Journal of Fluorine Chemistry 130 (2009) 317–320

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Chain-radical fluoroalkylation of thiophenols with freon $ClCF_2CFCl_2$ in the presence of sulfur dioxide

Vyacheslav G. Koshechko, Lydiya A. Kiprianova *, Ludmyla I. Kalinina

L.V. Pisarzhevsky Institute of Physical Chemistry of the National Academy of Sciences of Ukraine, Pr.Nauky 31, Kiev 03028, Ukraine

ARTICLE INFO

Article history:
Received 19 May 2008
Received in revised form 10 December 2008
Accepted 12 December 2008
Available online 25 December 2008

Keywords:
Polyfluoroalkylation
Thiophenols
Sulfur dioxide

ABSTRACT

A polyfluoroalkylation of thiophenols with $CF_2ClCFCl_2$ using substituted pyridine–sulfur dioxide system enables to obtain fluoroalkylated thioethers by a $S_{RN}1$-type free-radical route.

1. Introduction

The use of fluorohalocarbons as perfluoroalkyl group synthons for the synthesis of fluorine containing compounds attracted considerable interest [1–7]. Unlike iodine- and bromine-containing fluoroalkanes, chlorofluoroalkanes (CFCs) as the alkylating agents were explored to a much lesser extent, which is largely caused by their considerably lower reactivity due to stronger C–Cl bond compared to C–Br and C–I. At the same time, chlorofluoroalkanes usually are cheaper compared to their bromine- and iodine-containing analogues.

This paper describes a possibility of thiophenols fluoroalkylation with freon $CF_2ClCFCl_2$ (CFC113). Under standard conditions thiophenols do not react with freons, including CFC113, and thiophenol potassium salts are employed to activate such process [8–13]. $CF_2ClCFCl_2$–thiophenolates interaction is considered to be the halophilic process (Scheme 1).

Alternatively, for bromo- and iodofluoroalkanes, in some cases it is possible to implement thiophenols fluoroalkylation by a chain-radical route [8,14,15]. Such processes exhibit sufficiently high selectivity.

If it would be possible to perform thiophenols fluoroalkylation by $CF_2ClCFCl_2$ by a radical route, this will allow not only to improve the selectivity of the process, but also to produce $ArSCFClCF_2Cl$ instead of $ArSCF_2CFCl_2$ [8] according to the following hypothetical Scheme 2. It would be especially convenient to use thiophenols themselves, instead of their salts.

Taking this into account the possibility of thiophenols fluoroalkylation by freon $CF_2ClCFCl_2$ by the radical mechanism was studied.

2. Results and discussion

The $CF_2ClCFCl_2$–thiophenols interaction was intended to be activated in two ways: by increasing the electron-donating ability of the thiophenols and by introducing an electron transfer mediator into the system, which facilitates freon reduction and generation of active radicals.

Our strategy on the one hand was to create such fluoroalkylation conditions under which the basicity of the nucleophile would be not sufficient for separation off the bearing partial positive charge halogen from the freon to rule out the ionic process (Scheme 1) and, on the other hand, the nucleophile's electron-donating ability would be sufficiently high for electron transfer to the freon to enable the fluoroalkylation process by the radical route (Scheme 2).

We supposed that such substrate activation could be achieved by addition of organic nitrogen bases into the system, in particular pyridines, capable to form complexes with thiophenols through the hydrogen bond. This would contribute to increase of electron-

* Corresponding author. Tel.: +380 44 525 54 14; fax: +380 44 525 62 16.
E-mail address: lkipr@inphyschem-nas.kiev.ua (L.A. Kiprianova).

0022-1139/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2008.12.005

$$ArS^- + ClCF_2CFCl_2 \rightarrow ArSCl + {}^-ClCFCF_2Cl$$

$$^-ClCFCF_2Cl \rightarrow CF_2{=}CFCl + Cl^-$$

$$ArS^- + CF_2{=}CFCl \rightarrow ArSCF_2CFCl^-$$

$$ArSCF_2CFCl^- + ClCF_2CFCl_2 \rightarrow ArSCF_2CFCl_2 + ClCF_2CFCl^-$$

$$ArSCF_2CFCl^- + SH\ (solv.) \rightarrow ArSCF_2CFClH + S^-$$

Scheme 1.

donating ability of thiophenols due to equilibrium shift to their anionic forms with lower ionisation potential:

$ArSH + N{\equiv} \rightleftharpoons ArS^- \ldots {}^+HN{\equiv}$,
where $N{\equiv}$ are the nitrogen bases.

