Reactions of [2-iodo-3-(perfluoroalkyl)propyl]glycidyl ethers with alcohols under basic conditions

D. N. Bazhin, T. I. Gorbunova, A. Ya. Zapevalov, and V. I. Saloutin*

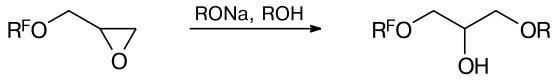
I. Ya. Postovsky Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 22 ul. S. Kovalevskoi, 620041 Ekaterinburg, Russian Federation. Fax: +7 (343) 362 3105. E-mail: bazhin@ios.uran.ru

On treatment with sodium alkoxides in the corresponding alcohols, [2-iodo-3-(perfluoroalkyl)propyl]glycidyl ethers are converted into 3-alkoxy-1-[3-(perfluoroalkyl)prop-2-enyloxy]propan-2-ols in 56—78% yields, while its reaction with 2,2,2-trifluoroethanol and phenol under phase transfer conditions (NaOH, CH_2Cl_2—H_2O, $Bu_4N^+I^-$, 35—40 °C) gives 3-alkoxy-1-[2-iodo-3-(perfluoroalkyl)propoxy]propan-2-ols (yields 45—72%).

Key words: glycidyl ethers, oxiranes, organofluorine compounds, phase transfer catalysis.

As a development of our studies of the regioselective opening of the oxirane ring[1] (Scheme 1), we considered for the first time the behavior of [2-iodo-3-(perfluoroalkyl)propyl]glycidyl ethers (**1** and **2**) in a similar reaction (Scheme 2).

Scheme 1



The reactions of substrates **1** and **2** with alcohols were carried out in a homogeneous alcohol medium or in a CH_2Cl_2—H_2O two-phase system containing alcohol, NaOH, and a phase transfer catalyst ($Bu_4N^+I^-$).

The study has shown that on refluxing with Na alkoxides in the corresponding alcohol, ethers **1** and **2** are converted into unsaturated fluorine-containing hydroxy ethers **3a,c,d** and **4a,c,d** in 56—78% yields (see Scheme 2). In order to suppress oligomerization,[2,3] the reactions of oxiranes **1** and **2** with phenol were carried out in diglyme at 100 °C; this gave hydroxy ethers **3b** and **4b**.

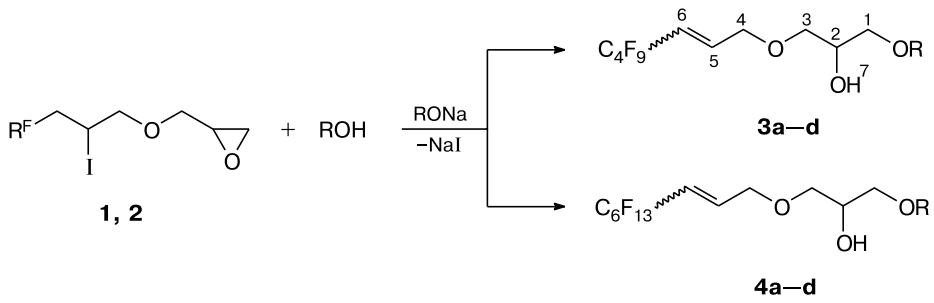
Hydroxy ethers **3a—d** and **4a—d** were obtained as mixtures of *E*- and *Z*-isomers (1 : 1), the isomer ratio was determined by comparing the integral intensities of the chemical shifts of olefinic protons in the ^1H NMR spectra.

Despite the differences in the basic and nucleophilic properties of the alkoxides used, they react with oxiranes **1** and **2** in the same way. The regioselective opening of the oxirane ring and dehydroiodination take place simultaneously.

It is noteworthy that previously[4] we carried out elimination of HI from compounds **1** and **2** with retention of the oxirane ring by treating them with DBU in CH_2Cl_2.

