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Journal of Fluorine Chemistry 107 (2001) 311–314

JOURNAL OF FLUORINE CHEMISTRY

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Nucleophilic perfluoroalkylation of diaryldisulfides with perfluorocarboxylate salts

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Received 3 April 2000; accepted 11 May 2000

Abstract

A new industrial and economical route to trifluoromethyl aryl sufides by thermal decarboxylation of trifluoroacetate salts has been recently developed. The possibility of generalising this reaction of ''trifluorodecarboxylation'' to R_fCO_2K (R_f: CCl_3, CF_2Cl, CF_3CF_2, $CF_3CF_2CF_2$) in order to synthesise R_fSAr has been studied. Thus, the reaction was effective with R_fCO_2K ($R_f = CCl_3$, CF_3CF_2) and a new route to aryl pentafluoroethyl sufides CF_3CF_2SAr has been briefly exemplified. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Trifluoromethylation; Perfluoroalkylation; Arylperfluoroalkylsulfide; Decarboxylation

1. Introduction

The proportion of trifluoromethylated products in life science chemicals is rapidly expanding [1], thus the challenge to develop trifluoromethylating reagents remains important. In this field, direct nucleophilic trifluoromethylation is an attractive reaction. In the past, we thought that the trifluoromethyl anion, due to its low stability, had to be generated in the presence of stoichiometric amounts of metal to prevent α-elimination (Scheme 1). Thus, the trifluoromethyl anion is stabilised due to a chemical bond with a transition metal (CF_3Cu [2] or CF_3ZnX [3]) or with the silicon (CF_3SiMe_3) [4].

During the last 5 years, we have established a new concept in nucleophilic trifluoromethylation stategies. Provided DMF is present, the trifluoromethyl anion can be obtained ''naked'' and used in organic synthesis without any stabilisation. CF_3^- is generated by trifluoromethane deprotonation [5–9] or thermal decarboxylation of trifluoroacetate salts [10,11]. This strategy allowed us to explore a new industrial and economical route to trifluoromethyl aryl sufides (Schemes 2 and 3).

In the present work, we have investigated the possibility of generalising this reaction of ''trifluorodecarboxylation'' to R_fCO_2K (R_f: CCl_3, CF_2Cl, CF_3CF_2, $CF_3CF_2CF_2$) in order to synthesise R_fSAr.

2. Results and discussions

First, the case of commercially available potassium perhaloacetates (CX_2YCO_2K, (**1a–c**)) has been studied (Table 1). Thermal decomposition of potassium trifluoroacetate in dimethylformamide, at 140°C, in the presence of diphenyldisulfide led to phenyltrifluoromethylsulfide (**2a**) with 84% yield (entry 1). The same reaction has been achieved with potassium trichloroacetate (**1b**) leading to $PhSCCl_3$ (**2b**) (entry 2, yield = 80%). A reaction temperature of 100°C was adequate, because the thermal decomposition of CCl_3CO_2K occurred at this point. In the case of potassium chlorodifluoroacetate (**1c**), a few percent of $PhSCF_2Cl$ (**2c**) and $PhSCF_2H$ have been detected by ^{19}F NMR and GC/MS analysis. An ^{19}F NMR analysis of the crude reaction mixture has shown that the $ClCF_2CO_2K$ conversion was total (entry 3). This result seemed to suggest that CF_2Cl^- might be less stable in DMF than CF_3^- or CCl_3^- and more difficult to trap by a disulfide (Scheme 4).

Potassium perfluorocarboxylates ($CF_3(CF_2)_nCO_2K$, $n = 1, 2$) were then investigated. The result of the thermal decarboxylation of these salts was not obvious because of the instability of the generated anions $CF_3(CF_2)_n^-$. These anions might decompose following a β-elimination process (Scheme 5).

As shown in Table 2, the thermal decarboxylation of potassium pentafluoropropionate (**1d**) succeeded (entry 4), leading to $PhSCF_2CF_3$ (**2d**) with 70% yield, whereas in the case of potassiumheptafluorobutyrate this was not so (entry 5). Indeed, the β-elimination process in this case led to a

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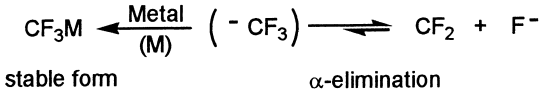
0022-1139/01/$ – see front matter
PII: S0022-1139(00)00374-2



Scheme 1. Trifluoromethyl anion behaviour.

mixture of the "linear sulfide" $PhSCF_2CF_2CF_3$ (**2e**) (yield = 29%) [12,13] and the "branched sulfide" $PhSCF(CF_3)_2$ (**3**) (yield = 33%) [12,13]. Another fluorinated compound (**4**) has been detected by ^{19}F NMR and GC/MS/IR analysis [12,13]. For this product a hypothetical structure has been proposed in Scheme 6.

