$S_{RN}1$ reactions of 2,2,2-trifluoroethyl halides with thiolate ions

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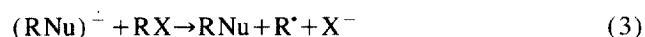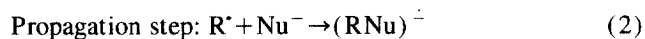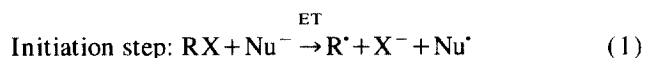
Abstract

2,2,2-Trifluoroethyl chloride, bromide, iodide but not fluoride react with thiolate ions in DMF under laboratory illumination at 30–50°C to give the 2,2,2-trifluoroethylthiol derivatives in high yields. The acceleration by UV irradiation, suppression by *p*-dinitrobenzene or hydroquinone and detection of trifluoroethyl radical by ESR spectroscopy show that the reactions occur by $S_{RN}1$ mechanism. The initiation step may be spontaneous or thermal electron transfer between thiolate and halides because the reactions can occur in dark. © 1998 Elsevier Science S.A. All rights reserved.
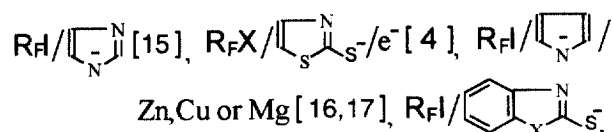
Keywords: 2,2,2-Trifluoroethyl halides; Thiolate ions; ESR spectroscopy

1. Introduction

The radical nucleophilic substitution of alkyl halides or $S_{RN}1$ mechanism is one of the most important parts of single electron-transfer (SET) reactions in organic chemistry [1,2]. The main steps are shown in Eqs. (1)–(3).

Initiation step: $RX + Nu^- \xrightarrow{ET} R^{\cdot} + X^- + Nu^{\cdot}$ (1)

Propagation step: $R^{\cdot} + Nu^- \rightarrow (RNu)^{\cdot -}$ (2)

$(RNu)^{\cdot -} + RX \rightarrow RNu + R^{\cdot} + X^-$ (3)

The initiation step can occur by photostimulation [3], electrochemical reduction [4] or spontaneous electron transfer from Nu^- to the substrate RX [5]. The alkyl radical $R^{\cdot}$ thus formed couples with Nu^- yielding a new radical anion $(RNu)^{\cdot -}$ (Eq. (2)), which by an intermolecular dissociative ET [6] to RX gives the substitution product and $R^{\cdot}$ to continue the chain propagation cycle (Eq. (3)). However, recently, a nonchain $S_{RN}1$ reaction of 1-iodoadamantane with arenthiolate ions was also reported [7]. In this context, per- and polyfluoroalkyl halides are very favorable to the $S_{RN}1$ mechanism because they have a low reactivity toward polar nucleophilic substitution, S_N1 and S_N2 [8–10]. Thus, a quite variety of $S_{RN}1$ reactions of perfluoroalkyl halides have been appeared since 1970s, for example: $R_FI/ArS^-/liqNH_3/h\nu$ [11], $R_FI/(CH_3)_2C^-NO_2$ [12], $R_FI/^-CH(CO_2R)_2$ [13], R_FI/CH_3COC^-HCOR [14],

$R_FI/\overset{N}{\underset{N}{[\ \ -]}}$ [15], $R_FX/\overset{N}{\underset{S}{[\ \ ]}}S^-/e^-$ [4], $R_FI/\overset{N}{\underset{N}{[\ \ -]}}/$

Zn,Cu or Mg [16,17], $R_FI/\overset{N}{\underset{X}{[\ \ ]}}S^-$,

$X = S, NH, O/h\nu$ [15–18], $BrCF_2Cl/ArS^-$ [19], R_FI/ArS^- [20]. Nevertheless, little attention has been devoted to their analogues, i.e., 2,2,2-trifluoroethyl halides, CF_3CH_2X (1) [X = Cl (a), Br (b), I (c), F (d)]. The polar nucleophilic substitution of 1c by sodium thiophenoxide in methanol was first established by Hine and Ghirardell in 1958 [21]. The S_N2 mechanism was supported later by comparing the relative reactivates of 1c with ArS^- versus ArO^- [22]. However, the explanation is suspect because it is known that the nucleophilic substitution of 1 could not occur due to the strong deactivation of the neighboring carbon by trifluoromethyl group [23]. In our opinion, there is no reason for sulfur nucleophile as an exception [24].