We also investigated the reactions of glycidyl ethers **1** and **2** with alcohols with phase transfer catalysis. The

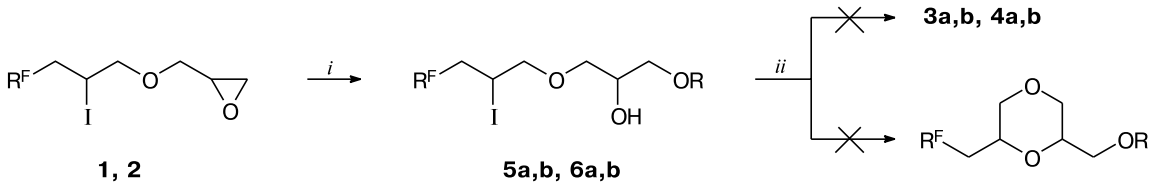
Scheme 2



$R^F = C_4F_9$ (**1**), C_6F_{13} (**2**)
$R = CF_3CH_2$ (**a**), Ph (**b**), Me (**c**), Pr^i (**d**)

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2279—2282, November, 2008.

Scheme 3



1, 2 **5a,b, 6a,b**

Reagents and conditions: *i*. ROH, NaOH, CH_2Cl_2—H_2O, $Bu_4N^+I^-$, 35—40 °C; *ii*. DMF, refluxing

R = CF_3CH_2 (**a**), Ph (**b**); R^F = C_4F_9 (**1**, **5**), C_6F_{13} (**2**, **6**)

process was performed in a CH_2Cl_2—H_2O two-phase system in the presence of NaOH and the phase transfer catalyst ($Bu_4N^+I^-$) at a temperature of 35—40 °C.

In the case of propan-2-ol and methanol, hydroxy ethers **3c,d** and **4c,d** were isolated in 48—65% yields. The ratio of *E* and *Z* isomers of compounds **3c,d** and **4c,d** is 25 : 1. The lower content of the *Z* isomer may be due to milder process conditions as compared with refluxing in alcohol (see Scheme 2).

Unexpected result was obtained when using 2,2,2-trifluoroethanol or phenol (Scheme 3), namely, the reaction gave iodine-containing hydroxy ethers **5a,b** and **6a,b**, while no subsequent elimination of HI took place. This can be attributed to the much lower basicity of the 2,2,2-trifluoroethoxide or phenoxide formed *in situ* compared to isopropoxide and methoxide, which is in line with the pK_a values of these alcohols.[5,6]

The presence of the active iodine atom and the hydroxyl groups in compounds **5a—b** and **6a—b** suggests the possibility of intramolecular Williamson reaction (*cf.* Ref. 7), which could result in 1,4-dioxane derivatives. However, refluxing of these compounds in DMF did not afford the desired products; unsaturated derivatives **3a,b** and **4a,b** were not formed either.

