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PERFLUOROTHIOALKANOYL HALIDES. PREPARATION FROM SULFIDES

THOAI NGUYEN and CLAUDE WAKSELMAN

CNRS-CERCOA
2, Rue Henri Dunant 94320 Thiais (France)

SUMMARY

Perfluorothioalkanoyl halides were generated from alkyl perfluoroalkyl sulfides by reaction with TiF_4, $TiCl_4$ or $ClSO_3H$. The alkyl groups were benzyl or methyl, the former was more suitable. An α-bromoperfluoroalkylsulfide gave a perfluorothioalkanoyl halide more easily than the corresponding α-chloro sulfide which gave the thioalkanoyl chloride. An exchange between the α-halogen atom X of the sulfide R_FCFXSR_H (X=Cl, Br) and the halogen atom of the Lewis acid can occur.

INTRODUCTION

An elegant way of access to perfluoroalkanoyl fluorides was the reaction of Lewis acid with perfluoroalkyl methyl ethers[1]. TiF_4 was the most practical Lewis acid for this purpose. The mechanism proposed for this reaction was an abstraction of fluorine from the C-F bond giving the acid fluoride, a metal fluoride anion, and a methyl cation. The last two ions unite to give methyl fluoride.

$$TiF_4 + R_F\text{-}CF_2OCH_3 \rightarrow R_FC(O)F + TiF_5^- + CH_3^+ \rightarrow R_FC(O)F + CH_3F + TiF_4$$

Based upon the ability of the sulfur atom to give a sulfonium ion, question arises about the possible extension of this reaction to sulfides for the preparation of perfluorothioalkanoyl halides.

$$TiF_4 + R_F\text{-}CFX\text{-}SR_H \rightarrow TiF_4 + R_HF + R_FC(S)X \text{ ; X=halogen}$$

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Not many studies have been made on the preparation of perfluorothio alkanoyl halides. Generally they are generated [2] by reactions of sulfur or of P_2S_5, at a temperature up to 500°C, with perfluoroalkyl mercury compounds, with perhalogenoethylenes $CF_2 = CX_2$ (X = F,Cl,Br,I) or with polyhalogeno-perfluoroalkanes R_FCFX_2, R_FCX_3 (X = Cl, Br, I). These reactions were not always simple. Thus, the transformation of sulfides into the thiocarbonyl halides would be interesting, since fluorinated alkyl sulfides were easily obtained [3].

RESULTS

We started our study with benzyl perfluorobutyl sulfide 1 [3b]. TiF_4 was inactive. $ClSO_3H$ or concentrated sulfuric acid led to benzyl-thioperfluorobutyrate 12. The sulfide was simply hydrolysed [4].

$$R_FCF_2SR_H \longrightarrow R_FC(O)SR_H. \quad ; R_F = C_3F_7$$

The breaking of the alkylsulfur bond, $R_H\!\not{-}\!S$, leading to a thiocarbonyl-halide did not occur. For this purpose, it seems that two factors ought to be satisfied : the ease of the alkyl group R_H to give the cation R_H^+, as would do the benzyl group, and the ability of the sulfur atom to leave its electron pair. The perfluoroalkyl group R_F-CF_2, by its attractive effect, retains tightly the sulfur doublet in the sulfur electronic cloud, the substitution of an α-fluorine atom by another halogen (Cl, Br) will make easier the formation of a donor-acceptor complex between the sulfide and the Lewis acid.

Benzyl 1-chloroperfluoroethyl sulfide 2 was then prepared [3b] and tried. When, this sulfide, mixed with TiF_4, was heated to about 100°C, a red liquid distilled. It was identified as trifluorothioacetyl chloride 8 [2]. It subsequently gave diethylamino trifluorothioacetamide $CF_3C(S)N(C_2H_5)_2$ [5] in 47% yield. The residue in the pot was tar. The benzyl 1-bromoperfluoro-ethyl sulfide 3 was yet more reactive than the 1-chloro derivative 2. It gave the unknown trifluorothioacetyl bromide 9 $CF_3C(S)Br$. Gentle heating to about 60°C was enough to split the benzyl sulfur bond. The reaction was autocatalytic; less than a stoïchiometric amount of TiF_4 can be used.

Methyl sulfides were less reactive than the benzyl derivatives. Compound 4 $CF_3CFClSCH_3$ did not react, but compound 5 $CF_3CFBrSCH_3$ did.

$TiCl_4$ was also efficient as a catalyst, but the reactions were complicated by a possible exchange between the chlorine atom of $TiCl_4$ and the halogen atom of the sulfide. For example compound 3 gave a 1/1 mixture of trifluorothioacetyl chloride 8 and trifluorothioacetyl bromide 9; compound 7 $CF_2BrCFBrSCH_2C_6H_5$ gave the bromodifluorothioacetyl chloride 15 $CF_2BrC(S)Cl$. The reactions with SbF_5 were violent and a lot of tar resulted.