To verify this assumption we studied the effect of various pyridines on the potentials of electrochemical oxidation of the thiophenols in acetonitrile, which characterise their electron-donating properties. It was found that addition of pyridines to acetonitrile led to a significant increase of the electron-donating capacity of the thiophenols, as evidenced by decrease of peak potentials of their electrochemical oxidation, for example, in the case of p-chlorothiophenol (Table 1).

In the absence of pyridine in acetonitrile solutions the peak potential (E_p) of p-chlorothiophenol is 1.87 V.

Increase of basicity of the pyridines, which is caused by hydrogen bond strengthening results in growth of the electron-donating capacity of p-chlorothiophenol. There is linear relationship between the E_p of the thiophenols and the pK_a of the pyridines (Fig. 1).

However enhancement of the substrate's electron-donating capacity alone, caused by the formation of complexes with pyridines, is an indispensable but insufficient condition for successful implementation of the process. In the presence of nitrogen bases only (pyridine, β-picoline), thiophenols fluoroalkylation with $CF_2ClCFCl_2$ in aprotic solvents at room temperature is not achieved. Donor strength of the complexes appears to be not enough for the electron transfer to the freon because of too broad gap between ionisation potentials of the complexes and electron affinity of the freon, which may be indirectly reflected by the corresponding electrochemical potentials (reduction potential of $CF_2ClCFCl_2$, $E_p = -2.3$ V vs. Ag/AgCl).

In order to activate electron transfer from the substrate–pyridine complexes to the freon, we used sulfur dioxide that is highly efficient as electron transfer mediator for the electrochemical and chemical processes involving per- and polyfluorohaloalkanes [16–20]. Sulfur dioxide capacity to act as the mediator of electron transfer to the CFC113 was demonstrated by catalytic current observed in the cyclic voltammogram of the sulfur dioxide (Fig. 2), when adding $CF_2ClCFCl_2$ to the system, owing to the SO_2 resumption in the near-electrode layer (Scheme 3).

We studied the interaction of different p-substituted thiophenols XC_6H_4SH (X = H, CH_3, Cl, NO_2, CF_3SO_2) with $CF_2ClCFCl_2$ in dimethylformamide in the presence of SO_2 as electron transfer

Table 1
Dependence of peak potentials of p-chlorothiophenol oxidation (E_p) in the mixtures of acetonitrile and substituted pyridine on pK_a of the pyridine. [p-chlorothiophenol] = 0.01 M; [pyridine] = 1.00 M; 0.1 M $NaClO_4$; Ag/AgCl; 25 °C.

Amine	pK_a	E_p, V
2-Chloropyridine	0.72	1.28
2-Bromopyridine	0.90	1.13
3-Bromopyridine	2.84	1.03
2,3-Lutidine	6.48	0.76
2,4-Lutidine	6.82	0.71
γ-Collidine	7.60	0.63

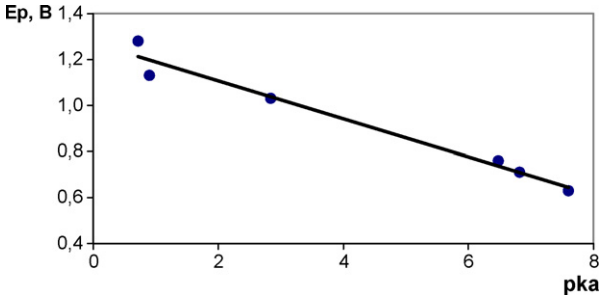


Fig. 1. Peak potentials of p-chlorothiophenol oxidation as a function of pK_a of the pyridines added to the system. [p-ClC_6H_4SH] = 0.01 M; [pyridine] = 1.0 M; Pt; $NaClO_4$ 0.1 M; Ag/AgCl; 25 °C.

mediator and of β-picoline added to enhance electron-donating capacity of the substrates to be fluoroalkylated. The reaction was conducted in a sealed ampoules at 35 °C for 5–6 h. It is found that sulfur dioxide–nitrogen base activation system allows to accomplish the thiophenols fluoroalkylation by $CF_2ClCFCl_2$ in mild conditions, and only one product—p-$XC_6H_4SCFClCF_2Cl$ is formed

