

Received: July 8, 1987; accepted: December 13, 1987

SOME DERIVATIVES OF 4-FLUOROBENZENETHIOL

SUSAN C. HERGETT and MICHAEL E. PEACH

Chemistry Department, Acadia University, Wolfville, NS, B0P 1X0 (Canada)

SUMMARY

Various metallic and organometallic derivatives of 4-fluorobenzenethiol have been prepared directly from the thiol. Its Ag(I), Ni(II) and Pb(II) salts were used to synthesize thioethers and thioesters. New compounds have been characterized by elemental analysis, NMR (H-1, F-19 and C-13) and mass spectroscopy.

INTRODUCTION

This paper is a continuation of a study of aromatic thiols containing various numbers of fluorine atoms on the aromatic ring. Previously some of the chemistry of pentafluorobenzenethiol [1,2,3], octafluorobiphenyl-4,4'-dithiol [4], 2,3,5,6-tetrafluorobenzenethiol [5] and benzenethiol [3,6] as well as pentachlorobenzenethiol [7] has been examined. The types of reaction studied were similar to previous work, involving primarily the reactions of the S-H bond rather than the C-S, C-H or C-F bonds, so that the effects, if any, of the fluorine on the reactivity of the S-H bond could be examined.

4-Fluorobenzenethiol is a colorless liquid, b.p. 164-8<sup>o</sup>, with a typical thiol odour, prepared by the reduction of 4-fluorobenzenesulfonic acid [8]. It is available commercially. It was first prepared by the reaction of 4-bromofluorobenzene with magnesium, followed by sulfur and subsequent acidification [9]. In aqueous solution the pK<sub>a</sub> is 8.1, being slightly more acidic than benzenethiol, pK<sub>a</sub> 8.6 [10].

The chemistry of 4-fluorobenzenethiol has been assumed to be similar to benzenethiol. Derivatives of the thiol have been prepared in studies of the toxicity of organic sulfides to the eggs and larvae of glass house red spider mite [11,12,13]; in studies of sulfur substituted derivatives of cysteine as anticancer agents [14], and in studies of derivatives of

mercapturic acid of biological interest [15]. Very recently the ability to detect the thiol by F-19 NMR has been utilized in a study of thiols as electron donors in molybdenum oxo-transferase analogue reaction systems [16]. The thiol was one of the thiols examined in a study of the para substituent dependance of the internal rotational barrier in benzenethiols [17] and in other NMR studies of benzenethiols [18,19].

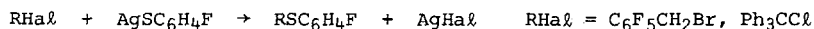
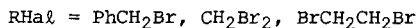
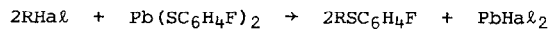
Various other derivatives of the thiol have been reported, including MeSR [8,20], CF<sub>3</sub>SR, CCl<sub>3</sub>SR [20], (RS)<sub>2</sub> [12,21], PhSR [22,23], AgSR, CuSR, and Hg(SR)<sub>2</sub> [21] (R = p-FC<sub>6</sub>H<sub>4</sub>S).

This paper describes some of the other chemical properties of 4-fluorobenzenethiol, which involve the preparation and characterization of some metallic, organometallic, aliphatic and aromatic derivatives of the thiol.

