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Synthesis of polyfluoroarylalkyl sulfide compounds

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Abstract

Syntheses of RC_6F_4SR' compounds (where R = F, C_6F_5, H, R' = alkyl, trifluorovinyl) have been accomplished through reaction between Ar_fSM (where M = Cu, MgX) and an alkyl or trifluorovinyl halide in dimethylacetamide solvent. Minor by-products from competing reactions have been partially characterized by GC–MS analysis.

Keywords: Synthesis; Polyfluoroarylalkyl sulfides; NMR spectroscopy; Mass spectrometry

1. Introduction

Metal polyfluorothiolates, e.g. Ar_fSNa [1], Ar_fSLi [2], Ar_fSCu [1,3–5], Ar_fSK [1,6] and $(Ar_fS)_2Pb$ [7] have been prepared and used as intermediates for the introduction of the polyfluoroarylthiolate group through their reaction with an appropriate aromatic halide (ArX).

$$Ar_fSM + ArX \longrightarrow MX + Ar_fSAr$$

An alternate synthesis method for the Ar_fSR compounds is through the reaction between a mercaptide RS^- and a polyfluoroaromatic compound by the nucleophilic displacement of an F^- [6,8,9] or replacement of a Br^- or I^- on a polyfluoroaromatic compound. Some of these reactions are solvent-dependent where both F and Br or I may be replaced along with protodebromination [5,8,10,11].

Cuprous pentafluorothiophenoxide (C_6F_5SCu, **I**), prepared by Belf, Buxton and Fuller [3], was shown to be a useful intermediate for the synthesis of polyfluoroaromatic sulfides on reaction with bromopolyfluoroaromatic compounds in dimethylformamide solvent. Subsequent research by Yakobson [4], Peach [5] and coworkers have involved the reactions of **I** with a variety of bromo- and iodo-polyfluoroaromatic compounds and have shown the generality of this reaction for the synthesis of polyfluoroaromatic sulfides.

2. Results and discussion

In our present study on the synthesis of Ar_fSR-type compounds we have extended the use of Ar_fSCu compounds to reactions with aliphatic bromides and iodides [Methods A and B]. We have also investigated the utility of Ar_fSMgX compounds as intermediates in the reactions with aliphatic bromides and iodides to yield Ar_fSR compounds [Methods C and D].

2.1. Method A

C_6F_5SCu (**I**) prepared in dimethylacetamide (DMAC) reacts with aliphatic bromo and iodo compounds to give C_6F_5SR compounds in excellent yield.

$$\underset{\textbf{(I)}}{C_6F_5SCu} + RX \xrightarrow{\text{DMAC}} C_6F_5SR + CuX$$

[RX = C_2H_5I (94 GC area%), C_4H_9Br (90 GC area%)]

Attempts to react **I** with $C_8F_{17}I$ to yield $C_6F_5SC_8F_{17}$ were unsuccessful. The major product from the reaction was $C_6F_5SCH_2C(O)N(CH_3)_2$ in addition to $C_6F_5SC_6F_5$ and $C_6F_5SSC_6F_5$ as determined by GC–MS analysis. On heating **I** in DMAC alone, the same products were obtained. In the absence of a reactive substrate (RX), **I** will react with the solvent. The nature of the reaction is unknown at this time.

Since a perfluoroalkyl iodide containing an sp^3 carbon–iodine bond was unreactive towards **I**, it was of interest to examine a perfluoroolefinic iodide con-

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taining an sp^2 carbon–iodide bond. On heating a mixture of **I** and $CF_2{=}CFI$ in DMAC to reflux temperature, the major product $C_6F_5SCF{=}CF_2$ (77 GC area%) was obtained along with a small yield of $C_6F_5SSC_6F_5$, probably formed by oxidation of **I** with free iodine present in the $CF_2{=}CFI$. In a similar manner, p-$CuSC_6F_4SCu$ (**II**) on reaction with $CF_2{=}CFI$ gave p-$CF_2{=}CFSC_6F_4SCF{=}CF_2$. It thus appears that both **I** and **II** may be useful intermediates in the synthesis of aryl, alkyl and fluoroolefinic sulfide compounds.