In order to prove the synthetic interest of the potassium pentafluoropropionate decarboxylation, the reaction has been generalised to other disulfides. As shown in Table 3, the experimental conditions have not been optimised but aryl pentafluoroethyl sufides are obtained with moderate yields. In the case of $(p\text{-}NO_2PhS)_2$, it was important to notice that the disulfide was only slightly soluble in the reaction mixture; this problem might explain the low yield.

So, a new and efficient synthesis of aryl pentafluoroethyl sufides has been developed by heating potassium pentafluoropropionate in the presence of diaryldisulfides. For an industrial application, for ecological reasons, this strategy does not suffer from the problem of the ozone depleting effect of the starting material. Indeed, the traditional strategy for the production of CF_3CF_2SAr, is the use of CF_3CF_2X (X = Br, I) [12,13], and chemists who are concerned by environmental problems know that due to their ozone depleting effects all these CF_3CF_2X compounds have been banned by the Montreal Protocol.

Table 1
Decarboxylation of CX_2YCO_2K in the presence of PhSSPh[a]

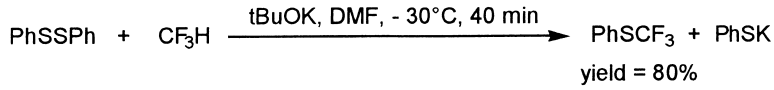
Entry	CX_2YCO_2K	θ (°C)	(**2a–c**), Yield (%)[b]
1	(**1a**) CF_3CO_2K	140	$PhSCF_3$ (**2a**), 84
2	(**1b**) CCl_3CO_2K	100	$PhSCCl_3$ (**2b**), 80
3	(**1c**) CF_2ClCO_2K	140	Traces of $PhSCF_2Cl$

[a] $\underset{(\mathbf{1a-c})}{CX_2YCO_2K} \xrightarrow[PhSSPh]{DMF,\theta^\circ C,6\,h} \underset{(\mathbf{2a-c})}{CX_2YSPh} + PhSK + CO_2$.

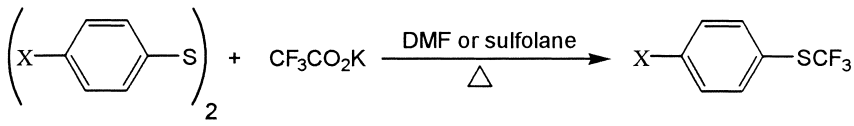
[b] Isolated yield.

3. Experimental

All reagents and solvents were commercial and used as received by using standard syringe techniques. ^1H NMR, ^{19}F NMR and ^{13}C NMR spectra were determined on a Bruker AM 300 spectrometer. Chemical shifts (δ) are expressed in ppm from external standard Me_4Si and CF_3CO_2H. GLC/MS analysis were performed using a Fison MD 800 spectrometer

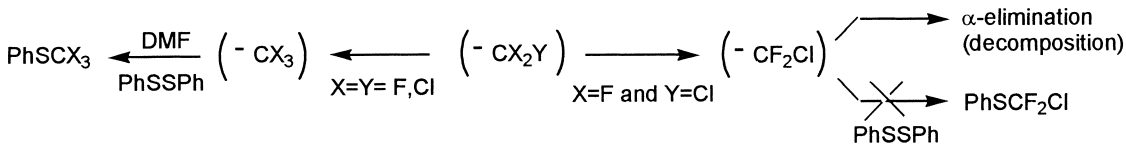


Scheme 2. Deprotonation of trifluoromethane.

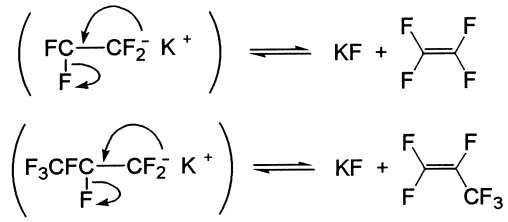


X	Yield %
H	84
Cl	56
Me	51
OMe	50

Scheme 3. Decarboxylation of potassium trifluoroacetate.



Scheme 4. CX_2Y anion behaviour.



Scheme 5. Decomposition of perfluoroalkyl carbanions via β-elimination process.

interfaced with a Fison GC 8000 gas chromatograph (DB1 column: 30 m × 0.23 mm i.d.). GLC analysis were performed using a Varian GC 3400 with a DB1 column (30 m × 0.53 mm i.d.).