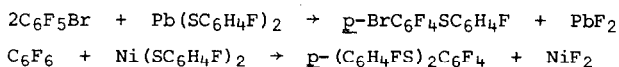
## RESULTS AND DISCUSSION

Many metallic thiolates precipitate when an aqueous solution of the metal ion is stirred with a suspension of a liquid thiol or a solution of the thiol in a water immiscible solvent [5]. It has been possible to  $Ag^+ + RSH \rightarrow AgSR\downarrow + H^+$  prepare the thiolates,  $M(SC_6H_4F)_x$ , M = Cu(I), Ag(I), Tl(I), Cd(II), Hg(II), Pd(II), Pb(II) and Bi(III) by this method. In some cases, such as copper (II), the thiol acts as a reducing agent and copper(I) thiolate is formed together with the disulfide. Other metallic and organometallic thiolates  $2Cu^{2+} + 4RSH \rightarrow 2CuSR\downarrow + (RS)_2 + 4H^+$  were prepared by literature methods, using the thiol; Ni(SC<sub>6</sub>H<sub>4</sub>F)<sub>2</sub> [1], Ph<sub>3</sub>SnSC<sub>6</sub>H<sub>4</sub>F [18]. The compounds AgSR, CuSR and Hg(SR)<sub>2</sub> (R = p-FC<sub>6</sub>H<sub>4</sub>) have been prepared previously, but not characterized [21]. These reactions are similar to those observed for other aromatic thiols.

Lead(II), copper(I), silver(I) and nickel(II) thiolates are useful reagents for the preparation of organic derivatives of thiols [2,23,3]. The monothioesters and thioethers may be obtained from the appropriate acyl or alkyl halide and silver or lead thiolate [2,3].

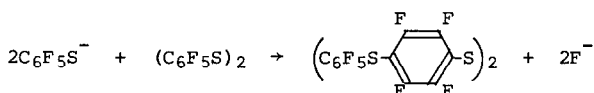


A thiolate group can be introduced onto an aromatic ring by displacement of fluorine using lead thiolate in DMF [6] or by displacement of bromine or iodine in bromo(iodo)fluorobenzenes with copper(I) thiolates in DMF [23]. Lead(II) and nickel(II) fluorobenzenethiolates have been used in



this way. It was not possible to displace the bromine of pentafluorobromobenzene with copper(I) thiolate, a known literature procedure [23]. These reactions show the utility of lead(II), nickel(II) and silver(I) thiolates as synthetic reagents. The relatively inert nature of copper(I) fluorobenzenethiolate was also observed in its non reactivity or very slow reactivity with triphenylmethyl chloride and pentafluorobenzyl chloride.

Pentafluorobenzenethiol is known to polymerize, particularly in alkaline solution in air. It has been postulated that this reaction occurs by initial oxidation of the thiol and subsequent nucleophilic attack by the thiolate anion, formed in the alkaline solution [1]. Such a reaction is

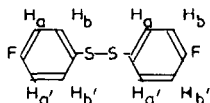
$$4C_6F_5SH + O_2 \rightarrow 2C_6F_5SSC_6F_5 + 2H_2O$$


observed with manganese dioxide [1]. This polymerization also occurs when lead(II) pentafluorobenzenethiolate is handled in warm DMF. Attempts to polymerize *p*-fluorobenzenethiol using manganese dioxide were unsuccessful. The reaction stopped at the disulfide stage. This inability to polymerize the thiol may be due to the difficulty of nucleophilic substitution of fluorine in derivatives of monofluorobenzene [6].

The new compounds have been characterized by elemental analysis, some by mass spectroscopy (when sufficiently volatile) and by NMR spectroscopy, both H-1 and F-19 (when sufficiently soluble). The C-13 NMR spectrum of the *p*-FC<sub>6</sub>H<sub>4</sub>S group has been assigned in several compounds. The presence of the various functional groups was confirmed in the infrared spectra. The mass spectra confirm the molecular weights and all have peaks at *m/z* 127, corresponding to FC<sub>6</sub>H<sub>4</sub>S<sup>+</sup>.