In order to clarify the mechanism, we repeated the literature work of thiolates with 1c [22] and extended to 1a, 1b and 1d. This paper presents the results.

2. Results and discussion

2,2,2-Trifluoroethyl chloride, 1a, HCFC-133a, was first chosen as a substrate reacting with thiolate ions because it is an important intermediate [25] for preparation of 1,1,1,2-tetrafluoroethane (HFC-134a) which is the main halogenated

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Table 1
The reactions of **1a** with **2** in DMF under laboratory illumination[a,b]

Entry	2	T (°C)	t (h)	Yield 3 (%)[c]
1	a	30	24	71
2	b	45	16	79
3	c	45	16	87
4	d	45	16	71
5	e	45	16	67
6	f	45	16	73

[a]**1a:2** = 1:1.1.
[b]The conversion of **1a** was 100% by ^{19}F-NMR.
[c]Isolated yields based on **1a**.

Table 2
Influences of additive on the reactions of **1a** with **2a** or **2d** in DMF at 35°C[a]

RS$^-$	Additive (mol)	t (h)	Conversion of **1a** (%)[c]
2a	lab.ill.[b]	2.5	30
	in dark	2.5	25
	lab.ill. + p-DNB (0.2)	2.5	4
	lab.ill. + HQ (0.2)	2.5	6
	$h\nu$	2.5	44
2d	lab.ill.	2	25
	lab.ill. + p-DNB (0.2)	2	5
	lab.ill. + HQ (0.2)	2	5

[a]**1a:2a** or **2d** = 1:1.1.
[b]lab.ill. = laboratory illumination.
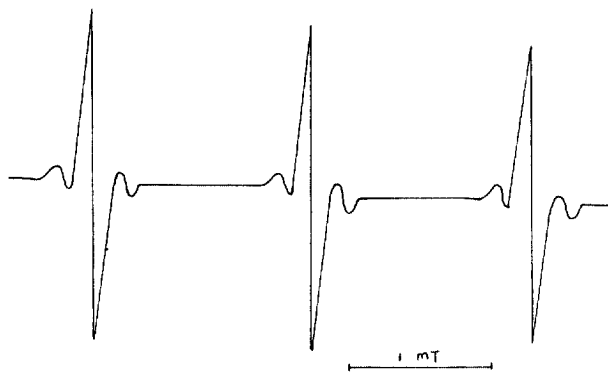[c]The conversion was determined by ^{19}F-NMR.

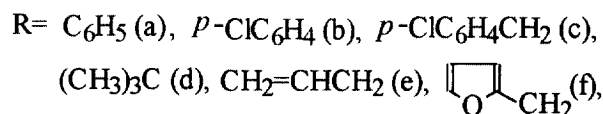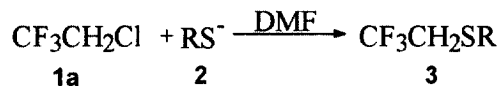Fig. 1. ESR of t-BuN(CH$_2$CF$_3$)O$^·$ + t-BuN(SC$_6$H$_5$)O$^·$. a_N = 1.57 MT, aH = 0.2 MT, g = 2.0055.

