Available online at www.sciencedirect.com
ScienceDirect
Journal of Fluorine Chemistry 128 (2007) 1376–1378
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Selective fluoroalkylation of thiophenols by 1,2-dibromotetrafluoroethane activated by sulfur dioxide

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

L.V. Pisarzhevsky Institute of Physical Chemistry of the National Academy of Sciences of Ukraine, Pr. Nauky 31, Kiev 01039, Ukraine

Received 4 April 2007; received in revised form 18 June 2007; accepted 20 June 2007
Available online 23 June 2007

Abstract

Treatment of 1,2-dibromotetrafluoroethane with thiophenols in DMF in the presence of sulfur dioxide and pyridines having $pK_a > 5$ gives fluoroalkylated thioethers in high yields under mild conditions. The influence of thiophenol reactant structure and medium basicity is discussed.

Keywords: Polyfluoroalkylation; Thiophenols; Sulfur dioxide

1. Introduction

Introduction of halocarbon fragments, containing other halogen atoms besides fluorine, into different organic substrates allows the synthesis of new polyfluoroalkyl substrates as well as transformation of fluorine containing substituents to more complex groups [1–14].

The fluoroalkylation of thiophenols, phenols and heterocyclic nitrogen compounds by 1,2-dibromotetrafluoroethane is usually performed by the interaction of the potassium salts of these compounds with $BrCF_2CF_2Br$ [3,10,15–18], as illustrated (Eq. (1)) for alkylation of thiophenols.

$$ArSK + BrCF_2CF_2Br \rightarrow ArSCF_2CF_2Br + ArSCF_2CF_2H \quad (1)$$

In addition to the product, $ArSCF_2CF_2Br$, this condensation yields diaryl disulfides and thioethers, containing the $-CF_2CF_2H$ group. Electron-withdrawing groups cause an increase of the yields of H-substituted product and a retardation of the whole reaction.

The aim of our study was to carry out the interaction of $BrCF_2CF_2Br$ with thiophenols, but not thiophenolates, as starting reagents and thereby to increase the selectivity of the process. Bromoderivatives, $ArSCF_2CF_2Br$, have high lipophilicity [17] and may be considered as potential physiologically active substances.

2. Results and discussion

The formation of two types of products in Eq. (1) can be rationalized by an ionic chain mechanism postulated in [10–18], including anionic intermediates $ArSCF_2CF_2^-$. Reaction with proton donors, including H_2O, gives the side product, $ArSCF_2CF_2H$, lowering the yield of the desired $ArSCF_2CF_2Br$. In [11,12] the hypothesis was proposed that one electron transfer from thiophenolates to perfluorohaloalkanes is followed by competition between a radical path and release of a ''positive'' halogen. In the case of 1,2-dibromotetrafluoroethane the thiophenoxides react by a carbanionic process.

We supposed that transformation of the process into a radical pathway ($S_{RN}1$ type) seems to increase its selectivity by excluding the formation of H-substituted products.

As thiophenols, unlike their salts, do not react with $BrCF_2CF_2Br$, it seemed reasonable to stimulate the radical decay of $BrCF_2CF_2Br$ using an electron transfer mediator, and to accelerate the electron transfer by a mediator to increase the nucleophility of thiopenols. It was demonstrated earlier [19–23] that sulfur dioxide can serve as an electron transfer mediator. The second aim was achieved by addition of organic nitrogen bases (such as pyridines) that increase the thiophenol nucleophility by complexation.

To verify this assumption we have studied the interaction of different thiophenols with $BrCF_2CF_2Br$ in dimethylformamide

* Corresponding author. Fax: +380 44 5256216.
E-mail address: lkipr@inphyschem-nas.kiev.ua (L.A. Kiprianova).

