stage in preparation of various polyfluorinated functional derivatives: ketones, acyl fluorides, esters, and substances of other classes of special importance, and also of perfluoropolyesters of high thermal and chemical resistance, good lubricants and release agents [1–6].

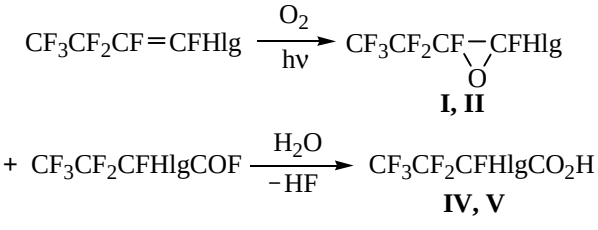
The mechanism of epoxy ring opening depends both on the structure of the polyfluorinated epoxide and on the bulk of the attacking nucleophile [1, 2, 7, 8]. Oxides of terminal fluoroolefins are known to give on reaction with primary and secondary alcohols α-alkoxypolyfluorocaboxylic acids esters resulting from the attack of the nucleophilic reagent on the central carbon atom of the epoxy ring [9–11].



In the present study we used as objects of investigation 1-chloro- and 1-bromo-1,2-epoxy-heptafluorobutanes (**I** and **II**) containing a chlorine or bromoine atom in the α-position. The reaction of compounds **I** and **II** with alcohols was compared with analogous reaction of the perfluorinated analog, 1,2-epoxyperfluorobutane (**III**), in order to elucidate further the relations between the structure and properties of fluoroolefins oxides and to synthesize functional organofluoric compounds based thereon.

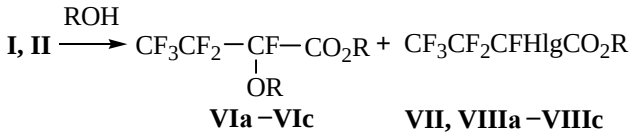
We prepared formerly epoxides **I** and **II** by oxidation of the corresponding fluoroalkenes with molecular oxygen

Scheme 1.



Hlg = Cl (**I, IV**), Br (**II, V**).

Scheme 2.



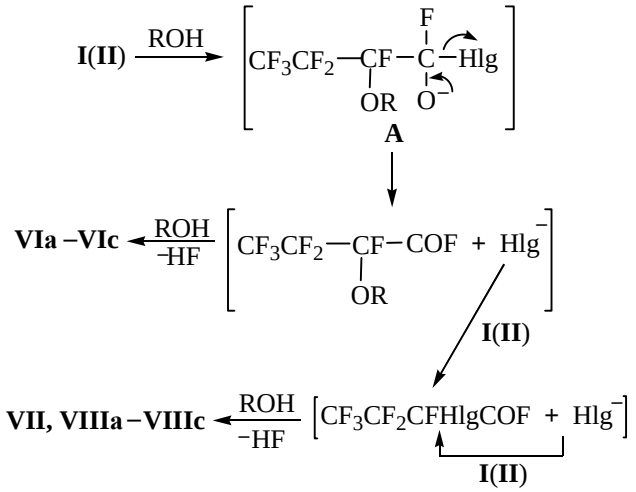
VI, VIII, R = CH_3 (**a**), C_2H_5 (**b**), $CH(CH_3)_2$ (**c**); **VII**, R = CH_3, Hlg = Cl; **VIII**, Hlg = Br.

under UV irradiation [12]. The isomeric acyl fluorides obtained alongside epoxides **I** and **II** were hydrolyzed by water into α-chloro(bromo)-hexafluorobutyric acids **IV** and **V** (Scheme 1).

On reacting polyfluoroepoxides **I** and **II** with methanol, ethanol, and 2-propanol we obtained a mixture of esters of α-alkoxy- and α-chloro(bromo)-hexafluorobutyric acids **VIa–VIc** and **VII**, **VIIIa–VIIIc**, where esters **VII** and **VIIIa–VIIIc** prevailed, and their fraction increased with the growing bulk of the nucleophilic reagent (Scheme 2).

The reaction mechanism, same as with perfluorinated α-oxides, apparently consists in a primary attack of the alcohol on the β-position of the epoxy ring yielding alkoxy anion **A** which is stabilized by ejection of chloride or bromide anions (because of lower strength of C–Cl and C–Br bonds compared with C–F). The formation of products mixture may originate from the concurrent attack of arising chloride and bromide anions which also open the epoxy ring in compounds **I** and **II** with elimination of Cl^- or Br^- anions (Scheme 3). Nucleophilicity of chloride and bromide anions is higher than that of alcohol [13] resulting in the prevalence of α-chloro(bromo)hexafluorobutyric acids esters in the product mixture obtained.

