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Synthesis of Polyfluorinated Ethers

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Abstract—Procedures for preparing polyfluorinated ethers $H(CF_2CF_2)_nCH_2OR$ by alkylation of the corresponding telomeric alcohols $H(CF_2CF_2)_nCH_2OH$ (n = 1–3) with alkyl halides and alkyl tosylates were examined.

The rising researchers' interest in synthesis of polyfluorinated ethers (PFEs) in the past decade is due to several factors. First, thanks to their physicochemical properties, compounds of this class are potential ozone-friendly substitutes of Freons [1]. Second, the majority of PFEs are inert low-freezing and, in some cases, relatively high-boiling liquids. These properties make them suitable as solvents, heat-transfer agents, and components of a new generation of power cells, improving the low-temperature characteristics of graphite electrodes [2]. An important property of PFEs is their adhesion to various materials, making these compounds promising as lubricants operating in a wide range of temperatures and loads.

Published procedures for PFE synthesis involve nucleophilic and radical addition of alcohols to polyfluoroalkenes, trifluoromethylation of polyfluorinated alcohols catalyzed by Lewis acids [3], alkylation of polyfluoroalkoxide anions with dimethyl sulfate [4] or polyfluoroalkyl chlorosulfites [5, 6], etc. Combinations of various reagents in PFE synthesis allow preparation of compounds of diverse structures. All the above-mentioned methods require anhydrous conditions, special equipment, and, frequently, difficultly available chemicals.

The classical route to ethers (Williamson reaction) involves the reaction of alcoholates with alkyl halides [7]. Among polyfluorinated alcohols commercially produced in Russia, telomeric alcohols of the general formula $H(CF_2CF_2)_nCH_2OH$ (n = 1–8) are the most readily available. However, conversion of telomeric alcohols into alcoholates for the Williamson reaction involves certain problems: reaction of these alcohols with alkali metals, developing with accumulation of the alcoholate or in the course of removal of excess alcohol, may cause self-ignition or even explosion of the reaction mixture; preparation of alcoholates using alkalis, followed by removal of water and excess alcohol, is not safe either [4]. At the same time, if the alcoholates are taken as solutions, the yields of the target compounds are low [8].

Within the framework of our study, the problem of raising the yields of PFEs derived from telomeric alcohols and alkyl halides is partially solved by performing the reaction in a DMSO + KOH mixture [see Experimental, method (a)] to enhance the basic and nucleophilic properties of the alcohol (n = 1):

$$HC_2CF_2CH_2OH + RX$$

$$\xrightarrow{100°C,\ 12\ h} HCF_2CF_2CH_2OR + HX,$$

$$\textbf{I–III},\ 45–55\%$$

where R = C_4H_9 (**I**), C_6H_{13} (**II**), $C_{10}H_{21}$ (**III**); X = Cl, Br.

However, even within the next telomeric alcohol (n = 2), this reaction yields no desired PFEs, apparently because of the formation of oligomeric products. The residue obtained after removing the excess KOH and solvent is undistillable in a rough vacuum.

Solov'ev *et al.* [9] reported on a one-step synthesis of fluorinated glycidol ethers under the conditions of phase-transfer catalysis. This method apparently facilitates the synthesis of a wide range of PFEs based on telomeric alcohols, but it is insufficiently versatile because of the different solubilities of the fluorine-containing components [10].

With the aim to raise the yields of PFEs, we chose appropriate solvent systems and prepared compound

IV–**IX** under relatively mild conditions [see Experimental, method (b)]:

$$H(CF_2CF_2)_nCH_2OH + RX$$

$$\xrightarrow{\text{A or B, catalyst, KOH}} H(CF_2CF_2)CH_2OR + HX,$$

$$\textbf{IV–IX},\ 40–70\%$$

conditions: (A) CH_2Cl, H_2O, 40°C, 5 h, $n = 2$; (B) THF, H_2O, 60°C, 5 h, $n = 3$. Catalyst: $[Et_3BzN]^+Cl^-$; X = Cl, Br; R = C_4H_9, $n = 2$ (**IV**); R = C_5H_{13}, $n = 2$ (**V**); R = $C_{10}H_{21}$, $n = 2$ (**VI**); R = C_4H_9, $n = 3$ (**VII**); R = C_6H_{13}, $n = 3$ (**VII**); R = $C_{10}H_{21}$, $n = 3$ (**IX**).