The *p*-fluorophenylthio group has characteristic NMR spectra in the aromatic proton region of the H-1 spectrum and in the fluorine and carbon-13 spectra. For example in the disulfide, (FC<sub>6</sub>H<sub>4</sub>S)<sub>2</sub>, the fluorine

spectrum is observed as a triplet of triplets, due to couplings to the two ortho hydrogen ( $J \sim 8\text{Hz}$ ) and two meta hydrogens ( $J \sim 5\text{Hz}$ ). In the proton spectrum two signals were observed, of relative intensity 1:1, due to  $H_a$  and  $H_b$ . This spectrum appears superficially as a triplet and a quartet (due to  $H_a$  and  $H_b$  respectively), although the fine structure indicates that this is a second order spectrum (AA'BB'X). Computer simulation of the spectrum using the values of  $J(H_a-F)$  and  $J(H_b-F)$  from the fluorine spectrum, shows that the values of  $J(H_a-H_b)$  and  $J(H_a,-H_b)$  are about 8 Hz, both  $J(H_a-H_a')$

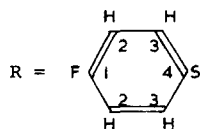


and  $J(H_b-H_b')$  are about 3 Hz and  $J(H_a-H_b')$  and  $J(H_b-H_a')$  are about 0.3 Hz, in accordance in literature values for compounds of the type  $p\text{-XC}_6\text{H}_4\text{SR}$  [24]. The carbon-13 proton decoupled spectrum can be assigned easily using the known values of the coupling constants C-F ( $\sim 250\text{Hz}$ ), C-C-F ( $\sim 20\text{Hz}$ ), C-C-C-F ( $\sim 8\text{Hz}$ ) and C-C-C-C-F ( $\sim 3\text{Hz}$ , which was not split in the observed spectrum) [25]. Some C-13 spectra are reported in Table 1 and details of the H-1 and F-19 spectra are shown in Table 2.

TABLE 1  
C-13 NMR spectra of the  $p\text{-FC}_6\text{H}_4\text{S}$  group

Compound	Chemical shifts (ppm) and C-C <sub>x</sub> -F coupling constants (Hz)*			
	C-1	C-2	C-3	C-4
RSSR	162.52 (248.0)	116.22 (22.1)	131.20 (7.8)	132.10
$p\text{-BrC}_6\text{F}_4\text{SR}^\dagger$	162.81 (249.5)	116.55 (22.2)	134.14 (8.9)	134.31
$\text{Ph}_3\text{CSR}$	162.99 (244.1)	115.33 (17.1)	137.62	144.48
$\text{C}_6\text{F}_5\text{COSR}$	164.07 (251.9)	117.01 (21.9)	136.82 (8.2)	136.16

\* Recorded in  $\text{CDCl}_3$  solution with TMS as internal standard; coupling constants in brackets.

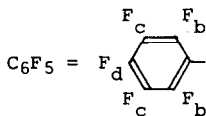
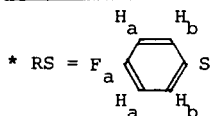