0022-1139/$ – see front matter
doi:10.1016/j.jfluchem.2007.06.006

Table 1
Condensation of $BrCF_2CF_2Br$ (0.024 mol L^{-1}) with thiophenols p-XC_6H_4SH (0.020 mol L^{-1}) in the presence of sulfur dioxide and β-picoline

X	β-Picoline (mol L^{-1})	SO_2 (mol L^{-1})	Yield[a] of p-$XC_6H_4SCF_2CF_2Br$ (%)
H	0.02	–	–
H	0.01	0.02	21.6
H	0.02	0.02	63.5
CH_3	0.04	0.02	82.4
CH_3	0.10	0.02	88.1
CH_3[b]	0.10	0.02	12.0
CH_3	0.10	0.06	78.8
CH_3	0.20	0.06	82.7
CH_3	0.20	0.10	76.4

[a] ^{19}F NMR yields.
[b] p-Dinitrobenzene was added.

(DMF) in the presence of sulfur dioxide as mediator and β-picoline as a base (Table 1).

In contrast to interaction of potassium salts of thiophenols with $BrCF_2CF_2Br$ only one product $ArSCF_2CF_2Br$ was formed (Table 1); hydrogenated by-product, $ArSCF_2CF_2H$, was absent. In the absence of sulfur dioxide and picoline, condensation of $BrCF_2CF_2Br$ with thiophenols did not occur. An excess of picoline strongly increases the yields of the desired product. Low yields of thioethers were obtained when β-picoline concentration was 0.01 mol L^{-1}, however the yield increased to 63.5% at equimolecular ratio of sulfur dioxide: β-picoline. Thiocresole demonstrates similar behavior. The yield of 76% of p-$CH_3C_6H_4SCF_2CF_2Br$ at twofold excess of picoline increases to 88% at a fivefold excess.

A sole product leads to the assumption that this conversion follows a radical pathway. It was demonstrated also by the absence of hydrogenated thioethers in the presence of water. The addition of free radical traps such as p-dinitrobenzene to the reaction mixture leads to inhibition of the process, lowering the yield from 88% to 12% (Table 1, entry 6) supporting the hypothesis of a radical pathway. We suppose that $S_{RN}1$ type mechanism (scheme (2)) is involved in the formation of aryl polyfluoroalkyl sulfides.

At the first step a single electron transfer takes place from the complexes of thiophenol with picoline. The ability of sulfur dioxide to induce some electrochemical and chemical processes of halofluorocarbon activation was demonstrated earlier [19–22]. In a few cases the presence of small amounts (1.5–4%) of tetrafluoroethylene was detected. Formation of this by-product can be explained by reduction of the radical $^{\bullet}CF_2CF_2Br$.

$$
\begin{aligned}
&1.\ XC_6H_4S^- + SO_2 \rightarrow XC_6H_4S^{\bullet} + {SO^{\bullet}}_2{}^-\\
&2.\ {SO^{\bullet}}_2{}^- + BrCF_2CF_2Br \rightarrow SO_2 + [BrCF_2CF_2Br]^{\bullet -}\\
&\quad \rightarrow {}^{\bullet}CF_2CF_2Br + Br^-\\
&3.\ XC_6H_4S^- + {}^{\bullet}CF_2CF_2Br \rightarrow [XC_6H_4SCF_2CF_2Br]^{\bullet -}\\
&4.\ [XC_6H_4SCF_2CF_2Br]^{\bullet -} + SO_2 \rightarrow XC_6H_4SCF_2CF_2Br + {SO^{\bullet}}_2{}^-\\
&5.\ [XC_6H_4SCF_2CF_2Br]^{\bullet -} + BrCF_2CF_2Br\\
&\quad \rightarrow XC_6H_4SCF_2CF_2Br + [BrCF_2CF_2Br]^{\bullet -}\\
&6.\ {SO^{\bullet}}_2{}^- + {}^{\bullet}CF_2CF_2Br \rightarrow SO_2 + Br^- + CF_2 = CF_2
\end{aligned}
\qquad (2)
$$

Table 2
Condensation of $BrCF_2CF_2Br$ (0.024 mol L^{-1}) with thiophenols p-XC_6H_4SH (0.020 mol L^{-1}) in the presence of sulfur dioxide (0.020 mol L^{-1}) and β-picoline (0.10 mol L^{-1})

X in p-XC_6H_4SH	CH_3	H	Cl	NO_2
σ	−0.17	0	+0.23	+0.78
Yields[a] (%) p-$XC_6H_4SCF_2CF_2Br$	88.0	61.7	42.5	21.9

[a] ^{19}F NMR yields.