Table 3
Influences of additive on the reactions of **1b** with **2a** in DMF at 30°C[a]

Additive (mol)	t (h)	Conversion of **1b** (%)[b]
lab.ill.	2	85
in dark	2	60
lab.ill. + p-DNB (0.2)	2	25
lab.ill. + HQ (0.2)	2	25
$h\nu$	2	95

[a]**1b:2a** = 1:1.1.
[b]The conversion was determined by ^{19}F-NMR.

replacement for ozone-depleting chlorofluorocarbons (CFCs) [25,26]. It was found that **1a** reacted with thiolate ions (**2**) in dimethylformamide (DMF) at 30–45°C for 16–24 h giving the corresponding 2,2,2-trifluoroethylthio derivatives, **3**, in good yields. The results are shown in Table 1.

$$CF_3CH_2Cl \; + RS^- \xrightarrow{\;\;DMF\;\;} CF_3CH_2SR$$

1a   **2**   **3**

R= C$_6$H$_5$ (a), p-ClC$_6$H$_4$ (b), p-ClC$_6$H$_4$CH$_2$ (c),

(CH$_3$)$_3$C (d),   CH$_2$=CHCH$_2$ (e), $\overset{\displaystyle \;}{\underset{O}{\bigcirc}}\!\!-CH_2$ (f),

The reaction could occur also in the dark and be accelerated under UV irradiation. Addition of single electron-transfer scavenger, p-dinitrobenzene (p-DNB) or free radical inhibitor, hydroquinone (HQ) to the reaction mixture (using **2a**, **2d** as representatives) decreased the conversion of **1a** significantly (see Table 2).

The existence of both CF$_3$CH$_2^·$ and C$_6$H$_5$S$^·$ through their adducts with t-BuNO when mixing **1a**, **2a** and t-BuNO in DMF at room temperature in 20 minutes has been observed by ESR technique (see Fig. 1).

Similarly, 2,2,2-trifluoroethyl bromide (**1b**) reacted with sodium benzenthiolate in DMF at 30°C for 6 h giving **3a** (yield, 78%) and 100% conversion of **1b**. Inhibitors, p-DNB and HQ depressed while UV irradiation increased the conversions of **1b** (see Table 3).

Finally, we have repeated the report of Nakai et al. [22] on the reaction of 2,2,2-trifluoroethyl iodide (**1c**) with **2a** and confirmed their results. However, the inhabitation by p-DNB or HQ and acceleration by UV irradiation were clear (see Table 4).

Like in the case of **1a**, ESR spectroscopy showed the presence of CF$_3$CH$_2^·$ and C$_6$H$_5$S$^·$ through their adducts with t-BuNO when mixing **1c**, **2a** and t-BuNO in DMF at room temperature in 3 min.

Table 4
Influences of additive on the reactions of **1c** with **2a** and **2d** in DMF at 35°C[a]

RSNa	Additive (mol)	t (h)	Conversion of **1c** (%)[b]	Yield of 3 (%)
2a	lab.ill.	1	100	82
	in dark	1	88	
	lab.ill. + p-DNB (0.2)	1	45	
	lab.ill. + HQ (0.2)	1	50	
	$h\nu$	0.6	100	
2d	lab.ill.	0.75	95	74
	in dark	0.75	85	
	lab.ill. + p-DNB (0.2)	0.75	27	
	lab.ill. + HQ (0.2)	0.75	30	

[a]**1c:2a** or **2d** = 1:1.1.
[b]The conversion was determined by ^{19}F-NMR.

Trifluoroethyl fluoride ($X = F$, HFC-134a), however, did not undergo the same reactions with thiolate ions under similar conditions.

The facts that the reactions are light catalyzed, UV irradiation accelerated, retarded by p-DNB and HQ and trifluoroethyl radical is detected by ESR spectroscopy provide unambiguous evidence that trifluoroethyl halides 1a–c react with thiolate ions by $S_{RN}1$ mechanism, not by S_N2. Comparing the conversion of 1a–d in their reactions with 2a and 2d under the laboratory illumination, under UV irradiation or in dark (see Table 2Tables 3 and 4) showed that the relative reactivity order is 1d ≪ 1a < 1b < 1c, which is consistent with the leaving ability of halide ions, $I^- > Br^- > Cl^- \gg F^-$ in the outer-sphere dissociative electron transfer mechanism [27]. This process could be initiated by spontaneous or thermal electron transfer between thiolate ion and 1a–c because the reactions can occur in dark [28]. The whole process may be described by Eqs. (1)–(3) if $R = CF_3CH_2$, $X = Cl$, Br, I, and $Nu^- = RS^-$.