3.1. General procedure

To a solution of $CF_3CF_2CO_2K$ (2.42 g, 12 mmol) in anhydrous DMF (25 ml) was added, at room temperature under nitrogen atmosphere, diaryldisulfide (10 mmol). The reaction mixture was then heated at 140–145°C over 5 h. At the end of the reaction, all the DMF and CF_3CF_2SAr were distilled under reduced pressure (40 Torr). This solution was poured into water and was extracted with ethyl ether. The combined organic fractions were washed with water, dried over $MgSO_4$, ethyl ether was evaporated and the crude material was then isolated.

3.2. Perfluoroethyl phenyl sulfide (2d)

This compound has been described in the literature by Wakselman [12,13] and the analytical data were identical.

3.3. Heptafluoropropyl phenyl sulfide (2e)

^{19}F NMR ($CDCl_3$, 282 MHz), δ: −4.0 ppm (3F, CF_3CF_2–), −11.6 ppm (2F, CF_3CF_2–), −47.5 ppm (2F, CF_2CF_2–SPh).

GC/MS (*m/z*): 278 (M, 49), 259 (M–F, 4), 159 (M–CF_3CF_2, 44), 109 (PhS, 100), 77 (C_6H_5, 40), 69 (CF_3, 26).

3.4. Heptafluoroisopropyl phenyl sulfide (3)

^{19}F NMR ($CDCl_3$, 282 MHz), δ: 2.5 ppm (6F, $(CF_3)_2CF$–), −80.5 ppm (1F, $(CF_3)_2CF$–).

GC/MS (*m/z*): 278 (M, 30), 209 (M–CF_3, 6), 109 (PhS, 100), 77 (C_6H_5, 8), 69 (CF_3, 18).

3.5. Fluorinated dihydrobenthiophène (4)

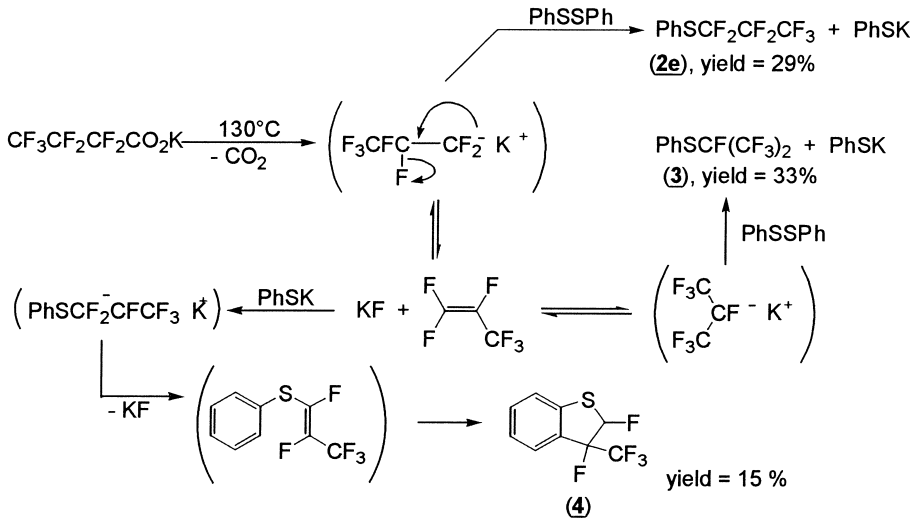
GC/MS/IR(*m/z*): 240 (M, 100), 220 (M–HF, 7), 177 (M–SCF, 22), 171 (M–CF_3, 36), 109 (PhS, 6), 77 (C_6H_5, 28), 69

Table 2
Decarboxylation of $CF_3(CF_2)_nCO_2K$ in the presence of PhSSPh[a]

Entry	$CF_3(CF_2)_nCO_2K$	θ (°C)	(**2d–e**), Yield (%)[b]	Comments
4	$CF_3CF_2CO_2K$	140	$PhSCF_2CF_3$ (**2d**), 70	–
5	$CF_3CF_2CF_2CO_2K$	130	$PhS(CF_2)_2CF_3$ (**2e**), 29	Two other fluorinated products detected including $PhSCF(CF_3)_2$ (**3**) (33%)

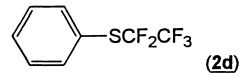
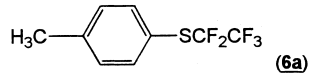
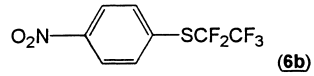
[a] $CF_3(CF_2)_nCO_2K$ (n=1,(**1d**);n=2,(**1e**)) $\xrightarrow[\text{PhSSPh}]{\text{DMF},\theta^\circ\text{C},6\,\text{h}}$ $CF_3(CF_2)_nSPh$ (n=1,(**2d**);n=2,(**2e**)) + PhSK + CO_2.