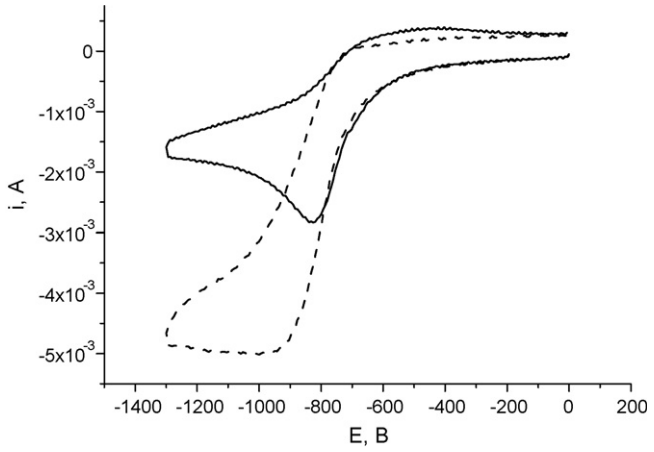


Fig. 2. Cyclic voltammogram of SO_2 (–) and $SO_2 + CF_2ClCFCl_2$ (- - -). $[SO_2] = 1 \times 10^{-2}$M; $[CF_2ClCFCl_2] = 2 \times 10^{-2}$M; $\nu = 0.2$ V/s; Ag/AgCl; 0.1 M Bu_4NBF_4 in DMFA.

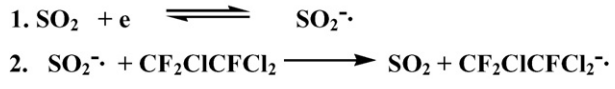
$$ArS^- + ClCF_2CFCl_2 \rightarrow ArS\cdot + [ClCF_2CFCl_2]^{-\bullet}$$

$$[ClCF_2CFCl_2]^{-\bullet} \rightarrow ClCF_2CFCl\cdot + Cl^-$$

$$ArS^- + ClCF_2CFCl\cdot \rightarrow [ArSCFClCF_2Cl]^{-\bullet}$$

$$[ArSCFClCF_2Cl]^{-\bullet} + ClCF_2CFCl_2 \rightarrow ArSCFClCF_2Cl + [ClCF_2CFCl_2]^{-\bullet}$$

Scheme 2.



Scheme 3.

Table 2
Product yields of thiophenol–$CF_2ClCFCl_2$ interaction in the presence of SO_2 [p-XC_6H_4SH] = 0.25 M; [$CF_2ClCFCl_2$] = 0.65 M, DMFA, 35 °C.

X in p-XC_6H_4SH	[SO_2], M	β-picoline, M	p-XC_6H_4S–$CFClCF_2Cl$ yield, %
CH_3	0.65	2.50	52
CH_3[a]	0.65	2.50	5
CH_3	0.12	1.25	37
CH_3	0.25	1.25	56
H	0.25	1.25	45
Cl	0.25	1.25	38
NO_2	0.25	1.25	–
CF_3SO_2	0.25	1.25	–

[a] p-Dinitrobenzene added.

in all cases. The yields of polyfluoroalkylarylsulfides are given in Table 2.

As it can be seen from Table 2, the efficiency of the thiophenols fluoroalkylation process depends on the concentration of the mediator (SO_2) and of the base (β-picoline). Only one single fluoroalkylation product, p-$XC_6H_4SCFClCF_2Cl$, evidently points to the fact that fluoroalkylation of thiophenols by $CF_2ClCFCl_2$ in SO_2–β-picoline activated system proceeds by a $S_{RN}1$-type free-radical route. The ionic mechanism (Scheme 1) would lead to p-$XC_6H_4SCF_2CFCl_2$ [8]. This may be relevant to diverse species involved in the ionic and free-radical routes: fluoroalkylation is accomplished with $CF_2{=}CFCl$ olefin for the former (Scheme 1) and with a $^{\bullet}CFClCF_2Cl$ free-radical for the latter. Assumed mechanism of thiophenols fluoroalkylation with $CF_2ClCFCl_2$ in the presence of SO_2 and β-picoline can be represented by the Scheme 4.

The first step of the process involves electron transfer from thiophenol complexes with β-picoline, rather than from the "pure" thiophenolate anions. Radical mechanism for thiophenols fluoroalkylation with $CF_2ClCFCl_2$ is evidenced by dramatic decrease in the fluoroalkylation product yields (from 52 to 5% for p-$CH_3C_6H_4SCFClCF_2Cl$) at the presence of radical trap, p-dinitrobenzene (Table 2).