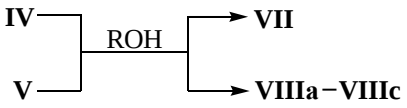
Scheme 3.



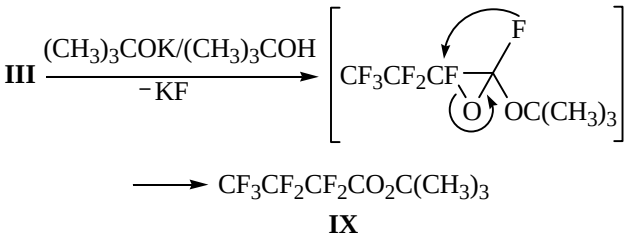
R = CH_3, C_2H_5, $CH(CH_3)_2$.
R = CH_3, C_2H_5, $(CH_3)_3CH$.

We prepared individual α-alkoxyesters **VIa–VIc** by an independent synthesis from alcohols and 1,2-epoxyperfluorobutane (**III**).

Esterification of previously obtained α-chloro(bromo)-hexafluorobutyric acids (**IV** and **V**) (Scheme 1) provided α-chloro(bromo)-containing esters **VII** and **VIIIa–VIIIc**.



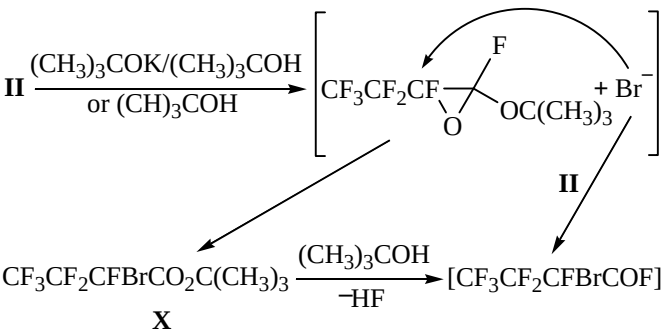
1,2-Epoxyperfluorobutane (**III**), same as hexafluoropropylene oxide [14], does not react with *tert*-butanol but with a stronger nucleophile, potassium *tert*-butylate, gives *tert*-butyl heptafluorobutyrate (**IX**).



IX

In contrast to the perfluorinated analogs, hexafluoropropylene oxide and epoxide **III**, epoxide **II** reacted both with *tert*-butanol and even more so, with potassium *tert*-butylate, giving *tert*-butyl α-bromohexafluorobutyrate (**X**). This difference is presumably due to the easy elimination of the bromide anion and to the higher nucleophilicity of bromide than fluoride anion in the alcoholic medium [13]. With epoxide **II** the *tert*-butoxy anion attacks the terminal carbon atom of the ring generating bromide anions which cause the opening of the epoxy ring leading to ester **X** (Scheme 4).

Scheme 4.



X

Apparently the driving force of the reaction of compounds **II** and **III** with potassium *tert*-butylate is the small volume of the halide ions forming in the first stage of reacion with bulky nucleophiles which are compelled to attack the terminal carbon atom of the ring, in keeping with the findings of [7, 14].

Thus basing on the oxidation products of 1-chloro-(bromo)heptafluoro-1-butenes, fluoroepoxides **I** and **II**, and α-chloro(bromo)hexafluorobutyryl fluorides (Scheme 1), hard-to-obtain polyfluorinated α-chloro-(bromo)acids and their esters can be prepared which are important intermediateds in organic synthesis [15, 16].

EXPERIMENTAL

^{19}F NMR spectra were registered on spectrometers Tesla BS-567 A (94.1 MHz), Tesla BS-587 A (75.3 MHz), and Bruker DRX-400 (376 MHz), internal reference C_6F_6, chemical shifts are presented from $CFCl_3$ and are regarded as positive in the growing field; ^1H NMR spectra were taken on a spectrometer Bruker DRX-400 (400 MHz), internal reference TMS. IR spectra were recorded on spectrophotometers Specord 75IR and Perkin Elmer One FT-IR in the range 400–4000 cm^{-1} from thin film or in the gas phase. GLC was carried out on a chromatograph LKhM-72, detector katharometer, carrier gas helium, steel columns 6500×4 mm with 15% SKTFT-100 or FS-1265 on carrier Chromosorb W.

Oxiranes **I** and **II** were prepared as described in [12]. The relative content of reaction products was determined by comparison of the integral intensities of the corresponding signals in the ^{19}F NMR spectra. The alcohols used in the study as reagents were purified and dried by standard procedures.