2.2. Method B

An alternate and simpler method for the synthesis of **I** and **II** has been developed. The cuprates can be prepared in situ and reacted with an alkyl iodide to give good yields of the fluoroarylalkyl sulfides. As an example, by placing all the reactants, p-HSC_6F_4SH [12], C_2H_5I, Cu_2O and DMAC, into a pressure vessel and heating the contents to 70 °C, the major product p-$C_2H_5SC_6F_4SC_2H_5$ was obtained. In a similar manner, p-HC_6F_4SH [6] gave p-$HC_6F_4SC_2H_5$.

$$p\text{-}HSC_6F_4SH + Cu_2O \xrightarrow[-H_2O]{DMAC}$$

$$[p\text{-}CuSC_6F_4SCu] \xrightarrow{C_2H_5I} \underset{(87\ \text{GC area\%})}{p\text{-}C_2H_5SC_6F_4SC_2H_5}$$

$$p\text{-}HC_6F_4SH + Cu_2O \xrightarrow[-H_2O]{DMAC}$$

$$[p\text{-}HC_6F_4SCu] \xrightarrow{C_2H_5I} \underset{(88\ \text{GC area\%})}{p\text{-}HC_6F_4SC_2H_5}$$

2.3. Method C

The metal–halogen exchange reaction is an excellent procedure for the preparation of C_6F_5MgBr [13].

$$C_6F_5Br + C_2H_5MgBr \xrightarrow{THF} C_2H_5Br + C_6F_5MgBr$$

In subsequent reactions of the Grignard reagent with other substrates the presence of C_2H_5Br is of no consequence since the Grignard does not react with the alkyl halide. However, reactions of the Grignard prepared by this method with certain other substrates, e.g. sulfur, give a different product than the expected mercaptan.

$$C_6F_5Br + C_2H_5MgBr \longrightarrow C_6F_5MgBr + C_2H_5Br \xrightarrow{S}$$

$$C_6F_5SMgBr \overset{H^+}{\rightsquigarrow} C_6F_5SH$$

$$+$$

$$C_2H_5Br \longrightarrow \underset{(92\ \text{GC area\%})}{C_6F_5SC_2H_5 + MgBr_2}$$

The thiol cannot be prepared by this method since the nucleophile $C_6F_5S^-$ reacts readily with C_2H_5Br to give good yields of the perfluoroarylalkyl sulfide.

Substituting CH_3MgBr in place of C_2H_5MgBr in the above example gave $C_6F_5SCH_3$ in excellent yield (94 GC area%). Similarly, by extending this type of reaction to i-C_3H_7MgBr, a lower yield (52 GC area%) of the product $C_6F_5SC_3H_7$-i was obtained. The rate of reaction between $C_6F_5S^-$ and the sterically hindered i-C_3H_7Br is lower than with the primarly alkyl halides. This allows $C_6F_5S^-$ to react with the product $C_6F_5SC_3H_7$-i by a nucleophilic displacement of the ring fluorine to yield additional products, e.g. $C_6F_5SC_6F_4SC_3H_7$-i and $C_6F_5S(C_6F_4S)_nC_3H_7$-i. Although not isolated, these by products were observed in a GC–MS analysis of the distillation residue.

$$C_6F_5SMgX + i\text{-}C_3H_7Br \longrightarrow \underset{(52\ \text{GC area\%})}{C_6F_5SC_3H_7\text{-}i} \xrightarrow{nC_6F_5S^-}$$

$$C_6F_5S(C_6F_4S)_nC_3H_7\text{-}i$$

The above results with the various Grignard reagents are consistent with an S_N2-type reaction, where the relative reaction rates of the alkyl halides towards the nucleophile $C_6F_5S^-$ are $CH_3X > C_2H_5X > i\text{-}C_3H_7X$.

2.4. Method D

Another variation in the use of perfluorophenyl Grignard reactions to yield C_6F_5SR compounds is shown in the following, whereby the Grignard reagent is prepared by the direct process using an aryl halide and elemental magnesium. In this manner, no alkyl halide exchange compound is formed.

$$C_6F_5Br + Mg \longrightarrow C_6F_5MgBr \xrightarrow[(2)\ S]{(1)\ CH_2=CHCH_2Br}$$

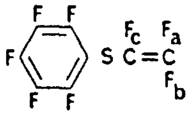
$$\underset{(93\ \text{GC area\%})}{C_6F_5SCH_2CH{=}CH_2}$$

By the addition of allyl bromide to a preformed C_6F_5MgBr followed by the addition of sulfur in small increments, a high yield of $C_6F_5SCH_2CH{=}CH_2$ (93 GC area%) can be obtained. This procedure allows the synthesis of a variety of C_6F_5SR compounds simply by varying the alkyl halide. It is also possible to prepare the Grignârd reagent without the concurrent formation of an alkyl halide, as in the alkyl halide-exchange reaction (Method C), by the metal–hydrogen exchange reaction (metalation reaction) [14].

$$C_6F_5H + C_2H_5MgBr \longrightarrow C_6F_5MgBr + C_2H_6$$

The above described procedures using the synthons C_6F_5SCu, p-$CuSC_6F_4SCu$, C_6F_5SMgBr and possibly $C_6F_4(SMgBr)_2$ provide convenient methods for the synthesis of a variety of mono- and specifically oriented di-substituted polyfluoroarylalkyl sulfide compounds.