Table 1. Yields, boiling points, and elemental analysis data for the products

Compound	Yield* (%)	B.p./°C (*P*/Torr)	Found / Calculated (%)			Molecular formula
			C	H	F	
1-(4,4,5,5,6,6,7,7,7-Nonafluorohept-2-enyloxy)-3-(2,2,2-trifluoroethoxy)propan-2-ol (**3a**)	78	120—122 (3)	33.20 / 33.35	2.67 / 2.80	52.61 / 52.75	$C_{12}H_{12}F_{12}O_3$
1-(4,4,5,5,6,6,7,7,7-Nonafluorohept-2-enyloxy)-3-phenoxypropan-2-ol (**3b**)	59	180—181 (4)	44.92 / 45.08	3.43 / 3.55	40.02 / 40.11	$C_{16}H_{15}F_9O_3$
3-Methoxy-1-(4,4,5,5,6,6,7,7,7-nonafluorohept-2-enyloxy)propan-2-ol (**3c**)	75 (59)	99—100 (3)	36.15 / 36.28	3.51 / 3.60	46.83 / 46.95	$C_{11}H_{13}F_9O_3$
3-Isopropoxy-1-(4,4,5,5,6,6,7,7,7-nonafluorohept-2-enyloxy)propan-2-ol (**3d**)	69 (65)	110—112 (3)	39.72 / 39.81	4.28 / 4.37	43.47 / 43.59	$C_{13}H_{17}F_9O_3$
3-(2,2,2-Trifluoroethoxy)-1-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)propan-2-ol (**4a**)	74	140—141 (5)	31.42 / 31.59	2.18 / 2.27	56.97 / 57.11	$C_{14}H_{12}F_{16}O_3$
1-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluorononon-2-enyloxy)-3-phenoxypropan-2-ol (**4b**)	56	202—203 (5)	40.93 / 41.08	2.76 / 2.87	46.79 / 46.93	$C_{18}H_{15}F_{13}O_3$
3-Methoxy-1-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)propan-2-ol (**4c**)	71 (55)	133—135 (3)	33.51 / 33.64	2.73 / 2.82	53.13 / 53.20	$C_{13}H_{13}F_{13}O_3$
3-Isopropoxy-1-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)propan-2-ol (**4d**)	64 (48)	135—136 (3)	36.47 / 36.60	3.32 / 3.48	50.03 / 50.17	$C_{15}H_{17}F_{13}O_3$
1-(2-Iodo-4,4,5,5,6,6,7,7,7-nonafluoroheptyloxy)-3-(2,2,2-trifluoroethoxy)propan-2-ol (**5a**)	72	158—159 (5)	25.62 / 25.73	2.23 / 2.34	40.59 / 40.70	$C_{12}H_{13}F_{12}IO_3$
1-(2-Iodo-4,4,5,5,6,6,7,7,7-nonafluoroheptyloxy)-3-phenoxypropan-2-ol (**5b**)	52	197—199 (5)	34.52 / 34.68	2.85 / 2.91	30.72 / 30.85	$C_{16}H_{16}F_9IO_3$
1-(2-Iodo-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoroheptyloxy)-3-(2,2,2-trifluoroethoxy)propan-2-ol (**6a**)	68	156—157 (5)	25.34 / 25.47	1.87 / 1.98	45.91 / 46.05	$C_{14}H_{13}F_{16}IO_3$
1-(2-Iodo-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoroheptyloxy)-3-phenoxypropan-2-ol (**6b**)	45	221—222 (5)	32.91 / 33.05	2.37 / 2.47	37.67 / 37.75	$C_{18}H_{16}F_{13}IO_3$

* The yields obtained with phase transfer catalysis are given in parentheses.