α-Alkoxyhexafluorobutyric acid esters VIa–VIc. General procedure. The reagents were charged into a glass ampule (at cooling with dry ice) and the ampule was sealed and maintained at room temperature with intermittent stirring, till the lower layer of oxirane disappeared. Then the cooled ampule was opened, the reaction mixture was poured into ice water, the organofluorine layer was separated, twice washed with water, dried over $MgSO_4$, and distilled.

Methyl α-methoxyhexafluorobutyrate (VIa). From 2.6 g (12 mmol) of epoxide **III** and 2.0 g (62 mmol) of methanol within 3 h we obtained 2.2 g (76%) of methoxyester **VIa**, bp 138–140°C. IR spectrum, ν, cm^{-1}: 1780 (C=O). ^1H NMR spectrum, δ, ppm: 3.63 d (3H, OCH_3, $^4J_{H,F}$ 1.4 Hz), 3.99 s (3H, $COOCH_3$). ^{19}F NMR spectrum, δ, ppm: 79.35 d (3F, CF_3, $^4J_{F,F}$ 10.7 Hz), 124.11 s (2F, CF_2), 130.47 q (1F, CF, $^4J_{F,F}$ 10.7 Hz). Found, %: C 30.25; H 2.62; F 47.16. $C_6H_6F_6O_3$. Calculated, %: C 30.00; H 2.50; F 47.50.

Ethyl α-ethoxyhexafluorobutyrate (VIb). From 2.7 g (12.5 mmol) of compound **III** and 2.2 g (48 mmol) of ethanol within 3 h we obtained 2.8 g (84%) of ethoxyester **VIb**, bp 158–160°C. IR spectrum, ν, cm^{-1}: 1770 (C=O). ^1H NMR spectrum, δ, ppm: 1.29 t (3H,$OCH_2\underline{CH_3}$, ^3J 7.0 Hz), 1.36 t (3H, $COOCH_2\underline{CH_3}$, ^3J 7.1 Hz), 3.89 m (2H, $O\underline{CH_2}CH_3$), 4.43 q (2H, $COO\underline{CH_2}CH_3$, ^3J 7.1 Hz). ^{19}F NMR spectrum, δ, ppm: 79.17 d (3F, CF_3, ^4J 10.7 Hz), 123.99 s (2F, CF_2), 127.14 q (1F, CF, ^4J 10.7 Hz). Found, %: C 35.43; H 3.95; F 42.96. $C_8H_{10}F_6O_3$. Calculated, %: C 35.82; H 3.73; F 42.54.

Isopropyl α-isopropoxyhexafluorobutyrate (VIc). From 2.5 g (11.6 mmol) of epoxide **III** and 2.9 g (48.0 mmol) of 2-propanol within 5 h we obtained 2.3 g (68%) of compound **VIc**, bp 169–171°C. IR spectrum, ν, cm^{-1}: 1760. ^1H NMR spectrum, δ, ppm: 1.30 d [6H, $COOCH(\underline{CH_3})_2$, ^3J 6.3 Hz], 1.35 d [6H, $OCH(\underline{CH_3})_2$, ^3J 6.1 Hz], 4.21 septet d [1H, $O\underline{CH}(CH_3)_2$, $^3J_{H,H}$ 6.1, $^4J_{F,H}$ 1.4 Hz], 5.24 septet [1H, $COO\underline{CH}(CH_3)_2$, ^3J 6.3 Hz]. ^{19}F NMR spectrum, δ, ppm: 79.00 d (3F, CF_3, $^4J_{F,F}$ 10.7 Hz), 122.70 q (1F, CF, $^4J_{F,F}$ 10.7 Hz), 123.41 d (1F, $C\underline{F}_AF_B$, $^2J_{A,B}$ 282.2 Hz), 124.41 d (1F, $CF_A\underline{F}_B$, $^2J_{A,B}$ 282.2 Hz). Found, %: C 40.76; H 4.27; F 38.92. $C_{10}H_{14}F_6O_3$. Calculated, %: C 40.54; H 4.73; F 38.51.