†		C-6	} 144.99ppm J(C-F) 253Hz
		C-7	
		C-5	} 133.36ppm J(C-C-F) 26Hz
		C-8	

TABLE 2

H-1 and F-19 NMR spectra

Compound*	Chemical Shifts (ppm) <sup>†</sup>				Coupling Constants (Hz) <sup>‡</sup>	
	H <sub>a</sub>	H <sub>b</sub>	F <sub>a</sub>	X	J(F-H <sub>a</sub> )	J(F-H <sub>b</sub> )
RSH	6.83	7.19	117.4	3.28S(SH)	8.8	5.2
RSSR	7.00	7.45	115.0		8.2	5.3
RSCH <sub>2</sub> SR	7.10	7.57	114.1	4.23S(CH <sub>2</sub> )	10.3	5.6
(RSCH <sub>2</sub> ) <sub>2</sub>	6.93	7.30	114.5	2.97S(CH <sub>2</sub> )	8.8	4.7
Ph <sub>3</sub> CSR	6.68	6.92	114.3	7.4M, 7.2M(Ph)	8.8	5.9
PhCH <sub>2</sub> SR	6.95	7.16 <sup>§</sup>	115.6	3.93S(CH <sub>2</sub> ) 7.16M(Ph) <sup>§</sup>	7.9	4.7
C <sub>6</sub> F <sub>5</sub> CH <sub>2</sub> SR	6.87	7.27	107.0	3.91S(CH <sub>2</sub> )	8.0	5.1
	137.2M(F <sub>b</sub> )	149.8TT(F <sub>d</sub> )	156.0M(F <sub>c</sub> )		J(F <sub>d</sub> -F <sub>c</sub> ) 20.0	J(F <sub>d</sub> -F <sub>b</sub> ) 4.2
MeCOSR	6.97	7.30	113.3	2.36S(Me)	9.0	5.4
PhCOSR	7.00	7.25	112.4	7.44M, 7.91M(Ph)	8.5	5.6
C <sub>6</sub> F <sub>5</sub> COSR	7.11	7.44	106.5			
	134.5M(F <sub>b</sub> )	146.2TT(F <sub>d</sub> )	157.0M(F <sub>c</sub> )		J(F <sub>d</sub> -F <sub>c</sub> ) 22.6	J(F <sub>d</sub> -F <sub>b</sub> ) 4.7
<i>p</i> -BrC <sub>6</sub> F <sub>4</sub> SR	7.00	7.45	113.9	132.4M(C <sub>6</sub> F <sub>4</sub> )		
<i>p</i> -(RS) <sub>2</sub> C <sub>6</sub> F <sub>4</sub>	6.92	7.20	113.7	133.4S(C <sub>6</sub> F <sub>4</sub> )		



<sup>†</sup> Recorded in CDCl<sub>3</sub> solution using TMS (H-1) and CFCℓ<sub>3</sub> or C<sub>6</sub>F<sub>6</sub> (corrected CFCℓ<sub>3</sub>) (F-19) as internal standards.

<sup>‡</sup> Derived from F-19 spectra.

<sup>§</sup> δH<sub>b</sub> and δC<sub>6</sub>H<sub>5</sub> superimposed.

The structure of the compound *p*-(FC<sub>6</sub>H<sub>4</sub>S)<sub>2</sub>C<sub>6</sub>F<sub>4</sub> is demonstrated unequivocally from its fluorine spectrum where a singlet and a triplet of triplets of intensity ratio 2:1 are observed. Similarly the structure of



*p*-BrC<sub>6</sub>F<sub>4</sub>SC<sub>6</sub>H<sub>4</sub>F can be deduced from comparison of its fluorine spectrum with that of *p*-BrC<sub>6</sub>F<sub>4</sub>SMe. The fluorine spectra of the *ortho* and *meta* isomers of BrC<sub>6</sub>F<sub>4</sub>SMe are totally different from the observed spectrum [26].

TABLE 3

Physical properties, yields and chemical analyses of new compounds

Compound	Color	m.p. (°C)	Method†	Found (%)		Calculated (%)	
		b.p. (°C/mm)		Yield (%)	C	H	C
CuSR*	yellow	274(d)	A 93	37.1	2.16	37.8	2.11
Ni(SR) <sub>2</sub> ·2/3H <sub>2</sub> O	red	325(d)	B 96	44.4	2.64	44.4	2.89
AgSR	yellow	350	A 96	30.6	1.68	30.7	1.72
Pd(SR) <sub>2</sub>	red-orange	350	A 95	39.7	2.22	40.0	2.24
Cd(SR) <sub>2</sub>	white	350	A 80	39.2	2.14	39.3	2.20
TlSR·2H <sub>2</sub> O	yellow	227-8	A 26	19.6	1.07	19.6	2.19
Pb(SR) <sub>2</sub>	yellow	235(d)	A 83	31.2	1.73	31.2	1.75
Hg(SR) <sub>2</sub>	white	188-190	A 98	30.9	1.71	31.7	1.77
Bi(SR) <sub>3</sub>	red-brown	140(d)	A 80	36.3	2.00	36.6	2.05
PhCOSR	white	47-9	C 86	67.2	3.87	67.2	3.91
Ph <sub>3</sub> CSR	white	107-9	D 73	80.6	5.13	81.0	5.17
MeCOSR	colorless	55-6/0.5	C 62	56.5	4.18	56.5	4.15
C <sub>6</sub> F <sub>5</sub> COSR	white	61-2	D 47	48.3	1.32	48.5	1.25
C <sub>6</sub> F <sub>5</sub> CH <sub>2</sub> SR	white	36-8	D 20	50.4	1.98	50.6	1.96
<u>p</u> -BrC <sub>6</sub> F <sub>4</sub> SR	white	68-70	E 45	41.1	1.18	40.6	1.14
<u>p</u> -(RS) <sub>2</sub> C <sub>6</sub> F <sub>4</sub>	white	112-6	F 42	53.6	2.15	53.7	2.00