Comparative analysis of the two procedures for preparing PFEs **I**–**IX** shows that none of them ensures quantitative yields of the desired compounds, and no correlation can be revealed between the substrate structure and PFE yield.

The highest yields of PFEs (up to 90%) are attained when a two-step procedure is used: first a fluorinated alcohol is converted to a sulfonate (mesylate, tosylate, triflate) by the reaction with appropriate sulfonyl derivative [10], after which the sulfonate group is readily replaced by the alcoholate ion formed from a nonfluorinated alcohol *in situ*. According to [10], this two-step process can be schematically represented as follows:

$$R^fCH_2OH \xrightarrow{R'SO_2Cl,\ NEt_3} R^fCH_2OSO_2R'$$

$$\xrightarrow{R''OH,\ NaH,\ 10\ h,\ 130°C} R^fCH_2OR'',$$

where $R^f = CF_3$, C_6F_{13}; R' = CH_3, CF_3, p-$C_6H_4CH_3$; R'' = p-$C_6H_4NO_3$.

The key step in this reaction is nucleophilic replacement of the RSO_3^- group, which can be performed in a virtually quantitative yield. However, the reaction of sulfo derivatives with a fluorinated alcohol involves the loss of a valuable chemical in the first step. Furthermore, the use of NaH requires anhydrous conditions, and the reaction requires heating at 130°C for 10 h.

Among the examined routes to PFEs, the most promising is, apparently, introduction of a labile leaving group into the hydrocarbon component. The resulting derivative in the modified Williamson reaction is a more active alkylating agent than alkyl halides.

Comparison of the reactivity of mesylates, triflates, and tosylates, taking into account the reaction conditions, shows that tosylates are not inferior to the other reagents, but are preferable from the viewpoint of convenience in handling and availability.

Tosylation of common alcohols by the nucleophilic substitution mechanism occurs under relatively mild conditions; the subsequent reaction of the resulting derivatives with telomeric alcohols gives the desired compounds **IV**–**IX** in high yields and does not require any anhydrous medium [see Experimental, method (c)]:

$$ROH + TsCl \xrightarrow[-HCl]{KOH,\ H_2O} [ROTs]$$

$$\xrightarrow{H(CF_2CF_2)_nCH_2OH,\ KOH,\ THF,\ H_2O,\ catalyst} \textbf{IV–IX} + TsOK.$$

$$87–96\%$$

It should be noted that isolation of the tosyl derivatives (ROTs) is not necessary for performing the second step of the synthesis successfully. Comparison of the yields of **IV**–**IX** in the processes whose second step was performed with isolated and crude ROTs shows that the difference in the yields is as small as 5–10%.

Thus, the latter procedure is the best from the viewpoint of conditions and results: reaction temperature 60°C, time (total of two steps) 8 h, and almost quantitative yields of the desired compounds.

The IR spectra of **I**–**IX** contain the following characteristic absorption bands, ν, cm^{-1}: 1111–1142 (C–F), 1200–1204 (C–O–C), and 2856–2879, 2927–2959, 2934–2966 (C–H).

The ^1H and ^{19}F spectra of all the PFEs prepared have common features.

EXPERIMENTAL

The IR spectra were recorded on a Perkin–Elmer Spectrum One Fourier spectrometer from thin films. The ^1H and ^{19}F NMR spectra were measured on a Bruker DRX-400 spectrometer in $CDCl_3$, internal references TMS and C_6F_6, respectively. The yields, boiling points, and elemental analyses of **I**–**IX** are given in Table 1, and the NMR data, in Table 2.