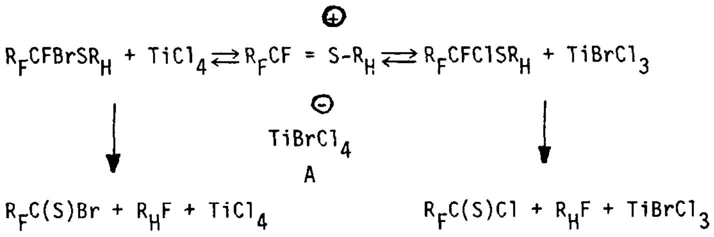
The table summarizes the results obtained with some typical sulfides. The reactions were carried out with TiF_4, $TiCl_4$ and $ClSO_3H$.

TABLE

Sulfides	TiF_4 (yield %)	$TiCl_4$ (yield %)	$ClSO_3H$ (yield %)
$C_3F_7CF_2SCH_2C_6H_5$ 1	No reaction		$C_3F_7C(O)SCH_2C_6H_5$ (37) 12
$CF_3CFClSCH_2C_6H_5$ 2	$CF_3C(S)Cl$ (47) 8	$CF_3C(S)Cl$ (58)	$CF_3C(S)Cl$ (48) $CF_3C(O)SCH_2C_6H_5$ (26) 13
$CF_3CFBrSCH_2C_6H_5$ 3	$CF_3C(S)Br$ (68) 9	$CF_3C(S)Cl$ $CF_3C(S)Br$ (71)[a]	$CF_3C(S)Br$ (60)
$CF_3CFClSCH_3$ 4	No reaction		$CF_3C(O)SCH_3$ (40) 14
$CF_3CFBrSCH_3$ 5	$CF_3C(S)Br$ (60)		$CF_3C(O)SCH_3$ (50)
$CF_2ClCFClSCH_2C_6H_5$ 6	$CF_2ClC(S)Cl$ (56) 10	$CF_2ClC(S)Cl$ (63)	$CF_2ClC(S)Cl$ (53)
$CF_2BrCFBrSCH_2C_6H_5$ 7	$CF_2BrC(S)Br$ (80) 11	$CF_2BrC(S)Cl$ (72) 15 $CF_2BrC(S)Br$ b	$CF_2BrC(S)Cl$ (65) $CF_2BrC(S)Br$ [c]

[a] in a 1/1 ratio, [b] in a ratio 4/1, [c] in a ratio 5/1. [8]

According to the table, benzyl sulfides were more suitable than methyl sulfides in the process of $R_H - \wr - S$ splitting, as also did the α-bromosulfides 3, 5, 7, as compared with the α-chloro sulfides 2, 4, 6. The fact that a thioacyl chloride was obtained along with a thioacyl bromide when an α-bromosulfide was used with $TiCl_4$, can be accounted for by the formation of a complex between this sulfide and the Lewis acid, which allowed a Br → Cl exchange to occur :



$$\begin{tikzcd} R_FCFBrSR_H + TiCl_4 \arrow[r, shift left] \arrow[d] & \overset{\oplus}{R_FCF = S-R_H} \arrow[l, shift left] \arrow[r, shift left] & R_FCFClSR_H + TiBrCl_3 \arrow[l, shift left] \arrow[d] \\ R_FC(S)Br + R_HF + TiCl_4 & \underset{A}{\overset{\ominus}{TiBrCl_4}} & R_FC(S)Cl + R_HF + TiBrCl_3 \end{tikzcd}$$

The complex A did not split, since in no case, was perfluorothioalkanoyl fluoride trapped.

EXPERIMENTAL

^1H NMR and ^{19}F NMR spectra were recorded on a Varian EM360 instrument at 60MHz and 56.4 MHz with TMS and $CFCl_3$ as external standards. Measurements were done on 10-20% solutions in $CDCl_3$. (s = singlet, d = doublet, t = triplet, q = quadruplet, dxd doublet of doublets).

Benzyl 1-bromotetrafluoroethyl sulfide 3

10g (67mM) of benzylthiocyanate, 6g (103mM) of potassium fluoride, 8ml of sulfolane were introduced in a stainless steel autoclave together with 12g (74.5mM) of bromotrifluoroethylene. The autoclave was closed and heated at 120°C during two days. After cooling to room temperature the autoclave's content was poured into 100ml of water, extracted with methylene chloride and dried. The solvent was removed, the residue was distilled under reduced pressure. 13g (39mM) of compound 3 were obtained b.p.:95°C; ^1H NMR (ppm), δ :4.2 (CH_2,s), 7.3 (C_6H_5,s), ^{19}F NMR (ppm), ϕ : -76(CF_3,d, J = 12Hz), -97 (CFBr, q).