We studied the influence of electronic reactant structure on the interaction of thiophenols with 1,2-dibromotetrafluoroethane (Table 2).

In all cases only thioethers p-$XC_6H_4SCF_2CF_2Br$ were obtained. Electron-donating groups promoted the reaction, but electron-withdrawing ones caused a decrease in the yield of thioethers; dependence on σ-constants of Hammett of thiophenol substituents was observed.

The yields' decrease is probably due to the retarding of electron transfer from thiophenols to SO_2 at the first, fourth and fifth stages of the scheme (2).

Fluoroalkylation of thiophenols by $BrCF_2CF_2Br$ yielding p-$XC_6H_4SCF_2CF_2Br$ may be performed also in DMSO; according to [24] this solvent stimulates the fragmentation of the anion-radical.

Addition of organic bases has an effect in fluoroalkylation of thiophenols by $BrCF_2CF_2Br$. These investigations were carried out using thiocresol as an example (Table 3).

The above results demonstrate that in the presence of rather weak bases as 2-chloropyridine and p-acetylpyridine there was no fluoroalkylation reaction. In contrast stronger bases efficiently stimulate thiocresol polyfluoroalkylation, producing p-$CH_3C_6H_4SCF_2CF_2Br$. The increase of pK_a of bases used resulted in higher yields of p-$CH_3C_6H_4SCF_2CF_2Br$; in the case of 2,5-lutidine and γ-collidine almost quantitative yields were attained.

It should be noted that fluoroalkylation process in the presence of γ-collidine occurred with simultaneous formation of precipitate due to the interaction of SO_2 with amine, however the yield of desired thioether was almost quantitative, probably the polyfluoroalkylation had enough time to be completed.

Hence polyfluoroalkylation of thiophenols by $BrCF_2CF_2Br$ may be efficiently performed in mild conditions in the presence

Table 3
Condensation of $BrCF_2CF_2Br$ (0.04 mol L^{-1}) with thiocresol (0.02 mol L^{-1}) in the presence of sulfur dioxide (0.03 mol L^{-1}) and substituted pyridines (0.10 mol L^{-1})

Pyridines	pK_a	Yields[a] of p-$CH_3C_6H_4SCF_2CF_2Br$ (%)
2-Chloropyridine	0.72	–
p-Acetylpyridine	3.18	–
Pyridine	5.23	78
2,5-Lutidine	6.25	98
γ-Collidine	7.60	99
Pyridine[b]	5.23	28
γ-Collidine	7.60	46

[a] ^{19}F NMR yields.
[b] p-Dinitrobenzene was added.

of strong nitrogen bases mediating the process by sulfur dioxide.

3. Experimental

^{1}H NMR and ^{19}F NMR spectra were recorded using a Bruker CXP-90 (90 MHz) instrument. ^{1}H and ^{19}F chemical shifts were recorded in δ(ppm) values relatively to hexamethyl disiloxane (^{1}H) and CCl_3F (^{19}F) as internal standard.

3.1. General experimental procedure: interaction of $BrCF_2CF_2Br$ with thiophenols in the presence of SO_2 and β-picoline

1,2-Dibromotetrafluoroethane (0.6 mmol) and sulfur dioxide (0.2 ml of SO_2 solution in DMF, 0.5 mmol) were added to a solution of 0.5 mmol of thiophenol in a mixture of DMF (2 ml) with β-picoline (0.25 ml, 2.5 mmol) under argon. The sealed ampoule was kept for 0.5–1 h at 35 °C. The yield of fluoroalkylated 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, organic layer washed with water, dried, ether was evaporated and the residue was purified by chromatography on a silica gel column with hexane as eluent. The characteristic properties of compounds obtained (^{1}H and ^{19}F NMR spectra, mp, bp) coincided with ones described in Ref. [17], as thioethers p-$XC_6H_4SCF_2CF_2Br$ with X = CH_3, H, Cl, NO_2 are already known.