Synthesis of polyfluorinated ethers. Method (a). A mixture of 0.1 mol of alkyl halide, 0.25 mol of KOH, and 50 ml of DMSO was heated with vigorous stirring to 100°C to obtain a uniform mixture, and 0.1 mol of telomeric alcohol ($n = 1$) was added dropwise at this temperature over a period of 30 min. The mixture was stirred for 8 h at 100°C. Then 150 ml of water was added, and the mixture was neutralized with HCl. The resulting neutral solution was extracted with $CHCl_3$ (2 × 30 ml). The chloroform extracts were combined and dried over $CaCl_2$; the solvent was distilled off. The residue was subjected to fractional distillation to obtain 1-(1,1,3-trihydroperfluoroprop-

Table 1. Yields, boiling points, and elemental analyses of ethers **I–IX**, $H(CF_2CF_2)_nCH_2O(CH_2)_mH$ (n = 1–3, m = 4, 6, 10)

Compound	Yield, %	bp, °C/*p*, mm Hg	Found, %/Calculated, %			Formula
			C	H	F	
I	45	140–141	$\frac{44.59}{44.68}$	$\frac{6.34}{6.43}$	$\frac{39.98}{40.39}$	$C_7H_{12}F_4O$
II	49	170–171	$\frac{50.15}{49.99}$	$\frac{7.40}{7.46}$	$\frac{34.93}{35.15}$	$C_9H_{17}F_4O$
III	55	105–107/6	$\frac{57.21}{57.34}$	$\frac{8.69}{8.88}$	$\frac{27.43}{27.91}$	$C_{13}H_{24}F_4O$
IV	87	179–180	$\frac{37.63}{37.53}$	$\frac{4.20}{4.17}$	$\frac{52.64}{52.75}$	$C_9H_{12}F_8O$
V	89	196–198	$\frac{41.58}{41.67}$	$\frac{5.28}{5.36}$	$\frac{47.05}{47.43}$	$C_{11}H_{17}F_8O$
VI	94	195–196/30	$\frac{48.56}{48.42}$	$\frac{6.56}{6.45}$	$\frac{40.39}{40.83}$	$C_{15}H_{24}F_8O$
VII	89	201–202	$\frac{34.35}{34.05}$	$\frac{3.12}{3.09}$	$\frac{58.24}{58.73}$	$C_{11}H_{12}F_{12}O$
VIII	88	160–161/30	$\frac{37.51}{37.44}$	$\frac{4.20}{4.08}$	$\frac{54.30}{54.65}$	$C_{13}H_{17}F_{12}O$
IX	96	217–220/30	$\frac{43.34}{43.25}$	$\frac{5.12}{5.08}$	$\frac{48.15}{48.28}$	$C_{17}H_{24}F_{12}O$