Methyl 1-chlorotetrafluoroethyl sulfide 4

36g (49mM) of methylthiocyanate, 6g (103mM) of potassium fluoride, 8ml of sulfolane, 8ml of methylene chloride, were introduced into a stainless steel autoclave together with 9g (77mM) of chlorotrifluoroethylene. The autoclave was heated at 120°C and agitated for two days. After cooling to room temperature the content of the autoclave was distilled. 5.5g (397mM) of 3 was obtained b.p.:72°C; yield 51%. ^1H NMR (ppm); δ :2.5 (CH_3,s); ^{19}F NMR (ppm), ϕ :-79 (CF_3,d,J = 9Hz); -101.5 (CFCl, q); Anal. Calcd. for $C_3H_3ClF_4S$: C, 19.73; H, 1.65; Cl, 19.45; F, 41.63; Found : C, 19.99; H, 1.72; Cl, 20.15; F, 41.83.

Methyl 1-bromotetrafluoroethyl sulfide 5

The same procedure was used. Starting from 4.4g (60mM) of methyl thiocyanate, 6g (103mM) of potassium fluoride, 8ml of sulfolane and 11.5g (71.4mM) of bromotrifluoroethylene, 7.5g (33mM) of 5 was obtained. b.p.:90°C; yield 46%. ^1H NMR (ppm), δ : 2.5 (CH_3,s); ^{19}F NMR (ppm), ϕ:-77 (CF_3,d, J = 12Hz); -100 (CFBr, q); Anal. Calcd. for $C_3H_3BrF_4S$: C, 15.88; H,1.33; Found : C,16.03; H, 1.37.

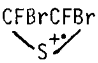
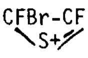
Benzyl-trifluorovinyl sulfide 16 (nc)

64ml of butyllithium (1.2N in hexane), 30ml of anhydrous tetrahydrofuran THF were cooled at -70°C in a three-necked flask. Under nitrogen and with stirring 9g (77mM) of chlorotrifluoroethylene were bubbled into the mixture. A solution of trifluorovinyllithium [9] was introduced portion wise under mechanical stirring into a solution of 7g (46.9mM) of benzylthiocyanate in 25ml of anhydrous THF. The temperature was kept around -15°C. After an hour, the cooled bath was removed, and the dark solution was acidified by dilute sulfuric acid, washed with brine and dried. After removal of the solvent, the residue was distilled under reduced pressure. 12g (58mM) of 16 was obtained. b.p.:80°-85°C/15 Torr; yield : 49%. ^1H NMR (ppm), δ :3.8 (CH_2,s); 7.15 (C_6H_5,s); ^{19}F NMR (ppm), ϕ : -87 (CF,dxd, J = 50 and 35Hz); -107 (CF,dxd, J = 130Hz); -149.5 (CF,dxd); Anal. Calcd. for $C_9H_7F_3S$: C, 52.96; H, 3.45; F, 27.92; Found : C, 53.00; H, 3.44; F, 27.63.

Benzyl 1,2- dichloro-trifluoroethyl sulfide 6 (nc)

3g (42.2mM) of chlorine were bubbled into a solution of 7g (34.3mM) of 16 in 100ml of methylene chloride cooled to -15°C. The solvent was removed under reduced pressure. 9g (32.7mM) of 6 were distilled from the residue, b.p.:100°C/15 Torr; yield 95%. ^{1}H NMR (ppm),δ:4.1 (CH_2,s); 7.25(C_6H_5,s); ^{19}F NMR (ppm),Φ:-63 (CF_2Cl,d, J = 14Hz); -91 (CFCl,t); MS : m/e 275,277, M^+; 91, $C_6H_5CH_2^+$.

Benzyl 1,2-dibromotrifluoroethyl sulfide 7 (nc)

A solution of 3.13g (19.6mM) of bromine in 5ml of CCl_4 was added dropwise at 0°C into a solution of 4g (19.6mM) of 16 in 5ml of CCl_4. After half an hour the solution was washed with water, dried, and distilled under reduced pressure. 6.4g of 7 (17.6mM) were obtained b.p.:123°C/5 Torr; yield 90%; ^{1}H NMR (ppm),δ:4.37 (CH_2,s); 7.45 (C_6H_5,s); ^{19}F NMR (ppm), Φ:-53.5 (CF_2Br,d, J = 20Hz); -87 (CFBr,t).MS:m/e 253, 255,257,

$\underset{\diagdown S^{+} \diagup}{CFBrCFBr}$ 173,175, 
$\underset{\diagdown S^{+} \diagup\!\!\diagup}{CFBr\text{-}CF}$; 91, $C_6H_5CH_2^+$.