Table 1
Properties and characterization of fluoroarylalkyl sulfides

Product [b]	Method [a]	Reference	B.p. (°C/mmHg)	MS	Yield (GC/isolated) (%)	Elemental analysis (Calc.) (Found) (%)				^{19}F NMR δ (ppm)	^{1}H NMR δ (ppm)
						C	H	F	S		
$C_6F_5SCH_3$ (**III**)	C	[1]	171–172	214 $(M)^+$	94/73	–	–	–	–		
$C_6F_5SC_2H_5$ (**IV**)	A, C	[15]	182–183 30.5/0.8	228 $(M)^+$	92/72	–	–	–	–		
$C_6F_5SC_3H_7$-i (**V**)	C	[15]	52/3.0	242 $(M)^+$	52/15	–	–	–	–		
$C_6F_5SCH_2CH{=}CH_2$ (**VI**)	D	nc	46.5/2.0	240 $(M)^+$	93/82	45.00 (45.21)	2.08 (2.23)	39.58 (42.00)	13.33 (14.00)		
$C_6F_5SC_4H_9$ (**VII**)	A	[10]	54/0.72	256 $(M)^+$	90/52	46.88 (47.13)	3.52 (3.65)	37.11 (37.38)	12.50 (13.10)		
$HC_6F_4SC_2H_5$ (**VIII**)	B	nc	187–189	210 $(M)^+$	88/75	45.71 (45.77)	2.86 (2.84)	36.19 (35.80)	15.23 (15.76)		
$C_6F_5SCF{=}CF_2$ (**IX**)	A	nc	155 24/0.92	280 $(M)^+$	95/65	34.28 (34.14)	0 (0)	54.28 (11.51)	11.42 (11.51)	85.5 (dofd) = F_a 103.1 (dofd) = F_b 152.2 (dofd) = F_c 132.3 (m) = o-F 149.6 (m) = p-F 160.2 (m) = m-F	
p-$C_2H_5SC_6F_4SC_2H_5$ (**X**)	B	[9]	m.p. 44–45	270 $(M)^+$	78/65	44.44 (44.36)	3.70 (3.56)	28.15 (31.00)	23.70 (23.59)		
p-$F_2C{=}CFSC_6F_4SCF{=}CF_2$ (**XI**)	A	nc	[c]	374 $(M)^+$	[c]	32.09 (31.95)	0 (0)	50.80 –	17.1 (17.60)	131.0 (s) = ArF 84.1 (dofd) = F_a 101.2 (dofd) = F_b 150.3 (dofd) = F_c	
$C_6F_5SCH_2C(O)N(CH_3)_2$ (**XII**)	A	nc	[c]	285 $(M)^+$	[c]	–	–	–	–	132.3 (m) = o-F 152.0 (m) = p-F 162.0 (m) = m-F	3.58 = SCH_2 3.13 and 2.90 = $(CH_3)_2$

[a] A = $Ar_fSCu + RX$; B = $Ar_fX + Cu_2O + RX + S$; C = $Ar_fX + RMgX + S$; D = $Ar_fX + Mg + RX + S$.

[b] Known compounds were characterized by GC–MS and comparing their b.p. and IR spectra with literature data.

[c] Isolated by preparative GC.

3. Experimental details

A dry nitrogen atmosphere, with the usual precautions to exclude air, was used. GLC analyses were performed on a Hewlett Packard model 5880 instrument using a flame ionization detector and a methyl silicone capillary column, Supelco SPB-1, 15 m, 0.53 mm i.d., 0.10 m film. GC mass spectral analyses were determined by chemical ionization and electron impact on a Finnigan model 4021 instrument. NMR were obtained on a Varian 56/60 spectrometer in CCl_4 solution using TMS and trichlorofluoromethane as internal standards. All known compounds were characterized by GC–MS analyses and by comparing their boiling points and infrared spectra with published data.

3.1. Preparation of trifluorovinyl pentafluorophenyl sulfide (IX) (Method A)

Into a metal pressure reactor were placed copper pentafluorophenylthiophenoxide [3] (5.3 g, 0.020 mol), iodotrifluoroethylene (5.0 g, 0.024 mol) and DMAC (20 ml). The reactor was sealed and heated to 70 °C for 20 h. On cooling, an aliquot sample was removed, added to diethyl ether which was repeatedly washed with water and then analyzed by GC. Analysis indicated a trace of DMAC and only one major product peak besides the solvent. The contents of the reactor were poured into a mixture of diethyl ether (50 ml) and water (100 ml). The mixture was filtered to remove the CuI and the diethyl ether separated, dried ($MgSO_4$) and subsequently concentrated under vacuum to yield the crude product (5.0 g). On distillation, the product **IX** was obtained in 65% yield (see Table 1).