Table 2. ^1H and ^{19}F NMR data for **I–IX**

Compound	Formula	^1H, δ, ppm (**I**)	^{19}F, δ, ppm	*J*, Hz
I	1 *b* *a* 2 3 4 5 6 $HCF_2CF_2CH_2OCH_2CH_2CH_2CH_3$	5.92 t.t (H^1), 3.76 t.t (H^2), 3.55 t (H^3), 1.57 m (H^4), 1.38 m (H^5), 0.92 m (H^6)	36.11 m (*a*), 21.52 d.m (*b*)	$J_{1,b}$ = 53.3, $J_{1,a}$ = 5.3, $J_{2,a}$ = 12.6, $J_{2,b}$ = 1.7, $J_{3,4}$ = 6.5
II	1 *b* *a* 2 3 4 5 6 7 $HCF_2CF_2CH_2OCH_2CH_2(CH_2)_2CH_2CH_3$	5.92 t.t (H^1), 3.79 t.t (H^2), 3.54 t (H^3), 1.58 m (H^4), 1.32 m (H^5, H^6), 0.89 t (H^7)	36.04 m (*a*), 21.51 d.m (*b*)	$J_{1,b}$ = 53.3, $J_{1,a}$ = 5.3, $J_{2,a}$ = 12.6, $J_{2,b}$ = 1.7, $J_{3,4}$ = 6.6, $J_{7,6}$ = 6.9
III	1 *b* *a* 2 3 4 5 6 7 $HCF_2CF_2CH_2OCH_2CH_2(CH_2)_6CH_2CH_3$	5.91 t.t (H^1), 3.79 t.t (H^2), 3.54 t (H^3), 1.57 m (H^4), 1.27 m (H^5, H^6), 0.88 t (H^7)	36.09 m (*a*), 21.49 d.m (*b*)	$J_{1,b}$ = 53.3, $J_{1,a}$ = 5.3, $J_{2,a}$ = 12.6, $J_{2,b}$ = 1.7, $J_{3,4}$ = 6.6, $J_{7,6}$ = 6.8
IV	1 *d* *c* *b* *a* 2 3 4 5 6 $HCF_2CF_2CF_2CF_2CH_2OCH_2CH_2CH_2CH_3$	6.06 t.t (H^1), 3.91 t (H^2), 3.59 t (H^3), 1.58 m (H^4), 1.39 m (H^5), 0.93 t (H^6)	41.94 m (*a*), 36.03 m (*b*), 31.38 m (*c*), 24.45 d.m (*d*)	$J_{1,d}$ = 52.0, $J_{1,c}$ = 5.5, $J_{2,a}$ = 13.8, $J_{3,4}$ = 6.5, $J_{6,5}$ = 6.8

Table 2. (Contd.)

Compound	Formula	^1H, δ, ppm (**I**)	^{19}F, δ, ppm	*J*,/Hz
V	1 *d* *c* *b* *a* 2 3 4 5 6 7 $HCF_2CF_2CF_2CF_2CH_2OCH_2CH_2(CH_2)_2CH_2CH_3$	6.06 t.t (H^1), 3.90 t (H^2), 3.58 t (H^3), 1.57 m (H^4), 1.33 m (H^5, H^6), 0.89 t (H^7)	41.91 m (*a*), 36.08 m (*b*), 31.34 m (*c*), 24.41 d.m (*d*)	$J_{1,\,d}$ = 52.0, $J_{1,\,c}$ = 5.5, $J_{2,\,a}$ = 13.9, $J_{3,\,4}$ = 6.5, $J_{7,\,6}$ = 6.9
VI	1 *d* *c* *b* *a* 2 3 4 5 6 7 $HCF_2CF_2CF_2CF_2CH_2OCH_2CH_2(CH_2)_6CH_2CH_3$	6.07 t.t (H^1), 3.91 t.t (H^2), 3.59 t (H^3), 1.57 m (H^4), 1.32 m (H^5, H^6), 0.89 t (H^7)	41.87 m (*a*), 35.83 t (*b*), 31.17 m (*c*), 24.32 d.m (*d*)	$J_{1,\,d}$ = 52.2, $J_{1,\,c}$ = 5.6, $J_{2,\,a}$ = 13.9, $J_{2,\,b}$ = 1.4, $J_{3,\,4}$ = 6.5, $J_{7,\,6}$ = 6.9, $J_{b,\,d}$ = 8.1
VII	1 *e* *d* *c* *b* *a* 2 3 4 5 6 $HCF_2CF_2(CF_2)_2CF_2CF_2CH_2OCH_2CH_2CH_2CH_3$	6.05 t.t (H^1), 3.92 t (H^2), 3.60 t (H^3), 1.57 m (H^4), 1.39 m (H^5), 0.93 t (H^6)	42.22 t.m (*a*), 39.58 m (*b*), 38.32 m (*c*), 32.22 m (*d*), 24.74 d.m (*e*)	$J_{1,\,e}$ = 51.9, $J_{1,\,d}$ = 5.2, $J_{2,\,a}$ = 13.9, $J_{3,\,4}$ = 6.5, $J_{6,\,5}$ = 7.2
VIII	1 *e* *d* *c* *b* *a* 2 3 4 5 6 $HCF_2CF_2(CF_2)_2CF_2CF_2CH_2OCH_2CH_2(CH_2)_3CH_3$	6.05 t.t (H^1), 3.92 t (H^2), 3.59 t (H^3), 1.58 m (H^4), 1.30 m (H^5), 0.89 m (H^6)	42.22 t.m (*a*), 39.44 m (*b*), 38.29 br.s (*c*), 32.20 br.s (*d*), 24.76 d.m (*e*)	$J_{1,\,e}$ = 51.9, $J_{1,\,d}$ = 5.2, $J_{2,\,a}$ = 14.0, $J_{3,\,4}$ = 6.5
IX	1 *e* *d* *c* *b* *a* 2 3 4 5 6 7 $HCF_2CF_2(CF_2)_2CF_2CF_2CH_2OCH_2CH_2(CH_2)_6CH_2CH_3$	6.05 t.t (H^1), 3.92 t (H^2), 3.59 t (H^3), 1.60 m (H^4), 1.31 m ($H^{5,6}$), 0.88 t (H^7)	42.22 t.m (*a*), 39.58 m (*b*), 38.32 br.s (*c*), 32.22 m (*d*), 24.76 d.m (*e*)	$J_{1,\,e}$ = 51.9, $J_{1,\,d}$ = 5.2, $J_{2,\,a}$ = 13.9, $J_{3,\,4}$ = 6.5, $J_{7,\,6}$ = 6.8