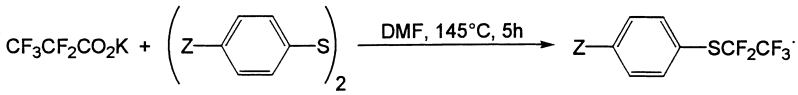
[b] Yield determined by ^{19}F NMR with an internal standard.



Scheme 6. Mechanism of the decarboxylation of $CF_3CF_2CF_2CO_2K$ in the presence of PhSSPh.

Table 3
Synthesis of $ArSCF_2CF_3$[a]

Entry	Z	(6a–c)	Yield (%)[b]
4	H	 (2d)	70
6	CH_3	 (6a)	50
7	NO_2	 (6b)	42

[a] 
(5a-c) (6a-c)

[b] Isolated yield.

(CF_3, 5) et IR: C–F (1350, 1219, 1169), C=C arom. (3081, 1581, 1479).

3.6. Perfluoroethyl p-tolyl sulfide (6a)

^{1}H NMR ($CDCl_3$, 300 MHz), δ: 7.49 (d, 2H, $^3J_{HF}$ = 8.25 Hz, 2H arom.), 7.26 (d, 2H, $^3J_{HF}$ = 8.25 Hz, 2H arom.), 2.29 (s, 3H, CH_3); ^{19}F NMR ($CDCl_3$, 282 MHz), δ: −6.87 (t, 3F, $^3J_{FF}$ = 3.81 Hz, CF_3), −16.66 (q, 2F, $^3J_{FF}$ = 3.81 Hz, CF_2); ^{13}C NMR ($CDCl_3$, 75 MHz), δ: 141.9 (s, C arom., C–CH_3), 136.8 (s, 2C, CH arom.), 130.4 (s, 2C, CH arom.), 119.95 (tq, $^1J_{CF}$ = 286.86 Hz et $^2J_{CF}$ = 39.67 Hz, 1C, CF_2), 117.93 (qt, $^1J_{CF}$ = 286.25 Hz et $^2J_{CF}$ = 37.23 Hz, 1C, CF_3), 117.70 (s, C arom.), 20.6 (s, 1C, CH_3).

GC/MS (*m/z*): 242 (M, 74), 173 (M–CF_3, 3), 123 (M–CF_3CF_2, 100), 91 (C_6H_4Me, 11), 69 (CF_3, 6).

3.7. p-Nitro perfluoroethyl sulfide (6b)

For this compound, the work up was different.

The reaction mixture was heated at 140–145°C over 5 h and at the end of the reaction, all the DMF was distilled off under reduced pressure (30–10 Torr). The residue was triturated in diisopropyl ether and the remaining solid was filtered off. The organic fraction was washed with water, dried over $MgSO_4$ and diisopropyl ether was evaporated. The crude material was then isolated.

^{1}H NMR ($CDCl_3$, 300 MHz), δ: 8.28 (d, 2H, $^3J_{HF}$ = 9.07 Hz, 2H arom.), 7.94 (d, 2H, $^3J_{HF}$ = 9.07 Hz, 2H arom.); ^{19}F NMR ($CDCl_3$, 282 MHz), δ: −3.83 (t, 3F, $^3J_{FF}$ = 3.05 Hz, CF_3), −12.05 (q, 2F, $^3J_{FF}$ = 3.05 Hz, CF_2); ^{13}C NMR ($CDCl_3$, 75 MHz), δ: 149.3 (s, 1C arom., C–NO_2), 137 (s, 2C, CH arom.), 129.3 (s, C arom.), 124.6 (s, 2C, CH arom.), 119.80 (tq, $^1J_{CF}$ = 286.86 Hz et $^2J_{CF}$ = 40.28 Hz, 1C, CF_2), 117.90 (qt, $^1J_{CF}$ = 286.86 Hz et $^2J_{CF}$ = 33.62 Hz, 1C, CF_3).

GC/MS (*m/z*): 273 (M, 100), 243 (M–NO, 37), 227 (M–NO_2, 5), 204 (M–CF_3, 8), 108 (C_6H_4S, 53), 69 (CF_3, 23).

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