3.2. Interaction of $BrCF_2CF_2Br$ with thiophenols in the presence of SO_2, β-picoline and p-dinitrobenzene

The interaction of reagents, further treatment of reaction mixture and determination of products were carried out similarly to the above mentioned, but 0.2 mmol of *p*-dinitrobenzene was added (Table 1).

3.3. Interaction of $BrCF_2CF_2Br$ with thiophenols in the presence of SO_2 and substituted pyridines

The interaction of reagents, further treatment of reaction mixture and determination of products were carried out similarly to 3.1, but instead of β-picoline other pyridines (Table 3) were added.

References

[1] F.-H. Wu, W.-Y. Huang, J. Fluorine Chem. 110 (2001) 59–61.
[2] L. Zang, J. Zang, Y. Wang, W. Fub, S.W. Eisbawer, J. Fluorine Chem. 88 (1998) 51–59.
[3] G. Nenajdenko, G.N. Varseev, V.N. Korotchenko, A.V. Shastin, E.S. Balenkova, J. Fluorine Chem. 125 (2004) 1339–1345.
[4] G.G. Furin, Russ. Chem. Rev. 69 (2000) 491–522.
[5] J. Ignatovska, W. Dmowski, J. Fluorine Chem. 127 (2006) 720–729.
[6] W. Dmowski, K. Piasecka-Maciejewska, J. Fluorine Chem. 123 (2003) 37–42.
[7] W. Dmowski, J. Ignatovska, J. Fluorine Chem. 123 (2003) 37–42.
[8] W. Dmowski, J. Ignatovska, K. Piasecka-Maciejewska, J. Fluorine Chem. 125 (2004) 1147–1151.
[9] A. Wolniewicz, W. Dmowski, J. Fluorine Chem. 109 (2001) 95–102.
[10] C. Wakselman, J. Fluorine Chem. 125 (2004) 1339–1345.
[11] C. Wakselman, M. Tordeux, J. Org. Chem. 50 (1985) 4047–4051.
[12] I. Rico, D. Cantacuzene, C. Wakselman, J. Org. Chem. 48 (1983) 1979–1984.
[13] M. Medebielle, M.A. Oturan, J. Pinson, J.-M. Saveant, J. Org. Chem. 61 (1996) 1331–1340.
[14] V.N. Boiko, G.M. Shchupak, J. Fluorine Chem. 69 (1994) 207–212.
[15] A.E. Feiring, J. Fluorine Chem. 24 (1984) 191–203.
[16] K.I. Petko, T.M. Sokolenko, A.V. Bezdudny, L.M. Yagupolski, J. Fluorine Chem. 126 (2005) 1342–1346.
[17] I. Rico, C. Wakselman, J. Fluorine Chem. 20 (1982) 759–764.
[18] X.-Y. Li, H.-Q. Pan, X.-K. Jiang, Tetrahedron Lett. (1984) 4937–4940.
[19] G. Koshechko, L.A. Kiprianova, L.I. Fileleeva, L.I. Kalinina, V.A. Khizhnyi, J. Fluorine Chem. 127 (2006) 1242–1244.
[20] V.G. Koshechko, L.A. Kiprianova, Theor. Exp. Chem. (translated from Russian) 35 (1999) 18–36.
[21] C.P. Andrieux, L. Gelis, J.M. Saveant, J. Am. Chem. Soc. 112 (1990) 786–791.
[22] V.G. Koshechko, L.A. Kiprianova, L.I. Filieleieva, Z.Z. Rozhkova, Theor. Exp. Chem. (translated from Russian) 29 (1993) 166–169.
[23] M. Tordeux, B. Langlois, C. Wakselman, J. Chem. Soc. Perkin Trans. I (1990) 2293–2297.
[24] Q.-Y. Chen, J. Org. Chem. 64 (1999) 4775–4781.