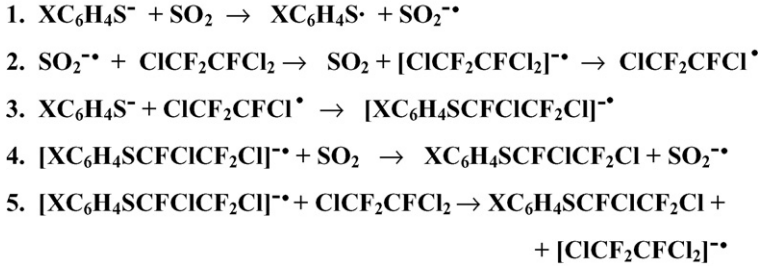
Scheme 5.

With increasing electron-withdrawing capacity of substituent X the yield of product p-$XC_6H_4SCFClCF_2Cl$ decreases and, in the case of NO_2 and CF_3SO_2 substituents, fluoroalkylation process fails to be accomplished under the present conditions. The observed dependence may be related to the fact that transition from electron-donating to electron-withdrawing substituents impedes the electron transfer from the thiophenol to the mediator, sulfur dioxide, in the first step of the process as well as during its follow-on development (Scheme 4).

In some cases we observed 3–4% of $CF_2{=}CFCl$ in the ^{19}F NMR spectrum along with the polyfluoroalkylarylsulfides $XC_6H_4SCFClCF_2Cl$. This species is seen as an intermediate for the ionic conversion route. However, we believe that in our case the formation of such olefin occurs due to further reduction of fluoroalkyl radical to have been obtained during the second step of the process (Scheme 5).

As it was pointed out above, unlike thiophenols fluoroalkylation with $CF_2ClCFCl_2$, activated using SO_2, interaction of thiophenolates and $CF_2ClCFCl_2$ results in a $XC_6H_4SCF_2CFCl_2$ product [8]. It was rather interesting to elucidate how SO_2 electron carrier can impact on the process with thiophenolates and whether it was possible to convert the latter from halophilic to free-radical one using SO_2. We found that, in the absence of SO_2, interaction of sodium thiophenolate and $CF_2ClCFCl_2$ results in $C_6H_5SCF_2CFCl_2$ (16%) and $C_6H_5SCF_2CFClH$ (16%) (Table 3). The lower yield compared to [8] is evidently related to the fact that we had used a sodium thiophenolate but not more active potassium salt as in [8].

Introduction of sulfur dioxide into the system in quantities equimolar or near-equimolar to thiophenolate, leads to dramatically changes: there is no hydrothioether, while the resulting product is $C_6H_5SCFClCF_2Cl$ (38%). A radical trap (p-dinitrobenzene) decreases this product's yield tenfold, which may confirm its radical origin.



Scheme 4.

Table 3
Product yields of sodium thiophenolate–$CF_2ClCFCl_2$ interaction in the presence of SO_2, DMFA, 35 °C.

[C_6H_5SNa], M	[$CF_2ClCFCl_2$] M	[SO_2] M	Product yields, %		
			C_6H_5S–CF_2CFCl_2	C_6H_5S–CF_2CFClH	C_6H_5S–$CFClCF_2Cl$
0.30	0.30	–	16.0	16.0	–
1.25	2.05	0.83	–	–	38
0.50	1.10	0.35	–	–	35
1.25[a]	2.05	0.83	–	–	3

[a] p-Dinitrobenzene added.

3. Conclusion

Thus a possibility of fluoroalkylating thiophenols with $CF_2ClCFCl_2$, using nitrogen base–sulfur dioxide system is shown, that enables not only to activate such process, setting it by free-radical route, but also to obtain fluoroalkylated products whose structure drastically differs from those which form in the course of fluoroalkylation of thiophenolates: p-$XC_6H_4SCFClCF_2Cl$ for the substituted pyridine-SO_2 system and p-$XC_6H_4SCF_2CFCl_2$ in the case of fluoroalkylation of alkaline salts of thiophenols.