Table 2. ^{1}H NMR data for the reaction products

Compound	δ (*J*/Hz)										
	$H_A(1)$	$H_B(1)$	H(2) (m)	$H_A(3)$	$H_B(3)$	H(4) (m)	H(5) (m)	$H_A(6)$	$H_B(6)$ (m)	H(7) (br.s)	R
3a	3.71 (m)	3.71 (m)	4.08	3.54 (m)	3.54 (m)	4.19 (*E*); 4.33 (*Z*)	5.90 (*E*); 5.62 (*Z*)	6.44 (dm, *E*, $J_{6,5}$ = 15.8); 6.28 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.64	3.89 (q, 2 H, CH_2CF_3 $J_{H,F}$ = 8.7)
3b	3.65 (dd, $J_{A,B}$ = 9.8, $J_{A,2}$ = 5.8)	3.68 (dd, $J_{B,A}$ = 9.8, $J_{B,2}$ = 4.6)	4.03	3.61 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 6.0)	3.57 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.5)	4.19 (*E*); 4.30 (*Z*)	5.93 (*E*); 5.61 (*Z*)	6.43 (dm, *E*, $J_{6,5}$ = 15.8); 6.30 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.76	7.07 (m, 5 H, Ph)
3c	3.44 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 6.1)	3.48 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.4)	3.99	3.55 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 6.0)	3.57 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.5)	4.19 (*E*); 4.33 (*Z*)	5.93 (*E*); 5.61 (*Z*)	6.45 (dm, *E*, $J_{6,5}$ = 15.8); 6.30 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.71	3.40 (s, 3 H, CH_3)
3d	3.46 (dd, $J_{A,B}$ = 9.5, $J_{A,2}$ = 6.3)	3.52 (dd, $J_{B,A}$ = 9.5, $J_{B,2}$ = 4.5)	3.95	3.59 (m)	3.59 (m)	4.20 (*E*); 4.34 (*Z*)	5.94 (*E*); 5.60 (*Z*)	6.45 (dm, *E*, $J_{6,5}$ = 15.8); 6.31 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.77	3.59 (m, 1 H, CH); 1.17 (d, 6 H, CH_3, J = 6.1)
4a	3.68 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 5.9)	3.73 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.4)	4.01	3.57 (dd, $J_{A,B}$ = 9.5, $J_{A,2}$ = 5.5)	3.58 (dd, $J_{B,A}$ = 9.5, $J_{B,2}$ = 4.3)	4.20 (*E*); 4.33 (*Z*)	5.91 (*E*); 5.62 (*Z*)	6.44 (dm, *E*, $J_{6,5}$ = 15.8); 6.27 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.40	3.89 (q, 2 H, CH_2CF_3, $J_{H,F}$ = 8.7)
4b	3.65 (dd, $J_{A,B}$ = 9.8, $J_{A,2}$ = 5.8)	3.68 (dd, $J_{B,A}$ = 9.8, $J_{B,2}$ = 4.6)	4.03	3.60 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 6.0)	3.57 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.5)	4.19 (*E*); 4.30 (*Z*)	5.93 (*E*); 5.61 (*Z*)	6.43 (dm, *E*, $J_{6,5}$ = 15.8); 6.30 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.73	7.08 (m, 5 H, Ph)
4c	3.44 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 6.1)	3.48 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.4)	3.99	3.55 (dd, $J_{A,B}$ = 9.7, $J_{A,2}$ = 6.0)	3.57 (dd, $J_{B,A}$ = 9.7, $J_{B,2}$ = 4.5)	4.19 (*E*); 4.33 (*Z*)	5.93 (*E*); 5.61 (*Z*)	6.45 (dm, *E*, $J_{6,5}$ = 15.8); 6.30 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.73	3.40 (s, 3 H, CH_3)
4d	3.46 (dd, $J_{A,B}$ = 9.5, $J_{A,2}$ = 6.3)	3.52 (dd, $J_{B,A}$ = 9.5, $J_{B,2}$ = 4.5)	3.95	3.59 (m)	3.59 (m)	4.20 (*E*); 4.34 (*Z*)	5.94 (*E*); 5.60 (*Z*)	6.45 (dm, *E*, $J_{6,5}$ = 15.8); 6.31 (dm, *Z*, $J_{6,5}$ = 12.4)	—	2.67	3.59 (m, 1 H, CH); 1.17 (d, 6 H, CH_3, J = 6.1)
5a	3.74 (m)	3.74 (m)	4.00	3.61 (m)	3.61 (m)	3.74	4.39	3.00 (m)	2.74	2.55	3.90 (q, 2 H, CH_2CF_3, $J_{H,F}$ = 8.7)
5b	3.71 (m)	3.71 (m)	4.19	3.71 (m)	3.71 (m)	4.05	4.36	2.98 (m)	2.71	2.74	7.10 (m, 5 H, Ph)
6a	3.74 (m)	3.74 (m)	4.01	3.61 (m)	3.61 (m)	3.74	4.39	3.00 (m)	2.74	2.35	3.90 (q, 2 H, CH_2CF_3, $J_{H,F}$ = 8.7)
6b	3.71 (m)	3.71 (m)	4.17	3.71 (m)	3.71 (m)	4.05	4.38	2.99 (m)	2.72	2.75	7.10 (m, 5 H, Ph)

Thus, similarly to other fluorine-containing glycidyl ethers,[1] [2-iodo-3-(perfluoroalkyl)propyl]glycidyl ethers tend to undergo regioselective epoxide ring opening under the action of alcohols under basic conditions. Depending on the process conditions and the nature of alcohol used, this may give either unsaturated or iodine-substituted hydroxy ethers.