oxy)butane **I**, 1-(1,1,3-trihydroperfluoropropoxy)hexane **II**, and 1-(1,1,3-trihydroperfluoropropoxy)decane **III**.

Method (b). A mixture of 50 ml of CH_2Cl_2 and 50 ml of 40% KOH (conditions A) [or 60 ml of THF and 30 ml of 50% KOH (conditions B)], 0.1 mol of telomeric alcohol [$n = 2$ (conditions A) or $n = 3$ (conditions B)], and 1 g of triethylbenzylammonium chloride was heated with vigorous stirring to 40°C (conditions A) or 60°C (conditions B). At this temperature, 0.1 mol of alkyl halide was slowly added over a period of 30 min, and the mixture was kept for 5 h. Then, for conditions A, the upper organic layer was separated, washed with dilute HCl (2 × 100 ml), and dried over $CaCl_2$; the solvent was distilled off. For conditions B, 150 ml of water was added, and the oil thus formed was extracted with $CHCl_3$ (2 × 30 ml). The combined chloroform extracts were dried over $CaCl_2$, and the solvent was distilled off. In both cases, the residue was subjected to fractional distillation to obtain 1-(1,1,5-trihydroperfluoropentoxy)butane **IV**, 1-(1,1,5-trihydroperfluoropentoxy)hexane **V**, 1-(1,1,5-trihydroperfluoropentoxy)decane **VI**, 1-(1,1,7-trihydroperfluoroheptoxy)butane **VII**, 1-(1,1,7-trihydroperfluoroheptoxy)hexane **VIII**, and 1-(1,1,7-trihydroperfluoroheptoxy)decane **IX**.

Method (c). A mixture of 0.15 mol of *p*-toluenesulfonyl chloride and 0.15 ml of ethanol was heated to 35–40°C, and 50 ml of 40% KOH was added dropwise over a period of 1 h with vigorous stirring. The resulting mixture was stirred for 3 h at 35–40°C and cooled, after which 200 ml of water was added. The oil thus formed was separated and treated under conditions A [method (b)].

CONCLUSION

The most efficient route to polyfluorinated ethers is a two-step process involving preparation of tosyl derivatives of alcohols, followed by their reaction with telomeric alcohols $H(CF_2CF_2)_nCH_2OH$ under the conditions of phase-transfer catalysis, which allows preparation of ethers $H(CF_2CF_2)_nCH_2OR$ (n = 2, 3) in high yields (87–96%).

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