\* R = p-FC<sub>6</sub>H<sub>4</sub>S† Modified literature methods: A[5], B[1], C[2], D[3], E[6], F as E using Ni(SR)<sub>2</sub>

From the reactions described here it can be concluded that the properties of p-fluorobenzenethiol are as expected for an aromatic thiol. The main difference from pentafluorobenzenethiol was its non polymerization. The metal salts Pb(SC<sub>6</sub>H<sub>4</sub>F)<sub>2</sub>, Ni(SC<sub>6</sub>H<sub>4</sub>F)<sub>2</sub> and AgSC<sub>6</sub>H<sub>4</sub>F have been shown to be useful synthetic reagents. The reactivity of CuSC<sub>6</sub>H<sub>4</sub>F will be studied further.

## EXPERIMENTAL

All reagents were available commercially. Microanalyses were performed by Canadian Microanalytical Services, New Westminster, B.C.. The analytical data and physical properties of the new compounds are shown in Table 3.

Mass spectra (70 eV) were recorded on a DuPont Model 21-104 Mass Spectrometer, using a direct introduction technique. The NMR spectra of  $\text{CDCl}_3$  solutions were recorded on a Varian EM 360 L (H-1 and F-19) and a Nicolet 360 MB (H-1 and C-13) Spectrometer, using TMS (H-1 and C-13) and  $\text{C}_6\text{F}_6$  (F-19) (reported values adjusted to  $\text{CFCl}_3$  as internal standard) as internal standards.

All reactions were studied on a 5-10 mmol scale. Metal thiolates were prepared by adding a stoichiometric amount of the neat liquid thiol to a well stirred aqueous solution of the metal salt. The precipitated thiolate was washed with water and hexane [5]. All other products were prepared by literature methods starting from the thiol or a metal thiolate. Known compounds were identified by comparison of the m.p. or b.p. with literature values:  $(\text{FC}_6\text{H}_4\text{S})_2\text{CH}_2$ , b.p.  $32^\circ/0.6\text{mm}$  (lit. b.p.  $141.7^\circ/1.1\text{mm}$  [11]) also confirmed by H-1 and F-19 NMR, yield 25% (method C);  $(\text{FC}_6\text{H}_4\text{SCH}_2)_2$ , m.p.  $69-70^\circ$  (lit. m.p.  $71^\circ$  [11]), yield 7% (method D);  $(\text{FC}_6\text{H}_4\text{S})_2$ , b.p.  $74-7^\circ/0.4\text{mm}$  (lit. b.p.  $131^\circ/1.0\text{mm}$  [12]) yield 79% (from the reaction of  $\text{Cu}^{2+}$  (aq) with RSH);  $\text{Ph}_3\text{SnSC}_6\text{H}_4\text{F}$ , m.p.  $114-6^\circ$  (lit. m.p.  $115-6^\circ$  [18]) method as ref. 5, yield 85%;  $\text{PhCH}_2\text{SC}_6\text{H}_4\text{F}$ , m.p.  $32-3^\circ$  (lit. m.p.  $32.5-33^\circ$  [13]), yield 72%, method E.