Experimental

IR spectra were recorded on a Perkin—Elmer Spectrum One spectrophotometer in thin film. ^{1}H and ^{19}F NMR spectra were measured on a Bruker DRX 400 spectrometer operating at 400.1 (^{1}H) and 376.5 MHz (^{19}F) using Me_4Si and C_6F_6, respectively, as internal standards.

Table 3. ^{19}F NMR data for the reaction products*

Compounds	R_F	Isomers	δ (*J*/Hz)
3a—d	$CF_3^dCF_2^cCF_2^bCF_2^a$	*E*	36.40—36.45 (m, 2 F^c); 37.92—37.97 (m, 2 F^b); 50.22—50.26 (m, 2 F^a); 81.01—81.06 (tt, 3 F^d, J = 9.7, J = 3.3)
		Z	36.13—36.18 (m, 2 F^c); 37.52—37.58 (m, 2 F^b); 54.08—54.12 (m, 2 F^a); 81.01—81.06 (tt, 3 F^d, J = 9.7, J = 3.3)
4a—d	$CF_3^fCF_2^eCF_2^dCF_2^cCF_2^bCF_2^a$	*E*	35.85—35.89 (m, 2 F^e); 38.71—38.75 (m, 2 F^d); 39.20—39.24 (m, 2 F^b); 40.43—40.46 (m, 2 F^c); 50.30—50.35 (m, 2 F^a); 81.13—81.17 (tt, 3 F^f, J = 10.7, J = 2.4)
		Z	35.85—35.89 (m, 2 F^e); 38.71—38.75 (m, 2 F^d); 39.20—39.24 (m, 2 F^b); 40.43—40.46 (m, 2 F^c); 54.12—54.17 (m, 2 F^a); 81.13—81.17 (tt, 3 F^f, J = 10.7, J = 2.4)
5a,b	$CF_3^fCF_2^dCF_2^cCF^bF^a$		37.95—37.99 (m, 2 F^d); 39.31—39.36 (m, 2 F^c); 49.62—49.65 (m, 1 F^a); 50.85—50.89 (m, 1 F^b); 82.60—82.65 (tt, 3 F, J = 9.7, J = 3.3)
6a,b	$CF_3^hCF_2^gCF_2^fCF_2^dCF_2^cCF^bF^a$		37.70—37.73 (m, 2 F^g); 40.21—40.26 (m, 2 F^f); 41.02—41.07 (m, 2 F^c); 42.12—42.16 (m, 2 F^d); 49.85—49.89 (m, 1 F^a); 50.90—50.94 (m, 1 F^b); 82.73—82.76 (tt, 3 F, J = 10.2, J = 2.5)

* In the ^{19}F NMR spectrum of compounds **3a**, **4a**, **5a**, and **6a**, the CF_3 group resonates at 87.45—87.57 ppm (t, $J_{F,H}$ = 8.7 Hz).

(4,4,5,5,6,6,7,7,7-Nonafluoro-2-iodoheptyl)oxymethyloxirane (**1**) and (4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-iodononyl)oxymethyloxirane (**2**) were prepared by a known procedure.[8]

3-Alkoxy-1-[3-(perfluorobutyl)prop-2-enyloxy]propan-2-ols (3a,c,d) and 3-alkoxy-1-[3-(perfluorohexyl)prop-2-enyloxy]-propan-2-ols (4a,c,d) (general procedure). Sodium metal (0.81 g, 35 mmol) was added to the corresponding absolute alcohol (0.35 mol), then epoxide **1** (or **2**) (10 mmol) was added with stirring at reflux over a period of 30 min, and the reaction mixture was refluxed and stirred for additional 2 h. The mixture was cooled, water (100 mL) was added, the mixture was acidified with HCl and extracted with Et_2O (2×50 mL), and the organic layer was washed with an aqueous solution of sodium carbonate, dried with $MgSO_4$, and concentrated. The reaction products were isolated by vacuum distillation (Table 1).