3.2. Preparation of ethyl-2,3,5,6-tetrafluorophenyl sulfide (VIII) (Method B)

Into a metal pressure reactor were placed 2,3,5,6-tetrafluorophenylthiophenol (10.0 g, 0.055 mol), cuprous oxide (4.32 g, 0.030 mol), ethyl iodide (10.2 g, 0.066 mol) and DMAC (20 ml). The reactor was sealed and heated to 70 °C for 20 h. On cooling, the mixture was added to diethyl ether (50 ml) and water (100 ml). The diethyl ether layer was separated, washed repeatedly with water and an aliquot sample on GC analysis indicated an 88 GC area% of a major product. The diethyl ether layer was dried ($MgSO_4$) and concentrated under vacuum to yield a crude material which on distillation gave the product **VIII** (see Table 1).

3.3. Preparation of ethyl pentafluorophenyl sulfide (IV) (Method C)

Ethylmagnesium bromide (0.105 mol, 105 ml of a 1.0 M THF solution) was slowly added to a cooled stirred solution of pentafluorophenyl bromide (24.7 g, 0.10 mol) in THF (15 ml) so as to keep the temperature at ca. −15 °C. After 1 h, an aliquot sample on GC analysis showed the absence of pentafluorophenyl bromide. Sulfur (3.36 g, 0.105 mol) was added in small increments over 4 min. A slight exotherm was noted. The reaction mixture was warmed to room temperature and stirred for 20 h. The mixture was then hydrolyzed with dilute hydrochloric acid and diethyl ether (100 ml) added. GC analysis showed a 92 GC area% of product. The ether layer was separated and washed repeatedly with water to remove the THF and then dried ($MgSO_4$). The solvent was removed under reduced pressure to give a crude product which on distillation yielded the product **IV** (16.6 g, 72%) (see Table 1).

3.4. Preparation of allyl pentafluorophenyl sulfide (VI) (Method D)

Under a nitrogen atmosphere, pentafluorophenyl bromide (12.35 g, 0.050 mol) was added slowly to a cooled, stirred mixture of magnesium (1.32 g, 0.055 mol) and THF (5 ml). When the reaction became exothermic (5 min), slow simultaneous addition of THF (45 ml) was started. The reaction temperature was controlled with an external ice bath (3 °C). After completion of addition, the reaction mixture was allowed to warm to room temperature. Allyl bromide (6.05 g, 0.050 mol) was added in one portion. Sulfur (1.76 g, 0.055 mol) was added in small portions over a period of 5 min. A slight exotherm of ca. 10 °C was noted. The reaction was allowed to proceed for 19 h with stirring. An aliquot sample of the reaction mixture on GC analysis showed primarily the major product peak (93 GC area%).

After hydrolysis with dilute hydrochloric acid, diethyl ether was added (100 ml), phase-separated and dried ($MgSO_4$). The diethyl ether was concentrated under vacuum and the residue distilled to give the product **VI** (9.3 g, 82%) (see Table 1).

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References

[1] P. Robson, M. Stacey, R. Stephens and J.C. Tatlow, *J. Chem. Soc.*, (1960) 4754.
[2] P.J. Eller and D.W. Meek, *J. Organomet. Chem.*, *2* (1970) 631.
[3] L.J. Belf, M.W. Buxton and G. Fuller, *J. Chem. Soc.*, (1965) 3372.
[4] G.G. Yakobson, G.G. Furin, L.S. Kobrina and N.N. Vorozhtsov, *J. Gen. Chem. (USSR)*, *37* (1967) 1221.

[5] L.J. Johnston and M.E. Peach, *J. Fluorine Chem., 12* (1978) 41.

[6] P. Robson, T.A. Smith, R. Stephens and J.C. Tatlow, *J. Chem. Soc.,* (1963) 3692.

[7] M.E. Peach and H.G. Spinney, *Can. J. Chem., 49* (1971) 644.

[8] W.J. Frazee and M.E. Peach, *J. Fluorine Chem., 13* (1979) 225.

[9] K.R. Langille and M.E. Peach, *J. Fluorine Chem., 1* (1971–72) 407.

[10] J. Burdon, P.L. Coe, C.R. Marsh and J.C. Tatlow, *J. Chem. Soc., Perkin Trans., 1* (1972) 763.

[11] M.E. Peach and J.D. Sutherland, *J. Fluorine Chem., 17* (1981) 225.

[12] R.H. Mobbs, *Chem. Ind. (London),* (1965) 1562.

[13] D.D. Denson, C.F. Smith and C. Tamborski, *J. Fluorine Chem., 3* (1973–74) 247.

[14] R.J. Harper, Jr., E.J. Soloski and C. Tamborski, *J. Org. Chem., 29* (1964) 2385.

[15] R.J. Neal and M.E. Peach, *J. Fluorine Chem., 1* (1971–1972) 257.