4. Experimental

Melting points were uncorrected. The dimethylformamide was distilled and stored over A4 sieves. 1,1,2-trichlorotrifluoroethane was distilled prior to use. Sodium thiophenoxide was prepared via sodium methylate–thiophenol interaction in methanol. The ^{19}F NMR spectra were recorded in δ (ppm) using Bruker-CXP-90 NMR spectrometer (DMSO-d_6, vs. CCl_3F), the ^{13}C NMR spectra using a Bruker AVANCE 400 ($CDCl_3$, vs. TMS). Cyclic voltammetry experiments were carried out in the undivided three electrode analytical cell; working electrode – disk cathode of platinum; auxiliary electrode – platinum wire; reference electrode – Ag/AgCl. The solvent of analytical grade (10 ml) contained supporting salt (0.1 M Bu_4NBF_4). The cell was purged for 15 min with nitrogen. The study was carried out using EP 20A potentiostate- and PC-based computerized electrochemical facilities.

4.1. General procedure for the interaction of thiophenol with $CF_2ClCFCl_2$ in the presence of sulfur dioxide

1,1,2-Trichlorotrifluoroethane $CF_2ClCFCl_2$ (0.15 ml, 13×10^{-4} M) and sulfur dioxide (0.17 ml of SO_2 solution in DMFA, 5×10^{-4} M SO_2) were added to a solution of thiophenol (0.055 g, 5×10^{-4} M) in a mixture of DMFA (1.5 ml) with β-picoline (0.25 ml, 2.5×10^{-3} M) under argon atmosphere. The sealed ampoule was kept at 35 °C for 4–5 h. The yield of polyfluoroalkylated product was calculated from ^{19}F NMR spectra. The reaction mixture was diluted with 30 ml of 17% solution of HCl, three times extracted with ether or hexane, organic layer washed with water and dried. After the ether had been removed, the product was distilled under reduced pressure. The similar procedures were carried out for other p-XC_6H_4SH–$CF_2ClCFCl_2$ interactions. The corresponding physical and spectral data of p-$XC_6H_4SCFClCF_2Cl$ are given below (X, b.p., ^{19}F NMR, ^{13}C NMR, the elemental analysis):

X = CH_3, colorless oil, b.p. 110 °C/9 mm Hg; ^{19}F NMR (84.79 MHz, Me_2SO-d_6): δ 89.9 (t, 1F, J = 14.3 Hz, SCFCl), 62.6 (d, 2F, J = 14.1 Hz, CF_2Cl); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 117.8; 120.7 (1C, dt, $^2J_{CF}$ = 294.9 Hz, $^1J_{CF}$ = 33.3 Hz, CFCl), 126.7 (1C), 126.4; 129.3; 132.4 (1C, td, $^1J_{CF}$ = 301.1 Hz, $^2J_{CF}$ = 35.9 Hz, CF_2Cl), 134.1 (2C), 141.3 (2C), 145.7 (1C). Anal. Calcd for $C_9H_7Cl_2F_3S$: C, 39.29; H, 2.54; F, 20.71. Found: C, 39.30; H, 2.40; F, 20.09.

X = Cl; colorless oil, b.p.107^{0}C/11 mm Hg; ^{19}F NMR (84.79 MHz, Me_2SO-d_6): δ 90.3 (tr, 1F, J_{FF} = 14.3 Hz, SCFCl), 62.8 (d, 2F, J_{FF} = 13.3 Hz, CF_2Cl); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 113.7; 116.6 (1C, dt, $^2J_{CF}$ = 294.3 Hz, $^1J_{CF}$ = 33.6 Hz, CFCl), 122.5; 125.3; 128.4 (1C, td, $^1J_{CF}$ = 300.3 Hz, $^2J_{CF}$ = 35.0 Hz, CF_2Cl); 124.9 (1C), 129.0 (1C), 129.4 (2C), 138,2 (1C), 138.6 (1C); Anal. Calcd for $C_8H_4Cl_3F_3S$: C, 32.51; H, 1.36; found: C, 32.00; H, 1.24.

X = H; b.p.101 °C/13 mm Hg; ^{19}F NMR (84.79 MHz, Me_2SO-d_6): δ 89.9 (tr, 1F, J = 14.3 Hz, SCFCl), 62.6 (d, 2F, J = 14.3 Hz, CF_2Cl); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 117.7; 120.7 (1C, dt, $^2J_{CF}$ = 295.3 Hz, $^1J_{CF}$ = 33.5 Hz, CFCl), 126.4; 129.3; 132.3 (1C, td, $^1J_{CF}$ = 301.3 Hz, $^2J_{CF}$ = 35.9 Hz, CF_2Cl); 130.2 (1C), 133.3 (2C), 135.1 (2C), 141.3 (1C); Anal. Calcd for $C_8H_5Cl_2F_3S$: C, 36.80; H, 1.93; F, 21.83. Found: C, 36.79; H, 2.05; F, 21.80.