3-Phenoxy-1-[3-(perfluorobutyl)prop-2-enyloxy]propan-2-ol (3b) and 3-phenoxy-1-[3-(perfluorohexyl)prop-2-enyloxy]propan-2-ol (4b) (general procedure). Sodium metal (0.81 g, 35 mmol) was added to phenol (400 mmol) in anhydrous diethylene glycol dimethyl ether (80 ml), the mixture was heated to 100 °C, then epoxide **1** (or **2**, 10 mmol) was added over a period of 30 min, and stirring was continued for 3 h at the same temperature. Pure **3d** and **4d** were isolated as described in the above procedure (see Table 1).

Synthesis of 3-alkoxy-1-[3-(perfluoroalkyl)prop-2-enyloxy]-propan-2-ols (3c,d and 4c,d) and 3-alkoxy-1-[2-iodo-3-(perfluoroalkyl)propoxy]propan-2-ols (5a,b and 6a,b) by phase transfer catalysis (general procedure). Epoxide **1** or **2** (10 mmol) was added at 35—40 °C to a stirred two-phase system consisting of CH_2Cl_2 (50 mL), 50% aqueous KOH (50 mL) containing alcohol (0.35 mol), and $Bu_4N^+I^-$ (0.1 g, 2 mol.%). After 4 h, the mixture was cooled, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic layers were washed with aq. HCl and dried with $MgSO_4$. Pure **3c,d**, **4c,d**, **5a,b**, and **6a,b** were isolated by vacuum distillation. The yields, boiling points, and elemental analysis data for compounds **3c,d**, **4c,d, 5a,b**, and **6a,b** are summarized in Table 1 and ^1H and ^{19}F NMR data are in Tables 2 and 3.

The IR spectra of compounds **3a—d** and **4a—d** exhibit common characteristic absorption bands in the ranges, ν/cm^{-1}: 3399—3431 (O—H), 2963—2859 (C—H), 1680—1682 (C=C), 1120—1122 (C—O—C, C—F); for compounds **5a,b** and **6a,b**: 3396—3432 (O—H), 2965—2859 (C—H), 1120—1122 (C—O—C, C—F).

References

1. D. N. Bazhin, T. I. Gorbunova, A. Ya. Zapevalov, V. E. Kirichenko, V. I. Saloutin, *Zh. Org. Khim.*, 2007, **43**, 661 [*Russ. J. Org. Chem.,* 2007, **43**, 656 (Engl. Transl.)].
2. D. V. Solov´ev, L. V. Kolomenskaya, A. A. Rodin, I. G. Zenkevich, A. N. Lavrent´ev, *Zh. Org. Khim*, 1991, **61**, 673 [*J. Gen. Chem. USSR*, 1991, **61** (Eng. Transl.)].
3. V. A. Petrov, *J. Fluorine Chem.*, 2004, **125**, 531.
4. D. N. Bazhin, T. I. Gorbunova, A. Ya. Zapevalov, V. I. Saloutin, *Izv. Akad. Nauk. Ser. Khim.*, 2007, 2160 [*Russ. Chem. Bull., Int. Ed.,* 2007, **56**, 2236 (Engl. Transl.)].
5. C. M. Timperley, W. E. White, *J. Fluorine Chem.*, 2003, **123**, 65.
6. A. Albert, E. Serjeant, *Ionisation Constants of Acids and Bases*, Methuen, London , 1962.
7. X. Yang, Z. Wang, Y. Zhu, X. Fang, X. Yang, F. Wu, Y. Shen, *J. Fluorine Chem.*, 2007, **128**, 1046.
8. D. N. Bazhin, T. I. Gorbunova, A. Ya. Zapevalov, V. I. Saloutin, *Izv. Akad. Nauk. Ser. Khim.,* 2007, 1476 [*Russ. Chem. Bull., Int. Ed.*, 2007, **56**, No. 8].

Received April 4, 2008;
in revised form May 27, 2008