***tert*-Butyl heptafluorobutyrate (IX).** Into a flask equipped with a magnetic stirrer, gas inlet tube, and dry-ice reflux condenser connected to a trap cooled to –78°C was charged 1 g (25.6 mmol) of potassium metal, it was dissolved in 40 ml of *tert*-butanol, and 4.3 g (20.0 mmol) of oxirane **III** was passed through the solution. Then the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was treated with water (~200 ml), the organofluorine layer was separated, twice washed with water, dried over $MgSO_4$, and distilled. Yield 3.9 g(72%), bp 115–116°C. IR spectrum, ν, cm^{-1}: 1776 (C=O). ^1H NMR spectrum, δ, ppm: 1.59 s [9H, $C(\underline{CH_3})_3$]. ^{19}F NMR spectrum, δ, ppm: 80.02 t (3F, CF_3, ^4J 8.6 Hz), 118.39 q (2F, $CF_3CF_2\underline{CF_2}$, ^4J 8.6 Hz), 126.11 br.s (2F, $CF_3\underline{CF_2}CF_2$). Found, %: C 53.87; H 3.18; F 48.85. $C_8H_9F_7O_2$. Calculated, %: C 53.56; H 3.33; F 49.26.

α-Chloro(bromo)hexafluorobutyric acid esters. General procedure. Into a flask equipped with

a dropping funnel and a reflux condenser capped with a drying tube packed with calcium chloride was charged alcohol, α-chloro-(bromo)hexafluorobutyric acid, and dropwise was added while stirring concn. H_2SO_4. The reaction mixture was heated at reflux for ~1 h, left overnight, then poured into ice water, the organofluorine layer was separated, washed with water, dried over $MgSO_4$, and distilled.

Methyl α-chlorohexafluorobutyrate (VII). From 11.5 g (50.0 mmol) of acid **IV**, 5.5 g (170 mmol) of methanol, and 5 ml of concn. H_2SO_4 we obtained 9.0 g (74%) of ester **VII**, bp 108–110°C. IR spectrum, ν, cm^{-1}: 1775 (C=O). ^{1}H NMR spectrum, δ, ppm: 4.07 s (3H, OCH_3). ^{19}F NMR spectrum, δ, ppm: 78.54 d (3F, CF_3, ^4J 11.7 Hz), 118.13 d.d (1F, C$\underline{F}_A$F$_B$, $^2J_{A,B}$ 281.3, ^3J 4.9 Hz), 121.15 d.d (1F, CF$_A\underline{F}_B$, $^2J_{A,B}$ 281.3, ^3J 7.8 Hz), 128.83 m (1F, CFCl). Found, %: C 24.32; H 1.46; Cl 14.90; F 46.17. $C_5H_3ClF_6O_2$. Calculated, %: C 24.54; H 1.23; Cl 14.52; F 46.63.

Methyl α-bromohexafluorobutyrate (VIIIa). From 7.0 g (25.5 mmol) of acid **V**, 4.8 g (150 mmol) of methanol, and 4 ml of concn. H_2SO_4 we obtained 5.9 g (80%) of ester **VIIIa**, bp 123–125°C. IR spectrum, ν, cm^{-1}: 1770 (C=O). ^{1}H NMR spectrum, δ, ppm: 4.05 s (3H, OCH_3). ^{19}F NMR spectrum, δ, ppm: 78.32 d (3F, CF_3, ^4J 10.7 Hz), 114.97 d.d [1F, C$\underline{F}_A$F$_B$, $^2J_{A,B}$ 280.0, ^3J(F$_A$, CFBr) 7.8 Hz], 117.79 d.d [1F, CF$_A\underline{F}_B$, $^2J_{A,B}$ 280.0, ^3J (F$_B$, CFBr) 12.7 Hz], 132.27 d.q.d [1F, CFBr, ^3J(F$_A$, CFBr) 7.8, ^3J(F$_B$, CFBr) 12.7, ^4J 10.7 Hz]. Found, %: C 20.34; H 1.23; Br 27.45; F 39.80. $C_5H_3BrF_6O_2$. Calculated, %: C 20.76; H 1.04; Br 27.68; F 39.45.

Ethyl α-bromohexafluorobutyrate (VIIIb). From 4.6 g (16.7 mmol) of acid **V**, 3 g (65 mmol) of ethanol, and 3 ml of concn. H_2SO_4 we obtained 3.6 g (72%) of ester **VIIIb**, bp 138–140°C. IR spectrum, ν, cm^{-1}: 1770 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH_3, ^3J 7.0 Hz), 4.49 q (2H, CH_2, ^3J 7.0 Hz). ^{19}F NMR spectrum, δ, ppm: 78.51 d (3F, CF_3, ^4J 11.7 Hz), 115.05 d.d [1F, C$\underline{F}_A$F$_B$, $^2J_{A,B}$ 280.3, ^3J(F$_A$, CFBr) 8.8 Hz], 117.89 d.d [1F, CF$_A\underline{F}_B$, $^2J_{A,B}$ 280.3, ^3J (F$_B$, CFBr) 12.7 Hz], 131.93 d.q.d [1F, CFBr, ^3J(F$_A$, CFBr) 8.8, ^3J (F$_B$, CFBr) 12.7, ^4J 11.7 Hz]. Found, %: C 23.51; H 1.70; Br 26.68; F 37.15. $C_6H_5BrF_6O$. Calculated, %: C 23.76; H 1.65; Br 26.40; F 37.62.