Reaction of sulfides with TiF_4 - general procedure.

A mixture of sulfide and anhydrous TiF_4 in stoïchiometric amounts was heated on an oil bath. When the reaction occurred, gas was evolved and the thioacyl halide distilled as a red liquid. It was trapped in a receiver cooled by a dry ice-acetone mixture. Diluted in CH_2Cl_2 it was identified by NMR and mass spectra and was subsequently converted into thioamide by reaction with diethylamine.

Trifluorothioacetyl chloride 8 [2]

Red liquid b.p.:28°C; ^{19}F NMR (ppm),Φ:-69.5; MS:m/e 148,150,M^+.

Diethylamino trifluoro thioacetamide [5]

^{1}H NMR (ppm),δ:1.25 (CH_3,t,7Hz); 3.8 (CH_2,q); ^{19}F NMR (ppm), Φ:-61, Anal. Calcd. for $C_6H_{10}F_3NS$: C,38.74; H, 5.42; N,7.52; Found: C, 38.74; H, 5.52; N,7.36.

Trifluorothioacetyl bromide 9 (nc)

Red liquid b.p.:45°C; ^{19}F NMR (ppm),Φ:-68 MS:m/e 192,194, M^+.

Chlorodifluorothioacetyl chloride 10 [7]

Red liquid b.p.:56°C (lit.E_{20} -10°C); ^{19}F NMR (ppm),Φ:-53. UV :λ_{max}:≃505nm, ε= 11 (lit. 500nm) (CH_2Cl_2 large).

Bromodifluorothioacetyl bromide 11 (nc)

Red liquid b.p.:75°C, ^{19}F NMR (ppm),Φ:48; MS :m/e 252,254, 256, M^+.

Diethylamino bromodifluorothioacetamide (nc)

^1H NMR (ppm), δ: 1.45 (CH_3,t,J = 7Hz); 4.05 (CH_2,q); ^{19}F NMR (ppm),Φ :-43; Anal. Calcd. for $C_6H_{10}BrF_2NS$: C,29.29; H,4.09; N, 5.69. Found : C, 29.85; H, 4.26; N, 5.51.

Diethylamino chlorodifluorothioacetamide (nc)

b.p.:110°C/15 Torr ^1H NMR (ppm), δ:1.35 (CH_3,t, J = 6Hz); 3.9(CH_2,q); ^{19}F NMR (ppm),Φ:-46; Anal. Calcd. for $C_6H_{10}ClF_2NS$: C, 35.75; H, 5.00; N, 6.94; Found : C, 35.78; H, 5.35; N, 6.53.

Reaction of sulfides with $TiCl_4$

By using the same method as with TiF_4, compound 3 gave a 1/1 mixture of 8 / 9. yield 71%. Compound 7 gave a 2 / 8 mixture of 11 / 15.

Bromodifluorothioacetyl chloride 15

^{19}F NMR (ppm),Φ :-49.5; MS : m/e 208, 210, 212, M^+.

Reaction of sulfides with chlorosulfonic acid-general procedure

5mM of sulfide were dissolved in 8ml of methylene chloride and cooled at 0°C. 8mM of chlorosulfonic acid dissolved in 4ml of methylene chloride were introduced dropwise with stirring. 5ml of pentane were then added. The upper layer was separated, washed with water and dried. The ^{19}F NMR of this solution gave the ratio of thioacyl halide over ester. Afterwards the halide was distilled with the solvent and converted into thioamide. The remaining benzylthioester was identified through its NMR spectrum by comparison with sample prepared from benzylmercaptan and the corresponding perfluoroalkanoyl chloride.

Benzylthio trifluoroacetate 13

b.p.:105°C/15 Torr; ^1H NMR (ppm), δ :5(CH_2,s), 6.9 (C_6H_5,s); ^{19}F NMR (ppm),Φ :-75 (CF_3,s).

Benzylthio heptafluorobutyrate 12

b.p.:98°C/3 Torr; ^1H NMR (ppm),δ :3.7 (CH_2,s); 7.34 (C_6H_5,s); ^{19}F NMR (ppm),Φ :-79 (CF_3,t, J = 8Hz), -116 (CF_2CO;q); -125 (CF_2).

Methylthio trifluoroacetate 14, [6]

b.p.:71°C; ^1H NMR (ppm),δ :2.5 (CH_3,s); ^{19}F NMR (ppm),Φ :-76.5 (CF_3,s).

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