3. Experimental details

^{1}H-NMR spectra were recorded on an FX-90Q instrument (90 MHz) using TMS as external standard. ^{19}F-NMR spectra were recorded on a Varian EM-360L instrument (60 MHz) using CF_3COOH as external reference with chemical shifts in ppm positive upfield. Mass spectra were recorded with a HP5989A instrument. IR spectra were taken on Perkin-Elmer 983 spectrometers. All reagents were purified prior to use.

The preparation of RSNa was according to the literature [29].

Typical procedure of the reaction of 1 with 2.

Under a nitrogen atmosphere, 1a (1.20 g, 10 mmol), 2b (1.83 g, 11 mmol) and DMF (30 ml) was added to a 50 ml three-necked round-bottomed flask equipped with stirrer and dry ice condenser. The mixture was then heated to 45°C for 16 h with stirring. The conversion of 1a was 100%, determined by ^{19}F-NMR. After cooling, the mixture was poured into ice water (30 ml). The aqueous layer was extracted three times with ether (3×30 ml). The combined extracts were washed with water (3×20 ml) and dried over Na_2SO_4. After removing ether, the residue was subjected to column chromatography on silica gel to give 3b (1.79 g, yield 79%). ^{19}F-NMR (CCl$_4$) δ: −11.6 ppm. ^{1}H-NMR (CCl$_4$) δ: 3.35 (q, J= 10 Hz, 2 H, CF$_3$CH$_2$), 7.29 (m, 4 H, Ar–H) ppm. Ms: 228 (M$^+$ +2, 60.73), 227 (M$^+$ + 1, 20.42), 226 (M$^+$, 100), 157 (M$^+$-CF$_3$, 53.86), 143 (M$^+$-CF$_3$CH$_2$, 39.00), 111 (M$^+$-CF$_3$CH$_2$S, 3.77), 69 (CF$_3^+$, 7.67). IR (film) (cm^{-1}): 2925, 1571, 1477, 1413, 1391, 1273, 1246, 1131, 1083, 862, 844, 747. Analysis: Calc. for C$_8$H$_6$ClF$_3$S: C, 42.40; H, 2.67; F, 25.15. Found: C, 42.54; H, 2.69; F, 25.22.

3a From Ref. [22]: ^{19}F-NMR (CCl$_4$) δ: −11.2 ppm. ^{1}H-NMR (CCl$_4$) δ: 3.35 (q, J= 9 Hz, 2H, CF$_3$CH$_2$), 7.10–7.60 (m, 5H, Ar–H) ppm. Ms: 192 (M$^+$, 100), 123 (M$^+$-CF$_3$, 59.18), 109 (M$^+$-CF$_3$CH$_2$, 2.25), 83 (CF$_3$CH$_2^+$,

3.70), 77 (C$_6$H$_5^+$, 11.70), 69 (CF$_3^+$, 9.83). IR (film) (cm^{-1}): 3062, 2946, 1674, 1580, 1482, 1440, 1272, 1246, 1129, 1086, 1029, 747, 693.

3c: ^{19}F-NMR (CCl$_4$) δ: −11.6 ppm. ^{1}H-NMR (CCl$_4$) δ: 3.13 (q, J= 10 Hz, 2H, CF$_3$CH$_2$), 4.02 (s, 2H, ArCH$_2$), 7.47 (m, 4H, Ar–H) ppm. Ms: 241 (M$^+$, 1.84), 240 (M$^+$-1, 14.17), 125 (M$^+$-CF$_3$CH$_2$S, 100), 83 (CF$_3$CH$_2^+$, 13.70), 69 (CF$_3^+$, 12.05). IR (film) (cm^{-1}): 2925, 1596, 1490, 1406, 1272, 1237, 1124, 1081, 832, 777. Analysis: Calc. for C$_9$H$_8$ClF$_3$S: C, 44.92; H, 3.35; F, 23.74. Found: C, 44.58; H, 3.09; F, 24.05.