Isopropyl α-bromohexafluorobutyrate (VIIIc). From 8.0 g (29 mmol) of acid **V**, 4.8 g (80 mmol) of 2-propanol, and 5 ml of concn. H_2SO_4 we obtained 4.8 g (52%) of ester **VIIIc**, bp 148–150°C. IR spectrum, ν, cm^{-1}: 1760 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.36 d [6H, CH($\underline{CH}_3$)$_2$, ^3J 6.3 Hz], 5.26 septet [1H, $\underline{CH}$(CH_3)$_2$, ^3J 6.3 Hz]. ^{19}F NMR spectrum, δ, ppm: 78.59 d (3F, CF_3, ^4J 11.7 Hz), 115.14 d.d [1F, C$\underline{F}_A$F$_B$, $^2J_{A,B}$ 280.3, ^3J(F$_A$, CFBr) 8.8 Hz], 117.88 d.d [1F, CF$_A\underline{F}_B$, $^2J_{A,B}$ 280.3, ^3J(F$_B$, CFBr) 12.7 Hz], 131.85 d.q.d [1F, CFBr, ^3J(F$_A$, CFBr) 8.8, ^3J(F$_B$, CFBr) 12.7, ^4J 11.7 Hz]. Found, %: C 26.13; H 2.48; Br 24.96; F 36.27. $C_7H_7BrF_6O_2$. Calculated, %: C 26.50; H 2.21; Br 25.24; F 35.96.

Reaction of epoxides I and II with alcohols. General procedure. The reagents were charged into a flask equipped with a magnetic stirred and a dry-ice a reflux condenser capped with a drying tube packed with calcium chloride. After boiling at reflux under stirring the reaction mixture was cooled, poured into ice water, the organofluorine layer was separated, washed with water, dried over $MgSO_4$, and distilled.

Reaction of epoxide I with methanol. From 1.0 g (4.3 mmol) of epoxide **I** and 1.5 g (47 mmol) of methanol by boiling for 1 h we obtained 0.85 g of products containing a mixture of methyl esters **VIa** and **VII**, 46:54 mol%.

Reaction of epoxide II with methanol. From 1.6 g (5.8 mmol) of epoxide **II** and 1.4 g (43.8 mmol) of methanol by boiling for 1 h we obtained 1.7 g of a mixture of methyl esters **VIa** and **VIIIa**, 25:75 mol%.

Reaction of epoxide II with ethanol. From 1.6 g (5.8 mmol) of epoxide **II** and 1.2 g (26 mmol) of ethanol by boiling for 1 h we obtained 1.8 g of a mixture of esters **VIb** and **VIIIb**, 14:86 mol%.

Reaction of epoxide II with 2-propanol. From 1.7 g (6.1 mmol) of epoxide **II** and 1.5 g (25 mmol) of 2-propanol we obtained 1.6 g of a mixture of esters **VIc** and **VIIIc**, 8:92 mol%.

***tert*-Butyl α-bromohexafluorobutyrate (X).** In 10 ml of *tert*-butanol was dissolved 0.5 g (12.8 mmol) of potassium metal, and 3.0 g (10.8 mmol) of epoxide **II** was added dropwise thereto. The reaction mixture was stirred for 3 h, then poured into ice water (~200 ml), the organofluorine layer was separated, twice washed with water, dried over $MgSO_4$, and distilled. Yield 2.2 g (61%), bp 153–155°C. IR spectrum, ν, cm^{-1}: 1760 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.56 s [9H, C(CH_3)$_3$]. ^{19}F NMR spectrum, δ, ppm: 78.14 d (3F, CF_3, ^4J 11.7 Hz), 114.95 d.d [1F, C$\underline{F}_A$F$_B$, $^2J_{A,B}$ 280.3, ^3J(F$_A$, CFBr) 9.8 Hz], 117.33 d.d [1F, CF$_A\underline{F}_B$, $^2J_{A,B}$ 280.3, ^3J (F$_B$, CFBr) 12.7 Hz], 130.75 m (1F, CFBr). Found, %: C 29.35; H 2.63; Br 24.50; F 34.83. $C_8H_9BrF_6O_2$. Calculated, %: C 29.00; H 2.72; Br 24.17; F 34.44.

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