4.2. Interaction of sodium thiophenolate with $CF_2ClCFCl_2$

1,1,2-Trichlorotrifluoroethane $CF_2ClCFCl_2$ (0.08 ml, 0.6×10^{-3} M) was added to a solution of sodium thiophenolate (0.079 g, 0.6×10^{-3} M) in 2 ml of DMFA under argon atmosphere. The sealed ampoule was kept at 35 °C for 5–6 h. The yield of polyfluoroalkylated product was calculated from ^{19}F NMR spectra. Further treatment of reaction products and their determination were carried out similarly to the above mentioned. The isolated products were found to be [(2,2-dichloro-1,1,2-trifluoroethyl)thio]benzene $C_6H_5SCF_2CFCl_2$ and $C_6H_5SCF_2CFClH$ [2].

4.3. Interaction of sodium thiophenolate with $CF_2ClCFCl_2$ in the presence of sulfur dioxide

$CF_2ClCFCl_2$ (0.47 ml, 4.1×10^{-3} M) and a sulfur dioxide (0.54 ml of sulfur dioxide solution in DMFA, 1.65×10^{-3}M SO_2) were added to a solution of sodium thiophenolate (0.33 g, 2.5×10^{-3}M) in 2 ml of DMFA under argon atmosphere. The sealed ampoule was kept at 35 °C for 5–6 h. The yield of polyfluoroalkylated product was calculated from ^{19}F NMR spectra. The subsequent treatment was carried out as specified above. The isolated product was found to be [(1,2-dichloro-1,2,2-trifluoroethyl)thio]benzene $C_6H_5SCFClCF_2Cl$ described in 3.1. The reaction was inhibited by addition 0.8×10^{-3} M of p-dinitrobenzene.

References

[1] F.-H. Wu, W.-Y. Huang, J. Fluorine Chem. 110 (2001) 59–61.
[2] C. Wakselman, C. Kaziz, J. Fluorine Chem. 33 (1986) 347–359.
[3] K. Wu, Q.-Y. Chen, J. Fluorine Chem. 113 (2002) 79–83.
[4] D.L.S. Brahms, W.P. Dailey, Chem. Rev. 96 (1996) 1585–1632.
[5] V.D. Pohodenko, V.G. Koshechko, V.E. Tytov, D.V. Sednev, Theor. Exp. Chem. 28 (1992) 85–99.
[6] V.G. Koshechko, L.A. Kiprianova, Theor. Exp. Chem. 39 (1999) 17–34.
[7] X.-T. Huang, Z.-Y. Long, Q.-Y. Chen, J. Fluorine Chem. 111 (2001) 107–113.
[8] C. Wakselman, M. Tordeux, J. Org. Chem. 50 (1985) 4047–4051.
[9] X.-Y. Li, X.-K. Jiang, H.-Q. Pan, J.-S. Hu, W.-M. Fu, Pure Appl. Chem. 59 (1987) 1015–1020.
[10] X.-Y. Li, H.-Q. Pan, X.-K. Jiang, Tetrahedron Lett. (1984) 4937–4940.
[11] I. Rico, C. Wakselman, Tetrahedron Lett. (1981) 323–326.
[12] I. Rico, C. Wakselman, J. Fluorine Chem. 20 (1982) 759–764.
[13] Z.-Y. Long, Q.-Y. Chen, J. Fluorine Chem. 91 (1998) 95–98.
[14] I. Rico, D. Cantacuzene, C. Wakselman, J. Org. Chem. 48 (1983) 1979–1982.
[15] V.N. Boiko, G.M. Shchupak, L.M. Yagupolski, J. Fluorine Chem. 69 (1994) 207–212.
[16] W.-Y. Huang, J. Fluorine Chem. 58 (1992) 1–8.
[17] C.P. Andrieux, L. Gelis, J.-M. Saveant, J. Am. Chem. Soc. 112 (1990) 786–791.
[18] V.G. Koshechko, L.A. Kiprianova, L.I. Fileleeva, K.G. Tzanov, Theor. Exp. Chem. 29 (1993) 166–169.
[19] V.G. Koshechko, L.A. Kiprianova, L.I. Fileleeva, L.I. Kalinina, V.A. Khizhnyi, J. Fluorine Chem. 127 (2006) 1242–1244.
[20] M. Tordeux, B. Langlois, C. Wakselman, J. Chem. Soc. Perkin Trans. I (1990) 2293–2299.