3d From Ref. [30]: ^{19}F-NMR (CCl$_4$) δ: −12.2 ppm. ^{1}H-NMR (CCl$_4$) δ: 1.35 (s, 9H, t-Bu), 3.07 (q, J= 11 Hz, 2H, CF$_3$CH$_2$) ppm. Ms: 172 (M$^+$, 26.30), 157 (M$^+$-CH$_3$, 13.18), 83 (CF$_3$CH$_2^+$, 3.70), 69 (CF$_3^+$, 1.98), 57 (t-Bu$^+$, 100). IR (film) (cm^{-1}): 2967, 1633, 1459, 1370, 1310, 1274, 1248, 1125, 1080.

3e: ^{19}F-NMR (CCl$_4$) δ: −11.0 ppm. ^{1}H-NMR (CCl$_4$) δ: 2.55–2.98 (m, 2H, CH$_2$C=), 3.12 (q, J= 10 Hz, 2H, CF$_3$CH$_2$), 5.08–5.34 (m, 2H, HC=CH$_2$), 5.67–6.20 (m, 1H, CH=CH$_2$) ppm. Ms: 157 (M$^+$ + 1, 100), 129 (M$^+$-CH=CH$_2$, 28.46), 115 (CF$_3$CH$_2$S$^+$, 6.07), 73 (CH$_2$=CHCH$_2$S$^+$, 19.85). IR (film) (cm^{-1}): 2963, 2925, 1631, 1450, 1413, 1271, 1245, 1127, 1083, 995. HRMS, Calc. for C$_5$H$_8$F$_3$S (M + 1): 157.0299, Found: 157.0290.

3f: ^{19}F-NMR (CCl$_4$) δ: −11.5 ppm. ^{1}H-NMR (CCl$_4$) δ: 3.15 (q, J= 10 Hz, 2H, CF$_3$CH$_2$), 4.03 (s, 2H, CH$_2$-SCH$_2$CF$_3$), 6.41(m, 2H, 2H$^\beta$), 7.50 (m, 1H, H$^\alpha$) ppm. Ms: 197 (M$^+$ + 1, 4.44), 196 (M$^+$, 38.62), 113 (M$^+$-CF$_3$CH$_2$, 12.25), 83 (M$^+$-CF$_3$CH$_2$S, 100), 69 (CF$_3^+$, 14.17). IR (film) (cm^{-1}): 2939, 1596, 1500, 1408, 1274, 1241, 1015, 941, 888, 845, 779. Analysis: Calc. for C$_7$H$_7$F$_3$SO: C, 42.85; H, 3.60; F, 29.28. Found: C, 42.58; H, 3.50; F, 29.52.

The typical inhibition experiment:

Under N$_2$ atmosphere, 2a (1.45 g, 11 mmol), and DMF (20 ml) was added to a three-necked round-bottomed flask equipped with a dry ice condenser. Then 1a (1.20 g, 10 mmol) was added through a gas inlet valve. After stirring for 2.5 h at 35°C under the laboratory light, ^{19}F-NMR analysis, i.e., integration ratio of peaks at −6.0 ppm (CF$_3$CH$_2$Cl) and −12.5 ppm (CF$_3$CH$_2$SPh) indicated that the conversion of 1a was 30%. When p-DNB (0.34 g, 2 mmol) was present, after stirring for 2.5 h at 35°C, ^{19}F-NMR analysis showed 4% conversion of 1a.

Similarly, when HQ (0.22 g, 2 mmol) was present instead of p-DNB and the reaction conducted for 2.5 h at 35°C, ^{19}F-NMR analysis showed 6% conversion of 1a.

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