#### ACKNOWLEDGEMENTS

This work was supported by the Natural Sciences and Engineering Research Council (Canada) through the award of an USRA (S.C.H.) Mass spectra were recorded at Dalhousie University, Halifax, N.S. (courtesy of Dr. S. Grossert) and 360 MHz proton and 90 MHz carbon-13 NMR spectra were recorded at the Atlantic Magnetic Resonance Centre, Halifax, N.S..

#### REFERENCES

- 1 M.E. Peach, *Can. J. Chem.*, **46** (1968) 2699.
- 2 M.E. Peach and H.G. Spinney, *Can. J. Chem.*, **49** (1971) 644.
- 3 N.G. Payne and M.E. Peach, *Sulfur Letters*, **4** (1986) 217.
- 4 K. Langille and M.E. Peach, *Can. J. Chem.*, **48** (1970) 1474.
- 5 J.A. Mahar and M.E. Peach, *J. Fluorine Chem.*, **27** (1986) 121.
- 6 M.E. Peach and K.C. Smith, *J. Fluorine Chem.*, **27** (1985) 105.
- 7 C.R. Lucas and M.E. Peach, *Can. J. Chem.*, **48** (1970) 1867.
- 8 H. Zahn and H. Zuber, *Chem. Ber.*, **86** (1953) 172.

- 9 M. Seyhan and S. Aksu, *Chem. Ber.*, 72 (1939) 594.
- 10 B. Dmuchovsky, F.B. Zienty and W.A. Vredenburgh, *J. Org. Chem.*, 31(1966) 865.
- 11 R.F. Brookes, J.E. Cranham, W.A.W. Cummings, D. Greenwood, B.S. Jackson and H.A. Stevenson, *J. Sci. Food Agric.*, 8 (1957) 31.
- 12 R.F. Brookes, J.E. Cranham, D. Greenwood and H.A. Stevenson, *J. Sci. Food Agric.*, 8 (1957) 561.
- 13 N.G. Clark, J.E. Cranham, D. Greenwood, J.R. Marshall and H.A. Stevenson, *J. Sci. Food Agric.*, 8 (1957) 566.
- 14 L. Goodman, L.O. Ross and B.R. Baker, *J. Org. Chem.*, 23 (1958) 1251.
- 15 N. Fuson, M-L. Josien and R.L. Powell, *J. Am. Chem. Soc.*, 74 (1952) 1.
- 16 J.P. Caradonna, E.W. Harlan and R.H. Holm, *J. Am. Chem. Soc.*, 108 (1986) 7856.
- 17 T. Schaffer and W.J.E. Parr, *Can. J. Chem.*, 55 (1977) 552.
- 18 A.N. Nesmeyanov, D.N. Krastov, B.A. Kvasov, E.M. Roklina, V.M. Pacherskaya, L.S. Golovchenko and E.I. Fedin, *J. Organometall. Chem.*, 38 (1972) 307.
- 19 T. Schaffer, T.A. Wildman and R. Sebastian, *Can. J. Chem.*, 60 (1982)1924.
- 20 L.M. Yagupolskii and M.S. Marenets, *Zhur. Obshchei Khim.*, 29 (1959) 278.
- 21 G. Olah and A. Pallath, *Acta Chim. Acad. Sci. Hung.*, 4 (1954) 111.
- 22 N.J. Leonard and L.E. Sutton, *J. Am. Chem. Soc.*, 70 (1948) 1564.
- 23 M.E. Peach and D.J. Sutherland, *J. Fluorine Chem.*, 17 (1981) 225.
- 24 L.J. Johnston and M.E. Peach, *J. Fluorine Chem.*, 12 (1978) 41.
- 25 F.J. Weigert and J.D. Roberts, *J. Am. Chem. Soc.*, 93 (1971) 2361.
- 26 W.J. Frazee and M.E. Peach, *J. Fluorine Chem.*, 13 (1979) 225.